New Heterogeneous Nano-Catalyst: Synthesis and Catalytic Effect on the Green Synthesis of 1-Substituted and 5-Substituted 1H-Tetrazole Derivatives

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Abstract

A novel heterogeneous catalyst containing Schiff base coordinated Cu(II) covalently attached to $Fe_3O_4@SiO_2$ nanoparticles through imidazolium linker [$Fe_3O_4@SiO_2$-Im(Br)-SB-Cu (II)] was synthesized and characterized by using various techniques. The catalytic efficiency of this nano-catalyst was tested in the synthesis of tetrazole derivatives. The investigation revealed that i) The catalyst is very efficient in the synthesis of tetrazole derivatives with high yield (97%) in aqueous medium; ii) The catalytic effectiveness is due the synergy between the metallic center and the imidazolium ion and iii) The reuse advantage of the catalyst without contamination or significant loss (12% of loss range) in the catalytic activity.

Introduction

Tetrazoles are essential class of poly-aza-heterocyclic compounds largely discovered in nature.[1] Recently, tetrazoles have received much attention due to their large spectrum of applications in the field of medicine and biology such as anticancer, antiviral, antiallergic, antibiotic, anti-HIV, etc,.[2−5] Homogeneous catalysts were predominantly used, due to their solubility and high activity, in the synthesis of tetrazole derivatives than there heterogeneous counterparts. However, homogeneous catalysts suffer from many drawbacks such as high-temperature working conditions, difficult recycling, product contamination, and deactivation through dimerization. To overcome these problems, methods were devised to heterogenized such catalysts, including polymerization[7,8], grafting them on organic[9] or inorganic supports[10,11,12]. One of the best solid support is magnetic nanoparticles, especially Fe_3O_4, due to several factors such as high active surface area, low toxicity, superparamagnetism,[13] ease of recycling,[14,15] high dispersion and reactivity, and chemical/thermal stability. Also, ease of surface modification and ligands coupling due to the chemical nature and accessible reactive groups on the surface of the nanoparticles.[24]

Our strategy was to design and synthesize a heterogenous catalyst that is suitable to work in aqueous conditions. To allow the catalyst to work in water, our design approach was based on the use of water-soluble linker or coupling spacer arm to bring the catalyst to aqueous medium during the catalytic process. We decided to prepare a Cu(II)-coordinated Schiff base nano-catalyst having an imidazolium linker to nanoparticles. The nano-catalyst efficiency was then successfully investigated in tetrazole derivatives synthesis in aqueous medium. The catalyst achieved high tetrazole derivatives yield in a short reaction time and, due to its magnetic characteristic, it was easily removed from the products without leaving behind any metallic contamination.

Experimental

Materials and apparatus

All solvents were purchased from Merck Co. and dried by standard procedures. All chemical reagents were purchased from Sigma-Aldrich chemical company and used without further purification. The

progress of reactions was monitored by TLC on Silica-gel Polygram SILG/UV254 plates. Fourier Transform Infrared (FT-IR) spectra were recorded on a PerkinElmer 780 FT-IR spectrometer (KBr tablets). The morphology (SEM) and elemental analysis (EDS) of the catalyst were determined by using the FE-SEM TESCAN MIRA3 instrument. Transmission Electron Microscopy (TEM) images were obtained with a Philips EM208 S electron microscope. X-ray Diffraction (XRD) patterns were collected using a Philips PW 1730 diffractometer using Cu Kα radiation (λ = 1.54 A°). Thermogravimetric Analysis (TGA) was performed on a Q600 TA instrument at 30−700 °C with a heating rate of 20 °C min^{-1} in an argon atmosphere. Vibrating Sample Magnetometer (VSM) analysis was performed at room temperature using an LBKFB instrument. Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-OES) analysis was performed using a Simultaneous VISTA-PRO instrument. Atomic Absorption Spectroscopy (AAS) analysis was performed using a Shimadzu AA6200 instrument.

The synthesis of modified silica coated Fe_3O_4 nanoparticles ($Fe_3O_4@SiO_2$)

The silica coated Fe_3O_4 magnetic nanoparticles were synthesized by previously reported methods.[26] $FeCl_3.6H_2O$ (6.8 g) and $FeCl_2.4H_2O$ (2.5 g) were added to deionized water (300 mL) and stirred under nitrogen gas at room temperature. Gradually, ammonia solution (25% w/w, 70 mL) was added to the vigorously stirred mixture. As soon as the solution's color turned black, the resulting nanoparticles were separated by an external magnet and washed several times with deionized water.

To synthesize silica-coated nanoparticles, Fe_3O_4 nanoparticles (3.0 g) were dispersed by sonication in a deionized water/ethanol solvent mixture (1:4 v/v, 500 mL) 30 minutes. Then a solution of ammonia (25% w/w) was gradually added until the pH reaches 10. The tetraethyl orthosilicate (TEOS, 20 mL) was slowly added to the mixture and stirred three hours at 50 °C. The silica-coated nanoparticles ($Fe_3O_4@SiO_2$) were collected by a permanent magnet and washed with deionized water and ethanol several times and dried in a vacuum oven at 50 °C for 24 hrs. In the final stage, $Fe_3O_4@SiO_2$ (1g) was sonicated in dry toluene (40 mL) for 30 min. Then, 3-Chloropropyl triethoxysilane (2.0 mL) was added dropwise and refluxed for 20 hours. The resulting chloro-modified $Fe_3O_4@SiO_2$ was removed from the reaction mixture by a strong magnet, washed with in toluene, ethanol and diethyl ether for several times. Then dried under vacuum at 60 °C for 12hrs.[27] The loading amount of Cl atom was 0.3 mmol per gram catalyst based on EDX.

The synthesis of $Fe_3O_4@ SiO_2$-Im nanoparticles

Imidazole (0.5 mmol, 0.034 g) was added to the dispersed solution of chloro-modified $Fe_3O_4@SiO_2$ (1.0 g) in dry toluene (40 mL) and triethylamine (NEt_3, 0.5 mmol, 0.05 g) was added dropwise and refluxed for 24 hrs. The resulting nanoparticles were separated with the external magnet and washed with distilled water and ethanol. The resulted $Fe_3O_4@ SiO_2$-Im nanoparticles were dried in a vacuum oven at 80 °C for 12hrs.

The synthesis of $Fe_3O_4@ SiO_2$-Im[Br] nanoparticles

The synthesized nanoparticles of $Fe_3O_4@SiO_2$-Im (1.0 g) in dry ethanol (40 mL) were dispersed for 30 mins by sonication. The ethanolic solution of 3-Bromopropylamin hydrobromide (0.5 mmol, 0.11 g) was gradually added to the stirred mixture and refluxed for 48 hours. The resulting nanoparticles were separated by the magnet, washed with distilled water, ethanol, and diethyl ether. Finally, nanoparticles were dried in a vacuum at 80 °C for 20 hrs.

The synthesis of $Fe_3O_4@ SiO_2$-Im[Br]-SB nanoparticles

The nanoparticles ($Fe_3O_4@ SiO_2$-Im [Br]-$PrNH_2$. HBr, 1.0 g) from the previous step were dispersed by sonication in dry ethanol (40 mL) followed by dropwise addition of salicylaldehyde (0.5 mmol, 56 µL) and sodium hydroxide (NaOH, 0.5 mmol, 0.02 g) solutions. The reaction mixture was then refluxed in ethanol 20 hours. The resulting nanoparticles were separated by the magnet and washed with distilled water, ethanol, and diethyl ether. Finally, nanoparticles were dried in a vacuum at 80 °C for 20 hrs.

