FULL PAPER



Magnetic Fe3O4 nanoparticles supported imine/Thiophene-nickel (II) complex: A new and highly active heterogeneous catalyst for the synthesis of polyhydroquinolines and 2, 3-dihydroquinazoline-4(1H)-ones

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Funding information Ilam University A new magnetically separable nickel catalyst $(Ni(NO_3)_2$ -Imine/Thiophene-Fe₃O₄@SiO₂) was readily prepared and structurally characterized by Fourier transform infrared spectroscopy (FT-IR), Scanning electron microscopy (SEM), Energy-dispersive X-ray spectroscopy (EDX), Vibrating sample magnetometer (VSM), X-Ray diffraction (XRD) and Atomic absorption spectroscopy (AAS). The Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂ exhibited efficient catalytic activity in the synthesis of 2,3-dihydroquinazoline-4(1H)-ones and polyhydroquinolines. Catalysis research under water and solvent-free conditions makes also this synthetic protocol ideal and fascinating from the environmental point of view. The catalyst can be magnetically recovered after the reaction and can be reused for many times without appreciable decrease in activity.

KEYWORDS

2,3-dihydroquinazoline-4(1H)-ones, magnetically nickel catalyst, magnetically separation, polyhydroquinolines, solvent-free condition, water

1 | INTRODUCTION

Catalysis research campaign is a hot research topic in modern organic synthesis. Compared with the heterogeneous catalysts, homogeneous catalysts exhibit high catalytic activities in chemical processes due to their solubility in reaction media, which increases catalytic site accessibility for the substrate.^[1,2] However, separating them from the reaction mixture to avoid contamination of the product requires expensive and tedious purification steps.^[3,4] In recent times. the immobilization of homogeneous catalysts on support materials (such as inorganic silica and organic polymers), for incorporate the preponderances of both heterogeneous and homogeneous catalysis, have emerged as an efficient catalytic strategy to overcome this drawback.^[5,6] Therefore, the search for finding new support materials and heterogenization techniques is a hot research topic in modern research in catalysis. Among various solid supports used for the immobilization of metallic catalysts, magnetic nanoparticles have emerged as a robust and high-surface-area heterogeneous catalyst support, because they could not only stabilize the reaction catalytic species, but also improve the catalytic activity^[7-12] The simple separation of MNPs-supported catalysts from products or mixture reaction by an external magnet is the most notable advantage of magnetic nanoparticles.^[13–15] It is noteworthy that magnetic-supported catalysts can be reused many times while keeping their initial activity. Among the various employed magnetic NPs as the core magnetic support, Fe₃O₄ nanoparticles have been widely studied both for their scientific interests and technological applications.^[15] In describing the magnetic nanoparticles can be said that in fact the magnetic separation is an admirable and valuable victory in the research campaign of chemistry catalysis.

In recent times, catalysis research under green mediums or in the absence of solvent has received special attention in both academic and industrial research.^[16]

2,3-dihydroquinazoline-4(1H)-ones and polyhydroquinolines are two important category of nitrogen-containing heterocyclic compounds that are broadly distributed in many natural products and bio-active molecules.^[17-21] 2. 3dihydroquinazoline-4(1H)-one and polyhydroquinoline structural motifs have been known to possess diverse biological activities such as antitumor, anticancer, antibiotic,

TEOS, PEG, EtOH

NH₃, H₂O, r.t, 36 h

ОНС

EtOH, reflux, N₂,16 h

well-known drugs for the treatment of cardiovascular and Alzheimer's diseases.^[31,32] Furthermore, polyhydroquinoline derivatives are well-known as Ca²⁺ channel blockers and drugs of NADH co-enzymes.^[33,34] The biological and pharmaceutical activities of 2,3-dihydroquinazoline-4(1H)-one and polyhydroquinoline derivatives have encouraged organic chemists to develop numerous one-pot, green strategies for their preparation. In recent times, search for finding new $_{\rm NH_2}$

antidiabetic, antibacterial, antidefibrillatory, antipyretic, and anticonvulsant agents.^[22-30] Polyhydroquinolines also are

SCHEME 1 Stepwise preparation of magnetic nanoparticles supported imine/ Thiophene nickel (II) complex (Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂)



Thiophene-Fe₃O₄@SiO₂ (E)

