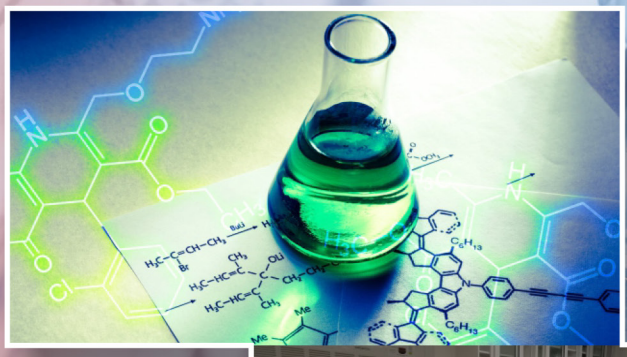
Practical Lab Manual of Pharmaceutical Organic Chemistry - II

As Per PCI Syllabus

B. Pharm 3rd Semester



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M. Pharm (Pharmaceutical Chemsitry), Ph.D.

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Practical Lab Manual of Pharmaceutical Organic Chemistry - II

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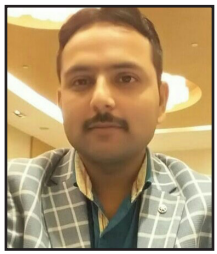
Dedicated

Affectionately to my Father Mr. Ramkhelawan Dwivedi, he is also a great teacher in a sky and my Mother Mrs. Phool Kumari Dwivedi.

Shivendra Kumar Dwivedi

About the Author



Dr. Shivendra Kumar Dwivedi, M. Pharm (Pharmaceutical Chemistry), Ph.D., presently working as an Assoc. Professor in University Institute of Pharmacy, Oriental University, Indore (M.P). He has 10 years of experience in academics and research. He is also the author of some of the other books for UG and PG in Pharmaceutical Chemistry and Practical manual. He has published more than 30 research papers in a different versatile International and National journals.

Acknowledgement

I am indebted to all my family members particularly to my wife **Mrs. Namrata Dwivedi**, my daughter **Shravi Dwivedi** who have always remained my source of inspiration and encouragement.

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Note for the Students

If you are a student, you will probably appreciate our effort to present you the book "Practical Lab manual of Pharmaceutical Organic Chemistry - II (Organic Chemistry - II)", which covers all practicals in the 3rd semester in organic chemistry.

The aim of this book is to give you an updated and comprehensive knowledge in a lucid manner. Considering your need, all the basic principles and concepts which underline the chemical reaction, have been explained.

Contents

Chapter 1

Introduction of the Laboratory Safety

Introduction

Before you begin working in the Chemistry laboratory, your instructor should review the safety rules and guidelines tell you what safety supplies, such as safety goggles and protective gloves you will need to use in the lab. In a first-time working in a during laboratory period, the instructor will show you where safety equipment is located and tell you how to use it. As you locate each item, check it off the following list and make a note of its location and proper working, which is not expire:

1. Fire extinguishers
2. Fire blanket
3. Safety shower
4. Eyewash fountain
5. First aid supplies
6. Spill cleanup supplies

Every Students and academician you should also learn the locations of chemicals, glassware consumable supplies (such as filter paper and boiling chips), waste containers, and various items of equipment such as balances and drying oven. If you find any glassware items with chips, cracks, or star fractures, you should have them replaced; they may cause cuts, break on heating, or shatter under stress. If necessary, clean up any dirty glassware and organize it neatly at this time.

Proper Working Efficiently

If all labs were geared to the slowest student, the objectives of the course could not be accomplished in the limited time available. Because of wide variations in individual working rates, it is usually not possible to schedule experiments so that everyone can finish in the allotted time. If you fall behind in the lab, you may need to put in extra hours outside your scheduled laboratory period in order to complete the course. The following suggestions should help you work more efficiently and finish each experiment on time:

Be prepared to start the experiment the moment you reach your work area: Don't waste precious minutes at the start of a laboratory period doing calculations, reading the experiment, washing glassware, or carrying out other activities that should have been done at the end of the previous period or during the intervening time. The first half hour of any lab period is the most important - if you use it to collect the necessary materials, set up the apparatus, and get the initial operation (reflux, distillation, etc) under way, you should have no trouble completing the experiment on time.

Organize your time efficiently: Schedule a time each week to read the experiment and operation descriptions and to complete the prelab assignment - an hour before the lab period begins is too late! Plan ahead so that you know approximately what you will be doing at each stage of the experiment. A written experimental plan is invaluable for this purpose

Organize your work area: Before performing any operation, arrange all of the equipment and supplies you will need during the operation neatly on your benchtop, in the approximate order in which they will be used. Place small objects and any items that might be contaminated by contact with the benchtop on a paper towel, laboratory tissue, or mat. After you use each item, move it to an out-of-the way location where it can be cleaned and returned to its proper location when time permits; for example put dirty glassware in a washing trough in the sink.

Getting Along in the Laboratory

You will get along much better in the laboratory if you can maintain peace and harmony with your coworkers – or at least keep from aggravating them - and stay on good terms with your instructor. Following these commonsense rules will help you do that.

Leave all chemicals where you can find them: You will understand the reason for this rule once you experience the frustration of hunting high and low for a reagent, only to find it at another's student's station in a far corner of the lab.

Take only what you need: Whenever possible, liquids and solutions should be obtained using pipets, graduated cylinders, or other measuring devices so that it will take no more than you expect to use for a given operation.

Prevent contamination of chemicals: Don't use your own pipet or dropper to remove liquids directly from stock bottles, and don't return unused chemicals to stock bottles. Be sure to close all bottles tightly after use – particularly those that contain dying agents and other anhydrous chemicals.

If you must use a burner, inform your neighbors: unless they are already using burners. This will allow them to cover any containers of flammable solvents and take other necessary precautions. In some circumstances, you may have to use a different heat source, move your operation to a safe location (for instance under a fume hood), or find something else to do while flammable solvents are in use.

Return all community equipment to the designated locations: This may include ring stands, lab kits, clamps, condenser tubing, and other items. Because such items will be needed by students in other lab sections, they should always be returned to the proper storage area at the end of the period.

Clean up for the next person: Clean off the benchtop with a towel or wet sponge; remove condenser tubing, other supplies, and debris from the sink; and thoroughly wash any dirty glassware that is to be returned to the stockroom. Clean up any spills and broken glassware immediately. If you spill a corrosive or toxic chemical, such as sulfuric acid or aniline, inform the instructor before you attempt to clean it up. It is advised to maximize the labor and minimize the oratory while in the laboratory. This does not mean that all conversation must come to a halt. Quiet conversation during a lull in the experimental activity is okay, but a constant stream of chatter directed at a coworker who is performing a delicate operation is distracting and can lead to an accident. For the same reason, radios, CD or MP3 players and other audio devices must not be brought into the laboratory.

Condition and Care About Yourself to Chemicals and Hazard Substances

Prime responsibility to the Lab in charge or academician are required to see that students know and follow established safety rules and guidelines, have access to and know how to use appropriate emergency equipment and are aware of hazards of hazards associated with specific experiments. The lab instructor alone cannot prevent laboratory accidents, however. You also have a responsibility to follow safe laboratory practices while performing experiments and to be ready to respond in case of accident.

People who work with chemicals should wear appropriate clothing and personal protective equipment (such as safety goggles) that reduce the likelihood of injury in case of an accident. Eye protection is always essential, and it should be the rule in every chemistry laboratory. Safety glasses provide only limited protection because they have no side shields, so it is best to wear safety goggles that protect your eyes from chemical splashes and flying particles from any direction.

If working a chemistry lab, you should proper wear clothing that is substantial enough and covers enough of your body to offer some protection against accidental chemical spills such as hazardous compounds and flying glass or other particles. Long-sleeved shirts or blouses and long pants or dresses are recommended, especially when they are made of denim or other heavy materials.

Some synthetic fabrics can be dissolved by chemicals such as acetone and could melt in contact with a flame or another heat source. Wear shoes that protect you from spilled chemicals and broken glass-not open sandals or cloth-topped athletic shoes. Always wear appropriate gloves when handling caustic chemicals, which can burn the skin, or toxic chemicals that can be absorbed through the skin. No single type of glove protects against all chemicals, but neoprene gloves offer good to excellent protection against many commonly used chemicals, and disposable nitrile gloves are adequate for use in most undergraduate labs. Latex gloves aren't recommended, because some people are allergic to latex because they are permeable to many hazardous chemicals.

To Preventing Laboratory Accidents

Most of the organic chemistry lab courses are completed without incident, apart from minor cuts or burns, and serious accidents are rare. Nevertheless, the potential for a serious accident always exists. To reduce the likelihood of an accident, you must learn the following safety rules and observe them at all times. Additional safety rules or revisions of these rules may be provided by your instructor.

Always wear approved eye protection in the laboratory: Even when you aren't working with hazardous materials another student's actions could endanger your eyes, so never remove your safety goggles or safety glasses until you leave the lab. Do not wear contact lenses in the laboratory because chemicals splashed into an eye may get underneath a contact lens and cause damage before the lens can be removed. Properly determine the location of the eyewash fountain nearest to you during the first laboratory session and learn how to use it.

Never smoke in the laboratory or use open flames in operations that involve low boiling flammable solvents: Anyone found smoking in an organic chemistry laboratory is subject to immediate expulsion. Before you light a burner or even strike a match, inform your neighbors of your intention to use a flame. If anyone nearby is using flammable solvents, either wait until he or she is finished or move to a safer location, such as a fume hood. Diethyl ether and petroleum ether are extremely flammable, but other common solvents, such as acetone and

ethanol, can be dangerous as well. When ventilation is inadequate, the vapours of diethyl ether and other highly volatile liquids can travel a long way; lighting a burner at one end of a lab bench that has an open bottle of ether at its other end has been known to start an ether fire.

Consider all chemicals to be hazardous and minimize your exposure to them: No and Never taste chemicals, do not inhale the vapors of volatile chemicals or the dust of finely divided solids, and prevent contact between chemicals and your skin, eyes and clothing. Many chemicals can cause poisoning by ingestion, inhalation, or absorption through the skin. Strong acids and bases, bromine, thionyl chloride, and other corrosive materials can produce severe burns and require special precautions, such as wearing gloves and lab coat. Some chemicals cause severe allergic reactions, and others may be carcinogenic (tending to cause cancer) or teratogenic (tending to cause birth defects) by inhalation, ingestion (swallowing) or skin absorption. To prevent accidental ingestion of toxic chemicals, don't bring food or drink into the laboratory or use mouth suction for pipetting, and wash your hands thoroughly after handling any chemical. To prevent inhalation of toxic or carcinogenic chemicals, work under an efficient fume hood or use a gas trap to keep chemical fumes out of the laboratory atmosphere. To prevent contact with corrosive or toxic chemicals, wear appropriate gloves and a lab coat.

Properly exercise great care when working with glass and when inserting or removing thermometers and glass tubing: Most of the common injuries in a organic chemistry lab are cuts in hand from broken glass and burns from touching hot glass. Protect your hands with gloves or a towel when inserting glass tubes or thermometers into stoppers or thermometer adapters, and when removing them. Grasp the glass close to the stopper or thermometer adapter and gently twist it in or out.

Properly wear appropriate clothing in the laboratory: Properly wear clothing that is substantial enough to offer some protection against accidental chemical spills, and shoes that can protect you from spilled chemicals and broken glass. Human hair is very flammable, to tie up your hair or wear a hair net while using a burner if you have long hair.

Properly dispose of chemicals: For reasons of safety and environmental protection, most organic chemicals shouldn't be washed down the drain. Except when your instructor or an experiment's directions indicate otherwise, place used organic chemicals and solutions in designated waste containers. Some aqueous solutions can be safely poured down the drain but consult your instructor if there is any question about the best method for disposing of a particular chemical or solution.

No and Never work alone in the laboratory or perform unauthorized experiments: If you wish to work in the laboratory when no formal lab period is scheduled, you must obtain permission from the instructor and be certain that others will be present while you are working.

In a Laboratory Operations

Students and laboratory instructor should read proper guidelines to the operation of practical in a Chemistry lab, which types of care in carried out during laboratory operation. Should still read the descriptions carefully because an operation may require different equipment or be performed in a different way in the organic chemistry lab.

Cleaning Glassware

Glassware must be clean in a water. clean glassware is essential for good results in the organic chemistry laboratory. Even small amounts of impurities can sometimes inhibit chemical reactions, catalyze undesirable side reactions, or invalidate the results of chemical tests or rate studies. Always clean dirty glassware at the end of each laboratory period, or as soon as possible after the glassware is used.

If you wait too long to clean glassware, residues may harden and become more resistant to cleaning agents; they may also attack the glass itself, weakening it and making future cleaning more difficult. It is particularly important to wash out strong bases such as sodium hydroxide promptly, because they can etch the glass permanently and cause glass joints to "freeze" tight. When glassware has been thoroughly cleaned, water applied to its inner surface should wet the whole surface and not form droplets or leave dry patches. However, used glassware that has been scratched or etched may not wet evenly.

You can clean most glassware adequately by vigorous scrubbing with water and a laboratory detergent, using a brush of appropriate size and shape to reach otherwise inaccessible spots. Organic residues that can't be removed by detergent and water will often dissolve in organic solvents such as technical-grade acetone (Never use reagent grade solvents for washing). For example, it is difficult if not impossible - to scrub the inside porcelain Büchner or Hirsch funnel, but squirting a little acetone around the inside of the funnel stem and letting it drain through the porous plate should remove chemical residues that may have lodged there. Use acetone sparingly and recycle it after use (don't pour it down the drain), as it is much more costly than water and may harm the environment. After washing, always rinse glassware thoroughly with water (a final distilled-water rinse is a good idea) and check it to see if the water wets its surface evenly rather than forming separate beads of water. If it doesn't pass

this test scrub it some more or use a cleaning solution. Note that some well-used glassware may not pass the test because of surface damage, but it may still be clean enough to use after thorough scrubbing.

Lubricating Joints

Most specialized glassware components used in organic chemistry have rigid ground-glass joints called standard-taper joints. The size of a tapered joint is designated by two numbers, such as 19/22, in which the first number is the diameter at the top of the joint and the second is the length of the taper, measured in millimeters. Glassware from a commercial organic lab kit, or its equivalent purshased as separate parts, can be used to construct apparatus for many different laboratory operations. For some operations, such as vacuum distillation, glass joints should be lubricated with a suitable joint grease. For most other operations, lubrication of glass joints is unnecessary and may be undesirable. Your instructor should inform you if lubrication will be necessary. To lubricate a ground-glass joint, apply a thin layer of joint grease completely around the top half of the inner (male) joint.

Do not lubricate the outer (female) joint. Be careful to keep grease away from the open end of the joint, where it may come into contact with and contaminate your reaction mixture or product. When you assemble the components, press the outer and inner joints together firmly, with a slight twist, to form a seal around the entire joint with no gaps. Grease should never extend beyond the joint inside the apparatus. After disassembling the apparatus, remove the grease completely by using a suitable organic solvent. You can remove petroleum-based greases with petroleum ether or hexanes, and silicone greases by thorough cleaning with dichloromethane.

An inner joint can be cleaned by wrapping a small amount of cotton loosely around the end of an applicator stick, dipping it in the solvent, and wiping the joint with the moist cotton. Assembling glassware Standard-taper joints are rigid, so a glassware apparatus must be assembled carefully to avoid strain that can result in breakage. First, place the necessary clamps and rings at appropriate locations on the ring stand (use two ring stands for distillations setups). Then, assemble the apparatus from the bottom up, starting at the heat source. Position the heat source on a ring or a Boy elevator so that it can be removed easily when the heating period is over; otherwise it may continue to heat a reaction mixture or an empty distilling flask even after it is switched off, causing a danger of breakage, tar formation, or even an explosion. Clamp the reaction flask or boiling flask securely at the proper distance from the heat source. As you add other components clamp them to the ring stand(s) but don’t tighten the clamp jaws completely until all of the components are in place and aligned properly.

Basic Safety Rules

These basic rules provide behavior, hygiene, and safety information to avoid accidents in the laboratory. Laboratory specific safety rules may be required for specific processes, equipment, and materials, which should be addressed by laboratory specific SOPs.

Basic safety rules for laboratory conduct should be observed whenever working in a laboratory. Many of the most common safety rules are listed below.

1. Know locations of laboratory safety showers, eyewash stations, and fire extinguishers. The safety equipment may be in the hallway near the laboratory entrance.
2. Know emergency exit routes.
3. Avoid skin and eye contact with all chemicals.
4. Minimize all chemical exposures.
5. No horseplay will be tolerated.
6. Assume that all chemicals of unknown toxicity are highly toxic.
7. Post warning signs when unusual hazards, hazardous materials, hazardous equipment, or other special conditions are present.
8. Avoid distracting or startling persons working in the laboratory.
9. Use equipment only for its designated purpose.
10. Combine reagents in their appropriate order, such as adding acid to water.
11. Avoid adding solids to hot liquids.
12. All laboratory personnel should place emphasis on safety and chemical hygiene at all times.
13. Never leave containers of chemicals open.
14. All containers must have appropriate labels. Unlabeled chemicals should never be used.
15. Do not taste or intentionally sniff chemicals.
16. Never consume and/or store food or beverages or apply cosmetics in areas where hazardous chemicals are used or stored.
17. Do not use mouth suction for pipetting or starting a siphon.
18. Wash exposed areas of the skin prior to leaving the laboratory.
19. Long hair and loose clothing must be pulled back and secured from entanglement or potential capture.
20. No contact lenses should be worn around hazardous chemicals – even when wearing safety glasses.

21. Laboratory safety glasses or goggles should be worn in any area where chemicals are used or stored. They should also be worn any time there is a chance of splashes or particulates to enter the eye. Closed toe shoes will be worn at all times in the laboratory. Perforated shoes or sandals are not appropriate.
22. Do not utilize fume hoods for evaporations and disposal of volatile solvents.
23. Perform work with hazardous chemicals in a properly working fume hood to reduce potential exposures.
24. Avoid working alone in a building. Do not work alone in a laboratory if the procedures being conducted are hazardous.
25. The PEL and the Threshold Limit Values (TLV) will be observed in all areas. If exposure above a PEL/TLV is suspected of an ongoing process, please contact EHS immediately.
26. Laboratory employees should have access to a chemical inventory list, applicable SDSs, department laboratory safety manual, and relevant SOPs.
27. Determine the potential hazards and appropriate safety precautions before beginning any work.
28. Procedures should be developed that minimize the formation and dispersion of aerosols.
29. If an unknown chemical is produced in the laboratory, the material should be considered hazardous.
30. Do not pour chemicals down drains. Do not utilize the sewer for chemical waste disposal.
31. Keep all sink traps (including cup sink traps and floor drains) filled with water by running water down the drain at least monthly.
32. Access to laboratories and support areas such as stockrooms, specialized laboratories, etc. should be limited to approved personnel only.
33. All equipment should be regularly inspected for wear or deterioration.
34. Equipment should be maintained according to the manufacturer's requirements and records of certification, maintenance, or repairs should be maintained for the life of the equipment.
35. Designated and well-marked waste storage locations are necessary.

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Chapter 2

To the Knowledge About the Basic Glassware are used in the Laboratory

Background

Glassware are basically used as laboratory apparatus offers a wide range of containment and transport functions for solutions and other liquids used in laboratories. Most laboratory glassware is manufactured with borosilicate glass, a particularly durable glass that can safely be used to hold chemicals being heated over a flame and to contain acidic or corrosive chemicals. All laboratory glassware should be cleaned immediately following use to prevent chemical residue from congealing or hardening.

Beakers

Beakers are glass containers that come in a variety of sizes and can be used for mixing and transporting fluids, heating fluids over an open flame and containing chemicals during a reaction. While most beakers have graduated volume, measurements etched into their glass, the measurements are an approximation that may deviate from the actual volume by five percent, making them unsuitable for use as a precision measurement tool.

Test Tube

Test tubes are the archetypal image of chemistry, whilst beakers also make frequent appearances in school practical.

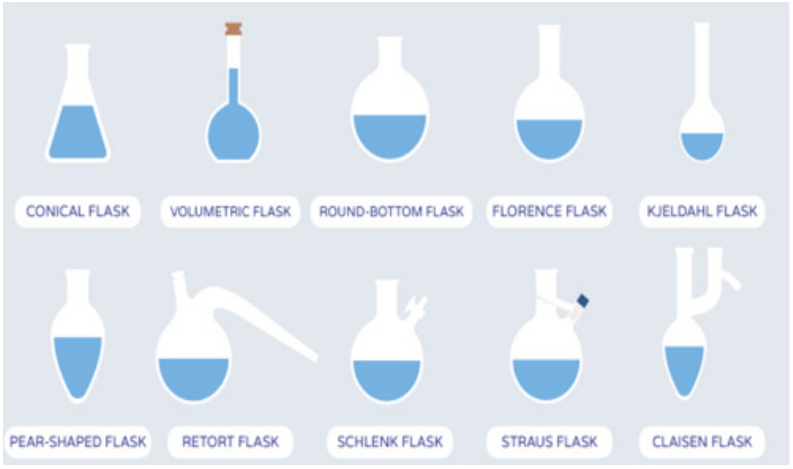
Boiling tubes are not that different from test tubes in appearance but are used when heating is required – they tend to be made of thicker glass and are slightly larger and wider.

