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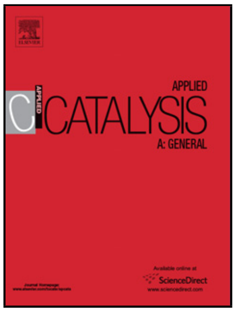

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PII: S0926-860X(13)00490-0
DOI: http://dx.doi.org/doi:10.1016/j.apcata.2013.08.006
Reference: APCATA 14387

To appear in: *Applied Catalysis A: General*

Received date: 11-6-2013
Revised date: 20-7-2013
Accepted date: 7-8-2013

Please cite this article as: S. Sobhani, M. Honarmand, Ionic liquid immobilized on γ-Fe_2O_3 nanoparticles: A new magnetically recyclable heterogeneous catalyst for one-pot three-component synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines, *Applied Catalysis A, General* (2013), http://dx.doi.org/10.1016/j.apcata.2013.08.006

Ionic liquid immobilized on γ-Fe_2O_3 nanoparticles: A new magnetically recyclable heterogeneous catalyst for one-pot three-component synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines

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Abstract

2-Hydroxyethylammonium sulphonate immobilized on γ-Fe_2O_3 nanoparticles (γ-Fe_2O_3-2-HEAS) was synthesized as a new supported ionic liquid by the reaction of *n*-butylsulfonated γ-Fe_2O_3 with ethanolamine. It was used as a magnetically recyclable heterogeneous catalyst for the efficient one-pot, three-component synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines. The catalyst was easily isolated from the reaction mixture by magnetic decantation using an external magnet and reused at least five times without significant degradation in the activity.

Keywords: Magnetic nanoparticles, Ionic liquids, Heterogeneous catalyst, 2-Amino-3,5-dicarbonitrile-6-thio-pyridines, One-pot

1. Introduction

Heterocycles containing 2-amino-3,5-dicarbonitrile-6-thio-pyridine ring system are known as interesting compounds in the pharmaceutical industry due to their various therapeutic applications [1,2]. One of the most significant existing methods for the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines involves one-pot three-component condensation of aldehyde, malononitrile and thiol. Acidic and basic catalysts were reported for the promotion of this condensation reaction [3-17]. The reaction has also been carried out in the presence of microporous molecular sieves [18] and nanocatalysts such as ZnO [19], CuI [20], MgO [21] and SiO_2 [22]. Moreover, ionic liquids including [bmIm]Br [23] and [bmIm]OH [24] were found as efficient catalysts for the synthesis of polysubstituted pyridines. However, the reported protocols suffer from one or more of the following drawbacks such as prolonged reaction time, formation of inevitable side products, harsh reaction conditions, low yields, tedious workup, time consuming methods for catalyst recovery, and use of expensive, unrecyclable and environmentally toxic catalysts and solvents. Therefore, in order to overwhelm these shortcomings, it is preferable to introduce a new procedure that applies a reusable non-hazardous catalyst for the efficient synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines.

Ionic liquids (ILs) have emerged as promising homogeneous catalysts [25] because of their unique physicochemical properties including negligible vapour pressure, wide liquid range, high ionic conductivity and excellent solubility [26]. Although ILs possess some advantages but their practical applications have been restricted by some difficulties in its recovery which lead to economical and environmental problems. On the other hand, their high viscosity not only limits their mass transfer during catalytic reactions but also makes their handling difficult. Moreover, the use of relatively large amounts of ILs is costly and may cause toxicological concerns. These problems can be overcome by immobilization of ILs onto solid supports to obtain heterogeneous catalysts [27-29].

Among different catalyst supports, in recent years, magnetic nanoparticles (MNPs) have attracted increasing attention because of their facile separation from the reaction mixture by using an external magnet [30-32]. Magnetic separation of MNPs is easy, economical, and saves time and energy. Moreover, MNPs such as γ-Fe_2O_3 have a high surface area, excellent thermal and chemical stability, surface modification ability, ease of synthesis and low toxicity and cost [33-36]. These attractive features have made γ-Fe_2O_3 as a promising support for ILs [37-39].

In our ongoing work on the development of efficient and environmentally benign procedures using ILs [40-43], we have recently synthesized silica supported 2-hydroxyethylammonium acetate and used it as a recyclable catalyst for the synthesis of phosphonate derivatives [44]. However, despite the high catalytic activity of silica supported IL, its application was limited due to the inevitable loss of the catalyst during recovery *via* filtration. To benefit the unique properties of ILs and the valuable applications of MNPs, herein, we report the synthesis of 2-hydroxyethylammonium sulphonate immobilized on γ-Fe_2O_3 (γ-Fe_2O_3-2-HEAS) as a new supported IL (Scheme 1). It is worthy to note that there is not any report on the supporting of 2-hydroxyethylammonium sulphonate on MNPs.

Scheme 1

To explore the catalytic activity of this catalyst in organic reactions, we have used γ-Fe_2O_3-2-HEAS as a magnetically recyclable heterogeneous catalyst for one-pot three-component synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines (Scheme 2). By using an external magnet, the supported IL is readily separated from the reaction mixture. This kind of separation eliminates the need of filtration and facilitates recycling of the catalyst.

