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Cu(II)-*N*-benzyl-amino-1*H*-tetrazole complex immobilized on magnetic chitosan as a highly effective nanocatalyst for C-N coupling reactions

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ABSTRACT

Herein, the synthesis of a novel catalytic nanosystem with high activity and easy recoverability through immobilization of Cu(II)-*N*-benzyl-amino-1*H*-tetrazole complex on magnetic chitosan (MCS-BAT-Cu(II)) is reported. The catalytic potential of MCS-BAT-Cu(II) catalyst has been assessed in C-N coupling reaction of 5-amino-1*H*-tetrazole with aryl halides. Various aryl iodides/bromides were successfully coupled using MCS-BAT-Cu(II) catalyst for the synthesis of 1-aryl-5-amino-1*H*-tetrazoles with excellent reaction yields. In addition, the magnetic catalyst was easily and effectively separated from the reaction mixture using an external magnet and reused five times without notable loss of catalytic activity.

1. Introduction

Tetrazoles constitute a privileged class of heterocycles with attractive characteristics such as a large number of nitrogen atoms, high acidity, low basicity, maximum dipole moment, good stability, high formation enthalpy, *etc*. These compounds are playing an important role in medicinal/pharmacological chemistry, material science, explosives/propellants, coordination chemistry [1–7], and versatile scaffolds for the synthesis of *N*-containing compounds, as well as being effective bioactive compounds, antihypertensive drugs, peptidase inhibitors, anti-HIV and anticancer/antitumor agents [8–10]. For instance, losartan and its analogues used as antihypertensive drugs and/or the peptidase inhibitor CGS-26303 are the most significant drugs comprising tetrazole rings [9,11-13]. Furthermore, 1,5-disubstituted tetrazoles utilized as the bioisostere (bioequivalent) of *cis*-amide bonds in peptides, show similar physicochemical features and improved metabolic stability in living organisms [14]. Generally, 5-substituted tetrazoles are widely used in medicine, pharmacology, biochemistry, fine organic synthesis, and in the industry as effective compounds in photography, military, imaging chemicals, *etc*. [5].

Widespread applications of tetrazoles; especially in medicinal and coordination chemistry, have attracted increasing attention and provided a recently expanding field of heterogeneous catalysis. Tetrazoles, in particular aminotetrazoles, have been applied as highly potent compounds in inorganic and/or organometallic chemistry for the synthesis of coordination complexes [15–17], metal organic frameworks (MOF) [18,19], coordination polymers [20,21], and various (photo)catalysts [22,23] in organic chemistry. They are a versatile starting material for multi-component reactions, asymmetric syntheses [24–26], and catalysts for organic reactions [27–29].

The classical methods to synthesize tetrazoles, in particular aminotetrazoles (Scheme 1), are based on the condensation of nitriles, thioureas, cyanamides, imidoyl chlorides, carbodiimides, and aminoiminomethanesulfonic acids with NaN_3. The reaction of cyanamides with HN_3, the reaction of $NaNO_2$ with aminoguanidine, thermal isomerization of 1-substituted aminotetrazoles in melt state or boiling ethylene glycol, the reaction of various amines with tetrazole comprising a leaving group in the 5th position, and conversion of 1-aryltetrazoles to 1-arylaminotetrazoles *via* single step ring opening and intramolecular cyclization processes using organolithium reagents and NaN_3 at -70 °C are some of the methods for the preparation of tetrazoles [30–34]. Due to their benefits and applications, the development of more efficient methods for preparing (amino)tetrazole scaffolds has received great attention. Each of the earlier methods has some drawbacks such as the utilization of stoichiometric quantities of homogeneous catalysts, moisture sensitive or harmful/expensive reagents, HN_3 generation, the formation of side products, low yields or tedious processes for

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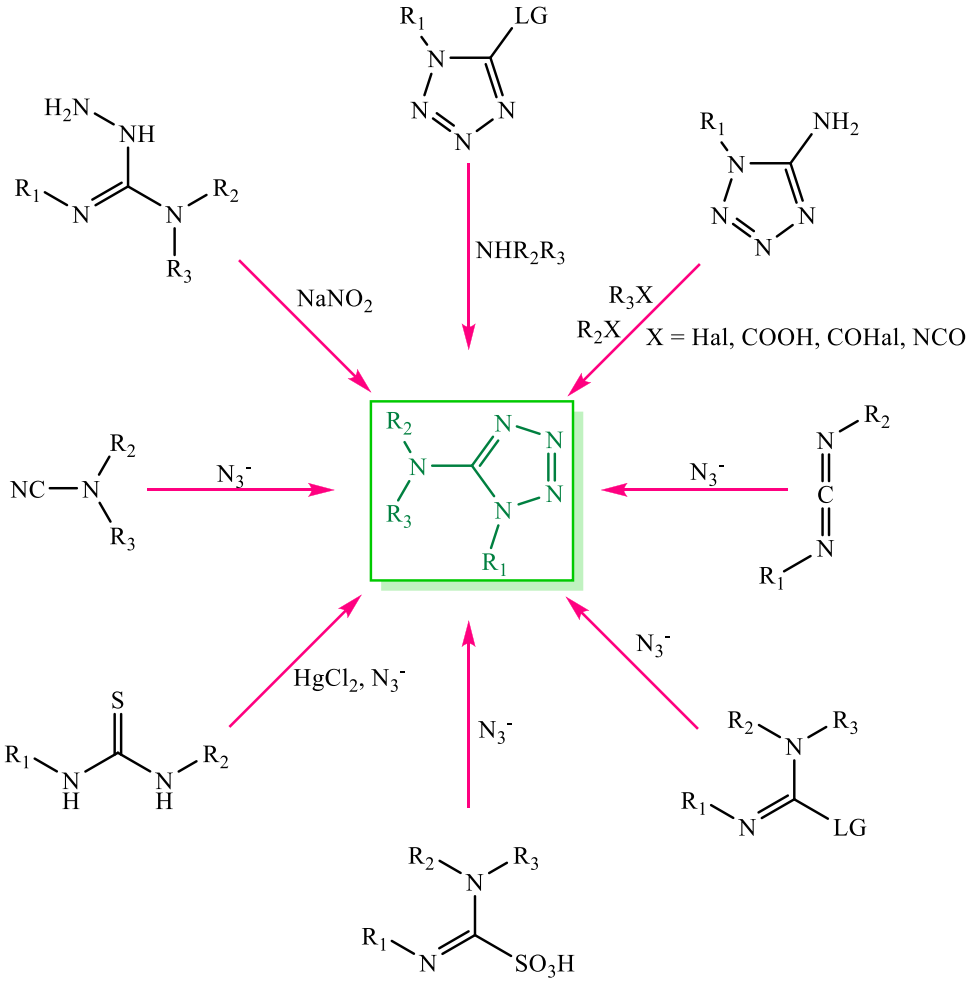


Scheme 1. Preparation of (aryl)aminotetrazoles using diverse methods.

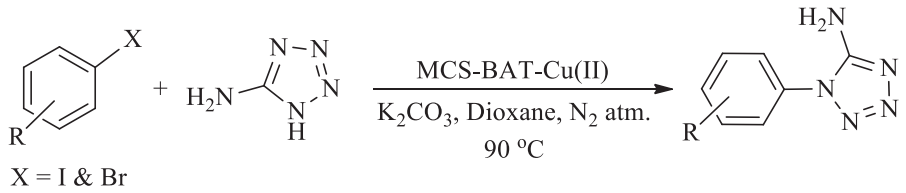
the synthesis of catalysts and work-up, *etc*. Hence, it is important to develop a more efficient and convenient technique to reduce and/or eliminate the utilization and generation of hazardous compounds [16,30,35].

[2 + 3]-cycloaddition reactions using homogeneous catalysts have turned into highly useful and synthetically attractive approaches for preparing tetrazoles [36]. Given the difficulties in the recovery of homogeneous catalysts [29], more efficient, convenient, and newer routes to prepare tetrazole based heterogeneous catalysts/complexes need to be explored. There are numerous reports/patents on the coordination of tetrazoles with various transition metals (*e.g.* copper, palladium, platinum, iridium, *etc*.) in the design or preparation and applications of the corresponding chelate complexes [28,37-40]. Choosing a suitable (nano)catalyst to fabricate these ligands and investigation of the more efficient techniques for the preparation of tetrazole containing metal complexes comprising a metal-nitrogen bond is of utmost significance. Furthermore, transforming tetrazoles into valuable heterogeneous catalysts extremely enhances sustainable economic development, as exemplified by the increasing demand for the (nano)catalysts and complexes using tetrazoles.

