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ARTICLE TYPE

Magnetically nano-Fe₃O₄@TiO₂/Cu₂O core-shell composite : An efficient novel catalyst for the regio-selective synthesis of 1,2,3-triazoles : A click reaction

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Magnetic nano-Fe₃O₄@TiO₂/Cu₂O core-shell composite, of Cu₂O, in various loading, has been successfully prepared and fully characterized, by analyzing of different obtained data, including FT-IR, XRD, XPS, FEG-SEM, EDS and VSM. The catalytic activity of nano-Fe₃O₄@TiO₂/Cu₂O core-shell composite was examined in a classical, one pot, and three component reaction of terminal alkynes, benzyal halides and sodium azide in water and observed, proceeding smoothly and completed in good yields and high regioselectivity. The catalyst was conventionally recovered using an external magnet and was reused at least in five successive runs, without appreciable loss of activity.

Introduction

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One of the most important development in the catalyzedorganic reactions, is the synthesis of novel catalysts or reagents, being readily available, inexpensive, selective, recyclable and environmentally benign.¹ In this context, nanoparticles find vast applications due to their high surface to volume ratio and their unique electronic properties, resulting in high catalytic activity and tenability.² Nano catalysts can often be isolated and recovered through filtration or centrifugation methods. However, it should be mentioned in spite of several advantages and merits, experienced in utilization of nano catalysts, the inconvenience and tedious separation, due to the nano size particles impose, few limitations to the sustainability of the nanocatalytic strategy in organic synthesis.³

To circumvent these problems, we contemplated to use an heterogeneous nanocatalyst which can be operationally separated, other than filtration. Magnetite nanoparicles (Fe₃O₄) have increasingly attracted interest in the past few years, due to their unique features, including, low preparation cost, high thermal and mechanical stability and adaptability for large-scale production. Furthermore, their paramagnetic nature allows their simple and efficient separation from the reaction mixture, without using standard filtration, required in separation of heterogeneous catalysts. Magnetite nanoparicles (Fe₃O₄) can be easily separated from reaction mixture by using just an external magnet.4-7 However, using naked, magnetic nano particles (MNPs) shows a serious drawback. The naked, magnetic nano particles (MNPs) are inherently, subjected to aggregation in the reaction mixture, mainly due to their small inter particle distance, high surface energy and the existence of van der Waals forces.8 This aggregation affects, their unique properties, associated with catalytic reactions. To solve this problem, MNPs are frequently, modified using suitable stabilizing coating materials in order to prevent irreversible aggregation, retain their nanoscale properties and preserve their finely dispersed active sites. Many materials have been explored, being outer shells of iron oxides, such as polymers,⁹ silica,¹⁰ titanium dioxide,¹¹ zeolites¹² and carbon.¹³ Recently, titanium dioxide have attracted great attention being employed as a support, due to its unique surface properties, its high chemical and thermal stability, non-toxicity, high catalytic activity, as well as its great accessibility and moderate cost. The appropriate electronic band structure and excellent surface activity endowed TiO2 with very promising potentials in hydrogen production, photovoltaic, photocatalysts, lithium-ion batteries, fuel cells, gas sensors, detoxification, and supercapacitors.¹⁴ Thus, further study on the performance of TiO₂-based nanostructures is still in much demands. Furthermore, the inclusion of Fe₃O₄ core into TiO₂ nanospheres makes them being easily recoverable by a magnetic field for further possible effective use. In recent years, multi component reactions (MCRs) have gained eminence as an efficient access to assemble molecular complexity with attractive biological features through the simple and readily available starting materials in a one-pot operation.15

Among them, Huisgen 1,3-dipolar cycloaddition, which is the reaction of a terminal alkyne and alkyl halide and sodium azide, providing 1,2,3-triazoles, has attracted much attention from biological and chemical points of view. The 1,2,3-triazole moieties are widespread in pharmaceutical, agrochemicals, dyes, corrosion inhibitors, phothostabilizers and phothographic matereials.¹⁶ Since its discovery, the regioselectivity of catalyzed-Huisgen reaction has been continuously under serious and wide

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investigations and has attracted enormous attention of organic chemists, worldwide. $^{17}\,$

There has been an ongoing interest to develop homogeneous and heterogeneous metal catalysis such as CuO–CeO₂,¹⁸ nano-Cu,¹⁹ Cu/C,²⁰ copper nanoparticles supported on agarose,²¹ Cu-MOF,²² Copper immobilized onto the triazole functionalized magnetic nanoparticle,²³ Cu/SiO₂,²⁴ ruthenium complex,²⁵ supported CuBr on graphene oxide/Fe₃O₄²⁶ and Mesoporous graphitic carbon nitride²⁷ for a regioselective, three-component reaction of alkyl halides, sodium azide and terminal alkynes. However, most of the above methods suffer from drawbacks such as the use of organic solvents, tedious experimental procedure to separate the catalyst as well as the requirement for reducing agents and stabilizing ligands. Therefore, there is still much demand to develop an efficient and well defined heterogeneous catalyst for a one pot, three component reaction of terminal alkynes, alkyl halides and sodium azide.

