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ARTICLE TYPE

Nano magnetite supported metal ions as robust, efficient and recyclable catalysts for green synthesis of propargylamines and 1, 4-disubstituted 1, 2, 3-triazoles in water

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Nano magnetite functionalized 2,2ˈ-Biimidazole complex of metal ions Cu(I), Cu(II), Ni(II) and Co(II) were successfully synthesized and characterized by different techniques such as elemental analysis, FT-IR spectroscopy, X-ray diffraction (XRD), thermo gravimetric analysis (TGA), transmission electron microscopy (TEM), scanning electron microscopy with energy dispersive X-ray spectroscopy (SEM with EDS), atomic absorption spectroscopy (AAS), inductively coupled plasma-optical emission spectrometry (ICP-OES) and vibrating sample magnetometer (VSM) instrument. The synthesized magnetic nanoparticles were used as heterogeneous catalysts in the synthesis of propargylamines via the three-component couplings reaction of aldehydes, alkynes and amines and one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles by click reaction of primary halides or tosylates, sodium azide and terminal acetylenes in aqueous media. The prepared nanocatalyst can be facilely recovered and reused many times without a significant decrease in activity and selectivity. The high catalytic activity, thermal stability and reusability, simple recovery and eco-friendly nature of catalyst make the present method to be particularly attractive in green chemistry.

Introduction

To develop experimental methods, reaction conditions, and the use of materials based on the principles of green chemistry is the challenging task in chemistry[1]. The use of safe solvents as well as efficient and cleanly reusable catalytic materials is considerable in the act of green chemistry. The use of aqueous media in transition-metal catalyzed reactions has become popular [2] because water is non-toxic, non-flammable, easily available and safer as well as being inexpensive. Moreover, the products can be separated simply by filtration. Magnetic nanoparticles (MNPs) have been extensively studied in the field of chemical catalysis, [3] magnetic biosensing[4] and contrast enhancement in magnetic resonance imaging. [5] The preparation and the use of MNPs in organic synthesis offer many advantages in sustainable chemistry as they can be non-toxic, readily accessible, and retrievable.[3,6] MNPs can be recovered from the reaction mixture with an external magnet which is typically more effective and simpler than separation with filtration or centrifugation. In addition, activity and selectivity of magnetic nanocatalysts can be manipulated by their surface modification.[7]

On the other hand, metal complexes have been extensively studied because of their potential use as homogenous catalysts in a wide range of reactions.[8] The 2,2ˈ-biimidazole (H_2Biim) is one of the most important derivatives of imidazole that can be coordinated to metal centers.[9] Some metal complexes of H_2Biim have been used as the efficient homogeneous catalysts in organic transformation reactions.[10-12] However, the major drawback of these complexes, in addition of their tedious separation, is decreasing of catalytic activities with time, due to the formation of dimeric species. [10-12] To overcome some of these issues, several metal complexes have been immobilized onto inorganic supports. A number of such supported nano magnetic Fe_3O_4 has been synthesized and applied in many organic reactions as catalyst. [7,13] Propargylamines, products of the three-component reaction of aldehydes, amines and alkynes (A^3-coupling), are versatile building blocks for the synthesis of *N*-containing biologically active compounds,[14] and key intermediates for the synthesis of natural products.[15]

Several homogenous catalysts like nickel[16] and copper salts, [17] CuI/ligand,[18] metal complexes[19] and heterogeneous systems such as Cu(0)-nanoparticles on montmorillonite,[20] silica-immobilized CuI, [21] copper ferrite nanoparticles, [22] CuNPs/MagSilica, [23] Au-

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SBA[24] and Au-CeO_2[25] have been developed for propargylamines synthesis. The scopes of these methodologies are limited due to the use of expensive [24,25] and moisture sensitive reagents,[19,21] use of alternative energy sources like ultrasound,[17] solvent toxicity[16, 19, 20] and difficulties in catalyst recyclability. [16-19] In our earlier reports, we described the synthesis of propargylamines using metal salen complex as an effective catalyst under solvent-free conditions. [26] In the last few years, metal oxide nanoparticles such as Fe_3O_4, [27] ferric hydrogensulfate, [28] impregnated copper on magnetite[29] and graphene-Fe_3O_4 [30] were reported as heterogeneous catalysts for the synthesis of propargylamines. Although all of these methods are relatively good yielding reactions, but some of them still suffer from disadvantages, such as, long reaction time [27,29,30] and using toluene [27,29] or acetonitrile[30] which are toxic solvents. Therefore, improvement of a catalytic system in terms of environmentally benign and economical approach is highly desirable.

Furthermore, 1,2,3-Triazole derivatives are important class of organic compounds for medicinal chemistry, which exhibit a wide range of biological activities such as antiepileptic, anticancer[31] and anti HIV.[32] In general, these compounds are prepared through Huisgen's dipolar cycloaddition of organic azides and alkynes. [33] However, because of the high activation energy (ca. 24 - 26 kcal/mol), these cyclo-additions are often very slow even at elevated temperature (80-120 °C for 12-24 h) and produce mixtures of regioisomers. The introduction of Cu (I) salts by Sharpless and co-workers led to a major improvement in both rate and regioselectivity of the reaction. [34] However, difficult separation process and recycling of the expensive catalyst, cytotoxicity and environmental pollution are problems homogeneous catalysis reaction. Removal of trace amounts of catalyst from the end product which is a difficult task in these reactions, is essential since metal contamination is highly regulated, particularly in the pharmaceutical industry.[35] Immobilization of the homogenous catalysts on organic and inorganic supports can investigate these problems. Recently, several methods have been developed to immobilize copper species on a wide variety of solid materials. [36-38] Nevertheless, the active sites in heterogeneous system are not as accessible as in a homogeneous catalyst, and thus the activity of the catalyst usually decreased. Furthermore, due to the diffusion of substrates and products through the pores of the support materials, a significant reduction in reaction rate is often observed compared to the homogeneous system. Thus, it is worthwhile to consider new materials as support for Immobilization of the homogenous catalysts. The magnetic support is one ideal solution to this problem because of high specific surface, the active sites which are mainly distributed on the "outer" surface of the support which avoids pore diffusion, and the application of an external magnetic field enables the removal of the particles in a simple way. [23, 39]

In our continuous study in the field of nano catalysts, [40] we recently reported Fe_3O_4 immobilized complex application as an efficient, recyclable and magnetically separable nanocatalyst in the imidazo[1,2-a]pyridines synthesis. [41] Because of the good performance of this catalyst in aqueous media, inspired us to prepare various nano magnetite functionalized 2,2ʹ-Biimidazole complexes and to investigate their catalytic activity, reusability and stability in the synthesis of propargylamines and 1,4-disubstituted 1,2,3-triazoles in green media.

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Results and discussion

Catalyst preparation and characterization

The nano Fe_3O_4 supported metal ion complexes were synthesized (Fig. 1) and characterized. Initially, Co-precipitation of $FeCl_3$ and $FeCl_2$ in an ammonia solution led to formation of Fe_3O_4 nanoparticles (MNPs). Then a layer of SiO_2 was coated on Fe_3O_4 surface to improve the chemical stability and biocompatibility of particles. Functionalization of MNPs@SiO_2 by 3-(chloropropyl)triethoxysilane (CPTES) afforded MNPs coated CPTES, which followed by reacting with biimidazole and subsequently with metal salts to produce biimidazole metal ion complexes immobilized on core-shell magnetic nanoparticles; MNP@BiimM M: Cu(I), Cu(II), Ni(II), Co(II). The structure of the synthesized nanoparticles were characterized by FT-IR, EDS, SEM, TEM, TGA, elemental analysis, XRD, VSM, AAS and ICP-AES techniques.

