New multicomponent approach for the synthesis of coumarin derivatives by using environmental-friendly core/shell nanocatalyst

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Abstract:

In this work, a three-component reaction of salicylaldehyde, diethylmalonate and phenylhydrazine in the presence of a core/shell nanocatalyst in EtOH was used to form a novel series of coumarin derivatives. This catalytic protocol was simply carried out in high yields and short reaction times. The remarkable magnetic properties of this nanocomposite provide easy separation of the catalyst from the reaction mixture without considerable loss of activity.

Keywords: Green chemistry, nanocatalyst, coumarin**,** salicylaldehyde, diethylmalonate, nanocomposite.

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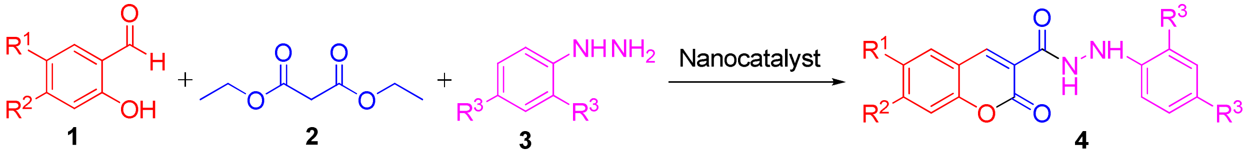
1. Introduction

The coumarin derivatives e.g. coumarin (2*H*-1-benzopyran-2-one) and are natural and essential chemical compounds in the perfume, cosmetic, and pharmaceutical industrial production.[1] Thus, development of novel and efficient methods for construction of these compounds will be a great challenge for the screening of novel biologically active molecules[2]. The typical methods for the preparation of coumarins comprise of three conventional approaches such as the Pechman reaction, the Wittig reaction, and the Knoevenagel condensation [3]. Coumarin applies as an intermediate in the synthesis of several organic productions such as furocoumarins, chromenes, coumarones and 2-acylresorcinols[4].

Multicomponent reactions (MCRs) are one pot processes in which at least three or more different simple reactant for the preparation of target materials. These reactions which have obtained much attention during the past years are frequently occurring not through a single-step procedure, but rather by several sequential steps or multicomponent cascade or main reactions.

These reaction include some advantages such as Simplicity, greater efficiency and atom economy with generation of molecular complexity and diversity in one-pot transformation because of their recyclability, sustainability, selective reactivity, high catalytic activity and ecological safety[5]. The catalysis by nanoparticles has gained more attention recently. In particular, catalysis by nanoparticles compounds of the first transition series metals Cu, Fe, Ni etc. has received much interest due to their large surface area and significant thermal, chemical, electronic, magnetic and optical properties[6]. Multifunctional nanomaterials with task-specific physicochemical properties, especially core–shell nanostructures with Fe_3O_4 core and NH_2-functional shells ($Fe_3O_4@SiO_2$–NH_2), have been widely investigated as high-performance adsorbents, catalysts and catalyst supports; and in several cases the controllable sol–gel method is the choice for fabrication of this kind of extensively served materials[7].

A new synthetic route for preparation of novel series of coumarin derivatives has been explored. To the best of our knowledge, this work presents the first simple direct route to the important class of coumarin derivatives. Herein, we report the synthesis of these new coumarin derivatives via a three-component reaction of salicylaldehyde **1**, diethyl malonate **2** and phenylhydrazine **3** in the presence of $Fe_3O_4@SiO_2@NH_2$ as a catalyst in EtOH.



Scheme 1. Preparation of 3-carboxyhydrazido coumarin derivatives.

2. Experimental

General

All the solvents, chemicals and reagents were purchased from Merck, Fluka and Aldrich. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IR-470 spectrometer by the method of KBr pellet.

Preparation of $Fe_3O_4@SiO_2$–NH_2 MNPs

The Fe_3O_4 MNPs were then modified sequentially with tetraethyl orthosilicate (TEOS) and 3-aminopropyl trimethoxysilane (APTMS) to introduce amine groups. Typically, 20 mL magnetofluid was diluted with 150 mL ethanol. The mixture was homogenized by ultrasonication for 15 min prior to the addition of 1–4 mL $NH_3.H_2O$. After stirring vigorously 30 min with a mechanical stirrer at 30 °C, 1.0 mL TEOS was dropped into the solution. The reaction was performed for 30–120 min and then 0.03–0.08 mL APTMS was introduced and lasted reaction for another 2–10 h. The optimized Fe_3O_4@SiO_2@NH_2 MNPs formulation was: 20 mL magnetofluid, 150 mL EtOH and 1.0 mL of $NH_3.H_2O$ was homogenized by ultrasonication for 15 min. Then, 1.0 mL of TEOS as the hydrolysis precursor was added into the mixture. After the mixture was hydrolyzed for 45 min, 0.07 mL APTMS was added to functionalize the MNPs with $–NH_2$ groups. During the mentioned stages, the pre-hydrolysis time of TEOS before addition of APTMS and the amount of APTMS were detailed investigated to correlate the variation of physicochemical properties of Fe_3O_4@SiO_2@NH_2 MNPs with the key preparation parameters[7].

