PRACTICAL ORGANIC CHEMISTRY

4th Year Students

Chem436

A. LABORATORY'S RULES

1. Practicians must wear laboratory uniform in every laboratory activities including during the discussion time.
2. Practicians must prepare the journal, report, and other tasks before practice begin.
3. Practicians not allowed eating, drinking and smoking in laboratory.
4. Practicians not allowed entering assistant room, storage and the research laboratory without permission from the assistant.
5. Except journal and laboratory kit, other should not be placed on the practice table.
6. Practice is done in definite workday and practicians not allowed working outside these days without pennission from the assistant.
7. Practicians should pay attention to sign (bell sound) at the beginning and at the end of practice time.
8. The fill up of attendance list will be done every workday including in every laboratory activities.
9. Practicing not allowed leaving the laboratory during the work hour without pennission from the assistant. Leaving more than 15' should be with written permission.
10. During the experiment activities, all windows should be opened.
11. Practicing that have finished the practice should ask for the signature of assistant.
12. Practicing not allowed taking chemistry compound from storage; the assistant will prepare the chemistry compounds. Every chemistry compound bottle should be clean and dry.
13. Liquid reagents test must be applied by pipette
14. Solid reagents test must be applied by spatula.

15. Reagents should be placed on reagents table and not allowed to remove.
16. Every tool should be used according to its utility.
17. Laboratory kit contains boiling chips, pipette, spatula, vial, matches, and stirring stick.
18. Cleanness kit contains napkin, tube brush and detergent.
19. Each tool must be clean and dry before the storage.
20. Practicing not allowed keeping chemical compounds in the drawer except with the pemlission from assistant.
21. Before leaving the laboratory, fume hood, weight room, laboratory, floor, washing stand, table and seat should be clean and neat. Water, gas, electricity and windows should be shut down.
22. Journal contents are experiment's number, procedure, chemical and physical properties of matter that used in the experiment, mechanism reaction, chemical and physical properties of the reaction, theory, reference, and table of result.
23. Report and tasks must be wrote on A4 paper and covered. Cover contents are practician code, experiment's number, name, NPM, date of experiment, name of the assistant.
24. Each journal must have agreement from assistant otherwise practician not allowed to do the experiment.
25. Journal, report and tasks should be handed over before the experiment begins. Practicing who don't hand over the journal, report and tasks on time won't be allowed to do the experiment.
26. Report and tasks that have been handed over can't be taking back by practicing.
27. In everything related with Organic Chemistry Laboratory practicing are not allowed to cheat. Any violation related to this rule, will caused

restitution of practicing back to his/her own department and will not allowed to practice for 1 or 2 semester, or the case will be handle by university.

28. Repeated warning that caused by repeated violation will affected to practice point.
29. Practicing must obey the rules without any exception.

NOTES

1. Practicing can have a final exam after completed all experiments, report, and tasks, collect all journals and finished all problems of tools and tables.
2. Each tool that returns to the laboratory should be in good and clean condition.
3. Tables should be returned in clean and neat condition. And so as the laboratory.
4. Anything related to the laboratory's rules that have not been written will be arranged later

B. INTRODUCTION TO THE LABORATORY

B.1 Laboratory Safety

B.1.1 Safety Equipment

A set *of* safety rules is written on the inside behind cover *of* this book. Careful observation *of* these rules will help to prevent accidents in the laboratory. However, from time to time accidents can occur. Therefore, safety equipment is installed for his eventuality in the laboratory. Safety equipment should include:

- An eye wash
- a safety shower
- Fire extinguishers

- Hoods
- First-aid kit

B.1.1.1 Eye Wash

The eyewash is designed to flush irritating chemicals from the eyes. It should be capable of providing a stream of water for at least 15 minutes. In the event of an eye accident, you should proceed to the eyewash at once and wash the eye for at least 15 minutes. During this process, the eye should be kept open. The eyes are the most vulnerable part of the body. In the event of any eye injury notify the instructor at once. All eye injuries should be immediately examined by a health professional.

Never use the eyewash for anything other than its intended purpose.

B.1.1.2 Safety Shower

The safety shower is designed for two purposes, namely, to extinguish clothing fires and to provide whole bodies wash if a large chemical spill occurs.

i. Clothing Fires: If your clothing catches fire, perhaps the best rule is to fall and roll. Never run to a shower with your clothes on fire, it will only fan the flames. Use the shower afterwards to squelch any residual embers.

ii. Large Chemical Spills: Large chemical spills on clothing or exposed parts of the body should be removed at once using the deluge shower. Contaminate clothing should be removed, and the affected body areas should be thoroughly washed to remove any chemical traces. Do not reuse contaminated clothing until it has been completely washed! Serious and avoidable injuries have resulted from wearing contaminated clothing.

B.1.1.3 Fire Extinguishers

In the laboratory, you will sometimes work with flammable materials. For most purposes, ABC fire extinguishers are adequate to extinguish most fires. Several of these extinguishers should be placed in the laboratory. Learn their location. Your instructor will demonstrate their use before you begin to work in the laboratory.

ABC-type extinguishers (e.g., lithium aluminum hydride or sodium) cannot extinguish any materials. In these circumstances, appropriate extinguishing materials will be provided and their use demonstrated before the experiment begins.

B.1.1.4 Hoods

If possible, do all experiments in a hood. The ventilation system draws the fumes generated by an experiment away from the experimenter. The walls of the hood enclose the experiment on five sides. Therefore, if on the explosion or spill occurs, the experiment can be contained. A sliding transparent sash augments all these features. The sash should always be kept between the individual's eyes and the experiment. In a modern organic laboratory, chemical! The reactions are always done in a hood.

B.1.1.5 First Aid Kits

First aid kits are used for minor injuries. Report all cuts and bums to the instructor, and at his/her discretion, visit the school physician for further treatment.

i. Cuts: All cuts should be cleaned carefully to remove any chemical residue or broken glass before a Band-Aid is applied.
ii. Bums: Immediately flush bums under cold water for 15 to 20 minutes to reduce the magnitude of the injury. Do not rub the affected area or

pack it in ice. If a seemingly minor injury appears to be getting worse, consult a physician.

B.1.2 Personal Protective Equipment

Wearing the proper clothing during an experiment is as important to an individual's safety as any other safety feature of the laboratory. This protective clothing should include the following.

B.1.2.1 Safety Glasses

Safety glasses or goggles must be worn from the time you enter the laboratory until the time you leave the laboratory. There are no exceptions to this regulation!

Some individuals wear contact lenses rather than corrective glasses. This practice is not recommended in the laboratory. Soft contact lenses actually accumulate organic vapors and hold them against the eye. Serious injury can result. Hard (J.e.,glass) contact lenses are somewhat better, however, in the event of a splash, the material can be drawn under the lens by capillary action. If during an experiment any irritation of the eye occurs, remove the contact lenses, wash the eye at the eyewash, notify the instructor, and leave the laboratory. A physician should be consulted as soon as possible. Ordinary glasses are not safety glasses. In the event of a splash, they do not provide lateral protection. In additions, street glasses are frequently made of plastic, and they can be ruined easily by the solvents in the laboratory.

B.1.2.2 Lab Coats

Lab coats are designed to removed quickly in case of a fire or chemical spill. Lab coats provide protection against the minor spills and splashes of the laboratory. The coat should at least protect the upper body from the neck to the waist, and preferably, it should protect it to the

knees. The lab coat should be made of cotton, not synthetic materials. During a clothing fire, a synthetic material melts and becomes incorporated into the burn. Synthetic lab coats tend to dissolve in organic solvents, therefore, they are not as durable as cotton ones.

B.1.2.3 Shoes

Proper laboratory footwear completely covers the foot. It may be either a street shoe or a sneaker, but sandals or open-toed shoes should not be worn. It is advisable to have a pair of sneakers in your locker and to change into them before the lab period begins.

B.1.2.4 Gloves

If toxic or colored (dyes) substances are used in the laboratory, the instructor may advise wearing gloves. Disposable gloves are preferred, and they should be worn only for as long as necessary.

B.1.3 Good Laboratory Practice

1. Food or Drink in the Laboratory: Food and drink should not be brought into the laboratory. Packaged materials (including lunches) can absorb materials from the air. Food consumed in the laboratory can easily become contaminated.
2. Also, beverages can easily absorb toxic vapors from the air. Serious cases of poisoning have resulted from this type of occurrence.
3. Smoking: Cigarette smoking is banned from the laboratory for two important reasons.

I. As with food consumption, material from the air, hands, and desk can be carried to the mouth during smoking.

II. Cigarettes represent an unacceptable ignition hazard in the laboratory Cleanliness: During a laboratory experiment, you are exposed to a wide variety of chemicals. They can be retained in the hands, especially

under the fingernails. It is a good laboratory practice to make sure your hands are clean before you leave the laboratory.

B.1.4 Safe Handling of Laboratory Equipment

Heat Sources: Gas burners, heating mantles, and steam baths are used as heat sources in the laboratory. Each source has its appropriate use and precautions.

B.1.4.1 Gas Burners (i.e., Bunsen Burners)

These devices provide instant high temperature (up to 1100 °C). However, the open flame represents a serious ignition hazard. For This reason, gas burners should not be used near volatile and easily ignited materials Furthermore, glass should not be heated directly in an open flame because the concentrated heat may cause it to crack.

B.1.4.2 Bunsen Burners

Bunsen burners are used infrequently in student labs. However, when they are used, a ceramic heating pad should be placed between the flame and the flask. Never leave a lit burner unattended.

B.1.4.3 Heating Mantles

These devices heat more slowly than a gas burner, and thus reach a lower temperature. Heating mantles use electricity as a source of heat, therefore, they should be kept dry, when used they should be connected to power only through a ground fault interrupter.

B.1.4.4 Steam baths

Steam baths provide a convenient source of heat for temperatures ranging from room temperature to 95°C. Steam, however, has a high heat of vaporization, and live steam can cause severe scalding.

B.1.5 Electrical Equipment

Electrical equipment represents two significant hazards in the organic laboratory.

