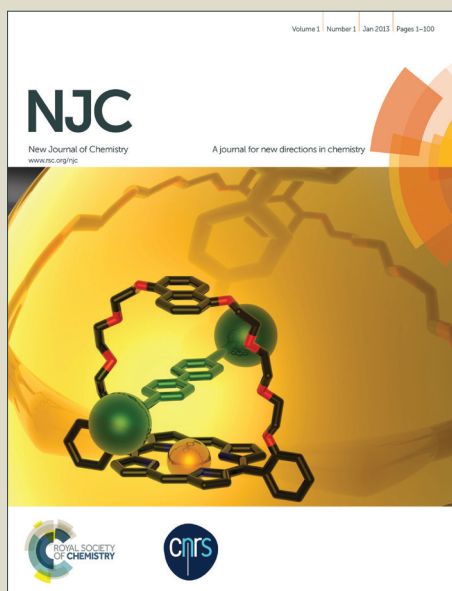


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Magnetically recoverable chitosan stabilised copper-iron oxide nanocomposite material as efficient heterogeneous catalyst for azide-alkyne cycloaddition reactions

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Received 00th January 20xx,
Accepted 00th January 20xx

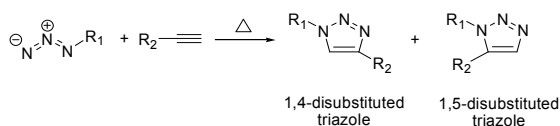
DOI: 10.1039/x0xx00000x

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Chitosan stabilised copper-iron oxide nanocomposite material is found to be a very efficient recyclable/reusable heterogeneous catalyst for azide-alkyne cycloaddition reaction under mild condition. The as-synthesized nanocomposite material is magnetically recoverable and reusable at least up to four times without significant loss in their catalytic activity. The catalytic system is found to be highly useful for the regioselective synthesis of a wide range of 1,2,3-triazoles from various azides and alkynes.

Introduction

The Huisgen^[1] 1,3-dipolar cycloaddition of alkynes and azides is the most convenient and straightforward approach for synthesis of 1,2,3-triazoles. This classical reaction usually requires higher temperatures and provides a mixture of 1,4- and 1,5-disubstituted 1,2,3-triazoles (Scheme 1). Sharpless et al.^[2] and Meldal et al.^[3] in 2002 independently published their pioneering work on Cu catalyzed azide alkyne cycloaddition (CuAAC) reaction leading to a mild and efficient synthesis of 1,4-disubstituted 1,2,3-triazoles. For reactions to be considered "click" they must fulfill a number of basic requirements: (i) they must demonstrate no sensitivity towards moisture or oxygen, (ii) they must afford products in high yields and with stereospecificity, and (iii) they must proceed in the absence of a solvent (or the use of a benign one) and led themselves to simple product isolation. CuAAC reaction satisfies the basic criteria of click chemistry and is increasingly used in diverse applications ranging from chemical and combinatorial synthesis, bioconjugation, and biology to materials science.^[4-7]



Scheme 1: Huisgen azide-alkyne cycloaddition

A good number of works have been done using copper (I) source in regioselective azide-alkyne cycloaddition. The copper (I) species required in the catalyzed version of the Huisgen cycloaddition are

usually generated from copper (II) salts with reducing agents (e.g. sodium ascorbate) or added directly as cuprous salts, usually with stabilizing ligands.^[8] Sometimes metallic copper or clusters are also employed. But these catalytic systems sometimes require oxidative agents. The reactions are relatively slow and a significant amount of catalyst is necessary. In some cases formation of diacetylenes and bistriazoles are also observed.^[9] In order to overcome these drawbacks, systems with heterogeneous catalyst have been developed. Heterogeneous catalyst exhibits possible advantages^[10] such as easy separation, reusability, the potential for incorporation in continuous reactors and microreactors and are becoming a trade in the present research works in chemistry. These days, works on click-compatible heterogeneous catalyst system is gaining more attention among the scientific community. In an effort to find efficient heterogeneous catalyst system, Cu (I) catalysts have been immobilized on polymers or zeolite, Cu (0) on charcoal, Cu (0) nanoparticles as well as CuO nanostructures, have also been successfully employed in azide-alkyne cycloaddition.^[11-15]

