Received: 16 April 2017 | Revised: 25 May 2017 | Accepted: 29 May 2017

DOI: 10.1002/aoc.3947

FULL PAPER

WILEY Applied Organometallic Chemistry

Click approach to the three-component synthesis of novel β-hydroxy-1,2,3-triazoles catalysed by new (Cu/Cu_2O) nanostructure as a ligand-free, green and regioselective nanocatalyst in water

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Copper nanostructures were produced as an effective and regioselective catalyst for the synthesis of 1,2,3-triazoles from a wide range of raw materials, such as sodium azide, epoxides and terminal alkynes, in water via a one-pot three-component click reaction. The new heterogeneous catalyst was prepared by a simple ball mill reduction of CuO with $NaBH_4$ using a ball-to-powder weight ratio of 50:1 under air atmosphere at room temperature. The catalyst was fully characterized using scanning electron microscopy, energy-dispersive X-ray analysis, Fourier transform infrared spectroscopy and X-ray diffraction. The copper nanostructures catalysed both ring opening and triazole cyclization steps. Products were obtained in high yields and short reaction times. The reactions were performed at ambient temperature in water as a green solvent. The Cu/Cu_2O nanostructures revealed high reusability and high stability via a simple recycling process.

KEYWORDS
click chemistry, copper nanostructures, epoxides, green chemistry, triazoles

1 | INTRODUCTION

The preparation of nanoparticles and their use in chemistry have led to big developments in the science of chemistry. This is a potent and growing research field in modern chemistry.[1] One of the features of nanostructures is their catalytic properties in organic synthesis.[2] Metallic nanocatalysts afford very high surface areas which are effective in catalytic performances.[3] Recyclable copper nanocatalysts also have been shown to be effective in organic chemistry reactions.[4]

1,2,3-Triazoles are an important and useful class of compounds in pharmaceuticals and agrochemicals.[5–7] Various substituents at 1- and 4-positions of triazoles provide biological activities such as anti-cancer, anti-bacterial and anti-HIV activities.[8,9] Triazoles have widespread use in synthesis.[10] In addition, triazoles are used in various industries to prevent corrosion.[11] One of the most efficient and widely used methodologies for selective C–N bond forming reactions is 'click' chemistry. Coined by Sharpless and Fokin, click chemistry offers extremely regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles with high yields.[12,13] 1,4-Disubstituted 1,2,3-triazoles were achieved via one-pot ring-opening and cycloaddition steps simultaneously, and finally purified. β-Hydroxy-1,4-disubstituted 1,2,3-triazoles were synthesized in the presence of Cu(I) catalyst from a wide range of terminal alkynes, epoxides and sodium azide through a three-component click reaction.[14,15]

Recently, β-hydroxy-1,2,3-triazoles have been synthesized via magnetic nano-iron oxide-catalysed reaction. This catalytic system needs harsh reaction conditions in comparison with those required for nanocopper catalysts.[16] The use of special catalysts such as the Cu(II)–azide complex $[Cu(H_2L)(N_3)]\cdot CH_3OH$ yielded two compounds through ring opening of an asymmetric epoxide in different positions. These compounds are formed by ring opening of asymmetric epoxide from two different positions.[17] Also, coupling alkynes, organic halides and NaN_3 in the presence of Cu_2O nanocrystals has been used to produce

various types of 1,4-disubstituted 1,2,3-triazoles with high regioselectivity under green conditions with high efficiency.[18,19] Also, CuO has rarely been used as a catalyst to provide 1,2,3-triazoles but Cu_2O is selective and its use is much more general.[20–22]

