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Mini-review

4-Thiazolidinone – A biologically active scaffold

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Abstract

The broad and potent activity of 4-thiazolidinones has established it as one of the biologically important scaffolds. This article is an effort to highlight the importance of the 4-thiazolidinones in the present context and promise they hold for the future.

Keywords: 4-Thiazolidinones; Solid-phase synthesis; Spectral studies; Stereochemistry; Biological activity

1. Introduction

One of the main objectives of organic and medicinal chemistry is the design, synthesis and production of molecules having value as human therapeutic agents. During the past decade, combinatorial chemistry has provided access to chemical libraries based on privileged structures [1], with heterocyclic structures receiving special attention as they belong to a class of compounds with proven utility in medicinal chemistry [2]. There are numerous biologically active molecules with five-membered rings, containing two hetero atoms. Thiazolidine (**A**) is an important scaffold known to be associated with several biological activities (Fig. 1) [3].

2. 4-Thiazolidinones

2.1. Chemistry of 4-thiazolidinones

4-Thiazolidinones are derivatives of thiazolidine with a carbonyl group at the 4-position (**1**). Substituents in the 2-, 3-, and 5-positions may be varied, but the greatest difference in structure and properties is exerted by the group attached to the carbon atom in the 2-position (R and R′ in **2** or X in **3**). Variations in the substituents attached to the nitrogen atom and the methylene carbon atom are possible for the structures represented by **2** and **3** (Fig. 2).

2.2. Syntheses of 4-thiazolidinones

Several protocols for the synthesis of 4-thiazolidinones are available in the literature [4–12]. Essentially they are three-component reactions involving an amine, a carbonyl compound, and a mercapto-acid. The process can be either a one-pot three-component condensation or a two-step process [13–15].

An improved protocol has been reported wherein *N*,*N*-dicyclohexyl carbodiimide (DCC) or 2-(1*H*-benzotriazo-1-yl)-1,1,3,3-tetramethyl uraniumhexafluorophospate (HBTU) (Scheme 1) is used as a dehydrating agent to accelerate the intramolecular cyclization resulting in faster reaction and improved yields [16,17]. The DCC/HBTU-mediated protocol has the advantage of mild reaction conditions, a very short reaction time, and product formation in almost quantitative yields. More importantly, yields of the 4-thiazolidinones are independent of the nature of the reactants. This modification is compatible with a solid-phase combinatorial approach to generate a library of compounds.

Cesur et al. and Vicini et al. have reported another method of synthesis of 4-thiazolidinones by the use of thiocyanate, alkylisothiocynate and ammonium thiocyanate with hydrazide/

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