Flask

Flasks are used in the chemistry lab is the most iconic is the conical (Erlenmeyer) flask. This also makes them useful for boiling liquids, and additionally their necks can support filter funnels.

Volumetric flasks are used to create precise quantities of solutions. A graduation line is etched into the volumetric flask's neck to indicate volume, and the lab worker begins to fill the flask by first adding the solute. She continues by

pouring in her solvent and then gradually adds drops of water as needed to bring the level of her solution up to the flask's graduated line. Which is also are used primarily in the preparation of standard solutions. To create a solution of a specific concentration, we need to know the volume of the solution; the narrow neck of the volumetric flask will have a thin graduation to show where a specific volume is reached.



Round-bottomed flasks and Florence flasks look very similar, but there is a slight difference between the two. Both have round bottoms, designed to spread out heat evenly when they are heated. They are frequently used by chemists for reactions and in rotary evaporators. Whereas round-bottomed flasks will usually have a ground glass joint on their neck, to allow connection to other apparatus, Florence flasks. They can also come with either a flat bottom, so they are free-standing, or a rounded bottom, and have longer necks.

Kjeldahl flask has an even longer neck, and was developed for use in the Kjeldahl method, which is used to determine the nitrogen content in a substance.

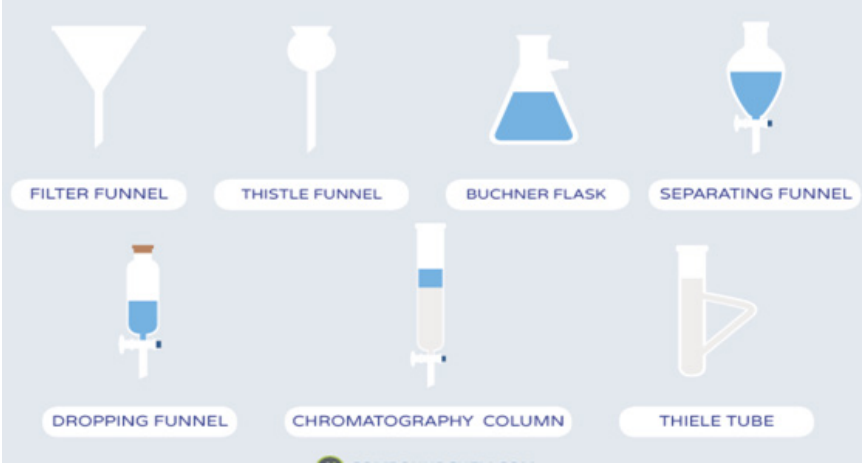
Pear-shaped flasks are usually rather small flasks, used for small-scale distillations. Their shape allows recovery of more material than the round-bottomed flasks.

Schlenk flask and the Straus flask are another two that look similar. Schlenk flasks are commonly used in air-sensitive chemistry, as the side arm allows an inert gas such as nitrogen to be pumped into the vessel. The Straus flask, on the other hand, is used to store dried solvents. The main neck is actually filled in halfway up and connected to a plugged smaller neck; this main neck can be connected to other apparatus and allows the solvent to be extracted when the plug is slightly withdrawn or removed entirely.

Claisen flask designed for vacuum distillation; distillation under vacuum produces problematic amounts of bubbles when solutions are boiled. Claisen's flask includes a capillary tube that inserts small bubbles into the liquid, easing the ferocity of boiling, whilst the branched portion of the flask hosts a thermometer.

Funnels, Analysis and Separation Funnels

Glass funnels can be used to guard against spillage when pouring chemicals from one vessel to another, and they can also be fitted with a filter to separate solids from liquids. Separatory funnels are also used for filtration and extraction, having a bulb-shaped enclosed body fitted with a stopper on top to prevent spillage when the funnel is inverted, along with a stopcock at the spout's base, which can be used to gradually lower the bulb's internal pressure.



Filter funnel into which filter paper can be placed, and a mixture can then be poured through. The smaller *thistle funnel* is not used for filtering at all, but to add liquids into apparatus.

Buchner funnel can be used in conjunction with a Buchner funnel in vacuum filtration and is a much quicker process than the gravity filtration used with normal filter funnels. A vacuum tube can be affixed to the flask's sidearm, which rapidly sucks through the solvent, leaving any solid in the Buchner funnel.

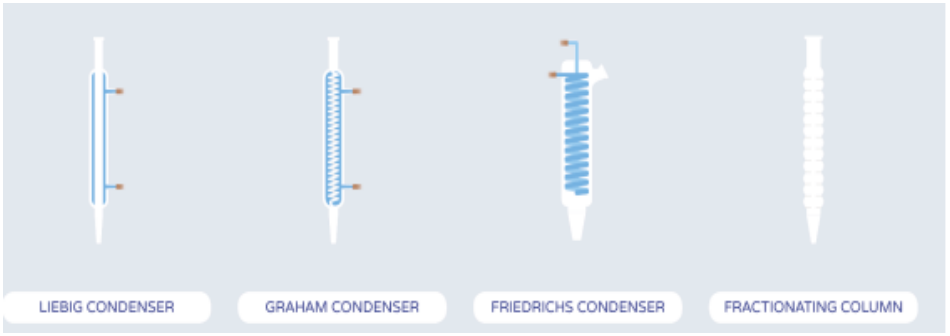
For separating solutions or liquids of different densities, separating funnels can be used. Liquids of a lower density will float to the top, then the mixtures can be tapped off separately. The similar-looking dropping funnel is used to add liquids or solutions to a reaction.

Another method of separating mixtures of compounds is column chromatography, which can be carried out using a chromatography column.

Thiele tube is a piece of apparatus used to determine the melting point of a solid compound. It contains and heats an oil bath, into which a sample can be placed along with a thermometer. Heating then allows melting point to be determined. The design of the flask allows the oil to circulate, ensuring even heating.

Condensers

A range of different condensers can be utilized in laboratories as important components of distillation apparatus. The most commonly seen condenser in schools is the *Liebig condenser*, which has an inner tube through which vapour flows, surrounded by a 'jacket' through which cool water passes and condenses the vapour.

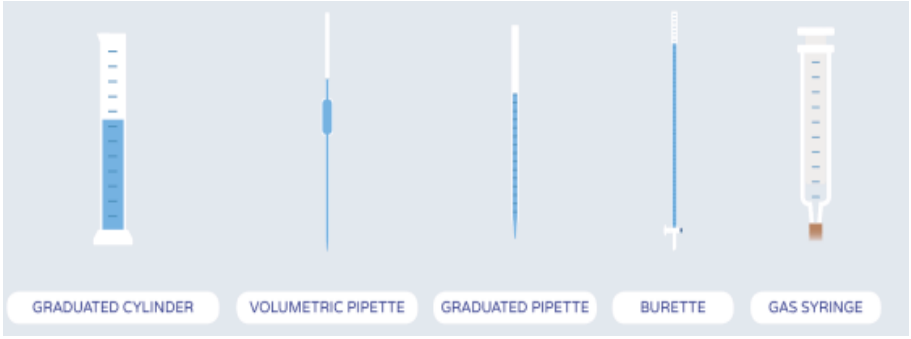


Graham condenser is like this but has a coiled path for the vapour to flow through and condense. Meanwhile, the *Friedrichs condenser* inverts the arrangement, having a spiral coil through which the coolant flows, with the vapour surrounding it. Other varieties of condenser are also available, though are not shown here.

Fractionating column which helps separate a mixture during distillation, as vapours collect and distill on the small glass 'trays' ascending the column. Only the most volatile gases will ascend all the way to the top of the column to be distilled off.

Measuring Apparatus

Graduated cylinders are tall, narrow containers used for measuring volume. While they are more accurate than beakers, measuring their contents to within one percent of actual volume, they're not used for quantitative analysis of fluids that require a high degree of precision. Graduated cylinders are fitted with a "bumper ring," a ring that shields the glass from impacting the work surface if the cylinder's knocked over. Bumper rings should be placed near the graduated cylinder's top for maximum protection.



Volumetric pipette which can be used to measuring volumes of solutions more precisely. These come in a variety of sizes, each measuring a fixed volume of solution.

Graduated pipettes can also be used, which allow various small volumes to be measured out. For measurement of volumes during titrations (the addition of one solution to another to determine an unknown concentration) *burettes* are used. These are long, narrow tubes, with incremental volume markings, which allow precise volumes of solutions to be dropped into another solution.

Gas syringe can be used to measuring the volume of gas produced in a reaction. This piece of apparatus can be attached to the top of a flask via a piece of tubing, and the gas produced pushes the plunger out of the syringe, allowing the gas volume to be measured.

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Chapter 3

Recrystallization of Given Sample Aspirin and Acetanilide

Recrystallization process is, also known as fractional crystallization, is a procedure for purifying an impure compound in a given solvent. The method of purification is based on the principle that the solubility of most solids increases with increased temperature. This means that as temperature increases, the amount of solute that can be dissolved in a solvent increase.

Principle

Recrystallization process is a laboratory technique for purifying different types of solids. The basic features of this technique are causing a solid to go into solution, and then gradually allowing the dissolved solid to crystallize. It is actually a very challenging process to get completely right. The goal is to obtain a compound in high purity as uniform crystals. Recrystallization is therefore a purification technique.

It is a crystallization technique used to purify a chemicals. By dissolving both impurities and a compound in an appropriate solvent, either the desired compound or impurities can be removed from the solution, leaving the other behind.

When an organic compound has been made it needs to be purified, particularly if it is a pharmaceutical chemical. This is because most organic reactions produce byproducts but, even if the reaction is a 'clean' one, the purity standards for many products are so stringent that small amounts of other compounds have to be removed. In the laboratory, this is often done by recrystallization. The general method is to find a solvent that dissolves the product more readily at high temperature than at low temperature, make a hot solution, and allow crystallizing on cooling. The crude product might contain.

1. Impurities which are insoluble in the solvent.
2. Impurities which are slightly soluble in the solvent; and
3. Impurities which dissolve readily in the solvent.
4. The solvent itself has also to be removed or it behaves as an impurity in its own right. It must not leave behind any residue.

Theory

The basic concept of purification technique. It works because of:

1. Different substances have different solubilities in the same solvent, and
2. Only molecules of the same compound will fit easily into the crystal lattice of that compound. Impurities remain in solution or stick on the outside of the crystal lattice.
3. In practice you purify by slowly cooling a hot, saturated solution of your compound. While cooling, molecules of the same type align in a crystal lattice, forming crystals.
4. After cooling, crystals are collected by vacuum filtration and washed by rinsing with ice-cold solvent.
5. There are also different recrystallization techniques that can be used such as:

Single-Solvent Recrystallization

Single solvent recrystallization is the most basic and commonly used recrystallization method.

An ideal solvent does NOT dissolve the solid at room temperature BUT dissolves the solid well in hot solvent.

Two Solvent Recrystallization

Two solvent recrystallizations is an alternative and very useful recrystallization method to single solvent recrystallization.

The first solvent should dissolve your crude product very well at room temperature (or in hot solvent). The second solvent should NOT dissolve your crude product at room temperature or in hot solvent.

The two solvents should be completely miscible and preferably have similar boiling points.

Key Points of Recrystallization Process to Carried Out

Choosing a Good Recrystallization Solvent

1. A good solvent for recrystallization is one that your compound not very soluble in at low temperatures, but very soluble in at higher temperatures.
2. For example, if the solubility of your compound in ethanol is 1 g/100 mL at 00 ºC and 2 g/mL at 500 ºC, then you won't be able to purify much more than 1 gram.
3. Conversely, if the solubility of your compound in ethanol is 10,000 g/100 mL at 0 ºC and 20,000 g/100 mL at 500 ºC, this is also equally useless.

4. When are you going to be purifying that much of your compound like 10 kg; In this case, ethanol is just too soluble?
5. Ethanol is a good solvent to recrystallize acetanilide because of the wide solubility range- 18 g/100 mL at 0 ºC and 80 g/mL at 500 ºC.

Like Dissolves Like

1. Polar compounds are soluble in polar solvents such as water, methanol, and ethanol. If your compound contains a polar group (see image below), it's best to use these solvents.
2. Nonpolar compounds are soluble in non-polar solvents such as hexanes and diethyl ether.

Crystal Size and Cooling Speed

1. The speed at which you allow a saturated solution to cool affects the size of the crystals that form.
2. If you take a hot solution and slam it into an ice bath, you'll get smaller crystals.
3. If you allow a hot solution to cool without any added heat for 10-20 minutes, and then place it in an ice bath, you'll get larger crystals.
4. This makes an important different- if you have smaller crystals, they are more likely to clog a filter! Everyone likes to get out of organic lab as soon as possible, but a clogged filter could add a good 30-40 minutes to your procedure.
5. It's worth it not to place your solution in an ice bath right away; let it cool close to room temperature first.

Removing Insoluble Impurities

1. Let's say you accidentally spilled group black pepper in a solution of acetanilide and ethanol. The black pepper won't dissolve.
2. So how do you remove it? By filtering the liquid- the black pepper will get stuck in the filter paper, and you can continue to recrystallize the liquid solution as normal.
3. The best way to get product to crash out is to add a seed crystal. This is just a small amount of pure material.
4. You can also try scratching the sides of the container with a stirring rod. This works because you pick up a small amount of solvent which evaporates and leaves behind a small amount of pure product.
5. So if you wanted to, you can allow some of the mother liquor to evaporate and collect more products.

The key features necessary for a successful recrystallization process, are a very controlled temperature decrease and enough time. Because most solids have a better solubility at higher temperatures, we can saturate or almost saturate a solution at high temperature (usually the boiling temperature of the solvent), and then slowly allow the solution to reach room temperature.

Recrystallization Works Best When

1. The quantity of impurities is small
2. The solubility curve of the desired solute rises rapidly with temperature

The slower the rate of cooling, the larger the crystals are that form. The disadvantage of recrystallization is that it takes a long time. Also, it is very important that the proper solvent is used. This can only be determined by trial and error, based on predictions and observations. The solution must be soluble at high temperatures and insoluble at low temperatures. The advantage or recrystallization is that, when carried out correctly, it is a very effective way of obtaining a pure sample of some product, or precipitate.

Requirements

Chemicals: as per specific requirement

1. Acetanilide = 5 gm
2. Aspirin = 20 ml
3. Ethanol = 100 ml
4. Distilled water = 100 ml

Glassware/Apparatus

1. Volumetric flask (200 mL)
2. Glass rod
3. Beaker
4. Measuring cylinder
5. Pipette
6. Burette
7. Tripod stand
8. Thermometer
9. Oil bath
10. Water Bath

Standard Procedure

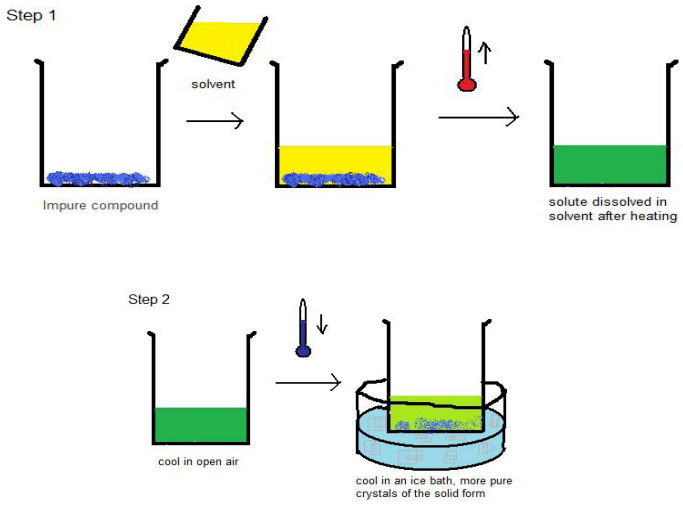
These are the important steps to the recrystallization process

Dissolve the solute in the solvent: Add boiling solvent to a beaker containing the impure compound. Heat the beaker and keep adding solvent until the solute is completely dissolved. **See Figure 1**

Cool the Solution: The solution is cooled in open air first, and then cooled in an ice bath. Slow cooling often leads to purer crystals. Crystals should form on the bottom of the beaker. The process of "seeding" can be used to aid the formation of crystals- this means adding a pure crystal of the compound. The pure crystal forms a surface for the solute to crystallize upon. **See Figure 2.**

Obtain the crystals of the solute: The more pure crystals of the solute are the desirable part of the mixture, and so they must be removed from the solvent. The process used for isolating the crystals that remain in the beaker still is called vacuum filtration. Suction is created using an aspirator, and whatever remains in the beaker is poured through a Buchner funnel. If for some reason there are no crystals visible, a gravity filtration can be performed. Activated carbon is added to the solution, the mixture is boiled, and a funnel system is used to transfer the new mixture to a new beaker of boiling solvent. Filter paper is used in the funnel to remove excess carbon. After this mixture cools slowly, there should be large crystals present.

Dry the resulting crystals: The crystals are dried by leaving them in the aspirator and then by removing them to a glass dish to wait a while longer. The purity of the crystals can be tested by performing a "melting point determination".



Examples

Procedure for Recrystallization of Acetanilide

1. The solubilities of most solids in solution increase as the temperature of the solution increases.
2. For example, the solubility of acetanilide in ethanol at 0 °C is about 18 g/100 mL.
3. This means that if you drop 50 grams of acetanilide in 100 mL of ethanol at 0 °C, about 18 grams will dissolve in the ethanol and the rest (~32g) will remain suspended in the solution.
4. But the solubility of acetanilide in ethanol increases to about 80 g/100 mL at 500 °C.
5. This means that if we heated up the same acetanilide-ethanol suspension to 500 °C, all of the acetanilide would dissolve.
6. In fact, we can add about another 30 grams of acetanilide to this solution and it would still dissolve, but once we added more than 80 g, additional solid acetanilide would no longer dissolve, and we would have a suspension once more.
7. At this point the solution is said to be saturated. So, let's say we had 50 g of acetanilide dissolved in 100 mL of ethanol at 500 °C.
8. What would happen if we allowed the temperature to cool back down again to 0 °C? At this point, we have more acetanilide dissolved in the ethanol that it should be able to hold, 50g vs. 18g, so the solution is said to be supersaturated.
9. That means that sooner or later, the extra ~32 grams of acetanilide should precipitate out of solution (also known as crashing out).
10. We then collect the acetanilide via vacuum (or gravity) filtration.
11. The liquid that remains after the filtration is known as the Supernatant Mother Liquor (or just Mother Liquor for short).
12. It's usually a good idea to save it. Because there were relatively little impurities compared with the relatively large amounts of acetanilide and ethanol used, those impurities should remain dissolved in the solution; the ~32 grams of acetanilide we collect should be pure.

Recrystallization of Salicylic Acid Contaminated Aspirin [Acetylsalicylic Acid (ASA)]

1. Aspirin does not like to dissolve in water. It sometimes dissolves slightly in hot alcohols.
2. To purify by recrystallization, place your crude aspirin (5 gm) in a 50 mL Erlenmeyer flask and dissolve it in a minimum amount of boiling propanol/ethanol (Do this in a water bath).
3. Remove the flask and add warm water drop wise until the solution becomes slightly cloudy.
4. Allow the solution to cool until crystallization starts then finish crystallizing in the ice-bath.
5. Collect your product by filtration, wash with small quantities of cold water. Place in the oven and complete its drying overnight.
6. Then Weigh and determine the melting point of the pure aspirin.

Result

The recrystallization of aspirin and acetanilide was done in a solvent ethanol.

Uses

Recrystallization is most important methods of purifying nonvolatile solids.

❑

Chapter 4

To Obtain Pure Components from a Mixture of Organic Compounds (Limonene) Using Steam Distillation

Principle

Steam distillation technique is used for separating substances which are immiscible with water, volatile in steam & having high vapour pressure at the boiling temperature of water. Consider two immiscible liquids. In the mixture one liquid cannot mix the properties of the other. So, each liquid behaves as if the other is not present. Therefore, each liquid will show it's on vapour pressure but the sum of the vapour pressures will be much higher than the vapour pressures of liquids. Hence the mixture of two immiscible liquid will boil at a lower temperature than the normal boiling point. So, this method can be used for purifying liquids with very high boiling points. e.g. Aniline.

If water is used as one of the immiscible liquids the method is called steam distillation. It is also used for purifying liquids which decompose at their normal boiling points. e.g. Glycerol.

This technique is used for separating organic compounds from plant parts. e.g. Lemon grass oil, Eucalyptus oil etc.

