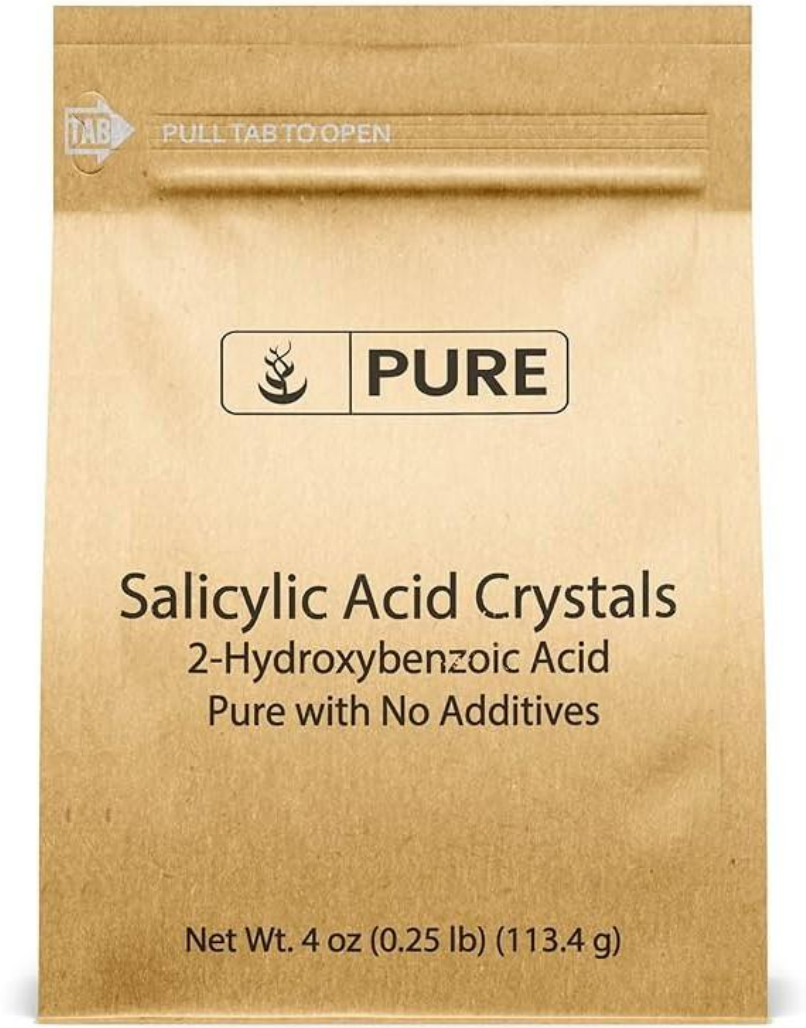
Preparation and Re-crystallization of Salicylic Acid

Undergraduate Organic Chemistry Lab

A step-by-step guide to synthesis, purification, and characterization.



Practical Organic Pharmaceutical Chemistry II & MSc.
Ameer A.Alameri

Learning Goals and Relevance

Learning Objectives

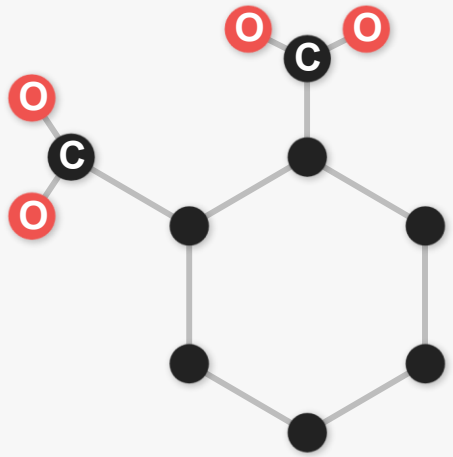
- Understand the chemical reaction involved in synthesizing salicylic acid.
- Accurately perform laboratory techniques for synthesis and purification.
- Calculate the percentage yield of the product.

Salicylic Acid at a Glance

Key Functional Groups

Carboxylic Acid COOH Imparts acidic properties and allows for esterification.

Phenolic Hydroxyl OH Also acidic, contributing to the compound's overall reactivity.



Chemical Structure

$C_7H_6O_3$

Solubility Profile

- Mostly insoluble in cold water, allowing for isolation by crystallization.
- Solubility increases significantly with temperature, crucial for recrystallization.

