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One-Pot Synthesis of 2,3-Dioxopyrrolidine Derivatives as Potential Anti-MRSA Agents

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Structured Abstract

Background: The rapid global spread of methicillin-resistant *Staphylococcus aureus* (MRSA) has become a serious public health concern due to its resistance to methicillin and most β-lactam antibiotics. The continuous rise of resistant strains has significantly limited current treatment options, emphasizing the urgent need for new antibacterial agents. Heterocyclic compounds are well-established scaffolds in medicinal chemistry due to their diverse biological activities. Among them, 2,3-dioxopyrrolidines possess structural similarity to biologically active pyrrolidine-based compounds and have demonstrated promising antimicrobial potential. However, studies combining environmentally friendly synthesis routes with anti-MRSA evaluation of 2,3-dioxopyrrolidine derivatives remain limited. This study aims to develop a one-pot synthetic approach for 2,3-dioxopyrrolidine derivatives following green chemistry principles while providing a foundation for future antibacterial evaluation.

Methods: A one-pot synthetic strategy was employed using sodium diethyl oxalacetate, methylamine, and substituted benzaldehydes in ethanol under reflux conditions. The reaction proceeds through sequential imine formation, enolate generation, nucleophilic addition, and intramolecular cyclization within a single reaction vessel. Four derivatives were synthesized using benzaldehyde, *p*-anisaldehyde, 4-bromobenzaldehyde, and 4-nitrobenzaldehyde as aromatic substrates. Product isolation was achieved through acidification and filtration without intermediate purification steps. Structural characterization of the synthesized compounds was performed using Fourier Transform Infrared (FTIR) spectroscopy and proton Nuclear Magnetic Resonance (^{1}H NMR) spectroscopy.

Results: Three of the four targeted 2,3-dioxopyrrolidine derivatives were successfully isolated as white crystalline solids with moderate yields ranging from 24.45% to 49.64%. FTIR spectra confirmed the presence of key functional groups, including hydroxyl, carbonyl, ester, and aromatic moieties. ^{1}H NMR analysis further verified the proposed molecular structures through characteristic chemical shifts and splitting patterns. The derivative synthesized from 4-nitrobenzaldehyde exhibited significant impurities, attributed to incomplete imine formation and insufficient purification during isolation.

Conclusion: To conclude, this study demonstrates that the one-pot synthetic approach is a viable, efficient, and environmentally friendly method for producing structurally diverse 2,3-dioxopyrrolidine derivatives. The findings provide a strong foundation for further optimization and future biological evaluation of these compounds as potential anti-MRSA agents.

Keywords: 2,3-dioxopyrrolidines, one-pot synthesis, green chemistry, MRSA, antibacterial agents

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