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ORIGINAL PAPER

Synthesis and cytotoxicity of novel chromenone derivatives bearing 4-nitrophenoxy phenyl acryloyl moiety

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Abstract This work describes synthesis of novel chromenone derivatives bearing 4-nitrophenoxy phenyl acryloyl moiety through the reaction of 4-(4-nitrophenoxy)benzaldehydes and 3-acetyl-2*H*-chromen-2-ones in refluxing toluene. Cytotoxicity of all compounds was evaluated using a tetrazolium (MTT) colorimetric assay against human breast cancer cell line, MDA-MB-231.

Keywords Chromenones · Cytotoxicity · 4-Nitrophenoxy

Introduction

Chalcones are the main component of a wide range of natural products as well as versatile starting materials for the construction of flavonoids and isoflavonoids [1]. The presence of the α,β-unsaturated moiety in chalcones induces significant biological activities such as anti-bacterial [2], antiamoebic [3], anti-fungal [4], anti-tumor [5], anti-malarial [6], and antiplasmodial [7] properties. The efficacy of chalcones is associated with their interaction with thiols instead of amino and hydroxyl groups of nucleic acids leading to the reduction of genotoxicity [8]. Hence, chalcones and efficient synthetic routes have absorbed the attention of medicinal chemists especially in the field of anti-cancer drugs development. Also, literature review demonstrated that the electronic properties of substituents on the benzylidene moiety play an important role in the biological activity of chalcones. It has been demonstrated that chalcones bearing nitro substituents depicted excellent cytotoxicity [9–12].

The Knoevenagel condensation, a nucleophilic addition of an active hydrogen compound to a carbonyl group followed by elimination of water, has been a versatile tool for the formation of C–C bond in organic synthesis and medicinal chemistry. Publishing a large number of reports on the development of various protocols and catalysts for the conduction of Knoevenagel condensation indicates the importance and efficiency of this reaction [13].

Among a large spectrum of *N*-heterocycles, chromenones are mainly attractive compounds due to their valuable biological properties such as bradykinin B1 antagonists [14], anti-proliferative [15], antidiabetic [16], carbonic anhydrases [17], interleukin-5 [18], and IRE-1 RNase inhibitory [19] activities. Recently, chalcone-based derivatives of chromenone (Fig. 1a) have shown significant medicinal activities. In this regard, they have been found as hA_3 adenosine receptor antagonists [20]. Also, they have shown anti-malarial [21], anti-cancer [22], antioxidant and trypanocidal [23] activities. It seems that combination of two valuable cores presents important biologically active scaffolds.

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