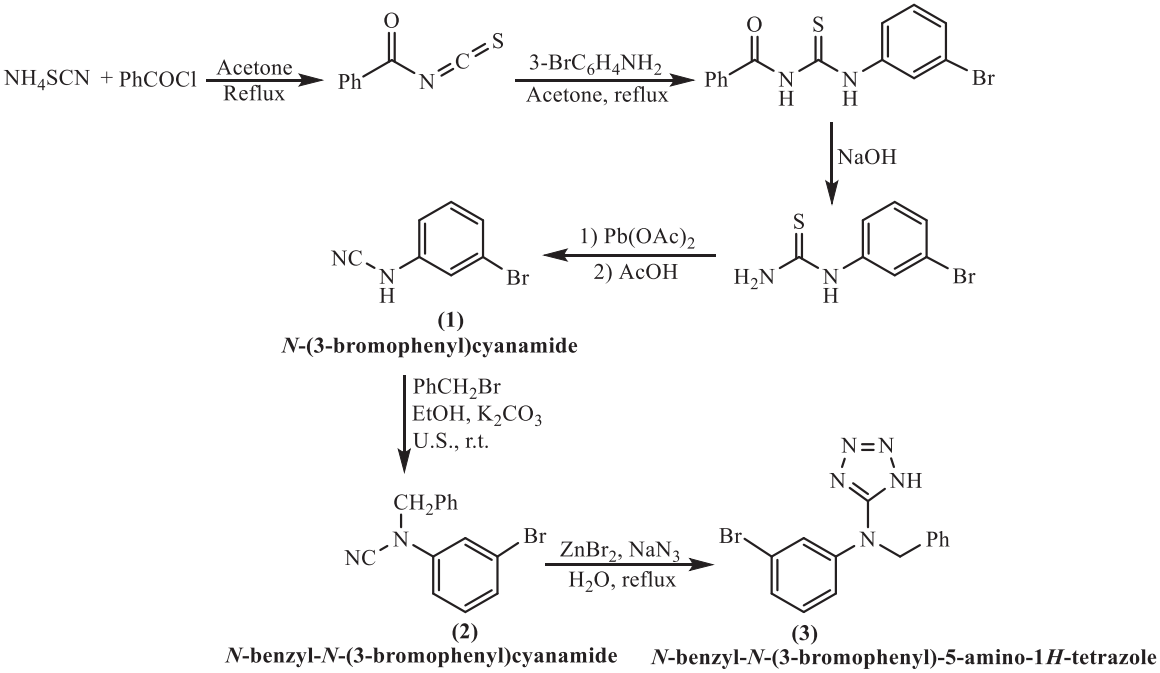
Several heterocycles containing embedded tetrazole ligands have been applied for environmental applications *via* the synthesis of heterogeneous nanocatalysts deploying diverse supports; namely, polymers, Fe_3O_4@SiO_2 nanoparticles (NPs), and other natural biomaterials [16,28,29]. Among diverse polymers, chitosan (CS) is a natural cationic polysaccharide with excellent efficiency as a support due to its biodegradability, biocompatibility, non-toxicity, environmentally benign nature, and availability [41]. The fusion of magnetic NPs and polysaccharides could afford one of the most interesting kinds of nanomagnetic supports for simple recovery of catalysts. Thus, the coating of CS about nanomagnetic core (MCS) is a valuable approach.

Transition metal catalyzed aryl C-N bond forming transformations are one of the most widely studied reactions in modern organic synthesis due to the importance of aromatic C-N bonds in different areas such as *e.g.* natural products, coordination chemistry, agrochemicals, pharmaceuticals, heterocycles, conjugated polymers and catalysis [42–46]. Nevertheless, many approaches have been developed for C-N coupling or *N*-arylation reactions between nitrogen based heterocycles and (pseudo)aryl halides to form N-C bonds, most of which need pre-functionalization of organic compounds and/or Pd catalysts [45,47-50].

In the light of our endeavors in the synthesis of tetrazole based heterogeneous complexes, in this study, we report here the preparation of Cu(II)-*N*-benzyl-amino-1*H*-tetrazole complex supported on magnetic chitosan (MCS-BAT-Cu(II); Scheme 2) and demonstrate its activity in the preparation of 1-aryl-5-amino-1*H*-tetrazoles in high yield *via N*-arylation of unsubstituted 5-amino-1*H*-tetrazole with aryl iodides/bromides in dioxane under nitrogen atmosphere. Moreover, MCS-BAT-Cu(II) showed high recyclability and was reused in five successive runs in C-N coupling reactions.



Scheme 2. MCS-BAT-Cu(II)-promoted preparation of substituted 5-amino-1*H*-tetrazoles.



Scheme 3. Preparation of *N*-benzyl-*N*-(3-bromophenyl)-5-amino-1*H*-tetrazole (**3**).

2. Experimental

2.1. Reagents and devices

Commercially available reagents, materials, and solvents were utilized as received. CS with 85% de-acetylation degree, 50000-80000 Da molecular weight (medium), solubility in 1% acetic acid in the 80-mesh size was purchased from Nano Novin Polymer company. FT-IR (Fourier transform infrared spectroscopy) spectra were recorded by a Thermo Nicolet 370 FT-IR spectrometer using KBr pellets. The NMR spectra were recorded on a Bruker spectrometer (Avance DRX-400 MHz). XRD (X-ray diffraction) and VSM (vibrating sample magnetometer) measurements were validated by Philips PW 1373 diffractometer (Cu Kα radiation = 0.15406 nm) and SQUID magnetometer (Quantum Design MPMS 20XL) at 298 K, respectively. The MCS-BAT-Cu(II) size and morphology were characterized utilizing TEM (JEM-F200 JEOL) and FESEM (Cam scan Mv2300). Energy Dispersive X-ray Spectroscopy (EDS) equipped in FESEM (TESCAN MIRA3-XMU) was extensively applied to determine the chemical composition of the catalyst. The loading and leaching of Cu were determined by inductively coupled plasma mass spectrometry (ICP-MS, Perkin Elmer, Optima 8000).

2.2. Synthesis of N-*benzyl*-N-*(3-bromophenyl)cyanamide* (***2***)

N-Benzyl-*N*-(3-bromophenyl)cyanamide (**1**) was synthesized (Scheme 3) according to our recent report by *N*-benzylation of (3-bromophenyl)cyanamide under ultrasonic irradiation [51].

2.3. Synthesis of N-*benzyl*-N-*(3-bromophenyl)-5-amino-1*H-*tetrazole* (***3***)

A mixture of *N*-benzyl-*N*-(3-bromophenyl)cyanamide (1.0 mmol), $ZnBr_2$ (1.0 mmol), and NaN_3 (1.5 mmol) in H_2O (20 mL) was stirred under reflux for 20 h (Scheme 3). Upon completion of the reaction, as monitored using TLC, the solid residues obtained were filtered from the reaction mixture, rinsed twice with water (20.0 mL) and subsequently treated with 3 mL of 3.0 N HCl. The as-prepared residue was purified/recrystallized with EtOH to afford the desired pure products.

2.4. Synthesis of MCS (***4***)

Fe_3O_4 NPs were fabricated *via* co-precipitation technique in basic media [52]. Next, a solution of CS (0.25 g) in acetic acid (1% V/V, 50 mL) was prepared to which were added 2.0 g of as-prepared Fe_3O_4 NPs at ambient temperature. The solution thus obtained was stirred for 0.5 h, followed by the slow addition of NaOH solution (1.0 M, 50 mL) and mechanically stirring the resulting solution for another 0.5 h. Finally, the formed Fe_3O_4-CS was easily collected using an external magnet and repeatedly washed with twice-distilled water and ethanol, and dried *in vacuo*.

2.5. Synthesis of N-*benzyl-amino-1*H-*tetrazole-trimethoxysilane* (***5***)

2.0 mmol of *N*-benzyl-*N*-(3-bromophenyl)-5-amino-1*H*-tetrazole (0.394 g) prepared and 2.0 mmol of TMOS [(3-chloropropyl)trimethoxysilane)] were added to a flask containing

40.0 mL of EtOH and the mixture obtained was stirred/refluxed for 24 h at 70 °C. The obtained product was soluble in EtOH.

2.6. Synthesis of MCS-$(CH_2)_3$-BAT (**6**)

MCS (0.5 g) was dispersed in 30.0 mL of EtOH for 0.5 h. Next, the soluble compound prepared in Section 2.5 was added dropwise to the mixture of dispersed aqueous MCS, followed by the addition of 2.0 mmol of K_2CO_3 (0.276 g) and mixing under reflux for 24 h at 60 °C. After cooling, the resulting MCS-$(CH_2)_3$-BAT was collected by an external magnet, rinsed two times with EtOH and distilled water, and dried to utilize as the magnetic support in the coordination of Cu(II).

2.7. Synthesis of MCS-BAT-Cu(II) (**7**)

Finally, a solution of $CuCl_2$ (0.25 g) was added to the obtained MCS-$(CH_2)_3$-BAT (0.5 g) in 25 mL of EtOH and the reaction mixture obtained was stirred at 75 °C for 24 h (Scheme 4). At the end of this process, MCS-BAT-Cu(II) complex was collected utilizing an external magnet, washed with EtOH, and subsequently dried to check its catalytic activity in *N*-arylation reactions.

2.8. General experimental procedure for C-N bond cross-coupling reactions

An appropriate aryl halide (1.0 mmol), MCS-BAT-Cu(II) (0.05 g), 5-amino-1*H*-tetrazole (1.0 mmol), K_2CO_3 (1.5 mmol), and dioxane (5 mL) were stirred at 90 °C under N_2 atmosphere for the adequate time. When the reaction was complete, as monitored using TLC, the mixture was cooled to ambient temperature, the magnetic catalyst was removed from the mixture utilizing an external magnetic field and rinsed twice with water and EtOH and the product was purified using ethyl acetate and aqueous EtOH. The obtained tetrazoles were characterized by FT-IR and NMR.

3. Results and discussion

3.1. Synthesis of the catalyst

N-(3-Bromophenyl)cyanamide (**1**) and *N*-benzyl-*N*-(3-bromophenyl)cyanamide (**2**) were synthesized from 3-bromoaniline according to Scheme 3. In continuation of our recent works on various tetrazoles [4,6], the preparation of *N*-benzyl-*N*-(3-bromophenyl)-5-amino-1*H*-tetrazole (**3**) in good yield was performed through $ZnBr_2$-catalyzed [2 + 3]-cycloaddition of (**2**; Scheme 3) and NaN_3 in H_2O under reflux conditions [16].