Chitosan is a natural, nontoxic, renewable biopolymer and possesses a great quantity of hydroxyl and amine groups, which can be coordinated with metal ions through chelate mechanism.^[16] It is widely used in many industrial and manufacturing processes and is commonly used for metal extraction and catalysis.^[17-22] Recently, functionalized magnetic nanoparticles represent as feasible alternatives to conventional materials as robust, easily available, high-surface-area heterogeneous catalyst supports. They offer an environmentally benign advantage of being magnetically separable and reduce the requirement of catalyst filtration after completion of the reaction.^[23] Magnetite is an ideal oxide support, having a very active surface for adsorptions or immobilization of metals and ligands with easy preparation system. It can be separated by simple magnetic decantation after the reaction which makes it a more sustainable catalyst.^[24] Catalysts with various metals like Pd, Ru, Co, Mo supported on magnetite have been developed for use in various

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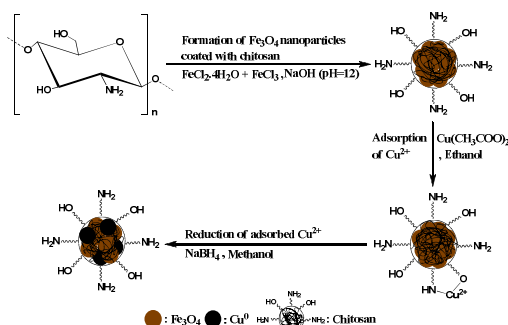
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reactions.^[25] Here, we developed a magnetic catalyst with Cu in order to use in azide-alkyne cycloaddition.

To continue our interest on click chemistry,^[26] here we applied magnetically recoverable and reusable chitosan stabilised copper iron oxide nanocomposite material as heterogeneous catalyst for regioselective synthesis of 1,2,3-triazoles. In the catalyst, Cu⁰ nanoparticles were attached on chitosan coated Fe₃O₄ (CS-Fe₃O₄-Cu⁰).

2. Results and Discussion:

The synthesis of CS-Fe₃O₄-Cu (Represented as Cu@Fe₃O₄) was depicted in Scheme 2 which consists of three steps. Firstly, we have synthesized CS-Fe₃O₄ by co-precipitation of Fe²⁺ and Fe³⁺ at pH 12. Secondly the Cu²⁺ ions were adsorbed by the amino and hydroxyl group of chitosan coated on Fe₃O₄. Finally the adsorbed Cu²⁺ ions were reduced to Cu⁰ by NaBH₄ and the Chitosan stabilized the Cu⁰ nanoparticles.



Scheme 2. Synthesis of Cu⁰ nanoparticles on chitosan coated Fe₃O₄

The TEM images of the CS-Fe₃O₄ showed that the diameters of the Fe₃O₄ nanoparticles are 10-15 nm and mostly spherical shape [Figure 1(a) & (b)]. The SAED pattern depicted in Figure 1 (b) inset confirmed the single crystallinity of the Fe₃O₄ nanoparticles. In case of CS-Fe₃O₄-Cu, the Cu⁰ nanoparticles can easily be recognized as it appears brighter than Fe₃O₄ nanoparticles in the TEM [Figure 1 (c) & (d)]. The Cu⁰ nanoparticles are spherical in shape and average diameters are 10 nm. The single crystalline nature of the Cu and Fe₃O₄ nanoparticles are seen from their SAED pattern [Figure 1(c) inset].

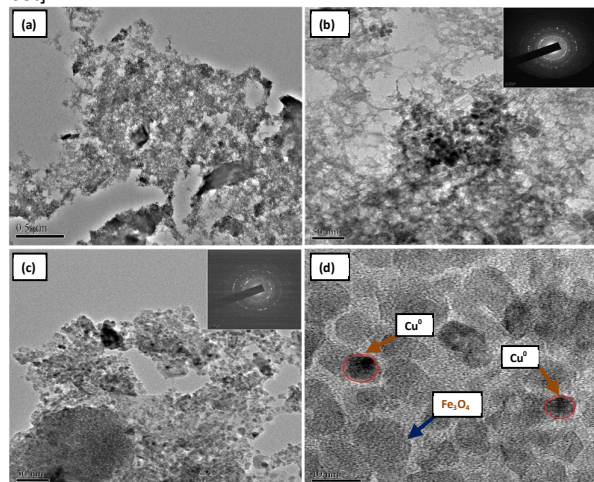


Figure 1: TEM images of (a) & (b) CS-Fe₃O₄ and SAED pattern (inset), (c) & (d) CS-Fe₃O₄-Cu and SAED pattern (inset).