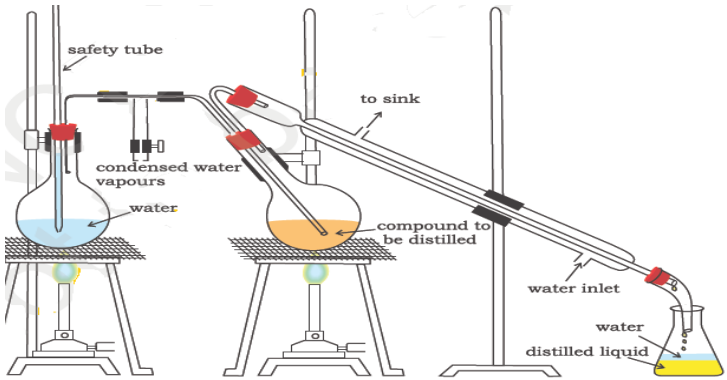
The steam distillation process works on the principle that when a mixture of two or more undissolved liquids are heated, while ensuring that the surfaces of both liquids are in contact with the atmosphere, the vapor pressure exerted by the system increases.

For example, the boiling point of **bromobenzene** is 156 °C and the boiling point of **water** is 100 °C, but a mixture of the two boils at 950 °C. Thus, **bromobenzene** can be easily distilled at a temperature 61 °C below its normal boiling point.

Basic Importance of Steam Distillation

1. Steam distillation is used to separate **heat-sensitive components**.
2. Steam is added to the mixture, causing some of it to vaporize. This vapor is cooled and condensed into two liquid fractions. Sometimes the fractions are collected separately, or they may have different density values, so they separate on their own.
3. An example is steam distillation of flowers to yield essential oil and a water-based distillate.

4. Steam distillation is employed in the isolation of essential oils, for use in perfumes.
5. Steam distillation also is an important means of separating fatty acids from mixtures and for treating crude products such as tall oils to extract and separate fatty acids, soaps and other commercially valuable organic compounds. Steam distillation was invented by the Persian chemist, **Ibn Sina** (known as **Avicenna** in the West), in the early 11th century. He invented it for the purpose of extracting essential oils, which are used in aromatherapy and the drinking and perfumery industries.



Steam distillation. Steam volatile component volatilizes, the vapours condense in the condenser and the liquid collects in conical flask.

Requirements

Chemicals: as per specific requirement:

1. Bromine water, no more than 0.2% v/v.
2. Potassium manganate (VII), 0.001 M.
3. Cyclohexene (Highly flammable, harmful if swallowed).
4. Cyclohexane (Highly flammable, skin and respiratory irritant).
5. Distilled water (100 ml).

Glassware/Apparatus

1. Eye protection
2. Grater
3. Bunsen burner
4. Heat resistant mat
5. Tripod and gauze
6. Oranges (2)

7. 1100 °C thermometer
8. Measuring cylinder (100 ml)
9. Measuring cylinder (50 ml)
10. Distillation apparatus
11. 250 ml round bottomed flask
12. Still head
13. Thermometer pocket
14. Condenser
15. Receiver adapter
16. Test tubes and bungs
17. Dropping pipette
18. Anti-bumping granules
19. Oil bath

Importance of Extracting Limonene from Oranges by Steam Distillation

1. The peel of oranges is boiled in water and the oil produced (limonene) distilled in steam at a temperature just below 100 oC, well below its normal boiling point. The immiscible oil can then be separated. Direct extraction by heating would result in decomposition whereas steam distillation does not destroy the chemicals involved.
2. Limonene (1-methyl-4-prop-1-en-2-yl-cyclohexene) is an unsaturated hydrocarbon, classed as a terpene. At room temperature it is a colourless oily liquid with the smell of oranges. Its molecular formula is $C_{10}H_{16}$ and its boiling point is 176°C.
3. Limonene is a chiral molecule with two optical isomers (enantiomers). The major biological form (d)limonene, the (R)-enantiomer, is used in food manufacture and medicines. It is also used as a fragrance in cleaning products, a botanical insecticide, and due to its flammability, a potential biofuel. The (S)-enantiomer, l-limonene, is also used as a fragrance but has a piney, turpentine odour.

Procedure

Step 1

1. Grate the outer orange coloured rind of two oranges and add to 100 ml of distilled water in the 250 ml round bottomed flask. Add anti-bumping granules to the round bottomed flask.

2. Set up the distillation apparatus as shown in the apparatus section.
3. Heat the flask so that distillation proceeds at a steady rate, approximately one drop per second of distillate. (Note: Take care not to let the liquid in the round bottomed flask boil too strongly).
4. Collect approximately 50 cm^3 of distillate in the measuring cylinder. The oil layer will be on the surface.
5. Using a dropping pipette carefully remove the oil layer into a test tube for the next stage.

Step 2

Odour: Cautiously smell the extracted oil by wafting the fumes towards the nose. Do not breathe in directly from the test tube.

Step 3

Action of bromine water

1. Measure out approximately 1 ml of bromine water into each of three test tubes.
2. Add a few drops of the limonene oil to one test tube, a few drops of cyclohexane to another, and a few drops of cyclohexene to the third. Place in the bungs and agitate. If the bromine water is decolourized the molecule contains double bonds.
3. 0.001 M potassium manganate (VII) can be substituted for the bromine water for class use.

Result

Extraction (steam distillation) of pure components from a mixture of organic compounds (Limonene) was performed, so the bromine water is decolourized hence confirm that the molecule contains double bond (Limonene) as compared to cyclohexane.

❑

Chapter 5

To Determination of Acid Value of the Given Oil/Fats Such as Ghee

Principle

Acid value which is defined as the number of mg of potassium hydroxide required to neutralize the free acid in 1 g of fat, fatty oil or other related substances is determined to assess the rancidity of the CMM samples. Sodium hydroxide may also be used. Here direct titration is done taking neutralized mixture of equal volumes of ethanol (95 %) and ether as solvent and phenolphthalein as indicator.

Acid number is a measure of the number of carboxylic acid groups in a chemical compound, such as a fatty acid, or in a mixture of compounds. The acid number is used to quantify the acidity of a substance. It is the quantity of base, expressed in milligrams of potassium hydroxide or sodium hydroxide, which is required to neutralize the acidic constituents in 1 g of sample.

Requirements

Chemicals: as per specific requirements

1. Sodium Hydroxide = 4 gm
2. Ether = 20 ml
3. Phenolphthalein Indicator = 1 gm
4. Ethanol = 5 ml
5. Potassium hydrogen phthalate = 0.6 gm
6. Distilled water = 200 ml

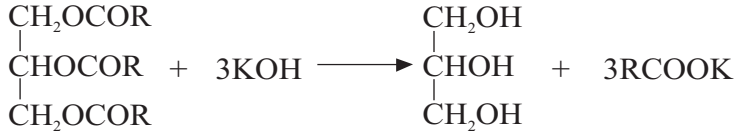
Glassware/Apparatus

1. Volumetric flask (200 mL)
2. Beaker
3. Pipette
4. Burette
5. Burette stand
6. Funnel
7. Measuring cylinder

8. Tripod stand
9. Water bath

Chemical Reaction

The acid value can be determined by the amount of free fatty acids in oil by integrating the carboxylic group proton (COOH) reacts with 3 moles of potassium hydroxide to give a glycerol and 3 moles of soap in the presence of ethanol.



Methods

Extraction of fatty oil Pulverize 30-50 g of CMM sample: Pass through No.2 sieve and mix well. Put the powdered sample in a cellulose extraction thimble. Place the cellulose extraction thimble in a Soxhlet extractor. Add 100-150 mL of n-hexane to a 500 mL round-bottomed flask. Perform the Soxhlet extraction using water bath for about 2 h. Cool down to room temperature. Filter through a No.3 sintered funnel. Transfer the filtrate to a 250 mL round-bottomed flask. Evaporate the solvent to dryness at reduced pressure in a rotary evaporator. Collect the fatty oil.

Determination of acid value (a) Reagents: Phenolphthalein indicator Weigh 1 g of phenolphthalein and dissolve in 100 mL of ethanol. Sodium hydroxide titrant Weigh accurately 4.0 g of sodium hydroxide and place it in a 1000- mL volumetric flask. Make up to the mark with water. Ethanol-ether solution Prepare a mixture of ethanol and diethyl ether (1:1, v/v). Neutralize with sodium hydroxide titrant and add 1.0 mL of phenolphthalein indicator until pink colouration is observed. Freshly prepare the solution.

(b): Standardization of sodium hydroxide titrant weigh accurately 0.6 g of potassium hydrogen phthalate, previously dried to constant weight at 105°C, and place it in a 250 mL conical flask, then add 50 mL of water. Shake it well. Add 2 drops of phenolphthalein indicator. Titrate the solution with the sodium hydroxide titrant until pink colouration can be observed. Towards the end of titration, potassium hydrogen phthalate should be completely dissolved. Calculate the concentration of the sodium hydroxide titrant.

Titration of test solution Unless otherwise specified: Weigh accurately a quantity of the fatty oil being examined as indicated in Table 1 and place it in a 250-mL conical flask, then add 50 mL of ethanol-ether solution. Shake it well. If necessary, reflux the mixture gently until the substance is completely dissolved. Titrate the

solution with sodium hydroxide titrant until pink colouration can be observed which persists for 30s. Measure the volume of sodium hydroxide titrant used and calculate the acid value according to the following equation:

$$\text{Acid value} = V_{NaOH} \times 5.61\,W$$

Where, V_{NaOH} = Volume of sodium hydroxide titrant used (mL)

W = Weight of the fatty oil being examined (g)

When the acid value is less than 10, it is suggested that a 10 mL semi-micro burette may be used for the titration.

Procedure

Reagents Preparation for Experiment

Phenolphthalein indicator: Weigh 1 g of phenolphthalein and dissolve in 100 mL of ethanol.

Sodium hydroxide titrant: Weigh accurately 4.0 g of sodium hydroxide and place it in a 1000 mL volumetric flask. Make up to the mark with water.

Ethanol-ether solution: Prepare a mixture of ethanol and diethyl ether (1:1, v/v). Neutralize with sodium hydroxide titrant and add 1.0 mL of phenolphthalein indicator until pink colouration is observed. Freshly prepare the solution.

Standardization of Sodium Hydroxide Titrant

1. Weigh accurately 0.6 g of potassium hydrogen phthalate, previously dried to constant weight at 105 °C, and place it in a 250 mL conical flask, then add 50 mL of water. Shake it well.
2. Then add 2 drops of phenolphthalein indicator.
3. Titrate the solution with the sodium hydroxide titrant until pink colouration can be observed.
4. Towards the end of titration, potassium hydrogen phthalate should be completely dissolved.
5. Calculate the concentration of the sodium hydroxide titrant.

Titration of Test Solution

1. Weigh accurately 1–10 gm of ghee and place it in a 250 mL conical flask, then add 50 mL of ethanol-ether solution.
2. Shake it well. If necessary, reflux the mixture gently until the substance is completely dissolved.
3. Titrate the solution with sodium hydroxide titrant until pink colouration can be observed which persists for 30 second.

4. Record the reading initial and final reading of burette. Calculate the difference value (ML) and acid vale.
5. Measure the volume of sodium hydroxide titrant used and calculate the acid value according to the following equation:

Acid Value = ml of alkali (titer volume) × N of alkali (NaOH)
× 28.2/Weight of sample (gm)
=% FFA × 1.99

Observation

No. of Observation	Initial Burette Reading (ml)	Final Burette Reading	Difference (ml)
1			
2			
3			

Calculation

Acid value = No of acid required to neutralize remaining KOH × 1000/w
= n × 0.00561 × 1000/w

Where, n = the no. of ml of 0.1 M potassium hydroxide required.
W = the weight of the fatty oil substance being examined (g).

Result

The Acid value of given oil or fat (Ghee) is …….

Uses

It is used as a determination of acid value of oils/fats, which may help to quality foods are serve to human being.

❑

Chapter 6

To Determination of Iodine Value of the Given Oil/Fats

Principle

The iodine value (or **iodine adsorption value** or **iodine number** or **iodine index**) in chemistry is the mass of iodine in grams that is consumed by 100 grams of a chemical substance. Iodine numbers are often used to determine the amount of unsaturation in fatty acids. This unsaturation is in the form of double bonds, which react with iodine compounds. The higher the iodine number, the more C=C bonds are present in the fat. It can be seen from the table that coconut oil is very saturated, which means it is good for making soap. On the other hand, linseed oil is highly unsaturated, which makes it a drying oil, well suited for making oil paints.

Fats and oils are a mixture of triglycerides. Triglycerides are made up of three fatty acids linked to glycerol by fatty acyl esters. Fatty acids are long chain hydrocarbons with carboxyl groups (COOH groups). These fatty acids can be classified into saturated or unsaturated based on the number of double bonds present in the fatty acid. Saturated fatty acids contain only single bond between the carbon atoms and tend to be solids at room temperature. Unsaturated fatty acids contain double bonds between the carbon atom in addition to the single bonds present in the fatty acid chain. They are likely to exists as liquids at room temperature. The double bonds present in the naturally occurring unsaturated fats are in the *Cis* form. Trans fatty acids are associated with health problems and cardiovascular diseases.

Requirements

Chemicals:

1. Carbon tetrachloride = 10 ml
2. Iodine monochloride = 20 ml
3. 0.1 M sodium thiosulphate = 50 ml
4. 1% Starch indicator Solution = 5 ml
5. Potassium iodide = 15 ml
6. Distilled water = 100 ml
7. Fat solution in carbon tetra chloride

Glassware/Apparatus

1. Volumetric flask (200 mL)
2. Beaker
3. Glass Pipette
4. Burette
5. Iodine flask
6. Burette stands with magnetic stirrer
7. Measuring cylinder

Chemical Reaction

Fatty acids react with a halogen [iodine] resulting in the addition of the halogen at the C=C double bond site. In this reaction, iodine monochloride reacts with the unsaturated bonds to produce a di-halogenated single bond, of which one carbon has bound an atom of iodine.

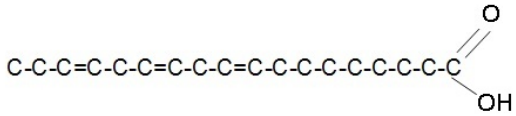
After the reaction is complete, the amount of iodine that has reacted is determined by adding a solution of potassium iodide to the reaction product.

$$ICl + KI \rightarrow KCl + I_2$$

This causes the remaining unreacted ICl to form molecular iodine. The liberated I2 is then titrated with a standard solution of 0.1N sodium thiosulfate.

$$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_2O_4$$

Saturated fatty acids will not give the halogenation reaction. If the iodine number is between 0–70, it will be a fat and if the value exceeds 70 it is an oil. Starch is used as the indicator for this reaction so that the liberated iodine will react with starch to give purple coloured product and thus the endpoint can be observed.



Procedure

Iodine monochloride (ICI) method or Wijs method

1. Arrange all the reagent solutions prepared and the requirements on the table.
2. Pipette out 10 ml of fat sample dissolved in chloroform to an iodination flask labelled as “TEST”.
3. Add 20 ml of Iodine Monochloride reagent into the flask. Mix the contents in the flask thoroughly.

4. Then the flask is allowed to stand for a half an hour incubation in dark.
5. Set up a BLANK in another iodination flask by adding 10 ml Chloroform to the flask.
6. Add to the BLANK, 20 ml of Iodine Monochloride reagent and mix the contents in the flask thoroughly.
7. Incubate the BLANK in dark for 30 minutes.
8. Meanwhile, take out the TEST from incubation after 30 minutes and add 10 ml of potassium iodide solution into the flask.
9. Rinse the stopper and the sides of the flask using 50 ml distilled water.
10. Titrate the "TEST" against standardized sodium thiosulphate solution until a pale straw colour is observed.
11. Add about 1ml starch indicator into the contents in the flask, a purple colour is observed.
12. Continue the titration until the colour of the solution in the flask turns colourless.
13. The disappearance of the blue colour is recorded as the end point of the titration.
14. Similarly, the procedure is repeated for the flask labelled 'BLANK'.
15. Record the endpoint values of the BLANK.
16. The procedure is repeated without the sample and the number of ml required is noted as (b).
17. Iodine value is calculated from the observed data.
18. Calculate the iodine number using the equation below:

Volume of Sodium thiosulphate used = [BLANK- TEST] ml

Observation

	No. of Observation	**Initial Burette Reading (ml)**
For TEST	1	
	2	
For BLANK	1	
	2	

Calculation

Iodine value = 1.269 (b-a)/W

Here, w = weight in grams of the sample.

Note: The approx. weight in grams of the sample to be taken can be calculated by dividing 20 by the highest expected iodine value. If more than half of the halogen is observed, the test must be repeated with a lesser quantity of sample.

Result

The Iodine value of given oil or fat is …….

Uses

The iodine value (or iodine adsorption value or iodine number or iodine index) in chemistry is the mass of iodine in grams that is consumed by 100 grams of a chemical substance. Iodine numbers are often used to determine the amount of unsaturation in fatty acids.

❑

Chapter 7

Determination of Saponification Value of the Given Oil/Fats

Principle

The saponification value corresponds to the mass in mg of potassium hydroxide (KOH - commonly known as potash) needed to neutralize the free fatty acids and saponify the esters contained in a gram of material.

Saponification value is a measure of the content of ester linkages. Saponification value is defined as the number of milligrams of potassium hydroxide (KOH) required to completely saponify (hydrolyze) one gram of the fat/oil under the conditions specified. It is a measure of the average molecular weight (or chain length) of all the fatty acids present. As most of the mass of a fat/tri-ester is in the 3 fatty acids, the saponification value allows for comparison of the average fatty acid chain length. The long chain fatty acids found in fats have a low saponification value because they have a relatively fewer number of carboxylic functional groups per unit mass of the fat as compared to short chain fatty acids. If more moles of base are required to saponify N grams of fat then there are more moles of the fat and the chain lengths are relatively small, given the following relation:

Number of moles = mass of oil/average molecular mass

Thus, it is a value that can be found experimentally. In the case of a pure triglyceride (containing only a single type of fatty acid), the saponification value can be obtained by the following formula (where MW is the molar mass of the substance):

$$\mathbf{Is = 56 \times 103/MW}$$

Soaps are an integral part to maintain good health and hygiene of the individuals. Soaps are essential to cleanse dirt and oil off the objects including skin surface. Soaps are widely used in bathing, cleaning, washing and in other household chores.

Fats and oils are the principle stored forms of energy in many organisms. They are highly reduced compounds and are derivatives of fatty acids.

Significance of Saponification Value

1. The magnitude of saponification value gives an idea about the average molecular weight of the fat or oil.

2. Higher the molecular weight of the fat, the smaller is its saponification value.
3. Saponification value also indicates the length of carbon chain of the acid present in that particular oil or fat.
4. Higher the saponification value, greater is the percentage of the short chain acids present in the glycerides of the oil or fats.

Requirements

Chemicals:

1. Oil or fat = 2 gm
2. 0.5 N HCl = 20 ml
3. Phenolphthalein indicator = 1 ml
4. 0.5 N Ethanoic KOH Solution = 25 ml
5. 0.5 N Potassium Hydroxide

Glassware/Apparatus

1. Round bottom flask (200 mL)
2. Beaker
3. Pipette
4. Burette
5. Water bath
6. Reflux condenser
7. Tripod stand

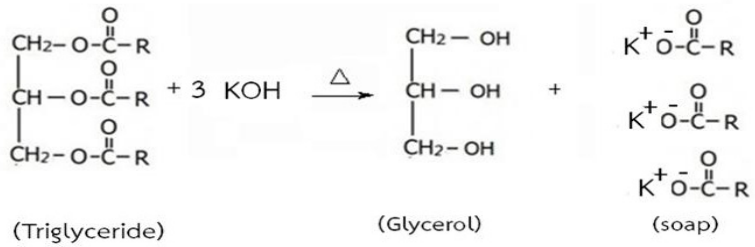
Chemical Reaction

Saponification is simply ***the process of making soaps***. Soaps are just potassium or sodium salts of long-chain fatty acids. During saponification, ester reacts with an inorganic base to produce alcohol and soap. Generally, it occurs when triglycerides are reacted with potassium or sodium hydroxide (lye) to produce glycerol and fatty acid salt, called 'soap'.

The saponification value is the number of mg of potassium hydroxide required to neutralize the fatty acids resulting from the complete hydrolysis of 1 g of the substance. In a practice a known amount of the oil or fat is refluxed with excess amount of standard alcoholic potash solution and the unused alkali is treated against a standard acid.

Reaction Takes Place in Two Steps

There can be either one-step saponification or two-step saponification process to convert triglycerides to soaps. The examples mentioned above are a one-step saponification process in which triglycerides, when treated with a strong base, splits from the ester bond to release glycerol and soaps (i.e. fatty acid salts).On the other hand, in the two-step saponification process, the steam hydrolysis of the triglyceride yields glycerol and carboxylic acid (rather than its salt). In the second step, alkali neutralizes fatty acid to produce soap.



Procedure

1. Take a 2 g of the test substance such as given oil or fats, accurately weighed, or the quantity specified in the monograph, in a conical flask with a capacity of about 200 mL.
2. Then add 25 mL of potassium hydroxide/ethanol, TS1 attach a reflux condenser, and heat in a boiling water-bath for 30 minutes, or the time specified in the monograph, frequently rotating the contents of the flask; immediately add 1 mL of phenolphthalein/ethanol TS and titrate the excess of alkali with hydrochloric acid (0.5 mol/l) VS.
3. Add 25 ml of 0.5 N alcoholic KOH and mix well, attach this to a reflux condenser.
4. Set up another reflux condenser as the blank with all other reagents present except the fat.
5. Place both the flasks in a boiling water bath for 30 minutes.
6. Cool the flasks to room temperature.
7. Now add phenolphthalein indicator to both the flasks and titrate with 0.5 N HCl.
8. Note down the endpoint of blank and test.
9. The difference between the blank and test reading gives the number of milliliters of 0.5 N KOH required to saponify 1 g of fat.
10. Calculate the saponification value.