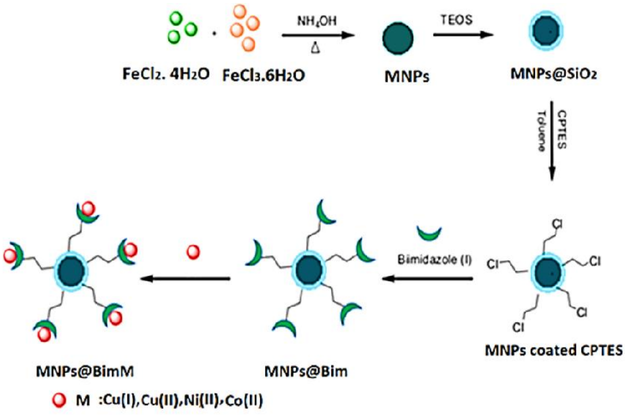
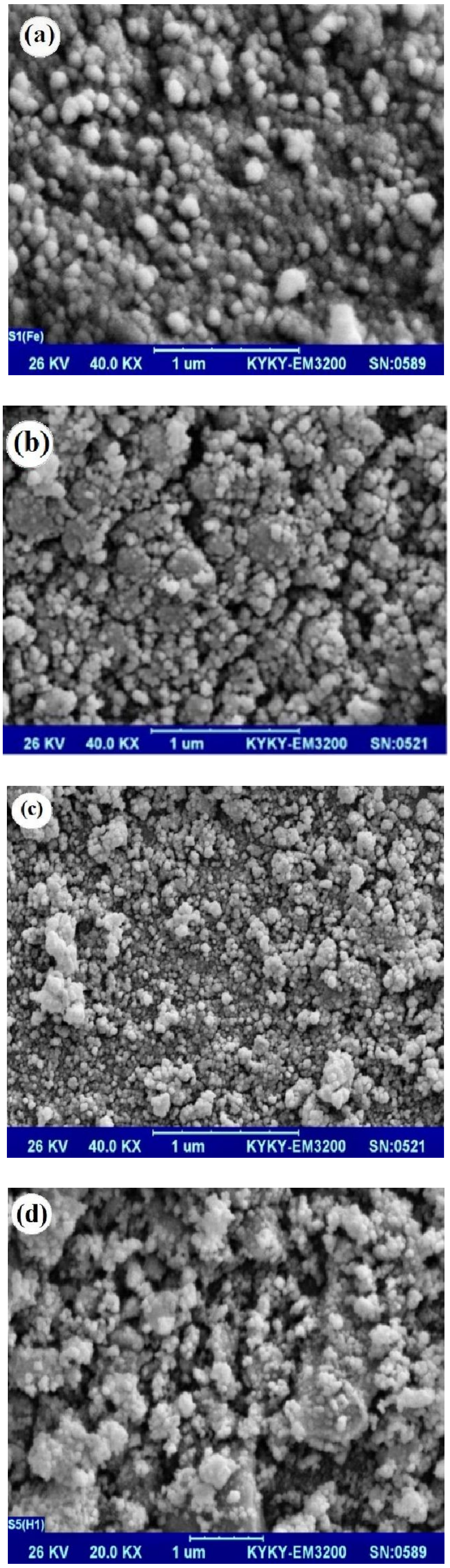


Fig. 1 Stepwise preparation of MNP@BiimM nanoparticles as a magnetically separable system

The average particles size and morphology of MNP@SiO_2, MNP@Biim and MNP@BiimCu(I) samples were investigated by means of scanning electron microscopy (SEM) and transmission electron microscopy (TEM). SEM image (Fig. 2a) of MNP@SiO_2 shows a smooth surface with diameters of approximately 15-20 nm with a narrow size distribution. SEM images (Fig. 2b and 2c) for upon coating the Fe_3O_4 particles are almost similar to that of the bare Fe_3O_4 except for a slightly larger particle size. These nanoparticles are also spherical in shape with slightly agglomeration.

TEM images reveal that the diameter of MNP@SiO_2 nanoparticles is about 15 nm and for MNP@Biim and MNP@BiimCu(I) nanoparticles are around 25 nm due to the agglomeration of Fe_3O_4 and surface growth of homogenous layer on the shell (Fig. 2e-g). HRTEM image of MNP@BiimCu nanoparticles clearly shows dark nano-Fe_3O_4 core surrounded by a grey silica shell (Fig. 2g).



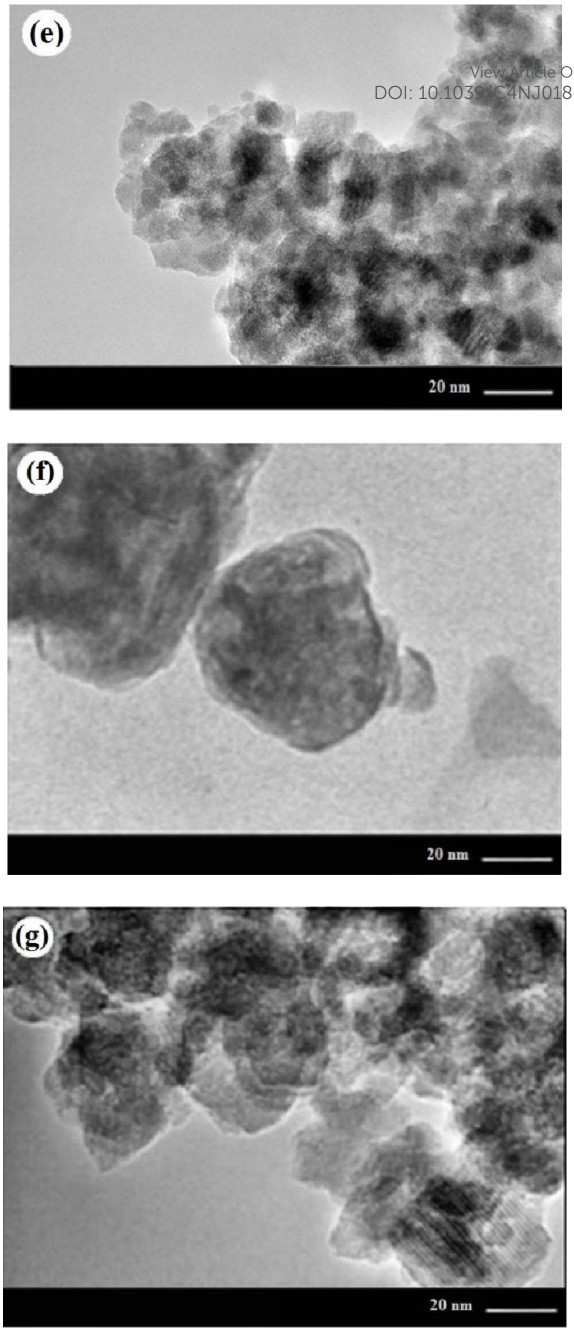


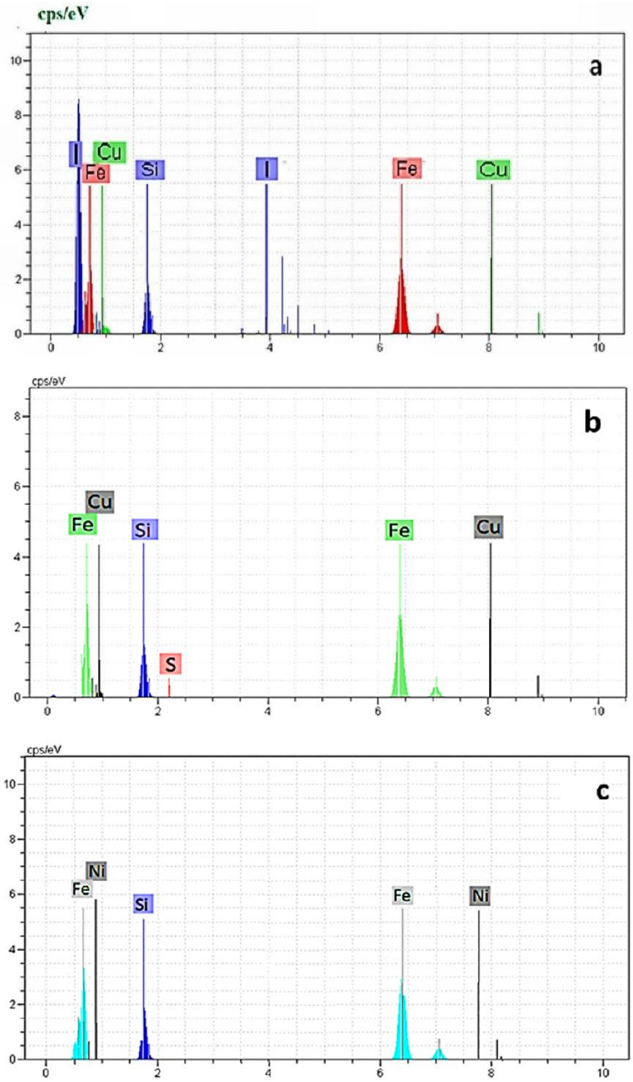
Fig. 2. SEM images of a) MNP@SiO_2, b) MNP@Biim, c) fresh MNPs@BiimCu d) recycled MNPs@BiimCu after 10 times, TEM images of e) MNP@SiO_2, f) MNP@Biim, g) MNPs@BiimCu(I)

FT-IR spectra of particles before and after each coating step were recorded and results reveal the existence of the organic compounds on core-shell magnetic nanoparticles (Fig. S1 in the Supporting Information). In addition, the crystalline structures of prepared nanoparticles were analyzed by X-ray powder diffraction. The XRD pattern of MNPs, showed peaks at 2Θ values 30.1°°, 35.4°, 43.1°, 53.4°, 57° and 62.6 ° related to (220), (311), (400), (422), (511) and (440) crystal planes in Fe_3O_4 cubic lattice (JCPDS 19-0629). The XRD patterns of the coated nanoparticles have the same characteristic peaks with an additional broad peak between 2-15 and 2-30 which is attributed to the amorphous silica shell and complex of metal (Fig. S3 in the Supporting Information).The average crystallite size was calculated by applying Scherrer's equation:

$$D = K\lambda/\beta\cos\theta$$

Where D is the grain size, β is the angular line width of half-maximum intensity in radians, θ is Bragg diffraction angle and λ is the X-ray wavelength used. The average size of MNP@Biim nanoparticles is found to be around 15 nm.

