



Journal of Coordination Chemistry

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/gcoo20

Cu(II) complex-decorated hybrid nanomaterial: a retrievable catalyst for green synthesis of 2,3dihydroquinazolin-4(1H)-ones

Mohammad Ali Bodaghifard & Somayeh Safari

To cite this article: Mohammad Ali Bodaghifard & Somayeh Safari (2021): Cu(II) complex-decorated hybrid nanomaterial: a retrievable catalyst for green synthesis of 2,3-dihydroquinazolin-4(1H)-ones, Journal of Coordination Chemistry, DOI: 10.1080/00958972.2021.1905803

To link to this article: <u>https://doi.org/10.1080/00958972.2021.1905803</u>



Published online: 13 Apr 2021.

|--|

Submit your article to this journal 🖸





View related articles



View Crossmark data 🗹



Check for updates

Cu(II) complex-decorated hybrid nanomaterial: a retrievable catalyst for green synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones

Mohammad Ali Bodaghifard^{a,b} and Somayeh Safari^a

^aDepartment of Chemistry, Faculty of Science, Arak University, Arak, Iran; ^bInstitute of Nanosciences and Nanotechnology, Arak University, Arak, Iran

ABSTRACT

The significant stability of magnetic core and – OH functional groups on the surface of silica-coated cobalt ferrite (CoFe₂O₄@SiO₂) nanoparticles make it a good candidate for functionalization and catalytic application. In this work, a surfacemodified magnetic solid support with Cu(II) complex was prepared. The structure of the new nanostructure was characterized by Fourier-transform infrared spectroscopy (FT-IR), X-ray powder diffraction (XRD), thermogravimetric analysis (TGA/DTG), vibrating sample magnetometer (VSM), the field emission scanning electron microscopy (FE-SEM), the electron-dispersive X-ray spectroscopy (EDS), and inductively coupled plasma optical emission spectrometry (ICP/OES) techniques. The catalytic activity of the prepared hybrid nanomaterial was evaluated in the synthesis of 2,3-dihydroguinazolin-4(1H)-ones and high yields of desired products were obtained with green media. Some advantages of this method are high yields, short reaction times, green solvent and conditions, easy workup procedure, negligible copper leaching, reusability without a significant diminish in catalytic efficiency and simple separation of nanocatalyst by using an external magnet alongside the environmental compatibility and sustainability.

ARTICLE HISTORY

Received 11 August 2020 Accepted 18 February 2021

KEYWORDS

Hybrid nanostructure; magnetic nanoparticles; heterogeneous catalysis; cobalt ferrite; 2,3-Dihydroquinazolin-4(1H)-one



CONTACT Mohammad Ali Bodaghifard (http://www.action.com, m-bodaghifard@araku.ac.ir (Department of Chemistry, Faculty of Science, Arak University, Arak, 38156-88138, Iran (2021 Informa UK Limited, trading as Taylor & Francis Group

1. Introduction

According to the principals of green chemistry, designing green reaction conditions have become an important subject for elimination of pollution from the environment. Use of solvent-free conditions or green solvents, especially water in organic reactions instead of hazardous solvents has developed in organic synthesis [1, 2].

Multicomponent reactions (MCRs) are a good way to produce complex and diverse combinations of interest [3–5]. MCRs have many advantages such as low reaction times, diminished work-up procedures, high efficiency, low cost, high selectivity and low environmental impact compared to methods of classical chemistry [5, 6]. MCRs are experimentally simple to perform, often without the need of dry conditions and inert atmosphere and provide huge chemical diversity; currently hundreds of different structurally varied chemical scaffolds have been described [7–9].

Mono- and disubstituted 2,3-dihydroquinazoline-4(1*H*)-ones have a broad range of biological and pharmacological properties such as analgesic, antitumor, anticancer, diuretic and herbicide activities [10–13]. These compounds can be easily oxidized to their quinazolin-4(3*H*)-one analogues [14], which also include important pharmacologically active compounds [15, 16]. Several methods have been reported for synthesis of 2,3-dihydroquinazolinones [17–30]. A general synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives involves three-component condensation reaction between aryl aldehydes, isatoic anhydride and amines [26–31]. However, these methods suffer from lengthy procedures and/or low yields, use of volatile and harmful solvents, and vigorous reaction conditions. So, the development of simple, high yield approaches and milder reaction conditions toward these valuable derivatives is desirable.

Magnetic nanoparticles (MNPs) have high surface area and can be easily separated by using an external magnetic field and do not have tedious separation procedures which result from small nanoparticles [32]. 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 [33]. Among inorganic compounds, SiO₂ 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 [34–40]. Using magnetic nanoparticles as catalysts is associated with other advantages including easy synthesis and functionalization, low toxicity and low cost [34–37].

Metal complexes have been used as homogenous catalysts in a wide range of reactions. However, most 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 with many reports for grafting and immobilization of metal complexes on magnetic nanosized inorganic supports that benefit from excellent catalytic activities, high selectivity and easy separation [34]. As part of our continuous effort to develop efficient heterogeneous magnetic nanocatalysts and green organic reactions to prepare valuable heterocyclic compounds [31, 34, 41–44], herein we report the preparation of a heterogeneous copper complex-supported hybrid nanostructure [CoFe₂O₄@SiO₂@BIMA@Cu] as a catalyst for synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives.

