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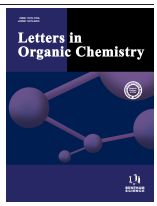
RESEARCH ARTICLE

Synthesis of Thiazolone Derivatives as Novel Soybean 15-LOX Inhibitors



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Abstract: ***Background***: Thiazole derivatives are known as important sulfur containing heterocycles which are present in a wide range of biologically active natural products.

Methods: A series of thiazolone derivatives were synthesized and evaluated for their soybean 15-LOX inhibitory activity. The title compounds were prepared by the reaction of 2-arylthiazol-4(5*H*)-ones and different aromatic aldehydes. All compounds were characterized and evaluated against soybean 15-LOX.

Results: Among the synthesized thiazolone derivatives, 5-(4-methoxybenzylidene)-2-((2-methoxyphenyl) amino)thiazol-4(5*H*)-one (**3l**) was found to be the most active compound comparing with quercetin as the reference drug.

Conclusion: It seems that prepared thiazolones having methoxy groups both on aryl and aminoaryl moieties can be considered for further drug discovery research.

Keywords: Heterocycles, inhibitory activity, 15-LOX, synthesis, thiazolones.

INTRODUCTION

Thiazole and its derivatives are important sulfur containing heterocyclic compounds, ubiquitous in many biologically active natural products such as trunkamide [1], thiostrepton [2], microcin B17 [3], and goadsporin [4]. Synthetic thiazoles have also attracted lots of attention due to versatile biological activities [5]. In this regard, they have depicted 15-lipoxygenase inhibitory activities [6]. Invaluable pharmaceutical properties of natural and synthetic compounds possessing thiazole moiety have encouraged organic and medicinal chemists to develop straightforward synthetic procedures starting from proper precursors for the synthesis of a wide range of thiazole derivatives [7-12]. For example, multi-component reaction of oxo components, primary amines, thiocarboxylic acids, and isocyanide afforded thiazoles as an efficient method for the total synthesis of definite naturally occurring thiazole derivatives [9]. Hetero-Diels-Alder reaction of 5-arylidene-4-thioxo-2-thiazolidinones and 2(5*H*)furanone gave novel thiopyrano[2,3-*d*]thiazoles [10]. Also, we have recently prepared various imidazo[2,1-*b*]thiazol-5-amines through four-component reaction of 2-bromoacetophenones, aromatic aldehydes, thiourea, and isocyanides as 15-LOX inhibitors [6].

Lipoxygenases (LOXs), nonheme ferroproteins catalyze dioxygenation of polyunsaturated fatty acids such as arachidonic acid (AA), linoleic acid, and linolenic acid. 5-, 12- and 15-LOXs are three main lipoxygenases characterized by the peroxidation site of AA [13, 14]. The enzyme isozymes and their metabolites play an important role in the pathogenesis of numerous illnesses such as inflammatory, hyperproliferative and neurodegenerative diseases. 15-LOX is also responsible for stroke-induced brain injury [15]. Similarly, recent studies demonstrated the presence of increased concentration of 15-LOX in human stroke [16]. In this respect, 15-LOX inhibition has emerged as anti-stroke therapy [17, 18]. Besides, 15-LOX has been known as the main aspect of rheumatoid arthritis inflammatory process [19] and cancer therapy [20]. Recently, Hofmann *et al.* introduced thiazolones as potent 5-LOX inhibitor through the preparation of 5-benzylidene-2-phenylthiazolinone derivatives [21]. All these studies confirm that design and synthesis of novel and

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