Hashemite University
Faculty of Pharmaceutical Sciences
Department of Pharmaceutical Chemistry

Practical Pharmaceutical Organic Chemistry

Manual

(131703212)

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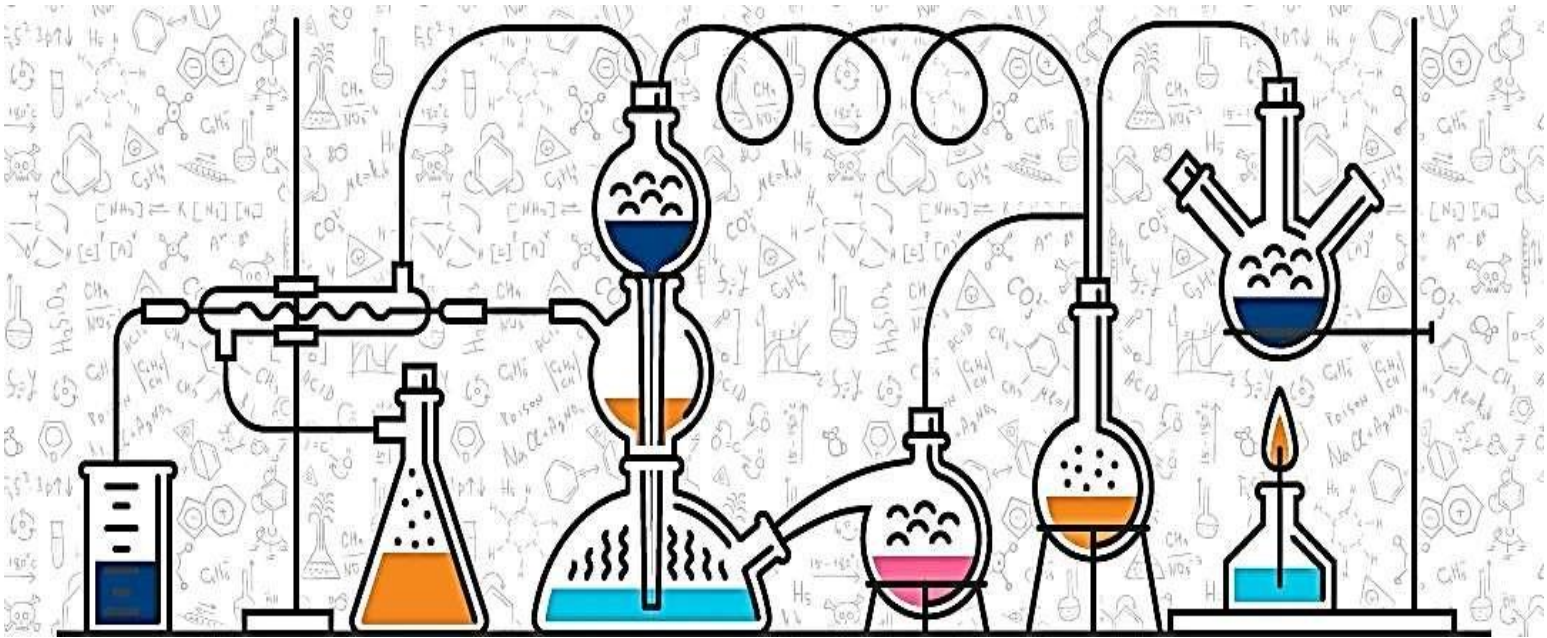
2024/2023



Course Description

This course is created to cover practical applications of various methods and techniques used for the identification of functional groups of organic compounds of pharmaceutical interest, giving more attention to chemical identification. The laboratory includes two parts; the first part includes the various separation and purification techniques of organic compounds such as crystallization, distillation, extraction, and chromatography. The second part concentrates on the identification of functional groups of organic compounds of pharmaceutical interest, giving more attention to chemical identification.

Course Objectives

1- Teach the student the principle of team-work and how to show respect for the students and teacher opinion.
2- Learn how to follow general policies and safety precautions in the lab.
3- Learn how to deal with heat sources in the lab.
4- Learn the student's various types of general and specific chemical reactions of certain organic compounds.
5- Learn the students how to perform the synthesis of organic compounds and the specific mechanism of organic reactions.
6- Learn the student's different lab techniques as recrystallization, melting point determination of the prepared chemical compound.
7- Adapt group discussion technique.

Course Learning Outcomes (CLOs)

A. Knowledge and Understanding: Student is expected to understand

A-1 Physical behavior and chemical identification of functional groups in organic compounds.
A-2 The importance of functional groups in pharmaceutical behavior of Drugs.
A-3. Practical experience in drugs synthesis and identification based on these functional groups.

B. Intellectual Analytical and Cognitive Skills: Student is expected to

B-1 Application of practical experience in identification of any unknown functional group or drugs incorporating these groups; such as Alcohols, Phenols, Ethers, Aldehydes, Ketons, Carboxylic acids and their derivatives, Nitro and Amino compounds.
B-2 Ability to synthesis some simple organic compounds and drugs such as Aspirin in organic laboratory implementing all techniques gained in this course.
B-3 Ability to understand and explain theoretical mechanism or behavior of certain drugs based on simple laboratory tests or reactions.

C. Subject-Specific Skills: Student is expected to

C-1 Chemical and physical identification of basic organic functional groups through basic practical test performed in any organic laboratory.
C-2 Acquaint practical skills regarding synthesis techniques, and preparation tools, in addition to methods of identification, classification, chemical and physical evaluation.
C-3 Practicing special techniques related to organic synthesis such as crystallization, melting point determination, distillation and refluxing.
C-4 Acquaint practical skills regarding to safe chemical handling and disposal.

C-5 Utilizing the concept of functional groups alteration, modification, derivitization in pharmaceutical drugs as tools for identification, characterization, purification, or even to improving the biological activity of a drug.

D. Transferable Key Skills: Students is expected to

D-1 Work in a team to organize and plan a synthetic experiment and fulfill course library requirements (writing scientific report). This must reflect positively on his future training of how to choose the right tools and approaches to conduct his experiment.
D-2 Master the rules of laboratory safety protocols and procedures needed for next laboratories.
D-3 Share, discuss and express ideas while working in group discussion sessions (Group discussion sessions to answer some questions.)
D-4 Gaining some electronic and internet experience while answering some problems through visiting specific web sites related to organic chemistry and answering preparing assignments using internet, and PC.
D-5 Developing problem solving approach.

Important regulations

- **On average, students need to spend 1 hrs of study and preparation weekly.**
- **Excellent attendence is expected. According to the university policy, students who miss more than 15% of the lecture hours with or without excuse will be dismissed from the course**
- **At the beginning of the lectures, be on time and don't leave before the end of the lecture without an accepted excuse**
- **If you missed a class, it is your responsibility to find out about any announcements or assignments you have missed**
- **For any clarification, please communicate your instructor at his posted office hours or by appointment**
- **Switch off your mobile or keep it silent throughout the lecture**
- **Listen well to the lecture and avoid side discussions, if you have a question, ask your instructor and not your collegue**
- **If you have any information, document your reference, if you didn't, then you broke the intellectual property rights law and the law will be applied**
  - **For more informations, visit the website:**
  - **http://www.plagiarism.org/**
- **Exams are scheduled to be given three times throughout the semester, your are expected to attend all. If not, make-up exams will be offered for valid reasons. It may be different from regular exams in content and format.**
- **Cheating, academic diconduct, fabrication and plagiarism will not be tolerated, and the university policy will be applied**

	Course Contents					
Date	**Week**	**Credit Hours**	**ILOs**	**Topics**	**Teaching Procedure**	**Assessment methods**
25/2-29/5	1	3	A B C D	Laboratory rules and safety precautions and	Lecturing discussion	Class participation
25/2-29/5	1	3	A B C D	Experiment 1: Melting Point Determination	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
3-7/3	2	3	A B C D	Experiment 2: Recrystallization	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
10-15/3	3	3	A B C D	Experiment 3: Identification of Alcohols and phenols	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
17-21/3	4	3	A B C D	Experiment 4: Identification of Aldehydes and ketones	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
24-28/3	5	***Off week (First exam duration "one week only")***				
31/3-4/4	6	3	A B C D	Experiment 5: Identification of Carboxylic acids	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
7-11/4	7	***Eid al-Fitr Holiday (23-24/4)***				
14-18/4	8	3	A B C D	Experiment 6: Chromatography	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
21-25/4	9	3	A B C D	Experiment 7: Boiling point and distillation	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
28/4-2/5		***Midterm Exam (30/4-3/5)***				
5-9/5	11	3	A B C D	Experiment 8: Extraction (Caffeine from tea leaves)	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
12-16/5	12	3	A B C D	Experiment 9: Synthesis of Aspirin (Acetylsalicylic Acid)	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment
19-23/5	13	3	A B C D	Experiment 10: Synthesis of Paracetamol (Acetaminophen)	Lecturing discussion Practical work	Class participation Laboratory Report Lab work evaluation Assignment

	14	***Final Exam***

Grade Distribution		
Assessment	**Grade**	**Date**
1. Quizzes	15%	➢ **Quiz 1 - week 2 (3-7/5):** Experiment 1 & Experiment 2 ➢ **-Quiz 2 - week 4 (17-21/3):** Experiment 3 & Experiment 4 ➢ **Quiz 3 - week 8 (14-18/4):** Experiment 6 & Experiment 7
2. Reports	10%	Weekly
3. Lab Evaluation (lab performance, readiness, etc)	10%	weekly
4. Mid Exam (Practical+Therotical)	25%	To be announced
5. Final Exam (Theoretical)	40%	The 14th week

Student Evaluation (out of 10):

Each student is evaluated weekly based on the following points:

A. Attendance punctuality **(2 mark)**
B. Behavior and adherence to basic lab requirements (e.g. Appearance: Lab-Coat, hair) **(1.5 mark)**
C. Availability of Gloves & Cleaning tools **(2 mark)**
D. Balance & Machines Use & Tools Use & their Cleaning **(2 mark)**
E. Teamwork **(1 mark)**
F. Procedure: Preparation & Adherence **&** Time frame **(1.5 mark)**

Reading List	
1. Textbook:	**Pharmaceutical Organic Chemistry-Laboratory Manual**
	I. Abdelnour L., Hussein A., Zahra J.: Selected Experiments in Organic Chemistry. 2th Ed. University of Jordan. **II. Gilbert J. C. and Martin S. F. (2011): Experimental Organic Chemistry A Miniscale and Microscale Approach. 5th Ed. Cengage Learning USA** **II. Shriner R.L., Herman C.K.F., Morill T.C., Curtin D.Y. and Fuson R.C. (1998): The Systematic Identification of Organic Compounds. , 7th Ed. A John Wiley & Sons, Ltd., Publication. England.**

CONTENT

GENERAL INFORMATION

1. Safety in Chemistry Labs (Safety Equipment)

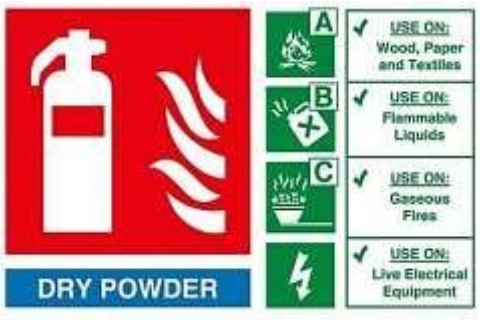
Chemistry is an experimental science. You cannot learn it without getting your hands dirty. All new chemistry students face the prospect of lab work with some apprehension and fear, and it would be untruthful to say that this is completely unwarranted. *Chemicals can be dangerous!* The more you study 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.

Protection for Your Eyes

Wearing safety goggles is compulsory in labs for eye protect actively experimenting. Eyewash fountains are available for in chemical splashes, emphasizing prompt action for safety.

Protection from Fire

hemistry labs have fire risks from flammable liquids and gas burners. Precautions include checking for nearby flammable chemicals and being cautious around sinks. Small fires can be smothered with a beaker, while larger ones may need CO2 extinguishers. Appropriate clothing is crucial, and emergency showers are available for clothing fires.



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

Handling corrosive substances in the lab requires proper care. Concentration levels determine the degree of danger, so even low concentrations can pose risks. Washing hands frequently, especially after spills, is crucial. Notify the instructor immediately if any corrosive substance comes in contact with skin, and seek medical attention if there's any sign of damage. In the event of a major spill, use the emergency shower without hesitation for safety.

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

common injuries in the chemistry lab include cuts and burns. Broken glassware should be handled with care using a broom and dustpan, and disposed of in designated areas. Avoid touching hot equipment; wait at least five minutes for cooling or use tongs. Be cautious when heating liquids in test tubes to prevent superheating accidents. Report all cuts and burns to the instructor immediately, as even minor injuries can become serious due to chemical exposure.

2. HAZARDS IN ORGANIC LAB CHEMISTRY

PRACTICES:

- Be aware of the nearest eyewash station and emergency shower. If a chemical splash occurs, flush immediately with running waterfor at least 15 minutes and seek medical attention.
- Use chemical splash goggles or other eye protection when working with acids/bases. Appropriate acid- and base- resistant protective clothing, including aprons, lab coats, and gloves, should also be worn.
- When diluting acids or bases with water, always pour the reagent slowly (while mixing) into the water, never the reverse.

3. COMMON PROBLEMS / EASY SOLUTIONS:

Summary of Safety Guidelines:

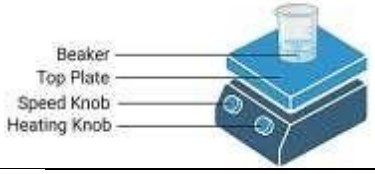
1. NH_4OH: Causes serious eye and mucous membrane damage.
2. Chlorinated solvents: Dispose in designated waste bottles.
3. Chlorosulfonic acid: Corrosive, causes severe burns and fatal if inhaled.
4. Alkali metals: Keep covered with inert solvent, treat with dry ethanol for disposal.
5. Mercury waste: Treat with solid sulfur powder, do not discard in waste basket.
6. Ether: Highly volatile and explosive, store in cold place.
7. Report broken glass, do not remove it yourself.
8. Avoid mouth pipetting or smelling chemicals.
9. Concentrated acids and bases: Keep in hood, wear gloves when using.
10. Maintain labels on containers, replace old ones.
11. Keep smelly chemicals in hood, dispose in closed bottles.

LABORATORY INSTRUCTIONS

1. Dispose of solids in wastepaper basket; avoid throwing matches, filter paper, broken glass, or insoluble chemicals in the sink. Organic liquids go in special residue bottles.
2. Double-check reagent bottle labels before use.
3. Use solutions from side shelves by pouring into a beaker; avoid carrying bottles to your bench to prevent crowding.
4. Never return chemicals to stock bottles.
5. Avoid laying down bottle stoppers to prevent contamination; close reagent bottles immediately after use.
6. Leave glassware clean and bench top dry at the end of each lab session.
7. Study experiment instructions thoroughly before lab; be prepared to explain procedures and purpose.
8. Work on experiments individually; no copying or collaboration unless instructed otherwise.
9. Bring required items to each lab session: laboratory manual, laboratory coat, matches, dish towel, and desk cleaning sponge.

HEATING SOURCES

There is different equipment that are used as a heating source in the laboratory which includes:

Bunsen Burner	Heating mantle	Hot plate
	 	 

Chemical Fume Hoods

A chemical fume hood is type of local ventilation device that is designed to limit exposure to hazardous or toxic fumes, vapors, or dusts. Many different types of fume hoods exist, but there are certain rules that should be followed for all types of chemical fume hoods.

Sash Height

You should keep the sash opened no further than 18 inches above the air foil. Typically, there is an arrow indicating where the sash should be opened to when working in the fume hood.

Proper Usage

Never store equipment or materials permanently in a hood. Do not place items that block the baffles. Always ensure the hood is working properly before beginning any work inside of it.

Certification

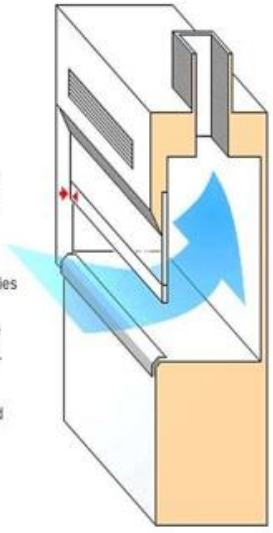
Chemical fume hoods must be certified annually by Facilities Operation and Development to ensure proper working order. If the fume hood needs repaired or certified, please contact Service2Facilities at 614-292-HELP or s2f.osu.edu.

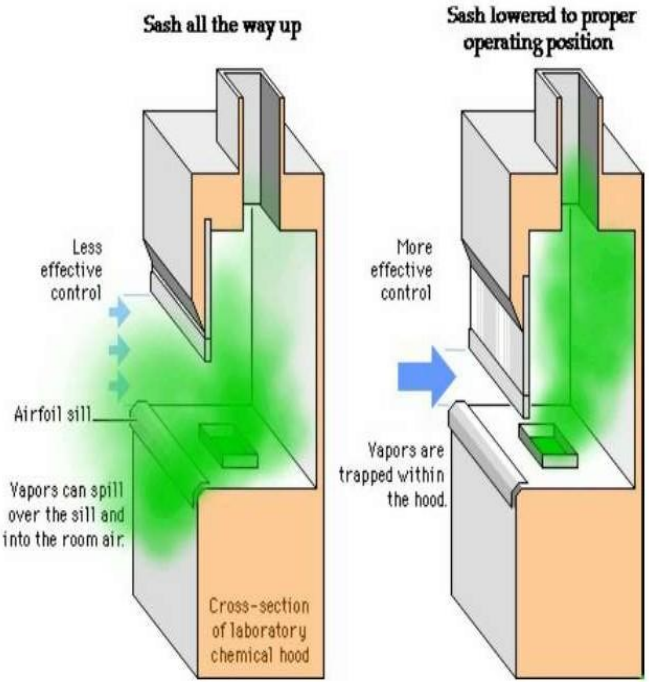
Energy Conservation

Fully close the sash when not actively working in the hood or all persons have left the room for the day.