2. Experimental

All reagents were purchased from chemical companies (Merck, Acros, Fluka) and were used without further purification. Melting points were measured by using an electrothermal digital apparatus and are uncorrected. Obtained products were identified with comparison of their melting points and spectral data reported in the literature. FT-IR spectra were recorded in a Unicom Galaxy Series. The ¹H and ¹³C NMR spectra for obtained products were reported on a Bruker DRX-300 spectrometer operating at 300 and 75 MHz, respectively, in DMSO- d_6 with TMS as an internal standard. The crystal was examined on a Philips Xpert Xray powder diffraction (XRD) diffractometer (Cu-Ka radiation and $\lambda = 0.15406$) in range of Bragg angle 10–80 using 0.05° as the step length. The thermal stability of CoFe₂O₄@SiO₂@PAF-IL was investigated by a thermogravimetric analyzer Mettler TA4000 System under an N₂ atmosphere at a heating rate of 10°Cmin⁻¹. The surface morphology and elemental content of CoFe₂O₄@SiO₂@PAF-IL were investigated on a Hitachi S-4160. 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. The loading amount of Cu on [CoFe₂O₄@SiO₂@BIMA@Cu] was determined with an inductively coupled plasma optical emission spectrometer (SPECTRO ARCOS).

2.1. Preparation of cobalt ferrite nanoparticles (CoFe₂O₄)

Magnetic cobalt ferrite nanoparticles were prepared by co-precipitation method according to procedure reported in the literature [37]. First, $CoCl_2 \cdot 6H_2O$ (5 mmol, 1.8 g) and $FeCl_3 \cdot 6H_2O$ (10 mmol, 2.7 g) were added to 50 mL of deionized water in a round bottom flask (100 mL) and the mixture was stirred at room temperature for 10 minutes. The pH was adjusted to 11 and 12 using NaOH (0.3 M) solution. The reaction mixture was stirred at 80 °C for 1 h. After cooling to room temperature, the precipitate was separated by magnet and washed with deionized water several times and finally washed with ethanol and dried in an oven at 80 °C.

2.2. Synthesis of silica-coated MNPs (CoFe₂O₄@SiO₂)

The silica shell was coated onto $CoFe_2O_4$ nanoparticles via hydrolysis of TEOS in basic solution [37]. Magnetic cobalt ferrite nanoparticles (1 g), ethanol (40 mL), deionized water (6 mL) and ammonia 25% (1.5 mL) were introduced in a 100 mL flask and sonicated for 20 min. Then, tetraethylorthosilicate (TEOS) (1.4 mL) was added. The reaction

4 🕳 M. A. BODAGHIFARD AND S. SAFARI



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

mixture was stirred at room temperature for 12 h. Finally, the precipitate was separated by magnet and washed with deionized water several times and ethanol, and dried in an oven at 80 °C.

2.3. Synthesis of 3-chloropropyl-funactionalized magnetic nanoparticles (CoFe₂O₄@SiO₂-PrCl)

 $CoFe_2O_4@SiO_2$ nanoparticles (1 g) were dispersed in 50 ml toluene for 10 minutes under sonication. Then, (3-chloropropyl)triethoxysilane (CPTES) (2 g) was added and refluxed for 24 h at 110 °C. Finally, the precipitate was separated by external magnet and washed with toluene several times and dried in an oven at 80 °C.

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

A mixture of 1,2-phenylenediamine (10 mmol, 1.08 g) and glycine (10 mmol, 0.75 g) in 20 mL toluene in a 100 mL round-bottomed flask was refluxed for 10 h at 110 °C [45–47]. Excess solvent was evaporated and the mixture diluted with ethyl acetate. The solid product was extracted using n-hexane and dried in a vacuum oven at 50 °C.

2.5. Preparation of CoFe₂O₄@SiO₂@BIMA

To synthesize the $CoFe_2O_4@SiO_2@BIMA$ nanocomposite, a mixture of (1H-benzo[d]imi-dazol-2-yl]methanamine, (0.5 g), triethylamine (0.5 g) and $CoFe_2O_4@SiO_2-PrCl$ (1 g) in 20 mL of DMF in a 100 mL round-bottomed flask was stirred under sonication. Then, the mixture was stirred with a magnetic stirrer for 24 h at 100 °C. After the reaction was complete, the precipitate was washed several times with hot ethanol and dried in an oven at 80 °C.

2.6. Stabilization of Cu complex on magnetic nanoparticles [CoFe₂O₄@SiO₂@BIMA@Cu]

In a 50 mL round-bottomed flask, 1 g of $CoFe_2O_4@SiO_2@BIMA$ in 20 mL EtOH (99%) and $Cu(OAc)_2 \cdot H_2O$ (0.1 mmol, 0.2 gr) was refluxed under N₂ for 12 h. The resulting mixture was washed with deionized water and ethanol. The resulting hybrid nanomaterial $[CoFe_2O_4@SiO_2@BIMA@Cu]$ was separated using a magnet and dried in a vacuum oven at 80 °C.

2.7. General procedure for one-pot synthesis of 2,3-dihydroquinazolin-4(1H)-ones

In a 25 mL round-bottomed flask, $[CoFe_2O_4@SiO_2@BIMA@Cu]$ (20 mg) was added to a mixture of aromatic aldehyde (1 mmol), isatoic anhydrides (1 mmol), ammonium acetate (2 mmol) or primary amine (1 mmol) in water (5 mL) and refluxed for an appropriate time. After completion, the resulting mixture 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. The purified products were obtained by recrystallization from ethanol-water (4:1).

