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Synthesis of new amides derived from pyrazinic and nicotinic acids via Steglich reaction

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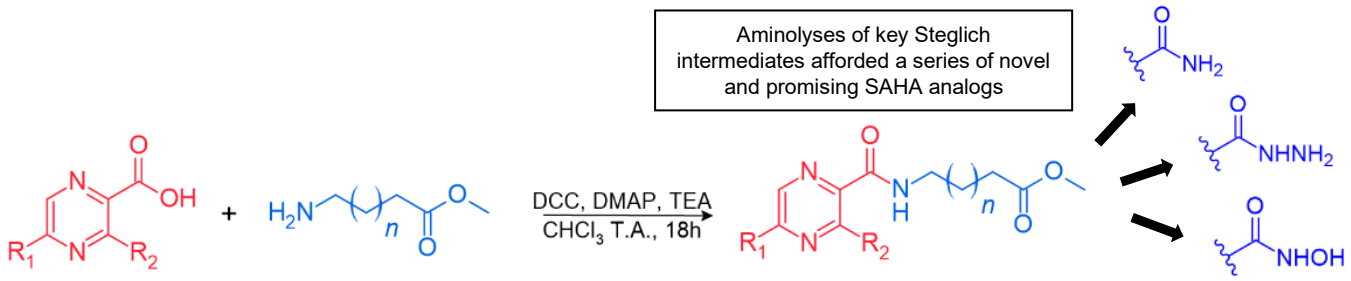
Palavras Chave: *Vorinostat, Pyrazine, Pyridine, Medicinal Chemistry, Steglich Reaction.*

Highlights

Novel SAHA analogs featuring pyrazine and pyridine scaffolds, Efficient synthesis via Steglich amidation strategy, Structural confirmation through FTIR and NMR analysis, Promising candidates for HDAC inhibition and anticancer testing, Innovative combination of heterocyclic chemistry and medicinal design.

Resumo/Abstract

The pyrazinic and nicotinic heterocyclic systems were selected for this study due to their prominent role in medicinal chemistry and their well-documented pharmacological versatility across various contexts.[1] The synthetic strategy employed Steglich amidation between pyrazinic or nicotinic acids and amino esters derived from 4-aminobutyric and 5-aminovaleric acids.[2] The resulting compounds include amide-methyl ester compounds incorporating both pyridine and pyrazine cores, exhibiting high purity and well-defined spectroscopic characteristics. The synthesized derivatives were characterized using Fourier-transform infrared spectroscopy (FTIR), proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR), and melting point determination. These molecules represent valuable intermediates for further functionalization into carbonyl-containing derivatives such as hydroxamic acids and related structures capable of chelating Zn^{2+} ions within histone deacetylase (HDAC) active sites. Such compounds serve as structural analogs of suberoylanilide hydroxamic acid (SAHA, Vorinostat®), a well-established HDAC inhibitor used in the treatment of cutaneous T-cell lymphoma. Incorporation of pyrazine and pyridine heterocycles into the SAHA molecular framework aims to enhance biological activity and selectivity toward cancer-associated enzymes. [1, 2]



1. ELMORSY, M. R. et. al. *BMC Chemistry*, v. 19, art. 164, **2025**.
2. JORDAN, A. et. al. *Green Chemistry*, v. 23, p. 6405–6413, **2021**.

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