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Salen complex of Cu(II) supported on superparamagnetic Fe_3O_4@SiO_2 nanoparticles: An efficient and recyclable catalyst for synthesis of 1- and 5-substituted 1H-tetrazoles

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ABSTRACT

An efficient and general method has been developed for synthesis of 1- and 5-substituted 1H-tetrazoles from nitriles and amines using magnetite nanoparticles immobilized Salen Cu(II) as an efficient and recyclable catalyst. The structural and magnetic properties of functionalized magnetic silica are identified by transmission electron microscopy (TEM), scanning electron microscopy (SEM) and vibrating sample magnetometer (VSM) instruments. NMR, FT-IR, elemental analysis and XRD were also used for identification of these structures.

Nanocatalyst can be easily recovered by a magnetic field and reused for subsequent reactions for at least 7 times with less deterioration in catalytic activity.

1. Introduction

In recent years, magnetic nanoparticles (MNPs) have gained an increasing interest because of their potential applications; examples include their uses for cell separation [1], magnetic resonance imaging [2], drug delivery systems [3], protein separation [4] and cancer treatments through hyperthermia [5].

Magnetite metal oxide nanoparticles, especially Fe_3O_4 nanoparticles have attracted increasing interest because of their unique physical properties including the high surface area, superparamagnetism, low toxicity and their potential applications in various fields [6]. Fe_3O_4 nanoparticles are easily prepared and surface functionalized and they can be recycled from the solution by external magnetic field. So, the catalyst supported on Fe_3O_4 nanoparticles can be easily separated from the reaction system and reused [7].

Currently, much attention is focused on the synthesis of magnetic core–shell structures by coating a SiO_2 shell around a preformed nanoparticle [8].

Homogeneous catalysts show higher catalytic activities than their heterogeneous counterparts because of their solubility in reaction media, which increases catalytic site accessibility for the substrate [9]. But, recycling homogeneous catalysts is often tedious and time consuming and there is also product contamination observed when these catalysts are used.

Schiff base transition metal complexes have been extensively studied because of their potential use as catalysts in a wide range of reactions [10]. Moreover homogenous metal Schiff base complex catalysts are deactivated easily through the formation of dimeric peroxo and μ-oxo species [11]. For overcoming the aforementioned drawbacks, recently our group reported Schiff base complex of metal ions supported on superparamagnetic Fe_3O_4@SiO_2 nanoparticles as an efficient, selective and recyclable catalyst for synthesis of 1,1-diacetates from aldehydes under solvent-free conditions [12].

Tetrazoles have attracted considerable interest in recent times because of their wide applications [13]. Mainly with the roles played by tetrazoles in coordination chemistry as ligands [14], in medicinal chemistry as a more favorable pharmacokinetic profile and a metabolically stable surrogate for carboxylic acid functionalities [15]. Tetrazoles have been successfully used in various material sciences and synthetic organic chemistry as analytical reagents [16] and synthons [17]. So synthesis of this heterocyclic nucleus is of much current importance.

Tetrazole rings can be prepared in several ways, 1-substituted 1H-tetrazoles are synthesized by reaction between hydrazoic acid and isocyanides [18], acid-catalyzed cycloaddition between isocyanides and trimethysilyl azide [19], cyclization between primary amines, or their salts, with an orthocarboxylic acid ester and

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sodium azide [20] and cyclizations from an amine, triethyl orthoformate, and sodium azide using AcOH [21], PCl_5 [22], $In(OTf)_3$ [23], $Yb(OTf)_3$ [24], SSA [25], $[HBIm]BF_4$ [26] and recently natrolite zeolite as a catalyst [27].

The conventional method of synthesizing 5-substituted 1H-tetrazoles is by addition of azide ions to organic nitriles. Different homogenous and heterogeneous catalysts such as $ZrOCl_2$ [28], $AlCl_3$ [29], $BF_3 \cdot OEt_2$ [30], $Pd(OAc)_2/ZnBr$ [31], ZnO [32], $ZnBr_2$ [33], $ZnCl_2$/tungstates [34], Zn/Al hydrotalcite [35], $Zn(OTf)_2$ [36], Zn hydroxyapatite [37], ZnS [38], Cu_2O [39a], nano $CuFe_2O_4$ [40], $CdCl_2$ [41], natural zeolite [42], nano ZnO/Co_3O_4 [43], $FeCl_3{-}SiO_2$ [44], $Fe(OAc)_2$ [45], $Fe(HSO_4)_3$ [46], Zeolite and sulfated zirconia [47] and γ-Fe_2O_3 [48] have been reported for the promotion of reaction between nitrile and NaN_3 or TMS-N_3. Recently, Ali Khalafi-Nezhad et al. have reported nano CSMIL as a novel heterogeneous catalyst for synthesis of tetrazole from nitrile [49].

Although most of these methods are worthwhile, many of them have one or more of the following drawbacks: tedious workup of the reaction mixture, difficulty in separation and recovery of the catalyst, expensive moisture sensitive reaction conditions, toxic metals, and hydrazoic acid which is highly toxic and explosive. So it is of great practical importance to develop a more efficient and environmentally benign method that avoids all these drawbacks.

In this work, our interest in this area led us to explore the Salen Cu(II) complex immobilized onto the surface of magnetic nanoparticles, which can be sufficiently applied even for synthesis of 1- and 5-substituted 1H-tetrazoles from nitriles and amines (Fig. 1). The catalyst can be easily separated from the reaction mixture to reuse.

2. Experimental

Chemical materials were purchased from the Merck Chemical Company in high purity. All the solvents were distilled, dried and purified by standard procedures. Fourier transform infrared (FT-IR) spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. The conversions % was determined by GC on a Shimadzu model GC-14A instrument. The NMR spectra were recorded on a Bruker avance DPX 250 MHz spectrometer in chloroform ($CDCl_3$) and dimethylsulfoxide (DMSO) using tetramethylsilane (TMS) as an internal reference. X-ray powder diffraction (XRD) spectra were taken on a Bruker AXS D8-advance X-ray diffractometer with Cu Kα radiation ($\gamma = 1.5418$). Field emission scanning electron microscopy (FE-SEM) images were obtained on HITACHI S-4160 and transmission electron microscopy (TEM) images were obtained on a Philips EM208 transmission electron microscope with an accelerating voltage of 100 kV. Magnetic properties were obtained on a BHV-55 vibrating sample magnetometer (VSM). Dynamic light scattering (DLS) was recorded on a HORIBA-LB550. Tetrazoles were characterized by their melting points, ^1H NMR and ^{13}C NMR and comparison with literature values. The progress of the reaction was monitored by TLC and purification was achieved by silica gel column chromatography.

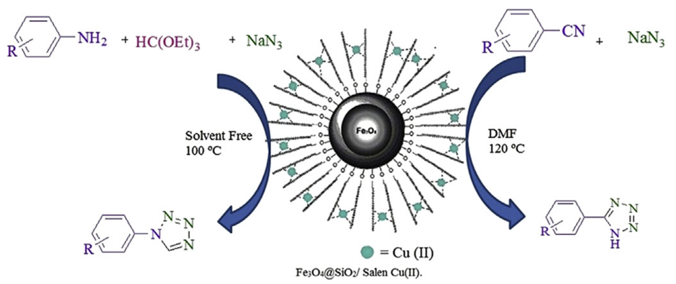


Fig. 1. Synthesis of 1- and 5-substituted 1H-tetrazoles in the presence of $Fe_3O_4@SiO_2$/Salen of Cu(II).

