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Research Article

Synthesis, Characterization and It's Antimicrobial Activity of Probenecid

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ABSTRACT

Probenecid was created by reacting 4-carboxybenzene sulfonamide with di-n-propylamine [1]. By promoting the excretion of uric acid, this uricosuric drug is used to treat hyperuricemia and gout [1]. The procedure creates probenecid by creating an amide link between the amine and the sulfonamide [2].

INTRODUCTION

By boosting the excretion of uric acid in the urine, the uricosuric medication Probenecid is used to treat hyperuricemia and gout [3]. Since its debut in the 1950s, it has been utilized extensively [4]. Probenecid is created when 4-carboxybenzene sulfonamide reacts with di-n-propylamine, forming an amide bond in the process [5]. 4-carboxy benzene sulfonamide is a chemical compound that is used as a starting material for the synthesis of probenecid. The synthesis of probenecid derivatives from 4-carboxy benzene sulfonamide is a multi-step process that requires careful control of the reaction conditions. However, the synthesis is relatively straightforward and can be carried out on a large scale. This project aims to synthesize probenecid through a modified version of this method, using readily available starting materials and reagents. The synthesized compound will be characterized by various analytical techniques, including infrared spectroscopy, nuclear magnetic resonance spectroscopy, and mass spectrometry. In this study, we aimed to synthesize a series of probenecid derivatives and evaluate their antimicrobial activity against a range of microorganisms. The synthesized derivatives were characterized using various spectroscopic

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techniques, and their antimicrobial activity was assessed using standard microbiological methods. This research aims to contribute to the development of novel antimicrobial agents, addressing the growing concern of antimicrobial resistance and providing new treatment options for infectious diseases.

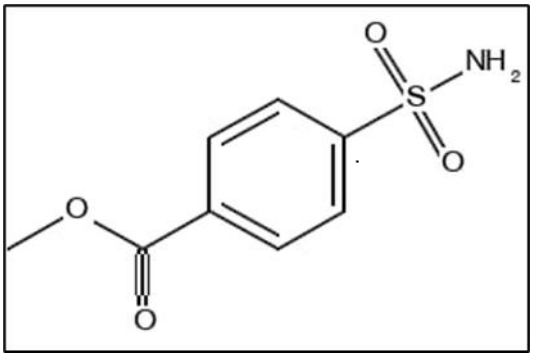


Fig no. 1: Structure of probenecid

MATERIAL AND METHODOLOGY:

Material:

Glassware: two- rounded flask, condenser, burner, pipette, stirrer, beaker.

Chemicals: Sulphuric acid, distill water, 4-carboxybenzoic acid, thionyl chloride, DMF, sulfonamide, pyridine, ethanol.

Methodology:

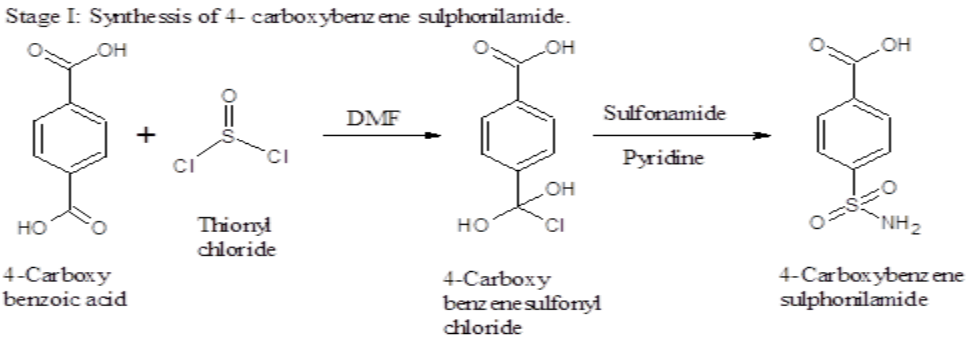
Synthesis of 4-carboxy benzene sulphonilamide:

Step 1: Synthesis of 4-Carboxybenzenesulfonyl Chloride

- React 4-carboxybenzoic acid (10 mmol) with thionyl chloride (20 mmol) in the presence of a catalyst (e.g., DMF) at 60°C for 2 hours.
- Distill the reaction mixture to obtain 4-carboxybenzenesulfonyl chloride.