The synthesis of $Fe_3O_4@ SiO_2$-Im[Br]-SB-Cu (II) Nano-complex

The ethanolic solution of Cu $(OAC)_2$. H_2O (0.8 mmol, 0.16 g) was added dropwise to the well dispersed $Fe_3O_4@ SiO_2$-Im [Br]-Schiff base nanoparticles (1.0 g)in ethanol and refluxed 12 hrs. The resulting Cu(II)-coordinated nanoparticles were separated by an external magnet and washed several times with ethanol, diethyl ether and dried in a vacuum at 60 °C for 10 hrs.

General procedure for the synthesis of 1-substituted 1H-tetrazole

aniline (1.0 mmol, 0.09 mL), Triethyl orthoformate (1.2 mmol, 0.2 mL), sodium azide (1.0 mmol, 0.06 g) in a water (1.0 mL) in the presence of $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) nano-catalyst (0.6 mol%, 0.008 g) were stirred at 40 °C. The reaction progression was monitored by thin-layer chromatography (TLC) at different interval of time using n-Hexane/Ethyl acetate (4:1) as eluent. At the end, the reaction mixture was cooled, and catalyst removed by an external magnet. The reaction mixture was extracted with 3x10mL of ethyl acetate. The organic phase was dried with anhydrous Na_2SO_4, filtered and then evaporated. The pure product was obtained by recrystallization in a mixture of n-Hexane/Ethyl acetate. The recovered yield was 97%.

General procedure for the synthesis of 5-substituted 1H-tetrazole

Benzaldehyde (1.0 mmol, 0.1 mL), hydroxylammonium chloride (1.0 mmol, 0.07 g), sodium azide (1.2 mmol, 0.08 g) in water (1.0 mL) in the presence of $Fe_3O_4@ SiO_2$-Im[Br]-SB-Cu (II) nano-catalyst (0.9 mol%, 0.012 g) were stirred at 40 °C. The reaction was followed by thin-layer chromatography (TLC) at different time intervals in (n-Hexane/Ethyl acetate: 4:1). The reaction mixture was cooled, and the catalyst removed by an external magnet. 5mL of HCl (5 N) was added to the reaction mixture and extracted with 3x10mL of ethyl acetate. The organic phase was extracted again with the HCl solution (1 N), followed by a saturated solution of NaCl. The organic phase was dried with the anhydrous Na_2SO_4, filtered and then

evaporated. The pure product was obtained in 97% yield by recrystallization with n-Hexane/Ethyl acetate solvent mixture.

Results And Discussion

Catalyst Characterization

Fe_3O_4@SiO_2-Im[Br]-SB-Cu(II) nano-catalyst was synthesized (Scheme 1) and investigated in the synthesis of tetrazole derivatives (Scheme 2). The prepared catalyst is characterized by various methods. The FT-IR spectra of the catalyst synthesis steps are shown in Fig. 1. The spectrum 1a, which corresponds to the Fe_3O_4 nanoparticles, show the peaks at 571 and 3442 cm^{-1} corresponding to stretching vibrations of Fe-O and OH groups, respectively.[28, 29] The appearance of new picks at 1077 and 1192 cm^{-1} are corresponding to Si-O (Symm.) and Si-O (Asymm.), respectively. These picks are a confirmation that the surface of nanoparticles is protected by silica coating layer (Fig. 1, 1b).[30] The transmittance of core shelled Fe_3O_4 nanoparticles was slightly lower than that of Fe_3O_4 nanoparticles due to silica coating. Absorbed picks in 2852 (Symm.), 2934 (Asymm.), 1420 (Bending) and 814 cm^{-1}, respectively, correspond to CH_2 and C-Cl are evidence of the modification of nanoparticles surface (Fig. 1, 1c).[31] The disappearing C-Cl pick and the appearance of new picks in 1632 and 1742 cm^{-1} indicate that the imidazole ring was coupled to the nanoparticles surface (Fig. 1, 1d).[32] The spectrum 1e shows pick in 3422 cm^{-1}, which correspond to NH of amine group. The new pick at 1636 cm^{-1} is evidence of the formation of imine (Fig. 1, 1f).[33] The new picks at 635 and 620 cm^{-1} correspond to Cu-N and Cu-O. Also, the transfer of imine peak to lower frequencies confirms the formation of the metal complex (Fig. 1, 1g).

The elemental composition of Fe_3O_4@SiO_2-Cl (Fig. 2) and the nano-catalyst Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) (Fig. 3) was estimated by Energy Dispersive X-rays (EDX) analysis. Absence of chlorine element in the nano-catalyst confirms the attachment of ionic metal Schiff base complex on the surface of modified nanoparticles leading to the nano-catalyst. Anticipated elemental composition: C (10.40%), N (3.77%), O (40.21%), Si (5.48%), Fe (36.49%), Br (0.57%) and Cu (3.10%).

The morphology of Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) nano-catalyst was determined by Scanning Electron Microscopy (SEM). SEM images show spherical and irregular shapes for the nanoparticles (Fig. 4).

The X-ray diffraction (XRD) patterns of Fe_3O_4, Fe_3O_4 @ SiO_2 and Fe_3O_4@SiO_2-Im [Br] -SB-Cu (II) are shown in Fig. 5. The XRD pattern of Fe_3O_4 magnetic nanoparticles is in accordance with (PDF # 88−0866, reference JCPDS card no. 19−629), which shows a crystalline cubic spinel structure.[34] XRD patterns of Fe_3O_4, Fe_3O_4 @ SiO_2 and Fe_3O_4 @ SiO_2-Im[Br]-SB-Cu (II) show the peaks in 2θ = 30.1°, 35.4°, 43.1°, 53.4°, 57°, and 62.6° which are related to the pages of (220), (311), (400), (422), (511), and (440), respectively and are in full agreement with the Fe_3O_4 pattern showing that their crystalline phase and position have not changed. These results indicate that the crystalline cubic structure of nanoparticles

Fe_3O_4 is preserved during the catalyst preparation process. In the $Fe_3O_4@SiO_2$ spectrum, a broad peak is observed in $2\theta = 10-20°$, which is related to amorphous silica. This broad peak for the nano-catalyst was shifted to lower angles due to the synergetic effect of amorphous silica and Cu(II)-coordinated Schiff base. The average size of nanoparticles was calculated by the Debye−Scherrer equation ($D = K.\lambda / \beta.\cos\theta$, λ (wavelength, 0.154 nm), K (a crystallized form factor, 0.94), β (Full width at half maximum, (rad)), θ (Bragg reflection angle, (°)) to be about 28 nm which correspond to the TEM results.

The magnetic property of nano-catalyst was measured at different steps of the synthesis by vibrating sample magnetometer (VSM) (Fig. 6). As shown in Fig. 6, the magnetic properties of nanoparticles are gradually reduced by the silica layer coating and the by the coupling of the Cu(II)-complex to the surface of the nanoparticles. Although the magnetic saturation values for Fe_3O_4, $Fe_3O_4@SiO_2$ and $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) are 80, 58 and 38 emu g^{-1}, respectively, nano-catalyst has still a strong magnetic property for its removal from the reaction mixture by an external magnet.

The thermal stability of $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) nano-catalyst was examined by TGA technique (Fig. 7). In the thermogram diagram of this catalyst, the maximum weight loss occurs in the range of 414 to 500°C (15%), which is related to removing organic groups from the surface of the catalyst. The two weight losses before 414°C and 138°C, are related to removing hydroxyl groups (5%) and adsorbed water molecules on the surface of iron oxide nanoparticles, respectively. Based on this graph and the ICP-OES analysis, the ligand to metal ratio was estimated to be 2: 1.