Scheme 2

2. Experimental

2.1. Large scale synthesis of γ-Fe_2O_3 NMPs

γ-Fe_2O_3 nanoparticles were synthesized by a reported chemical co-precipitation technique of ferric and ferrous ions in alkali solution with minor modification [45-47]. In this procedure $FeCl_2.4H_2O$ (9.25 g) and $FeCl_3.6H_2O$ (15.8 g) were dissolved in deionized water (200 mL) under Ar atmosphere at room temperature. Then a solution of NH_4OH (25%, 100 mL) was added dropwise (drop rate = 1 mL min^{-1}) to the stirring mixture to reach the reaction pH of 11. The resulting black dispersion was continuously stirred for 1 h at room temperature and then refluxed for another 1 h to yield a brown dispersion. The MNPs were then purified by a repeated centrifugation (1730-3461 ×g, 20 min) and decantation followed by 3 times redispersion. The as-synthesized sample was heated in air at 2 °C min^{-1} up to 200 °C and then kept in the furnace for 3 h to give a reddish-brown powder.

2.2. Synthesis of n-butylsulfonated γ-Fe_2O_3 (γ-Fe_2O_3-n-BS)

In order to enrich the hydroxyl group on γ-Fe_2O_3 MNPs, ammonium hydroxide (100 ml, 25%, v/v aqueous solution) was added to a sonicated mixture of γ-Fe_2O_3 MNPs (6.2 g) in ethanol and water (400 ml, 1:1 by volume). The resulting mixture was stirred vigorously at 60 °C for 24 h. γ-Fe_2O_3 MNPs were then isolated by magnetic decantation and washed with copious amounts of deionized water, ethanol, and *n*-hexane. The resulting solid (6 g) was suspended in 600 mL of 0.1 M toluene solution of 1,4-butanesultone. This colloidal solution was refluxed for 48 h. The modified γ-Fe_2O_3 were isolated and purified by repeated washing (first in CH_3CN and then in water) and centrifugation. The *n*-butylsulfonated γ-Fe_2O_3 (γ-Fe_2O_3-*n*-BS) was obtained as reddish-brown powder. By elemental analysis and TGA, the loading amount of *n*-butylsulfonated on γ-Fe_2O_3 was determined and it was 0.19 mmol g^{-1}.

2.3. Synthesis of 2-hydroxyethylammonium sulphonate immobilized on γ-Fe_2O_3 (γ-Fe_2O_3-2-HEAS)

A mixture of γ-Fe_2O_3-*n*-BS (5.8 g) in dry CH_2Cl_2 (100 mL) was sonicated for 30 min. Ethanolamine (0.07 g) was added to the dispersed γ-Fe_2O_3-*n*-BS in dry CH_2Cl_2 and stirred at room temperature for 8 h. The resulting solid was separated by an external magnet and washed 3 times with CH_2Cl_2, ethanol and H_2O. After drying at room temperature in vacuum, γ-Fe_2O_3-2-HEAS was obtained as reddish-brown powder.

2.4. General procedure for the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines in the presence of γ-Fe_2O_3-2-HEAS

γ-Fe_2O_3-2-HEAS (0.08 g) was added to a stirred mixture of aldehyde (1 mmol), malononitrile (2 mmol) and thiol (1 mmol). The reaction mixture was stirred at 50 ˚C for the appropriate time (Table 2). The progress of the reaction was monitored by TLC. After completion of the reaction, EtOAc (10 mL) was added to the cooled reaction mixture. The catalyst was separated by an external magnet, washed with EtOAc, dried and re-used for a consecutive run under the same reaction conditions. Evaporation of the solvent of the filtrate under reduced pressure gave the crude products. Pure product was obtained by recrystallization in aqueous EtOH.

3. Results and Discussion

3.1. Characterization of γ-Fe_2O_3-2-HEAS

In the XRD pattern of the synthesized γ-Fe_2O_3 MNPs (Figure 1), diffraction patterns had a good agreement with the cubic structure of maghemite (JCPDS file No 04-0755), a unit cell dimension of 8.35 Å and the space group of P4132 (213). The average crystallite size was calculated to be 13.1 nm using Scherrer equation in which $K = 0.9$ and $\lambda = 0.154$ nm.

Figure 1

The synthesized γ-Fe_2O_3-2-HEAS was fully characterized by TEM, FT-IR, TGA, elemental analysis, N_2 adsorption–desorption and VSM. The particle size distribution of γ-Fe_2O_3-2-HEAS was evaluated using transmission electron microscopy (TEM) (Figure 2) and showed that the mean diameter of MNPs is 14 nm (Figure 2b).

Figure 2

FT-IR spectra of γ-Fe_2O_3 and γ-Fe_2O_3-2-HEAS (Figure 3) showed broad bands around 450-600 cm^{-1}, which were attributed to Fe-O vibration [48]. FT-IR spectrum of γ-Fe_2O_3-2-HEAS showed the typical bands at 2960, 2933 and 2866 cm^{-1} attributed to C-H stretching vibrations of alkyl chains. Moreover, the broad peak at 1111 cm^{-1} belonged to S=O stretching vibrations in the sulphonate functional groups. Bands at 1600, 1502 cm^{-1} were related to N-H bending vibrations in the ammonium groups. These results indicated that IL was successfully immobilized on γ-Fe_2O_3 MNPs.