MCS-$(CH_2)_3$-BAT (**6**) was synthesized *via* functionalization of MCS (**4**) with *N*-benzyl-amino-1*H*-tetrazole-trimethoxysilane (**5**), followed by the incorporation of $CuCl_2$ with the resulting MCS-$(CH_2)_3$-BAT (**6**) in EtOH under mild conditions to fabricate the highly effective and magnetically separable MCS-BAT-Cu(II) (**7**) complex. The complex was prepared *via* a systematic sequence (Scheme 4). Firstly, the aqueous solution of Fe^{2+} and Fe^{3+} was added to the CS acidic solution at ambient temperature, followed by the dropwise addition of NaOH to grow Fe_3O_4 NPs on the chitosan cationic surface to prepare MCS (**4**) *via* a one pot co-precipitation route. The obtained MCS (**4**) was dispersed for 30 min to form narrow black particles, followed by the reaction with *N*-benzyl-amino-1*H*-tetrazole-trimethoxysilane (**5**) to prepare MCS-$(CH_2)_3$-*N*-benzyl-*N*-(3-bromophenyl)-5-amino-1*H*-tetrazole (**6**). Finally, MCS-BAT-Cu(II) (**7**) was fabricated *via* incorporation of MCS-$(CH_2)_3$-BAT (**6**) with copper ions under reflux conditions. The catalytic activity of MCS-BAT-Cu(II) catalyst was evaluated in the preparation of various 1-aryl-5-amino-1*H*-tetrazoles through the C-N cross-coupling of unsubstituted 5-aminotetrazole with aryl halides at 90 °C.

3.2. Characterization of the catalyst

MCS-BAT-Cu(II) (**7**) catalyst was characterized by XRD, VSM, FE-SEM, FT-IR, TEM, EDS, and ICP-MS analyses. The phase and crystalline nature of MCS-BAT-Cu(II) (**7**) were assessed by XRD analysis (Fig. 1a). As shown in Fig. 1a, the XRD spectrum of the catalyst displayed typical diffraction pattern at 2θ = 16.8°, 20.1°, 30.1°, 35.8°, 43.3°, 54.0°, 57.7° and 63.0°, which are assigned to [110], [111], [220], [311], [400], [422], [511] and [440] crystal planes of magnetic NPs, respectively (JCPDS file, File No. 19-0629). These peaks confirmed the successful preparation of Fe_3O_4 particles. The patterns at 2θ values of 43.5°, 50.3° and 74.7° can be assigned to [111], [200] and [220] crystal planes, respectively, in Cu cubic structure.

Fig. 1b depicts the FT-IR spectrum of MCS-BAT-Cu(II) (**7**). In the spectrum, characteristic adsorption peaks were observed at about 3200-3400 cm^{-1} (-OH and/or -NH stretching), 2927 cm^{-1} (-CH stretching), 1497 cm^{-1} (-NH bending vibration), 1405 cm^{-1} (-C-H stretching), and 1070 cm^{-1} (-C-O-C stretching) [53,54]. The band at 1405 cm^{-1} is ascribed to the CH_2OH stretching of the chitosan matrix in Fe_3O_4-CS. Additionally, the band at 1634 cm^{-1} is due to the imine C=N stretching vibration modes, confirming the formation of MCS supported copper(II)-tetrazole complex. In addition, the peak at 630 cm^{-1} is attributed to the Fe-O stretching vibration of magnetite NPs.

The elemental composition of MCS-BAT-Cu(II) (**7**) was studied by EDS analysis (Fig. 2a). The EDS spectrum of MCS-BAT-Cu(II) (**7**) showed the presence of O, Fe, C, N, and Cl as well as Cu elements (Fig. 2a) indicating the grafting of Cu(II)-*N*-benzyl-*N*-(3-bromophenyl)-1*H*-tetrazole-5-amine on the surface of magnetic CS. The 'N' element in the complex could confirm the grafting of *N*-benzyl-arylaminotetrazoles on magnetic NPs. Moreover, the total content of copper in the MCS-BAT-Cu(II) (**7**) was determined to be about 5.2 wt.% by ICP-MS measurement. Furthermore, Fig. 2b shows the FESEM images of MCS-BAT-Cu(II) (**7**). It could be concluded that the surface of MCS is covered with Cu(II)-*N*-benzyl-*N*-(3-bromophenyl)-5-amino-1*H*-tetrazole complex. Furthermore, MCS-BAT-Cu(II) (**7**) has an average particle size in the ~13-21 nm range. The images indicated that the MCS-BAT-Cu(II) (**7**) catalyst was fabricated (Fig. 2b).

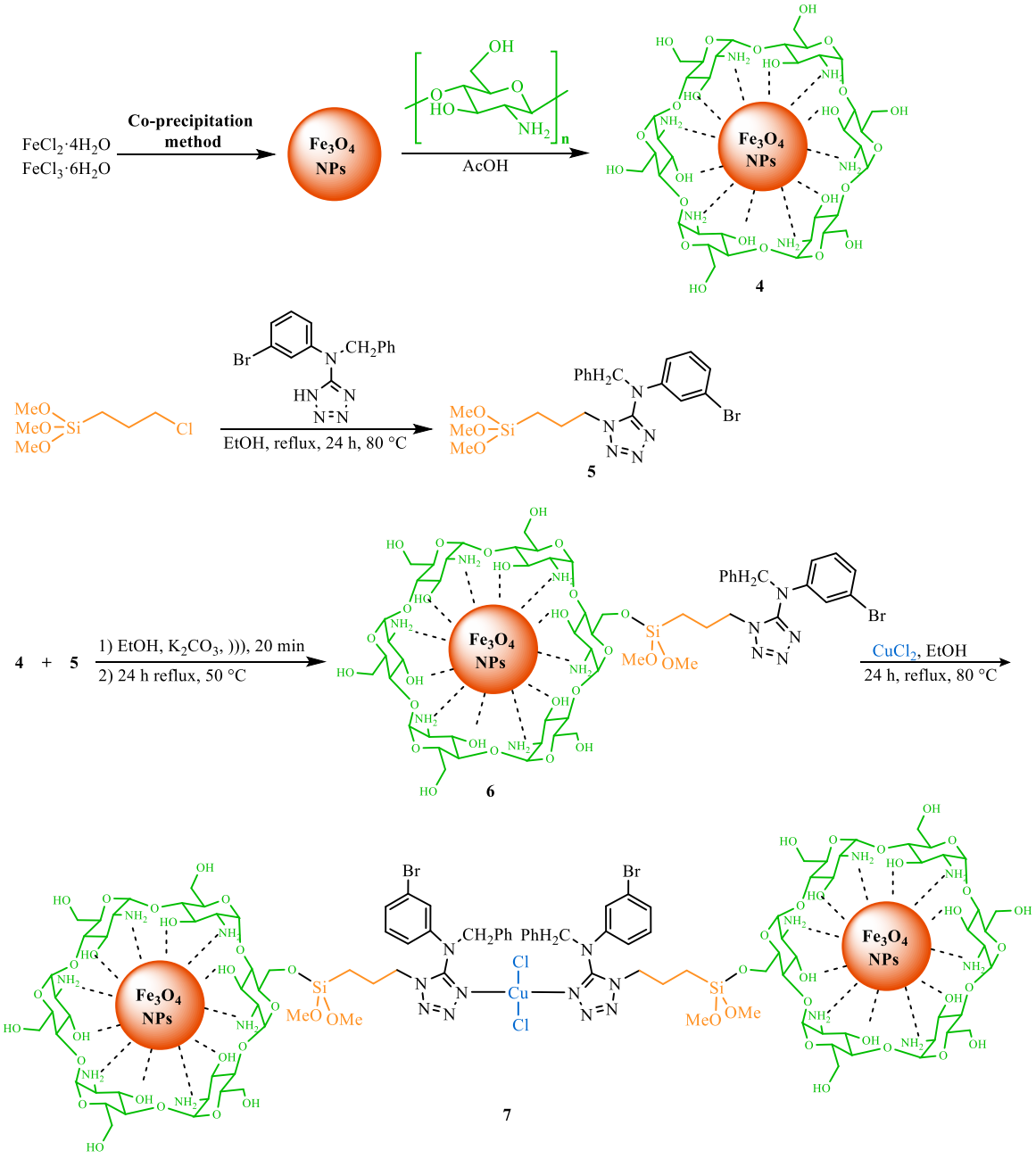
The TEM analysis of MCS-BAT-Cu(II) (**7**) was performed for further identification and the obtained TEM micrographs are depicted in Fig. 3. The TEM micrographs displayed that Cu(II)-*N*-benzyl-aminotetrazole complex were successfully immobilized/stabilized on Fe_3O_4/chitosan and the average particle size was around ~18 nm.

The magnetic property and magnetic hysteresis loop of the produced MCS-BAT-Cu(II) (**7**) were examined by VSM technique with field sweeping in the -15000 to +15000 Oe range. According to Fig. 3, the magnetization saturation (M_s) value of MCS-BAT-Cu(II) (**7**) was 50.0 emu g^{-1}. Thus, the coordination of Cu(II)-*N*-benzyl-aminotetrazole on the magnetic CS was verified by VSM analysis.

3.3. Investigation of catalytic prowess of MCS-BAT-Cu(II) (**7**) in C-N coupling reactions

The present work affords Cu(II)-*N*-benzyl-amino-1*H*-tetrazole complex supported on magnetic chitosan as a novel heterogeneous catalyst for C-N cross-coupling reactions. This catalytic system does not require expensive, conventional, difficult to synthesize, and air or moisture sensitive ligands. The MCS-BAT-Cu(II) (**7**) catalytic activity was evaluated in the C-N coupling reaction of 5-amino-1*H*-tetrazole with iodobenzene as a model reaction.

To optimize the parameters of the reaction of 5-amino-1*H*-tetrazole (1.0 mmol) with PhI (1.0 mmol) using MCS-BAT-Cu(II) (**7**), the effects of various bases (1.5 mmol), solvents (5 mL) and catalyst amount in the model coupling reaction were studied (Table 1).



Scheme 4. Synthesis of MCS-BAT-Cu(II) (**7**) catalyst.

