الجامعة الألمانية الأردنية
German Jordanian University

School of Medical Sciences

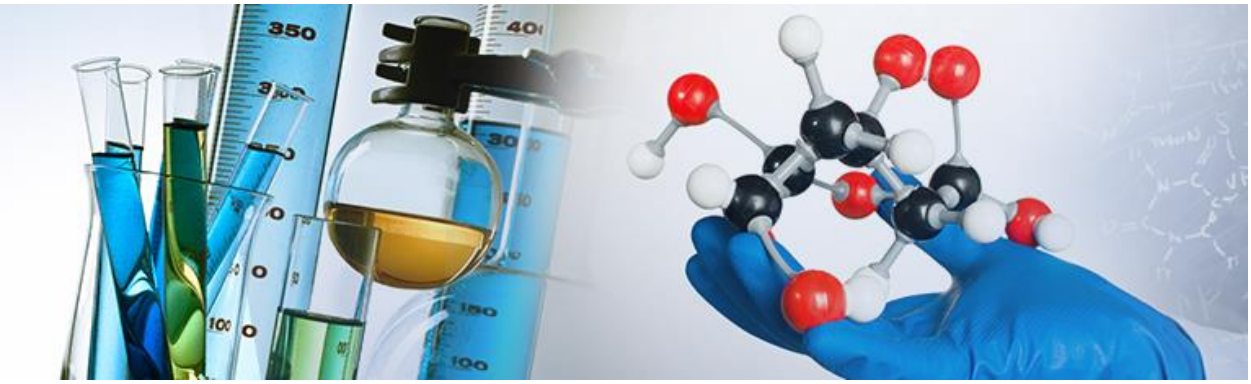
Pharmaceutical and Chemical Engineering Department

Laboratory Manual

for

Pharmaceutical Organic Chemistry

PCE371



Edition: 2021

Contents

Preface

This practical course is a 2nd year level that is co-requisite to Pharmaceutical Organic Chemistry course. This lab is a 1 credit hour course but scheduled to be given for 3 hours once a week.

This lab covers the following:

Separation, purification and identification of organic compounds through their physical properties: melting point, distillation, crystallization, extraction, and chromatography; preparation of simple pharmaceutical organic compounds; qualitative tests for selected classes of organic compounds, and analysis of different spectral data.

It is not the role of your instructor or TA to do the lab for you. You are responsible for coming to lab prepared and ready to work during each session. During the lab sessions you must complete an experimental procedure and solve the questions related to the experiment. It is your responsibility to ensure you have all the necessary results and to have completed any calculations before leaving the lab.

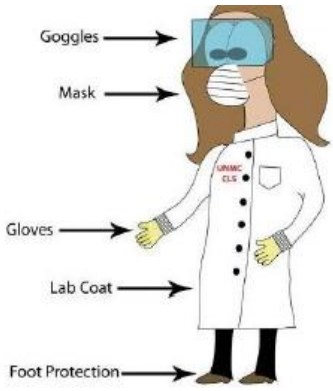
During the first lab session, you will be introduced to some of the safety equipment in the lab as well as the rules and regulations for your class. Pay close attention to this discussion so that you can react properly in case of an emergency!

What Will You Need to Bring With You to Lab?

It is important to come prepared for your laboratory session. You will be required to bring:

Your manual, a lab-coat and protective eyewear (goggles or glasses with side-shields) as well as a calculator.

Please note you will not be allowed to enter the lab if you do not come prepared with a lab-coat, goggles and solved Pre-lab.



Lab Reports

Each lab session is divided into three main parts:

the **Pre-laboratory section** which should be completed before attendance. Sometimes these pre-laboratory questions will include numerical problems similar to those you will encounter in processing the data you will be collecting in the experiment. Obviously, if you review a calculation before lab, things will be much easier when you are actually in the lab!

Pre-lab assignments MUST be graded AT THE BEGINNING of the lab session. If you do not complete the pre-lab assignment and turn it in at the beginning of the lab, you will NOT be allowed to participate in the lab that day.

the **Experimental results** which are to be recorded while following the experimental methodology.

the **Post-laboratory questions**.

Your final lab report including all three sections must be submitted to your TA or instructor before leaving the lab.

Assessment Policy		
Reports	The least graded report will not be counted	**40%**
Evaluation	Participation, following lab rules	**10%**
Quizzes	The least graded quiz will not be counted	**20%**
Final Exam**	Including all experiments	**40%**

** Final Exam might be a written exam or divided into two parts: a written part and a practical part.

Regulations	
Signing the Consent Form	During your first lab session you have to read and sign the consent form given in the next page of this manual and hand it to your TA (or instructor).
Attendance	Lab session attendance is mandatory. The student is allowed maximally 15% absentia of the total module hours. According to the rules you are allowed to be absent maximum for 2 lab session (even with excuses). More than this percentage, a student with an excuse will be drawn from the module. Otherwise, the student will be deprived from the module with zero mark assigned.
Online-sessions	Regarding the online-given lab sessions: If you don't submit your report on the assigned time, you will be considered 'absent' on that session.
Reports	You have to depend on yourself to prepare your report. Copying from each other is NOT allowed. **Similar copies of reports will be graded ZERO.** You may discuss together, search for the solution or ask your instructor or TA; but at the end you should write the answers in your own language.

School of Applied Medial Sciences

Pharmaceutical Organic Chemistry Lab. – PCE371

Consent Form

Student Full Name:	Student ID Number:
Student Emergency Contact Telephone Number:	

I hereby acknowledge receipt of safety codes and procedures that are required in the current edition of SAMS/PCE department safety regulations, all of which I have read, instructed, viewed, understood and agree to observe. Moreover, I will be aware of my special risks with the work I am doing and that should use protective equipment without any exemption. My own health and that of safety and that of others depend on this. In addition, it is my responsibility to cooperate with safety measures and seek consultation from lab supervisor about any unclear procedure/statement. I understand that I have registered in this practical course with the number of students decided by the PCE administrative department and I understand that the instructors in this course applied their best to keep people apart to help reduce the spread of coronavirus (COVID-19). On that aspect I will be committed to 1) have face covering to minimize the time of sharing breathing zone; 2) to be apart from my colleagues or staff by 2 meters through following floor tapes or signage to remember this social distancing; 3) to work side by side or facing away rather than face to face; 4) to limit the movement and follow the instructor regulations to rotate between equipment/tools; 5) to limit touching of surfaces or any stuff I will not use and to keep myself belongings without sharing ; 6) to report your concern of developing any of COVID 19 symptoms*; 7) to safely discard disposable items and clean reusable ones thoroughly; and 8) to ensure washing my hand thoroughly with soap and water (20 seconds) or an alcohol-based hand sanitizer as soon as possible before and after entering the laboratory assigned hall. Otherwise of all the above I understand that my activity will be stopped, and the staff will end my class.

Signed…… Date……

Instructor:

TA:

*The main symptoms of coronavirus are:

- a high temperature – this means you feel hot to touch on your chest or back (you do not need to measure your temperature)
- a new, continuous cough – this means coughing a lot for more than an hour, or 3 or more coughing episodes in 24 hours (if you usually have a cough, it may be worse than usual)
- a loss or change to your sense of smell or taste – this means you've noticed you cannot smell or taste anything, or things smell or taste different to normal.

Most people with coronavirus have at least one of these symptoms. Once you report any of these symptoms you are recommended to kindly leave the class and visit the **university clinic** and we will give you all the support needed, so please keep us posted so we can assist you and trace your case.

Safety in Chemistry Labs

Chemistry is an experimental science. You cannot learn it without getting your hands dirty. All new chemistry students face the prospect of lab work with some apprehension and fear, and it would be untruthful to say that this is completely unwarranted. *Chemicals can be dangerous!* The more you study chemistry, the more danger you will face, but also the more knowledge you will have to protect yourself. If you approach your lab work calmly and studiously, you will minimize any risk.

During your first lab session, you will be given a brief tour of your laboratory. You will be shown the locations of various pieces of emergency equipment that are there for your safety. If you have other specific questions about your safety in the lab consult with your laboratory instructor.

Protection for Your Eyes

It is a requirement for the labs (and it is just common sense!!) that you must wear **protective eyewear (safety goggles)** while you are in the laboratory. Such eyewear must be worn even if you are personally not working on an experiment.

In addition to protective goggles, an **eyewash fountain** provides eye protection in the laboratory. Should a chemical splash near your eyes, you should use the eyewash fountain before the material has a chance to run in behind your safety glasses. A typical eyewash fountain is shown in the accompanying Figure. If you ever need to use the eyewash fountain, don't be afraid or modest – *use it immediately!!*

Protection from Fire

The danger of fire in a chemistry laboratory is real, since the lab usually has a large number of flammable liquids in it, and open-flame gas burners are sometimes used for heating. With careful attention, though, the danger of fire can be reduced considerably, and even avoided completely.

Always check the lab before lighting a gas burner (Bunsen burner) to be sure than no one is pouring or using flammable chemicals near you. Since the vapors of most flammable liquids are heavier than air, be especially careful around sinks as they tend to concentrate there.

In spite of all the precautions you take, fires may still occur. The method you use to fight them depends on their size and on the substance that is burning. If only a small amount of flammable material has caught fire and there is no chance it can spread, depriving it of oxygen is the best and safest method to extinguish the flames. To do this, put a beaker over the fire and it will quickly go out. Leave the beaker in place for several minutes to ensure that the flammable material has cooled and will not flare up again.

In the unlikely event that a larger chemical fire occurs, carbon dioxide fire extinguishers are available in front of the lab door. When using a **CO_2 fire extinguisher**, direct the spray at the base of the fire. This not only deprives it of oxygen, but also cools the flammable material quickly. If this does not quickly work to extinguish the fire, immediately evacuate the laboratory and call the fire department. Be aware that the CO_2 fire extinguishers should not be used on fires in which magnesium (or other reactive metals) are burning – this may only make the fire worse. Consult your instructor before using a fire extinguisher to be certain you have chosen the correct method.

One of the most frightening and potentially dangerous accidents in the chemistry laboratory is the igniting of a person's clothing or hair. For this reason, certain types of clothing should never be worn in the lab, including long flowing sleeves; clothing made of silk or other flammable fabrics; and long hair should be tied back. In the unlikely event that a student's hair or clothing catches fire, his or her lab-mates must act quickly to extinguish the flames and prevent serious burns. The Figure on the side shows the kind of **emergency shower** you will find in our labs. This type of equipment provides a very large amount of water very quickly to put out most types of fires.

Protection from Chemical Burns

Most acids, alkalis (bases) and oxidizing and reducing agent are corrosive to the skin. Since it is impossible to avoid using these substances completely, you must learn how to handle them properly and safely. As a general rule, a material's corrosiveness is related to its concentration – the higher the concentration, the more dangerous it will be. Even though the concentrations of the chemicals you will be dealing with in this lab are generally small, this does not completely remove the danger. You should wash your hands frequently during lab, especially if any chemical substance is spilled on your skin.

After working with a substance that you know to be particularly dangerous or corrosive, wash your hands, even if you did not spill the substance – you don't know if the student using the bottle before you spilled any on the outside of the container. Whenever you spill a corrosive substance on your skin you should tell your instructor immediately. If there is any sign whatsoever of damage to your skin, you should see a doctor as soon as possible.

In the event of a major chemical spill, in which substantial portions of your body or clothing are affected, use the emergency shower – this is not the time for modesty, your health and safety are much more important!!!

Protection from Toxic Fumes

Many chemical substances are volatile (easily become a gas) and have toxic vapors. As a rule, in the chemistry lab, be careful that "if you can smell it, it can hurt you!" Some toxic fumes can overpower you immediately (like ammonia), whereas some fumes are even more dangerous and can cause harm without you even knowing it. There is no need to expose yourself to these toxic fumes in the lab. Our chemistry labs are equipped with **fume hoods** (figure on the side) that have exhaust fans to pull the vapors into the hood and away from you. Flammable solvents should also be stored in the hood to reduce the risk of fire.

Protection from Cuts and Burns

The most common injuries to students in the general chemistry lab are simple cuts and burns. You will use thermometers and glassware for nearly every experiment, and they are often not used properly.

Broken glassware should not be touched with your bare hands. Use a broom and dustpan to clean up the spills and shards of glass. Each lab has a designated place to put broken glass – do not throw it in the garbage, someone else may get injured if you do!

Simple burns occur in the laboratory when students forget that an apparatus is hot and touch it. Never touch a piece of equipment that has been heated until it has cooled for at least five minutes. Use tongs if you are unsure! Perhaps the

most common accident in the lab is the tipping over of a flask or beaker while it is being heated or handled.

Another common mistake occurs while heating liquids in test tubes. If the contents of the tube are heated too quickly, they can super-heat and blow out of the test tube like a bullet from a gun!! Ideally, heat a test tube in a beaker of boiling water, or if you must heat it directly over a heat source (like a Bunsen burner) hold it at a 45º angle, pointed away from yourself and anyone else in the lab. Gently move the tube through the flame, only briefly should it come in contact with the fire.

Report any cuts or burns to your instructor immediately, no matter how minor they seem. If there is a damage to your skin, you will likely be sent to see a doctor. What may seem like a scratch could become infected from the chemicals you were using and should be treated by a professional.

Safety Rules and Regulations

General Lab Rules

- Do not enter the laboratory before your instructor or TA arrives.
- Wear safety goggles and lab coat at all time when you are in the laboratory.
- Do not wear short skirts, shorts, or open-toed shoes in the laboratory.
- Do not wear scarves or neckties in the lab, because they may accidentally be ignited in the flame of a Bunsen burner.
- Jewelry should be removed. Chemicals can cause a severe irritation if concentrated, under a ring, wristwatch, or bracelet; chemicals on fingers or gloves can cause irritation around earrings, necklaces, and so on. It is just a good practice of laboratory safety to remove jewelry.
- Girls with long hair should tie it back before entering the lab, it, too, may accidentally catch fire.
- Never chew gum, eat, drink, or smoke in the laboratory.
- Contact lenses should not be worn in the lab, even if goggles are worn. Lenses can absorb vapors and are difficult to remove in an emergency.
- Prepare your work area Before you begin a lab, clear the lab bench or work area of all your personal items, such as backpacks, books, sweaters, and coats. Find a storage place in the lab for them. All you will need is your laboratory manual, a calculator, a pen or pencil, and equipment from your lab drawer.

Heating Safety Tips

- Never leave a lighted Bunsen burner unattended.
- Never heat solutions to dryness, this can sometimes cause an explosion.
- Never heat a "closed system" such as a stoppered flask.

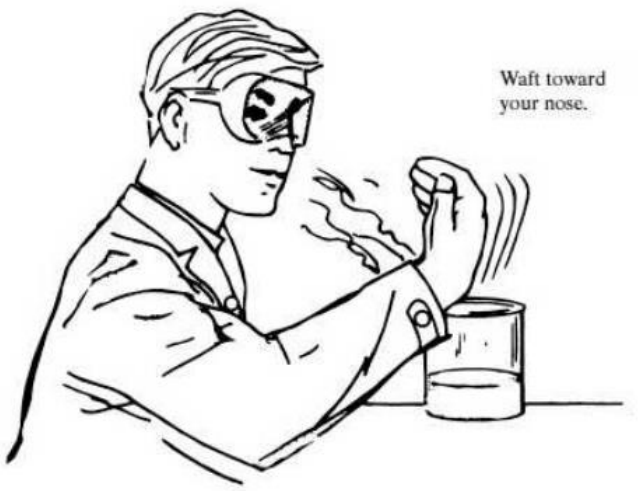
- To heat liquids, add 2-3 boiling stones to help it heat evenly and boil smoother.

Waste Disposal

- Always use the smallest amount of substance required for an experiment; more is never better in chemistry.
- Never return unused portions of chemicals to their original bottle – use a waste container.
- Dispose of all reaction products as directed by your instructor. In particular, observe the special disposal techniques necessary for flammable or toxic substances.
- Dispose of all glass products in the special container provided.

Other Rules

- Do not leave your experiment unattended during the laboratory period: This is often a time when accidents occur.
- Never remove any chemical substance from the laboratory. This is grounds for expulsion from our class and from the university.
- Handle chemicals carefully. Check the labels of all bottles before removing the contents. Read the labels three times: before you pick up the container, when the container is in your hand, and when you put the bottle back.
- Do not insert droppers into reagent bottles. Pour a small amount of the chemical into a beaker.
-
- Keep your work area clean and help keep the common areas of the laboratory clean. If you spill something in a common are, remember that this substance may injure someone else.
- Never fully inhale vapors of any substance. Waft a tiny amount of the vapor toward your nose if you need to smell it.



- Never add water to a concentrated reagent (like an acid) when diluting the reagent. Always add the reagent to water. The reverse may cause it to splash out on you.
- Never perform any experiment that is not specifically authorized by your instructor. DO NOT play games with chemicals!
- Don't use any glassware that has any cracks, chips, star fractures, or any other deformity.

Lab Safety Rules

Science labs offer great opportunities for learning, teaching, and research. They also pose hazards that require proper safety precautions.

Stay safe when conducting your labs by following these guidelines.

Dress appropriately

Tie back long hair, and wear suitable gloves, goggles, and other protective equipment.

Proper supervision

Don't perform lab experiments without instructor supervision (unless given permission to do so).

Know location of emergency numbers & safety equipment

Know the location of safety equipment and emergency phone numbers (such as poison control) so you can access them quickly if necessary.

No food

Don't eat or drink in the lab—and never taste chemicals.

ID hazards

Identify hazardous materials before beginning labs.

Be attentive

Be attentive while in the lab. Don't leave lit Bunsen burners unattended or leave an experiment in progress.

Be careful when handling hot glassware

Turn off all heating appliances when not in use. Keep flammable objects away from your workspace.

Keep a clean workspace

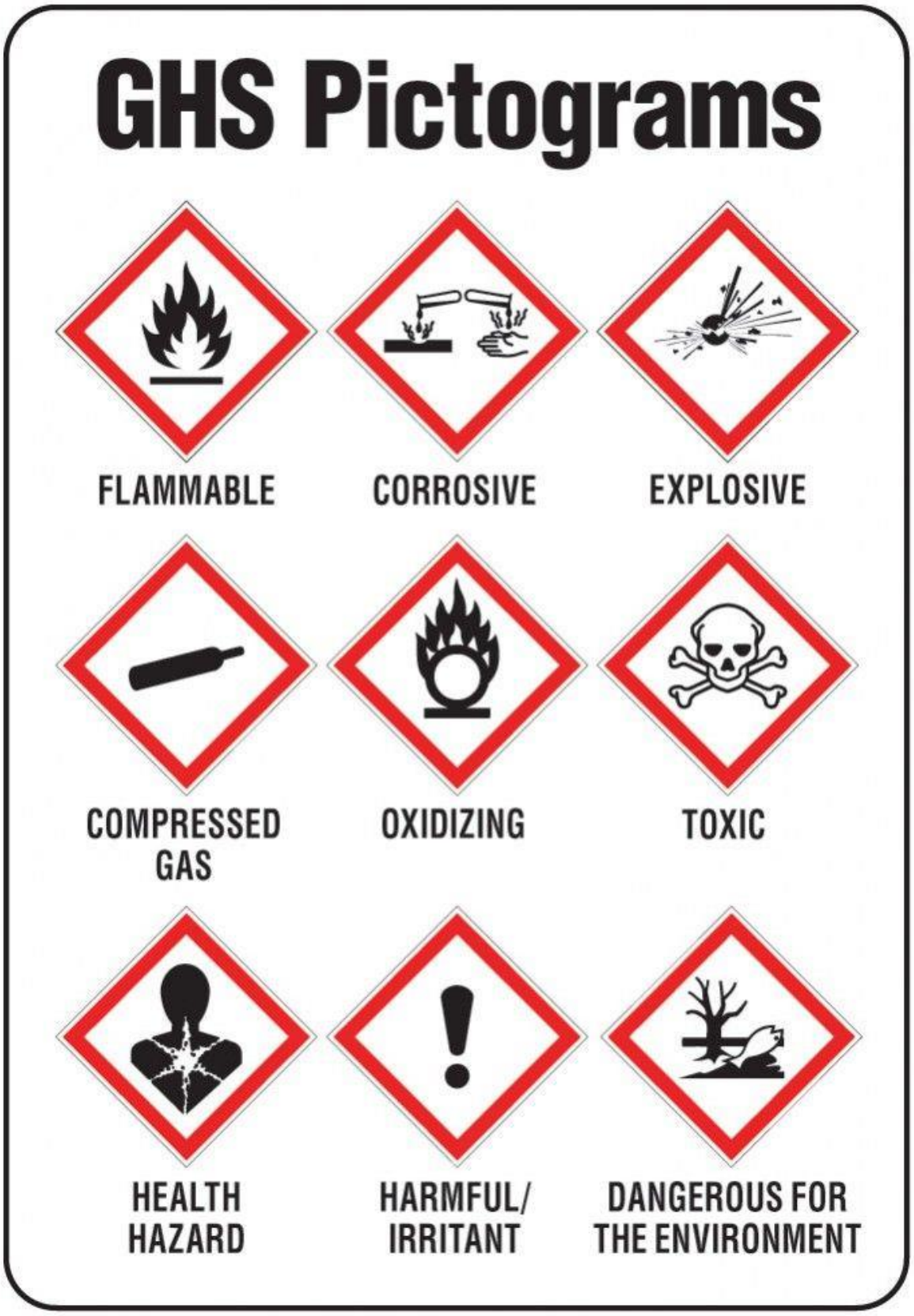
Don't obstruct work areas, floors, or exits. Keep coats, bags, and other personal items stored in designated areas away from the lab. Don't block sink drains with debris.

Handle glassware carefully

Properly dispose of anything that breaks. Report cuts, spills, and broken glass to your instructor immediately.

Clean up

After completing the lab, carefully clean your workspace and the equipment, and wash your hands.


GHS Pictograms
FLAMMABLE
CORROSIVE
EXPLOSIVE
COMPRESSED GAS
OXIDIZING
TOXIC
HEALTH HAZARD
HARMFUL/ IRRITANT
DANGEROUS FOR THE ENVIRONMENT

Student Name:	**Student ID no.:**
Date:	**Section:**
Instructor Name:	**TA name:**

Safety Quiz

This quiz will test you on the preceding safety discussion. Circle the correct answer(s) in each of the following questions:

1. Approved eye protection is to be worn

   a) for certain experiments
   b) only for hazardous experiments
   c) all the time

2. Eating in the laboratory is

   a) not permitted
   b) allowed at lunch time
   c) all right if you are careful

3. If you need to smell a chemical, you should

   a) inhale deeply over the test tube
   b) take a breath of air and fan the vapors toward you
   c) put some of the chemical in your hand, and smell it

4. When heating liquids in a test tube, you should

   a) move the tube back and forth through the flame
   b) look directly into the open end of the test tube to see what is happening
   c) direct the open end of the tube away from other students

5. Unauthorized experiments are

a) all right as long as they don't seem hazardous
b) all right as long as no one finds out
c) not allowed

6. If a chemical is spilled on your skin, you should

a) wait to see if it stings
b) flood the area with water for 10 minutes
c) add another chemical to absorb it

7. When taking liquids from a reagent bottle,

a) insert a dropper
b) pour the reagent into a small container
c) put back what you don't use

8. In the laboratory, open-toed shoes and shorts are

a) okay if the weather is hot
b) all right if you wear a lab apron
c) dangerous and should not be worn

9. When is it all right to taste a chemical used in the lab?

a) never
b) when the chemical is not hazardous
c) when you use a clean beaker

10. After you use a reagent bottle,

a) keep it at your desk in case you need more
b) return it to its proper location
c) play a joke on your friends and hide it

11. Before starting an experiment,

a) read the entire procedure
b) ask your lab partner how to do the experiment
c) skip to the laboratory report and try to figure out what to do

12. Working alone in the laboratory without supervision is

a) all right if the experiment is not too hazardous
b) not allowed
c) allowed if you are sure you can complete the experiment without help

13. You should wash your hands

a) only if they are dirty
b) before eating lunch in the lab
c) before you leave the lab

14. Personal items (books, clothes, etc.) should be

a) kept on your lab bench
b) left outside
c) stored out of the way, not on the lab bench

15. When you have taken too much of a chemical, you should

a) return the excess to the reagent bottle
b) store it in your lab locker for future use
c) discard it using proper disposal procedures

16. In the lab, you should wear

a) practical, protective clothing
b) something fashionable
c) shorts and loose-sleeved shirts

17. If a chemical is spilled on the table,

a) clean it up right away
b) let the stockroom help clean it up
c) use appropriate adsorbent if necessary

18. If mercury is spilled,

a) pick it up with a dropper
b) call your instructor
c) push it under the table where no one can see it

19. If a student's hair or shirt catches on fire,

a) use the safety shower to extinguish the flames
b) get the student to the floor and roll
c) roll the student in a fire blanket

20. Hazardous waste should be

a) placed in a special waste container
b) washed down the drain
c) placed in the wastebasket

Experiment 1

Melting Point Determination: Purity and Identity of Crystalline Organic Compounds

Objectives

- Determine the melting points of pure organic compounds.
- Determine the melting points of a mixture of two organic compounds.
- Identify an unknown organic compound by determining its melting point and by finding a mixture melting point.

Background

Most crystalline organic compounds have characteristic melting points that are sufficiently low (50-300 °C) to be conveniently determined with simple equipment. Organic chemists routinely use melting points

(a) to get an indication of the purity of crystalline compounds
(b) to help identify such compounds.

The **melting point** of a pure crystalline substance is a physical constant or property of that substance. A physical property of a substance is one of that is intrinsic to a

given substance in its pure form. Pure crystalline compounds usually have a sharp melting point. That is, the **melting point range** - *the difference between the temperature at which the sample begins to melt and the temperature at which the sample is completely melted* - is small (narrow). Impurities, even when present in small amounts, usually lower the melting point and broaden the melting point range. A wide melting point range (more than 5 ℃) usually indicates that the substance is impure; a narrow melting point range (0.5-2 ℃) usually indicates that the substance is fairly pure. Small differences in melting point (on the order of 2-3 ℃) may also result from variations in technique, thermometer accuracy, and the experience of the person doing the melting point determination.

Melting point can be used in the following way to help identify a compound. Say a sharp-melting, unknown substance X is suspected of being identical to some known substance A. If the two are identical, they should have the same melting point. Thus, if A is reported in the chemical literature to have a melting point significantly different from that observed for X, we can be quite certain that X does not have the same structure as A. On the other hand, if A is reported to have a melting point within a few degrees of that observed for X, the two substances may be identical (the small difference being due to variations in technique and purity).

To make certain that X and A are identical, one can determine the **mixture melting point** - that is, the melting point of a mixture of X and A (when a sample of A is available). If X and A are identical, the mixture should have the same melting point as X or A alone. On the other hand, if X and A are not the same substance (even though they separately have the same melting point), then a mixture of the two usually has a lower melting point and a broader melting point range than either substance alone. This is because each substance acts as an impurity in the other.

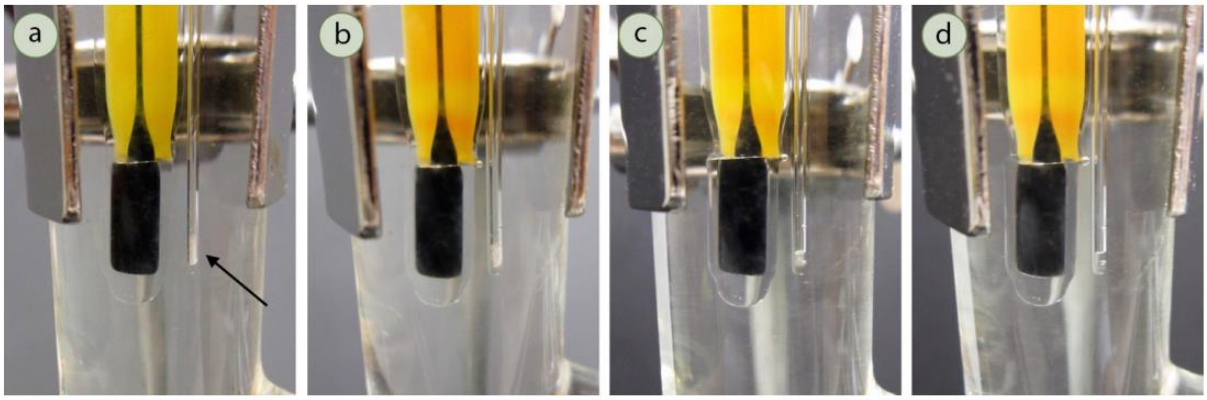
To summarize, if a crystalline substance is pure, its melting point range is likely to be narrow. If two samples have identical structures, their mixture melting point is not depressed and the melting point range is not broadened.

General Technique for Melting Point Determination:

To determine the melting point of a crystalline substance, we introduce a small amount of the finely powdered material into a thin – walled capillary tube that is

sealed at one end. The capillary tube is inserted into a melting point apparatus and heated. Two temperatures are recorded: the temperature at which the substance begins to liquefy and the temperature at which it becomes completely liquified. The observed melting point range is the interval between these two temperatures. The melting point is a characteristic property of a pure chemical substance.

The following figure indicates the melting of a solid white sample in a silicon oil bath.



a) Solid sample inside the oil, as indicated with an arrow, b) Initial melting of the sample, c) Midway, d) Melted sample.