2.8. Selected spectroscopic data

2-(4-Bromophenyl)-2,3-dihydroquinazolin-4(1H)-one (4b)

FT-IR (KBr), $v_{max} = 3307$, 3187, 3058, 1659, 1609, 1385, 752 cm⁻¹; ¹H NMR (DMSO- d_6): $\delta = 8.35$ (1H, s, NH), 7.60 (1H, d, J = 7.8 Hz, ArH), 7.44-7.52 (4H, m, ArH), 7.27 (1H, t, J = 7.8 Hz, ArH), 7.15 (1H, s, NH), 6.72 (1H, d, J = 8.2 Hz,ArH), 6.66 (1H, t, J = 7.8 Hz, ArH), 5.76 (1H, s, CH) ppm. Anal. Calcd. for C₁₄H₁₁BrN₂O: C, 55.47; H, 3.66; N, 9.24. Found: C, 55.55; H, 3.73; N, 9.32.

2-(4-(Dimethylamino)phenyl)-2,3-dihydroquinazolin-4(1H)-one (4j)

FT-IR (KBr), $v_{max} = 3291$, 3191, 3052, 2890, 2805, 1655, 1612, 1512, 1354, 1161, 818, 752, 520 cm⁻¹. ¹H NMR (DMSO- d_6): $\delta = 8.13$ (1H, s, NH), 7.63 (1H, d, J = 7.5 Hz, H_{Ar}), 7.23-7.34 (3H, m, H_{Ar}), 6.96 (1H, s, NH), 6.66-6.76 (4H, m, H_{Ar}), 5.66 (1H, s, CH), 2.91 (6H, s, 2CH₃) ppm.; ¹³C NMR (DMSO- d_6): $\delta = 164.3$, 151.1, 148.6, 133.6, 131.8, 129.1, 128.2, 127.8, 117.4, 115.5, 114.8, 112.4, 67.1, 40.6 ppm. Anal. Calcd. for C₁₆H₁₇N₃O: C, 71.89; H, 6.41; N, 15.72. Found: C, 71.78; H, 6.49; N, 15.81.

2,3-Diphenyl-2,3-dihydroquinazolin-4(1H)-one (5a)

FT-IR (KBr), $v_{max} = 3296$, 3059, 1633, 1508, 1390, 1159, 752, 696 cm⁻¹. ¹H NMR (DMSOd₆): $\delta = 7.75$ (1H, d, J = 7.5 Hz, ArH), 7.70 (1H, s, NH), 7.19-7.42 (11H, m, ArH), 6.75 (2H, m, ArH), 6.32 (1H, s, CH) ppm. Anal. Calcd. for C₂₀H₁₆N₂O: C, 79.98; H, 5.37; N, 9.33. Found: C, 79.89; H, 5.44; N, 9.45.

2-(4-Bromophenyl)-3-(p-tolyl)-2,3-dihydroquinazolin-4(1H)-one (5 l)

FT-IR (KBr), $v_{max} = 3302$, 1636, 1609, 1512, 1389, 1087, 822, 755, 512 cm⁻¹. ¹H NMR (300 DMSO- d_6): $\delta = 8.45$ (1H, s, NH), 6.54-7.77 (12H, m, H_{Ar}), 6.07 (1H, s, CH), 2.13 (3H, s, CH₃) ppm. Anal. Calcd. for C₂₁H₁₇BrN₂O: C, 64.13; H, 4.36; N, 7.12. Found: C, 64.27; H, 4.41; N, 7.17.

3-Benzyl-2-(4-chlorophenyl)-2,3-dihydroquinazolin-4(1H)-one (5n)

FT-IR (KBr), $v_{max} = 3472$, 3358, 3302, 1630, 1539, 1449, 1269, 752, 727, 696 cm⁻¹. ¹H NMR (300 DMSO- d_6): $\delta = 8.5$ (1H, s, NH), 7.36 (1H, s, CH), 6.22-7.12 (13H, m, H_{Ar}), 4.23 (2H, s, CH₂). Anal. Calcd. for C₂₁H₁₇ClN₂O: C, 72.31; H, 4.91; N, 8.03. Found: C, 72.23; H, 4.97; N, 8.11.



Fe₃O₄@SiO₂@BIMA@Cu

Scheme 2. Schematic steps for construction of CoFe₂O₄@SiO₂@BIMA@Cu hybrid nanostructure.

2-(4-Chlorophenyl)-3-propyl-2,3-dihydroquinazolin-4(1H)-one (50)

FT-IR (KBr), $v_{max} = 3303$, 2963, 2870, 1628, 1508, 1304, 1088, 852, 744, 517 cm⁻¹. ¹H NMR (DMSO- d_6): $\delta = 7.67$ (1H, d, J = 7.7 Hz, ArH), 7.35-7.46 (5 H, m, ArH and NH), 7.22 (1H, t, J = 7.3 Hz, ArH), 6.64-6.71 (2 H, m, ArH), 5.90 (1H, s, CH), 3.83-3.92 (1H, m, CH₂), 2.70-2.80 (1H, m, CH₂), 1.45-1.62 (2H, m, CH₂), 0.86 (3H, t, J = 7.3 Hz, CH₃) ppm. ¹³C NMR (DMSO- d_6): $\delta = 162.6$, 146.5, 140.7, 133.6, 133.3, 128.9, 128.4, 127.9, 117.7, 115.5, 114.8, 69.7, 46.6, 21.3, 11.6 ppm. Anal. Calcd. for C₁₇H₁₇ClN₂O: C, 67.88; H, 5.70; N, 9.31. Found: C, 67.73; H, 5.81; N, 9.41.