As illustrated in Table 1, the C-N coupling reaction was first carried out without any catalyst at 90 °C (Entry 1), which resulted in no coupling product formation. The optimum amount of the MCS-BAT-Cu(II) (**7**) was 0.05 g (Table 1, entry 4). As shown in Table 1, the choice of the base (Na_2CO_3, NaOH, KOAc, NEt_3 and K_2CO_3) or solvent (MeCN, toluene, EtOH, acetone, NMP, DMF, and dioxane) affects the reaction. The best result could be obtained using dioxane and K_2CO_3 as the solvent and base, respectively (Table 1, entry 10). As a result, other solvents such as DMF and toluene were found to afford moderate yields in the coupling reaction (Table 1, entries 5, 6). In addition, no organic co-solvents, surfactants, or ligands were required. According to the results of the control experiment, excellent yield of coupling products was obtained when the reaction conditions were as follows; catalyst amount: 0.05 g, base: K_2CO_3, solvent: dioxane, reaction temperature: 90 °C, reaction time: 4 h, and under nitrogen atmosphere. No significant improvements in yields were observed using higher amounts of the MCS-BAT-Cu(II) (Entry 14).

The effect of the substituent in the structure of tetrazole on the catalytic activity was also examined. In order to evaluate the efficiency of other catalysts in C-N cross-coupling reaction, the activity of Fe_3O_4@SiO_2-aminotet-Cu(II) (copper(II)-aminotetrazole complex immobilized on silica coated Fe_3O_4) catalytic system was investigated in a model reaction (entry 15). Fe_3O_4@SiO_2-aminotet-Cu(II) was prepared according to our previous report (Fig. 4) [16]. According to Table 1, the nature of the substituent was not effective and the product was obtained in good yield (entries 10 and 15).

The MCS-BAT-Cu(II)-catalyzed *N*-arylation of 5-amino-1*H*-tetrazole with aryl iodides/bromides to prepare 1-aryl-5-amino-1*H*-tetrazoles were carried out in dioxane at 90 °C under nitrogen atmosphere. Various aryl halides containing either electron withdrawing or donating groups (-H, -OMe, -Me, and $-NO_2$) were

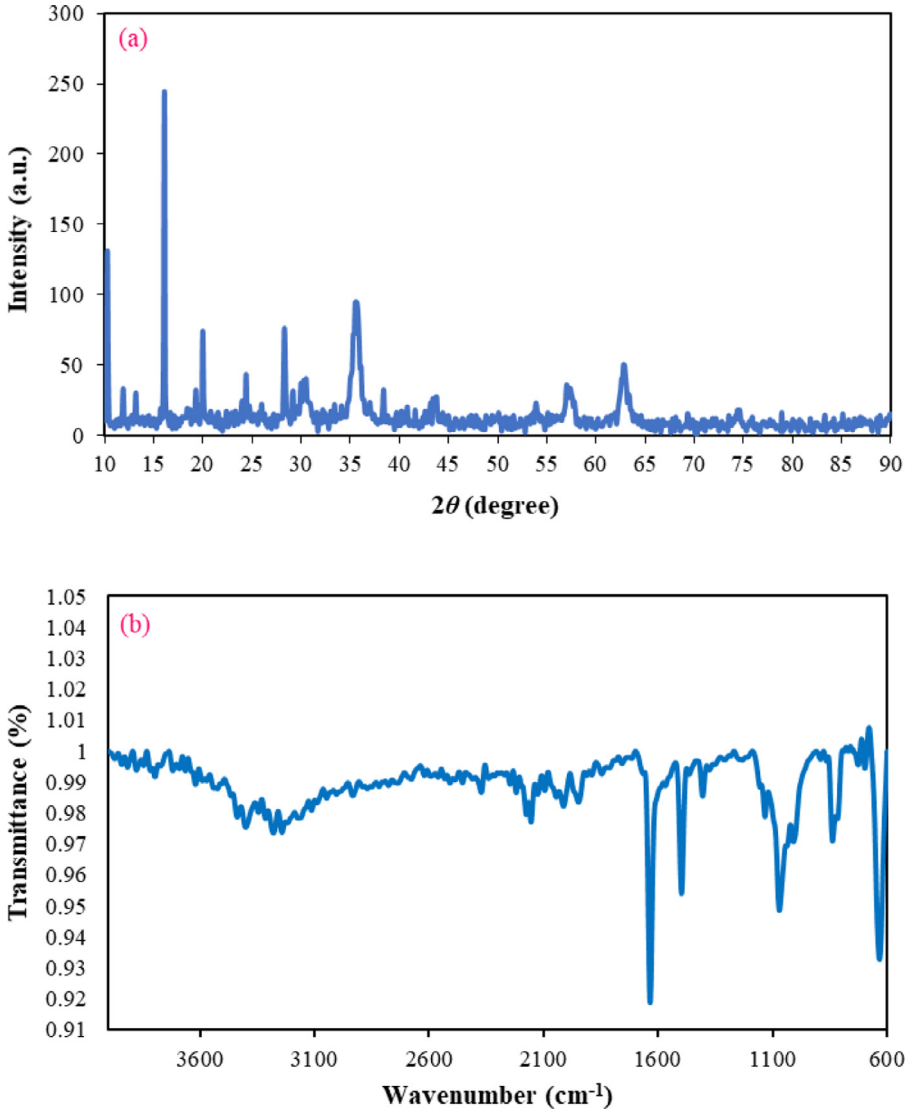


Fig. 1. (**a**) XRD pattern and (**b**) FT-IR spectrum of MCS-BAT-Cu(II) (**7**).

Table 1
Optimization of *N*-arylation of iodobenzene with 5-amino-1*H*-tetrazole using MCS-BAT-Cu(II).[a]

Entry	MCS-BAT-Cu(II) (**7**) (g)	Solvent	Base	Yield[b] (%)
1	MCS-BAT-Cu(II) (0.0)	MeCN	K_2CO_3	0.0
2	MCS-BAT-Cu(II) (0.01)	MeCN	K_2CO_3	0.0
3	MCS-BAT-Cu(II) (0.01)	Acetone	K_2CO_3	18
4	MCS-BAT-Cu(II) (0.05)	Acetone	K_2CO_3	29
5	MCS-BAT-Cu(II) (0.05)	DMF	K_2CO_3	78
6	MCS-BAT-Cu(II) (0.05)	Toluene	K_2CO_3	62
7	MCS-BAT-Cu(II) (0.05)	Ethanol	K_2CO_3	0.0
8	MCS-BAT-Cu(II) (0.05)	NMP	K_2CO_3	44
9	MCS-BAT-Cu(II) (0.05)	Dioxane	Na_2CO_3	61
10	**MCS-BAT-Cu(II) (0.05)**	**Dioxane**	**K_2CO_3**	**92**
11	MCS-BAT-Cu(II) (0.05)	Dioxane	Et_3N	0.0
12	MCS-BAT-Cu(II) (0.05)	Dioxane	KOAc	58
13	MCS-BAT-Cu(II) (0.05)	Dioxane	NaOH	28
14	MCS-BAT-Cu(II) (0.07)	Dioxane	K_2CO_3	92
15	Fe_3O_4@SiO_2-aminotet-Cu(II) (0.05)	Dioxane	K_2CO_3	91

[a] Reaction conditions: 5-amino-1*H*-tetrazole (1.0 mmol), phenyl iodide (1.0 mmol), base (1.5 mmol), solvent (5.0 mL), 90 °C, 4 h, N_2 atmosphere.
[b] Isolated yield.

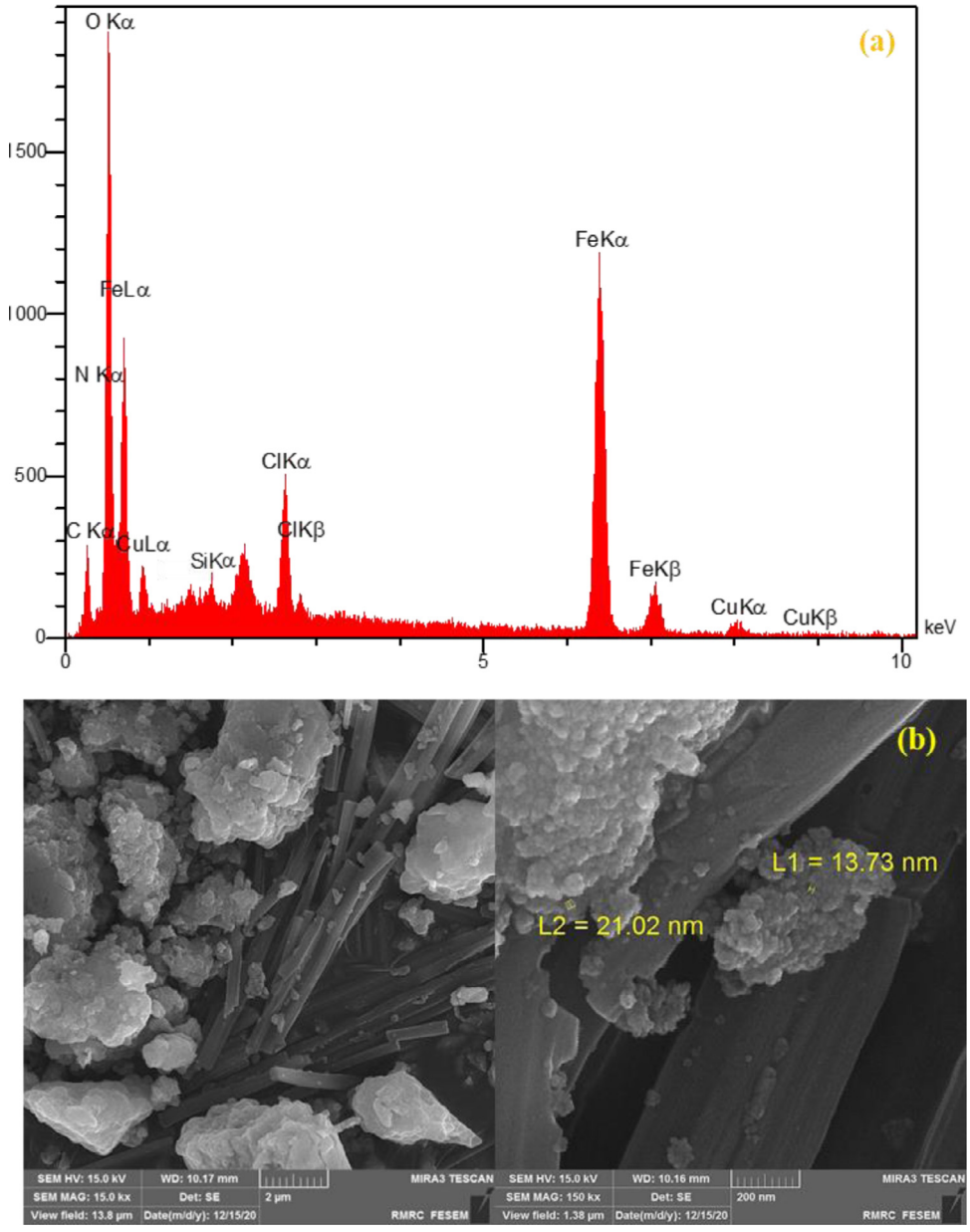


Fig. 2. (**a**) EDS spectrum and (**b**) FESEM images of MCS-BAT-Cu(II) (**7**) catalyst.