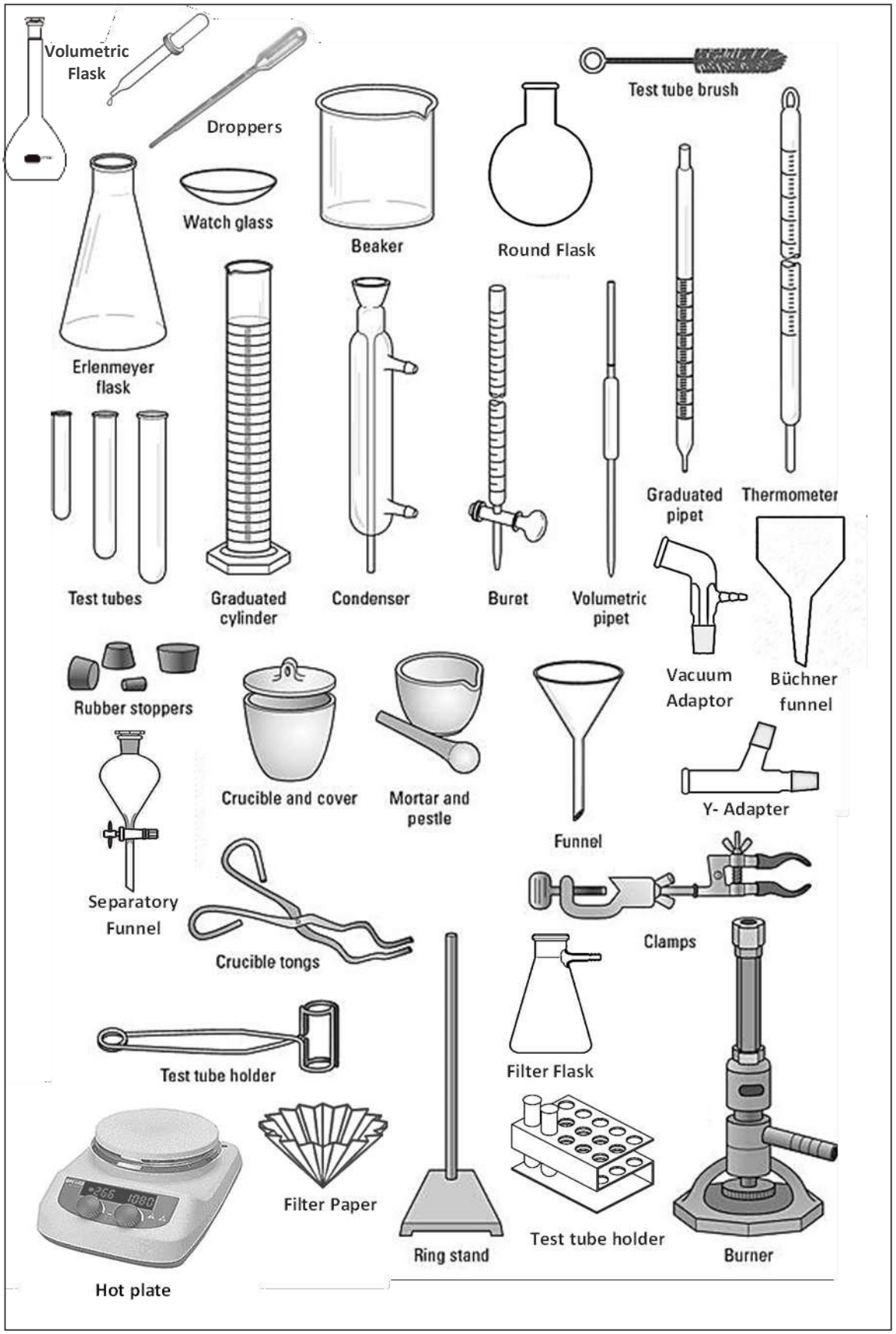
Training

An online safety training module (Fume Hood Safety) is available on the EHS website.





COMMON LABORATORY EQUIPMENT



EXPERIMENT 1: MELTING POINTS

Identity and Purity of Solid Organic Compounds

INTRODUCTION

The melting point of a solid is the temperature at which transition fromsolid to liquid occurs at atmospheric pressure; or the temperature at which solid and liquid phases are in equilibrium at a pressure of one atmosphere. The melting point is practically unaffected by changes in external pressure, making it a convenient physical constant for the identification of solids.

Many organic compounds are solids at room temperature as a result of strong intermolecular forces which hold the individual molecules together in a crystal lattice. The nature and strength of these intermolecular forces are responsible for the observed differences in melting point. In general, if the forces are strong, the melting point will be high, and if they are relatively weak, the melting point will be low.

A pure solid has a sharp melting point and will melt within a narrow range of 1-2 ^{o}C. Soluble impurities affect the melting point of a solid in the following manner:

a. Lower the melting point of the substance, with the upper limit considerably below the true melting point. The presence of an impurity in the molten compound, reduces its vapor pressure thus lowering the melting point of the compound. The greater the amount of impurity, the greater is the melting point depression.

b. Broaden the melting point range. Depending on the amount of impurity, the melting process may extend over a range of 2-20 ^{o}C or more. Insoluble impurities (*e.g.*, glass, sand ...*etc*.) do not affect the melting point or the melting point range.

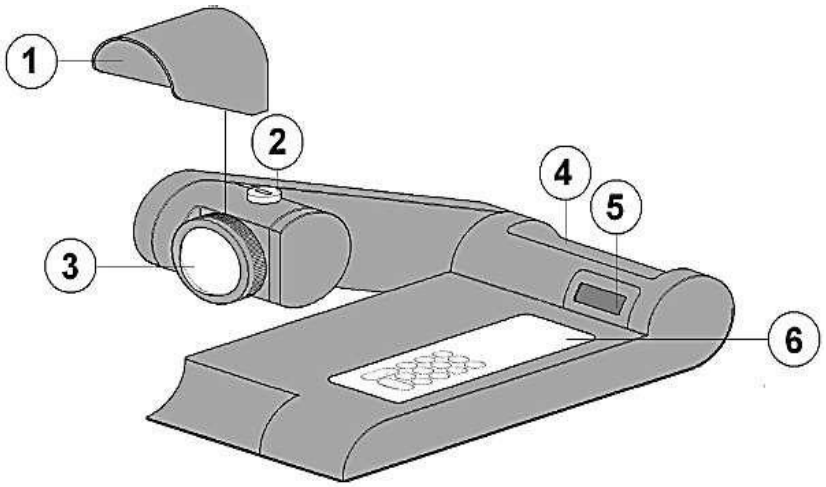
Mixture melting points can be used in the following manner to determine whether two compounds are the same or different even though they have similar melting points. If a given organic compound (A) meltssharply at 120 ^{o}C, and benzoic acid (compound B) also has a melting pointof 120 ^{o}C. Is compound (A) benzoic acid or a different compound?

If compound (A) is benzoic acid, then a mixture melting point of (A) and (B) will melt sharply at 120 ^{o}C, i.e., the same as each individual compound alone. If, on the other hand, compound (A) is not benzoic acid, then the mixture melting point of (A) and (B) will be lowered and the melting range will be broadened. Since they are different compounds, each behaves as an impurity in the other.

MELTING POINT DETERMINATION PROCEDURES

- ***USING DIGITAL MELTING POINT APPARATUS***

Digital Melting Point Apparatus has been designed for general purpose laboratory use in which samples submitted for analysis are enclosed in a glass capillary tube and brought to a melting point condition under strict controlled parameters of time and temperature. Figure 7 shows a graphical representation for the digital melting point and its components.



Number	Description
1	Lens hood
2	Capillary Guide
3	Lens
4	Capillary tube Holder
5	Digit display
6	Keypad

Figure 7. digital melting point apparatus

GENERAL PROCEDURE

1. The digital melting point apparatus units must always be kept upright.
2. Place a small quantity (about 0.5 cm in tube) of the solid to be melted in a capillary tube (labeled melting point tubes).
3. Tap the closed end of the tube on the desk, clean the outside, and compact the solid down to the closed end of the melting point capillary tube.
4. Drop the tube (closed end down) down a section of glass tubing to compact the solid in the bottom or closed end of the tube even more.
5. Place the tube loaded with the sample into the sample holder of the apparatus with the closed end down. The crystals can be ground up if they are too big to fit into the capillary tube.
6. Melting point capillary tubes are placed (closed end down) in the slots directly in front of the magnifying lens where they are viewed during melting. (Up to three samples can be viewed at once).
7. Record the temperature that the crystals begin to melt; crystals will look wet, (this is the melting start point), and the temperature at which the substance becomes a clear liquid; no solid material remaining (this is the melting end point).
8. Determine the melting range (Starting point – End point).
9. Calculate the melting point by taking the average point between the start point and the end point.

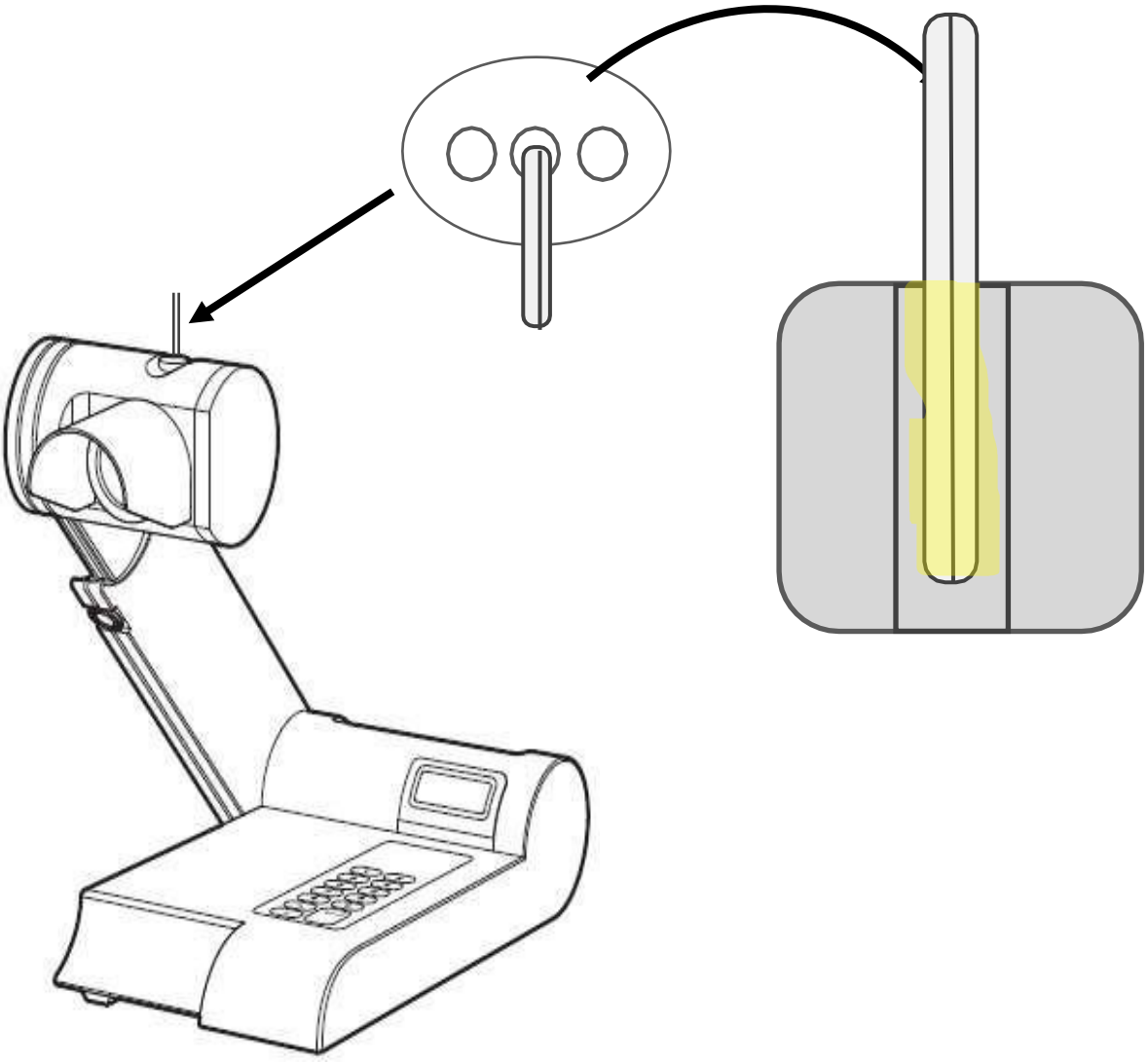
Note

The heating rate of the digital apparatus is adjusted by setting a temperature ramp along with a start and end temperature following the "Quick Start Instructions" on the front of the digital apparatus. A ramp of 20 °C per minute will result in a rapid temperature rise while a ramp of say 2 °C per minute will give a slower rise that will more accurately measure the melting range of a solid.

OBJECTIVES

1. Determining the melting point of a pure known organic solid.
2. Identifying an unknown from its melting point.

Having done this experiment, you will have seen the effect of an impurity on the melting point of a solid substance and the use of the melting point in characterizing organic solids.



EXPERIMENTAL

MATERIALS NEEDED	Equipment: digital melting point apparatus Glassware: Capillary tubes (open one side only) Chemicals: Binzillide, Salicylic acid, Citric acid, Paracetamol, Caffeine, Urea.

DETERMINATION OF MELTING POINTS OF PURE COMPOUNDS

Each group should obtain a small amount (about 0.1 g) of one of the following solid compounds:

1. Cinnamic acid
2. Salicylic acid
3. Citric acid.
4. Paracetamol
5. Caffeine
6. Urea

Measure the melting point by using the digital Melting point apparatus but you must first measure its melting range.

1. Tap a small amount of your unknown into two different capillary tubes. Just a few crystals are adequate. You may need to grind some of your unknown into a powder if it is too coarse to fit into the capillary tube.
2. Find the melting point range of the pure unknown substance by first quickly determining an approximate melting range on a fast ramp (20 ^{o}C/min from 70-210 ^{o}C)
3. Conduct a slow, careful melting range with the second capillary tube you prepared (use a ramp of 2 ^{o}C/min and start about 15 ^{o}C below the melting range to 10 ^{o}C above the range). Make sure the Digital Melting apparatus is below 70 ^{o}C before starting the first melting range and 10-20 ^{o}C below the compound's melting range before doing a slow careful melting range.
4. After determining the range, now you can calculate the approximate melting point midpoint as follows:

Melting Point Range = (Start Point → End Point)

Melting point Midpoint= (Start Point + End Point)/ 2

IDENTIFICATION OF AN UNKNOWN

Obtain an unknown (from instructor) and determine its melting point as described before. Using the melting points listed in the table on the previous page determine which possible compounds are within ±10 °C of your unknown's melting range.

Table 1. Melting points of some organic compounds

Compound	mp (°C)	Compound	mp (°C)
Acetanilide	114	Maleic acid	135
Mandelic acid	117	Adipic acid	152
2-Naphthol	121	Citric acid	154
Benzoic acid	122	Salicylic acid	158
Urea	132	Benzanilide	161
Cinnamic acid	133	Sulfanilamide	165
Benzoin	133	p-Toluic acid	182

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

EXPERIMENT 2: **RECRYSTALLIZATION**

A Purification Technique for Solids

INTRODUCTION

Crystallization may be defined as the process in which a solid compound precipitates from a saturated solution in the form of crystals. Saturation is usually affected through cooling or evaporation. In certain cases, ***recrystallization*** may be used for the **separation** of a solid mixture and **purification** of a desired impure crystalline substances (fractional recrystallization). Impure crystalline substances can be purified by recrystallization from a suitable solvent.

This process depends on two facts:

a. Different solids have different solubilities in a given solvent (impurities have solubilities different from those of the desired compound).

b.Most solids are more soluble in hot than in cold solvents.

When the impure solid is dissolved in a minimum volume of a suitable hot solvent and the resulting solution is gradually cooled, saturation and eventual crystallization of the pure compound occurs.

Impurities in a solid are of two kinds: soluble and insoluble and recrystallization involves the removal of both to purify a solid. Insoluble impurities are first removed by gravity filtration of the hot solution. While soluble impurities remain dissolved in the cold saturated solution (mother liquor) after precipitation of the desired compound. The pure crystals are separated from the supernatant liquid by suction filtration. After drying, the purity is checked by a melting point determination.

Crystal formation is a selective process and only molecules of the same substance can fit into the crystal lattice, excluding foreign molecules (impurities) which remain in solution (Figure 14).

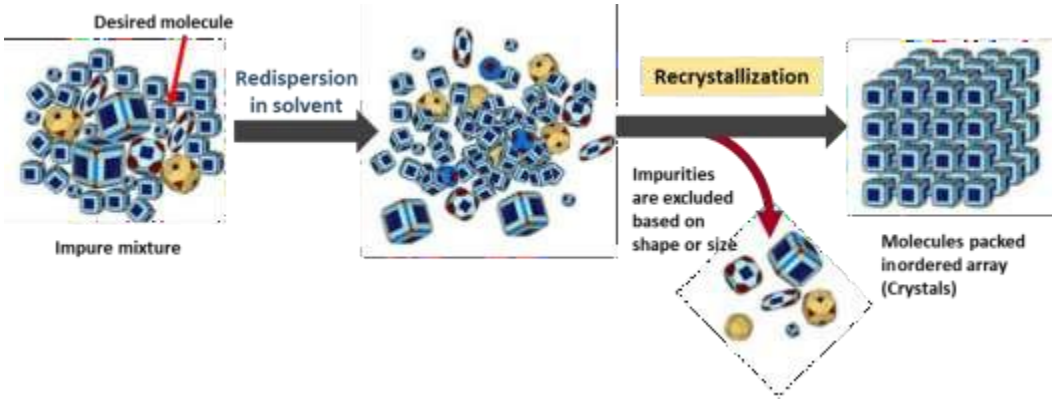


Figure 14. The crystallization process.

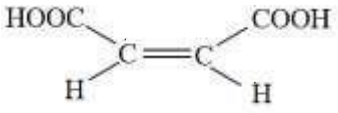
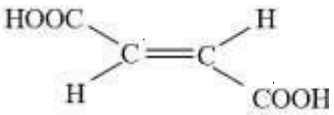
The solubility of a solid solute in a solvent is determined by two factors:

a. The relative polarities of the solvent and solute. "Like dissolves like" is the best summary of solubility behavior.

Polar solvents dissolve polar solutes and non-polar solvents dissolve non-polar solutes. For example, solutes that contain polar groups like OH, NH_2, and COOH dissolve in polar solvents like water, methanol, and ethanol while hydrocarbons and their halogenated derivatives are non-polar and dissolve in non-polar solvents like chloroform, carbon tetrachloride, hexane, and petroleum ether.

b. The lattice energy of the crystalline solute. The crystal lattice, holding solute molecules together in the solid state, is broken down upon dissolution.

The necessary energy is provided through *"solvation"* of the solute bysolvent molecules. The stability of a crystal lattice is roughly reflected by the melting point: a high melting point indicates a high lattice energy, and *vice versa*. For a given set of isomers, *the higher the melting point, the less soluble the substance is in a given solvent.*

	 maleic acid	 fumaric acid
Melting point ^{o}C	130	288
Solubility (g/100 mL water)	78.8	0.70

A suitable solvent for recrystallization should possess the following important properties:

a. Dissolve a large amount of the solid to be purified at high temperatures, but very little at room temperature.

b. Dissolve impurities readily at low temperatures or not at all even atthe boiling point.

c. Not react with the substance to be purified.

d. Evaporate readily from the crystals, i.e., be relatively volatile.

If two or more solvents appear to be equally suitable, it is preferable tochoose a solvent which is non-flammable, non-toxic, and cheap.

GENERALIZED EXPERIMENTAL PROCEDURE

Recrystallization involves the following sequence of steps:

1. *Selection of a suitable solvent.*
2. *Preparation of the hot solution and "decolorization" if necessary.*
3. *Filtration of the hot solution to remove insoluble impurities (and charcoal).*
4. *Cooling to effect crystallization.*
5. *Collection (cold filtration), washing, and drying of the crystals.*

Each step will now be discussed more fully.

1. ***Selection of the Solvent.*** The suitable solvent is determined experimentally through solubility tests.

This is done by shaking about 0.1 g of the powdered solid with 2 mL of the given solvent in a dry test tube. If all the solid has nearly dissolved in the cold solvent, the solvent is considered unsuitable.

If not, the mixture is heated gently to the boiling point with stirring (water bath for flammable solvents). If most of the solid did not dissolve, the solvent is also unsuitable.

If a substance is found to be too soluble in one solvent and insoluble in another, then a mixture of both solvents (solvent pair) may be used. In such cases the two solvents must be completely miscible. The compound to be recrystallized is first dissolved in the solvent in which itis very soluble, then the other solvent is added gradually, with heating,until a slight turbidity occurs. The solution is then allowed to stand at room temperature to effect slow crystallization before chilling in ice.

Table 2. Common solvents for recrystallization.