Recently, we have used nano-Fe₃O₄ as an efficient and easily separable catalyst in different organic reactions.²⁸ As a part of our continued interest to multi-component reactions,²⁹ and our efforts to develop the regioselective synthesis of 1,4-disubstituated 1,2,3triazoles, via click reaction,³⁰ herein, we wish to report the preparation of novel and recyclable catalyst system, composing of a magnetic Fe₃O₄ core and TiO₂ shell with microctystals of Cu₂O. The Fe₃O₄@TiO₂/Cu₂O composite is conveniently prepared and its structure was fully characterized by XRD, FTIR, XPS, SEM, TEM, EDX and VSM analysis. The catalytic activity of this catalyst system was examined in the reaction of phenyl acetylene, benzyl bromide and sodium azide, in water as a model reaction, which proceeded smoothly to afford the corresponding, 1,4- substituted 1,2,3-triazole as sole product, regioselectively.

Experimental

Material and Instruments

Chemical reagents in high purity were purchased from Merck and Aldrich and were used without further purification. Melting points were determined in open capillaries using an Electrothermal 9100 without further corrections.¹H NMR and ¹³C NMR spectra were recorded using a Bruker DRX-400 spectrometer at 400 and 100 MHz respectively. FT-IR spectra were obtained with potassium bromide pellets in the range of 400-4000 cm⁻¹ using a Shimadzu 8400s spectrometer. The purity of the compounds, synthesized was monitored by TLC on commercial aluminum-backed plates of silica gel 60 F254, visualized , using ultraviolet light. X-ray diffraction (XRD) was detected by Philips using Cu-Ka radiation of wavelength 1.54Å. Scanning electron Microscopy, FE-SEM-EDX, analysis was performed using Tescanvega II XMU Digital Scanning Microscope. Samples were coated with gold at 10 mA for 2 min prior to analysis. The magnetic properties were characterized using a vibrating sample magnetometer (VSM, Lakeshore7407) at room temperature. XPS Spectra of the sample using a Gammadata-scienta ESCA200 hemispherical analyzer equipped with an Al Kα (1486.6 eV) Xray source were obtained.

Preparation of composite

Preparation of Fe₃O₄

The nano-Fe₃O₄ particles were prepared in accordance to our earlier report.²⁸ View Article Online DOI: 10.1039/C5RA06810J

Preparation of nano-Fe₃O₄@TiO₂

Nano-Fe₃O₄@TiO₂ was synthesized according to a previously reported method,³¹ subjected to modification. The prepared nanomagnetic Fe₃O₄ particles were dispersed in a mixture of solvent 250 mL of absolute ethanol / 90 mL of acetonitrile. This mixture was sonicated for 15 min, and then 1.5 mL of NH₃·H₂O solution (25 wt.%) was added. After the continuous mechanical stirring for 30 min, 3 mL of tetrabutyl titanate (TBOT), dissolved in 20 mL of absolute ethanol was added drop-wise to the above suspension, under the continuous mechanical stirring at 30 °C. The reaction mixture was further mechanically stirred for 1.5 h to obtain Fe₃O₄@TiO₂ core/shell nanoparticles. The obtained product was collected by magnetic separation and washed, three times with absolute ethanol.

Preparation of nano-Fe₃O₄@TiO₂/Cu₂O coreshell magnetic composite

Four types of composite with different molar ratio of Fe₃O₄@TiO₂:Cu₂O were synthesized. Nano- Fe₃O₄@TiO₂ (0.036-0.324 g) was dispersed in 80 mL of deionized water. 5 mL of (0.1 mol/L) CuCl₂ solution was added into the aqueous Fe₃O₄@TiO₂ and sonicated for 15 min. Then, 1.8 mL of (1.0 mol/L) NaOH solution was added drop wise under ultra sonic radiation. The resulting solution turned into light blue instantly, indicating the formation of Cu(OH)2. Eventually, 12 mL of (0.1 mol/L) NH2OH.HCl was immediately injected over 5 sec. into the solution. The solution was kept in the water bath for 1 h and centrifuged for 3 min .Then the solution was decanted as much as possible. After the top solution was decanted, the precipitate was washed with 6 mL of a 1:1 volume ratio of water and ethanol for three times. The nano-Fe₃O₄@TiO₂/ Cu₂O was collected as a brown solid which can be stored in a tight vessel for several months without any changes in color and activity.

Synthesis of 1,2,3-triazoles :General procedure

In a round-bottomed flask, an appropriate, *alpha*-haloketone (1 mmol) or alkyl halide (1 mmol), terminal alkyne (1 mmol), sodium azide (1.1 mmol), in water (10 ml) were placed. Then, to this mixture, nano-Fe₃O₄@TiO₂/Cu₂O magnetic composite (0.01 g) was added. The suspension was magnetically stirred under reflux for the indicated time (Table 3). The progress of the reaction was monitored by TLC (n-hexane: ethyl acetate; 7:3). After the completion of the reaction, the solution was decanted as much as possible. The left over residue, diluted with hot ethanol. Then the catalyst was separated from this mixture by an external magnet and washed with acetone (2×10 ml), dried in oven and stored for use in subsequent run under the same conditions. After separation of catalyst, the solution was evaporated to dryness, and crude product was obtained. The crude products in some cases were washed with 10 ml of ether and was re-crystallized from EtOH/ H₂O (3:1 v/v) to afford pure crystalline products. Some

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products had to be purified by chromatography on silica gel , using a short column (Table 3) $% \left(\left(\left(T_{a}^{2}\right) \right) \right) \right) =0$