converted to 1-aryl-5-amino-1*H*-tetrazoles in 72-92% yields within 3-8 h and the results are shown in Table 2. It was found that the presence of electron withdrawing groups in the aryl halides promoted the Cu(II)-catalyzed *N*-arylation reactions with less reactivity compared to those bearing electron donating substituents and resulted in lower product yields [46]. Generally, the aryl halides with electron donating substituents (-OMe, and -Me) were more reactive than those with electron withdrawing substituents ($-NO_2$) in the preparation of arylaminotetrazoles (Table 2, entries 2-5,9). For example, 4-iodonitrobenzene and 4-bromonitrobenzene (Table 2, entries 6,10) resulted in lower yields in longer coupling reaction times. As shown in Table 2, aryl iodides containing electron donating groups (entries 2-5) reacted at 90 °C after 3-4.5 h, while the species containing the NO_2- electron withdrawing group (entry 6) requires higher reaction time (7 h). The results revealed that the coupling reactions of aryl iodides proceeded smoothly with high reaction yields in the presence of MCS-BAT-Cu(II) (**7**) compared with those of aryl bromides. Due to the presence of the two I groups, 1,4-diiodobenzene (Table 2, entry 7) interestingly afforded the double addition product. In order to optimize the synthesis of 1,4-phenylene-bis(1*H*-tetrazol-5-amine) (Table 2, entry 7), an additional experiment was conducted using excess 5-amino-1*H*-tetrazole (2.0 mmol), catalyst (0.1 g), and K_2CO_3 (3.0 mmol).

A plausible mechanism is represented in Scheme 5, wherein the C-N coupling reaction of aryl halides with 5-amino-1*H*-tetrazole using the base leads to the formation of 1-aryl-5-amino-1*H*-tetrazoles. In the first step, intermediate (**A**) is formed by the oxidative addition of the aryl halide to the catalyst (ArCuX). The reaction between the deprotonated aminotetrazole with the intermediate (**A**) is then followed by a nucleophilic attack in the presence of the base. Finally, the formation of the desired product and the regeneration of Cu catalyst occur *via* a reductive elimination stage [46,55].

After purification, the desired products were characterized by ^{1}H NMR, ^{13}C NMR, and FT-IR spectra [16,30,56]. The disappear-

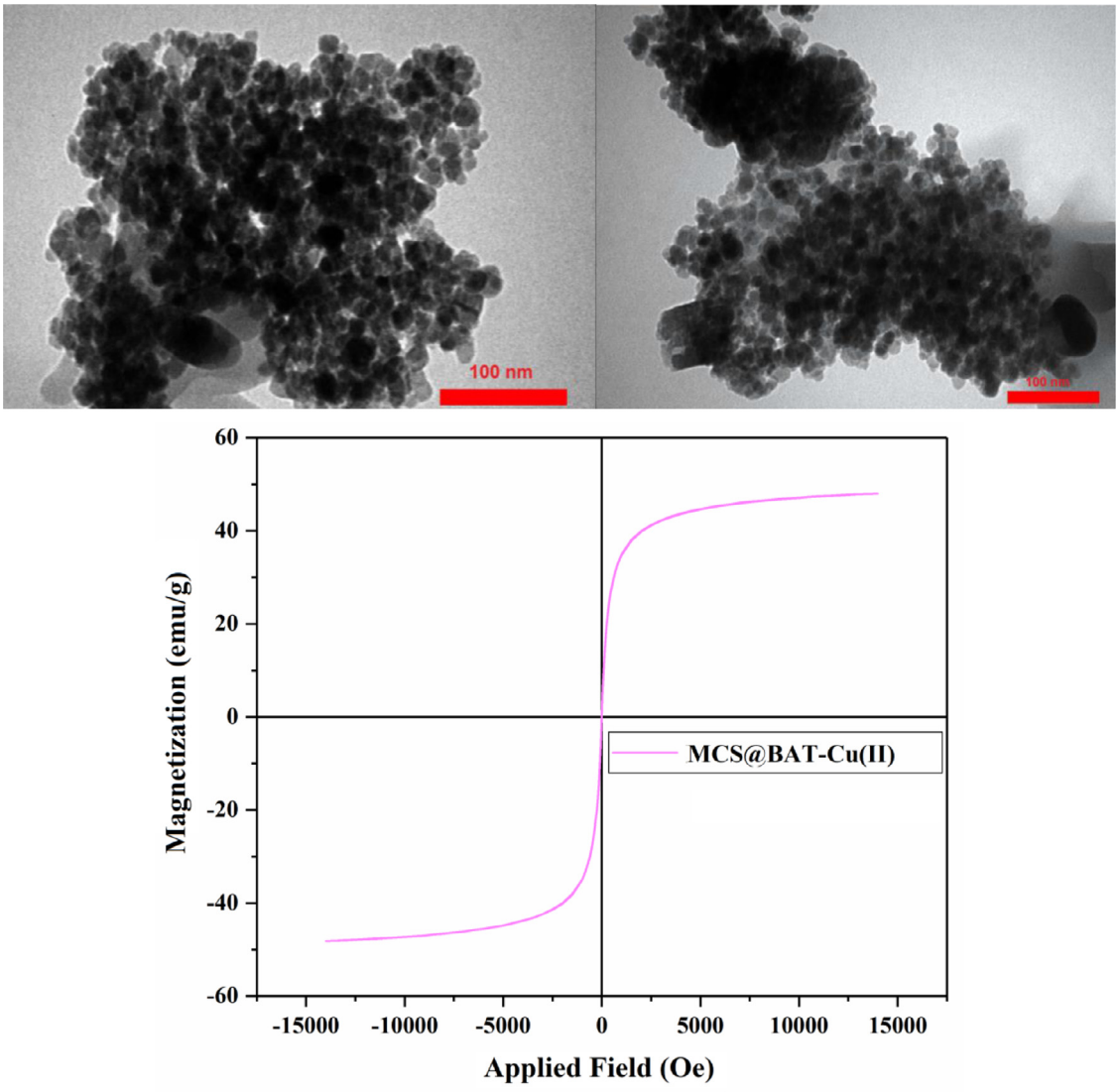


Fig. 3. TEM images and magnetization curve of MCS-BAT-Cu(II) (**7**) catalyst.

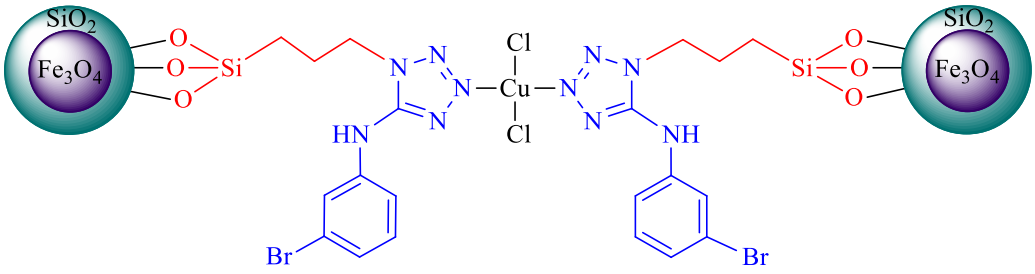


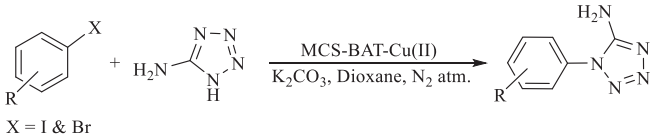
Fig. 4. Structure of Fe_3O_4@SiO_2-aminotet-Cu(II).

ance of N-H stretching of the aminotetrazole ring and the presence of two NH_2 stretching signals in the FT-IR spectra provided clear evidence for the preparation of substituted aminotetrazoles (Fig. 5). The ^{1}H NMR spectrum of unsubstituted 5-amino-1*H*-tetrazole showed two NH peaks corresponding to the NH_2 and NH groups while the ^{1}HNMR spectrum of the substituted aminotetrazoles (Fig. 6a) indicated the appearance of one NH_2 signal (6.6-7 ppm). Furthermore, the ^{13}C NMR spectrum of the pure products (Fig. 6b) showed one peak for the carbon of the tetrazole ring at 145-160 ppm.