The amount of supported copper on the $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) nano-catalyst was determined by AAS & ICP-OES analyzes. AAS analysis showed 0.83 mmol/g of Cu (II) on the nano-catalyst surface. This Cu(II) content was confirmed by the ICP-OES analysis which showed a 0.72 mmol of Cu(II) per gram of nano-catalyst.

The catalytic activity of $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) was investigated in the synthesis of 1-phenyl and 5-phenyl 1-H tetrazole derivatives. The synthesis of 1-phenyl 1-H tetrazole derivatives was optimized using the reaction model of aniline, triethyl orthoformate, and sodium azide (Scheme 3). The results of this investigation are summarized in Table 1. Firstly, the reaction efficiency in polar solvents is higher than in non-polar solvents (Entries 1−8). This is probably due to the ionic nature of catalyst. The reaction was run in the presence of different level of catalyst and the best result was obtained with 0.6 mol% of catalyst. A control reaction with 0 mol% of catalyst was run and as expected no product was obtained (Entry 9). Other reactions controls were tried in the presence of Fe_3O_4 and $Fe_3O_4@SiO_2$-Im[Br] (Entries 14, 15) with very low efficiency. The effect of the temperature and time on the reaction were also investigated (Entries 16−21) and we concluded that the best conditions are: H_2O solvent, 0.6 mol% of the catalyst loading, time 20 min and 40°C.

The synthesis of 1-phenyl 1-H tetrazole derivatives

Table 1
Optimization of the reaction conditions for the synthesis of 1-phenyl- 1H tetrazole derivatives

Entry	Solvent	Catalyst (mol %)	Temperature (^{0}C)	Time (min)	Yield (%)[b]	TON[c]	TOF (h^{-1})[d]
1	H_2O	0.6	40	20	97	162	486
2	MeOH	0.6	40	20	75	125	375
3	EtOH	0.6	40	20	70	117	9.8
4	THF	0.6	40	20	30	50	150
5	CH_3CN	0.6	40	20	60	67	201
6	$CHCl_3$	0.6	40	20	40	67	201
7	CH_2Cl_2	0.6	40	20	40	80	240
8	Solvent-free	0.6	40	20	85	142	426
9	H_2O	-	40	24 h	-	-	-
10	H_2O	0.4	40	20	80	133	399
11	H_2O	0.9	40	20	90	150	450
12	H_2O	1	40	20	85	142	426
13	H_2O	1.4	40	20	78	130	390
14[e]	H_2O	0.008 gr	40	24 h	30	50	2.08
15[f]	H_2O	0.008 gr	40	24 h	50	83	3.5
16	H_2O	0.6	rt	20	60	100	300
17	H_2O	0.6	60	20	95	158	474
18	H_2O	0.6	80	20	85	142	426
19	H_2O	0.6	100	20	70	117	351
20	H_2O	0.6	40	10	70	117	702
21	H_2O	0.6	40	30	92	153	306

a Aniline (1.0 mmol), Triethyl orthoformate (1.2 mmol), Sodium azide (1mmol) and $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II).

Entry	Solvent	Catalyst (mol %)	Temperature (⁰C)	Time (min)	Yield (%)[b]	TON[c]	TOF (h⁻¹)[d]

After optimizing the reaction conditions, different 1-phenyl 1H-tetrazole derivatives were synthesized by using different aniline derivatives under the same conditions (Table 2). The reaction in the presence of electron-donating and electron-withdrawing groups on benzaldehyde and the spatial barrier on aniline have significant impact on the reaction efficacy (Entries 2, 3 & 7, 8).

Table 2. Synthesis of 1-phenyl-1H-tetrazole derivatives in the presence $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) catalyst[a]

Entry	R	Product	Time (min)	Yield (%) [b]	MP found (Lit.) (°C) [34]
1	H	4a	20	97	64−66 (64−65)
2	2-Cl	4b	30	86	127−130 (127−131)
3	4-Cl	4c	30	95	156−158 (157−158)
4	4-CH₃	4d	15	92	92−94 (94−95)
5	4-OCH₃	4e	10	92	115−117 (114−115)
6	4-NO₂	4f	60	92	200−204 (201−202)
7	2-OH	4g	45	90	205−207 (-)
8	4-OH	4h	15	95	215−218 (-)
9	4-Br	4i	30	90	181−184 (183−185)

[a] Reaction conditions: Aniline (1.0 mmol), Triethyl orthoformate (1.2 mmol), Sodium azide (1.0 mmol) and $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) (0.5 mol %) in the water at 40 ºC.

[b] Isolated yield.

The plausible mechanism for the synthesis of 1-phenyl- 1H tetrazole derivatives by using $Fe_3O_4@SiO_2@Im[Br]$-SB-Cu (II) nano-catalyst is depicted in Scheme 4.[36]

The reaction model using benzaldehyde, hydroxy amine hydrochloride and sodium azide was selected to optimize the conditions for the synthesis of 5-phenyl- 1H-tetrazole derivatives (Scheme 5). The results of this investigation are shown in Table 3. Firstly, water was identified as the solvent of choice (Entries 1−8). As in the case of 5-phenyl 1-H tetrazole derivatives, we confirmed that the reaction needs the catalyst to proceed and no product was obtained in the absence of the catalyst (Entries 9−13). In this reaction model, the highest conversion rate was obtained in the presence of 0.9 mol% of catalyst (Entry 1). Also in the presence of the precursor of our catalyst (Fe_3O_4 and $Fe_3O_4@SiO_2$-Im[Br]), the reaction conversion rate was very low (Entries 14, 15). The effect of temperature and reaction time was also investigated (Entries 16−21) and the best conditions are: H_2O as solvent, 0.9 mol% of the catalyst, time 20 min and 40°C.

Table 3

Optimization of the reaction conditions for the synthesis of 5-phenyl- 1H tetrazole derivatives [a]

Entry	Solvent	Catalyst (mol %)	Temperature (^0C)	Time (min)	Yield (%)[b]	TON[c]	TOF[d]
1	H_2O	0.9	40	20	97	108	323
2	MeOH	0.9	40	20	80	88.9	267
3	EtOH	0.9	40	20	70	77.8	233
4	THF	0.9	40	20	20	22.2	66.6
5	CH_3CN	0.9	40	20	40	44.4	133.3
6	$CHCl_3$	0.9	40	20	30	33.3	100
7	CH_2Cl_2	0.9	40	20	30	33.3	
8	Solvent-free	0.9	40	20	70	77.8	233
9	H_2O	-	40	24 h	-	-	-
10	H_2O	0.4	40	20	70	140	420
11	H_2O	0.6	40	20	85	94	282
12	H_2O	1	40	20	90	100	300
13	H_2O	1.4	40	20	75	83	249
14[e]	H_2O	0.9	40	24 h	30	33.3	1.4
15[f]	H_2O	0.9	40	24 h	50	55.5	2.3
16	H_2O	0.9	rt	20	60	66.6	200

[a] Benzaldehyde (1.0 mmol), hydroxy amine hydrochloride (1.0 mmol), Sodium azide (1.2 mmol) and $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) (0.9 mol%, 0.012 g).

[b] Isolated Yield.

[c] Turnover numbers (TONs) defined as mmol of products reacted per mmol of catalyst.

