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# Immobilized copper(II) on nitrogen-rich polymer-entrapped Fe<sub>3</sub>O<sub>4</sub> nanoparticles: a highly loaded and magnetically recoverable catalyst for aqueous click chemistry

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Nasrin Zohreh<sup>a</sup>\*, Seyed Hassan Hosseini<sup>b</sup>, Ali Pourjavadi<sup>b</sup> and Craig Bennett<sup>c</sup>

A heterogeneous magnetic copper catalyst was prepared via anchoring of copper sulfate onto multi-layered poly(2dimethylaminoethyl acrylamide)-coated magnetic nanoparticles and was characterized using various techniques. The catalyst was found to be active, effective and selective for one-pot three-component reaction of alkyl halide, sodium azide and alkyne, known as copper-catalyzed click synthesis of 1,2,3-triazoles. As little as 0.3 mol% of catalyst was found to be effective under the optimum conditions. The catalyst could also be recycled and reused up to seven times without significant loss of activity. Thermal stability, high loading level of copper on catalyst, broad diversity of alkyl/benzyl/allyl bromide/chloride and alkyl/aryl terminal alkynes without isolation of azide intermediate, and good to excellent yields of products make this procedure highly economical. Copyright © 2015 John Wiley & Sons, Ltd.

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Keywords: polymeric catalyst; magnetic separation; Cu-catalyzed click reaction

### Introduction

No doubt one of the most significant developments in the catalysis realm is heterogenization of homogeneous catalysts.<sup>[1,2]</sup> Easy handling and separation minimizing the cost of production, excellent reusability, and chemical and thermal stability of catalysts are outstanding qualities making heterogeneous catalysts environmentally benign.<sup>[3–5]</sup> Heterogenization has been achieved by functionalization or immobilization of homogeneous catalysts on the surface of insoluble solids such as silica,<sup>[6,7]</sup> polymers,<sup>[8]</sup> magnetic nanoparticles<sup>[9]</sup> and carbon materials.<sup>[10,11]</sup> Compared to others, magnetic nanoparticles are special. They are in a superparamagnetic state at room temperature, resulting in unique opportunities for excellent separation simply using an external magnet.<sup>[12–15]</sup> They have also good stability, high surface area as well as low toxicity and price.<sup>[16,17]</sup>

After introducing the heterogenization concept, the conditions of numerous catalyzed chemical reactions or industrial processes have been modified using many heterogeneous catalytic systems.<sup>[18–21]</sup> Among these transformations, the copper-catalyzed azide/alkyne cyclization (CuAAC) reaction is one of the most important in the realm of click reactions. This is because the resulting triazoles function as rigid linking units that can mimic the atom placement and electronic properties of a peptide bond without the same susceptibility to hydrolytic cleavage.<sup>[22,23]</sup> Triazoles are also multipurpose building blocks in materials science, medicinal chemistry, drug discovery,<sup>[24,25]</sup> organic chemistry and polymer science.<sup>[26–29]</sup>

Various heterogeneous systems have been realized by the covalent and non-covalent immobilization of copper species onto a variety of supports for CuAAC. Most of them include supported copper nanoparticles on solid beds.<sup>[30-34]</sup> Moreover, various Nor C-ligand/Cu(I) complexes have been covalently immobilized

on solid supports for CuAAC.<sup>[27,35-41]</sup> Although these catalysts are efficient, each of them suffers from some drawbacks such as multi-step catalyst preparation,<sup>[35,36]</sup> low loading (low amount of active catalyst species on the solid support),<sup>[41]</sup> long reaction time,<sup>[35]</sup> tedious workup of catalyst<sup>[30]</sup> and product<sup>[32]</sup> and harsh reaction conditions.<sup>[34,39,40]</sup> In most cases, the low loading problem of heterogeneous copper-based catalysts leads to the use of a larger amount of catalyst or higher temperature<sup>[36]</sup> and longer reaction time.<sup>[31,34,35,39,41]</sup> Immobilization of copper species onto the surface of polymers is a good way to overcome this limitation, since a large number of functionalities can be linked to copper. In contrast to the use of polymers as supports used only for heterogenization,<sup>[38]</sup> polymerization of a desired structure on the surface of the support followed by immobilization of copper species on it is an effective way to increase loading. However, only a few examples of polymer-supported copper catalysts have been reported based on this strategy for CuAAC reaction.<sup>[39,42,43]</sup> In a recent study,<sup>[44]</sup> a very high-loading polymer-based copper catalyst was reported, resulting in the use of parts per million amount of catalyst for CuAAC reaction.