Benchmark Properties

Melting Point as a Purity Indicator

Pure Salicylic Acid

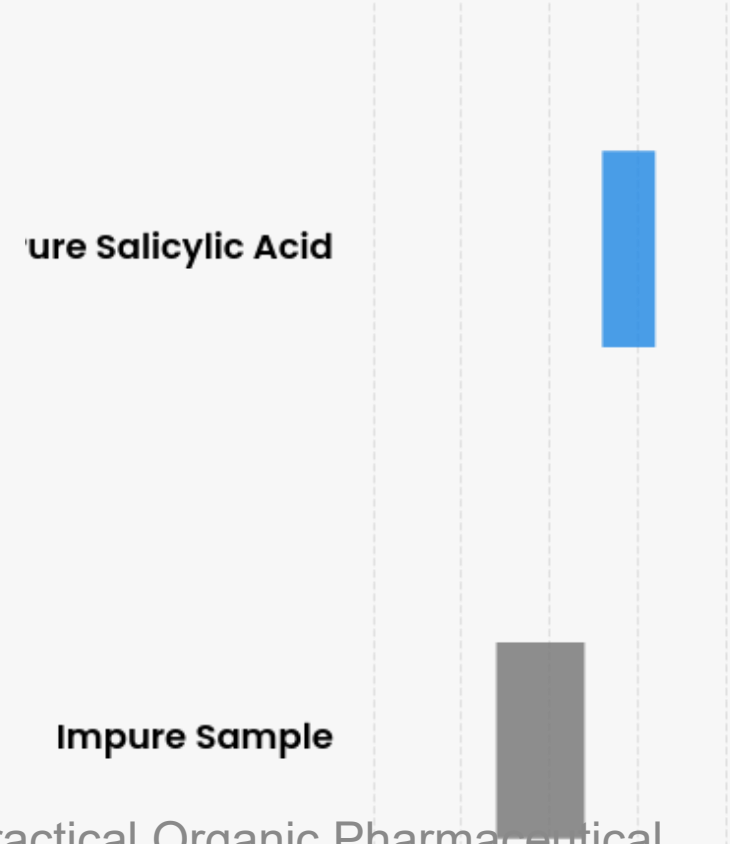
- Melts sharply within the range of 158 161 °C.

Impure Samples

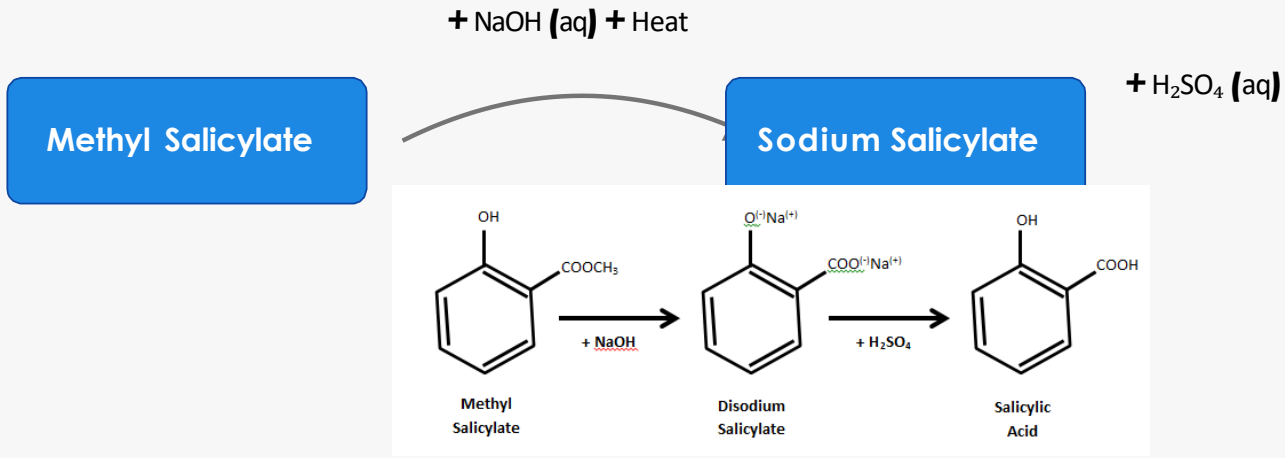
- Exhibit a lower melting point and a broader melting range (e.g., 3°C .

Wet Samples

- Can also depress and broaden the melting point range.