[d] Turnover frequencies (TOFs) defined as mmol of products reacted per mmol of catalyst per hour.

[e] Fe_3O_4 (0.012 gr).

[f] $Fe_3O_4@SiO_2$-Im[Br] (0.012 gr).

Entry	Solvent	Catalyst (mol %)	Temperature (°C)	Time (min)	Yield (%)[b]	TON[c]	TOF[d]
17	H_2O	0.9	60	20	97	108	323
18	H_2O	0.9	80	20	85	94.4	283
19	H_2O	0.9	100	20	75	83.3	250
20	H_2O	0.9	40	10	75	83	498
21	H_2O	0.9	40	30	90	100	200

[a] Benzaldehyde (1.0 mmol), hydroxy amine hydrochloride (1.0 mmol), Sodium azide (1.2 mmol) and Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) (0.9 mol%, 0.012 g).

[b] Isolated Yield.

[c] Turnover numbers (TONs) defined as mmol of products reacted per mmol of catalyst.

[d] Turnover frequencies (TOFs) defined as mmol of products reacted per mmol of catalyst per hour.

[e] Fe_3O_4 (0.012 gr).

[f] Fe_3O_4@SiO_2-Im[Br] (0.012 gr).

Different 5-phenyl 1H-tetrazole derivatives were synthesized using different benzaldehyde derivatives under the optimized conditions (Table 4). The results show that the reaction efficiency is impacted by the electronic properties and the position of the substituents groups on the benzaldehyde ring.

Table 4. Synthesis of 5-Phenyl-1H-Tetrazole derivatives in presence of Fe3O4@SiO2-Im[Br]-SB-Cu (II) catalyst [a]

Entry	R	Product	Time (min)	Yield (%)	MP Found (Lit.) ($^{\circ}$C)
1	H	4a	20	97	214–216 (215–216) [36]
2	2-Cl	4b	45	80	230–233 (-)
3	4-Cl	4c	20	80	260–262 (261–263) [37]
4	4-CH3	4d	20	82	253–254 (250–251) [41]
5	4-OCH3	4e	20	86	232–234 (231–232) [38]
6	4-NO2	4f	60	75	218–220 (218–219) [36]
7	2-OH	4g	30	82	221–223 (220–222) [39]
8	4-OH	4h	20	90	235–236 (233–234) [40]
9	4-Br	4i	20	92	264–266 (265) [42]

Reaction conditions: Benzaldehyde (1.0 mmol), hydroxy amine hydrochloride (1.0 mmol), Sodium azide (1.2 mmol) and $Fe_3O_4@SiO_2$-Im[Br] -SB-Cu (II) (0.9 mol %, 0.012 g) in water at 40 $^{\circ}$C.

b Isolated yield.

The hypothetical mechanism for the formation of 5-phenyl- 1H-tetrazole derivatives using $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) nano-catalyst is illustrated in Scheme 6.[44]

We studied the reusability of $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) in the synthesis of tetrazole derivatives. After completing the reaction, the catalyst was separated by an external magnet from the reaction mixture, washed with ethyl acetate, dried, and reused in subsequent catalytic cycles under the same reaction conditions. The recycled catalyst was successfully reused for eight runs (Fig. 8). The FT-IR comparison of fresh and reused catalysts is shown in Fig. 9 with no change in the catalyst structure.

To investigate the heterogenous nature of our catalyst, the hot filtration test was performed.

A hot filtration test was performed to evaluate the metal leaching rate and assess if the catalytic activity of our catalyst is not due to leached Cu(II) species in the reaction mixture (Fig. 10). In the model reaction for the synthesis of 1-Phenyl- 1H-tetrazole derivatives after the half reaction time in which the reaction conversion rate is 50%, the reaction was stopped and catalyst was removed with an external magnet. The reaction mixture without the catalyst was then allowed to proceed further (60 min). After the separation of catalyst from the reaction mixture, no increase in conversion was observed. This is a strong indication that the catalytic process is taking place only in the presence of the nano-catalyst and confirms the heterogeneity of the catalytic process (Fig. 10). The test also indicate that there is no active copper metal species in the synthesis of tetrazole was leached into the reaction mixture.

Our catalyst was benchmarked against published catalyst for the synthesis of tetrazole derivatives (Table 5). The data in Table 5 show that our catalyst (Entry 7) is more efficient than the other reported

catalysts in terms of yield and reaction time.

Table 5

Comparison of $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) with other catalysts in synthesis of tetrazole derivatives

Entry	Catalyst	Conditions	Time (min)	Yield (%) a	Ref.
1	Cu (OAC)$_2$	EDS (chcl-urea), 100°C	720	90	[44]
2	$Fe_3O_4@WO_3$-EAE-SO$_3$H	H_2O, 60°C	30	95	[45]
3	Pd-isatin-boehmite	PEG-400, 120°C	480	94	[46]
4	Cu (II) immobilized on $Fe_3O_4@SiO_2@L$-Arginine	PEG, 120°C	180	95	[47]
5	$Fe_3O_4@SiO_2$/Salen Cu (II)	DMF, 120°C	420	90	[48]
6	Nano CSMIL [b]	Solvent-free, 70°C	420	87	[49]
7	$Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II)	H_2O, 40°C	20	97	This work c

a Isolated Yield.

b Chitosan derived magnetic ionic liquid.

c Aniline (1.0 mmol), Triethyl orthoformate (1.2 mmol), Sodium azide (1.0 mmol) and $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) (0.6 mol %, 0.008 g). Benzaldehyde (1.0 mmol), hydroxy amine hydrochloride (1.0 mmol), Sodium azide (1.2 mmol) and $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) (0.9 mol %, 0.012 g).

Conclusion

A novel and green heterogenous nano-catalyst was prepared. Its catalytic efficiency in water was demonstrated in the synthesis of tetrazole derivatives. This catalyst showed better performance than published catalysts for tetrazole synthesis. The catalyst is easy to recycle with high catalytic efficiency and its intrinsic design allowing for its use in water with high performance may be used as a guidance for the preparation of other useful heterogenous catalytical systems.

Declarations

Acknowledgment

Conflicts of interest

There are no conflicts to declare.

Data availability / Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to the continuation of the work at Faculty of Science, University of Birjand, Iran, but are available from the corresponding author on reasonable request.

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Figures
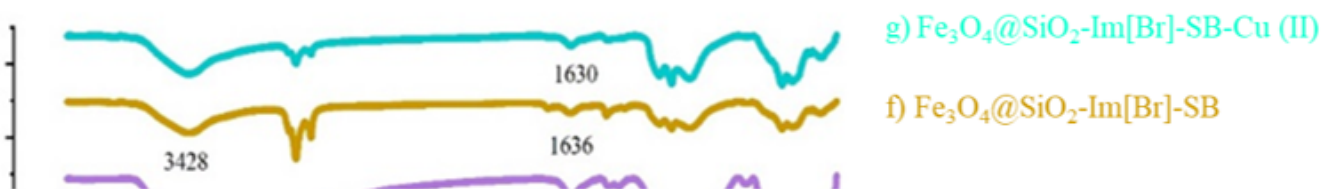
Figure 1