The XRD pattern of CS-Fe₃O₄ [Figure 2 (a)] contains a sharp peak at 2 θ = 21.2 which is characteristic for chitosan. The diffraction peaks appeared at 2 θ = 18.6, 30.9, 35.7, 38.5, 43.7, 52.6, 57.5, and 63.1 were assigned to (111), (220), (311), (222), (400), (422), (511) and (440) reflections respectively, which are indexed to the Fe₃O₄ (JCPDS Card No. 19-0629). For CS-Fe₃O₄-Cu nanocomposite material, the characteristic peaks due to chitosan and Fe₃O₄ was retained with a little shift in their peak position which is depicted in Figure 2 (b). The characteristic peak due to metallic Cu was observed at 2 θ = 43.7, 50.3 and 74.1 which is assigned to (111), (200) and (220) indexed to the face centered cubic (fcc) lattice of metallic Cu (JCPDS Card No. 4-0836). But peak due to (111) reflection of metallic Cu merged with the (400) reflection of Fe₃O₄.

The FT-IR spectra (Figure 3a) of CS-Fe₃O₄ exhibited characteristic peaks for chitosan and Fe₃O₄.^[16] The peak at 3385 cm⁻¹ was assigned as the asymmetric stretching vibration of N-H and O-H. The C-H stretching vibration appears at 2930 and 2864 cm⁻¹. The other characteristic peaks at 1640, 1383, 1119, 613 cm⁻¹ correspond to NH (bending), C-N (stretching), bridging C-O-C (asymmetric), Fe-O-Fe (stretching). In case of CS-Fe₃O₄-Cu all characteristic peaks due to chitosan and Fe₃O₄ are retained with little shift of their position [Figure 3 (a) & (b)].

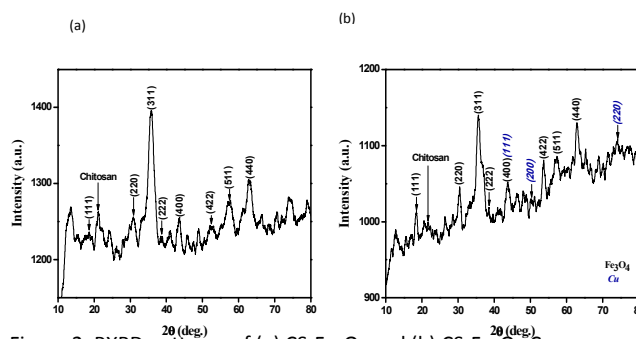


Figure 2: PXRD patterns of (a) CS-Fe₃O₄ and (b) CS-Fe₃O₄-Cu.

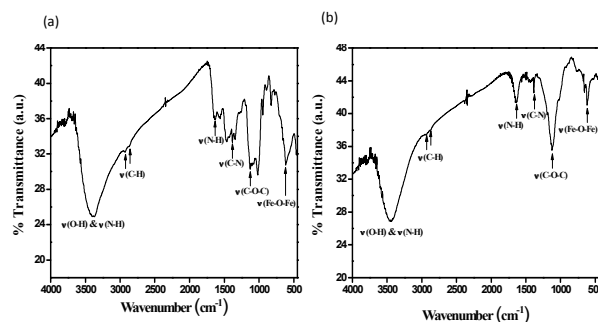
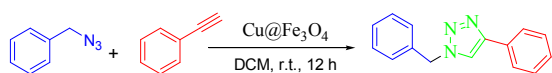


Figure 3: FT-IR spectra of (a) CS-Fe₃O₄ and (b) CS-Fe₃O₄-Cu.