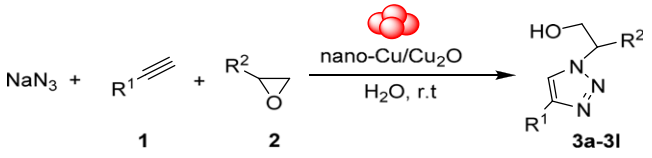
Ball milling is a simple method to prepare a wide range of nanocatalysts through the solid state with the possibility of use on a large scale.[23] Other methods that provide copper nanoparticles from reduced Cu(II) (chemical and electrochemical methods) cannot be used on a large scale. Conventional chemical methods generate impurity products and isolation of products is difficult and time-consuming.[24–27]

In the work reported here, Cu/Cu_2O nanostructures (NSs) were synthesized via a ball mill reduction method for first time and investigated in the one-pot three-component regioselective synthesis of novel 1,4-disubstituted 1,2,3-triazoles (Scheme 1). This catalytic system revealed an excellent performance. 1,4-Disubstituted 1,2,3-triazoles were synthesized in water as a green solvent at room temperature and in high yield. The Cu/Cu_2O NSs as a heterogeneous catalyst can be separated from a reaction mixture via simple filtration and reused three times without loss of catalytic activity.

2 | EXPERIMENTAL

2.1 | Instrumentation and reagents

All reagents were obtained from Merck and used without further purification. The melting points of products were obtained with an Electrothermal Type 9100 melting point apparatus. The ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker DRX 300 Avance spectrometer at 300 and 75 MHz, applying DMSO-d_6 or $CDCl_3$ as deuterated solvents. Chemical shifts were measured in ppm downfield from tetramethylsilane as internal standard. Phase characterization and microstructure of the catalyst were investigated using X-ray diffraction (XRD) with a Philips X'Pert X-ray diffractometer using Cu Kα radiation (λ = 0.154056 nm). The diffraction data were obtained over a 2θ range of 5–95° with a step width of 0.02°. Fourier transform infrared (FT-IR) spectra were collected with a Thermo Nicolet (USA) Avatar 370 infrared spectrometer, using KBr pellets at room temperature. The morphology of the catalyst and elemental compositions were investigated with scanning electron microscopy (SEM) and energy-dispersive X-ray (EDX) analysis using a TESCAN Mira 3 scanning electron microscope, operated at 20 kV.



SCHEME 1 Multicomponent synthesis of β-hydroxy-1,2,3-triazoles from epoxides

2.2 | Synthesis of Cu/Cu_2O NSs

In a typical experiment, 2.69 g (33.8 mmol) of CuO was mixed with 0.32 g (8.46 mmol) of $NaBH_4$ to give a CuO-to-$NaBH_4$ molar ratio of 4. The mixture was loaded into a hardened steel vial along with hardened steel balls (10 mm in diameter) to give a ball-to-powder weight ratio of 50:1. The milling method was conducted with a high-energy planetary ball mill in ambient atmosphere with a rotating speed of 250 rpm for 1 h. In the purification step, before using the catalyst in the click reaction for 1,2,3-triazole synthesis, the product was washed with distilled water (2 × 10 ml) and methanol (2 × 10 ml) to eliminate boron oxides and unused $NaBH_4$.

2.3 | Synthesis of β-Hydroxy-1,2,3-triazoles (3a–**3 l**)

Terminal alkyne (1.0 mmol), epoxide (1.0 mmol) and sodium azide (0.078 g,1.2 mmol) were stirred in water(5 ml) in the presence of the Cu/Cu_2O NSs (0.01 g).The reaction mixture was monitored by TLC using *n*-hexane–ethyl acetate (4:1). After completion of the reaction, the mixture was diluted with ethyl acetate (3 ml). In the following the whole reaction mixture was centrifuged for separation of the catalyst. The heterogeneous catalyst was washed three times with methanol and dried at room temperature. The reaction mixture was added to water (5 ml) and extracted with ethyl acetate (3 × 10 ml). Organic phases were washed with saturated brine and dried with anhydrous Na_2SO_4. The solvent was removed under vacuum and the required triazole was obtained. To increase the purity of products we used column chromatography with a silica gel column and ethyl acetate–hexane as eluent. Products **3b**, **3e**, **3 g**, **3 h**, **3 k** and **3 l** are reported for the first time, but products **3a**, **3c**, **3d** and **3f** have been reported in the literature, previously. All products (**3a**–**3 l**) were confirmed using ^{1}H NMR, ^{13}C NMR and FT-IR spectra.