FT-IR spectra: a) Fe_3O_4 ; b) $Fe_3O_4@SiO_2$; c) $Fe_3O_4@SiO_2$-$(CH_2)_3Cl$; d) $Fe_3O_4@SiO_2$-Im; e) $Fe_3O_4@SiO_2$-Im[Br]; f) $Fe_3O_4@SiO_2$-Im[Br]-SB; g) $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II)
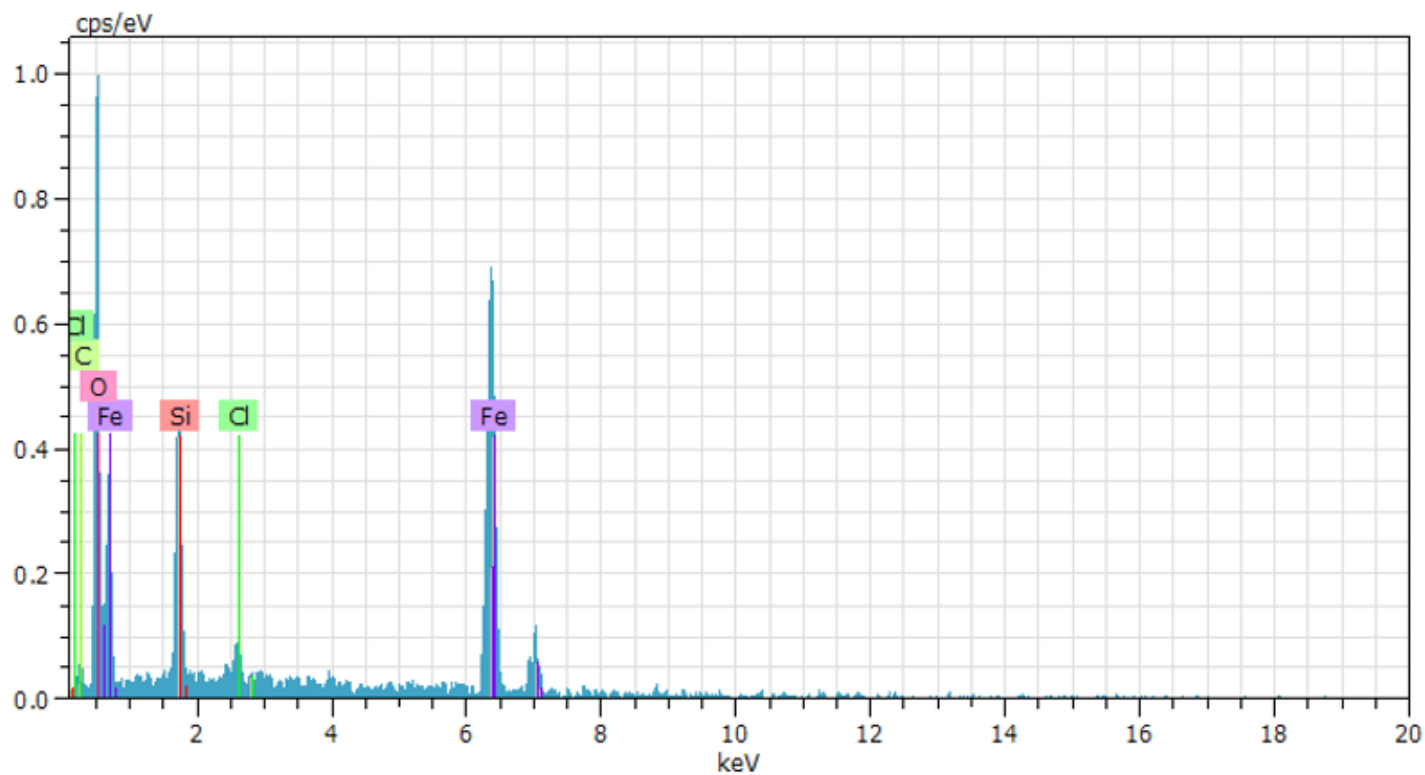
Figure 2

EDX Spectrum of $Fe_3O_4@SiO_2$-Cl
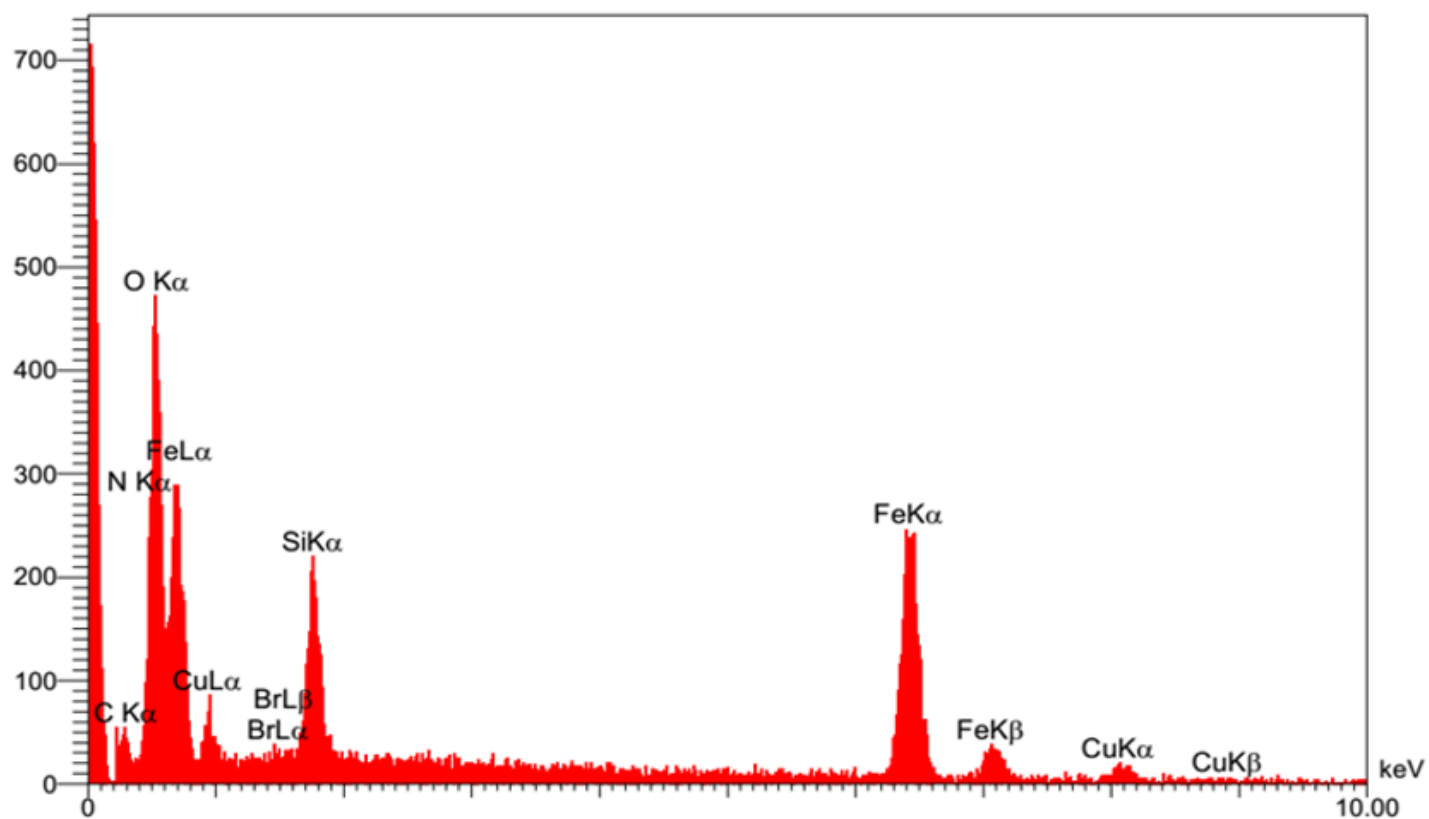
Figure 3