Correspondence to: Nasrin Zohreh, Department of Chemistry, Faculty of Science, University of Qom, PO Box 37185-359, Qom, Iran. E-mail: n.zohreh@qom.ac.ir

a Department of Chemistry, Faculty of Science, University of Qom, PO Box 37185-359, Qom, Iran

b Polymer Research Laboratory, Department of Chemistry, Sharif University of Technology, Tehran, Iran

c Department of Physics, Acadia University, Wolfville, Nova Scotia, Canada



Scheme 1. Synthesis of catalyst MNP@PDMA-Cu.

In this context, we investigated the development of a novel heterogeneous copper catalyst based on poly(2-dimethylaminoethyl acrylamide)-encapsulated magnetic nanoparticles purposing a high loading of copper and easy magnetic recoverability. Also investigated was a small library of 1,2,3-triazoles prepared in the presence of the catalyst via three-component reaction of alkyl halide, sodium azide and terminal alkynes under simple and mild reaction conditions.

## **Materials and methods**

Ferric chloride hexahydrate (FeCl<sub>3</sub>·6H<sub>2</sub>O), ammonia (25%), ferrous chloride tetrahydrate (FeCl<sub>2</sub>·4H<sub>2</sub>O), 3-(trimethoxysilyl)propylmethacrylate (MPS), *N*,*N*-dimethylethylenediamine and methylenebisacrylamide (MBA) were obtained from Merck without further purification. 2,2'-Azobisisobutyronitrile (AIBN; Kanto, 97%) was recrystallized from ethanol and methyl acrylate (Sigma-Aldrich) was distilled before use. TLC was performed with silica gel 60 F254 plates and UV light was used for visualization. Fourier transform infrared (FT-IR) spectra of samples were obtained using an ABB Bomem MB-100 FT-IR spectrophotometer. NMR spectra were recorded with a Bruker 500 MHz NMR instrument. Thermogravimetric analysis (TGA) was conducted under a nitrogen atmosphere with a TGA Q 50 thermogravimetric analyzer. Morphology of the catalyst was observed with a scanning electron microscopy (SEM) instrument (Philips XL30). Transmission electron microscope. The magnetic properties of the catalyst were measured using a vibrating sample magnetometer (model 7400). Copper ions were measured using atomic absorption spectrometry (AAS; Shimadzu 680 A) or inductively coupled plasma optical emission spectrometry (ICP-OES; Perkin-Elmer DV 4300).



Figure 1. FT-IR spectra of (a) MNP, (b) MNP@MPS, (c) MNP@PMA, (d) MNP@PDMA and (e) MNP@PDMA-Cu.



Figure 2. (a) XRD pattern and (b) RDP of MNP@PDMA.





Figure 3. TGA curves of (a) MNP@MPS, (b) MNP@PMA, (c) MNP@PDMA and (d) MNP@PDMA-Cu.

#### Synthesis of modified magnetic nanoparticles (MNP@MPS)

Magnetic Fe<sub>3</sub>O<sub>4</sub> nanoparticles were prepared using a chemical coprecipitation method. An iron salt solution was obtained by mixing 13.6 g of FeCl<sub>3</sub>·6H<sub>2</sub>O (50.3 mmol) and 5 g of FeCl<sub>2</sub>·4H<sub>2</sub>O (25.1 mmol) in 500 ml of deionized water under nitrogen at room temperature. By dropwise addition of NH<sub>3</sub> solution, the pH was adjusted to 12. A black precipitate was formed after continuously stirring for 1 h. The precipitate was magnetically separated and washed four times with deionized water and two times with ethanol and was dried under vacuum at 50 °C overnight (5.5 g of product).

The resulting Fe<sub>3</sub>O<sub>4</sub> nanoparticles (3 g) were ultrasonically suspended in 400 ml of an ethanol–water mixture (4:1) and the pH of the solution was adjusted to 9 by adding ammonia solution. Tetraethyl orthosilicate (15 ml) was added dropwise to the solution at 50 °C in the presence of a constant nitrogen flow. The mixture was stirred for 6 h. The silica-coated nanoparticles were then magnetically separated and washed three times with deionized water and two times with ethanol. The final dark brown product (MNP) was dried at 50 °C under vacuum for 24 h (7.8 g of product).

Subsequently, 1.0 g of MNP was dispersed in 40 ml of a 4:1 mixture of ethanol-water, and then 2 ml of ammonium hydroxide solution (25%) was added. Then, an excess amount (10 mmol per gram of MNP) of MPS was added dropwise over a period of 10 min, and the reaction mixture was stirred at 50 °C for 48 h. The modified MNP@MPS were magnetically separated and washed three times with methanol to remove any excess reagent and salts (0.96 g of product).