2.1. General procedure

2.1.1. Preparation of Fe_3O_4 nanoparticles

The mixture of $FeCl_3 \cdot 6H_2O$ (1.3 g, 4.8 mmol) in water (15 mL) was added to the solution of polyvinyl alcohol (PVA 15,000) (1 g), as a surfactant, and $FeCl_2 \cdot 4H_2O$ (0.9 g, 4.5 mmol) in water (15 mL), which was prepared by completely dissolving PVA in water followed by addition of $FeCl_2 \cdot 4H_2O$. The resultant solution was left to be stirred for 0.5 h in 80 °C. Then hexamethylenetetramine (HMTA) (1.0 mol/L) was added drop by drop with vigorous stirring to make a black solid product when reaction media reaches pH 10. The resultant mixture was heated on water bath for 2 h at 60 °C and the black magnetite solid product was filtered and washed with ethanol three times and was then dried at 80 °C for 10 h [12].

2.1.2. Preparation of $Fe_3O_4@SiO_2$ core–shell

The core–shell $Fe_3O_4@SiO_2$ nanospheres were prepared by a modified Stober method [50]. Briefly, Fe_3O_4 (0.50 g, 2.1 mmol) was dispersed in the mixture of ethanol (50 mL), deionized water (5 mL) and tetraethoxysilane (TEOS) (0.20 mL), followed by the addition of 5.0 mL of NaOH (10 wt%). This solution was stirred mechanically for 30 min at room temperature. Then the product, $Fe_3O_4@SiO_2$, was separated by an external magnet, and was washed with deionized water and ethanol three times and dried at 80 °C for 10 h. FT-IR (KBr pellets, cm^{-1}): 3400 (O–H), 1000–1150 (Si–O–Si) and 556 (Fe–O) [12].

2.1.3. General procedure for preparation of the salen ligand

To the solution of 3-aminopropyl (triethoxy) silane (1 mmol, 0.176 g) in 25 mL ethanol, the stoichiometric amount of salicylaldehyde (1 mmol, 0.122 g) in ethanol (25 mL) was added dropwise

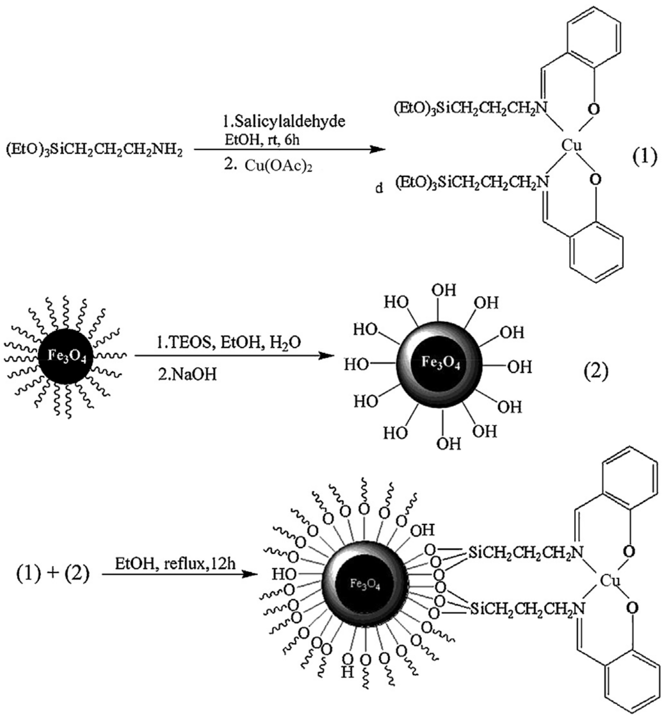


Fig. 2. Preparation process of salen complex of Cu(II) supported on superparamagnetic $Fe_3O_4@SiO_2$ nanoparticles.

to the yellow solution obtained, because of imine formation, then the solution was stirred at room temperature for 6 h. The resulting salen ligand, as the bright yellow precipitate, was separated by filtration and washed with ethanol (5 mL) and then dried in vacuum. The crude product was recrystallized from ethanol to obtain the pure product in 98% yield (0.271 g). Anal. found (%): C, 58.36; H, 8.52; N, 4.48. Calc. for $C_{16}H_{27}NO_4Si$ (%): C, 59.04; H, 8.36; N, 4.30. ^1H NMR (250 MHz, $CDCl_3$): $\delta = 0.7$ (t, 2H, CH_2, $J = 8.5$ Hz); 1.22 (t, 9H, CH_3, $J = 7.0$ Hz); 1.82 (m, 2H, CH_2); 3.59 (t, 2H, CH_2, $J = 6.5$ Hz); 3.81 (q, 6H, CH_2, $J = 7.0$ Hz); 6.85–6.96 (m, 2H, CH aromatic); 7.21–7.29 (m, 2H, CH aromatic); 8.33 (s, 1H, CH); 13.59 (s, 1H, OH). ^{13}C NMR (63 MHz, $CDCl_3$): $\delta = 7.94$, 18.32, 24.37, 58.43, 62.05, 117.03, 118.38, 118.81, 131.12, 132.05, 161.40 and 164.78.

2.1.4. General procedure for the preparation of the salen complex of Cu(II)

$Cu(OAc)_2$ (0.182 g, 1 mmol) was added to the solution of the salen ligand (0.651 g, 2 mmol) in ethanol (25 mL) and the mixture was refluxed to complete the reaction. The progress of the reaction was monitored by TLC. After the completion of complex formation, a color change was observed. Resulting product was filtered and washed with ethanol. Then the product was purified by recrystallization from ethanol and the resulting pure salen complex was obtained. FT-IR spectrum of the complex showed the expected bands, including a distinctive band due to C=N stretching, which is lowered in frequency on complexation to metal ion.

2.1.5. General procedure for salen complex of metal ion functionalized magnetite@silica nanoparticles

$Fe_3O_4@SiO_2$ (2 g) was added to the solution of salen complex of Cu(II) (1 mmol) in ethanol (10 mL) and the resultant mixture was reflux for 12 h. Hot ethanol and water were added to the product, $Fe_3O_4@SiO_2$/Salen of Cu(II), and then nanocatalyst was separated by an external magnet and dried at 80 °C for 6 h.

2.1.6. General procedure for the synthesis of 1-substituted-1H-tetrazoles from amines

A mixture of amine (1 mmol), sodium azide (1.2 mmol), triethyl ortho-formate (1.2 mmol) and catalyst (0.02 g, contains 0.4 mol% of Cu(II)) was taken in a round-bottomed flask and stirred at 100 °C. The progress of the reaction was followed by thin-layer chromatography (TLC). After completion of the reaction, the reaction mixture was cooled to room temperature and diluted with ethyl acetate (3 × 20 mL). The catalyst was removed by using magnetic field or filtration and then the resulting solution was washed with water, dried over anhydrous Na_2SO_4 and was evaporated. The residue was concentrated and recrystallized from EtOAc–hexane (1:9).

All products were characterized by ^1H, ^{13}C NMR, FT-IR, and melting point which were in agreement with literature. We have reported the spectral data of some aromatic and heteroaromatic synthesized compounds.