Results and discussion

Synthesis of Composite

Scheme 1 shows the schematic illustration for the synthesis of the $Fe_3O_4@TiO_2/Cu_2O$ core-shell magnetic composite. The $Fe_3O_4@TiO_2$ based on Cu_2O composite was prepared from commercially inexpensive available materials. In the first step, the magnetic Fe_3O_4 nanoparticles were prepared by co-perecipitation of iron (II) and iron (III) ions in alkali medium. The TiO₂ shell was prepared by the hydrolysis of tetrabutyl titanate (TBOT) in an absolute ethanol/acetonitrile mixture in the presence of the well dispersed $Fe_3O_4@TiO_2$ nanoparticles were removed by magnetic separation. The $Fe_3O_4@TiO_2/Cu_2O$ composite was obtained by reducing copper (II) hydroxide using hydroxylamine hydrochloride in the presence of $Fe_3O_4@TiO_2$. The structure of



Scheme 1. Preparation of nano-Fe₃O₄@TiO₂/Cu₂O core-shell composite.

Fe₃O₄@TiO₂/Cu₂O composite was fully characterized using, the corresponding data, provided by FT-IR, SEM, TEM, XRD, XPS and VSM techniques

Structure characterization of the composite

FT-IR spectra

Fig. 1 gives the FT-IR spectra pattern of Fe₃O₄, Fe₃O₄@TiO₂ and Fe₃O₄@TiO₂/Cu₂O in the range of 4000-500 cm⁻¹. FT-IR spectra shows a broad peak in 700-500 cm⁻¹, which is attributed to the vibration of Metal-O functional group. The peak appeared around 545 cm⁻¹ can be assigned to the vibration of Fe-O functional group.³² The Ti-O and Cu-O absorption peaks appeared in ~500 and 625 cm⁻¹ respectively. Notably, in the Fe₃O₄@TiO₂ and Fe₃O₄@TiO₂/Cu₂O samples the observed peak is relatively broader. This may be attributed to the overlapping of Fe-O, Ti-O and Cu-O peaks. The peaks appeared at 1118 and 1465 cm⁻¹ for the Fe₃O₄@TiO₂ and Fe₃O₄@TiO₂/Cu₂O samples could associated with the presence of stretching vibrations of Ti-O and Fe-O-Ti bonds.³³ The bands at 1628 cm⁻¹ belong to H-O-H bending vibration, indicating that several OH groups are present in the sample as a result of TiO₂ coating.



Figure 1. The FT-IR spectra of Fe₃O₄, Fe₃O₄@TiO₂ and Fe₃O₄@TiO₂/Cu₂O.

X-ray diffraction spectra

Figure 2 shows X-ray diffraction patterns of Fe₃O₄@TiO₂ and as-made samples with different Cu2O molar ratios (from 9:1 to 6:4 mole ratio of Fe₃O₄@TiO₂ to Cu₂O). The typical diffraction peaks located approximately at 30.1, 35.5, 43.2, 53.4, 57.1 and 62.7 can be well assigned to the diffraction of Fe₃O₄ nanoparticles with cubic phase from the (220), (311), (400), (422), (511) and (440) planes, respectively. In addition, a broad diffraction peak appeared at 2θ = 20-30 nm can be indexed to amorphous TiO₂.³⁴ The main peaks for the Fe₃O₄@TiO₂ are similar to the standard Fe₃O₄ particles (JCPDS card No. 19-629), which reveals that the crystal structure of Fe₃O₄@TiO₂ is well coated. No obvious diffraction peak for the TiO₂ is observed, suggesting amorphous TiO₂ coating is formed by the hydrolysis of tetrabutyl titanate (TBOT) in the presence of the well dispersed Fe₃O₄ nanocrystals by a sol-gel process. Compared to Fe₃O₄@TiO₂, new diffraction peaks located at 29.5 (110), 36.7 (111), 42.5 (200), 52.7 (211), 61.6 (220), and 73.7 (311) can be indexed to the diffraction of Cu₂O rhombic dodecaheadral crystals in the cubic phase (JCPDS card no. 05-0667), which suggest the presence of Cu₂O in the desired prepared composites. No additional diffraction peaks were observed, indicating the complete reduction of copper(II) to copper(I). It was also observed that by increasing content of Cu₂O in samples, the intensity of XRD patterns becomes gradually stronger due to the increase of the Cu₂O / Fe₃O₄@TiO₂ weight ratio.



Figure 2. XRD patterns of $Fe_3O_4@TiO_2$ and $Fe_3O_4@TiO_2/Cu_2O$ with different weight ratio.

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FE-SEM-EDS and TEM analysis

The morphology and chemical purity of Fe₃O₄, Fe₃O₄@TiO₂ and Fe₃O₄@TiO₂/Cu₂O core/shell composite (optimized amount) were visualized by SEM and EDX analysis (Figure 3). Appearance of Au element in EDX analysis shows, the material being coated by layer of Au proved by EDX and SEM characterization. The SEM image of Fe₃O₄ shows that nearly spherical nano particles were obtained with an average diameter of about 15-20 nm. Moreover, the energy-dispersive X-ray (EDAX) spectrum depicted in Figure 4(b), indicated that the product is mainly composed of nano-Fe₃O₄. It can be observed from Figure 3c that the as-synthesized Fe₃O₄@TiO₂ core/shell still keeping the morphological properties of Fe₃O₄ except for a slightly larger particle size and stifle surface, where TiO2 are coated on the Fe₃O₄ particles, uniformly. EDAX spectrum of Fe₃O₄@TiO₂ (Fig. 3d) core/shell nanoparticles shows the elemental compositions are Fe, Ti and O.



