

Synthesis of Betulinic Acid-2-Pyridine-Carboxaldehyde Hydrazone

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Structured Abstract

Background: Betulinic acid, a pentacyclic triterpene found in plants like birch and eucalyptus, exhibits diverse biological activities, including anti-inflammatory, antiviral, antimalarial, anticancer, and antidiabetic effects. However, its clinical use is limited by poor bioavailability and low water solubility. This study aims to synthesize a new derivative of betulinic acid by introducing a hydrazone group, specifically 2-pyridine-carboxaldehyde hydrazone, through an efficient synthetic pathway. The modification is expected to enhance its solubility and therapeutic potential, offering a more effective and versatile alternative to unmodified betulinic acid for pharmaceutical applications.

Methods: In this study, betulinic acid hydrazone was synthesized through a sequence of three chemical reactions. Firstly, betulinic acid was subjected to esterification with diazomethane under reflux conditions, resulting in the formation of a methyl ester derivative. In the second step, the obtained methyl ester was reduced to a hydrazide using hydrazine hydrate under reflux, facilitating the introduction of the hydrazone precursor group. Lastly, the hydrazide underwent a condensation reaction with substituted 2-pyridine-carboxaldehyde in methanol, leading to the formation of the desired betulinic acid hydrazone derivative. All final products were purified using column chromatography to ensure high purity for further characterization.

Results: The structure of the synthesized compound was confirmed through comprehensive spectroscopic analysis, including Fourier-Transform Infrared Spectroscopy (FTIR), Proton and Carbon Nuclear Magnetic Resonance (¹H and ¹³C NMR). The ¹H and ¹³C NMR spectra provided detailed information on the chemical environment of hydrogen and carbon atoms, respectively, while the FTIR analysis confirmed the presence of key functional groups, such as the hydrazone linkage and other characteristic bonds. These combined spectroscopic techniques verified the successful formation of the target compound with the expected structural features. Following purification through column chromatography, the final betulinic acid hydrazone derivative was obtained as a pure product with an overall yield of 32.7%.

Conclusion: In conclusion, this study demonstrated an efficient synthetic approach for producing hydrazone derivatives of betulinic acid. The development of betulinic acid-2-pyridine-carboxaldehyde hydrazone may help overcome the limitations of the parent compound by enhancing its biological properties. This novel derivative holds promise for improving the therapeutic potential of betulinic acid and may contribute to future advancements in clinical applications.

Keywords: Betulinic acid, hydrazone, esterification, derivative synthesis, spectroscopy

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