Synthesis and Characterization of Sulfanilamide: A Review of the Preparation, Percentage Yield, and Melting Point

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Abstract

Sulfanilamide is an aromatic sulfonamide compound that played an important role in the early development of antibacterial chemotherapy. Its synthesis is a useful experiment in organic and pharmaceutical chemistry because it demonstrates electrophilic aromatic substitution, functional-group protection, amination, and hydrolysis. The conventional preparation involves the conversion of acetanilide into an activated sulfonyl chloride intermediate, followed by reaction with ammonia and removal of the acetyl protecting group. The synthesized product can be evaluated by its physical appearance, percentage yield, and melting point. These measurements provide an initial indication of product recovery and purity. This review discusses the general synthetic pathway, the chemical principles involved, the evaluation of the isolated product, and relevant literature supporting the procedure.

Keywords: Sulfanilamide, acetanilide, chlorosulfonation, sulfonamide, percentage yield, melting point, characterization.

1.Introduction

Sulfanilamide, also known as 4-aminobenzenesulfonamide, belongs to the sulfonamide class of compounds. It is historically significant because the development of sulfonamide drugs marked an important advance in the treatment of bacterial infections. Its chemical structure contains an amino group attached to a benzene ring and a sulfonamide group, making it a useful starting compound for the preparation of other sulfonamide derivatives.

The synthesis of sulfanilamide from acetanilide is a well-established experiment in practical organic chemistry. The preparation illustrates how a protecting group can be used to control the reactivity of a functional group during a multistep reaction. The acetyl group temporarily protects the amino group, allowing sulfonyl substitution to take place preferentially at the para position of the aromatic ring. The protecting group is removed during the final hydrolysis step to obtain sulfanilamide.

The traditional synthetic route and its intermediate compounds are described in practical organic chemistry literature and in research on sulfonyl chloride preparation .These sources provide a basis for understanding both the reaction sequence and the subsequent evaluation of the product. [1]

2. Review of the Literature

The preparation of sulfanilamide has been studied since the early development of sulfonamide chemistry. Gelmo's work in 1908 is cited in historical accounts as an early report concerning sulfanilamide. Subsequent practical organic chemistry texts established laboratory procedures for preparing the compound and related sulfonamide derivatives.

A commonly described route begins with acetanilide. Chlorosulfonation introduces the sulfonyl chloride functionality into the aromatic ring, producing 4-acetamidobenzenesulfonyl chloride. Reaction of this intermediate with ammonia forms 4-acetamidobenzenesulfonamide. Acidic hydrolysis then removes the acetyl group and produces sulfanilamide. This sequence is described in the laboratory procedure published by Przybył and colleagues (2020) and in the classical Organic Syntheses procedure for preparing the sulfonyl chloride intermediate.[2]

Research has also examined improvements to the preparation of sulfonyl chloride intermediates. investigated an alternative chloro sulfonation process intended to reduce the amount of chlorosulfonic acid required. Their findings demonstrate that reaction conditions and reagent ratios can influence the efficiency of intermediate preparation. However, the reported yield for that intermediate should not be confused with the overall yield of sulfanilamide, because the two values refer to different products and reaction stages.

The literature therefore supports the use of the conventional multistep route for understanding sulfanilamide synthesis, while also highlighting the importance of reaction conditions, isolation techniques, and product characterization.[3]

3. Aim and Objectives

Aim: To synthesize sulfanilamide from acetanilide and evaluate the isolated product using physical characteristics, percentage yield, and melting-point determination.

The objectives are:

- To understand the chemical reactions involved in the preparation of sulfanilamide.
- To observe the physical appearance and crystalline nature of the product.
- To calculate the percentage yield from the actual mass of the product obtained.
- To determine the melting point and compare it with a reported reference value.
- To assess the likely purity of the synthesized product using these preliminary measurements.

4. Principle of Synthesis

The conventional preparation of sulfanilamide involves three main chemical transformations.

➢ Step 1 — Chlorosulfonation

Acetanilide is converted into 4-acetamidobenzenesulfonyl chloride using chlorosulfonic acid.

➢ Step 2 — Formation of sulfonamide

The sulfonyl chloride intermediate reacts with ammonia to form 4-acetamidobenzenesulfonamide.

➢ Step 3 — Hydrolysis

The acetyl protecting group is removed under acidic hydrolysis conditions to obtain sulfanilamide.