Solvent	b.p	Particulars of Solvent
Water	100	to be used whenever suitable
Methanol	65	flammable; toxic
Ethanol	78	flammable
Acetone	56	flammable
Ethyl acetate	78	flammable
Chloroform	61	non-flammable; vapor toxic
Benzene	80	flammable; vapor highly toxic
Cyclohexane	81	flammable

2. ***Preparation of the Solution.*** To prepare the hot solution, the solid is placed in an Erlenmeyer flask and the selected solvent is added in small portions. The mixture is stirred and heated to boiling after each addition, until the solid dissolves completely. A slight excess of the solvent is usually added to compensate for any losses (through evaporation) during filtration.

Decolorizing charcoal may be added at this stage if the solution is colored due to colored impurities. The flask should be removed from the heat source before adding charcoal to it, otherwise bumping will occur.

3. ***Hot Filtration (Gravity Filtration).*** Filtration of the hot solution is necessary to remove insoluble impurities. A fluted filter paper and a short-stem funnel (Figure 15) allow rapid filtration and avoidpremature crystallization inside the stem and on the filter paper.

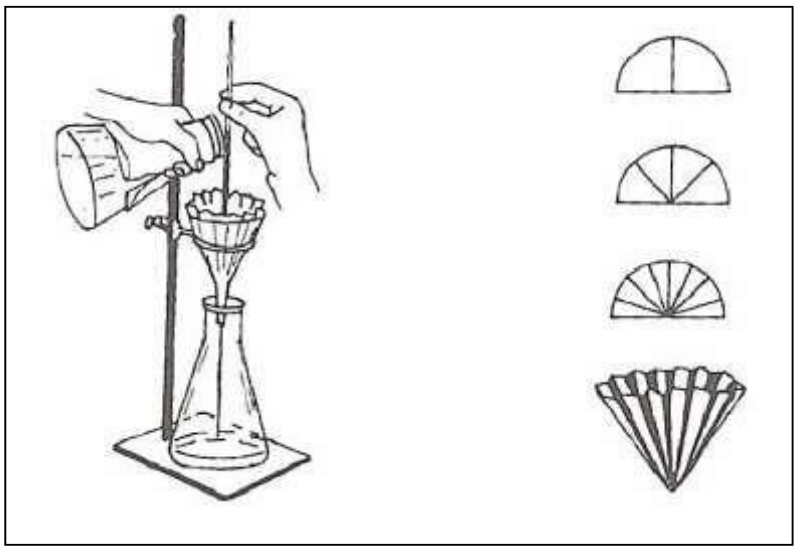


Figure 15. Rapid filtration of a hot solution using a fluted filter paper.

4. ***Cooling***. To induce crystallization, the clear, hot filtrate is allowed to cool down to room temperature, undisturbed, until a large number of crystals has formed. The mixture is finally chilled in ice to complete crystallization.

5. ***Collecting and Drying of Crystals.*** The crystals are collected by suctionfiltration (cold filtration) using a Buchner funnel to ensure rapid and complete removal of the solvent. The crystals are then washed with a few milliliters of fresh, ice-cold solvent to get rid of the last traces of mother liquor. The crystals are finally dried in an oven or allowed to air-dry, in case the melting point is low, by spreading them over a sheet of paper.

OBJECTIVES

1. Selection of suitable solvents for recrystallization.
2. Recrystallization of an unknown compound.

EXPERIMENTAL

MATERIALS NEEDED	Glassware: 3 test tubes, 2 Erlenmeyer flasks (100 mL), filter flask, filter funnel, Buchner funnel, clamp, hot water bath, filter papers, ice water bath, watch glass, spatula - glass rod. boiling stones (boiling chips): inert material with small pores that provide sites where bubbles can form, thus inducing even boiling. Melting point apparatus & capillary tubes Chemicals: 10 mL of each of acetone, ethanol, 1.0 g of unknown, Activated charcoal

PART 1: SELECTION OF SOLVENT

Perform solubility tests on the unknown in water, alcohol, and acetone as follows:

With a spatula take about 0.1 g of the powdered solid and place in a dry test tube. Start by dissolving it in 2 mL of solvent with stirring. Ifinsoluble, heat the mixture to boiling (water bath for flammable solvents) and observe the solubility. The results should allow the selection of a suitable solvent for each compound.

PART 2: RECRYSTALLIZATION OF AN UNKNOWN

Obtain an unknown and perform solubility tests as described above to choose the best crystallizing solvent. Recrystallize 1.5 g of this unknown from the solvent you have selected. Make sure you use only the minimum volume of solvent, otherwise the amount of recovered product will be small. Determine the weight and melting point of the purified unknown compound.

PROCEDURE

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

2. *Place the rest of the unknown in a 100-mL conical flask, add boiling suitable solvent till no more solid appears to dissolve.*

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

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

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

6. *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.*

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

8. *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.*

9. *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.*

10. *Transfer the crystals to an oven or store them in your locker for drying until the next laboratory period.*

11. *Weigh the dried product and determine its % yield and melting point.*

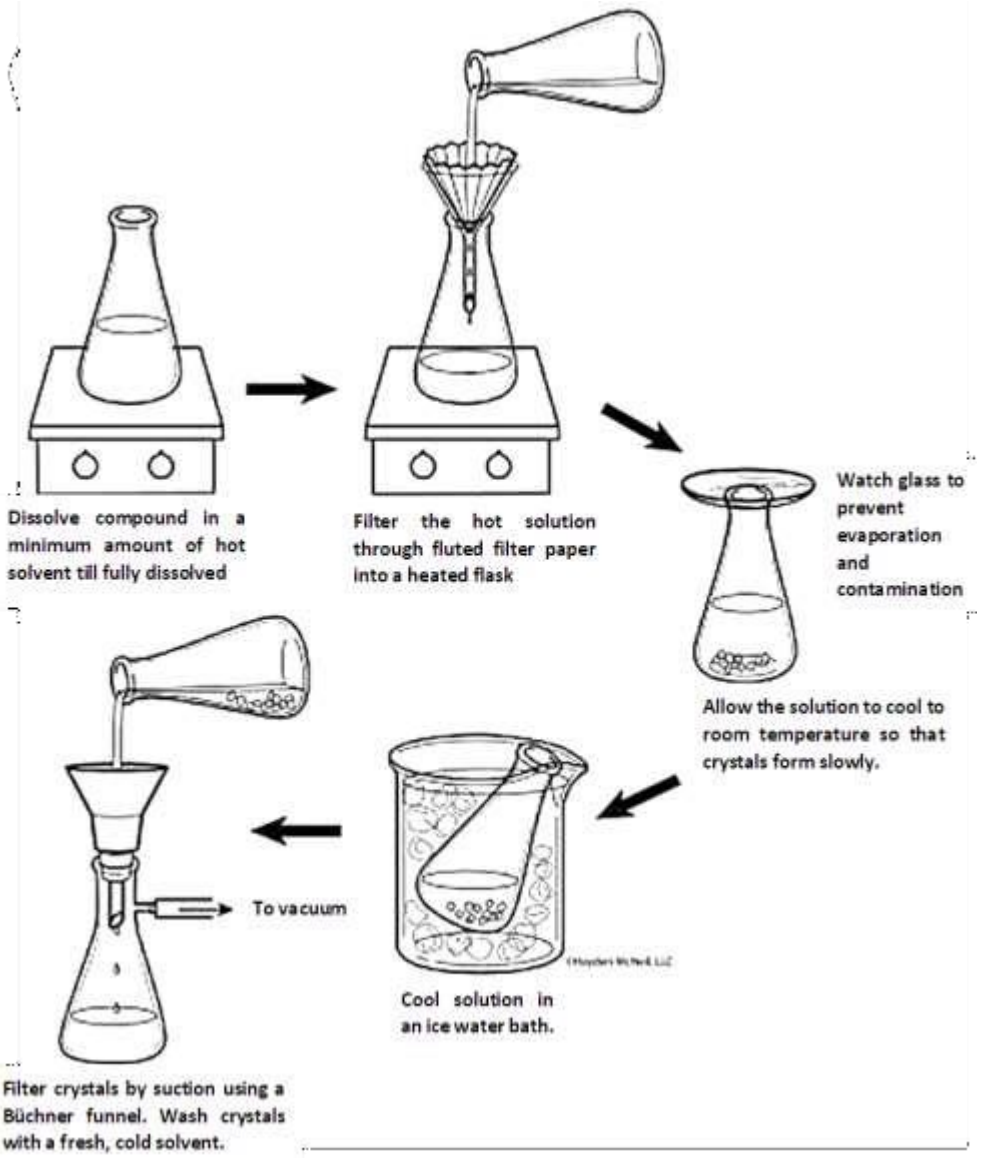
12.

$$\textbf{\% Yield} = \frac{mass\ of\ purified\ products}{mass\ of\ crude\ sample}\ x\ 100$$

NOTE

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

PROCEDURE SUMMARY DIAGRAM:



Useful links

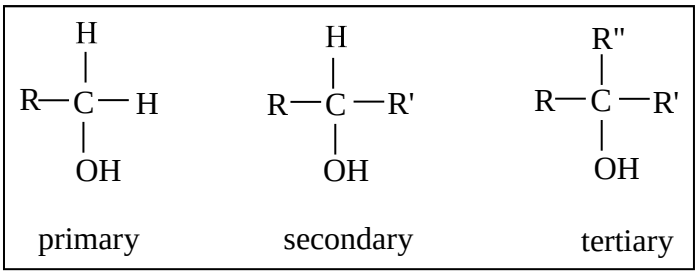
Recrystallization of Organic Compounds
https://www.youtube.com/watch?v=qJLvB6NFnoA

EXPERIMENT 3: ALCOHOLS AND PHENOLS

Classification and Tests

I. ALCOHOLS

Alcohols are classified as primary, secondary and tertiary according to the number of alkyl groups directly attached to the carbinol carbon.



Reactions of alcohols involve the breaking of either of two bonds: the O- H bond as in reactions with bases and esterification reactions, or the C-OH bond leading to dehydration and substitution reactions. In breaking the C-OH bond, protonation of the -OH group is essential to convertit from apoor leaving group to a better one.

Some physical and chemical properties of alcohols are examined in the following tests.

EXPERIMENTAL

MATERIALS NEEDED	Glassware: 4 Test tubes. Chemicals: 1 mL each of: ethanol,1-butanol, 2-butanol, 2-methyl-2-propanol, ethylene glycol,, sodium metal, phenolphthalein indicator, 15 mL potassium dichromate (1%), 0.5 mL sulfuric acid, 6.0 mL Lucas reagent, 15 mL iodoform reagent, 6 mL NaOH (10%),

1. Solubility in Water

Alcohols of low molecular weight are water soluble due to their ability toform hydrogen bonds with water. Solubility in water decreases with

increasing molar mass but increases with branching and with the number of hydroxyl (OH) groups.

PROCEDURE

Glassware: 4 test tubes
The following alcohols to be tested*:* 1- butanol, ethanol, ethylene glycol, or 2-methyl-2-propanol.

1. In each test tube, add **10** drops of one of the alcohols to be tested**.**
2. Add **2** mL of water to each test tube.
3. Shake very well.
4. Record your observations **and** result.

2. Acid Properties of Alcohols

Alcohols react with metallic sodium with the evolution of hydrogen. The relative acidities of alcohols and consequently their relative rates of reaction with sodium are in the order:

primary > secondary> tertiary.

$$2R{-}OH + 2Na \longrightarrow 2RO^{-}Na^{+} + H_2$$

PROCEDURE

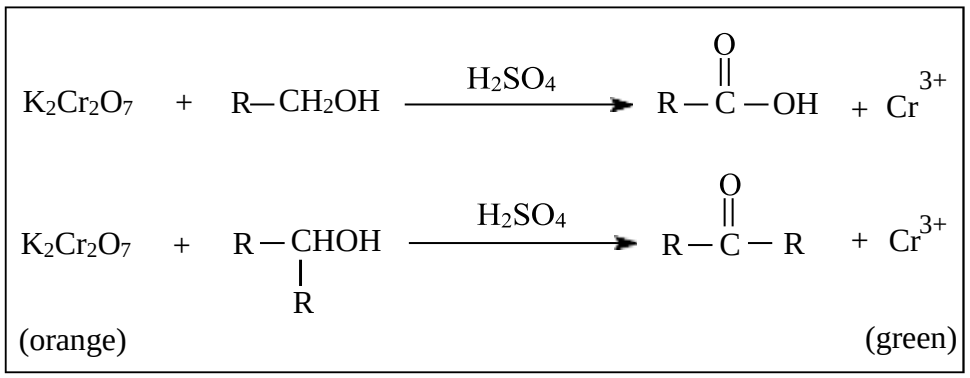
Glassware: 3 test tubes
The following alcohols to be tested*:* 1- butanol, 2-butanol, or 2-methyl-2-propanol.

1. In each test tube, place a small piece of sodium.
2. Add **2** mL of one of the alcohols to be tested.
3. Add (up to **10** drops) of concentrated **sulfuric acid.**

4. Shake.
5. Compare the rates of evolution of hydrogen gas and record your results.
6. After all the sodium has reacted in the test tube containing the 1-butanol, add 3 drops of phenolphthalein indicator solution and observe the color change.
7. Record your observations **and** result.

3. Chromic Acid Oxidation of Alcohols

Primary and secondary alcohols are oxidized by chromic acid to the corresponding carboxylic acids and ketones respectively. Tertiary alcohols are generally unreactive under similar conditions. When alcohols are oxidized, they reduce chromium (VI) to Cr (III) changing the color of the solution from orange to green. Oxidation therefore offers a method for distinguishing primary and secondary alcohols from tertiary alcohols.



PROCEDURE

Glassware: 3 test tubes
The following alcohols to be tested*:* 1- butanol, 2-butanol, or 2-methyl-2-propanol.

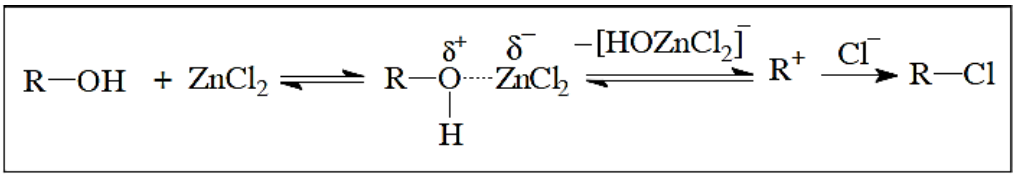
8. In each test tube, place **5** mL of **Chromic Acid Reagent (1% potassium dichromate solution)**.
9. Add (up to **10** drops) of concentrated **sulfuric acid.**
10. Mix thoroughly and add **2** drops of one of the alcohol to be tested and shake.
11. Record your observations **and** result.

Positive results → Green solution will be formed.

4. The Lucas Test

A solution of zinc chloride in concentrated hydrochloric acid (Lucas reagent) can be used to distinguish between primary, secondary and tertiary alcohols.

With this reagent the order of reactivity is typical of compounds reacting by the S_N1 mechanism. The zinc chloride (a Lewis acid) assists in breaking the C-OH bond as illustrated in the equation below:



Alcohols (of no more than six carbons) are soluble in the Lucas reagent while the corresponding alkyl chlorides are not. Tertiary alcohols react rapidly with the reagent forming an insoluble alkyl chloride layer almost immediately. Secondary alcohols react within 5-10 minutes, while primary alcohols require several hours to react at room temperature (S_N2 mechanism).

PROCEDURE

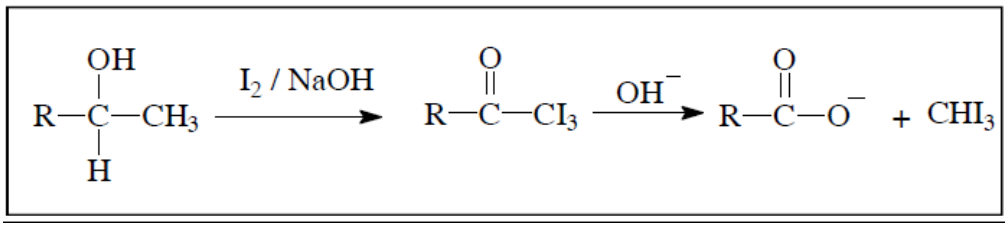
Glassware: 3 test tubes
The following alcohols to be tested*:* 1- butanol, 2-butanol, or 2-methyl-2-propanol.

1. In each test tube, place **2** mL of **Lucas' reagent**
2. Add **6** drops of one of the alcohols to be tested.
3. Close the tubes with a piece of parafilm and shake well.
4. If no change occurs immediately, then place in water bath at (**100ºC**) for **5-13** minutes.
5. Record your observations **and** result.

Positive results → White to cloudy mixture (immediately with 3° alcohols & within 5-10 min with 2° alcohols)

5. The Iodoform Test

is is a test for methyl carbinols having the structure CH_3CHOH- and methyl ketones (CH_3CO-). Methyl carbinols are first oxidized by the reagent to methyl ketones which become iodinated and then cleaved by base to give a bright yellow precipitate of iodoform.



PROCEDURE

Glassware: 3 test tubes
The following alcohols to be tested*:* 1- butanol, 2-butanol, or 2-methyl-2-propanol.

5. In each test tube, add **3** mL of **5% sodium hydroxide**.
6. Add 10 drops of one of the alcohols to be tested**.**
7. Add **5-10** drops of **iodine solution (**or up to **0.5** mL) gradually.
8. Shake very well.
9. Allow to stand for **3-5** minutes.
10. Record your observations **and** result.

Positive results → Bright yellow precipitate

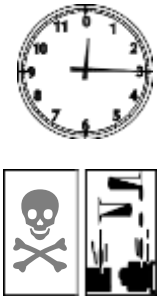
II. PHENOLS

The most common reactions of phenols involve breaking the O-H bond and the usual electrophilic aromatic substitution at the aromatic ring. Protonation of the hydroxyl group and loss of a water molecule as in alcohols would give a phenyl cation which is very unstable and difficult to form. Since the aromatic nucleus is electron rich, direct attack by nucleophiles as in $S_N1$or S_N2 reactions is not possible. Consequently, phenols do not undergo substitution of the hydroxyl group either by the $S_N1$or S_N2 mechanisms.

The characteristic property that differentiates phenols from alcohols is acidity. Phenols are stronger acids than alcohols and react with sodium hydroxide, whereas alcohols do not. The reason for this difference isthat the phenoxide ion is resonance-stabilized whereas the alkoxide ion is not.

EXPERIMENTAL

MATERIALS NEEDED	Glassware: 4 Test tubes. Chemicals: cyclohexanol, phenol, *p*-cresol, 4 mL bromine water solution, 0.5 mL ferric chloride solution (1%), 6 mL of 10% NaOH solution .

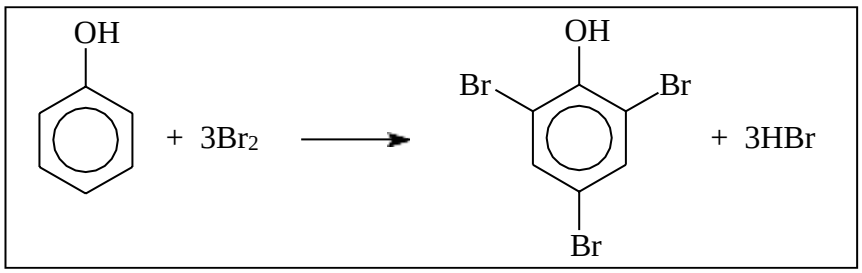


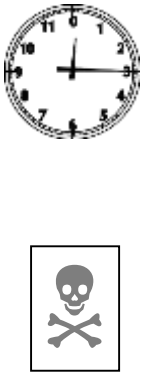
1. Acidity of Phenols

Procedure In each of three test tubes add 0.4 mL or 0.2 g of cyclohexanol, phenol, or *p*-cresol. Add 1 mL of water to each tube, shake and note whether the compound dissolves. If not add 2 mL of 10% NaOH solution and observe the result.