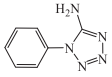
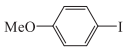
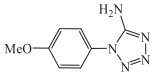
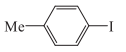
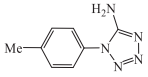
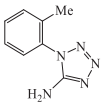
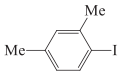
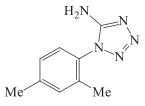
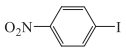
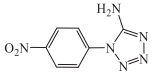
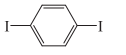
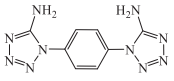
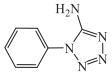
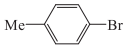
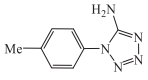
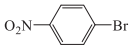
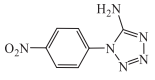
3.4. Catalyst recyclability

Recyclability/reusability is one of the significant properties of a catalytic (nano)system from practical, commercial, industrial, and economic aspects. Therefore, the reusability of MCS-BAT-Cu(II) (**7**) for the preparation of substituted tetrazoles was tested in C-N bond cross-coupling of 5-amino-1*H*-tetrazole with iodobenzene. The catalyst could be simply collected from the reaction mixture by an external magnet, rinsed twice with EtOH, and dried at 70 °C for 9 h for further catalytic runs. After the 5th run, MCS-BAT-Cu(II)

Table 2
MCS-BAT-Cu(II)-catalyzed C-N cross-coupling reaction of 5-amino-1*H*-tetrazole with various aryl halides.[a]



X = I & Br

Entry	Aryl halide	Product	Time (h)	Yield[b] (%)	TON	TOF (h^{-1})
1			4	92	22488	5622
2			3	93	22732	7577
3			4	92	22488	5622
4			4.5	90	21999	4888
5			4.5	89	21755	4834
6			7	82	20043	2863
7			7.5	88	10755	1434
8			6	84	20532	3422
9			6	86	21021	3503
10			8	72	17599	2199

[a] Reaction conditions: MCS-BAT-Cu(II) (0.05 g), aryl halide (1.0 mmol), 5-amino-1*H*-tetrazole (1.0 mmol), K_2CO_3 (1.5 mmol), Dioxane (5.0 mL), 90°C, nitrogen atmosphere.
[b] Isolated yield.

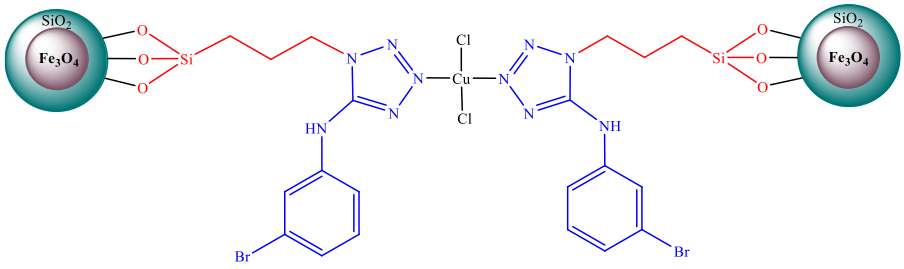


Fig. 5. FT-IR spectrum of 1-(4-methylphenyl)-5-amino-1*H*-tetrazole.

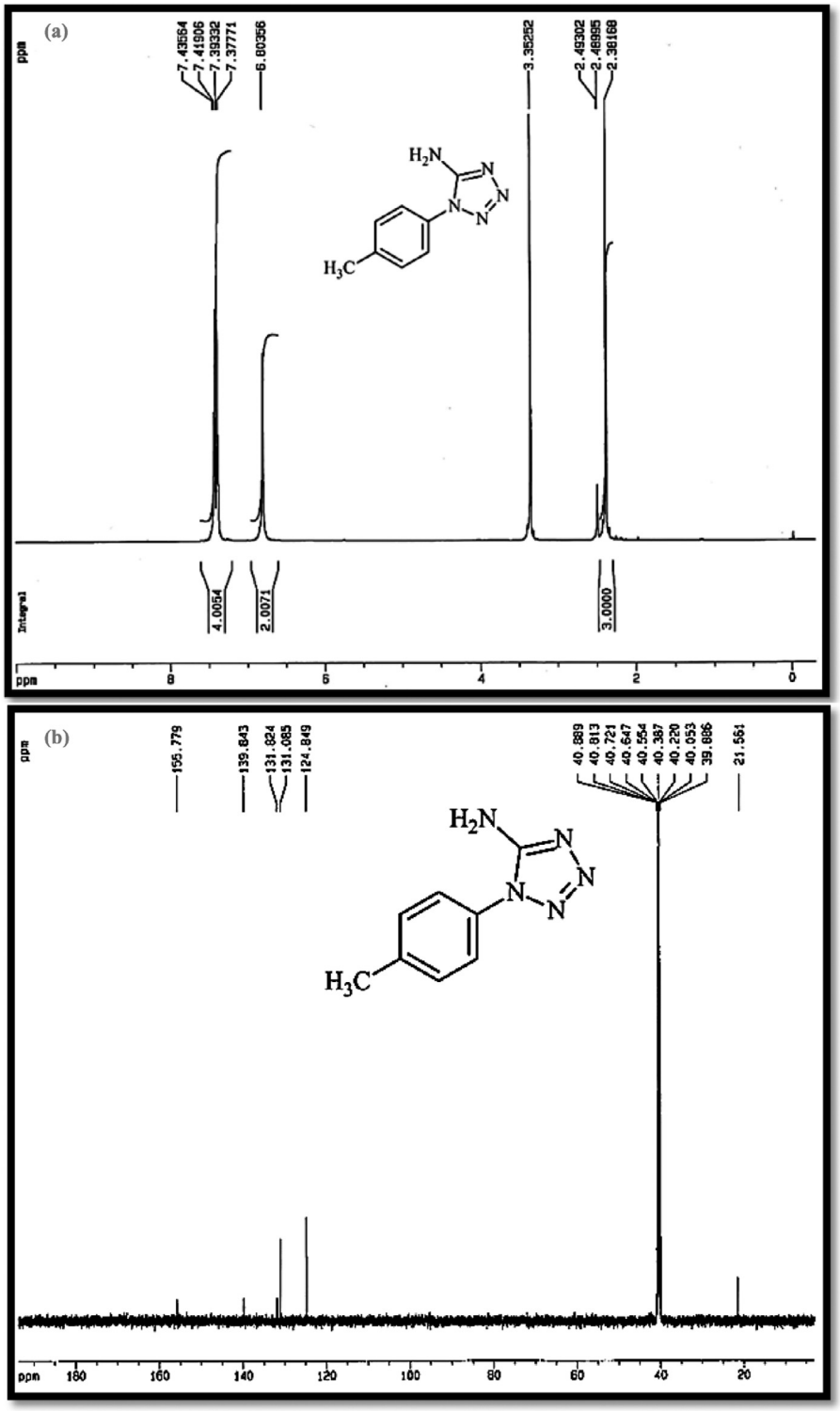
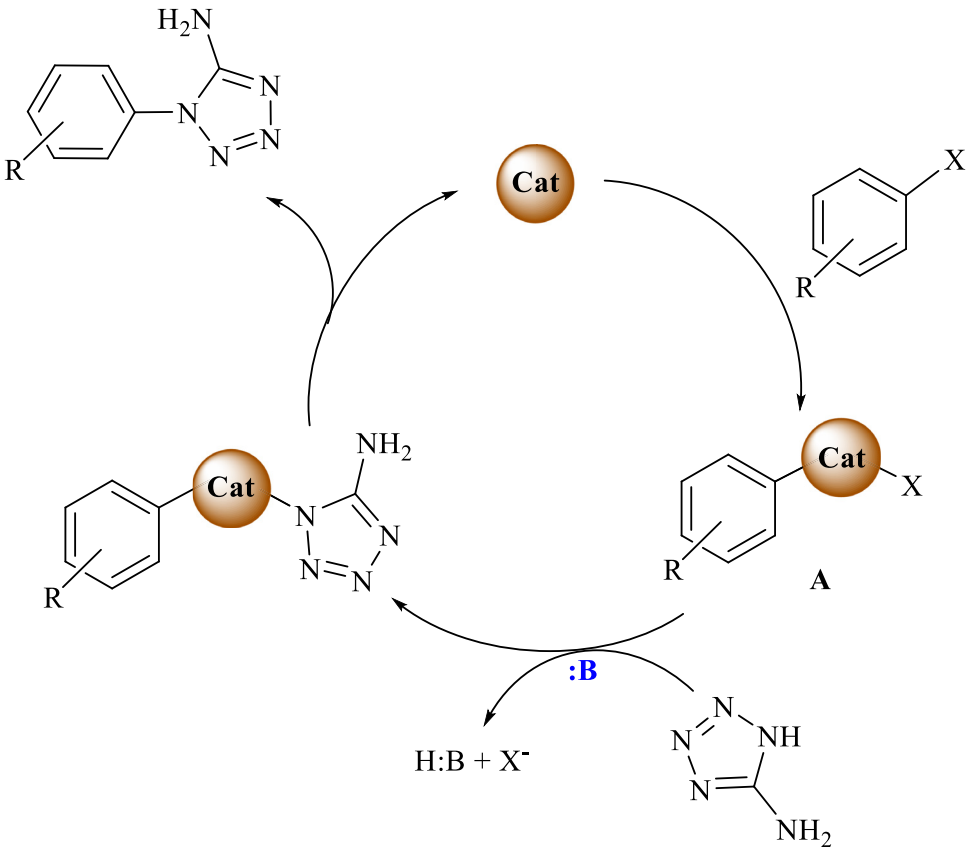


Fig. 6. (a) ^{1}H NMR and (b) ^{13}C NMR spectra of 1-(4-methylphenyl)-5-amino-1*H*-tetrazole.

(**7**) can be reused with a minor decrease in the catalytic prowess (Fig. 7). As depicted in Fig. 7, the magnetic catalyst presented excellent product yields even after the 5th reaction sequence. The XRD analysis of the recycled catalyst (after five cycles) revealed that the recycled MCS-BAT-Cu(II) (**7**) complex had the same peaks as the fresh catalyst (Fig. 8). To check the heterogeneity of the recycled catalyst, the leaching phenomenon was examined by ICP-MS analysis of the resulting solution of the coupling reaction and less than 0.1% of the total content of Cu was observed.

4. Conclusion

In summary, we report the C-N bond cross-coupling of 5-amino-1*H*-tetrazole with aryl halides by a novel heterogeneous copper complex (Cu(II)-*N*-benzyl-amino-1*H*-tetrazole) on Fe_3O_4-



Scheme 5. Proposed mechanism for the *N*-arylation reaction using MCS-BAT-Cu(II) (**7**).