Step 2: Synthesis of 4-Carboxybenzene Sulphonilamide

- React 4-carboxybenzenesulfonyl chloride (10 mmol) with sulfonamide (10 mmol) in the presence of a base (e.g., pyridine) at room temperature for 2 hours.
- Filter the reaction mixture and wash the product with cold water.
- Recrystallize the product from a suitable solvent (e.g., ethanol or acetone).[6].

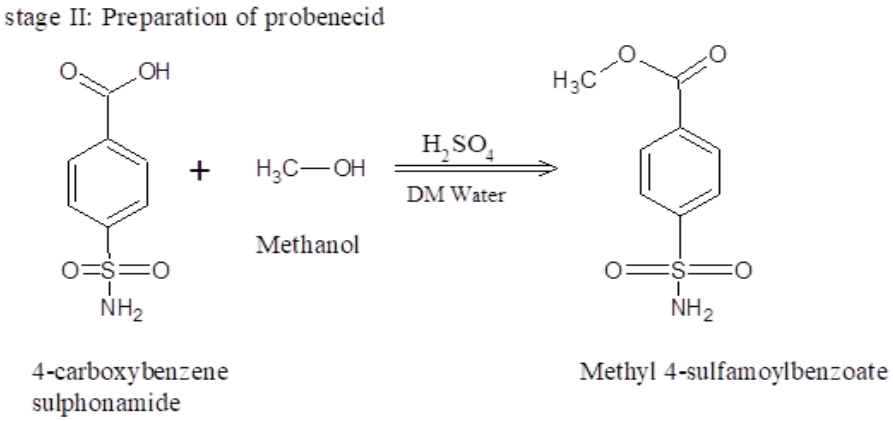


Scheme no.1 : Synthesis of 4-carboxy benzene sulphonilamide.

Synthesis of methyl 4-sulfamoylbenzoate:

- Take a clean dry 4 neck round bottom flask 1 lit with TP, reflux condenser on water bath.
- Charge Methanol (t-1) (4.5ml) under stirring at 25 to 30 °C.
- Charge 4-Carboxy benzene sulfonamide (PSBA) (1.5 g) under stirring at 25 to 30°C.
- Charge Methanol (lot-2) (3ml) under stirring at 25 to 30°C.
- Add drop wise Sulphuric acid (1.5ml) under stirring at 15 to 25°C.

- After addition heat the reaction mass under stirring at 60 to 65°C.
- Maintain the reaction mass at 60 to 65°C for 8 hours under stirring.
- Distill out Methanol atmospherically at 60 to 65°C and then apply high vacuum at 60 to 70^0
- Cool the reaction mass under stirring to 25 to 30^0C.
- Charge DM water (4.5 mL) (lot-1) under stirring at 25 to 30°C
- Stir the reaction mixture for 30 minutes at 25 to 30°C.
- Filter the reaction mixture at 25 to 30°C.
- Wash wet cake with DM water (lot-2) (4 x150 mL).
- Suck dry for 30 mins under vacuum.
- Dry the solid in a hot air oven at temperature 50 to 60°C for 6 hours.



Scheme no.2: synthesis of methyl 4-sulfamoylbenzoate.

Fig no.3: Reflux condensation of synthesis of methyl 4-sulfamoylbenzoate.

Fig no.4: Product of methyl 4-sulfamoylbenzoate

Characterization:

FTIR:

1. The sulfonamide group shows strong absorption peaks in the range of 1335-1370 cm^-1 due to S=O stretching.

2. The carboxylic acid group exhibits a strong, broad peak around 2500-3300 cm^-1 due to O-H stretching.
3. A peak around 1706-1720 cm^-1 due to C=O stretching.[7]

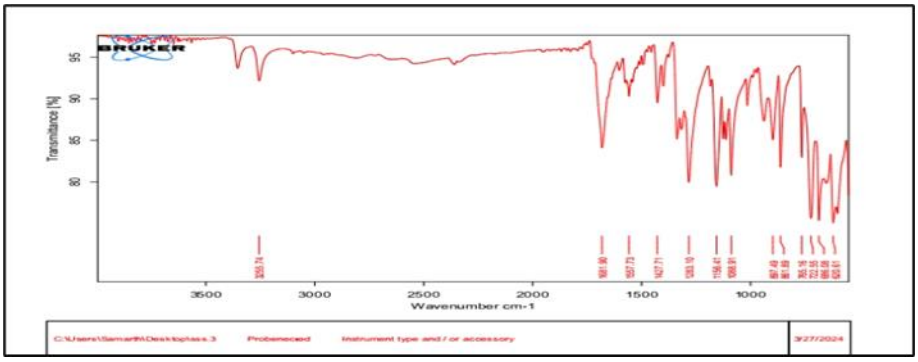


Fig no.5: Probenecid FTIR

NMR:

- Aromatic protons (1H NMR): 7-8 ppm
- Methylene protons (1H NMR): 2-4 ppm
- Methyl protons (1H NMR): 0.5-2 ppm
- Carbonyl carbon (13C NMR): 170-180 ppm
- Aromatic carbons (13C NMR): 120-150 ppm[8]

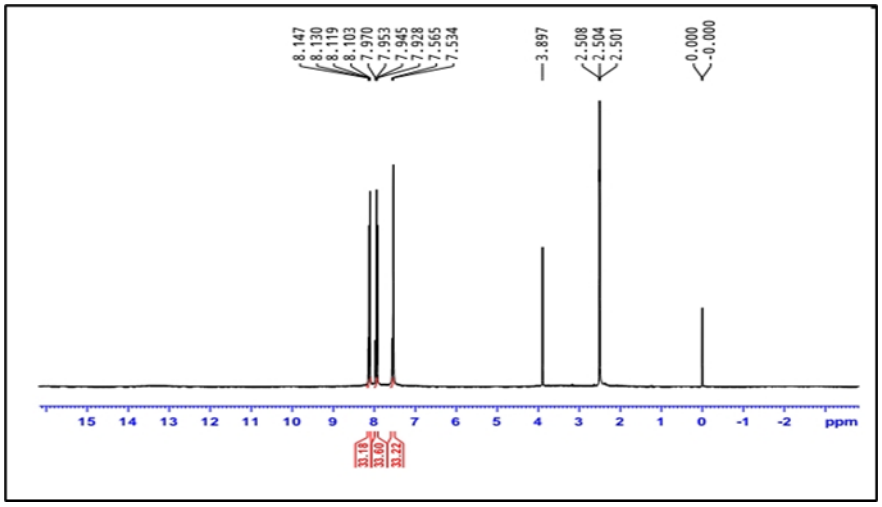


Fig no.6: NMR of pobenecid.

Anti- fungal activity:

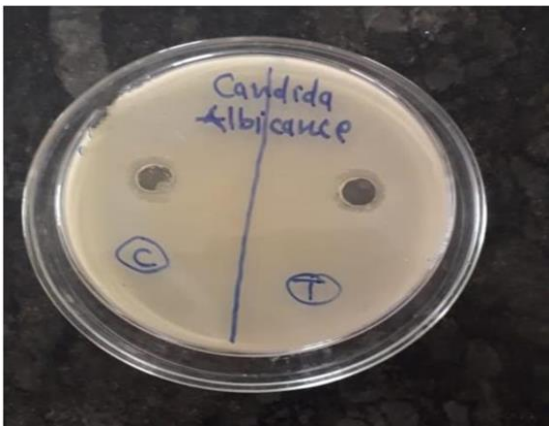


Fig no.7: anti-fungal activity against candida albicans

TLC:

Probenecid's Thin Layer Chromatography (TLC) analysis involves separating the compound using aluminum TLC plates precoated with silica gel G.F 254 as the stationary phase and ethyl acetate–methanol–33% ammonia (8:1:1, by volume) as the mobile phase. The obtained chromatograms are scanned at 254 nm, and probenecid's Rf value is

reported to be 0.36 with a concentration of 15 µg/band.[9]

Fig no.8: TLC of probenecid.

ACKNOWLEDGEMENT:

The synthesis of probenecid from 4-carboxybenzene sulfonamide is a crucial process for producing this uricosuric agent. The reaction with di-n-propylamine forms an amide bond, resulting in the production of probenecid. This synthesis route is significant for the development of new methods and improvement of existing ones.

CONCLUSION:

The synthesis of probenecid from 4-carboxybenzene sulfonamide involves a reaction with di-n-propylamine, resulting in the formation of an amide bond. This process is crucial for producing probenecid, a uricosuric agent used to treat gout and hyperuricemia. Understanding the synthesis of probenecid can help in the development of new methods and improvement of existing ones, ultimately contributing to the availability of this important medication.

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