

# 1<sup>th</sup> National Seminar of Development of Nanotechnology in Basic Science and Engineering

## Green Synthesis of 1-Amidoalkyl-2-naphtholes Using the Cu (II) Complex Immobilized on Hybrid Nanomaterial as a Reusable Catalyst

Mohammad Ali Bodaghifard<sup>a,b\*</sup>

<sup>a</sup> Department of Chemistry, Faculty of Science, Arak University, 38156-88138, Arak, Iran.

<sup>b</sup> Institute of Nanosciences and Nanotechnology, Arak University, 38156-88138, Arak, Iran.

\* Email: mbodaghi2007@yahoo.com; m-bodaghifard@araku.ac.ir

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# Introduction

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According to the principals of green chemistry, designing the green reaction conditions has become an important subject for the elimination of pollutions from environment in recent years. In this regard, the use of solvent-free conditions or green solvents especially water in organic reactions instead of hazardous solvents has been developed enormously in organic synthesis [1, 2].

The multicomponent reactions are a good way to produce complex and diverse combinations with high interest rates [3-5]. The MCRs have many advantages as low reaction times, diminished work-up procedures, high efficiency, cheapness, high selectivity, low environmental impact compared to different methods of classical chemistry [5, 6]. MCRs are mostly experimentally simple to perform, often without the need of dry conditions and inert atmosphere. Recently MCRs provide a huge chemical diversity and currently more than hundreds different structurally varied chemical scaffolds have been described in the chemical literature [7-9].

The magnetic nanoparticles (MNPs) not only have high surface area but also they can be easily separated by using an external magnetic field and do not have tedious separation procedures which resulted from the small sizes of nanoparticles [10]. However, magnetic nanoparticles can easily aggregate into larger clusters because of their anisotropic dipolar attraction. In addition, they have other deficiencies such as leaching under acidic conditions and being susceptible to autoxidation and toxicity. Therefore, it is necessary to protect the surface of MNPs in order to reduce these undesirable features. For this purpose, MNPs are usually coated with a polymeric or inorganic matrix [11]. Among inorganic compounds, SiO<sub>2</sub> can be a suitable candidate for protecting the surface of MNPs due to its high chemical and thermal stability and most importantly its easy modification by a wide range of functional groups, which increase chemical and colloidal stability of these compounds [12-18]. Besides, using magnetic nanoparticles as catalysts is associated with other advantages including easy synthesis and functionalization, low toxicity and low cost [12-15].



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Studies have shown that 1-amidoalkyl-2-naphthols and their derivatives are important compounds for the synthesis of many natural and pharmacological products, including antibiotics and HIV-protease inhibitors [19-21], anticonvulsant [22], anticancer [23], anti-rheumatism [24], anti-viral (malaria) [25]. 1-amidoalkyl-2-naphthols can be also converted to 1,3-oxazine derivatives by an amide hydrolysis reaction, which exhibit anti-depression and anti-bradycardia effects [26]. There are many reported methods for synthesis of these compounds. However, these methods have many defects such as long reaction times, the use of quantitative amounts of catalysts, expensive and non-recyclable catalysts, use of volatile and harmful solvents contradictory to green chemistry, reflux conditions, and difficult separation of the products. So, the development of simpler and high yield approaches and milder reaction conditions toward this valuable nucleus is very desirable.

Metal complexes have been used as homogenous catalysts in the wide range of organic reactions. However, most of them are precious and expensive and have drawbacks such as tedious separation and decreasing of catalytic activities with time. To overcome some of these issues, several metal complexes have been immobilized onto inorganic supports. So many works have been reported in the literature for grafting and immobilization of metal complexes on magnetic nanosized inorganic supports that benefit from excellent catalytic activity, high selectivity and easy separation [12].

As part of our continuous effort to develop efficient heterogeneous magnetic nanocatalysts and green organic reactions to gain the valuable heterocyclic compounds [12, 27-31], herein we have reported the preparation of a novel heterogeneous copper complex-supported hybrid nanostructure  $[\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}]$  as an impressive catalyst for synthesis of 1-amidoalkyl-2-naphthol derivatives (Scheme 3).