We applied this magnetically recoverable and reusable catalyst for carrying out CuAAC reactions leading to regioselective formation of

1,2,3-triazoles. The experiments began with the intention of optimizing the reaction conditions for dipolar cycloaddition of benzylazide and phenylacetylene. To find out the most effective solvent for the CuAAC reaction using our catalyst, the reaction of benzyl azide and phenyl acetylene was carried out in different solvent systems (Table 1, Entries 1-8). Dichloromethane was found to be the best solvent system for the azide-alkyne cycloaddition reaction with our catalyst (Table 1, Entry 6). At room temperature with 20 mg (1.54 mol%) of the catalyst the reaction seemed to proceed very well to give the desired triazole product in excellent yield in 12 h.

Table 1. Solvent optimization study^a



Entry	Solvent	% Yields ^b
1	H ₂ O/t-BuOH (1:1)	30
2	THF	30
3	THF/H ₂ O (1:1)	60
4	Acetonitrile	<10
5	H ₂ O	60
6	DCM	92
7	DMF	<10
8	DMSO	<10

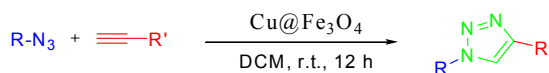
^a Reagents and reaction conditions: benzyl azide (1 mmol), phenyl acetylene (1.1 mmol), catalyst {20 mg (1.54 mol%), 4.89 wt%} in the given solvent was stirred at room temperature for 12 h; ^b Isolated yields

Therefore, further reactions were performed using dichloromethane as the solvent. Reactions using CS-Fe₃O₄ (without the Cu nanoparticles) and the CS-Fe₃O₄-Cu(CH₃COO)₂ (before the reduction) were also performed to be sure that the observed catalytic activity is only a result of the supported Cu nanoparticles. The use of CS-Fe₃O₄ shows no conversion and use of CS-Fe₃O₄-Cu(CH₃COO)₂ gives lower yields under our reaction conditions. Therefore it is found that only CS-Fe₃O₄-Cu⁰ has good catalytic activity for the azide-alkyne cycloaddition.

After finding the best reaction condition, CuAAC reactions were carried out with various azides and alkynes. Under this reaction

condition, various alkynes-both aromatic and aliphatic react with azides to afford 1,2,3-triazoles in good to excellent yields (Table 2, Entries 1-11). Moreover, the catalyst was found to be effective for non terminal alkynes also (Table 2, Entry 12).

Table 2. Study of azide-alkyne cycloaddition of a variety of azides and alkynes^a



Entry	Azides	Alkynes	Product	% Yields ^b	TOF (per hour)
1			a	92	4.98
2			b	77	4.17
3			c	96	5.19
4			d	78	4.22
5			e	95	5.14
6			f	86	4.65
7			g	79	4.27
8			h	88	4.76
9			i	93	5.03
10			j	90	4.87
11			k	89	4.82
12			l	96	5.19

^a All reactions were carried out using azide (1 mmol), alkynes (1.1 mmol), Catalyst (20 mg, 1.54 mol%, 4.89 wt%), in DCM (3 mL) at room temp, 12 h.

^b Isolated yields.

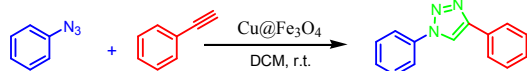
For the useful applications of such heterogeneous systems, the lifetime of the catalyst and its level of reusability are very significant factors. In order to find out whether our catalyst fulfils its applicability or not, a set of experiments were performed for the cycloaddition of phenyl azide and phenylacetylene using the recycled CS-Fe₃O₄-Cu catalyst. After the completion of the first reaction, the product was extracted and the catalyst was recovered easily which, due to its magnetic nature, got stuck with magnetic

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bead used in the reaction. A fresh reaction was then performed with new reactants, under the same conditions. The results obtained in our experiment confirmed that it was possible to recycle and reuse the catalytic system for at least up to four times without losing any catalytic activity (Table 3, Entries 1-4).

Table 3. Recyclability of the catalytic system^a



Entry	Run	% Yield ^b	TON
1	1 st	96	62.3
2	2 nd	96	62.3
3	3 rd	94	61.0
4	4 th	91	59.1

^a) Reagents and reaction conditions: phenyl azide (1 mmol), phenyl acetylene (1.1 mmol), catalyst (20 mg) in DCM was stirred at room temperature for 12 h.