B.1.5.1 Ignition Hazard

Electrical motors spark frequently during operation. These sparks can cause fires or explosions. For this reason In areas where solvents are located, only spark-free motors should be used. The problem of sparking also exists with switches and plug connections. These devices should be on the outside of the hood where the concentration of solvent vapor is low and where the danger of igniting it is minimal.

B.1.5.2 Shock Hazard

Do not use poorly maintained equipment (e.g., frayed cords, loose plugs, etc.). Keep these devices dry and away from the puddles of water that may collect in a hood. All these devices should be connected through ground-fault interrupters to minimize shock hazards.

B.1.6 Waste Disposal

Every laboratory experiment generates by products (e.g., spent solvents, pot residues, etc.) that must be disposed of. The proper disposal of laboratory wastes is as much a part of the experiment as the synthesis and isolation of the product. Some general rules follow for disposing of chemical wastes.

B.1.6.1 Chemical Spills

Chemical spills should be cleaned up as soon as they occur. The residues from the clean up should be placed in a properly labeled container for later disposal. Do not attempt to clean up a large spill (i.e., 100 ml or more).

B.1.6.1.1 Solids

Sweep up the solids and dispose of them in an appropriately labeled container.

B.1.6.1.2 Liquids

Spilled solvents can be adsorbent on commercially available spill control materials such as vermiculite, clay, and so forth. Very small spills can be cleaned up with paper towel. Exercise car where the paper towel may react chemically with the spilled material (Le. oxidizing agents or reactive metals). Place the clean-up material Wet with the solvent, in a labeled waste bag for later disposal. Wear gloves when cleaning up the spill, unless you are absolutely certain that the spilled material is nontoxic. Neutralize spilled acids or bases and then rinse them down the drain.

B.1.6.1.3 Mercury

Broken thermometers are a common source of spilled mercury in the laboratory. Clean up such spills immediately. Amalgamating agents are commercially available to remove such spills completely. Place the spent clean-up material and any free mercury in a separate waste container reserved for the disposal of mercury wastes. Dusting the spill with elemental sulfur is not an adequate clean-up procedure.

B.1.6.1.4 Broken Glass

Broken laboratory equipment often produces fragments wit razor-sharp edges and needlepoint. Place this broken glassware in a specially labeled container not in the common trash.

WARNING: Do not combine residues from chemical spills unless specifically told by the instructor. Violent chemical reactions can result from these mixtures.

1. Chemical Reaction Wastes: Chemical reaction wastes are usually of known composition, and disposal can be planned ahead of time. Instructions for such disposal are found in the note column of each experiment. It is imperative that wastes be placed in the correct container. These containers should be used for only one experiment. The mixing of

waste stream from various experiments should be used for only one experiment. Only the instructor should do the mixing of the waste streams from various experiments. Violent chemical reactions can result from the careless mixing of such waste streams.

2. Spent Acids and Bases: Carefully neutralizes these materials and pour them down the drain. This procedure should be followed only if the resulting salt is non hazardous. Otherwise, the spent material should be placed in a container for disposal. Solids

a. Nonhazardous: If the materials are water soluble, dissolve them in water and flush them down the drain. Insoluble materials should be labeled and disposed of as nonhazardous solid waste.

b. Hazardous: Place these materials in a properly labeled container and save them for hazardous waste disposal.

Liquid Wastes, Waste-mixed Solvents: hazardous waste disposal, these materials should be placed in a container for

LABORATORY METHODS

1. General Directions to the Student.-Before beginning an experiment read through to the end the directions which are to be followed. Many mistakes which involve additional work can be prevented by understanding beforehand just what is to be done. The import of the experiment should be clear, and the chemical reactions involved at each step should be understood before the work is started. References are given in each experiment to the section in the author's textbook "The Principles of Organic Chemistry" in which the chemical reactions involved are discussed. Keep a clear and concise record of the laboratory work. The notes should be written as soon as the experiment has been performed, and care should be taken to have the original record, made

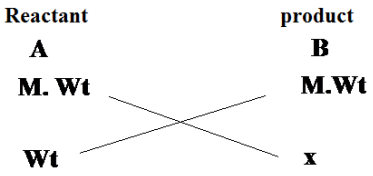
during the course of the experiment, of such a character that it serves as the permanent record of the work. Notes should not be taken on loose pieces of paper and afterward written out in the notebook; they should be written carefully in good English, and should state briefly what was done and what was observed. It is necessary for the student to recognize what the experiment is to teach-why he was asked to do it. If the work consists in the preparation of some compound the details for which are given in the laboratory guide, it is not advisable to take time to copy these details in the notebook. References to the pages in the book where the preparation is described should be given, and a statement made of the amounts of the substances used. If any unexpected difficulties arose, or if any improvement in the way of carrying out the preparation was used, these facts should be noted. Write equations for all reactions taking place in the experiment, and record the yield of the compound obtained. The substance should be put in a clean, dry, glass stopper bottle of appropriate size, and be labeled. The student's name, the name, weight, and the boiling-point or melting-point of the substance should be recorded on the label. The boiling-point or melting-point should be that observed by the student for the sample itself, and not the points recorded in the book. The student should use reasonable care in his manipulations.

He should endeavor to get as large a yield as possible of the product sought, but should use judgment as to whether it is advisable to spend a large amount of time to increase by a small amount the yield of the product. The processes should not be carried out in the manner used with a quantitative analysis-a few drops may be lost here and there if they form but a very small portion of the total amount formed, and their recovery entails the expenditure of much extra time. It is not meant by this that the student be careless; be should develop judgment as to the

relative value of a slightly higher yield of the product and the time required to obtain it.

2. Calculation of Yield.-The student should calculate in each preparation the percentage yield obtained. From the chemical equation for the reaction can be calculated the so-called theoretical yield. The percentage of thus obtained is called the percentage yield. The latter is never equal to 100 per cent for many reasons. It is often advisable to use an excess over the theoretical amount of one of the substances used in the preparation. The student should, before calculating the percentage yield obtained, determine whether an excess of one reagent has been employed.

When one substance used in a preparation is much more expensive than the rest, it is customary to take the substances in such amounts that the largest yield possible calculated from the more expensive substance is obtained. For example, preparations involving the use of iodine are so carried out that the largest amount of the halogen possible is obtained in the substance prepared. In this case the test of the skill with which the preparation is carried out is determined by this fact; the percentage yield should be calculated, accordingly, from the weight of iodine used.



$$\text{x (theortical yield)} = \frac{\text{Wt (A) x M. Wt (B)}}{\text{M. Wt (A)}}$$

$$\%\ \text{yield} = \frac{experimental\ yeild}{theortical\ yeild}\ x\ 100$$

3. CRYSTALLIZATION

The steps involved in recrystallization may be defined as follows:

1. Select the solvent.
2. Dissolve the material in the hot solvent.
3. Filter the solution if necessary.
4. Allow crystallization to take place.
5. Collect the crystals.
6. Wash the crystals.
7. Dry the crystals.

When an organic compound has been prepared it must be purified from the by-products which are formed at the same time. In the case of solid substances crystallization is ordinarily used for this purpose, although with certain compounds purification can be more readily effected by sublimation or distillation, processes which are described below.

Choice of Solvent.-The separation of two substances by means of crystallization is based on the fact that they are present in the mixture to be separated into its constituents in different amounts, or on the fact that the two substances possess different solubilities in the liquid used as a solvent. When it is desired to purify a substance by crystallization a solvent should be selected, if possible, in which the impurity is readily soluble, and in which the substance sought is more or less difficultly soluble. Purification is effected most easily when the substance to be purified is appreciably soluble in the hot solvent, and much less soluble in it when cold. If the two conditions stated above can be combined-and this is possible in many cases-purification is readily accomplished. The solvents most commonly used in crystallization are water, alcohol, ether, benzene, petroleum ether, ligroin, carbon bisulphide, chloroform, acetone, and glacial acetic acid. In certain cases hydrochloric acid, carbon tetrachloride, ethyl acetate, toluene, and nitrobenzene have been found of

particular value as solvents. In order to crystallize a compound the solubility of which is not known, preliminary tests should be made with the solvents enumerated above; about 0.1 gram or less of the substance should be used in each test. The solid is placed in a small test-tube, and the solvent is added a drop at a time and the tube is shaken. After the addition of about 1 cc. of the liquid, if the substance has not dissolved, the tube should be heated until the liquid boils. If the substance does not dissolve, more liquid should be added in small quantities until solution occurs. If a very large amount of the liquid is required for solution, or the substance proves insoluble, another solvent must be used. When solution takes place the tube is cooled by running water. If the substance separates, it is redissolved by heating, and the contents set aside to cool slowly, when crystals will probably form. If the substance does not separate to a considerable degree when the hot solution is cooled, similar tests should be made with other liquids. If none of the solvents can be used in this way, either the substance must be obtained by spontaneous evaporation, or a mixture of liquids must be used-a method described below.

If the compound is to be crystallized by spontaneous evaporation, cold saturated solutions, prepared by dissolving about 0.1gram or less of the substance in a number of solvents, are poured onto watch-glasses and left to evaporate slowly.

4. EXTRACTION

4.1 Introduction

There are two main application of extraction on organic laboratory: (1) the separation and isolation of substances from mixtures of solids,

typically those that occur in nature and (2) the selective isolation of substances from solutions of mixtures that arise in synthetic chemistry.

Extraction of Solids. Examples of extractions of solid mixtures are the extraction of alkaloids from leaves and bark, flavoring extracts from seeds, perfume essence from flowers, and sugar from sugar cane. Solvents commonly used for this purpose are ether, dichloromethane, chloroform, acetone, various alcohols, and water. In the laboratory, a common form of apparatus for continuous extraction of solids by means of volatile solvents is the Soxhlet extractor (Figure 1.1), meanwhile discontinuous one is Maceration extractor.

Extraction of Solutions. A more common application of extraction is in "liquid-liquid" extraction, which is used to isolate a substance dissolved in one solvent by shaking the solution another solvent, immiscible with the first, in a separatory funnel and continuous extractors (Figure 1.1).