Figure 4. (a) TEM and (b) SEM images of MNP@PDMA-Cu.

#### Synthesis of catalyst

An amount of 500 mg of MNP@MPS was dispersed ultrasonically in 200 ml of methanol in a 500 ml single-necked flask for 10 min. Then, a mixture of 2 g of methyl acrylate (20 mmol), 500 mg of MBA (3.2 mmol) and 70 mg of AIBN (0.43 mmol) was added to the flask to initiate the polymerization. The mixture was completely deoxy-genated by bubbling purified argon for 30 min. The flask, sub-merged in a heating oil bath, was equipped with a fractionating column, Liebig condenser and receiver. The reaction mixture was heated from ambient temperature to boiling within 1 h and the reaction was ended after about 100 ml of methanol was distilled from the reaction mixture within 5 h. The obtained cross-linked polymethacrylate-coated MNP (MNP@PMA) were collected by magnetic separation and washed two times with water and three times with methanol to eliminate excess reactants and a few generated copolymer microspheres (1.40 g of product).

An amount of 500 mg of MNP@PMA was dispersed ultrasonically in 20 ml of methanol in a 50 ml single-necked flask for 10 min. Then, 15 ml of *N*,*N*-dimethylethylenediamine (16 mmol) was added and the mixture was stirred at 60 °C until the stretching vibration band of carbonyl groups of polymethacrylate disappeared (about 48 h). Poly(dimethylaminoethyl acrylamide)-coated MNP (MNP@PDMA) was magnetically separated and washed three times with methanol to remove any excess reagent and then dried at 60 °C for 12 h (0.53 g of product).

Table 1. Results of CHNS analysis							
Entry	Sample	C (%)	H (%)	N (%)	S (%)	Loading (mmol $g^{-1}$ )	
1	MNP@MPS	3.19	0.62	0.09	_	0.38 <sup>a</sup>	
2	MNP@PMA	13.27	1.97	0.87	—	$0.28^{b}$ for MBA; $1.61^{c}$ for CO <sub>2</sub> Me	
3	MNP@PDMA	18.15	3.09	5.05	—	1.49 <sup>d</sup> for NMe <sub>2</sub>	
4	MNP@PDMA-Cu	17.12	4.50	4.83	1.63	0.51 for SO <sub>4</sub> ; 0.51 <sup>e</sup> for Cu	

<sup>a</sup>Based on carbon atom.

<sup>b</sup>Based on nitrogen atom.

<sup>c</sup>Based on carbon atom after subtracting the %C of MBA. %C of MBA can be calculated from the loading amount of MBA (0.28 mmol g<sup>-1</sup>) which is 2.35%. <sup>d</sup>Based on nitrogen atom after subtracting the %N of MBA which is 0.78% (0.87 - 0.09 = 0.78%).

<sup>e</sup>Based of sulfur atom in complexed CuSO<sub>4</sub>.

The resulting powdered material was subjected to an anchoring (complexation) reaction. An amount of 0.5 g of MNP@PDMA was added to 30 ml of water and an excess of CuSO<sub>4</sub> (1.5 g, 6 mmol) was added to the solution. The mixture was vigorously stirred for 3 days at 70 °C. The solid catalyst (MNP@PDMA-Cu) was then magnetically separated, washed with water (5 × 50 ml) and methanol (2 × 20 ml) and dried under vacuum at 50 °C (0.49 g of product).

#### General procedure for synthesis of 1,4-disubstituted triazoles

Primary halides (1 mmol),  $NaN_3$  (1.5 mmol) and terminal alkynes (1 mmol) were placed in a 10 ml round-bottom flask in water (2 ml). Subsequently, MNP@PDMA-Cu (5.26 mg, 0.3 mol%) and



Figure 5. Vibrating sample magnetometry curves for (a)  ${\rm Fe}_3{\rm O}_4$  and (b)  ${\rm MNP}@{\rm PDMA-Cu}.$ 

ascorbic acid (10 mol%) were added to the solution. The reaction mixture was stirred at room temperature and the completion of the reaction was monitored using TLC. After completion of the reaction, the catalyst was magnetically separated and washed several times with ethanol followed by water and dried under vacuum. The corresponding triazole was easily isolated by simple filtration of the reaction mixture and crystalized from EtOAc-hexane. All synthesized triazoles are known compounds.<sup>[42,43,45]</sup> However, characterization data for some derivatives are given in the supporting information.