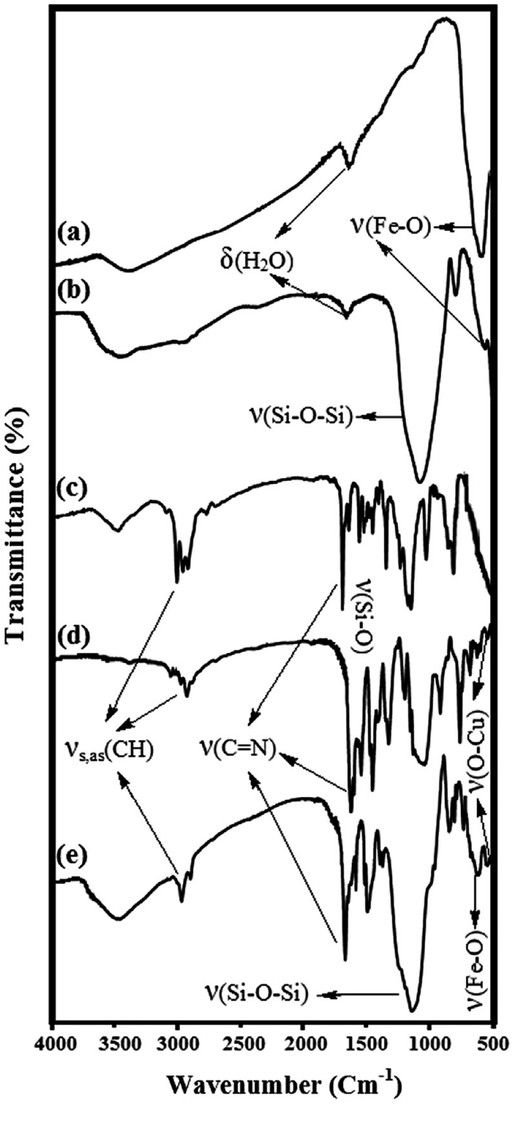


Fig. 3. a) Fe_3O_4, b) $Fe_3O_4@SiO_2$, c) Salen ligand, d) Salen complex of Cu(II), e) $Fe_3O_4@SiO_2$/Salen of Cu(II).

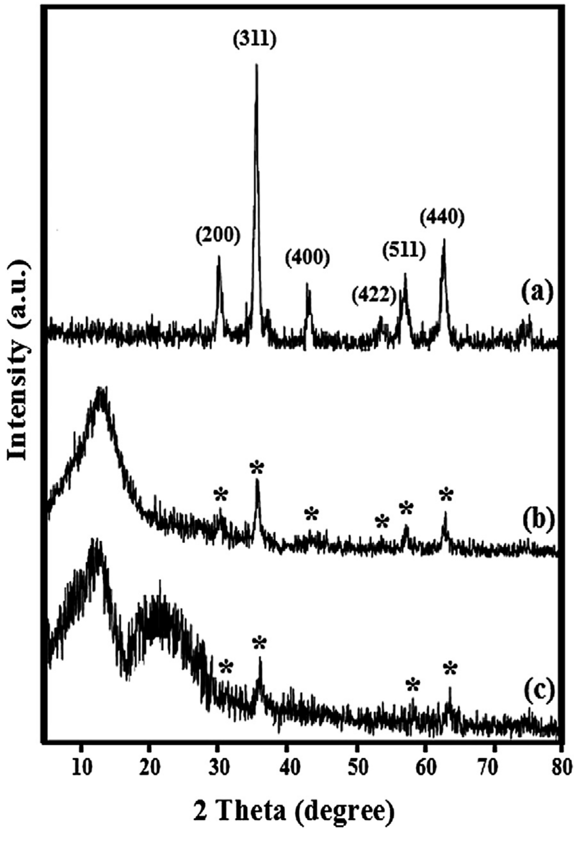


Fig. 4. XRD patterns of (a) Fe_3O_4 [12], (b) $Fe_3O_4@SiO_2$ [12] and (c) $Fe_3O_4@SiO_2$/Salen of Cu(II).

2.1.6.1. 1-(4-Bromophenyl)-1H-tetrazole (Table 2, entry 4). White solid (83% yield); m.p. 183–184 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 7.00$ (d, $J = 8.7$ Hz, 2H), 7.54 (d, $J = 7.5$ Hz, 2H), 8.07 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 153.5, 137.0, 128.9, 125.3, 118.0 ppm. FT-IR (KBr) (ν_{max} cm^{-1}): 3532, 3167, 3058, 2863, 1675, 1591, 1575, 1488, 1415, 1319, 1284, 1235, 1200, 1153, 1100, 1098, 1013, 992, 834 cm^{-1}.

2.1.6.2. 1-(4-Acetylphenyl)-1H-tetrazole (Table 2, entry 9). Yellow solid (78% yield); m.p. 175–176 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.76$ (s, 3H), 7.78–7.97 (d, $J = 8.7$ Hz, 2H), 8.12–8.31 (d, $J = 8.7$ Hz, 2H), 9.32 (s, 1H) ppm. ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ 26.58, 122.32, 131.12, 136.00, 138.67, 142.22, 194.11 ppm. FT-IR (KBr) (ν_{max} cm^{-1}): 3024, 1712, 1675, 1634, 1600, 1576, 1532, 1500, 1243, 1056, 976 cm^{-1}.

2.1.6.3. 2-Methyl-6-(1H-tetrazol-1-yl) pyridine (Table 2, entry 7). White solid (85% yield); m.p. 106–107 °C. ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 2.90$ (s, 3H), 7.21–7.43 (m, 1H), 7.84–8.02 (m, 2H), 9.32 (s, 1H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 123.4, 129.4, 130.2, 137.0, 155.3 ppm. FT-IR (KBr) (ν_{max} cm^{-1}): 3025, 1632, 1587, 1555, 1511, 1497, 1254, 1065, 973 cm^{-1}.

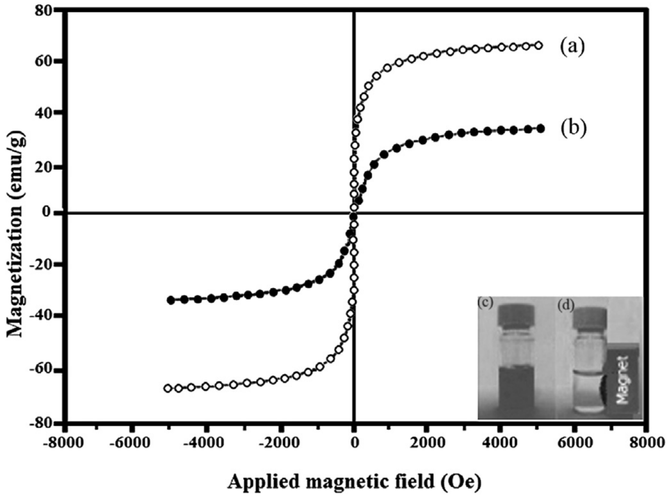


Fig. 6. Magnetization curves at 300 K for Fe_3O_4 (a), $Fe_3O_4@SiO_2$/Salen of Cu(II) (b). The dispersion (c) and separation (d) process of magnetic $Fe_3O_4@SiO_2$/Salen of Cu(II) nanocatalyst.