Route 1: Hydrolysis of Methyl Salicylate



Reaction Overview

Methyl salicylate (oil of wintergreen) is hydrolyzed under basic conditions to yield sodium salicylate, which is then acidified to form salicylic acid.

Reagents and Stoichiometry

Methyl Salicylate: Starting material 0.050 mol).

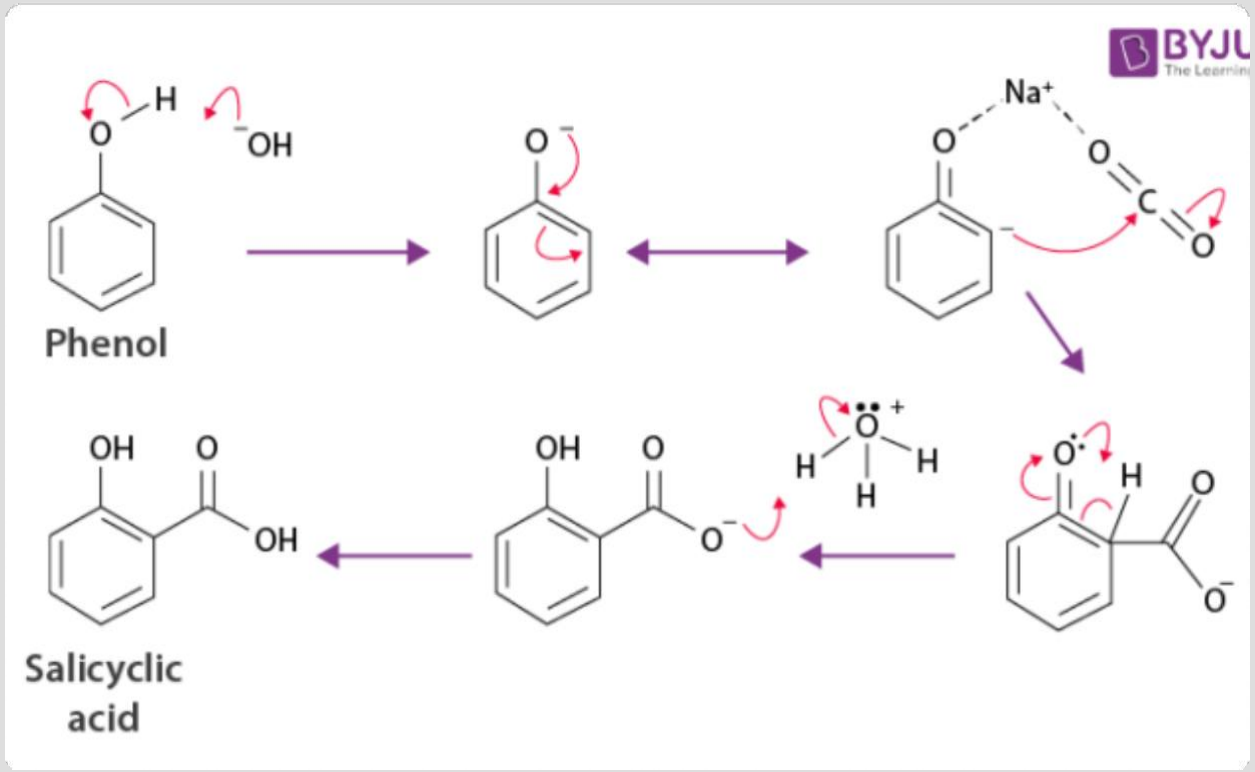
Sodium Hydroxide NaOH Strong base for hydrolysis.

Sulfuric Acid H_2SO_4): Strong acid for acidification.

Stoichiometry: 1 mole of methyl salicylate yields 1 mole of salicylic acid.

Industrial Synthesis of Salicylic Acid

Route 2: Kolbe–Schmitt (Overview)



The Kolbe-Schmitt reaction is a carboxylation chemical reaction that proceeds by treating phenol with sodium hydroxide to form sodium phenoxide, then heating sodium phenoxide with carbon dioxide under pressure.

Key Conditions

- **Phenol + NaOH** Forms sodium phenoxide.
- **CO_2 under Pressure:** Carboxylation at high pressure 100 atm) and temperature 125 °C .
- **Acid Treatment:** The resulting salicylate is treated with sulfuric acid to yield salicylic acid.

