A Novel Method for the Synthesis of Spiro[indoline- Pyrazolo[4' ,3' :5,6]pyrido[2,3- d]pyrimidine]tr iones by Alum as a Reusable Catalyst

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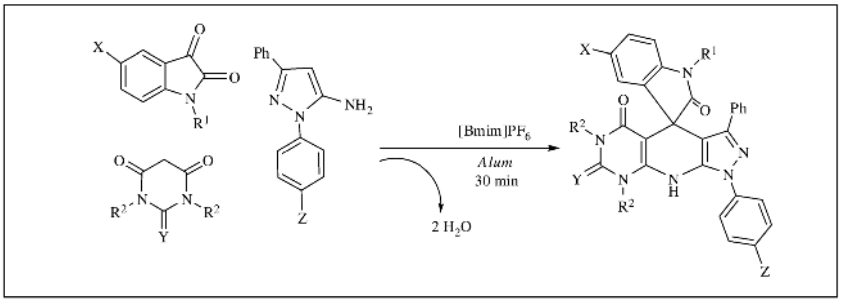

Synthesis of spiro[indoline- pyrazolo[4' ,3' :5,6]pyrido[2,3- d]pyrimidine]trione derivatives by a cyclo- condensation reaction of indolin- 2- ones, barbituric acids, and 1,3- diphenyl- 1H- pyrazol- 5- amines with the ionic liquid as an effective green reaction media and in the presence of Alum as a reusable catalyst was reported. Excellent yields of products, green media, use of a reusable catalyst, and short reaction time are the main advantages of this new method.

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INTRODUCTION

With the emphasis on the search for atom- efficient transformations of easily available starting materials into complex organic molecules, reactions that provide maximum diversity are especially desirable. Here, expeditious domino and multicomponent reactions (MCRs) have emerged as powerful strategies. These methodologies have great utility, particularly when they lead to the formation of privileged medicinal heterocyclic compounds. MCRs are economically and environmentally very advantageous, because multistep syntheses produce considerable amounts of waste mainly due to complex isolation procedures often involving expensive, toxic, and hazardous solvents after each step [1–3].

In recent years, the synthesis of combinatorial small-molecule heterocyclic libraries has emerged as a valuable tool in the search for novel lead structures. Thus, the success of combinatorial chemistry in drug discovery is considerably dependent on further advances in heterocyclic MCR methodology [4].

Polyfunctionalized heterocyclic compounds play important roles in the drug discovery process, and analysis of drugs in late development or on the market shows that 68% of them are heterocycles. Therefore, it is not surprising that research in the field of synthesis of polyfunctionalized heterocyclic compounds has received special attention [1].

Spirocyclic systems containing one carbon atom common to two rings are structurally interesting [5]. The asymmetric characteristic of the molecule due to the chiral spiro carbon is one of the important criteria of the biological activities. The presence of the sterically constrained spiro structure in various natural products also adds to the interest in the investigations of spiro compounds [6]. Spiro compounds represent an important class of naturally occurring substances characteristic by their highly pronounced biological properties [7,8].

The heterocyclic spirooxindole ring system is a widely distributed structural framework present in a number of pharmaceuticals and natural products [9], including such cytostatic alkaloids as spirotryprostatins A, B, and strychnophylline (Fig. 1) [10–12]. The unique structural array and the highly pronounced pharmacological activity displayed by the class of spirooxindole compounds have made them attractive synthetic targets [13].