

Area: ORG

Optimization of a Synthetic Route and Methodologies for the Synthesis of Eugenol-derived Chalcones

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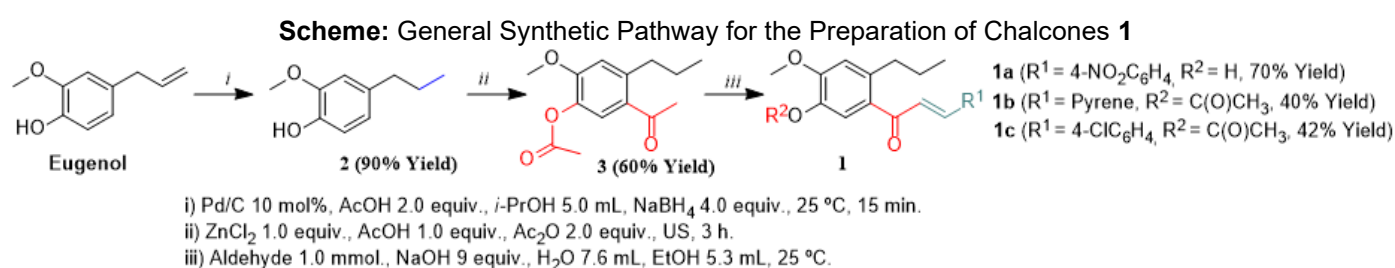
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Highlights

Three-step synthesis of chalcones from eugenol. Ultrasound-assisted one-pot methodology for phenolic group protection and Friedel-Crafts acylation in a single step.

Abstract

Eugenol is a natural compound with a functionalized structure and can undergo various chemical modifications, making it an excellent precursor for the synthesis of bioactive molecules. Another class of compounds with a broad spectrum of biological activities includes chalcones. Therefore, in this work, we optimized a synthetic route for the synthesis of eugenol-derived chalcones **1** with potential antimicrobial activity. The synthesis was carried out in three reaction steps starting from eugenol (Scheme). The initial step yielded product **2** under reducing conditions in 90% yield without further purification. The subsequent step involved an optimization of the ultrasonic (US)-assisted HO-protection and Friedel-Crafts acylation methodology to form product **3**. To optimize this reaction conditions, different reaction times (20, 60, 90, 120, 150, and 180 min) were evaluated, with reaction carried out for 180 min affording compound **3** in highest conversion (100%). The product was then isolated in 60% yield after purification by recrystallization from ethanol. Finally, chalcones **1** were obtained via Claisen-Schmidt condensation reaction in yields ranged from 42 to 70% (Scheme).



Thus, we optimized a route and synthetic methodologies for the synthesis of eugenol-derived chalcones **1**. Chalcone **1a** was obtained with the phenolic OH group already deprotected, while the others require an additional deprotection step (currently being characterized). The synthetic pathway will be extended to the synthesis of a series of chalcones **1**, whose bioactivity has been previously investigated through *in silico* studies.

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