NO₂ 95 85 (A) 75 2879 625 101 65 90 (B) 70 1400.73 3391.42 2972.56 2877.26 1629.70 1084.67 954.80 799.13 589.78 454.27 50 100 80 (C) 60 625.73 324.88 38 **M35.25** 002.64 144.35 2821 40 100 (D) 60 1425.22 1625.85 097.84 798.24 159.71 20 100 (E) 80 88 8 3365.60 **1378.09** 463.20 1612.25 5.8 2003 8 38 60 3500 3000 2500 2000 1000 500 1500 Wavenumber cm-1

(MeO)₃Si <

0-

EtOH/H2O, 40 °C, 8 h

Fe₃O₄@SiO₂



FeCl_{3.}6H₂O

FeCl₂4H₂O

NH₄OH N₂, r.t

Ni(NO₃)_{2.}3H₂O

EtOH, reflux, 6 h



and efficient synthetic routs toward the preparation of 2, 3dihydroquinazoline-4(1H)-one and polyhydroquinoline derivatives have been focused on using highly active and reusable catalysts under environmentally benign mediums.

Now, as a part of our research program directed toward the utility of magnetic nanoparticles,^[6,33] herein we wish to report that Imine/Thiophene-functionalized silica-coated magnetic Fe₃O₄ nanoparticles is a new support for the immobilization of nickel (II) complex (Ni(NO₃)₂). The activity of this magnetically nickel catalyst was investigated in the synthesis of 2,3-dihydroquinazoline-4(1H)-ones and polyhydroquinolines.

2 | RESULT AND DISCUSSION

2.1 | Preparation and characterization of Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂

The magnetic nanoparticles supported Imine/Thiophene nickel (II) complex was successfully fabricated by the concise route outlined in Scheme 1. Silica-coated magnetic Fe_3O_4 nanoparticles ($Fe_3O_4@SiO_2$) were prepared by chemical co-precipitation strategy.^[35] The $Fe_3O_4@SiO_2$ -propyl chloride was prepared by the reaction of $Fe_3O_4@SiO_2$ with 3-aminopropyltrimethoxysilane (APTMS) in thermal EtOH/ H_2O for 8 h.^[5] Next, the imine bond was formed through the condensation between $Fe_3O_4@SiO_2$ -propyl amine with thiophene-2-carbaldehyde in refluxing ethanol under

nitrogen conditions. Ultimately, the Imine/Thiophene-Fe₃O₄@SiO₂ reacted with Cu(NO₃)₂.3H₂O in refluxing ethanol for 6 h to provide the target catalyst (Ni(NO₃)₂-Imine/ Thiophene-Fe₃O₄@SiO₂).

As-prepared catalyst was characterized by several characterization techniques such as FT-IR, SEM, EDX, VSM, XRD, TGA, AAS and ICP/OES analysis.

The FT-IR spectra for the Fe₃O₄ MNPs (a), Fe₃O₄@SiO₂ APTMS-Fe₃O₄@SiO₂ Imine/Thiophene-(b), (c), Fe₃O₄@SiO₂ (d) and Ni(NO₃)₂-Imine/Thiophene- $Fe_3O_4@SiO_2$ (e) are displayed in Figure 1. The FT-IR analysis of the Fe₃O₄ MNPs exhibits a characteristic peak at 579 cm⁻¹, which is attributed to the Fe-O stretching vibration. Also the broad band at around 3400 cm⁻¹ is attributed to bound water O-H stretching vibration adsorption. In the curve of $Fe_3O_4@SiO_2$ (b), two peaks at 954 and 1084 cm⁻¹ can be attributed the Si-O-Si stretching vibration of silica shell. The FT-IR analysis of the APTMS-Fe₃O₄@SiO₂ (c) exhibits that broad bond at 3435 cm^{-1} is assigned to NH₂ group and two weak peaks at 2921 and 2858 cm⁻¹ are ascribed to the C-H stretching vibration of alkyl chain of amine. In the curve of Imine/Thiophene-Fe₃O₄@SiO₂ (d), stretching vibrations of imine bond appeared at 1625 cm^{-1} , while this band shifts to lower frequency (1612 cm⁻¹) in the Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂ catalyst. This band shifts to lower frequency confirmed the formation of metal-ligand bonds. Therefore, it can be concluded that Ni (II) complex was



FIGURE 2 SEM image of the Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂



FIGURE 3 EDX spectrum of the Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂

supported successfully on the surface of Imine/Thiophene-functionalized silica-coated magnetic Fe_3O_4 nanoparticles.

