INVESTIGATION OF THE REACTIONS BETWEEN BUTYL ESTER OF MONOCHLOROACETIC ACID AND PYRIDINE.

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Abstract. This study investigates the synthesis of quaternary ammonium salts via the reaction of esters of monochloroacetic acid with tertiary amines. The effects of solvent type, molar ratios, and reaction temperature on product yield were systematically examined. Optimal conditions were established at 50–60°C with a 1:2 molar ratio of pyridine to ethyl ester of monochloroacetic acid. The resulting quaternary ammonium salts were isolated, dried under vacuum, and characterized for their physicochemical properties. The synthesized compounds exhibited potential biological activity, including antibacterial effects against Gram-positive and Gram-negative bacteria.

Keywords: Quaternary ammonium salts, tertiary amines, monochloroacetic acid esters, pyridine, solvent effects, reaction temperature.

Annotatsiya. Ushbu ishda monoxlorsirka kislotasi efirlari bilan uchlamchi aminlar o‘rtasidagi reaksiyalar orqali to‘rtlamchi ammoniy tuzlarini sintez qilish o‘rganildi. Mahsulot unumi ustiga erituvchi tabiatining, reagentlarning molyar nisbati va reaksiyaning harorati ta’siri tizimli ravishda tahlil qilindi. Optimal sharoitlar 50–60°C harorat va piridin:etil ester nisbatida 1:2 ekanligi aniqlangan. Olingan to‘rtlamchi ammoniy tuzlari ajratilib, vakuum ostida quritildi va ularning fizik-kimyoviy xossalari o‘rganildi. Sintez qilingan birikmalar Gram-manfiy va Gram-musbat bakteriyalarga qarshi biologik faollikni ko‘rsatdi.

Kalit so‘zlar: To‘rtlamchi ammoniy tuzlari, uchlamchi aminlar, monoxlorsirka kislotasi efirlari, piridin, erituvchi ta’siri, reaksiyaning harorati.

Аннотация. В данной работе изучен синтез четвертичных аммониевых солей путем реакции эфиров монохлоруксусной кислоты с третичными аминами. Влияние природы растворителя, молярного соотношения реагентов и температуры реакции на выход продукта было систематически исследовано. Оптимальные условия были установлены при 50–60°C и молярном соотношении пиридин:этиловый эфир монохлоруксусной кислоты 1:2. Полученные четвертичные аммониевые соли были выделены, высушены под вакуумом и охарактеризованы по физико-химическим свойствам. Синтезированные соединения проявили потенциальную биологическую

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активность, включая антибактериальные свойства против грамотрицательных и грамположительных бактерий.