^b) Isolated yields

In order to establish the heterogeneity of the catalyst, the following technique was followed which confirmed that during the progress of the reaction, metal loss from the solid surface did not occur. To perform this test, an experiment was carried out for the cycloaddition of benzyl azide (1 mmol) and phenyl acetylene (1.1 mmol) in presence of the catalyst using dichloromethane as solvent. The reaction was allowed to run for 6 h. Then the progress of the reaction was noticed and catalyst was removed from the reaction mixture.

After that the reaction mixture was again allowed to run for another 6 h. It was found that there was no progress of the reaction after the removal of the catalyst. It clarifies that our catalyst does not undergo any loss of metal from the solid support during reaction which proves its useful applicability to a wide extent.

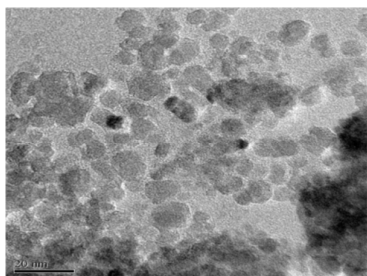


Figure 4: TEM images of recovered CS-Fe₃O₄-Cu catalyst (after 4th cycle)

The TEM image of recovered catalyst after 4th cycle was depicted in Figure 4. The sizes and shape Fe₃O₄ and Cu nanoparticles seemed to be retained from the TEM spectra.

Experimental section

Reagents and solvents were obtained from commercial suppliers and used without further purification. All reactions were carried out in oven dried glassware under atmospheric conditions otherwise noted. All reported yields are isolated yields.

Synthesis of chitosan coated Fe₃O₄ (CS-Fe₃O₄):

The chitosan coated Fe₃O₄ nanoparticles were synthesized by a little modification of the reported procedure.^[16] In a typical experimental procedure, 2 g of chitosan was dissolved in 5 % acetic acid solution. Then anhydrous FeCl₃ (4.8660 g) and FeCl₂·4H₂O (2.9820 g) were added to the chitosan solution and sonicated for 30 minutes (Scheme 2). Then the mixture was magnetically stirred at 1400 rpm for 3 h. After 3 h of stirring, a solution of 4M NaOH solution was added drop wise to the stirring solution until the pH became 12. The products from this step were washed by centrifugation with double distilled water until the neutral pH was obtained. The brown solid product was then dried in a desiccator. The as-synthesized material was designated as CS-Fe₃O₄.

Synthesis of Cu⁰ nanoparticles on chitosan coated Fe₃O₄ (CS-Fe₃O₄-Cu):

0.5 g of CS-Fe₃O₄ was taken into a 100 ml round bottom flask and dispersed in 25 ml ethanol then 25 ml (0.25 mmol) ethanolic solution of Cu(CH₃COO)₂ was added slowly under vigorous stirring condition. The stirring was continued for another 4 h. After 4 h of stirring, Cu²⁺ ions were completely adsorbed by chitosan and CS-Fe₃O₄-Cu(CH₃COO)₂ composite was separated by an external magnet and dried in a desiccator. The dry CS-Fe₃O₄-Cu(CH₃COO)₂ composite was again dispersed in 50 ml of methanol and 15 ml solution of NaBH₄ (5 mmol) in methanol was then added slowly in a nitrogen environment under constant stirring conditions. The reaction started immediately and the colour changed from brown to black, due to conversion of adsorbed Cu (II) into Cu (0)-nanoparticles. The black solid material was recovered using an external magnet and washed with distilled methanol for several times and then dried in a desiccator. The as-synthesized material was designated as CS-Fe₃O₄-Cu. The material was characterized by PXRD, FT-IR, TEM etc.