Comparing Routes

Why Hydrolysis is Preferred for Teaching Labs

Simplicity & Accessibility

- Uses readily available reagents and standard equipment.
- Less complex reaction conditions than Kolbe–Schmitt.

Safety Considerations

- Avoids high pressures and specialized equipment.
- Reagents have established undergraduate safety protocols.

Educational Value

- Demonstrates ester hydrolysis and acid–base chemistry.
- Provides experience with key lab techniques.

Reagent Hazards and PPE

Understanding Chemical Risks

Sodium Hydroxide (NaOH) & Sulfuric Acid (H_2SO_4)

Hazard: Corrosive, causes severe skin burns and eye damage.

Handling: Use caution, wear appropriate PPE, handle under a fume hood.

Methyl Salicylate / Methanol

Hazard: Can be absorbed through skin; methanol is toxic if ingested/absorbed.

Handling: Avoid skin contact, use in well-ventilated area.

Personal Protective Equipment

Safety Goggles
Always wear to protect eyes.

Nitrile Gloves
Wear to protect hands.

Lab Coat
Use to protect clothing and skin.

Waste and Spill Response

Waste Segregation

Aqueous Waste

- Neutralized acidic and basic solutions collected in designated containers.
- Ensure pH is neutral before disposal if not specified otherwise.

Organic Waste

- Any organic residues or solvents (e.g., methanol by-product) placed in separate containers.

Solid Waste

- Contaminated filter paper, used capillary tubes, and dried product in solid waste.
- Broken glassware must be placed in a dedicated broken glass container.

Spill Response

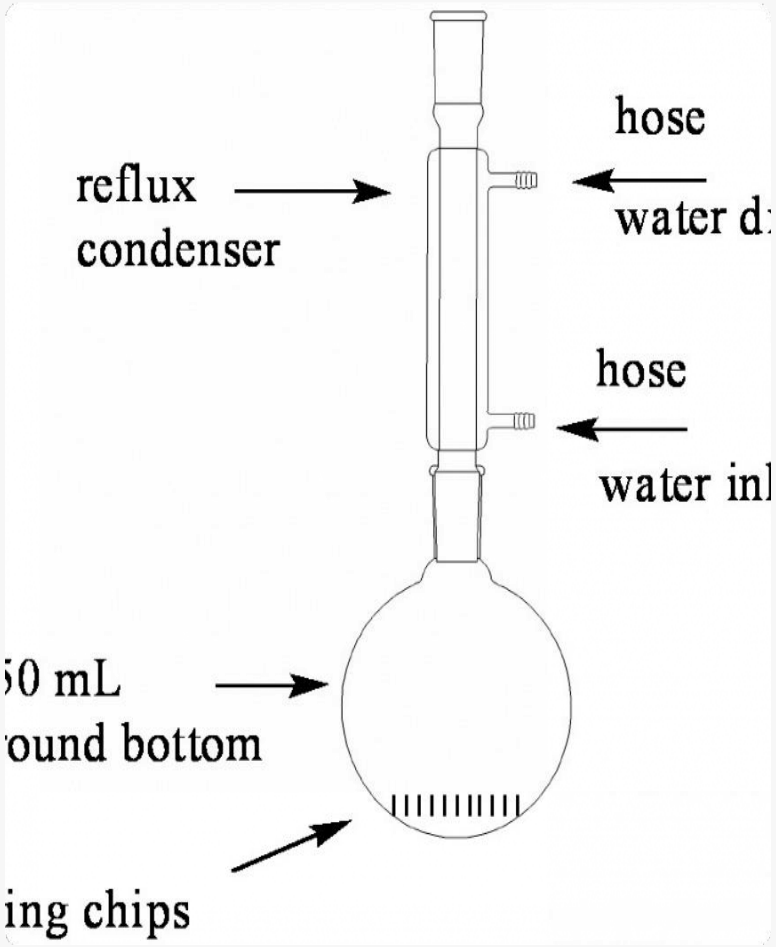
Minor Spills

Notify instructor immediately. Use appropriate spill kit (acid/base neutralizer).

Major Spills

Evacuate area, notify instructor and emergency personnel.