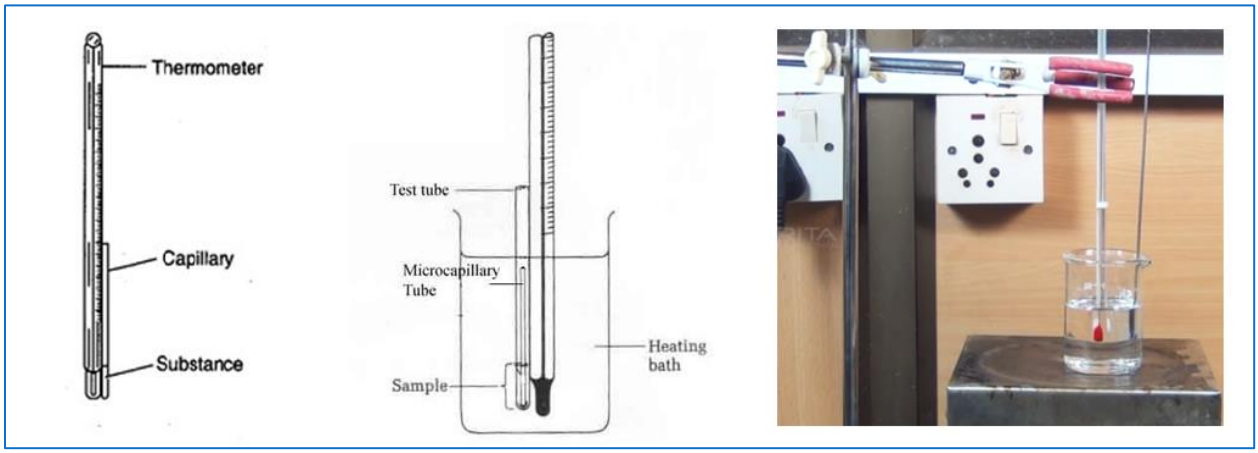
The observed melting point range can be influenced not only by the purity of the material but also by the size of the crystals, the amount of the material, the density of its packing in the tube, and the rate of heating. A finite time is required to transfer heat from a hot liquid bath or metal block through the walls of the capillary tube and throughout the mass of the sample. When the bath is heated too quickly, its temperature rises several degrees during the time required for melting to occur. This can result in an observed range that is higher than the true one.

When the temperature of the bath or block approaches the melting point of the sample, *it is essential for good results to raise the temperature slowly and at uniform rate*, usually about 2 °C/min. **The sample should be small, finely powdered, and packed tightly in a thin-walled capillary tube of small diameter**. The column of solid in the capillary tube should be just high enough to be seen clearly during melting (about 1-2 mm).

The behavior of a material upon melting should be observed and recorded carefully. Write, for example “melts sharply at 89.0-89.5 °C or “mp 131-133 °C, with decomposition” or “Discolors at 65 °C; melts slowly at 67-69 °C”.

There are two common methods for determining melting point:

- Oil bath method:



- Using a melting point apparatus

Apparatus/Reagents Needed

- Stand
- 50 ml beaker
- Hotplate with stirrer
- Thermometer
- Capillary tubes (open from one side)
- Cinnamic acid
- 50:50 (Cinnamic acid: Urea) mixture
- 25:75 (Cinnamic acid: Urea) mixture
- 75:25 (Cinnamic acid: Urea) mixture
- Unknown solid organic compound
- Clamp
- Clamp holder
- Rubber band or tape
- Oil (silicon or paraffin)
- Urea

Procedure

Part A: Determination of Melting Points

1- Pulverize 50-100 mg of urea by crushing it with a spatula against the walls of a small dry beaker.

2- Fill a melting point tube with a sample of dry urea by thrusting the open end into the beaker several times. To work the plug of solid material down to the sealed end to the tube, vigorously tap the sealed end on the table or lightly draw a file or stem of a test tube brush across the tube held loosely in the hand. Repeat the procedure until the tube contains a 1-2 mm column of densely packed powder at the bottom.

The following figure shows how to fill the melting point capillary tube.

a) Depositing sample into the open end of a capillary tube, b) Inverting and tapping the tube on the benchtop, c) Dropping the sample through a long tube, d) Correct height of sample in the tube.

3- Insert the tube into the melting point apparatus and start heating. The temperature may be allowed to rise fairly rapidly to within 15-20 ℃ below the compound's expected melting point. However, during determination of the actual melting point range, the temperature should not rise more rapidly than 1-2 ℃/min. Therefore, decrease the rate of heating when the temperature is about 15 ℃ below the expected melting point. The melting point of urea is approximately 130 ℃.

4- Record the melting point range of urea on the report sheet.

5- In a similar way, determine and record the melting point range of a sample of *trans*-cinnamic acid. This compound also melts at approximately 130 ℃.

6- To demonstrate the effect of impurities on the melting point of a pure substance, determine the melting point range of a 50:50 mixture by weight (use about 50 mg of each compound) of urea and cinnamic acid. Repeat the procedure with 75:25 and 25:75 mixtures. Using midpoints of the melting point ranges, the data on the report sheet.

Part B: Identification of an Unknown

** When the melting point of an unknown substance is to be determined, you can save time if you first obtain its approximate melting point using a rapid heating rate-say, 15-20 ℃/min. Then allow the temperature of the thermometer to drop to 15-20℃ below the approximate melting point.

Obtain an unknown sample (of one of the substances listed in table 1.1) from your instructor. Fill the melting point tube with the unknown sample, use the data in table 1.1 to make preliminary identification of your unknown. Then confirm its identity by the mixture melting point technique: mix about 50 mg of the unknown with an equal weight of the substance you suspect it to be from the side shelf and determine the mixture melting point. Repeat the procedure, if necessary, to determine with certainty the identity of the unknown.

Table 1.1 Melting points of some organic compounds

Compound	mp, °C	Compound	mp, °C
Biphenyl	70-71	2-Naphthol	121-122
ε- Caprolactam	69-71	Benzoin	132-133
Vanillin	81-82	*trans*-Cinnamic acid	132-133
Glutaric acid	97-99	Urea	132-133
Dibenzothiophene	99-100	Cholesterol	148-150
Acetanilide	113-114*	Salicyclic acid	156-158
(±)-Mandelic acid	119-120	Benzanilide	164-166
Benzoic acid	121-122	Sulfanilamide	165-166

*If the acetanilide was recrystallized from water and not thoroughly dried, it may melt at 83-84^{0}C.

Useful Links

Melting point of an organic compound-Oil bath method
https://www.youtube.com/watch?v=nQNaTfqXECk

Mixed melting point-melting point apparatus
https://www.youtube.com/watch?v=cLHdm8wJJIw

Student Name:	Student ID no.:
Date:	Section:
Instructor Name:	TA name:

Experiment 1: Melting Point Determination

Pre-lab Questions

1. Determine the term *melting point range*.

2. When determining the melting point of an unknown substance, it is a common practice to first determine a rough melting point by quickly heating the sample followed by a careful determination of the melting point by gradually heating the sample at the rate of 1-2 ℃/min. What is the advantage of this two-step determination of the melting point?

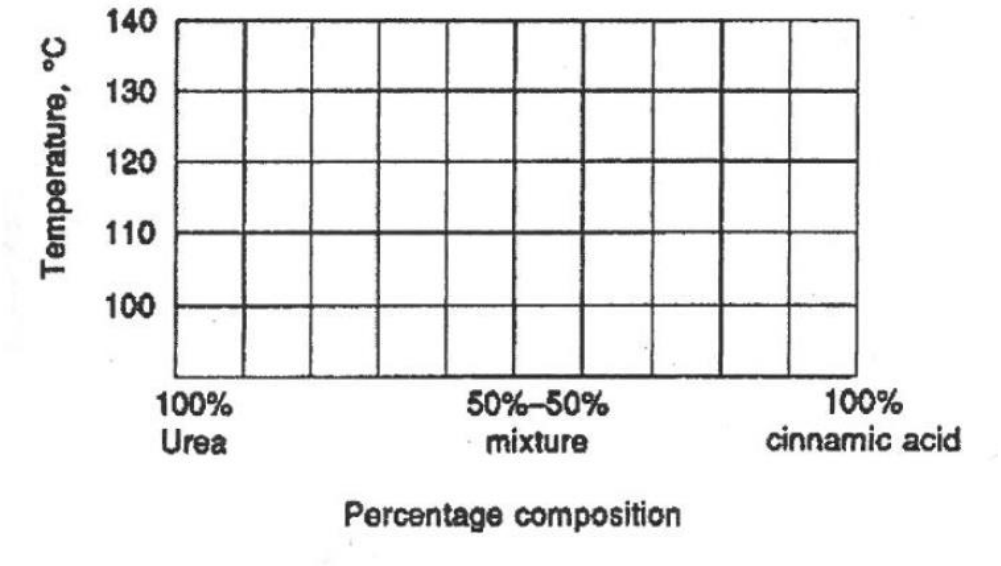
3. What two effects do impurities have on the melting point of an organic compound?

Results and Observation

1. Record the observed melting points in the table.

	Melting Point, °C		
Compound	start	Finish	Range
Urea			
Cinnamic acid			
50:50 mixture			
75:25 mixture			
25:75 mixture			

2. Graph the midpoints of the melting ranges of urea, cinnamic acid, and mixtures of the two.



3. **Identification of your unknown**

Identity number of your unknown: ----------

Melting point range: ----------

Melting point mixed with ---------- : ----------

Melting point mixed with ---------- : ----------

My unknown compound is: ----------

Post-lab Questions

1. Look at the following melting point ranges and tick the box to show whether the substance is likely to be a mixture or a pure substance.

Substance	Starts melting (°C)	Finishing melting (°C)	Pure	Mixture
A	99.1	100.4		
B	0	9.1		
C	132.2	132.4		
D	-188.2	-183.8		

2. Why is it essential to:

(a) pack the sample tightly in the melting point tube

(b) heat the sample slowly and steadily as the melting point temperature is approached?

2. What is the effect of using too large a sample when determining a melting point?

3. Research chemists when determining the melting points of newly synthesized compounds often fill a second capillary tube with a known substance (of similar melting point range) and co-determine the melting points of the two substances using the same apparatus. What purpose does the determination of the melting point of the known substance serve?

4. For what two purposes are melting points routinely used?

   a.

   b.

5. Three test tubes contain white crystalline organic solids A, B and C, each of which melts at 149-150 °C. A 50:50 mixture of A and B melts at 130-139 °C. A 50:50 mixture of A and C melts at 149-150 °C.

   In what range would a 50:50 mixture of B and C probably melt?

   What can you say about the identities of A, B and C?

Experiment 2

Analgesics and Thin-Layer Chromatography

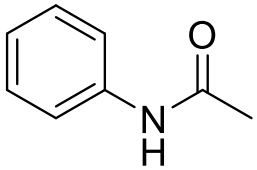
Objectives

- Describe the technique of thin-layer chromatography (TLC).
- Identify the structure of a few known analgesics.
- Calculate R_f values.
- Develop a readable TLC plate.
- Identify unknown analgesics by using TLC.

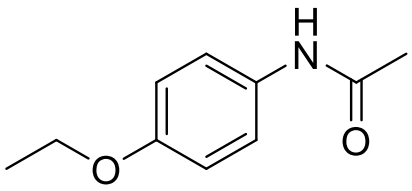
Background

During a lifetime, almost everyone uses some type of over-the-counter pain reliever. These drugs are often taken to relieve pain (analgesic) or to reduce a fever antipyretic). Over the years, other substances have been added to drugs; these additives include caffeine, muscle relaxers, sedatives, and antihistamines, to mention a few.

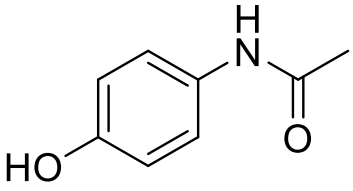
The discovery of antipyretics began by mistake in 1886. The compound found to reduce fevers was **acetanilide**.



As research advanced, the compound **phenacetin** was found to be more effective antipyretic and analgesic. This eventually led to the discovery of **acetaminophen**, which is widely used today. Note the similarity in structure of these two compounds.



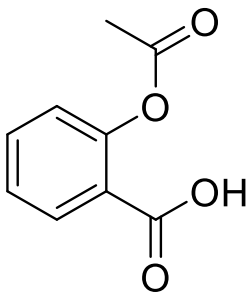
phenacetin



acetaminophen

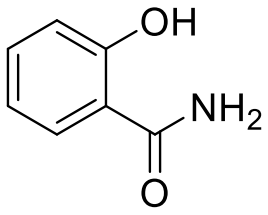
Both of these substances are more effective in their relief than acetanilide. But the excessive use of either acetaminophen or phenacetin can lead to an anemic-like side effect. Acetaminophen is a viable alternative to **aspirin** as a pain-killer or a fever reducer since it does not cause stomach irritation. On the other hand, acetaminophen is lacking in two areas where aspirin is beneficial. Acetaminophen does not possess anti-inflammatory properties, and it has no effect on the cardiovascular system.

While aspirin is a very effective analgesic and antipyretic, it has been proved to cause hemorrhaging of the stomach lining. People with ulcers or other stomach-lining sensitivity cannot tolerate aspirin. Aspirin is widely used by arthritic people since it acts upon the discomfort and swelling of inflamed tissue. Furthermore, aspirin is believed to provide protection against heart attacks and strokes when used on an every-other-day basis. For young children, however, aspirin should be avoided. A known link exists between aspirin and Reye's syndrome.



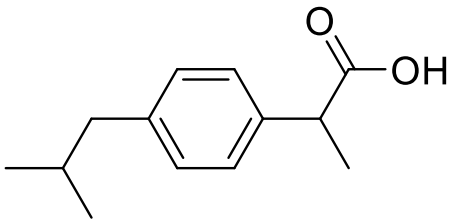
aspirin
(acetylsalicylic acid)

Salicylamide is similar to aspirin in its structure and was at one time widely used as an analgesic. It is no longer found as an over-the-counter preparation.



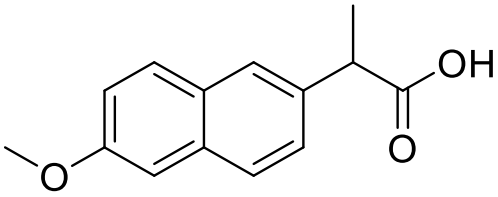
salicylamide

Ibuprofen was introduced in the United States in 1974 as a prescription analgesic. This compound is now found in the market as both a prescription and nonprescription drug. It is available over the counter as Advil, Nuprin, and in generic brands. Its main action targets inflamed tissue, but it still has analgesic and antipyretic properties. When taken with food, ibuprofen should not cause much stomach upset. Unlike aspirin, it does not provide protection against heart attacks. Those people who do not tolerate aspirin well are advised against this drug, as well as those with heart disease, kidney problems, hypertension, or asthma. Ibuprofen's biggest selling point is its potency in reducing pain.

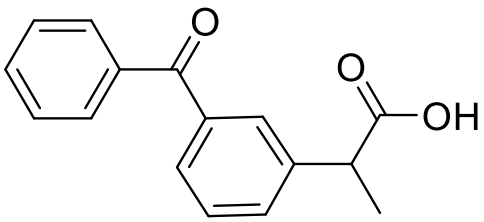


ibuprofen

The two latest analgesics approved for nonprescription use are **naproxen**, which is patented and sold as Aleve, and **ketoprofen**, patented as sold as both Actron and Orudis KT. Naproxen's long-lasting relief, claimed by the manufacturer (Syntex Corp. and Procter & Gamble Co.) to be 8-12 hours, is its strongest selling point. Ketoprofen's selling points include its fast onset, short half-life, and potency; Bayer (manufacturer of Actron) claims that ketoprofen gets into the body quickly to perform its relief and exits the body quickly. Like ibuprofen and aspirin, naproxen and ketoprofen offer anti-inflammatory relief for ailments such as arthritis.



naproxen



ketoprofen

Chromatography

Chromatography is a technique used widely to purify, to separate, or to identify substances. While several types of chromatography are available, the basic theory behind each type is the same. Chromatography involves two phases:

- The **stationary phase** which works to adsorb the substances; the most often used solid adsorbents in TLC are silica gel ($SiO_2.xH_2O$) and aluminum oxide.
- The **mobile phase (eluent)**, which functions to move the substances along the stationary phase.

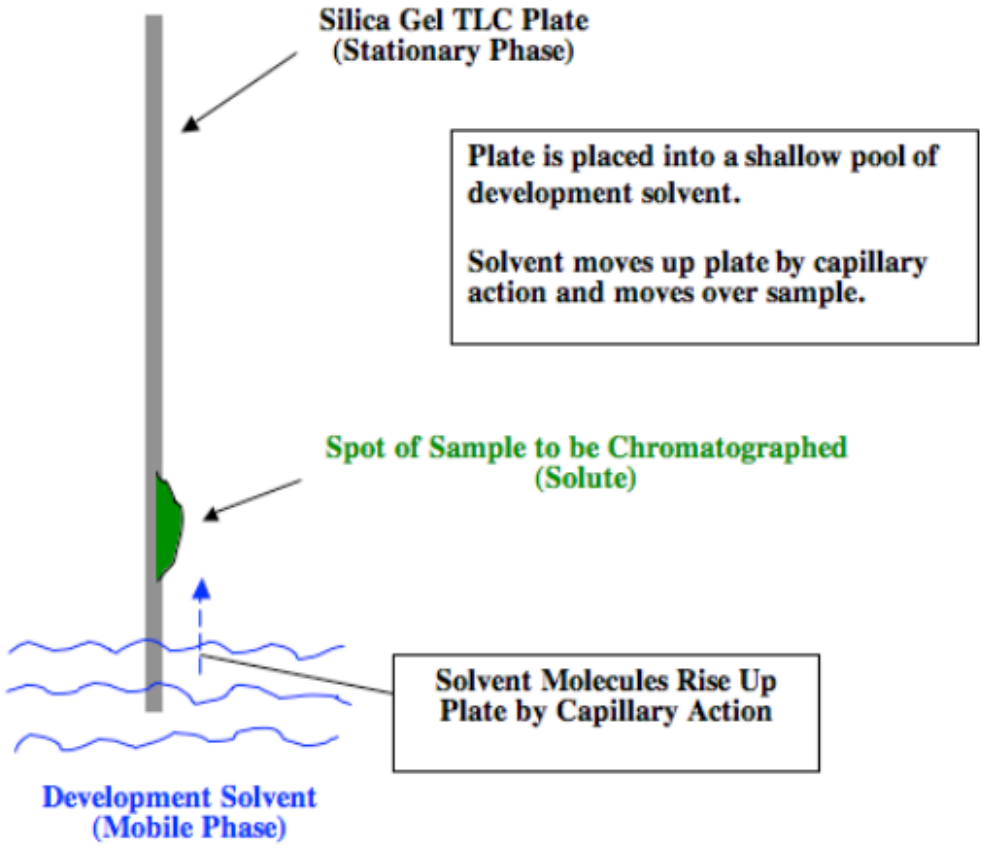
This technique works on the concept that compounds of similar structure or polarity attract and tend to hold together. For example, if the stationary phase is made up of a very polar compound(s), a substance being tested that possesses polar groups will tend to be held to this stationary phase. Polar substances, in this case, will not be carried well by the mobile phase. Nonpolar substances, on the other hand, will move easily along stationary phase. They will not be readily adsorbed by the polar stationary phase.

The mobile phase in chromatography needs to 'complement' the stationary phase for successful separation of components. When the stationary phase is polar, a solvent that is too polar will move all the components of polar nature along the solvent from without adequate separation. Additionally, a solvent that is too polar may bind stronger to a polar adsorbent than the substances to be separated, causing them to remain in the mobile phase. Conversely, a solvent that is too nonpolar may not be able to move any of the components along the stationary phase. Often, a mixture of solvents is required for separation of components. the choice of mobile

phase solvent typically arises through the testing of different solvents or solvent combinations. Solvents of intermediate polarity include dichloromethane (DCM, CH_2Cl_2) and hydrocarbon/ ether mixtures.

Thin-layer chromatography (TLC) procedures can utilize commercial chromatography plates that have some type of chemical coating that functions as the stationary phase. The plates for this experiment possess a silica gel coating, which is polar, along with a fluorescent indicator. The substances to be tested will be spotted on this plate using capillary tubes. Then the plate will be set in a covered glass jar or chamber that contains a small amount of solvent (mobile phase). This is called the **developing chamber**.

The concept behind TLC is illustrated in the following figure:

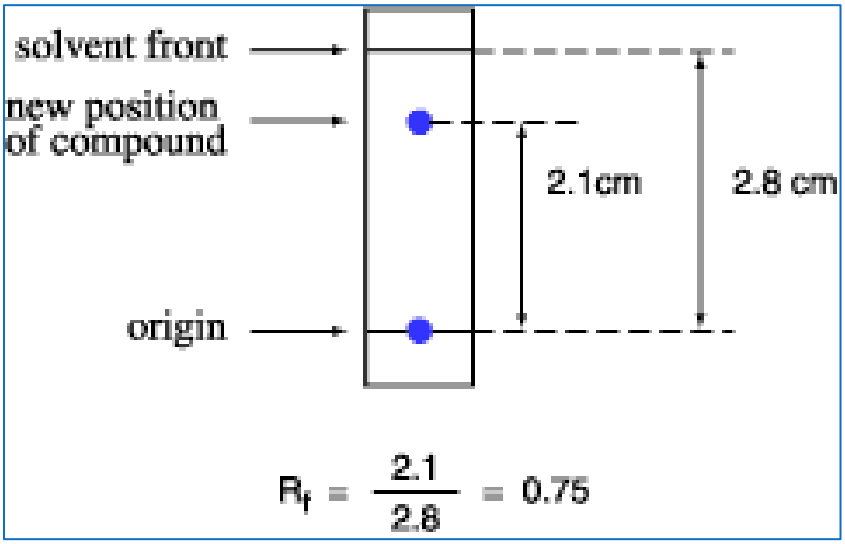


The solvent makes up the mobile phase, as it functions to carry the substances up the TLC plate. When the solvent nears the top of the plate, the plate is removed from the jar and the **solvent front** (the place where the solvent stops) is marked. If the spots are not colored, upon illumination with ultraviolet light, spots are seen on the TLC plates. These spots represent how far the substances traveled and should be marked or circled lightly with a pencil. Remember that the more similar the substance is to the silica gel, the shorter the distance it moves.

By knowing the distance that the solvent moves and the distance that each substance moves**, R_f values (retardation factor)** can be calculated. R_f values have no units and are a solvent-dependent physical property.

$$R_f = \frac{distance\ substance\ traveled}{distance\ solvent\ traveled}$$

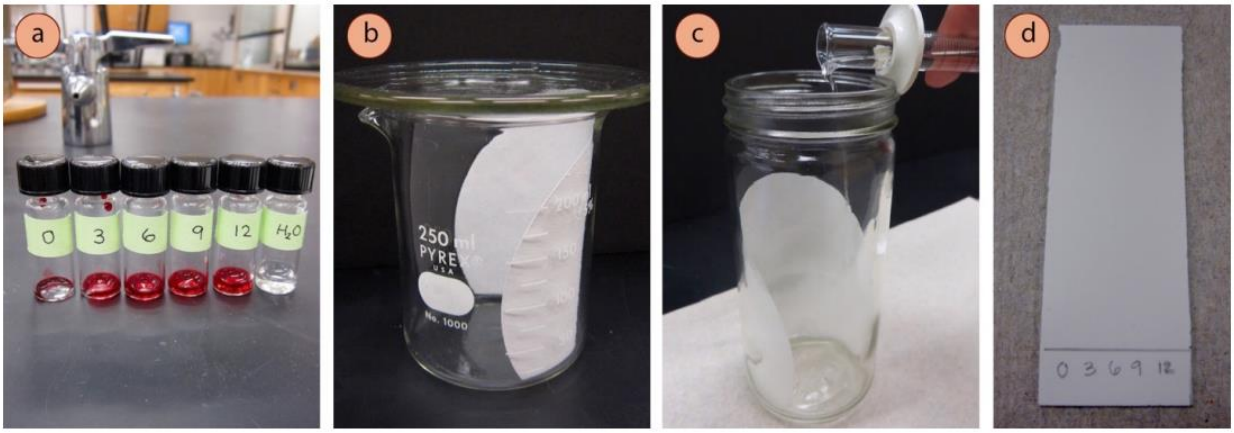
Example:



These R_f values are helpful in the identification of drugs from urine and blood samples when all chromatography conditions are constant (mobile phase system, adsorbent, thickness of adsorbent, relative amount of spotted material). But since many compounds can have the same R_f value, other data tests may be necessary to confirm the identification.

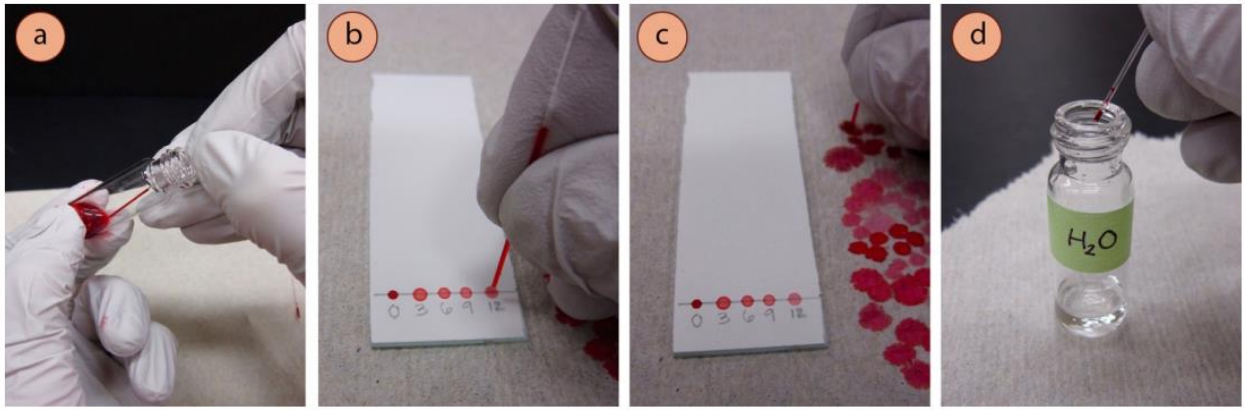
Here are the main steps of TLC.

Step 1: Prepare the samples (by dissolving them in a volatile solvent), the developing chamber and the TLC plate.



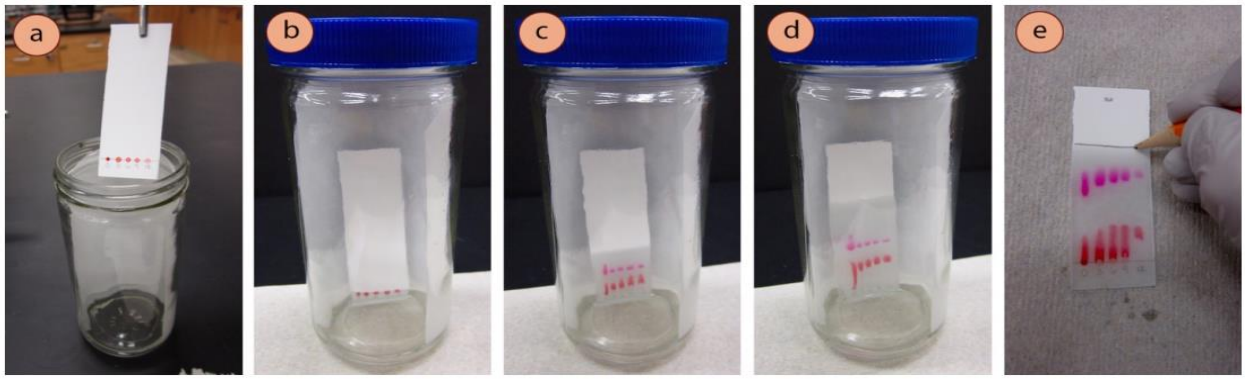
a) Prepared samples, b) TLC chamber made with a beaker and watch glass, c) Adding mobile phase to a TLC chamber, d) Prepared plate (use pencil to mark the origin and spots).

Step 2: Spot the **TLC** plate.



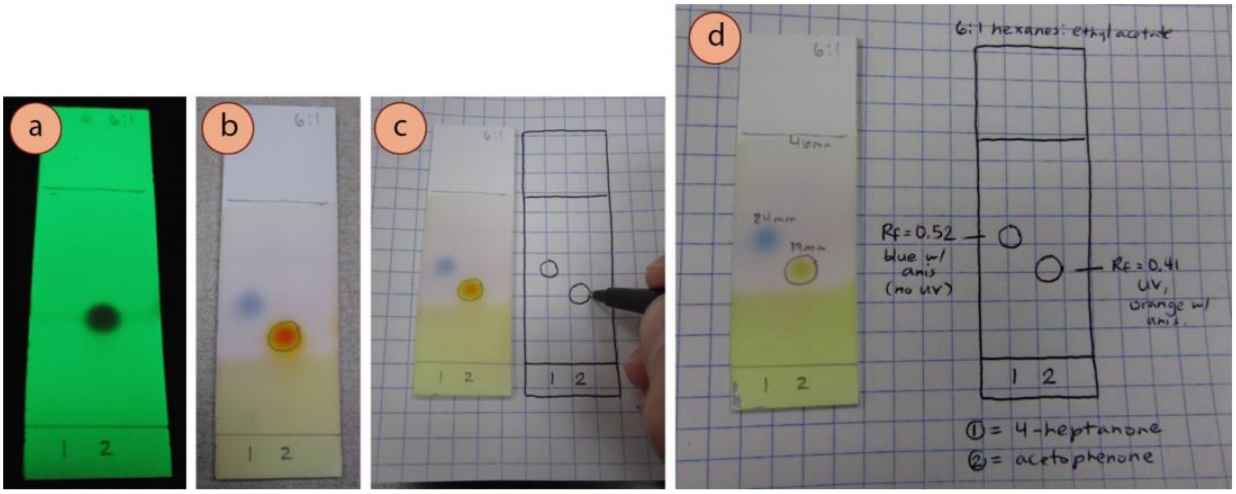
a) Tipping the vial to withdraw liquid into the capillary tube, b) Spotting samples onto a TLC plate, c) Excess sample drained on a paper towel, d) Rinsing the capillary tube with solvent (water in this case).

Step 3: Develop the plate.



a) Using forceps to place the TLC plate into the chamber, b-d) Elution, e) Marking the solvent front with a pencil.