FE-SEM: The FESEM images [Figure 5 (a) & (b)] showed an aggregate morphological structure of CS-Fe₃O₄ due to magnetic attraction among chitosan coated Fe₃O₄. The EDX pattern determined the elemental compositions and spatial distributions of different

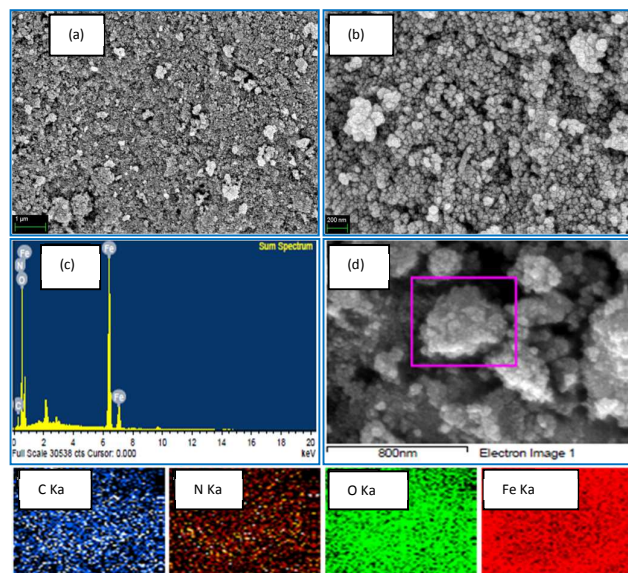


Figure 5: FESEM images (a) & (b) of CS-Fe₃O₄, (c) EDX pattern of CS-Fe₃O₄ (d) EDS mapping analysis from the selected rectangle in Figure (c).

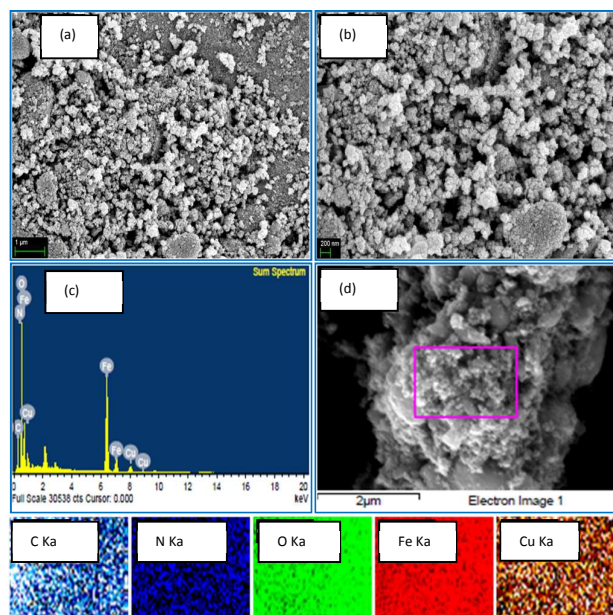


Figure 6: FESEM images (a) & (b) of CS-Fe₃O₄-Cu, (c) EDX pattern of CS-Fe₃O₄-Cu (d) EDS mapping analysis from the selected rectangle in Figure (c).

elements in the of CS-Fe₃O₄ sample [Figure 5 (c)]. The characteristic peaks of C, N, O and Fe confirmed that the CS-Fe₃O₄ sample is composed of C, N, O and Fe elements. Furthermore, the EDS mapping analysis [Figure 5 (d)] demonstrates the uniform

dispersion of all elements across the CS-Fe₃O₄. In case of CS-Fe₃O₄-Cu, no change in morphological structure was observed [Figure 6 (a) & (b)]. The corresponding EDX pattern determined the Cu along with C, N, O and Fe elements of CS-Fe₃O₄ [Figure 6 (c)]. The amount of Cu obtained from EDX analysis is 4.66 (wt%). Further confirmation on uniform dispersion of elements obtained from EDS mapping analysis [Figure 6 (d)].

The FESEM-EDS analysis was performed in Carl Zeiss Ultra 55 FE-SEM.

AAS analysis:

The amount of Cu was derived from AAS analysis of CS-Fe₃O₄-Cu sample which is 4.89 (wt%). This amount of Cu is quite resemble with EDX data which confirmed the uniform dispersion of Cu and its presence mostly in the surface of CS-Fe₃O₄-Cu as SEM scans only surface topography of a sample.

The Atomic absorption spectroscopy (AAS) measurement was carried out using PerkinElmer (Model-AAnalyst-700) spectrometer. Prior to analysis the sample was digested in aqua regia.