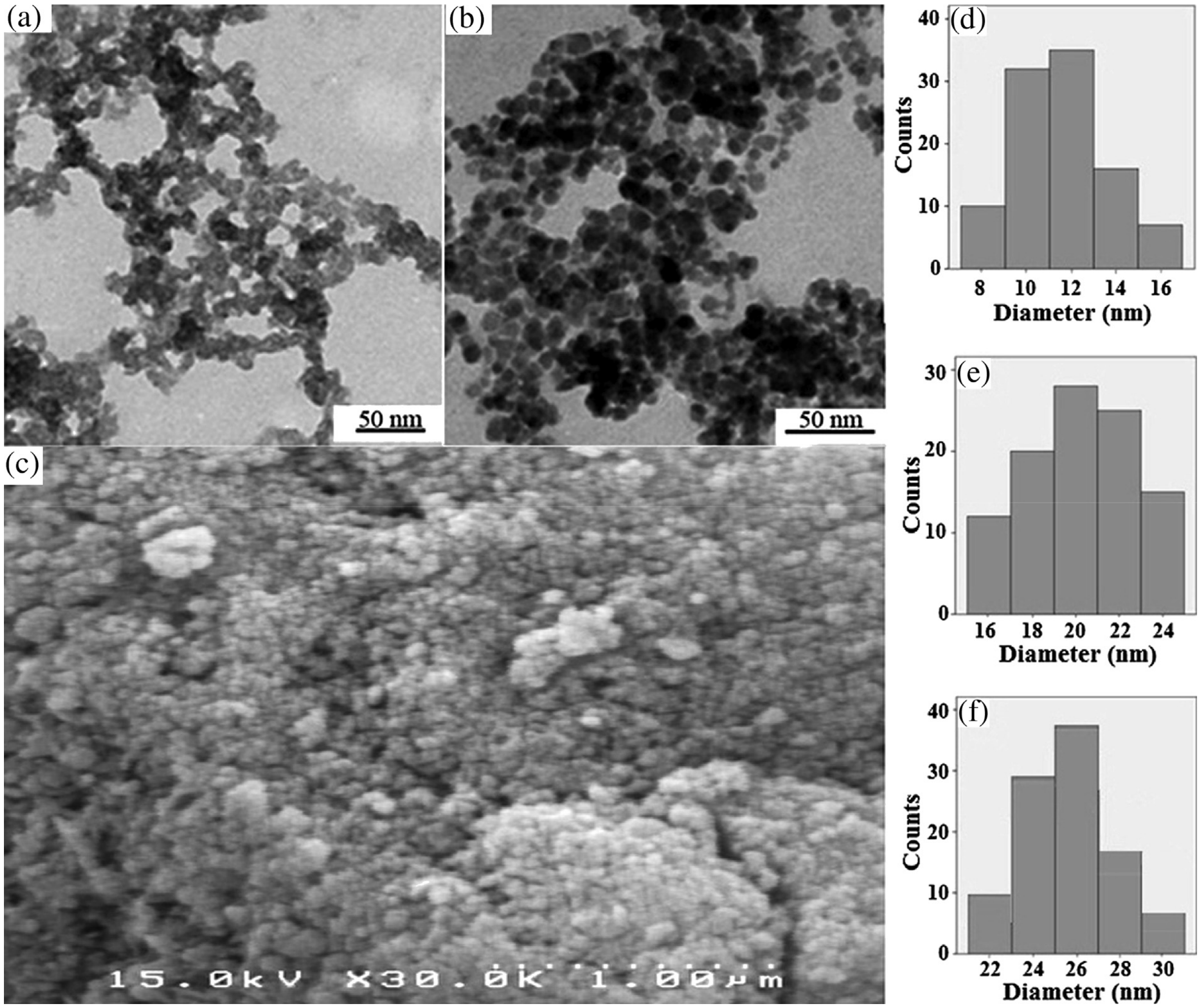
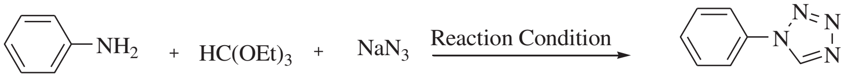


Fig. 5. TEM images of Fe_3O_4 (a) and $Fe_3O_4@SiO_2$ (b). FE-SEM image of $Fe_3O_4@SiO_2$/Salen of Cu(II) (c). DLS of Fe_3O_4 (d), $Fe_3O_4@SiO_2$ (e) and $Fe_3O_4@SiO_2$/Salen of Cu(II) (f) respectively.

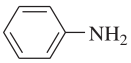
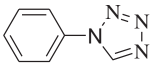
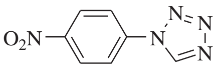
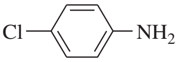
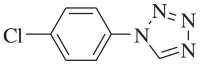
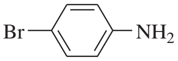
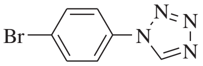
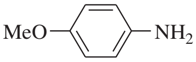
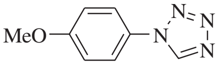
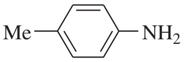
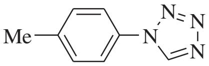
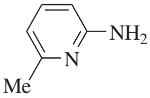
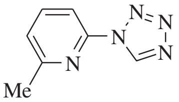
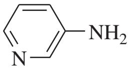
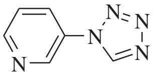
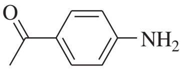
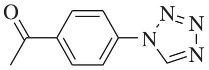
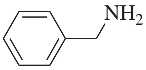
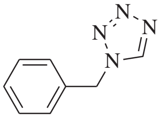
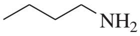
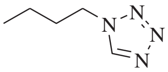
Table 1
Effect of catalysts and solvents on formation of 1-substituted 1H-tetrazoles.[a]



Entry	Solvent/catalyst amount (g)	Temp. (°C)	Time (min)	Yield[b] (%)
1	Neat/0.005	100	90	60
2	Neat/0.01	100	90	73
3	Neat/0.015	100	90	85
4	Neat/0.02	100	75	92
4	Neat/0.025	100	75	92
5	DMF/0.02	Reflux	100	78
6	DMSO/0.02	Reflux	100	75
7	EtOH/0.02	Reflux	120	40
8	MeOH/0.02	Reflux	100	50

[a] Conditions: aniline (1 mmol), triethyl orthoformate (1.2 mmol), and sodium azide (1 mmol).
[b] Yields refer to isolated pure product.

Table 2
Preparation of 1-substituted 1H-tetrazoles in the presence of Fe_3O_4@SiO_2/Salen Cu(II).[a]

Entry	Substrate	Product	Time (h)	Yield[b] (%)	Mp. (°C) (Lit.)[c]	Ref.
1			1	92	63–64 (64)	[49]
2			3	75	200–201 (200)	[49]
3			1.5	85	152–155 (153)	[49]
4			1.5	87	168–170 (170)	[49]
5			1	96	115 (115)	[49]
6			1	90	91–101 (92)	[49]
7			3	80	165–166 (166)	[49]
8			2.5	80	77 (77)	[49]
9			3	77	175–177 (175)	[49]
10			3	83	128–130 (130)	[49]
11			3.5	75	142–144 (144)	[49]

[a] Conditions: amines (1 mmol), triethyl orthoformate (1.2 mmol), and sodium azide (1 mmol).
[b] Yields refer to isolated pure product.
[c] Melting points reported in the parenthesis refer to the literature melting points.

Table 3
Comparison of various catalysts in synthesis of 1-substituted 1H-tetrazoles.[a]

Entry	Catalyst	Solvent	T (°C)	Yield[b] (%)	Time (h)	Ref.
1	Natrolite zeolite	Neat	120	82	4	[27]
2	$In(OTf)_3$	Neat	100	89	1.5	[23]
3	Silica sulfuric acid	Neat	120	95	5	[25]
4	$[HBIm]BF_4$	Neat	100	91	0.33	[26]
5	Fe_3O_4@SiO_2/Salen Cu(II)	Neat	100	96	1.0	–

[a] Conditions: *p*-methoxy aniline (1 mmol), triethyl orthoformate (1.2 mmol), and sodium azide (1 mmol), solvent free, 100 °C.
[b] Yields refer to isolated pure product.