Step 4: Visualize the spots and calculate R*f* values. If the substances are not colored UV light can be used to visualize them. Alternatively, the TLC late can be stained with a suitable staining solution to see the spots.



a) Plate under UV light, b) Plate stained with p*-anisaldehyde staining solution, as it appeared directly after heating, c) Copying the TLC into the notebook, d) calculating R_f values.*

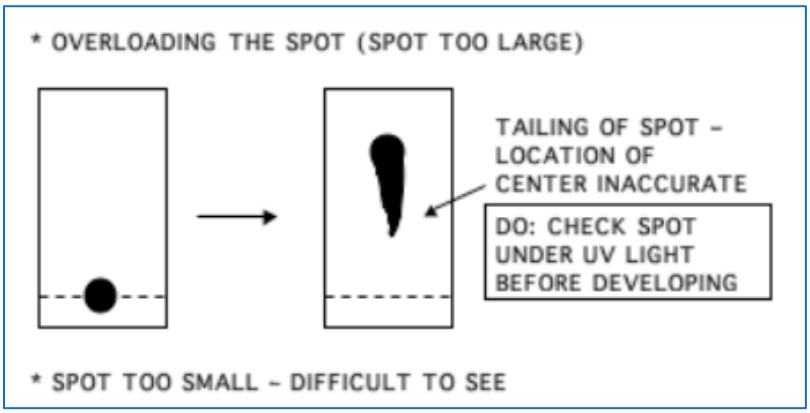
Important tips regarding TLC:

- Do not touch the TLC plate on the side with the white surface.

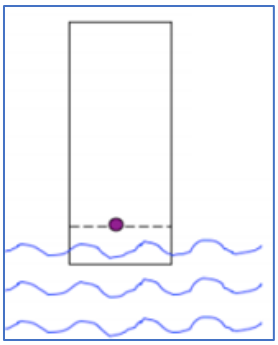
- You can only spot/label/mark TLC plates using a pencil. You can't use a pen because the ink will travel up the TLC plate with the TLC solvent, just like your chemical samples do. The graphite in a pencil will not run up the plate!

- Place a filter paper inside the developing chamber. The filter paper keeps the chamber saturated with vapors so when the eluent rises on the plate it doesn't easily evaporate but continues to climb and undergo the chromatography. If the eluent evaporated, movement would stop, but could also change the local composition of a mixed eluent and affect the results.

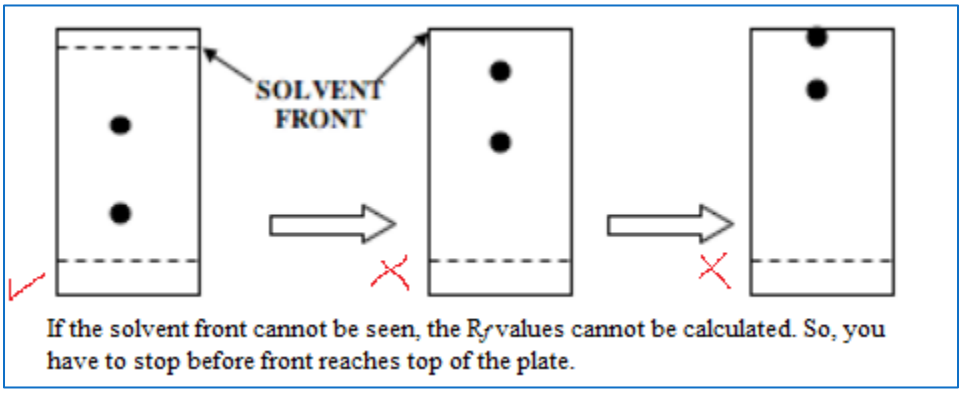
- Spotting sizes of your sample should not be larger than 1-2 mm in diameter. Try to avoid spotting too much material, because this will deteriorate the quality of the separation considerably ('tailing'). The spots should be far enough away from the edges and from each other as well.



- The liquid level must be below the pencil line where the samples are spotted, or the compounds will dissolve in the pool of eluent instead of traveling up the plate.

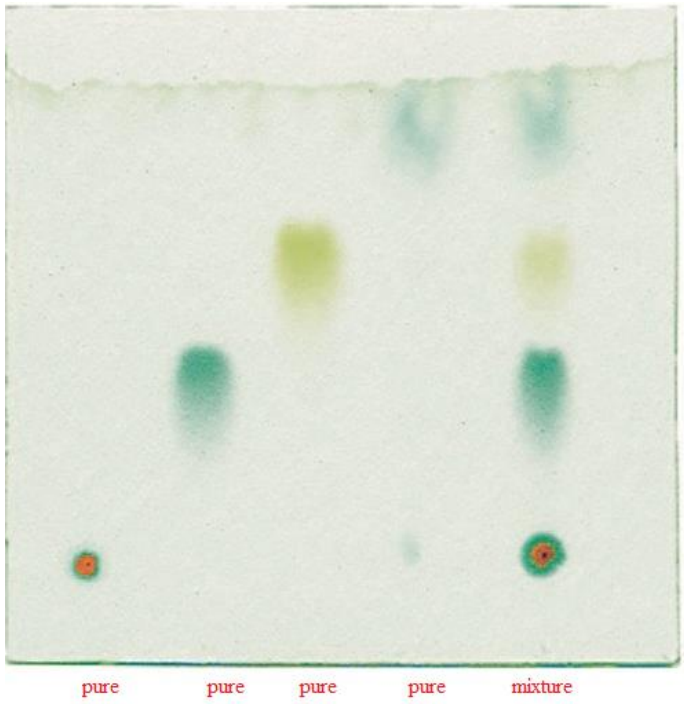


- Allow the plate to develop until the solvent is about half a centimeter below the top of the plate. Remove the plate from the beaker and immediately mark the solvent front with a pencil.



If the solvent front cannot be seen, the R_f values cannot be calculated. So, you have to stop before front reaches top of the plate.

- A pure substance produces one spot on the TLC plate while an impure substance produces two or more spots.



- Although a pure substance would show only one spot on a developed TLC plate, if you got one spot in an experiment, this does not necessarily mean your substance is pure, because this spot may refer to more than one substance having the same R_f value.

We will test some pain reliever ingredients such as: aspirin, acetaminophen, ibuprofen, salicylamide, naproxen and ketoprofen, along with unknown generic preparation. You should be able to identify which analgesic compound is contained in the generic drug by TLC analysis. Then an unknown mixture will be tested and analyzed.

Apparatus/Reagents Needed

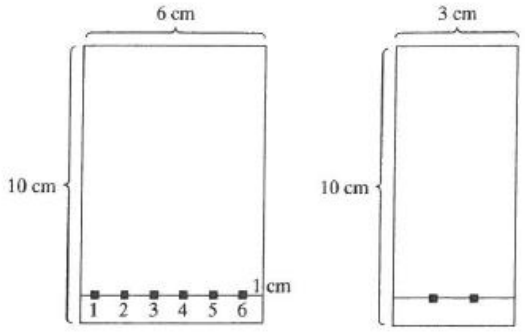
- TLC plates (silica gel) with fluorescent indicator (6 cm x10 cm).
- capillary tubes (open both ends).
- pencil
- ruler
- Filter paper
- developing chamber (glass jar with lid)
- UV lamp
- Various analgesic solutions (1-5 mg analgesic in 5 mL CH_2Cl_2 and 5 mL ethanol: aspirin, acetaminophen, salicylamide, ibuprofen, naproxen, ketoprofen, over-the-counter analgesic, unknown mixture). A solution of caffeine.
- Solvent (mobile phase): ethyl acetate / hexane (50:50) with 0.3% glacial acetic acid.

Procedure

1- Obtain a developing chamber. Put a filter paper in it then put a few milliliters of the mobile phase (eluent).

2- Obtain three TLC-plates (one 10 cm x 3 cm and two 10 cm x 6 cm). Handle them carefully and only at the edges to avoid contamination.

3- Draw a light pencil line across the short parts of the plates, 1 cm from the bottom. On larger plates mark 6 spots on the line with a pencil, equal distances apart. On the smaller plate mark 3 spots on the line with a pencil, equal distances apart.



4- **Spot the analgesic solution** as follows with capillary tubes. Use a separate capillary tube for each substance. Let the spot dry and then reapply the solution. Spot 1-aspirin, spot 2-acetaminophen, spot 3-salicylamide, spot 4-ibuprofen, step 5-naproxen, spot 6-ketoprofen.

5- Check spots under UV light then allow the spots to dry.

6- Carefully place the TLC plate in the developing chamber. Cover the jar. Don't disturb the glass chamber while development of the plate takes place.

7- When the solvent has reached ~1-2 cm from the top, remove the plate from the jar and immediately mark the solvent front.

8- Visualize the pots under a UV lamp and circle each spot using a pencil. Calculate R_f values of each substance.

9- Make a solution for TLC analysis using unknown, generic analgesic tablet (crush the tablet first then dissolve it in DCM/ethanol).

10- **Spot the smaller TLC plate with a spot for the generic analgesic and another spot for the unknown mixture**.

11- Calculate the R_f values and identify each substance in the mixture. Decide, according to your data, which pain-relieving substance is in your unknown generic preparation. Your decision s should be based both on the Rf values and the appearance of the spots. Decide what are the substances present in the unknown mixture too.

12- **Spot the 2nd large TLC plate** with a spot for the unknown generic analgesic, a spot of the unknown mixture and spots for susceptible components of each.

13- Check if your decision regarding the components of both the generic analgesic and the unknown mixture is correct.

Useful links

TLC of Analgesics Experiment Part 1, Prelab:

https://www.youtube.com/watch?v=5ECpK5iRj30&t=6s

TLC of Analgesics Experiment Part 2, Spotting and Developing:

https://www.youtube.com/watch?v=uqyDBRHxfGw

TLC of Analgesics Experiment Part 3, Visualizing Spots:

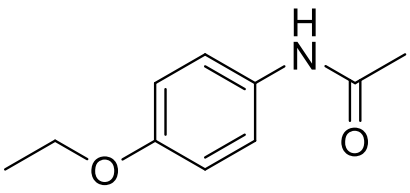
https://www.youtube.com/watch?v=kgcMFpRFSR4

Student Name:	Student ID no.:
Date:	Section:
Instructor Name:	TA name:

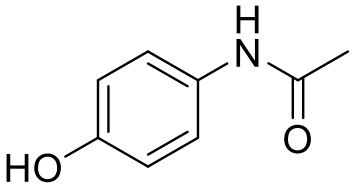
Experiment 2: Analgesics and Thin-Layer Chromatography

Pre-lab Questions

2. Look at the structures of acetaminophen and phenacetin. What functional group is found on acetaminophen and not on phenacetin?



phenacetin



acetaminophen

2. Thin-layer chromatograph was performed on an unknown substance. The substance traveled 5.85 cm while the solvent front was measured to be 6.92 cm from the initial spotting. Calculate the R_f value.

3. In your own words, define the following terms:

a. analgesic

b. Thin-layer chromatography

c. Developing chamber

d. solvent front

e. Ibuprofen

4. What is the role of the stationary phase in chromatography?

5. What makes up the stationary phase in thin-layer chromatography?

Results and Observations

1- Draw your TLC plate here and stick the original one,
Then fill in the table below.

Substance code	**Substance**	**R_f value** *(Show calculations)*
A	Acetaminophen	
B	Aspirin	
C	caffeine	
D	ibuprofen	
E	Unknown #9	

What is the identity of the unknown? Explain your answer.

Post-lab Questions

1. Using your TLC data, decide which substance is:

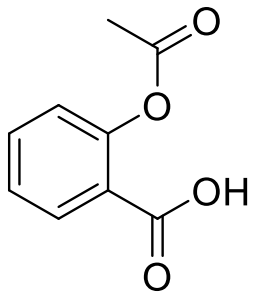
   a. most chemically similar to silica gel (stationary phase).

   b. most chemically different from the silica gel.

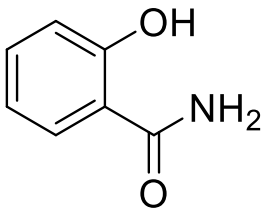
2. In the TLC lab experiment, a student added 14 mL of the solvent to his developing chamber instead of 4 mL as stated in his procedure. Explain the effect this mistake will have on his experiment.

3. A term used recently in describing aspirin, ibuprofen, and naproxen is NSAIDs; this stands for nonsteroidal anti-inflammatory drugs. Why is acetaminophen *not* included in this group?

4. Here are the structures of aspirin and salicylamide:



aspirin
(acetylsalicylic acid)



salicylamide

a. What are the functional groups in the aspirin molecule?

b. What functional groups does salicylamide possess?

5. You tested an unknown mixture in the lab that was to be made up of two substances that you tested at a previous time. After the TLC plate was developed, three spots were seen.

a. Draw a picture of what this plate looked like under the UV lamp.
(draw on Paint then copy your drawing from there and paste it here)

b. How could you determine which of the three spots was due to an impurity?

6. Based on what you have read in the background of the experiment, fill in the following table:

	Advantages	**Disadvantages**
Acetaminophen		
Aspirin		
Ibuprofen		

Experiment 3

Recrystallization:

Purification of Crystalline Organic Compounds

Objectives

• Understand the concept behind recrystallization and its usefulness in organic synthesis.

• Learn how to choose the correct solvent for recrystallization.

Background

Impure crystalline substances can be purified by recrystallization from a suitable solvent. This process depends on two facts: Most compounds are more soluble in hot solvents than in cold ones, and impurities have solubilities different from those of the desired compound.

The procedure involves:

(1) **dissolving** the impure material in a minimum amount of boiling solvent,
(2) **filtering** the hot solution to remove insoluble impurities,
(3) allowing the solution to **cool slowly** to deposit crystals of the compound,
(4) **filtering** the crystals from the solution (called the mother liquor),
(5) **washing** the crystals with a little cold solvent to remove the mother liquor,
(6) **drying** the crystals to remove the last traces of solvent.

If recrystallization is to be effective, the solvent must be properly selected. A good recrystallization solvent should

(l) dissolve a moderate quantity of the substance being purified at an elevated temperature, but only a small quantity at low temperature

(2) not react with the substance being purified,

(3) dissolve impurities readily at a low temperature or not dissolve them at all, and

(4) be readily removable from the purified product. This last requirement usually means that the solvent should have a fairly low boiling point and evaporate readily.

** If a single solvent cannot be found that meets all these requirements, a mixture of two solvents may be used.

Solvents suitable for recrystallizing a known compound are usually reported in the chemical literature. If none is reported, or if the substance is a new compound, several solvents can be tested in the following way. Place about 10 mg (a small spatula tipful) of the substance to be purified in each of several small test tubes, and add about 0.25 mL of a different solvent to each. Then observe the solubility of the sample in each solvent, when cold and when heated. Also note whether abundant, well-formed crystals are produced as the hot solution cools.

To obtain a good recovery of purified material, it is best to avoid using unnecessarily large volumes of solvent. Dissolving the substance in the smallest possible amount of hot solvent minimize the amount of material lost by retention in the mother liquors. In practice, 3-5% more solvent than the minimum required is used so that the hot solution will be not quite saturated. This helps to prevent separation of the crystals and clogging of the filter paper during filtration of the hot solution.

Traces of coloring matter or resinous impurities can sometimes be removed with selective adsorbents, such as finely divided **charcoal**. To do this, add a small amount of decolorizing charcoal to the warm solution before filtering it. Avoid using excess decolorizing agent, however, because it may also adsorb appreciable amounts of the substance being purified.

Some substances are readily form supersaturated solutions, and crystallization may not occur spontaneously when the hot solution is cooled. In such situations, it is sometimes possible to initiate crystallization by scratching the walls of the vessel beneath the surface of the solution with a stirring rod. Though the effect of scratching the inside walls of the vessel in inducing crystallization is not well understood, two possible explanations are:

- the fine glass particles produced through such scratching may act as nuclei on which crystallization may begin, or more likely,

- small amounts of the solution drawn onto the sides of the vessel during scratching evaporate to produce dry solutes that are pushed back into the solution.

These finely divided solute particles act as nuclei for crystallization to start. The best way to induce crystallization is to ‘seed’ the cold solution with one ow two crystals of the substance being purified.

Although some compounds crystallize readily, others may separate from solutions as oils, and it may take some time before they crystallize.

To remove insoluble impurities and decolorizing charcoal, it is necessary to filter the solution while it is hot. Otherwise, when the solution cools, crystals deposit prematurely. Rapid filtration can be accomplished by using fluted filter paper (paper folded with many pleats to give a large surface) or by using a vacuum to increase the filtration rate.

** Do not add decolorizing charcoal to a hot solution. If a solution is at or near its boiling point, the addition of finely divided charcoal (which acts as thousands of boiling chips) will cause rapid boil over.

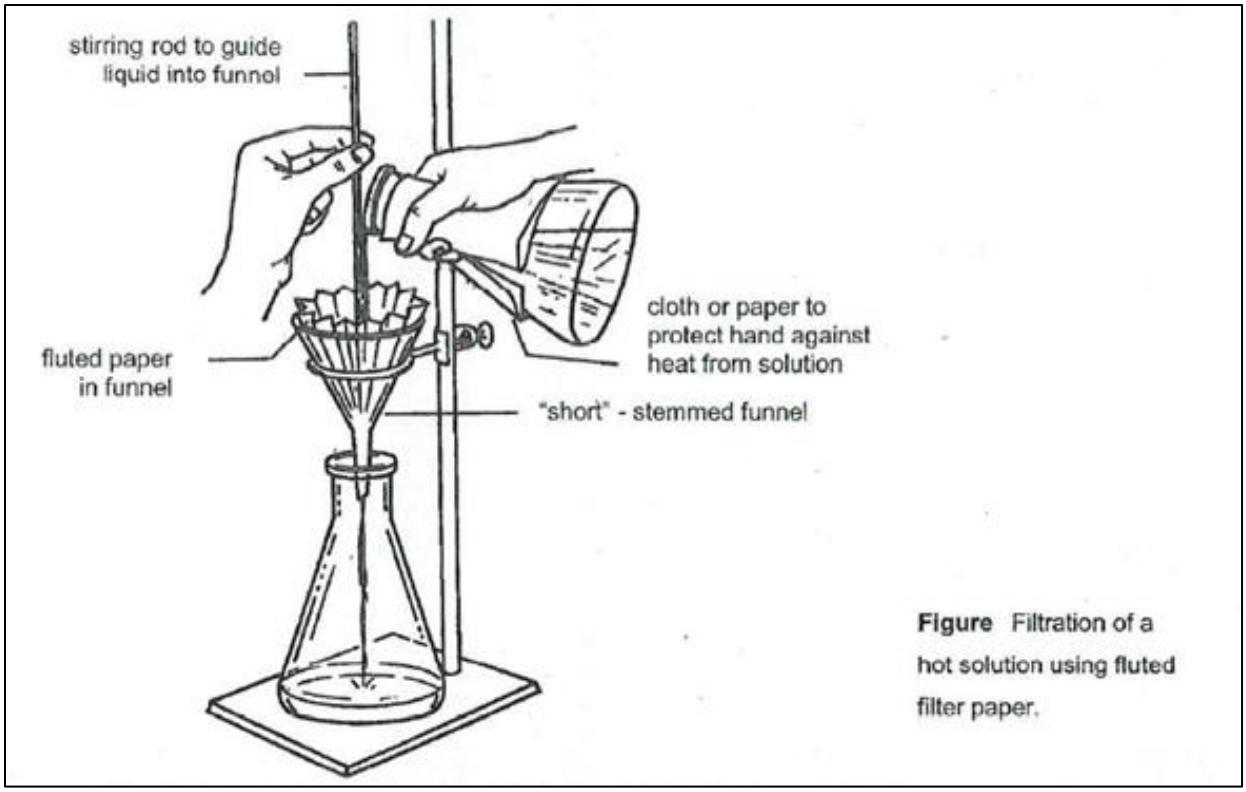
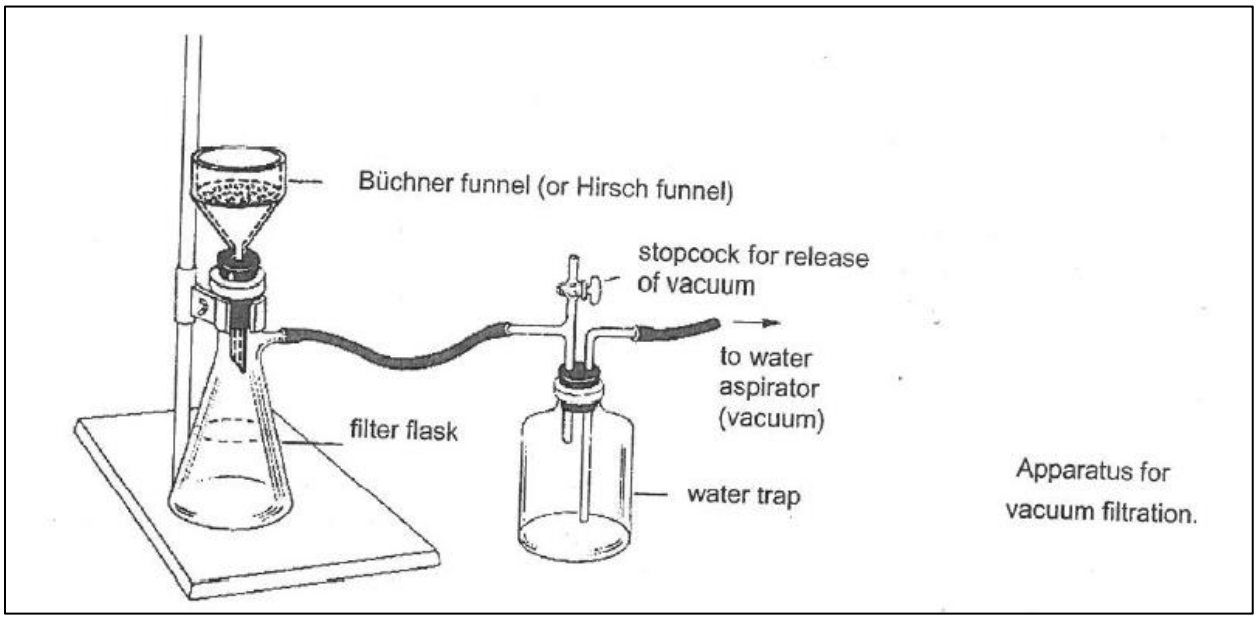


Figure Filtration of a hot solution using fluted filter paper.

Vacuum Filtration is generally used to remove soluble impurities and solvent from the crystals of the purified substance. The following Figure shows the apparatus for vacuum filtration.



Apparatus for vacuum filtration.

A Büchner or a Hirsch funnel is fitted to a filter flask with a tight-fitting rubber stopper. A disc of filter paper just large enough to cover all the holes in the funnel is placed in the funnel and moistened with some of the solvent used in the recrystallization. The filter flask is then connected to the aspirator by thick-walled rubber tubing through a water trap, and vacuum is applied. When the filter paper is drawn tightly to the funnel, the solution and crystals are transferred to the funnel. The solution passes through the paper, while the crystals deposit on the paper.

Recrystallization of Acetanilide

In this experiment a sample of impure acetanilide will be recrystallized from water. Pure acetanilide recrystallizes out as white leaflets from water. You will weigh the crude sample and the pure product and percentage recovery and the melting point before and after recrystallization to illustrate the efficiency of the process.

** In a recrystallization procedure, the maximum amount of material that can be recovered is the weight of the crude sample. In fact, only a fraction of this sample is obtained as purified crystals. The efficiency of the recrystallization (or the percentage recovery) is given by:

$$\% \text{ Recovery} = \frac{mass\ of\ purified\ products}{mass\ of\ crude\ sample}\ x\ 100$$

The value should be less than 100%. If it is greater, your recrystallized material is wet or impure.

Apparatus/Reagents Needed

- Top loading balance
- Büchner funnel
-2 Erlenmeyer flasks
- Filter papers
- Spatula
- ice
- Activated charcoal
- Hot plate stirrer
- funnel
- Filter flask connected to Vacuum pump
- Watch glass
- glass rod
- impure sample of acetanilide
- boiling stones (boiling chips): inert material with small pores that provide sites where bubbles can form, thus inducing even boiling.

Procedure

- Weigh out a 1.5-g sample of impure acetanilide and use a few milligrams to determine the melting point. Record the melting point on the report sheet.

- Place the rest of the acetanilide in a 100-mL conical flask, Add boiling water till no more solid appears to dissolve.

- Remove the heat source, allow the flask to cool a few moments.

- Add a small amount (about 0.2 g) of decolorizing charcoal to the contents of the flask.

- Meanwhile, set up the hot filtration (gravity filtration) apparatus shown up, using fast-flow fluted filter paper and a 125-mL Erlenmeyer flask as the receiver, then pour 15—20 mL of boiling water through the funnel to warm it and to wet the filter paper. Discard this water.

- Heat the acetanilide solution again for a few seconds then filter the hot solution without delay. If particles of charcoal pass through the filter paper, return the filtrate to the original flask, heat the solution to boiling, and filter it again through the same piece of filter paper.

- As the filtrate cools, crystals will begin to form immediately. Place the Erlenmeyer flask in a pan of ice to complete the crystallization.

- Meanwhile, set up the vacuum-filtration apparatus using a 125-mL filter flask. Set a piece of filter paper (Use only the correct size filter paper that completely

covers the inside of the Büchner funnel) in place, connect the flask to the aspirator, and turn it on. Pour 15—20 mL of cold water through the funnel to wet the filter paper. Discard this water. Reconnect the Flask to the aspirator.

- When crystallization is complete, collect the crystals by vacuum filtration. Rinse the crystals (with the vacuum on) with a few milliliters of ice-cold water. Use a clean spatula to press the crystals as dry as possible on the funnel.

- Transfer the crystals to a piece of clean, white paper, spread them in a thin layer, and cover the crystals with a watch glass.

- Store them in your locker for drying until the next laboratory period.

- Weigh the dried product and determine its melting point.

Useful Links

Recrystallization of Organic Compounds

https://www.youtube.com/watch?v=qJLvB6NFnoA

Student Name:	**Student ID no.:**
Date:	**Section:**
Instructor Name:	**TA name:**

Experiment 3: Recrystallization

Pre-lab Questions

Recrystallization of an impure solid must be carried out using a minimum amount of the required solvent(s) at or near its boiling point.

1. Why is it necessary to use only a minimum amount of the required solvent for recrystallization?

2. Why is it necessary to carry out the recrystallization at or near the boiling point of the solvent used?

3. How are insoluble impurities removed during recrystallization?

4. What purpose does the addition of finely divided charcoal serve during the recrystallization of impure solids?

5. Put the following recrystallization steps in the correct order:

a. Cool in ice-bath

b. Hot filtration

c. Heat the mixture to boiling

d. Suction filtration

e. Allow the filtrate to cool down to room temperature

f. Dissolve the material in the minimum amount of the suitable solvent.

g. Add charcoal

h. Check the solubility of the compound in different solvents (cold and hot) to choose the most suitable solvent for recrystallization.

Results and Observations

Recrystallization of Acetanilide

- Describe the appearance crude acetanilide and recrystallized acetanilide.

Mass of crude sample to be purified	
Mass of purified compound	
Percent recovery (*Show calculations*)	
Melting point of crude acetanilide	
Melting point of purified acetanilide	

- Comment on the difference between the melting point ranges for the crude sample and the purified one.

- Explain how thin-layer chromatography can help you to know if your recrystallization was good.

Post-lab Questions

1. What is the purpose of recrystallization?

2. How are soluble impurities removed during a recrystallization?

3. Crystallization may be induced by scratching the vessel beneath the surface of the solution with a glass rod. How does scratching the inside of the vessel with a glass rod induce crystallization?

4. What properties are desirable in a recrystallization solvent?

5. Give two reasons why vacuum filtration is sometimes preferable to ordinary gravity filtration.

    1.

    2.

6. Why is water a good solvent for the recrystallization of acetanilide?
(*Hint*: The solubility of acetanilide in hot water is 5.5 g/100 mL at 100 °C and its solubility in cold water is 0.53 g/100 mL at 0 °C)

7. Why must the funnel be heated before the hot acetanilide solution is filtered?

8. Assuming that charcoal and sugar are the main impurities in a sample of crude acetanilide, explain how recrystallization from water would remove each.

9. Why can we use a water-ethanol mixture but not a water-hexane mixture as a recrystallizing solvent?

Experiment 4

Distillation:

Separation and Purification of Organic Liquids

Objectives

• Distill a pure liquid and observe that it has a constant boiling point.

• Distill a two-component mixture twice, first using a simple distillation then using a fractionating column.

• Compare the efficiency of these two types of apparatus by evaluating the separation of the mixtures.

Background

Distillation is a technique used to separate and purify liquids. It consists of heating a liquid to its boiling point, conducting the vapors to a cooling device where they are allowed to condense, and collecting the condensate.

In a sealed container partially filled with a liquid, some molecules escape from the liquid's surface into the space above. In their random motion, molecules that have escaped to the vapor may strike the liquid surface again and stick to it. At equilibrium, the number of molecules that leave the liquid surface equals the number of vaporized molecules that strike the liquid surface and stick. The molecules in the vapor also strike the walls of the container and exert a pressure, which is called the **vapor pressure** of the liquid. If the temperature of the liquid is raised, more molecules escape to the vapor until equilibrium is once again established. *The vapor pressure of a liquid, therefore, increases with increasing temperature*. The following Figure shows a typical vapor pressure-temperature curve and the Figure afterwards illustrates the concept of vapor pressure.