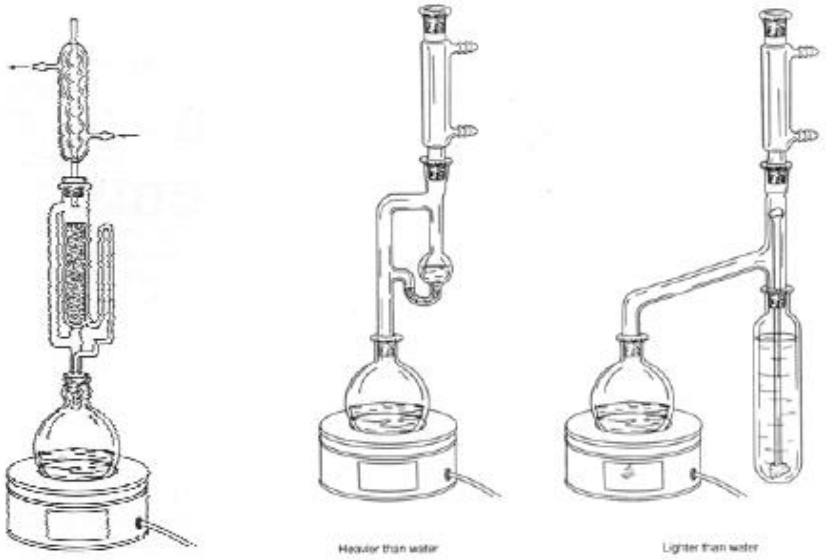


Figure 1.1 Soxhlet Extractor and Continuous Extractor Assembly

In this course, the term "extraction" refers to the process whereby a component in a mixture is transferred into another solvent phase: The operation involves shaking an immiscible pair of liquids, whereby a

solute passes from one liquid to the other. Commonly, one of the liquids will be an aqueous (water) solution and the other, an organic solvent (e.g.diethyl ether or CH_2CI_2) or a solution involving an organic solvent).

Before using the separating funnel, apply a thin coat of grease or, when dichloromethane is used as solvent, a film of water, to the glass tap (DO NOT grease Teflon taps). Check for leaks by adding a small volume of the solvent to be used to the separating funnel with the tap inserted and closed.

4.2 Using the separating funnel (Figure 1.2):

1. Close the tap.
2. With the separating funnel supported in a ring clamp, add the two liquid phases and insert the stopper.
3. Remove funnel from ring clamp and, holding the stopper firmly with the palm of one hand, invert the funnel and release pressure through the tap.
4. After closing the tap, shake the funnel several times whilst holding both the stopper and the tap.
5. At frequent intervals during an extraction, release excess pressure through the tap. Take care not to point the stem, at your neighbor during this operation.
6. When the extraction is completed, replace the separating funnel in the ring clamp, remove the stopper and allow the phases to settle.
7. Drain the lower phase into an appropriate container, and then pour out the upper phase through the neck of the funnel into another container.

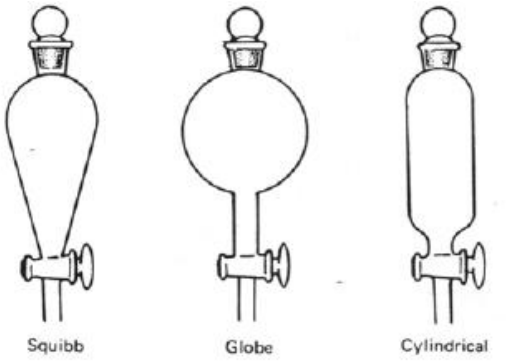


Figure 1.2 Extraction Funnel

Extraction is based on the differential solubility of compounds in various solvents. The solvents (used in pairs) for extraction must be immiscible. Water is frequently used as one of the pair because its solvent ability can be dramatically altered by changing its pH during the course of an extraction sequence. It has the further advantage of being insoluble (immiscible) in most organic solvents.

In a typical extraction, a mixture of two compounds is dissolved one solvent placed in a separator funnel and then shaken (extracted) with a second, immiscible solvent. Ideally, one of the compounds in the mixture will be preferentially extracted into the new solvent leaving the other compound behind in the original solvent. The new solvent can then be separated from its immiscible partner. Solvent removal from the two layers will yield two separate compounds in a reasonably pure state.

4.3 Procedure

In a 500 mL Erlenmeyer flask place 30 g of ordinary dry tea, 300 mL of water and 15 g of powdered calcium carbonate. After boiling the mixture gently with occasional swirling for 20 minutes, add 5 g of Celite or other filter aid filter the hot mixture on a Buchner funnel and press the filter cake firmly with a large cork to obtain as much as possible of the liquid. Cool the aqueous extract to 15-20°C, transfer it to a separator

funnel and extract the caffeine with three successive 25 mL portions of methylene chloride (Chloroform).

Pour the combine chloroform extract into an Erlenmeyer flask and add 0,5 g sodium sulphate. Decant the chloroform solution from sodium sulfate indicant flask. Evaporate the solvent on the steam bath. Scrape the dry product from the flask and weight the crude caffeine.

I.1.4 Question

1. Define Polarity!!!

2. What are some of advantages and disadvantages of ether as an extraction solvent?

3. Why is it inadvisable to filter a hot solution of chloroform by suction filtration?

4. Boiling chips should never be added to a liquid that is near its boiling point. Why?

5. The distribution coefficient for a certain organic compound between ether and water is 1. Show the amount of the compound extracted from

II.2 MELTING POINTS

II.2.1 Introduction

The Theory of Melting-Point Depression. The molecules of a crystal are aligned in regular patterns. As the temperature of the crystal is raised, the increasing vibrational motions of the molecules make it more difficult for the regularity to be preserved. Eventually a temperature is reached (the melting temperature or melting point) at which the pattern is broken and the solid melts and turns into a disordered liquid. A pure crystalline substance usually possesses a sharp melting point; i.e., it melts

completely over a very small temperature range (in practice, not more than 0.5-1.0°). The presence of even small amounts of impurities soluble in the molten compound will usually produce a marked depression of the temperature at which melting begins as well as a smaller depression at which the last crystal disappears, resulting in a large increase in the melting-point range. The amount of lowering of the final temperature at which the last crystal disappears is called the melting-point depression.

The situation is entirely different in the solid phase. Here the original substance and the impurities usually form a heterogeneous mixture of crystals of each substance. The crystals are so intimately mixed that it is impractical to try to separate them, yet at a molecular level, they behave as though they were independent of each other. As a consequence, the vapor pressure of the solid substance is essentially unaltered by the presence of impurities, which may be thousands of angstroms (Å) away. This behavior is shown in Figure 2.1 as a vapor pressure curve for the solid that is independent of the presence of impurities. Since by definition the temperature at which melting ends is the temperature at which the solid and melt have the same vapor pressure (the point of intersection of the solid and liquid curves), that temperature will be depressed by the presence of an impurity. The greater the amount of impurity (at least up to a point, to be described later), the larger is the melting-point depression.

II.2.2 Apparatus for Melting-Point Determination

One common method for determining melting points is to use the Thiele apparatus illustrated in Figure 2.2. The sample is contained in a capillary tube. The thermometer is inserted into a drilled cork or rubber stopper and supported by means of a buret clamp. The thermometer

position is adjusted so that it is centered vertically in the Thiele tube. with the upper end of the mercury bulb about 1 cm below the side arm. The capillary tubes usually come with one end sealed. If yours do not, a tube can be sealed by touching one end to a small, hot flame.

A small amount of the material to be examined (0.05 g is sample) is pulverized finely by crushing it with a spatula or knife blade on a piece of smooth, hard paper or a watch glass. The crushed material is collected into a small mound, and the open end of the capillary tube is thrust into it. The tube is then inverted, and the solid is shaken down into the tube by tapping the lower end on the desk top; alternatively, the solid may be forced down by dropping the tube (sealed end downward) through a 2-ft length of ordinary glass tubing onto the desk top. Further increments of the sample are introduced in the same way, until the material forms a compact column 3-5 mm high at the bottom of the tube after repeated tapping. It is essential that the material be pulverized finely and packed tightly to ensure rapid transfer of heat throughout the sample.

Although the capillary tube will usually adhere to the thermometer by capillary action of a thin film of bath liquid, it should be attached more firmly by means of a thin slice of rubber tubing or a small rubber band. The tube should be adjusted so that the sample is just alongside the mercury bulb of the thermometer, and the rubber fastening should be above the level of the bath liquid (to avoid softening of the rubber and discoloration of the bath).

The Thiele tube is heated at its lowest point. The resulting convection currents will circulate the oil in a counterclockwise direction if the apparatus is set up as shown in Figure 2.2. The tube may be heated at a fairly rapid rate until the bath temperature approaches within 15-20° of the melting point (roughly determined in a preliminary trial, if necessary).

Heating is then continued with a very small flame, adjusted so that the temperature rises slowly and regularly, at a rate of about 2°/min. The observed melting point is reported as the temperature range beginning with the thermometer reading when the substance starts to liquefy and ending with the reading when the melt becomes clear. The temperature readings and any other observations are recorded at once in the notebook.

Ideally, the observed temperature readings should be corrected for the exposure of the mercury column to atmospheric cooling, but usually this stem correction is omitted, even in research. Whether or not this correction has been made should be indicated by a notation such as, "mp 172-173° (uncorrection)" or "mp 172-173° (correction)".

