



FULL PAPER

Synthesis and characterization of Fe₃O₄@THAM-SO₃H as a highly reusable nanocatalyst and its application for the synthesis of dihydropyrano[2,3-*c*]pyrazole derivatives

Homayoun Faroughi Niya | Nourallah Hazeri | Malek Taher Maghsoodlou

Department of Chemistry, Faculty of Science, University of Sistan and Baluchestan, P.O. Box 98135-674, Zahedan, Iran

Correspondence

Nourallah Hazeri, Department of Chemistry, Faculty of Science, University of Sistan and Baluchestan, P.O. Box 98135-674, Zahedan, Iran.
Email: nhazeri@chem.usb.ac.ir; n_hazeri@yahoo.com

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University of Sistan and Baluchestan

In this work, a new, green and beneficial nanomagnetic catalyst was easily fabricated using sulfuric acid as an acidic group on Fe₃O₄ nanoparticles coated with tris (hydroxymethyl) aminomethane (THAM). The synthesized catalyst was characterized by FT-IR, TGA/DTG, XRD, TEM, EDS, VSM, and SEM analyses. Next, its catalytic activity was studied for the synthesis of dihydropyrano[2,3-*c*]pyrazole derivatives. This catalyst has advantages such as high catalytic activity, non-toxicity, easy separation from the reaction mixture using an external magnet and reuses for several times without significantly reducing in its catalytic activity.

KEYWORDS

Fe₃O₄@THAM-SO₃H, heterogeneous nanocatalyst, magnetite nanoparticles, multicomponent reaction

1 | INTRODUCTION

In recent years, magnetic nanoparticles (MNPs) (especially superparamagnetic Fe₃O₄ nanoparticles) are used in various applications in pharmaceutical industries and green chemistry such as drug delivery vehicles,^[1,2] sensors,^[3] and catalysts.^[4,5] MNPs received considerable attention due to their superior characteristics such as high surface energies, high surface to volume ratios, easy recoverability, enhanced dispersion, high catalytic performance, and reusing without loss of their catalytic activity.^[6–12] One of the most essential abilities of MNPs in organic chemistry is their catalyst role in multicomponent reactions (MCRs). The use of heterogeneous magnetic nanocatalyst has been widely reported. These nanocatalysts have small size and large external surface areas that allow great accessibility of substrates to the surface-bound active catalytic sites.^[13–15] Also, their applications are increased due to their superior characteristics such as easily removable from the reaction mixture using an external magnet and reuse for several times

without significantly reducing in its catalytic activity.^[16–20]

As a review of previous studies, many methods have been reported for sulfuric acid coupling as an acidic group on magnetic nanoparticles. Among them, Fe₃O₄@APTES@isatin-SO₃H,^[21] CoFe₂O₄@SiO₂-SO₃H,^[22] Fe₃O₄@BNPs@SiO₂-SO₃H,^[23] Fe₃O₄@zeolite-SO₃H,^[24] Fe_{3-x}Ti_xO₄-SO₃H^[25] and Fe₃O₄@GO-naphthalene-SO₃H^[26] are examples of catalysts.

Pyranopyrazoles and their derivatives such as dihydropyrano[2,3-*c*]pyrazole derivatives are an important class of heterocyclic compounds which have significant biological activities, such as anticancer,^[27] vasodilatory^[28] and bactericidal^[29] activities. These molecules are also used as biodegradable agrochemicals and pharmaceutical ingredients.^[30] Furthermore, dihydropyrano[2,3-*c*]pyrazole derivatives have attracted attention as molluscicidal agents^[31,32] and potential insecticidal.^[33]

In continue the development of synthesis of MNPs as a green catalyst for the production of pharmaceutical

compounds in one pot synthesis, we wish to propose a nanomagnetic catalyst using sulfuric acid as an acidic group on Fe_3O_4 nanoparticles coated with THAM. Then, the synthesized nanocatalyst was used as a recyclable catalyst sorbents for one-pot synthesis of dihydropyrano[2,3-*c*]pyrazole derivatives from reaction between benzaldehyde (**1**), malononitrile (**2**) and 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (**6**) or hydrazine hydrate (**3**) and acetoacetate (**4**) (Scheme 1).

2 | EXPERIMENTAL

2.1 | General

Melting points and FT-IR spectra of compounds were measured with an Electrothermal 9100 apparatus. The ^1H NMR spectra were obtained on BRUKER DRX 300 and 400 MHz, using DMSO as a solvent. Ferrous chloride tetrahydrate ($\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$) and ferric chloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$) were obtained from Aldrich. Other reagents and solvents were obtained from Aldrich and Merck and were used without further purification.

2.2 | Synthesis of the magnetic Fe_3O_4 nanoparticles

Fe_3O_4 nanoparticles (NPs) have been synthesized by chemical coprecipitation method. Briefly, $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (0.994 g, 5.0 mmol) and $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (2.703 g, 10.0 mmol) were dissolved in 100 ml deionized water under nitrogen flow. Thereafter, 25% ammonia solution was added dropwise to the solution under vigorous stirring at 1000 rpm. After reaching the pH of 11, the mixture was stirred vigorously for 1 hr at room temperature. Finally, the nanoparticles obtained were separated and washed several times with ethanol and diethyl ether and dried for 2 hr at 60 °C in an oven.