2.3.1 | 1-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethanol (3a)[14,16,20,28]

White solid; yield 75%; m.p. 121.5–124.5 °C. IR (KBr, ν, cm^{-1}): 764, 1043, 1078, 1226, 1429, 1460, 1489, 1610, 2928, 3091, 3124, 3385. ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.76 (s, 1H), 7.73 (dd, 2H, J_1 = 7.0,

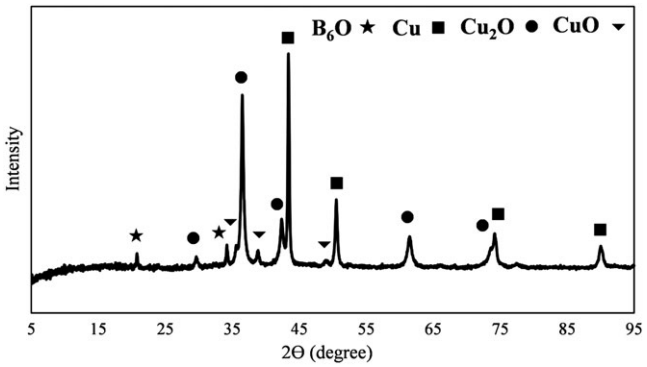


FIGURE 1 XRD pattern of Cu/Cu_2O nanostructures

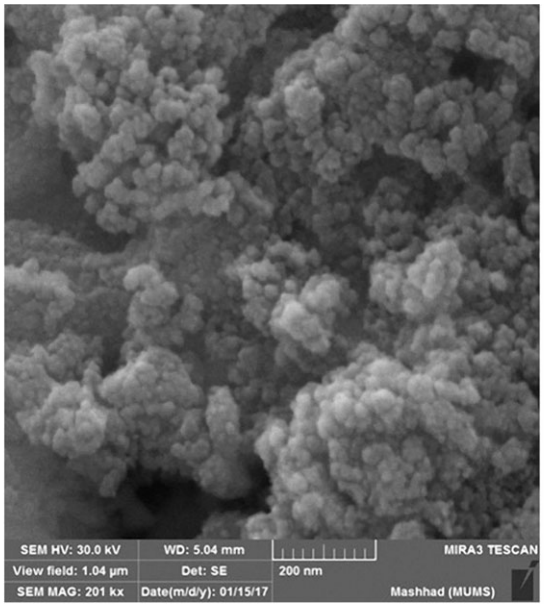
J_2 = 1.5 Hz), 7.29–7.41 (m, 8H), 5.71 (dd, 1H, J_1 = 8.2, J_2 = 3.8 Hz), 4.61–4.68 (m, 1H), 4.35 (b, OH), 4.23–4.27 (m, 1H), 3.85 (t, 1H).

2.3.2 | 2-(4-phenyl-1*H*-1,2,3-triazol-1-yl) butane (3b)