This sequence is consistent with the classical synthetic procedure described for the intermediate and the laboratory synthesis.[4]

The overall transformation can be summarized as:

Acetanilide
↓ Chlorosulfonation
Sulfonyl chloride intermediate
↓ Ammonia
Protected sulfonamide
↓ Hydrolysis
Sulfanilamide

Chlorosulfonic acid is highly corrosive, and the reaction can release hydrogen chloride. This synthesis should therefore be performed only in a properly equipped laboratory under qualified supervision, with appropriate protective equipment and fume-hood controls.

5. Evaluation of the Synthesized Product

5.1 Physical characteristics

Sulfanilamide is generally described as a white or nearly white crystalline solid. Its appearance and crystalline nature can be recorded after the product has been isolated and dried.

The following characteristics should be documented during the experiment.

Property	Observation or reference
Physical state	Solid
Colour	White or nearly white
Appearance	Crystalline powder or crystals
Odour	Record the observation without directly smelling the sample
Solubility	Record the solvent used and the observed solubility
Molecular formula	$C_6H_8N_2O_2S$
Molar mass	Approximately 172.20 g/mol

The physical description is consistent with historical pharmaceutical literature, which describes sulfanilamide as a white crystalline powder.[5]

5.2 Percentage yield

Percentage yield indicates how much product was recovered relative to the maximum amount theoretically obtainable from the limiting reactant.

The formula is:

$$\% \text{ Yield} = \frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100$$

For a multistep synthesis, the theoretical yield should be calculated from the limiting reactant and the overall reaction stoichiometry. The isolated product must be weighed after appropriate drying.

Example calculation format

Assume that the theoretical yield calculated from the starting material is 1.50 g and the actual mass of dried sulfanilamide obtained is 1.05 g.

$$\% \text{ Yield} = \frac{1.05}{1.50} \times 100$$

$$\boxed{\% \text{ Yield} = 70\%}$$

This is an illustrative calculation only, not a reported experimental result.

A lower yield may result from incomplete reaction, product loss during filtration or transfer, incomplete crystallization, or losses during purification. Conversely, a high apparent yield does not necessarily indicate high purity because residual solvent, moisture, or other impurities may increase the measured mass.

5.3 Melting-point determination

Melting-point determination is a simple and useful preliminary method for assessing the identity and purity of a crystalline organic compound.

Historical literature reports a melting point of approximately 165°C for sulfanilamide [5]

The melting point should be measured using a suitable laboratory melting-point apparatus. The temperature at which melting first becomes visible and the temperature at which the sample becomes completely liquid should both be recorded.

Measurement	**Experimental result**
Reported reference melting point	Approximately 165°C
Observed initial melting temperature	_____ °C
Observed complete melting temperature	_____ °C
Observed melting range	– °C

A relatively narrow melting range close to the reference value supports the expected identity and suggests reasonable purity. A broad or substantially depressed melting range may indicate impurities, residual solvent, incomplete drying, or the presence of another compound. Melting point alone, however, cannot conclusively establish chemical identity or purity.

6. Results and Discussion

The synthesized sulfanilamide should be evaluated by considering the physical appearance, percentage yield, and melting-point range together.

A white crystalline product would be consistent with the reported physical description of sulfanilamide. The percentage yield would indicate the efficiency of product recovery, whereas the melting point would provide preliminary evidence concerning the product's identity and purity.

These measurements have different purposes. A good percentage yield does not automatically mean that the product is pure, and a melting point close to the literature value does not independently confirm its chemical structure. Additional analytical methods, such as infrared spectroscopy (IR), can provide stronger evidence by identifying characteristic functional groups.

demonstrated the relevance of reaction conditions to the preparation of sulfonyl chloride intermediates, while the classical procedure of Smiles and Stewart (1925) documents the preparation of the protected intermediate used in this synthetic route. These studies help explain why the reaction conditions, work-up, and purification procedure can influence the final result.

For the final report, replace the blank fields in the results table with your actual experimental measurements. This will allow the discussion to be linked to the results obtained in your own laboratory rather than to assumed values.[6]

7. Conclusion

Sulfanilamide can be prepared from acetanilide through chlorosulfonation, reaction of the resulting sulfonyl chloride with ammonia, and hydrolysis of the acetyl protecting group. The preparation demonstrates important principles of multistep organic synthesis and functional-group protection.

The product is evaluated through its physical characteristics, percentage yield, and melting point. A white crystalline appearance and a melting point close to the reported value of approximately 165°C are consistent with sulfanilamide. The percentage yield provides information about the efficiency of the preparation, while the melting-point range offers a preliminary indication of purity. Final conclusions about the synthesized material should be based on the actual experimental results and, where available, additional analytical evidence.

The following references are presented in a conventional academic style and can be used to support the review. The first two are particularly relevant to the synthetic procedure.

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