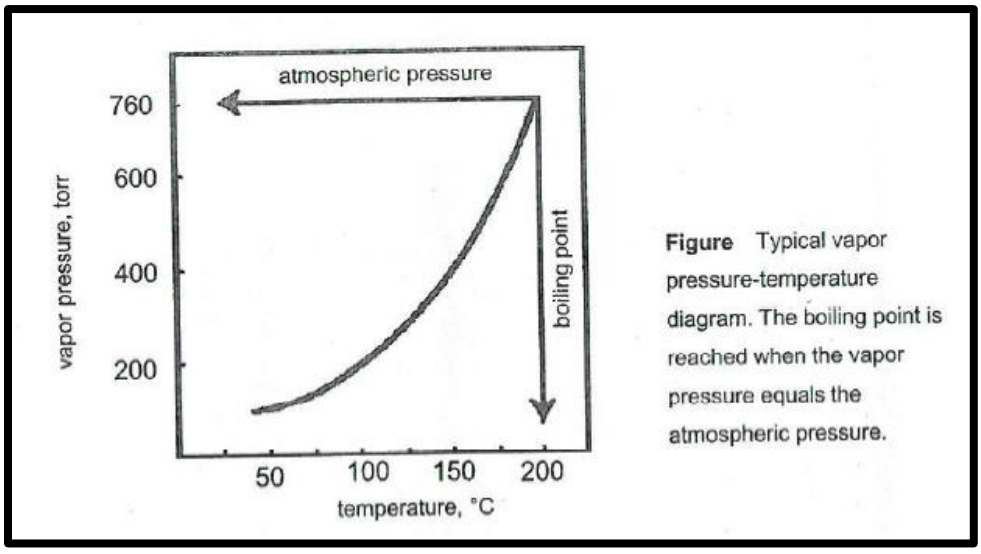
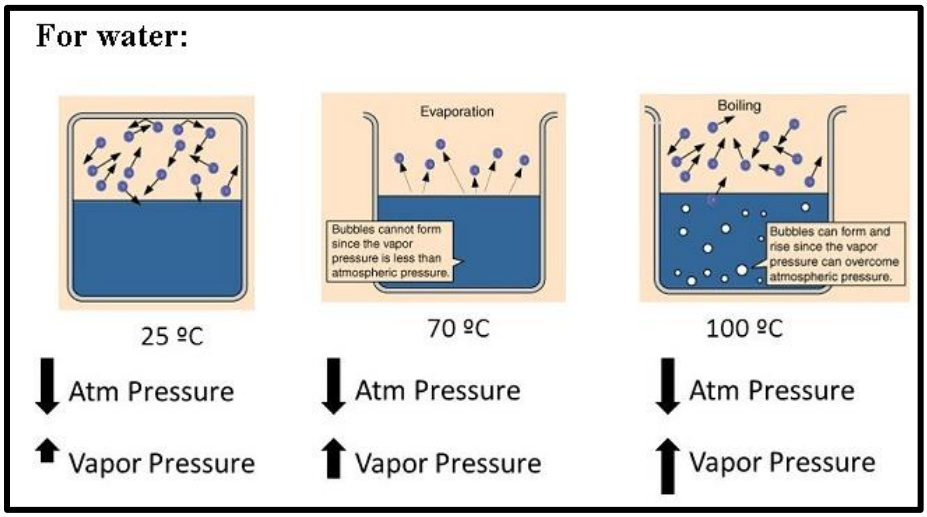


Figure Typical vapor pressure-temperature diagram. The boiling point is reached when the vapor pressure equals the atmospheric pressure.



The **boiling point** of a liquid is that temperature at which the vapor pressure of the liquid becomes equal to the pressure exerted by its surroundings. If the liquid is open to the atmosphere, the boiling point is the temperature at which the vapor pressure of the liquid becomes equal to the atmospheric pressure. The vapor pressure of a pure liquid rises steadily as the temperature is increased until the boiling point is reached. A thermometer placed in the vapor of a boiling pure liquid registers that liquid's boiling point. The temperature remains constant throughout the distillation of a pure liquid. This is because at the boiling point, vapor and liquid are in equilibrium; if the phase composition of the vapor and liquid remains constant throughout the process, the temperature also remains constant. The boiling point (at a given pressure) is a characteristic property of a pure liquid, just as the melting point is a characteristic property of a pure crystalline solid.

A Mixture of Ideal Liquids

When a mixture of two miscible liquids with different boiling points is heated, the vapor does not have the same composition as the liquid. Instead, the vapor is richer in the more volatile component. The following Figure describes the behavior of the mixture of A and B, two miscible volatile liquids with boiling points T_A and T_B, respectively. The lower of the two curves represents the boiling points of mixtures of A and B.

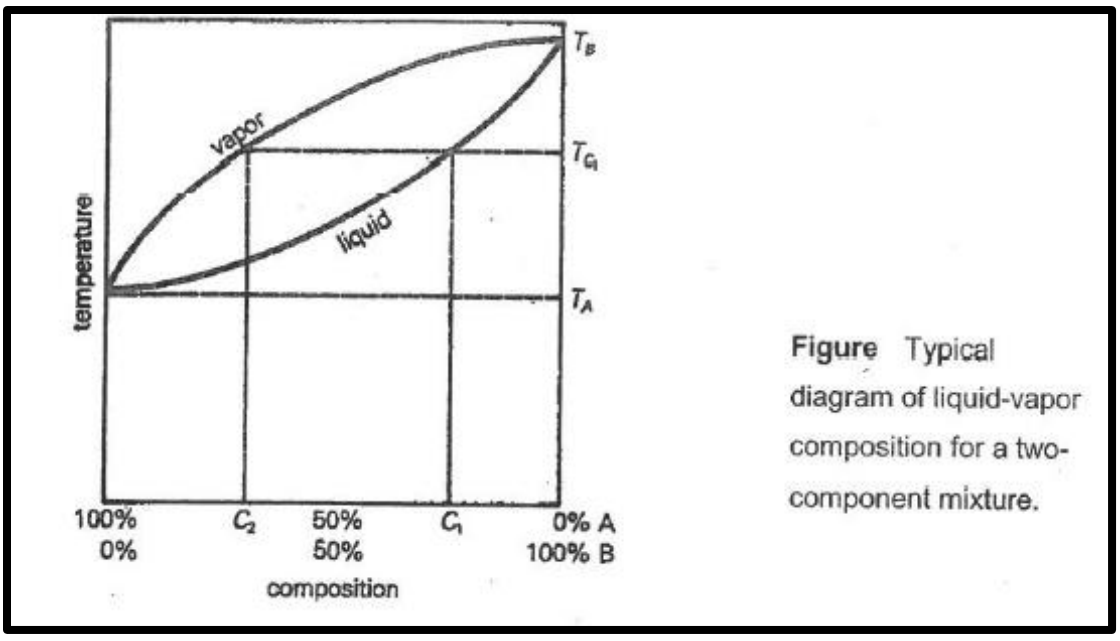


Figure Typical diagram of liquid-vapor composition for a two-component mixture.

The boiling point gradually rises as the mixture becomes richer in the higher-boiling component, B. The upper curve represents the composition of the vapor that is in equilibrium with the liquid at its boiling point. At 100% A or 100% B, the curves meet, because pure A (at T_A) can have only pure A vapor in equilibrium with it. The same applies to pure B (at T_B).

When a mixture of A and B with composition C_l is heated, it boils at TC_1. Reading horizontally on the graph to the vapor curve, you can see that the vapor at TC_1 has the composition C_2. This means that if mixture C_l were placed in a distillation apparatus and heated to its boiling point, the vapor (and therefore the first drop of liquid to be condensed) would have the composition G; it would be much richer in A, the more volatile of the two components, than was the original liquid.

As the distillation proceeds, A is selectively removed from the liquid. The composition of the liquid changes gradually from C_l to 100% B. The boiling point of the liquid gradually rises from TC_1, to TB. At the same time, the composition of the distillate gradually changes from C_2 (rich in A) to 100% B. Thus, in the simple distillation of a mixture, the first material to distill (sometimes called the **first cut** or the **first fraction**) is rich in the more volatile or lower-boiling component, and the last material (**last cut** or **last fraction**) is rich in the less volatile or higher-boiling component.

Fractional distillation and the Fractionating Column

Even the first drop of distillate obtained when an A-B mixture with composition C_l is distilled is not pure A but rather a mixture of composition G, which contains mainly A but some B. If we were to combine and redistill the first fractions, the first vapor to be condensed would be even richer in A. Repetition of this process (vaporization, condensation, and revaporization) can gradually lead to isolation of pure A from the A-B mixture. Similarly, redistillation of the higher-boiling fractions can lead to isolation of pure B in the final fractions. However, such repeated redistillation is a laborious process.

A fractionating column is a device used to increase the efficiency of distillations. It consists of a vertical tube that either is packed with inert material (such as glass beads or glass helices) or has some other device (such as indentations) to increase the surface on which the rising vapors can condense. As the hot vapors rise through the column, they condense, and the liquid flows back down the column. As this liquid reaches the lower, hotter portions of the column, it is revaporized, and the more volatile components once again proceed up the column. If the column efficient, this process is repeated many times, and the distillate consists of the lowest-boiling component of the mixture in nearly pure form. The following Figure illustrates this process graphically. The original A-B mixture with composition C_l boils at temperature TC_1, and the vapors enter the column at that temperature.

Fractionating Column

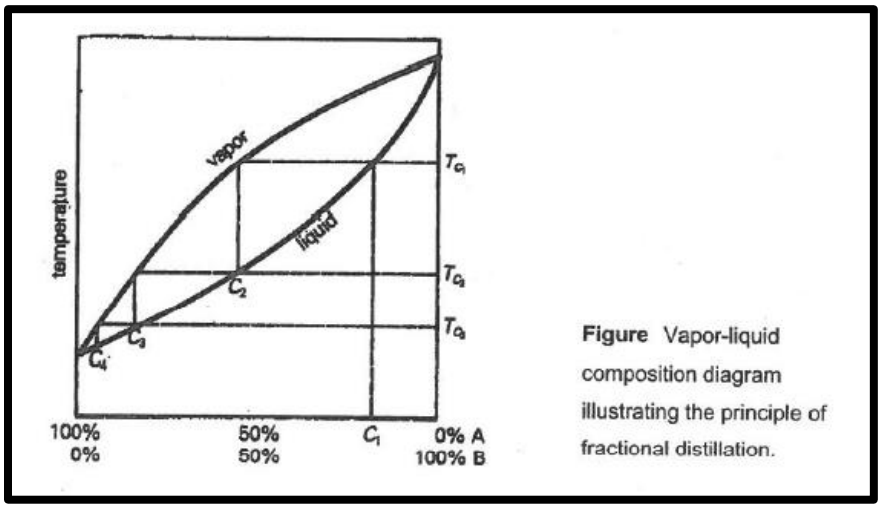
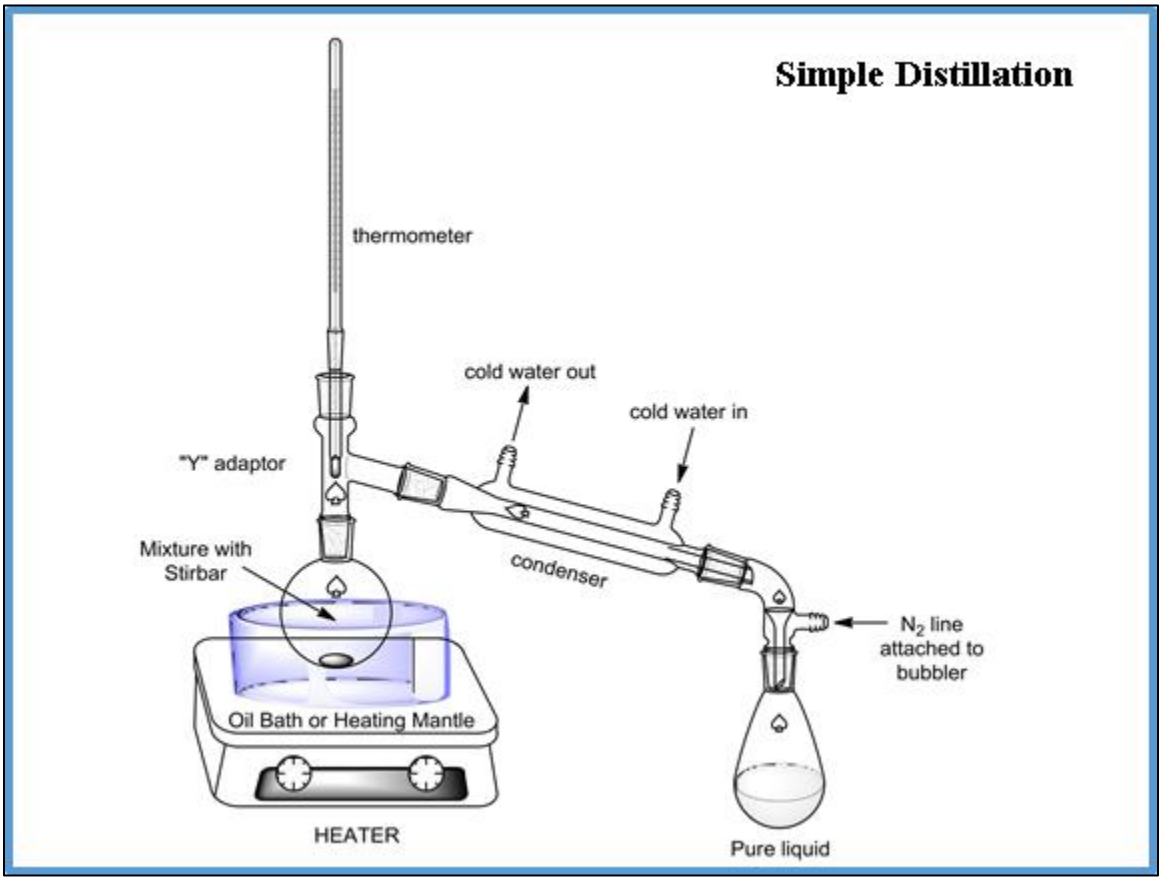


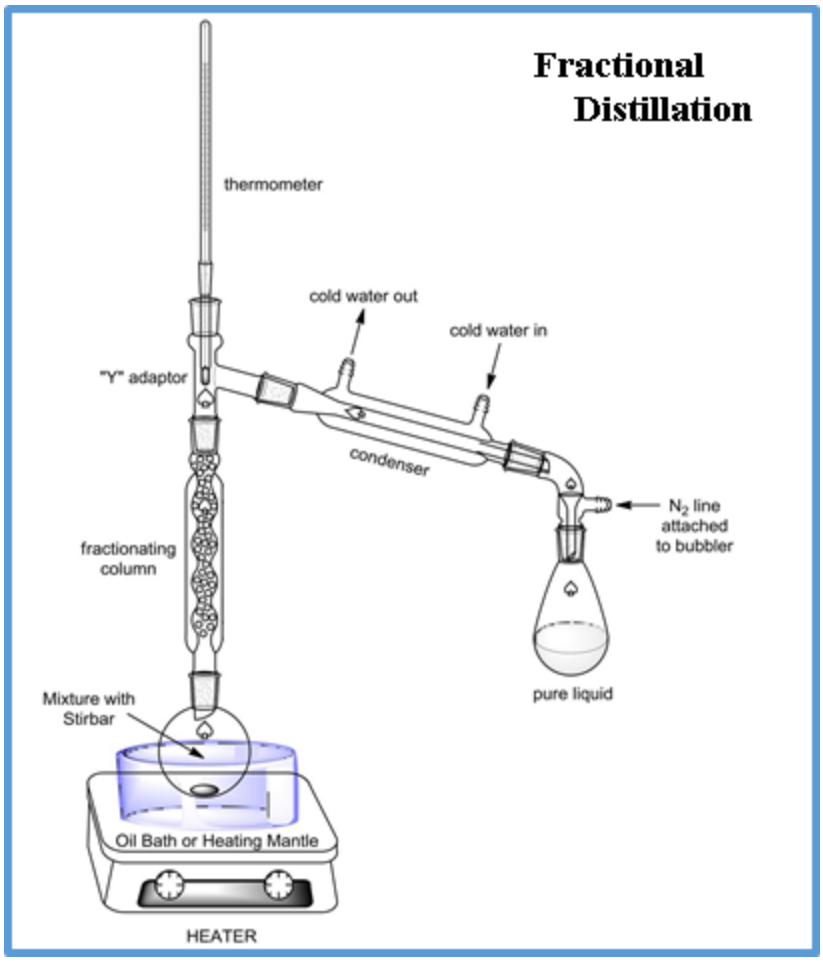
Figure Vapor-liquid composition diagram illustrating the principle of fractional distillation.

If they condense somewhere in the column, the condensate has composition C_2. This condensate drops back down the column and vaporizes nearer the bottom at temperature T_{C2}, producing vapors with composition G. These vapors may condense somewhat farther up the column at temperature T_{C3}. Vaporization yields vapor with composition Q, and so on. If the column is sufficiently high, or if it contains enough surface area for many successive vaporizations and condensations, the distillate that comes over the top is nearly pure A. Distillation yielding pure A continues until all of A is removed, after which the temperature rises to the boiling point of B. In practice, fractionating columns are not 100% efficient.

Columns have been designed, however, that can separate liquids with boiling points within as little as 2°C of each other.

The following Figures show the apparatus of both simple distillation and fractional distillation.





Apparatus/Reagents Needed

- Round Bottom flask 50 mL
- Y-adapter and receiving adapter
- 2 Erlenmeyer flasks
- Thermometer / thermometer adapter
- Stands, clamps, and clamp holders
- Condenser
- Boiling stones
- Acetone
- Heating mantle
- funnel
- 25-mL Graduated cylinders
- Rubber Tubes
- Clips
- Fractional column
- Grease
- Distilled water

Procedure

1- Distillation of Acetone

You will first distill a pure liquid in a simple distillation apparatus. Assemble the apparatus (distilling flask, thermometer, condenser, adapter, and graduated receiver) as illustrated in before, using a 50-mL distilling or round-bottomed flask. *Be sure that the thermometer bulb is positioned just below the side arm* so that it can measure

the temperature of the vapor as that vapor passes out of the flask into the condenser and receiver.

Place 20 mL of acetone in the flask, add a boiling stone (to prevent "bumping" due to superheating), put the thermometer in place, and start water circulating through the condenser.

Start heating the flask and increase the heat gradually until the acetone boils. When liquid begins to drip into the receiver, adjust the heat so that the drops come slowly and steadily at a rate of about one per second. Record the temperature after you have collected 1,3,5,7,9 and 11 mL of distillate, then stop the distillation. The temperatures you have recorded should not vary by more than 2°C and should collectively represent the boiling point range of acetone. Keep the distillate for the next part.

** *Always stop a distillation before the flask becomes completely dry*. When the flask is dry, its temperature can rise sharply. Some organic compounds may contain peroxide impurities that become concentrated and can explode at dryness.

** If during a distillation the temperature should drop below the boiling point of the liquid in the flask, liquid will fill the pores of the boiling stone and it will no longer be effective. In this event, the liquid can be cooled and a fresh stone cautiously added. The new stone should not be added when the liquid is at or near the boiling point because it may initiate uncontrolled boiling.

2- Separation of a Binary Mixture by Simple Distillation

Use the simple distillation apparatus to distill a mixture of 10 mL acetone + 10 mL water. Adjust the heat during the distillation so that the distillate drips slowly and steadily into the receiver. Record the temperature after every 1-2 mL as the distillation proceeds until you have collected ~ 10 mL of distillate.

3- Separation of a Binary Mixture by Using a Fractionating Column

Assemble the fractional distillation apparatus as shown above. Place 10mL water + 10 mL acetone in a 50-mL round-bottomed flask, connect this flask to the distilling column, and proceed as before. Again, record the temperature every 1-2 mL as the distillation proceeds until you have collected ~10 mL of distillate.

** Discard the collected fractions as advised by your instructor.

Useful Links

An Introduction to Simple Distillation:

https://www.youtube.com/watch?v=T4eIc_v-SrI

A Brief Introduction to Fractional Distillation:

https://www.youtube.com/watch?v=Z6OyNB8V7Hc

Simple Distillation and Fractional Distillation (Experiment):

https://www.youtube.com/watch?v=sLom1F_1K1Y

Student Name:	Student ID no.:
Date:	Section:
Instructor Name:	TA name:

Experiment 4: Distillation

Pre-lab Questions

1- High boiling liquids are often distilled under reduced pressure by applying vacuum to the distillation set up. What practical benefit does one obtain by carrying out the distillation under reduced pressure?

2- Why is it necessary to add a boiling chip or two during the distillation of a liquid?

3- Define the terms vapor pressure and boiling point of a liquid.

4- Does the vapor pressure of a liquid change with temperature and if so, why?

Results and Observations

Distillation of Acetone

Quantity Distilled, mL	2	4	6	8	10
Temperature, ℃					

Separation of a Binary Mixture

Quantity Distilled, mL	2	4	6	8	10
Temperature, ℃ **Without column**					
Temperature, ℃ **With column**					

1- The known boiling point of acetone is 56℃. Comment on the difference between the known and the measured values.

2- True of False:

( ) - The water should enter the condenser from the lower inlet to keep the jacket of the condenser full of water so that the cooling is very efficient.

( ) - There should be a drop of liquid all the time of distillation to get accurate results.

( ) - The thermometer should be immersed into the liquid which presents in the round bottom flask.

( ) - When distilling a pure liquid the temperature will remain nearly constant throughout the distillation process.

( ) - Continue distillation until the round bottom flask is completely dry.

( ) - The best method to separate 2 liquids of close boiling points is simple distillation.

( ) - During the distillation of a binary mixture of liquids, the less volatile liquid will be collected first in the receiving flask.

Post-lab Questions

1- Which procedure is more efficient at separating the mixture into its components?

2- A pure liquid has a constant boiling point, but a liquid with a constant boiling point is not necessarily pure. Explain.

3- What effect does a reduction in the atmospheric pressure have on the boiling point of a liquid?

4- Why doesn't a pure liquid in a distilling flask vaporize all at once when the boiling temperature is reached?

5- Why is it dangerous to heat a liquid in a distilling apparatus that is closed tightly at every joint and has no vent to the atmosphere?

6- Why is it important that the cooling water in a distillation apparatus enter the condenser jacket at the lower end and exit at the upper end, and not vice versa?

7- Why should a distilling flask be filled to not more than two-thirds of its capacity at the beginning of a distillation procedure?

Experiment 5

Extraction:

Separation and isolation technique

Objectives

- Extract caffeine from tea leaves.

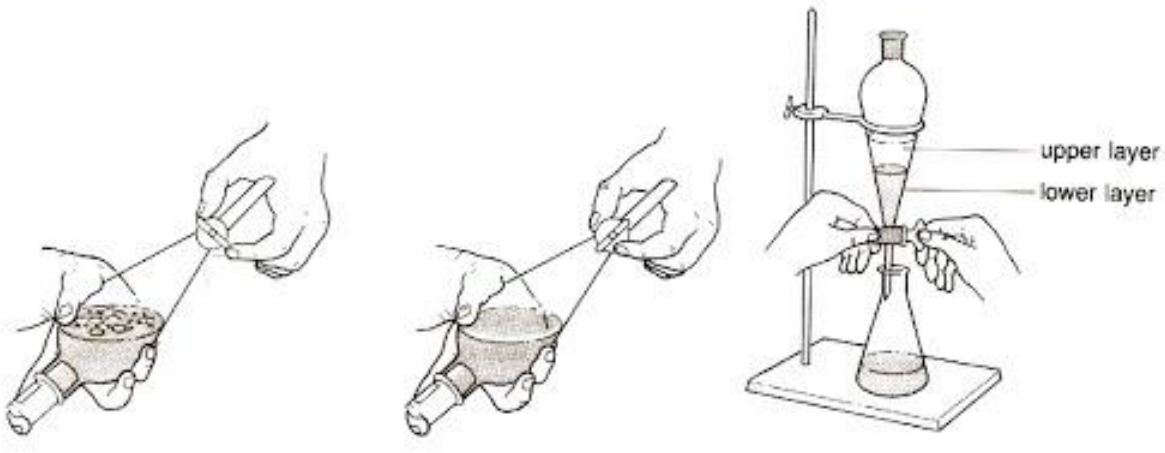
Background

In synthesis, the desired product must be separated from the by-products, excess reactants, impurities, and other substances that may be present in the reaction mixture. Similarly, substances in nature are always mixed with other substances. Extraction is the most common technique used to separate a desired organic product from a reaction mixture or to isolate an organic substance from its natural source.

Extraction usually involves shaking a solution that contains the desired substance with an immiscible solvent in which the desired substance is more soluble than it is in the starting solution. Upon standing, the solvents form two layers that can be separated. Extraction may have to be repeated several times to effect complete separation.

Most commonly, one of the solvents is organic and the other is aqueous. Inorganic compounds can usually be separated from organic compound in this way. The former dissolve in the aqueous phase and the later in the organic solvent. In such cases, a single extraction may suffice to affect a satisfactory separation. However,

many organic compounds (particularly oxygen-or nitrogen containing compounds, such as aldehydes, alcohols, esters and amines, (which can form hydrogen bonds) are partially soluble in water. They distribute themselves between the aqueous phase and (*w*, for water) and the organic solvent (*o*) in proportion to their relative solubilities (S) in the two solvents.



The ratio of the concentrations of a substance in the two solvents (C_o/C_w) at equilibrium is called its **distribution coefficient, K_D**:

$$K_D = \frac{K_o}{K_w} = \frac{S_o}{S_w}$$

The magnitude of K_D is an indication of the efficiency of extraction:

- *The larger the value of K_D, the more efficient the extraction.*

If a compound has a low K_D for a given extraction, it is better to search for a different organic solvent in which the compound is more soluble in order to do liquid-liquid extraction. If this is not feasible, doing multiple extractions can increase the amount of compound extracted.

Example:

Suppose the solubility of compound A is 0.6 g/ 100mL in ether and 0.12 g/ 100 mL in water. K_D is then 0.60/0.12 = 5.

To illustrate how the distribution coefficient K_D can be used, let us calculate the amount of A that is removed from a solution containing 60 mg of A in 60 mL of water by extracting with 100 mL of ether. If we let x be the number of milligrams of A extracted into the ether layer, then (60 – x) represents the milligrams of A remaining in the water. The equation for K_D is, therefore,

$$K_D = \frac{C_0}{C_w} = 5 = \frac{\frac{x}{100}}{\frac{60-x}{60}}$$

Solving for x, we find that 53.5 mg of A will be extracted by the ether and, consequently, that 6.5 mg of A (60 - x) will remain in the water.

It is easy to show that if we had extracted A twice with 50 mL of ether instead of once with 100 mL of ether, we would have removed 48.4 + 9.4 mg = 57.8 mg of A from the water. In general, performing several extractions using smaller volumes of solvent is more efficient than performing a single extraction with a larger volume of solvent.

When equal volumes of the two solvents are used, one can solve for the amount of material extracted by simple inspection because in this case, K_D is simply the ratio of the weights of the solute in each solvent. For example, if $K_D = 5$, then 5/6 of the solute will be in the organic phase and 1/6 in the aqueous phase when the volumes of the two solvents are equal.

An extraction solvent must readily dissolve the substance to be extracted, yet it must be only sparingly soluble in the solvent from which the desired substance is to be extracted. Also, it should extract only the desired substance or as small an amount as possible of any other substance present; it should not react chemically with the solute in an undesirable way, and it should be easily separated from the desired solute after extraction. This last requirement can be met if the solvent is low-boiling and easily removed by distillation.

Common organic solvents that fulfill these requirements include many hydrocarbons and their chloro derivatives, such as petroleum ether (a mixture of low-boiling alkanes), dichloromethane, chloroform, and carbon tetrachloride. If chlorinated hydrocarbons are used, however, it is important to avoid breathing their vapors because these compounds are toxic, and some are carcinogenic. They can be used

safely if we carry out operations in an efficient hood and take care to avoid getting them on the skin. Diethyl ether is another common extraction solvent, but here, too, care is necessary. Diethyl ether (usually referred to simply as ether) is highly flammable and, upon standing in air, its solutions may develop dangerous concentrations of explosive peroxides. Furthermore, ether is slightly water-soluble (about 7 g/ 100 mL), Nevertheless, because most organic compounds are highly soluble in it and because of its low boiling point (35°C), ether is frequently used despite its drawbacks.

Sometimes we can use desirable, easily reversed chemical reactions such as acid-base reactions to effect separations by extraction. For example, dilute sodium hydroxide (an inorganic base) converts organic acids to their sodium salts:

$$RCO_2H + Na^+OH^- \rightarrow RCO_2^- Na^+ + H_2O$$

Although a particular acid may not be soluble in water, its more polar sodium salt usually is. When a mixture of a neutral compound and an acidic, water-insoluble compound in an organic solvent is shaken with dilute aqueous sodium hydroxide, the acid is converted to its sodium salt, which dissolves in the aqueous layer, and the neutral compound remains in the organic layer. After the layers are separated, the acid is recovered by acidifying the aqueous layer with a strong acid.

$$RCO_2^- Na^+ + HCl \rightarrow \quad RCO_2H + Na^+Cl^-$$

Thus, acids can easily be separated from neutral (or basic) contaminants by extraction with aqueous alkali.

Phenols also form salts when treated with an inorganic base:

$$ArOH + Na^+ OH^- \rightarrow \quad ArO^- Na^+ + H_2O$$

However, most phenols are less acidic than the carboxylic acids. Aqueous sodium bicarbonate is usually alkaline enough to convert carboxylic acids to their salts, but not alkaline enough to convert phenols to their salts. Thus, carboxylic acids and phenols can sometimes be separated by extraction first with aqueous sodium bicarbonate (to remove carboxylic acids) and then with aqueous sodium hydroxide (to remove phenols).

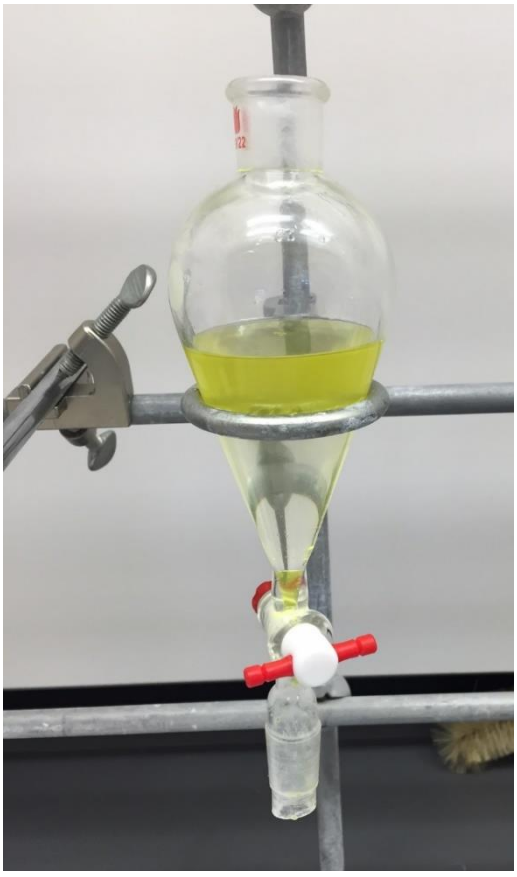
Dilute aqueous acid can be used to extract basic compounds, particularly amines, from neutral or acidic substances by converting them to water-soluble alkylammonium salts:

$$RNH_2 + H^+Cl^- \rightarrow RNH_3^+ Cl^-$$

After separating the organic and aqueous layers, we can recover the amine from the aqueous layer by making the solution alkaline with a strong base.

$$RNH_3^+ Cl^- + Na^+OH \rightarrow RNH_2 + H_2O + Na^+Cl^-$$

Use of separatory Funnel



Extractions are usually performed with a separatory funnel. Improperly handed, this moderately expensive piece of glassware is easily broken. Always follow proper handling technique.