2.3 | Synthesis of magnetite nanoparticles coated by tris (hydroxymethyl) aminomethane

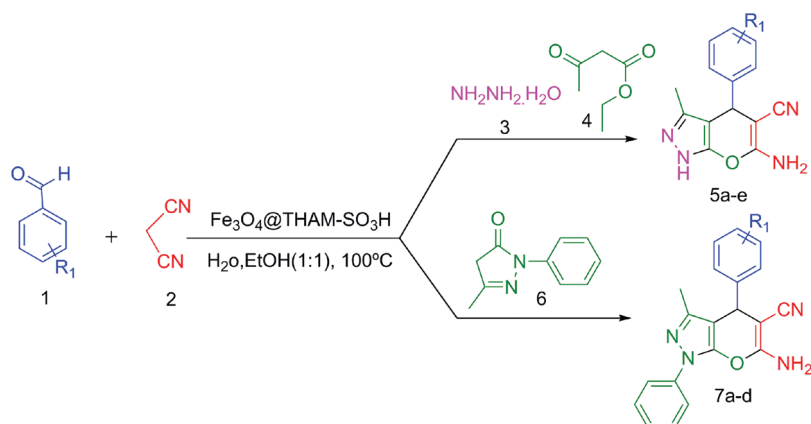
THAM-capped Fe_3O_4 were prepared according to previous reports.^[34] The synthesized Fe_3O_4 (1.0 g) and 50 ml of ethanol were ultrasonically dispersed for 30 min. Then, to this suspension, 2.0 g of tris (hydroxymethyl) aminomethane (THAM) was added. The reaction mixture was stirred for 24 hr at 100 °C under N_2 atmosphere. Finally, The resulting nanoparticles ($\text{Fe}_3\text{O}_4@\text{THAM}$) were separated by an external magnet and washed several times with water to remove unreacted material and dried at 60 °C.

2.4 | Synthesis of $\text{Fe}_3\text{O}_4@\text{THAM-SO}_3\text{H}$

An amount of 1.0 g of the prepared magnetite $\text{Fe}_3\text{O}_4@\text{THAM}$ nanoparticles was dispersed in 50 ml chloroform by ultrasonic bath for 20 min. Then, subsequently, chlorosulfonic acid (1.5 ml) was added dropwise and the resulting reaction mixture was stirred for 4 hr at room temperature under N_2 atmosphere. The resulting nanoparticles ($\text{Fe}_3\text{O}_4@\text{THAM-SO}_3\text{H}$) were separated by an external magnet and washed several times with ethanol to remove the remaining acid and dried at 60 °C.

2.5 | General procedure for four-component synthesis of dihydropyrano[2,3-*c*]pyrazole derivatives

Initially, the reactant ethyl acetoacetate (1.0 mmol) and hydrazine hydrate (1.0 mmol) were taken at room temperature until 3-methyl-2-pyrazoline-5-one was precipitated as white solid. Then, malononitrile (1.0 mmol), aromatic aldehyde (1.0 mmol) and $\text{Fe}_3\text{O}_4@\text{THAM-SO}_3\text{H}$ (10 mg) in ethanol/water (1:1) was added to the reaction mixture at 100 °C and stirred for the appropriate time.



SCHEME 1 $\text{Fe}_3\text{O}_4@\text{THAM-SO}_3\text{H}$ catalyzed the one-pot synthesis of dihydropyrano[2,3-*c*]pyrazoles derivatives

After the completion of the reaction which was monitored by TLC, the product was dissolved in hot ethanol and the catalyst separated by an external magnet, and the resulting solution was cooled to room temperature, the desired product precipitated and crystalized, then it was filtered.

2.6 | General procedure for three-component synthesis of dihydropyrano[2,3-*c*]pyrazole derivatives

A mixture of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (1.0 mmol), malononitrile (1.0 mmol), aldehydes (1.0 mmol) and $\text{Fe}_3\text{O}_4@\text{THAM-SO}_3\text{H}$ (10 mg) in ethanol/water (1:1) was stirred at 100 °C for the appropriate time. After the completion of the reaction which was monitored by TLC, the product was dissolved in hot ethanol and the catalyst separated by an external magnet, and the resulting solution was cooled to room temperature, the desired product precipitated and crystalized, then it was filtered. The spectra of selected compounds have been reported in supporting information.

2.7 | Selected spectra for seven known products are given below

2.7.1 | 6-Amino-1,4-dihydro-3-methyl-4-(2-chlorophenyl)pyrano[2,3-*c*]pyrazole-5-carbonitrile (5b)

FT-IR (KBr, ν_{max} , cm^{-1}): 3391 (NH_2), 3357 (NH_2), 3314 (NH), 2925 ($\text{C-H}_{\text{aliphatic}}$), 2190 (CN), 1654 (C=N), 1272 (C-O). ^1H NMR (300 MHz, DMSO) δ = 1.82 (s, 3H, CH_3), 5.12 (s, 1H, C-H), 7.00 (s, 2H, NH_2), 7.22–7.66 (m, 4H, Ar-H), 12.18 (s, 1H, NH).

2.7.2 | 6-Amino-1,4-dihydro-3-methyl-4-(2-nitrophenyl)pyrano[2,3-*c*]pyrazole-5-carbonitrile (5c)

FT-IR (KBr, ν_{max} , cm^{-1}): 3414 (NH_2), 3376 (NH_2), 3315 (NH), 2186 (CN), 1158 (C-O). ^1H NMR (300 MHz, DMSO) δ = 1.79 (s, 3H, CH_3), 5.11 (s, 1H, CH), 7.05 (s, 2H, NH_2), 7.33–7.92 (m, 4H, Ar-H), 12.22 (s, 1H, NH).