3. Results and discussion

3.1. Preparation and characterization of the hybrid nanostructure

The magnetic hybrid nanoparticles were prepared sequentially as depicted in Scheme 2. First, $CoFe_2O_4$ prepared easily by the co-precipitation method from reaction of Co^{2+} and Fe³⁺ ions in basic conditions [37]. Then, CoFe₂O₄ nanoparticles were coated with silica layer using the Stöber method [37]. The chloropropyl-modified silica-coated $CoFe_2O_4$ nanoparticles were prepared by reaction of $CoFe_2O_4@SiO_2$ with (3-chloropropyl)triethoxisilane (CPTES) which can bind covalently to free-OH groups at the particles surface and afforded the Fe₃O₄@SiO₂-PrCl. The reaction of (1H-benzo[d]imidazol-2vl)methanamine with CoFe₂O₄@SiO₂-PrCl resulted in construction of CoFe₂O₄@SiO₂@BIMA nanostructure. Finally, Cu(OAc)₂ was stabilized on the modified magnetic nanoparticles. The resulting precipitate was washed with ethanol and dried in the vacuum oven to gain [CoFe₂O₄@SiO₂@BIMA@Cu]. 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 magnetometry (VSM) and inductively coupled plasma optical emission spectrometry (ICP/OES) were employed to characterize the prepared hybrid nanostructure.



Figure 1. FT-IR spectra of $CoFe_2O_4$ (a), $CoFe_2O_4@SiO_2$ (b), $CoFe_2O_4@SiO_2$ -PrCl (c), $CoFe_2O_4@SiO_2@BIMA$ (d) and $CoFe_2O_4@SiO_2@BIMA@Cu$ (e).

The FT-IR spectra of $CoFe_2O_4$ (a), $CoFe_2O_4@SiO_2$ (b), $CoFe_2O_4@SiO_2@Pr-Cl$ (c), $CoFe_2O_4@SiO_2@BIMA$ (d) and $CoFe_2O_4@SiO_2@BIMA@Cu$ (e) are shown in Figure 1. The FT-IR spectrum of magnetic $CoFe_2O_4$ nanoparticles show the characteristic Fe-O and Co-O absorption bands at 594 and 389 cm^{-1} (Figure 1(a)). Also, a broad band at 3380 cm^{-1} refers to stretching vibrations of H-O-H groups on the surface of nanoparticles. $CoFe_2O_4@SiO_2$ shows characteristic FT-IR bands at 1084 cm^{-1} , 798 cm^{-1} and 457 cm^{-1} which are attributed to the asymmetric stretch, symmetric stretch, in plane bending and rocking mode of the Si–O–Si group, respectively, that confirm the formation of the SiO₂ shell (Figure 1(b)). The absorption band at 1620 cm^{-1} is from stretch of Si-OH groups. The weak absorptions at 2850 and 2980 cm⁻¹ are attributed to symmetric and asymmetric stretching modes of the attached alkyl groups (Figure 1(c)–(e)). Thus, the results confirm that the functional groups were grafted on the surface of $CoFe_2O_4$ nanoparticles.

The X-ray powder diffraction (XRD) patterns were used to study the crystallinity of the prepared nanostructure (Figure 2). The XRD patterns of CoFe₂O₄ (a) and CoFe₂O₄@SiO₂@BIMA@Cu (b) show characteristic peaks at 74.5, 63.0, 57.3, 53.9, 43.3, 35.8 and 30.4°, attributed to the 533, 440, 511, 422, 400, 311 and 220 planes of CoFe₂O₄, respectively (Figure 2(a)). These data are according to the standard CoFe₂O₄ sample (standard JCPDS no. 22-1086) and confirm a cubic spinel structure for CoFe₂O₄ nanoparticles [37]. The broad peak at $2\theta = 20-27^{\circ}$ can be attributed to the amorphous SiO₂ coated on the surface of CoFe₂O₄ core in CoFe₂O₄@SiO₂@BIMA@Cu nanostructure (Figure 2(b)). The average crystallite sizes were estimated using Scherrer's equation (D = 0.9 λ/β cos θ) with CoFe₂O₄@SiO₂@BIMA@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 (Figure 3).

8 🛞 M. A. BODAGHIFARD AND S. SAFARI



Figure 2. XRD patterns of CoFe₂O₄ (a) and CoFe₂O₄@SiO₂@BIMA@Cu (b).



Figure 3. FE-SEM image of CoFe₂O₄@SiO₂@BIMA@Cu nanomaterial.



Figure 4. TGA/DTG thermogram of CoFe₂O₄@SiO₂@BIMA@Cu.



Figure 5. EDX analysis of CoFe₂O₄@SiO₂@BIMA@Cu.

The thermal stability of CoFe₂O₄@SiO₂@BIMA@Cu was determined by thermal analysis (TGA/DTG) from 50 °C to 950 °C (Figure 4). The magnetic nanomaterial shows three weight loss steps and total weight loss of MNPs in three steps was 19% wt. The first stage, including a small (4%) weight loss at T < 200 °C, was due to the removal of physically adsorbed solvent, water and surface hydroxyl groups. The second step at 200 °C to nearly 500 °C is attributed to decomposition of the organic layer in the nanocomposite. Therefore, the weight loss between 200 and 500 °C gives the organic moiety ratio grafted on the prepared nanomaterial. The organic moiety grafted on the $CoFe_2O_4$ (SiO_2) BIMA (Cu was approximately 10% wt. The third step shows weight loss 5% at T > 500 °C attributed to destruction and deformation of silica layer. The exact amount of copper in CoFe₂O₄@SiO₂@BIMA@Cu was measured using the ICP/OES technique and the amount of copper in the hybrid nanocatalyst is $1.87 \times 10^{-3} \text{ mol g}^{-1}$.