Lubricate the stopcock of the funnel with a thin layer of grease so that the stopcock turns easily, but be sure that the bore does not become clogged. (If the separatory funnel has a Teflon plug, lubrication is unnecessary.) Support the funnel in an iron ring padded with plastic or rubber tubing. Close the stopcock, and add the liquids to be separated. Insert the stopper (which has been lightly greased if it is not Teflon) and invert the funnel, being sure to hold the stopper in with one hand and the stopcock in with the other (as shown below). Then, with the barrel pointed up and away from you and from anyone else in the vicinity, slowly open the stopcock. This will relieve any pressure that may have built up inside the funnel. Pressure buildup is quite common when volatile solvents such as ether are used because the vapor pressure of the solvent adds to the atmospheric pressure already present. This situation is further aggravated when the funnel is

warmed by the heat of your hands or when a gas is generated during the extraction, as happens when an ether solution of an acid is extracted with sodium bicarbonate.

After the pressure is released, close the stopcock, shake the funnel gently two or three times, and again invert the funnel and release the pressure by opening the stopcock. Repeat this process until the pressure buildup is slight. Then shake the contents vigorously to complete the extraction.

Replace the funnel in the iron ring and remove the stopper immediately. Allow the funnel to stand until the layers separate cleanly. Then slowly draw off the lower layer through the stopcock into a flask or beaker of appropriate size. As the boundary between the two layers approaches the stopcock, slow the flow. Close the stopcock just as the upper layer enters the stopcock bore. If the upper layer is to be transferred to another vessel, pour it out through the top of the funnel. Do not run the upper layer through the stopcock. The relative positions of the aqueous and organic layers in the separatory funnel depend on their densities. The more dense solvent forms the lower layer. Hydrocarbons and ether are less dense than water, whereas chlorinated hydrocarbons (chloroform, dichloromethane, and carbon tetrachloride) are more dense than water. If you have any doubt about which is the organic layer and which is the aqueous layer, withdraw a few drops of the lower layer and determine whether or not they dissolve in water.

Sometimes, especially with alkaline solution, it is difficult to obtain a sharp separation of layers because an **emulsion** has formed. Gentle swirling of the funnel

in a near-upright position, gentle stirring with a glass rod, addition of salt to the aqueous layer, or addition of certain defoaming agents may overcome this difficulty.

To improve the extraction of organic compounds from aqueous mixtures, it is advisable to saturate the aqueous phase with a salt such as NaCl or Na_2CO_3. This phenomenon which is called **salting-out** has the following effects:

1) Decreases the solubility of organic compounds in the saturated aqueous phase.

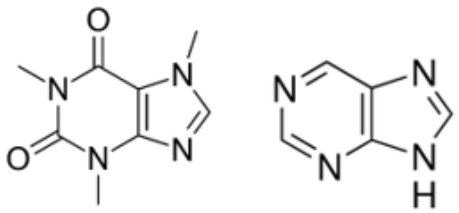
2) Decreases the solubility of the organic and aqueous phases in each other, thus improving their separation. This is particularly useful in *breaking up emulsions*.

Since the organic solution has been extracted or washed with aqueous solutions, it will contain some water. The last traces of water have to be removed by treatment with a **drying agent**. Common drying agents are *anhydrous inorganic salts which readily take up water to become hydrated* (as shown in the equation below). At the end of the drying process, the hydrated salt is removed from the organic solutions by filtration. When dry, the organic phase becomes clear. Anhydrous $CaCl_2$, $MgSO_4$, or Na_2SO_4 are some common drying agents.

$$MgSO_4 + H_2O \rightarrow MgSO_4.7H_2O$$

Extraction of Caffeine

Caffeine is an alkaloid present in tea, coffee, cola nuts, and several other plants. It is a mild stimulant and may be used medically for this purpose (NoDozTM tablets are an example). Structurally, caffeine belongs to a class of nitrogen bases called purines. It is a colorless, crystalline solid that melts at 235-236 °C, but it can be sublimed readily under reduced pressure at temperatures below its melting point. It is moderately soluble in water (2.2 g/ 100 mL) but more soluble in common organic solvents.



Caffeine purine

In this experiment you will extract caffeine with hot water from tea leaves, where it is present to the extent of about 5%. This treatment also extracts the tannins, another class of compounds present in tea. It will therefore be necessary to separate the caffeine from the tannins. You will do so by adding sodium carbonate to the solution. Tannins are acidic and remain in solution. The caffeine is extracted from the aqueous alkaline solution with dichloromethane. It can then be purified by sublimation or recrystallization.

Apparatus/Reagents Needed

- Tea leaves
- Sodium carbonate
- Anhydrous sodium sulfate
- Distilled water
- DCM (Dichloromethane)
- Heating mantle
- Separatory funnel
- funnel
- 100-mL Beakers
- 600-mL beaker

Procedure

Make a large tea bag by wrapping and tying 15 g of dry tea leaves in a double thickness of cheesecloth. (Alternatively, you can use 8—10 ordinary tea bags.) Place the tea in a solution of 20 g of sodium carbonate in 150 mL of water contained in a 400-mL beaker and boil the mixture for 20 min. Remove the bag of tea and squeeze it with tongs (to avoid finger stains) so as to obtain the maximum amount of extract. Cool the aqueous solution to room temperature, transfer it to a separatory funnel,

and extract three times with 20 mL portions of dichloromethane (DCM, CH_2Cl_2). Do not shake the funnel vigorously or an emulsion may form. Instead shake gently and swirl the layers in the funnel for several minutes during each extraction.

Dichloromethane is more dense than water and forms the lower layer. Combine the dichloromethane extracts and wash any emulsion that may have formed with 20 mL of water, swirling the layers as before.

Drain the DCM extract through the funnel into a 100-mL beaker, add anhydrous sodium sulfate then filter in another pre-weighed beaker. Put the beaker on hot plate so the DCM will evaporate leaving the solid white caffeine.

Useful Links

Extraction of Caffeine from tea leaves:

https://www.youtube.com/watch?v=5K1t4-1TDdo

How to use the separatory funnel:

https://www.youtube.com/watch?v=EFiFPoOzqtk&t=161s

Student Name:	**Student ID no.:**
Date:	**Section:**
Instructor Name:	**TA name:**

Experiment 5: Extraction

Pre-lab Questions

1- What are the important criteria one has to consider in selecting a solvent for extraction?

2- A mixture of carboxylic acid and a phenol can often be separated by extracted with aqueous sodium bicarbonate and suitable organic solvent. What difference in the chemical properties of the carboxylic acid and the phenol makes this separation process?

3- What safety precautions should one take when using chlorinated solvents for extraction?

4- What is the practical advantage of using dichloromethane (density= 1.325 g/mL) over diethyl ether (density =0.706 g/mL) for extracting organic compounds from a aqueous solution using a separatory funnel?

5- What purpose does sodium carbonate serve during the extraction of caffeine from tea leaves?

Results and Observations

Mass of tea leaves= 15 g

Mass of isolated caffeine = ?

Mass % of Caffeine in tea leaves=

If you know that caffeine exists in tea leaves with a 5%.

What is the max. amount of caffeine that you can isolate from 15 g tea leaves?

(show calculations)

Post-lab Questions

1- What purpose does a 1-cm layer of anhydrous sodium sulfate in the apex of the funnel serve while transferring the dichloromethane extract into the beaker?

2- What are the advantages and the disadvantages of using ether as an extraction solvent?

3- What is the practical advantage of having the organic solvent be more dense than water when one is extracting an organic compound from an aqueous solution in a separatory funnel?

4- Why must the stopper at the top of the separatory funnel be removed before liquid can be withdrawn through the stopcock?

5- Verify the conclusion (that two extractions of A with 50-mL portions of ether yield 57.8 mg of A, whereas one extraction with 100 mL of ether yields only 53.5 mg of A.

6- The solubility of suberic acid is 0.14 g/100 mL of water or 0.56 g/100 mL of ether. Calculate the volume of ether needed to remove 90% of the suberic acid from 100 mL of a saturated aqueous solution in a single extraction.

7- Explain the chemical meaning of sublimation.

Experiment 6

Steam Distillation:

A method for Purification and Separation of Liquids and Solids

Objectives

- Isolate essential oils from cloves or the seeds of one of the following: anise, caraway, or cumin.
- Examine the theoretical features of steam distillation to the isolation of essential oils from plants.

Background

Steam distillation is the separation of slightly volatile, water-insoluble substances from non -volatile material by means of steam.

For a mixture of two completely immiscible compound A and B, the total vapor pressure (P_T) can be expressed, as usual, in terms of partial pressure P_A and P_B:

$$P_T = P_A + P_B = P°_A X_A + P°_B X_B$$

X_A and X_B are the mole fractions of A and B in the liquid mixture. However, since A and B are immiscible, each behaves independently of the other and therefore $X_A = X_B = 1$, the above expression thus becomes:

$$P_T = P_A + P_B = P°_A + P°_B = \text{constant}$$

This means that the total vapor pressure of such a heterogeneous (two-phase) mixture is constant and depends only on the vapor pressure of pure A ($P°_A$) and pure B ($P°_B$) at a given temperature. These vapor pressures are completely independent of the relative amounts of A and B in the mixture. Unless either P_A or P_B is zero, the vapor pressure of the mixture (at a given temperature) is higher than the vapor pressure of either component alone. The boiling point of the mixture will be the temperature at which the total vapor pressure equals atmospheric pressure, and it is obviously lower than the boiling point of either pure A or pure B.

Steam distillation always takes place at a temperature below the boiling point of water. This makes it possible to distil high- boiling, steam-volatile, organic compound at temperatures below 100 °C. Thus, avoiding possible decomposition of such compounds.

At equilibrium, the composition of the vapor above the liquid mixture can be expressed as:

$$\frac{moles\ of\ A}{moles\ of\ B}\ in\ vapor = \frac{P_A}{P_B} = \frac{P°_A * X_A}{P°_B * X_B} = \frac{P°_A}{P°_B}$$

$$(remember\ X_A = X_B = 1)$$

The weight ratio of A and B in the vapor will depend not only on their molar ratios but also on their molar masses. Since the molar mass of the organic substance is usually much higher than that of water, significant amounts of the organic substance will distil over, even though its vapor pressure may be relatively low. From the relationship between mole, mass and molar mass we obtain:

$$\frac{moles\ of\ A}{moles\ of\ B} = \frac{mass\ of\ A/\ MW_A}{mass\ of\ B/\ MW_B} = \frac{P°_A}{P°_B}$$

Therefore

$$\frac{mass\ of\ A}{mass\ of\ B} = \frac{P^{\circ}_{A} * MW_A}{P^{\circ}_{B} * MW_B}$$

Steam distillation is convenient for the purification of high-boiling compounds by low-temperature distillation and so replaces vacuum distillation. However, an inherent disadvantage of this technique is that it is limited to substances with the following properties:

1- Steam-volatile, those that have appreciable vapor pressure at the temperature of steam distillation (between 90 and 95° C).

2- Immiscible with water.

3- Inert toward steam and stable under the conditions of steam distillation.

Steam distillation finds application in the separation of such compounds from mixtures containing nonvolatile impurities, as well as in the isolation of steam-volatile compounds from natural sources (plants). This technique is not restricted to liquids but can be applied to solids as well, provided they fulfill the above-mentioned conditions.

Essential oils

The characteristic aromas of plants are due to volatile essential oils, which are used as a source of fragrances and flavorings. These oils, which occur in all parts of the plant, are generally complex mixtures of hydrocarbons, alcohols and carbonyl compounds. Essential oils are best isolated from the plant tissue by steam distillation.

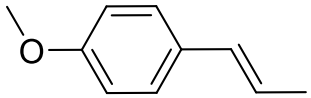
In this experiment, the essential oils of one of four widely used spices (anise, caraway, cumin or cloves) will be isolated by steam distillation.

Anise oil. The essential oil obtained from anise, a popular flavoring for cookies, is predominantly trans-1-(*p*-methoxyphenyl)propene (anethole) which comprises 80-90% of the oil. A minor component is the double bond isomer, 3-(p-methoxyphenyl)propene (*p*-allylanisole). Anethole has a melting point near room temperature and the oil crystallizes on chilling.

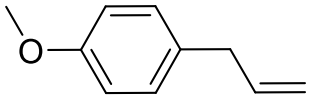
Caraway oil. The essential oil of caraway, comprising 1-3% by weight of the dry seeds, contains two principal compounds which are carvone and limonene.

Cumin oil. The major volatile constituent of cumin is *p*-isopropyl-benzaldehyde (cuminaldehyde). Cumin also contains limonene.

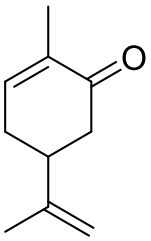
Clove oil. Oil of cloves comprising between 14% and 20% of the cloves, is rich in 4-allyl-2-methoxyphenol (eugenol) which is used medicinally as dental antiseptic and analgesic.



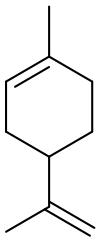
anethole



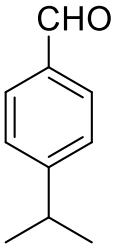
p-allylanisole



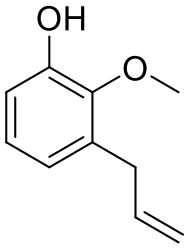
carvone



limonene



cuminaldehyde



euginol

Apparatus/Reagents Needed

- Round Bottom flask 50 mL
- Y-adapter and receiving adapter
- 2 Erlenmeyer flasks
- Thermometer / thermometer adapter
- Stands, clamps, and clamp holders
- Condenser
- Boiling stones
- sodium chloride
- Gloves, anise, caraway or cumin seeds
- Heating mantle
- funnel
- Clips
- Rubber Tubes
- Grease
- Distilled water
- separatory funnel
- DCM (Dichloromethane)
- anhydrous sodium sulfate

Procedure

** The apparatus is basically the same as that used for simple distillation except for the need for a large distillation flask containing a large volume of water to provide the steam.

Place 25g of the ground spice and 200-mL of water in a 500-mL round-bottomed flask. Connect the flask to distillation apparatus and boil the mixture vigorously. Collect the distillate until no more droplets of oil come over; a minimum of 150 ml should be collected. Add 10-15g of sodium chloride and stir until completely dissolved.

Cool the distillate to room temperature, transfer to a 250 ml separatory funnel, and extract with 15 mL of dichloromethane (DCM).

Separate the layers and collect the organic layer in a small flask. Repeat the extraction twice with another 15 mL each of dichloromethane and combine the organic extract. Dry the organic phase with anhydrous sodium sulfate until the solution is clear. Decant the dichloromethane solution into a small pre-weighed beaker. Evaporate the solvent on the steam bath, in the fume hood, until the solution

has been concentrated to an oily residue. Weigh the oil and calculate the percentage yield based on the weight of the dried spice.

** Note: steam distillation is vigorous so take care to avoid the material boiling over into the receiver.

** Note: If the substance being distilled is a solid, it often solidifies and accumulates inside the condenser. In such cases, use an air condenser (without water flow) or stop the flow of cooling water until the solid melts and eventually collects in the receiver.

Useful Links

An Introduction to Steam Distillation:
https://www.youtube.com/watch?v=7g4e3dhtgjI

Isolation of Euginol from Cloves:
https://www.youtube.com/watch?v=qLq6AE9M4_U

Student Name:	Student ID no.:
Date:	Section:
Instructor Name:	TA name:

Experiment 6: Steam Distillation

Pre-lab Questions

1- Find out the plant origin for the following essential oils:

(a) limonene

(b) menthol

(c) citral

(d) myrcene

(e) eugenol

(f) anethole

2- Regarding the essential oil that can be isolated from Cloves:

- Give its structure.
- Give its molecular formula.
- What are the functional groups present in it?

3- Choose the best choice for each of the following:

- In steam distillation, the liquid boils when the sum of vapor pressure due to organic liquid and due to water becomes _____

  a) Greater than atmospheric pressure
  b) Equals to atmospheric pressure
  c) Lesser than atmospheric pressure
  d) None of the mentioned

- The organic liquid in steam distillation vaporizes at _____

  a) Higher temperature than its boiling point) Lower temperature than its boiling point
  c) At its boiling point
  d) None of the mentioned

- Steam distillation process is used to separate substances which are_____

  a) Steam volatile
  b) Steam volatile and miscible with water
  c) Steam volatile and immiscible with water
  d) All of the mentioned

Results and Observations

Suppose you got the following data:

Mass of seeds= 25 g

Mass of collected essential oils = 2.75 g

Calculate the percent of essential oils in these seeds.

Post-lab Questions

1- How is steam distillation different from simple distillation?

2- Explain why the distillate from the steam distillation was turbid.

3- Why is steam distillation a preferred technique to purify high boiling liquids that are water insoluble?

4- Why does distilling an essential oil using steam help avoid decomposition?

5- You are given an authentic sample of the essential oil. Propose a simple experiment to confirm that the isolated essential oil is identical to the given authentic sample.

Experiment 7

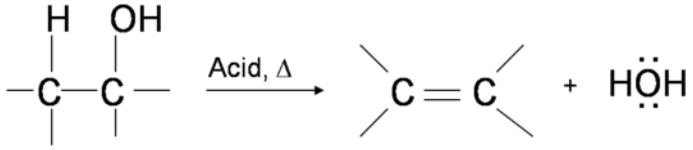
Preparation of Alkenes from Cyclohexanol or 2-Methyl-2-butanoI, and Tests for Unsaturation

Objectives

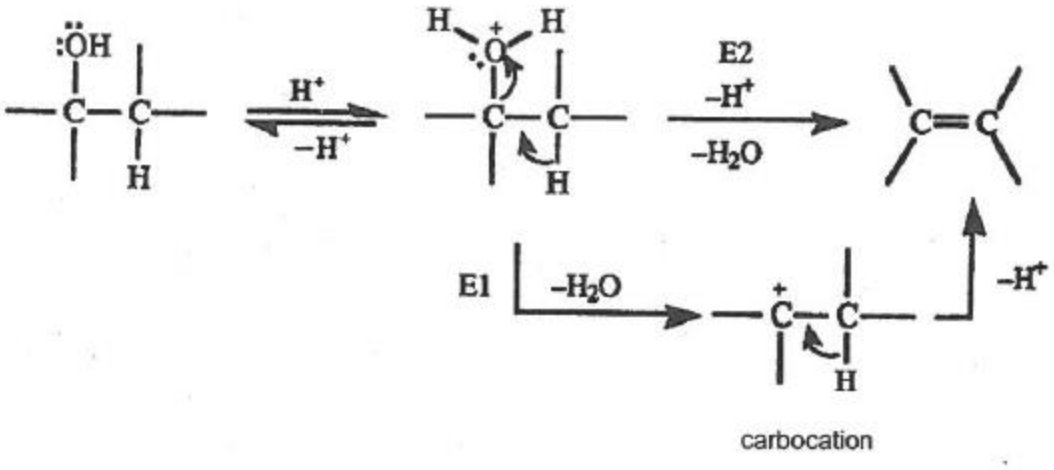
- Synthesize alkenes from their original alcohol
- Test the unsaturation of alkenes

Background

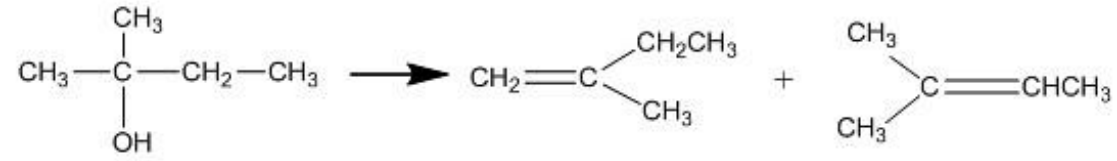
One general synthetic method used to prepare alkenes involves dehydration of an alcohol:



A strong and high-boiling mineral acid, such as sulfuric or phosphoric acid, is the catalyst for the reaction. The acid protonates the alcohol. Subsequently, a molecule of water and a proton are eliminated.

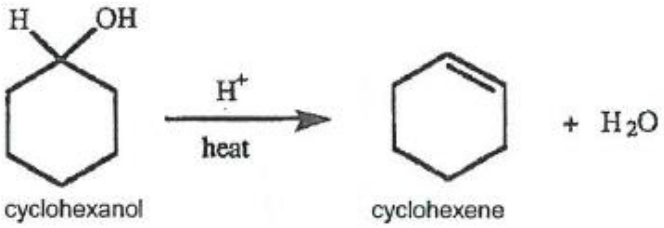


If the alcohol is tertiary or has other structural features that stabilize the corresponding carbocation, the elimination usually proceeds stepwise (El mechanism). Alternatively, if the alcohol is primary, the loss of H_2O and usually occurs in one step (E2 mechanism). If the alcohol is secondary, either mechanism is possible. If the alkyl groups attached to the hydroxyl-bearing carbon atom are different from one another, it is possible to obtain two or more different alkenes as seen in the following example:



PART A. CYCLOHEXENE FROM CYCLOHEXANOL

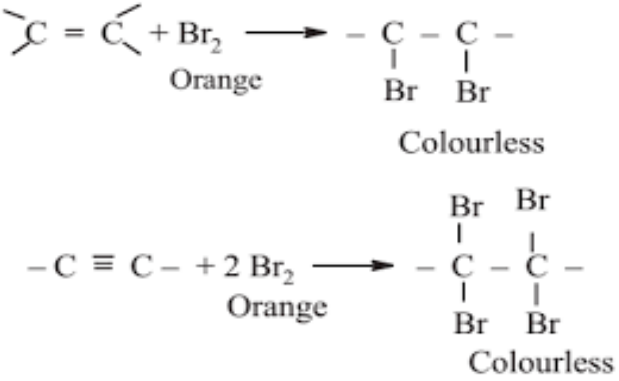
In this experiment, the secondary alcohol cyclohexanol will be dehydrated to cyclohexene:

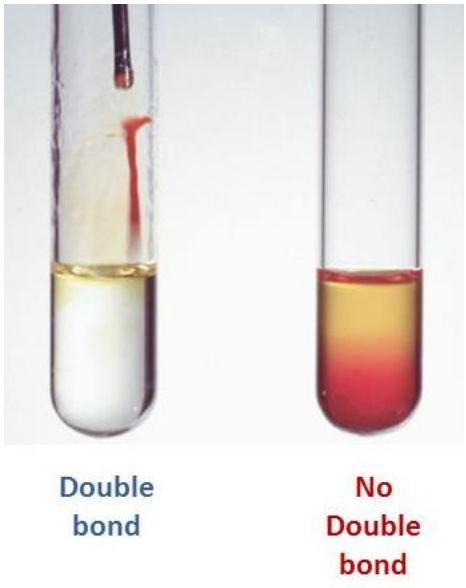


Experimentally, advantage is taken of the fact that alkenes boil at much lower temperatures than the alcohols from which they are prepared. The alcohol is heated (with acid) to a temperature above the boiling point of the alkene but below that of the alcohol. The alkene and water distill from the reaction flask as they are formed, whereas the unchanged alcohol remains behind to be further acted on by the acid. In the present case, the dehydration is carried out at 130-140℃, which is above the boiling point of cyclohexane (83℃) but below that of cyclohexanol (161℃).

PART B. TESTS FOR UNSATURATION

Bromine decolorization is used as a simple qualitative test for unsaturation. Bromine is a dark red-brown liquid, but alkenes and dibromoalkanes are colorless.



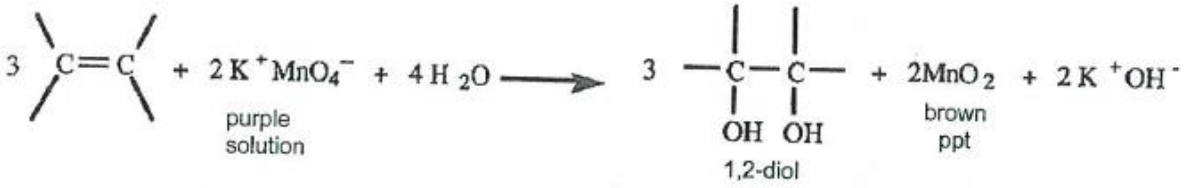


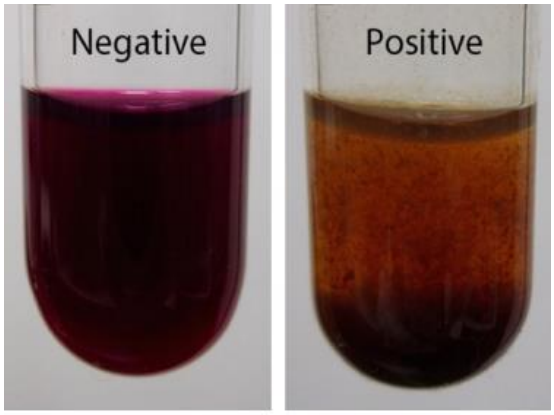
Thus, a dilute solution of bromine in some inert colorless solvent, such as tetrachloromethane or dichloromethane, is rapidly decolorized when it is added to

an alkene. In contrast, most saturated compounds do not decolorize bromine solutions.

Oxidizing agents also react with carbon-carbon double bonds. This reaction can be used to distinguish alkenes from alkanes. In the Baeyer test, the reagent is alkaline permanganate.

When the alkene is oxidized, the reagent is reduced to manganese dioxide. The color change observed is from purple (MnO_4^-) to brown (MnO_2):

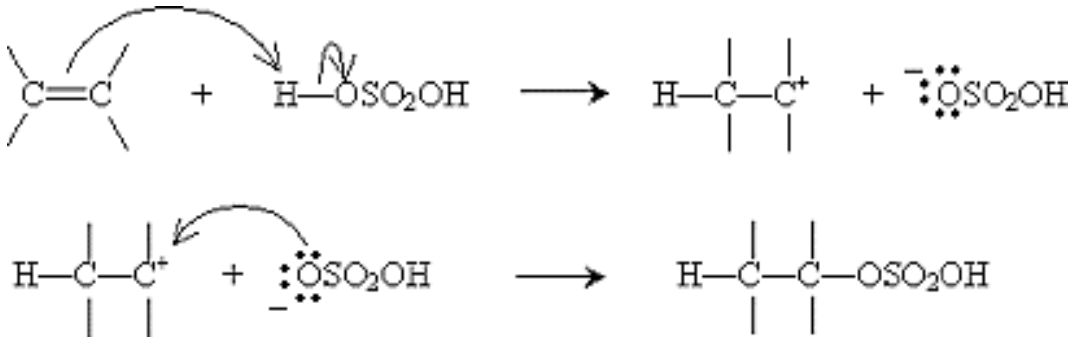




Baeyer test

Most alkanes, on the other hand, do not react with permanganate under the test conditions.

Although alkanes are inert to cold concentrated sulfuric acid, alkenes react. Either they dissolve to form an alkyl hydrogen sulfate or they produce polymers or tars, which are often dark in color.



In this part of the experiment, you will apply these three tests to the alkene you prepared in order to demonstrate that it does contain a carbon—carbon double bond. For comparison, you will also test a structurally similar but saturated hydrocarbon alkane.

Apparatus/Reagents Needed

- 50-mL Round bottom flask
- Y-adapter
- Receiving adapter
- Thermometer and thermometer adapter
- Erlenmeyer Flask
- Condenser
- Separatory funnel
- Heating mantle
- Test tubes
- plastic droppers
- boiling stones
- Cyclohexanol
- funnel
- drying agent

Procedure

PART A. CYCLOHEXENE FROM CYCLOHEXANOL

1. Arrange a simple distillation apparatus.
2. Add 16 g (16.7 mL, 0.16 mol) of cyclohexanol (density = 0.96) and 4 mL of concentrated sulfuric acid to a 50-mL round-bottomed flask. Mix the contents thoroughly by swirling before connecting the flask to the distillation setup.
3. Add two boiling stones.
4. Heat the flask gently so that the temperature of the distilling vapor does not exceed 100°C.
5. Continue the distillation until only a few milliliters of high-boiling residue remain in the flask. If white fumes appear near the end of the distillation, stop heating at once by lowering the heating mantle; these fumes are oxides of sulfur.
6. When cool, disconnect the distillation flask.
7. Pour the acidic residue into a beaker containing 50 mL of water, and neutralize the solution by cautiously adding cold sodium bicarbonate until the solution is just basic to litmus. Then pour the contents of the beaker into a waste container provided by your instructor.
8. Rinse the flask with water, then finally rinse it with acetone until it is clean. Dispose of the acetone rinses in a bottle for non-halogenated organic waste provided by your instructor.

** Note that the distillate in the receiver consists of two layers.

9. Transfer the distillate to a small separatory funnel and add 4 mL of saturated sodium chloride solution (to decrease the solubility of cyclohexene in the water layer). Then slowly add 4 mL of 10% sodium carbonate solution to neutralize any traces of acid. Swirl or shake the mixture gently. Allow the layers to separate, then draw off and discard the lower layer. Pour the upper layer (crude cyclohexene) out the top of the separatory into a small Erlenmeyer flask.
10. Add 0.5 g of anhydrous calcium chloride granules to the cyclohexene and allow it to stand for 10-15 min, swirling it occasionally. The calcium chloride is used to dry (that is, remove traces of water from) the cyclohexane. The product should be clear, not cloudy.
11. Reassemble the clean, dry distillation apparatus. Be sure that the inner tube of the condenser is also clean and dry. Decant or filter the cyclohexene from the

calcium chloride into the round-bottomed flask, add two boiling stones, connect the flask to the apparatus, and distill. Collect the product that boils in the range 79-84°C in a receiver of known weight.