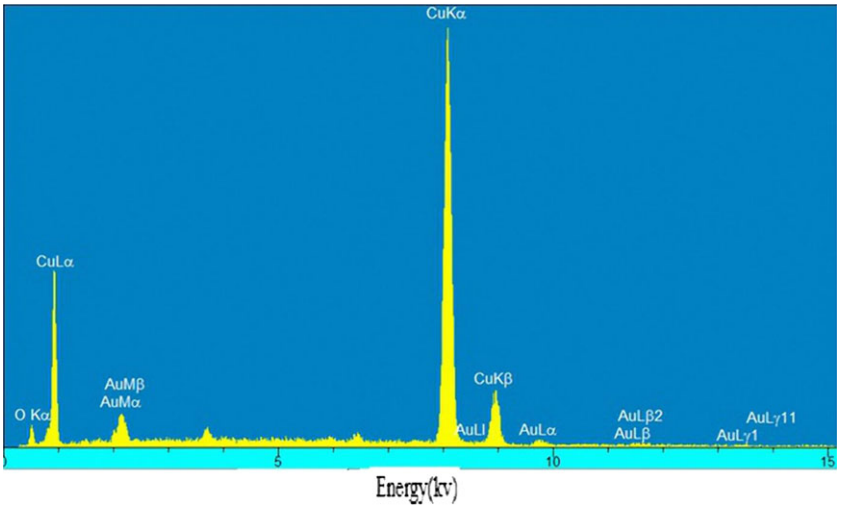
Colourless solid; yield 72%; m.p. 71.5–72.8 °C. IR (KBr, ν, cm^{-1}): 698, 721, 860, 957, 1076, 1165, 1358, 1458, 2970, 3128, 3356. ^1H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.75 (s, 1H), 7.61–7.64 (dd, 2H, J_1 = 9, J_2 = 6.9 Hz), 7.19–7.32 (m, 3H), 4.39–4.45 (dd, 2H, J_1 = 22.8, J_2 = 11 Hz), 4.12–4.20 (dd, 1H, J_1 = 13.8, J_2 = 5.7 Hz), 3.99 (b, OH), 1.48–1.54 (m, 2H), 0.98 (t, 3H).

2.3.3 | 2-(4-phenyl-1*H*-1,2,3-triazol-1-yl) cyclohexanol (3c)[14,28]

Bright solid; yield 68%; m.p. 177–179 °C. IR (KBr, ν, cm^{-1}): 873, 960, 1001, 1029, 1070, 1146, 1230, 1295, 1363, 1450,



(a) SEM image of Cu/Cu_2O nanostructures (NSs)



(b) EDS spectrum of Cu/Cu_2O nanostructures (NSs)

FIGURE 2 (a) SEM image of Cu/Cu_2O nanostructures. (b) EDX spectrum of cu/Cu_2O nanostructures

1568, 1743, 2857, 2933, 3133, 3304, 3382. ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.67 (s, 1H), 7.57–7.64 (dd, 2H, J_1 = 13.8, J_2 = 6.3 Hz), 7.19–7.44 (m, 3H), 3.96–4.16 (m, 1H), 1.08–2.13 (m, 8 H).

2.3.4 | 3-Phenoxy-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)propane (3d)[14,16,28]

Brown oily compound; yield 78%. IR (KBr, ν, cm^{-1}): 691, 754, 1044, 1115, 1175, 1245, 1495, 1599, 1733, 2947, 2929, 3062, 3351. ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.87 (s, 1H), 7.70–7.73 (d, 2H), 7.29–7.42 (m, 4H), 6.94–7.04 (m, 4H), 4.71–4.77 (m, 1H), 4.25 (dd, 1H, J_1 = 14, J_2 = 7.8 Hz), 3.97 (dd, 1H, J_1 = 11, J_2 = 5.4 Hz), 3.37–3.39 (m, 1H), 2.93 (m, 1H), 2.78 (dd, 1H, J_1 = 4.8, J_2 = 2.1 Hz). ^{13}C NMR ($CDCl_3$, 75.6 MHz, δ, ppm): 53.2, 68.8, 68.8, 114.5, 121.4, 121.5, 125.5, 128.2, 128.8, 129.5, 130.1, 147.3, 158.