Figure 3

The thermal behaviour of γ-Fe_2O_3-2-HEAS was investigated by thermogravimetric analysis (TGA) (Figure 4). As shown in Figure 4, the weight loss around 180 $^{\circ}$C was related to the loss of adsorbed water molecules. The organic parts were decomposed completely at 487 $^{\circ}$C. According to the TGA, the amount of IL supported on γ-Fe_2O_3 was evaluated to be 0.15 mmol g^{-1}. The loading amount of IL on γ-Fe_2O_3 was also quantified *via* elemental analysis and it was 0.15 mmol g^{-1} based on nitrogen and sulfur determination (0.21% and 0.48%, respectively).

Figure 4

N_2 adsorption–desorption isotherms of γ-Fe_2O_3-2-HEAS (Figure 5) showed a type IV curve (IUPAC classification) and revealed that the adsorption–desorption process was not reversible [49,50]. This is a result of the hysteresis loops due to capillary condensation. Using BET method, values of 91 m^2 g^{-1} and 14.3 nm were found for surface area and mean pore diameter of γ-Fe_2O_3, respectively. Reducing surface area to 67 m^2 g^{-1} and increasing mean pore diameter to 18.2 nm for γ-Fe_2O_3-2-HEAS confirmed the immobilization of IL on the surface of γ-Fe_2O_3.

Figure 5

The magnetic properties of γ-Fe_2O_3 and γ-Fe_2O_3-2-HEAS were characterized by vibrating sample magetometer (VSM) at room temperature (Figure 6). γ-Fe_2O_3 and γ-Fe_2O_3-2-HEAS displayed a superparamagnetic behaviour, as evidenced by a zero coercivity on the magnetization loop. The saturation magnetizations of γ-Fe_2O_3 and γ-Fe_2O_3-2-HEAS were 68.9 and 63.4 emu g^{-1}, respectively. A slight decrease of the saturation magnetization of γ-Fe_2O_3-2-HEAS was due to the immobilization of IL on the surface of γ-Fe_2O_3 MNPs.

Figure 6

3.2. Synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines catalyzed by γ-Fe_2O_3-2-HEAS

At first, the reaction of benzaldehyde, malononitrile and thiophenol was chosen as a model reaction to optimize the reaction conditions such as molar ratio of the catalyst, temperature and solvent (Table 1). It was found that the best yield of the product was obtained at 50 °C under solvent-free conditions in the presence of 1.2 mol% of γ-Fe_2O_3-2-HEAS (Table 1, entry 2). Three separated reactions were examined in the absence of any catalyst and in the presence of γ-Fe_2O_3 and γ-Fe_2O_3-*n*-BS. The results of these studies showed that any amount of the desired product was not formed, and α,β-unsaturated malonate was detected as the sole product of these reactions (Table 1, entries 15-17). A similar reaction in the presence of 2-hydroxyethylammonium methansulfonate (2-HEAMS) as a non-supported IL gave the desired product in moderate yield (69%) due to the formation of by-products (Table 1, entry 18). This result indicated that the catalytic efficiency of IL was increased by immobilization onto γ-Fe_2O_3.

In order to establish the generality of this method, the synthesis of various 2-amino-3,5-dicarbonitrile-6-thio-pyridines was studied using different aldehydes and thiols under optimized reaction conditions (Table 2).

Table 1

Synthesis of 2-amino-4-phenyl-6-phenylsulfanyl-pyridine-3,5-dicarbonitrile under different conditions.

Entry	Catalyst (mol %)	Temperature (°C)	Solvent	Time	Yield[a] (%)
1	γ-Fe_2O_3-2-HEAS (1.4)	50	-	10 min	91
2	γ-Fe_2O_3-2-HEAS (1.2)	50	-	10 min	91
3	γ-Fe_2O_3-2-HEAS (1)	50	-	30 min	80
4	γ-Fe_2O_3-2-HEAS (0.8)	50	-	1 h	78
5	γ-Fe_2O_3-2-HEAS (1.2)	60	-	10 min	91

6	γ-Fe_2O_3-2-HEAS (1.2)	40	-	1 h	84
7	γ-Fe_2O_3-2-HEAS (1.2)	30	-	3 h	82
8	γ-Fe_2O_3-2-HEAS (1.2)	25	-	4 h	81
9	γ-Fe_2O_3-2-HEAS (1.2)	50	EtOH	24 h	40
10	γ-Fe_2O_3-2-HEAS (1.2)	50	MeOH	24 h	50
11	γ-Fe_2O_3-2-HEAS (1.2)	50	CH_3CN	24 h	10
12	γ-Fe_2O_3-2-HEAS (1.2)	50	$CHCl_3$	24 h	40
13	γ-Fe_2O_3-2-HEAS (1.2)	50	EtOAc	24 h	10
14	γ-Fe_2O_3-2-HEAS (1.2)	50	H_2O	24 h	0
15	-	50	-	24 h	0
16	γ-Fe_2O_3 (0.08 g)	50	-	24 h	0
17	γ-Fe_2O_3-*n*-BS (1.2)	50	-	24 h	0
18	2-HEAMS (1.2)	50	-	10 min	69[b]

[a]Isolated yields. Conditions: aldehyde/malononitrile/thiol: 1/2/1. [b]The desired product plus a mixture of by-products were obtained.