2.1.7. General procedure for the synthesis of 5-substituted-1H-tetrazoles

A mixture of nitrile (1 mmol), sodium azide (1.5 mmol) and catalyst (0.02 g, contains 0.4 mol% of Cu(II)) in DMF (3 mL) was taken in a round-bottomed flask and stirred at 120 °C. The progress of the reaction was followed by thin-layer chromatography (TLC). After completion of the reaction, the reaction mixture was cooled to room temperature and diluted with ethyl acetate (3 × 20 mL). The catalyst was removed by using magnetic field or filtration and then the resulting solution was washed with 1 N HCl, dried over anhydrous Na_2SO_4 and then was evaporated. The crude products were obtained in excellent yields. All products were characterized by ^1H, ^{13}C NMR, FT-IR, and melting point which were in agreement with literature. We have reported the spectral data of some aromatic and heteroaromatic synthesized compounds.

2.1.7.1. 2-(1H-tetrazol-5-yl) pyridine (Table 5, entry 9). White solid (90% yield); m.p. 210–211 °C. ^1H NMR (250 MHz, DMSO-d_6): $\delta = 7.69$ (m, 1H), 8.23 (m, 1H), 8.21 (d, $J = 8.2$ Hz, 1H), 8.78 (d, $J = 5.0$ Hz, 1H) ppm. ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 120.4, 138.4, 137.8, 150.6 ppm. FT-IR (KBr) (ν_{max} cm^{-1}): 3434, 2865, 2716, 1635, 1596, 1510, 1383, 1367, 1045, 867 cm^{-1}.

2.1.7.2. 5-(4-Chlorophenyl)-1H-tetrazole (Table 5, entry 6). White solid (84% yield); m.p. 261–263 °C. ^1H NMR (250 MHz, DMSO-d_6): $\delta = 7.72$ (d, $J = 8.6$ Hz, 2H), 8.12 (d, $J = 8.6$ Hz, 2H) ppm. ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 123.5, 129.3, 130.2, 136.3, 156.4 ppm. FT-IR (KBr) (ν_{max} cm^{-1}): 3423, 2931, 2822, 2745, 1612, 1468, 1445, 1398, 1356, 1173, 1089, 1043, 878, 773 cm^{-1}.

2.1.7.3. 5-(Naphthalen-1-yl)-1H-Tetrazole (Table 5, entry 12). White solid (90% yield); m.p. 263 °C. ^1H NMR (250 MHz, DMSO-d_6): $\delta = 7.66$–7.81 (m, 3H), 7.91–8.03 (m, 1H), 8.09–8.12 (m, 1H), 8.19–8.23 (m, 1H), 8.62–8.72 (m, 1H) ppm. ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 125.9, 126.7, 127.9, 128.0, 128.8, 131.3, 132.8, 169.0 ppm. FT-IR (KBr) (ν_{max} cm^{-1}): 3429, 3061, 2817, 2720, 1628, 1601, 1523, 1491, 1385, 1358, 1252, 1128, 1100, 958, 869 cm^{-1}.

2.1.7.4. 5-(Phenanthren-9-yl)-1H-tetrazole (Table 5, entry 11). White solid (83% yield); m.p. 213–215 °C. ^1H NMR (250 MHz, DMSO-d_6): $\delta = 7.50$–7.70 (m, 4H), 7.99 (d, $J = 8.3$ Hz, 2H), 8.43 (d, $J = 8.2$ Hz, 2H), 8.52 (s, 1H) ppm. ^{13}C NMR (62.5 MHz, DMSO-d_6): δ 125.3, 126.8, 128.2, 130.9, 131.8, 133.6, 134.0, 134.9, 161.0 ppm. FT-IR (KBr) (ν_{max} cm^{-1}): 3448, 3063, 2823, 2743, 1622, 1594, 1511, 1490, 1381, 1361, 1253, 1125, 1100, 969, 867 cm^{-1}.

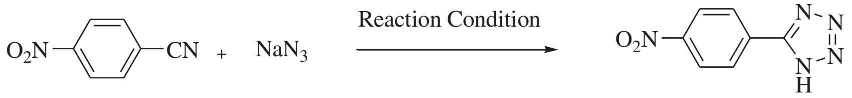
3. Result and discussions

Salen complex of Cu(II) was prepared by refluxing stoichiometric amounts of Schiff base ligand and copper acetate in ethanol. The complexes were insoluble in water but soluble in most organic solvents (Fig. 2).

Determination of Cu content was performed by Inductively Coupled Plasma (ICP) analyzer. According to the ICP analysis, the Cu content in the magnetic nanocatalyst was determined which revealed the presence of 0.21 mmol/g for this catalyst.

The IR spectra of complex show important bands from the free salen ligand. The free ligand exhibits a ν (C=N) stretch at 1634 cm^{-1} while in the complex, this band shifts to lower frequency and appears at 1622 cm^{-1} because of coordination of the nitrogen with Cu(II). Vibrations in the range of 1480–1600 cm^{-1} are attributed to the aromatic ring. The presence of vibration bands in 559–588, 1100 and 3400 cm^{-1}, which are caused by Fe–O, Si–O–Si, and OH respectively, demonstrates the existence of Fe_3O_4 and SiO_2 components in the synthesized complex. The presence of several bands with medium intensity in 2750–3000 cm^{-1} region is allocated to C–H stretching of methylene group. The presence of two or three bands in the low frequency region between 420 and 550 cm^{-1} indicates the coordination of phenolic oxygen in addition to azomethine nitrogen. C–O stretching vibrations shows a peak centered at 1200–1320 cm^{-1}. The OH stretching vibration, ν(O–H) found as a medium band at 3410 cm^{-1} in free Schiff base ligand, disappears in the spectra of the complex (Fig. 3).

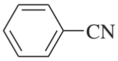
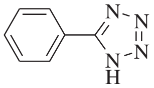
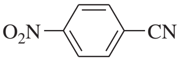
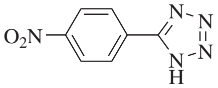
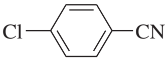
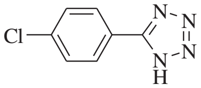
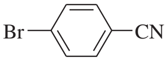
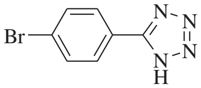
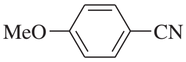
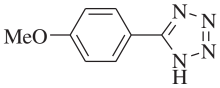
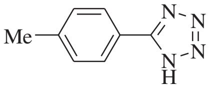
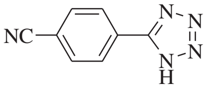
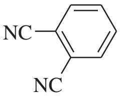
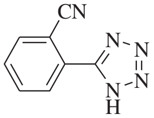
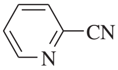
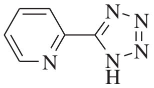
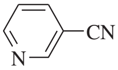
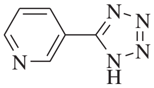
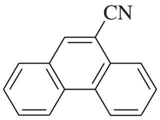
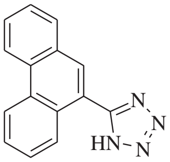
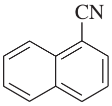
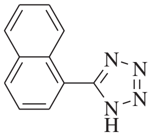
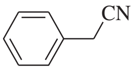
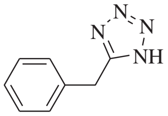
Table 4
Effect of catalysts and solvents on forming 5-substituted 1H-tetrazoles.[a]



Entry	Solvent/catalyst amount (g)	Temp. (°C)	Time (h)	Yield[b] (%)
1	EtOH/0.02	90	24	40
2	MeOH/0.02	100	24	55
3	DMSO/0.02	120	10	87
4	Toluene/0.02	120	12	65
5	Neat/0.02	120	12	70
6	THF/0.02	100	12	70
7	DMF/0.005	120	12	75
8	DMF/0.01	120	12	82
9	DMF/0.015	120	8	87
10	DMF/0.02	120	6	92
11	DMF/0.025	120	6	92

[a] Conditions: *p*-nitro benzonitrile (1 mmol) and NaN_3 (1 mmol).
[b] Yields refer to isolated pure product.