The EDS spectra of the prepared nanoparticles are depicted in Fig. 3(a-d) and all the samples show the presence of iron and silicone together with the peaks of the related metal ions in the structure of the nanoparticles. The EDS patterns clearly gave the pivotal evidence of the immobilization of metal ions on the surface of silica-coated iron oxide nanoparticles.



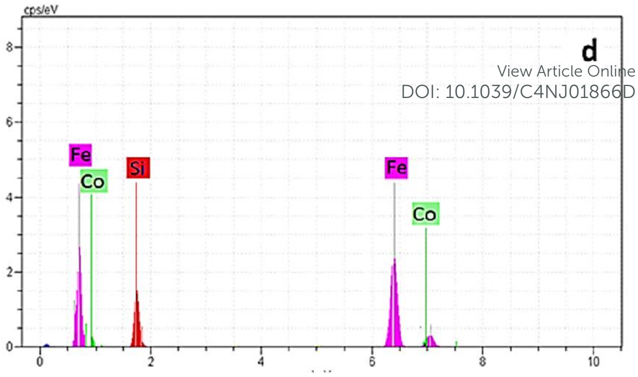


Fig.3. EDS patterns of a) MNPs@BiimCu(I), b) MNPs@BiimCu(II), c) MNPs@BiimNi(II), d) MNPs@BiimCo(II)

Thermogravimetric analysis (TGA) and differential thermal analysis (DTA) were performed at the range of 25 to 800 ˚C, to determine the loading of organic groups coated on the surface of the magnetite (Fig. 4). In case of MNPs@SiO_2 (Fig. 4a), the weight loss around 5% is due to the physically adsorbed water molecules and hydroxyl groups on the magnetite surface.

The TGA curve of magnetite coated CPTES sample (Fig. 4b), shows a weight loss of ~ 2% in temperature range of 25-150 °C attributed to the loss of moisture and a weight decrease of ~ 16% at ~ 250-450 °C, associated to the thermal decomposition of chloropropyl group. Considering the results, the CPTES loading calculated using Eq. (1) to be 2.07 mmol/g. For MNPs@Biim, two-stage weight losses are observed (Fig. 4c). The first weight loss (below 150 ˚C ~1%) can be ascribed to the evaporation of water molecules and the other weight loss above 250 °C (~ 30%) could be assigned due to the decomposition of biimidazolypropyl moiety grafted on the MNPs@SiO_2 surface. This was confirmed by DTA diagram of MNPs@Biim (Fig. 4c). The amount of adsorbed biimidazolypropyl calculated by Eq. (2) is 1.7 mmol g^{-1}.

For the MNPs@BiimCu(I) sample (Fig. 4d), TGA curve shows a weight loss about 1% within 25–150 ˚C relating to the physically adsorbed moisture followed by the second weight loss corresponding to the thermal decomposition of the organic spacer group and the third weight loss above 600˚ C could be assigned to the sublimation of iodine (melting point of CuI: 602 ˚C).[42] DTA diagram confirms the two steps thermal decomposition at 250 and 600 ˚C (Fig. 4d). Comparing TGA curve of MNPs@BiimCu(I) (Fig. 4d) with MNPs@Biim (Fig. 4c), the mass fraction of copper iodine on the surface of MNPs@SiO_2 could be deduced to be 38% and the amount of adsorbed copper iodide calculated by Eq. (3) is 1.9 mmol/g. These results could prove not only the attachment of biimidazolypropyl moiety but also indicate the amount of CuI onto the surface of MNPs@SiO_2.

Eq. (1):

mmol CPTES = (weight loss / 100 × Mw hydrolyzed CPTES) × 1000 = (16/ 100 × 77) × 1000

= 2.07 mmol

Eq. (2):

mmol biimidazolypropyl = (weight loss / 100 × Mw biimidazolypropyl) × 1000 = (30/ 100 × 176) × 1000

= 1.7 mmol

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Eq. (3): 45
mmol CuI = (weight loss of copper iodide) / 100× Mw copper iodide) × 1000 = (38 / 100 × 190) × 1000
= 1.9 mmol

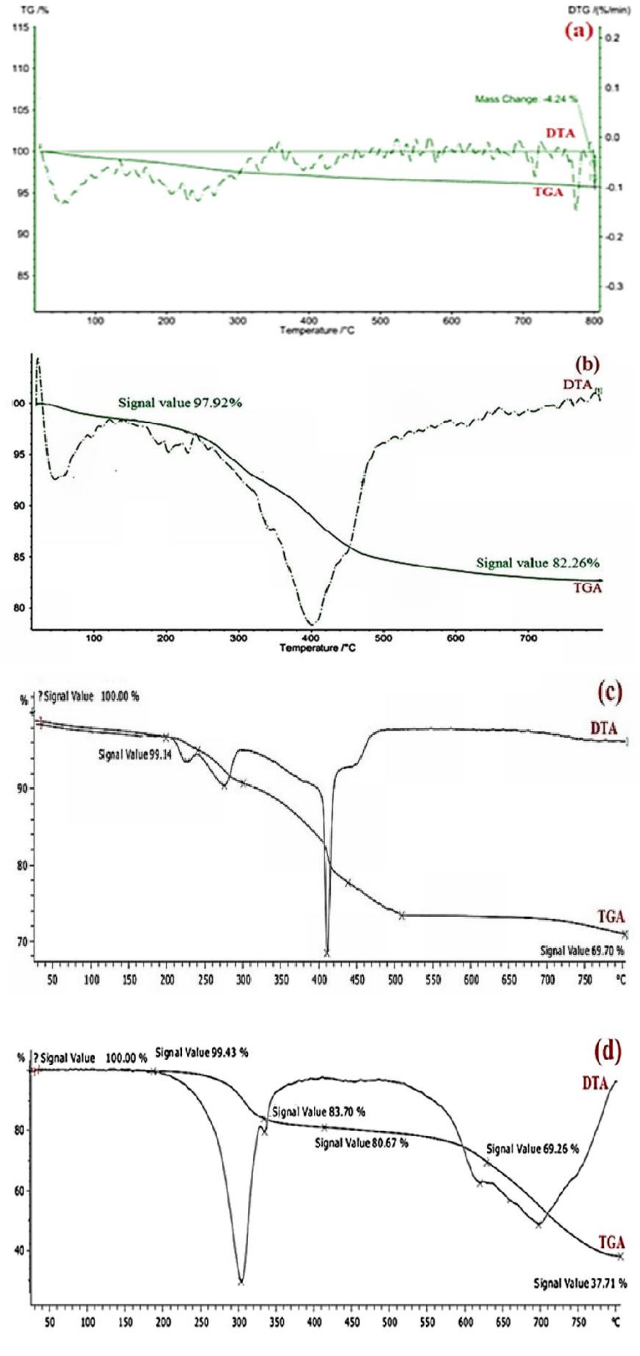


Fig. 4. The TGA/DTA curves of a) MNPs@SiO$_2$ b) MNPs coated CPTES, c) MNPs@Biim d) MNPs@BiimCu(I), 10˚C/min under N$_2$

The elemental analysis of the samples (Table in the Supporting Information) is in good agreement with result obtained from TGA data. The amount of loaded copper iodide on MNPs@BiimCu(I) surface was also measured by inductively coupled plasma-optical emission spectrometry (ICP-OES) and atomic absorption spectrophotometer (AAS) to be 1.73 mmol/g and 1.71 mmol/g, respectively ((Table in the Supporting Information) which is in good agreement with the calculated value from TGA data of the MNP@BiimCu(I) nanoparticles.