12. Weigh the product and calculate the percentage yield.

** For a good preparation, the yield should be about 8-9 g.

PART B. TESTS FOR UNSATURATION

- The Bromine Test

In 10 drops of dichloromethane (CH_2Cl_2, DCM), dissolve 2 drops of the alkene you prepared. Add to this solution, dropwise, a solution of bromine in tetrachloromethane (CCl_4) or DCM. Observe the result. For comparison, repeat the test using the saturated alkane in place of the alkene.

* Discard the tube contents in a waste bottle for halogenated organic liquids provided by your instructor.

- The Baeyer Test

Add 2 drops of the alkene you prepared to 10 drops of 0.5% of potassium permanganate solution, shake the tube for 1-2 min, and note the results. For comparison, repeat the test using the saturated alkane.

* Pour the contents of the tubes through a filter into a bottle provided by your instructor.

- The Sulfuric Acid Test

To 10 drops of concentrated sulfuric acid in a test tube, add 2 drops of your alkene. Shake the tube well but carefully and note the result. For comparison, repeat the test with the saturated alkane.

* Discard the tube contents into a beaker containing at least 20 mL of water. Neutralize the solution with aqueous 10% sodium hydroxide and pour the resulting solution into a waste container provided by your instructor.

Useful Links

Preparation of cylcohexene from cyclohexanol

https://www.youtube.com/watch?v=-ZsRW6Ils24

Tests for Unsaturation

https://www.youtube.com/watch?v=08v40LxePK0

https://www.youtube.com/watch?v=JmlDkC6IdKA

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Experiment 7: Preparation of Alkenes from Cyclohexanol or 2-Methyl-2-butanoI, and Tests for Unsaturation

Pre-lab Questions

1- Explain why alcohols generally have a high boiling point than alkenes derived from them through dehydration reaction?

2- What are the structures of the major and minor products obtained when 1-methylcyclohexanol is dehydrated using conc sulfuric acid?

3- Can the products from question 2 be differentiated from each other using any of the tests for unsaturation described in the procedure? If yes, how? If not, why not?

Results and Observations

PART A. CYCLOHEXENE FROM CYCLOHEXANOL

- write a balanced equation for the preparation of cyclohexene from cyclohexanol.

- Fill in the following table.

alcohol (reactant)	**cyclohexanol**
Molar mass	
volume	
Density	0.96 g/mL
mass	
moles	
alkene (Product)	**cyclohexene**
Molar mass	
Theoretical yield, **moles**	
Theoretical yield, **g**	
Actual (Experimental Yield), **g**	
Yield%	

PART B. TESTS FOR UNSATURATION

Fill in the following table with your observations.

Bromine Test	
cyclohexane	
cyclohexene	
Baeyer Test	
cyclohexane	
cyclohexene	
Sulfuric Acid Test	
cyclohexane	
cyclohexene	

- Write a balanced equation for the reaction of cyclohexene with bromine, with potassium permanganate, and with cold sulfuric acid.

Post-lab Questions

1- Write the equation for the mechanistic steps in the dehydration of cyclohexanol. Assume E1 mechanism.

2- List several factors the contribute to your actual yield being less than 100%.

3- Why was it necessary to wash the crude cyclohexene product (Part A) with aqueous sodium carbonate? (Give an equation)

4- Would the dehydration of 2-methylcyclohexanol yield a single alkene? Explain, using equations.

5- Acid-catalyzed dehydration of unsymmetrically substituted alcohols usually favors formation of the most stable alkene. Based on that, which of the two alkenes formed in Q4 is more stable?

Experiment 8

Synthesis of Aspirin (Acetylsalicylic Acid)

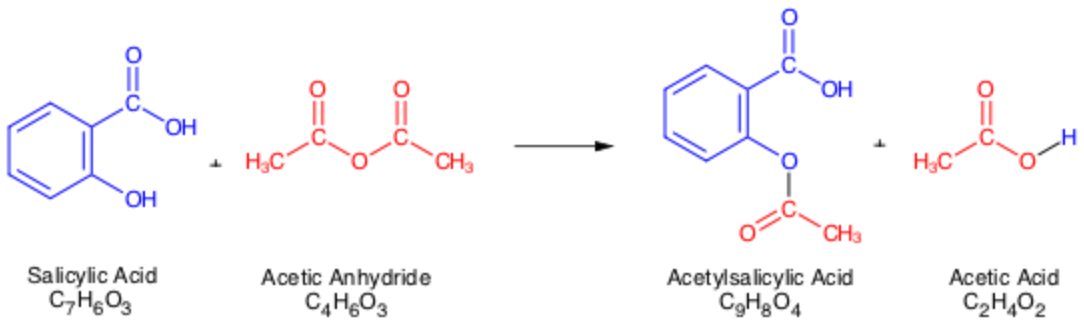
Objectives

- Prepare aspirin from salicylic acid and acetic anhydride.

Background

Salicylic acid (*o*-hydroxybenzoic acid) has been used in medicine for many years, either as the sodium salt or as an ester. Salicylates are antipyretics; that is, they lower the body temperature of one who has a fever, but they have little effect if the temperature is normal. Salicylates are also mild analgesics, which relieve certain types of pain (such as a headache, neuralgia, and rheumatism).

Unfortunately, sodium salicylate has an irritating effect on the stomach lining. This is why various esters are now used in place of the free acid or salt. These esters pass through the stomach largely unchanged but are hydrolyzed in the alkaline medium of the intestine, liberating the salicylic acid. Aspirin is the most common salicylate used in medicine today. It is the sodium salt of acetylsalicylic acid, in which the phenolic group has been converted to its acetate ester. Aspirin can be prepared from salicylic acid and acetic anhydride.



Annual production of aspirin in the United States is approximately 50 million pounds, which is enough to make over 50 billion standard tablets, or more than 200 tablets per person per year. Consumption of one-half tablet per day is said to reduce the risk of heart attack.

In this preparation you will heat a mixture of salicylic acid and acetic anhydride with a little sulfuric or phosphoric acid as catalyst. Aspirin is not very soluble in water; its solubility is only about 0.25 g/100 mL. Consequently, you can isolate the aspirin by diluting the reaction mixture with water.

Caution

1. Acetic anhydride is irritating in the liquid or vapor state. Avoid contact with skin and eyes.
2. When handling concentrated sulfuric or phosphoric acid be careful to avoid contact with skin and clothing. Wear disposable gloves.

Apparatus/Reagents Needed

- 125 mL Erlenmeyer flask
- 500 mL Beaker
- Disposable dropper
- Salicylic acid
- Concentrated sulfuric acid
- Glass rod
- Hot plate
- Vacuum filtration set-up
- Büchner funnel
- Acetic anhydride
- ice water

Procedure

Place 3.0 g of salicylic acid in a 125-mL Erlenmeyer flask. Carefully add, stirring constantly, 6 mL of acetic anhydride, followed by 10 drops of concentrated sulfuric acid. Swirl the contents of the flask so that the reactants are thoroughly mixed. Stopper the flask with a one-hole cork fitted with an inverted Pasteur pipet to prevent condensation of water in the reaction flask during heating on the steam bath. Heat the flask in a boiling-water or steam bath for 15 min. Remove the flask from the bath. While the contents are still hot, cautiously add 5 mL of ice water all at once. (The purpose here is to hydrolyze the excess acetic anhydride. If you allow the flask to cool before adding water, this hydrolysis is rather slow).

After the reaction subsides, add 35 mL of water and chill the contents of the flask in an ice bath. Use a stirring rod to break up any lumps that may form.

Collect the product by vacuum filtration, using a Büchner funnel. In the funnel, rinse the product with 15 mL of ice water; then draw air through the product for several minutes. Transfer the solid to a sheet of dry filter paper, and allow it to dry thoroughly. Weigh the dry solid to determine the yield, and determine its melting point.

- You can recrystallize the product by dissolving it in a few milliliters of ether, adding an equal volume of petroleum ether and cooling the mixture in an ice bath.

Waste disposal

Dispose of the aqueous filtrate in the container designated for aqueous waste. Discard the recrystallization filtrate in a waste bottle for non-halogenated organic solvents.

** Test:

In a separate test tubes, dissolve in 1 mL of methanol a few crystals of salicylic acid and a few crystals of aspirin that you synthesized and apply the ferric chloride test for phenols to each.

(Note: salicylic acid has a phenolic hydroxyl group, whereas acetylsalicylic acid does not).

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Experiment 8: Synthesis of Aspirin (Acetylsalicylic Acid)

Pre-lab Questions

1. What is the purpose of sulfuric acid or phosphoric acid used in the acetylation reaction? Use equations to explain this purpose.

2. The procedure calls for cautious addition of water to the reaction mixture while it is still hot. What purpose does the addition of water serve and why should the addition be done while the reaction mixture is hot? Provide an equation for the reaction involved.

3. Using the quantities of salicylic acid and acetic anhydride noted in the procedure and any other necessary data, calculate the theoretical yield in moles and grams of aspirin.

4. Describe how and why the ferric chloride test can be used to detect whether your reaction has gone to completion.

Results and Observations

Reagent	Molecular weight	Grams	Moles
Salicylic acid			
Acetic anhydride			

- The limiting reagent (show calculations):

- Theoretical yield of aspirin ……..mol

……g

- Actual yield ……..g

- Percentage yield …….%

- Results of ferric chloride test:

Post-lab Questions

1. What impurity is most likely to be present in the sample of aspirin you prepared? What effect would this impurity have if the product were intended for human consumption?

2. Write an equation for the reaction that occurs when aspirin is hydrolyzed in the body.

3. Upon heating with acid, salicylic acid can form a polymer. What is its structure likely to be?

Experiment 9

Esters: Synthesis and Saponification of Methyl Benzoate

Objectives

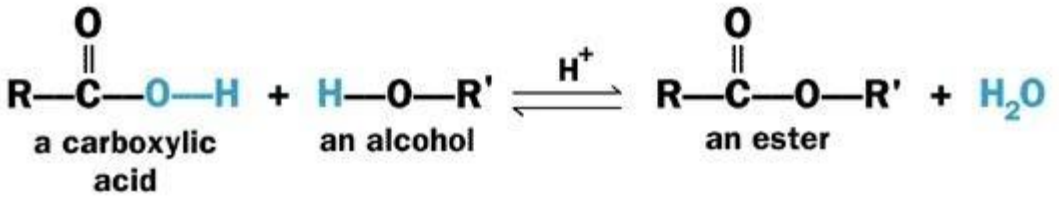
- Synthesize an ester.
- Study the saponification of esters.

Background

Esters are pleasant-smelling substances responsible for the flavor and fragrance of many fruits and flowers. In this experiment, you will synthesize an ester in Part A and, in Part B, study an important reaction of esters—saponification.

PART A. SYNTHESIS OF METHYL BENZOATE

Esters can be prepared by the reaction of an alcohol with an acid.



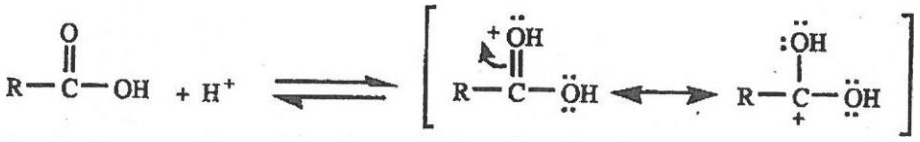
(Where R and R' are general hydrocarbon groups)

Esterification is reversible, and equilibrium is reached slowly unless the reaction is catalyzed by a little mineral acid, such as sulfuric acid. For many acid-catalyzed esterifications, the equilibrium constant is about 4:

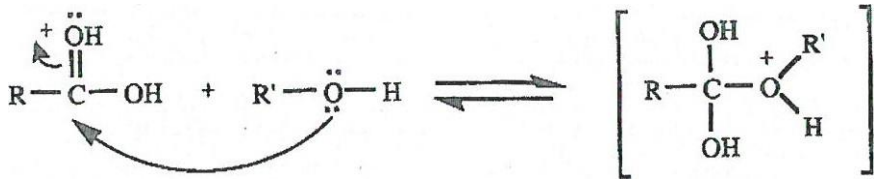
$$K_{eq} = \frac{[ester][water]}{[alcohol][acid]}$$

If equal initial concentrations of alcohol and acid are used, the yield of ester is about 66% according to the above equation. But this percentage yield can be increased to nearly 100% by using an excess of one reagent (usually the alcohol) or by removing the water that forms during the reaction. In these ways, the equilibrium can be shifted in favor of ester formation.

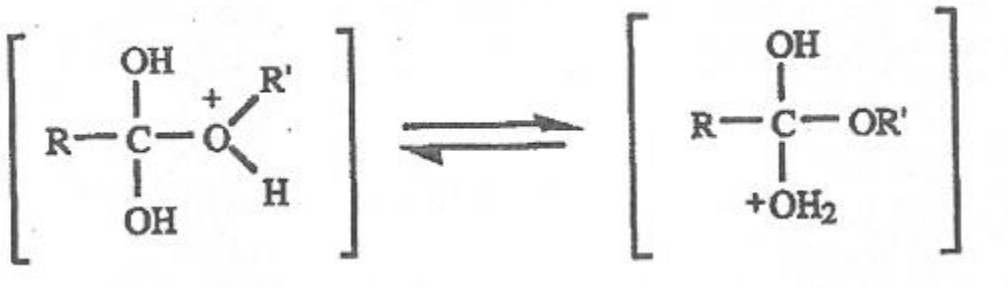
Mineral acid catalyzes the reaction by protonating the carbonyl oxygen of the organic acid.



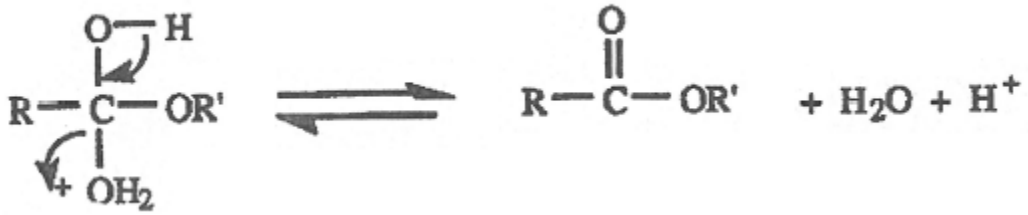
Protonation increases the positive charge on the carbonyl carbon atom and makes it more susceptible to nucleophilic attack by the alcohol.



Originally trigonal, the carbonyl carbon atom becomes tetrahedral. The tetrahedral intermediate, as formed above, is protonated on the alkoxy group, but it is in equilibrium with another form, with the proton on one of the hydroxyl groups.



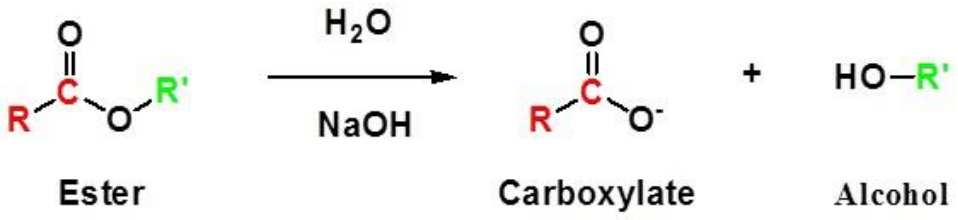
The reaction is completed by elimination of a proton and a water molecule.



In this experiment, you will prepare methyl benzoate by the sulfuric acid-catalyzed esterification of benzoic acid with methanol. You will use one of the two reactants in considerable excess of the equimolar amount to drive the equilibrium toward the desired product.

PART B. SAPONIFICATION OF METHYL BENZOATE

An ester can be converted to its component alcohol and acid by boiling it with aqueous base. The reaction is called **saponification** because it is analogous to the process used to convert fats to soaps. The overall reaction is:



The reaction proceeds to completion because the carboxylate ion, being negatively charged, is not readily attacked by nucleophiles such as R'OH, the other saponification product.

In this experiment you will saponify a portion of the methyl benzoate you synthesized in Part A. The products are methanol and benzoate ion. You will then recover benzoic acid from the benzoate ion by acidification. The overall process is the reverse of the synthesis that you performed in part A.

Apparatus/Reagents Needed

- 250 mL Round bottom flask
- 50 mL Round bottom flask
- condenser
- Disposable dropper
- 25 mL graduated cylinder
- 250 mL Beaker
- Dichloromethane (DCM)
- 15% NaOH solution
- Benzoic acid
- Concentrated Sulfuric acid
- Heating mantle
- pH paper
- Tubber tubes
- Separatory funnel
- 50 mL Erlenmeyer flask
- Boiling stones
- Ice
- Büchner funnel
- Methanol
- Concentrated hydrochloric acid

Procedure

PART A. SYNTHESIS OF METHYL BENZOATE

Arrange a reflux apparatus using a 250-mL RB-flask. Place 15 g of benzoic acid and 20 mL (16 g) of methanol in the flask. While swirling the contents of the flask to ensure thorough mixing, cautiously add 3 mL of concentrated sulfuric acid. The contents of the flask will heat up somewhat, but cooling is not necessary. Add two boiling stones, connect the flask to the condenser, turn on the cooling water, and heat the reaction mixture at gentle reflux for 30 min.

After cooling the reaction mixture, dilute it with 25 mL of water, transfer it to a separatory funnel, and add 10 mL of dichloromethane. Shake, vent to release pressure, and then allow the layers to separate. Draw off the lower (organic) layer

into a dry 50-mL Erlenmeyer flask and add to it about 1 g of anhydrous sodium carbonate.

Assemble a simple distillation apparatus using a 50-mL RB-flask. Transfer the dry organic solution to the flask through a funnel containing a small cotton plug at the apex to retain the drying agent. Rinse with 1-2 mL of dichloromethane. Add a boiling stone and distill. Discard the first fraction, which is recovered dichloromethane (bp 40℃), into a beaker, and collect the product, methyl benzoate, boiling between 195℃ and 201℃. Weigh the product to determine your yield. Save the product for use in Part B.

PART B. SAPONIFICATION OF METHYL BENZOATE

Place 5 mL (5.5 g) of methyl benzoate, 25 mL of 15% sodium hydroxide solution, and two boiling stones in a 250-mL round-bottomed flask. Attach a condenser to the flask, greasing the joint lightly. Heat the mixture at reflux until the ester layer disappears (20-30 min). Remove the flask and transfer the contents to a 250-mL beaker cooled in an ice bath. Cautiously acidify the reaction mixture (test with litmus paper or pH paper) by adding concentrated hydrochloric acid in small portions, stirring constantly (about 12-15 mL of acid will be required). Use a Büchner funnel to filter the white solid (benzoic acid), wash with cold water, and spread it on filter paper to dry. Weigh the dry product and determine its melting point.

Student Name:	Student ID no.:
Date:	Section:
Instructor Name:	TA name:

Experiment 9: Esters: Synthesis and Saponification of Methyl Benzoate

Pre-lab Questions

1. Using the quantities of benzoic acid and methanol noted in the procedure, calculate the theoretical yield in moles and grams of methyl benzoate.

2. Use of concentrated sulfuric acid (a source of protons) as a catalyst is recommended in the procedure. Will the use of dilute sulfuric acid (still a good source of protons) hinder the reaction, and if so, how?

3. Write and name the structures of the products of saponification of methyl benzoate.

Results and Observations

PART A. SYNTHESIS OF METHYL BENZOATE

Reagent	Molecular weight	Grams	Moles
Methanol			
Benzoic acid			

- The limiting reagent (show calculations):

- Theoretical yield of ester ……..mol

……g

- Actual yield ……..g

- Percentage yield …….%

PART B. SAPONIFICATION OF METHYL BENZOATE

Reagent	Molecular weight	Grams	Moles
Methyl benzoate			

- Theoretical yield of benzoic acid……..mol

……g

- Actual yield ……..g

- Percentage yield …….%

Post-lab Questions

1. In the preparation of methyl benzoate, which reagent was used in excess? Why?

2. What would have been the effect of omitting the sulfuric acid from the methyl benzoate preparation?

3. Write out all the steps in the mechanism for the esterification of benzoic acid with methanol. Mark the oxygen of the methanol with an asterisk (*) in each step and note where (in the ester or in the water) this oxygen ends up.

4. The equilibrium constant for the formation of methyl benzoate from methanol and benzoic acid at 25°C is 3.77. Use the equation for the equilibrium constant to calculate the theoretical yield of methyl benzoate for the following conditions.

i) With equal initial amounts of the reactants

ii) With a five-fold excess of methanol

5. Write equations for the mechanism for saponification of methyl benzoate. (Hint: Begin with nucleophilic attack of hydroxide ion on the carbonyl group of the ester.)

6. Write an equation for the reaction that occurred when you acidified the saponification reaction mixture with hydrochloric acid.

Experiment 10

Reactions of Alcohols and Phenols

Objectives

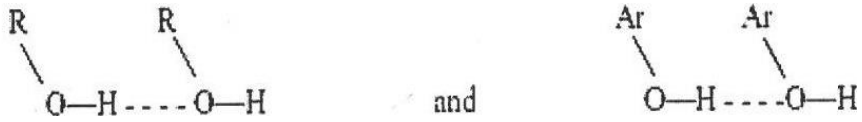
- Perform tests of alcohols and phenols to demonstrate their properties and reactions.

Background

Alcohols and phenols are organic analogs of water, H-OH, in which one hydrogen is replaced by an aliphatic (R-OH) group in the alcohols and by an aromatic (Ar-OH) group in the phenols. The following tests and experiments illustrate some properties and reactions of alcohols and phenol.

1. Solubility in water

Alcohols and phenols, like water, form strong intermolecular hydrogen bonds:



The lower-molecular-weight alcohols can easily replace water molecules in the hydrogen-bonded network of water and are thus readily soluble in water.

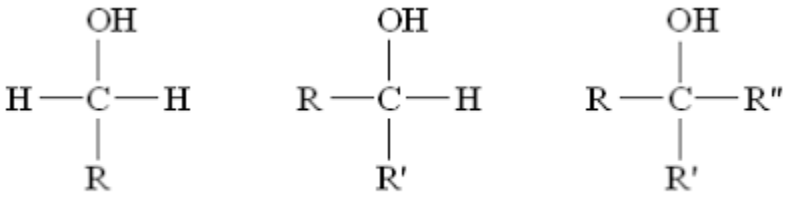
The solubility of alcohols in water gradually decreases as the alkyl group becomes longer and larger. In this part of the experiment, you will test the solubility of several alcohols in water.

Procedure

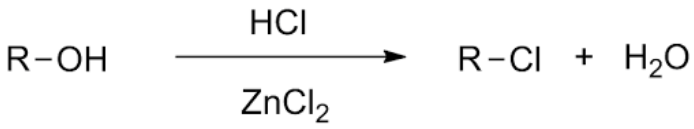
In separate test tubes, place 0.5 mL of each of the following alcohols: ethanol, 1-butanol, 2-methyl-2-propanol, cyclohexanol. Add 2 mL of water to each test tube, mix, and observe. Record your results for each alcohol on the report sheet as very soluble, moderately soluble, slightly soluble, or insoluble.

2. The Lucas test

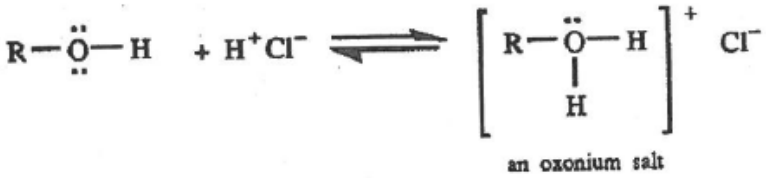
Alcohols are classified as primary, secondary, or tertiary, depending on whether the hydroxyl-bearing carbon is bound to one, two, or three carbon atoms. When treated with a particular reagent, alcohols may differ in the rates at which they react, or indeed even in the type of product obtained, depending on the class to which they belong. Tests that distinguish among the three classes can be useful in determining the structure of an unknown alcohol.



The **Lucas reagent** is a solution of zinc chloride in concentrated hydrochloric acid. The Lucas test is based on the different rates at which primary, secondary, and tertiary alcohols are converted to chlorides with this reagent.



The lower alcohols all dissolve in the reagent to form oxonium salts.



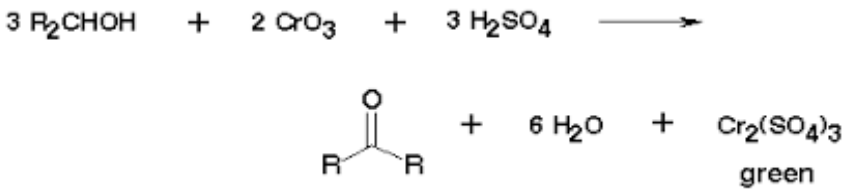
The corresponding alkyl chlorides, however, are insoluble in the reagent. Tertiary alcohols react so rapidly that it is impossible to detect their dissolution; the alkyl chloride separates immediately as a cloudy dispersion or separate layer. Secondary alcohols dissolve to give a clear solution (provided the R group does not have too many carbon atoms in the chain) and then form alkyl chlorides (cloudy solution) within a few (usually 4-5) minutes. Primary alcohols are not converted to chlorides with this reagent at room temperature until several hours have elapsed.

Procedure

Place 2 mL of Lucas reagent in each of four test tubes. Test each alcohol by adding about 5 drops of the alcohol to the reagent. Shake the test tube and note the length of time it takes for the mixture to become cloudy or separate into two layers. Test 1-butanol, cyclohexanol, and 2-methyl-2-propanol, and record the results for each. The fourth tube, containing only the reagent, is used as a comparison control.

3. The Bordwell- Wellman Test

Primary and secondary alcohols are oxidized rapidly by chromic acid, whereas tertiary alcohols are not. Primary and secondary alcohols are oxidized to aldehydes and to ketones, respectively.



In the Bordwell-Wellman test, an acetone solution of the alcohol to be tested is treated with a solution of chromic anhydride, CrO_3, in sulfuric acid. Alcohols that are oxidized reduce the Cr(VI) to Cr(III), causing the solution to become opaque and to take on a greenish cast.

Caution	Chromic acid is toxic and corrosive. Do not get Bordwell-Wellman reagent on your skin.

Procedure

Place 1 mL of acetone in each of three test tubes. (The best results are obtained with acetone that has been distilled from potassium permanganate to remove traces of isopropyl alcohol.) Add 1 drop or a few crystals (10 mg) of one of the following alcohols to each of five test tubes: 1-butanol, 2-methyl-2-propanol. The third tube is used as a comparison control. Then, while shaking each tube, add 1 or 2 drops of the Bordwell-Wellman reagent. Note any changes that take place.

4. Esters

Alcohols react with acids to form esters. The process is called esterification. The products are usually pleasant-smelling substances. Esters are responsible for the flavors and fragrances of many fruits and flowers.

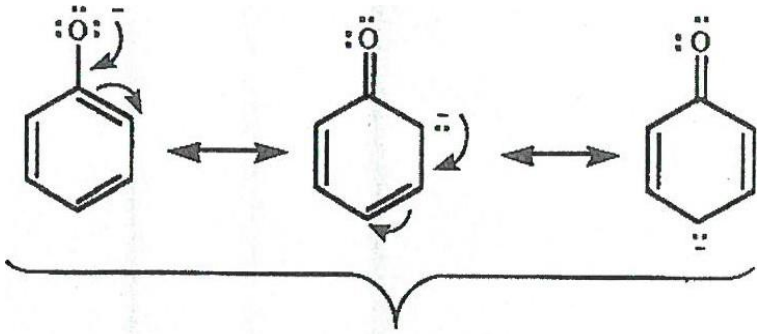
In this experiment you will convert two alcohols to their acetates (R' = CH_3) by treatment with acetic acid using an acid catalyst (H_2SO_4).

Procedure

Place 1 mL of glacial acetic acid in each of two test tubes. To one tube add 1 mL of ethanol, and to the other add 1 mL of isopentyl alcohol (3-methyl-l -butanol). Shake the tubes to effect dissolution. While shaking, cautiously add 1 mL of concentrated sulfuric acid to each tube, and then place the tubes in a beaker of warm (50°C) water for 5 min. Pour each reaction mixture into a separate beaker containing 10 g of crushed ice, stir, and cautiously note the odor in each case.

5. The Acidity of Phenols

Phenols are stronger acids than alcohols or water. The principal reason is that the negative charge in phenoxide ions can be delocalized into the aromatic ring, through resonance, whereas the negative charge in alkoxide or hydroxide ions is localized on the oxygen atom.



charge delocalization in phenoxide ion

The approximate acidity constants are 10^{16} for ethanol, 10^{15} for water, and 10^{10} for phenols. Thus, phenols can be converted to their salts (phenoxides) by treatment with sodium hydroxide.

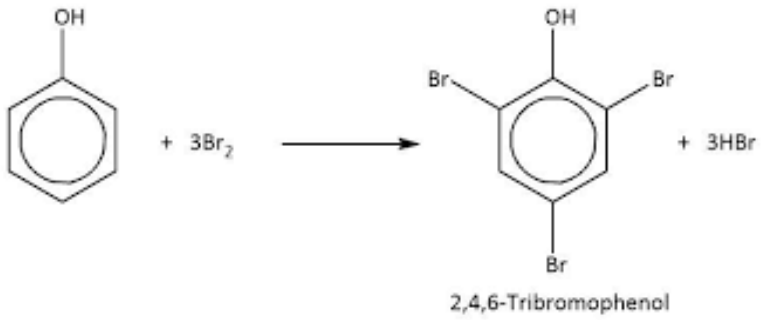
Procedure

Caution	Phenols are corrosive. Wear disposable gloves when working with phenols in the next three procedures. If you get any phenols on your skin, wash the area immediately with plenty of water.

Place 0.2 g or 0.5 mL of each of the following compounds in a separate test tube: 1-hexanol and phenol. Add 1 mL of water to each tube, shake, and note whether the compound dissolves. Then add 2 mL of 15% sodium hydroxide solution to each tube, shake again, and note whether the compound now dissolves.

6. Reaction of phenol with Bromine water

The hydroxyl group of phenols activates the aromatic ring toward electrophilic substitution. This activation can be seen in the reaction of phenol with bromine water. No catalyst (such as $FeBr_3$) is required, and the reaction proceeds directly to the tribromophenol product.



2,4,6-Tribromophenol

Procedure

To 0.5 mL of 3% aqueous phenol solution add bromine water, and shake until the yellow color persists. Observe and record the results.