Observation

	Samples No.	Initial Burette Reading (ml)	Final Burette Reading	Difference (ml)
For excess KOH remaining	1			
	2			
For Blank	1			
	2			

Calculation

Saponification value = No of acid required to neutralize remaining KOH × 1000/W

= (b-a) × 0.02805/W

Result

The saponification value of given oil or fat is …….

Uses

Soaps are essential to cleanse dirt and oil off the objects including skin surface. Soaps are widely used in bathing, cleaning, washing and in other household chores. Soaps are an integral part to maintain good health and hygiene of the individuals. It is also used in:

Wet chemical fire extinguishers: To extinguish cooking oils and fats, we use a saponification reaction. This is because cooking oils and fats have a flashpoint which is above 37^{o} which render regular fire extinguishers useless.

Creating hard and soft soaps: By using different types of alkali in the process the type of reaction product can be altered between hard and soft:

1. Using KOH: We can obtain soft soaps.
2. Using NaOH: We can obtain hard soaps.

❑

Chapter 8

Synthesis and Characterization of Benzanilide from Aniline by Acetylation Reaction

Principle

Amine compounds on treatment with benzoyl chloride gives benzoyl derivatives, the reaction is known as **Schotten-Baumann Reaction**. The benzanilide is prepared by insertion of benzoyl moiety instead of an active hydrogen atom present in primary amino ($-NH_2$) or secondary amino group (-NH) is usually termed as benzoylation reaction.

This reaction essentially bears a close resemblance to the phenomenon of acetylation except that in specific instance the reagent (benzoyl chloride) which reacts in the present pyridine or 10% NaOH and not benzoic anhydride. The amines are more soluble in acid chloride than in NaOH, the reaction occurs preferably between benzoyl chloride and amine. In the preparation of benzanilide, NaOH neutralizes the liberated HCl and catalyzed the reaction. It is a base-catalyzed (aqueous sodium hydroxide or pyridine) reaction that is necessary to encourage an equilibrium shift towards the formation of amides. The base also neutralizes the hydrochloric acid, which is formed in the process, thereby preventing the further protonation of the amide product formed.

Requirements

Chemicals:

1. Aniline = 2 ml
2. Benzoyl chloride = 2.8 ml
3. Hot Ethanol = 50 ml
4. 10% sodium hydroxide = 30 ml
5. Cold water = 100 ml

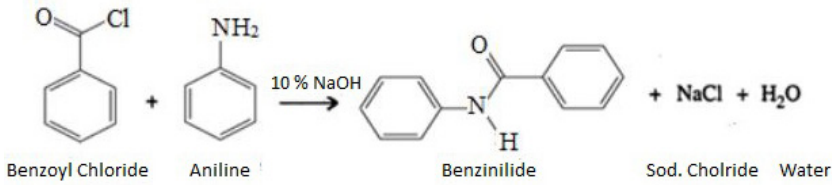
Glassware/Apparatus

1. Erlenmeyer flask (250 mL)
2. Volumetric flask
3. Pipette
4. Glass stirring rod

5. Buchner funnel
6. Suction pump
7. Filter papers
8. Measuring cylinder
9. Rubber clock
10. Fume hood

Chemical Reaction

In this reaction benzoyl chloride is react with aniline in the presence of 10% sodium hydroxide solution. Benzoylation of compounds those are containing active hydrogen such as phenol, aniline, alcohol etc. form benzoyl chloride in the presence of aqueous NaOH (Schotten Baumann reaction).



Procedure

1. Take a 2.0 mL (2.04 g) of aniline and 30 mL of 10% sodium hydroxide solution in 250 mL Erlenmeyer flask with a good rubber cork and shake well at room temperature.
2. Sincerely add 2.8 mL (3.39 g) of benzoyl chloride (**using fume hood**), cork the flask and shake the mixture vigorously with intermittent pressure release (**perform under a fume hood**) for at least 15-20 minutes.
3. Reaction mixture is diluted with cold water, filter out the crude benzanilide with suction pump on a Buchner funnel, and wash with a cold water/ice water.
4. The reaction mixture is a recrystallizing from hot alcohol in a at least 2 times.
5. The crude product of benzanilide is obtained.
6. Dried the product and calculate the practical yield about 3.2 gm.

Calculation

The basic reagent is aniline; hence give a yield should be calculated from its amount taken.

1. Molecular formal of aniline = C_6H_7N
2. Molecular formal of benzanilide = $C_{13}H_{11}NO$
3. Molecular weight of aniline = 93 g/mol
4. Molecular weight of benzanilide = 197 g/mol

Theoretical Yield

As per specific quantity used in this reaction:

Here 93 g of aniline reacts with a benzoyl chloride to gives a 197 g of benzanilide.

Therefore, 2.04 g of aniline will give?..... (X) g of crude product of benzanilide.

$$X = (197 \times 2.04)/93 = 4.32\ g$$

Theoretical yield = 4.32 g

Practical yield = assume 3.2 g

Percentage practical yield = (Practical yield×100)/Theoretical yield

= (3.2 × 100)/4.32

= 74.07 %

Properties

1. White crystalline solid.
2. Insoluble in water and soluble in 85 % acetic acid and ethanol.
3. Boiling point is about 117 °C.
4. Melting point is 163 °C.

Result

Benzanilide was synthesized by the reaction of aniline and benzoyl chloride and give the crude product. The practical yield was found to be 3.2 gm and % yield about 74.07 % and melting point of benzanilide was measured and found to be 163 °C.

Uses of Benzimidazole

Benzimidazole was used as amide model compound to study the reaction between the amide and epoxy. It is also used to study the influence of β-cyclodextrin on photo rearrangement of acetanilide, benzanilide and ethyl phenyl carbonate.

Safety and precautions must be taken during perform practical:

1. Properly wear gloves and goggles throughout this experiment perform in a laboratory.
2. Aniline is more toxic and can be easily absorbed through the skin. Hence the mixing of aniline is done in a use in a fume cup hood/Fuming chamber.
3. Benzoyl chloride is very toxic. It is lachrymatory and should be handled with care under the reaction the mixture in fume cup hood.
4. If any problems occur you spill a lot of either of these, wash it off with lots of water and notify your laboratory instructor or teacher.
5. In a reaction mixture freshly, distilled aniline should be used to get a better result, or a small amount of zinc can be added in the reaction mixture

Questions

1. What is the purpose of the addition of NaOH to the benzoylation of aniline with benzoyl chloride?
2. What is benzoylation?
3. What are the advantages of benzoylation over acetylation?

❑

Chapter 9

Synthesis and Characterization of Phenyl Benzoate from Phenol by Acetylation Reaction

Principle

Synthesis of phenyl benzoate from phenol is an example of Schotten-Baumann Reaction where phenols react with an aromatic acid chloride in the presence of an excess of a base at room temperature to form an ester. In this reaction, phenol is shaken with benzoyl chloride and excess amount of sodium hydroxide solution, it is benzoylated to give the ester, phenyl benzoate. The phenol is first converted into the ionic compound sodium hydroxide to give sodium phenoxide (sodium phenate) by dissolving in sodium hydroxide solution. The phenoxide ions reacts more rapidly with benzoyl chloride than the original phenol does, but even so you have to shake it with benzoyl chloride for about 15 minutes. Solid phenyl benzoate is formed to give phenyl benzoate.

The introduction of a benzoyl group in place of the active hydrogen of hydroxyl, amino group is known as benzoylation reaction. The reaction is somewhat like acetylation except that here the reagent used is benzoyl chloride in presence of NaOH and not the benzoic anhydride.

Requirements

Chemicals: as per specific quantity require to reaction.

1. Phenol = 1 gm
2. Benzoyl chloride = 2 ml
3. Ethanol = 50 ml
4. 10% sodium hydroxide = 15 ml
5. Cold water = 100 ml
6. Methanol = 100 ml

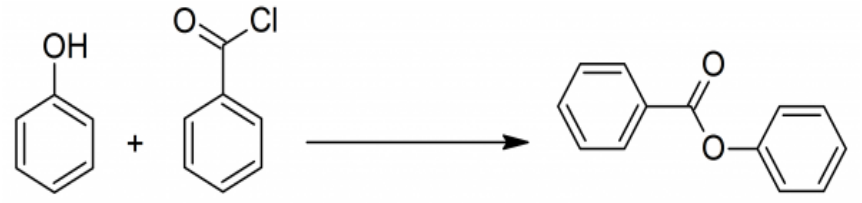
Glassware/Apparatus

1. Erlenmeyer flask (250 mL)
2. Volumetric flask
3. Pipette
4. Glass stirring rod

5. Buchner funnel
6. Suction pump
7. Filter papers
8. Measuring cylinder
9. Rubber cork
10. Fume hood
11. Spatula

Chemical Reaction

Phenyl benzoate is a phenyl ester of benzoic acid. Phenol is treated with benzoyl chloride in presence of sodium hydroxide for preparation phenyl benzoate.



Procedure

1. Take a 1.0 g of phenol and add a 15 mL of 10% sodium hydroxide solution in 250 ml Erlenmeyer flask with a good rubber cork and shake well at room temperature.
2. Carefully add 2.0 mL of benzoyl chloride (under fume cup hood), cork the flask and shake the mixture vigorously with intermittent pressure release for at least 15-20 minutes.
3. The reaction should be complete, and a solid product obtained is filter off with suction pump on Buchner funnel, breaking up any lumps occurs in a crude product on the filter with a spatula, and then wash thoroughly with ice water.
4. Erlenmeyer flask rinse with cold water in 2 times to remove any residual crystals which may be present in a crude product.
5. Phenyl benzoate as possible from the Buchner funnel to a clean, dry 250 mL beaker and recrystallize it from methanol.
6. Weigh the recrystallized phenyl benzoate and calculate the practical yield about 1.8 gm.
7. Determine the melting point of the synthesized phenyl benzoate.
8. It's obtained as colourless needles; melting point is 68–69 ^{o}C.

Calculation

Here limiting reagent is phenol; hence yield should be calculated from its amount taken.

1. Molecular formal of phenol = C_6H_6O
2. Molecular formal of phenyl benzoate = $C_{13}H_{10}O_2$
3. Molecular weight of phenol = 94 g/mol
4. Molecular weight of phenyl benzoate = 198 g/mol

Theoretical Yield

94 g of phenol reacts with benzoyl chloride to gives a 198 g of phenyl benzoate.

Therefore, 1.0 g of phenol will give? (X)……. g of phenyl benzoate.

$$X = (198 \times 1.0)/94 = 2.11 \text{ g}$$

Theoretical yield = 2.11 g

Practical yield = assume 1.8 gm.

Percentage practical yield = (Practical yield ×100)

= (1.8×100)/2.11

= 85 %

Properties

1. White solid powder.
2. Insoluble in water and soluble in other organic solvent.
3. Boiling point is about 158 °C.
4. Melting point is 68–69 °C.

Result

Phenyl benzoate was synthesized by the reaction of phenol and benzoyl chloride, crude product was obtained, and the practical yield was found to be 1.8 gm and% yield about 85%.

The melting point of phenyl benzoate was found to be 68–69°C.

Uses

1. Phenyl Benzoate is used an excellent starting material for the production of optical components, particularly high-quality lenses for still and motion picture cameras.
2. It is also used in a variety of polyesters, which have application in products from clothing to heavy industry to the preparation of new generation of cloths. Phenyl benzoate is a white powdery organic compound that falls

into the broad category of chemicals known as esters.

3. The compound is formed in a reaction between phenol, sodium hydroxide and benzonyl chloride.
4. The compound is solid at room temperature but can form an oily liquid at a relatively low temperature.
5. One use that takes advantage of the electrical properties of phenyl benzoate is the development of liquid crystal displays.
6. Phenyl benzoate based liquid crystals have excellent compatibility characteristics with other materials used in liquid crystal displays, such as biphenyl, phenyl cyclohexane, bicyclohexane and fluorine types, especially at low temperatures.

Safety and Precautions must be taken during reaction performed:

1. Properly Wear gloves and goggles throughout this experiment.
2. Phenol is very toxic substance; if contact with sin may cause severe burns or systemic poisoning as phenol is readily absorbed through the skin, which cause irritation on skin.
3. Benzoyl chloride is very toxic; it's lachrymatory.
4. Phenol and Benzoyl chloride should be handled with care under a fume cup board.
5. If any problems occur you spill a lot of either of these, wash it off with lots of water and notify your laboratory instructor or teacher.

Questions

1. What is the basic purpose of the addition of 10 % sodium hydroxide to the benzoylation of phenol with benzoyl chloride?
2. What is benzoylation reaction?
3. Explain the basic mechanism and reaction of Schotten-Baumann reaction.
4. Which solvent may be used to the recrystallization of crude product?
5. Define the melting point and recrystallization process of phenyl benzoate.

❑

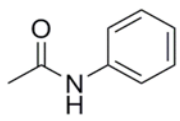
Chapter 10

Synthesis and Characterization of Acetanilide from Aniline by Acetylation Reaction

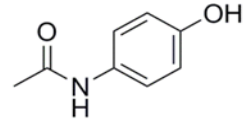
Principle

Primary amines react with acid chlorides or anhydrides to form mono acetyl derivatives. Acetanilide is an organic chemical compound (meaning it›s composed of carbon and hydrogen mostly) that is classified as an amide in terms of its functional group. This means that it has the carbonyl group (carbon-oxygen double bond) bonded directly to a nitrogen atom. It also contains an aromatic ring, which is a ring composed of six carbon atoms and an alternating double-single-double-single bonding pattern all around the ring. Acetanilide is an analgesic, which was formally known as Antifebrin, and is structurally like acetaminophen (or Tylenol). However, unlike acetaminophen, acetanilide is toxic. Acetanilide is prepared from aniline using an acetylation reaction. Acetylation is often used to place an acetyl protecting group on primary or secondary amines to reduce their reactivity toward oxidizing agents or electrophiles. Acetamides are usually crystalline solids which can be a help in purification by recrystallization.

The melting points can be used for characterization and identification of the corresponding compounds.



acetanilide



acetominophen (Tylenol)

Requirements

Chemicals: as per specific quantity required

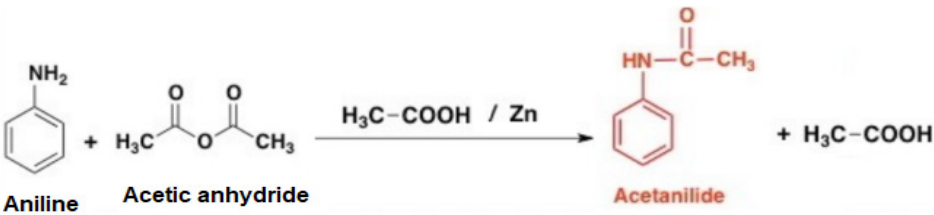
1. Aniline = 1 gm
2. Glacial acetic acid = 2 ml
3. Acetic anhydride = 50 ml
4. Zinc dust = 15 ml
5. Distilled water = 100 ml

Glassware/Apparatus

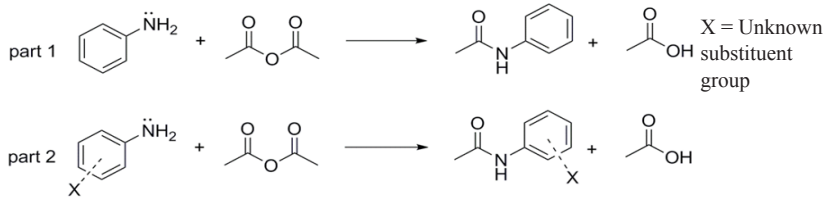
1. Erlenmeyer flask (250 mL)
2. Conical flask
3. Pipette
4. Reflux condenser
5. Glass stirring rod
6. Buchner funnel
7. Suction pump
8. Filter papers
9. Measuring cylinder
10. Rubber cork
11. Fume hood
12. Spatula

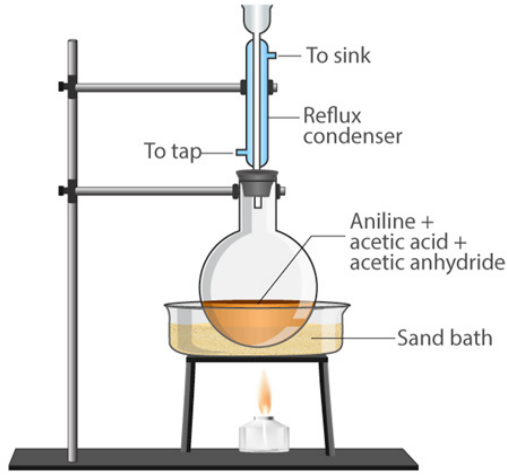
Chemical Reaction

Acetanilide is prepared from aniline when it acylating with acetic anhydride in presence of glacial acetic acid and zinc dust. Aniline or phenylamine is a primary amine and basic in nature. Acetic anhydride as anhydride of acetic acid, act as a source of acyl group. Aniline reacts with acetic anhydride to form acetanilide by nucleophilic substitution reaction and the reaction is called acylation reaction. In this reaction aniline acts as a nucleophile and acyl (CH_3CO-) group from acetic anhydride act as a electrophile. Hence the hydrogen atom of NH_2 group is replaced by the acyl group. Zinc is used to prevent the oxidation of aniline during the chemical reaction. Acetanilide is medicinally important, and it is used as *febrifuge*.



Other Names– N-phenyl acetamide, N-phenylethanamide, Acetanil.





Procedure

1. Wash out all the apparatus with distilled water before starting the experiment.
2. Prepare a mixture of 10 ml of glacial acetic acid and 10 ml acetic anhydride in a beaker.
3. Place 10 ml (10.3 gm) of aniline in a round bottom flask and carefully add 20 ml of acetic anhydride and glacial acetic acid mixture (equal volumes) and add a zinc dust.
4. Set up the reflux condenser with the round bottom flask.
5. Heat the reaction mixture gently for about 15–20 minutes on oil bath.
6. Reaction mixture quickly crystallize.
7. Pour the hot reaction mixture in a beaker containing ice cold water with constant stirring.
8. Carefully stir the reaction mixture vigorously to hydrolyze excess of acetic anhydride.
9. Reaction mixture was recrystallized from about 60 ml mixture of one volume of acetic acid and two volumes of water.
10. Crude product of acetanilide is precipitated, collect and filter of the colourless crystals at the suction pump, again wash thoroughly with water.
11. Dried the crude product of acetanilide.
12. Recrystallization the crude product by using a 30 ml ethanol.
13. Weigh the crude product and calculate the practical yield and obtained 12 gm and measure the melting point about 114 ^{o}C.

Calculation

Here limiting reagent is aniline; hence yield should be calculated from its amount taken.

1. Molecular formal of acetanilide = $C_8H_9O_1N_1$
2. Molecular formal of aniline = $C_6H_7N_1$
3. Molecular weight of aniline = 93 g/mol
4. Molecular weight of acetanilide = 135 g/mol

Theoretical Yield

93 g of aniline reacts with acetic anhydride to gives a 135 g of acetanilide.

Therefore, 10.3 g of aniline will give? (X)…… g of acetanilide

$$X = (135 \times 10.3)/93 = 14.95\ g$$

Theoretical yield = 14.95 gm.

Practical yield = assume 12 gm.

Percentage practical yield = (Practical yield ×100)

= (12 × 100)/14.95

= 93.6 %

Properties

1. It is a white solid with a flaky appearance. This is an odorless compound.
2. Insoluble in water and soluble in other organic solvent.
3. The boiling point for this substance is 304 °C.
4. Melting point is 114 °C.

Result

Acetanilide was synthesized by the reaction of aniline, acetic anhydride, and glacial acetic acid. The crude product is obtained, practical yield was found to be 12 gm and % yield to be 80.26 %.

The melting point of phenyl benzoate was found to be 114°C.

Uses

1. Acetanilide is used in the synthesis of penicillin and in other pharmaceuticals.
2. It is also used as an antipyretic agent means fever reducing agent.
3. It was used in the past to treat fever and headache and was known as *Antifebrin*.

4. Acetanilide is used as an inhibitor of hydrogen peroxide decomposition and is used to stabilize cellulose ester varnishes. It is also found uses in the intermediation in rubber accelerator synthesis, dyes and dye intermediate synthesis, and camphor synthesis.
5. Acetanilide is used for the production of 4-acetamidobenzenesulfonyl chloride, a key intermediate for the manufacture of the sulfa drugs.
6. It is also a precursor in the synthesis of penicillin and other pharmaceuticals.
7. In the 19th century acetanilide was one of a large number of compounds used as experimental photographic developers.
8. Acetanilide was the first aniline derivative found to possess analgesic as well as antipyretic properties.