2. Bromination of Phenols with Bromine Water

The hydroxyl group strongly activates thearomaticring towards electrophilic aromatic substitution. Phenol readily forms a tribromo derivative when treated with a solution of bromine-water at room temperature.

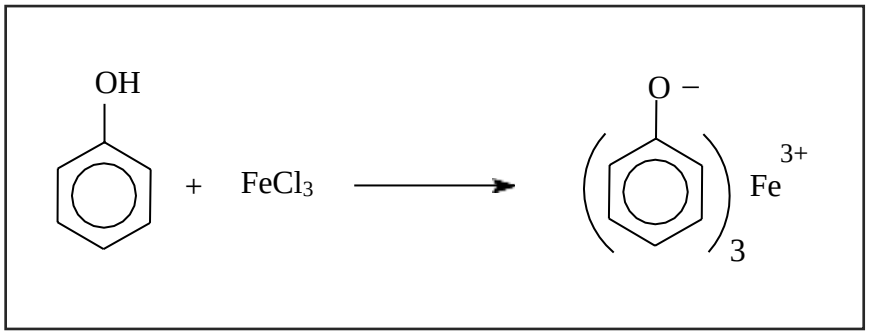




Procedure. In a test tube introduce 1 mL of water and about 0.2 g of phenol. Add enough bromine-water and shake until the yellow color persists. Observe the formation of a precipitate.

3. Ferric Chloride Test

The presence of a phenolic (or enolic group) in a compound is indicated by the formation of a violet (or red) iron complex when treated with a ferric chloride solution.



PROCEDURE

Glassware: 1 test tube
The following alcohols to be tested*:* phenol, and cyclohexanol.

1. In a test tube, place **3** mL of **water.**
2. Add **5** drops of the **Unknown**.
3. Add **1-2** drops of **1% ferric chloride solution**.
4. Shake well and allow to stand for **1-2** minutes.
5. Record your observations **and** result.

Positive results → violet solution will be formed

Useful links

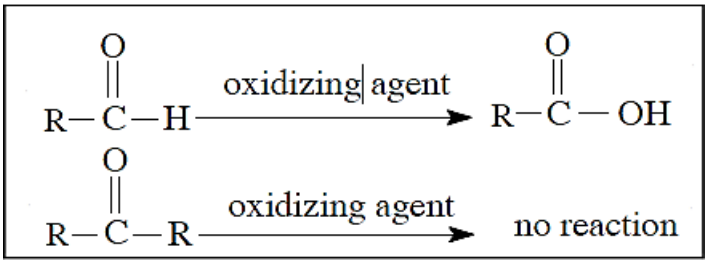
Alcohols (Classification and Tests)
https://www.youtube.com/watch?v=dinNjEiqxcg
Organic Chemistry Experiment: Solubility of Alcohol and Phenol
https://www.youtube.com/watch?v=ilVEmFOweVA

EXPERIMENT 4: ALDEHYDES AND KETONES

Classification, Tests and Derivatives

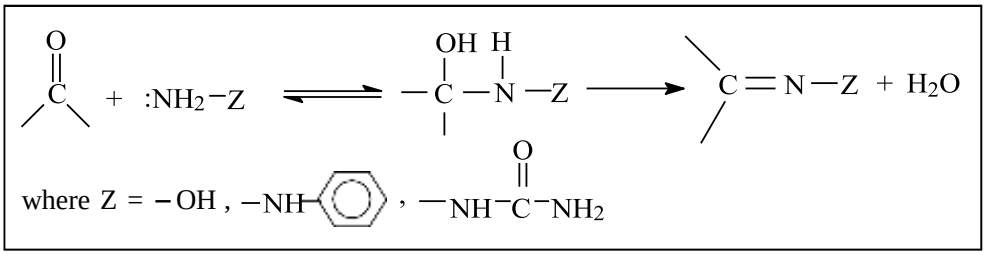
INTRODUCTION

The carbonyl group is common to both aldehydes and ketones, and as a result, both classes of compounds react similarly with many reagents. 2,4-Dinitrophenylhydrazine is commonly used to test for both types of compounds. However, a distinguishing behavior of aldehydes is their reaction with mild oxidizing agents which oxidize them to carboxylic acids while ketones, which are more difficult to oxidize, remains unchanged.



Several laboratory tests that distinguish between aldehydes and ketones, therefore, take advantage of this difference in behavior towards oxidants. One of these is *Tollens*' silver mirror test, in which a silver ammonia complex ion is reduced, by aldehydes, to metallic silver. *Fehling's* and *Benedict's* solutions are also distinguishing reagents where the $Cu_{(II)}$ ion, complexed to tartarate or citrate respectively, is reduced to red cuprous oxide (Cu_2O) by aldehydes but not ketones.

Carbonyl compounds (aldehydes and ketones) are conveniently identified through a number of easily prepared derivatives. These include oximes, phenylhdrazones, 2,4-dinitrophenylhydrazones and semicarbazones. These derivatives are ideal because they are easily purified, crystalline solids with sharp melting points. The mechanism of formation of these closely related derivatives involves a typical nucleophilic addition at the carbonyl carbon followed by eliminationof a water molecule.



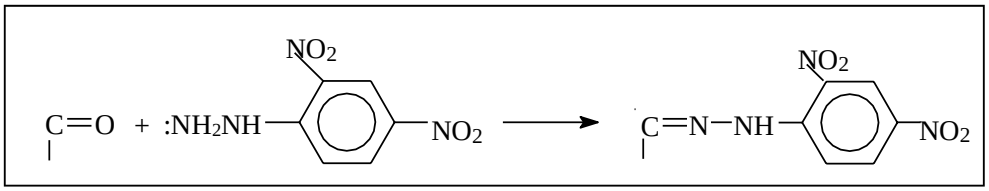
For further structural identification of methyl carbonyl compounds, the iodoform reaction, using iodine and aqueous sodium hydroxide is used. Compounds containing the CH3CO group give a bright yellow precipitate of CHI3 (*iodoform*).

EXPERIMENTAL

MATERIALS NEEDED	Glassware: 4 test tubes, Erlenmeyer flask (50 mL), ice bath, graduated cylinder (10 mL), Buchner funnel, filter flask, melting point apparatus. Chemicals: 15 mL Tollens' reagent, 0.5 mL each of: formaldehyde, benzaldehyde, acetone, 2-propanol, 2-pentanone, 3-pentanone, 15 mL Fehling's or Bendict's solution, 12 mL sodium hydroxide(5%), 40 mL iodoform reagent, 1.0 g hydroxylamine hydrochloride, 3 g sodium acetate, 2.3 mL cyclohexanone, 30 mL petroleum ether, 5.0 mL phenylhydrazine reagent, 50 mL ethanol, 16 mL 2,4-dinitrophenylhydrazine reagent, 1.0 g semicarbazide hydrochloride and 1.0 g unknown.

I. TESTS AND DERIVATIVES

1. 2,4-Dinitrophenylhydrazine Test



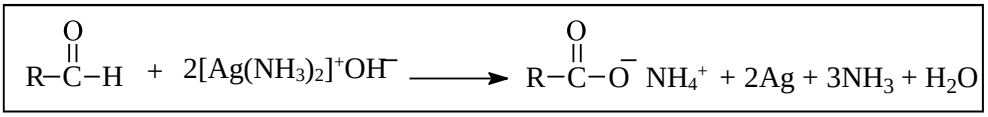
PROCEDURE

Glassware: 2 test tubes
The following carbonyl compounds to be tested: Acetone, or benzaldehyde.

1. In each test tube, add **2** mL of ethanol.
2. Add **5** drops of the carbonyl compounds to be tested and mix.
3. Add **2** mL of **2,4-dinitrophenylhydrazine** reagent and shake well.
4. Record your observations **and** result

Positive results → Bright orange to yellow precipitate

2. Tollens' Silver Mirror Test



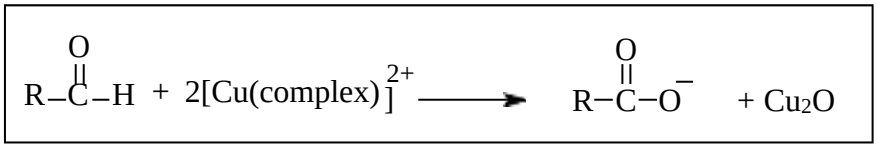
PROCEDURE

Glassware: 3 test tubes
The following carbonyl compounds to be tested*:* Acetone, formaldehyde, or benzaldehyde.

1. In each test tube, add 3 mL of **Tollens' reagent**.
2. Add **3-4** drops of the carbonyl compounds to be tested and mix.
3. Shake the tubes vigorously and allow to stand for **5** minutes.
4. Place the tube in a hot water bath (**50ºC**) for **3-5** minutes.
5. Record your observations **and** result.

Positive results → Dark grey precipitate to silver mirror

3. Fehling's and Benedict's Tests



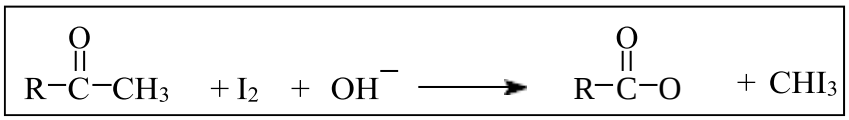
PROCEDURE

Glassware: 2 test tubes
The following carbonyl compounds to be tested*:* Acetone, or benzaldehyde.

1. In each test tube, add <u>both</u> **2** mL of **Fehling's reagent A** and **2** mL of **Fehling's reagent B** and mix.
2. Add **3-5** drops of the <u>carbonyl compounds to be tested</u> and mix.
3. Place the test tube in a beaker of boiling water for **15-20** minutes.
4. Record your observations **and** result.

Positive results → Dark red to dark brown precipitate

4. The Iodoform Test



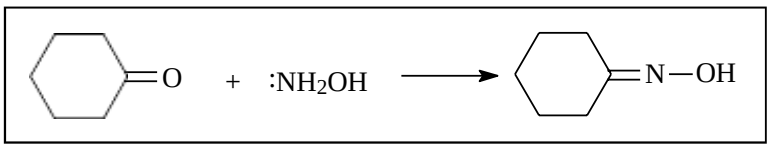
PROCEDURE

Glassware: 5 test tubes
The following alcohols to be tested*:* Acetone, formaldehyde, 2-propanol, 2-pentanone, and 3-pentanone.

1. In each test tube, add **3** mL of **5% sodium hydroxide**.
2. Add 10 drops of one of the <u>alcohols to be tested</u>**.**
3. Add **5-10** drops of **iodine solution (**or up to **0.5** mL) gradually.
4. Shake very well.
5. Allow to stand for **3-5** minutes.
6. Record your observations **and** result.

Positive results → Bright yellow precipitate

5. Cyclohexanone Oxime

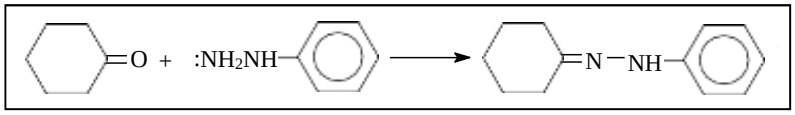


PROCEDURE.

Dissolve 1 g of hydroxylamine hydrochloride and 1.5 g of sodium acetate in 4 mL of water in a test tube. Warm the solution to about 40 ^{o}C and then add 1 mL of cyclohexanone. Stopper the flask and shake for 1-2 minutes. Cyclohexanone oxime begins to separate as fine colorless crystals. Cool the tube thoroughly in an ice bath to complete precipitation. Filter the crystals using a small Buchner funnel then wash with a little ice-cold water. Air-dry the crystals and determine their melting point.

Oximes of some carbonyl compounds will crystallize more slowly. They may require longer cooling and scratching the walls of the flask to induce crystallization. Oximes can be recrystallized nicely from petroleum ether (bp 40-50).

6. Cyclohexanone Phenylhydrazone

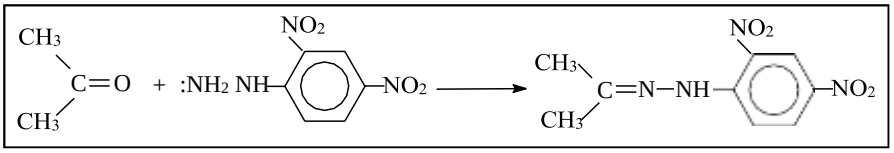


PROCEDURE.

Add 10 drops of cyclohexanone to 5 mL of ethanol and 5 mL of phenylhydrazine reagent Shake the mixture until a clear solution is obtained. Heat the mixture on a water bath for 10 minutes then cool in an ice bath and filter the crystals.

The crude phenylhydrazone may be recrystallized by dissolving it in hot ethanol and adding water to the hot solution until a faint turbidity persists. The solution is then cooled and the crystals are collected.

7. Acetone 2,4Dinitrophenylhydrazone

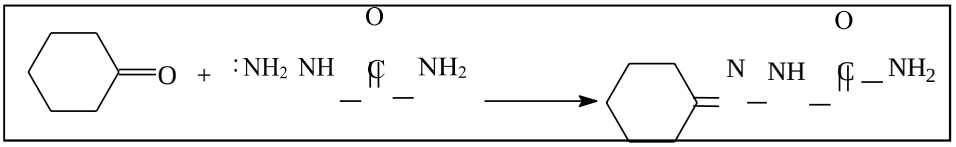


PROCEDURE.

Add 10 mL of 2, 4-dinitrophenylhydrazine reagent to 10 drops of acetone in 10 mL of ethanol and allow the mixture to standat room temperature for a few minutes. Precipitation of the acetone 2, 4-dinitrophenylhdrazone usually occurs immediately; other carbonyl compounds may require 5-6 minutes or even several hours. When crystallization is complete, cool the mixture in an ice bath, and collect the crystals. Recrystallize from ethanol, dry the resulting crystals and determine their melting point.

NOTE: Derivatives of phenylhydrazine are suspected carcinogens.
Handle with care and avoid skin contact.

8. Cyclohexanone Semicarbazide



PROCEDURE.

In a test tube dissolve 1g semicarbazide hydrochloride and 1.5 g sodium acetate in 10 mL of water, add 1 mL of cyclohexanone and shake vigorously. Place the test tube in a beakerof boiling water for 5 minutes then cool to room temperature. Place inan ice bath and scratch the sides of the tube with a glass rod until crystallization is complete. Filter the crystals, wash with a little water, and recrystallize from ethanol. Dry the crystals and determine their melting point.

II. IDENTIFICATION OF AN UNKNOWN CARBONYL COMPOUND

Procedure. While the various derivatives are drying, obtain

anunknown from your instructor and proceed to identify it as follows: Use *Tollen's* test to determine whether the compound is an aldehyde or a ketone. If the unknown is a ketone, perform the iodoform test to determine if it is a methyl ketone.

Finally prepare a crystalline derivative of the unknown to determine its identity. The unknown is selected from the aldehydes and ketones listed below:

Table 3. Derivatives of some aldehydes and ketones

Compound	Formula	Oxime	Phenyl-hydrzone	2,4-DNP	Semi-carbazone
Ethyl methyl ketone	$CH_3CH_2COCH_3$	oil	oil	116	136
Diethyl ketone	$CH_3CH_2COCH_2CH_3$	69	oil	156	139
Furfural	$C_4H_3O.CHO$	75	79	229;212	202
Crotonaldehyde	$CH_3CH = CHCHO$	119	56	190	199
Benzaldehyde	C_6H_5CHO	35	158	237	224
Cyclohexanone	$C_6H_{10}O$	91	81	162	167
2-Heptanone	$CH_3(CH_2)_4COCH_3$	oil	207	89	127
n-Heptanal	$CH_3(CH_2)_5CHO$	57	oil	108	109
Acetophenone	$C_6H_5COCH_3$	59	105	239	199
2-Octanone	$CH_3(CH_2)_5COCH_3$	oil	oil	58	123
Salicylaldehyde	$C_6H_4(OH)CHO$	63	143	252	231

Useful links

Aldehydes and Ketones (Tests)/Organic Chemistry Lab)
https://www.youtube.com/watch?v=1IaaMeGQwdg

EXPERIMENT 5: IDENTIFICATION OF CARBOXYLIC ACIDS

General and Individual Identification Tests

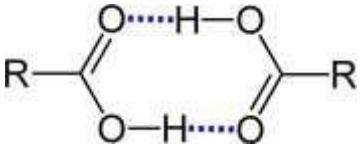
INTRODUCTION

Carboxylic acids are organic acids characterized by the presence of at least one carboxyl group. The general formula of a carboxylic acid is R-COOH. Carboxylic acids are Brønsted-Lowry acids, they are proton donors. They are the most common type of organic acid. Among the simplest examples are the formic acid H-COOH, that occurs in ants, and acetic acid CH3-COOH group, that gives vinegar its sour taste.

Physical and Chemical Properties of Carboxylic Acids:

- ✓ ***Solubility in water***

Carboxylic acids usually exist as dimeric pairs in nonpolar media due to their tendency to "self-associate. But in the presence of water, the carboxylic acids don't dimerize. Instead, hydrogen bonds are formed between water molecules and individual molecules of acid. The solubility of the bigger acids decreases very rapidly with size. This is because the longer hydrocarbon "tails" of the molecules get between water molecules and break hydrogen bonds. In this case, these broken hydrogen bonds are only replaced by much weaker van der Waals dispersion forces.



- ✓ ***Boiling Point***

Carboxylic acids tend to have higher boiling points than water, not only because of their increased surface area, but because of their tendency to form stabilized dimers. Carboxylic acids tend to evaporate or boil as these dimers. For boiling to occur, either the dimer bonds must be broken, or the entire dimer arrangement must be vaporized. Higher boiling points than similar alcohols due to dimer formation. (Acetic acid, b.p. 118 °C)

- ✓ ***Melting Point***
  - Aliphatic acids with more than 8 carbons are solids at room temperature.

- Double bonds (especially cis) lower the melting point.
- Note these 18-C acids:
  - Stearic acid (saturated): 72°C
  - Oleic acid (one cis double bond): 16°C
  - Linoleic acid (two cis double bonds): -5°C

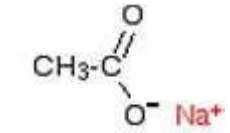
✓ *Acidity of carboxylic acid*

Carboxylic acids are typically weak acids, meaning that they only partially dissociate into H+ cations and RCOO– anions in neutral aqueous solution. For example, at room temperature, only 0.02 % of all acetic acid molecules are dissociated. Electronegative substituents give stronger acids.

Carboxylic Acids	***pKa***
Formic acid (HCO_2H)	*3.77*
Acetic acid (CH_3COOH)	*4.76*
Chloroacetic acid (CH_2ClCO_2H)	*2.86*
Dichloroacetic acid ($CHCl_2CO_2H$)	*1.29*
Trichloroacetic acid (CCl_3CO_2H)	*0.65*
Trifluoroacetic acid (CF_3CO_2H)	*0.5*
Oxalic acid (HO_2CCO_2H)	*1.27*
Benzoic acid ($C_6H_5CO_2H$)	*4.2*

❖ *Salts of Carboxylic Acids*

When the acids form salts, this is lost and replaced by a metal. Sodium ethanoate, for example, has the structure:



sodium ethanoate

- Sodium hydroxide removes a proton to form the salt.
- Adding a strong acid, like HCl, regenerates the carboxylic acid.