The morphology and size of the nickel nano-solid was investigated by Scanning electron microscope (SEM) as shown in Figure 2 The SEM image of $Ni(NO_3)_2$ _Imine/Thiophene-Fe₃O₄@SiO₂ shows that the catalyst is formed of nanometre-sized particles.

Energy-dispersive X-ray spectroscopy (EDX) is an efficient spectra technique to characterize the components of catalyst. The EDX analysis of Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂ is shown in Figure 3. As shown in Figure 3, characteristic peaks containing Si, O and Fe are indicative of the formation of silica coated magnetic support. The results confirmed the presence of Fe (74.72%), O (7.98%), Si (2.35%), C (4.03%), N (1.08%), S (0.96%) and Ni (8.88%) in the sample. Also, another point taken from the EDX analysis is that there are no any extra peaks related to any impurity. As a result of the analysis, the Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂ catalyst has been successfully synthesized.

The magnetic property of the catalyst was investigated by vibrating sample magnetometer (VSM) at ambient temperature. The curves of magnetization for the Fe_3O_4 MNPs (green line) and Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂ (blue line) are depicted in Figure 4. According to the magnetization curves, the saturation of the nanoparticles decreased from 55 emu/g in the initial Fe_3O_4 sample to 34 emu/g in the final Ni(NO₃)₂-Imine/Thiophene-



FIGURE 4 Magnetization curves for Fe_3O_4 MNPs (green line) and $Ni(NO_3)_2$ _Imine/Thiophene-Fe₃O₄@SiO₂ (blue line) at room temperature



FIGURE 5 The XRD pattern of the $Ni(NO_3)_2$ -Imine/Thiophene-Fe₃O₄@SiO₂

 $Fe_3O_4@SiO_2$ catalyst. The decrease of the saturation magnetization can be related to the presence of Ni(NO₃)₂-Imine/ Thiophene on the surface of the Fe₃O₄@SiO₂ nanoparticles supports.

X-ray diffraction (XRD) is an efficient spectra technique to the better reorganization of the major properties of the magnetite structures. In fact, the formation of magnetite crystal phase in the nanomagnetic catalyst in aggregate powder form can be as well identified by the X-ray diffraction (XRD). X-ray diffraction (XRD) spectrum of



FIGURE 6 TGA thermogram of the Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂

Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂ is displayed in Figure 5 the strong characteristic diffraction peaks at $2\theta = 35.1^{\circ}$, 41.4° , 50.6° , 63.3° , 67.5° and 74.4° were observed for Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂ nanoparticles, in which are related to the (220), (311), (400), (422), (511) and (440) planes. These results are similar to those of the standard JCPDS 89–3854 exhibiting the iron oxide characteristic peaks with cubic structure^[36] Accordingly, XRD analysis confirmed as well that the Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂ have been fabricated successfully without damaging the crystal structure of Fe₃O₄ core.

The thermal stability of Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂ was investigated by thermogravimetric analysis (TGA), and the results is shown in Figure 6. As shown in Figure 6, the small amount of weight loss below 140°C is due to desorption of physically adsorbed solvents and surface hydroxyl groups. Organic groups have been reported to desorb at temperatures above 220°C. The last stage of degradation in the region of 250-550°C, probably is due to thermal decomposition of the complex.

Atomic absorption spectroscopy (AAS) of the catalyst showed that the amount of nickel loaded on the surface of magnetic Fe_3O_4 nanoparticles is about 15×10^{-5} mmol.g⁻¹. Also, the Ni amount was measured by atomic absorption spectroscopy (AAS), which the

	O I NH4C	H Catalyst Solvent, Temperature		
Entry	Catalyst (mg)	Solvent (Temp. ^o C)	Time (min)	Yield (%) ^a
1	25	Peg (100 °C)	20	70
2	25	DMF (100 °C)	20	67
3	25	CH ₃ CN (reflux)	20	16
4	25	EtOH (reflux)	20	56
5	25	EtOH/H ₂ O (1:1) (80 °C)	20	45
6	25	H ₂ O (reflux)	20	50
7	25	Solvent-free (100 °C)	20	96
8	20	Solvent-free (100 °C)	20	96
9	15	Solvent-free (100 °C)	20	90
10	10	Solvent-free (100 °C)	20	78
11	20	Solvent-free (r.t)	20	Trace
12	20	Solvent-free (60 °C)	20	55
13	20	Solvent-free (90 °C)	20	87
14	20	Solvent-free (110 °C)	20	95
15		Solvent-free (100 °C)	120	Trace

TABLE 1 Optimization of the reaction conditions ^a

^aReactions conditions: aldehyde (1 mmol), dimedone (1 mmol), ethyl acetoacetate (1 mmol) and ammonium acetate (1.2 mmol). ^b Isolated yield.



results were very close to ICP-OES method $(15.37 \times 10^{-5} \text{ mmol.g}^{-1})$.