# Experimental

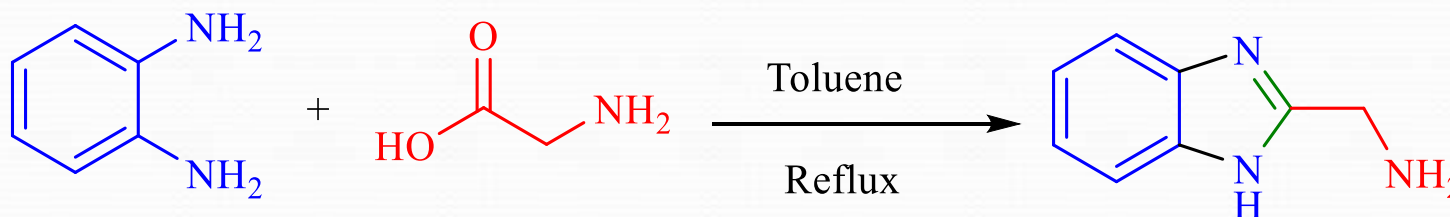
All reagents were purchased from reputable chemical companies (Merck, Across, Fluka) and were used without further purification. Melting points were measured by using electrothermal digital apparatus and are uncorrected. Obtained products were identified with comparison of their melting points and spectral data reported in the literature. The FT-IR spectra were recorded by Unicom Galaxy Series. The  $^1\text{H}$ ,  $^{13}\text{C}$ NMR spectra for obtained products were reported on Bruker DRX-300 spectrometer operating at 300 and 75 MHz respectively in  $\text{DMSO-}d_6$  with TMS as an internal standard. The crystal structure was carried out on by Philips Xpert Xray powder diffraction (XRD) diffract meter ( $\text{Cu-K}\alpha$  radiation and  $\lambda = 0.15406$ ) in range of Bragg angle 10-80 using  $0.05^\circ$  as the step length. The thermal stability of  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  was investigated by a thermogravimetric analyzer with model Mettler TA4000 System under an  $\text{N}_2$  atmosphere at a heating rate of  $10^\circ\text{Cmin}^{-1}$ . The surface morphology and elemental content of  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  was investigated on a Hitachi S-4160. The Elemental chemical analysis [energy dispersive X-ray spectroscopy (EDS)] coupled with SEM was reported for characterization of chemical elements of the prepared hybrid nanomaterial. The magnetization and hysteresis loop for the synthesized magnetic nanoparticles were measured at room temperature using a 7300 VSM system with a maximum field of 10 kOe. In addition, the loading amount of Cu on  $[\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}]$  was determined with an inductively coupled plasma optical emission spectrometer (SPECTRO ARCOS).



# Experimental

## Synthesis of (1*H*-benzo[*d*]imidazol-2-yl)methanamine (BIMA, Scheme 1)

A mixture of 1,2-phenylenediamine (10 mmol, 1.08 g), glycine (10 mmol, 0.75 g) in 20 mL toluene in 100 mL round-bottomed flask was refluxed for 10 h at 110 °C [32-33]. The excess solvent was evaporated and the mixture diluted with ethyl acetate. The solid product was extracted using n-hexane and dried in vacuum oven at 50 °C.



**Scheme 1:** Synthesis of (1*H*-benzo[*d*]imidazol-2-yl)methanamine (BIMA)

# Experimental

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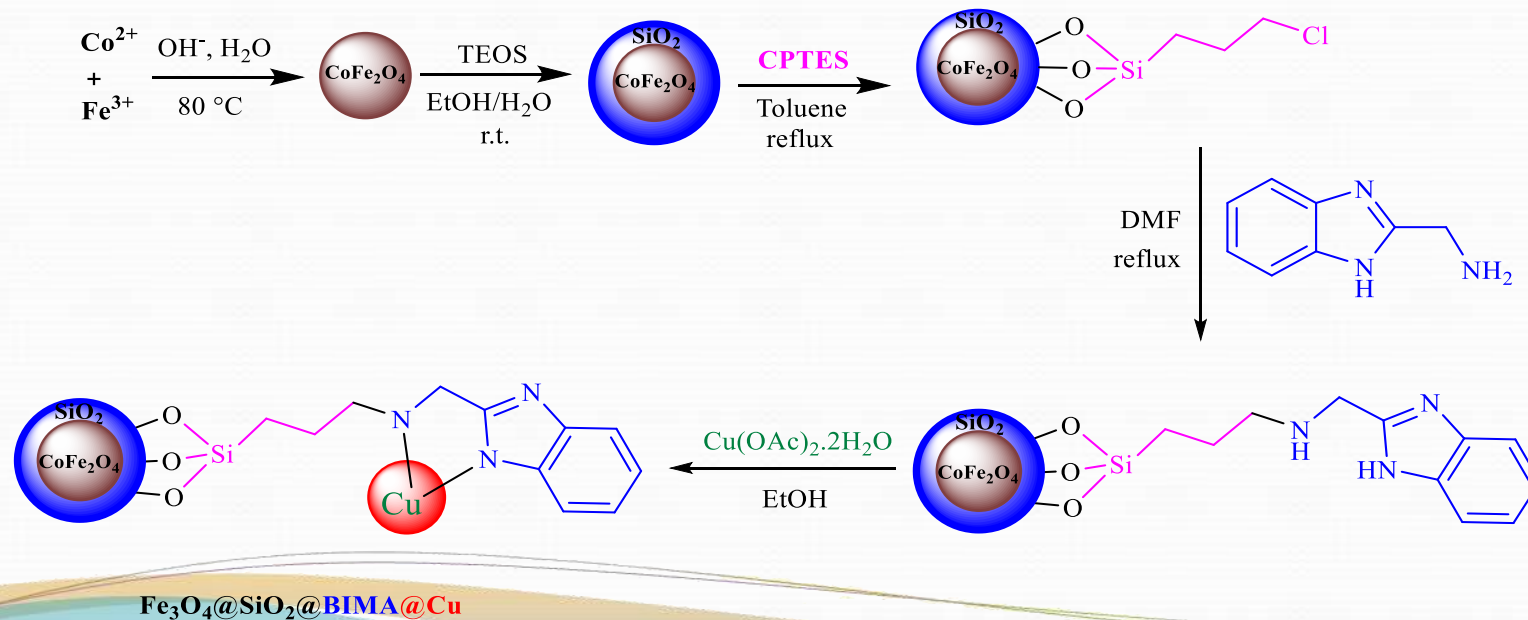
## **General procedure for One-pot Synthesis of 1-amidoalkyl-2-naphthols**