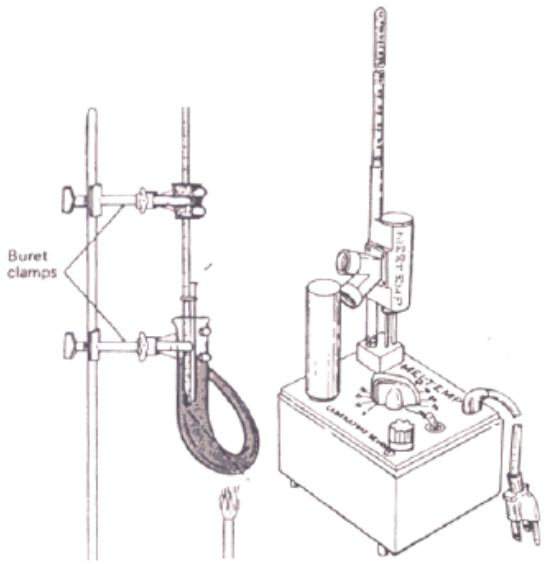


Figure 2.2 Melting-Point Apparatus

II.2.3 Procedure

The components must be powdered finely and each sample mixed very thoroughly, on a piece of smooth hard paper or a watch glass, by means of a clean spatula or knife blade. Introduce caffeine crystal (product of previously experiment) into a melting point tube marked appropriately for

identification and determine the melting point by the following procedure. Apply heat at a moderate rate until the bath liquid is within 15-20° of the melting point (for this pair of compounds to about 100°; when necessary, make a rough preliminary determination). Continue the heating so that the temperature rises slowly and at a uniform rate (about 2°/ min). Observe carefully the sample in the melting-point tube and the thermometer reading. Record as the observed melting-point the range between the thermometer reading when the sample starts to liquefy and that when the melt is clear. Note also if the sample undergoes preliminary fusing together (sintering) or discoloration, melts sharply or slowly over a wide range, and so on. Repeat this process for each of the other samples, but be sure to allow the bath to cool below 100° before the next sample is inserted into the bath. If care is taken, it is possible to observe the melting behavior of all three samples at once.

Melting-point tubes are discarded into the waste crock (not into the sink) after a single use. Record the observed melting points directly in your note book and compare with literature.

Experiment: Determine the melting point of the following compounds

1-Benzoic acid 2- Salicylic acid

3- A mixture of benzoic and salicylic acid

CHROMATOGRAPHY

1. Introduction

Chromatography is an exceptionally versatile separation technique that in one or more of its numerous forms is used by just about every research chemist. In any chromatographic separation there are two phases (solid, liquid, or gas); these move relative to each other while maintaining intimate contact. The sample is introduced into the moving phase, and the

sample components distribute themselves between the stationary phase and the mobile one. The components spend different amounts of time in the stationary phase as determined by the structures of the components and the two phases. If one component spends a larger fraction of the time in the mobile phase, it will move along quickly; if it spends more time in the stationary phase it will move slowly. As with extraction, the relative amounts in the two phases is determined by a distribution coefficient, which is related to the same structural factors that control solubility. The degree of separation of a mixture is controlled by the differences in the distribution coefficient of the components.

The first chromatographic technique to be considered is liquid-solid chromatography. The stationary phase is made up of very small particles of solid packed in a column (hence, the common name column chromatography), and the mobile phase is a liquid that percolates through the column and past the surfaces of the solid particles. Solid surfaces adsorb thin layers of foreign molecules as a result of electrostatic and van der Waals forces. Since adsorption strengths differ with the character of the solid surface, a properly chosen solid may adsorb selectively one component of a mixture.

A common variation of liquid-solid chromatography is the use of a thin film of solid (mixed with a binder such as plaster of paris) on a sheet of glass or plastic. The solution is added as a spot at the bottom of the plate and the plate is dipped vertically into a shallow layer of solvent, which ascends (against gravity) by capillary action and moves the solutes with it. Thin-layer chromatography is restricted to very small samples.

1.2 Laboratory Practice

1.2.1 Thin-Layer Chromatography

A convenient type of commercial TLC plate comes as 20x20-cm sheets consisting of a 100-μm layer of adsorbent bound to a 200 μm sheet of plastic. With reasonable care these can be cut with ordinary (sharp) scissors or a paper cutter into 2x 10-cm strips suitable for analytical separations.

A convenient developing chamber for TLC plates can be prepared from an ordinary wide-mouthed, screw-cap bottle. The inside of the bottle is lined with a folded circle of filter paper, which acts as a wick to transfer the developing solvent to the upper portions of the chamber. As shown in Figure 3.1, the circle of filter paper is folded to form a rectangle, which is inserted in the wide- mouthed bottle with the folds against the walls of the bottle. The size of filter paper should be chosen so that the folded paper comes close to the top of the bottle, but there must be a gap between the paper and the top of the bottle so that the approach of the solvent front to the upper line on the plate can be seen without removing the cap. Sufficient solvent is added to the bottle to saturate the liner and leave a layer 2-4 mm deep at its shallowest point. The spotted end of the plate is centered in the bottom of the chamber with its upper edge leaning against the wall; the spotted face of the plate should face the gap in the filter paper lining so that the rising spots will be visible. The bottle is capped and gently set aside until the rising solvent front has just reached the upper line. The plate is then removed and the solvent is allowed to evaporate from it. Since the solvent vapors may be harmful, it is good practice to do the evaporation in a hood.

If one or more of the components to be identified is colorless, a convenient visualization technique is to place the plate in another screw-cap bottle containing a few crystals of iodine mixed with about. a table

spoon of sand which serves to disperse the iodine. The capped bottle is held horizontally and rotated for a few seconds to bring the plate in contact with the iodine and sand mixture. Iodine vapor is absorbed on the plate wherever there is a concentration of organic material and produces a brown spot (commercial plastic plates do not absorb a significant amount of iodine under these conditions; some organic compounds also do not absorb iodine vapor). After the color has developed, the plate is removed and a circle penciled around each spot. On exposure to air, the brown iodine spots gradually evaporate.

Another method for visualization, which works with compounds that absorb ultraviolet (UV) light, is to use thin-layer plates that have been impregnated with a fluorescent dye. When the plate is exposed to UV light, the dye will glow; if the organic compound absorbs UV light, it will preve the light from reaching the dye and make a dark spot at that point against the glowing background. While the plate is glowing, the dark spots should be circled carefully with a pencil so that their positions can be measured and recorded after the ultraviolet light has been withdrawn. When handling the UV lamp, take care to avoid looking directly at the light source because unfiltered UV light could damage your eyes.

1.2.2 Column Chromatography

A simple apparatus for liquid-solid column chromatography is a glass tube that has been constricted at one end (Figure 3.2). For separation of 0.1- to 0.5-g samples, a convenient tube size is 60 cm of 15-mm diameter tubing. This size will hold about 50 g of solid support and give a 100: 1 ratio of packing to sample. Other sample sizes may be used with appropriately scaled apparatus.

1.2.3 Pencil Columns

When you are working with only a few milligrams of sample, the column just described is much too large. TLC could be used, but an interesting option is to do column chromatography with a Pasteur pipet for the column. A small wad of glass wool is pushed into the constricted neck of the pipet, followed by enough adsorbent to produce a column about 3-5 cm high. The sample and solvent are added in the way described previously. Frequently, the solvent will not flow through the column on its own and must be forced through (slowly) with a rubber bulb.

1.3 Procedure

1.3.1 Separation of Ink Pigments by Thin-Layer Chromatography

Prepare two 2x 10-cm thin-layer plates by drawing two horizontal pencil lines across each plate 7 mm from each end. On the bottom line of each plate, about 5 mm from the left-hand edge, make a single, sharp dot of ink from a black Flair pen; in the center of the line make a second spot about 2 mm in diameter by momentarily holding the pen tip on the plate; on the right-hand side of the line, about 5 mm from the edge, make a third spot about 5 mm in diameter. Add sufficient acetone to an 8-oz, wide-mouth, screw-cap bottle containing a filter paper lining until a 3-mm-deep layer is produced. Center one of the spotted plates in the bottle with the upper edge leaning against the side and screw the cap tightly onto the bottle. When the solvent front reaches the upper pencil line, remove the plate and allow the solvent to evaporate. While the first plate is developing, repeat the process with the other plate and a second 8-oz bottle using a 1 : 1 mixture of acetone and 95% ethanol.

Determine and record the Rf values for all of the colored spots. Determine which spots, if any, are UV active. Determine which spots are stained by I2. Make a sketch of the two plates in your laboratory

notebook showing the location and shape of the spots with side notes on their response to UV and I_2.

The experiment can be repeated with other colors of Flair pens to determine if the same dyes are used that were found in the analysis of the pen with black ink.

1.3.2 Separation of Plant Pigments by Thin-Layer Chromatography

In a mortar place 1 g of spinach, 1 g of clean sand, 5 mL of acetone, and 5 mL of mixed "hexanes." Grind the spinach until the green chlorophyll appears to have been extracted completely. Decant the solution into a small beaker.

Prepare two thin-layer plates as described in (A) and in the center of each bottom line place a microdrop of the chlorophyll extract. Blow gently on the spot so that the solvent evaporates quickly. Repeat the addition of the extract several times until a distinct green spot is visible. The additions should superpose as closely as possible.

Develop one plate with 1:4 (v: v) mixture of acetone and mixed "hexanes"s as described in (A). Develop the second plate with a 1: 6: 1 (v: v: v) of aceton, mixed hexanes and ethanol 95%.

1.3.3 Separation of a Dye Mixture

Insert a small wad of glass wool into the constricted end of a 30-cm length of 10-mm diameter tubing and clamp the tube in an upright position (see Figure 3.2). Add a 5-mm layer of coarse sand to the tube. In a 100-mL beaker, prepare a slurry of 6 g of aluminum oxide in 10 mL of hot water, and transfer the slurry in small batches to the tube (swirl between additions). The water that filters through the sand and glass wool should be collected and used to transfer any column material that remains in the beaker. After the packing has settled, add a second 5-mm layer of sand, followed by a small filter paper circle.

When the last drop of water penetrates the column, add 4 drops of the dye solution to the top of the column. When the dye solution has penetrated, add a few drops of water to wash down any dye adhering to the walls. After the wash water has penetrated, fill the tube with water and allow the chromatogram to develop.

1.4 Questions

1. Arrange the following compounds in the order of their elution from a silica gel column, with benzene as eluent.

   $CH_3(CH_2)_{10}CH_3$ CH_3CO_2H $CH_3CH_2CH_2OH$ $CH_3COCH_2CH_3$

2. Suggest suitable liquid phases for separation of carboxylic acids by liquid-liquid chromatography.
3. Lists several classes of solvents arranged in order of increasing eluting ability. Give a practical example of each class.

DISTILLATION

1. Introduction

Distillation is the most important *means* of separating and purifying liquid compounds on a large scale. It consists of vaporizing the liquid and condensing the vapor in a separate receiver. There are several kinds of distillation processes; simple**,** fractional, steam and distillation under reduced pressure. Simple distillation will be discussed first since it depends upon principles and concepts which will be needed to understand the other techniques.