All together, these analyses are indicative of the successful immobilization of Ni (II) complex onto the Imine/Thiophene-Fe₃O₄@SiO₂ nanoparticles.

2.2 | Catalytic studies

After characterization of the catalyst, the catalytic activity of $Ni(NO_3)_2$ -Imine/Thiophene-Fe₃O₄@SiO₂ was studied in the synthesis of polyhydroquinoline and 2,3-dihydroquinazoline-4(1H)-one derivatives.

2.2.1 | Polyhydroquinolines

Four-component reaction of benzaldehyde (1a), ethyl acetoacetate, dimedone and ammonium was chosen as a simple model substrate to optimize the reaction conditions. First, the effect of solvent and solvent-free condition on the four-component reaction, catalyzed by 25 mg of Ni(NO₃)₂₋Imine/Thiophene-Fe₃O₄@SiO₂, was investigated (Table 1, Entries 1-7). A number of solvents such as PEG, DMF, CH₃CN, EtOH, EtOH/H₂O and H₂O were tested. In all cases, the reaction afforded the desired product in poor to moderate yields. As shown in Table 1, the maximum yield was observed in the absence of solvent (Table 1 , Entry 7). Next, under solvent-free conditions, the effect of catalyst loading on the four-component reaction was investigated (Table 1, Entries 7–10). As seen in Table 1, the best results in terms of reaction time and isolated yield were observed in the presence of 20 mg of Ni(NO₃)₂_Imine/ Thiophene-Fe₃O₄@SiO₂ (Table 1, Entry 8). The effect of temperature on the reaction was then studied. The reaction was evaluated at different temperatures including r.t, 60, 90 and 110°C (Table 1, Entries 11-14). As seen in Table 1, higher reaction temperature (110°C) did not improve the reaction time and product yield, while lower reaction temperatures (r.t, 60 and 90°C) decreased the product yield. Finally, to clarify the role of catalyst in the process, the reaction was carried out at in the absence of catalyst. But, only a trace amount of the product 2a was observed after 120 min (Table 1, Entry 15). Accordingly, 20 mg of Ni(NO₃)₂₋Imine/Thiophene-Fe₃O₄@SiO₂ in the

absence of solvent at 100°C was considered as the standardized reaction conditions (Table 1, Entry 8).

Under the standardized conditions, the generality of the catalytic system was evaluated by the reaction of various

TABLE 2Ni(NO3)2-Imine/Thiophene-Fe3O4@SiO2 catalyzed thesynthesis of polyhydroquinolines at 100 °C under solvent-freeconditions