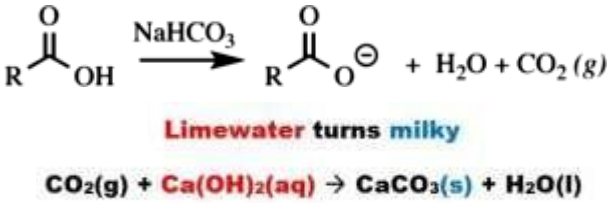
➢ *Properties of acid Salts*

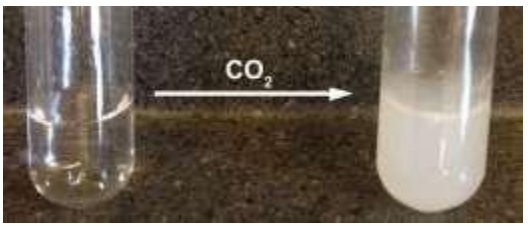
- Usually solids with no odor.
- Carboxylate salts of Na+, K+, Li+, and NH4+ are soluble in water.
- Soap is the soluble sodium salt of a long chain fatty acid.
- Salts can be formed by the reaction of an acid with NaHCO3, releasing CO2.
- The bond between the sodium and the ethanoate is ionic.

❖ *GENERAL TESTS FOR CARBOXYLIC ACIDS:*

1. Sodium Carbonate test (Demonstration Only)

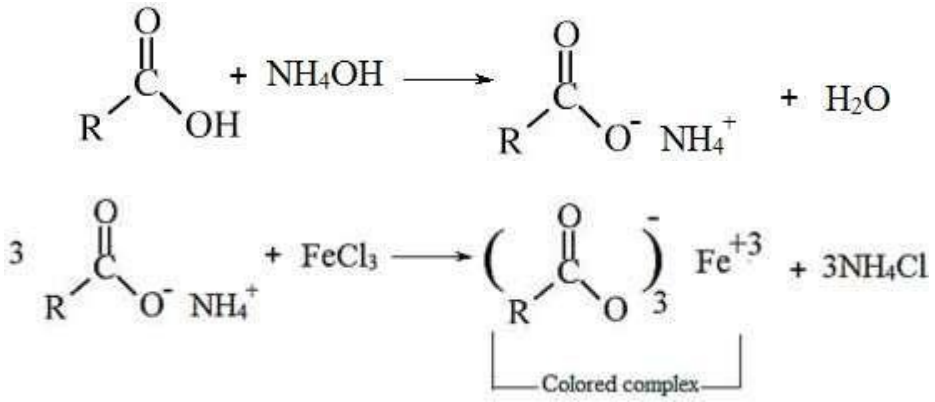
They are soluble in both dilute sodium hydroxide and sodium carbonate (Na2CO3) or sodium bicarbonate solutions (NaHCO3). Sodium hydrogen carbonate (NaHCO3) or sodium carbonate (Na2CO3) reacts with carboxylic acids to give the sodium salt of the acid and liberates carbon dioxide. If the acid is insoluble in water and the reaction is sluggish dissolve the acid in methanol and add carefully to a saturated sodium hydrogen carbonate solution, when a vigorous effervescence will be observed.

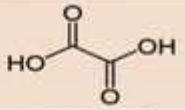
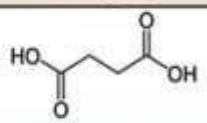
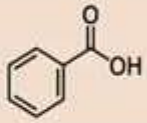
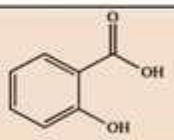
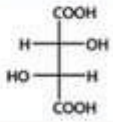
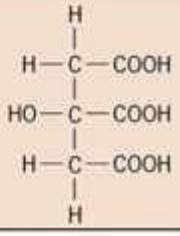




2. Ferric chloride test

Neutral carboxylic acids form colored complexes with ferric chloride solution. The carboxylic acids are first neutralized using ammonia. The color of the complex depends on the kind of acid.



Acids	Structure	Use/Presence	Result
Formic	HCOOH	Ants and venoms	Red sol>brown ppt with heating
Acetic	CH_3COOH	Vinegar	Red sol>brown ppt with heating
Oxalic		Cleaning, bleaching, removal of rust	Faint yellow ppt
Succinic		Sweetener	Brick red ppt
Benzoic		Preservative	Buff to brown ppt
Acids	**Structure**	**Use/Presence**	**Result**
Salicylic		Keratolytic, antifungal	Violet sol
Tartaric		Sour taste	Yellow sol
Citric		Citrus fruit	Yellow sol

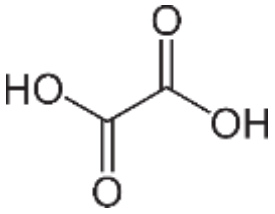
PROCEDURE

1. Place 2 mL of each of the following neutral acid solutions in separate test tubes; Sodium acetate solution, Sodium succinate solution, Sodium benzoate solution, Sodium salicylate solution, Sodium oxalate solution, Sodium citrate solution, Sodium tartarate solution and Formicacid.
2. Add excess Ammonium hydroxide solution till the solution is justalkaline to litmus paper.
3. Boil the solution till the odor of ammonia is completely removed.
4. Add few drops of neutral Ferric chloride solution.
5. Note the results.

Remember same test with phenol give violate color.

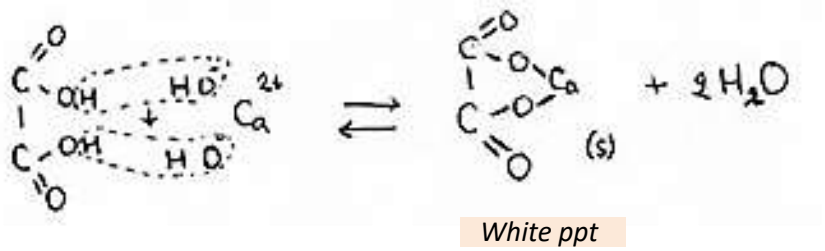
❖ *INDIVIDUAL REACTIONS OF CARBOXYLIC ACIDS:*

➢ *Oxalic Acid*

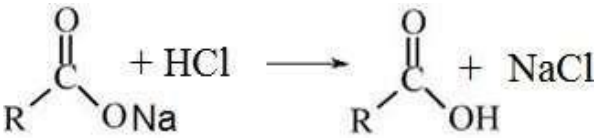


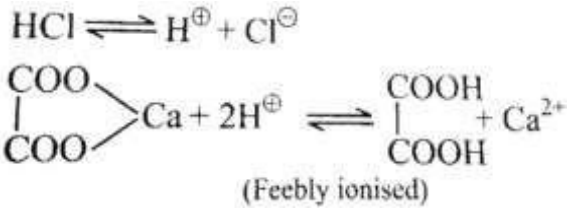
Calcium chloride test

Carboxylic acid salts react with strong mineral acids w liberate free organic acid. If the freed carboxylic acid is water insoluble, it will precipitate.



White ppt

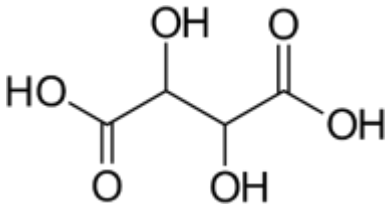




PROCEDURE

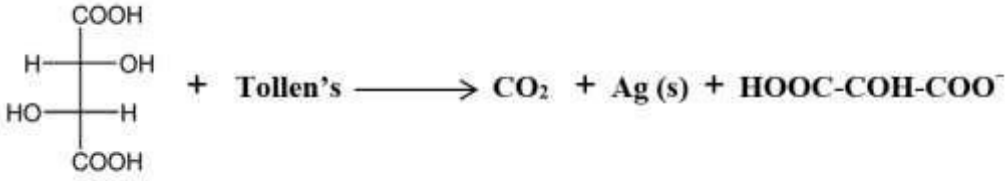
Add Calcium chloride solution to Oxalate solution. Try the solubility of the ppt in acetic acid and dilute HCl.

➢ ***Tartaric Acid***



Tollen's test

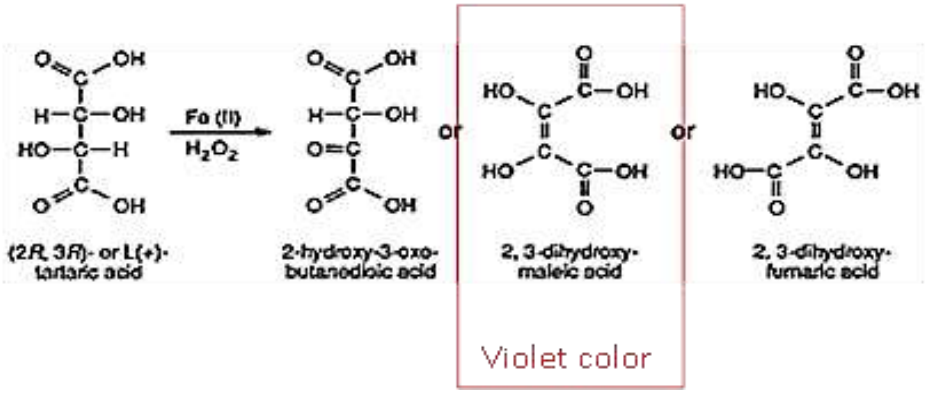
Reducing property of tartaric acid is tested with Tollen's reagent (Reduction of Ammonical Silver nitrate).



PROCEDURE

Prepare the Tollen's reagent then a dd to 5 mL of that reagent, few drops of neutral tartarate solution and place the mixture in a warmwater bath. Note the formation of a mirror.

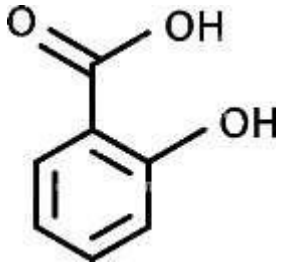
Reaction with Fenton's reagent



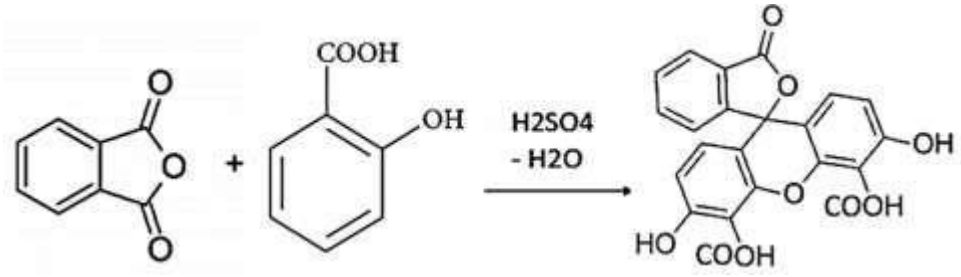
PROCEDURE

Add to few mLs of a tartarate solution one drop of freshly prepared Ferrous sulphate and 2 drops of Hydrogen peroxide solution followed by excess Sodium hydroxide. Notice the color.

- ***Salicylic Acid***



Phthalein formation



PROCEDURE

Prepare In a dry test tube fuse together few crystals of Salicylic acid with the same amount of Phthalic anhydride and few drops of conc. Sulfuric acid, cool then dissolve in water and add excess Sodium hydroxide. Notice the color.

EXPERIMENT 6: CHROMATOGRAPHY

A Separation and Purification Technique

INTRODUCTION

Chromatography is a technique that may be used to separate the components of a mixture as well as to identify organic substances and examine their purity. Chromatography encompasses several techniques such as column, thin-layer, paper, gas liquid, etc. chromatography. Two principles are basically involved in chromatography: adsorption (as in thin- layer chromatography) and partition (as in paper chromatography), andcertain terms are common to both types of chromatography.

In adsorption chromatography, separation depends on the selective desorption of the components of a mixture by the eluent (mobile phase) from the surface of a solid adsorbent (stationary phase). The adsorbent maybe packed in a column (column chromatography) or spread as a thin layer on a glass plate as in thin-layer chromatography.

In partition chromatography, separation depends on partition of the components of a mixture between the stationary and mobile phases. The mobile phase may be a liquid (liquid-liquid partition chromatography) or a gas (gas-liquid partition chromatography).

ANALYSIS OF CHROMATOGRAMS

In thin layer and paper chromatography, substances are characterized by their R_f-values (retardation factor). The R_f-value is a number (less than one) which is characteristic of a compound for a given adsorbent and developing solvent. It is defined as:

$$R_f = \frac{\text{distance traveled by the compound}}{\text{distance traveled by the solvent}}$$

In gas-liquid chromatography, compounds are characterized by their retention times.

THIN-LAYER CHROMATOGRAPHY (TLC)

This is one application of adsorption chromatography in which an adsorbent, usually silica gel or alumina, is spread out as a thin layer on an inert surface, such as a glass plate or microscope slide. The mixture is applied at one end of the coated plate and, as the mobile phase (a liquid) moves up the solid adsorbent by capillary action, the adsorbed components of the mixture get desorbed and carried along at different rates by the moving solvent.

Adsorption of the components of the mixture, on the surface of the adsorbent, occurs to differing extents depending on their structural features and polarity. The more strongly adsorbed a given compound is, the slower it is transported by the mobile phase, and conversely, the more weakly adsorbed the compound is, the faster it is transported up thestationary phase. The result is that the components of the mixture are separated into different zones or spots (Figure 20).

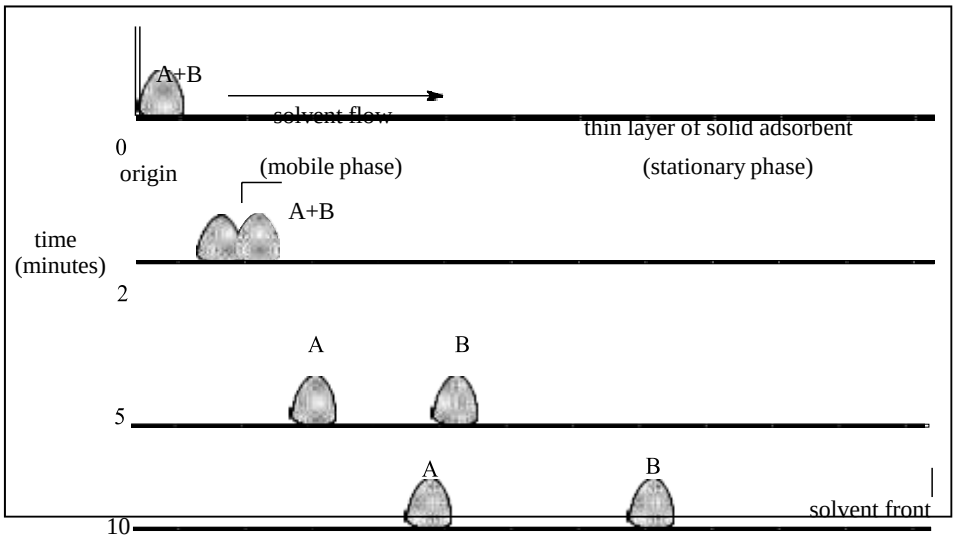


Figure 20. Separation by thin-layer chromatography

Separation by thin-layer chromatography depends on the kind and activity of the adsorbent (stationary phase), the polarity of the eluent (mobile phase) and on the chemical nature of the components of the mixture. The most common adsorbents employed in *TLC* are silica (SiO_2.

xH_2O) and alumina (Al_2O_3. xH_2O), and the activity of these adsorbents is largely determinedby their water content. For a given adsorbent and compound, the greater the polarity of the eluent, the greater is its ability to dislodge a compound from the surface of the adsorbent, and therefore the higher the R_f-value.

Eluting power of solvents:

Acetic acid > Ethyl alcohol > Acetone > Diethyl ether > Dichloromethane >Hexane.

GENERALIZED EXPERIMENTAL PROCEDURE

PREPARATION OF TLC PLATES

Large glass plates (20x20 cm) are commonly used for quantitative separations, while microscope slides are usually used for qualitative purposes. A homogeneous slurry of the adsorbent in a volatile organic solvent (chloroform or dichloromethane) is poured over the glass plates and allowed to air-dry at room temperature. Microscope slides can be coated, two at a time, by dipping them into the slurry for some time then holding them vertically to air-dry. The jar of adsorbent must be shaken thoroughly before each use to homogenize the slurry. Three steps are involved in TLC: **spotting, developing, and visual**

Spotting. The mixture to be analyzed is dissolved in a suitable solvent (1% solution). With a drawn capillary tube, a small amount of this solution is spotted on the *TLC* plate about 1 cm from the bottom (Figure 21). The spotsshould have a diameter not larger than 1-2 mm, since larger spots result in "tailing" and overlapping of close spots. Once the solvent evaporates from the spots, the plate is ready for developing.

Development of the Chromatogram. The eluent, also called developing solvent, is chosen based on the nature and polarity of the compounds being studied. It is best to choose the solvent that will give a satisfactory separation within the range of 0.2-0.8 R_f values. The plate is

placed in a developing chamber (*e.g.*, a covered beaker) containingthe solvent and lined with filter paper soaked in the solvent to help saturate the atmosphere with solvent vapors. When the solvent front reaches the finish line, the plate is removed from the beaker and placed onthe bench top to air-dry.

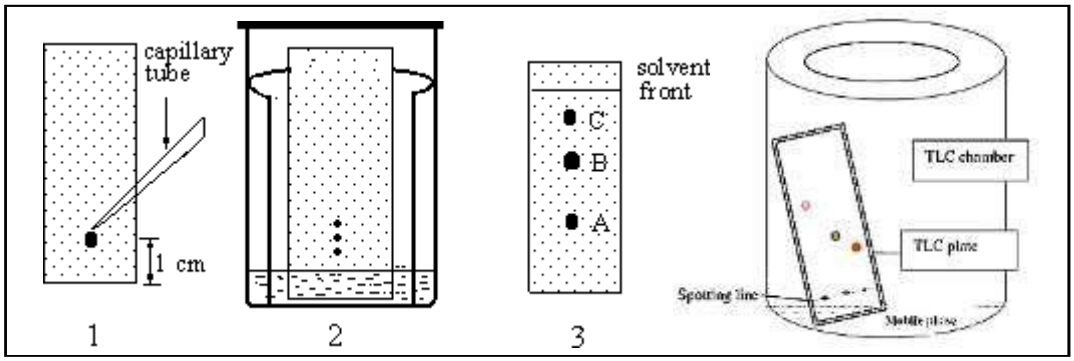


Figure 21. Steps in the TLC technique

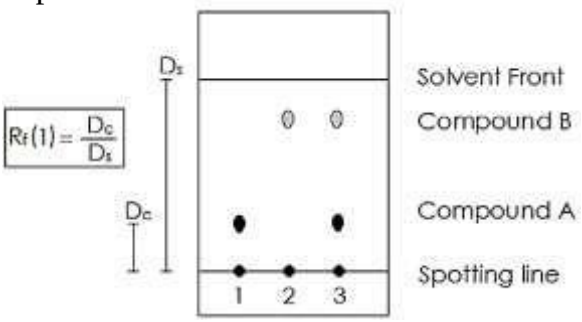
Visualization of Spots. Compounds on the plate are located according to their characteristics:

a. If the spots are colored, they can be observed in ordinary light.

b. If the compounds are colorless, they can be seen under *UV*-light or using iodine staining where they appear as dark spots on a white background.