### **Results and discussion**

Preparation of the copper catalyst MNP@PDMA-Cu was carried out in a few steps as illustrated in Scheme 1. Magnetic Fe<sub>3</sub>O<sub>4</sub> nanoparticles were synthesized by typical chemical co-precipitation of FeCl<sub>3</sub> and FeCl<sub>2</sub> in alkaline pH and coated with silica using a sol–gel process to obtain core–shell magnetic nanoparticles (Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>).<sup>[46]</sup> Generally, coating of Fe<sub>3</sub>O<sub>4</sub> nanoparticles with SiO<sub>2</sub> layer can prevent the Fe<sub>3</sub>O<sub>4</sub> core from aggregation and can also provide Si–OH groups for fine chemical functionalization and modification using available alkoxysilane materials. Subsequently, the MNP substrate was treated with MPS to produce MNP@MPS support. Coating with MPS generates vinyl groups on the surface of the nanoparticle surface.

Distillation-precipitation copolymerization is the key step conducted with MNP@MPS as the seed, methyl acrylate as monomer, MBA as cross-linker and AIBN as initiator in methanol without any surfactant. The resulting cross-linked polymers are insoluble in methanol and continuously precipitate from the solution while

Table 2. Optimization of conditions for the click synthesis of triazoles using MNP@PDMA-Cu catalyst <sup>a</sup>							
	$Ph \sim Br + NaN_3 + Ph = H \sim MNP@PDMA-Cu \rightarrow N \sim N$						
Entry	Solvent	Catalyst (mol%)	T (°C)	Time (h)	NaN <sub>3</sub> (eq.)	Na ascorbate (mol%)	Yield (%) <sup>b</sup>
1	_	1.0	r.t.	7	1	10	20
2	CH <sub>3</sub> CN	1.0	r.t.	7	1	10	Trace
3	CHCl <sub>3</sub>	1.0	r.t.	7	1	10	Trace
4	DMF	1.0	r.t.	7	1	10	33
5	MeOH	1.0	r.t.	7	1	10	78
6	H <sub>2</sub> O	1.0	r.t.	7	1	10	89
7	MeOH-H <sub>2</sub> O (1:1)	1.0	r.t.	7	1	10	88
8	<sup>t</sup> BuOH–H <sub>2</sub> O (1:1)	1.0	r.t.	7	1	10	92
9	H <sub>2</sub> O	1.0	50	1.5	1	10	95
10	H <sub>2</sub> O	0.5	50	1.5	1	10	91
11	H <sub>2</sub> O	0.3	50	2	1	10	93
12	H <sub>2</sub> O	0.3	70	2	1	10	93
13	H <sub>2</sub> O	0.3	90	2	1	10	92 <sup>c</sup>
14	H <sub>2</sub> O	0.3	50	3	1	10	94
15	H <sub>2</sub> O	0.3	50	2	1	20	91
16	H₂O	0.3	50	2	1.5	10	96
17	H <sub>2</sub> O	0.2	50	2	1.5	10	93
18	H <sub>2</sub> O	0.1	50	4.5	1.5	10	93

<sup>a</sup>Benzyl bromide: 1 mmol; phenylacetylene: 1 mmol; solvent: 2 ml.

<sup>b</sup>lsolated yield.

<sup>c</sup>Mixture of isomers.

covalently grafting to the surface of the MNP@MPS. Grafting becomes very efficient in the presence of vinyl groups of MPS on the surface of MNP. In other words, without MPS modification, only a minor part of the magnetic nanoparticles can be coated with a complete layer of polymer chains instead of all of them. Simultaneous distillation of methanol generates multilayer polymeric shell-grafted MNP (MNP@PDMA). Subsequently, amidation of esteric groups with *N*,*N*-dimethylethylenediamine provides the desired functional groups. We believe that the *N*,*N*-dimethylethylenediamine on the surface of the polymer layer can act as a ligand because of strong coordination of its *N*,*N*-dimethyl group with copper, as shown in Scheme 1. Finally, anchoring of

Cu(II) obtained via complexation of copper sulfate and polymer chains on the surface of MNP@PDMA affords the catalyst MNP@PDMA-Cu.