As the results of Table 2 indicate, 2-amino-3,5-dicarbonitrile-6-thio-pyridines **1a-g** were produced from the reaction of various substituted benzaldehyde and thiophenol in good to high yields (Table 2, entries 1-7). 2-Naphthaldehyde as a polynuclear aldehyde and pyridine-3-carbaldehyde as a heteroaromatic aldehyde underwent the condensation reaction to afford the corresponding pyridines in good yields (Table 2, entries 8 and 9). Interestingly, γ-Fe_2O_3-2-HEAS efficiently promoted the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines using aliphatic aldehydes and thiols (Table 2, entries 10-12).

The practical synthetic efficiency of this method was highlighted by the reaction of both carbonyl groups in terephthalaldehyde with malononitrile and thiophenol to give a structurally complex pyridine derivative **1m** in 84% yield after 10 min (Scheme 3).

Scheme 3

Table 2

Synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridine derivatives in the presence of γ-Fe_2O_3-2-HEAS.

Entry	R	R′	Product	Time (min)	Yield[a] (%)
1	Ph	Ph	**1a**	10	91
2	Ph	4-ClC_6H_4	**1b**	10	81
3	Ph	4-$MeOC_6H_4$	**1c**	20	79
4	Ph	4-MeC_6H_4	**1d**	10	84
5	4-MeC_6H_4	Ph	**1e**	10	81
6	4-ClC_6H_4	Ph	**1f**	5	87
7	4-ClC_6H_4	4-MeC_6H_4	**1g**	10	80
8	2-Naphthyl	Ph	**1h**	10	79
9	3-Pyridinyl	Ph	**1i**	5	89
10	3-Phenylpropanal	Ph	**1j**	5	88

11	Me	Ph	**1k**	10	90
12	Ph	*n*-Bu	**1l**	10	83

[a]Yields refer to those of pure isolated products characterized by their spectral data (see supplementary information). Conditions: aldehyde/malononitrile/thiophenol/γ-Fe_2O_3-2-HEAS: 1/2/1/0.012, 50 °C, solvent-free.

A plausible mechanism for the formation of 2-amino-3,5-dicarbonitrile-6-thio-pyridines catalyzed by γ-Fe_2O_3-2-HEAS is shown in Scheme 4. The first step of the process involves Knoevenagel condensation of aldehyde with malononitrile to form the corresponding α,β-unsaturated malonate (**A**). The reaction proceeds through the addition of thiolate to the nitrile of **A** followed by Michael addition of the second molecule of malononitrile to the adduct. Aromatization and oxidation of dihydropyridines **B** by air under the reaction conditions give pyridines **1a-m**. It is supposed that dual activation of substrates by γ-Fe_2O_3-2-HEAS has been taken place in this three-component reaction. The hydroxyl group of the catalyst as a basic moiety has activated malononitrile and thiol, and ammonium group as an acidic moiety has activated nitrile of α,β-unsaturated malonates (**A**).

To show the role of the hydroxyl group in the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines **1a**, the reaction of benzaldehyde, malononitrile and thiophenol in the presence of γ-Fe_2O_3-2-HEAS and 2-ethylammonium sulphonate immobilized on γ-Fe_2O_3 (γ-Fe_2O_3-2-EAS) was studied. The results showed that the reaction in the presence of γ-Fe_2O_3-2-EAS proceeded in a longer reaction time (4 h) compared with γ-Fe_2O_3-2-HEAS (10 min) and produced the desired product in 85% yield. These results depicted the specific role of hydroxyl group of γ-Fe_2O_3-2-HEAS in imparting the catalytic property and indicated that γ-Fe_2O_3-2-HEAS would take a part in the reaction as a functionalized ionic liquid.

Scheme 4

The recovery and reuse of a catalyst is highly preferable for a catalytic process. In this regard the recyclability of γ-Fe_2O_3-2-HEAS was investigated in a model reaction of benzaldehyde, malononitrile and thiophenol under optimized reaction conditions. After the reaction was completed, EtOAc was added to the reaction mixture and the whole amount of γ-Fe_2O_3-2-HEAS simply separated from the product by an external magnet (Figure 7). The recovered catalyst washed with ethylacetate, dried at room temperature and reused for a similar reaction. It is worth to note that the magnetic property of γ-Fe_2O_3-2-HEAS facilitates the efficient recovery of the catalyst from the reaction mixture during work-up procedure so that the catalyst could be recycled and reused for five consecutive trials without loss of its catalytic activity (Figure 8).

Figure 7

Figure 8

The recyclablity test was stopped after five runs. Comparison of TEM images (Figure 9) and FT-IR spectra of used catalyst (Figure 10) with those of the fresh catalyst (Figure 2b and 3) showed that the morphology and structure of γ-Fe_2O_3-2-HEAS remained intact after five recoveries.

Figure 9

Figure 10

In order to show the merit of the present method for the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines, we have compared our results obtained using γ-Fe_2O_3-2-HEAS with some of those reported in the literature for the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines (Table 3). These results indicate well the superior activity of γ-Fe_2O_3-2-HEAS than those of other promoters especially for the synthesis of 2-amino-3,5-

dicarbonitrile-6-thio-pyridines from aliphatic aldehydes or thiols. Most of the reported methods suffer from lack of generality for the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines from arylaldehydes/arylthiols, alkylaldehydes/arylthiols and arylaldehydes/alkylthiols. Requiring a small amount of γ-Fe_2O_3-2-HEAS and short reaction time are the other advantageous of this catalyst compared with the reported methods.

Table 3

Synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines in the presence of reported reagents or catalysts.