Distillation consists of boiling a liquid and condensing the vapor in such a manner that the condensate (distillate) is collected in a separate container. A simple apparatus assembly for this operation is shown in Figure 4.1. When a pure substance is distilled at constant pressure, the temperature of

the distilling vapor will remain constant throughout the distillation provided that sufficient heat is supplied to ensure a uniform rate of distillation and superheating is avoided. In actual practice these ideal conditions are not obtained; drafts in the laboratory can cause momentary condensation of vapors before they reach the thermometer, which lowers the temperature sensed by the thermometer. On the other hand, after they leave the surface of the liquid the distilling vapors may be heated above the liquid's boiling point (superheating), which increases the temperature sensed by the thermometer. Because of these two contrary effects, a distillation range of 1-20 actually represents an essentially constant boiling point. With somewhat more refined apparatus and technique, a distillation range of 0.10 can be observed for a pure compound.

The temperature reading of a thermometer in the distilling vapor represents the boiling point of that particular portion of the distillate. This temperature will be the same as the boiling point of the liquid in the distilling flask only if the distilling vapor and the boiling liquid are identical in composition. Since a pure liquid fulfills this condition, a constant thermometer reading is sometimes used as a criterion of purity of a liquid. It should be noted, however, that certain mixtures (such as azeotropes) also give constant thermometer readings. Occasionally two liquids have such similar boiling points that no appreciable change in the thermometer readings will be observed when a mixture of them is distilled.

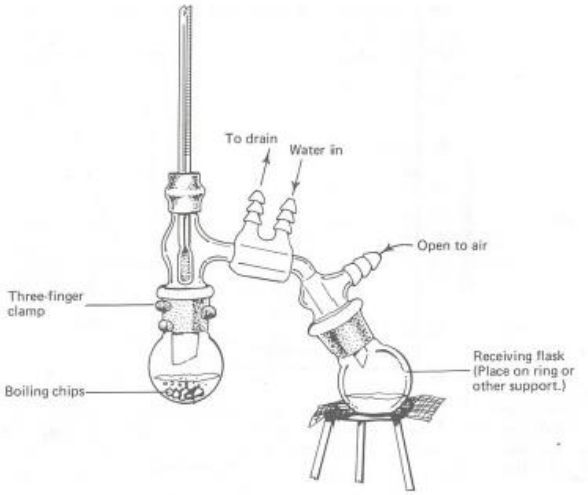


Figure 4.1 Apparatus for Simple Distillation

1.2 Fractional Distillation

The common use of the term *fractional distillation* refers to a distillation operation in which *a fractionating column* has been inserted between the boiler and the vapor takeoff to the condenser. The effect of this column is to give in a single distillation a separation equivalent to several successive simple distillations (Figure 4.2).

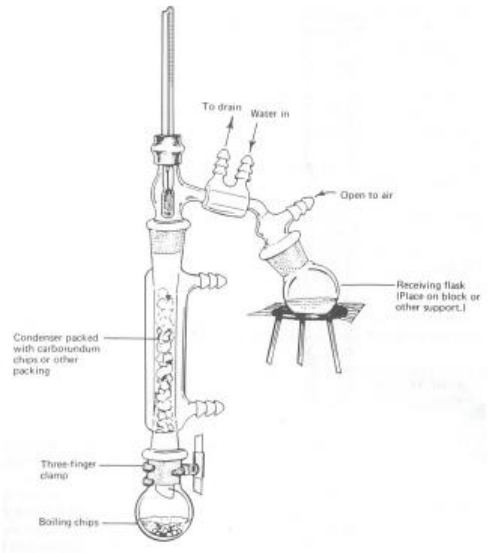


Figure 4.2 Apparatus Fractional Distillation

In addition to packed columns, special columns are available that achieve; mixing of the ascending vapor and the descending condensate by

their special construction. One of the simplest, least expensive, and most widely used is the Vigreux column (Figure 4.3). It is essentially an empty tube with many finger-like indentations that point downward at a 450 angle. The rising vapors condense on the fingers and any excess liquid drips down to lower parts of the column. The film of condensate on each finger equilibrates with the rising vapor. Under normal working conditions the Vigreux column has a relatively low efficiency (high HETP of 10 cm), but its low resistance to vapor flow permits a large throughput (volume of distillate per unit of time) that makes the column well suited to distillation of bulk solvents. Because of its small surface area the column has a low holdup and is sometimes used for preliminary purification of small samples.

1.3 Vacuum Distillation

Since the boiling temperature of a liquid is decreased by diminishing the pressure on its surface, you can distill at a lower temperature by using an apparatus that is connected to a vacuum pump that maintains a lower inside pressure. This procedure is useful for Purifying liquids (or low-melting solids) that decompose at elevated temperatures (Figure 4.4).

1.4 Steam Distillation

Steam distillation consists of distilling a mixture of water and an insoluble or partly soluble substance. The practical advantage of steam distillation is that the mixture usually distills at a temperature below the boiling point of the lower-boiling component. Consequently, it is possible to steam distill a high boiling organic compound at a temperature much below its boiling point (in fact, below 100°) without resortin, to vacuum distillation. Steam distillation is useful also in separating mixtures when one component has an appreciable vapor pressure (at least 5 mm) in the

vicinity of 100° and the other has a negligible vapor pressure. The process of steam distillation is widely employed in the laboratory and in industry; e.g., for the isolation of a-pinene, aniline, nitrobenzene, and many natural essences and flavoring oils (Figure 4.5).

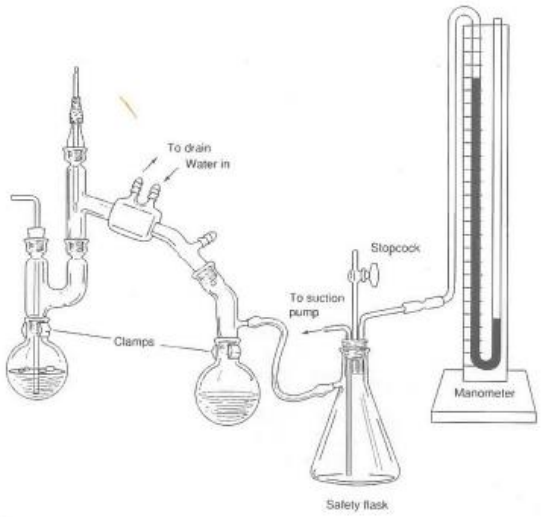


Figure 4.4 Apparatus Vacuum Distillation

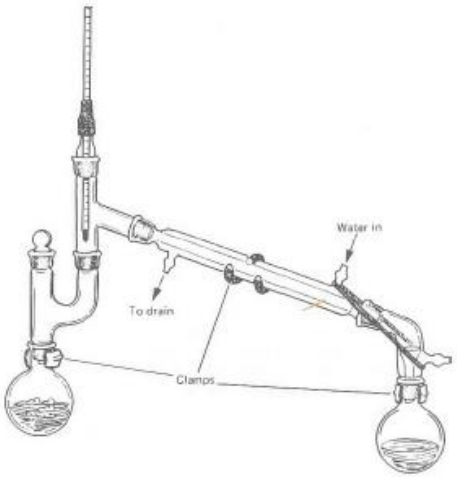


Figure 4.5 Small-Scale Steam Distillation Assembly

1.5 Laboratory Practice

The purpose of this section is to provide sufficient practice in purification of liquids by distillation so that this operation can

subsequently be carried out skillfully and without reference to detailed directions. Usually only one or two of these procedures will be assigned.

1.5.1 Simple Distillation

Arrange a distillation assembly similar to the one shown in Figure 4.1.

Distillation of a Pure Compound

Into the 250-mL boiling flask introduce 100 mL of pure methanol (caution- *flammable liquid)* by means of a clean, dry funnel. Add one or two tiny boiling chips, attach the boiling flask, and make certain that all connections are tight. Place a graduated cylinder beneath the drip tip to serve as receiver. Heat the flask gently until the liquid begins to boil. Adjust the heating rate until the ring of vapor condensation moves up the wall of the flask and past the thermometer into the condenser. Record the temperature when the first few drops of distillate are collected. Continue to distill the liquid slowly (not over 2 mL/min) and record the distilling temperature at regular intervals during the distillation when the total distillate amounts to 1, 2, 3, etc. mL. Discontinue the distillation (and turn off the heat source) when all but 1 mL of the liquid has distilled. Record the temperature range from the beginning to the end of the distillation; this is the observed boiling point. If the boiling point differs from the literature value, record the correction in your laboratory notebook for future reference.

Transfer the used methanol to a bottle provided for this purpose. From your data, draw a distillation graph for pure methanol, plotting distilling temperatures on the vertical axis against total volume of distillate on the horizontal axis.

1.5.2 Fractional Distillation

Arrange an assembly for fractional distillation as shown in Figure 4.2.

(A) Methanol and Water

For the separation of a 50:50 mixture (by volume) of methanol and water, the following temperature ranges are satisfactory for the fractions: A, 64-70; B, 70-80; C, 80-90; D, 90-95; and E, residue. Plot your data for the distillation temperature versus volume distilled and by selecting the curve closest to your data estimate the number of theoretical plates obtained.

(B) Acetic Acid and Water

In this experiment you will fractionally distill a mixture of glacial acetic acid and water (100: 31.5 by volume, 1: 1 mole ratio) and follow the progress of separation by titrating 0.5-mL portions of several fractions against standardized aqueous sodium hydroxide with phenolphthalein indicator to determine the acetic acid content. The acetic acid content of the original mixture should be determined in the same way before the material is fractionated. If a column having a large number of plates is used, it will be desirable to use larger portions of the early fractions.

Obtain a 35-mL supply of a 1: 1 molar solution of acetic acid and water. Fill a 50-mL buret with 1.0 *N* sodium hydroxide solution. With the aid of a 0.5-mL or 1.0-mL pipet, place 0.5 mL of the 1: 1 molar solution of acetic acid and water in a 50-mL Erlenmeyer flask and add 10 mL of water and a few drops of phenolphthalein indicator. Titrate to a slightly pink end point and record the volume of titrant. Repeat the titration on two more 0.5-mL samples of the 1: 1 molar solution of acetic acid and water and compute the average titer.