Precautions

1. Prolonged heating and uses of excess of anhydride should be avoided, otherwise variable amount of the diacetyl would result.
2. Recrystallization of the product from an aqueous solvent such as dilute alcohol avoids the diacetyl derivatives because the latter hydrolyses to the mono acetyl compound in the presence of water.
3. Do not inhale the fumes of acetic anhydride.
4. Always carry out experiments in fuming chamber or near the window.
5. Use the water condenser for refluxing the reaction mixture.
6. Dry the crystals of acetanilide before finding the weight and its melting point.

Questions

1. Name any two-acetylating agent.
2. What is the need to add zinc during the preparation of acetanilide?
3. What is nitrating mixture?
4. What is the IUPAC name for acetanilide?
5. Mention any two uses of acetanilide.

❑

Chapter 11

Synthesis and Characterization of 2,4,6-Tribromoaniline from Aniline by Halogenation (Bromination) Reaction

Principle

Electrophilic aromatic substitution reaction is an important class of synthesis of organic compound. Substituents already present in the benzene nucleus determine the position and extent of substitution of the new incoming groups. These substituents are generally classified as strongly activating (NH_2), moderately activating ($NHCOCH_3$) and deactivating (NO_2). Bromination of aniline provides a good example to study orientation of the incoming electrophile on a strongly activate aromatic nucleus. The amino group of aniline directs the electrophile to the two ortho and one para position.

$$C_6H_5NH_2 + 3Br_2 \rightarrow C_6H_2(Br)_3NH_2 \text{ (2,4,6-tribromoaniline)} + 3HBr$$

Requirements

Chemicals:

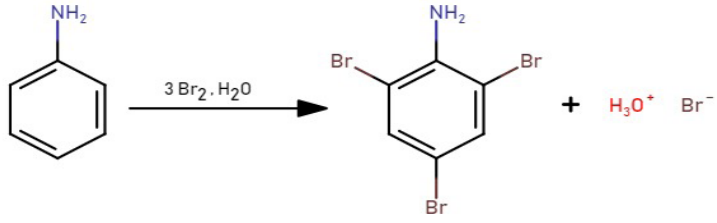
1. Aniline = 5 ml
2. Bromine = 8 ml
3. Glacial acetic acid = 50 ml
4. Ethanol = 20 ml

Glassware/Apparatus

1. Conical flask (250 mL)
2. Beaker
3. Pipette
4. Glass rod
5. Buchner funnel
6. Filter paper
7. Thermometer

Chemical Reaction

Aniline undergoes electrophilic substitution reaction with bromine even in cold water. Tribromo aniline can be prepared by dissolving aniline in glacial acetic acid and then treating it with bromine dissolved in glacial acetic acid in the cold.



Procedure

1. Take a 4.66 g (5 ml) aniline is dissolved in glacial acetic acid (20 mL) in a 100 mL round bottomed flask equipped with a magnetic stirrer.
2. Then added a dropwise solution of 8 ml of bromine solution in a 20 ml of glacial acetic acid from an addition funnel at such a rate, that complete decolourization is achieved between each drop.
3. Then mixture solution is cooled on an ice water bath.
4. During the addition, the reaction mixture is stirred continuously with magnetic stirring (if the acetic acid solidifies, remove the flask from the ice/water bath momentarily) and cooled in ice.
5. When all the bromine is added the reaction, mixture is stirred 10 minutes before it is poured into water (250 mL) containing a pinch of sodium bisulphite ($NaHSO_3$). The yellow coloured mass is obtained.
6. The precipitate is filtered off and washed with water.
7. The product is recrystallized from a minimum of hot ethanol with a spoonful of activated charcoal.
8. The approximate yield expected in this experiment is 3.0 grams and the melting point of the compound is 119 °C.

Calculation

Here limiting reagent of aniline; hence yield should be calculated from its amount.

1. Molecular Formula of Aniline = $C_{14}H_{12}O_2$
2. Molecular Formula of 2,4,6-tribromoaniline = $C_{14}H_{10}O_2$
3. Molecular weight of 2,4,6-tribromoaniline = 329.81 g/mole
4. Molecular weight of aniline = 93.13 g/mole

Theoretical Yields

93.13 gm of aniline and 3 g mole of bromine forms of 329.81 gm of 2,4,6-tribromoaniline.

Therefore, 4.66 gm of aniline will form…… (X) gm of 2,4,6-tribromoaniline.

$$X = 329.81 \times 4.66/93.13 = 16.50\,gm$$

Hence the theoretical yield about 16.5 gm.

If practical yield is 15 gm, hence percentage yield is:

$$\% \text{ yield} = \text{Practical yield/Theoretical Yield} \times 100$$

$$\% \text{ Yield} = 15/16.5 \times 100$$

$$= 90.9\,\%$$

Properties

1. It is a needle shape solid.
2. Insoluble in water and soluble in Alcohol.
3. The boiling point for this substance is 300 °C.
4. Melting point is 120–122 °C.

Result

2,4,6-tribromoaniline was synthesized by the reaction of aniline and bromine. The crude product was obtained about 15 gm and the percentage yield was found to be 96.9 %.

Uses

It is used in the organic synthesis of pharmaceuticals, agrochemicals, and fire extinguishing agents.

Precautions taken throughout the Experiment

1. Do not inhale the fumes of bromine.
2. Always carry out experiments in fuming chamber or near the window.
3. Dry the crystals of 2,4,6-tribromoaniline before finding the weight and its melting point.

Questions

1. Name any two-acetylating agent.
2. What is the Bromination reaction?
3. What is the IUPAC name for aniline?
4. Mention any two uses of 2,4,6 tribromo aniline.

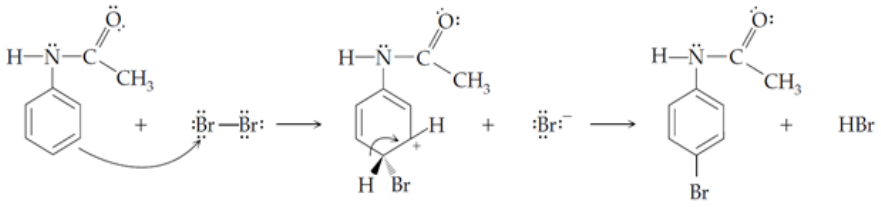
❑

Chapter 12

Synthesis and Characterization of Para Bromo Acetanilide from Acetanilide by Halogenation (Bromination) Reaction

Principle

Acetanilide on treatment with bromine gives a mixture of *o*- and *p*-bromo acetanilide (As compared with aniline which gives a tribromo derivatives). In this case it is the inductive effect of the carbonyl group of the acetyl group, which is slightly deactivates of the benzene ring. This mechanism is a classic example of electrophilic aromatic substitution. An amine may lead to di- and tri- substituted products. If an amide is used in place of the amine, mono substitution usually predominates (the electron-withdrawing carbonyl group makes the benzene ring less nucleophilic). This ortho-, para- directing group will tend to only add groups para- to itself because of the steric bulk of the amide group.



Requirements

Chemicals:

1. Acetanilide = 3 gm
2. Bromine = 1.5 ml
3. Glacial acetic acid = 10 ml
4. Distilled Water = 100 ml
5. Sodium meta bisulphite = enough quantity
6. Rectified Spirit = 100 ml

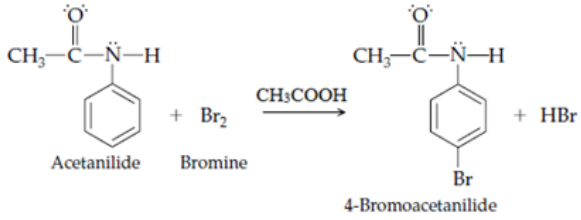
Glassware/Apparatus

1. Conical flask (100 mL)
2. Beaker

3. Burette
4. Pipette
5. Measuring cylinder
6. Glass rod
7. Buchner funnel
8. Filter paper
9. Water bath
10. Suction pump

Chemical Reaction

The synthesis of *p*-Bromo acetanilide from acetanilide in the presence of bromine using glacial acetic acid as a catalyst is a classic example of nuclear Bromination (electrophilic aromatic substitution). Bromination of acetanilide occurs at the para/ortho position due to the amide substituent (electron releasing group), which is a para/ortho director. Along with *p*-Bromo acetanilide, *o*-Bromo acetanilide is also formed as a minor product (due to steric hindrance of amide group), however, and being more soluble in alcohol than the *para* compound can be readily eliminated by recrystallization.



Bromination of acetanilide is important because the resulting 4-bromoacetanilide is a precursor to anti-cancer agents, kinase inhibitors, and other important pharmaceutical compounds.

Procedure

1. Place a dissolve 2.7 g of finely powdered acetanilide in 9.0 mL of glacial acetic acid in a 125 mL Erlenmeyer flask.
2. Take in another Erlenmeyer flask dissolve carefully dropwise 1 ml of bromine in 5.0 mL of glacial acetic acid and transfer the solution to a burette under fume cup board.
3. Carefully add dropwise the bromine solution slowly and with constant shaking to ensure thorough mixing; stand the flask in cold water (perform under a **FUME HOOD**) as the reaction exothermic.

4. After the addition is over, the solution will have an orange colour due to the slight excess of bromine; a part of the reaction product may crystallize out.
5. The solution is allowed to stand at room temperature for 30 minutes with occasional shaking.
6. Pour the reaction mixture into 80 mL of water; rinse the flask with about 20 ml of water.
7. Stir the reaction mixture well and if it is appreciably coloured, add just sufficient sodium metabisulphite solution to remove the orange colour.
8. Filter the crystalline precipitate with suction on a Buchner funnel, wash thoroughly with cold water and press as dry as possible with a wide glass stopper.
9. Finally, recrystallize from dilute methanol or rectified spirit.
10. Weigh the recrystallized p-Bromo acetanilide and calculate the practical yield.
11. Measure the melting point of the synthesized p-Bromo acetanilide.
12. It's obtained as colourless crystals, m.p. 167 °C.

Calculation

Here limiting reagent is aniline; hence yield should be calculated from its amount taken.

1. Molecular formal of acetanilide = C_8H_9NO
2. Molecular formal of p-bromoacetanilide = C_8H_8BrNO
3. Molecular weight of acetanilide = 135 g/mol
4. Molecular weight of p-bromoacetanilide = 214 g/mol

Theoretical Yield

135 g of acetanilide gives 214 g of p-bromoacetanilide

Therefore, 2.7 g of acetanilide will give? (X) g of p-bromoacetanilide

$$X = (214 \times 2.7)/135 = 4.28\ g$$

Theoretical yield = 4.28 g

Practical yield = 4 g

Percentage practical yield = (Practical yield × 100)/Theoretical yield

= 4 × 100/4.28

= 93.45%

Properties

1. It is a white to light beige crystalline (white to off white) solid.
2. Insoluble in cold water and soluble in benzene and chloroform and moderately soluble in alcohol.
3. The boiling point for this substance is 353.4 °C.
4. Melting point is 165–169 °C.

Result

p-Bromo acetanilide was synthesized and the practical yield was found to be 93.45 %.

The melting point of p-Bromo acetanilide was found to be 167 °C.

Uses

1. It is used as an inhibitor of hydrogen peroxide decomposition and is used to stabilize cellulose ester varnishes.
2. Acetanilide was the first aniline derivative found to possess analgesic as well as antipyretic properties and was quickly introduced into medical practice under the names of Antifebrin. It has also found uses in the intermediation in rubber accelerator synthesis, dyes and dye intermediate synthesis, and camphor synthesis.
3. Acetanilide is used for the production of 4-acetamidobenzenesulfonyl chloride, a key intermediate for the manufacture of the sulfa drugs.
4. It is also a precursor in the synthesis of penicillin and other pharmaceuticals.

Precautions

1. Wear gloves and goggles throughout this experiment.
2. Glacial acetic acid can cause bad burns.
3. When working with bromine keep the safety rules with special care. The valve of the burette should be bromine-tight (for greasing a grinded glass valve, apply sulfuric or phosphoric acid). Notice the colour change on dropping the bromine.
4. Use them only in the fume hood and be sure the hood fan is on! If you spill a lot of either of these, **wash it off with lots of water** and **notify your instructor**.
5. During the bromine addition period keep the temperature at 25-35 °C by proper cooling. Lower temperature results in decreased reaction rate and conversion, higher temperature results in higher amounts of undesired by-products.

Questions

1. What is the limiting reactant in the bromination of acetanilide?
2. What type of reaction is the addition of bromine to acetanilide?
3. Provide a reason why p-bromo acetanilide the major product in this reaction over o-bromoacetanilide?
4. Why glacial acetic acid is used in the bromination of acetanilide?
5. Identify what is the electrophile in this reaction?
6. Why does the sodium metabisulphite make the solution colourless?

❑

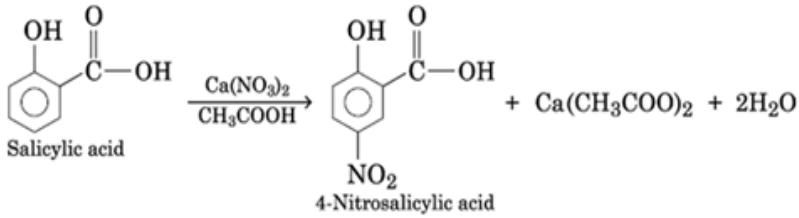
Chapter 13

To Synthesis and Characterization of 5- Nitro Salicylic Acid from Salicylic Acid by Nitration Reaction

Principle

Nitration are among the most common reactions carried out at industrial scale. Nitration on salicylic acid occurs by placing a nitro group on the aromatic ring system via an electrophilic aromatic substitution reaction. Here the calcium nitrate is used as the nitrating agent in the presence of acetic acid. Two groups -COOH and -OH in salicylic acid complement each other since they both direct the entering nitro group to the 5th position. The 5th position and the 3rd position are both electronically favored since the -COOH group is meta directing and -OH group is ortho para directing. The nitro group is attached at the 5th position, not at the 3rd position, due to steric effect.

We can also use anhydrous nitric acid or concentrated and nitric acid and concentrated sulphuric acid as nitrating agent.



Requirements

Chemicals:

1. Salicylic acid = 2 gm
2. Acetic acid = 10 ml
3. Calcium nitrate tetrahydrate = 3 gm

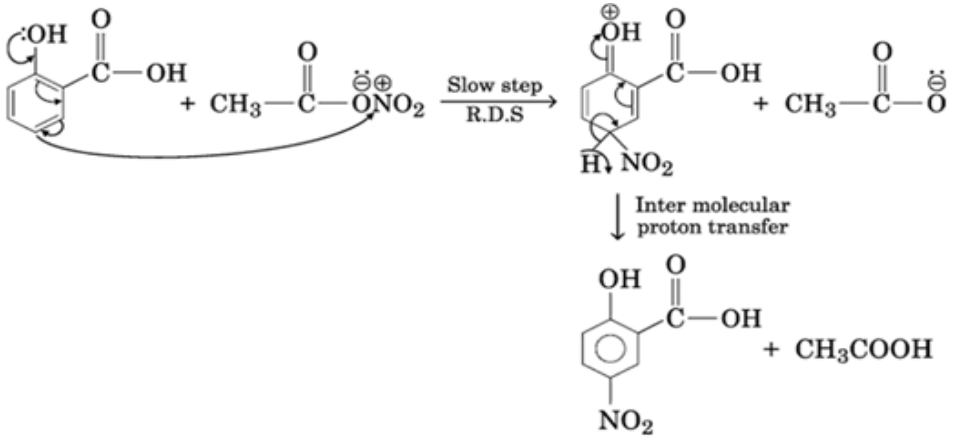
Glassware/Apparatus

1. Conical flask (250 mL)
2. Beaker
3. Pipette

4. Glass rod
5. Reflux condenser
6. Buchner Funnel
7. Filter paper
8. Measuring cylinder
9. Suction pump

Chemical Reaction

The 5-nitrosalicylic acid is synthesized by nitration (generates the intermediate 2-Chloro-5-nitrobenzoic acid, and hydrolysis (generates the target product) of o-chlorobenzoic acid. The influences of the nitration of temperature, proportion of mixed acid and of the hydrolysis of temperature, reaction occurs.



Procedure

1. Place a 3 gm of calcium nitrate tetrahydrate is dissolved in a 10 ml of acetic acid in a 250 ml of conical flask by gently heating in a water bath.
2. Then added 2 gm of salicylic acid is added, and the reaction mixture is heated on boiling water bath (below 80 °C) for few minutes.
3. A dark red solution is formed. Then the dark red colour solution mixture is poured into 100 ml beaker containing 20 ml ice water.
4. A turbid dark red coloured solution is form which is kept in refrigerator and after 4–5 hours, yellow crystal of 5-Nitrosalicylic acid separate out.
5. Crude product is filtered at a suction pump wash with cold water and dried.

6. Yellow precipitate of 5- Nitro salicylic products obtained with a yield of 132 gm, m.p. 234 °C.

Calculation

Here limiting reagent is aniline; hence yield should be calculated from its amount taken.

1. Molecular formal of salicylic acid = $C_7H_6O_3$
2. Molecular formal of 5-nitro salicylic acid = $C_7H_5NO_5$
3. Molecular weight of salicylic acid = 138 g/mol
4. Molecular weight of 5-nitro salicylic acid = 198 g/mol

Theoretical Yield

138 g of salicylic acid gives 198 g of 5-nitro salicylic acid

Therefore, 2 g of salicylic acid will give? (X)…….. g of 5-nitro salicylic acid

$$X = (138 \times 2)/198 = 2.87\ g$$

Theoretical yield = 2.87 g

Practical yield = assume 2.5

Percentage practical yield = (Practical yield × 100)/Theoretical yield

= 2.5 × 100/2.87

= 90 %

Properties

1. It is a clear yellow beige to orange brown solid.
2. Soluble in cold water moderately soluble in alcohol.
3. The boiling point for this substance is 316.77 °C.
4. Melting point is 234 °C.

Result

5-nitro salicylic acid was synthesized, and the practical yield was found to be 2.5 gm and% of yield 90 %.

The melting point of 5-nitro salicylic acid was found to be 234 °C.

Uses

1. Nitration products are used directly or as intermediates in dyes, explosives, pesticides, and the pharmaceutical industry.
2. It is also used as intermediate in manufacture of APIs, Dyes and Pigments.

Precautions

1. Wear gloves and goggles throughout this experiment.
2. When working with keep the safety rules with special care.
3. Use them only in the fume hood and be sure the hood fan is on! If you spill a lot of either of these, **wash it off with lots of water** and **notify your instructor**.

Questions

1. What is the limiting reactant in the nitration of salicylic acid?
2. What type of reaction is the addition of salicylic acid to 5-Nitro salicylic acid?
3. Why salicylic acid is used in the nitration of 5-Nitro salicylic acid?
4. Identify what is the electrophile in this reaction?

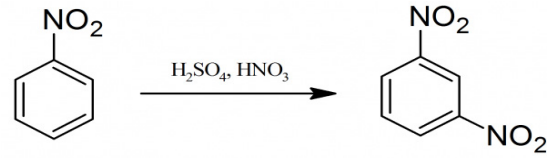
❑

Chapter 14

Synthesis and Characterization of Meta-Di Nitro Benzene from Nitrobenzene by Nitration Reaction

Principle

Nitration are among the most common reactions carried out at industrial scale. Nitration on nitrobenzene occurs by placing a nitro group on the aromatic ring system via an electrophilic aromatic substitution reaction. It is prepared nitration of nitrobenzene with concentrate nitric acid in the presence of sulphuric acid. Here the functional group of sulphuric acid is convert to the nitric acid into the highly reactive, electrophile, nitronium ion (NO_2^+), which is the effective nitrating agent. Nitration of aromatic hydrocarbon is usually is carried out with nitrating reagent at comparatively low temperature. Unnecessary higher temperature is avoided since poly nitration is more likely and oxidative break down of the aromatic system may occurs.



Requirements

Chemicals:

1. Con. Sulphuric acid = 20 mL
2. Nitrobenzene = 12.5 ml
3. Nitric acid = 15 ml
4. Distilled water = 100 ml

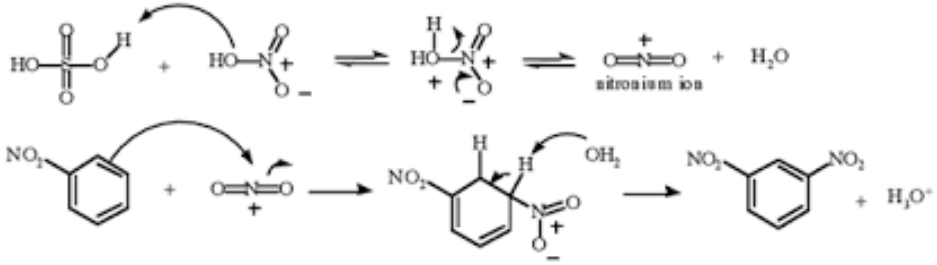
Glassware/Apparatus

1. Round bottom flask (250 mL)
2. Beaker
3. Pipette

4. Glass rod
5. Reflux condenser
6. Funnel
7. Filter paper
8. Measuring cylinder

Chemical Reaction

The nitration of nitrobenzene containing a electron withdrawing NO_2 group does not readily occurs under the above condition, in which use forcing condition which requires the use of fuming of nitric acid and concentrate sulphuric acid is employed. The deactivating effect of the nitro group is largely as the result of its mesomeric interaction (-M effect) with the pie electron system of the benzene ring which is supplemented by the inductive effect. The overall electron withdrawal from the ring system result in the rate of attack of nitronium ion being substantially retarded compared to the benzene. Moreover the representation of the canonical forms of nitrobenzene, the ortho and para position are subjected to the greatest reduction in electron density, so energetically unfavorable the mesomeric stabilization of this intermediate is less than that of the corresponding intermediate resulting from attack in the m- position. Because of this reason, the incoming nitro group oriented towards the m-position of the nitrobenzene.