Entry	Catalyst or reagent	Aldehyde:malononitrile:thiol (mmol)/Catalyst or reagent	Aldehyde/Thiol	Time	Yield (%)[a] [ref]
1	H_3BO_3	1:2:1/15 mol%	Aryl/Aryl	8-50 min	80-94 [3]
2	$ZnCl_2$	1:2:1/20 mol%	Aryl/Aryl	2 min-2.5 h	50-77 [4]
			Alkyl/Aryl	3 min-2.5 h	46 [4]
3	$ZrOCl_2.8H_2O$	1:2:1/20 mol%	Aryl/Aryl	2-20 min	90-98 [5]
4	IBX	1:2:1/10 mol%	Aryl/Aryl	1.5-2.5 h	69-83 [6]
5	Et_3N or DABCO	1.5:3.1:1.6 or 1.5:2.25:0.75/10 mol%	Aryl/Aryl	2 h [7], 40-90 min [8]	20-48 [7], 55-96 [8]
			Alkyl/Aryl	2 h [7], 40-90 min [8]	20-29 [7], 39-55 [8]
			Aryl/Alkyl	2 h [7], 40-90 min [8]	21-47 [7], 42-92 [8]
6	Piperidine or TBAH	2:3:1/piperidine (30 mol%) or TBAH (50 mol%)	Aryl/Aryl	1-24 h	40-67 [9]
			Alkyl/Aryl	1-24 h	5-6 [9]

7	DBU	1:2:1/5 mol%	Aryl/Aryl	10-40 min	75-91 [10]
8	Basic alumina	1:2:1/10% aqueous suspension of basic alumina (2 mL)	Aryl/Aryl	50-100 min	79-90 [11]
9	KF/alumina	1:2:1/10 mol%	Aryl/Aryl	5-70 min	56-93 [12]
10	TBAF	1:2:1/10 mol%	Aryl/Aryl	45-120 min	87-96 [13]
			Alkyl/Aryl	420-630 min	62-64 [13]
11	Sodium silicate	1:2:1/5 mol%	Aryl/Aryl	1 h	78-82[b] [14]
12	K_2CO_3	1:2:1/20 mol%	Aryl/Aryl	40-180 min	70-89 [15]
			Alkyl/Aryl	90 min	80 [15]
			Aryl/Alkyl	75-90 min	60-61 [15]
13	KOH	3:6:3/10 mol%	Aryl/Aryl	30-60 min	71-90 [16]
			Alkyl/Aryl	90 min	76 [16]
			Aryl/Alkyl	30 min	82-89 [16]
14	NH_4OH	1:2.1:1/12 mol%	Aryl/Aryl	6 h	60-90 [17]
15	Microporous molecular sieves	1:2:1/200 mg	Aryl/Aryl	30-120 min	78-91 [18]
16	Nano-ZnO	1:2.2:1/20 mol%	Aryl/Aryl	80-150 min	75-94 [19]
17	Nano-CuI	1:2.2:1/10 mol%	Aryl/Aryl	85-150 min	80-94 [20]
			Alkyl/Aryl	85-200 min	70-75 [20]
			Aryl/Alkyl	145-165 min	

				min	78-82 [20]
18	Nano-MgO	1:2.1:1.1/100 mg	Aryl/Aryl Aryl/Alkyl	2-9 h 4-8 h	48-69 [21] 41-56 [21]
19	Nano-SiO_2	1:2:1/14 mg	Aryl/Aryl Alkyl/Aryl Aryl/Alkyl	2.5-3 h 6 h 6 h	70-85 [22] 60 [22] 60-65 [22]
20	[bmlm]Br	1:2:1/60 mol%	Aryl/Aryl	4 -12 min	75-86 [23]
21	[bmlm]OH	1:2:1/50 mol%	Aryl/Aryl	0.5-1.5 h	62-92 [24]
22	2-HEAA	1:2:1/0.5 mL	Aryl/Aryl Alkyl/Aryl Aryl/Alkyl	5 min 5 min 5 min	76-96 [42] 72-90 [42] 70 [42]
23	γ-Fe_2O_3-2-HEAS	1:2:1/1.2 mol%	Aryl/Aryl Alkyl/Aryl Aryl/Alkyl	5-20 min 5-10 min 10 min	79-91[c] 88-90[c] 83[c]

[a]Isolated yield. [b]GC yield. [c]This work.

4. Conclusions

In summary, in this paper, 2-hydroxyethylammonium sulphonate immobilized on γ-Fe_2O_3 (γ-Fe_2O_3-2-HEAS) was successfully synthesized as a new supported IL from readily available starting materials. It was applied as a magnetically recyclable heterogeneous catalyst for the one-pot three-component synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines. This catalyst efficiently promoted the condensation of both aromatic and aliphatic aldehydes and thiols with malononitrile leading to 2-amino-3,5-dicarbonitrile-6-thio-pyridines in good to high yields under solvent-free conditions. Product separation and catalyst recycling are easy and simple with the assistance of an external magnet. The catalyst can be recovered and reused for five times without significant degradation in activity.

Acknowledgement

We are thankful to University of Birjand Research Council for their support on this work.

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Figure captions

Figure 1. XRD spectra of γ-Fe_2O_3 MNPs.

Figure 2. (a) TEM images of γ-Fe_2O_3-2-HEAS and (b) γ-Fe_2O_3-2-HEAS particle size distribution histogram.