The size and morphology of the CoFe₂O₄@SiO₂@BIMA@Cu particles were investigated by field emission scanning electron microscopy (Figure 3). The SEM image shows CoFe₂O₄@SiO₂@BIMA@Cu particles are nearly spherical shapes with mean diameter 30 nm. The electron dispersive X-ray spectrum (EDS) confirms the presence of carbon (C), silicon (Si), nitrogen (N), oxygen (O), cobalt (Co), iron (Fe), and copper (Cu) in CoFe₂O₄@SiO₂@BIMA@Cu nanostructure (Figure 5). The higher intensity of the Si peak compared to the Fe and Co peaks exhibits the CoFe₂O₄ nanoparticles have been trapped by the SiO₂ layer. So, based on the results, the CoFe₂O₄@SiO₂@BIMA@Cu nanocomposite has been fabricated.

The magnetic properties for $CoFe_2O_4$ (a) and $CoFe_2O_4@SiO_2@BIMA@Cu$ (b) nanoparticles are measured by a 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 (Ms) for $CoFe_2O_4$ and $CoFe_2O_4@SiO_2@BIMA@Cu$ were observed at 45 and 20 Oe, respectively. These results show the functionalization led to decrease in the magnetic properties of the nanostructure.



Figure 6. VSM analysis of CoFe₂O₄ (a) and CoFe₂O₄@SiO₂@BIMA@Cu (b).



Scheme 3. The synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones in the presence of $CoFe_{2}O_{4}@SiO_{2}@BIMA@Cu$ as a catalyst.

Table	 Optimization 	of	the	reaction	conditions	for	synthesis	of	2,3-dihydroquinazolin-
4(1H)-0	ones.ª								

Entry	Catalyst (mg)	Solvent	Temperature (°C)	Time (min)	Yield (%)
1	CoFe2O4@SiO2@BIMA@Cu (10)	EtOH	70	80	80
2	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (10)	EtOH	Reflux	60	85
3	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (10)	DMF	Reflux	60	43
4	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (10)	CH ₃ CN	Reflux	60	41
5	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (10)	EtOH:H ₂ O	Reflux	60	85
6	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (10)	Solvent-free	100	80	67
7	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (10)	H ₂ O	r.t	90	40
8	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (10)	H ₂ O	70	60	87
9	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (10)	H ₂ O	Reflux	40	93
10	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (5)	H ₂ O	Reflux	40	81
11	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu (20)	H ₂ O	Reflux	30	95
12	$CoFe_{2}O_{4}$ (20)	H ₂ O	Reflux	90	81
13	$CoFe_2O_4@SiO_2$ (20)	H ₂ O	Reflux	90	73
14	CoFe ₂ O ₄ @SiO ₂ @BIMA (20)	H ₂ O	Reflux	90	79
15		H ₂ O	Reflux	120	25

^a4-chlorobenzaldehyde, isatoic anhydride, ammonium acetate, catalyst.

3.2. Synthesis of 2,3-dihydroquinazolin-4(1H)-ones using $CoFe_2O_4@SiO_2@BIMA@Cu$ as a catalyst

After preparation and characterization of CoFe₂O₄@SiO₂@BIMA@Cu, its catalytic activity was considered in the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives. The

						M.p.(°C)	
Entry	R ¹	$\rm NH_4OAc~or~R^2 \rm NH_2$	Product	Time (min)	Yield (%) ^a	Found ^b	Reported [26-31]
1	C ₆ H₅	NH₄OAc	4a	30	93	290–293	290–292
2	4-Br-C ₆ H ₄	NH₄OAc	4b	30	91	269–271	275-276
3	$4-OCH_3-C_6H_4$	NH₄OAc	4c	35	90	226-227	224-226
4	3,4-(OCH ₃) ₂ -C ₆ H ₃	NH₄OAc	4d	40	91	273–275	271–273
5	$4-CH_3-C_6H_4$	NH₄OAc	4e	30	93	274–275	274–276
6	3-NO ₂ -C ₆ H ₄	NH₄OAc	4f	35	92	223–224	221–224
7	4-NO ₂ -C ₆ H ₄	NH₄OAc	4g	35	90	>300	318-320
8	4-CI-C ₆ H ₄	NH₄OAc	4h	30	95	285–287	288-290
9	4-OH-C ₆ H ₄	NH₄OAc	4i	35	90	265–267	264–265
10	4-(N(CH ₃) ₂)-C ₆ H ₄	NH₄OAc	4j	30	90	218–221	227–229
11	2-pyridyl	NH₄OAc	4k	45	87	274–277	275–278
12	C_6H_5	PhNH ₂	5a	40	93	105–107	113–115
13	4-CI-C ₆ H ₄	PhNH ₂	5b	30	95	84–85	88-89
14	2-CI-C ₆ H ₄	PhNH ₂	5c	30	90	120–121	120-121
15	4-Br-C ₆ H ₄	PhNH ₂	5d	30	92	269–271	275–278
16	4-OH-C ₆ H ₄	PhNH ₂	5e	40	87	230-232	231–233
17	$4-OCH_3-C_6H_4$	PhNH ₂	5f	40	90	253–255	261-262
18	$4-CH_3-C_6H_4$	PhNH ₂	5g	30	95	140–142	144–146
19	$4-NO_2C_6H_4$	PhNH ₂	5h	35	90	221–223	225-227
20	$3-NO_2C_6H_4$	PhNH ₂	5i	40	92	284–286	284-286
21	2-pyridyl	PhNH ₂	5j	50	85	209–212	211-213
22	4-CI-C ₆ H ₄	4-MePhNH ₂	5k	50	92	273–275	270–274
23	4-Br-C ₆ H ₄	4-MePhNH ₂	51	35	93	251–253	-
24	Isatine	4-MePhNH ₂	5m	50	95	272–275	271–273
25	4-CI-C ₆ H ₄	$PhCH_2NH_2$	5n	30	94	126–128	122–124
26	4-CI-C ₆ H ₄	PrNH ₂	5o	50	93	175–177	173–174