Powder XRD patterns were recorded on a Rigaku, Ultima IV X-ray diffractometer in the 2θ range of 10-90° using Cu Kα source (λ = 1.54 Å). FTIR spectra (4000-400 cm⁻¹) were recorded as KBr pellets in a Shimadzu IR affinity-1 spectrophotometer. The Transmission electron microscopy (TEM) images were taken using JEOL (Model JEM-2011).

Thin layer chromatography (TLC) was carried out using aluminium sheets pre-coated with silica gel 60F254 (Merck) and was visualized under 254 nm UV light. ¹H NMR (300 MHz), ¹³C NMR (75 MHz) were measured on a Bruker Avance 300 MHz spectrometer. Chemical shifts are reported in parts per million (ppm,) downfield from residual solvents peaks and coupling constants are reported as Hertz (Hz). Splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), broad (br) etc. Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m). ESI-MS spectra were recorded on an Agilent 6510 ESI-QTOF LC/MS mass spectrometer. Melting points were measured with a Büchi B-540 melting point apparatus.

Azides. All azides were synthesized according to the reported procedure.^[27]

A typical CuAAC procedure for the preparation of 1,2,3-triazole: To a mixture of catalyst (20 mg, 1.54 mol%) and azide (1 mmol) in dichloromethane (3 ml), alkyne (1.1 mmol) was added at room temperature. The resultant mixture was stirred until the reaction was complete. Then the reaction mixture was washed with H₂O and brine, and dried over anhydrous Na₂SO₄. Removal of the solvent yielded a residue, which was purified by column chromatography over silica gel.

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1-Benzyl-4-phenyl-1H-1,2,3-triazole (a). White solid, mp 128–130 °C, 92% yield. ^1H NMR (300 MHz, CDCl_3): δ 7.81 (d, J = 7.2 Hz, 2H), 7.66 (s, 1H), 7.43–7.30 (m, 5H), 5.59 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3): δ 148.2, 134.6, 130.4, 129.1, 128.8, 128.2, 128.0, 125.7, 119.5, 54.2.

1-Benzyl-4-butyl-1H-1,2,3-triazole (b). White solid, mp 64–66 °C, 77% yield. ^1H NMR (300 MHz, CDCl_3): δ 7.41–7.26 (m, 6H), 5.50 (s, 2H), 2.73 (t, J = 7.5 Hz, 2H), 1.68–1.58 (m, 2H), 1.42–1.30 (m, 2H), 0.93 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 148.8, 134.8, 128.9, 128.7, 128.4, 127.8, 120.3, 53.8, 31.3, 25.2, 22.2, 13.7.

1-(4-Diphenyl)-1H-1,2,3-triazole (c).

Pale yellow solid, mp 183–184 °C, 96% yield. ^1H NMR (300 MHz, CDCl_3): δ 8.52 (s, 1H), 8.22 (d, J = 5.4 Hz, 2H), 7.93 (d, J = 6.9 Hz, 2H), 7.81–7.28 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 148.3, 136.9, 130.1, 129.6, 128.8, 128.6, 128.3, 125.7, 120.4, 117.5.

4-Butyl-1-phenyl-1H-1,2,3-triazole (d). Colorless liquid, 78% yield. ^1H NMR (300 MHz, CDCl_3): δ 7.73 (d, J = 8.1 Hz, 2H), 7.53–7.39 (m, 3H), 7.48 (s, 1H), 2.83–2.78 (t, 2H), 1.77–1.67 (m, 2H), 1.49–1.37 (m, 2H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 149.0, 137.1, 129.4, 128.3, 120.4, 118.7, 31.4, 25.2, 22.2, 13.7.

1-Octyl-4-phenyl-1H-1,2,3-triazole (e). White solid, mp 74–76 °C, 95 % yield. ^1H NMR (300 MHz, CDCl_3): δ 7.84 (d, J = 7.3 Hz, 2H), 7.74 (s, 1H), 7.44–7.29 (m, 3H), 4.40 (t, J = 7.2 Hz, 2H), 1.96 (t, J = 7.0 Hz, 2H), 1.34–1.26 (m, 10H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 147.5, 130.6, 129.0, 128.7, 127.9, 125.5, 119.3, 50.3, 31.5, 30.2, 28.9, 28.8, 26.3, 22.4, 13.9.