EDX Spectrum & data of Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II)
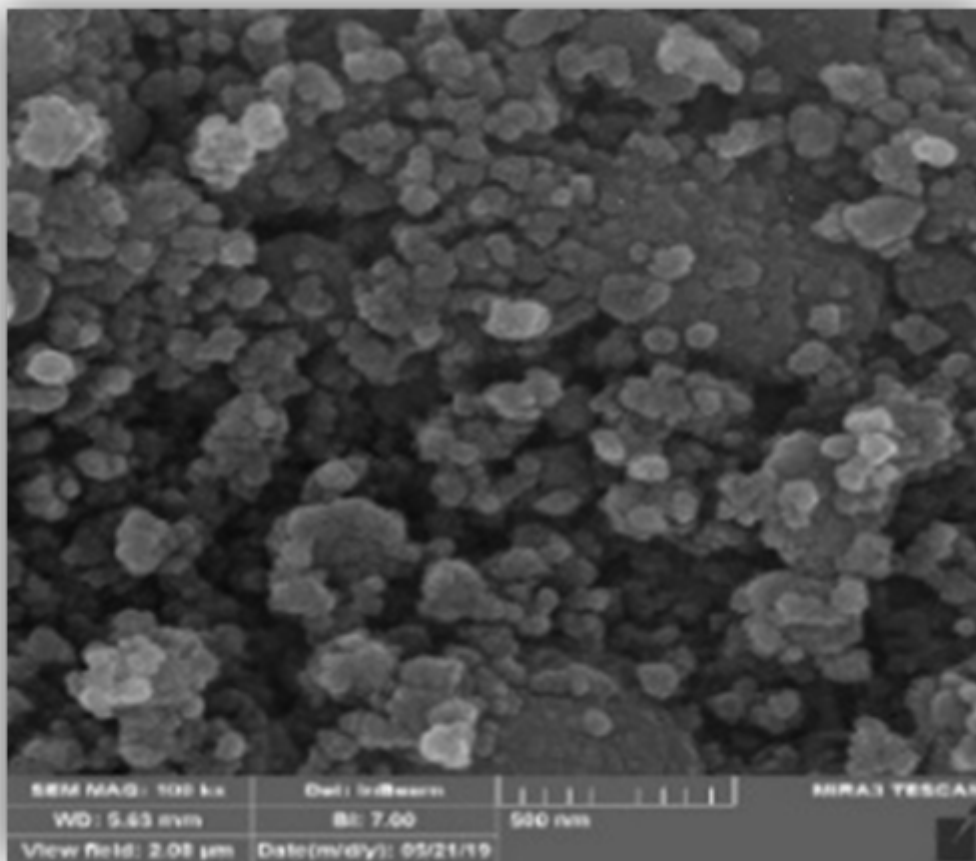
Figure 4

SEM image of Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) nanocomplex
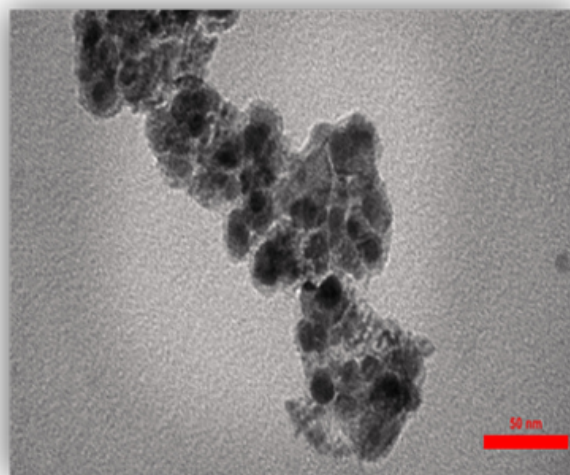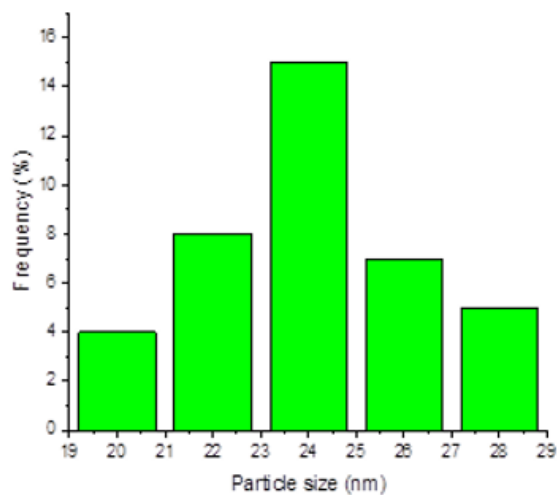
Figure 5

a) TEM image and b) histogram of Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) nano complex
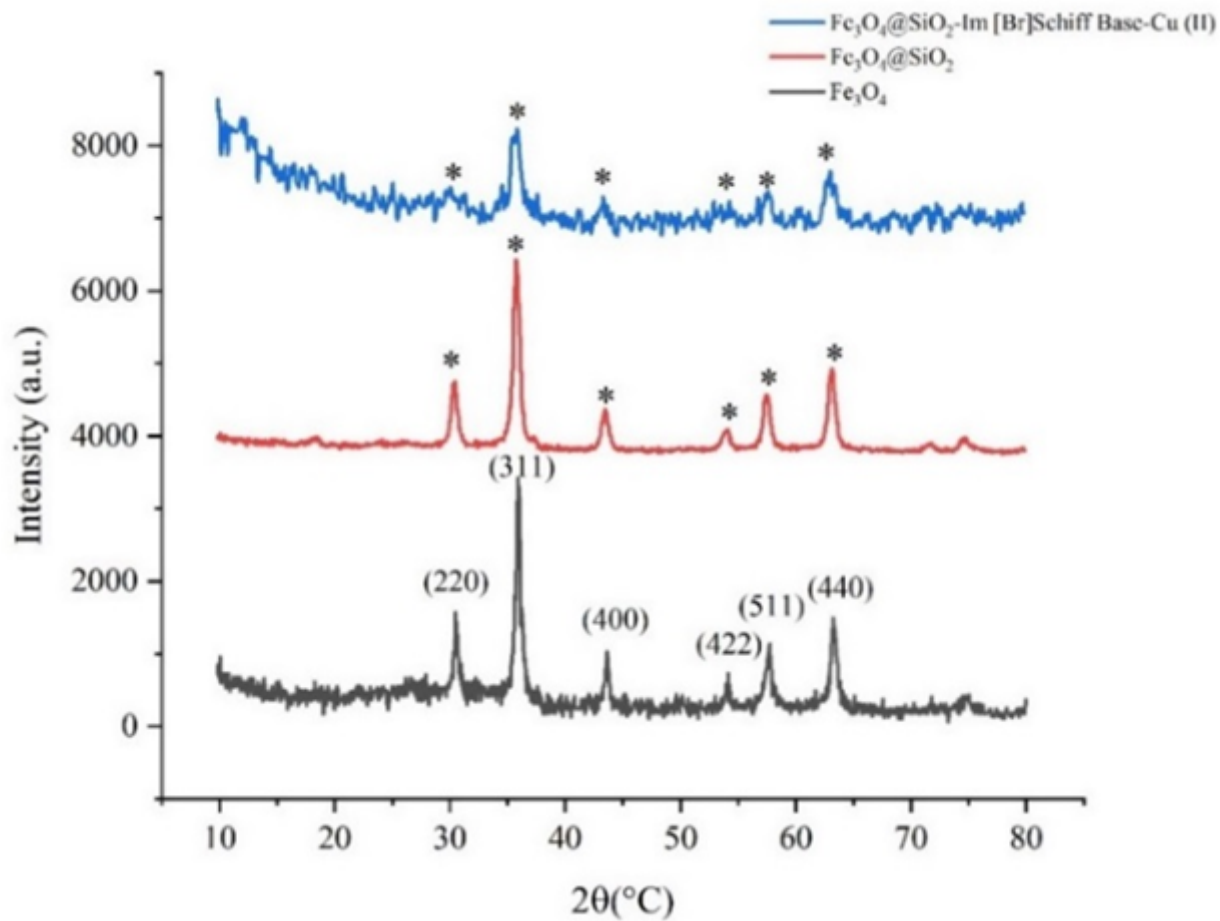
Figure 6