Assemble a fractional distillation apparatus using a 50-mL round-bottomed flask for the boiler and a 25-mL graduated cylinder for the receiver. Place 30 mL of the 1: 1 mixture in the flask and add a boiling chip. You will need a small test tube that has been marked to show the liquid level when it contains exactly 0.5 mL of liquid.

Heat the mixture until it boils and then adjusts the heating rate so that the mixture distills at a *maximum* rate of 1 drop/sec. Note the temperature at which the first drop distills. Collect the first 0.5 mL of distillate in your marked test tube and the next 4.5 mL in the graduated cylinder. Record the distillation temperatures at each 1-mL interval. Transfer the 0.5-mL sample to a 50-mL Erlenmeyer flask (rinse the tube with a total of 10 mL of distilled water and add the rinse to the Erlenmeyer flask). Mark the flask to indicate the sample it contains.

When the volume of distillate reaches 5 mL, collect another 0.5-mL sample in the test tube and transfer it in the same manner to another Erlenmeyer flask. Collect the next 4.5 mL of distillate in the graduated cylinder, recording the distillation temperatures at each 1-mL interval. Repeat this process at 10 mL, 15 mL, 20 mL, and 25 mL of distillate. Titrate the six samples with the sodium hydroxide solution (the early samples will require very little titrant) and calculate the mole fraction of acetic acid present. In the calculations assume that the volumes of acetic acid and water are additive so that the mole fraction in any sample is simply proportional to the titer value obtained for the initial 0.5 mole fraction mixture.

A)*O*-AND *N*-ACYLATION

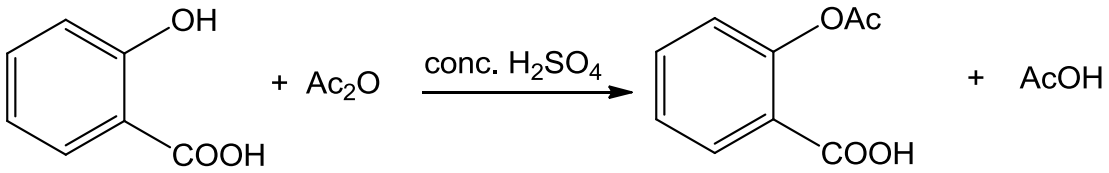
EXPERIMENT 1:

Preparation of Acetylsalicylic Acid (Aspirin)

Materials:

- Salicylic acid 5 g
- Acetic anhydride 10 ml
- Conc. Sulphuric acid 1 ml

Reaction:



Salicylic acid

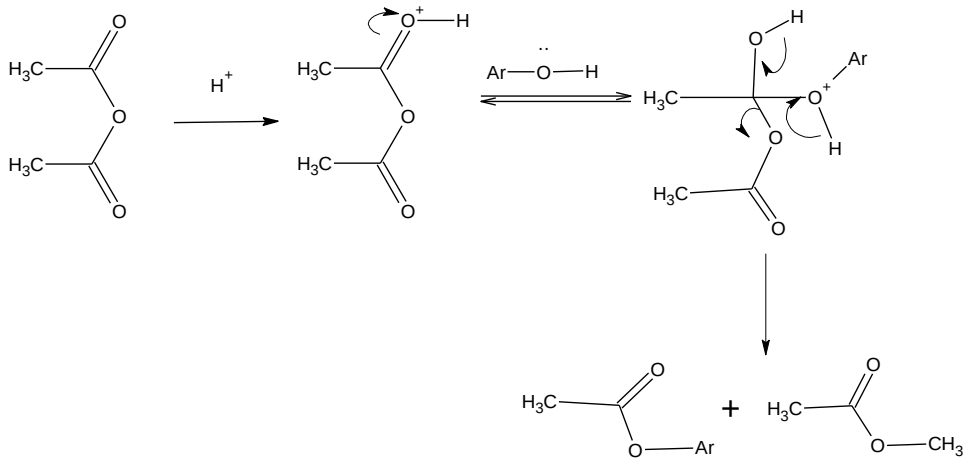
Acetylsalicylic acid
Aspirin

Method:

A. In a conical flask, place salicylic acid (5 g), acetic anhydride (10 ml) and conc. Sulphuric acid (1 ml). Shake the mixture thoroughly and heat the contents on a water-bath at 50-60°, with occasional stirring, for about 15 minutes. Cool, add water (100 ml) into it and filter under suction. Recrystallize the elude product with 50 % ethanol. The yield is 5-5.5g and the m.p. is 130-135° (various because of partial decomposition). Check the purity by TLC also. Record IR spectra of salicylic acid and the product and compare.

B. In an alternative method, mix salicylic acid (5 g) with pyridine (4 ml) in a conical flask. Cool the mixture in ice-bath and cautiously add acetyl chloride (3.5 ml) in a dropwise manner into it with continuous stirring. The rest of the procedures is the same as given in **A**.

Mechanism of reaction



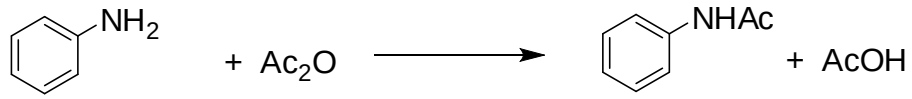
Experiment 2:

Preparation of Acetanilide

Materials:

Aniline	10 ml
Acetic acid (glacial)	10 ml
Acetic anhydride	10 ml

Reaction:



Aniline **Acetanilide**

Procedure

1. In a dry, round-bottomed flask, fitted with a reflux water condenser, place aniline (10 ml), acetic anhydride (10 ml), glacial acetic acid 10 ml). Boil the mixture gently for 10-15 minute and pour the hot liquid, with stirring, into ice-cold water (250 ml).

2. Filter the crude product at the pump, wash with cold water and recrystallize it from boiling water to which some methylated spirit has been added. The yield is 10 g and the m.p. is 114° Check the purity by TLC also. Record IR spectra of aniline and the product and compare.

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B) CONDENSATION REACTIONS

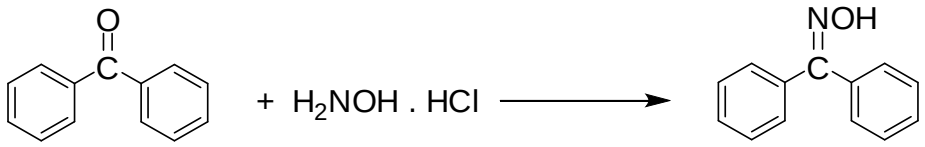
EXPERIMENT 3:

Preparation of benzophenone oxime

Materials:

- benzophenone 5 g
- hydroxylamine 3 g
- Sodium hydroxide 28 g

Reaction:



Procedure

1- Place a mixture of 5 g of benzophenone , 3 g of hydroxylamine HCl in 50 ml of rectified spirit and 10 ml of water in a 500 ml R. B. flask.

2- Add 28 g of NaOH (Pellet form) in portions with shaking and cool the flask with tap water. When all sod. Hydroxide has been added attach a reflux condenser to the flask, heat to boiling and reflux for 5 minutes.

3- Cool and pour the contents of the flask into a solution of 75 ml of conc. HCl in 500 ml of water contained in a one liter beaker.

4- Filter the precipitate at the pump, wash with cold water, dry it and recrystallize it from methanol.

5- The yield is 26.5 g and the m.p. is 142^{o}. Check purity by TLC also record IR spectra of benzophenone and the product and compare.

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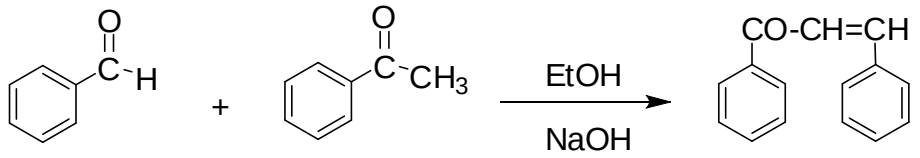
EXPERIMENT 4:

Preparation of benzalacetophenone (*Chalcone*)

Materials:

- Benzaldehyde 4.5 ml
- Acetophenone 5 ml
- Ethanol 15 ml
- Sodium hydroxide 10 percent, 25 ml

Reaction:



Procedure:

1. In a round –bottomed flask, Place ethanol (15 ml). Add into it 10 percent NaOH (25 ml), shake and place the flask in an ice bath with magnetic stirrer.
2. Pour of 5 ml of acetophenone, and then add 4.5 ml of pure benzaldehyde. Continuously stirring the mixture for 2-3 hours at 15-30 ^{o}C until the mixture become quite thick that stirring is no longer effective.
3. Romove the stirrer and leave the reaction mixture on a Buchner funnel, wish with cold water until the washings are neutral to litmus.
4. The crude chalcone, after drying in air, weighs 7-8 g and M.P. 56-57 ^{o}. Recrystallise from ethanol.
5. Record IR and UV spectra of bezaldehyde and the product and compare.

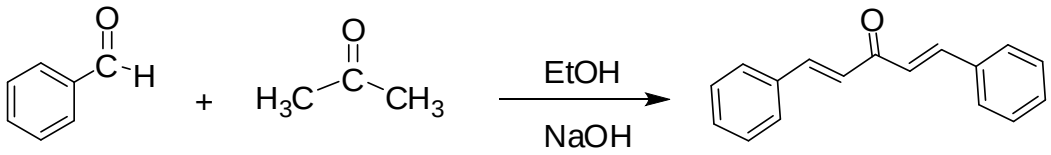
EXPERIMENT 5:

Preparation of dibenzalacetone (*Chalcone*)

Materials:

- Benzaldehyde 8 ml
- Acetone 4 ml
- Ethanol 60 ml
- Sodium hydroxide 10 percent, 80 ml

Reaction:



Procedure:

1. In a round –bottomed flask, Place ethanol (60 ml). Add into it 10 percent NaOH (80 ml), acetone (4 ml) and benzaldehyde (8 ml) and boil the solution gently for 5 minutes, shaking the flask.
2. Cool, filter the product at the pump; wash with cold water, drain well dry in air.
3. Recrystallize the cured product from hot ethyl acetate or ethanol. The yield is 6.5 g and the m.p. is 112^{o}.
4. Record IR and UV spectra of bezaldehyde and the product and compare.