Setup and Reflux



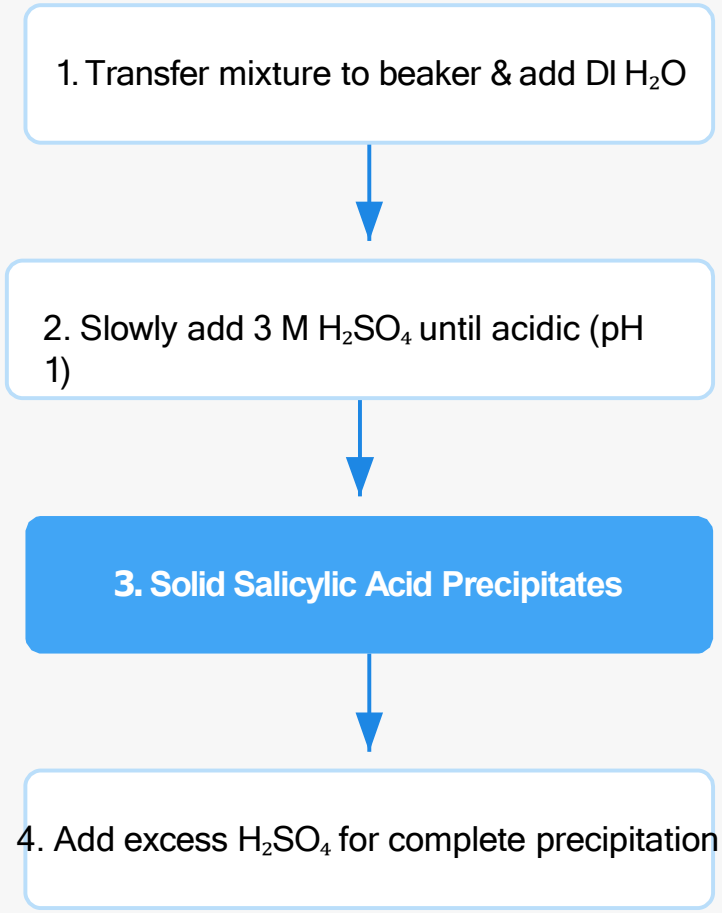
Reflux Apparatus Setup

- Charge a 100-mL round bottom flask with 25 mL of 5 M NaOH and 2 ml) of methyl salicylate.
- Add 3_ 4 boiling stones to prevent bumping.
- Attach a reflux condenser to the flask and ensure cooling water is flowing through it.

Heating and Reflux

- Heat the reaction mixture to boiling using a heating mantle.
- Maintain reflux for approximately 20 minutes, ensuring continuous boiling.

Workup and Acidification



Dilution and Acidification

After reflux, transfer reaction mixture to a 250-mL beaker.

Add 50 mL of deionized water.

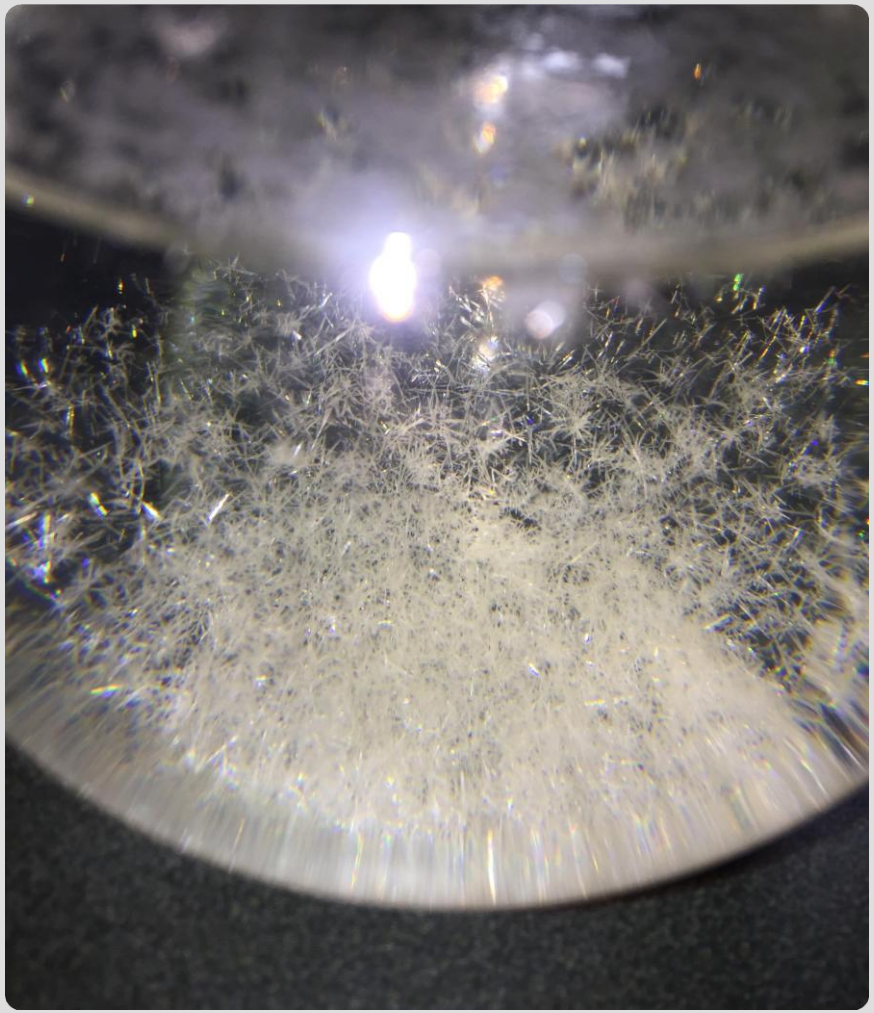
Slowly add 3 M H_2SO_4 until solution is acidic to litmus paper (pH 1).