In a test tube, a mixture of aldehydes (1 mmol),  $\beta$ -naphthol (1 mmol), amides (1.2 mmol) and nano-CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@BIMA@Cu (20 mg) as a catalyst stirred under solvent free conditions at 80 °C for the appropriate time. After completion of the reaction as monitored by TLC, the precipitate was diluted with hot ethanol (10 ml) and the catalyst was separated by an external magnet. The reaction mixture was cooled to room temperature and filtered to afford the crude products. Products were purified by re-crystallization from ethanol-water mixture (4:1).



# Results and Discussion

The magnetic hybrid nanoparticles were prepared sequentially as depicted in Scheme 2. Firstly,  $\text{CoFe}_2\text{O}_4$  prepared easily by the co-preparation method from chemical reaction of  $\text{Co}^{2+}$  and  $\text{Fe}^{3+}$  ions in the base conditions [15]. Then,  $\text{CoFe}_2\text{O}_4$  nanoparticles were coated with silica layer using the stöber method [15]. The chloropropyl-modified silica-coated  $\text{CoFe}_2\text{O}_4$  nanoparticles were prepared by reaction of  $\text{CoFe}_2\text{O}_4@SiO_2$  with (3-chloropropyl)triethoxysilane (CPTES) which can bind covalently to the free-OH groups at the particles surface and afforded the  $\text{Fe}_3\text{O}_4@SiO_2\text{-PrCl}$ . The reaction of (1*H*-benzo[*d*]imidazol-2-yl)methanamine with  $\text{CoFe}_2\text{O}_4@SiO_2\text{-PrCl}$  resulted to construction of  $\text{CoFe}_2\text{O}_4@SiO_2@BIMA$  nanostructure. Finally,  $\text{Cu}(\text{OAc})_2$  was stabilized on the modified magnetic nanoparticles. The resulting precipitate was washed with ethanol and dried in the vacuum oven to gain the final hybrid nanomaterial [ $\text{CoFe}_2\text{O}_4@SiO_2@BIMA@Cu$ ]. The Fourier transform infrared (FT-IR) spectroscopy, X-ray powder diffraction (XRD), field emission scanning electron microscopy (FE-SEM), energy dispersive X-ray spectroscopy (EDS), thermogravimetric analysis (TGA/DTG), vibrating sample magnetometer (VSM) and inductively coupled plasma optical emission spectrometry (ICP/OES) were employed to identify and characterize the prepared hybrid nanostructure.