Figure 3. The FEG-SEM-EDS analysis of (a,b) Fe₃O₄; (c,d) Fe₃O₄@TiO₂ and (e,f) Fe₃O₄@TiO₂/Cu₂O (8:2) composite.



Figure 4. TEM image of Fe₃O₄@TiO₂/Cu₂O (8:2) composite.

Figure 3e shows the SEM image of Fe₃O₄@TiO₂/Cu₂O composite with the optimized amount of Cu₂O required for catalytic activity in synthesis of 1,4-disubstitured 1,2,3-triazoles. The Cu₂O shows rhombic dodecahedral structure and can be easily distinguished in the hybrid material by their different shape as marked in Fig. 3e. The EDX analysis on the obtained Fe₃O₄@TiO₂/Cu₂O composite reveals the existence of Fe, Ti, Cu and O elements, re-confirming the formation of Cu₂O species on the Fe₃O₄@TiO₂ nano-spheres.

TEM image illustrated as Figure 4, shows, vividly, a uniform coating of TiO₂ thin layer (~4nm) around the whole surface of $Fe_3O_4(\sim 20 \text{ nm})$. The Cu₂O as a bigger and dark particle can be seen and distingushed in TEM image.

Magnetization study

Magnetic properties of synthesized Fe₃O₄, Fe₃O₄@TiO₂ and Fe₃O₄@TiO₂/Cu₂O core/shell composite were assessed by a vibrating sample magnetometer at ambient temperature. As illustrated in Figure 5 the saturation magnetization of the Fe₃O₄@TiO₂ and MNPs are 61.6 emu/g and those for Fe₃O₄@TiO₂ and Fe₃O₄@TiO₂/Cu₂O core/shell composite are 29.9 and 24.11 emu/g, respectively. The decrease of the saturation magnetization of Fe₃O₄ MNPs after surface coating with TiO₂ and Cu₂O can be ascribed to the contribution of the non-magnetic materials. Nonetheless, this magnetic property is adequate and the Fe₃O₄@TiO₂/Cu₂O core/shell composite could be completely, efficiently and rapidly, separated from the reaction mixture.



Figure 5. The magnetization curves of Fe₃O₄, Fe₃O₄@TiO₂ and Fe₃O₄@TiO₂/Cu₂O.

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XPS analysis

The XPS elemental survey scans of the surface of Fe₃O₄@TiO₂/Cu₂O composite are shown in Figure 6. The peaks, corresponding to oxygen, titanium and copper were clearly observed (Fig 6).



Figure. 6. XPS pattern of as-synthesized Fe₃O₄@TiO₂/Cu₂O composite.



Figure 7. High resolution XPS spectra of Fe₃O₄@TiO₂/Cu₂O composite which shows (a) Ti2p (b) Cu₂p (c) O1s.

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The corresponding high resolution XPS spectra of Ti2p, O1s and Cu2p regions are shown in Figure 7. The Ti2p XPS spectra showed two major peaks with binding energies of ca. 466.5 and 472.1, corresponding to Ti2p3/2 and Ti2p1/2, respectively, characteristic of presence of TiO₂ phase (Fig. 7a).³⁵ The Fe signals were not observed, indicating that the Fe₃O₄ core has well been coated by the TiO2 shell. The carbon peak observed belongs to the carbon tape, used for XPS analysis. The peak at 931.8 ev is assigned to Cu2p3/2 and the other peak at 952.54 ev is assigned to Cu2p1/2. The additional peaks to Cu2p3/2 and Cu2p1/2 are the two shake-up satellite peaks, appearing at binding energies of 942.3 and 962.5 ev. These are expected for an open 3d⁶ shell, corresponding to Cu⁺¹ state and assigned to Cu₂O in accordance with data given in literature³⁶ The O1s peak at 538.3 ev was found over the catalyst surface can be assigned to OH species in composite.

Catalytic application of Fe₃O₄@TiO₂/Cu₂O core-shell magnetic composite

After the successful preparation and fully characterized, Fe₃O₄@TiO₂/Cu₂O core-shell magnetic composite, its catalytic activity in different weight ratios of Cu₂O were examined by a model reaction of benzyl bromide, phenyl acetylene and sodium azide (Huisgen cycloaddtion reaction), to obtain 1-benzyl-4phenyl-1H-1,2,3-triazole 4a (Scheme2), as sole product ,using 0.01 g magnetic composite under reflux in water. The products were obtained in high yield and excellent regioselectivity . The result showed, this click reaction is proceeding regioselectively, among the other merits concluded from the use of this novel catalyst system for the aforementioned model reaction. In order to establish the strategy, various terminal alkynes, different substituted benzyl bromides and sodium azide were reacted in the presence of catalytic amounts of Fe₃O₄@TiO₂/Cu₂O core-shell to afford the corresponding 1,4-disubstituted-1,2,3-triazoles, regioselectively in good yields (Table 3).



Scheme 2. Click reaction catalysed by nano-Fe₃O₄@TiO₂/Cu₂O core-shell composite.