Precipitation of Salicylic Acid

As the solution becomes acidic, solid salicylic acid will precipitate.

Add 1 2 mL excess 3 M H_2SO_4 to ensure complete precipitation.

Cooling and Filtration



Crystallization in Ice Bath

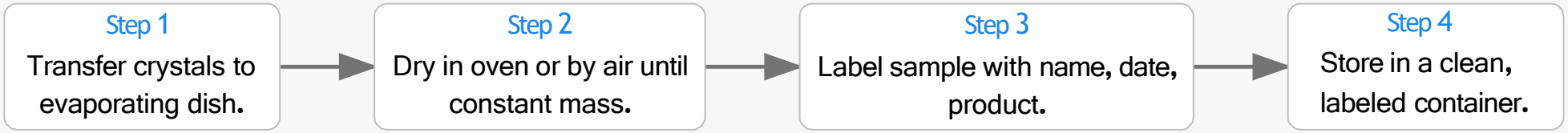
Cool the mixture in an ice-water bath to approximately 0°C for about 15 minutes to maximize crystal formation.

Ensure the solid forms a slurry; add a small amount of water if necessary for free flow.

Büchner Filtration Best Practices

- Set up a Büchner funnel with filter paper on a vacuum flask, securing it with a clamp.

Drying and Labeling



⚠ Caution: Do not store filter paper with the chemical if collected from an acid solution.

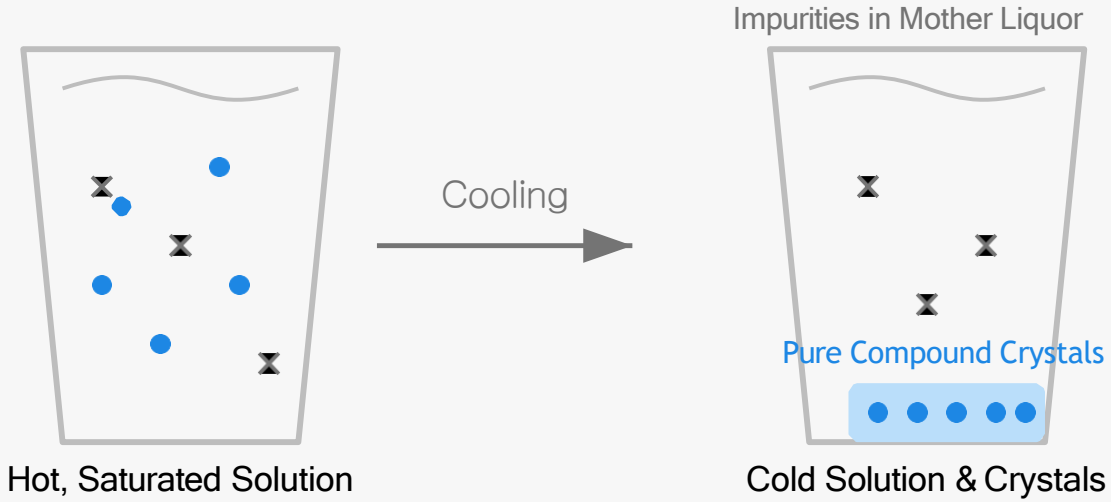
Recrystallization Principles

Solubility-Temperature

Recrystallization relies on the principle that most solids are more soluble in a hot solvent than in a cold solvent. As a hot, saturated solution cools, the solubility decreases, causing the desired compound to crystallize out.