7. Reaction of Phenols and Enols with Ferric Chloride

Phenols and compounds with a hydroxyl group attached to an unsaturated carbon atom (enols) give a coloration (pink, violet, or green, depending on the structure of the phenol or enol) when mixed with ferric chloride, $FeC1_3$. The color is due to the formation of coordination complexes with the iron. Ordinary alcohols do not react. This test can be used to distinguish most phenols from alcohols.

Procedure

In three separate test tubes, dissolve one or two crystals, or 1 or 2 drops, of phenol, 2,4-pentanedione, and 2-propanol in 5 ml of water. In a fourth test tube, place 5 ml of water as a comparison control. To each test tube, add 1 or 2 drops of 1% ferric chloride solution, shake, and observe and record the results.

Apparatus/Reagents Needed

- Clean test tubes
- Plastic droppers
- 100 ml beaker
- Hot plate
- crushed ice
- Litmus paper

1. Solubility in water

   Ethanol, 1-Butanol, 2-Methyl-2-propanol, Cyclohexanol

2. The Lucas Test

   1-Butanol, Cyclohexanol, 2-Methyl-2-propanol, Lucas reagent.

3. The Bordwell-Wellman Test

   1-Butanol, 2-Methyl-2-Butanol, Cyclohexanol, Acetone,

4. Esters

   Ethanol, Isopentyl Alcohol

5. The Acidity of Phenols

   Distilled water, NaOH solution, 1-Hexanol, Phenol

6. Reactions of Phenol with Bromine Water

   3% aqueous phenol solution, Br_2/H_2O

7. Reaction of Phenols and Enols with Ferric Chloride

   Phenol, 2,4-pentanedione, 2-propanol

Student Name:	**Student ID no.:**
Date:	**Section:**
Instructor Name:	**TA name:**

Experiment 10: Reactions of Alcohols and Phenols

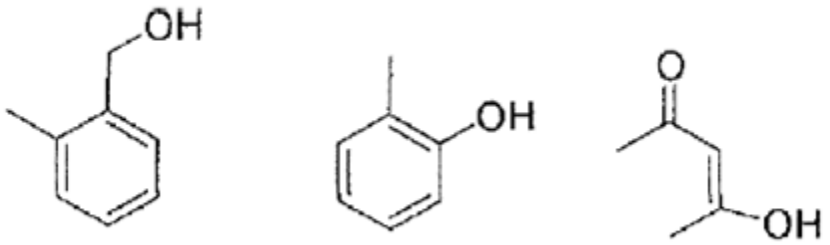
Pre-lab Questions

1. Provide the structures of 1 -pentanol, 2-pentanol, 3-pentanol and 2-methyl-2-butanol, and classify these as primary, secondary or tertiary alcohols.

2. Among the alcohols listed for question 1, which ones would give a positive Bordwell-Wellman test?

3. Among the compounds listed for question l, which one is expected to react the fastest with Lucas reagent to produce a cloudiness in the test tube and why?

4. Among the structures shown below, which one is not expected to give a positive test with ferric chloride and why?



Results and Observation

1. Solubility in water

Compound	structure	Solubility in water
Ethanol		
1-Butanol		
2-Methyl-2-propanol		
Cyclohexanol		

2. The Lucas Test

Compound	structure	Result and observation
1-Butanol		
Cyclohexanol		
2-Methyl-2-propanol		
Control		

3. The Bordwell-Wellman

compound	structure	Result and observation
1-Butanol		
2-Methyl-2-propanol		
Acetone		
Cyclohexanol		

4. Esters

Ethanol : …….

Isopentyl alcohol : …….

5. Acidity of Phenols

Compound	Structure	Solubility	
		Water	NaOH solution
1-Hexanol			
Phenol			

6. Reactions of Phenol with Bromine Water

Observations:

……

7. Reaction of Phenols and Enols with Ferric Chloride

Compound	Structure	Result
Phenol		
2,4-pentanedione		
2-propanol		
Control		

Post-lab Questions

1. What general conclusions can you draw about the solubility of alcohols in water on the basis of your results in Section 1?

2. Which is less soluble in water, 1-pentanol or 1-heptanol? Explain.

3. Write an equation for the reaction of 2-butanol with the Lucas reagent.

4. What would be the result of treating each of the following compounds with the Lucas reagent? Explain.

a). 2-Methyl- I -propanol

b). Cyclopentanol

c). 1-Methylcyclopentanol

5. Which of the alcohols listed in Question 4 would not be oxidized in the Bordwell-Wellman test? Explain.

6. Describe the odor of the product derived from mixing isopentyl alcohol and acetic acid (Sec. 5) and write the equation for its formation.

7. Write an equation that explains the solubility of *p*-chlorophenol in 15% sodium hydroxide.

8. From the results of this experiment, would you say that 1-hexanol is more acidic or less acidic than phenol? Explain.

9. Write an equation for the equilibrium between 2,4-pentanedione and its major enolic form.

10. Using tests performed in this experiment, tell how you would distinguish between the members of each of the following pairs of compounds. Give equations when appropriate.

1-Propanol and 2-propanol

4-Chlorophenol and 4-chlorocyclohexanol

1 -Butanol and 2-methyl-2-propanol

2,4-Pentanedone and 2-pentanone

Experiment 11

Reactions of Aldehydes and Ketones

Objectives

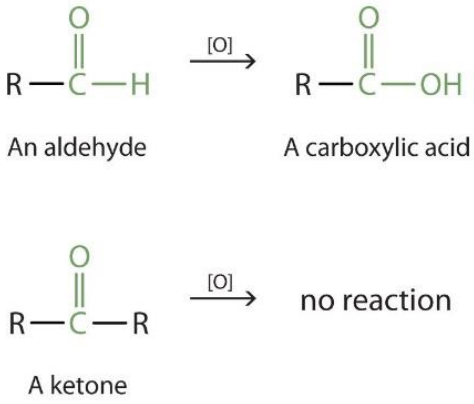
- Perform tests of aldehydes and ketones to demonstrate their properties and reactions.

Background

The functional group in aldehydes and ketones is the carbonyl group, a carbon and an oxygen joined by a double bond. In aldehydes, at least one of the other two bonds on the carbonyl carbon is to a hydrogen atom, whereas in ketones, both other atoms that are attached to the carbonyl carbon are carbon atoms. Aldehydes and ketones often react similarly. With the same reagent, aldehydes usually react faster than ketones, mainly because there is less crowding at the carbonyl carbon. Aldehydes are also more easily oxidized than ketones. In this experiment, you will perform reactions that illustrate the similarities and differences between aldehydes and ketones.

Part A. Oxidation

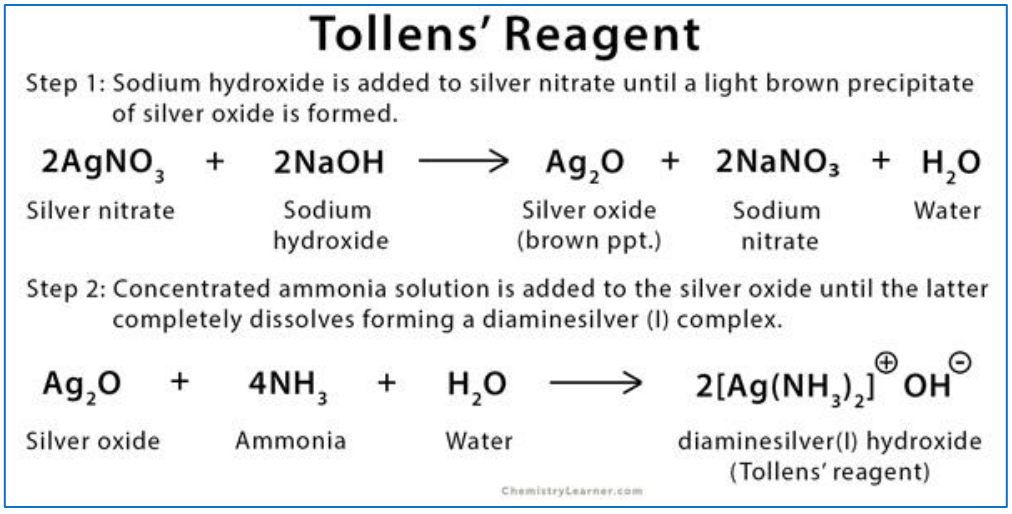
Aldehydes and ketones behave differently toward oxidizing agents. Aldehydes are easily oxidized to acids with the same number of carbon atoms.



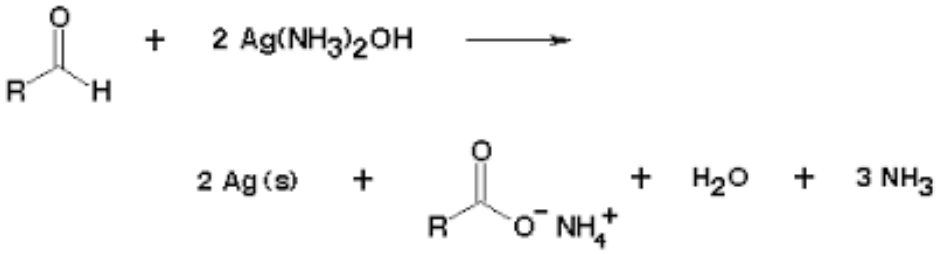
Ketones may be oxidized only under more severe conditions (stronger reagents and higher temperatures), because their oxidation to an acid requires the rupture of a carbon-carbon bond. Several laboratory tests that distinguish aldehydes from ketones are based on the fact that they are oxidized under different conditions.

- Tollen's silver mirror

Tollens' reagent is an ammoniacal solution of silver ion prepared by dissolving silver oxide in ammonia:



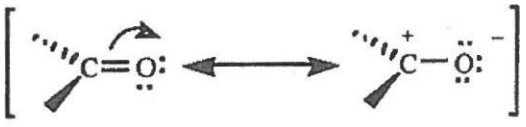
Tollens' reagent is reduced to metallic silver by aldehydes. The aldehyde is oxidized to the corresponding acid as Tollens' reagent is reduced. Ketones are not usually oxidized by this reagent.



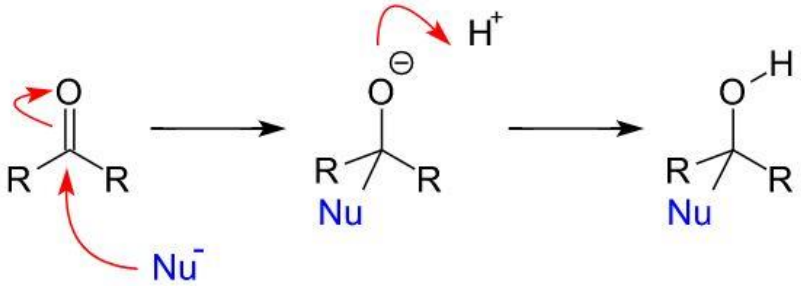
When the test is carried out with dilute solutions of reagents in scrupulously clean glassware, the silver deposits finely in the form of a mirror on the walls of the vessel. Otherwise, the silver deposits as a black precipitate.

Part B. Addition

The most common reaction of carbonyl compounds involves addition of various reagents to the carbon-oxygen double bond. Because of the electronegativity of oxygen, the carbonyl group can be described as a resonance hybrid between these two structures:

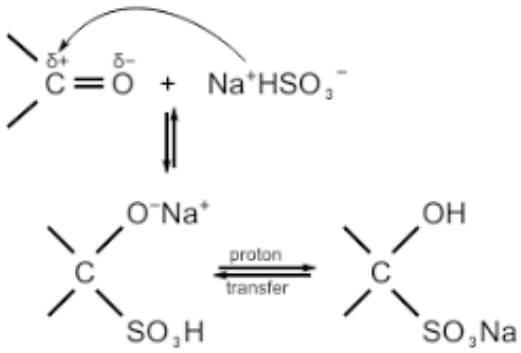


The carbonyl carbon atom carries a partial positive charge, so it is susceptible to attack by nucleophiles-reagents that can supply an electron pair. A nucleophile forms a bond with the carbonyl carbon and displaces the π electrons to the oxygen, thus converting the carbonyl carbon atom from a trigonal to a tetrahedral structure.



- Bisulfite Addition Compounds

Aldehydes and certain ketones that are not sterically hindered by having large groups attached to the carbonyl carbon atom react with saturated aqueous sodium bisulfite to form white crystalline addition products. The nucleophile is the bisulfite ion. Excess bisulfite shifts this equilibrium to the right.



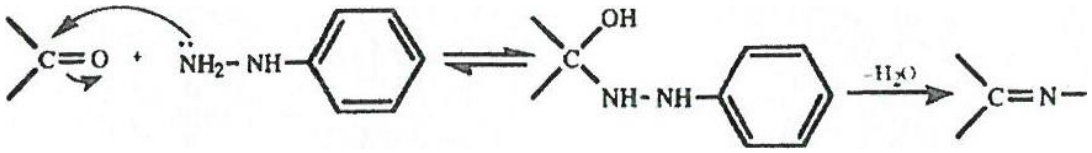
The addition compounds can be reconverted to the original carbonyl compound by treatment with acid. The reaction can therefore be used to separate carbonyl compounds from mixtures containing other substances.

- Shiff's fuchsin-Aldehyde test

Fuchsin is a magenta dye, the aqueous solution of which can be decolorized by sulfur dioxide. In the presence of aldehydes, but not ketones, the color reappears. The reaction with aldehydes is not merely a combination with sulfur dioxide and regeneration of the original fuchsin. Instead, the color is due to various addition products of the aldehyde and the dye. For that reason, the color varies from one aldehyde to another, but generally the color is pink with a blue or purple cast. The test is extremely sensitive and can detect small traces of aldehydes.

- Phenylhydrazones

Phenylhydrazine reacts with aldehydes and ketones to form phenylhydrazones.

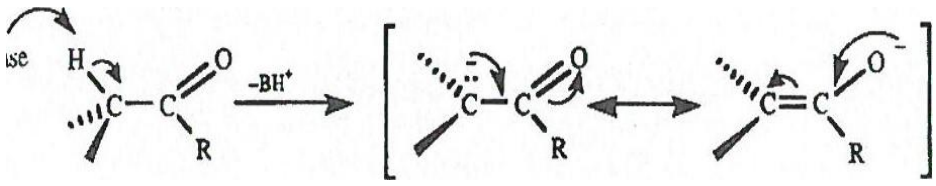


The products are frequently crystalline and can be used (via their melting points) to identify aldehydes or ketones. If 2,4-dinitrophenylhydrazine is used in place of phenylhydrazine itself, the products usually have higher melting points. Tables of such melting points are available for use in identifying unknowns.

Caution	Derivatives of phenylhydrazine are suspected carcinogens. Handle these reagents with care and avoid skin contact. Wear disposable gloves.

Part C: REACTIONS OF ENOLATE ANIONS

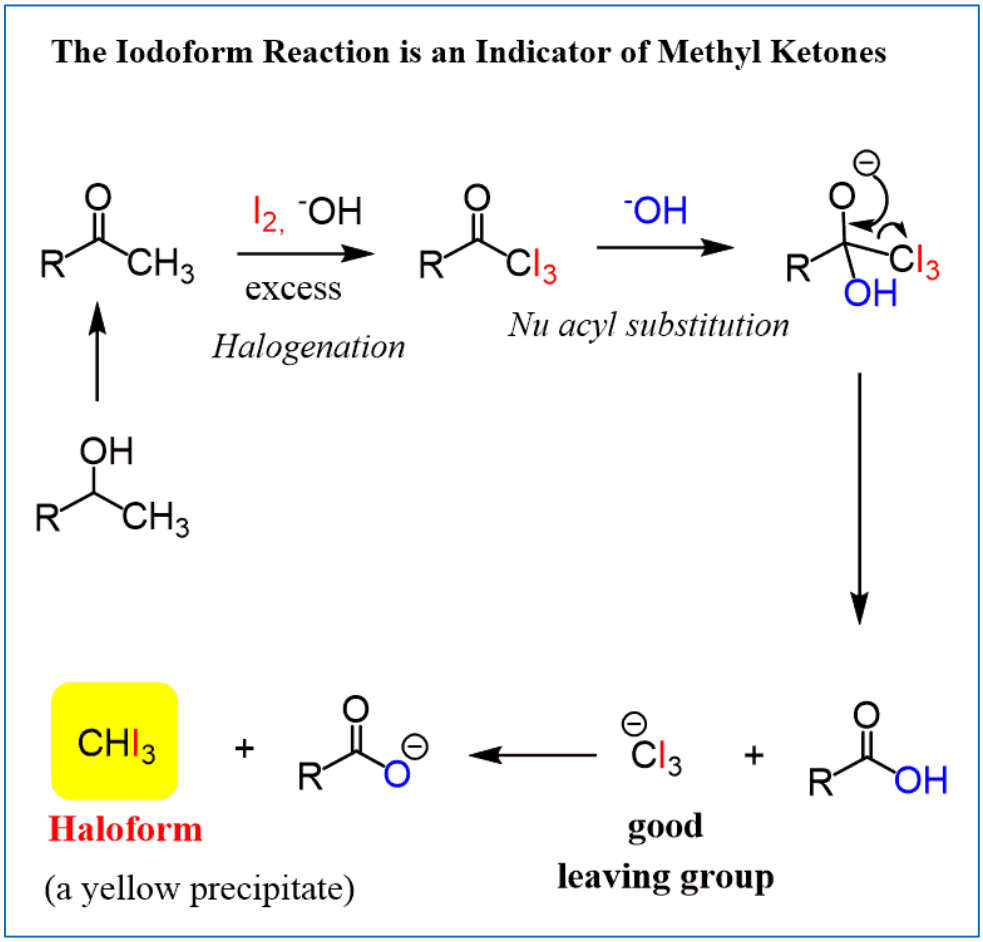
The acidity of a C-H bond a to a carbonyl group is enhanced because the carbonyl carbon, which carries a partial positive charge, acts as an electron-withdrawing and hence acidity increasing substituent on the α-carbon. Also, the negative charge in the carbanion that results from proton removal can be delocalized by resonance.



Enolate anions can act as nucleophiles in many reactions, two of which are illustrated in this part of this experiment.

- The Haloform Reaction and the Iodoform Test

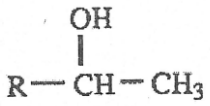
Because of the electron-withdrawing effect of the first halogen, any remaining α-hydrogens become even more acidic and are rapidly replaced by halogens. In this way, a methyl group adjacent to a carbonyl group is rapidly converted to a trihalomethyl group by the halogen and base. With iodine, the reaction is:



Because of the presence of strong electron-withdrawing groups on adjacent carbon atoms, the resulting trihalo compound is readily cleaved by a base, a reaction that leads to iodoform (haloform).

If bromine is used instead of iodine, the product is bromoform; if chlorine is used, the product is chloroform.

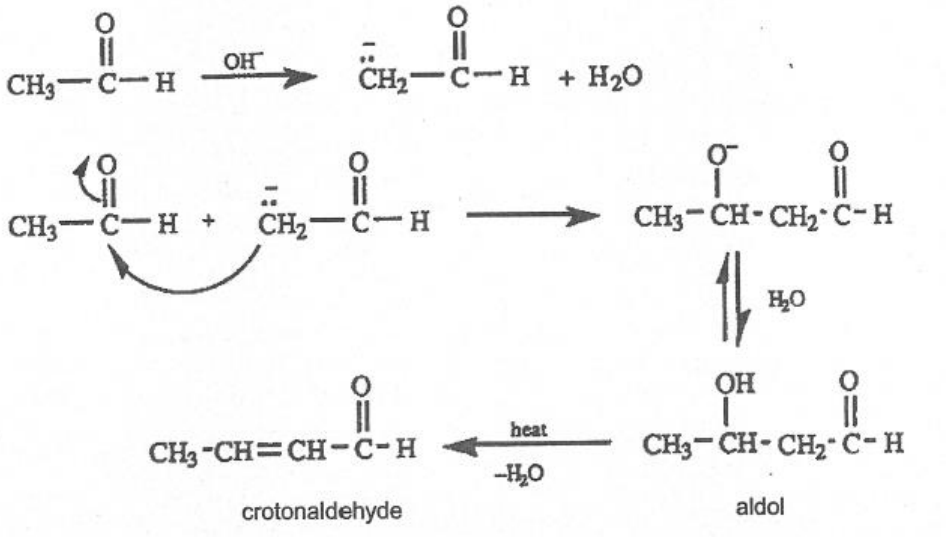
Most commonly, this reaction is used to test for the presence of compounds known as methyl ketones. When such compounds are treated with iodine and a base, iodoform deposits as a yellow crystalline compound with a typical medicinal odor. A positive test also results from alcohols with the structure:



because iodine is an oxidizing agent, and such alcohols are easily oxidized by it to methyl ketones, which then give iodoform.

- The Aldol condensation

Being nucleophiles, enolate anions can add to carbonyl groups. Such reactions lead to new carbon-carbon bonds and are extremely useful in synthesis. When acetaldehyde is treated with a dilute base, it condenses with itself to give aldol. Upon heating, the aldol loses water, giving the unsaturated aldehyde crotonaldehyde.



Apparatus/Reagents Needed

- Clean test tubes
- Beakers
- Hot plate
- Büchner funnel
- Distilled water
- 5% sodium hydroxide
- 2% ammonium hydroxide
- Benzaldehyde
- Acetone
- Nitric acid
- 20% sodium bisulfite
- Ethanol
- Hydrochloric acid
- Sodium carbonate
- Cyclohexanone
- Phenylhydrazine
- 2,4dinitrophenylhydrazine
- 2-propanol
- 2-pentanone

Procedure

1. Tollens' test

Clean a test tube thoroughly with soap and water, and rinse it with distilled water. To 2 mL of 5%silver nitrate solution, add 0.5 mL of 5% sodium hydroxide solution and mix thoroughly. Then, while stirring vigorously, add enough 2% ammonium hydroxide to just dissolve the precipitate. The test will fail if you add too much ammonium hydroxide. If all the precipitate has not yet dissolved when the test tube is half full, do not continue to add ammonium hydroxide. Let the undissolved precipitate settle and decant the clear liquid for use.

Divide the Tollens' reagent equally among five test tubes, one of which is to serve as a comparison control. Test each of the following carbonyl compounds by adding 2 drops of it to one of the test tubes: benzaldehyde, acetone and formaldehyde (prepared by adding 5 drops of formalin to 5 mL of water). Shake each mixture, and then allow it to stand for 10 min. If no reaction occurs, place the tube in a beaker of warm water (35-50°C) for 5 min. Record your observations.

2. Bisulfite Addition

Place 5 mL of a 20% aqueous solution of sodium bisulfite in a 50-mL Erlenmeyer flask and cool the solution in an ice bath. Add 2.5 mL of acetone drop by drop, constantly stirring. If after 5 min a precipitate does not appear, add a few milliliters of ethanol to promote crystallization. Filter the adduct with vacuum (Büchner funnel). In a test tube, treat the crystals (in the hood) with a few drops of concentrated hydrochloric acid, and note what happens.

3. Schiff's fuchsin-Aldehyde test

In three test tubes prepare dilute test solutions by adding 2 or 3 drops of the following carbonyl compounds to 5 mL of water: formaldehyde, benzaldehyde, acetone. Now add 2 or 3 drops of these solutions to separate test tubes containing I mL of Schiff's reagent, and note the results.

4. Phenylhydrazine

Test benzaldehyde and cyclohexanone. To 5 mL of phenylhydrazine reagent in a test tube, add about 10 drops of the compound to be tested. Stopper the tube and shake vigorously for 1-2 min (until the product crystallizes). Filter the crystalline phenylhydrazone with vacuum (Büchner funnel), rinse the crystals with a little cold water, and recrystallize them from a minimum volume of methanol or ethanol. Allow the purified crystals to dry and determine their melting point. Record your results for each compound tested.

5. The Haloform Reaction and the Iodoform Test

To 2 drops of acetone in 1 mL of 5% sodium hydroxide solution, add iodine solution and shake until the color of iodine barely persists (about 4 mL of iodine solution is required). The yellow precipitate of iodoform should be apparent (note its medicinal odor). Repeat the test using 2-propanol and 2-pentanone and record your observations for each.

Student Name:	Student ID no.:
Date:	Section:
Instructor Name:	TA name:

Experiment 11: Reactions of Aldehydes and Ketones

Pre-lab Questions

1. Why are aldehydes more reactive towards nucleophiles than ketones?

2. It is not advisable to prepare and store Tollens' reagent in advance for tests described in this experiment. Why?

3. Why does the nitrogen atom of the NH_2 (and not the nitrogen atom of the NH) group of phenylhydrazine act as the nucleophilic site in the formation of phenylhydrazones?

Results and Observation

1. Tollens' Silver Mirror Test

Compound	Structure	Result
Benzaldehyde		
Acetone		
Cyclohexanone		
Formaldehyde		

2. Bisulfite Addition

Observations:……

3. Schiff's Fuchsin-Aldehyde Test

Compound	Color
Formaldehyde	
Benzaldehyde	
Acetone	

4. Phenylhydrazones

Compound	Phenylhydrazone	2,4-Dinitrophenylhydrazone
Benzaldehyde		
Cyclohexanone		

5. Haloform Test

Compound	Structure	Result
Acetone		
Isopropyl alcohol		
2-Pentanone		

Post-lab Questions

1. Write an equation for the preparation of the acetone-bisulfite addition compound.

2. What gas was evolved when you treated the acetone-bisulfite addition compound with hydrochloric acid?

Write an equation for the reaction.

3. Write an equation for the reaction of benzaldehyde with phenylhydrazine.

4. How can you account for the difference between the colors of the benzaldehyde and cyclohexanone phenylhydrazones? Explain using formulas.

5. Explain why, in the base-catalyzed halogenation of acetone, the second and third halogenations occur on the same carbon as the first, and not on the carbon of the other methyl group.

6. Only one aldehyde and only one primary alcohol give a positive iodoform test. What are their structures?

7. Write out all the steps in the mechanism for the base-catalyzed condensation of acetone with 2 mol of benzaldehyde.

8. Explain how you could use the simple laboratory tests performed in this experiment to distinguish between the following compounds.

a. 2-Pentanone and 3-pentanone

b. 3-Pentanone and pentanal

c. Benzaldehyde and acetophenone

d. Acetaldehyde and propionaldehyde

Experiment 12

Infrared and NMR Spectroscopy

Objectives

- Understand and analyze different types of spectra.

Background

- IR spectroscopy

IR spectroscopy is particularly useful for determining the types of bonds that are present in a molecule. Infrared frequency is usually expressed in units of wavenumber, defined as the number of waves per centimeter. Ordinary instruments scan the range of about 700 cm^{-1} to 5000 cm^{-1}.

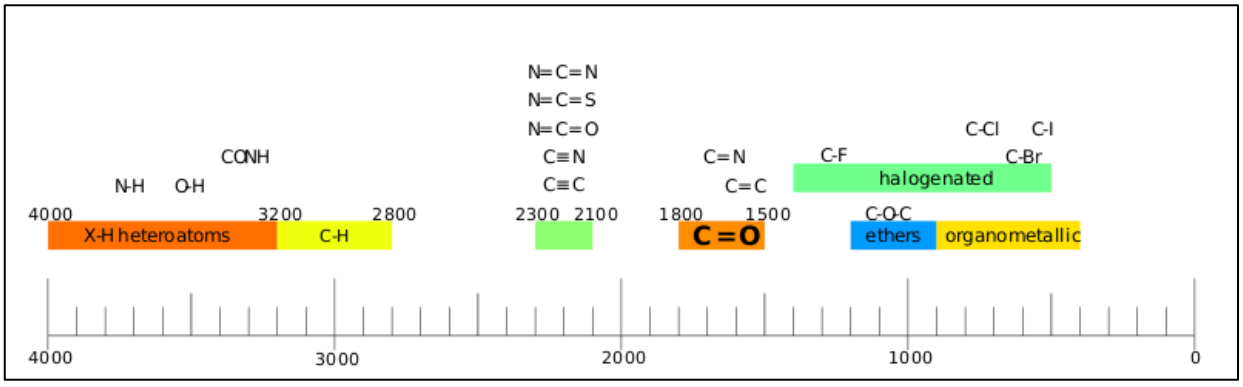
IR spectrum consists of two regions:

- Functional groups region: from 1500 cm^{-1} to 4000 cm^{-1}. Bands in this region reflect different functional groups in a certain compound.

- Fingerprint region: from 700 cm^{-1} to 1500 cm^{-1}. Bands are unique for each particular compound.

To summarize, IR spectra can be used to tell what types of bonds might be present in a molecule (by using the functional group region) and to tell whether two substances are identical or different (by using the fingerprint region).

IR chart



- ^{1}H-NMR spectroscopy

^{1}H NMR spectroscopy can give us the following kinds of structural information:

1. The number of signals and their chemical shifts can be used to identify the kinds of chemically different ^{1}H nuclei in the molecule.
2. The peak areas tell us how many ^{1}H nuclei of each kind are present.
3. The spin–spin splitting pattern gives us information about the number of nearest ^{1}H neighbors that a particular kind of ^{1}H nucleus may have.

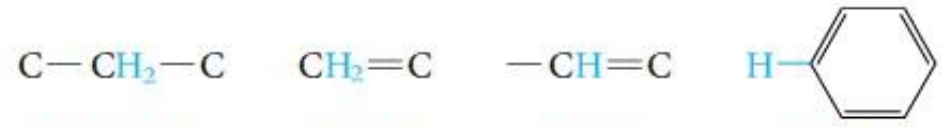
The chemical shifts are the positions of the peaks measured in δ (delta) units with respect to the peak of a reference compound, tetramethylsilane (TMS), $(CH_3)_4Si$.