The magnetic properties of MNPs@SiO$_2$, MNPs coated CPTES and MNPs@BimCu(I) were determined by a vibrating sample magnetometer, VSM, (Fig. S4 in the Supporting Information). The saturation magnetization values were 52.3 emu/g for MNP@Bim and 47.4 emu/g for MNPs@BimCu(II) without the observation of hysteresis curves, indicating the typical superparamagnetic behavior. The saturation magnetization of these nanoparticles is smaller than that of MNPs@SiO$_2$ due to entrapment of MNPs into the nonmagnetic materials. However, the magnetization is still large enough for separation of the catalyst by magnetic stirring bar in the reaction mixture (Fig. 5).

Catalytic application of MNP@BiimM nanoparticles

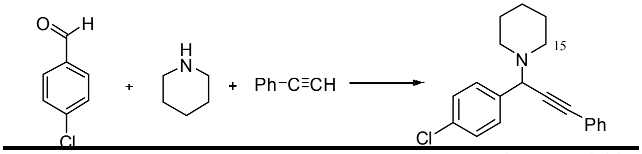
The catalytic activity of synthesized magnetic nanoparticles was tested in two different terminal-alkyne transformations: the multicomponent 1,3-dipolar cycloaddition of terminal alkynes, with sodium azide and alkyl halides, and the three-component synthesis of propargylamines from aldehydes, amines and terminal alkynes (A^3 coupling). The optimal reaction conditions were determined independently for both reactions studied.

A^3 coupling reaction based one-pot synthesis of propargylamines

Initially, in order to investigate the catalytic activity of MNPs@BiimCu(I) in synthesis of propargylamines, the reaction of piperidine (1 mmol) with *p*-chloro benzaldehyde (1 mmol) and phenylacetylene (1 mmol) were examined under different conditions as a model reaction, and the results are presented in Table 1. It can be seen that when the model reaction was carried out at 100˚C in the aqueous medium in the absence of any catalyst, no desired product was formed after 24h (Table 1, entry 1), and only 23% yield was observed with Fe$_3$O$_4$ as the catalyst in water after 10 h (Table 1, entry 2). On the other hand, CuI and biimidazole/CuI(Bim/CuI) equivalent to that deposited on MNPs@BimCuI, 0.017 mmol (calculated by ICP analysis), resulted in 34% and 78% yields in water after a long time (Table 1, entry 3 and 4). Excellent yield of propargylamine was observed in the presence of 10 mg MNPs@BiimCu(I) as the catalyst after 1.5 hr (Table 1, entry 5). When the reaction was conducted at 80 °C, lower yield of the product was obtained compared with reaction at 100 ˚C (Table 1, entry 6). Using the other solvents such as EtOH, THF, CH$_3$CN and toluene under reflux temperature did not increase the yield even in longer reaction time (Table 1, entries

7-10). In the absence of solvent, 87% yield in 5 h was obtained (Table 2, entry 11). Increasing the amount of catalyst to 20 mg showed no further increase in the yield. Decreasing the loading of catalyst leads to lower product yield (Table 1, entries 12 and 13). Finally, from Table 1 it can be seen that treating piperidine (1 mmol) with *p*-chloro benzaldehyde (1 mmol) and phenylacetylene (1 mmol) using MNPs@BiimCu(I) (10 mg) in water (2 mL) at 100 ºC, an excellent yield of the desired propargylamine can be achieved (Table 1, entry 5). On the other hand, it is interesting to note that the present experimental condition no other byproducts were observed.

Table 1. Effect of temperature, solvent and catalyst on A^3 coupling reaction[a]



Entry	Catalyst (10 mg)	Solvent/ Temp(°C)	Time (h)	Yield (%)[b]
1	-	H_2O/ Reflux	24	-
2	MNPs	H_2O/ Reflux	10	23
3	CuI (3.2 mg)[c]	H_2O/ Reflux	10	34
4	Biim/CuI (5.5 mg)[c]	H_2O /Reflux	7	78
5	**MNPs@BiimCu(I)[c]**	**H_2O /Reflux**	**1.5**	**99**
6	MNPs@BiimCu(I)	H_2O/ 80 °C	1.5	75
7	MNPs@BiimCu(I)	EtOH /Reflux	10	65
8	MNP@BiimCu(I)	THF/ Reflux	10	trace
9	MNP@BiimCu(I)	MeCN / Reflux	10	44
10	MNP@BiimCu(I)	Toluene/ Reflux	10	85
11	MNP@BiimCu(I)	-/100°C	5	87
12	MNP@BiimCu(I),20 mg	H_2O/ Reflux	1.5	99
13	MNP@BiimCu(I),5 mg	H_2O/ Reflux	1.5	75

Bold in entry highlight the optimal reaction conditions.[a] All reactions were carried out with *p*-chloro benzaldehyde (1mmol), piperidine (1mmol) and phenyl acetylene (1mmol) in 2 mL solvent, [b]Isolated yield, [c] Containing Cu 0.017 mmol or 1.7 mol%

The catalytic activity of MNPs@BiimCu(I) was compared with other synthesized MNPs@Bim complex of metal ions ,Cu(II), Ni(II) and Co(II). These complexes were examined in the reaction of piperidine (1 mmol) with *p*-chloro benzaldehyde (1 mmol) and phenylacetylene (1 mmol) (Table 2) under the optimal reaction conditions. It can be seen that although copper (I) showed highest efficiency but the other metal ions showed also promising catalytic activities as heterogeneous catalysts in the A^3 coupling reaction. In comparison with some of those reported in literature, [16,19] we observed that the MNPs@BiimCo(II) gives better yield in shorter reaction time than some homogenous catalysts such as $CoCl_2(PPh_3)_2$ complex.[19] Also, MNPs@BiimNi(II) is comparable with $NiCl_2$ catalyst that reported by Samai et al.[16] MNPs@BiimCu(II) nanoparticles was less reactive than other coated nanoparticles. Therefore, we chose MNPs@BimCu(I), for synthesis of propargylamines from aldehydes, amines and terminal alkynes (Table 2).

Table 2 The effect of MNPs@Bim complex of metal ions on the A$_3$ coupling reaction[a]

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Entry	Catalyst (10 mg)	Time (h)	Yield (%)[b]
1	MNPs@BiimCu(I)	1.5	99
2	MNPs@BiimCu(II)	5	75
3	MNPs@BiimNi(II)	5	86
4	MNPs@BiimCo(II)	3	91

[a]Reaction conditions: *p*-chloro benzaldehyde (1mmol), piperidine(1mmol) and phenyl acetylene (1mmol), catalyst (10 mg, 1.7 mol%) and H_2O (2 mL), reflux [b]Isolated yield

In order to explore the generality and applicability of this catalyst a variety of aldehydes and secondary amines with phenylacetylene were coupled under the optimal reaction conditions, and the results are summarized in Table 3. The results indicated that both aromatic and aliphatic aldehydes were transformed to the corresponding propargylamines in excellent yields. Aryl aldehydes with both electron-donating and electron-withdrawing substituents showed high reactivity and generated the desired products in good to excellent yields (Table 3, entries 1-9).

In addition, heteroaromatic aldehydes such as thiophene-2-carbaldehyde and furan-2-carbaldehyde as well as 2-naphthaldehyde also participated well in this reaction (Table 3, entries 11-13). To extend the scope of the reaction, various amines were used and the results are also tabulated in Table 3. All the amines gave excellent yields of the desired propargylamines (Table 3, entries 14-26). Similarly, terephthalaldehyde reacted with two equivalents of piperidine or morpholine and phenyl acetylene to afford the disubstituted products in high yields (Table 3, entries 19 and 20). Attempt to synthesize the monosubsituted product was not successful. Reaction of cinnamaldehyde with morpholine and phenyl acetylene afforded the expected product in high yield (Table 3, entry 27). To show the practical applicability of the catalyst, the model reaction was repeated in l0 mmol scale under similar optimized reaction conditions. *p*-chloro benzaldehyde with piperidine and phenylacetylene in presence of 100 mg of MNPs@BiimCu catalyst (Cu content 0.17 mmol) were allowed to stir in 10 mL water at 100 ˚C. The reaction proceeds well with 87% isolated yield in 1.5 h (Table 3, entry 1[c]).

