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ORIGINAL PAPER

Microwave-assisted green synthesis, antimicrobial activity, and drug-likeness of novel isoindolinone derivatives

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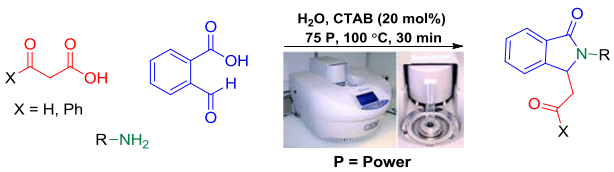
Abstract

An efficient and green microwave method has been developed for the synthesis of novel isoindolinone derivatives with good yields. The framework of these derivatives was constructed from *β*-ketocarboxylic acids, various primary amines, and 2-carboxybenzaldehyde via cetrimonium bromide salt-promoted multicomponent cascade of decarboxylation/lactamization reaction. This methodology features a simple, environmentally friendly approach, employing water as a green solvent and using a one-pot, three-component reaction. The synthesized compounds were evaluated for their antimicrobial activity in vitro against six microorganisms, namely *Escherichia coli*, *Serratia*, *Staphylococcus aureus, Bacillus subtilis*, *Aspergillus niger*, and *Fusarium oxysporum*. The results revealed that these derivatives have a significant antimicrobial activity. In addition, the drug-likeness of these derivatives has been evaluated.

Graphic abstract



Keywords Microwave-assisted synthesis · Green solvent · Cetrimonium bromide · Isoindolinone derivatives · Antimicrobial activity

Introduction

Isoindolinone skeleton is an important privileged class in exhibiting a broad range of potent therapeutic and pharmacological activities [1, 2]. The isoindolinone moiety is found in natural products and biologically active compounds [3, 4]. Examples of biological activities of isoindolinone derivatives include therapeutic agents such as pagoclone (**A**) and pazinaclone (**B**) which showed anxiolytic and hypnotics activities [5, 6]. Zopiclone (**C**) is found to be clinically useful in the treatment of sedative effects [7] and compound **D** exhibited an inhibitory potency toward aldose reductase [8]. Furthermore, compound **E** appears to be an important agent to evaluate the potential therapeutic of ELOVL6 and ELOVL3 inhibitors [9] (Fig. 1).

Several methodologies for the synthesis of isoindolinone derivatives have been reported in the literature, including Mukaiyama/Mannich lactamization [10], Ugi/Diels–Alder reaction [11], Sonogashira coupling, followed by ring closure and redox reactions [12] and cascade reactions [13, 14]. Reportedly, in some methods various catalysts have been explored in the synthesis of isoindolinone derivatives such as camphorsulfonic acid (±)-CSA [15], DBU [16], bis(triphenylphosphine)palladium(II) dichloride [17], rhodium(III) [18], L-proline [19], Ru(II) [20], and $In(OTf)_3$ [21]. Nevertheless, the reported methodologies generally

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