The synthesized MNP@PDMA-Cu was characterized in detail using a combination of methods. As shown in Fig. 1, to verify the successful incorporation of the organic components, the chemical compositions of MNP, MNP@MPS, MNP@PMA, MNP@PDMA and MNP@PDMA-Cu were characterized using FT-IR spectroscopy. The stretching vibrations at 582 and 1083 cm<sup>-1</sup>, in all spectra, confirm the maintenance of the Fe–O and Si–O bonds during the synthesis processes. The absorption peaks at 2929, 1707 and 1404 cm<sup>-1</sup> in Fig. 1(b) show successfully coating of MPS onto MNP and are

Table 3.      MNP@PDMA-Cu-catalyzed three-component synthesis of 1,2,3-triazoles <sup>a</sup>						
	5 7	MNP@PDM (0.3 mol	MA-Cu I%) N=N			
	$R-X + NaN_3 +$	Na ascorbate (	(10 mol%) R <sup>-N</sup>			
	1	2 H <sub>2</sub> O, 50	P°C 3			
Entry	R	R'	Time (h)	Yield of <b>3</b> (%) <sup>b</sup>		
1	PhCH <sub>2</sub>	Ph	2(X = Br)	<b>3a</b> : 96		
	- 2		2.5 (X = CI)	<b>3a</b> : 90		
2	4-MePhCH₂	Ph	2 (X = Br)	<b>3b</b> : 91		
3	4-CIPhCH <sub>2</sub>	Ph	2 (X = Br)	<b>3c</b> : 95		
4	4-NO <sub>2</sub> PhCH <sub>2</sub>	Ph	1.5 (X = Br)	<b>3d</b> : 97		
			1.5 (X = CI)	<b>3d</b> : 93		
5	4-BrPhCH₂	Ph	2.5 (X = Br)	<b>3e</b> : 90		
6	PhCH <sub>2</sub>	Ph	1.5 (X = OTs)	<b>3a</b> : 94		
7	1-Naphthylmethyl	Ph	3 (X = Cl)	<b>3f</b> : 91		
8	PhCOCH <sub>2</sub>	Ph	2.5 (X = Br)	<b>3 g</b> : 87		
9	EtOCOCH <sub>2</sub>	Ph	3 (X = Br)	<b>3 h</b> : 85		
10	MeCH <sub>2</sub> CH <sub>2</sub>	Ph	3 (X = Br)	<b>3i</b> : 88		
11	-CH <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> -	Ph	3 (X = Br)	<b>3j</b> : 90		
12	$Me(CH_2)_5CH_2$	Ph	3.5 (X = Br)	<b>3 k</b> : 80		
			4 (X = CI)	<b>3 k</b> : 76		
13	H <sub>2</sub> NCOCH <sub>2</sub>	Ph	2.5 (X = Br)	<b>3  </b> : 84		
14	$(Me)_2C = CCH_2$	Ph	2 (X = Br)	<b>3 m</b> : 91		
			2 (X = CI)	<b>3 m</b> :90		
15	PhCH <sub>2</sub>	MeO <sub>2</sub> C	4.5 (X = $CI$ )	<b>3n</b> : 86		
	-	_	4 (X = OTs)	<b>3n</b> : 85		
16 <sup>c</sup>	4-NO <sub>2</sub> PhCH <sub>2</sub>	MeO <sub>2</sub> C	3.5 (X = Br)	<b>30</b> : 86		
17 <sup>c</sup>	Allyl	MeO <sub>2</sub> C	4 (X = Br)	<b>3p</b> : 87		
18 <sup>d</sup>	PhCOCH <sub>2</sub>	EtO <sub>2</sub> C	4.5 (X = Br)	<b>3q</b> : 80		
19	PhCH <sub>2</sub>		4.5 (X = Br)	<b>3r</b> : 92		
20	4-NO <sub>2</sub> PhCH <sub>2</sub>	HOCH <sub>2</sub>	3 (X = Br)	<b>3 s</b> : 85		
21	$Me(CH_2)_2CH_2$	HOCH <sub>2</sub>	4 (X = Br)	<b>3 t</b> : 80		
22	PhCH <sub>2</sub>	Me(CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub>	3.5 (X = Br)	<b>3u</b> : 92		
	-		3.5 (X = Cl)	<b>3u</b> : 89		
23	4-BrPhCH <sub>2</sub>	Me(CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub>	3 (X = Br)	<b>3v</b> : 85		
24	$Me(CH_2)_5CH_2$	$Me(CH_2)_3CH_2$	4 (X = Br)	<b>3w</b> : 77		
		2.5 2	4 (X = CI)	<b>3w</b> : 75		
25	PhCOCH <sub>2</sub>	Me(CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub>	3.5 (X = Br)	<b>3x</b> : 82		
26	Allyl	$Me(CH_2)_3CH_2$	3.5 (X = Br)	<b>3y</b> : 86		
	-		3.5 (X = Cl)	<b>3y</b> : 81		
27	EtOCOCH <sub>2</sub> CH <sub>2</sub>	$Me(CH_2)_3CH_2$	4 (X = Br)	<b>3z</b> : 81		

<sup>a</sup>Reaction conditions: alkyl halide (1 mmol), NaN<sub>3</sub> (1.5 mmol), acetylene (1 mmol), MNP@PDMA-Cu (0.3 mol%), H<sub>2</sub>O (2 ml).