Table 5
Preparation of 5-substituted 1H-tetrazoles in the presence of $Fe_3O_4@SiO_2$/Salen complex of Cu(II).[a]

Entry	Substrate	Product	Time (h)	Yield[b] (%)	Mp. (°C) (Lit.)[c]	Ref.
1			7	90	215 (215)	[49]
2			6	92	219 (219–220)	[39]
3			6	88	261–263 (262)	[49]
4			6.5	88	265–266 (266)	[49]
5			12	85	233 (231–233)	[39]
6			9	85	248–249 (248–249)	[39]
7			6	92	256 (255)	[39]
8			7	90	209–210 (208–210)	[39]
9			6	90	210–211 (211)	[49]
10			6	90	239 (238–240)	[47]
11			12	80	213–215 (215)	[49]
12			8	85	263 (264)	[49]
13			9	83	123 (123–124)	[39]

[a] Reaction conditions: nitrile compounds (1 mmol), NaN_3 (1 mmol), $Fe_3O_4@SiO_2$/Salen Cu(II) (0.02 g), DMF, 120 °C.

[b] Isolated yield.

[c] Melting points reported in the parenthesis refer to the literature melting points.

The crystalline structures of the Fe_3O_4 particles, Fe_3O_4@SiO_2 and Fe_3O_4@SiO_2/Salen Cu(II) were determined by powder X-ray diffraction (XRD). As shown in Fig. 4, it can be seen that the Fe_3O_4 obtained has highly crystalline cubic spinel structure which agrees with the standard Fe_3O_4 (cubic phase) XRD spectrum (PDF#88-0866). The patterns indicate a crystallized structure at 2θ: 30.1°, 35.4°, 43.1°, 53.4°, 57° and 62.6°, which are assigned to the (220), (311), (400), (422), (511) and (440) crystallographic faces of magnetite (reference JCPDS card no. 19-629). The XRD pattern of Fe_3O_4@SiO_2 prepared by the Stöber process, shows an obvious diffusion peak at $2\theta = 15–25°$ that appeared because of the existence of amorphous silica. For Fe_3O_4@SiO_2/Salen Cu(II) nanoparticles, the broad peak was transferred to lower angles due to the synergetic effect of amorphous silica and salen complex of Cu(II).

According to the result calculated by Scherrer equation, it was found that the diameter of Fe_3O_4 nanoparticles obtained was about 12 nm and Fe_3O_4@SiO_2 microspheres were obtained with a diameter of about 20 nm due to the agglomeration of Fe_3O_4 inside nanospheres and surface growth of silica on the shell [51].

The morphology and sizes of (a) Fe_3O_4 and (b) Fe_3O_4@SiO_2 particles were observed by transmission electron microscopy (TEM) as shown in Fig. 5.

Fig. 5(b) displays the TEM images of Fe_3O_4 nanoparticles coated with silica layers. The mesoporous silica shell on the surface of Fe_3O_4 is quite homogeneous and exhibits good monodispersity with estimated thickness of 8 nm. The morphology of Fe_3O_4@SiO_2/Salen of Cu(II) was also observed by FE-SEM (Fig. 5(c)).

In this study, Dynamic light scattering (DLS) was used for particle size analyzing of the catalyst. The average diameters of particles are evaluated to be about 12 nm for Fe_3O_4 Fig. 5(d), 20 nm for Fe_3O_4@SiO_2 Fig. 5(e) and 26 nm for Fe_3O_4@SiO_2/Salen of Cu(II) Fig. 5(f). The histogram was proposed according to the results obtained from the XRD and TEM images.

The magnetic properties of the sample containing a magnetite component were studied by a vibrating sample magnetometer (VSM) at 300 K (Fig. 6).

Fig. 6 shows the absence of hysteresis phenomenon and indicates that product has superparamagnetism at room temperature. The saturation magnetization values for Fe_3O_4 (a) and Fe_3O_4/SiO_2/Salen complexes of Cu(II) (b) were 64.8 and 35.2 emu/g, respectively. These results indicated that the magnetization of Fe_3O_4 decreased considerably with the increase of SiO_2 and salen complex of Cu(II). Nevertheless, the metal ion complex supported on Fe_3O_4@SiO_2 can still be separated from the solution by using an external magnetic field on the sidewall of the reactor Fig. 6(c,d).

At the first stage for 1-substituted 1H-tetrazoles, the reaction of aniline (1 mmol), triethyl orthoformate (1.2 mmol), and sodium azide (1 mmol) was investigated in presence of Fe_3O_4@SiO_2/Salen Cu(II) as a catalyst in various solvents and under neat conditions in the presence of various amount of catalyst. The results were summarized in Table 1.

As it was shown in Table 1, solvent free condition at 100 °C with 0.02 g catalyst (contains 0.4 mol% of Cu(II)) (Table 1, entry 4) is the best choice for these reactions. Other organic solvents like DMF, DMSO, MeOH and EtOH afforded the desired product in lower yields.

After optimizing the reaction conditions, we next investigated the generality of this condition using triethyl orthoformate, sodium azide, and several amines. The results are summarized in Table 2. A wide range of anilines containing electron-withdrawing and electron-donating groups such as, chloro, bromo, methyl, methoxy, acetyl and nitro underwent condensation in short reaction times with excellent isolated yields (Table 2). The catalytic system also worked well with heterocyclic amine such as amino pyridines (Table 2, entries 7, 8) to generate the corresponding tetrazoles. Also for aliphatic amines such as benzyl amine and n-butylamine (Table 2, entry 10, 11) a good yield of desired product was obtained.

To show the advantage of Fe_3O_4@SiO_2/Salen Cu(II) over some of the reported catalysts in the literature, we showed a reaction of *p*-methoxy aniline with triethyl orthoformate, and sodium azide in the presence of 0.02 g Fe_3O_4@SiO_2/Salen Cu(II) (Table 3). In comparison with the other reported catalysts in literature, we observed that the Fe_3O_4@SiO_2/Salen Cu(II) gives better yield in shorter reaction time and lower temperature than SSA and natrolite zeolite. Also this catalyst is comparable with [HBIm]BF_4 and In(OTf)$_3$.

The first step for the 5-substituted 1H-tetrazoles synthetic approach involved optimization of reaction conditions and exploring the catalytic activity of Fe_3O_4@SiO_2/Salen complex of Cu(II). The reaction of *p*-nitro benzonitrile (1 mmol) and NaN_3 (1 mmol), was investigated in the presence of Fe_3O_4@SiO_2/Salen Cu(II) as a catalyst in various solvents and temperatures in present of various amount of catalyst. The results were summarized in Table 4.

As it was shown in Table 4, DMF as a solvent at 120 °C with 0.02 g catalyst (contains 0.4 mol% Cu(II)) (Table 4, entry 10) is the best choice for these reactions. Other organic solvents like DMSO, THF, Toluene, EtOH, MeOH and neat condition afforded the desired product in lower yields (Table 4, entries 1–4, 6).