As shown in Table 1, the catalytic performance of $Fe_3O_4@TiO_2/Cu_2O$ magnetic composite with a weight ratio of 8:2 gave the best result. It was found that no change in yield was obtained with increase of Cu_2O loading in magnetic composite. Therefore, the weight ratio of $Fe_3O_4@TiO_2:Cu_2O$ 8:2 were selected as one of optimal reaction conditions. The reaction of benzylbromide (1 mmol), phenylacetylene (1 mmol) and sodium azide (1.3 mmol) was also conducted in various solvents, different temperatures and various loading of magnetic composite.

action.			
Entry	Fe ₃ O ₄ @TiO ₂ (%)	Cu ₂ O (%)	Yield ^b (%)
1	60	40	93
2	70	30	93
3	80	20	93
4	90	10	82

 Table 1 Optimization of Cu₂O for magnetic composite in model reaction.

^a Reaction conditions: benzylbromide (1 mmol), sodium azide (1.3 mmol),phenylacetylene (1 mmol), and catalyst (0.010 g) in Water under reflux.

^b Isolated yield.

The results for the optimization of the reaction conditions are summarized in Table 2. In our delight, the reaction performed in refluxing water, gave the highest yield of product which an inert atmosphere is non-required (Table 2, entry 7). We carried out the model reaction in the presence of Fe₃O₄@TiO₂ as a catalyst under reflux in water and the poor yield of product was formed even after 2 h (Table 2, entry 8). As expected, the reaction did not proceed in the absence of the catalyst, even after prolonged reaction time (Table 2, entry 9). This indicates that the magnetic composite as catalyst plays a crucial role in the regioselective synthesis of 1-benzyl-4-phenyl-1H-1,2,3-triazole **4a**. A higher reaction temperature or the catalyst amount does not make an obvious difference in the yield of product (Table 2, entries 6, 10). But, a lower amount of catalyst decreased the yield of the reaction.

Table 2 Optimization of the three-component click synthesis of4-phenyl-1H-1,2,3-triazole,**4a**, using Fe₃O₄@TiO₂/Cu₂Omagnetic composite^a

-	-			
Entr	Catalyst (9)	Condition	Time	Yield ^b
у	Catalyst (g)	Condition	(h:min)	(%)
1	Fe ₃ O ₄ @TiO ₂ /Cu ₂ O (0.020)	H ₂ O/ r.t	2	Trace
2	$Fe_{3}O_{4}@TiO_{2}/Cu_{2}O$ (0.020)	$H_2O/60\ ^\circ C$	0:15	43
3	$Fe_{3}O_{4}@TiO_{2}/Cu_{2}O$ (0.020)	H ₂ O/ 80 °C	0:15	79
4	$Fe_3O_4@TiO_2/Cu_2O$ (0.020)	H ₂ O/ 110 °C	0:15	91
5	$Fe_3O_4@TiO_2/Cu_2O$ (0.010)	H ₂ O/ Reflux	0:15	69
6	$Fe_3O_4@TiO_2/Cu_2O$ (0.015)	H ₂ O/ Reflux	0:15	82
7	$Fe_{3}O_{4}@TiO_{2}/Cu_{2}O$ (0.020)	H ₂ O/ Reflux	0:15	93
8	$Fe_3O_4@TiO_2(0.020)$	H ₂ O/ Reflux	2	Trace
9	-	H ₂ O/ Reflux	24	-
10	$Fe_{3}O_{4}@TiO_{2}/Cu_{2}O$ (0.025)	H ₂ O/ Reflux	0:15	93
11	$Fe_3O_4@TiO_2/Cu_2O$ (0.020)	$H_2O/DMSO$ (2:1)/ Reflux	1:40	58
12	$Fe_3O_4@TiO_2/Cu_2O$ (0.020)	CH ₃ CN/ Reflux	1	75
13	$Fe_{3}O_{4}@TiO_{2}/Cu_{2}O$ (0.020)	EtOH/ Reflux	0:45	86
14	$Fe_{3}O_{4}@TiO_{2}/Cu_{2}O$ (0.020)	DMF/ 100 °C	1:45	46
15	$Fe_3O_4@TiO_2/Cu_2O$ (0.020)	DMSO/ 100 °C	1:45	50
16	$Fe_3O_4@TiO_2/Cu_2O$ (0.020)	Solvent free/ 100 °C	2	65

^a Reaction condition: Benzyl bromide(1 mmol), Sodium azide (1.3 mmol), Phenylacetylene (1 mmol).

Thus, with the optimized reaction condition in hand, the substrate scope of reaction was extended to various structurally diverse terminal alkynes and benzylhalides (Table 3). In an attempt to broaden the generality of the Fe₃O₄@TiO₂/Cu₂O magnetic composite, we further investigated the possibility of seast and sodium azide phenacyl bromide with various terminal alkynes and sodium azide in the presence of our novel catalyst, and found it promising and fruitful (Scheme 3). The results are listed in Table 4. Under optimal conditions for this one-pot, multi-component reaction, phenacyl bromide 1 mmol, phenylacetylene 1 mmol and sodium azide 1.3 mmol were reacted in the presence of 0.01 g magnetic composite under reflux in water.



Scheme 2. Click reaction of phenacyl bromide, phenyl acetylene and sodium azide.

In general, different substituted phenyl acetylenes and benzyl halides bearing electron-donating substituents as well as electronwithdrawing groups provided an array of 1,4-disubstituted 1,2,3triazoles smoothly and cleanly, in good to excellent yields (75-93%) within relative short times 15-80 min of reaction times. As shown in Tables 3 and 4, the aliphatic terminal alkynes bearing hydroxyl as functional group gave the desired triazoles in higher yields.