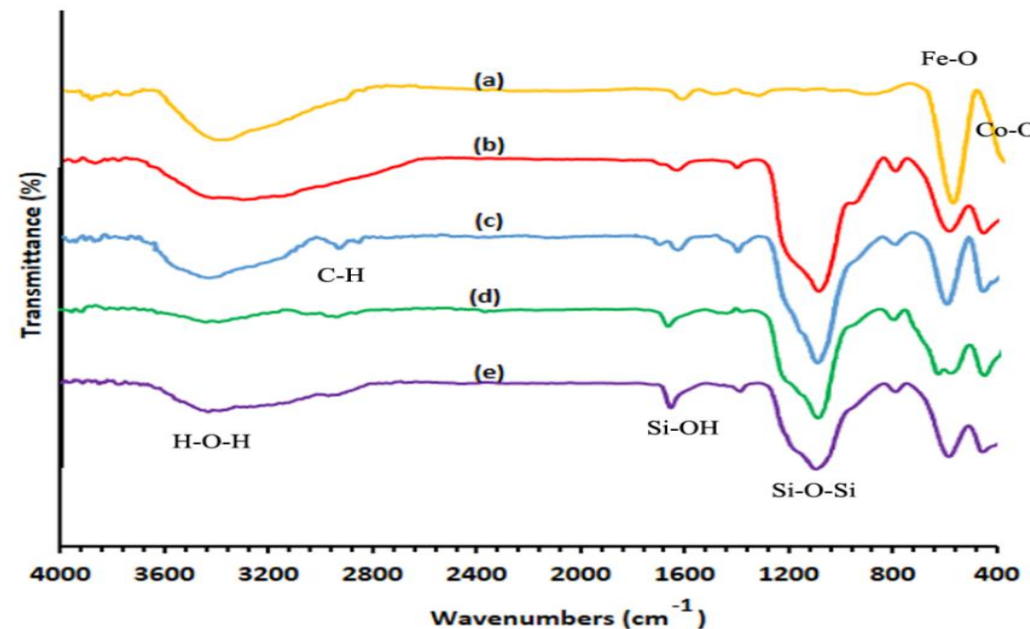


**Scheme 2:** Schematic steps for the construction of  $\text{CoFe}_2\text{O}_4@SiO_2@BIMA@Cu$  hybrid nanostructure



# Results and Discussion

The FT-IR spectra of  $\text{CoFe}_2\text{O}_4$  (a),  $\text{CoFe}_2\text{O}_4@\text{SiO}_2$  (b),  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{Pr-Cl}$  (c),  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}$  (d) and  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  (e) are shown in Figure 1. The FT-IR spectrum of magnetic  $\text{CoFe}_2\text{O}_4$  nanoparticles show the characteristic Fe-O and Co-O absorption bands around  $594$  and  $389$   $\text{cm}^{-1}$  (Fig. 1a). Also, broad band around  $3380$   $\text{cm}^{-1}$  refers to the stretching vibration vibrations of H-O-H groups on the surface of nanoparticles.  $\text{CoFe}_2\text{O}_4@\text{SiO}_2$  shows characteristic FT-IR bands at around  $1084$   $\text{cm}^{-1}$ ,  $798$   $\text{cm}^{-1}$ , and  $457$   $\text{cm}^{-1}$  which are attributed to the asymmetric stretching, symmetric stretching, in plane bending and rocking mode of the Si-O-Si group, respectively, that confirm the formation of  $\text{SiO}_2$  shell (Fig. 1b). The absorption band at  $1620$   $\text{cm}^{-1}$  is referred to stretching vibration mode of Si-OH groups. The weak absorptions at  $2850$  and  $2980$   $\text{cm}^{-1}$  are attributed to symmetric and asymmetric stretching modes of the attached alkyl groups (Fig. 1c-e). Thus, the results confirm that the functional groups were successfully grafted on the surface of  $\text{CoFe}_2\text{O}_4$  nanoparticles.



**Fig. 1:** FT-IR spectra of  $\text{CoFe}_2\text{O}_4$  (a),  $\text{CoFe}_2\text{O}_4@\text{SiO}_2$  (b),  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{PrCl}$  (c),  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}$  (d) and  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  (e)



# Results and Discussion

The X-ray powder diffraction (XRD) patterns was used to study the crystallinity of prepared nanostructure (figure 2). The XRD patterns of  $\text{CoFe}_2\text{O}_4$  (a) and  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  (b) show characteristic peaks at 74.5, 63.0, 57.3, 53.9, 43.3, 35.8, and 30.4°, which attributed to the 533, 440, 511, 422, 400, 311, and 220 planes of  $\text{CoFe}_2\text{O}_4$  respectively (Figure 2a). These data are according to the standard  $\text{CoFe}_2\text{O}_4$  sample (standard JCPDS no.22-1086) and confirm a cubic spinel structure for  $\text{CoFe}_2\text{O}_4$  nanoparticles [15]. The broad peak at  $2\theta= 20\text{-}27^\circ$  can be attributed to the amorphous  $\text{SiO}_2$  coated on surface of  $\text{CoFe}_2\text{O}_4$  core in  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  nanostructure (Figure 2b). The average crystallite sizes estimated using Scherrer's equation ( $D = 0.9 \lambda/\beta\cos\theta$ ). The crystallite size of  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  calculated from the width of the peak at  $2\theta= 35.8^\circ$  (311) is 35 nm, which is in the range determined using FE-SEM analysis (Fig. 4A).

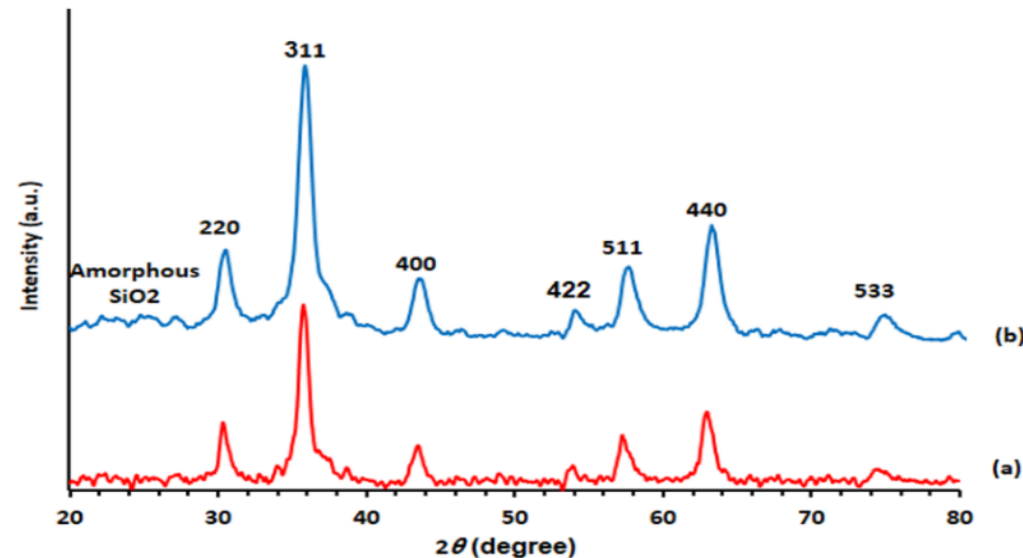


Fig. 2: XRD patterns of  $\text{CoFe}_2\text{O}_4$  (a) and  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  (b)