Aldehyde	Product	Time (min)	Yield (%) ^a	Mp (°C) [ref.]
C ₆ H ₅ CHO	2a	20	96	214-216 ^[33]
4-ClC ₆ H ₅ CHO	2b	40	98	235-237 ^[33]
4-OMeC ₆ H ₅ CHO	2c	65	93	252-255 ^[33]
4-FC ₆ H ₅ CHO	2d	25	92	184–186 ^[33]
4-NO ₂ C ₆ H ₅ CHO	2e	60	86	232-236 ^[33]
4-OHC ₆ H ₅ CHO	2f	100	85	230-231 ^[33]
4-OEtC ₆ H ₅ CHO	2 g	55	91	182–185 ^[33]
3-NO ₂ C ₆ H ₅ CHO	2 h	60	83	174–177 ^[5]
3-OHC ₆ H ₅ CHO	2i	70	88	216-218 ^[5]
3-BrC ₆ H ₅ CHO	2j	50	87	230-232 ^[33]
2-OMeC ₆ H ₅ CHO	2 k	30	91	250-251 ^[5]
2-NO ₂ C ₆ H ₅ CHO	21	45	90	207-209 ^[5]
	Aldehyde C ₆ H ₅ CHO 4-ClC ₆ H ₅ CHO 4-OMeC ₆ H ₅ CHO 4-FC ₆ H ₅ CHO 4-FC ₆ H ₅ CHO 4-OMC ₆ H ₅ CHO 4-OHC ₆ H ₅ CHO 4-OHC ₆ H ₅ CHO 3-OHC ₆ H ₅ CHO 3-BrC ₆ H ₅ CHO 3-BrC ₆ H ₅ CHO 2-OMeC ₆ H ₅ CHO 2-NO ₂ C ₆ H ₅ CHO	Aldehyde Product C ₆ H ₅ CHO 2 a 4-CHC ₆ H ₅ CHO 2 b 4-OMC ₆ H ₅ CHO 2 c 4-FC ₆ H ₅ CHO 2 c 4-FC ₆ H ₅ CHO 2 c 4-NO ₂ C ₆ H ₅ CHO 2 c 4-OHC ₆ H ₅ CHO 2 c 4-OHC ₆ H ₅ CHO 2 c 3-NO ₂ C ₆ H ₅ CHO 2 c 3-NO ₂ C ₆ H ₅ CHO 2 c 3-BC ₆ H ₅ CHO 2 c 3-BC ₆ H ₅ CHO 2 c 3-BC ₆ H ₅ CHO 2 c 2-OMC ₆ H ₅ CHO 2 c 2-NO ₂ C ₆ H ₅ CHO 2 c	High Time Aldehyde Porden (min) Cafbachyde Ca 20 4-ChCafbach Ca 40 4-Ordeafbach Ca 40 4-Ordeafbach Ca 60 4-Ordeafbach Ca 60 4-Stabachyschen Ca 60 4-Stabachyschen Ca 60 4-Stabachyschen Ca 60 4-Ordeafbach Ca 60 4-Ordeafbach Ca 60 4-Ordeafbach Ca 60 4-Ordeafbach Ca 60 3-Ordeafbach Ca 60	Time Yield Aldehyde Poduci (m) (m) ² C ₆ H ₅ CHO 2a 20 96 4-ChC ₆ H ₅ CHO 2b 92 93 4-OMeC ₆ H ₅ CHO 2b 92 93 4-OMeC ₆ H ₅ CHO 2c 65 93 4-FC ₆ H ₅ CHO 2c 62 92 4-NO ₂ C ₆ H ₅ CHO 2c 63 93 4-OHC ₆ H ₅ CHO 2c 63 93 4-OHC ₆ H ₅ CHO 2c 93 93 3-NO ₂ C ₆ H ₅ CHO 2c 63 93 3-NO ₂ C ₆ H ₅ CHO 2c 70 88 3-SHC ₆ H ₅ CHO 2c 70 89 3-SHC ₆ H ₅ CHO 2c

^aIsolated yield.



SCHEME 3 Proposed mechanism for the synthesis of polyhydroquinolines catalyzed by Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂

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aromatic aldehydes (bearing electron-donating and electronwith drawing groups) with ethyl acetoacetate, dimedone and ammonium acetate (Scheme 2). The results are listed in Table 2. As seen in Table 2, a diverse range of the 1,4-DHP products were synthesized in high to excellent yields in less than 100 min. Aromatic aldehydes containing nitro group on aromatic ring were applicable to this reaction and the desired products were afforded in lower yields and longer reaction times (Table 2, Entry 4, 8 and 12).

A proposed mechanistic path for the synthesis of polyhydroquinolines using $Ni(NO_3)_2$ -Imine/Thiophene-Fe₃O₄@SiO₂ as catalyst is depicted in Scheme 3.

2.2.2 | 2,3-dihydroquinazoline-4(1H)-ones

In order to establish the optimum condition for the synthesis of 2,3-dihydroquinazoline-4(1H)-ones, the cyclocondensation

of anthranilamide with banzaldehyde was chosen as a model substrate, and the effect of various parameters (such as solvent type, catalyst and temperature amount) on the model reaction was studied. First, the effect of solvent on the model reaction was tested. Among all tested solvents (Table 3, Entries 1-7), water was found to be the best solvent in terms of the product yield (Table 3, Entry 7). Next, the effect of catalyst loading (3, 5, 6, 7, 8, and 10) on the model reaction was evaluated (Table 3, Entries 8–12). The results in Table 3 showed that the best results were obtained in 50 min in the presence of 5 mg of catalyst (Table 3, Entry 9). The yield remained unchanged when the catalyst loading was increased from 5 to 10 mg (Table 3, Entries 10–12). The reaction at lower reaction temperatures (r.t, 60, 80 and 90°C) was also tested, but, the obtained results were disappointing (Table 3, Entries 13-16). Only a trace amount of the desired product (4a) was obtained in the absence of the Ni catalyst (Table 3, Entry 17). Ultimately, the reaction