Recycling and leaching of the catalyst

One of the main advantages of heterogeneous catalysis is the ease of separation and their possible reusability in further runs.³⁷ In this line the recyclability of Fe₃O₄@TiO₂/Cu₂O magnetic composite was practically examined in a one-pot synthesis of 1benzyl-4-phenyl-1H-1,2,3-triazole 4a under optimized conditions. No significant loss in catalytic activity was observed after five runs, suggesting that Cu₂O leaching is not meaningful for Fe₃O₄@TiO₂/Cu₂O magnetic composite (Figure 8). Another test was done to determine that catalytic activity of Fe₃O₄@TiO₂/Cu₂O composite is not due only to dissolved Cu^I species in the solution. In this light, we performed an unfinished experiments. First, we took starting materials and catalyst, Fe₃O₄@TiO₂/Cu₂O composite in 3 mL water and refluxed the mixture for 5 min to simulate the actual conditions. Then at this point the catalyst was removed by an external magnet, while we allow the reaction normally proceed, then we permitted, the mixture being refulxed in the absence of the removed catalyst, magnitically. No apperaciable progress was observed even after 2 h (monitored bt TLC). Thus it can be concluded that the dissolved Cu^I species is not actually, involved in catalysis at least by itsef alone.



Figure. 8. Recycling results of the Fe₃O₄@TiO₂/Cu₂O composite.

^b Isolated yield.

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Table 3. Three-component click reaction of benzylhalides, terminal alkynes and sodium azide using Fe ₃ O ₄ @TiO ₂ /Cu ₂ O magnetic composite ^a						
Enters	Halida muanuman	A 11-1-1-0	Droduct	Time	Yield ^b	Mrs °C Lit
Entry	Hande precursor	Aikyne	Product	(min)	(%)	Mp. C ²
1	Br			15	93	127-128 (126-127) ^{30d}
2	Me		Me N=N	20	89	104-106 (105-106) ³⁹
3	O ₂ N Br			30	84	153-156 (156-157) ³⁹
4	Br	Me	N=N / N_Me	20	87	147-149 (150) ⁴⁰
5	Br	OH	N=N / N	20	91	77-79 (78-78.5) ³⁹
6	Br	Me Me OH	$ \begin{array}{c} N = N \\ N \\ N \\ Me \\ Me \end{array} $	20	85	76-77 (77) ³⁹
7	Cl			20	89	127-128 (126-127) ^{30d}
8	Me		Me N=N	25	83	104-106 (105-106) ³⁸
9	CI		ClN=N	25	84	143-146 (142-145) ⁴¹
10	Cl	Me	N=N NMe	25	84	147-149 (150) ⁴⁰
11	Cl	OH	N=N / N	20	89	77-79 (78-78.5) ³⁹
12	Cl	Me Me OH	$ \begin{array}{c} N = N \\ N \\ N \\ Me \\ Me \end{array} $	25	86	76-77 (77) ³⁹

 $^{a} Reaction \ condition: \ alkyl halide \ (1\ mmol), \ NaN_{3} \ (1.3\ mmol), \ acetylene \ (1\ mmol), \ Fe_{3}O_{4}@TiO_{2}/Cu_{2}O \ (0.020\ g), \ H_{2}O \ (2\ ml), \ reflux.$ ^b Isolated yield.

Δ	rti	\mathbf{c}	
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composite	-				DOI:1	0 1039/C58406810-1
Entry	phenacylhalide	Alkyne	Product	Time (min.)	Yield ⁶	Mp.°C ^{Lit.}
1	Br			20	89	169-171 (171-172) ^{30d}
2	Br		Br	25	83	115-118 (116-119) ^{30d}
3	O Cl			25	86	102-104 (100-103) ^{30d}
4	Br			30	87	157-159 (156-158) ^{30d}
5	O Br	OH	O N=N OH	50	76	111-113 (110-113) ^{30d}
6	Br	OH	O N=N OH	60	75	180-183 (180-183) ^{30d}
7	Br Br	OH	NIC O N=N OH	50	82	156-158 (157-160) ^{30a}
8	O Cl Br	Me Me OH	O N=N OH N Me Me	75	80	153-155 (151-154) ^{30a}
9	O Me	Me Me OH	O N=N OH N Me Me	70	78	154-155 (154-155) ^{30d}
10	Br Br	Me Me OH	Br O N=N OH Me Me	80	76	168-171 (167-170) ^{30d}

 Table 4. Three-component click reaction of phenacylhalides, terminal alkynes and sodium azide using Fe₃O₄@TiO₂/Cu₂O magnetic view Article Online

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^a Reaction condition: α-haloketones (1 mmol), NaN₃ (1.3 mmol), acetylene (1 mmol), Fe₃O₄@TiO₂/Cu₂O (0.020 g), H₂O (2 ml), reflux. ^b Isolated yield.

Conclusion

In summary, we have developed an efficient method for the regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles through a one-pot multi-component reaction of alkyl halides or phenacyl bromide, terminal alkynes and sodium azide,catalyzed by novel and well characterizid nano-Fe₃O₄@TiO₂/Cu₂O coreshell magnetic composite under reflux in water. Using,

commercially and readily available starting materials and the green and abundent, water as solvent are the merits of this method. Conducting the reaction in conventional conditions, convenient work up procedure, easy recovery and efficient reusability of catalyst are conspicuous features of this methodology. Further studies on the scope and application of nano- Fe₃O₄@TiO₂/Cu₂O magnetic composite are underway in our laboratory.