<sup>b</sup>lsolated yield.

<sup>c</sup>MeOH as solvent.

<sup>d</sup>EtOH as solvent.

attributed to C–H, esteric C=O and C=C bonds of MPS. The FT-IR spectrum of MNP@PMA (Fig. 1(c)) shows a strong vibration band at 1735 cm<sup>-1</sup> associated with esteric C=O of polymethacrylate. Comparing Figs. 1(c) and (d), disappearance of the stretching band at 1735 cm<sup>-1</sup> and appearance of amidic C=O band at 1638 cm<sup>-1</sup> can be observed indicating total substitution of CO<sub>2</sub>Me group with *N*,*N*-dimethylethylenediamine via amidation. On complexation with copper, the FT-IR spectrum of MNP@PDMA-Cu (Fig. 1(e)) shows a new band at 1120 cm<sup>-1</sup> attributed to S=O of CuSO<sub>4</sub>. These results confirm that the catalyst had been successfully prepared.

The crystallinity and phase composition of the resulting catalyst were investigated using X-ray diffraction (XRD) and ring diffraction pattern (RDP). The high-angle XRD pattern of MNP@PDMA is shown in Fig. 2(a). Comparing with the XRD pattern of pure Fe<sub>3</sub>O<sub>4</sub> nanoparticles, it can be seen that all peaks are in the same region and intensity. There is a broad diffraction peak at  $2\theta = 20^{\circ}$  assigned to amorphous silica coated on the surface of Fe<sub>3</sub>O<sub>4</sub> nanospheres.<sup>[47]</sup> This indicates that not all modifications cause a phase change in Fe<sub>3</sub>O<sub>4</sub>. The RDP of the catalyst also shows the crystalline planes of Fe<sub>3</sub>O<sub>4</sub> (Fig. 2(b)).

In order to investigate the thermal stability and organic content of MNP@MPS, MNP@PMA, MNP@PDMA and MNP@PDMA-Cu, TGA was carried out (Fig. 3). Obvious weight losses below 150 °C are assigned to the loss of the physically adsorbed water on the surface of nanostructure materials. A weight loss of 4.1% in the TGA curve of MNP@MPS (Fig. 3(a)) shows that organic content loaded on the surface of MNP (loading of MPS) is 0.32 mmol g<sup>-1</sup>. Since both MNP@PMA and MNP@PDMA contain monomer and cross-linker, calculation of accurate loading amount of  $-CO_2Me$  or  $-NMe_2$  based on TGA curves is not possible. However, according to the weight losses between 200 and 900 °C in their TGA curves (Figs. 3(b) and (c)), it is calculated that the content of PMA and PDMA on the surface of MNP is about 21.5 and 29 wt%, respectively. TGA also shows that the catalyst has high thermal stability of over 200 °C.

The amount of NMe<sub>2</sub> groups on MNP@PDMA was calculated using the back-titration method. MNP@PDMA (50 mg) was dispersed in water and an excess of HCl (0.1 M) was added. The mixture was stirred for 3 h until neutralization of all amine groups on the surface of the catalyst. The excess HCl in solution was titrated using NaOH (0.1 M) in the presence of phenolphthalein. The amount of NMe<sub>2</sub> ligand loaded on the surface of MNP@PDMA is found to be 1.58 mmol g<sup>-1</sup>. CHNS elemental analysis also served to calculate *N*,*N*-dimethylaminoethyl acrylamide or NMe<sub>2</sub> loading amount (see supporting information). According to the elemental analyses (Table 1), NMe<sub>2</sub> loading is calculated as about 1.49 mmol g<sup>-1</sup> which is in good agreement with the calculated loading amount from titration.

The amount of Cu(II) ions loaded in MNP@PDMA-Cu was calculated with AAS using standard samples. It is found that the amount of Cu(II) ions loaded in MNP@PDMA-Cu is 0.57 mmol g<sup>-1</sup>. This loading level of copper on the surface of the magnetic support is quite high for a nonionic supported ligand.