XRD patterns of Fe_3O_4, Fe_3O_4@SiO_2 and Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) nanocomplex
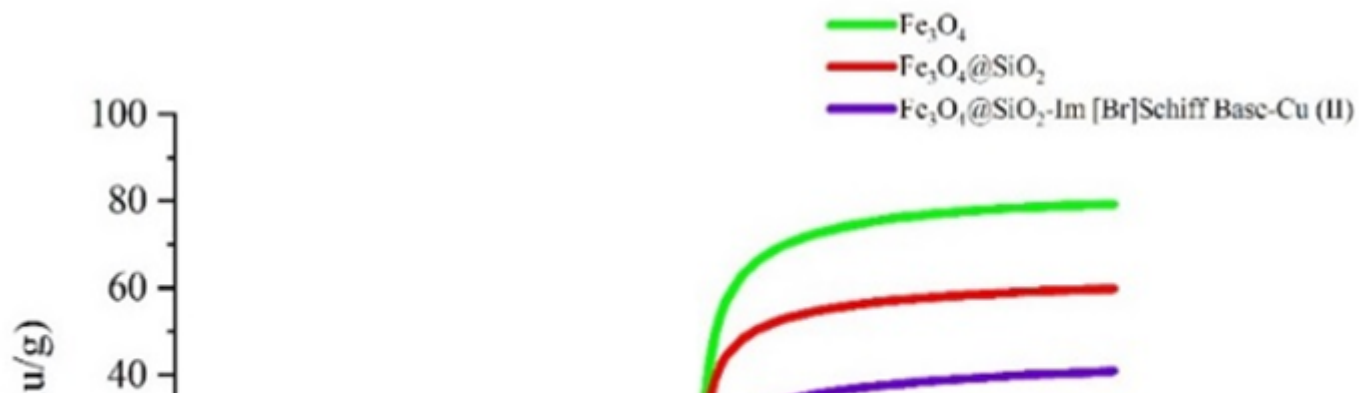
Figure 7

Magnetization curves of Fe_3O_4, Fe_3O_4@SiO_2 and Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) nano complex
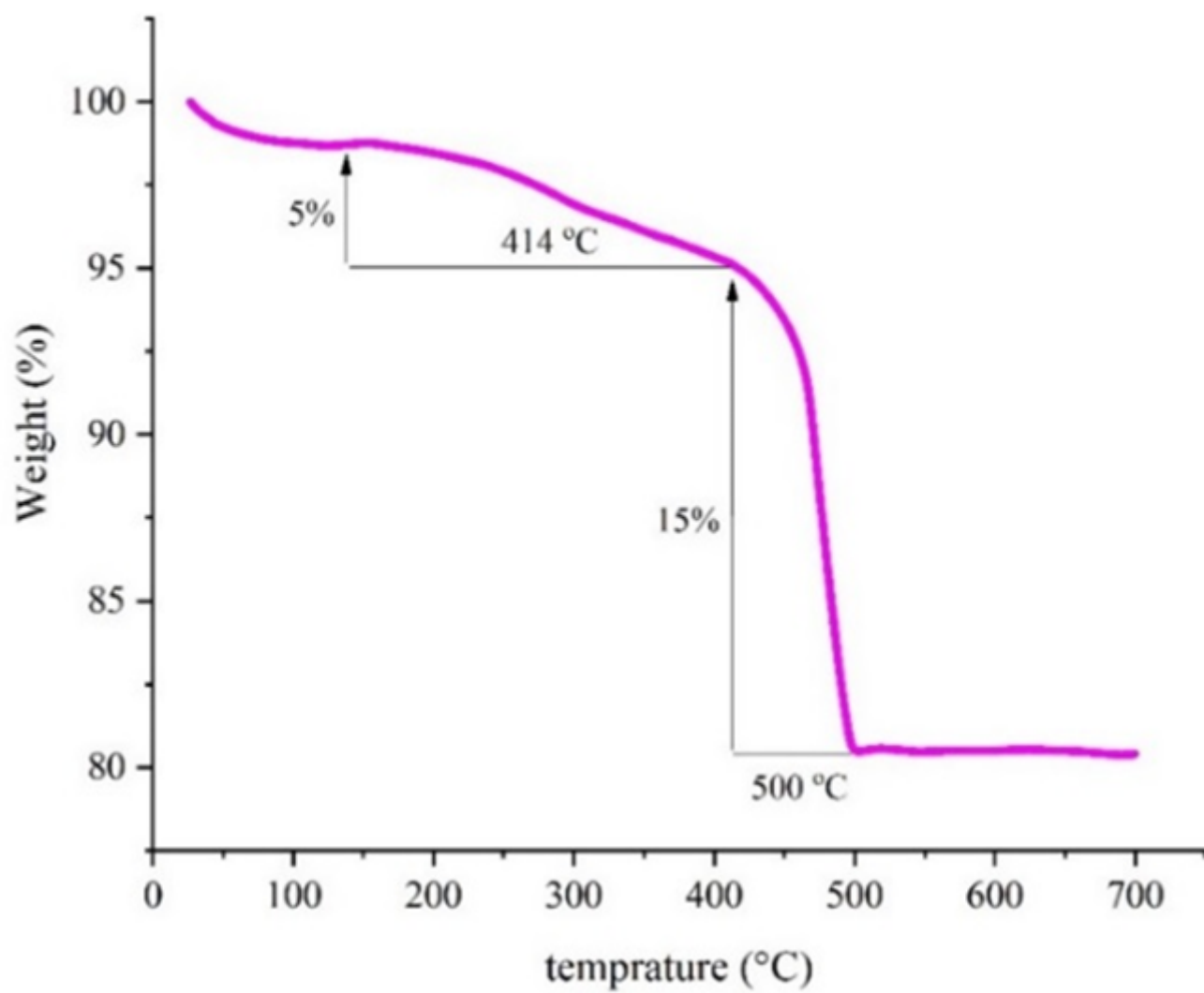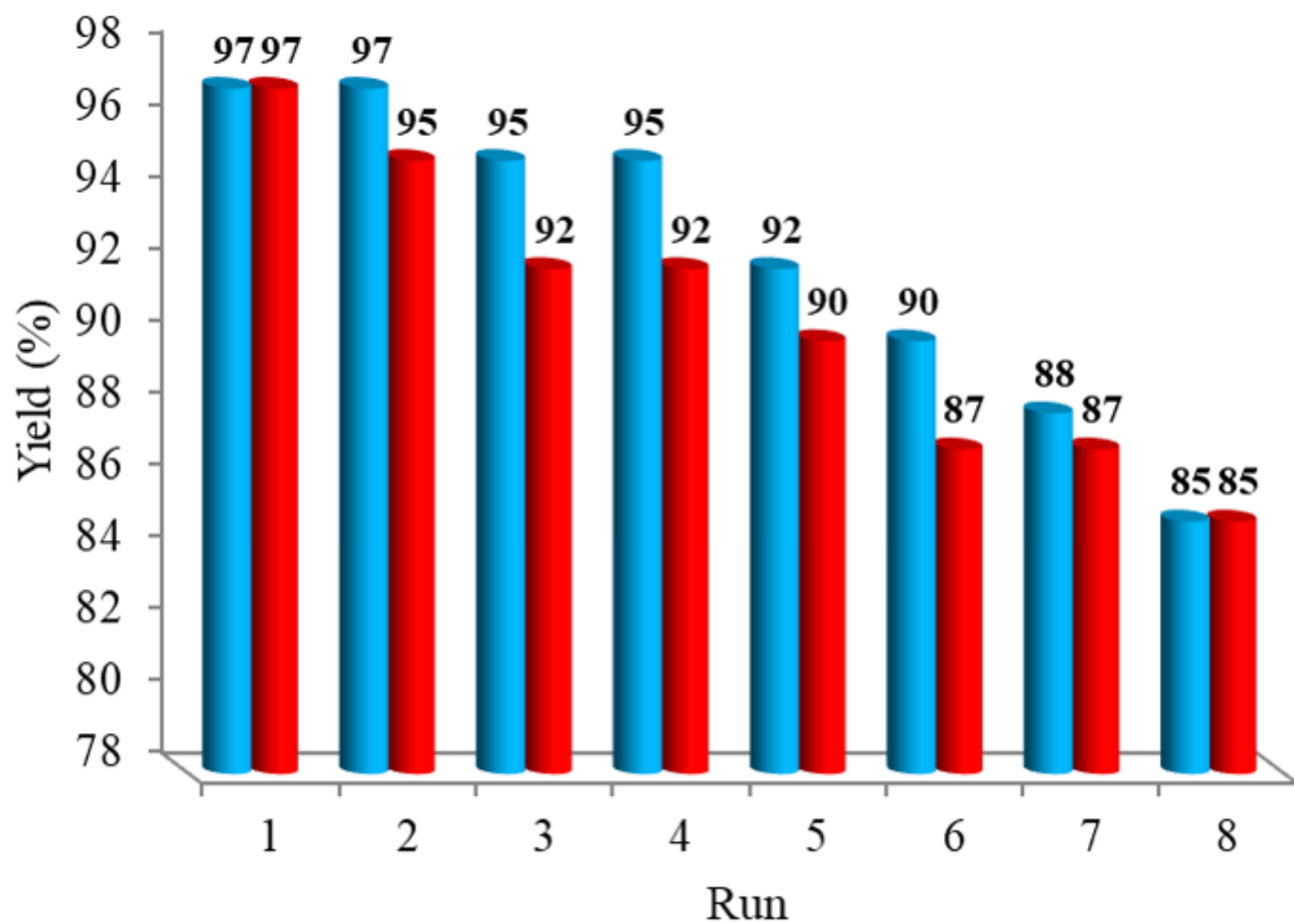
Figure 8