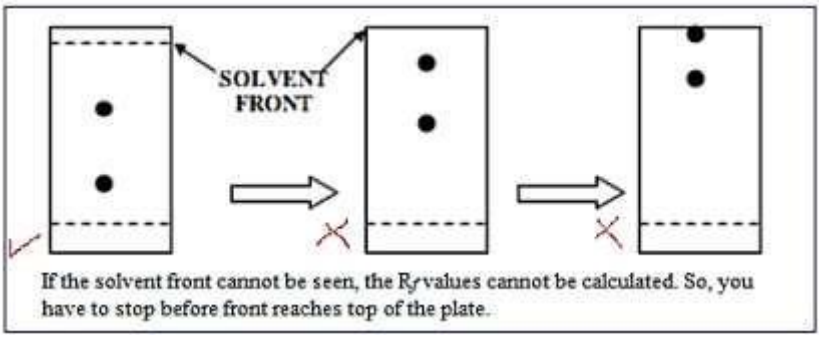
c. Colorless spots may also be located with an indicator. Most organic compounds form complexes with iodine giving dark brown spots whenthe plate is exposed to iodine vapor.

Sulfuric acid may also be used to make colorless spots visible. Most organic compounds turn black when sprayed with sulfuric acid.



Notes:

○ 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.



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

OBJECTIVES

1. Determining the R_f-value for *o*- and *p*-nitroaniline by *TLC*.
2. Separating a mixture of two dyes by paper chromatography.
3. Determining the constituents of an analgesic drug by *TLC*.

Having done this experiment, you will have seen the use of *TLC* and paper chromatography in the separation of mixtures and in the characterization of organic compounds.

EXPERIMENTAL

MATERIALS NEEDED	Glassware: 2 Microscope slides,, capillary tubes, beaker (200 mL), Petri dish with cover, filter paper, UV lamp. Chemicals: stock solutions (1% in acetone) of *o*-nitrophenol, and *p*-nitrophenol, green dye, 5 mL dichloromethane, 20 mL isoprophyl alcohol, 1 mL methanol, 6 mL benzene, 3 mL ether, 1 mL acetic acid and analgesic tablet (Remin, Revanin, Paracetamol or Excedrin), stock solutions (5% in acetone) of aspirin, phenacetin, salicylamide, caffeine, acetaminophen.

TLC EXAMINATION OF ISOMERIC NITROANILINES

Prepare the developing chamber by placing a filter paper inside a 200mL beaker and adding 5 mL dichloromethane. Cover the beaker while preparing the *TLC* plates as described before. Dip a capillary tube into a 1% solution of *p*-nitroaniline in acetone and touch it to the *TLC* plate at the origin.

After the solvent has evaporated from the spot, place the slide in the developing chamber. When the solvent front has reached the finish line, remove the slide and allow the solvent to evaporate. Locate the center of the spot and calculate the R_f-value. Repeat the procedure with *o*-nitroaniline.

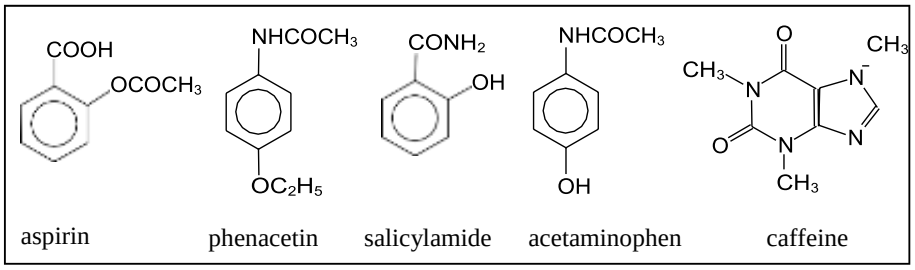
On a new slide, place the spots of *p*-nitroaniline and *o*-nitroanilineside by side at the origin so that the two compounds run parallel on the same slide. Calculate the R_f-value for each. Repeat using amixture of the two compounds in addition to the single compounds as references. Place one spot of the mixture in the middle and a spot of

each isomer on either side of the mixture. Note the resolution of the mixture into two spots and compare the R_f-values obtained for the mixture and for the individual compounds.

ANALYSIS OF ANALGESIC DRUGS BY TLC

In many non-prescription analgesic drugs such as Remin, Revacod, Revanin, Paracetamol, Excedrin etc.., the active ingredient is one or more of the compounds listed below. The constituents of an analgesic drug may be qualitatively determined by *TLC* using suitablereference samples. Introduce a small piece of an analgesic tablet intoa test tube, add 1 mL of methanol and stir well. Allow the insoluble material to settle and use the supernatant liquid for spotting on the *TLC* plate.

Make dilute methanolic solutions of the reference compounds and spot as many of them as possible on the same plate. Use a solvent mixture of benzene: ether: acetic acid (2:1:0.3) to develop the chromatograms. Examine the developed plates under ultraviolet light and determine the composition of the analgesic tablet.



aspirin phenacetin salicylamide acetaminophen caffeine

PAPER CHROMATOGRAPHIC ANALYSIS OF A DYE

In this experiment green food coloring (composed of a yellow and a blue component) will be examined by paper chromatography using a Petri dish (10 cm in diameter) as a developing chamber (figure 22).

Locate the center of a circular piece of filter paper by folding it in half. Make sure that the filter paper has a diameter slightly larger than that of the Petri dish. Using a melting point capillary tube with both sides open, apply a small spot of food coloring at the center of the paper.

Punch a small hole at the center and through it insert a small strip of filter paper rolled together to make a wick (Figure 22). Put 20-30 mL of the developing solvent (isopropyl alcohol - water 2:1) into the Petri disk and rest the filter paper on the rim of the dish making sure that the wick dips into the solvent.

Cover the paper with the Petri dish cover and leave the chromatogram to develop undisturbed for 10 minutes until the colors separate into distinctcircles. Remove the paper chromatogram and allow to air-dry.Calculate the R_f-values for the yellow and the blue dye.

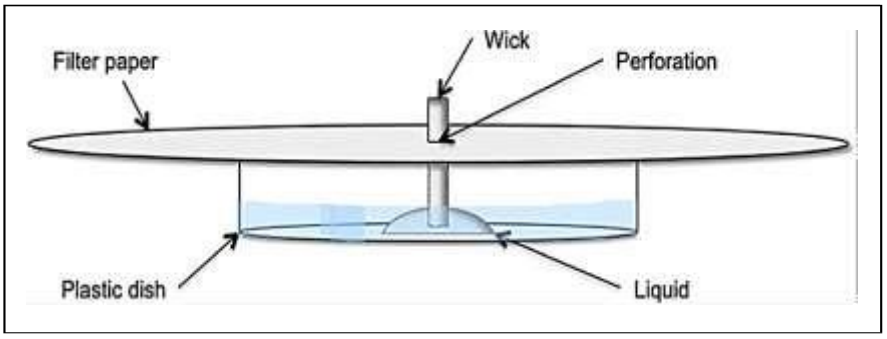
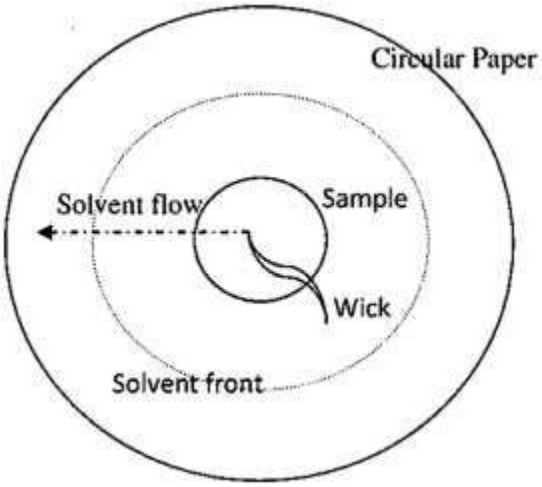


Figure 22. Paper chromatography using a Petri dish



Useful links

Thin Layer and Paper Chromatography
https://www.youtube.com/watch?v=w65S1dqrSAY

EXPERIMENT 7: BOILING POINTS AND DISTILLATION

Identity and Purity of Liquid Organic Compounds Distillation as a Method for the Separation of Liquids

INTRODUCTION

If a liquid is kept in a sealed container, equilibrium is eventually established between the liquid and gaseous molecules. The pressure exerted by these gaseous molecules is called the vapor pressure and it increases with increasing temperature of the liquid (Figure 7).

The boiling point of a liquid is defined as the temperature at which the vapor pressure of the liquid equals the external pressure (usually 1 atmosphere). It is also defined as the temperature at which vapor and liquidare in equilibrium at a given pressure.

The boiling point, like the melting point, is a physical constant and may be used to identify unknown organic liquids.

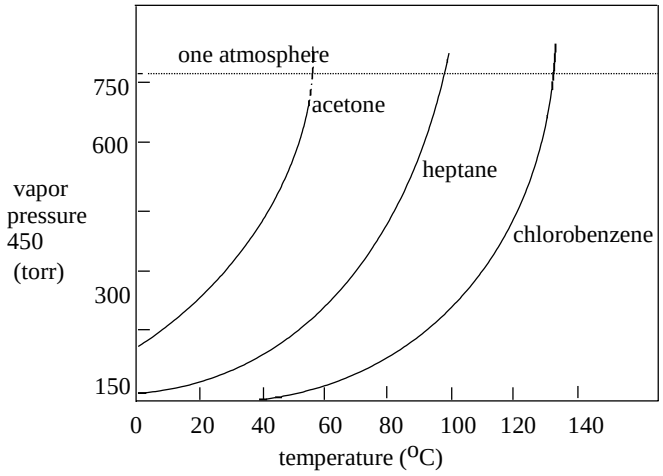


Figure 7. Vapor pressure-temperature curves.

Boiling Points of Pure Liquids. The boiling point of a pure liquid dependson the following variables:

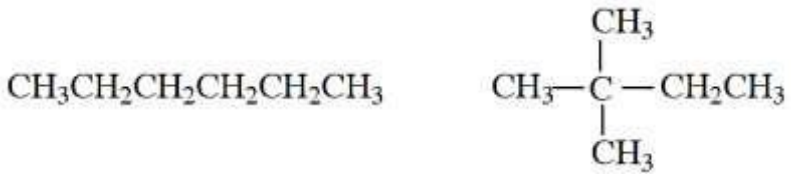
a) Nature of intermolecular attractive forces: H-bonding, dipole-dipole, orLondon forces.

$CH_3CH_2CH_2CH_2CH_2CH_2{-}OH$ bp 157 (H-Bonding,)

$CH_3CH_2CH_2{-}O{-}CH_2CH_2CH_3$ bp 57 (no H-bonding,)

b) Molar mass: boiling point increases with molar mass.

c) Shape of molecules: among isomeric compounds, having the same functional group, straight chain molecules have higher boiling points than the corresponding branched ones (less molecular surface area).



(bp 68) (bp 50)

Boiling Points of Solutions. For solutions, the boiling point is defined as the temperature at which the total vapor pressure is equal to the external (atmospheric) pressure. The effect of any solute, A, on the boiling point of a liquid B, will depend on the nature of A (Figure 8). If A is less volatile thanB, then the total vapor pressure of the solution is lower at any giventemperature, and its boiling point is higher than that of pure B (*e.g.*, a solution of sugar in water). If, on other hand, solute A is more volatile than B, then the total vapor pressure of the solution, at any given temperature, is higher and its boiling point is lower than that of pure B (*e.g.*, a solution of acetone and water).

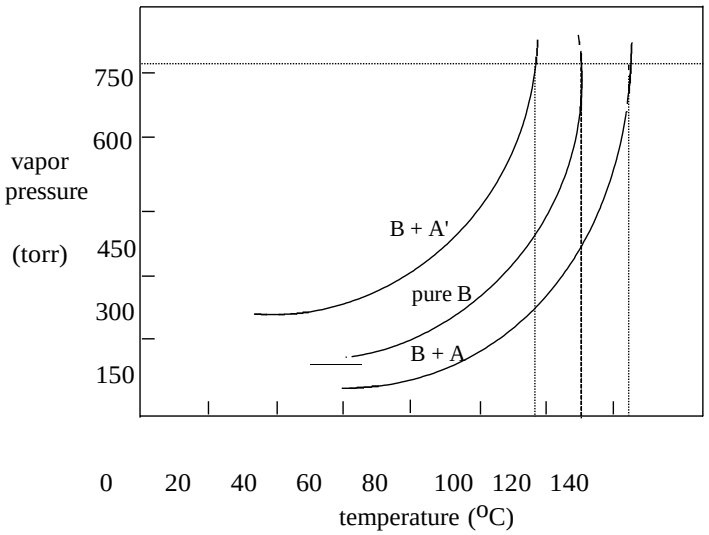


Figure 8. Vapor pressure-temperature diagram for a pure liquid and different solutions.

The behavior of a solution of two miscible liquids, A and B, is best explained by referring to Raoult's law which states that the partial pressure of liquid A (p_A) in a mixture is equal to the vapor pressure of pure liquid A (P^o_A) multiplied by the mole fraction of A in the mixture (X_A). The same applies to liquid B. Therefore:

$$p_A = X_A . P^o_A \qquad \text{and} \qquad p_B = X_B . P^o_B$$

From Dalton's law, the total vapor pressures of the solution (P_T) is the sumof the partial pressures of A and B:

$$P_T = p_A + p_B = X_A . P^o_A + X_B . P^o_B \qquad (X_A + X_B = 1)$$

A vapor pressure-composition diagram for the ideal two-component mixture is shown below (Figure 9).

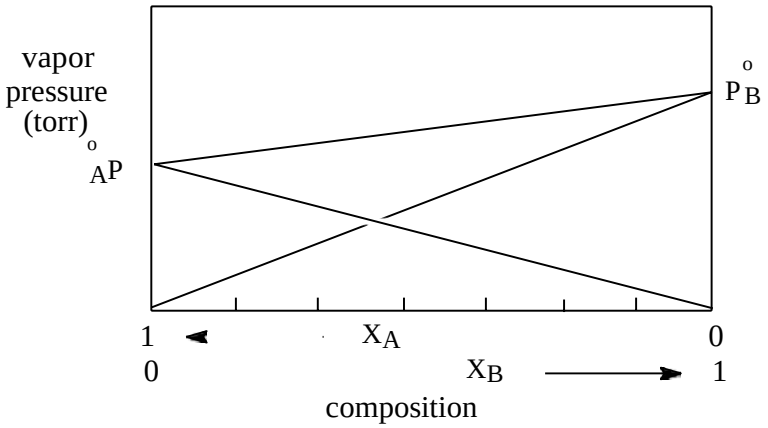


Figure 9. Vapor pressure-composition diagram for two miscible liquids

A solution of A and B will boil when the total vapor pressure (P_T) equals the external pressure. This occurs at a temperature which is intermediate between the boiling points of the two pure liquids (lower curve in Figure 10).

In order to understand the separation of a pair of miscible liquids A and B by simple and fractional distillation, a boiling point diagram is helpful (Figure 10).

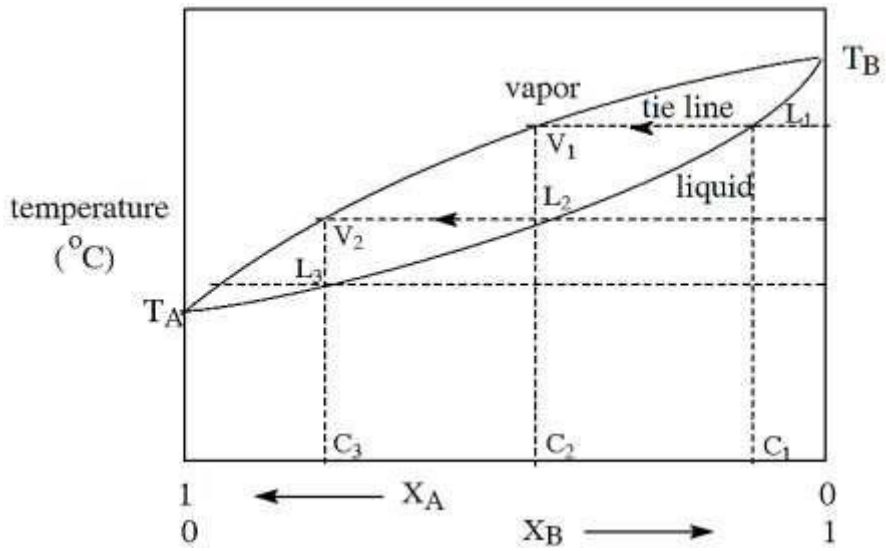


Figure 10. Temperature-composition diagram of two miscible liquids.

This diagram shows the temperature at which mixtures of A and B of various composition boil (lower curve). The composition of the vapor in equilibrium with the liquid is given by the tie line connecting the liquid and vapor curves. It is clear from Figure 10 that the vapor will always be richer than the liquid in the more volatile component. This makes sense, since the molecules of the component with the higher vapor pressure(more volatile) will escape more readily, and thus be in higher proportion in the vapor phase.

Simple and Fractional Distillation.

Distillation is the process of heating a liquid to its boiling point, condensing the vapor by cooling, and collecting the liquid distillate. It is a technique for the purification of liquids and for the separation of liquid mixtures. The principals involved in distillation (simple / fractional) may be explained by referring to Figure 10.

If a liquid mixture of A and B with composition C_1 ($X_A = 0.2$) is heated to boiling (L_1), then the vapor in equilibrium with it (V_1) will have the composition C_2 ($X_A = 0.4$), i.e., the vapor will contain more of the volatile component A, than the original liquid. If this vapor is condensed (L_2) and redistilled, the distillate ($V_2 \rightarrow L_3$) will be much

richer in A (composition C_3). As the distillation progresses, the mixture will gradually have less of the more volatile component and its boiling point will gradually rise. Consequently, the distillate will contain a continually decreasing proportion of the more volatile component until finally all has been collected and the less volatile component is left as a residue.

In practice, separation of a liquid mixture into its components by a single distillation (simple distillation) is possible only when the boiling points of the components are 80 degrees or more apart. For mixtures of liquids having boiling points much less than 80 degrees apart, separation can be achieved only by fractional distillation. Such a distillation is equivalent to several repeated simple distillations.

It uses a fractionating column which provides a large surface area for continuous heat exchange between the hot ascending vapor and the cooler descending liquid, thus resulting in a series of evaporations and condensations leading to separation of the two components.

Vacuum distillation is a technique for the distillation of high boiling liquids,and for compounds that decompose at atmospheric pressure. At the low pressures employed, those compounds distil at much lower temperatures.

GENERAL PROCEDURE

A typical set-up for simple and fractional distillation is given in Figures 11 and 12, respectively.

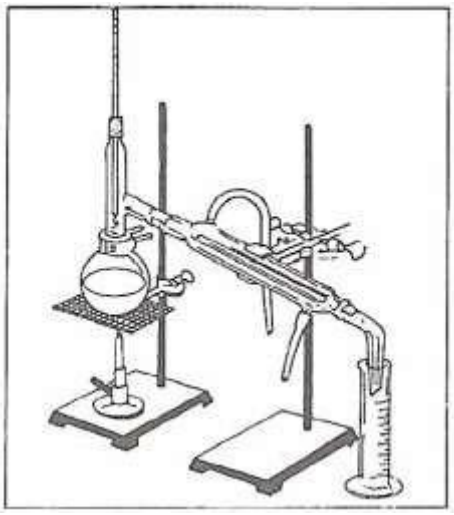


Figure 11. Simple distillation apparatus

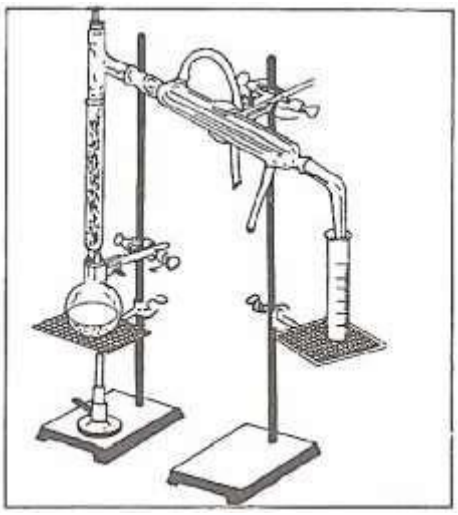


Figure 12. Fractional distillation apparatus.