TEM imaging of MNP@PDMA-Cu (Fig. 4(a)) provides strong evidence that MNP (black cores) are encapsulated within multilayer polymer (grey shell). The TEM image (Fig. 4(a)) also shows the good dispersion of spherical nanoparticles onto the copolymer matrix, with a size distribution and an average particle size of 6 nm. The surface morphology of MNP@PDMA-Cu was also examined using SEM. As indicated in Fig. 4(b), a bulk polymeric structure with rough surface is seen. The rough surface of the catalyst is due to the presence of magnetic nanoparticles increasing the catalytic surface and activity.

The magnetization curves of bare  $Fe_3O_4$  nanoparticles and MNP@PMDA-Cu are shown in Figs. 5(a) and (b), respectively. It can be seen that  $Fe_3O_4$  and MNP@PDMA particles are superparamagnetic with magnetic saturation values of about 64.1 and 24.3 emu g<sup>-1</sup>, respectively. The 39.8 emu g<sup>-1</sup> reduction of saturation magnetization is attributable to the presence of SiO<sub>2</sub>/PDMA shell on  $Fe_3O_4$  particles. However, the level of catalyst magnetizations is still sufficient to strongly respond to an external magnet during catalyst recovery.

To evaluate the effectiveness of MNP@PDMA-Cu as a heterogeneous copper catalyst, one-pot three-component cycloaddition of benzyl bromide, sodium azide and phenylacetylene was selected as a model reaction for synthesis of 1,2,3-triazoles. The reaction was evaluated under various optimizations (Table 2). In the preliminary experiments, a variety of solvents were screened for exploring their suitability as reaction media in the presence of a fixed catalyst amount (1.0 mol%). As evident from Table 2 (entries 1-8), a significant effect on time and product yield is observed by changing the solvents from aprotic to protic ones. This effect is probably because of the poor solubility of NaN<sub>3</sub> or ionic intermediates in aprotic solvents. Among the protic solvents, water exhibits the greatest effect and 89% of desired product 3a is obtained. However, using a mixture of <sup>t</sup>BuOH and water gives better product yield, but the low cost and green nature of water convinced us to use pure water as solvent. Optimization of catalyst amount was then examined in the reaction of equimolar ratio of reactant and 10 mol% sodium ascorbate. Increasing the reaction temperature to 50 °C increases the reaction yield to 95% in shorter reaction time (entry 9). Decreasing the catalyst amount from 1.0 to 0.3 mol% does not significantly change the yield of product (entries 9–11). Increasing the reaction temperature to 90 °C results in a mixture of cis- and trans-triazole isomers (27%:73%; entries 11-13). It is also observed that increasing the amount of NaN<sub>3</sub> enhances the yield of product up to 96%, while increasing the amount of sodium ascorbate reduces the yield of product (entry 16). Consequently, in the presence of 0.3 mol% MNP@PDMA-Cu catalyst, the reaction of benzyl bromide, sodium azide and phenylacetylene in a ratio of 1:1.5:1 and 10 mol% sodium ascorbate gives the best yield of 1,2,3-triazole **3a** at 50 °C after 2 h. These conditions were selected as the optimum ones (entry 16).

Inspired by the excellent catalytic activity of MNP@PDMA-Cu in the model reaction under optimum conditions, scope of substrates and limitations of CuAAC reaction were investigated for the synthesis of a small library of 1,4-disubstituted 1,2,3-triazoles (Table 3). A wide range of diversely substituted benzyl, allyl and alkyl halides and dihalides were successfully subjected to the one-pot CuAAC reaction. It is found that all reactions produce corresponding triazoles; however, the reaction rates for chlorides are lower than those for



Figure 6. Results of recycling experiment.

Table 4. Comparison of MNP@PDMA-Cu with reported catalysts in the synthesis of triazoles <sup>a</sup>							
Entry	Catalyst	Copper loading on catalyst (mmol $g^{-1}$ )	Catalyst loading (mol%)	Time (h)	T (°C)	Yield (%)	Ref.
1	Functionalized chitosan/Cu	0.6	0.1	12	70	99	[49]
2	lonic polymer/Cu	0.25	5	2.5	r.t.	99	[50]
3	Nanoferrite-glutathione-Cu	0.25	2.5	0.17	120; MW	99	[34]
4	MNP–CuBr	0.44	1.46	0.3	80; MW	96	[51]
5	Cu/Al <sub>2</sub> O <sub>3</sub>	0.29	10	1	r.t.	92	[31]
6	Cu(II)/clay	1.5	2	0.25	r.t.; sonic	98	[52]
7	Cu/SiO <sub>2</sub>	2.59	10	0.17	70, 50; MW	92	[53]
8	CuNPs/MagSilica	1.07	4.3	1	70	98	[53]
9	Cu NP/activated carbon	0.25	0.5	3	70	98	[54]
10	MNP@PDMA-Cu	0.57	0.3	2	50	96	This work
<sup>a</sup> Click reaction of benzylbromide, sodium azide and phenylacetylene.							