Table 2. Synthesis of 2,3-dihydroquinazolin-4(1H)-ones using $CoFe_2O_4@SiO_2@BIMA@Cu$ as a catalyst.

^alsolated yield.

^bThe melting points are not corrected.

reaction of 4-chlorobenzaldehyde, isatoic anhydride, and ammonium acetate was selected as model substrates and the reaction was carried out in various conditions to optimize the reaction (Scheme 3). The different solvents as well as solvent-free medium, temperatures and catalyst amounts were examined on the model reaction and the results are shown in Table 1. The refluxing aqueous condition, and use of 20 mg of CoFe₂O₄@SiO₂@BIMA@Cu as a catalyst, serves as the best condition with respect to green nature and clean workup procedure for this synthesis (Table 1, entry 11). To define the role of CoFe₂O₄@SiO₂@BIMA@Cu as the catalyst, the model reaction was performed under the same conditions with CoFe₂O₄, CoFe₂O₄@SiO₂@BIMA, and without any catalyst. With respect to reaction time and yield of product, the best result is achieved using CoFe₂O₄@SiO₂@BIMA@Cu as the catalyst (Table 1, entry 11–15).

After optimization of reaction conditions, in order to determine the generality and efficacy of the hybrid nanocatalyst, various aldehydes carrying either electron-donating or electron-withdrawing groups were reacted under the optimized reaction conditions (Scheme 3). Reactions for all of the various substrates proceed efficiently to obtain the corresponding 2,3-dihydroquinazolin-4(1*H*)-ones in good to excellent yields without formation of side products (Table 2). Arylaldehydes with electron-withdrawing substituents produced higher yields of desired products compared to arylaldehydes bearing electron-donating substituents (Table 2).



Figure 7. (a) The recyclability of hybrid nanocatalyst ($CoFe_2O_4@SiO_2@BIMA@Cu$) in the model reaction during six runs, (b) FT-IR spectrum, and (c) XRD patterns for fresh and reused catalyst.

The recovery and reusability of the catalyst are very important for commercial and industrial applications as well as green aspects. Recovery and reusability of $CoFe_2O_4@SiO_2@BIMA@Cu$ was investigated in the model reaction (benzaldehyde, ammonium acetate and isatoic anhydride, Figure 7). After completion of the reaction, the resulting solid mixture was diluted with hot EtOH (15 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 95%) could be obtained from each run. As seen in Figure 7a, the recycled catalyst could be reused six times without additional treatment or appreciable reduction in catalytic activity. In Figures 7b and c, the FT-IR spectra and XRD patterns of the fresh (a) and reused (b) catalyst are compared. 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 1.81×10^{-3} molg⁻¹ after six cycles based on ICP/OES measurement. The copper content in CoFe₂O₄@SiO₂@BIMA@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 CoFe₂O₄@SiO₂@BIMA@Cu catalyst confirms its stability, recyclability and performance for the synthesis of desired products.

Based on a literature survey, a tentative mechanism for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones in the presence of $CoFe_2O_4@SiO_2@BIMA@Cu$ is depicted in Scheme 4. The reaction may proceed via carbonyl group activation (1) by hybrid catalyst. The subsequent condensation with amine (2) leads to the ring opened intermediate (IN 1). The intermediate IN 1 undergoes decarboxylation to form the antranilamide (IN 2). The condensation of amine group with aldehyde (3) produces



Scheme 4. The proposed path for synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones using $CoFe_2O_4@SiO_2@BIMA-Cu$ as a hybrid catalyst.

Table 3. The comparison of $CoFe_2O_4@SiO_2@BIMA@Cu$ as a catalyst in the synthesis of 2,3-dihy-droquinazolin-4(1H)-ones with some other reported catalysts.

Entry	Catalyst	Condition	Time (min)	Yield (%)
1	Nano Fe ₃ O ₄	H ₂ O, Reflux	120	80 ^[36]
2	SBSSA	EtOH, 80 °C	130	90 ^[51]
3	Nano ZnO	Solvent-free, 70 °C	180	92 ^[52]
4	TBAB	H₂O, 70 °C	30	90 ^[31]
5	Nano-CuO	$H_2^{-}O:EtOH$, Reflux	180	85 ^[53]
6	β-Cyclodextrin-SO ₃ H	H ₂ O, 80 °C	60	90 ^[54]
7	Fe ₃ O ₄ @SiO ₂ -imid-PMA ⁿ	$H_2O:EtOH$, Reflux	120	82 [55]
8	Co-Am-benzamid@Al-SBA-15	EtOH, Reflux	25	94 ^[56]
9	[PyPS] ₃ PW ₁₂ O ₄₀	Solvent-free, MW, 80 °C	15	90 ^[57]
10	CoFe ₂ O ₄ @SiO ₂ @BIMA@Cu	H ₂ O, Reflux	30	93 ^[This work]

the imine intermediate **IN 3**. The nucleophilic attack of second amino group on activated imine double bond affords the corresponding 2,3-dihydroquinazolin-4(1*H*)-ones [36]. So, it is proposed that the Cu(II) ions act as Lewis acids and activate the carbonyl functional groups and facilitate the condensation reactions [48–50]. The porosity and high surface area of nanostructure (CoFe₂O₄@SiO₂@BIMA@Cu) provide suitable support for the chemical reactions and increase the catalytic performance of the prepared hybrid nanomaterial.