In order to study the role of catalyst in this reaction, a few experiments were carried out. Reaction of phenylacetylene with piperdine without aldehyde in the presence of catalyst, homocoupling product, 1,4-diphenylbuta-1,3-diyne was produced in 91% yield in short time (Table 3, entry 28). Thus, this procedure can also be utilized for homocoupling reactions. A significant decrease of product yield in the absence of the catalyst, clearly demonstrates the effect of catalyst in homocoupling reaction (Table 3, entry 29). However, phenylacetylene in the presence of catalyst without adding piperidine gave the expected homocoupling product in 55% yield (Table 3, entry 30).

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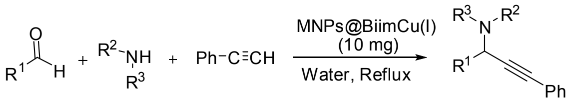
Table 3 MNP@BiimCu(I) nanoparticles catalyst A^3 coupling reaction of aldehyde, amine and alkyne[a]



Entry	R^1	R^3, R^4	Yield (%)[b]	TON /TOF	Ref
1	4-ClC_6H_4	$(CH_2)_5$	99, 87[c]	82/0.91,	44
2	C_6H_5	$(CH_2)_5$	99	82/0.91	44
3[h, i]	C_6H_5	$(CH_2)_5$	99 (2h[h],3h[i])	82/ 0.7[h], 82/0.4 [i]	44
4	4-MeC_6H_4	$(CH_2)_5$	91	76/0.84	44
5	4-BrC_6H_4	$(CH_2)_5$	99	82/0.91	25
6	3-BrC_6H_4	$(CH_2)_5$	98	82/0.9	45
7	4-CNC_6H_4	$(CH_2)_5$	91	76/0.84	44
8	2-OHC_6H_4	$(CH_2)_5$	91	76/0.84	43
9	2,4-$DiMeC_6H_3$	$(CH_2)_5$	80	67/0.74	26
10	$CH_3CH_2CH_2$	$(CH_2)_5$	81	670.74	44
11	Furyl	$(CH_2)_5$	84	70/0.77	26
12	Thiophyl	$(CH_2)_5$	87	72/0.8	43
13	2-Naphthyl	$(CH_2)_5$	85	71/0.78	43
14	C_6H_5	$(CH_2)_2O(CH_2)_2$	98	82/0.91	28
15	4-CNC_6H_4	$(CH_2)_2O(CH_2)_2$	84	70/0.85	43
16	4-FC_6H_4	$(CH_2)_2O(CH_2)_2$	96	80/0.88	45
17	4-$CF_3C_6H_4$	$(CH_2)_2O(CH_2)_2$	99	82/0.9	43
18	3-OHC_6H_4	$(CH_2)_2O(CH_2)_2$	89	74/0.82	43
19	4-$CHOC_6H_4$	$(CH_2)_2O(CH_2)_2$	81[d]	67/0.74	26
20	4-$CHOC_6H_4$	$(CH_2)_5$	86[d]	72/0.8	26
21	$CH_3CH_2CH_2$	$(CH_2)_2O(CH_2)_2$	83	69/0.76	26
22	$(CH_3)_2CH$	$(CH_2)_2O(CH_2)_2$	80	67/0.74	43
23	C_6H_5	$(CH_2)_4$	91	76/0.84	28
24	2-Naphthyl	$(CH_2)_4$	81	67/0.74	43
25	4-FC_6H_4	Et, Et	95	79/0.87	26
26	C_6H_5	$PhCH_2$, $PhCH_2$,	91	76/0.84	44
27	PhCH=CH_2	$(CH_2)_2O(CH_2)_2$	89	74/0.82	45
28	-	$(CH_2)_5$	99[e]	**homo coupling product**	46
29	-	$(CH_2)_5$	35[f]		
30	-	-	55[g]		

[a] Aldehyde(1mmol), amine(1mmol), phenylacetylene (1mmol), catalyst (10 mg, 1.7 mol%) and H_2O (2 mL) for 1.5 h, [b] Isolated yields, [c] Scale-up to 10 mmol scale, [d] Disubstitued product, [e, f, g] Homocoupling product, for 20 min, [f] Without catalyst, [g] Without piperidine, [h] After fifth and [i] tenth run.

Click reaction based one-pot synthesis of 1,2,3-triazole

The catalytic activity of the MNP@BiimCu(I) nanoparticles was also examined in the multicomponent 1, 3-dipolar cycloaddition reaction of terminal alkynes with organic azides generated in situ from sodium azide and alkyl halides. Table 4 shows the results of the reaction of phenylactelylene with benzyl bromide and NaN_3 under different reaction conditions. Interestingly, from the different solvents and solvent/co-solvent mixtures tested, water was found to be the most effective medium for this reaction (Table 4, entries 2-6). After finding the best solvent, other parameters such as temperature (entries 7–8) and amount of catalyst (entries 9 and 10) were optimized. The highest yield of 1-benzyl-4-phenyl-1H-1,2,3-triazole was achieved when phenylacetylene, benzyl bromide and sodium azide using 5 mg catalyst stirred in water for only 0.5 h at room temperature (Table 4, entry 2), Lack of reaction in the absence of the catalyst, clearly demonstrates the effect of catalyst in this reaction (Table 4, entry 1).

Table 4 Optimization of reaction conditions for synthesis of 1,4-disubstituted 1,2,3 triazole[a]

Entry	Catalyst (5 mg)	Solvent / Temp(°C)	Yield (%)[b]
1	-	H_2O/ rt	-[c]
2	**MNP@BimCu(I)**[e]	**H_2O /rt**	**99**
3	MNP@BimCu(I)	H_2O: EtOH(1:1)/rt	75
4	MNP@BimCu(I)	EtOH /rt	30
5	MNP@BimCu(I)	THF/ rt	trace
6	MNP@BimCu(I)	MeOH / rt	65
7	MNP@BimCu(I)	H_2O/ 50	99
8	MNP@BimCu(I)	H_2O/ 70[d]	99
9	MNP@BimCu(I),10 mg	H_2O/ rt	99
10	MNP@BimCu(I),3 mg	H_2O/ rt	82
11	CuI, (1.6 mg) [e]	H_2O/ rt	trace
12	Biim/CuI (2.7 mg)[e]	H_2O/ rt	45

Bold in entry highlight the optimal reaction conditions. [a] All reactions were carried out with benzyl bromide (1mmol), NaN_3 (1.1 mmol) and phenyl acetylene (1mmol) in 1 mL solvent, for 0.5 h, [b] Isolated yield [c] For 6 h, [d] For 20 min, [e] containing Cu 0.0085 mmol or 0.85 mol%.

In order to study the catalytic activity of other MNPs@Bim complex of metal ions in comparison to MNPs@BimCu(I), These complexes were tested in the reaction of phenylactelylene with benzyl bromide and NaN_3 and results are shown in Table 5. The catalytic activity of nanoparticles was found to be of the order Cu(I)> Cu(II)>>Ni(II)> Co(II). Although MNP@BimCu(II), showed excellent performance within a short reaction time but Cu(I) species is more effective than other prepared nanoparticles. As a result, MNPs@BimCu(I) was used in the subsequent investigations.

Table 5 The effect of MNPs@Bim complex of metal ions on the click reaction[a]

Entry	Catalyst (5 mg)	Time (h)	Yield (%)[b]
1	MNPs@BiimCu(I)	0.5	99
2	MNPs@BiimCu(II)	1	92
3	MNPs@BiimNi(II)	3	65
4	MNPs@BiimCo(II)	3	37

[a] Reaction condition: benzyl bromide (1mmol), NaN_3 (1.1 mmol), phenyl acetylene (1mmol)), catalyst (0.85 mol%) and H_2O (1 mL), [b] Isolated yield.