TABLE 3 Optimization of the reaction conditions ^a

	NH ₂	+ CHO Catalyst Solvent, Temperature		
Entry	Catalyst (mg)	Solvent (Temp. ^o C)	Time (min)	Yield (%) ^a
1	7	Peg (100 °C)	50	75
2	7	PhMe (100 °C)	50	15
3	7	1,4-dioxane (100 °C)	50	10
4	7	CH ₃ CN (reflux)	50	55
5	7	EtOH (reflux)	50	70
6	7	EtOH/H2O (80 °C)	50	87
7	7	H ₂ O (reflux)	50	97
8	3	H ₂ O (reflux)	50	90
9	5	H ₂ O (reflux)	50	97
10	6	H ₂ O (reflux)	50	97
11	8	H ₂ O (reflux)	50	96
12	10	H ₂ O (reflux)	50	93
13	5	$H_2O(r.t)$	50	5
14	5	H ₂ O (60 °C)	50	58
15	5	H ₂ O (80 °C)	50	82
16	5	H ₂ O (90 °C)	55	92
17		H ₂ O (reflux)	120	Trace
18		Solvent-free (100 °C)	240	No

^aReaction conditions: anthranilamide (1.05 mmol) and 4-chlorobenzaldehyde (1 mmol) in the presence of catalyst and solvent (2 ml). ^b Isolated yield.

SCHEME 4 Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂ catalyzed the cyclocondensation of anthranilamide with aldehydes



TABLE 4	Ni(NO ₃) ₂ _Imine/Thiop	phene-Fe ₃ O ₄ @SiC	₂ catalyzed the sy	nthesis of 2, 3-dihy	droquinazolin-4(1H)	-ones in refluxing water

Entry	Aldehyde	Product	Time (min)	Yield (%) ^a	Mp (°C) [ref.]
1	C ₆ H ₅ CHO	4a	50	97	216-218 ^[33]
2	4-ClC ₆ H ₅ CHO	4b	40	99	198-200 ^[33]
3	4-OMeC ₆ H ₅ CHO	4c	55	92	181–184 ^[33]
4	4-FC ₆ H ₅ CHO	4d	45	91	198-201 ^[33]
5	4-MeC ₆ H ₅ CHO	4 e	75	90	222-225 ^[33]
6	4-NO ₂ C ₆ H ₅ CHO	4 f	110	94	199-200 ^[33]
7	4-OEtC ₆ H ₅ CHO	4 g	70	93	185–187 ^[33]
8	3-BrC ₆ H ₅ CHO	4 h	100	87	173–175 ^[33]
9	3-NO ₂ C ₆ H ₅ CHO	4i	125	91	212-214 ^[33]
10	2-OMeC ₆ H ₅ CHO	4j	85	95	169–172 ^[33]
11	2-ClC ₆ H ₅ CHO	4 k	80	86	203-205 ^[33]
12	3,4-(OMe) ₂ C ₆ H ₄ CHO	41	150	88	213-215 ^[33]

^aIsolated yield.

did not occur in the absence of catalyst and solvent even after a long reaction time (240 min) (Table 3, Entry 18).

After evaluation of the solvent nature, catalytic loading, the reaction time, and the reaction temperature, the best result



was obtained in the presence of 5 mg of the catalyst in refluxing water (Table 3, Entry 9).

To determine the scope of the protocol, a nice collection of aromatic aldehydes subjected to react with anthranilamide under the optimized reaction conditions (Scheme 4). All results are listed in Table 4. As shown in Table 4, the reactions proceeded smoothly to give the 2,3dihydroquinazoline-4(1H)-one products in admirable yields over suitable reaction times. High reaction yield was obtained when disubstituted aromatic aldehyde vg was targeted as a substrate (Table 4, Entry 12).

A plausible mechanistic path for the cyclocondensation of aldehydes with anthranilamide is depicted in Scheme 5. It seems that enhancing the electrophilicity of the carbonyl group in aldehyde has occurred using supported metal. Thus, the intermediate A is formed by the reaction of 2aminobenzamide and activated aldehyde. After dehydration of intermediate A, the imine intermediate B is produced. The intramolecular nucleophilic attack of the amide nitrogen on activated imine group following by a proton transfer leads to the desired 2,3-dihydroquinazolinones.