Comparison of the $CoFe_2O_4@SiO_2@BIMA@Cu$ nanostructure as catalyst with some previously reported catalysts for synthesis of 2,3-dihydroquinazolin-4(1*H*)-one

derivatives is shown in Table 3. The data confirm that the CoFe₂O₄@SiO₂@BIMA@Cu is a comparable, suitable and efficient catalyst for the synthesis of desired 2,3-dihydroquinazolin-4(1*H*)-ones.

4. Conclusion

Surface-modified magnetic nanoparticles were functionalized with Cu(II) complex tags. The Cu-complex decorated hybrid nanostructure ($CoFe_2O_4@SiO_2@BIMA@Cu$) was characterized using various techniques and its catalytic activity was considered in the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives. The desired products were synthesized by three component reaction of isatoiac anhydride, amine, and aldehyde in high yields within short reaction times. This strategy offers several key characteristics such as using a green solvent, high yield and purity, easy work-up and eco-friendly process, simple separation of catalyst by an external magnetic field. Cu grafting with organic functional groups on the inorganic support limit Cu leaching and particle growth, which permitted this hybrid nanocatalyst to be reused several times with only a slight diminish in its activity.

Funding

The authors acknowledge the financial support of the Research Council of Arak University.

References

- [1] R.C. Cioc, E. Ruijter, R.V. Orru. Green Chem., 16, 2958 (2014).
- [2] L.J. Yan, Y.C. Wang. ChemistrySelect, 1, 6948 (2016).
- [3] J. Zhu, Q. Wang, M.-X. Wang. *Multicomponent Reactions in Organic Synthesis*, 1st Edn, Wiley-VCH, Weinheim, Germany (2015).
- [4] J. Zhu, H. Bienayme. *Multicomponent Reactions*, 1st Edn, Wiley-VCH, Weinheim, Germany (2005).
- [5] J. Montgomery. Acc. Chem. Res., 33, 467 (2000).
- [6] H. Bienayme, K. Bouzid. Angew. Chem., Int. Ed., 37, 2234 (1998).
- [7] R.V. Orru, M. de Greef. Synthesis, 10, 1471 (2003).
- [8] L. Chen, X.-J. Huang, Y.-Q. Li, M.-Y. Zhou, W.-J. Zheng. Monatsh. Chem., 140, 45 (2009).
- [9] L.F. Tietze, A. Modi. Med. Res. Rev., 20, 304 (2000).
- [10] V.S. Misra, V.K. Saxena, R. Srivastava. Indian J. Pharm. Sci., 45, 207 (1983).
- [11] J.K. Padia, M. Field, J. Hinton, K. Meecham, J. Pablo, R. Pinnock, B.D. Roth, L. Singh, N. Suman-Chauhan, B.K. Trivedi, L. Webdale. J. Med. Chem. , 41, 1042 (1998).
- [12] Y. Xia, Z.Y. Yang, M.J. Hour, S.C. Kuo, P. Xia, K.F. Bastow, Y. Nakanishi, P. Namrpoothiri, T. Hackl, E. Hamel, H.K. Lee. *Bioorg. Med. Chem. Lett.*, **11**, 1193 (2001).
- [13] M.-J. Hour, L.-J. Huang, S.-C. Kuo, Y. Xia, K. Bastow, Y. Nakanishi, E. Hamel, K.H. Lee. J. Med. Chem., 43, 4479 (2000).
- [14] S.E. Lopez, M.E. Rosales, N. Urdaneta, M.V. Godoy, J.E. Charris. J. Chem. Res.(s), 2000, 258 (2000).
- [15] S.K. Krishnan, S. Ganguly, R. Veerasamy, B. Jan. Eur. Rev. Med. Pharmacol. Sci., 15, 673 (2011).
- [16] H. Georgey, N. Abdel-Gawad, S. Abbas. *Molecules*, 13, 2557 (2008).