2.3.5 | 3-Butoxy-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)propanol (3e)

Light brown oily compound; yield 80%. IR (KBr, ν, cm^{-1}): 696, 766, 829, 988, 1089, 1116, 1229, 1437, 1466, 1744, 2868, 2930, 2956, 3060, 3260. ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.90 (s, 1H), 7.77–7.79 (m, 2H), 7.29–7.44 (m, 3H), 4.60 (dd, 2H, J_1 = 13.8, J_2 = 10.2 Hz), 4.44 (dd, 2H, J_1 = 14, J_2 = 7 Hz), 4.28 (b, OH), 3.40–3.55 (m, 3H), 1.54–1.63 (m, 2H), 1.33–1.45 (m, 2H), 0.94 (t, 3H). ^{13}C NMR ($CDCl_3$, 75.6 MHz, δ, ppm): 13.9, 19.2, 31.6, 53.2, 69.2, 71.4, 71.5, 121.2, 125.6, 128.1, 128.8, 130.4, 147.5.

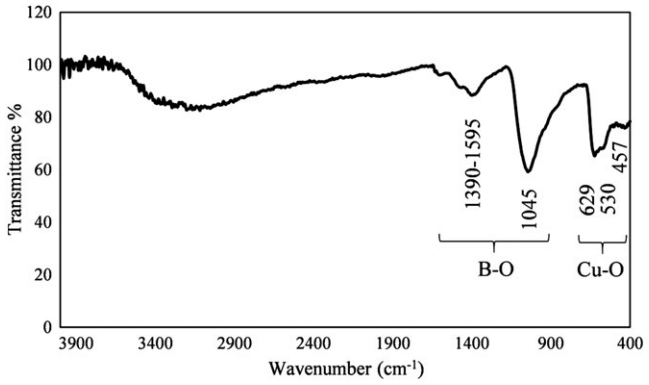


FIGURE 3 FT-IR spectrum of Cu/Cu_2O nanostructures

2.3.6 | 2-(4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)-2-phenylethanol (3f)[14]

Colourless solid; yield 84%; m.p. 110–111.8 °C. IR (KBr, ν, cm^{-1}): 657, 735, 845, 1012, 1061, 1115, 1229, 1461, 1638, 1742, 2868, 2932, 2962, 3154, 3355. ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.99 (s, 1H), 7.10–7.17 (m, 5 H), 5.61 (dd, 1H, J_1 = 9, J_2 = 5.1 Hz), 5.15 (b, 2H, OH) 4.36 (s, 2H), 4.08–4.12 (dd, 1H, J_1 = 11.4, J_2 = 9 Hz), 3.85 (dd, 1H, J_1 = 11.4, J_2 = 5.1 Hz). ^{13}C NMR ($CDCl_3$, 75.6 MHz, δ, ppm): 55.6, 63.5, 66.5, 122.8, 127.6, 128.6, 129.0, 138.0, 148.2.

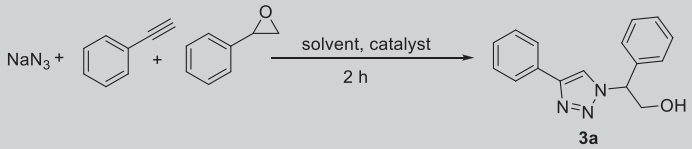
2.3.7 | 3-Phenoxy-2-(4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)propanol (3 g)

Brown oily compound; yield 80%. IR (KBr, ν, cm^{-1}): 698, 721, 860, 957, 1076, 1165, 1358, 1458, 2970, 3128, 3356. ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.79 (s, 0.4H), 7.75 (s, 0.6H), 7.26 (m, 2H), 6.99 (m, 1H), 6.86 (m, 2H), 3.60–4.69 (m, complex, 9H). ^{13}C NMR ($CDCl_3$, 75.6 MHz, δ, ppm): 53.5, 68.9, 71.3, 72.3, 121.0, 125.4, 128.7, 129.7, 134.2, 147.0.