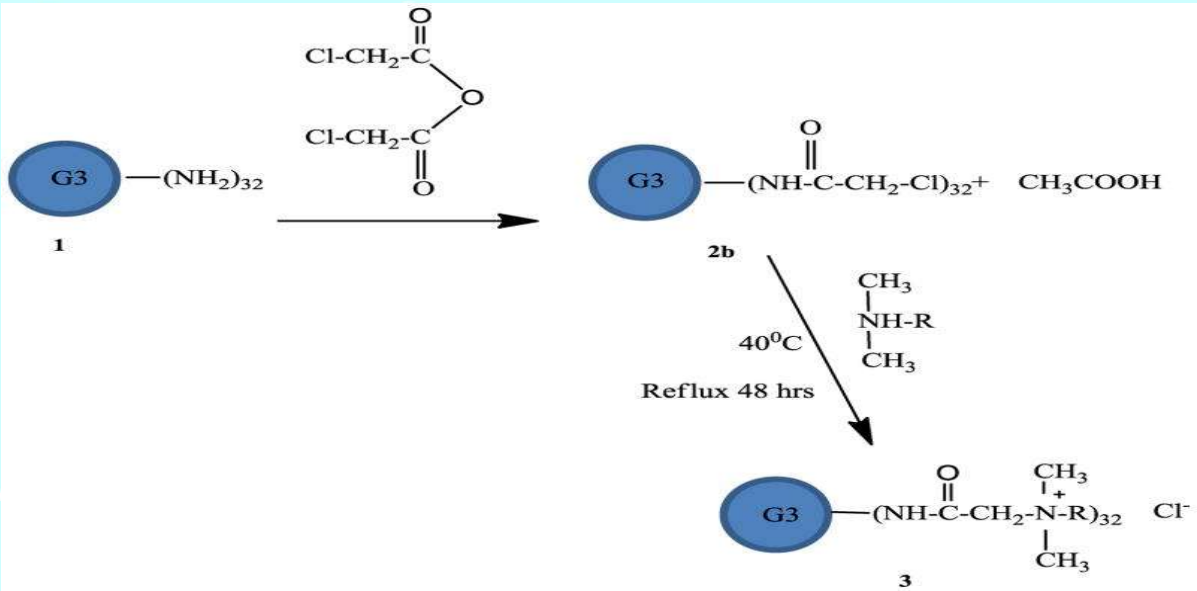
Ключевые слова: Четвертичные аммониевые соли, третичные амины, эфиры монохлоруксусной кислоты, пиридин, влияние растворителя, температура реакции.

Introduction

Alkylation and acylation reactions introduce alkyl and acyl groups into molecular structures, redistributing electron density and significantly altering the physicochemical properties of compounds. Quaternary ammonium salts are widely used in pharmaceuticals, polymers, and antimicrobial materials. Previous studies have reported the biological activity of quaternary ammonium salts derived from geminal diamines, triamines, azaphenothiazines, tetrahydropyridines, and γ-carbolines [1–5].

Notably, quaternary ammonium salts based on epoxypropyl dodecyl dimethylammonium chloride (EPDDMAC) and gelatin demonstrate antibacterial activity several times higher than gelatin alone [6]. Recent research highlights the use of polymeric quaternary ammonium compounds as antimicrobial agents. For example, PAMAM dendrimers modified with tertiary amines of varying chain lengths (dimethyldodecylamine, dimethylhexylamine, dimethylbutylamine) exhibit activity against Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa [14,15].

The current research aims to optimize the synthesis of quaternary ammonium salts from monochloroacetic acid esters and tertiary amines, focusing on isolation, structural characterization, physicochemical properties, and preliminary biological evaluation.



The synthesized quaternary ammonium salts exhibited notable antimicrobial activity against both Gram-positive and Gram-negative bacteria. Specifically, they

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were effective against Staphylococcus species and Escherichia coli [14; pp. 6670–6675], as well as against Staphylococcus aureus (Gram-positive) and Pseudomonas aeruginosa (Gram-negative) [15; pp. 918–927]. These findings are consistent with the previously reported biological activity of quaternary ammonium compounds, which are widely recognized for their broad-spectrum antibacterial properties.

The preparation of quaternary ammonium salts is a complex process that necessitates careful control of reaction parameters. Key factors influencing the success of these syntheses include the nature of the solvent, the molar ratio of the reactants, and the reaction temperature. In most experimental protocols, volatile solvents such as ethyl acetate, acetone, or ethanol are employed, often under controlled low-temperature conditions to prevent side reactions and decomposition of the products. The selection of an appropriate solvent is crucial, as it affects the solubility of the reagents, the kinetics of the nucleophilic substitution, and the ease of product isolation.

An excess of alkyl halide or anion-containing reagents can complicate the crystallization process of the target quaternary ammonium salt and hinder its subsequent purification. Additionally, since many organic solvents contain trace amounts of water, the reaction mixtures must be carefully dried under vacuum in a desiccator after completion. This step is essential because quaternary ammonium salts are generally highly soluble in water, and residual moisture can significantly reduce product yield and purity.