1-(4-Chlorophenyl)-4-phenyl-1H-1,2,3-triazole (f). Yellow solid, mp 225–227 °C, 86% yield. ^1H NMR (300 MHz, CDCl_3): δ 8.17 (s, 1H), 7.92 (d, J = 7.5 Hz, 2H), 7.77 (d, J = 8.6 Hz, 2H), 7.54–7.36 (m, 5H). ^{13}C NMR (75 MHz, CDCl_3): δ 134.4, 129.8, 128.8, 128.4, 125.7, 121.5, 117.2.

1-(4-Bromophenyl)-4-phenyl-1H-1,2,3-triazole (g).

White solid, mp 231–233 °C, 79 % yield. ^1H NMR (300 MHz, CDCl_3): δ 8.17 (s, 1H), 7.91–7.35 (m, 9H). ^{13}C NMR (75 MHz, CDCl_3): δ 135.9, 132.8, 130.8, 129.8, 128.8, 128.7, 128.5, 125.7, 122.3, 121.7, 117.2.

[1-(4-Bromo-phenyl)-1H-[1,2,3]triazol-4-yl]-methanol (h).

Yellowish solid, mp 135–137 °C, 88% yield. ^1H NMR (300 MHz, CDCl_3): δ 8.00 (s, 1H), 7.72–7.59 (m, 4H), 4.89 (s, 2H), 2.14 (brs, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 135.9, 132.8, 122.4, 121.8, 56.3.

(1-Phenyl-1H-[1,2,3]triazol-4-yl)-methanol (i). White solid, mp 115–118 °C, 93% yield. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 8.68 (s, 1H), 7.92 (d, J = 7.8 Hz, 2H), 7.61–7.45 (m, 3H), 4.64 (d, J = 5.2 Hz, 2H), 2.50 (brs, 1H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$): δ 149.6, 137.2, 130.3, 128.9, 121.4, 120.4, 55.4.

[1-(4-Chloro-phenyl)-1H-[1,2,3]triazol-4-yl]-methanol (j).

Yellowish solid, mp 146–148 °C, 90% yield. ^1H NMR (300 MHz, CDCl_3): δ 8.01 (s, 1H), 7.68 (d, J = 8.5 Hz, 2H), 7.50 (d, J = 8.5 Hz, 2H), 4.88 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3): δ 135.5, 134.6, 129.9, 121.7, 56.2.

(1-Benzyl-1H-1,2,3-triazol-4-yl) methanol (k). White solid, mp 75–78 °C, 89% yield. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 8.02 (s, 1H), 7.40–7.31 (m, 5H), 5.50 (s, 2H), 4.52 (s, 2H), 2.50 (s, 1H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$): δ 148.7, 136.6, 129.1, 128.5, 128.3, 123.2, 55.5, 53.1.

1-Phenyl-1H-[1,2,3]triazole-4,5-dicarboxylic acid dimethyl ester (l). White solid, mp 106–108 °C, 95% yield. ^1H NMR (300 MHz, CDCl_3): δ 7.77–7.23 (m, 5H), 4.15–3.66 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 160.0, 159.3, 138.6, 135.4, 129.8, 129.7, 129.6, 129.5, 52.6, 52.2.

Conclusions

In conclusion, we have developed a simple and efficient heterogeneous catalytic system for the [3+2] cycloaddition of azides and alkynes. This heterogeneous method offers a wide scope giving excellent results with various azides and alkynes (including internal alkynes) and provides a very high regioselectivity, with only the 1,4-disubstituted 1,2,3-triazole regioisomer being formed. Moreover, this heterogeneous $\text{CS-Fe}_3\text{O}_4\text{-Cu}$ catalyst can be recovered magnetically and reused at least up to 4 times without losing catalytic activity. The easy recoverability of the catalyst and milder reaction condition for regioselective synthesis of 1,2,3-triazoles lead to its applicability towards various scientific prospects.

Acknowledgements

DS is thankful to CSIR, New Delhi for a research grant [No. 02(0154)/13/EMR-II]. The authors also acknowledge the Department of Science and Technology for financial assistance under DST-FIST programme and UGC, New Delhi for Special Assistance Programme (UGC-SAP) to the Department of Chemistry, Dibrugarh University.

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