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References

- 1 P. Hu, J. V. Morabito and C. K. Tsung, ACS Catal., 2014, 4, 4409-4419.
- 2 F. Shirini and F. Absdini, J. Nanosci. Nanotechnol. 2013, 13, 4838-4860.
- 3 T. Cheng, D. Zhang, H. Li and G. Liu, Green Chem., 2014, 16, 3401-3427.
- 4 R. Mr'owczy'nski, A. Nanb and J. Liebscher, RSC Adv., 2014, 4, 5927–5952.
- 5 A. Kumar, R. Parella, S. A. Babu, Synlett., 2014, 25, 835-842.
- 6 S. Shylesh, V. Schünemann, W. R. Thiel, Angew. Chem. Int. Ed., 2010, 49, 3428-3459.
- 7 M. B. Gawande, P. S. Branco, R. S. Varma, Chem, Soc. Rev., 2013, 42, 3371-3393.
- 8 R. Hudson, Y. Feng, R. S. Varma and A. Moores, Green Chem., 2014,16, 4493-4505.
- 9 X. Zhu, J. Niu, F. Zhang, J. Zhou, X. Li and J. Ma, New J. Chem., 2014, 38, 4622-4627.
- 10 S. P. Pujari, L. Scheres, A. T. M. Marcelis and H. Zuilhof, Angew. Chem. Int. Ed., 2014, 53, 6322-6356.
- 11 S. Xuan, W. Jiang, X. Gong, Y. Hu and Zuyao Chen, J. Phys. Chem. C., 2009, **113**, 553-558.
- 12 T. A. Salah El-Din, A. A. Elzatahry, D. M. Aldhayan, A. M. Al-Enizi and S. S. Al-Deyab, *Int. J. Electrochem. Sci.*, 2011, **6**, 6177-6183.
- 13 Z. Chen, Z. Xue, L. Chen, Z. Geng, R. Yang, L Chena and Zhilin Wang, *New J. Chem.*, 2013, **37**, 3731-3736.
- (a) X. Wang, Z. Li, J. Shi and Y. Yu, *Chem. Rev.*, 2014, **114**, 9346-9384; (b) M. Pelaeza, N. T. Nolanb, S. C. Pillai b, M. K. Seeryc, P. Falarasd, A. G. Kontosd, P. S. M. Dunlope, J. W. J. Hamiltone, J. Anthony Byrnee, K. O'Sheaf, M. H. Entezarig and D. D. Dionysioua, *Appl. Catal.*, *B*, 2012, **125**, 331-349.
- (a) C. Allais, J.-M. Grassot, J. Rodriguez and T. Constantieux, *Chem. Rev.*, 2014, **114**, 10829-10868; (b) H. G. O. Alvim, E. N. J. da S. Jumior and B. N. D. Neto, *RSC Adv.*, 2014, **4**, 54282-54299; (c) H. Y. Cho and J. P. Morken, Chem. *Soc. Rev.*, 2014, **43**, 4368-4380; (d) V. Estevez, M. Villacampa and J. C. Menendez, Chem. Soc. Rev., 2014, **43**, 4633-4657.
- 16 (a) M. K. Singh, R. Tilak, G. Nath, R. S. K. Awasthi and A. Agarwal, *Eur. J. Med. Chem.* 2013, **63**, 635-644; (b) M. Whiting, J. Muldoon, Y. C. Lin, S. M. Silverman, W. Lindstrom, A. J. Olson, H. C. Kolb, M. J. Fine, K. B. Sharpless, J. H. Elder and V. V. Fokin, *Angew. Chem. Int. Ed.*, 2006, **45**, 1435-1439; (c) Z. Ke, H. F. Chow, M. C. Chan, Z. Liu and K. H. Sze, *Org. Lett.*, 2012, **14**, 394-397; (d) Y. Hua and A. H. Flood, *Chem. Soc. Rev.*, 2010, , 1262-1271;
- (a) A. Lauria, R. Delisi, F. Mingoia, A. Terenzi, A. Martorana, G. Barone and A. M. Almerico, *Eur. J. Org. Chem.*, 2014, **79**, 3289-3306; (b) X. Xiong, L. Cai, *Catal. Sci. Thecnol.*, 2013, **3**, 1301-1307; (c) B. Kaboudin, R. Mostafalu, T. Yokomatsu, *Green Chem.*, 2013, **15**, 2266-2274; (d) N. Aslam, N. A. Babu, S. Arulanda, D. Kuma, R. Ameet, *Synlett.*, 2014, **25**, 2201-2207.
- 18 J. Albadi, J. Abbasi Shiran and Azam Mansurnezhad, J. Chem. Sci., 2014, 126, 147-150.
- 19 L. Huang, W. Liu, J. Wu, Y. Fu, K. Wang, C. Huo and Z. Du, *Tetrahedron Lett.*, 2014, 55, 2312-2316.
- 20 F. Alonso, Y. Moglie, G. Radivoy and Miguel Yusv. Adv. Synth. Catal., 2010, 352, 3208-3214.
- 21 M. Gholinejad and N. Jeddi, ACS Sustainable Chem. Eng., 2014, 2, 2658-2665.
- 22 P. Li, S. Regati, H. Huang, H. D. Arman, J. C. G. Zhao and B. Chen, *Inorg. Chem. Front.*, 2015, 2, 42-46.
- F. Matloubi Moghaddam, S. E. Ayati, *RSC Adv.*, 2015, 5, 3894-3902.
 C. Schwartz Radatz, L. Amaral Soares, E. Roberto Vieira, D. Alves,
- D. Russowsky and P. Henrique Schneider, New J. Chem., 2014, 38, 1410-1417.
- 25 H. X. Siyang, H. L. Liu, X. Y. Wu and P. N. Liu, RSC Adv., 2015, 5, 4693-4697.
- 26 X. Xiong, H. Chen, Zh. Tang, Y. Jiang, RSC Adv., 2014, 4, 9830-9837.
- 27 S. Dadashi-Silab, B. Kiskan, M. Antonietti and Y. Yagci, *RSC Adv.*, 2014, 4, 52170-52173.