- [17] J.A. Moore, G.J. Sutherland, R. Sowerby, E.G. Kelly, S. Palermo, W. Webster. J. Org. Chem., 34, 887 (1969).
- [18] W.K. Su, B.B. Yang. Aust. J. Chem. , 55, 695 (2002).
- [19] J.M. Khurana, G. Kukreja. J. Heterocycl. Chem., 40, 677 (2003).
- [20] L.-Y. Zeng, C. Chun. J. Heterocyclic Chem., 47, 1035 (2010).
- [21] D. Shi, L. Rong, J. Wang, Q. Zhuang, X. Wang, H. Hu. Tetrahedron Lett., 44, 3199 (2003).
- [22] D. Shi, C. Shi, J. Wang, L. Rong, Q. Zhuang, X. Wang. J. Heterocycl. Chem., 42, 173 (2005).
- [23] C.L. Yoo, J.C. Fettinger, M.J. Kurth. J. Org. Chem., 70, 6941 (2005).
- [24] Y.S. Sadanandam, K.R.M. Reddy, A.B. Rao. Eur. J. Org. Chem., 22, 169 (1987).
- [25] V.B. Reo, C.V. Ratnam. Indian J. Chem., 18, B, 409 (1979).
- [26] M. Dabiri, P. Salehi, S. Otokesh, M. Baghbanzadeh, G. Kozehgary, A.A. Mohammadi. Tetrahedron Lett., 46, 6123 (2005).
- [27] P. Salehi, M. Dabiri, M.A. Zolfigol, M. Baghbanzadeh. Synlett, 1155 (2005).
- [28] S.Y. Abbas, K.A.M. El-Bayouki, W.M. Basyouni. Synth. Commun., 46, 993 (2016).
- [29] J. Chen, W. Su, H. Wu, M. Liu, C. Jin. Green Chem., 9, 972 (2007).
- [30] J. Chen, D. Wu, F. He, M. Liu, H. Wu, J. Ding, W. Su. Tetrahedron Lett., 49, 3814 (2008).
- [31] M.A.B. Fard, A. Mobinikhaledi, M. Hamidinasab. Synth. React. Inorg. Met.-Org. Nano-Met. Chem., 44, 567 (2014).
- [32] W. Injumpa, P. Ritprajak, N. Insin. J. Magn. Magn. Mater., 427, 60 (2017).
- [33] S.H. Araghi, M.H. Entezari. Appl. Surf. Sci., 333, 68 (2015).
- [34] M.A. Bodaghifard, M. Hamidinasab, N. Ahadi. Curr. Org. Chem., 22, 234 (2018).
- [35] M.B. Gawande, P.S. Branco, R.S. Varma. Chem. Soc. Rev., 42, 3371 (2013).
- [36] Z.-H. Zhang, H.-Y. Lü, S.-H. Yang, J.-W. Gao. J. Comb. Chem., 12, 643 (2010).
- [37] Z. Mahhouti, H.E. Moussaoui, T. Mahfoud, M. Hamedoun, M.E. Marssi, A. Lahmar, A.E. Kenz, A. Benyoussef. J. Mater. Sci: Mater. Electron., 30, 14913 (2019).
- [38] S. Shylesh, V. Schünemann, W.R. Thiel. Angew. Chem. Int. Ed. Engl., 49, 3428 (2010).
- [39] Y. Leng, K. Sato, Y. Shi, J.G. Li, T. Ishigaki, T. Yoshida, H. Kamiya. J. Phys. Chem. C, 113, 16681 (2009).
- [40] A.L. Morel, S.I. Nikitenko, K. Gionnet, A. Wattiaux, J. Lai-Kee-Him, C. Labrugere, B. Chevalier, G. Deleris, C. Petibois, A. Brisson, M. Simonoff. ACS Nano, 2, 847 (2008).
- [41] M.A. Bodaghifard, Z. Faraki, A.R. Karimi. Curr. Org. Chem., 20, 1648 (2016).
- [42] A. Mobinikhaledi, M. Zendehdel, M. Hamidinasab, M.A. Bodaghifard. *Heterocycl. Commun.*, 15, 451 (2009).
- [43] A. Mobinikhaledi, S. Asadbegi, M.A. Bodaghifard. Mol. Divers., 20, 461 (2016).
- [44] N. Ahadi, M.A. Bodaghifard, A. Mobinikhaledi. Appl. Organometal. Chem., 33, e4738 (2019).
- [45] R.-H. Chen, J.-F. Xiong, P. Peng, G.-Z. Mo, X.-S. Tang, Z.-Y. Wang, X.-F. Wang. Asian J. Chem., 26, 926 (2014).
- [46] P. Peng, J.F. Xiong, G.Z. Mo, J.L. Zheng, R.H. Chen, X.Y. Chen, Z.Y. Wang. Amino Acids, 46, 2427 (2014).
- [47] C. Chen, H. Liu, B. Zhang, Y. Wang, K. Cai, Y. Tan, C. Gao, H. Liu, C. Tan, Y. Jiang. *Tetrahedron*, **72**, 3980 (2016).
- [48] L. Álvarez-Miguel, I. Álvarez-Miguel, J.M. Martín-Álvarez, C.M. Álvarez, G. Rogez, R. García-Rodríguez, D. Miguel. *Dalton Trans.*, 48, 17544 (2019).
- [49] F.-Y. Cheng, C.-Y. Tsai, B.-H. Huang, K.-Y. Lu, C.-C. Lin, B.-T. Ko. Dalton Trans., 48, 4667 (2019).
- [50] K. Ojaghi Aghbash, N. Noroozi Pesyan, H. Batmani. ACS Omega, 5, 22099 (2020).
- [51] K. Niknam, M.R. Mohammadizadeh, S. Mirzaee. Chin. J. Chem., 29, 1417 (2011).
- [52] I. Yavari, S. Beheshti. J. Iran. Chem. Soc., 8, 1030 (2011).
- [53] J. Zhang, D. Ren, Y. Ma, W. Wang, H. Wu. Tetrahedron, 70, 5274 (2014).
- [54] J. Wu, X. Du, J. Ma, Y. Zhang, Q. Shi, L. Luo, B. Song, S. Yang, D. Hu. Green Chem., 16, 3210 (2014).
- [55] M. Esmaeilpour, J. Javidi, S. Zahmatkesh, N. Fahimi. Monatsh. Chem., 148, 947 (2017).
- [56] J. Safaei-Ghomi, R. Teymuri, A. Bakhtiari. BMC Chem., 3, 26 (2019).
- [57] Y. Yang, R. Fu, Y. Liu, J. Cai, X. Zeng. Tetrahedron, 76, 131312(2020).