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Gold(III) chloride ($HAuCl_4 \cdot 3H_2O$) in PEG: A new and efficient catalytic system for the synthesis of functionalized spirochromenes

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ABSTRACT

Gold(III) chloride ($HAuCl_4 \cdot 3H_2O$) in PEG 400 was found to be an efficient catalytic system for the synthesis of biologically important functionalized spirochromene derivatives *via* one-pot three-component reaction of isatins/acenaphthoquinone, active methylene compounds and cyclic 1,3-diketones/4-hydroxycoumarin. A new catalytic system, recyclability of reaction medium, little reaction times and excellent yields with easy workup render this protocol more attractive and economically viable.

1. Introduction

The evaluation of eco-friendly synthetic methodologies to facilitate the preparation of compound libraries is a pivotal focal point of research activity in the field of modern medicinal and combinatorial chemistry [1]. One approach to address this challenge involves the development of multicomponent reactions (MCRs) in which at least three easily accessible components react to each other to form a single product in a one-pot reaction flask, incorporating essentially all atoms of the starting materials [2]. As one-pot reaction, MCRs show high atom-economy, high selectivity and procedural simplicity due to the formation of C–C and C-heteroatom bonds [3]. The growing interest for an environmentally benign multicomponent procedure is closely related to the development for the synthesis of combinatorial small-molecule heterocyclic libraries which is becoming an important and promising area of current organic synthesis [4].

Compounds containing indole moiety exhibit antibacterial and antifungal activities [5]. Furthermore, it has been reported that using of the indole 3-carbon in the formation of spiroindoline derivatives highly enhances biological activity [6]. The heterocyclic spirooxindole ring system is a widely distributed structural framework of many pharmaceuticals and natural products [7]. For example, spirotryprostatins A, B are a natural alkaloids isolated from the fermentation broth of *Aspergillus fumigates* in which spirotryprostatins B has been shown to completely inhibit the G2/M progression of mammalian tsFT210 cells at concentrations over 12.5 μg/mL [8] and polycyclic alkaloids pteropodine and isopteropodine have a long history for its medicinal applications in modulating the function of muscarinic serotonin receptors [9] (Fig. 1). Among them oxygen-containing heterocycles fused with spirooxindole ring system, functionally substituted 4*H*-chromenes have been received considerable attention due to a wide range of biological properties like anticoagulant, diuretic, anticancer and antianaphylactic activities [10].

There are several methods have been reported for the synthesis of spirooxindoles with fused chromenes in which conventional synthesis involves one-pot, three-component condensation of isatin with cyclic 1,3-diketones and malononitrile or 2-aminobenzothiazole [11]. Shanthi et al. has reported a three-component reaction for the synthesis of spirooxindole derivatives catalyzed by $InCl_3$ with 70–90% yields [12]. This reaction was also carried out in the presence of *p*-TSA within 1 h under reflux conditions [13]. Other more effective procedure for the synthesis of spirooxindoles employed quaternary cationics [14], and electrochemical methods [15]. Thus, each of the known procedures for the synthesis of corresponding spiro[(4*H*-chromene)-4,3′-oxindole] has its merits, however, further studies are still necessary for the

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