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Dehydrozingerone based 1-acetyl-5-aryl-4,5-dihydro-1*H*-pyrazoles: Synthesis, characterization and anticancer activity

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ABSTRACT

A small series of 1-acetyl-5-aryl-4,5-dihydro-1*H*-pyrazoles (aryl = 4-hydroxy-3-methoxyphenyl and 4-alkoxy-3-methoxyphenyl) was prepared, starting from 4-(4-hydroxy-3-methoxyphenyl)-3-buten-2-one, dehydrozingerone, and its alkyl derivatives. Their *in vitro* cytotoxic activity against some cancer cell lines was tested, showing significant anticancer activity. All the new compounds were well characterized by IR, ^{1}H, ^{13}C NMR and ESI-MS spectroscopy and physical data, whereas structures of two of them were determined by single crystal X-ray analysis.

1. Introduction

Many natural products, such as vanillin, were used as starting materials in the new drug design, and consequently a plethora of newly introduced medicals were originated from known natural sources. Sometimes, these starting materials undergo only to small chemical changes allowing them to remain certain biological activity, but improving certain feature, like hydrophilicity, lipophilicity, etc.

Chalcones, 1,3-diaryl-2-propen-1-ones, are an important class of natural occurring compounds, since they often represent core structure of many natural products and pharmaceuticals. Chalcones and its derivatives exhibit different pharmacological and biological activities such as antifungal [1,2], antimicrobial [3–5], anticonvulsant [6], antioxidant [7–10], anti-malarial [11–14], antiprotozoal [15], anti-inflammatory [16–19], anticancer [20–28].

Starting from vanillin, a pungent constituent of ginger rhizome 4-(4-hydroxy-3-methoxyphenyl)-3-buten-2-one, dehydrozingerone **1a**, was prepared [29]. In this phenolic compound, the enone function is conjugated, its structure is however different from standard chalcones, as the methyl group is linked to the carbonyl and not to the aryl group. This compound, as a half analogue of curcumin, also exhibits a wide range of biological activities, among which antitumor features were found to be well expressed [30–32].

On the other hand, dihydropyrazoles are important five-membered heterocycles which are present in different bioactive compounds, showing broad spectrum of biological activities, such as anti-inflammatory, anti-depressant, anti-bacterial, anti-viral, anti-cancer activities [33–35] and antidiabetic activities [36]. Moreover, functionalized dihydropyrazoles are also of significance for the preparation of compounds similar to natural products and extensive efforts have been directed toward the synthesis of these scaffolds.

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