## Results and Discussion

The thermal stability of  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  was determined by thermal analysis (TGA/DTG) at 50-950 °C range (Figure 3). The magnetic nanomaterial shows three weight loss steps and total weight loss of MNPs in three steps was estimated to be 19% wt. The first stage, including a low amount (4%) of weight loss at  $T < 200$  °C, was due to the removal of physically adsorbed solvent, water and surface hydroxyl groups. The second step at about 200 °C to nearly 500 °C is attributed to the decomposition of the organic layer in the nanocomposite. Therefore, the weight loss between 200 and 500 °C gives the organic moiety ratios grafted on the prepared nanomaterial. The organic moiety grafted on the  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  was approximately 10% wt. The third step show weight loss 5% at  $T > 500$  °C attributed to destruction and deformation of silica layer. The exact amount of copper in  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  was measured using the ICP/OES technique and the amount of copper in the hybrid nanocatalyst is  $2.19 \times 10^{-3} \text{ mol g}^{-1}$ .



# Results and Discussion

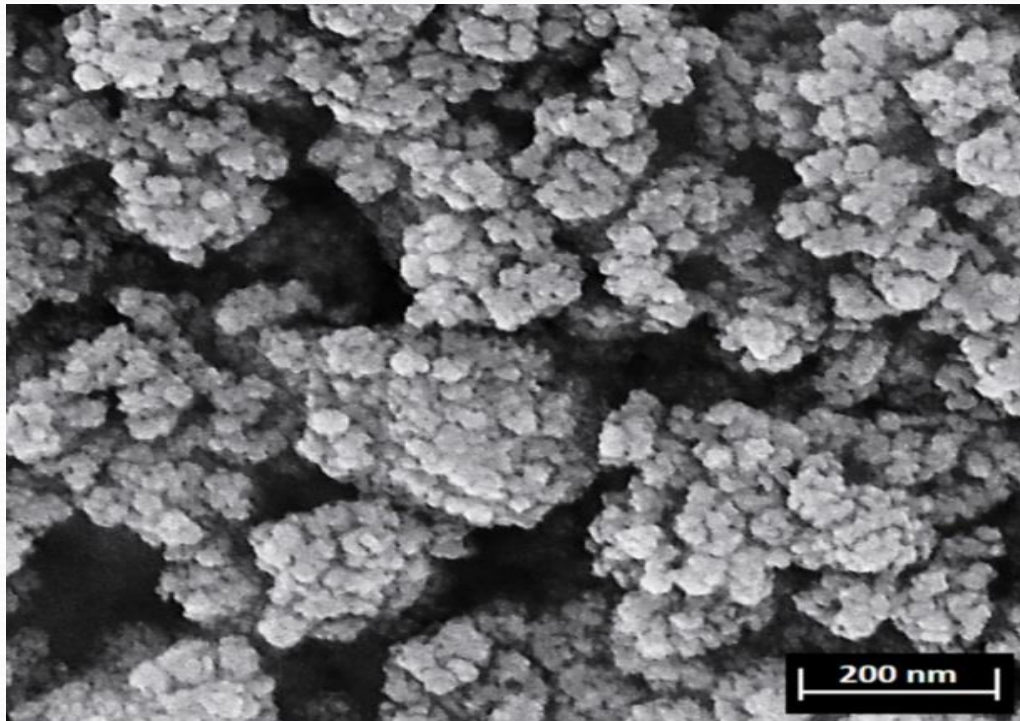


Fig. 4: FE-SEM image of CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@BIMA@Cu nanomaterial