Figure 3. FT-IR spectra of γ-Fe_2O_3 and γ-Fe_2O_3-2-HEAS.

Figure 4. Thermogravimetric analysis (TGA) of γ-Fe_2O_3-2-HEAS.

Figure 5. Nitrogen adsorption–desorption isotherms of γ-Fe_2O_3-2-HEAS.

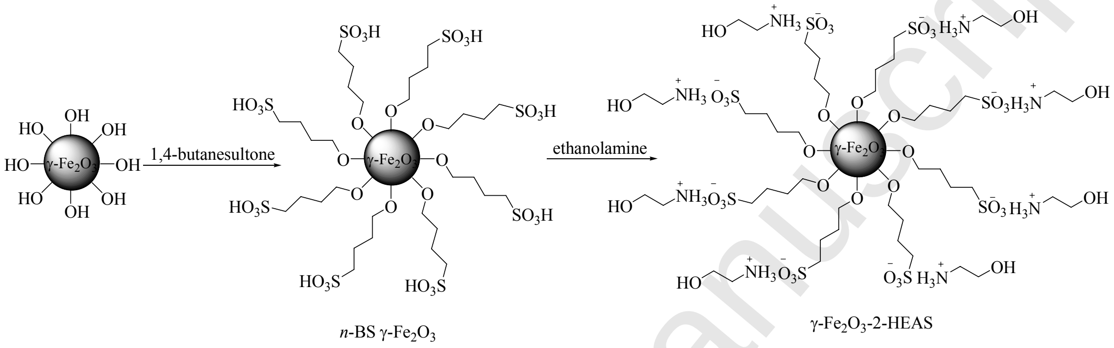
Figure 6. Magnetization curves of γ-Fe_2O_3 and γ-Fe_2O_3-2-HEAS.

Figure 7. Separation of γ-Fe_2O_3-2-HEAS from the reaction mixture using an external magnet.

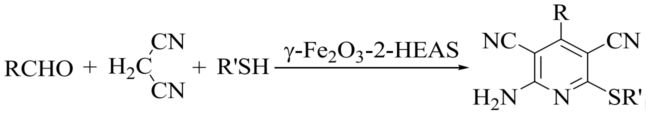
Figure 8. Recycling experiment of γ-Fe_2O_3-2-HEAS.

Figure 9. TEM image of γ-Fe_2O_3-2-HEAS after five reuses.

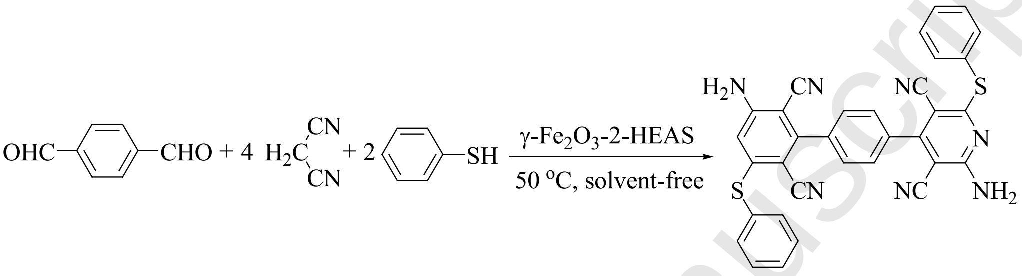
Figure 10. FT-IR spectrum of recovered γ-Fe_2O_3-2-HEAS.



Scheme 1. Synthesis of γ-Fe_2O_3-2-HEAS.



Scheme 2. Synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines catalyzed by γ-Fe_2O_3 MNPs.



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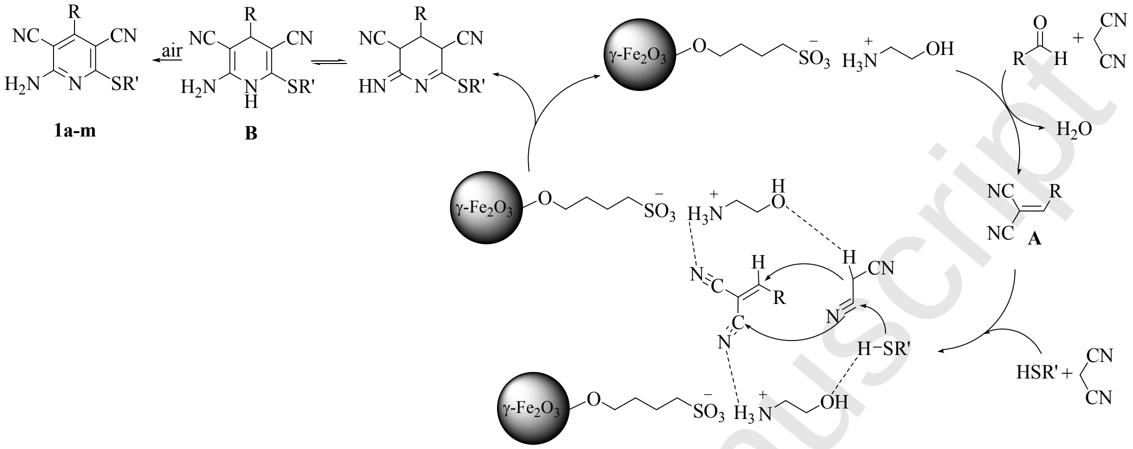
Scheme 3. Synthesis of 1,4-bis(2-amino-6-phenylsufanyl-4-pyridyl-3,5-dicarbonitrile)benzene.