TGA of Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) nanocomplex

Figure 9

Recycling chart of Fe_3O_4@SiO_2-Im[Br]-SB-Cu (II) MNP catalyst for the synthesis of 1-Phenyl-1H-tetrazole (blue) and 5-Phenyl-1H-tetrazole (red) derivatives

Figure 10
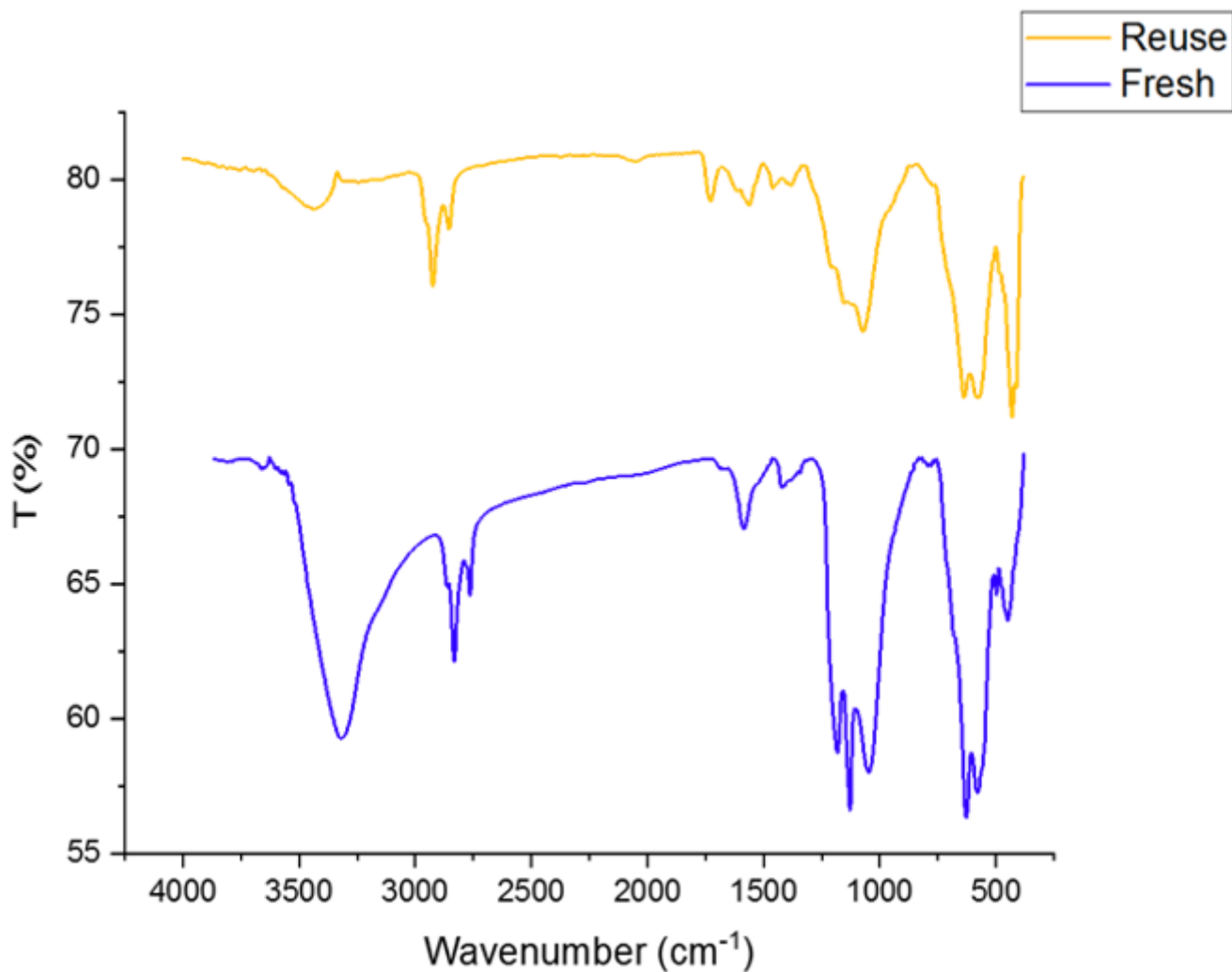
FT-IR spectra of fresh (blue) and reuse (orange) of $Fe_3O_4@SiO_2$-Im[Br]-SB-Cu (II) MNP catalyst

Supplementary Files

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- scheme1.png
- scheme2.png
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- scheme5.png
- SCHEME6.png