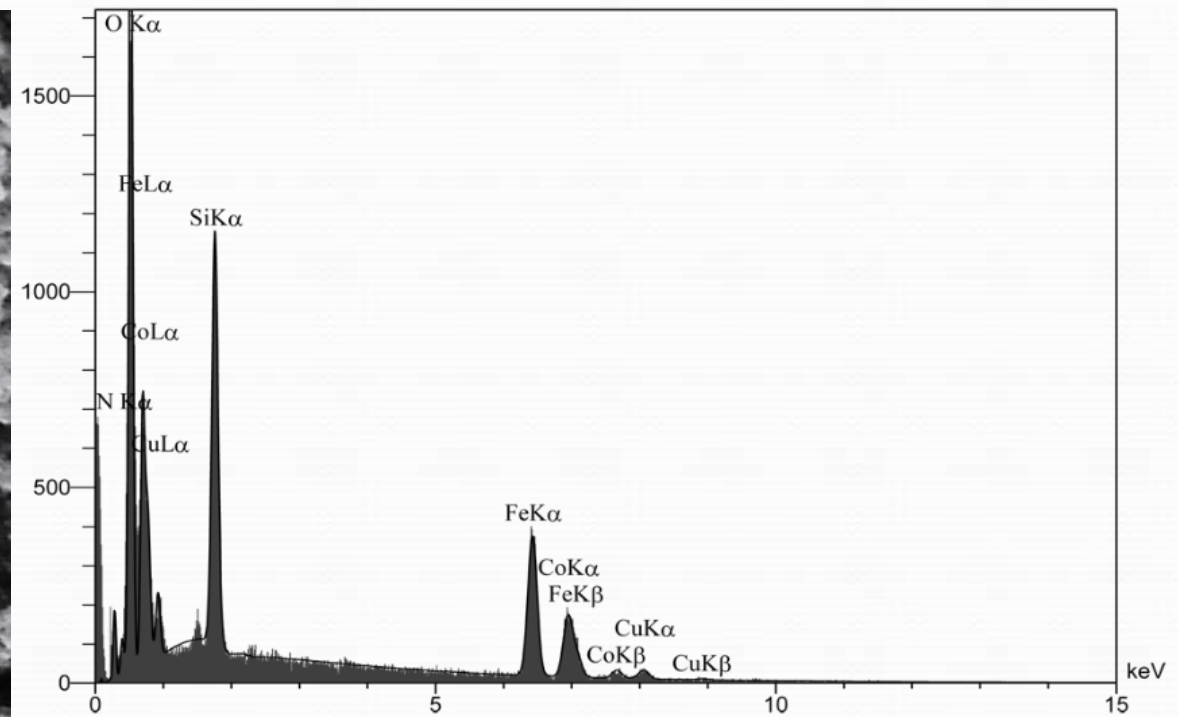
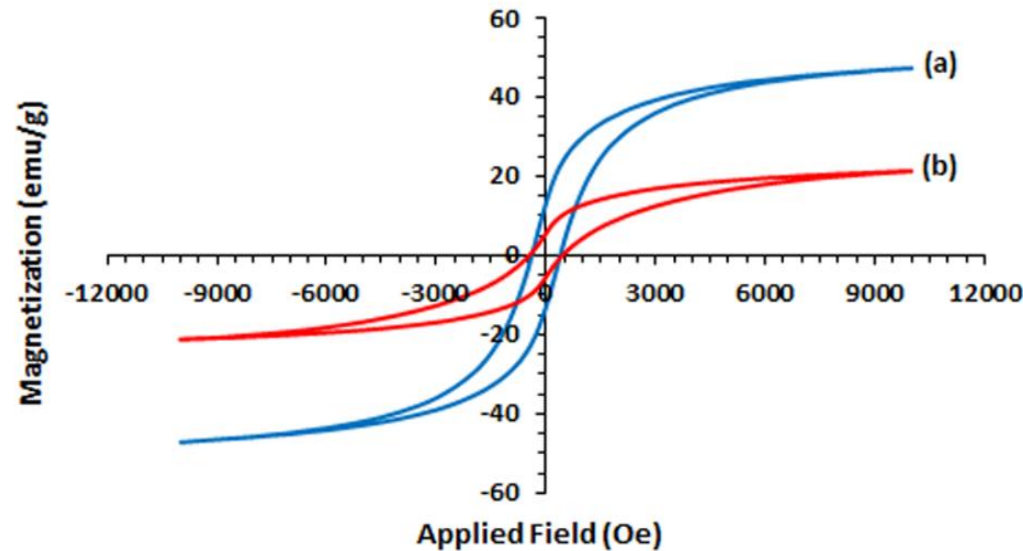


Fig. 5: EDX analysis of CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@BIMA@Cu



# Results and Discussion

The magnetic properties for  $\text{CoFe}_2\text{O}_4$  (a) and  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  (b) nanoparticles are measured by vibrating sample magnetometer (VSM) in -12000 to 12000 Oe range at room temperature (Figure 6). The hysteresis loops show superparamagnetic behavior in two samples and no hysteresis phenomenon was observed. The obtained saturation magnetizations ( $M_s$ ) for  $\text{CoFe}_2\text{O}_4$  and  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  were observed at 45 and 20 Oe, respectively. These results show the functionalization led to decrease in the magnetic properties of the nanostructure.