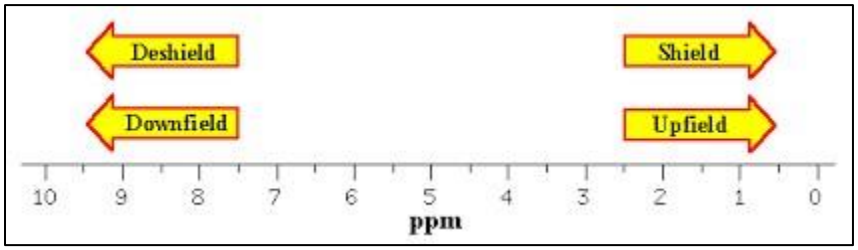
Factors that influence chemical shifts:

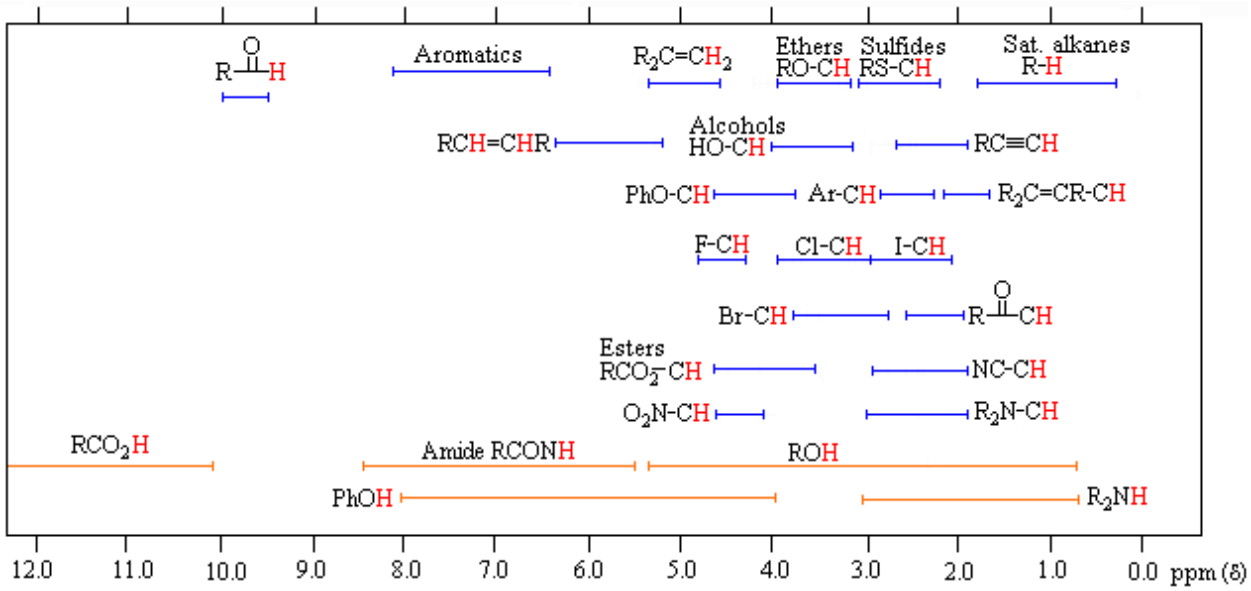
1. the electronegativity of groups in the immediate environment of the ^{1}H nuclei. Electron- withdrawing groups generally cause a downfield chemical shift.

$-CH_3$	$-CH_2Cl$	$-CHCl_2$
~ 0.9	~ 3.7	~ 5.8

2. the presence of pi electrons. Hydrogens attached to a carbon that is part of a multiple bond or aromatic ring usually appear downfield from hydrogens attached to saturated carbons.





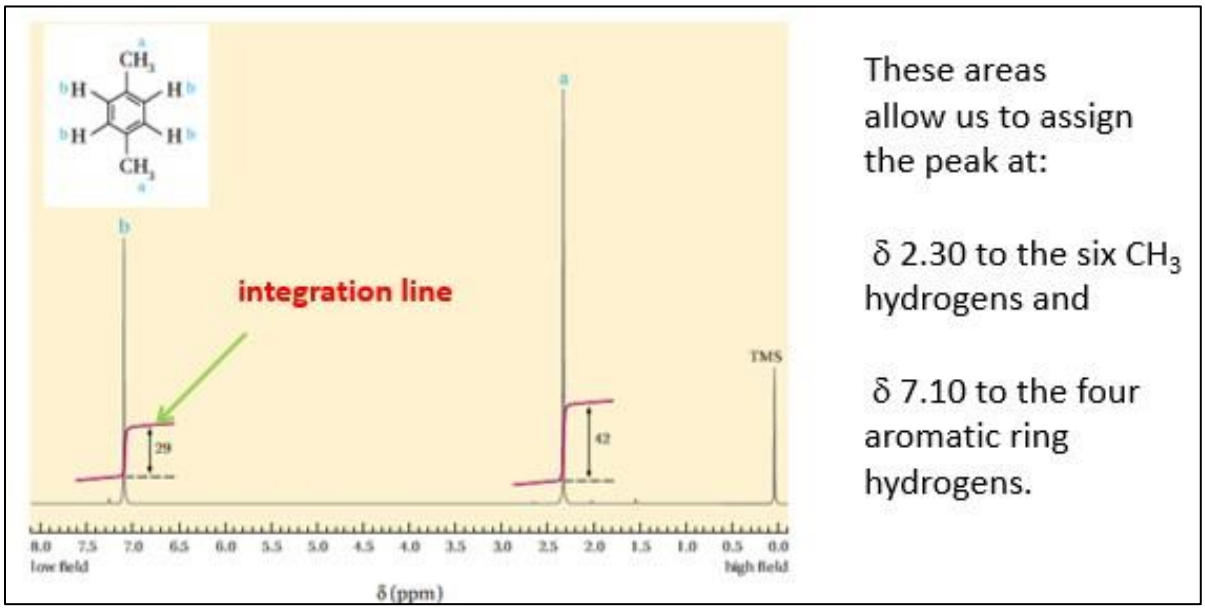


** notice that the chemical shifts in 1H-NMR are normally 0-12 ppm.

Integration

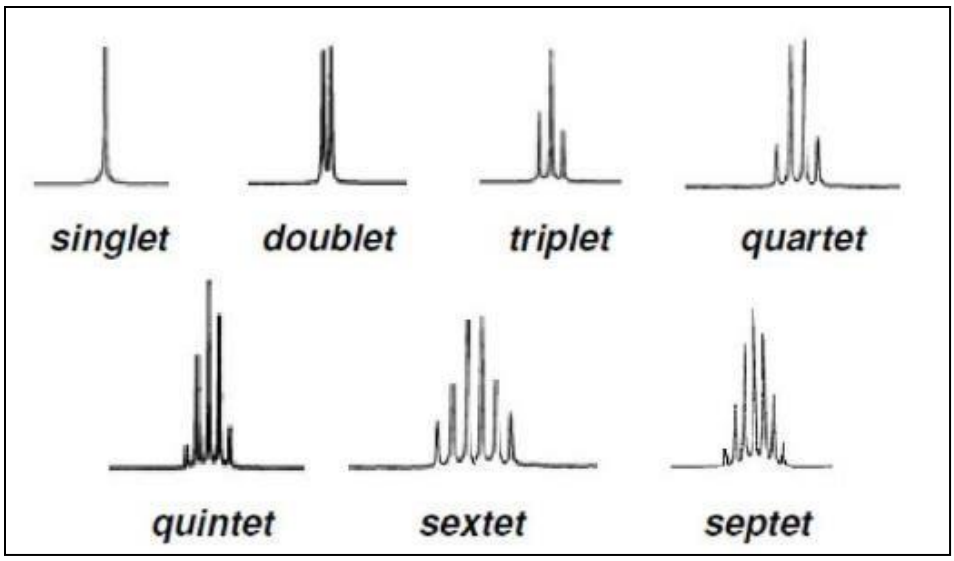
The peak area is directly proportional to the number of ^{1}H nuclei responsible for the particular peak.

The ratio of heights of the vertical parts of the integration line is the ratio of peak areas → in the *p*-xylene spectrum the ratio is 3 : 2 (or 6 : 4).



Spin-Spin Splitting

- A ^{1}H nucleus with no ^{1}H neighbors gives a singlet peak.
- Neighboring ^{1}H nuclei cause spin–spin splitting (multiplicity) of the ^{1}H signal.



How to predict the splitting pattern?

By n+1 rule

If a ^{1}H nucleus has a n ^{1}H neighbors with a different chemical shift, its NMR signal is split into n+1 peaks.

In $CH_3CH_2OCH_2CH_3$: each CH_3 hydrogens has two ^{1}H neighbors (on the CH_2 group)

→ CH_3 signal is split into 2+1= 3 peaks

Each CH_2 hydrogen has three ^{1}H neighbors (on the CH_3 group) → CH_2 signal is split into 3 +1= 4 peaks.

- By analyzing the splitting pattern of a signal in the ^1H NMR, you can determine the number of equivalent protons on adjacent carbons

Number of Neighbors	Multiplicity	Relative Intensities of Individual Peaks
1	doublet	1:1
2	triplet	1:2:1
3	quartet	1:3:3:1
4	quintet	1:4:6:4:1
5	sextet	1:5:10:10:5:1
6	septet	1:6:15:20:15:6:1

Example:

$CH_3CH_2OCH_2CH_3$

Have a look on the strucrure of diethyl ether.

- How many different hydrogens do you see? 2 types then the ^1H NMR should have 2 peaks.

- Which hydrogens are downfield? CH_2OCH_2 since they are deshielded by the oxygen.

- So the ^1H NMR spectrum of diethylether consists of 2 peaks.

CH_3 at δ 0.9 and OCH_2 at δ 3.5

triplet quartet

1:2:1 1:3:3:1 (relative areas)

- ^{13}C-NMR Spectroscopy

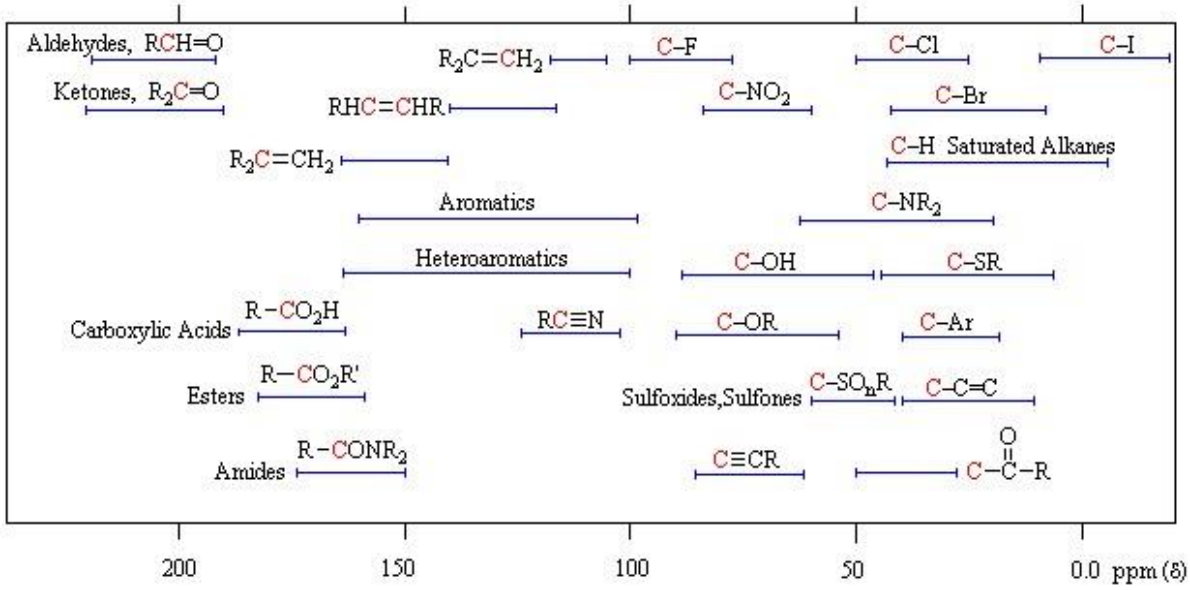
^{13}C chemical shifts are measured against the same reference compound (TMS) whose methyl carbons are all equivalent → 1 sharp signal.

Sheilding and desheilding occur here too.

Differences between ^{13}C NMR and ^{1}H NMR:

^{13}C chemical shifts occur over a **wider range** than those of ^{1}H nuclei.

^{13}C- ^{13}C splitting is ordinarily not seen.



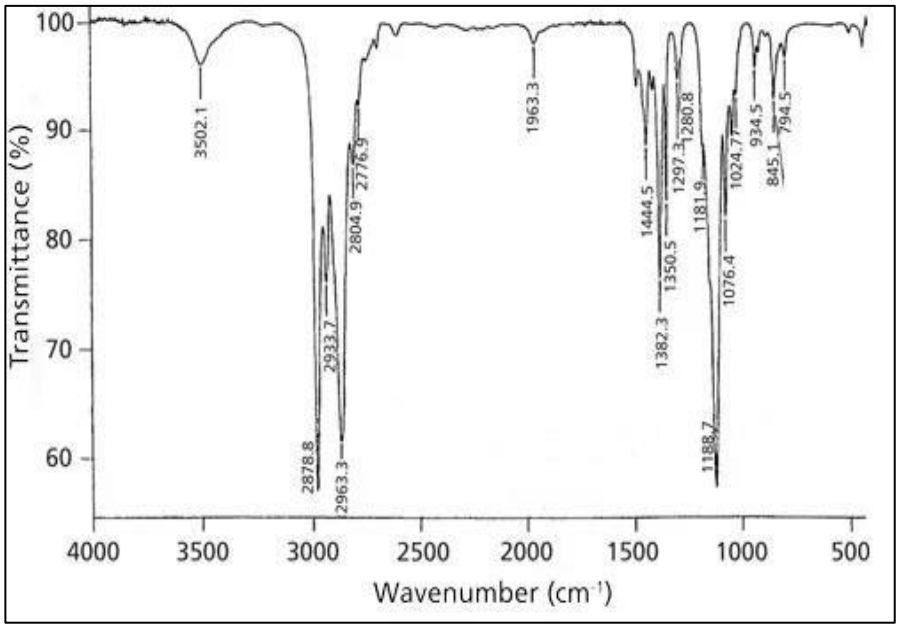
** notice that the chemical shifts in ^{13}C-NMR are normally 0-220 ppm.

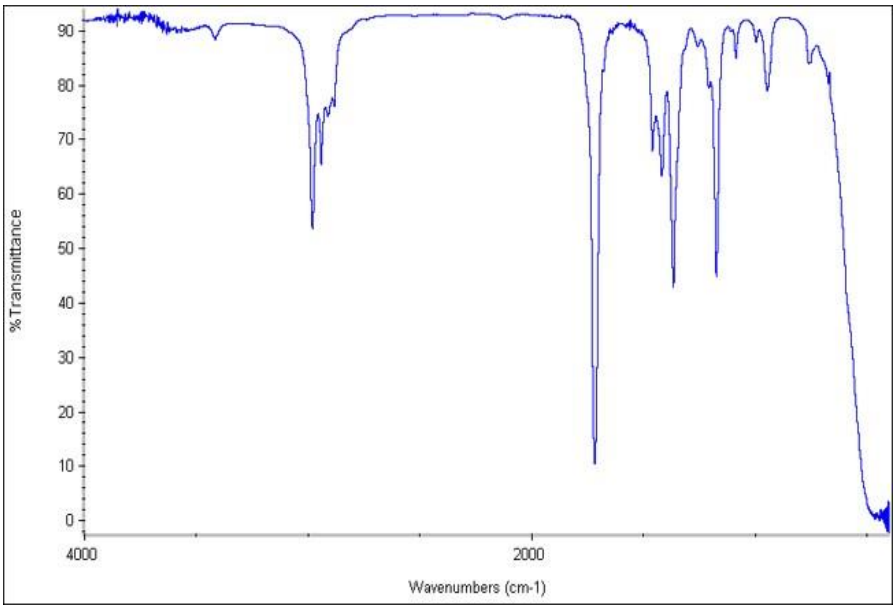
Student Name:	Student ID no.:
Date:	Section:
Instructor Name:	TA name:

Experiment 12: Infrared and NMR Spectroscopy

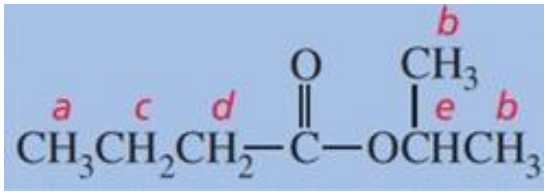
Results and Observation

1. You have two compounds, a ketone and an ether, each of them has 4 carbon atoms and one oxygen atom. Here are the IR spectra of both compounds. Which of them is for the ketone and which one is for the ether? Explain.

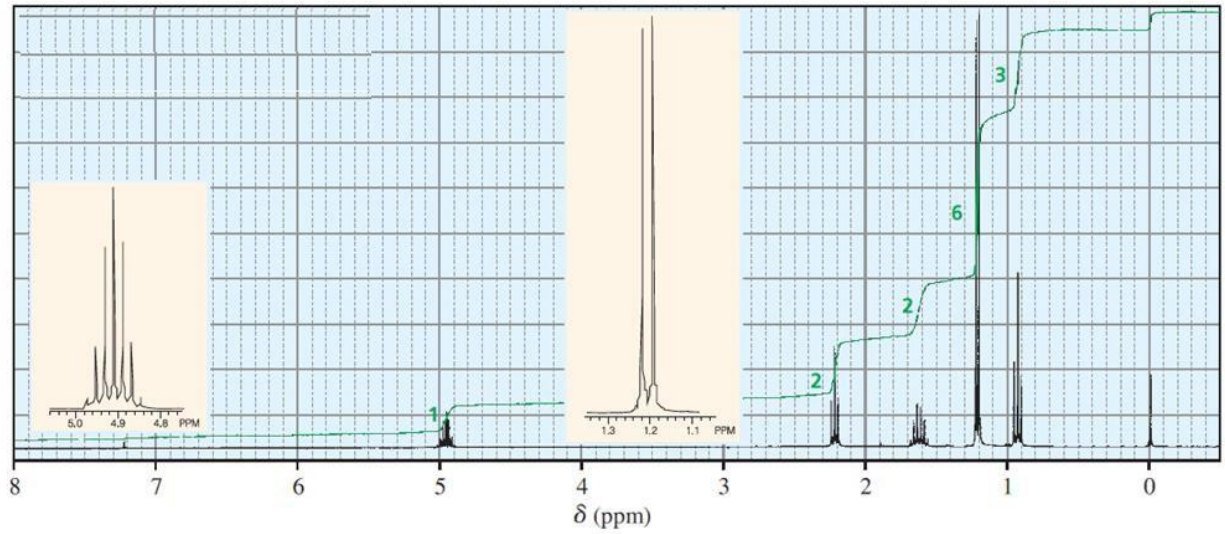




2. Here is the 1H-NMR spectrum of



Assign all the peaks and splitting.
Pay attention to the integration in green.
(Fill in the table below the spectrum)



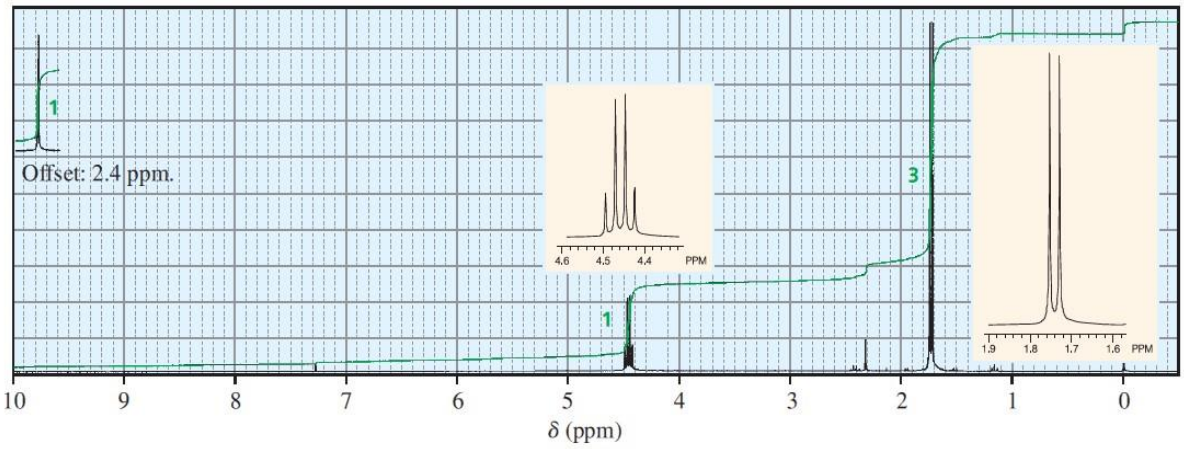
Protons	Number of protons	Chemical shift, δ (ppm)	Multiplicity (singlet, doublet, …..)
a	3		
b	6		
c	2		
d	2		
e	1		

The most downfield proton/s is/are:

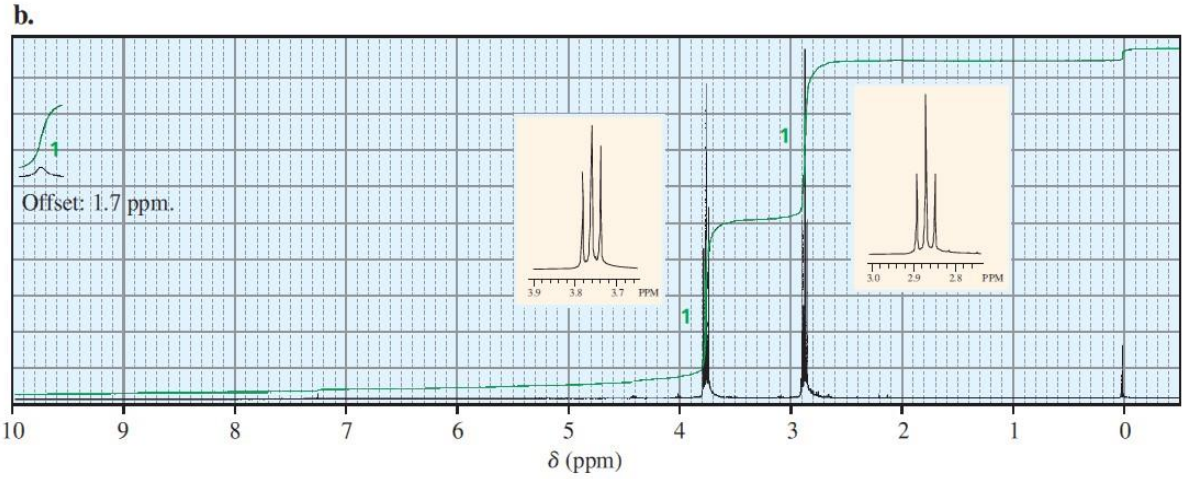
Why?

3. You have two carboxylic acid with the molecular formula $C_3H_5O_2Cl$. The ^{1}H-NMR spectra of both compounds are given below. Based on the spectra, draw the structure of each carboxylic acid. **Explain your solution and identify all peaks**.

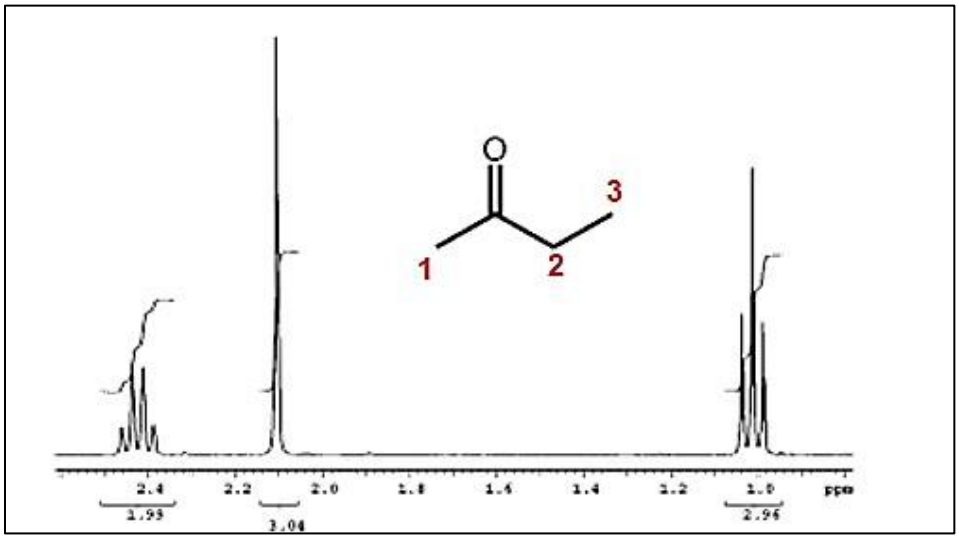
a.



b.

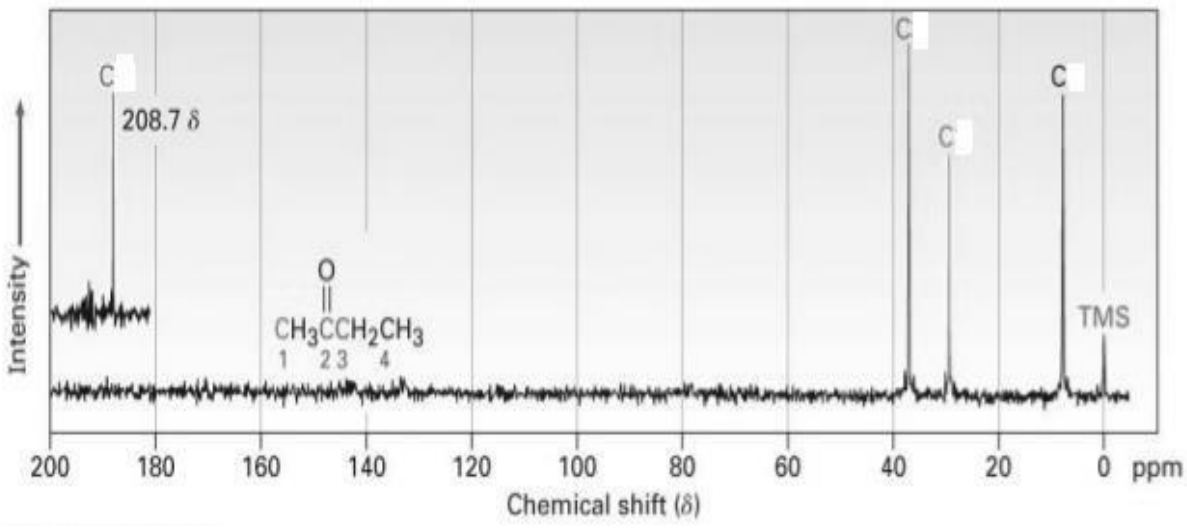


4. Have a look on the following spectra of the given compound and assign the peaks. Fill in the tables.



Protons	Integration	Chemical shift δ (ppm)	Multiplicity (singlet, doublet, …..)
1	3		
2	2		
3	3		

Account for the difference in chemical shift of both 1 and 3 hydrogens.

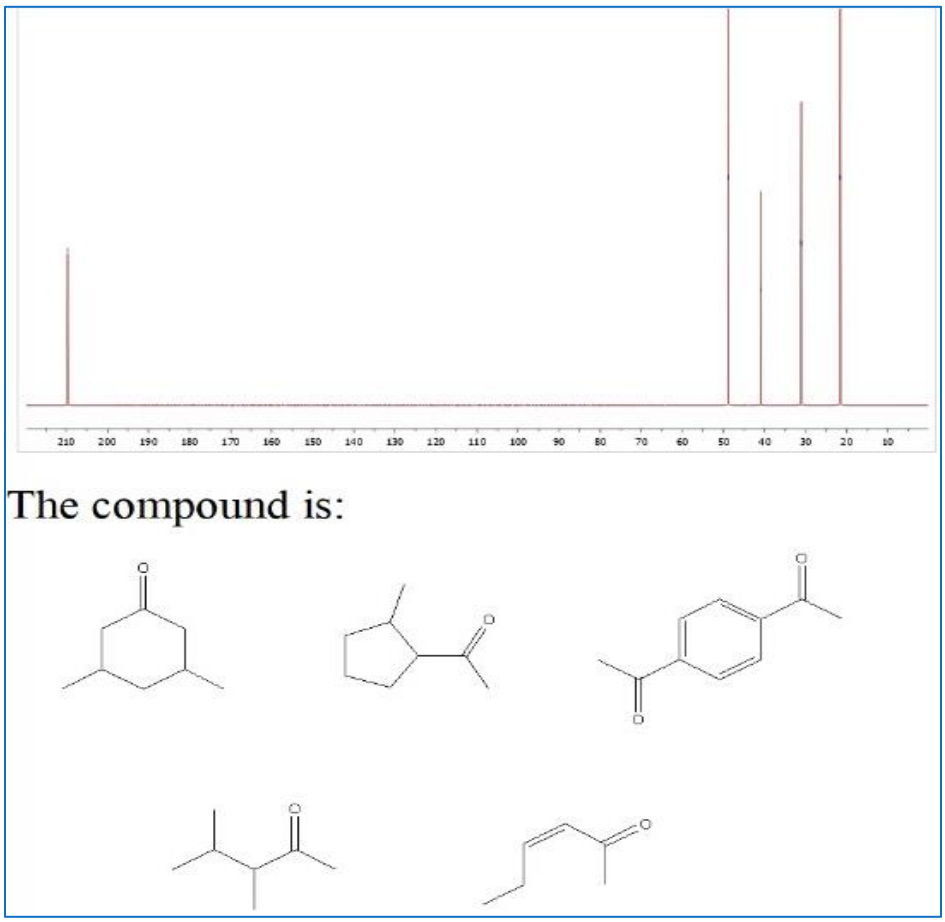


Carbons	Chemical shift δ (ppm)
1	
2	
3	
4	

The most downfield carbon is ------?

Why?

5. Have a look on the following ^{13}C-NMR spectrum and decide which compound is represented by this spectrum. **Explain your answer**.



Questions

1. What type of structural information does one obtain from the IR spectrum of a compound?

2. Which regions of the IR spectra of 3-hydroxycyclohexanone and 4-hydroxycyclohexanone will help you (a) identify the functional groups present in these compounds and (b) allow you to make a complete identification of the compounds?

3. Chemical shift and multiplicity of peaks are two frequently analyzed parameters from the NMR spectrum of a compound. What structural information does one receive from (a) the chemical shift of a peak and (b) the multiplicity of a peak?

4. Briefly explain how you could differentiate ethyl acetate from methyl propionate, structures by using the NMR spectral information of the two compounds.