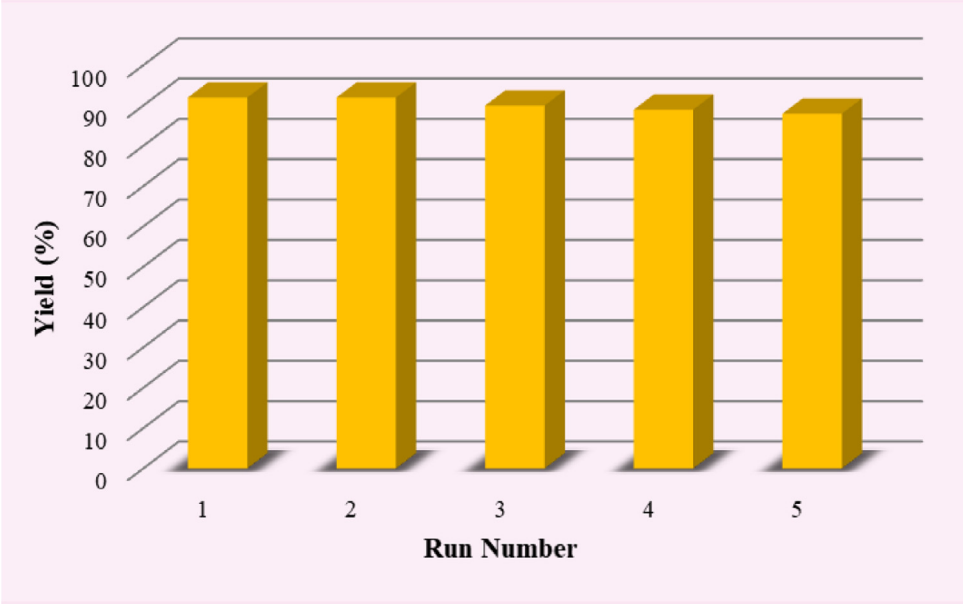


Fig. 7. Recycling performance of MCS-BAT-Cu(II) (**7**) in *N*-arylation of 5-amino-1*H*-tetrazole with iodobenzene.

chitosan as a stabilizer/support. The synthesized MCS-BAT-Cu(II) catalyst was characterized by various techniques such as XRD, FT-IR, EDS, VSM, FESEM, TEM, and ICP-MS. Efficient preparation of 1-aryl-5-amino-1*H*-tetrazole derivatives was carried out in excellent yields. The present work reports an unprecedented instance of aminotetrazole grafted on magnetic chitosan as a magnetically recoverable catalyst, which could be recycled/reused five times without any noticeable changes in the reaction time and yield. The designed catalytic nanosystem showed advantages such as easy recycling, high stability, long life, good dispersibility, facile work-up, and high catalytic activity within short reaction times. The efficacy of the developed catalytic system (MCS-BAT-Cu(II)) is superior to those of other catalytic systems in terms of reaction time, yield, work-up, and amount of catalyst. Furthermore, the good structural characteristics of MCS-supported copper(II)-tetrazole complex make it potentially useful in other catalytic transformations.

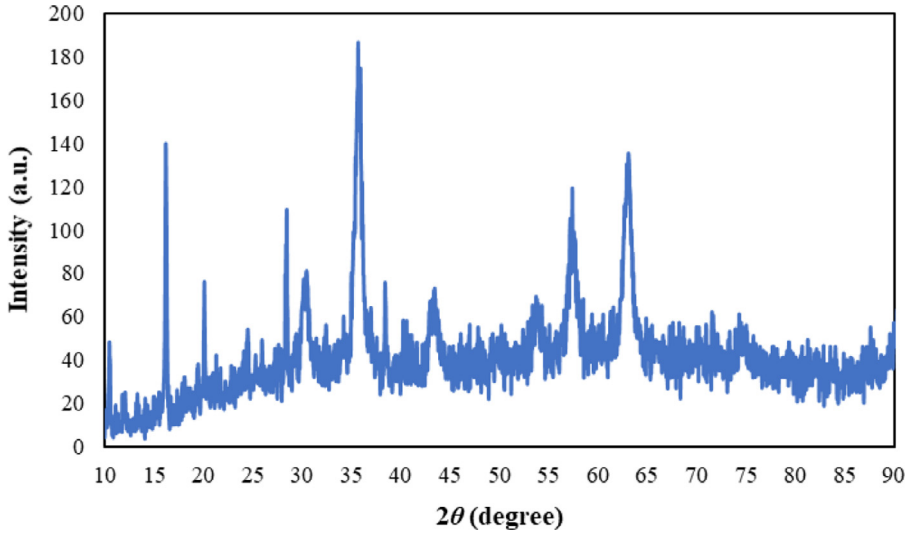


Fig. 8. XRD pattern of reused MCS-BAT-Cu(II) catalyst after fifth recycle.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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References

[1] C.-X. Wei, M. Bian, G.-H. Gong, Tetrazolium compounds: synthesis and applications in medicine, Molecules 20 (4) (2015) 5528–5553.
[2] D. Ichinari, A. Nagaki, J.-i. Yoshida, Generation of hazardous methyl azide and its application to synthesis of a key-intermediate of picarbutrazox, a new potent pesticide in flow, Bioorganic & Medicinal Chemistry 25 (23) (2017) 6224–6228.
[3] M.S. Pino-Gonzalez, A. Romero-Carrasco, S. Calvo-Losada, N. Oña-Bernal, J.J. Quirante, F. Sarabia, Synthesis of tetrazole fused azepanes and quantum chemical topology study on the mechanism of the intramolecular cycloaddition reaction, RSC Advances 7 (79) (2017) 50367–50371.
[4] A.R. Modarresi-Alam, M. Nasrollahzadeh, Synthesis of 5-arylamino-1*H*(2*H*)-tetrazoles and 5-amino-1-aryl-1*H*-tetrazoles from secondary arylcyanamides in glacial acetic acid: a simple and efficient method, Turkish Journal of Chemistry 33 (2) (2009) 267–280.
[5] C.G. Neochoritis, T. Zhao, A. Dömling, Tetrazoles via multicomponent reactions, Chemical Reviews 119 (3) (2019) 1970–2042.
[6] X.-M. Kang, Me.-H. Tang, G.-L. Yang, B. Zhao, Cluster/cage-based coordination polymers with tetrazole derivatives, Coordination Chemistry Reviews 422 (2020) 213424.
[7] J.A. Eremina, E.V. Lider, D.G. Samsonenko, L.A. Sheludyakova, A.S. Berezin, L.S. Klyushova, V.A. Ostrovskii, R.E. Trifonov, Mixed-ligand copper(II) complexes with tetrazole derivatives and 2,2′-bipyridine, 1,10-phenanthroline: Synthesis, structure and cytotoxic activity, Inorganica Chimica Acta 487 (2019) 138–144.
[8] P. Kushwaha, S. Fatima, A. Upadhyay, S. Gupta, S. Bhagwati, T. Baghel, M.I. Siddiqi, A. Nazir, K.V. Sashidhara, Synthesis, biological evaluation and molecular dynamic simulations of novel benzofuran-tetrazole derivatives as potential agents against Alzheimer's disease, Bioorganic & Medicinal Chemistry Letters 29 (1) (2019) 66–72.
[9] T. Tanaka, T. Okuda, Y. Yamamoto, Characterization of the CYP3A4 active site by homology modeling, Chemical and Pharmaceutical Bulletin 52 (7) (2004) 830–835.
[10] S.M. Bayomi, M.A. Moustafa, A.R. Maarouf, M.H. Abutaleb, Design, synthesis, biological activity and molecular modeling of new heterocyclic tetrazole derivatives, Journal of American Science 12 (1) (2016) 40–56.
[11] R.R. Wexler, W.J. Greenlee, J.D. Irvin, M.R. Goldberg, K. Prendergast, R.D. Smith, P.B. Timmermans, Nonpeptide angiotensin II receptor antagonists: the next generation in antihypertensive therapy, Journal of Medicinal Chemistry 39 (3) (1996) 625–656.
[12] B. Schmidt, B. Schieffer, Angiotensin II AT1 receptor antagonists. Clinical implications of active metabolites, Journal of Medicinal Chemistry 46 (12) (2003) 2261–2270.
[13] S. DeLombaert, R.D. Ghai, A.Y. Jeng, A.J. Trapani, R.L. Webb, Pharmacological profile of a non-peptidic dual inhibitor of neutral endopeptidase 24.11 and endothelin-converting enzyme, Biochemical and biophysical research communications 204 (1) (1994) 407–412.
[14] J. Zabrocki, G.D. Smith, J.B. Dunbar, H. Iijima, G.R. Marshall, Conformational mimicry. 1. 1,5-Disubstituted tetrazole ring as a surrogate for the cis amide bond, Journal of the American Chemical Society 110 (17) (1988) 5875–5880.
[15] L. Zeisel, N. Szimhardt, M.H.H. Wurzenberger, T.M. Klapötke, J. Stierstorfer, 2-Methyl-substituted monotetrazoles in copper(II) perchlorate complexes: Manipulating coordination chemistry and derived energetic properties, New Journal of Chemistry 43 (2) (2019) 609–616.
[16] M. Nasrollahzadeh, M. Sajjadi, H.A. Khonakdar, Synthesis and characterization of novel Cu(II) complex coated Fe_3O_4@SiO_2 nanoparticles for catalytic performance, Journal of Molecular Structure 1161 (2018) 453–463.
[17] M. Arshad, A.R. Bhat, S. Pokharel, J.-E. Kim, E.J. Lee, F. Athar, I. Choi, Synthesis, characterization and anticancer screening of some novel piperonyl-tetrazole derivatives, European Journal of Medicinal Chemistry 71 (2014) 229–236.
[18] Y. Li, X. Zhang, J. Lan, P. Xu, J. Sun, Porous Zn (Bmic)(AT) MOF with abundant amino groups and open metal sites for efficient capture and transformation of CO_2, Inorganic Chemistry 58 (20) (2019) 13917–13926.
[19] L.A. Kondacs, S. Orenga, R.J. Anderson, E.C.L. Marrs, J.D. Perry, M. Gray, C-Terminal 1-aminoethyltetrazole-containing oligopeptides as novel alanine racemase inhibitors, Molecules 25 (6) (2020) 1315.
[20] T.P. Kilpeläinen, J.K. Tyni, M.K. Lahtela-Kakkonen, T.S. Eteläinen, T.T. Myöhänen, E.A.A. Wallén, Tetrazole as a replacement of the electrophilic group in characteristic prolyl oligopeptidase inhibitors, ACS Medicinal Chemistry Letters 10 (12) (2019) 1635–1640.
[21] X.-S. Wang, Y.-Z. Tang, X.-F. Huang, Z.-R. Qu, C.-M. Che, P.W.H. Chan, R.-G. Xiong, Syntheses, crystal structures, and luminescent properties of three novel zinc coordination polymers with tetrazolyl ligands, Inorganic Chemistry 44 (15) (2005) 5278–5285.
[22] L.M.T. Frija, A. Ismael, M.L.S. Cristiano, Photochemical transformations of tetrazole derivatives: applications in organic synthesis, Molecules 15 (5) (2010) 3757–3774.
[23] X. Jiang, B. Yang, Q.-Q. Yang, C.-H. Tung, L.-Z. Wu, Cu(II) coordination polymers with nitrogen catenation ligands for efficient photocatalytic water oxidation, Chemical Communications 54 (2018) 4794–4797.
[24] S. Firoj Basha, T.N. Prasad, V.B. Gudise, V.S. Kumar, N. Mulakayala, S. Anwar, An efficient, multicomponent, green protocol to access 4,7-dihydrotetrazolo [1,5-a] pyrimidines and 5,6,7,9-tetrahydrotetrazolo [5,1-b] quinazolin-8(4*H*)-ones using PEG-400 under microwave irradiation, Synthetic Communications 49 (22) (2019) 3181–3190.
[25] Q. Xiong, S. Dong, Y. Chen, X. Liu, X. Feng, Asymmetric synthesis of tetrazole and dihydroisoquinoline derivatives by isocyanide-based multicomponent reactions, Nature Communications 10 (1) (2019) 1–10.
[26] A.V. Dolzhenko, 5-Aminotetrazole as a building block for multicomponent reactions (Review), Heterocycles 94 (10) (2017) 1819–1846.
[27] Y. He, C. Cai, Tetrazole functionalized polymer supported palladium complex: an efficient and reusable catalyst for the room-temperature Suzuki cross-coupling reaction, Catalysis Letters 140 (3) (2010) 153–159.
[28] J. Yang, Mono- and dinuclear palladium(II) complexes containing both *N*-heterocyclic carbenes and tetrazole ligands as catalysts for Hiyama coupling, New Journal of Chemistry 40 (2016) 14234–14241.
[29] N. Motahharifar, M. Nasrollahzadeh, A. Taheri-Kafrani, R.S. Varma, M. Shokouhimehr, Magnetic chitosan-copper nanocomposite: A plant assembled catalyst for the synthesis of amino-and *N*-sulfonyl tetrazoles in eco-friendly media, Carbohydrate polymers 232 (2020) 115819.