2.7.3 | 6-amino-1,4-dihydro-3-methyl-4-(3,4-dimethoxyphenyl)pyrano[2,3-*c*]pyrazole-5-carbonitrile (5d)

FT-IR (KBr, ν_{max} , cm^{-1}): 3456 (NH_2), 3346 (NH_2), 3229 (NH), 2971 ($\text{C-H}_{\text{aliphatic}}$), 2209 (CN), 1568, 1642 (C=C),

752, 853 (C-H). ^1H -NMR (300 MHz, DMSO) δ = 1.83 (s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 4.94 (s, 1H, CH), 6.54 (d, J = 3 Hz, 1H, Ar-H), 6.79 (dd, J_1 = 8.7 Hz, J_2 = 3 Hz, 1H, Ar-H), 6.84 (s, 2H, NH_2), 6.95 (d, J = 9 Hz, 1H, Ar-H), 12.03 (s, 1H, N-H).

2.7.4 | 6-amino-1,4-dihydro-3-methyl-4-(4-bromophenyl)pyrano[2,3-*c*]pyrazole-5-carbonitrile (5e)

^1H -NMR (300 MHz, DMSO) δ = 1.80 (s, 3H, CH_3), 4.63 (s, 1H, CH), 6.96 (s, 2H, NH_2), 7.15 (d, J = 8 Hz, 2H, Ar-H), 7.54 (d, J = 8 Hz, 2H, Ar-H), 12.17 (s, 1H, N-H).

2.7.5 | 6-Amino-3-methyl-1,4-diphenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (7a)

FT-IR (KBr, ν_{max} , cm^{-1}): 3471 (NH_2), 3324 (NH), 3063 ($\text{C-H}_{\text{aromatic}}$), 2919 ($\text{C-H}_{\text{aliphatic}}$), 2198 (CN), 1592, 1516 (C=C), 685, 753 (C-H). ^1H -NMR (300 MHz, DMSO): (δ , ppm): 1.80 (s, 3H, CH_3), 4.70 (s, 1H, CH), 7.23 (s, 2H, NH_2), 7.26–7.40 (m, 6H, Ar-H), 7.51 (t, J = 8 Hz, 2H, Ar-H), 7.81 (d, J = 9 Hz, 2H, Ar-H).

2.7.6 | 6-Amino-1,4-dihydro-3-methyl-4-(2,4-dichlorophenyl)-1-phenylpyrano[2,3-*c*]pyrazole-5-carbonitrile (7b)

^1H NMR (400 MHz, DMSO): δ = 1.81 (s, 3H, CH_3), 4.74 (s, 1H, CH), 7.31–7.44 (m, 5H, NH_2 and ArH), 7.48–7.52 (m, 2H, ArH), 7.62 (s, 1H, ArH), 7.78 (d, J = 8 Hz, 2H, ArH).

2.7.7 | 6-amino-1,4-dihydro-3-methyl-4-(4-chlorophenyl)-1-phenylpyrano[2,3-*c*]pyrazole-5-carbonitrile (7c)

^1H NMR (400 MHz, DMSO): δ = 1.79 (s, 3H, CH_3), 5.16 (s, 1H, CH), 7.28–7.79 (m, 9H, ArH), 7.81 (s, 2H, NH_2).

3 | RESULTS AND DISCUSSION

3.1 | Synthesis and characterization of catalyst

In this work, we prepared a new nanocatalyst ($\text{Fe}_3\text{O}_4@\text{THAM-SO}_3\text{H}$) by following the method shown

in Scheme 2. In the first step, The Fe_3O_4 MNPs were prepared by chemical coprecipitation method. Then, chlorosulfonic acid was coated on the surface of magnetite nanoparticles using tris (hydroxymethyl) aminomethane. The synthesized nanocatalyst was characterized using several techniques, including Fourier transform infrared (FT-IR), X-ray diffraction (XRD), thermogravimetric (TGA), differential thermal analysis (DTA), vibrating sample magnetometer (VSM), field emission scanning electron microscopy (FE-SEM), X-ray spectroscopy (EDS), and TEM analyses.

The determination of the size and morphology of the $\text{Fe}_3\text{O}_4@$ THAM- SO_3H was performed by FESEM. As shown in Figure 1, The particles of uncoated Fe_3O_4 and $\text{Fe}_3\text{O}_4@$ THAM- SO_3H are uniform in both shape and size. The FESEM image of the nanocatalyst ($\text{Fe}_3\text{O}_4@$ THAM- SO_3H) showed the spherical-shaped nanoparticles and an average size of approximately 14 nm. The size histogram of Fe_3O_4 (a) and $\text{Fe}_3\text{O}_4@$ THAM- SO_3H (b) was constructed by measuring 200 particles that appear in the FESEM image (Figure 2).

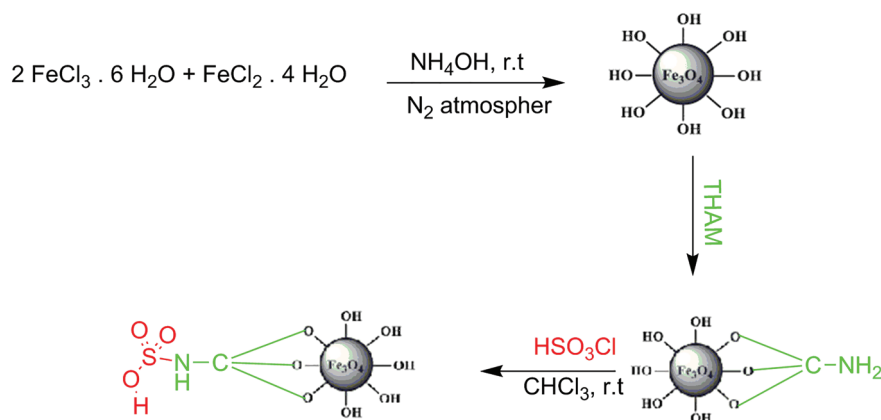
The EDS spectrum of $\text{Fe}_3\text{O}_4@$ THAM- SO_3H exhibited in Figure 3. This spectrum showed the presence of oxygen (O, 25%), sulfur (S, 2.2%), nitrogen (N, 1.2%), carbon (C, 17.3%) and iron (Fe, 54.3%) elements. This spectrum is proof for the fact that the organic layer (THAM- SO_3H) was immobilized onto the Fe_3O_4 nanoparticles.