When carrying out a distillation, the following practical points should beobserved:

a. The boiling flask should not be more than half full.

b. Boiling stones are added to the liquid to prevent bumping.

c. Each ground joint should be greased to ensure a completely sealed system.

d. Cooling water in the condenser should enter at the lower end and exit at the upper end. This ensures that the condenser jacket is always full of water.

e. The bulb of the thermometer should be below the opening of the side arm so as to measure the temperature at which liquid and vapor are in equilibrium.

f. Heat sources used depend on the nature of the liquid. A water bath is used to distil low-boiling and flammable liquids, while a burner with a wire gauze is used for higher boiling and less flammable liquids.

OBJECTIVES

1. Distilling a pure liquid (acetone) and determining its boiling point.
2. Separating a mixture of acetone and water by simple distillation.
3. Separating a mixture of acetone and water by fractional distillation.

Having done this experiment, you should be able to compare the efficiencyof each type of distillation.

EXPERIMENTAL

MATERIALS NEEDED	Glassware: Round-bottomed flasks (50 and 100 mL), distillation head, adapter, condenser, 2 Erlenmeyer flasks (50 mL), fractionating column, 2 stands, wiregauze, 2 clamps, 2 clamp holders, large beaker forwater bath, graduated cylinder (10 mL). Chemicals: 30 mL acetone, boiling stones, grease

DETERMINATION OF BOILING POINT OF PURE ACETONE

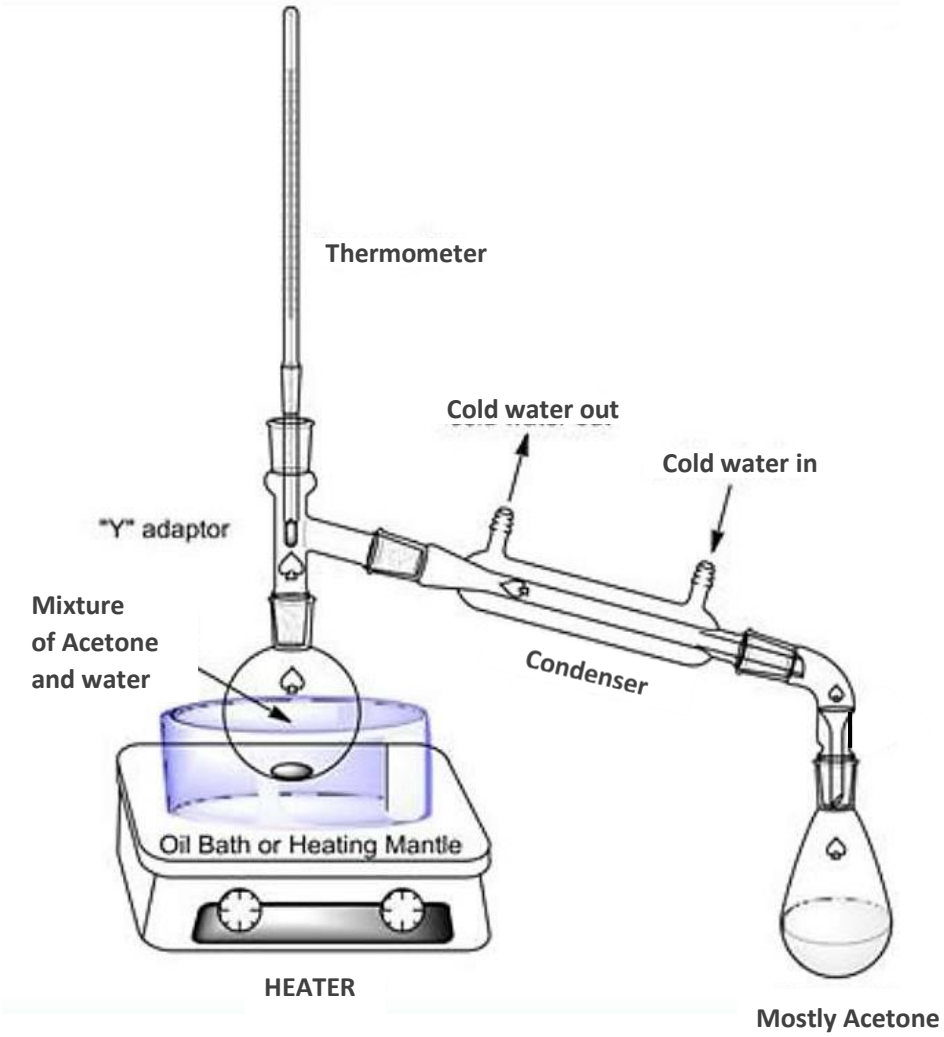
Arrange a simple distillation apparatus as shown in Figure 11 using a water bath as a heat source. Introduce about 20 mL of a liquid (e.g. acetone) and a few boiling stones in a 50 mL round-bottomed flask. Heat gently so that the distillate collects in the receiver drop by drop.Make surethat there is a drop of liquid hanging from the bulb of the thermometer to ensure that the thermometer is reading the correct boiling point. Absence of this drop indicates superheating. Wait until 1-2 mL of the distillate have been collected before recording the temperature. Continue the distillation until about 2 mL of residue are left in the distillation flask, and record the temperature again. Keep the acetone for the following part.

SEPARATION OF A MIXTURE

1. Simple Distillation. Make a mixture of two liquids (e.g. acetone-water) 20 mL each and pour it into a 100 mL round-bottomed flask. Carryout a simple distillation as before and collect five fractions in the following boiling ranges: 50-62, 62-72, 72-82, 82-95 plus the fifth fraction which is the residue. Measure the volume of each fraction and record the results in the report sheet.

2. Fractional Distillation. Combine the five fractions and pour into a 100 mL round-bottomed flask, attach the fractionating column and proceed as for simple distillation. Measure the volume of each fraction as before and record your results.

PROCEDURE SUMMARY DIAGRAM



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

EXPERIMENT 8: EXTRACTION

A Separation and Isolation Technique

INTRODUCTION

Extraction is the separation of a substance from a mixture by means of a solvent that preferentially dissolves that substance. If the substance is extracted from a solid phase, the process is called solid-liquid extraction, asin the isolation of caffeine from tea leaves by means of hot water.

Extraction of a substance from a liquid phase is called liquid-liquid extraction. The most common applications of this latter technique are:

a. The recovery of an organic product from a reaction mixture containing excess unreacted materials and by-products.
b. Isolation of an organic substance from its natural source, such as a plant.

Liquid-Liquid Extraction. This is the most common type of extraction. It involves shaking the liquid mixture with an immiscible solvent which preferentially dissolves the desired compound. On standing, the two immiscible phases (usually organic and aqueous) form two separate layers (upper and lower) that can be separated by means of a separatoryfunnel. The various solutes in the mixture distribute themselves between theorganic and aqueous phases according to their relative solubilities in each solvent. At equilibrium, the ratio of the concentration (C) or solubility (S)of the substance in the organic phase, (C_o or S_o) to that in the aqueous phase(C_w or S_w) is called the distribution coefficient (K_D).

$$K_D = \frac{C_o}{C_w} = \frac{S_o}{S_w}$$

A large distribution coefficient implies that the compound is much more soluble in the organic phase than in the aqueous one and, in this case, a single extraction suffices to remove the desired compound from the mixture. When K_D is small, it means that the compound distributes itself

more evenly in both phases, so that repeated extractions are required to recover such a compound from the aqueous mixture.

In general, it is more efficient to divide the total volume of extracting solvent over several extractions than to use the whole volume in a single extraction.

GENERAL EXPERIMENTAL CONSIDERATIONS

Choice of Solvent. A solvent used for extraction should have the following characteristics:

1. Immiscible with the liquid in which the solute is present.
2. Readily dissolve the solute to be extracted.
3. Extract little or none of the impurities and other compounds present in the mixture.
4. Non-flammable, nontoxic, cheap and easily removable from the solute after extraction (*i.e*., volatile).

Salting-out. Extraction of organic compounds from aqueous mixtures is usually improved by saturating the aqueous phase with a salt such as NaCl or Na_2CO_3. This phenomenon is called salting-out and 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.

Emulsions. In certain cases, the two immiscible phases do not separate cleanly into two distinct layers; instead, they form an emulsion which, once formed, is usually difficult to break. It is therefore advisable to prevent the formation of emulsions during extraction. This is best achieved by avoiding vigorous shaking of the layers whenever an emulsion is expected to form

(*e.g.*, when alkaline aqueous solutions are extracted with chloroform or dichloromethane). If an emulsion still forms one can often break it by:

1. Stirring the emulsified layer gently with a glass rod.
2. Saturating the aqueous layer with a salt.
3. Centrifugation.

Drying Agents. The organic phase often shows turbidity due to the presence of traces of water from the aqueous phase. Anhydrous $CaCl_2$, $MgSO_4$, or Na_2SO_4 may be used as drying agents which absorb the traces of water present in the organic phase. When dry, the organic phase becomes clear.

ACID-BASE EXTRACTION

Mixtures of organic acids and bases are commonly separated by acid-base extraction. Such compounds are converted to their salts by treatment with acid or base. Unlike the original compounds, the corresponding salts are usually soluble in water, thus enabling their transfer from the organic phase to the aqueous layer. After separation of the layers, the organic acid or base is recovered by neutralization of the aqueous layer. Since the acid or base is insoluble in water it precipitates out, and is collected by filtration. A flow diagram for such a separation is shown in Figure 16.

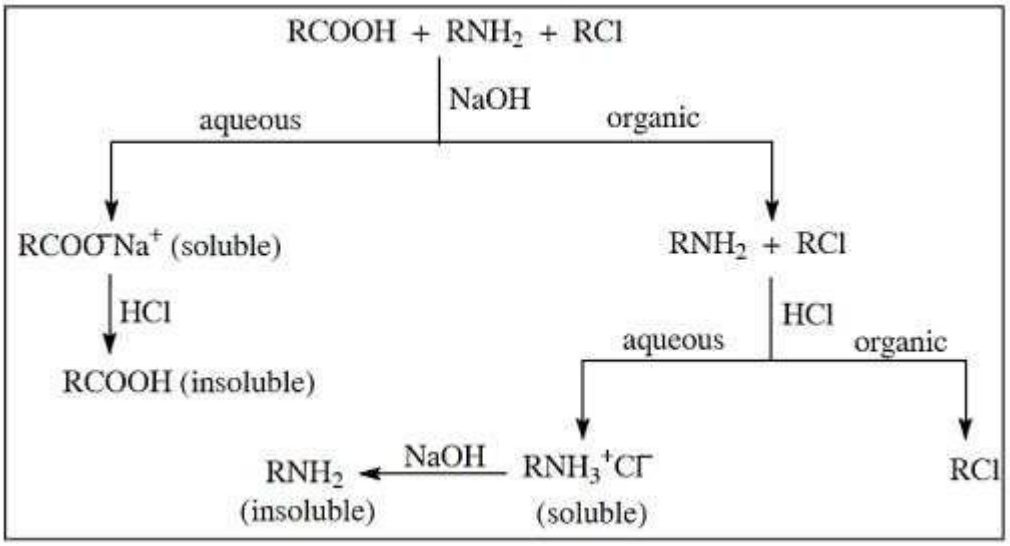


Figure 16. Flow chart for separation of a mixture by acid base extraction.

APPARATUS AND PROCEDURE

The set-up for an extraction using the separatory funnel is shown in Figure 17. The stopcock and stopper should be greased before use. The separatory funnel is held upside down in both hands, such that the stopper is firmly held in the left hand, while the right hand controls the stopcock (Figure 17). The funnel is shaken gently at the beginning and vented periodically through the stopcock to release excess pressure which builds up inside. Once there is no more pressure build-up in the funnel, shaking may be more vigorous to ensure goodextraction.

Figure 17. Correct position for holding a separatory funnel.

The mixture is left standing for some time until the two layers are well separated. The lower layer is drained through the stopcock, while the upper layer is poured through the top of the funnel into a separate container.

To determine whether a given layer is organic or aqueous, place a few drops of it on a watch glass containing a few milliliters of water and check the solubility. As a precaution, never discard any layer before you get your product.

OBJECTIVES

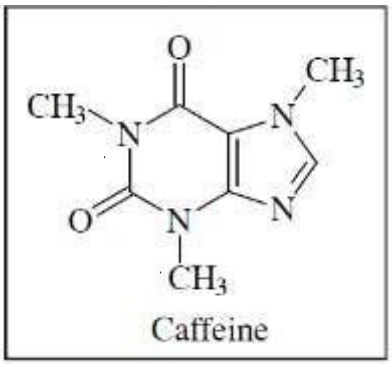
1. Isolating caffeine from tea leaves.
2. Separating a two-component mixture (acid and neutral).

EXPERIMENTAL

MATERIALS NEEDED	Glassware: Beaker (600 mL), 2 beakers (100 mL), 2 Erlenmeyer flasks (100 mL), stand, wire gauze, clamp, ring, clamp holder, graduated cylinder (10 mL), separatory funnel (100 mL), cheesecloth 20x20 cm. Chemicals: 15 g Tea leaves, 10 g sodium carbonate, 30 mL dichloromethane, 1.0 g anhydrous sodium sulfate, 1 g benzoic acid, 1 g p-dichlorobenzene, 25 mL ether, 40 mL of 10% sodium hydroxide, 20 mL concentrated hydrochloric acid, anhydrous calcium chloride, blue litmus paper.

➢ *EXTRACTION OF CAFFEINE FROM TEA LEAVES*

Caffeine is an organic compound present in the fruit and bark of some plants, as well as in tea leaves, coffee, cocoa and cola beans. The caffeine content in dried tea leaves is about 3-4%.



Caffeine

Caffeine belongs to a family of basic, nitrogen-containing, cyclic compounds called alkaloids. It is a mild stimulant and is used as such in many drugs and analgesics. The solubility of caffeine at room temperature is 2.2 g/100 mL of water and 18 g/100 mL of chloroform.

In this experiment, you will extract caffeine from tea leaves with hot water. This treatment also extracts tannins, a class of acidic organic compounds, also present in the leaves. Sodium carbonate is used to remove the acidic tannins by converting them to water-soluble salts.

Procedure. You will be provided with a large tea bag containing about 15 g dry tea leaves. Place the tea bag in a 600 mL beaker, add 10 g of sodium carbonate and 150 mL of water, and boil the mixture gently for 20 minutes. Cool the dark brown aqueous solution to room temperature and

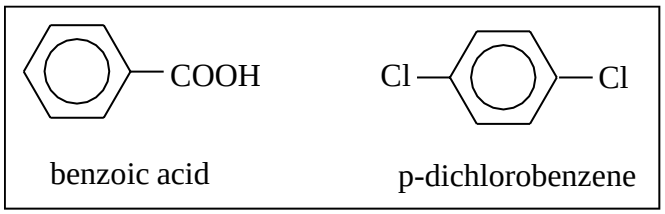
squeeze the tea bag to extract the liquid fully before discarding the bag.

Transfer the dark solution to a separatory funnel and extract twice with 15 mL portions of dichloromethane.

Avoid vigorous shaking of the funnel since emulsions may form readily; instead, swirl the funnel gently or turn it upside down several times. After each extraction drain the denser dichloromethane layer into a small flask. Dry the combined organic extracts with anhydrous sodium sulfate until the solution is clear. Decant the dichloromethane into a small beaker andevaporate to dryness over a water bath in the fume hood. Do not heat the residue any longer than necessary since caffeine decomposes readily. Weigh the crude caffeine and calculate its percentage in the tea leaves. Determine the melting point of your product.

➢ *SEPARATION OF A TWO COMPONENT MIXTURE*

In this part, a mixture of benzoic acid and *p*-dichlorobenzene (or any other neutral compound such as naphthalene, *p*-dimethoxybenzene or diethoxybenzene) will be separated into its components by means of extraction.



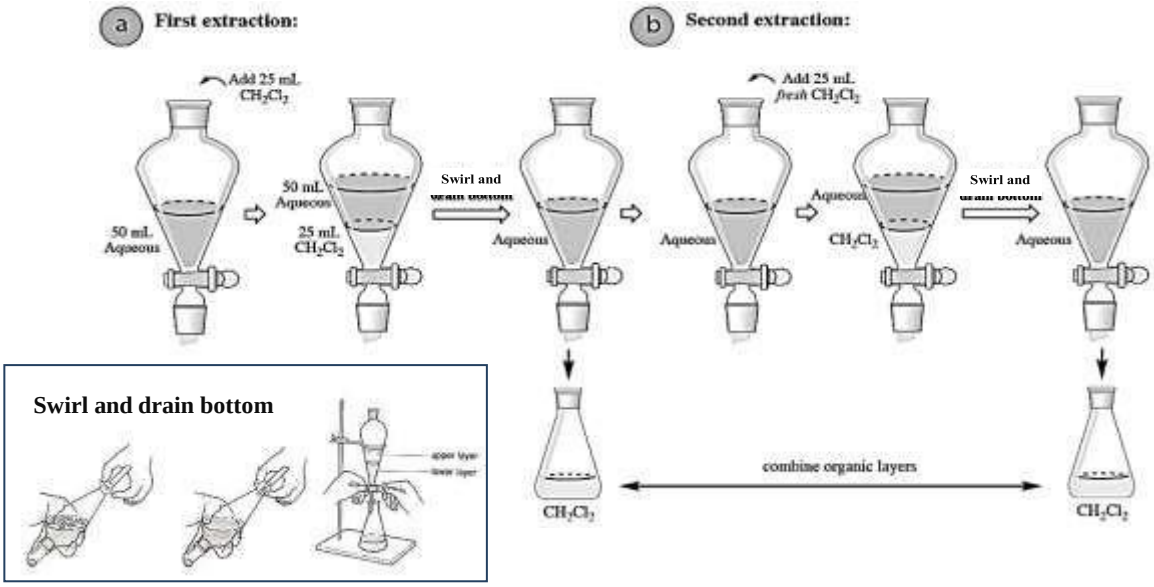
Procedure. Obtain from your instructor a 2.0 g sample of the two-component mixture, dissolve it in 25 mL of ether, and pour the solution into a 100 mL separatory funnel. To extract the benzoic acid from the mixture, shake the ether solution with 20 mL of 10% NaOH solution.

Draw off the lower (aqueous) layer into a flask and repeat extractionof the ether solution with another 20 mL of 10% NaOH solution followed by 10 mL of water. Combine the three aqueous extracts and cool in an ice

bath. Neutralize the cold aqueous phase by adding concentrated HCl until the solution is acid to blue litmus paper (about 8 mL). Collect the precipitated benzoic acid by suction filtration.

Dry the product, determine its weight and its melting point. Pour the remaining ether solution (which contains the neutral component) into a small flask and add enough anhydrous calcium chloride to remove any traces of water. Decant the dry ether solution into a small, weighedbeaker and evaporate the solvent in the fume hood (use a low temperature water bath since *p*-dichlorobenzene may sublime). Determine the weight of yourproduct.