TABLE 5 Comparison of the activity of various catalysts in the synthesis of products 2b (Entries 1–5) and 4b (Entries 6–10)

Entry	Catalyst	Condition	Time (min)	Yield (%)	[ref.]
1	PdCl ₂	THF, reflux	240	87	[25]
2	K ₇ [PW ₁₁ CoO ₄₀]	CH ₃ CN, reflux	30	80	[37]
3	Cu-SPATB/Fe ₃ O ₄	Peg-400, 80°C	65	96	[38]
4	[TBA] ₂ [W ₆ O ₁₉]	Solvent-free, 110°C	20	95	[39]
5	This catalyst	Solvent-free, 100°C	40	98	This work
6	$KAl(SO_4)_2.E_{12}H_2O$	EtOH, reflux	300	80	[40]
7	Glycerosulfonic acid	Glycerol, 80°C	360	97	[41]
8	Silica sulfuric acid	H ₂ O,80°C	180	81	[42]
9	SBNPSA	EtOH, reflux	150	87	[43]
10	This catalyst	H ₂ O, reflux	40	99	This work

In order to show the efficiency of present work, the obtained results for the synthesis of synthesis of products 2b and 4b were compared with the previously reported procedures in the literature (Table 5). As shown in Table 5, this methodology is superior to some of the reported previously procedures in terms of product yield, reaction time and reaction conditions.

2.2.3 | Reusability of the catalyst

The recovery and reusability of catalyst is a valuable advantage in modern catalysis research, in which makes them very notable from commercial and economical points of view. In this respect, the reusability of Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂ in the synthesis of products 2b and 4b (as the model reactions) was investigated. After completion of the reaction, the catalyst was separated easily and rapidly from the product by exposure to an external magnet (Figure 7). The remaining nano-magnetic catalyst was washed several times with ethyl acetate and dried to remove residual product, and subjected to the next run. The magnetically separation minimizes the loss of catalyst during separation. The recovered catalyst could be reused seven times without any significant loss in catalytic efficiency (Figure 8).



FIGURE 7 (A) reaction mixture and (B) recovery of catalyst from the reaction mixture using an external magnet



FIGURE 8 Reusability of Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂ in the synthesis of products2b and 4b

The loading amount of Ni in the recovered catalyst after seven times was about 13.47×10^{-5} mmol.g⁻¹, which is determined by ICP/OES analysis.

3 | CONCLUSION

In summary, from obtained experimental results we can conclude that the Ni(NO₃)₂_Imine/Thiophene-Fe₃O₄@SiO₂ is a versatile and efficient heterogeneous catalyst for the synthesis of *N*-heterocyclic compounds (2,3-dihydroquinazoline-4(1H)-ones and polyhydroquinolines). It is noteworthy that the catalyst can be readily separated and recovered from the reaction system by a magnet, and reused for at least seven times without noticeable loss of its activity. Good to excellent yields, simplicity of operation, high catalytic activity, catalysis research under water or solvent-free conditions, easy magnetically separation and reusability of the solid catalyst are notable advantages of this protocol. As a result of this study, this catalytic system can act as an efficient strategy for the synthesis of biologically and pharmaceutically active molecules.

4 | EXPERIMENTAL

4.1 | Materials

Chemicals were purchased from Fisher and Merck. The reagents and solvents used in this work were obtained from Sigma-Aldrich, Fluka or Merck and used without further purification. The infrared spectra (IR) of samples were recorded in KBr disks using a NICOLET impact 410 spectrometer. ¹HNMR and ¹³CNMR spectra were recorded with a Bruker DRX-400 spectrometer at 400 and 100 MHz respectively. Nanostructures were characterized using a Holland Philips X, pert X-ray powder diffraction (XRD) diffractometer (Co K α , radiation = 0.154056 nm), at a scanning speed of 2° min⁻¹ from 10° to 80° . Scanning electron microscope (SEM) was performed on a FEI Quanta 200 SEM operated at a 20 kV accelerating voltage. The thermogravimetric analysis (TGA) curves are recorded using a PL-STA 1500 device manufactured by Thermal Sciences. The magnetic measurements were carried out in a vibrating sample magnetometer (VSM, BHV-55, Riken, Japan) at room temperature.