Impurity Rejection

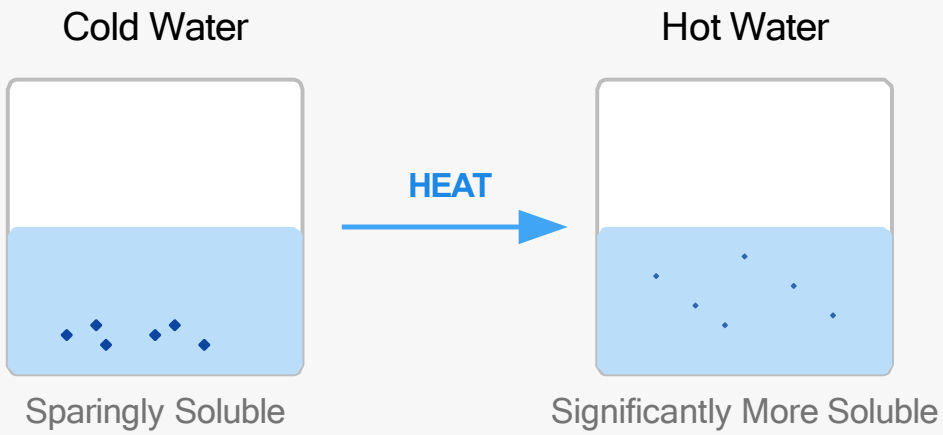
Impurities either remain dissolved in the cold solvent or do not dissolve in the hot solvent, allowing for separation. The goal is to leave impurities in the mother liquor.



Choosing Solvent and Volume

Water as Primary Solvent

Water is ideal for salicylic acid due to its temperature-dependent solubility and non-toxicity.



Minimum Hot Solvent Rule

A critical principle for maximizing product recovery.

- Dissolve crude solid in the **minimum amount of hot solvent** required.
- Using **too much solvent** will reduce the recovery of the purified product upon cooling.
- **Add solvent slowly** while heating and stirring until all solid dissolves.

Hot Filtration and Cooling Profile

Hot Filtration to Remove Insoluble Impurities

If insoluble impurities are present, perform a hot filtration to remove them before cooling.

Collect, Wash, and Dry Crystals

Collection by Vacuum Filtration

- Use a Büchner funnel and vacuum filtration.
- Ensure filter paper is seated and moistened.

Washing the Crystals

- Wash with a small amount of ice-cold solvent.
- Removes surface impurities without dissolving product.

Drying to Constant Mass

- Draw air through the funnel to remove solvent.
- Dry in an oven or air-dry until mass is constant.

Melting Point Analysis

Determination

- Load a small amount of powdered, dry sample into a capillary tube.
- Use a melting point apparatus to observe the temperature range.