TEM images, which is presented in Figure 4, clearly demonstrates that the nanocatalyst was composed of two parts, brighter and darker parts (core-shell structure). The brighter parts of the image are likely related to the organic layer anchored to the surface of the Fe_3O_4 NPs and the darker parts correspond to magnetic nanoparticles. Also, the TEM image of $\text{Fe}_3\text{O}_4@$ THAM- SO_3H exhibits that the morphology of nanoparticles is almost spherical with a narrow size distribution of about 11 nm (Figure 5), which confirmed the achieved SEM data.

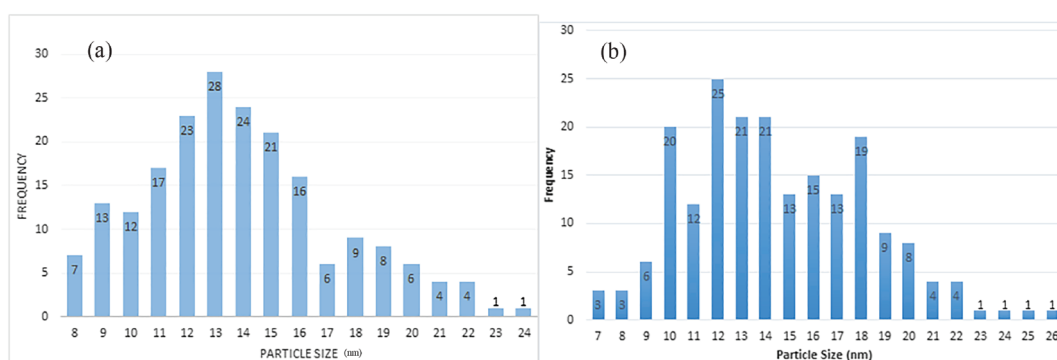
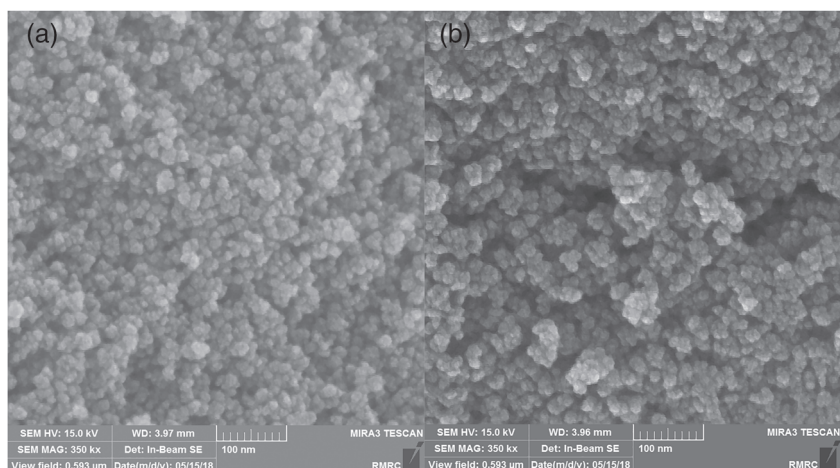
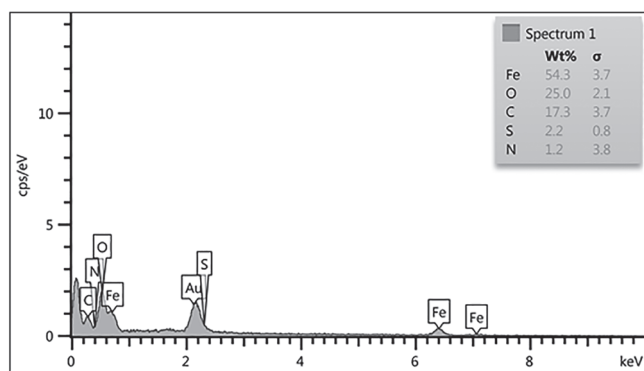
The characterization of $\text{Fe}_3\text{O}_4@$ THAM- SO_3H was confirmed by FT-IR spectrum (Figure 6) which showed spectra of Fe_3O_4 (a) and $\text{Fe}_3\text{O}_4@$ THAM- SO_3H (b). In Figure 6a can be seen the Fe-O stretching vibration of Fe_3O_4 at $550\text{--}650\text{ cm}^{-1}$. Also, two peaks at 1618 cm^{-1} and 3374 cm^{-1} are attributed to bending vibration and stretching vibration of the OH functional groups on the surface of Fe_3O_4 , respectively. The spectrum of $\text{Fe}_3\text{O}_4@$ THAM- SO_3H (Figure 6b) shows some bands in $1000\text{--}1250\text{ cm}^{-1}$ which are attributed to the absorption S-O and S=O stretching bands of $-\text{SO}_3\text{H}$ moiety on $\text{Fe}_3\text{O}_4@$ THAM- SO_3H surface. In addition, the peak at 3405 cm^{-1} in the spectrum of $\text{Fe}_3\text{O}_4@$ THAM- SO_3H was probably attributed to the $-\text{SO}_2\text{-OH}$ groups, which is overlapped by the Fe-OH stretching vibration.^[21]