- (a) F. Nemati, M. M. Heravi and R. Saeedi rad, *Chin. J. Catal.*, 2012, 33, 1825-1831; (b) F. Janati, M. M. Heravi and A. M. Shökraletidynthline *React. Inorg. Met. Org. Chem.*, 2015, 45, 1-59(c) 071/Africhfred A10J Oskooei and M. M. Heravi, Synth. Commun., 2013, 43, 3357-3362.
- (a) M. M. Heravi and Z. Faghihi, J. Iran. Chem. Soc., 2014, 11, 209-224; (b) M. M. Heravi and S. Moghimi, Tetrahedron Lett., 2012, 53, 392-394; (c) M. M. Heravi and S. Moghimi, J. Iran. Chem. Soc., 2011, 8, 306-373; (d) M. M Heravi, F. K. Behbahani, M. Daraie and H. A. Oskooie, Mol. Diversity. 2009, 13, 375-378; (e) M. M. Heravi, E. Hashemi, Y. Sh. Beheshtiha, Kh. Kamjou, M. Toolabi and N. Hosseintash, J. Mol. Cat. A: Chem., 2014, 392, 173-180; (f) M. M. Heravi, F. Mousavizadeh, N. Ghobadi and M. Tajbakhsh, Tetrahedron Lett., 2014, 55, 1226-1228; (g) M. M. Heravi, Sh. Asadi and B. M. Lashkariani, Mol. Diversity, 2013, 17, 389-407.
- (a) A. Fazeli, H. A. Oskooie, Y. S. Beheshtiha, M. M. Heravi1 and H. Valizadeh, *Lett. Org. Chem.*, 2013, 10, 738-743; (b) A. Fazeli, H. A. Oskooie, Y. S. Beheshtiha, M. M. Heravi, H. Valizadeh and F. F. Bamoharram, *Monatsh Chem.*, 2013, 144, 1407-1410; (c) M. M. Heravi, A. Fazeli, H. A. Oskooie, Y. S. Beheshtiha and H. Valizadeh, *Synlett.*, 2012, 23, 2927-2930; (d) E. Hashemi, Y. S. Beheshtiha, S. Ahmadi, M. M. Heravi, *Transition Met Chem.*, 2014, 39, 593-601; (e) M. M. Heravi, H. Hamidi and V. Zadsirjan, *Curr. Org. Synth.*, 2014, 11, 647-675; (d) R. Mirsafaei, M. M. Heravi, Sh. Ahmadi, M. S. Moslemin and T. Hosseinnejad, *J. Mol. Catal. A: Chem.* 2015, 402, 100-108.
- 31 W. Hu, B. Liu, Q. Wang, Y. Liu, Y. Liu, P. Jing, S. Yu, L. Liua and J. Zhang, *Chem. Commun.*, 2013, **49**, 7596-7598.
- 32 R. J. Watts, S. Kong and W. Lee. J. Environ. Eng., 1995, 121, 730-735.
- 33 T. Xin, M. Ma, H. Zhang, J. Gu, S. Wang, M. Liu and Q. Zhang, *Appl. Surf. Sci.*, 2014, 288, 51-59.
- 34 H. Yin, Y. Wada, T. Kitamura, S. Kambe, S. Murasawa, H. Mori, T, Sakatac and S. Yanagida, *J. Mater. Chem.*, 2001, 11, 1694-1703.
- 35 F. Niu, Y. Jiang and W. Song, *Nano Res.*, 2010, **3**, 757-763.
- 36 C. H. Kuo, Y. T. Chu, Y. F. Song and M. H. Huang, Adv. Funct. Mater., 2011, 21, 792-797.
- 37 (a) D. Diaz, D. Kuehbeck and R. Koopmans, J. Chem. Soc. Rev., 2011,
 40, 427-448; (b) M. M. Heravi and S. Sadjadi, J. Iran Chem. Soc.,
 2009, 6, 1-54.
- 38 J. Gonz´alez, V. M. P´erez, D. O. Jim´enez, G. Lopez-Valdez, D. Corona and E. Cuevas-a˜nez, *Tetrahedron Lett.*, 2011, **52**, 3514-3517.
- 39 H. Sharghi, R. Khalifeh and M. M. Doroodmand, *Adv. Synth. Catal.*, 2009, **351**, 207-218.
- 40 Z. Gonda and Z. Novak, *Dalton Trans.*, 2010, **39**, 726-729.
- 41 P. V. Chavan, K. S. Pandit, U. V. Desai, M. A. Kulkarni and P. P. Wadgaonkar, *RSC Adv.*, 2014, 4, 42137-42146.

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