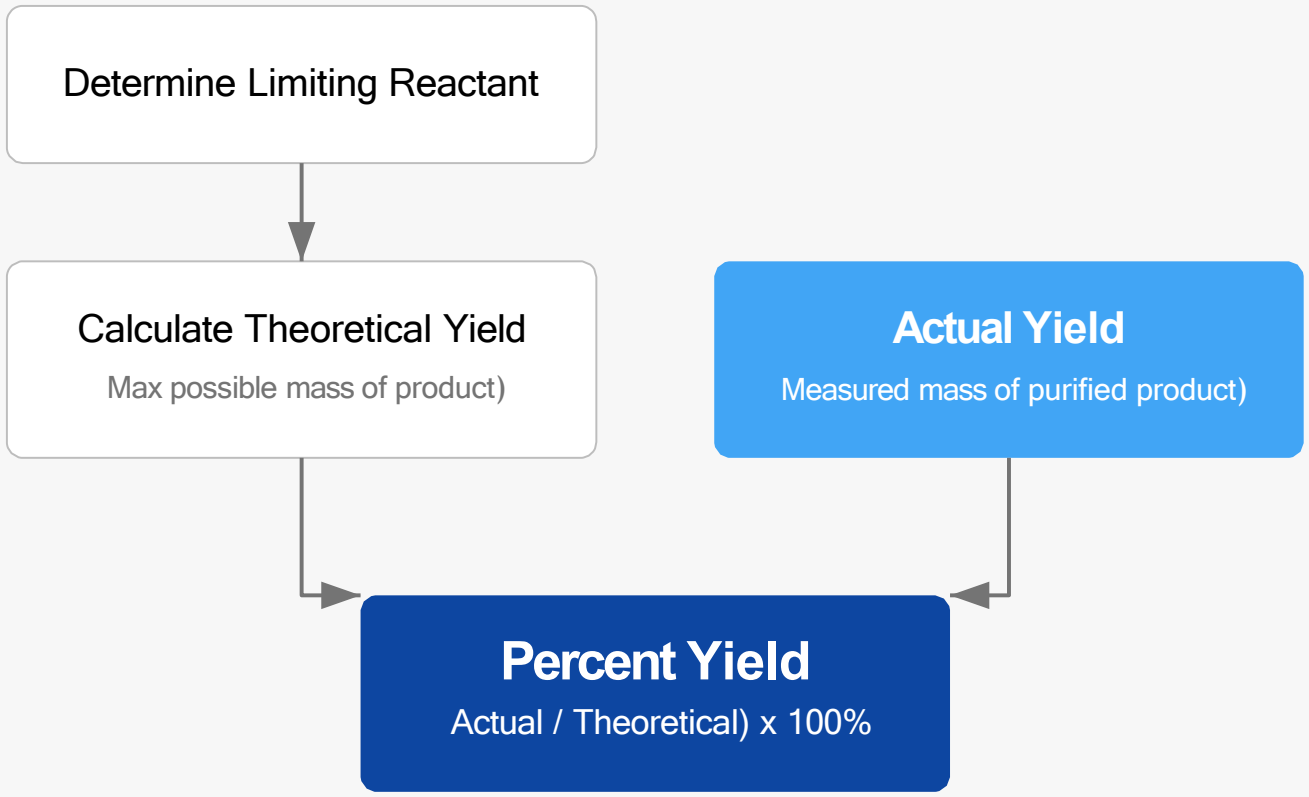
Interpreting Results

Sharp Melting Point 158 161 °C Indicates a pure substance.

Broad Melting Range 3°C Suggests impurities are present.

Depressed Melting Point 158 °C Also indicates impurities.

Yield Calculations



Actual Yield and Percent Yield

Actual Yield: The mass of purified salicylic acid obtained after recrystallization and drying.

Percent Yield: Actual Yield / Theoretical Yield) x 100%.

Common Loss Points

- Incomplete reaction during hydrolysis.
- Loss during transfers between glassware.
- Solubility losses during recrystallization.
- Incomplete drying of the final product.

Lab Notebook and Reporting

Essential Record-Keeping

- Record all masses (starting materials, crude product, purified product).
- Document all experimental conditions (reflux time, cooling method, solvent volumes).
- Note observations (color, crystal formation, melting point range).

Error Analysis and Reflection

- Identify potential sources of error in your experiment.
- Discuss how these errors might have affected your yield and purity.
- Suggest improvements for future experiments.

Troubleshooting Non-Crystallization

No Crystals Forming

Cause

Too much solvent used, solution not sufficiently cooled.

Solution

Reheat and evaporate some solvent, then re-cool slowly, or scratch the inside of the flask with a glass rod (seeding).

Oiling Out

Cause

Impurities or solvent choice causing the compound to separate as an oil instead of crystallizing.

Solution

Reheat, add a small amount of a different solvent or adjust the solvent ratio, then re-cool very slowly.

Low Yield or Impure Product

Causes of Low Yield

Excess Solvent

Issue:
Too much solvent used during recrystallization means more product remains dissolved in the mother liquor.

Mitigation:
Use the minimum amount of hot solvent to dissolve the crude product.

Incomplete Acidification

Issue:
Not enough H_2SO_4 was added, leaving some salicylic acid as the more soluble sodium salt.

Causes of Impure Product

Hot Filtration Timing

Issue:
Solution cooled too much during hot filtration, causing product to crystallize with impurities.

Mitigation:
Keep solution hot, work quickly, or use pre-heated apparatus.

Rapid Cooling

Issue:
Fast cooling leads to rapid crystallization, trapping impurities within the crystal lattice.