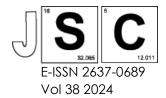
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Synthesis of 3,4-dimethoxybenzohydrazide with 4-nitrophenyl isothiocyanate and 4-nitrobenzenesulfonyl chloride derivatives

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Structured Abstract

Background: In pharmaceutical chemistry, the sulfonamide moiety is an extremely useful carboxylic group bioisostere. The addition of a thiadiazole moiety with a sulfur atom increases chemical solubility and biological activity. The purpose of this research is to develop a method for synthesizing novel derivatives of 3,4-dimethoxybenzohydrazide with 4-nitrophenyl isothiocyanate and 4-nitrobenzenesulfonyl chloride derivatives, which could potentially serve as lead molecules for biological targets and to create an optimized single-step method for synthesizing sulfonamide and thiadiazole derivatives from 3,4-dimethoxybenzohydrazide.

Methods: 3,4-dimethoxybenzoic acid was esterified with methanol using concentrated H₂SO₄ at 200°C overnight. The solvent was removed using a rotary evaporator after completed. The ester went through a further reaction with hydrazide hydrate in methanol at 200°C for overnight. After the solvent was removed, hexane and ethyl acetate confirmed the removal of water. The hydrazide was subsequently reacted with 4-nitrophenyl isothiocyanate in chloroform. The product was collected, rinsed, and dried. Finally, the pure product was obtained by reacting 4-nitrobenzenesulfonyl chloride in pyridine, and then neutralizing and washing.

Results: In this study, sulfonamide and thiadiazole derivatives were successfully synthesized and purified. The proposed cyclization for thiadiazole derivatives employed the sulfonyl group as a nucleophile, resulting in a stable 5-membered ring. The 1H NMR exhibits a 13H signal, which indicates cyclization. The FTIR spectrum shows that the hydrazide group has disappeared from the compound, indicating that the reaction is complete. The sulfonamide derivatives produce a 15H signal in 1H NMR analysis, indicating that they are comparable to the expected structure, but no methoxy group peaks exist in 13C NMR. The FTIR spectrum shows a broad peak of carbonyl group.

Conclusion: In conclusion, this research was successful in developing a new and efficient method for synthesizing 3,4-dimethoxybenzohydrazide derivatives from 4-nitrophenyl isothiocyanate and 4-nitrobenzenesulfonyl chloride derivatives and the synthesis efficiently paves the way to further exploration of the molecular properties of these sulfonamide and thiadiazole derivatives.

Keywords: Sulfonamide, Thiadiazole, 3,4-dimethoxybenzoic acid, 3,4-dimethoxybenzohydrazide