Procedure

1. Place a 21 ml (37.5 gm) of concentrated sulphuric acid and 15 ml (22.5 gm) of fuming nitric acid in a 250 ml of round bottom flask with a few smaller pieces of porcelain.
2. Reflux condenser is attached, and the apparatus is placed in a fuming cupboard.
3. Then carefully added 12.5 ml (15 gm) of nitrobenzene in portions of about 3 ml is added slowly and after each addition the flask is shaken thoroughly.

4. Reaction mixture is heated on water bath for 30 minutes with constant shaking.
5. Then it can cool and poured into about 250 ml of cold water a cautiously with vigorous stirring. The dinitrobenzene soon solidifies.
6. Crude product is filtered by using a Buchner funnel, washed with water and allow to drain as much as possible.
7. The crude product is transferred to a 250 ml RB flask fitted with a reflux condenser, 80-100 l of rectified spirit is added and heated on a water bath to dissolve all the solid for 20 minutes.
8. If the solution is not clear, it is filtered using a warm Buchner funnel.
9. About 15 gm of m-dinitrobenzene is deposited on cooling as colourless crystals.
10. A second recrystallization is usually necessary in order to eliminate traces of o- and p-dinitrobenzene, and thus pure m-nitrobenzene obtained and m.p. 90 ^{o}C.

Calculation

Here limiting reagent is aniline; hence yield should be calculated from its amount taken.

Molecular formal of Nitrobenzene = $C_6H_5NO_2$
Molecular formal of m-dinitrobenzene = $C_6H_4N_2O_4$
Molecular weight of Nitrobenzene = 123 g/mol
Molecular weight of m-dinitrobenzene = 168 g/mol

Theoretical Yield

123 g of Nitrobenzene react with nitric acid to gives a 168 g of m-dinitrobenzene.
Therefore, 15 g of Nitrobenzene will give? (X) g of m-dinitrobenzene.

$$X = (123 \times 15)/168 = 20.48\ g$$

Theoretical yield = 20.48 g
Practical yield = assume 19 gm
Percentage practical yield = (Practical yield × 100)/Theoretical yield
= 19×100/20.48
= 92.77 %

Properties

1. It is a clear yellow solid.
2. Insoluble in cold water and soluble in a organic solvent.

3. The boiling point for this substance is 297 °C.
4. Melting point is 89.6 °C.

Result

m-dinitrobenzene was synthesized, and the practical yield was found to be 19 gm and% of yield to be found 92.77 %.

The melting point of m-dinitrobenzene was found to be 89.6 °C.

Uses

It is used an organic drug synthesis. Mainly uses as synthetic intermediates in pharmaceuticals.

Precaution

1. Wear gloves and goggles throughout this experiment.
2. When working with keep the safety rules with special care.
3. Use them only in the fume hood and be sure the hood fan is on! If you spill a lot of either of these, **wash it off with lots of water** and **notify your instructor**.
4. Nitrobenzene is readily absorbed in the skin, and the concentrate mineral acid is corrosive, gloves should be worn when transferring these reagents.

Questions

1. What is the limiting reactant in the nitration of nitrobenzene?
2. What type of reaction is the addition of nitrobenzene to m-dinitrobenzene?
3. Why nitrobenzene is used in the nitration of m-dinitrobenzene?
4. Identify what is the electrophile in this reaction?
5. Define nitration process.

❑

Chapter 15

Synthesis and Characterization of Benzoic Acid from Benzyl Chloride by Oxidation Reaction

Principle

In this reaction a side chain oxidation reaction is performed. If oxidation occurs an aromatic compound having an aliphatic side chain then, fission of the side chain occurs between the first and second carbon atom from the benzene ring and the first carbon atom thus becoming part of a carboxyl (-COOH) group.

The oxidation process is carried out with a mixture of potassium permanganate and sodium carbonate in aqueous solution or dilute nitric acid. The reaction is quite slow if the side chain a simple alkyl group. The side chain containing chlorinated alkyl group is more susceptible to oxidation. Hence in comparison to toluene, benzyl chloride more rapidly oxidizes in the presence of an aqueous oxidizing agent. Here benzyl chloride is first hydrolyzed to benzyl alcohol and undergoes oxidation of a primary alcohol to the corresponding carboxylic acid. In order to achieve this benzyl chloride is mixed with sodium carbonate solution and is oxidized with potassium permanganate solution. The sodium salt of benzoic acid is formed, this is acidified with concentrated hydrochloric acid when benzoic acid crystallizes out.

Requirements

Chemicals:

1. Benzyl chloride = 5 mL (5.5 gm)
2. Sodium sulphite = 20 gm
3. Potassium permanganate = 10 gm
4. Anhydrous sodium carbonate = 5 gm
5. Con. Hydrochloric acid = 50 mL

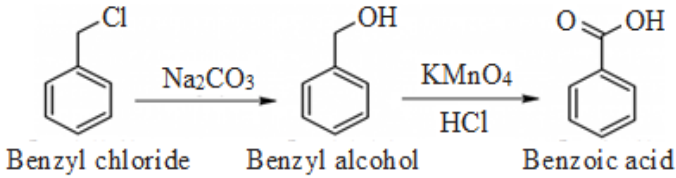
Glassware/Apparatus

1. Round bottom flask (250 mL)
2. Beaker
3. Pipette
4. Glass rod

5. Reflux condenser
6. Buchner Funnel
7. Filter paper
8. Measuring cylinder

Chemical Reaction

In this mechanism of reaction benzyl chloride is first hydrolyzed to benzyl alcohol in the presence of sodium carbonate in aqueous solution of nitric acid and undergoes oxidation of a primary alcohol to the corresponding carboxylic acid. In order to achieve this benzyl chloride is mixed with sodium carbonate solution and is oxidized with potassium permanganate solution. The sodium salt of benzoic acid is formed, this is acidified with concentrated hydrochloric acid when benzoic acid crystallizes out.



Procedure

1. 5 ml (5.5 gm) of benzyl chloride is added to a solution of about 5 grams of anhydrous sodium carbonate dissolved in 100 ml of distilled water in a round bottom flask.
2. Then round bottom flask is fitted with a water reflux condenser.
3. Added 10 grams of potassium permanganate in 80 ml of water in small quantities through the water condenser until a permanent pink colour persists even after continuous boiling.
4. Then it is boiled gently for 1 to 1.5 hours to complete the reaction.
5. During the boiling time, the permanganate is slowly reduced, and manganese dioxide is separates as a dark brown precipitate.
6. After the flask is cooled, and 50 ml of conc. hydrochloric acid is added cautiously until the mixture is strongly acidic, and all the benzoic acid precipitate is formed.
7. Then added about 20 grams of sodium sulfite are added to this mixture slowly with shaking until the manganese dioxide is completely dissolved and only the white precipitate of benzoic acid is remains.
8. Reaction mixture is cooled, precipitated of benzoic acid is filtered and washed the suction pump.

9. Crude product of benzoic acid is recrystallized from using of boiling water.
10. Benzoic acid is obtained a colourless needle, the melting point is 121°C.
11. Care should be taken while setting up the equipment's, the hydrochloric acid used in converting the sodium salt of benzoic acid is concentrated, so extreme care should be taken while handling the chemicals and using them. Wear goggles, gloves and apron while performing the experiment.

Calculation

Here limiting reagent of Benzyl chloride; hence yield should be calculated from its Benzoic acid.

1. Molecular Formula of Benzyl chloride = C_7H_7Cl
2. Molecular Formula of Benzoic acid = $C_7H_6O_2$
3. Molecular weight of Benzyl chloride = 140.57 g/mole
4. Molecular weight of Benzoic acid = 122.12 g/mole

Theoretical Yields

140.57 gm of Benzyl chloride gives of 122.12 gm of benzoic acid

Therefore, 5.5 gm of benzyl chloride will form…… (X) gm of benzoic acid.

$$X = 122.12 \times 5.5/140.57 = 4.78 \text{ gm}$$

Hence the theoretical yield about 4.78 gm.

If practical yield is 4.1gm, hence percentage yield is:

$$\% \text{ yield} = \text{Practical yield}/\text{Theoretical Yield} \times 100$$

$$\% \text{ Yield} = 4.1/4.78 \times 100$$

$$= 85.77$$

Properties

1. It is a White to yellow beige to sweet orange smelling, colourless, liquid.
2. It is soluble in organic solvents such as 95% of ethanol but slightly soluble in water.
3. The boiling point for this substance is 249 °C.
4. Melting point is 121 °C.

Result

Benzoic acid was synthesized, and the practical yield to be 4.1 gm and percentage yield was found to be 85.77%. The melting point of benzoic acid was found to be 121 °C.

Uses

1. It is used as a topical agent with salicylic acid to treat the skin problem such as irritation and inflammation which may causes by burns, insect bites, fungal infection, and eczema.
2. It is a sweet smelling, colourless, liquid used in perfumery under the name Essence de Niobe; in the manufacture of Peau d'Espagne; and as an artificial fruit essence.
3. Benzoic acid is most found in industrial settings to manufacture a wide variety of products such as perfumes, dyes, topical medications, and insect repellents.
4. Benzoic acid's salt (sodium benzoate) is commonly used as adjustor and preservative in food, preventing the growth of microbes to keep food safe.

Precaution

1. Wear gloves and goggles throughout this experiment.
2. When working with keep the safety rules with special care.
3. Care should be taken while setting up the equipment's, the hydrochloric acid used in converting the sodium salt of benzoic acid is concentrated, so extreme care should be taken while handling the chemicals and using them. Wear goggles, gloves and apron while performing the experiment.

Questions

1. What is the limiting reactant in the oxidation of benzoyl chloride?
2. What type of reaction is the addition of benzoyl chloride to benzoic acid?
3. What do you think the purpose was to filter the hot product solution through the fluted filter paper?
4. Write a good definition for what a catalyst is. Is the sodium hydroxide a catalyst in this experiment? Explain.
5. You could say that the reaction you have completed is "oxidation".

❑

Chapter 16

Synthesis and Characterization of Benzoic Acid from Ethyl Benzoate by Hydrolysis Reaction

Principle

This process is called base hydrolysis (or saponification) of an ester and is used in this experiment to first obtain sodium benzoate solution, and then benzoic acid from ethyl benzoate. Ethyl benzoate belongs to a class of compounds called esters. Esters are hydrolyzed either by an acid or a base. Alkaline hydrolysis of ester is irreversible which is also called as saponification. Acid hydrolysis of ester is reversible reaction. Acid hydrolysis of ester is can occurs by more than one type of mechanism, the common mechanism is: Alkaline hydrolysis, which occurs through a nucleophilic acyl substitution. Here ethyl benzoate on hydrolysis with sodium hydroxide gives benzoic acid and ethyl alcohol, where OH ion of sodium hydroxide act as a nucleophile. When ethyl benzoate is shaken with water two liquid layers form. The upper layer is ethyl benzoate (less dense) and the lower layer is water. There is no clear indication of any reaction taking place. A more careful study shows that ethyl benzoate reacts very slowly with water and is hydrolyzed to give benzoic acid and ethanol, but the reaction does not go to completion. However, ethyl benzoate is found to react much faster with aqueous sodium hydroxide, the reaction going to completion, to give sodium benzoate (water soluble) and ethanol (miscible with water). The ethanol may be recovered by simple downward distillation from the reaction mixture and collected as a solution in water.

Requirements

Chemicals:

1. Ethyl Benzoate = 2 mL
2. 10% sodium Hydroxide solution = 100 ml
3. Hydrochloric acid = Sufficient

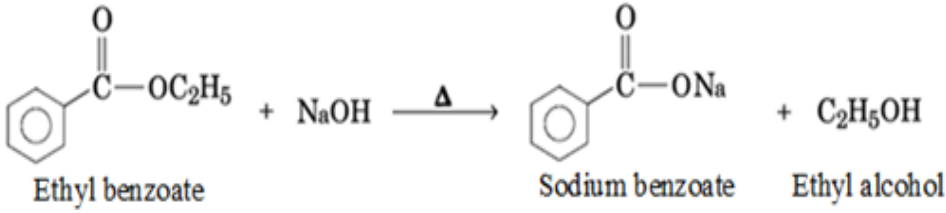
Glassware/Apparatus

1. Round bottom flask (250 mL)
2. Beaker
3. Pipette
4. Glass rod

5. Reflux condenser
6. Funnel
7. Filter paper
8. Measuring cylinder

Chemical Reaction

Ethyl benzoate is heated with aqueous sodium hydroxide. At the start of the reaction the flask contains two immiscible layers, a liquid layer of the water insoluble ethyl benzoate floating on the aqueous sodium hydroxide layer. reaction mixture to as the ethyl benzoate reacts, water soluble products are formed and the upper layer decreases in size until a homogeneous solution is obtained and the reaction is complete.



Procedure

1. Properly clean the glassware and lightly grease the ground glass joints. Use only a small amount of the lubricant supplied (on the upper bench top) to grease the joints, then rotate them together to form a smooth seal. Excess grease may be wiped off with a towel.
2. Set up the apparatus with the condenser attached to the round bottom flask in the reflux position. Do not clamp too tightly or the glass may break. Never store glassware with the joints connected as they may "freeze" together.
3. Then carefully detach the 100 ml round-bottomed flask from the apparatus and dispense 2.0 ml of ethyl benzoate into it.
4. Then transfer 15 ml (graduated cylinder) sodium hydroxide followed by 3 or 4 boiling granules to the ethyl benzoate in the flask and reattach it to the apparatus.
5. Then heat can be gently over a low flame so that the liquid refluxes for 30 minutes at a temperature at 90–100 °C.
6. Reaction mixture in the flask should be shaken by using glass rod almost continuously to speed up the hydrolysis reaction.

7. All of the oily drops of ester have disappeared (about 15 minutes) and the solution is almost clear when shaken, stop heating and cool the room temperature for minutes.
8. Reactive solution is acidified with HCl. The resultant acidified solution is cooled is an ice water bath.
9. Collect the crystals by vacuum filtration using a Buchner flask and funnel. Rinse the crystals with a little ice water and allow them to dry under suction in the Buchner funnel for a few minutes.
10. Dried the crude product of benzoic acid by pressing them between filter papers.
11. Crude product crystals to a pre-weighed, labelled sample vial and reweigh to determine the mass of product obtained and give a yield about 1.3 gm.

Calculation

Here limiting reagent of ethyl benzoate; hence yield should be calculated from its Benzoic acid.

1. Molecular Formula of ethyl benzoate = $C_9H_{10}O_2$
2. Molecular Formula of benzoic acid = $C_7H_6O_2$
3. Molecular weight of ethyl benzoate = 150 g/mole
4. Molecular weight of Benzoic acid = 112 g/mole

Theoretical Yields

150 gm of ethyl benzoate gives of 112 gm of benzoic acid

Therefore, 2 gm of ethyl benzoate will form…… (X) gm of benzoic acid.

$$X = 112 \times 2/150 = 1.49 \text{ gm}$$

Hence the theoretical yield about 1.49 gm.

If practical yield is 1.3 gm, hence percentage yield is:

$$\% \text{ yield} = \text{Practical yield}/\text{Theoretical Yield} \times 100$$

$$\% \text{ Yield} = 1.3/1.49 \times 100$$

$$= 87.24\%$$

Properties

1. It is a White to yellow beige to sweet orange smelling, colourless, liquid.
2. It is soluble in organic solvents such as 95% of ethanol but slightly soluble in water.
3. The boiling point for this substance is 249 °C.
4. Melting point is 121 °C.

Result

Benzoic acid was synthesized, and the practical yield to be 1.3 gm and percentage yield was found to be 87.24%. The melting point of benzoic acid was found to be 121 °C.

Uses

It is used as a topical agent with salicylic acid to treat the skin problem such as irritation and inflammation which may causes by burns, insect bites, fungal infection and eczema.

It is a sweet smelling, colourless, liquid used in perfumery under the name *Essence de Niobe*; in the manufacture of *Peau d'Espagne*; and as an artificial fruit essence. Benzoic acid is most found in industrial settings to manufacture a wide variety of products such as perfumes, dyes, topical medications, and insect repellents. Benzoic acid's salt (sodium benzoate) is commonly used as adjustor and preservative in food, preventing the growth of microbes to keep food safe.

Precaution

1. Wear goggles, gloves and apron while performing the experiment.
2. When working with keep the safety rules with special care.
3. Care should be taken while setting up the equipment's, o extreme care should be taken while handling the chemicals and using them.

Questions

1. What is the limiting reactant in the hydrolysis of ethyl benzoate?
2. What type of reaction is the addition of Ethyl benzoate to benzoic acid?
3. What do you think the purpose was to filter the hot product solution through the fluted filter paper?
4. Write a good definition for what a catalyst is. Is the sodium hydroxide a catalyst in this experiment? Explain.
5. You could say that the reaction you have completed is hydrolysis reaction.

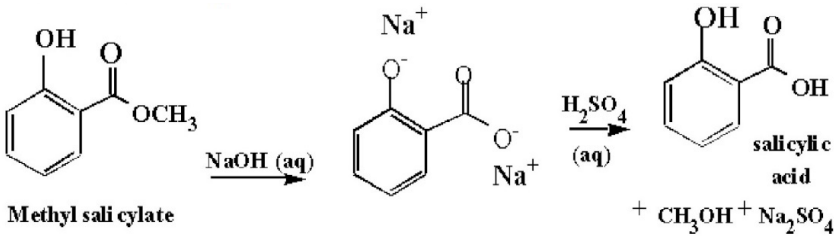
❑

Chapter 17

Synthesis and Characterization of Salicylic Acid from Alkyl Salicylate by Hydrolysis Reaction

Principle

Methyl salicylate is an ester easily recognized by its odor and is known as oil of wintergreen because of its natural source. This ester will be treated with aqueous base. The hydrolysis reaction that occurs will form methanol, water, and the sodium salt of salicylic acid. Salts of organic compounds usually are soluble in water or will dissolve in water with a bit of heating. Later in the work-up, the salt is acidified with sulfuric acid to convert the organic salt into the protonated carboxylic acid. Therefore, the major organic products of this reaction are methanol and salicylic acid. The salicylic acid is a solid that can be isolated and purified by crystallization. The chemical equations that describe this experiment are:



Because the phenolic hydroxyl group is acidic, it is also converted to the corresponding sodium salt during the basic hydrolysis. In the subsequent acidification, this group also becomes reprotonated.

Requirements

Chemicals:

1. Methyl Salicylate = 3 mL
2. Sodium Hydroxide (6M) = 100 ml
3. Sulphuric acid = Sufficient

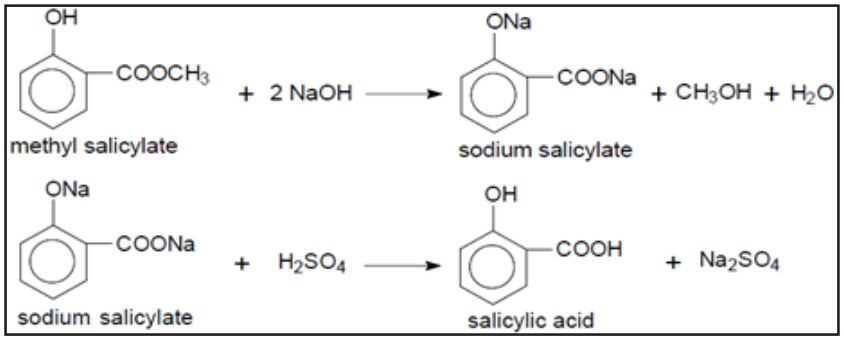
Glassware/Apparatus

1. Round bottom flask (200 mL)
2. Beaker (200 ml)

3. Pipette
4. Glass rod
5. Reflux condenser
6. Funnel
7. Filter paper
8. Measuring cylinder

Chemical Reaction

Alkaline hydrolysis of ester is called a saponification and is an irreversible process. Here one mole of methyl salicylates (oil of wintergreen) reacts with 2 moles of sodium hydroxide to form sodium salicylate with methanol and water, each of one mole. Sodium salicylate is reached with sulphuric acid or hydrochloric acid to remove the sodium ion and forms salicylic acid with sodium sulphate as a by-product.



Procedure

1. Place 10 g sodium hydroxide into 50 mL of deionized water in a 250 mL Erlenmeyer flask. While this solution cools a bit, remove the round-bottom flask from your reflux set up.
2. Added 3 ml (3.5 gm) of the methyl salicylate liquid into a small beaker, then pour this liquid into your round-bottom flask. Add one or two small boiling stones to the round bottom.
3. Finally, add the sodium hydroxide solution to this same round-bottom.
4. Reassemble the apparatus for reflux for 30–40 minutes from the point the mixtures start to boil.
5. If the reaction mixture still has oil or cloudy, continue to reflux. Start water flowing through the condenser, turn on the mantle, and bring the mixture to boil. Continue heating under vigorous reflux for 30 minutes.