Scheme 4. Suggested mechanism for the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines in the presence of γ-Fe_2O_3-2-HEAS.

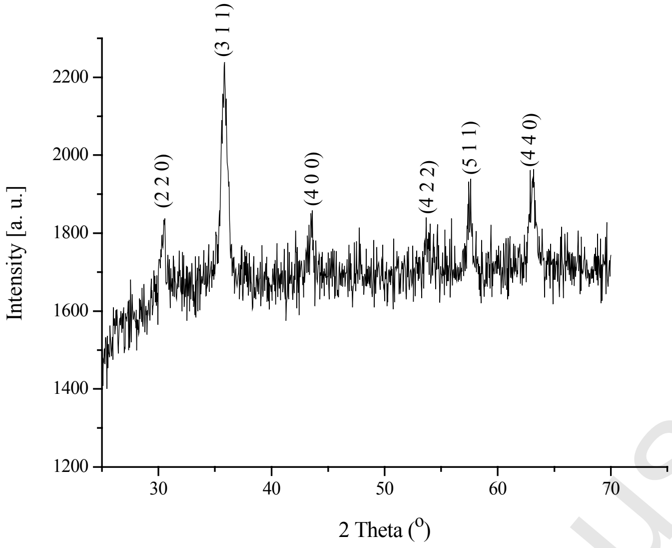
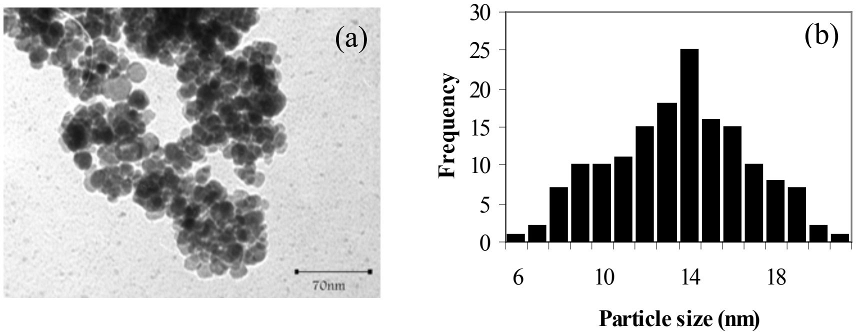


Figure 1. XRD pattern of γ-Fe_2O_3 MNPs.



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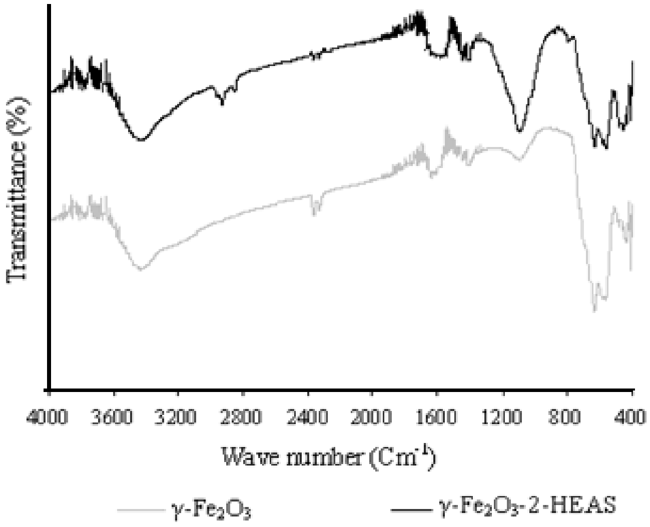
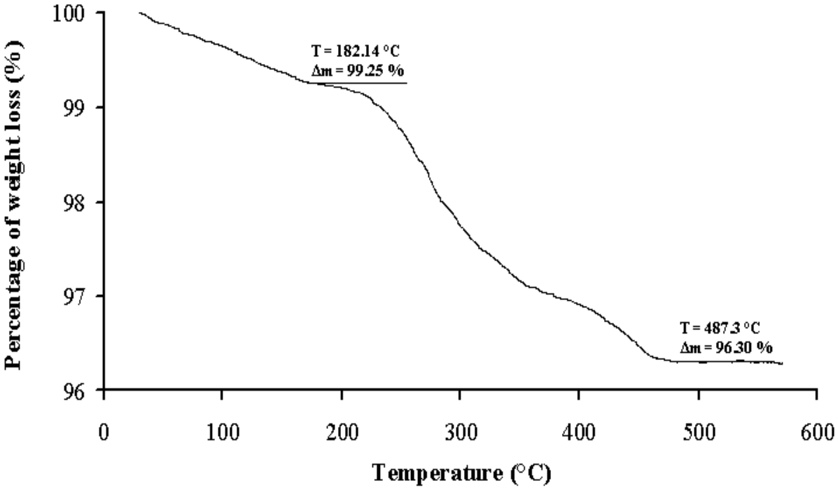


Figure 3. FTIR spectra of γ-Fe_2O_3 and γ-Fe_2O_3-2-HEAS.



