

Synthesis of Betulinic Acid-2-Hydroxy-5-Methoxybenzylidene Hydrazone

Nur Anishafiqah Maswadi, Mohd Tajudin Mohd Ali*

Structured Abstract

Background: Betulinic acid is a natural pentacyclic triterpenoid with notable pharmaceutical and therapeutic properties, including anticancer, antiviral, anti-inflammatory, and antimicrobial activities. However, its potential is limited by poor solubility, low bioavailability, and low extraction yield from natural sources. To enhance its biological potential, the synthesis of novel derivatives is necessary.

Methods: In this study, a new derivative of betulinic acid, betulinic acid-2-hydroxy-5-methoxybenzylidene hydrazone, was successfully synthesised through a three-step reaction. Firstly, betulinic acid was esterified with diazomethane in diethyl ether under cold conditions to yield methyl betulinate. This was followed by reduction with hydrazine hydrate in methanol under reflux to produce the hydrazide intermediate. Finally, condensation of the hydrazide with 2-hydroxy-5-methoxybenzaldehyde in the presence of glacial acetic acid and methanol under reflux produced the target hydrazone derivative.

Results: The final product was obtained as a solid and purified using column chromatography. The structure of the compound was confirmed through spectroscopic analyses, including ¹H and ¹³C Nuclear Magnetic Resonance (NMR), Fourier-Transform Infrared Spectroscopy (FTIR), and High-Resolution Mass Spectrometry (HR-MS). The yield of the final product was 28%, based on the limiting reagent.

Conclusion: The successful synthesis and characterisation of betulinic acid-2-hydroxy-5-methoxybenzylidene hydrazone demonstrates the feasibility of chemically modifying betulinic acid to obtain new derivatives. This contributes to the advancement of betulinic acid-based compounds for future pharmaceutical applications.

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

*Correspondence: tajudinali@uitm.edu

School of Chemistry & Environment, Faculty of Applied Sciences, Universiti Teknologi MARA, Shah Alam, Malaysia