A DIC Mediated Expeditious Small Library Synthesis and Biological Activity of Thiazolidin-4-one and 1,3-Thiazinan-4-one Derivatives

Amit Verma, Shweta S Verma, and Shailendra K Saraf*

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Northern India Engineering College, Lucknow 227105, Uttar Pradesh, India
*E-mail: v.amit28@gmail.com

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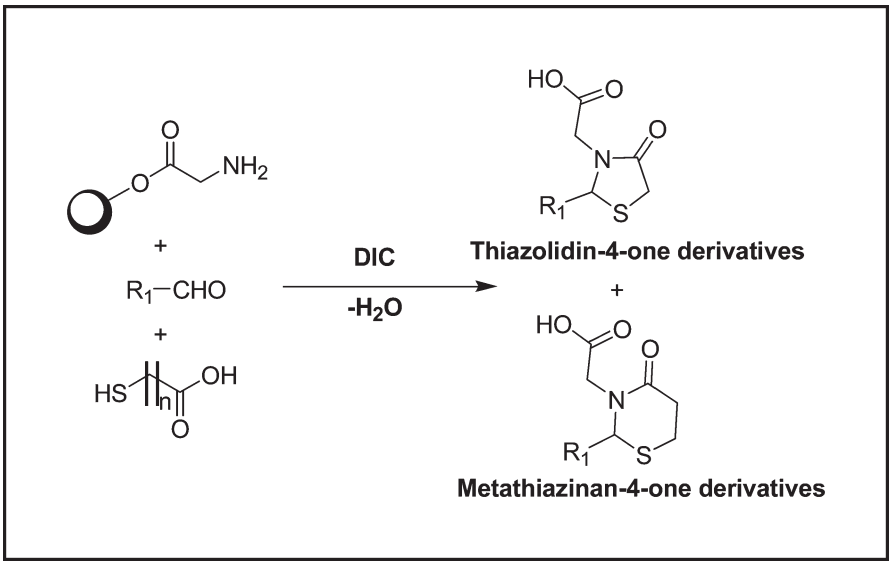

A diisopropylcarbodiimide (DIC) mediated small library of thiazolidin-4-one and 1,3-Thiazinan-4-one derivatives were efficiently synthesized using one pot three component condensation of amino acid, aldehyde, and mercapto carboxylic acid on a polymer support. The study shows significantly higher yields of the thiazolidin-4-one derivatives thereby indicating a lower dependence on the nature of the amino acid and aldehyde components. As an obvious extension of this protocol, the reactions were performed using heterocyclic aldehydes and substituted hindered aromatic aldehydes instead of simple aromatic aldehydes. The synthesized library compounds were also screened for their antifungal acitivity against these three pathogenic fungi: *Candida albicans (Ca), Candida parapsilosis (Cp)*, and *Cryptococcus neoformans (Cn)*.

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INTRODUCTION

The categorical imperative of modern drug discovery is to produce better clinical candidates that are less prone to failure at later stage. Solid phase organic synthesis is regarded as one of the key disciplines for providing constant supply of chemical compounds that may be monitored for their biological activity on the vastly increasing number of biological targets. Solid phase organic synthesis together with high throughput synthesis and efficient data management, undoubtedly lead to acceleration in the process of drug discovery [1].

There are numerous biologically active molecules whose framework includes a five-membered and six-membered ring containing two hetero atoms. Thiazolidin-4-one and thiazinan-4-one are biologically important scaffolds known to be associated with several biological activities. These structures contain one **S** and one **N** atom in skeleton as heterocyclic atoms [2–3].

Several protocols for the synthesis of thiazolidin-4-one and thiazinan-4-one derivatives are available in the literature [4–12] (Scheme 1). Essentially these 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. The reaction has been suggested to proceed via imine formation followed by the attack of sulfur nucleophile on the imine carbon. The last step involves intramolecular cyclization with the elimination of water to give the final compound. This step appears to be