The thermal stability of $\text{Fe}_3\text{O}_4@$ THAM- SO_3H nanoparticles was studied by TG/DTG analysis in the decomposition area of $0\text{--}600\text{ }^\circ\text{C}$ with a heating rate of $10\text{ }^\circ\text{C}$ per minute under nitrogen atmosphere (Figure 7). As can be seen, $\text{Fe}_3\text{O}_4@$ THAM- SO_3H nanoparticles displayed four weight-loss steps. The initial weight loss (4.82%) from room temperature to $180\text{ }^\circ\text{C}$ is related to loss of physically adsorbed solvent and the surface hydroxyl groups. The second weight loss (5.09%) between 180 and $330\text{ }^\circ\text{C}$ is due to thermal decomposition of acidic functional groups (SO_3H) of the nanocatalyst. The other organic moiety grafted on the Fe_3O_4 NPs decomposed at elevated temperatures (weight loss 11.41%). The total weight loss was computed to be 16.5%. In accordance with this mass loss, it was computed that the amount of 0.85 mmol of the organic layer (THAM- SO_3H) was loaded on 1 g of Fe_3O_4 nanoparticles. Furthermore, the DTG curve shows that the decomposition of the organic structure mainly happened at $250\text{ }^\circ\text{C}$. So, the $\text{Fe}_3\text{O}_4@$ THAM- SO_3H is stable below this temperature.

The XRD pattern of $\text{Fe}_3\text{O}_4@$ THAM- SO_3H and Fe_3O_4 was investigated in the domain of $5\text{--}80$ degrees (Figure 8). The powder XRD pattern of the Fe_3O_4



SCHEME 2 Preparation of $\text{Fe}_3\text{O}_4@$ THAM- SO_3H

FIGURE 1 SEM images of Fe₃O₄ (a) and Fe₃O₄@THAM-SO₃H (b)**FIGURE 2** The size histogram of Fe₃O₄ (a) and Fe₃O₄@THAM-SO₃H (b)**FIGURE 3** EDS spectrum of Fe₃O₄@THAM-SO₃H

(Figure 8a) exhibited diffraction peaks at $2\theta = 30.03^\circ$, 35.68° , 43.36° , 53.85° , 57.35° , 62.79° and 74.43° , which are associated with corresponding indices of (2 0 2), (3 1 1), (4 0 0), (4 2 2), (5 1 1), (4 4 0) and (6 6 0), respectively. In the XRD pattern of Fe₃O₄@THAM-SO₃H (Figure 8b), an additional broad peak at region lower than 20° is seen which can be attributed to the existence of amorphous organic layer (THAM-SO₃H) that was immobilized onto the Fe₃O₄ nanoparticles.

The magnetic properties of Fe₃O₄ NPs and Fe₃O₄@THAM-SO₃H were analyzed *via* VSM at room temperature (Figure 9). The M(H) hysteresis loop was completely reversible. Hence, these results indicate that nanocatalyst possesses sufficient superparamagnetism. The magnetic saturation (M_s) values of Fe₃O₄ NPs and Fe₃O₄@THAM-SO₃H are 116.6 and 42.3 emu g⁻¹, respectively. The decrease of M_s for the synthesized nanocatalyst (Fe₃O₄@THAM-SO₃H) is due to the non-magnetic nature of the organic layer anchored to the surface of the Fe₃O₄ NPs.

3.2 | Catalytic application of Fe₃O₄@THAM-SO₃H

In order to evaluate the catalytic activity of the Fe₃O₄@THAM-SO₃H nanoparticles, they were used in the synthesis of dihydropyran[2,3-*c*]pyrazole derivatives (Scheme 1). To find the optimal reaction conditions, the four-component reaction of benzaldehyde (1), malononitrile (2), hydrazine hydrate (3) and acetoacetate (4) was chosen as a model reaction. Initially, the influence of a variety of solvents was investigated using