PROCEDURE SUMMARY DIAGRAM



Useful links

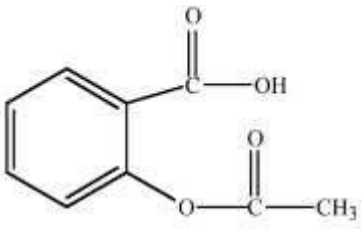
Extraction of Caffeine from tea leaves:
https://www.youtube.com/watch?v=5K1t4-1TDdo
How to use the separatory funnel:
https://www.youtube.com/watch?v=EFiFPoOzqtk&t=161s

EXPERIMENT 9: SYNTHESIS OF ASPIRIN (ACETYLSALICYLIC ACID)

Prepare aspirin from salicylic acid and acetic anhydride by esterification.

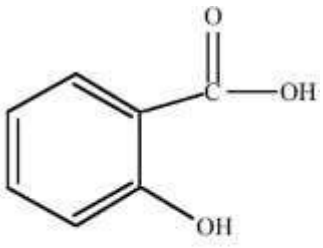
INTRODUCTION

Aspirin is an effective analgesic (pain reliever), antipyretic (fever reducer) and anti-inflammatoryagent and is one of the most widely used non- prescription drugs. The use of aspirin had its origin in the 18th century, when it was found that an extract from the bark of willow trees was useful in reducing pain and fever. The active ingredient in willow bark was later found to be salicylic acid.



Acetylsalicylic acid (aspirin)
$C_9H_8O_4$

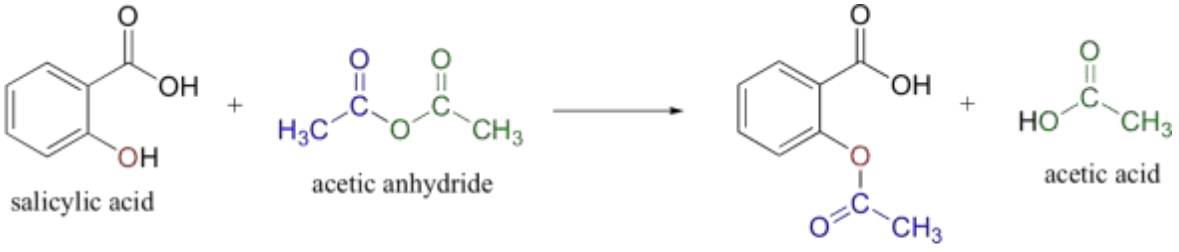
Salicylic acid (o-hydroxybenzoic acid) has been used in medicine for many years, either as the sodium salt or as an ester. The structure of salicylic acid is shown below. Salicylates are antipyretics; that is, they lower the body temperature of one who has a fever, but they have little effect if the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



Salicylic Acid
$C_7H_6O_3$

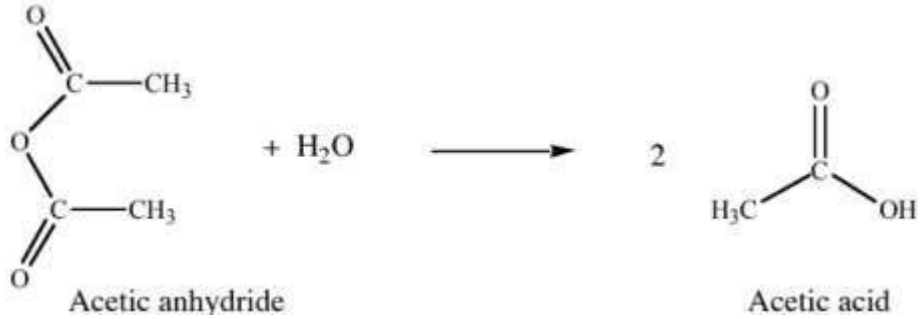
Unfortunately, sodium salicylate has an irritating effect on the stomach lining. This is why various esters are now used in place of the free acid or salt. These esters pass through the stomach largely unchanged but are hydrolyzed in the alkaline medium of the intestine, liberating the salicylic acid. In 1899, the Bayer Company in Germany patented a drug they called

aspirin, which was a modification of 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.



acetylsalicyic acid
(aspirin)

In this experiment, the salicylic acid is the limiting reactant, and the acetic anhydride is in excess. After the reaction heating period is over, the excess unreacted acetic anhydride will be destroyed by the addition of water to the mixture: water reacts with acetic anhydride to form 2 molecules of acetic acid, according to the reaction shown below. When the esterification reaction is complete, water will be added to the mixture. This will cause the precipitation of the acetylsalicylic acid and will react with any remaining acetic anhydride. The solid aspirin will be collected using vacuum filtration. Any other reaction ingredients that are soluble (this includes acetic acid, phosphoric acid, and water) will pass through the filter paper.



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.

The collected aspirin will be tested for its purity using ***$FeCl_3$ (aq)***. Iron (III) ion reacts with phenols to form ***a purple complex***. Salicylic acid contains a phenol group, but acetylsalicylic acid does not. Therefore, if you add ***$FeCl_3$*** to an aspirin sample and you see ***a purple color***, it means that there is still some salicylic acid present, and the sample is ***impure*.**

The aspirin collected will then be purified by ***recrystallization.*** In this purification method, the crude aspirin will be dissolved in a small amount of ***warm ethanol.*** Water will then be added, and the solution will be cooled slowly and then chilled. The acetylsalicylic acid will recrystallize, and the solid impurities (unreacted salicylic acid) should remain dissolved in the solution. The solid aspirin will again be collected using vacuum filtration and tested for purity. This aspirin should be purer than the original aspirin.
The final product will be dried and weighed, and ***the theoretical and percent yields*** will be calculated.

SAFETY PRECAUTIONS (CAUTION):

- ***Acetic anhydride*** is irritating to the nose and sinuses in the liquid or vapor state. Always keep this compound under the **fume hood** and avoid breathing the vapors. Avoid contact with skin and eyes.
- When handling concentrated ***sulfuric or phosphoric acid*** be careful to avoid contact with skin and clothing. Wear disposable gloves.
- The ***aspirin*** that you make in this lab is NOT pure enough to be taken internally! Do not ingest the aspirin!
- Avoid touching the chemicals.
- Wear your safety goggles.
- All waste must be placed in the organic waste containers.

EXPERIMENTAL (SYNTHESIS)

MATERIALS NEEDED	Glassware: 150 mL and 125 mL Erlenmeyer flask, Hotplate, 500 mL Beaker, Vacuum filtration set-up, Disposable dropper, Büchner funnel, Glass rod, melting apparatus, ice bath, watch glass, 3 test tubes Chemicals: Salicylic acid, Acetic anhydride, Concentrated sulfuric acid, ice water, 0.2M $FeCl_3$, ethanol

PROCEDURE

PART 1: Preparation of Aspirin

1. *Weigh out about **3 grams** of salicylic acid on a piece of weighing paper. To do this, first weigh a piece of weighing paper. Place some salicylic acid on the weighing paper and weigh again. Add or remove solid until you have about 3 grams of it on the paper. Record the mass of the weighing paper plus the solid. Subtract to determine the mass of the salicylic acid. Place this solid into a **125-mL** Erlenmeyer flask.*
2. *In the hood, measure out **6.0 mL** of acetic anhydride in a small, graduated cylinder and add it to the flask. From this point on, **keep your flask under the fume hood**, because it now contains acetic anhydride (the vapors of acetic anhydride are very irritating).*
3. *Add **10 drops** of concentrated (85%) phosphoric acid. This will be the catalyst for the reaction. Add a magnetic stirring bar to the flask.*
4. ***In the hood,** set up a ring stand and set a hot plate/magnetic stirrer on the base of the ring stand. Put some water in a glass crystallization dish and set this on the hot plate – this will be your hot water bath. Put your reaction flask in the water bath and secure it in place with a utility clamp attached to the ring stand. (See the picture)*

Reaction mixture setup

5. *Start heating the reaction and turn on the magnetic stirrer. Once the water bath starts boiling, start timing the reaction. When the mixture has been allowed to react at 100°C (the temperature of boiling water) for **15 minutes,** you can consider the reaction to be complete. During the heating*

time, put 3 mL of water in each of two test tubes and chill these two test tubes in an ice bath. (These tubes of cold water will be used to rinse the solid aspirin after you collect it on the filter paper.)

6. *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). Keep the mixture under the hood for a few more minutes – some of the acetic acid that is produced at this step will vaporize, and the vapor is irritating.*
7. *At this point, the flask no longer needs to be under the hood, since the acetic anhydride is now gone. Add ~35 mL of water to the flask and swirlit around to mix it. As the flask cools, crystals of aspirin will start to form. When you see crystals, chill the flask in an ice bath for 10 minutes.(Aspirin, like many other substances, is more soluble in hot water than in cold water. Therefore, to maximize the number of crystals, it is best to coolthe mixture as much as possible.) Use a stirring rod to break up any lumpsthat may form.*
8. *Collect the product by vacuum filtration, usinga 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.*

Vacuum Filtration Setup

9. *Weigh the dry solid to determine the yield and set aside a small amount of the crude aspirin– you will test its purity later. (You will need enough to test its melting point and to test its reactivity with FeCl3).*

PART 2: Recrystallization of Aspirin

10. *Transfer the rest of the crude aspirin to a 150-mL Erlenmeyer flask. Add **10 mL** of 95% ethanol and warm the flask on a hot plate until all the solid dissolves. Immediately remove the flask from the heat and slowly add **25 mL** of cold water. Crystals should form. Chill this solution in an ice-water bath and collect the crystals using vacuum filtration as you did in steps 8.*

11. *Carefully lift the filter paper with the crystals on it and transfer it on a clean watch glass. Leave this aspirin to completely dry then weigh the aspirin on a piece of weighing paper or a weighing boat. (You will need to scrape it off of the filter paper.)*

PART 3: Determination of Aspirin purity

12. *Using a **melting point apparatus**, determine the melting point of your crude aspirin and your recrystallized aspirin. (In order to get a meaningful result for the melting point determination, the solids must be dry.) The melting point of pure aspirin is 135°C, and the melting point of salicylic acid is 158°C. Comment on the purity of your aspirin based on its melting point.*
13. *For the **$FeCl_3$** test, the samples do not have to be dry. To do the test, get 3 test tubes. Place **1 mL** of ethanol and **2 drops of $FeCl_3$** solution in each tube. Add a few crystals of salicylic acid to one test tube. Add a few crystals of your crude aspirin product to the second tube. In the third tube, place a few crystals of the recrystallized aspirin. A purple color is indicative of the presence of the phenol group of salicylic acid. Record your observations.*

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

EXPERIMENT 10: SYNTHESIS OF PARACETAMOL (ACETAMINOPHEN)

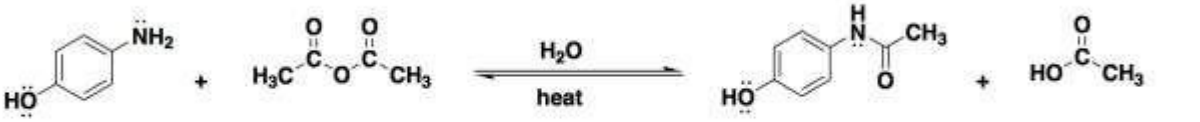
Prepare paracetamol by reacting p-aminophenol with acetic anhydride (acylation).

INTRODUCTION

Paracetamol (Acetaminophen) is an analgesic compound used to reduce pain. It also acts as antipyretics compound which is used to reduce fever. Another popular drug that does both is aspirin, whereas acetaminophen is often used by people who have unwanted, harmful side effects to aspirin.

The purpose of this experiment is to produce and purify acetaminophen by first reacting p-aminophenol with acetic anhydride to produce a crude acetaminophen. It is then purified by recrystallization using ethanol, the %yield will be calculated for pure product produced and its purity will be measured by determining its melting point and comparing it to the value listed in the literature.

The Reaction:



p-Aminophenol
MW 109.13 g/mol
MP 187-190 ^{0}C

Acetic anhydride
MW 102.09 g/mol
BP 140 ^{0}C
d 1.08 g/mL

p-Acetylaminophenol
(Acetaminophen)
MW 151.16 g/mol
MP 168-179 ^{0}C

Acetic acid
MW 60.05 g/mol
BP 119 ^{0}C
d 1.05 g/mL

Practical grade p-aminophenol contains impurities that must be removed at the beginning of the synthesis. We will use decolorizing charcoal (Norite) and water for that purpose. The sequence involves first solubilizing the water insoluble amine by converting it into a water-soluble amine hydrochloride, then decolorizing. In order to acylate the amine, it is necessary first to neutralize the amine hydrochloride which is accomplished with a sodium acetate buffer, immediately followed by addition of the

acylating agent. The neutralization converts the amine hydrochloride back to the free amine which can react with acetic anhydride.

SAFETY PRECAUTIONS (CAUTION):

- ***p-aminophenol*** is hazardous to skin.
- *Concentrated* **HCl** is caustic.

EXPERIMENTAL (SYNTHESIS)

MATERIALS NEEDED	Glassware: 150 mL and 125 mL Erlenmeyer flask, Hotplate, 500 mL Beaker, Vacuum filtration set-up, Disposable dropper, Büchner funnel, Glass rod, melting apparatus, ice bath, watch glass, 3 test tubes Chemicals: p-aminophenol, Acetic anhydride, Concentrated HCl, charcoal, sodium acetate trihydrate

PROCEDURE

PART 1: Preparation of Acetaminophen

1. *Weigh out about **2.1 g** of p-aminophenol into a 125-mL Erlenmeyer flask and add **35 mL** of water followed by **1.5 mL** of **concentrated hydrochloric acid**. Swirl the flask to dissolve the amine hydrochloride. Add a few more drops of concentrated acid if necessary to dissolve the amine completely as the hydrochloride (it will be difficult to determine since the solution is very dark).*
2. *Add **0.3-0.4 g** of decolorizing charcoal to the solution (this is much more than usual but necessary because the crude p-amino-phenol contains a lot of polymeric material), swirl the solution on a steam bath for 4-8 minutes and periodically check to see if the solution is decolorizing (it will be difficult to determine since the solution is dark).*
3. *Remove the charcoal by **gravity filtration** into another secured 125-mL Erlenmeyer flask using fluted filter paper while the solution is warm. The flask is secured to prevent tipping.*

4. *Rinse the filter paper with **1 mL** of water. If the charcoal comes through the filter paper it may be necessary to refilter or to use a filter aid, Celite. The filtrate may be clear or, more likely, a tea color. If the solution is a dark brown, add **0.1 g** of charcoal, heat on the steam bath for a few minutes and filter. The filtrate will darken with time!*
5. *While decolorizing the p-aminophenol, prepare a buffer solution by dissolving **2.5 g** of sodium acetate trihydrate in **7.5 mL** of water which will give 8.8 mL of solution. Clarify the solution by gravity filtration, if necessary.*
6. *Warm the filtered aqueous p-aminophenol hydrochloride solution on a steam bath, then add the buffer solution in one portion with swirling. Immediately add **2.0 mL** of acetic anhydride while continuing to swirl the solution. Continue heating on the steam bath while swirling vigorously for 10 minutes.*
7. *Cool the solution in an ice-water bath, stirring with a glass rod until the crude acetaminophen begins to crystallize. A little bit of rubbing/scratching with a glass rod near the surface often stimulates the crystallization.*
8. *After crystallization begins, allow the solution to sit in the ice bath for almost an hour. Filter your product using a Buchner funnel and the water aspirator or house vacuum line. Wash (rinse) the crystals once with a minimum amount of cold water (a few mL should suffice). Allow thecrystals to air dry under vacuum. Collect the crude crystalline product andweigh to the nearest tenth of a gram. Record the weight.*

PART 2: Recrystallization of Acetaminophen

9. *Recrystallize all but **100 mg** of your crude acetaminophen from water by first dissolving the solid in the minimum amount of hot (boiling) water. Do thiscarefully adding small amounts of hot water. You do not want to have excess water. Work on a steam bath to keep the solution hot.*
10. *Add another 2 mL of hot water. If there are no insoluble particles in the solution, you can allow it to cool slowly without having to first filter. If not, decant the hot solution or try to remove the particles with a spatula or Pasteur pipette while keeping the solution warm.*

11. *After crystallization begins, cool the solution more rapidly using an ice bath. When crystallization ceases (15 minutes), collect the crystals as before, rinsing once with a few mL of cold water, and air drying.*
12. *Record the weight of the dry, recrystallized acetaminophen and the % recovery from recrystallization (eg; if you obtain 0.75 g recrystallized product after starting with 1.0 g crude product you have 0.75/1.0 x 100 = 75% recovery. Record the percent theoretical yield of dry recrystallized product.*

PART 3: Determination of Acetaminophen purity

13. *Using a melting point apparatus, determine the melting point of your crude acetaminophen and compare it to the literature (lit mp 169-170.5).*

الجامعة الهاشمية
كلية العلوم الصيدلانية

ارشادات السلامة العامة للمختبرات

على جميع الطلاب مراعاة التعليمات التالية، لما لها من أهمية كبيرة على سلامة العامة في المختبرات:

في حال وجود اي حالة طارئة يرجي الاتصال بالأرقام التالية: 4666 ,4791, 4790.

1. عدم دخول المختبر قبل الوقت المحدد في البرنامج، وعد العمل في المختبر بدون وجود المشرف.
2. ارتداء مريول المختبر مع (tag name) قبل دخول المختبر، وارتداء والنظارات الواقية للعينين طيلة فترة تواجد في المختبر.
3. من اجل سلامتك الرجاء عدم ارتداء القبعات والملابس القصيرة كالشورت والتنورة والأحذية المكشوفة (مثل الصندل). وعدم ارتداء العدسات اللاصقة للعينين.
4. من اجل سلامتك يفضل ارتداء القفازات المخبرية أثناء عمل التجارب.
5. من اجل سلامتك على الطالب اعلام المدرس في حالته الصحية بشكل سري إذا كان يعاني من بعض الامراض التي تستدعي انتباه المدرسة كالأمراض المناعية او تناوله لأدوية تضعف جهاز المناعة او في حال كانت الطالبة حامل.
6. التعرف على الاماكن وجود الطفايات الحريق ومعرفة كيفية استخدامها وكذلك مكان وجود الدش وبطاني الحريق.
7. المحافظة على جو من المسؤولية والجد والنظام.
8. الامتناع عن الاكل والشرب والتدخين داخل المختبر.
9. عدم شم او تذوق المواد الكيمانية.
10. عدم الاسراف في استعمال المواد الكيميائية.
11. عدم تغير أماكن وجود المواد الكيميائية خصوصا المواد الموضوعة في خزانة الابخرة.
12. يجب اضافة الحامض الي الماء وليس العكس.
13. عدم فتح حنفية الغاز قبل اشعال عود الثقاب.
14. عدم جعل فوهة أنبوب الاختبار باتجاه الوجه، او باتجاه شخص اخر اثناء عمل التجارب.
15. يجب عدم تسخين المواد المتطايرة او القابلة للاشتعال على اللهب المباشر، وعدم رج الزجاجات التي تحتوي عليها.
16. يجب اجراء التفاعلات التي تنتج عنها غازات السامة في خزانة الابخرة.
17. يجب سكب كمية كافية من الماء بعد سكب الاحماض والقواعد في المغسلة.
18. التعامل مع الادوات الزجاجية بحذر لان جروحها عادة ما تكون بليغة، ووضع مادة التشحيم عند وصل أداتين ببعضها البعض.
19. عدم إلقاء النفايات الصلبة في المغاسل أو وضع فراشي التنظيف في المحاليل الحوامض أو القواعد.
20. عدم وضع الاغراض الشخصية والملابس على طاولة العمل في المختبر.
21. المحافظة على مكان العمل في المختبر نظيفا.
22. التأكد من اغلاق حنفيات الغاز والماء وغسل اليدين قبل المغادرة.

اللهم علمني ماينفعني
وانفعني بما علمتني
وزدني علما