4.2 | Preparation of the magnetic Fe₃O₄-nanoparticles

The mixture of FeCl₃.6H₂O (5.838 g, 0.0216 mol) and FeCl₂.4H₂O (2.147 g, 0.0108 mol) were dissolved in 100 ml of deionized water in a three-necked bottom (250 mL) under N₂ atmosphere. After that, under rapid mechanical stirring, 10 ml of NH₃ was added into the solution within 30 min with vigorous mechanical stirring. After

-WILEY-Organometallic Chemistry being rapidly stirred for 30 min, the resultant black dispersion was heated to 80°C for 30 min. The black precipitate formed was isolated by magnetic decantation, washed with doubledistilled water until neutrality, and further washed twice with ethanol and dried at room temperature.^[29,44]

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4.3 | Preparation of the Fe₃O₄@SiO₂:

Then the obtained Fe₃O₄ MNPs (2 g) were dispersed in 20 ml of water by sonication for 30 min, and then 2-propanol (200 ml) was added to the reaction mixture. The reaction mixture was stirred using a magnetic stirrer at room temperature. Under continuous stir-ring, PEG (5.36 g), water (20 ml), ammonia solution (10 ml, 28 wt.%) and 2 ml of tetraethyl orthosilicate (TEOS) were respectively added into the suspension, and continuously reacted for 38 h under stirring at room temperature. Then the products ($Fe_3O_4@SiO_2$) were isolated with an external magnet and washed two times with ethanol and distilled water.^[35]

4.4 | Preparation of APTMS-Fe₃O₄@SiO₂

The obtained Fe₃O₄@SiO₂ nanoparticles (1.5 g) was dispersed in 250 ml ethanol/water (volume ratio, 1:1) by sonication for 30 min, and then APTMS (2.5 ml) was added to the mixture reaction. The reaction mixture was stirred using mechanical stirring under N₂ atmosphere at 40°C for 8 h. then, the nanoparticles was re-dispersed in ethanol by sonication for 5 times and separated through magnetic decantation. The nanoparticles product (APTMS-Fe₃O₄@SiO₂) was dried at room temperature.^[2]

4.5 | Preparation of imine/Thiophene-Fe₃O₄@SiO₂

The APTMS-Fe₃O₄@SiO₂ (3 g) were dispersed in EtOH (60 ml) by ultrasonic bath for 10 min. Thiophene-2carbaldehyde (6 mmol, 672 g) was added and stirred at reflux temperature for 12 h under N₂ atmosphere. Then, the prepared functionalized magnetic nanoparticles were separated by magnetic decantation and washed five times with ethanol to remove the unattached substrates. The resulting product was dried at room temperature.

4.6 | Preparation of Ni(NO₃)₂_Imine/ Thiophene-Fe₃O₄@SiO₂

In the last step, Ni(NO₃)₂.3H₂O (5 mmol, 1.45 g) was added to Imine/Thiophene-Fe₃O₄@SiO₂ (2.5 g) in absolute ethanol (50 mL) and the resultant mixture was stirred under reflux for 6 h. Finally, the synthesized nano-solid (Ni(NO₃)₂-Imine/ Thiophene-Fe₃O₄@SiO₂) was separated by magnetic decantation. The nano-magnetic catalyst washed several times with

absolute ethanol, and dried under vacuum at room temperature (Scheme 1).

4.7 | General procedure for the synthesis of polyhydroquinolines

A mixture of aldehyde (1 mmol), dimedon (1 mmol), ethylacetoacetate (1 mmol), ammonium acetate (1.2 mmol) and Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂ (20 mg) was stirred at 100°C under solvent-free conditions. Reaction progress was monitored by TLC (acetone: n-hexane, 3:7). After completion of the reaction, the catalyst was separated using an external magnet and washed with ethyl acetate. Then, the solvent was evaporated and all products were recrystallized from ethanol. The pure polyhydroquinoline derivatives were obtained in excellent yields (83-98%).

4.8 | General procedure for the synthesis of 2,3-dihydroquinazolin-4(1H)-ones:

A mixture of anthranilamide (1.05 mmol, 142 mg), aldehyde (1 mmol) and Ni(NO₃)₂-Imine/Thiophene-Fe₃O₄@SiO₂ (5 mg) in water (2 ml) was stirred at reflux temperature. Reaction progress was monitored by TLC (acetone: n-hexane, 2:8). After time specified in Table 4, reaction mass was allowed to cool down to room temperature. CH₂Cl₂ $(3 \times 5 \text{ ml})$ was added to reaction mixture and the catalyst was separated by an external magnet. CH₂Cl₂ was evaporated under reduced pressure to afford the crude products. The obtained crude products were further recrystallized from ethanol to get the pure 2,3-dihydroquinazolin-4(1H)-ones (86-99%).

All the products reported here are known compounds and their spectroscopic data are reported in the literature.

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