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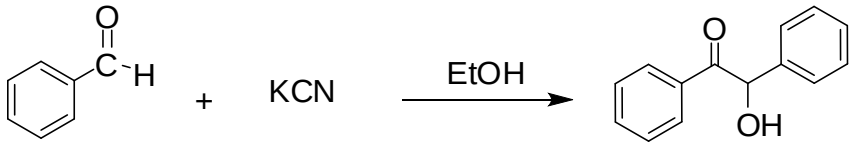
C) OXIDATION AND REDUCTION

Experiment 6: Preparation of benzoin

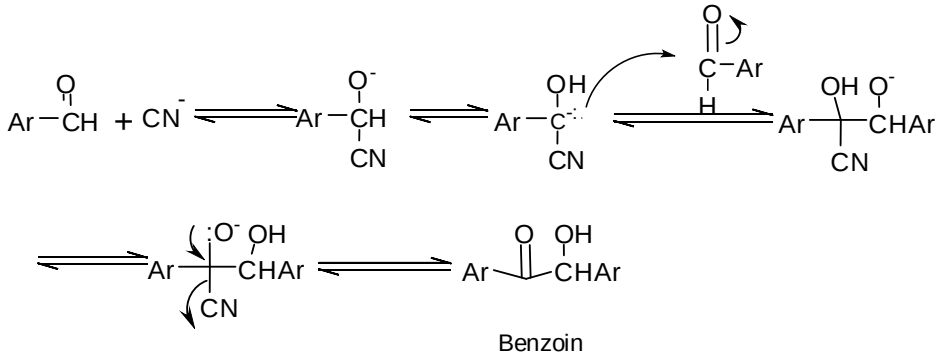
Materials:

Benzaldehyde	12 ml
Rectified spirit	25 ml
Potassium cyanide	1.5 g

Reaction:



Mechanism:



Benzoin

Method:

1. In a round bottom flask, fitted with a reflux water condenser, place ethanol (25 ml), pure benzaldehyde (12 ml) and a solution of potassium or sodium cyanide (1.5 g) in water (12 ml).

2. Boil the mixture gently for half an hour and then cool in an ice-water bath. Filter the crude product at the pump, wash with cold water, drain well and dry. Recrystallize it from hot rectified or methylated spirit.

3. The yied is 10-11 g and the m.p. is 137^{o}.

4. Record IR spectra of benzaldehyde and product and compare them.

Precaution:

Potassium cyanide is very poisonous; handle it with great care (use hand-gloves), dispose of the filtrate directly in the sink and wash with a large quantitv of water.

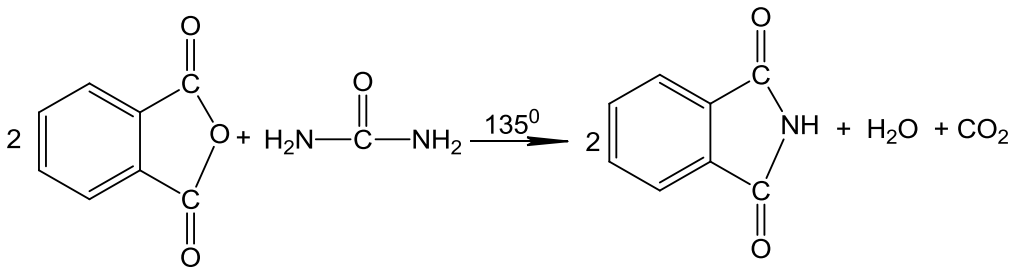
D)AMIDES AND IMIDES FORMATION

EXPERIMENT 7: Preparation of Phthalimide

Materials:

- Phthalic anhydride 15 g
- Urea 3.5 g

Reaction:



Method:

1. In a round-bottomed flask fitted with an air condenser place a well mixed of phthalic anhydride (15 g) and urea (3.5 g) and heat the flask at 130-135° on a sand-bath for 15-20 minutes.
2. The reaction begins with the melting of the contents, effervescence commence which gradually increase in vigor, and thereafter, the mass suddenly froths up and the temperature rise spontaneously to 160°.
3. Allow the mass (a spongy solid) to cool and add water to disintegrate the solid in the flask. Filter the solid at the pump, wash with a little water and dry at 100°. Normally, the product is sufficiently pure and does not need recrystallization. The yield is 12-12.5 g and the m.p. is 233°.
4. Record IR and UV spectra of bezaldehyde and the product and compare.

In an ***alternative method***, place finely powdered phthalic anhydride (10 g) in a round-bottomed flask. Add into it conc. Ammonia solution (10.5 ml) and heat the mixture over a wire-gauze with occasional shaking until the mass fuse quietly and form a homogeneous melt (generally 1.5-2 h heating is required to achieve this stage). Pour the content of the flask, a hot, into a porcelain basin; allow cooling and grinding the mass to fine particles in a mortar.

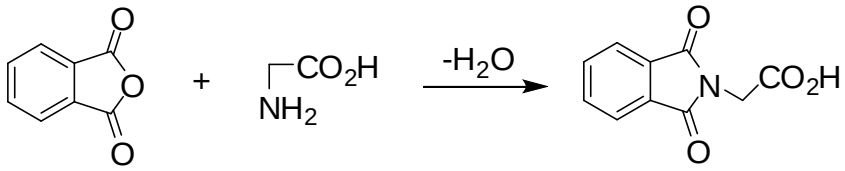
EXPERIMENT 8:

Preparation of Phthalylglycine

Materials:

- Phthalic anhydride 6 g
- Glycine 3 g

Reaction:



Method:

1. In a boiling tube, place phthalic anhydride (6 g) and glycine (3 g) and fuse the mixture at 150-190^{o} for 15-20 minutes.

2. Allow to cool and recrystallize the product from water. The yield is 7.5-8 g and the m.p. is 192-193^{o}.

3. Record IR and UV spectra of bezaldehyde and the product and compare.

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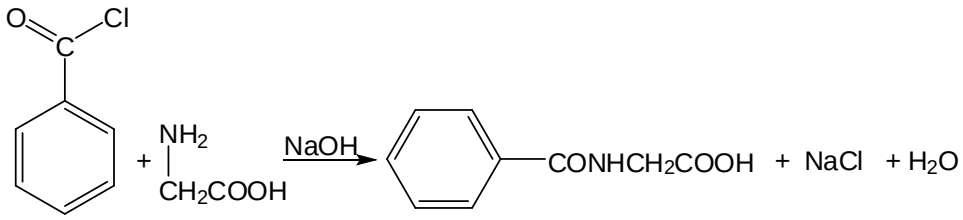
EXPERIMENT 9:

Preparation of hippuric acid (benzoylglycine)

Materials:

- Glycine 7.5 g
- Benzoyl chloride 14 ml
- Sodium hydroxide solution (aq.) 10% 75 ml (10%)
- Carbon tetrachloride 25 ml

Reaction:



Hippuric acid

Method:

1. In a conical flask, dissolve glycine (7.5 g) in an aqueous sodium hydroxide solution (10%, 75 ml) and add to it benzoyl chloride (14 ml) in a five or six installments.
2. After each addition, stopper the flask and shake vigorously until all chloride has reacted (the content may be warmed gently and thoroughly shaken until the smell of benzoyl chloride disappears). Transfer the solution to a beaker containing crushed ice and add conc. HCl slowly and with stirring until the solution becomes acidic. Filter the crude product (containing a little benzoic acid as impurity) by suction, wash well on the filter with cold water and boil the impure product gently with carbon tetrachloride (25 ml) for 10 minutes to remove the benzoic acid.

3. Cool the mixture slightly and filter by gentle suction. Wash the residue with carbon tetrachloride (3-4 ml) and recrystallize from hot water. The yield is 13 g and the m.p. is 187°. Check purity by TLC also. Record IR spectra of glycine and the product and compare.

D) ELECTROPHILIC SUBSTITUTION

Experiment 10: Haloform Reaction

All methyl ketones (CH_3-CO-R), acetaldehyde, ethanol and secondary methylcarbinols CH_3-CH(OH)-R, when treated with halogen (X2) and a base, are cleaved to yield a carboxylic acid(salt) and haloform (CHX_3)

Preparation of iodoform

$$CH_3\text{-}CO\text{-}CH_3 + 3I_2 + 4NaOH \longrightarrow CH_3I + CH_3COONa + 3NaI + 3H_2O$$

Materials:

Acetone 3 ml

Iodine solution: (Dissolve 12.5 gm iodine in a solution of 25 gm of potassium iodide in 100 ml of water.

Sodium hydroxide solution 10%, 15 ml

Procedure:

1. In a conical flask, place acetone (3 ml), water (30 ml) and sodium hydroxide solution (10%, 15 ml).
2. Now add into it, a drop at a time, iodine solution, all the while shaking the flask until the yellow color of iodine persists.
3. Heat the contents to 60^o in a water bath. If the solution becomes colorless after 2 minutes, add more iodine solution and heat again.
4. Cool the mixture, filter the yellow precipitate of iodoform and recrystallize from methanol: water mixture (1:1). The yield is 5 gm and the m.p. is 119^{o}C.

