Synthesis of 3,4-dihydropyrimidin-2(1H)-thiones in the presence of $FeCo_2O_4$ NPs

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Abstract

In this research, we report here an efficient and green method for Biginelli condensation reaction of aldehydes, β-ketoesters and thiourea catalyzed by $FeCo_2O_4$ under solvent-free conditions. Compared to the classical Biginelli reaction conditions, the present method has the advantages of giving good yields, short reaction times. The as-synthesized nanostructures were characterized by spectroscopic analysis including FE- SEM, EDAX and XRD.

Keywords: Biginelli reaction; dipyrimidinones; solvent-free; $FeCo_2O_4$; nanoparticles.

Introduction

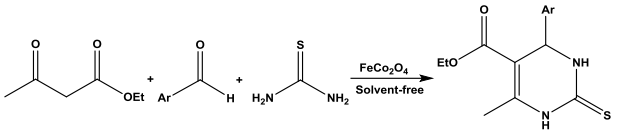
One of the interesting scientific and technological challenges associated with the use of nanoparticles as catalysts is the understanding of how the composition and atomic-scale structure of nanoparticles produce the best catalytic activity [1].

Multi-component reactions (MCRs) are of increasing importance in organic and medicinal chemistry [2]. In times where a premium is put on speed, diversity, and efficiency in the drug discovery process, MCR strategies offer significant advantages over conventional linear-type syntheses. In such reactions, three or more reactants come together in a single reaction vessel to form new products that contain portions of all the components. In an ideal case, the individual building blocks are commercially available or are easily synthesized and cover a broad range of structural variations. MCRs can provide products with the diversity needed for the discovery of new lead compounds or lead optimization employing combinatorial chemistry techniques [3].

Among six-membered aromatic heterocycles, pyrimidines play central and peculiar roles as three nucleobases found in nucleic acids, cytosine (C), thymine (T), and uracil (U). In nature, pyrimidine is an important subunit in numerous natural products [4]. Both natural and synthetic pyrimidines demonstrate various biological and pharmacological activities such as anticonvulsant, cardiotonic, vasorelaxant , and antitumor properties [5,6].

In recent years, new methods for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones have been developed by different catalysts such as VCl_3 [7], $Zn(OTf)_2$ [8], LiBr [9].

Consequently, synthesis of 3,4-dihydropyrimidin-2(1H)-thione derivatives with the aim to develop new drug molecules has been an active area of the research. Herein we wish to report a novel and effective method to the synthesis of pyrimidines via multi-component coupling of ethyl acetoacetate, thiourea with various aryl aldehydes in the presence of $FeCo_2O_4$ NPs "Scheme1".



Scheme 1: Preparation of 3,4-dihydropyrimidin-2(1H)-thiones

Experimental:

Chemicals were purchased from the Sigma-Aldrich and Merck in high purity. All of the materials were of commercial reagent grade and were used without further purification. All melting points are uncorrected and were determined in capillary tube on Boetius melting point microscope. ^1H NMR and ^{13}C NMR spectra were obtained on Bruker 400 MHz spectrometer with DMSO-d_6 as solvents using TMS as an internal standard. FT-IR spectrum was recorded on Magna-IR, spectrometer 550. Microscopic morphology of products was visualized by SEM (LEO 1455VP). The compositional analysis was done by energy dispersive analysis of X-ray (EDX, Kevex, Delta Class I).

Synthesis of $FeCo_2O_4$ nanoparticles:

The Co-precipitation process was performed as follows: a solution containing 0.01M of $FeCl_3$ and 0.02M of $CoCl_2 .6H_2O$ was added drop wise to a solution of sodium hydroxide having a concentration of 0.5M and pH 9 with continuous stirring for 2 hours at 90° C. The precipitate was formed immediately and remained in the mother solution which was placed in a water bath for 4 hours. After cooling, the precipitate was filtered and washed repeatedly with distilled water until traces of sodium chloride formed during the reaction was removed. The precipitate was dried in a hot air oven for 2 hours and then it was ground well and was calcined at 350°C for 4 hours to get $FeCo_2O_4$ nanoparticles.