After optimizing the reaction conditions, we next used different nitriles as the substrates for this reaction. The results are summarized in Table 5. As the entries in Table 5 show, the catalysis proceeded well for a wide variety of aryl nitriles, providing the corresponding tetrazoles in high yields. The substituents on the nitriles had a significant effect on the tetrazole formation reaction. Reactions of electron poor aromatic and heteroaromatic nitriles, such as 4-nitrobenzonitrile, 2-cyanopyridines, 3-cyanopyridines, 1,2-dicyanobenzene and 1,4-dicyanobenzene were completed within a few hours (Table 5, entries 2, 7–10). Some electron rich nitriles required longer reaction time (Table 5, entries 5, 6). The best percentage conversions were observed for nitriles with electron withdrawing substituents. Interestingly 1,4-dicyanobenzene and 1,2-dicyanobenzene (Table 5, entries 7, 8) afforded the mono-addition product, though in the reaction between sodium azide with 1,4-dicyanobenzene and 1,4-dicyanobenzene in the presence of Zn(II) salts the double addition products were reported [33].

To show the advantage of Fe_3O_4@SiO_2/Salen Cu(II) over some of the reported catalysts in the literature, we showed a reaction of *p*-nitro benzonitrile (1 mmol) and NaN_3 (1 mmol) in the presence of 0.02 g Fe_3O_4@SiO_2/Salen Cu(II) Table 6. In comparison with the other reported catalysts in literature, we observed that the Fe_3O_4@SiO_2/Salen Cu(II) is comparable with some of these catalysts such as nano ZnO/Co_3O_4 and Zn/Al-HT (Table 6, entries 2, 4) and gives better yield in shorter reaction time than another ones.

The reusability of the catalyst is an important benefit especially for commercial applications. So, the recovery and reusability of nanocatalyst was investigated using the reaction of *p*-methoxy aniline, triethyl orthoformate, and sodium azide in the presence of Fe_3O_4@SiO_2/Salen complex of Cu(II) under optimized conditions (Fig. 7(a)). The catalyst was recovered by a magnetic field and was

Table 6
Comparison of various catalysts in synthesis of 5-substituted 1H-tetrazoles.[a]

Entry	Catalyst	Solvent	T (°C)	Yield[b] (%)	Time (h)	Ref.
1	Natural zeolite	DMF	120	90	14	[42]
2	Nano ZnO/Co_3O_4	DMF	120	90	12	[43]
3	ZnHAP	DMF	120	78	12	[37]
4	Zn/Al-HT	DMF	120	84	12	[35]
5	Fe_3O_4@SiO_2/Salen Cu(II)	DMF	120	92	6	–

[a] Conditions: *p*-nitro benzonitrile (1 mmol) and NaN_3 (1 mmol).
[b] Yields refer to isolated pure product.

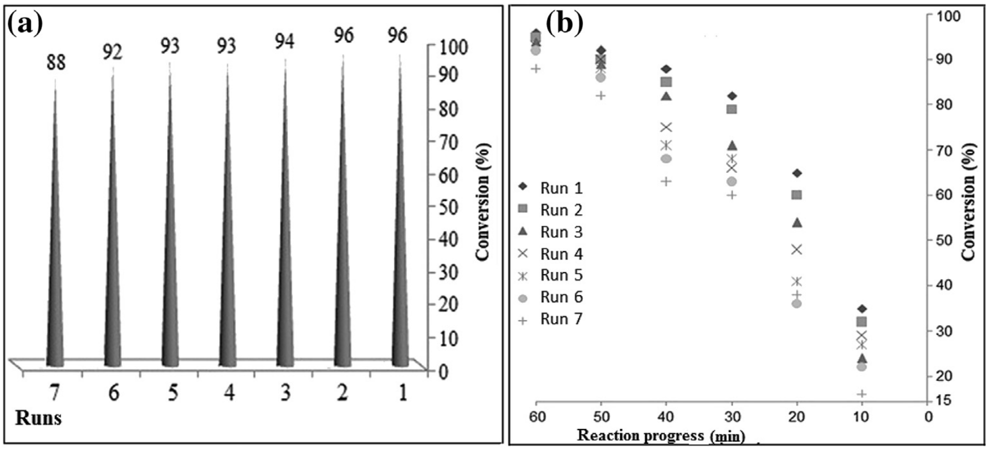


Fig. 7. Reusability of the catalyst (a), reaction progress *vs.* conversion of the reaction of *p*-methoxy aniline, triethyl orthoformate, and sodium azide at different cycles of the reaction under optimized conditions (b). (The conversion was determined by GC.)

washed with ethyl acetate (3 × 10 mL), dried and the catalyst reused for subsequent reactions for at least 7 times with less activation process.

We also decided to perform the kinetic studies to estimate the reaction rates at different cycles according to some reported paper in the literature [52]. For this purpose we selected the reaction of *p*-methoxy aniline, triethyl orthoformate, and sodium azide in the presence of $Fe_3O_4@SiO_2$/Salen complex of Cu(II) under optimized conditions to evaluate the reactivity of nanocatalyst at different time at every cycle. The results were summarized in (Fig. 7(b)).

The amounts of Cu leaching into solution for the reaction was detected by checking the Cu loading amount before and after each reaction cycle through ICP. The amount of Cu leaching after the first run was determined by ICP analysis to be only 0.2%, and after 7 repeated recycling was 5.4%.

4. Conclusion

In this study, an efficient, and general method has been developed for synthesis of 1- and 5-substituted 1H-tetrazoles from nitriles and amines using magnetite nanoparticles immobilized Salen Cu(II) as an efficient and recyclable catalyst. Nanocatalyst can be easily recovered by a magnetic field and reused for subsequent reactions for at least 7 times with less deterioration in catalytic activity.