**Fig. 6:** VSM analysis of  $\text{CoFe}_2\text{O}_4$  (a), and  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  (b)



# Results and Discussion

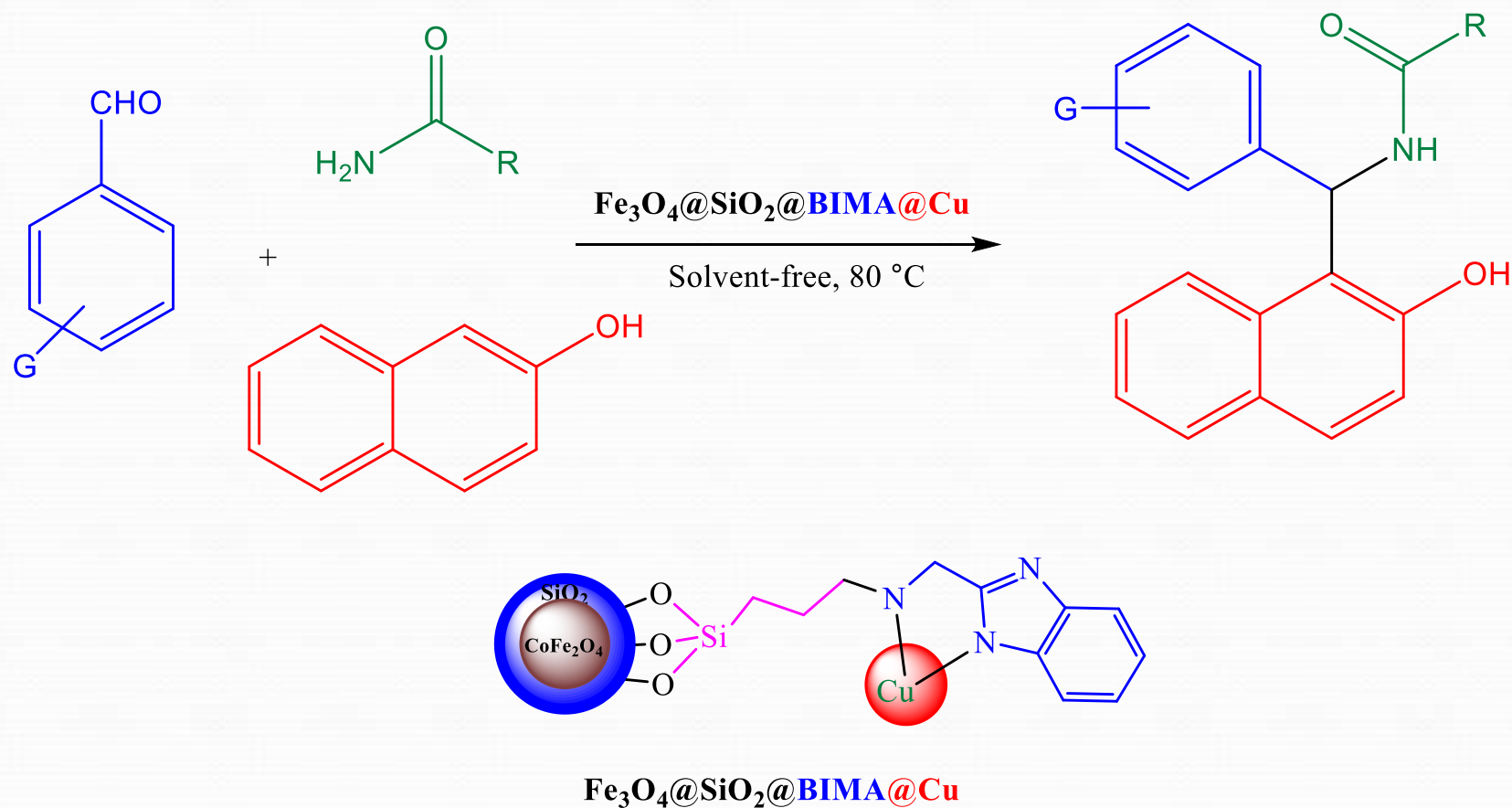
After the successful preparation and characterization of  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$ , its catalytic activity was considered in the synthesis of 1-amidoalkyl naphthol derivatives. The reaction of 4-chlorobenzaldehyde (1 mmol),  $\beta$ -naphthol (1 mmol) and urea (1.2 mmol) was selected as a model reaction (Scheme 3), and parameters affecting the reaction yields such as temperature, solvent, catalyst amount, and the solvent-free conditions were investigated. Using the  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  as a catalyst, conventional heating at 80 °C under solvent-free conditions is the efficient and best condition. It was found that this reaction did not proceed significantly without catalyst and heating, even in a long time.

With the optimized conditions in hand, different amides and substituted aldehydes were reacted with  $\beta$ -naphthol in the presence of  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  (20 mg) via the one-pot multicomponent reaction to obtain substituted amidoalkyl naphthol derivatives. The results were summarized in Table 1. These reactions were very efficient and the desired products (**4a–l**) obtained in good to excellent yields (90-95%) in relatively short reaction times, without byproducts. Arylaldehydes with electron-donating or electron-withdrawing groups could lead to favorite products with no reasonable difference in their reactivity. The structure of 1-amidoalkyl naphthols was confirmed by FT-IR,  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$  spectroscopies and comparison with those reported in the literature. The comparison of the  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  nanostructure as catalyst with some previously reported catalysts for the synthesis of 1-amidoalkyl naphthol derivatives, confirm that the  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  is a comparable, suitable and efficient catalyst for synthesis of these compounds. Based on the literature survey, it is proposed that the Cu (II) ions act as Lewis acids and activate the carbonyl functional groups and facilitate the condensation reactions. The porosity and high surface area of nanostructure ( $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$ ) providing suitable support for the chemical reactions and increase the catalytic performance of the prepared hybrid nanomaterial.