The scope and limitation of the reaction were investigated by reacting various primary halides with alkynes and NaN_3, and results are presented in Table 6. Different benzyl bromides reacted well with alkynes and NaN_3 to afford the corresponding triazoles in nearly quantitative yields. In the case of activated functionalized organic halides such as *p*-bromo phenacyl bromide and phenacyl bromide, the reactions proceeded smoothly and the products were isolated in high yields (Table 6, entries 5, 8). Allyl bromide reacted as well as its benzyl counterpart (Table 6, entry 9). As it is clear from this table, aliphatic bromides tolerated well in this reaction (Table 6, entries 6,18,21). Aliphatic alkynes, such as 1-heptyne also gave the expected triazoles in good to high yields, although in longer reaction times compared with their aryl counterparts (Table 6, entries 12,14,16 and 19). Other electrophiles such as alkyl chlorides and alkyl tosylates classically used in nucleophilic substitution reaction for comparison with alkyl bromides were also screened in this reaction. The lower yields of triazoles derived from chlorides in water compared with high yields obtained using ethanol as co-solvent (Table 6, entries 2,7,11,13 and 17), is probably due to the less solubility of the chloride in water. However, tosylate derivatives proved more reactive than corresponding chlorides in pure water and gave the desired triazoles in high yields. (Table 6, entries 3,10,15 and 20).

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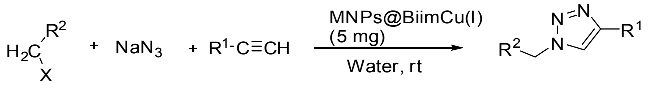
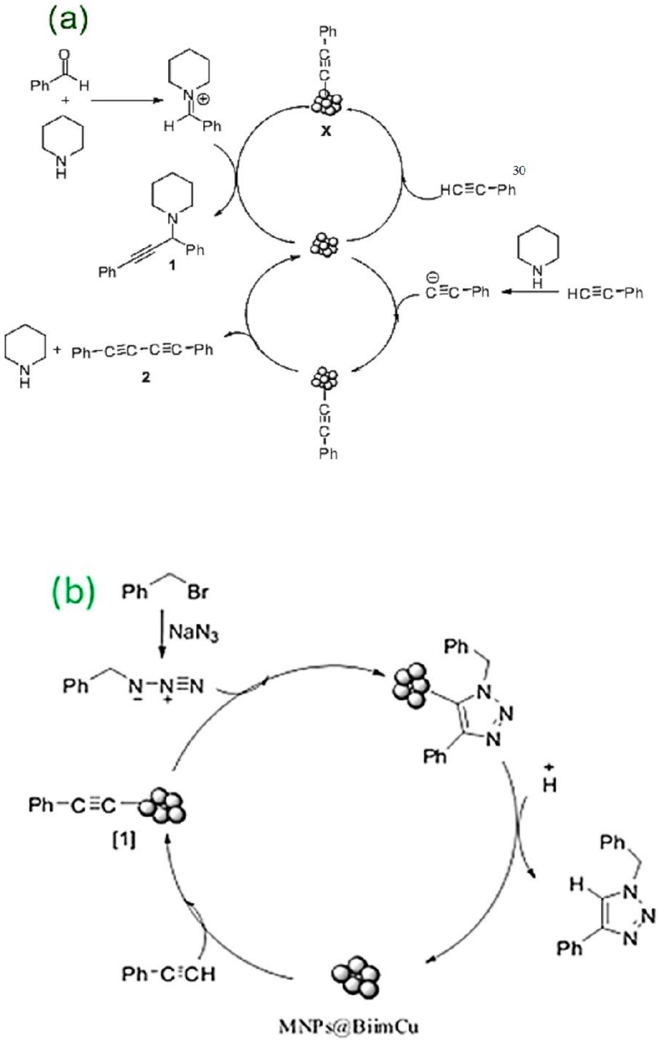
Table 6 Huisgen 1,3-dipolar cycloaddition reaction catalyzed by MNPs@BiimCu(I)[a]



Entry	R^1	R^2/X	Time (h)	Yield (%)[b]	TON[d]/ TOF[e]	Ref
1	Ph	C_6H_5/Br	0.5	99	165/5.5,165/4.1[f]	46
2	Ph	C_6H_5/Cl	1	75,93[c]	155c/2.5	46
3	Ph	C_6H_5/OTS	1	99	165/2.7	46
4	Ph	4-BrC_6H_4/Br	0.5	97	162/5.4	47
5	Ph	4-BrC_6H_4CO/Br	1	91	152/2.5	47
6	Ph	$CH_3(CH_2)_5$/Br	2	92	152/1.27	36
7	Ph	$CH_3(CH_2)_5$/Cl	2	70, 98[c]	163c/1.3c	36
8	Ph	C_6H_5CO/Br	1	94	157/2.6	48
9	Ph	CH_2=CH/Br	0.5	96	160/5.3	46
10	Ph	CH_2=CH/OTS	1	99	165/2.7	46
11	Ph	CH_2=CH/Cl	2	80, 97[c]	162[c] /1.3	46
12	$CH_3(CH_2)_4$	CH_2=CH/Br	2	99	-	-
13	$CH_3(CH_2)_4$	2-Naphthyl/Cl	2	65, 88[c]	147c/1.2	49
14	$CH_3(CH_2)_4$	C_6H_5/Br	1.5	99	165/1.8	50
15	$CH_3(CH_2)_4$	C_6H_5/OTS	1.5	95	158/1.75	50
16	$CH_3(CH_2)_4$	4-BrC_6H_4/Br	1.5	97	162/1.8	-
17	$CH_3(CH_2)_4$	4-BrC_6H_4/Cl	2	68, 91[c]	152c/1.3[c]	-
18	Ph	CH_3CH_2 /Br	1.5	98	163/1.8	46
19	$CH_3(CH_2)_4$	CH_3CH_2/Br	3	94	157/0.9	-
20	$CH_3(CH_2)_4$	CH_3CH_2/OTS	3.5	91	151/0.7	-
21	Ph	$CH_3(CH_2)_4$/Br	2	96	160/1.3	36
22	COOEt	C_6H_5/Br	2	99	165/1.4	46

[a] Reaction condition: primary halide (1mmol), NaN_3 (1.1mmol), alkyne (1mmol) catalyst (5 mg, 0.85 mol%) and H_2O (1 mL), [b] Isolated yield. [c] performed in a 1:1 mixture of water and ethanol, [d]TON: turn over number (mol of product/mol of catalyst), [e]TOF: turn over frequency [mol of product/(mol of catalyst × reaction time(min)]. [f] After fifth run.

Based on reports in the literature,[20, 24] a tentative mechanism is proposed for three-component synthesis of propargylamines using MNPs@BiimCu(I) catalyst in Scheme 1(a). It is assumed that, due to high alkynophilicity of copper (I) ion for terminal alkyne; phenylacetylene is coordinated to copper (I) supported on magnetic nanoparticles to activate the C–H bond and generate the acetylide complex (**X**). Then the copper acetylide complex reacts with iminium ion, formed in situ by condensation of aldehyde with the secondary amine, to afford desired propargylamines (1), and the catalyst is regenerated. The catalytic cycle repeats until the completion of substrates. Furthermore, based on obtained results from Table 3 (entries 28-30), in the absence of aldehyde, it is postulated that the generation of acetylide complex (X) is facilitated in presence of piperidine as base and thus homocoupling product (2) is formed in excellent yield in short reaction time. This observation is in consistent with the results reported in the literature.[51, 52, 53]



Scheme 1. Tentative mechanism for (a) A^3 coupling and homocoupling reaction of phenylacetylene (b) Click reaction catalyzed by MNPs@BiimCu(I)

Furthermore, according to the previous studies,[36,54] a possible mechanism for click reaction is proposed in Scheme 1(b). The 1,2,3-triazole formation proceeds through the formation of copper acetylide (**1**) followed by coordination of the organic azide, formed in situ by click chemistry, to the copper center of the acetylide initiates an azide-alkyne 1,3-dipolar cycloaddition reaction.