Acknowledgments

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References

[1] J. Ying, R.M. Lee, P.S. Williams, J.C. Jeffrey, S.F. Sherif, B. Brian, Z. Maciej, Biotechnol. Bioeng. 96 (2007) 1139–1154.
[2] J. Lee, Y. Jun, S. Yeon, J. Shin, Angew. Chem. Int. Ed. 45 (2006) 8160–8162.
[3] N. Tobias, S. Bernhard, H. Heinrich, H. Margarete, V.R. Brigitte, J. Magn. Mater. 293 (2005) 483–496.
[4] H. Gu, K. Xu, C. Xu, B. Xu, Chem. Commun. 9 (2006) 941–949.
[5] I. Akira, T. Kouji, K. Kazuyoshi, S. Masashige, H. Hiroyuki, M. Kazuhiko, S. Toshiaki, K. Takeshi, Cancer Sci. 94 (2003) 308–313.
[6] (a) Y.S. Lin, C.L. Haynes, Chem. Mater. 21 (2009) 3979–3986;
(b) L.M. Rossi, I.M. Nangoi, N.I.J.S. Costa, Inorg. Chem. 48 (2009) 4640–4642.
[7] (a) Z. Wang, P. Xiao, B. Shen, N. He, Colloids Surf. A: Physicochem. Eng. Asp. 276 (2006) 106–116;
(b) A. Schätz, M. Hager, O. Reiser, Adv. Funct. Mater. 19 (2009) 2109–2115;
(c) F. Zhang, J. Jin, X. Zhong, S. Li, J. Niu, R. Li, J. Ma, Green Chem. 13 (2011) 1238–1242;
(d) J. Mondal, T. Sen, A. Bhaumik, Dalton Trans. 41 (2012) 6173–6181.
[8] (a) T.J. Yoon, K.N. Yu, E. Kim, J.S. Kim, B.G. Kim, S.H. Yun, B.H. Sohn, M.H. Cho, J.K. Lee, S.B. Park, Small 2 (2006) 209–215;
(b) D.K. Yi, S.S. Lee, J.Y. Ying, Chem. Mater. 18 (2006) 2459–2461;
(c) D.K. Yi, S.S. Lee, G.C. Papaefthymiou, J.Y. Ying, Chem. Mater. 18 (2006) 614–619.
[9] (a) A. Corma, H. Garcia, Adv. Synth. Catal. 348 (2006) 1391–1412;
(b) J.A. Widegren, R.G. Finke, J. Mol. Catal. A: Chem. 198 (2003) 317–341.
[10] (a) L. Canali, D.C. Sherrington, Chem. Soc. Rev. 28 (1999) 85–93;
(b) T. Katsuki, Coord. Chem. Rev. 140 (1995) 189–214.
[11] (a) K.J. Ballus Jr., A.K. Khanmamedova, K.M. Dixon, F. Bedioui, Appl. Catal. A: Gen. 143 (1996) 159–173;
(b) C. Heinrichs, W.F. Holderich, Catal. Lett. 58 (1999) 75–80.
[12] M. Esmaeilpour, A.R. Sardarian, J. Javidi, Appl. Catal. A: Gen. 445–446 (2012) 359–367.
[13] R.N. Butler, A.R. Katritzky, C.W. Rees, E.F.V. Scriven (Eds.), Comprehensive Heterocyclic Chemistry, fourth ed., Pergamon, Oxford, UK, 1996.
[14] (a) V.V. Nilulin, T.V. Artamonova, G.I. Koldobskii, Russ. J. Org. Chem. 39 (2003) 1525–1529;
(b) V.V. Nilulin, T.V. Artamonova, G.I. Koldobskii, Russ. J. Org. Chem. 41 (2005) 444–445.
[15] L.V. Myznikov, A. Hrabalek, G.I. Koldobskii, Chem. Heterocycl. Compd 43 (2007) 1–9.
[16] L.B. Moskvin, A.V. Bulatov, G.L. Griogorjev, G.I. Koldobkij, Flow Injection Anal. 20 (2003) 53–58.
[17] A. Burger, Prog. Drug Res. 37 (1991) 287–371.
[18] (a) D.M. Zimmerman, R.A. Olofson, Tetrahedron Lett. 58 (1969) 5081–5084;
(b) F.G. Fallon, R.M. Herbst, J. Org. Chem. 22 (1957) 933–936.
[19] T. Jin, S. Kamijo, Y. Yamamoto, Tetrahedron Lett. 45 (2004) 9435–9437.
[20] Y. Satoh, N. Marcopulos, Tetrahedron Lett. 36 (1995) 1759–1762.
[21] A.K. Gupta, C.H. Oh, Tetrahedron Lett. 45 (2004) 4113–4116.
[22] W. Su, Z. Hong, W. Shan, X. Zhang, Eur. J. Org. Chem. (2006) 2723–2726.
[23] K. Dhiman, M. Adinath, H. Alakananda, Tetrahedron Lett. 50 (2009) 2668–2670.
[24] T.M. Potewar, S.A. Siddiqui, R.J. Lahoti, K.V. Srinivasan, Tetrahedron Lett. 48((2007) 1721–1724.
[25] D. Habibi, H., Nabavi., M. Nasrollahzadeh, J. Chem. (2012) 1–4.
[26] D. Kundu, A. Majee, A. Hajra, Tetrahedron Lett. 50 (2009) 2668–6770.
[27] D. Habibi, M. Nasrollahzadeh, T.A. Kamali, Green Chem. 13 (2011) 3499–3504.
[28] M.R.M. Bhoje, M.A. Gowd Pasha, J. Chem. Sci. 123 (2011) 75–79.
[29] D.P. Green, J.E.A.J. Shuker, J. Comb. Chem. 2 (2000) 19–23.
[30] A. Kumar, R. Narayanan, H. Shechter, J. Org. Chem. 61 (1996) 4462–4465.
[31] Z. Yizhong, R. Yiming, C. Chun, Helv. Chim. Acta 92 (2009) 17–175.
[32] M.L. Kantam, K.B. Shiva Kumar, C. Sridhar, Adv. Synth. Catal. 347 (2005) 1212–1214.
[33] Z.P. Demko, K.B. Sharpless, J. Org. Chem. 66 (2001) 7945–7950.
[34] S. Rostamizadeh, H. Ghaieni, R. Aryan, A. Amani, Chin. Chem. Lett. 20 (2009) 1311–1314.
[35] M.L. Kantam, K.B. Shiva Kumar, K.J. Phani Raja, J. Mol. Catal. A: Chem. 247 (2006) 186–188.
[36] S. Hajra, D. Sinha, M. Bhowmick, J. Org. Chem. 72 (2007) 1852–1855.
[37] M.L. Kantam, V. Balasubrahmanyam, K.B. Shiva Kumar, Synth. Commun. 36 (2006) 1809–1814.
[38] L. Lang, B. Li, W. Liu, L. Jiang, Z. Xu, G. Yin, Chem. Commun. 46 (2010) 448–450.
[39] (a) T. Jin, F. Kitahara, S. Kamijo, Y. Yamamoto, Tetrahedron Lett. 49 (2008) 2824–2827;
(b) T. Jin, F. Kitahara, S. Kamijo, Y. Yamamoto, Chem. Asian J. 3 (2008) 1575–1580.
[40] B. Sreedhar, A. Suresh Kumar, Divya Yada, Tetrahedron Lett. 52 (2011) 3565–3569.

[41] G. Venkateshwarlu, A. Premalatha, K.C. Rajanna, P.K. Saiprakash, Synth. Commun. 39 (2009) 4479–4485.
[42] M. Nasrollahzadeh, D. Habibi, Z. Shahkarami, Y. Bayat, Tetrahedron 65 (2009) 10715–10719.
[43] S.M. Agawane, J.M. Nagarkar, Catal. Sci. Technol. 2 (2012) 1324–1327.
[44] M. Nasrollahzadeh, Y. Bayat, D. Habibi, S. Moshaee, Tetrahedron Lett. 50 (2009) 4435–4438.
[45] J. Bonnamour, C. Bolm, Chem. Eur. J. 15 (2009) 4543–4545.
[46] H. Eshghi, S.M. Seyedi, E. Rahimi Zarei, ISRN Org. Chem. (2011) 1–5.
[47] A. Teimouri, A. Najafi Chermahini, Polyhedron 30 (2011) 2606–2610.
[48] G. Qi, Y. Dai, Chin. Chem. Lett. 21 (2010) 1029–1032.
[49] A. Khalafi-Nezhad, S. Mohammadi, RSC Adv. 3 (2013) 4362–4437.
[50] Y.H. Deng, D.W. Qi, C.H. Deng, X.M. Zhang, D.Y. Zhao, J. Am. Chem. Soc. 130 (2008) 28–29.
[51] J. Kim, J.E. Lee, J. Lee, J.H. Yu, B.C. Kim, K. An, Y. Hwang, C.H. Shin, J.G. Park, J. Kim, T. Hyeon, J. Am. Chem. Soc. 128 (2006) 688–689.
[52] (a) X. Zhu, K. Venkatasubbaiah, M. Weck, Ch. W. Jones, ChemCatChem 2 (2010) 1252–1259;
(b) X. Zhua, K. Venkatasubbaiaha, M. Weckb, Ch. W. Jonesa, J. Mol. Catal. A: Chem. 329 (2010) 1–6.