6. After the thirty minutes of reflux, stop heating, lower the heating mantle if possible, and shut down the water flow.
7. Once the mixture is clear and homogenous, then the solution is checked whether it no longer having smell of oil of wintergreen. If the smell still exists, then continued to reflux for some more minutes. Boiling chips are removed, and the solution is transferred to a 250 ml beaker.
8. A 6 M sulphuric acid is added slowly with stirring until the PH 2.0. The mix solution is cooled is an ice bath for 10 minutes, vacuum filtered and rinsed with ice cold water.
9. The product is recrystallized from hot water, yield 3 gm and m.p.158–159 °C.

Calculation

Here limiting reagent of methyl salicylate; hence yield should be calculated from its salicylic acid.

1. Molecular Formula of methyl salicylate = $C_8H_8O_3$
2. Molecular Formula of salicylic acid = $C_7H_6O_3$
3. Molecular weight of methyl salicylate = 152 g/mole
4. Molecular weight of salicylic acid = 138 g/mole

Theoretical Yields

152 gm of methyl salicylate gives of 138 gm of salicylic acid

Therefore, 3.5 gm of methyl salicylate will form…… (X) gm of salicylic acid.

$$X = 138 \times 3.5/152 = 3.1 \text{ gm}$$

Hence the theoretical yield about 3.1 gm.

If practical yield is 3.0 gm, hence percentage yield is:

$$\% \text{ yield} = \text{Practical yield}/\text{Theoretical Yield} \times 100$$

$$\% \text{ Yield} = 3.0/3.1 \times 100$$

$$= 96.77\%$$

Properties

1. It is a white to off white solid.
2. It is soluble in organic solvents such as ethanol but slightly soluble in water.
3. The boiling point for this substance is 211 °C.
4. The melting point is 158–159 °C.

Result

Salicylic acid was synthesized, and the percentage yield was found to be 96.77%. The melting point of salicylic acid was found to be 158–159 °C.

Uses

1. Salicylic acid as a medication is used most commonly to help remove the outer layer of the skin. It is used to treat warts, psoriasis, acne, ringworm, dandruff, and ichthyosis.
2. Similar to other hydroxy acids, salicylic acid is a key ingredient in many skincare products for the treatment of seborrhoeic dermatitis, acne, psoriasis, calluses, corns, keratosis pilaris, acanthosis nigricans, ichthyosis and warts.
3. Salicylic acid is used in the production of other pharmaceuticals, including 4-aminosalicylic acid, sandulpiride, and landetimide.
4. Salicylic acid was one of the original starting materials for making acetylsalicylic acid (aspirin).
5. Bismuth subsalicylate, a salt of bismuth and salicylic acid, is the active ingredient in stomach relief aids such as Pepto-Bismol, is the main ingredient of Kaopectate and «displays anti-inflammatory action (due to salicylic acid) and also acts as an antacid and mild antibiotic».
6. Salicylic acid is used as a food preservative, a bactericidal and an antiseptic.
7. Aspirin (acetylsalicylic acid or ASA) can be prepared by the esterification of the phenolic hydroxyl group of salicylic acid with the acetyl group from acetic anhydride or acetyl chloride.

Precaution

1. As a use of methyl salicylate to wear gloves and avoid skin contact, eye contact, or inhalation which is a toxic, irritant, hazardous in case of skin contact, eye contact, or inhalation.
2. Prolonged contact can cause target organ damage.
3. Let the instructor know if any is spilled. • Sulfuric acid. Corrosive and causes burns. Wear gloves. Immediately neutralize any spills. • Salicylic acid. Irritant. Hazardous in case of skin contact, eye contact, or inhalation. Wear gloves.

Questions

1. What is the white solid that formed immediately when the methyl salicylate was introduced to the aqueous solution of sodium hydroxide?
2. Suppose a student forgot to turn on the reflux condenser water and proceeded to heat the reaction mixture for a long period of time. This student ended up with a disappointing yield of product. What could have happened?
3. What do you think the purpose was to filter the hot product solution through the fluted filter paper?
4. Write a good definition for what a catalyst is.

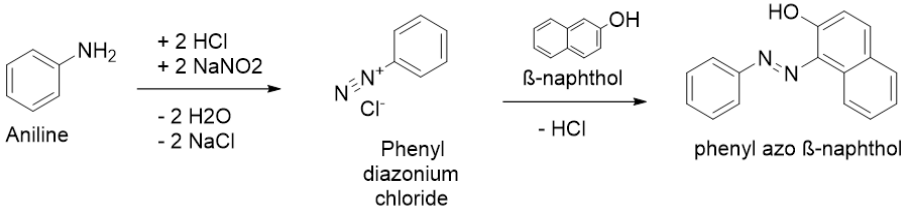
❑

Chapter 18

Synthesis and Characterization of 1-Phenyl-Azo-2-Naphthol from Aniline by Diazotization and Coupling Reaction

Principle

2-Naphthol aniline dye or Phenyl azo 2-Naphthol is an orange red dye with an azo compound. It belongs to a large class of azo compounds, all of which contain a -C-N=N-C. Azo compounds have an extended system of conjugation and are often coloured and used as colours. The reaction known as the coupling reaction prepares these compounds. 2-Aniline naphthol dye is made from aniline. It is a scarlet dye can be prepared by coupling reaction. Aniline reacts with sodium nitrite in the presence of hydrochloric acid forms benzene diazonium chloride. Further benzene diazonium chloride reacts with 2-naphthol forms a bright orange colour 2-naphthol aniline dye.



Requirements

Chemicals:

1. Aniline = 5 mL
2. Sodium nitrite = 4 gm
3. 2-Naphthol = 7 gm
4. Conc. HCl = 10 ml
5. Glacial acetic acid = 40 ml
6. Sodium hydroxide solution = 40 ml
7. Distilled water = 100 ml

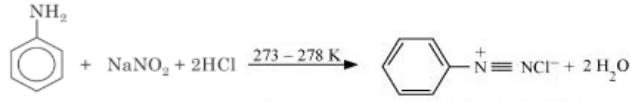
Glassware/Apparatus

1. Conical flask (100 mL)
2. Beaker (100 ml)
3. Pipette
4. Glass rod
5. Funnel
6. Filter paper
7. Test tube
8. Buchner funnel
9. Thermometer
10. Capillary tube

Chemical Reaction

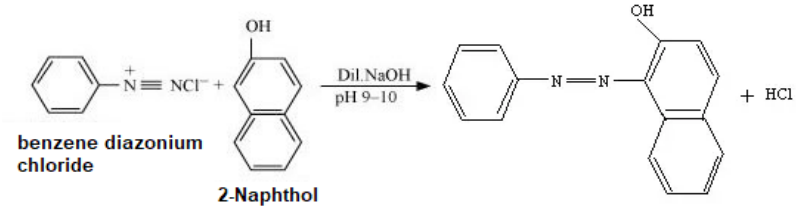
Azo compounds are prepared by the reaction of diazonium salts with phenol under alkaline conditions. Primary aromatic amines react with nitrous acid at 0 °C to give a diazonium salt. Nitrous acid is in turn formed by the reaction of sodium nitrite with hydrochloric acid. The active reagent is nitrous anhydride or dinitrogen trioxide. Nitrous anhydride reacts with aniline to give nitro amine derivative which is unstable and isomerizes to form a di acetic acid which in turn converted to a diazonium salt. Finally, this diazonium salt reacts with 2-naphthol in the presence of sodium hydroxide give 2-naphthol aniline which is an aniline dye.

Step-1:



benzene diazonium chloride

Step-2:

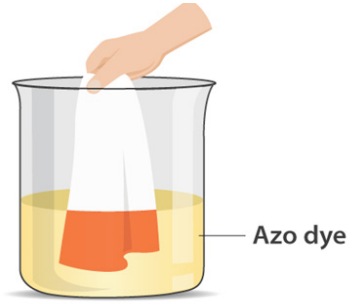


benzene diazonium chloride

2-Naphthol

2-Naphthol Aniline Dye (Orange colour)

Apparatus Setup



Procedure

1. Place 100 ml of conical flask and add 5 ml of aniline, 10 ml concentrated hydrochloric acid and 10 ml of water.
2. Then cool the solution in ice bath between 0–5 °C.
3. In a 100 ml of beaker add a solution of 4 gm sodium nitrite in 15 ml of water dropwise with continuous shaking and controlling the temperature below 5 °C.
4. Then slowly add sodium nitrite solution to the solution of aniline I conc. HCl.
5. Take another flask to dissolve 8 gm of 2-naphthol in a solution of 5 gm sodium hydroxide solution in 50ml of water.
6. Cool the solution in the ice bath to 0–5°C.
7. Now add the diazotized solution dropwise with constant stirring.
8. Continue the stirring at least half an hour without allowing the temperature to rise above 10 °C.
9. The mixed solution immediately develops a red colour and the 1-phenyl-azo-2-naphthol rapidly separates as orange red crystals.
10. When the addition of diazo solution is complete, allow the mixture to stand in ice salt mixture for 30 minutes. Filter the crude sample and wash it with cold water.
11. Dry and recrystallize the product it from ethyl alcohol or glacial acetic acid.
12. Filter the crystal obtained the pump. Wash with a few ml of ethanol to remove acetic acid.
13. 1-Phenyl-azo-2-Naphthol is obtained as orange red crystals.
14. Expected yield is 14 gm and melting point is 131–133 °C.

Calculation

Here limiting reagent of methyl salicylate; hence yield should be calculated from its salicylic acid.

1. Molecular Formula of aniline = $C_{14}H_{12}O_2$
2. Molecular Formula of 1-Phenyl azo 2-naphthol = $C_{16}H_{12}N_2O$
3. Molecular weight of aniline = 93 g/mole
4. Molecular weight of 1-Phenyl azo 2-naphthol = 258 g/mole

Theoretical Yields

93 gm of aniline on reacting with 144 gm of 2- Naphthol yields of 258 gm of 1-Phenyl azo 2-naphthol.

Therefore, 5.5 gm of aniline will form…… (X) gm of 1-Phenyl azo 2- naphthol.

$$X = 258 \times 5.5/93 = 15.25 \text{ gm}$$

Hence the theoretical yield about 15.25 gm.

If practical yield is 14 gm, hence percentage yield is:

$$\% \text{ yield} = \text{Practical yield/Theoretical Yield} \times 100$$

$$\% \text{ Yield} = 14/15.25 \times 100$$

$$= 91.80\%$$

Properties

1. It is a orange red solid.
2. It is soluble in organic solvents such as ethanol but insoluble in water.
3. The boiling point for this substance is 192 °C.
4. The melting point is 131–133 °C.

Result

1-Phenyl azo 2-naphthol was synthesized, and the percentage yield was found to be 91.80 %.

The melting point of 1-Phenyl azo 2-naphthol was found to be 131–133 °C.

Uses

Azo dyes are used to dye textile fibers, especially cotton, as well as silk, wool, viscose and synthetic fibers.

Precautions

1. The solution must be cooled to 5 °C. Do not raise the temperature.
2. Not to touch the dye otherwise it will stick to hands.

3. Not to touch the concentrated acids otherwise it will cause irritation.
4. Wash the crude sample repeatedly with cold water in order to remove soluble impurities.
5. Maintain the pH between 4–5.

Questions

1. What is coupling reaction?
2. Give the formula of 2-naphthol aniline dye.
3. What is diazotization reaction?
4. What is the colour of pure aniline?
5. Mention the uses of azo dyes.

❑

Chapter 19

Synthesis and Characterization of Benzil from Benzoin by Oxidation Reaction

Principle

Benzil (systematically known as 1,2-diphenylethane-1,2-dione) is the organic compound with the formula $(C_6H_5CO)_2$, generally abbreviated $(PhCO)_2$. This yellow solid is one of the most common diketones. Its main use is as a photo initiator in polymer chemistry. Here alcohol group of benzene is oxidized to ketone from forming bezil in the presence of nitric acid. Nitration of aromatic ring is not occurring as sulphuric acid is totally absent in this reaction.

Requirements

Chemicals:

1. Benzoin = 20 gm
2. Concentrate Nitric Acid = 100 ml
3. Ethanol = 150 ml

Glassware/Apparatus

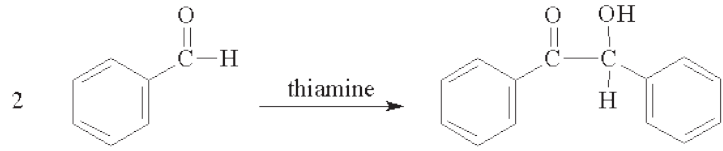
1. Round bottom flask (125 mL)
2. Beaker
3. Pipette
4. Glass rod
5. Buchner funnel
6. Filter paper
7. Hood

Chemical Reaction

This reaction takes place in two steps:

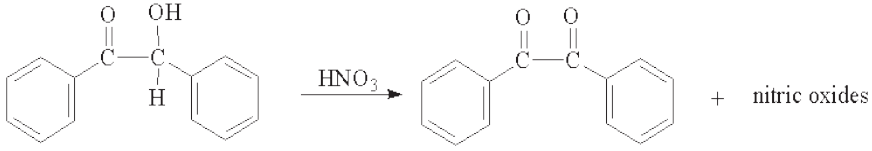
1. In the first step conversion of benzaldehyde to benzoin using the vitamin, thiamin, as a catalyst.
2. In the second step, the benzoin is oxidized to benzil using an oxidizing agent.

Step 1: Synthesis of Benzoin



This reaction is a classic--the conversion of two molecules of an aldehyde to an alpha-hydroxy ketone. The reaction is known as a benzoin condensation ("condensation" because two molecules become condensed to one molecule). This reaction, which requires a catalyst, if often performed with cyanide ion. We will use thiamine as a catalyst. It is heat-sensitive and may decompose if heated too vigorously. Instead of running this reaction at elevated temperatures for a few hours, we will allow the reaction to proceed closer to room temperature for 24 hours or more. Benzaldehyde is easily oxidized to benzoic acid which can impede the desired reaction so freshly distilled benzaldehyde is used. The concentration of reactants and temperatures of solutions are critical to obtaining a good yield so procedures must be followed carefully. Too much water will force benzaldehyde out of solution preventing an efficient reaction. Too little water prevents the thiamine hydrochloride from dissolving. Some of the base reacts with the thiamine hydrochloride to produce thiamine which is the active catalyst.

Step 2: Oxidation of Benzoin to Benzil



CAUTION: Concentrated Nitric Acid is extremely caustic and will burn exposed skin.

Procedure

Step I - Preparation of benzaldehyde to benzil

1. Place 1.5 mL of 5 M NaOH (CAUTION: extremely caustic) in a 10 mL Erlenmeyer flask and cool in an ice bath.
2. In a 50 mL Erlenmeyer flask dissolve 0.80 g of thiamine hydrochloride (MW = 337) in 2.5 mL of water.
3. Add 7.5 mL of 95% ethanol to the thiamine and cool the solution for several minutes in an ice bath.

4. While keeping both flasks in the ice bath, add the 1.5 mL of previously cooled 5 M sodium hydroxide dropwise (3–5 minutes) to the thiamine solution with swirling so that the solution stays below room temp.
5. Remove the 50 mL flask from the ice bath, add 5.0 mL of benzaldehyde (d = 1.044 g/mL) at one time, swirling the flask so that the benzaldehyde mixes with the yellow, aqueous, basic layer. The solution becomes milky but then clears*.
6. Seal the flask with Parafilm and place it in your drawer until the next lab period.
7. Filter the crystals, wash them free of mother liquor with 10-15 mL of a cold 2:1 mixture of water and 95% ethanol, and air dry the solid for 15 min.
8. Weigh your crude yield, break up any clumps of solid and recrystallize from hot 95% ethanol (8 mL per gram).
9. You should not have to filter the hot solution. After cooling, the recrystallized benzoin should be filtered, washed with a minimum of a cold 2:1 mixture of water and 95% ethanol, and air dried for 15 min or left until the next lab period.

Step II – Preparation of benzil to benzoin

1. Take a 125 mL Erlenmeyer flask, add 20 gm of benzoin (weighed to the nearest tenth of a gm) and carefully add 100 mL of concentrated nitric acid.
2. Carry out the reaction under the hood.
3. Heat the mixture on a steam bath with occasional slow swirling for 1.5 hours or until the brown-red nitric oxide gases are no longer evolved. The fumes are toxic and noxious so be certain that the fume hood safety shield is pulled down.
4. Carefully cool the flask in a 300 – 400 ml ice cold water and (keep the flask covered with a plastic seal or a cork), then pour into 35 mL of cool water and swirl to coagulate the precipitated product.
5. Collect the yellow solid using Buchner funnel and wash twice with 50 mL of cool water to remove some of the nitric acid present.
6. Press the crystals to remove more water or moisture by placing another piece of filter paper over the crystals and pushing with a beaker or cork.
7. This crude product can be recrystallized from 95% ethanol while it is still slightly wet (4 mL/g).

8. Dissolve it in hot ethanol, add water dropwise to reach the cloud point, and allow it to slowly crystallize. Once the product has recrystallized, collect it on a Buchner funnel filter and dry it.
9. Weigh the practical yield and the melting point and theoretical yield of product.

Testing for the presence of unoxidized benzoin

1. Dissolve about 5 mg of the purified benzil in 0.5 ml of 95 % of ethanol and add I drop of 10 % sodium hydroxide. If benzoin is present in the solution will acquire a purplish colour.
2. If no colours appear in 2–3 minutes, an indication that the sample is free of benzoin, add a small amount of benzoin and observe the colour are develops.
3. Did your product contain unoxidized benzoin?
4. Dispose of the waste in the organic waste container.

Calculation

Here limiting reagent of benzoin; hence yield should be calculated from its amount.

1. Molecular Formula of Benzoin = $C_{14}H_{12}O_2$
2. Molecular Formula of Benzil = $C_{14}H_{10}O_2$
3. Molecular weight of Benzoin = 212 g/mole
4. Molecular weight of Benzil = 210 g/mole

Theoretical Yields

212 gm of benzoin forms of 210 gm of benzil

Therefore, 20 gm of benzoin will form…… (X) gm of benzil.

$$X = 210 \times 20/212 = 19.8 \text{ gm}$$

Hence the theoretical yield about 19.8 gm.

If practical yield is 19 gm, hence percentage yield is:

% yield =Practical yield/Theoretical Yield × 100

% Yield = 19/19.8 × 100

= 95.9%

Properties

1. It is pale yellow crystalline powder.
2. It is soluble in organic solvents such as ethanol, benzene and diethyl ether but insoluble in water.

3. The boiling point for this substance is 346–348 °C.
4. The melting point is 94.8 °C.

Result

Benzil was synthesized and the practical yield found to be 19 gm and percentage yield was found to be 95.9 %. The melting point of benzil was found to be 94.8°C.

Uses

1. Benzil is a potent inhibitor of human carboxylesterases, enzymes involved in the hydrolysis of carboxyl esters and many clinically used drugs.
2. Benzil is used in the free-radical curing of polymer networks. Ultraviolet radiation decomposes benzil, generating free-radical species within the material, promoting the formation of cross-links.
3. It is also a relatively poor photo initiator and is seldom used. It absorbs at the 260 nm wavelength. It undergoes photobleaching, which allows the curing light to reach deeper layers of the material on longer exposure.
4. It is used in the manufacture of glycollate pharmaceuticals as a benzillic acid, clidinium, Dilantin and flutropium.

Precautions

1. The preparation must be carried out in a fume cup board as nitrous fumes are evolved during the reaction.
2. The condenser and flask should be clamped separately, if the two are joined through a park cork.
3. The solution must be used carefully. Wear a glove to handling of chemicals.
4. Not to touch the dye otherwise it will stick to hands.
5. Not to touch the concentrated acids otherwise it will cause irritation.
6. Wash the crude sample repeatedly with cold water in order to remove soluble impurities.

❑

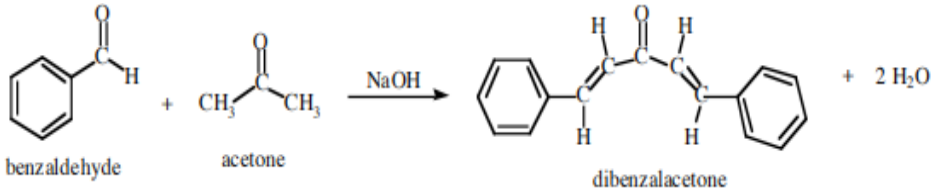
Chapter 20

Synthesis and Characterization of Dibenzal Acetone from Benzaldehyde by Claisen-Schmidt Reaction

Principle

The reaction of an aldehyde with a ketone employing sodium hydroxide as the base is an example of a mixed aldol condensation reaction, the Claisen-Schmidt reaction. According to Claisen aldehydes in the presence of sodium hydroxide can condense with another aldehyde or ketone eliminating a water molecule. Thus, moles of benzaldehyde condense with one mole of acetone to give Dibenzal acetone.