For a heterogeneous catalyst, it is essential to study its ease of separation, recoverability and reusability. To study on the stability and the reusability of MNPs@BiimCu(I) was investigated in A^3-coupling reaction via *p*-chlorobenzaldehyde, phenyl acetylene and piperidine and one-pot click reaction of benzylbromide with phenyl acetylene and sodium azide under the optimized reaction conditions (Table 7). After completion of the reaction, catalyst was easily removed from the reaction mixture by magnetic stirring bar as shown in Fig. 5 and recovered simply by washing with EtOH, and vacuum drying. The colours of the reaction mixtures are related to the products. In order to rule out the possible contribution of any free metal in the reaction solution and to check the stability of the nanomagnet supported catalyst against the so-called "leaching-out" of catalyst molecules from the supporter, the actual content of metal ions in reaction solution (water) and washing solution (ethanol) was measured by AAS. No significant amount of copper was detected from the product solution after the removed of the catalyst. FT-IR spectra of nanomagnet supported catalyst before and after the catalytic reaction did not show any significant differences (Fig S2 in the supporting information). The recovered catalyst was reused for many times without a significant decrease in its catalytic activity (Table 7). Moreover, no appreciable change in textural properties of the catalyst was detected after several runs, as clearly evidenced from ICP analysis and SEM analysis of the recycled catalyst. In the Click reaction, the amount of copper loss calculated by ICP analysis is 0.08% after five cycles; while it is 0.2% in the A^3 coupling reaction after 10 repeated recycling. These results may partly explain the yield decreasing slightly with increasing the recycles for the both coupling reactions. SEM images also did not show a significant change in the morphology (Fig. 2d) in the surface of recovered catalyst after the 10th recycles in the A^3-coupling reaction. Based on these experimental results, however, it can be corroborated that Cu ions existing on the nanomagnet surface show a good stability against the “leaching-out” phenomena, to be used as an immobilized recyclable catalyst in the solvent system investigated. After several cycles, when the reaction rates were reduced, the recovered catalyst was retreated and the thus regenerated catalyst resumed the initial activity of the fresh one, showing conversion of 99%. This demonstrates a good regenerate capability for MNPs@BimCu(I).(Table 7, Regenerated catalyst).

Table 7: Recyclability of the catalyst

Run	[A] Yield(%)^b/Time(h)	[B] Yield(%)^b/Time(min)
Fresh	99/1.5	99/30
1	99/1.5	99/30
2	96/1.5	99/30
3	99/2	99/30
4	99/2	93/30
5	99/2	96/40
6	93/2	-
7	99/2.5	-
8	91/2.5	-
9	89/3	-
10	89/3.5	-
Regenerated catalyst	99/1.5	99/30
Cu leached ^{a}	0.23% (after 10 th)	0.08% (after 5 th)

[A] A^3 coupling: *p*-chlorobenzaldehyde (1 mmol), piperdine (1 mmol), phenyl acetylene (1 mmol), catalyst (10 mg, 1.7 mol%) and H_2O (2 mL) at 100 ºC, [B] Click reaction: benzyl bromide(1 mmol), NaN_3(1.1 mmol), phenyl acetylene (1 mmol), catalyst (5 mg, 0.85 mol%) and H_2O (1 mL) at r.t. ^{a} Cu leaching was determined by ICP ,Cu content in product phase in % of initial Cu loading of the catalysts, ^{b} Isolated yield.

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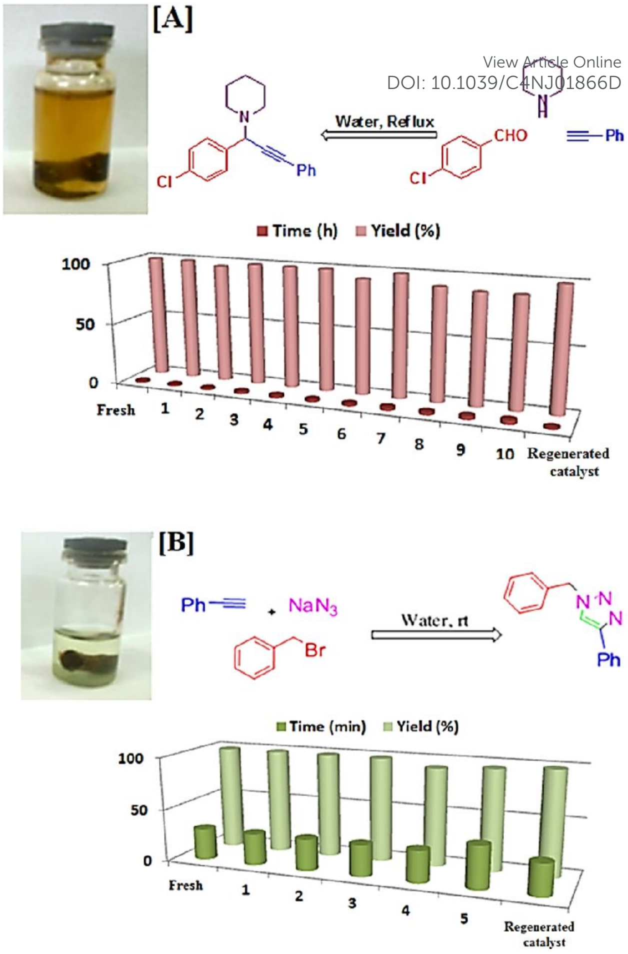

Fig 5. Column graph of recyclability of the catalyst

Comparison with other reported systems

To show the merit of the current protocol for the synthesis of propargylamines and 1,2,3-triazoles, the results obtained for A^3 coupling reaction of benzaldehyde, piperidine and phenylacetylene and click reaction of benzylbromide, sodium azide, and phenylacetylene were compared with some of those reported in the literature using other catalysts (Table 8).

Among the heterogeneous catalysts in Table 7 for A^3 coupling reaction, the present method comparatively affords a truly green process using water as reaction media and magnetically separable nanoparticles as the catalyst with high yield of the product in shorter reaction time (Table 7, bold in entries).Although, other catalysts gave high yield of the product but they suffer from drawbacks such as using organic solvents (Ag-graphene, Graphene-Fe_3O_4, Cu(0)-MM clay) or high temperatures and long reaction times (Fe_3O_4, Au-SBA , Au/CeO_2). For the click reaction, although, other copper catalysts afford high yield of the product, they need organic solvent (Cu NP), higher temperature (CuNPs/MagSilica, $CuFe_2O_4$, Cu/SiO_2, MNP-CuBr) and using mw irradiation (Cu/SiO_2, MNP-CuBr) or ball-milling (Cu/Al_2O_3). However, compare in other catalysts, the present catalytic system for click reaction, exhibited higher activity with lower amount of catalyst, without using any organic solvent in the work up procedure under green and mild conditions (Table 8, bold in

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entries).

Table 8 Comparison of catalytic activity of the MNPs@BiimCu(I) catalyst in the A^3 coupling and click reactions with some other reported methods

Reaction	Catalyst, (mol%)	Reaction conditions	Yield (%)	Ref
A^3coupling[a]	Ag-graphene, 0.1	CH_2Cl_2, 60 ˚C, 24 h	86	55
	Graphene-Fe_3O_4, 5	CH_3CN, 80˚C, 24 h, Ar	trace	30
	Fe_3O_4, 20	Toluene, 110˚C, 16 h	75	27
	Cu(0)-MM clay, 0.05	Toluene, 110˚C,3 h	94	20
	Cu(OH)x–Fe_3O_4 , 0.1	Solvent-free, 120˚C, 3 h	99	29
	Au-SBA, 0.04	Solvent-free, 100˚C, 8 h	95	24
	Au/CeO_2, 0.127	H_2O, 100 ºC, 6 h	99	25
	MNP@BiimCu(I), 1.7	**H_2O,Reflux, 1.5 h**	**99**	-[c]
Click [b]	CuNPs/MagSilica, 4.3	H_2O, 70ºC, 1 h	98	23
	$CuFe_2O_4$, 5	H_2O, 70ºC, 3 h	93	56
	Cu/Al_2O_3, 10	ball-milling, 1 h	92	37
	Cu/SiO_2, 10	H_2O, 70ºC, mw, 10 min	92	38
	Cu NP, 5	MeOH, r.t, 8 h	93	54
	MNP-CuBr, 1.46	H_2O/PEG, 80ºC, mw,0.3h	96	39
	MNP@BiimCu(I), 0.85	**H_2O/ r.t, 0.5 h**	**99**	-[c]

[a] A^3 coupling reaction of benzaldehyde, piperidine and phenylacetylene, [b] Click reaction of benzylbromide, sodium azide, and phenylacetylene, [c] Bold in entries, this work

Conclusion

Nano magnetite functionalized 2,2ˈ-Biimidazole complex of metal ions were synthesized, characterized and employed as heterogeneous catalysts for synthesis of propargylamines and 1,4-disubstituted 1,2,3-triazoles. Considering the importance of these catalysts, it was shown that the prepared nano magnetite specially Cu(I) are highly efficient catalysts for synthesis of propargylamines via A^3 coupling reaction and also one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles in water without using any toxic solvent or co-catalyst. This protocol is clean and safe process and can be used to generate a diverse range of products in good to excellent yields. Moreover, this nano-catalyst is stable showing no aggregation and metal leaching, and can be recycled many times without loss of catalytic activity

Experimental

Reagents and materials

Chemical materials were purchased from Merck and Aldrich Chemical Companies in high purity. All the solvents were distilled, dried and purified by standard procedures.