The present research focuses on the synthesis of quaternary ammonium salts through the reaction of esters of monochloroacetic acid with tertiary amines. The study aims not only to optimize the reaction conditions for maximum yield but also to isolate the resulting products and investigate their structural, physicochemical, and biological characteristics.

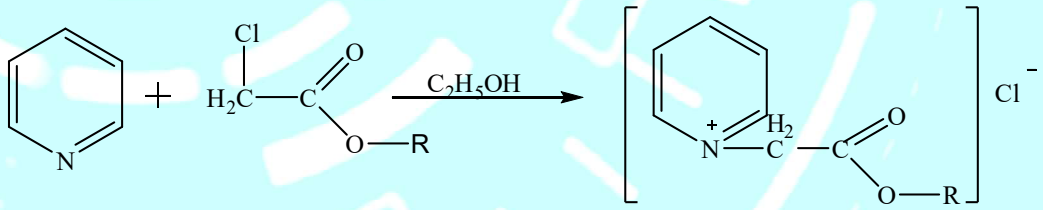
In this context, the reaction of pyridine with the ethyl ester of monochloroacetic acid was thoroughly investigated to determine the optimal conditions for the formation of the corresponding quaternary ammonium salt. The reaction follows a nucleophilic substitution mechanism, in which the lone pair of electrons on the nitrogen atom of pyridine attacks the electrophilic carbon atom of the ester, resulting in the formation of a stable quaternary ammonium species.

For this synthesis, pyridine and the ethyl ester of monochloroacetic acid were dissolved in ethanol and combined in a 1:2 molar ratio. Upon gradual addition of the ester to the pyridine solution, the reaction mixture exhibited a noticeable increase in temperature, accompanied by the evolution of white fumes. These observations indicate the exothermic nature of the reaction and the formation of the intermediate species. The effect of reaction temperature was systematically studied

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within the ranges of 30–40°C, 50–60°C, and 70–80°C. Experimental results revealed that the highest yield of the quaternary ammonium salt was consistently obtained within the 50–60°C range. Consequently, all subsequent syntheses were conducted at this optimal temperature with continuous stirring for a period of 2–4 hours.

After completion of the reaction, the resulting quaternary ammonium salts were isolated by filtration and dried under vacuum for 24 hours. This procedure ensures the removal of residual solvent and water, thereby producing a pure, crystalline product suitable for further physicochemical and biological studies. The optimization of these parameters, including solvent selection, molar ratio, and temperature, is critical for the efficient and reproducible synthesis of quaternary ammonium salts, which are of significant interest due to their diverse chemical and biological applications.



For the synthesis, pyridine and the ethyl ester of monochloroacetic acid were accurately measured and dissolved in ethanol, maintaining a 1:2 molar ratio of pyridine to ester. The ethyl ester was then gradually added to the pyridine solution under constant stirring. Upon addition, the reaction mixture exhibited a noticeable rise in temperature, accompanied by the evolution of white fumes, indicating the exothermic nature of the reaction and the formation of intermediate species.

The influence of reaction temperature on product yield was systematically investigated within three temperature ranges: 30–40°C, 50–60°C, and 70–80°C. Experimental results demonstrated that the highest yields of quaternary ammonium salts were consistently achieved in the 50–60°C range. Based on these findings, all subsequent syntheses were conducted at this optimal temperature, with continuous heating for 2–4 hours to ensure complete conversion of reactants.

Upon completion of the reaction, the resulting quaternary ammonium salts were isolated by filtration and subsequently dried under vacuum for 24 hours to remove any residual solvent and moisture. This step is essential due to the high solubility of quaternary ammonium salts in water and the presence of traces of moisture in organic solvents.

The effect of reaction temperature on the yield of the synthesized quaternary ammonium salts was carefully analyzed, and the results are presented graphically below, clearly demonstrating the dependence of product yield on temperature and confirming 50–60°C as the optimal condition for efficient synthesis.

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