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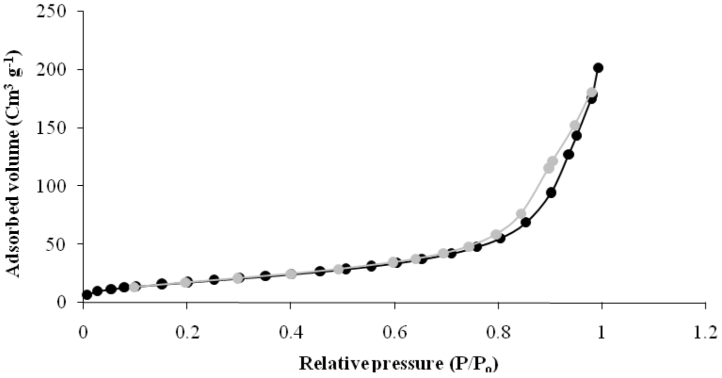

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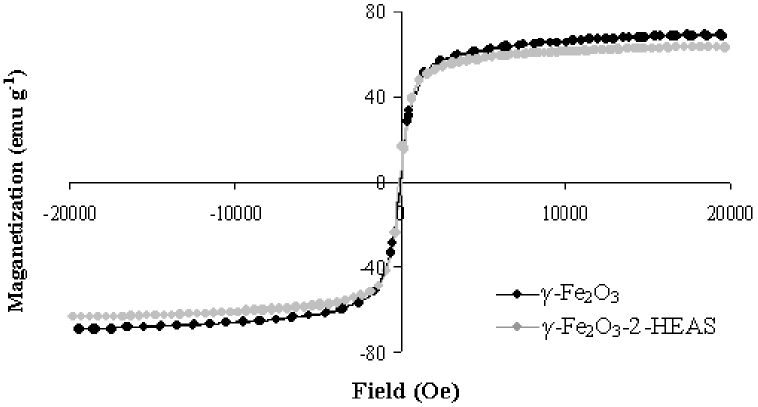

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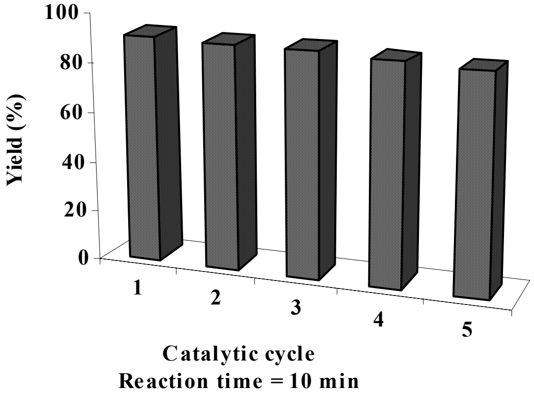

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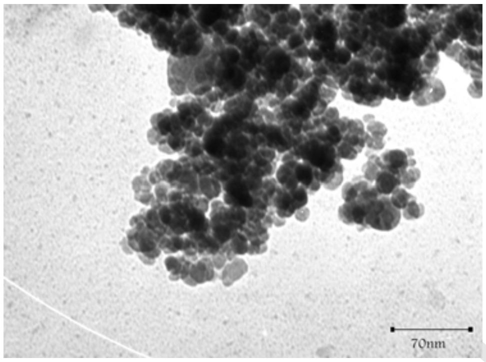


Figure 9. TEM image of γ-Fe_2O_3-2-HEAS after five reuses.

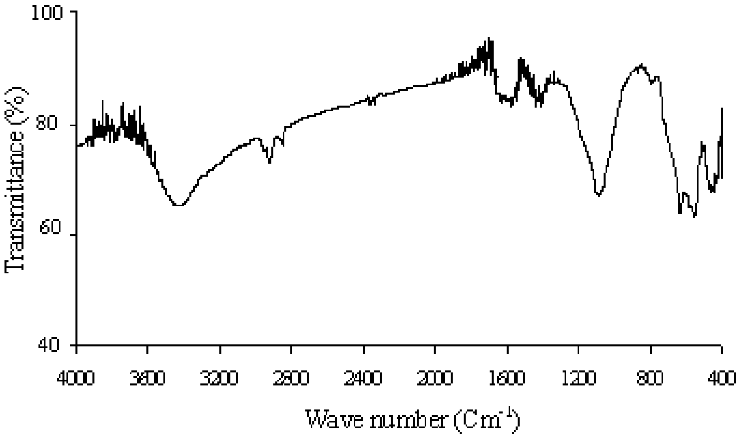
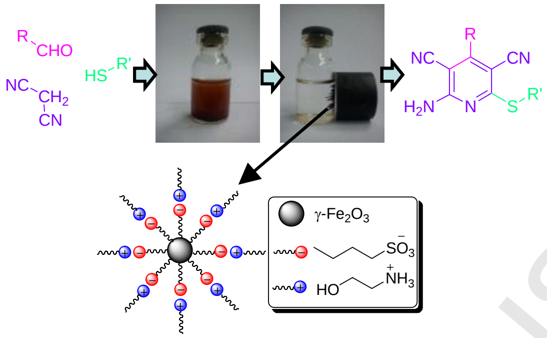


Figure 10. FT-IR spectrum of recovered γ-Fe_2O_3-2-HEAS.

Graphical Abstract



Research Highlights:

- Ionic liquid immobilized on γ-Fe_2O_3 magnetic nanoparticles was synthesized.
- It was used as a heterogeneous catalyst for the synthesis of pyridine derivatives.
- Pyridine derivatives were obtained in good to high yields.
- In this method, catalyst separation was easily performable by a magnetic bar.
- This catalyst was reused at least five times with sustained catalytic activity.