bromides, so that the reaction time must be enhanced for an equivalent transformation. It is also found that benzyl halides containing electron-donating groups give products in lower yields or longer reaction times. Aromatic and aliphatic acetylenes are also quantitatively converted to their corresponding triazoles in the presence of 0.3 mol% MNP@PDMA-Cu. However, less reactive aliphatic alkynes require longer reaction times compared to their aryl counterparts. It is pleasing that electron-deficient acetylenes, which are normally difficult substrates for CuAAC reaction,<sup>[48]</sup> react smoothly to produce the desired products with acceptable time and yield. These results show that MNP@PDMA-Cu is an active and selective heterogeneous copper catalyst which effectively catalyzes threecomponent cycloaddition of alkyl halide, alkyne and azide for triazole synthesis.

The stability, recoverability and reusability of heterogeneous metal-anchored catalysts are important in terms of practical application and green chemistry. To address this concern, recycling experiments were performed in consecutive runs of the reaction under optimized conditions. After each run, the catalyst is easily removed using an external magnet and easily recovered by washing with ethanol, and vacuum drying. As indicated in Fig. 6, MNP@PDMA-Cu can be successfully recovered and reused for up to seven runs without significant loss of activity. However, after each run the reaction takes a longer time to complete than the first run, but this is attributed to mass loss of catalyst during catalyst separation and recycling and not to loss of catalyst activity. For this concern, turnover frequency (TOF) of fresh catalyst and final recycled catalyst was compared. After the seventh run the remaining catalyst was separated and weighed. Based on this experiment, TOF of recycled catalyst is  $142 h^{-1}$  which is almost equal to TOF of fresh catalyst (160  $h^{-1}$ ). ICP analysis of recovered catalyst shows that loading of copper is  $0.54 \text{ mmol g}^{-1}$  which is almost same as fresh catalyst loading (0.57 mmol  $g^{-1}$  analyzed using ICP).

In order to investigate the possible leaching of species into the reaction solution from the catalyst, two sets of experiments were performed. Magnetic recovery of catalyst from hot reaction mixture followed by ICP analysis of reaction solution shows that no detectable metal ions exist in the reaction solution after all seven runs. In the second experiment, the model reaction of sodium azide, phenylacetylene and benzyl bromide was performed under optimized conditions and the MNP@PDMA-Cu catalyst was completely removed from the reaction mixture using an external magnet after 60 min. Then, the reaction was allowed to stir for 4 h and no further production of **3a** was observed. These observations confirm that

insoluble catalyst promotes the reaction under heterogeneous conditions and that no copper species are released into the reaction mixture.

The MNP@PDMA-Cu catalyst was compared with other previously reported supported copper catalysts. The loading amounts and catalytic performances of MNP@PDMA-Cu and other catalysts are compared in Table 4. As is evident, compared to traditional supported copper catalysts, the MNP@PDMA-Cu catalyst shows relatively high loading amount of copper on the surface. However, in some cases (entries 6–8), where copper ions are adsorbed onto non-modified supports, loading amounts are higher than for our catalyst. But in those catalysts the leaching of copper is markedly high because of weak interaction of copper with the unmodified support surface. Also, the activity of MNP@PDMA-Cu is higher than those high-loaded catalysts and as little as 0.3 mol% catalyst is enough for completion of the reaction. This feature of the catalyst is especially useful in large-scale applications where the amount of expensive catalyst should be low.

# Conclusions

We have developed copper-loaded nitrogen-rich polymerentrapped magnetic nanoparticles as an efficient heterogeneous copper catalyst. The resulting catalyst was applied in regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles through one-pot reaction of sodium azide, alkyl halide and terminal acetylenes in water at 50 °C. A low amount of the catalyst showed excellent performance for a variety of alkyl/benzyl/allyl halide/tosylate and acetylenes resulting from high loading of copper on the polymeric layer. High stability and efficiency, easy magnetic recyclability and reusability, simple reaction performance without sensitivity to air and moisture, excellent yields and ease of product separation are the most important aspects of the developed catalyst.

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26

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