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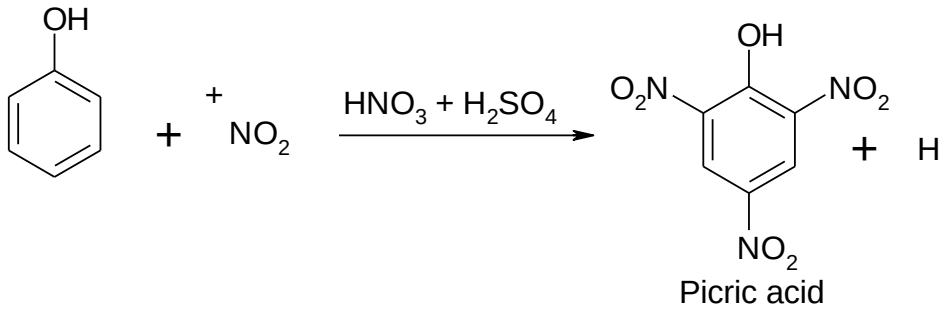
Experiment 11:

Preparation of picric acid

Materials:

Phenol	7.5 g
Conc. Sulphuric acid	20 ml
Conc. Nitric acid	22 ml

Reaction:



Picric acid

Method:

1. In a round bottom flask, place phenol (7.5 g) and conc. sulphuric acid (20 ml), shake well and then heat the mixture on aboiling water-bath for half hour until a clear solution of phenolsulphonic acid is obtained.

2. Cool the flask thoroughly in an ice-water mixture, add conc. Nitric acid (22 ml) into it whilst the phenolsulphonic acid are still viscous syrup and immediately mix the liquids by shaking. A vigorous reaction sets in within 1-2 min. copious red fumes (oxides of nitrogen) evolve and the liquid becomes deep red in colour.

3. After the reaction has subsided, heat the mixture in a boiling water-bath for about 2 hours with occasional shaking, cool, and add water (50 ml) into it. Again cool in ice-water, filter under suction, wash the residue well with water, and recrystallize from water: alcohol (2:1) mixture. The

yield is 11-12 g and the m.p. is 122^{o}. Check purity of the compound by TLC also. Record U.V. spectra of phenol and the product and compare them.

Precaution:

Picric acid is an explosive compound and hence should not be ground.

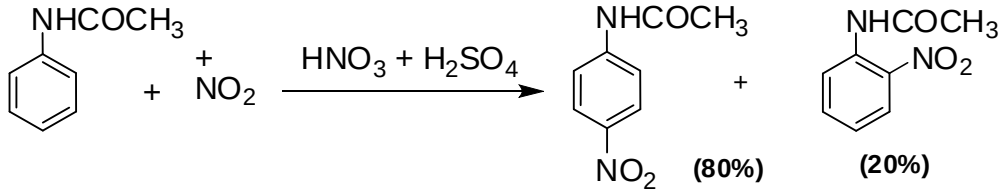
Experiment 12:

Preparation of *p*-nitroactanilide

Materials:

Acetanilide	12 g
Acetic acid (glacial)	12 ml
Conc. Sulphuric acid	28 ml
Conc. Nitric acid	6 ml

Reaction:



Method:

1. In a beaker, place glacial acetic acid (12 ml) and add into it finely powdered dry acetanilide in small portions, stirring constantly. Then add gradually, while stirring, conc. sulphuric acid (24 ml). The mixture becomes warm and the result is a clear solution.

2. Cool the mixture to 0-2^{o} C in a pan of crushed ice, and when sufficiently cold (below 5^{o}), add into it a cold acid mixture containing conc. or fuming nitric acid (6 ml) and conc. sulphuric acid (4 ml) drop by drop, stirring continuously. When all the nitrating acid has been added, remove the beaker from the ice-bath and let it stand at room temperature for 30-40 min.

3. Pour the reaction mixture into crushed ice and stir. The *o*-nitroacetanilide, being soluble, remains in the solution, while *p*-nitroacetanilide being insoluble, precipitates as a solid. Filter the crude product, wash thoroughly with cold water and recrystallize it from hot

alcohol or methylate spirit. The yield is 9-10 g and the m.p. is 214°. Check purity by TLC also record IR spectra of acetanilide and the product and compare.

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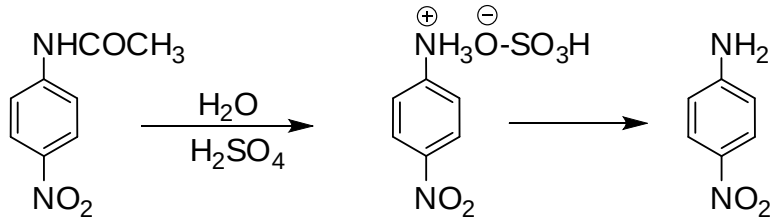
Preparation of *p*-nitroaniline

Materials:

p-nitroacetanilide	15 g
Sulphuric acid	(70 percent), 80 ml
Sodium hydroxide	(10 percent) 6 ml

Reaction:



1. In a round-bottomed flask, fitted with a reflux condenser, place 15 g of *p*-nitroacetanilide and 80 ml of 75% H_2SO_4. Stir the mixture into a thin

paste, boil the contants for 20 minutes (or more until the test sample remains clear upon dilution with 2-3 times its volume of water) and then pour the contents into a beaker.

2. Add crushed ice into the beaker and precipitate *p*-nitroaniline by adding into it, with stirring, an excess of 10 % NaOH or concentrated ammonia solution.

3. Cool the mixture in ice for some time, then filter the product by suction, wash with cold water and recrystallize the product from 50% EtOH or from hot water. The yield is 10 g and m.p. is 148^{o}. Check purity by TLC. Record IR spectra.

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E) AZOIC DYES SYNTHESIS

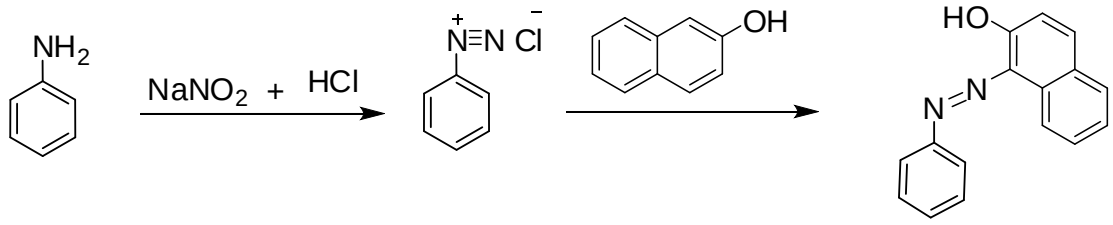
Experiment 13:

Preparation of Phenylazo-β-naphthol

Materials:

Aniline	5 ml
Sodium nitrite	4 g
Conc. HCl	16 ml
β-naphthol	8 g
Sodium hydroxide	(50 ml, 10%)

Reaction:



Method:

1. In a beaker, dissolve pure aniline (5 ml) in a mixture of conc.HCl (16 ml) and water (16 ml), coolin ice bath to 0^{o} C and add into it a solution of $NaNO_2$ (4 g) in water (20 ml) drop by drop while shaking the beaker (maintain the tempreture of the mixture below 5^{o}).

2. In another beaker, dissolve pure β-naphthol (8 g) in warm 10 % NaOH (50 ml) cool the solution to below 5^{o} in an ice bath and add into it , drop by drop , with vigorous stirring, the prepared cold diazonium salt solution.

3. After all diazonium salt solution has been added, allow the reaction mixture to stant in the ice bath (below 10^{o}) for about 30 minute, occasionally stirring the mixture.

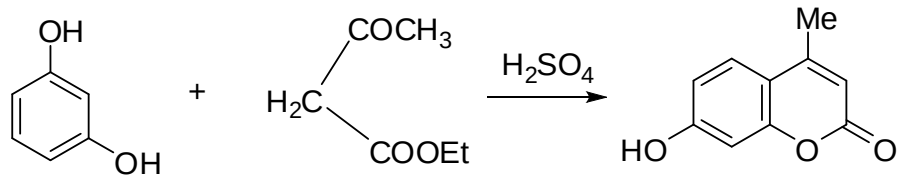
4. Filter the product with gentle suction, wash well with water and recrystallize with EtOH. The yield is 11 g and the m.p. is 131^{o}.

F) HETEROCYCLIC COMPOUNDS

Experiment 14:

Preparation of 7-Hydroxy-4-methylcoumarin

Umbelliferone occurs in a variety of plants, both as the free phenol and combined as glycosides sugar derivatives. Umbelliferone is a fluorescent compound. So that it is often found in sun-lan lotions, the retionate being that solar u.v. radiation, instead of exerting damaging effects on the skin, becomes trapped before reachin the skin.



Materials:

Resorcinol	5.6 gm
Ethyl acetoacetate	6.5 ml
Conc. H_2SO_4	(75%, 50 ml)

Procedure:

In a conical flask, dissolve resorcinol (5.6 gm) and ethyl acetoacetate (6.5 g) with 75% H_2SO_4 (50 ml) and stir continuously. Heat the mixture on water-bath at 100 ^oC for 30 min. cool the resulting solution and stir into crushed ice (250 gm). Filter of the crude product, and wash cold with water and dry at 60^o. Recrystallizes the crude product from EtOH, the yield of product is 8 g, m.p. 185-186^o.

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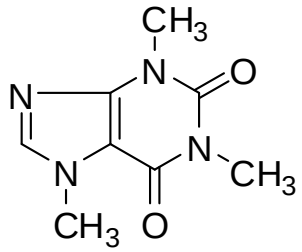
G)NATURAL PRODUCTS

Experiment 15:

Isolation of caffeine from tea

Caffeine (1,3,7-trimethylxanthine) occurs in tea leaves in 1.0 to 4.8%. Being soluble in boiling water, it can be extracted by means of boiling water and using chloroform as a slolvent. From aqueous solution, it can crystallize in long silky needles with one molecule of water.



Caffeine

Procedure

Boil nearly 50 gm of tea leaves with 250 ml of water in 500 ml flask fitted with an air condenser for ½ hr. Filter the hot solution and wash the residue with boiling water. Added basic lead acetate solution to the filtrate with constant stirring till complete precipitation is obtained. Again filter the hot solution, add dilute sulfuric acid till the whole of lead acetate is removed as lead sulfate. Remove the lead sulfate by filtration, and nearly 0.5 gm of animal charcoal to decolorize the filtrate and then concentrate the solution nearly to half of its volume. Filter the resulting solution and extract caffeine from filtrate by adding 75ml of chloroform in three times (25 ml each) using a separating funnel. Distill of the solvent (chloroform) from organic layer using a distillation flask and a water bath. Dissolve the residue in least amount of hot water and then cool the solution when long silky needles of caffeine separate.

Record the yield and melting point of caffeine.