# Results and Discussion

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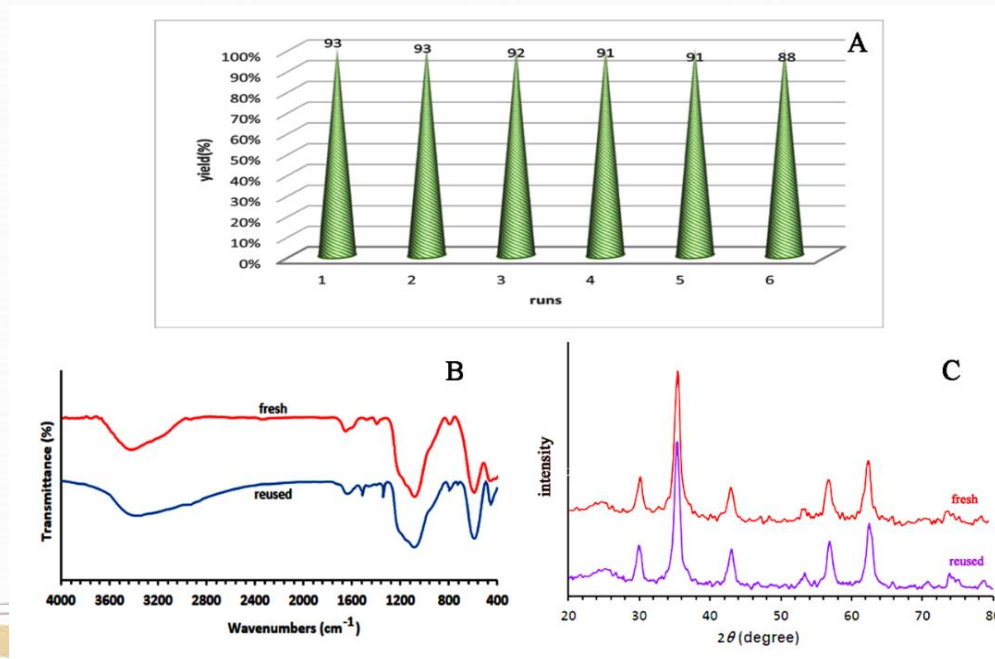


**Scheme 3:** Synthesis of 1-amidoalkyl naphthol derivatives in the presence of  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  hybrid nanocatalyst



# Results and Discussion

The recovery and reusability of  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  was investigated in the model reaction (benzaldehyde, urea, and 2-naphthol, Figure 7). After completion of the reaction, the resulting solidified mixture was diluted with hot EtOH (10 mL). Then, the catalyst was easily separated, washed with hot EtOH, dried under vacuum and reused in a subsequent reaction. Nearly, quantitative recovery of catalyst (up to 97%) could be obtained from each run. As seen in Figure 7a, the recycled catalyst could be reused six times without any additional treatment or appreciable reduction in catalytic activity. In Figure 7b and 7c, the FT-IR spectra and XRD patterns of the fresh (a) and reused (b) catalyst are compared respectively. Potential Cu leaching into the reaction mixture was also analyzed with ICP/OES analysis after six runs. The amount of copper in the catalyst is found to be  $2.08 \times 10^{-3} \text{ mol g}^{-1}$  after six cycles based on ICP/OES measurement. The copper content in  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  after six runs is comparable to that of fresh catalyst, confirming that the leaching of copper in the reaction mixture is negligible. The consistent structure and activity of recovered and reused  $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$  catalyst confirms its stability, recyclability and performance for the synthesis of desired products.



**Fig. 7:** (A) The recyclability of hybrid nanocatalyst ( $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$ ) in synthesis of 1-amidoalkyl-2-naphthols during six runs, (B) FT- IR spectrum, and (C) XRD patterns for fresh and reused catalyst

## Conclusions

In this work, a surface-modified magnetic nanoparticles were functionalized with the Cu (II) complex tags. The novel Cu-complex decorated hybrid nanostructure ( $\text{CoFe}_2\text{O}_4@\text{SiO}_2@\text{BIMA}@\text{Cu}$ ) was characterized successfully using various techniques and its catalytic activity was considered in the synthesis of 1-amidoalkyl-2-naphthol derivatives. The desired products were synthesized by three component reaction of 2-naphthol, amides, and aldehydes in high yields within short reaction times. This strategy offers several key characteristics such as high yield and purity of products, easy work-up and eco-friendly process, and simple separation of catalyst. It is noteworthy that the Cu grafting with organic functional groups on inorganic support efficiently limit Cu leaching and particle growth, which permit this hybrid nanocatalyst to be reused several times with only a slight diminish in its activity.