[30] M. Maham, M. Khalaj, Synthesis of thiotetrazoles and arylaminotetrazoles using rutile TiO_2 nanoparticles as a heterogeneous and reusable catalyst, Journal of Chemical Research 38 (2014) 502–506.
[31] W.L. Garbrecht, R.M. Herbst, The synthesis of certain 5-aminotetrazole derivatives. II. The action of hydrazoic acid on monoalkylcyanamides, The Journal of Organic Chemistry 18 (8) (1953) 1014–1021.
[32] W.G. Finnegan, R.A. Henry, E. Lieber, Preparation and isomerization of 5-alkylaminotetrazoles, Journal of Organic Chemistry 18 (7) (1953) 779–791.
[33] A.N. Vorobiov, P.N. Gaponik, P.T. Petrov, O.A. Ivashkevich, One-pot syntheses of 5-amino-1-aryltetrazole derivatives, Synthesis (08) (2006) 1307–1312 (2006).
[34] M.S. Congreve, Synthesis of 5-*N*-substituted tetrazole derivatives of the potent NK1 receptor antagonist GR203040, Synlett (04) (1996) 359–360 (1996).
[35] M. Nasrollahzadeh, M. Sajjadi, M.R. Tahsili, M. Shokouhimehr, R.S. Varma, Synthesis of 1-substituted 1*H*-1,2,3,4-tetrazoles using biosynthesized Ag/sodium borosilicate nanocomposite, ACS Omega 4 (5) (2019) 8985–9000.
[36] Z.P. Demko, K.B. Sharpless, Preparation of 5-substituted 1*H*-tetrazoles from nitriles in water, The Journal of Organic Chemistry 66 (24) (2001) 7945–7950.
[37] G. Aromí, L.A. Barrios, O. Roubeau, P. Gamez, Triazoles and tetrazoles: prime ligands to generate remarkable coordination materials, Coordination Chemistry Reviews 255 (5-6) (2011) 485–546.
[38] E.A. Popova, R.E. Trifonov, V.A. Ostrovskii, Advances in the synthesis of tetrazoles coordinated to metal ions, ARKIVOC (1) (2012) 45–65 2012.
[39] M. Massi, S. Stagni, M.I. Ogden, Lanthanoid tetrazole coordination complexes, Coordination Chemistry Reviews 375 (2018) 164–172.
[40] M. Saha, K.M. Vyas, L.M. Martins, N.M.R. Martins, A.J.L. Pombeiro, S.M. Mobin, D. Bhattacherjee, K.P. Bhabak, S. Mukhopadhyay, Copper(II) tetrazolato complexes: role in oxidation catalysis and protein binding, Polyhedron 132 (2017) 53–63.
[41] H. Peniche, C. Peniche, Chitosan nanoparticles: a contribution to nanomedicine, Polymer International 60 (6) (2011) 883–889.
[42] D.A. Horton, G.T. Bourne, M.L. Smythe, The combinatorial synthesis of bicyclic privileged structures or privileged substructures, Chemical Reviews 103 (3) (2003) 893–930.
[43] A. Quintás-Cardama, H. Kantarjian, J. Cortes, Flying under the radar: the new wave of BCR-ABL inhibitors, Nature Reviews Drug Discovery 6 (10) (2007) 834–848.
[44] A.O. King, N. Yasuda, Palladium-catalyzed cross-coupling reactions in the synthesis of pharmaceuticals, in: Organometallics in Process Chemistry, Springer, 2004, pp. 205–245.
[45] P. Ruiz-Castillo, S.L. Buchwald, Applications of palladium-catalyzed C–N cross–coupling reactions, Chemical Reviews 116 (19) (2016) 12564–12649.
[46] S.N.M. Boddapati, A.E. Kola, S.B. Kesana, H.B. Bollikolla, Temperature dependent regioselective synthesis of aryl tetrazole amines using copper source, Journal of Organometallic Chemistry 866 (2018) 177–183.
[47] J. Bariwal, E. Van der Eycken, C–N bond forming cross-coupling reactions: an overview, Chemical Society Reviews 42 (24) (2013) 9283–9303.
[48] J.F. Hartwig, Transition metal catalyzed synthesis of arylamines and aryl ethers from aryl halides and triflates: scope and mechanism, Angewandte Chemie International Edition 37 (15) (1998) 2046–2067.
[49] L. Zhu, G. Li, L. Luo, P. Guo, J. Lan, J. You, Highly functional group tolerance in copper-catalyzed N-arylation of nitrogen-containing heterocycles under mild conditions, The Journal of Organic Chemistry 74 (5) (2009) 2200–2202.
[50] J.C. Antilla, J.M. Baskin, T.E. Barder, S.L. Buchwald, Copper-diamine-catalyzed *N*-arylation of pyrroles, pyrazoles, indazoles, imidazoles, and triazoles, The Journal of Organic Chemistry 69 (17) (2004) 5578–5587.
[51] M. Nasrollahzadeh, M. Sajjadi, R.S. Varma, A catalyst-free and expeditious general synthesis of *N*-benzyl-*N*-arylcyanamides under ultrasound irradiation at room temperature, Ultrasonics Sonochemistry 56 (2019) 481–486.
[52] P.L. Hariani, M. Faizal, R. Ridwan, M. Marsi, D. Setiabudidaya, Synthesis and properties of Fe_3O_4 nanoparticles by co-precipitation method to removal procion dye, International Journal of Environmental Science and Development 4 (3) (2013) 336–340.
[53] Z. Liu, H. Wang, C. Liu, Y. Jiang, G. Yu, X. Mu, X. Wang, Magnetic cellulose-chitosan hydrogels prepared from ionic liquids as reusable adsorbent for removal of heavy metal ions, Chemical Communications 48 (59) (2012) 7350–7352.
[54] T. Parandhaman, N. Pentela, B. Ramalingam, D. Samanta, S.K. Das, Metal nanoparticle loaded magnetic-chitosan microsphere: water dispersible and easily separable hybrid metal nano-biomaterial for catalytic applications, ACS Sustainable Chemistry & Engineering 5 (1) (2017) 489–501.
[55] H. Alinezhad, K. Pakzad, C-S cross-coupling reaction using novel and green synthesized CuO nanoparticles assisted by *Euphorbia maculata* extract, Applied Organometallic Chemistry 33 (10) (2019) e5144.
[56] K. Lakshmi, M.S. Babu, D. Ramachandran, Cobalt-promoted regioselective preparation of aryl tetrazole amines, Journal of Chemical Sciences 130 (5) (2018) 46.