Instrumentation

Melting points were measured on an Electrothermal 9100 apparatus. The samples were analyzed using FT-IR spectroscopy (Bruker Vector in KBr matrix). The X-ray powder diffraction (XRD) of the catalyst was carried out on a Philips PW 1830 X-ray diffractometer with CuKα source (λ=1.5418 Å) in a range of Bragg's angle (10-80°) at room temperature. Scanning electron microscope (SEM) pictures-EDS analyses were taken using VEGA//TESCAN KYKY-EM3200 microscope (acceleration voltage 26 kV). Transmission electron microscopy (TEM) experiments were conducted on a Philips EM 208 electron microscope. ^1H, ^{13}C NMR spectra were recorded on a BRUKER DRX-400 AVANCE spectrometer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 20 eV. Elemental analyses for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. Thermo gravimetric analysis (TGA) was recorded on a Stanton Redcraft STA-780 (London, UK). Magnetic measurements were performed using vibration sample magnetometry (VSM, MDK, and Model 7400) analysis. A simultaneous ICP-OES (Varian Vista-Pro, Springvale, Australia) coupled to a V-groove nebulizer and equipped with a charge-coupled device (CCD) was applied for determination of the trace.

Preparation of 2,2ˈ-biimidazole (Biim)

To a mixture of ammonium acetate (35.4 g, 0.46 mol) and H_2O (6.5 mL) was added drop wise aqueous glyoxal solution (20%, 10.0 g, 0.173 mol) at 40 °C over a period of 3 h. Then the mixture was allowed to stir for an additional 5h at room temperature. The reaction mixture was filtered and then washed with distilled water (3 ×20 mL) and acetone (3 ×20 mL) to give a brown residue. The residue was dissolved in 130 ml of hot ethylene glycol, and decolorized with activated carbon. After hot filtration, the product precipitated instantly to provide 3.2 g (42%) of compound, biimidazole as white crystals[11].

Preparation of MNP coated CPTES nanoparticles

$FeCl_3.6H_2O$ (2.35 g, 8.7 mmol) and $FeCl_2.4H_2O$ (0.86 g, 4.3 mmol) were dissolved in 40 mL deionized water, and the resultant solution was left to stir for 0.5 h at 80º C. Then 5 mL of NH_4OH solution (25%) was added with vigorous stirring to produce a black solid, and the reaction was continued for another 0.5 h. The black magnetite nanoparticles were isolated by magnetic decantation, washed several times with deionized water and subsequently dried at 80 ºC for 10 h. 0.5 g of dried Fe_3O_4 nanoparticles was suspended in a solution of 50 mL ethanol and 5 mL of NH_3 (25%). Then, 0.2 mL of tetraethoxysilane (TEOS) was added to the above suspension, and the mixture was ultrasonicated for two h. Afterward silica coated MNPs (MNPs@SiO_2) was magnetically separated, washed three times with ethanol and dried at 80 ºC for 10 h. MNPs@SiO_2 (100 mg) was dispersed in 15 mL of dry toluene by ultrasonication under nitrogen atmosphere. Next, 3-chloropropyltriethoxysilane (0.2 mL, 0.8 mmol) was added dropwise into the MNPs@SiO_2 dispersed solution under reflux conditions for 48 h. The CPTES functionalized magnetic nanoparticles (MNPs coated CPTES) was washed with 30 mL of toluene and ethanol before being dried at 60 ºC for 12 h.

Preparation of MNP@Biim nanoparticles

Sodium hydroxide (0.2 g, 5 mmol) was dissolved in 20 mL of ethylene glycol (EG) at 60 ºC. To this solution, biimidazole (0.5 g, 4 mmol) was added and stirred for 30 minutes. The MNPs coated CPTES (2 g) was added to this suspension and stirred at 60 ºC for 24h. Formed precipitate was collected with a permanent magnet, washed with water and methanol and subsequently soxhlet extraction by hot methanol to remove unreacted specie and dried under vacuum.

Preparation of MNP@BiimCu(I) nanoparticles

A mixture of magnetic nanoparticles supported Biimidazole (MNPs@Biim) (0.5 g), copper iodide (0.4 g), and acetonitrile (10 ml) was stirred at 60 ºC for two days. The brown solid was separated by an external magnet and washed with acetonitrile several times. The residue was dried for 24 h to afford the magnetic nanoparticles supported Biimidazole Cu(I) Complex (MNPs@BiimCu(I)). The exact metal content of MNP@P BiimCu(I) was measured using ICP-OES to be 10.9 wt% (1.7 mmol/g)

Preparation of MNP@BiimCu(II) nanoparticles

To the mixture of MNPs@Biim (0.5 g) in water (10 mL) was added copper sulfate (0.3 g) and the mixture was stirred at 60 ºC for two days. The precipitates were separated by magnetic decantation and washed with water and dried under reduced pressure to give MNP@BimCu(II). The metal content of MNP@P BiimCu(II) was measured using ICP-OES to be 8.27 wt% (1.31 mmol/g)

Preparation of MNP@BiimNi(II) and Co(II) nanoparticles

To the mixture of MNPs@Biim (0.5 g) in ethanol (10 mL) was added metal chloride ($NiCl_2$ or $CoCl_2$) (2 mmol) and the mixture was stirred at 60 ºC for two days. The resulting solid was separated by an external magnet and washed with ethanol several times. The residue was dried to afford the magnetic nanoparticles supported Biimidazole Complex of metal ions Ni(II) and Co(II); MNPs@BiimNi(II) and MNPs@BiimCo(II). The metals content of MNPs@BiimNi(II) and MNPs@BiimCo(II) was measured using ICP-OES to be 7.19 wt% (1.23 mmol/g) and 9.14 wt% (1.57 mmol/g), respectively.

General procedure for the synthesis of propargylamines

In a 10 mL round bottomed flask, a mixture of aldehyde (1 mmol), amine (1 mmol) and magnetic nanoparticles supported complex of metal ion (0.01 g, 1.7 mol%) was stirred for 10 min. Phenylacetylene (1 mmol), and 2 mL H_2O were added to the above mixture and allowed to stir under reflux conditions for 1.5 h. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the catalyst was separated using magnetic stirring bar. After evaporation of the solvent, the desired product was isolated by silica gel flash column chromatography with a mixture of petroleum ether/ethyl acetate as eluent. Propargylamines derivatives were characterized with IR, ^{1}HNMR and ^{13}CNMR spectroscopies (pages S8-40 in Supporting Information).

General procedure for the synthesis of 1,2,3-triazoles

Primary halides (1 mmol), NaN_3 (72 mg, 1.1 mmol) and terminal alkynes (1 mmol) were placed in a 10 ml round-bottomed flask in H_2O (1 mL). Sequentially, magnetic nanoparticles supported complex of metal ion (5 mg, 0.85 mol %) was added. The reaction mixture was stirred at room temperature and monitored by TLC. After completion of the reaction, the catalyst was separated using magnetic stirring bar. The corresponding triazole can be easily isolated by simple filtration of the reaction mixture without any further purification. The products were characterized with IR, ^{1}HNMR and ^{13}CNMR spectroscopies (pages S8-40 in Supporting Information).

Percent yields of the products were calculated as follows:
% yield = actual yield (g)/ theoretical yield (g) × 100

Recycling of the catalyst

The feasibility of repeated use of catalyst was also examined for the model reactions (Scheme 1). The recovery of the catalyst was very easy. After completion of the reaction, the catalyst remains insoluble. The catalyst can be separated from reaction mixture using magnetic stirring bar and washed several times with EtOH (5 mL), dried under vacuum and reused in subsequent runs. No fresh catalyst was added. The recovered catalyst was tested for 5 subsequent runs for model click reaction and 10 runs for model A^3 coupling reaction.

The retreatment of the recovered catalyst

After several cycles, when the reaction rates were reduced, the recovered catalyst in the both reactions was retreated with copper iodide solution. For this purpose, 0.05 gr recovered catalyst was stirred in 0.5 M solution of copper iodide in acetonitrile (1 ml) at 60 ºC for 6 h. The brown residue was separated by an external magnet and washed with acetonitrile several times. The catalyst was dried for 24 h and reused in the next reaction (Table 7, Regenerated catalyst).

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Supporting Information Available: IR spectra, elemental analysis, XRD patterns, AAS, ICP-OES analysis, VSM curves, data and Copies of ^{1}HNMR, ^{13}CNMR spectra for products.

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