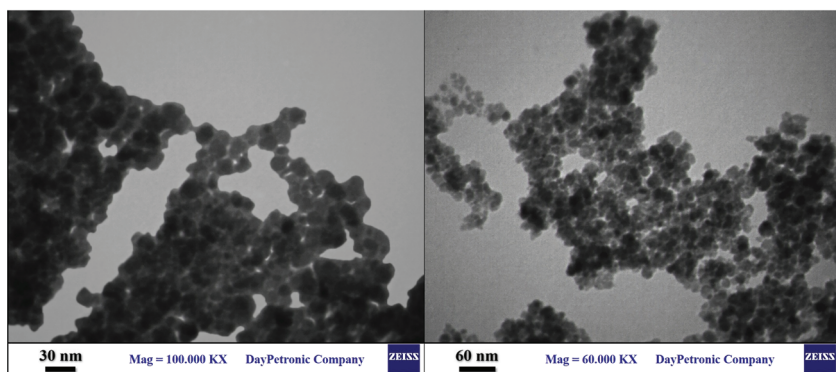


FIGURE 4 TEM images of Fe₃O₄@THAM-SO₃H

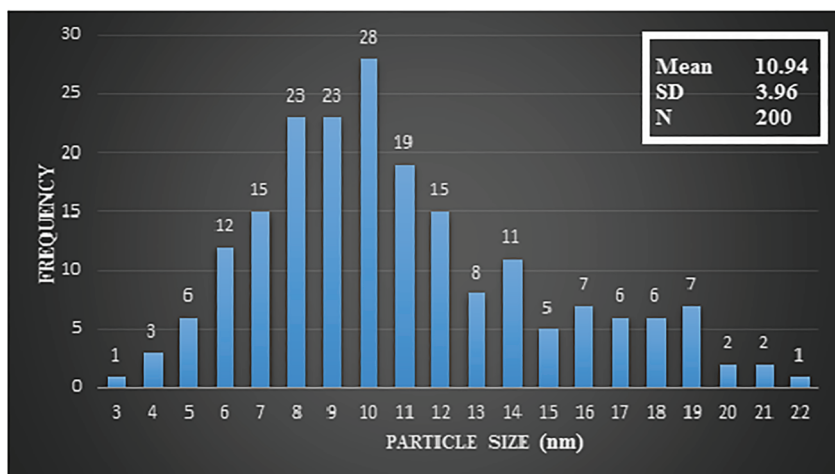


FIGURE 5 The size histogram of Fe₃O₄@THAM-SO₃H

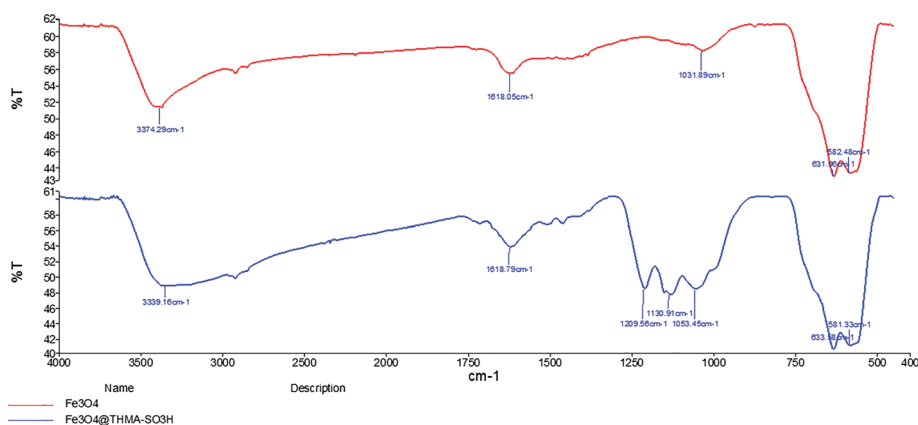


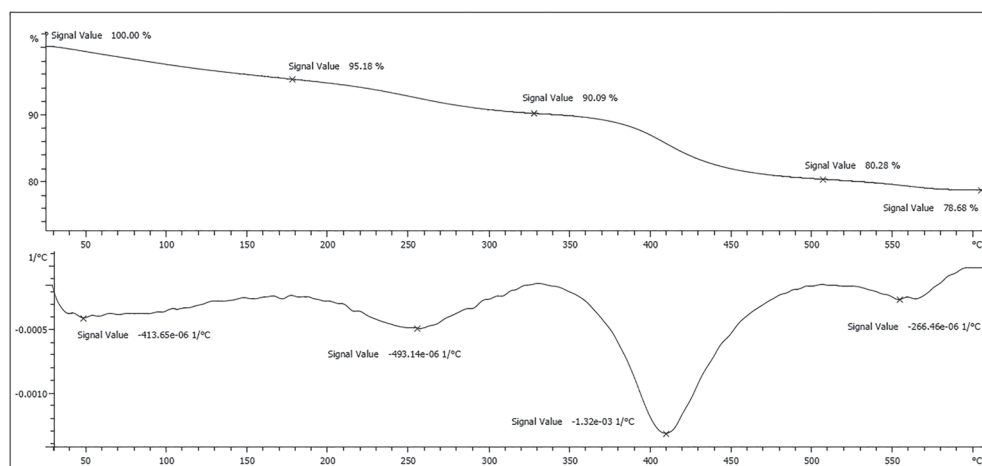
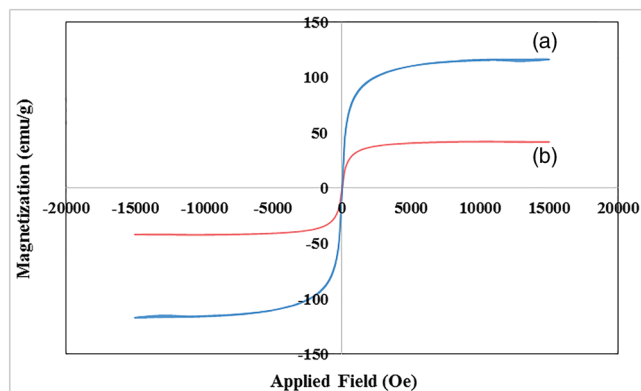
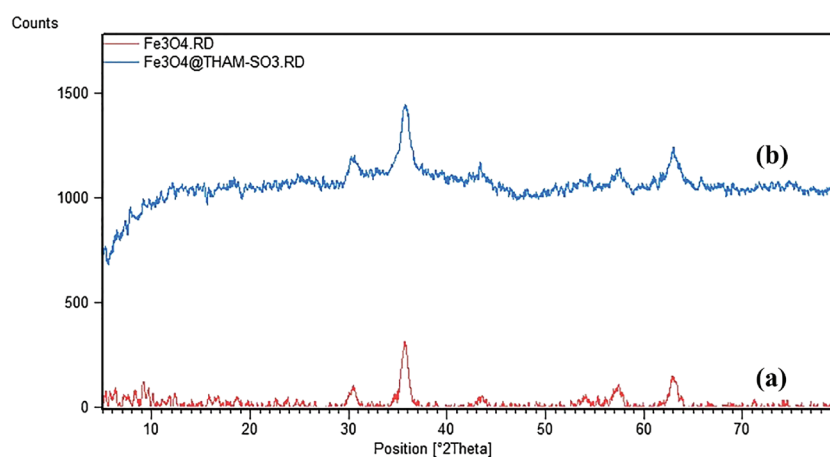
FIGURE 6 FT-IR spectra of Fe₃O₄ (a) and Fe₃O₄@THAM-SO₃H (b)

various solvents such as ethanol, water, or mixture of ethanol:water (1:1). All of the results are registered in Table 1. Among the studied solvents, mixture of ethanol:water (1:1) exhibited the most potent effect on the model reaction (Table 1, entry 2).