An aldol condensation is a reaction that is named based on the type of product formed when two aldehydes (or ketones), in the presence of dilute base, yields a molecule having both aldehyde (ald-) and alcohol (-ol) functional groups. The aldol products are β-hydroxy aldehyde (or β-hydroxyketone). This reaction is used extensively for the synthesis of new C-C bonds and to make larger organic molecules. In every case, the product results from the addition of one molecule of an aldehyde (or ketone) to a second aldehyde (or ketone) in such a way that the α-carbon (in the form of an enolate ion) of the first becomes attached to the carbonyl carbon of the second.



benzaldehyde + acetone → dibenzalacetone + 2 H_2O

Other names- 5-Diphenylpenta-,4-dien-3-one, trans Dibenzylideneacetone

Requirements

Chemicals:

1. Acetone = 4 mL
2. Benzaldehyde = 10.5
3. Methanol = 10 ml
4. 10% Sodium hydroxide solution = 2 ml

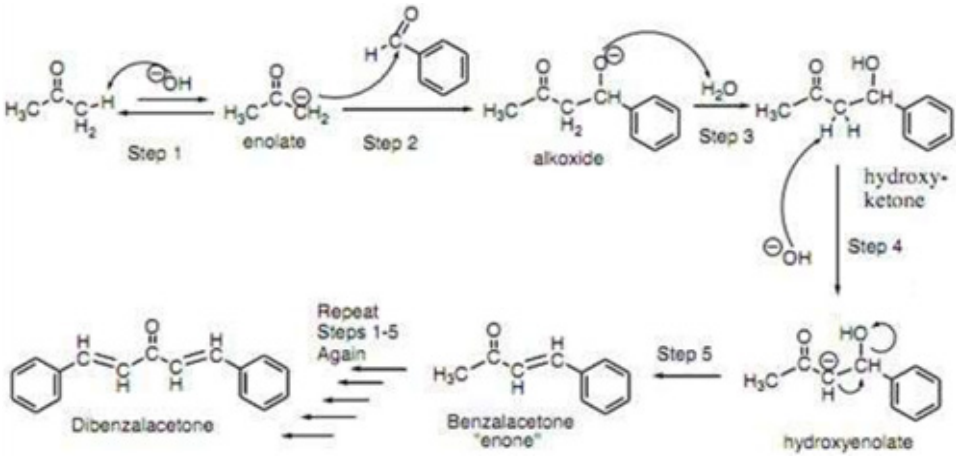
5. Distilled water = 100 ml
6. Dilute HCI = 20 ml

Glassware/Apparatus

1. Conical flask (100 mL)
2. Beaker (100 ml)
3. Pipette
4. Glass rod
5. Funnel
6. Filter paper
7. Buchner funnel
8. Thermometer
9. Measuring cylinder

Chemical Reaction

Aromatic aldehyde undergoes condensation reaction with aldehyde or ketone which contain alpha hydrogen atoms in the presence of an alkali. This reaction is called Claisen-Schmidt reaction. The double mixed-aldol condensation reaction between acetone and benzaldehyde was carried out. Acetone has α-hydrogens (on both sides) and thus can be deprotonated to give a nucleophilic enolate anion. The alkoxide produced is protonated by solvent, giving a β-hydroxyketone, which undergoes base-catalyzed dehydration. The elimination process is particularly fast in this case because the alkene is stabilized by conjugation to not only the carbonyl but also the benzene. In this experiment, excess benzaldehyde such that the aldol condensation can occur on both sides of the ketone.



Dibenzalacetone is readily synthesized by condensation of acetone with two equivalents of benzaldehyde. The aldehyde carbonyl is more reactive than that of the ketone and therefore reacts rapidly with the anion of the ketone to give a β-hydroxyketone, which easily undergoes base catalyzed dehydration. Depending on the relative quantities of the reactants, the reaction can give either mono- or dibenzalacetone.

Procedure

1. Place a 100 ml of conical flask add 10 ml (10.4 gm) freshly distilled benzaldehyde and 4 ml of pure acetone.
2. Place the flask in cold water bath and then add 2 ml of 10% sodium hydroxide solution dropwise with constant stirring.
3. The reaction mixture temperature should not be raised beyond 30 °C. Should be maintain the temperature at 30 °C.
4. After completing the addition of sodium hydroxide stir the mixture and allow to stand for 30 minutes.
5. Occasionally shaking reaction mixture and finally cooled the mixture in ice water. During the shaking Dibenzal acetone separates initially as a fine emulsion and then forms yellow crystals.
6. The reaction mixture is filtered with at the pump, washed well with a water to eliminate traces of alkali.
7. Filter out the pale-yellow crystals with cold water, dried the crude product and recrystallize with using of 30 ml of ethanol.
8. Crude Dibenzal acetone is obtained, yield 10 gm and m.p. 112 °C.

Calculation

Here limiting reagent of benzaldehyde; hence yield should be calculated from its Dibenzal acetone.

1. Molecular formula of benzaldehyde = C_7H_6O
2. Molecular formula of Dibenzal acetone = $C_{17}H_{14}O$
3. Molecular weight of benzaldehyde = 106 g/mole
4. Molecular weight of Dibenzal acetone = 234 g/mole

Theoretical Yields

2×106 =212 gm of benzaldehyde (2 moles) yields of 234 gm of Dibenzal acetone

Therefore, 10.4 gm of benzaldehyde will form…… (X) gm of Dibenzal acetone.

$$X = 234 \times 10.4/212 = 11.5 \text{ gm}$$

Hence the theoretical yield about 11.5 gm.

If practical yield is 9gm, hence percentage yield is:

$$\% \text{ yield} = \text{Practical yield/Theoretical Yield} \times 100$$

$$\% \text{ Yield} = 9/11.5 \times 100$$

$$= 78.26\%$$

Properties

1. It is pale yellow crystalline solid.
2. It is soluble in organic solvents such as ethanol and diethyl ether but insoluble in water.
3. The boiling point for this substance is 130 °C.
4. The melting point is 112 °C.

Result

Dibenzal acetone was synthesized, and the practical yield to be 9 gm and percentage yield was found to be 78.26%. The melting point of dibenzal acetone was found to be 112 °C.

Uses

1. Dibenzalacetone used as a component in sunscreens, and some industrial organometallic compounds because it bonds to metals and helps form a stable chemical structure.
2. Dibenzalacetone is a pale-yellow solid that does not dissolve in water, but dissolves in ethanol. This is because it is a symmetrical, non-polar molecule

Precautions

1. Primary precaution may be carefully taken, whenever vigorous reaction is taking place inside the flask, release the pressure from time to time by opening the cork of the flask.
2. The reaction mixture temperature should not be raised beyond 30^{o}C.
3. Ethanol and acetone should be kept away from the flame throughout the reaction.

Questions

1. What is condensation reaction?
2. What is the IUPAC name for dibenzal acetone?
3. Dibenzal acetone preparation is based on which naming reaction.
4. Why to lose the cork on the mouth of the flask during heating?
5. What is the formula for dibenzal acetone?

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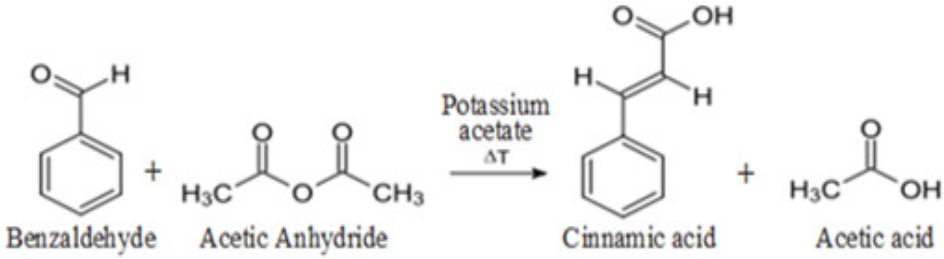
Chapter 21

To Synthesis and Characterization of Cinnamic Acid from Benzaldehyde by Perkin Reaction

Principle

Cinnamic acid derivatives synthesizes from the thermal condensation between aromatic aldehydes (Benzaldehyde) and aliphatic carboxylic acid anhydrides or carboxylic derivatives (e.g., amide) in the presence of a basic compound functioning as a catalyst is generally known as the Perkin reaction. It has been reported that the carbonates, acetates, phosphates, sulfites, and sulfides of sodium or potassium are all effective for this reaction. In addition, even a strong organic base such as tertiary amine and pyridine are good catalysts for the Perkin reaction. The higher-order aliphatic acid anhydrides normally give low yields. This reaction has importance for the preparation of cinnamic acid derivatives.



Requirements

Chemicals:

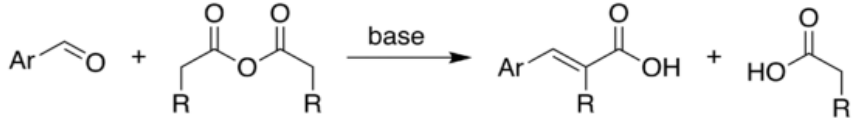
1. Potassium acetate = 6 gm
2. Benzaldehyde = 10.5 gm
3. Acetic anhydride = 15 gm
4. Sodium carbonate = 20 gm
5. Rectified spirit = 50 ml
6. Con. HCI = q.s.

Glassware/Apparatus

1. Double necked round bottom flask with guard tube system (250 mL)
2. Round bottom flask (500 ml)
3. Pipette
4. Glass rod
5. Funnel
6. Filter paper
7. Reflux condenser set
8. Buchner funnel
9. Thermometer
10. Measuring cylinder

Chemical Reaction

Cinnamic acid can be synthesized from aromatic aldehydes such a benzaldehyde and aliphatic carboxylic anhydrides (acetic anhydride) capable of providing an "active methylene" moiety in the presence of bases catalyst, such as acetate ion and hydronium ion which yields in carboxylic acid moiety. Particularly with sodium or potassium salts of the carboxylic acids corresponding to the anhydrides used in reactions as reagents.

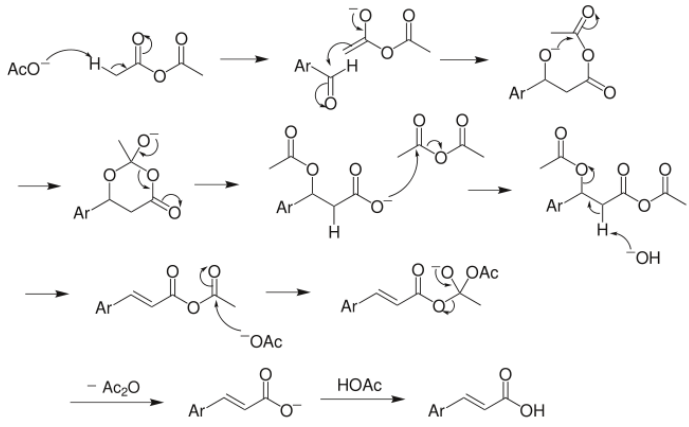


One of the most important applications of the Perkin reaction is the laboratory synthesis of phytoestrogenic stilbene resveratrol. The Perkin reaction can be considered as a type of condensation reaction.

Mechanism

Under the influence of the base, the anhydride gives the carbanion. This carbanion now attacks the carbonyl carbon of the aldehyde. This attack yields an intermediate. The abstraction of a proton from the active methyl group of the intermediate by the given base and the subsequent elimination of the hydroxyl group gives unsaturated anhydride.

This product is now hydrolyzed to finally give alpha, beta-unsaturated acid. The illustration of the Perkin reaction mechanism is given below.



Thus, the required alpha, beta-unsaturated acid is formed.

It is important to note that the above-given mechanism is not universally accepted as there are many other variations to the mechanism of Perkin reaction. One of these other mechanisms includes decarboxylation without the transfer of an acetyl group.

Procedure

1. Place 10 ml (10.5 gm) grams of benzaldehyde, 14 ml (15 gm) of acetic anhydride, both freshly distilled in a 250 ml round bottom flask, and added 6 grams of anhydrous pulverized potassium acetate, provided with $CaCl_2$ guard tube at its top end.
2. A mixture of round bottom flask is mixed properly, and the reaction mixture is heated in a RB flask fitted with a reflux condenser, for 60 minutes at 160 °C in oil bath, further at an elevated temperature of 180 °C for about 3 hours.
3. After the reaction is complete, the hot reaction product is poured into a large flask.
4. Distilled water is added and then distilled with steam distillation, until no more benzaldehyde passes over. The quantity of water used here is large enough so that all of the cinnamic acid dissolves except a small portion of an oily impurity.
5. The solution is then boiled a short time, with some activated charcoal, and filtered.
6. On cooling, the cinnamic acid separates out in lustrous leaves.
7. Recrystallization the crude product of cinnamic acid from ethanol. Crude cinnamic acid is obtained, yield 12 gm and m.p. 133 °C.

Calculation

Here limiting reagent of benzaldehyde; hence yield should be calculated from its Cinnamic acid.

1. Molecular formula of benzaldehyde = C_7H_6O
2. Molecular formula of Cinnamic acid = $C_9H_8O_2$
3. Molecular weight of benzaldehyde = 106.12 g/mole
4. Molecular weight of Cinnamic acid = 148.16 g/mole

Theoretical Yields

106.12 gm of benzaldehyde yields of 148.16 gm of Cinnamic acid

Therefore, 10.5 gm of benzaldehyde will form…… (X) gm of Cinnamic acid.

$$X = 148.16 \times 10.5/106.12 = 14.66 \text{ gm}$$

Hence the theoretical yield about 14.66 gm.

If practical yield is 12 gm, hence percentage yield is:

$$\% \text{ yield} = \text{Practical yield}/\text{Theoretical Yield} \times 100$$

$$\% \text{ Yield} = 12/14.66 \times 100$$

$$= 81.9\%$$

Properties

1. It is white crystalline powder.
2. It is soluble in organic solvents such as ethanol but slightly soluble in water.
3. The boiling point for this substance is 300 °C.
4. The melting point is 133 °C.

Result

Cinnamic acid was synthesized by the reaction of benzaldehyde and acetic anhydride. The crude product was obtained and the percentage yield about 12 gm and % yield to be 81.9 %.

The melting point of Cinnamic acid was found to be 133 °C.

Uses

1. Cinnamic acid are used in macromolecular synthesis as very important building blocks for various classes of polymers, having attractive properties, especially a high photo reactivity due to the presence, in the main or side chains, of the cinnamoyl group, well known as photo responsive unit.

2. Cinnamic acids is compose a relatively large family of organic acids which appear to have antibacterial, antifungal and anti-parasitical activities.
3. Cinnamic acid contain polymer moiety in a structure. Polymers containing cinnamoyl moieties are used in a wide range of applications in emerging fields such as advanced microelectronics, photolithography, non-linear-optical materials, integrated circuit technology and photocurable coatings.
4. It is also used in the perfume production, the food industry, pharmaceuticals, medicine and technical applications, cinnamic acids are synthesized on a commercial scale.

Precautions

1. The solution must be used carefully. Wear a glove in hands and eyeglasses to throughout the experiment.
2. Never touch the dye otherwise it will stick to hands.
3. Never to touch the concentrated acids otherwise it will cause irritation on the skin, they can easily absorb and occurs wounds in skin.
4. Carefully wash the crude reaction mixture repeatedly with cold water in order to remove soluble impurities.

Questions

1. Describe Perkin reaction.
2. What catalysts may be used in the Perkin reaction?
3. What is the use of this named reaction?
4. Which solvent are used to recrystallization of crude product in this reaction?

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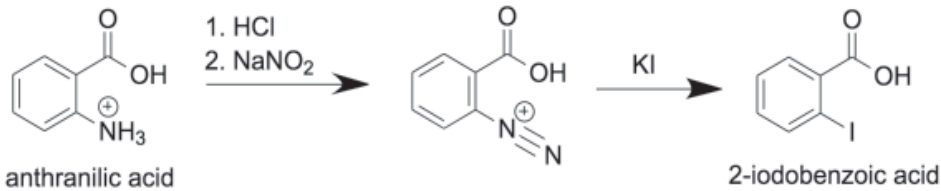
Chapter 22

Synthesis and Characterization of **P-Iodo Benzoic Acid** from **P-Amino Benzoic Acid**

Principle

The Sandmeyer reaction is a versatile synthetic tool by which an amino group on an aromatic ring is replaced with a wide range of substituents by converting an amino group attached to an aromatic ring into a diazonium salt that can be transformed into several functional groups. In this experiment, the 2-iodobenzoic acid is synthesized from 2-aminobenzoic acid by this reaction.



anthranilic acid 2-iodobenzoic acid

Requirements

Chemicals:

1. p-amino benzoic acid = 10 ml
2. Potassium iodide = 15 gm
3. Conc. HCl = 10 ml
4. Sodium nitrite = 10 gm
5. Rectified spirit = 50 ml
6. Distilled water = 100 ml

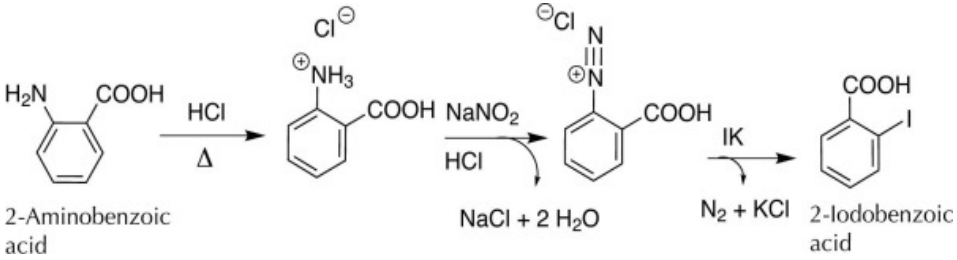
Glassware/Apparatus

1. Round bottom flask (250 mL)
2. Beaker (100 ml)
3. Glass rod
4. Funnel
5. Filter paper

6. Buchner funnel
7. Measuring cylinder
8. Pump

Chemical Reaction

p-Iodobenzoic acid can be synthesized via a Sandmeyer reaction consisting of the diazotization of anthranilic acid followed by a diazo replacement. First anthranilic acid is treated with nitrous acid in order to convert the amino group into the diazo group. The diazo group is ejected, yielding a carbocation which is then attacked by highly nucleophilic I^- anion.



Procedure

1. Place 10 ml of p-amino benzoic acid (PABA) in a 250 ml of round bottom flask.
2. Add 10 ml of 3 M HCl in RB flask.
3. Warm gently while stirring until reaction mixture is dissolves properly.
4. Dissolve 10 gm of $NaNO_2$ in 10 ml water in a 100 ml of beaker.
5. Cool both solutions in ice baths until both are below 5 ºC.
6. Add sodium nitrite solution to round bottom flask, keep below 10 ºC.
7. Test with starch-iodide paper, add minute amounts of urea to give a negative test.
8. Dissolve 15 ml of KI in 100 ml water in another beaker.
9. Pour diazonium salt into 500 ml beaker with the KI solution, stir.
10. Heat gently, pop foam with stirring of glass rod.
11. Collect product with vacuum filtration, wash with a cold water.
12. Recrystallize with 80% ethanol/20% water.
13. Obtained crude product.

Calculation

Here limiting reagent of p-amino benzoic acid; hence yield should be calculated from its p-iodo benzoic acid

1. Molecular formula of p-amino benzoic acid = $C_7H_7NO_2$
2. Molecular formula of p-iodo benzoic acid = $C_7H_5IO_2$
3. Molecular weight of p-amino benzoic acid = 137.14 g/mole
4. Molecular weight of p-iodo benzoic acid = 248.02 g/mole

Theoretical Yields

137.14 gm of p-amino benzoic acid yields of 248.02 gm of p-iodo benzoic acid

Therefore, 10 ml (11 gm) of p-amino benzoic acid will form…… (X) gm of p-iodo benzoic acid.

$$X = 248.02 \times 11/137.14 = 19.89 \text{ gm}$$

Hence the theoretical yield about 19.89 gm.

If practical yield is 18 gm, hence percentage yield is:

$$\% \text{ yield} = \text{Practical yield}/\text{Theoretical yield} \times 100$$

$$\% \text{ Yield} = 18/19.89 \times 100$$

$$= 90.5\%$$

Properties

1. It is off white to light brown colour powder.
2. It is soluble in organic solvents such as ethanol and ether but slightly soluble in water.
3. The boiling point for this substance is 318.5 °C.
4. The melting point is 273 °C.

Result

p-iodo benzoic acid was synthesized, and the percentage yield was found to be 90.5 %.

The melting point of p-iodo benzoic acid was found to be 273 °C.

Uses

4-Iodobenzoic acid is used as anti-infective, contraceptive agent and x-ray contrast medium for diagnostic radiology.

Precautions

1. The solution must be used carefully. Wear a glove to handling of chemicals.
2. Not to touch the dye otherwise it will stick to hands.
3. Not to touch the concentrated acids otherwise it will cause irritation.
4. Wash the crude sample repeatedly with cold water in order to remove soluble impurities.

Questions

1. Describe Sandmeyer reaction.
2. What catalysts are used in the Sandmeyer reaction?
3. What are the applications of this named reaction?

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