2.3.8 | 3-Phenoxy-2-(4-(phenoxymethyl)-1*H*-1,2,3-triazol-1-yl)propanol (3 h)

Light brown oily compound; yield 73%. IR (KBr, ν, cm^{-1}): 884, 994, 1039, 1079, 1122, 1173, 1243, 1292, 1457, 1495, 1598, 1731, 2847, 2928, 3040, 3063, 3290, 3370. ^{1}H NMR

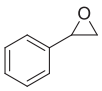
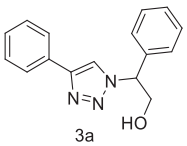
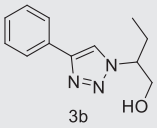
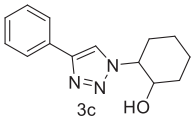
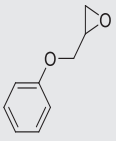
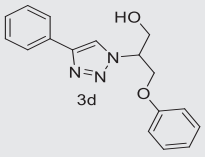
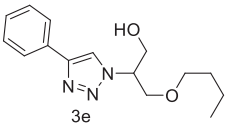
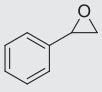
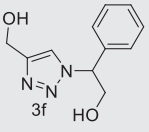
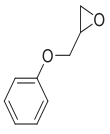
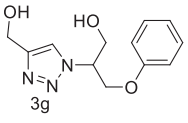
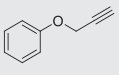
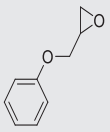
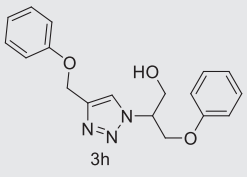
TABLE 1 Optimization of reaction conditions



3a

Entry	Solvent	Temperature (°C)	Catalyst loading (mg)	Yield (%)
1	Toluene	25	0	0
2	DMF	25	10	40
3	Ethanol	25	10	55
4	Water	25	0.5	47
5	Water	25	1	75
6	Water	25	1.5	78

TABLE 2 Synthesis of 1,4-disubstituted β-hydroxy-1,2,3-triazoles (**3a–3 l**)

	Alkyne	Epoxide	Product	Yield (%)
1			 3a	75
2			 3b	72
3			 3c	68
4			 3d	78
5			 3e	80
6			 3f	84
7			 3g	80
8			 3h	73

(Continues)

TABLE 2 (Continued)

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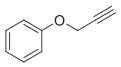
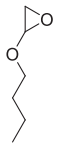
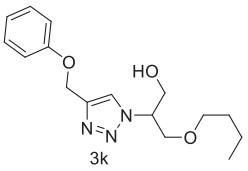
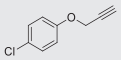
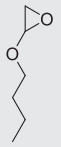
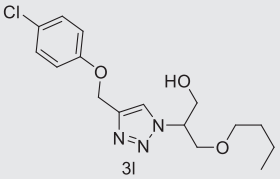
9			 3k	70
10			 3l	65

($CDCl_3$, 300 MHz, δ, ppm): 7.81 (s, 1H), 7.28–7.41 (m, 4H), 6.92–7.03 (m, 6H), 4.72 (AB, q, 2H), 4.25 (dd, 1H, $J_1 = 12$, $J_2 = 3$ Hz) 3.97 (dd, 1H, $J_1 = 12$, $J_2 = 6$ Hz), 3.36–3.41 (m, 1H), 2.93 (dd, 1H, $J_1 = 9$, $J_2 = 6$ Hz), 2.78 (dd, 1H, $J_1 = 6$, $J_2 = 3$ Hz) 2.85 (b, OH). ^{13}C NMR ($CDCl_3$, 75.6 MHz, δ, ppm): 45.1, 51.4, 56.6, 68.5, 114.5, 115.5, 122.1, 122.5, 124.5, 129.6, 130.0, 143.5, 158.3, 158.9.