In the next step, the model reaction was performed with various amounts of nanoparticles (5, 7.5, 10, 15 mg). All of the results are registered in Table 2. The best result was obtained in the presence of 10 mg of Fe₃O₄@THAM-SO₃H as a catalyst which confirmed the catalytic activity of Fe₃O₄@THAM-SO₃H nanoparticles. Finally, the effect

of temperature was studied. Based on our experimental results, the best result is obtained in ethanol:water (1:1) at 100 °C in the presence of 10 mg of Fe₃O₄@THAM-SO₃H for 10 min. In these conditions, the desired product was obtained at 80% yields (Table 2, entry 9).

After optimizing the reaction conditions, of benzaldehyde (1), malononitrile (2), hydrazine hydrate (3) and acetoacetate (4) under optimized conditions for preparation of dihydropyrano[2,3-*c*]pyrazole derivatives was investigated. Interestingly, a variety of aromatic aldehydes including, *para*, *meta*, *ortho*-substituted were used

FIGURE 7 TGA and DTG curves of Fe₃O₄@THAM-SO₃H**FIGURE 8** XRD pattern of Fe₃O₄ (a) and Fe₃O₄@THAM-SO₃H (b)**FIGURE 9** VSM spectra of Fe₃O₄ (a) and Fe₃O₄@THAM-SO₃H (b)**TABLE 1** Optimization of solvent at 60 °C

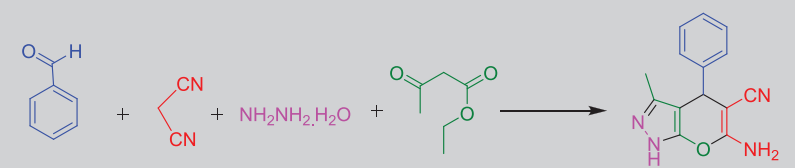
Entry	Solvent	Time (min)	Yield (%)
1	EtOH	50	37
2	H ₂ O:EtOH (1:1)	30	67
3	H ₂ O	35	66

and corresponding products were synthesized in excellent yields at short reaction times (Table 3).

A proposed mechanism for the synthesis of dihydropyrano[2,3-*c*]pyrazoles is provided in Scheme 3. In the first step, the electrophilicity of the carbonyl group of aldehyde (**1**) was increased by the proton from Fe₃O₄@THAM-SO₃H. Next, the Knoevenagel condensation of malononitrile (**2**) with activated aldehyde generates 2-benzylidenemalononitrile intermediate (**a**). In the second step, Michael addition of 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (**6**) or pyrazolone (**b**) (from the reaction between ethyl acetoacetate (**4**) and hydrazine hydrate (**3**)) to 2-benzylidene malononitrile intermediate (**a**), followed by continuous intramolecular cyclization happen to give the intermediate (**d**). Finally, tautomerization affords the corresponding product.

3.3 | Catalyst recovery and reuse

The recyclability and stability of the catalyst was checked using the three-component reaction of

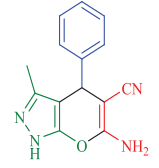
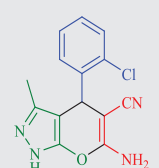
TABLE 2 Effect of the catalyst amount and temperature on the model reaction


Entry	Catalyst (gr)	Temperature (°C)	Time (min)	Yield (%)
1	No catalyst	60	40	56
2	0.005	60	40	50
3	0.0075	60	40	53
4	0.01	60	30	67
5	0.015	60	30	55
7	0.01	70	30	70
8	0.01	90	20	68
9	0.01	100	10	80
10	0.01	110	10	75

4-chlorobenzaldehyde, malononitrile, and 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one, using the recycled catalyst under the optimized conditions. After completion of the reaction, the product was dissolved in hot ethanol (30 ml) and the catalyst separated by an external magnet and washed with ethanol for three

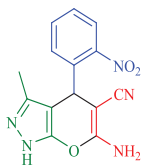
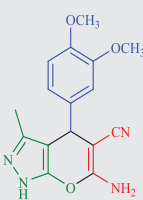
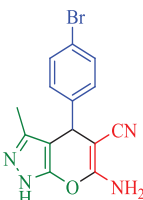
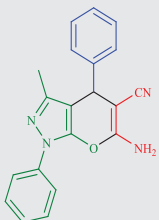
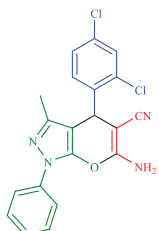
times to remove any organic moieties present and dried at 60 °C. The catalyst was used directly in the next run. As shown in Figure 10, the catalyst could be reused eight times with no significant reduction in its activities. This small decrease can be attributed to the loss of catalyst after every recycling.