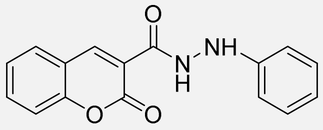
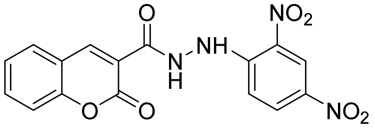
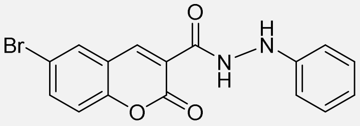
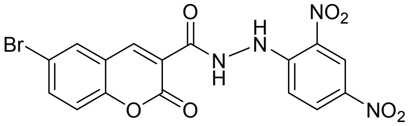
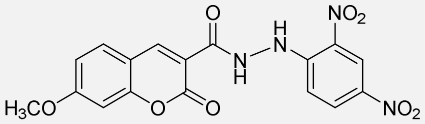
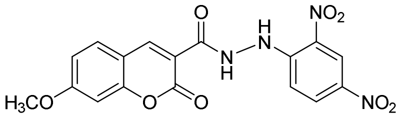
General procedure for the synthesis of 3-carboxyhydrazido coumarin derivatives

A mixture of salicylaldehyde derivatives **1** (1 mmol) and diethyl malonate **2** (1 mmol) and phenylhydrazine derivatives **3** (1 mmol) in the presence of a catalytic amount of Fe_3O_4@SiO_2@NH_2 (0.15 g) in 10 mL ethanol was stirred for 5 h at 50 °C. After the completion of the reaction, according to the TLC (ethyl acetate/*n*-hexane, 1/3) resulted. Then, the catalyst separated by using an external magnet. The precipitated solid was then collected and recrystallized from ethanol (96%) to give highly pure 3-carboxyhydrazido coumarin derivatives.

3. Results and discussion

In this work, coumarin derivatives were synthesized by the reaction of salicylaldehyde derivatives, diethyl malonate and phenylhydrazine derivatives in present of magnetic nanocatalyst. The results are reported in Table 1. This process offer attractive advantage like operational simplicity and environmentally benign nature.

Table 1. Synthesis of 3-carboxyhydrazido coumarin derivatives by using $Fe_3O_4@SiO_2@NH_2$ nanocatalyst in ethanol.

Entry	R^1	R^2	R^3	Product	Time (h)	Yield (%)
1	H	H	H	 **4a**	5	85
2	H	H	NO_2	 **4b**	4.5	88
3	Br	H	H	 **4c**	4.5	88
4	Br	H	NO_2	 **4d**	4	90
5	H	OCH_3	H	 **4e**	5.5	83
6	H	OCH_3	NO_2	 **4f**	5	85

An important parameter in heterogeneous catalysis is the reusability of the catalyst. Hence, a set of experiments was performed to check the reusability of the present nanocatalyst for the synthesis of 2-oxo-2H-chromene-3-carboxylic acid N-phenylhydrazide **4a**. Due to magnetic properties, the catalyst was easily separated, washed three times with ethanol and water; and reused efficiently for at least six times without significant loss in its activity

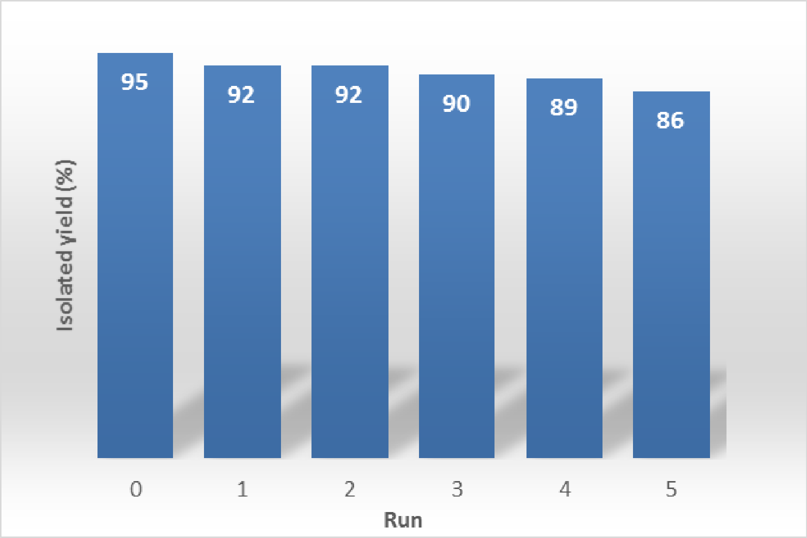


Fig1. Reusability of $Fe_3O_4@SiO_2@NH_2$ for the synthesis of **4a**.

4. Conclusions

In summary, we have developed a highly efficient and environmental friendly method for the synthesis of 3-carboxyhydrazido-coumarin derivatives via $Fe_3O_4@SiO_2@NH_2$-catalyzed multicomponent reactions in significant yields. The remarkable advantages of this method include mild reaction conditions, short reaction times, avoiding hazardous organic solvents, high yields of the products and the superparamagnetic catalyst was easily removed from the reaction mixture by an external magnet. In addition, this procedure had some further advantages such as simple catalyst recyclability. So, it could have promising applications as a recyclable and renewable catalyst in industrial large-scale production.

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