One-pot synthesis of 1,4-dihydropyridine derivatives using magnetic nanocomposite catalyst under solvent-free conditions

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ABSTRACT

A green and efficient synthesis of Hantzsch 1,4-dihydropyridine derivatives using magnetic nanocomposite (Fe_3O_4-Ch-SO_3H) as a recyclable catalyst under solvent-free conditions was performed. The catalyst was characterized by FT-IR, VSM, and SEM analysis. One-pot three-components Hantzsch synthesis 1,4-dihydropyridine derivatives using magnetic nanocomposite has the advantages of short reaction times, little catalyst loading, high yields, easy recovery and reusability of the catalyst.

Keywords: Solvent free; 1,4-dihydropyridine; magnetic nanocomposite catalyst.

1. INTRODUCTION

1,4-dihydropyridine (DHP) derivatives contain a large family of medicinally important compounds that have attracted much attention due to their several pharmacological and therapeutic properties, such as vasodilator, hepatoprotective, antiatherosclerotic, bronchodilator, antitumor, geroprotective, antidiabetic activity. Also 4-substituted 1,4-dihydropyridines (1,4-DHPs) are well known as calcium channel blockers and have emerged as one of the most important class of drugs for the treatment of cardiovascular diseases. In view of the biological, industrial and synthetic importance of 1,4-dihydropyridines, several methods for their synthesis have been reported [1-7]. Most of processes have distinct advantages, the use of high temperatures, expensive metal precursors, environmentally harmful catalysts, harsh reaction conditions, long reaction times and large quantity of volatile organic solvents limit the use of these methods. So in green point of view the search for the possibility of performing multicomponent reactions under solvent-free conditions with recoverable catalysts for the synthesis of these compounds is an active ongoing research area and there is scope for further improvement toward milder reaction conditions and higher yields. Nanocomposites have high surface-to-volume ratio and coordination sites compared to their bulk analogs, which provide a larger number of active sites per unit area. In recent years, as an important family of separation materials, magnetic nanocomposite have attracted considerable interest in chemistry due to easy separated with an external magnet. Recently, magnetic nanocomposites were used as an efficient catalyst in many organic reactions. Hence, we decided to green synthesis 1,4-dihydropyridine derivatives using Fe_3O_4-Ch-SO_3H under solvent-free conditions [8, 9].

2. EXPERIMENTAL

2.1. Preparation of magnetic chitosan nanocomposites: Fe_3O_4-Ch NCs

Fe_3O_4-chitosan nanocomposites (Fe_3O_4-Ch NCs) were prepared by chemical co-precipitation of $Fe^{3+}$and Fe^{2+} ions with molar ratio 2:1, in presence of chitosan, followed by the hydrothermal treatment. Specifically 1 g of chitosan is dissolved in 100 mL of 0.05 M acetic acid solution; to which $FeCl_3 \cdot 6H_2O$ (3.51 g, 0.013 mol) and $FeCl_2 \cdot 4H_2O$ (1.29 g, 0.0065 mol) are added. Consequently, 6 mL of 25% NH_4OH is injected drop wise into the reaction mixture with constant stirring. After 30 min, the mixture is cooled to room temperature and chitosan coated over magnetic nanoparticles are separated by an external magnet, first washed with distilled water, then ethanol, and finally dried under vacuum at room temperature.

2.2. Synthesis of Fe_3O_4-chitosan-SO_3H nanocomposites: Fe_3O_4-Ch-SO_3H NCs

0.5 gr of Fe_3O_4-Ch NCs is dispersed in CH_2Cl_2 (10 mL) in an ultrasonic bath for 20 min, then chlorosulfonic acid (0.8 mL) is added drop-wise over, at room temperature under N_2 atmosphere. Finally, functionalized magnetic Fe_3O_4-Ch-