TABLE 3 Synthesis of dihydropyrano[2,3-c]pyrazole derivatives in the presence of Fe₃O₄@THAM-SO₃H (0.01 g) in water/ethanol (1:1) at 100 °C

Entry	Product	Time (min)	Yield (%)	M.p (°C)	M.p (°C) [Lit.]Ref.
1		10	80	244–246	243–245 ^[35]
2		15	75	143–145	145–147 ^[35]
3		25	69	226–228	227–228 ^[36]

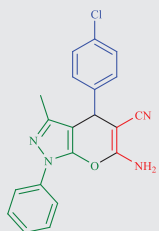
(Continues)

TABLE 3 (Continued)

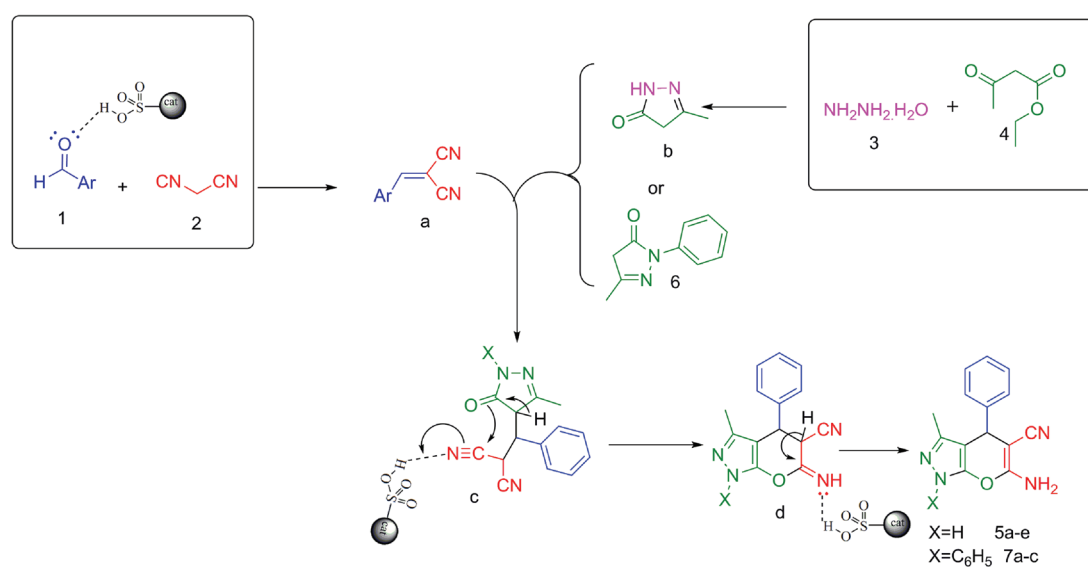
Entry	Product	Time (min)	Yield (%)	M.p (°C)	M.p (°C) [Lit.]Ref.
	 <p>5c 5c</p>				
4	 <p>5d 5d</p>	10	81	190–193	189–193 ^[35]
5	 <p>5e 5e</p>	5	85	180–181	178–180 ^[35]
6	 <p>7a 7a</p>	20	82	165–168	167–169 ^[35]
7	 <p>7b 7b</p>	10	88	182–184	181–183 ^[35]

(Continues)

TABLE 3 (Continued)

Entry	Product	Time (min)	Yield (%)	M.p (°C)	M.p (°C) [Lit.]Ref.
8		5	98	169–171	170–172 ^[35]

7c
7c



SCHEME 3 Proposed mechanism for the synthesis of dihydropyrano[2,3-c]pyrazoles

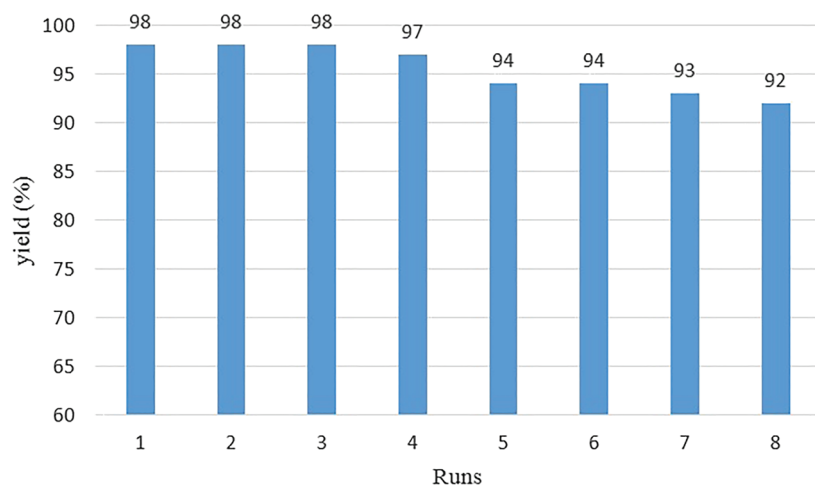


FIGURE 10 Reusability of the nanocatalyst in the synthesis of 6-amino-1,4-dihydro-3-methyl-4-(4-chlorophenyl)-1-phenylpyrano[2,3-c]pyrazole

4 | CONCLUSIONS

In this study, The Fe₃O₄ nanoparticles (NPs) was synthesized easily by chemical coprecipitation method at room temperature. The synthesis of Fe₃O₄ NPs at room temperature has some advantage such as better magnetic properties and avoids Fe₃O₄ to γ -Fe₂O₃ conversion. Then, Fe₃O₄@THAM-SO₃H as a magnetically retrievable nanocatalyst was synthesized and characterized by several analyses including FT-IR, XRD, SEM, EDS, TEM, VSM, and TG/DTG. The synthesized nanocatalyst was successfully employed in the synthesis of dihydropyrano[2,3-c]pyrazole derivatives. This heterogeneous nanocatalyst has the following advantages: easy product separation and purification, reusability for eight reactions cycles without any significant decrease in catalytic activity, eco-friendly nature that make it sustainable, attractive and economic in agreement with some green chemistry protocols.

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ORCID

Nourallah Hazeri  <https://orcid.org/0000-0002-0560-7245>

Malek Taher Maghsoodlou  <https://orcid.org/0000-0002-4454-8049>

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SUPPORTING INFORMATION

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