2.3.9 | 3-Butoxy-2-(4-(phenoxymethyl)-1*H*-1,2,3-triazol-1-yl)propanol (3 k)

Dark brown oily compound; yield 70%. IR (KBr, ν, cm^{-1}): 883, 992, 1011, 1034, 1119, 1173, 1241, 1299, 1377, 1456, 1459, 1599, 2870, 2932, 2957, 3149, 3327. ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.79 (s, 1H), 7.15–7.36 (m, 2H), 6.69–7.07 (m, 3H), 5.17 (b, 1H), 4.71 (AB, q, 2H), 4.56 (dd, 1H, $J_1 = 12$, $J_2 = 3$ Hz),4.40 (dd, 1H, $J_1 = 20.0$, $J_2 = 9.0$ Hz), 4.21 (m, 1 H), 4.05 (m, 1H), 3.36–3.63 (m, 3H), 1.51–1.65 (m, 2H), 1.27–1.42 (m, 2H), 0.92 (t, 3H, $J = 7.5$ Hz). ^{13}C NMR ($CDCl_3$, 75.6 MHz, δ, ppm): 13.9, 19.2, 31.6, 53.1, 55.7, 61.7, 69.1, 71.4, 114.8, 114.9, 121.3, 124.4, 129.5, 143.9, 158.1.

2.3.10 | 3-Butoxy-2-[4-((4-chlorophenoxy)methyl)-1*H*-1,2,3-triazol-1-yl]propanol (3 l)

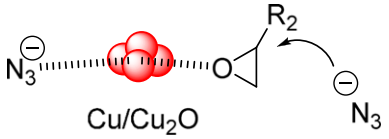
Light brown oily compound; yield 65%. IR (KBr, ν, cm^{-1}): 508, 666, 822, 915, 1006, 1037, 1093, 1244, 1491, 1595, 2867, 2928, 3063, 3097, 3424. ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 7.77 (s, 1H), 7.21–7.29 (m, 2H), 6.89–6.92 (m, 2H), 5.17 (b, 1H), 4.67 (AB, q, 2H), 4.56 (dd, 1H, $J_1 = 12$, $J_2 = 3$ Hz), 4.41 (dd, 1H, $J_1 = 20.0$, $J_2 = 9.0$ Hz), 4.19 (m, 1 H), 3.89–3.96 (m, 1H), 3.34–3.48 (m, 3H), 1.51–1.60 (m, 2H), 1.25–1.41 (m, 2H), 0.91 (t, 3H). ^{13}C NMR ($CDCl_3$, 75.6 MHz, δ, ppm): 13.8, 19.2, 31.6, 53.5, 64.3, 69.1, 69.6, 116.1, 124.4, 126.1, 129.3, 143.5, 156.7.

3 | RESULTS AND DISCUSSION

Ball-milled reduction of CuO with $NaBH_4$ gave Cu/Cu_2O NSs which were characterized using XRD, SEM, EDX and FT-IR. The XRD pattern of the catalyst, presented in Figure 1, reveals crystalline copper. It is obvious that CuO is reduced to Cu_2O and Cu NSs. The Cu_2O characteristic diffraction peaks are at $2\theta = 36.5°$, 42.2°, 61.24° and 74.1° in the XRD pattern, indexed to (111), (200), (220) and (311),[29] and characteristic diffraction peaks of Cu nanoparticles are observed at $2\theta = 43°$, 50.32°, 74° and 90° in the XRD pattern. XRD peaks indexed to (111), (200) and (220) represent face-centred cubic structure and agree well with Miller index.[29,30] Peaks at $2\theta = 23.5°$ and 34° in the XRD pattern are related to B-containing compounds such as B_6O. Weak peaks at $2\theta = 36.5°$, 39° and 49° are related to CuO.[30,31]

Figure 2(a) shows a SEM image of the catalyst particles. The SEM image of the synthesized catalyst confirms that Cu nanoparticles are spherical but not very well defined, and the particle size is in the nanometre size range. The EDX spectrum shows Cu and O elements (Figure 2b).

The FT-IR spectrum of the catalyst (Figure 3).shows the presence of bands at 457 and 530 cm^{-1} corresponding to



SCHEME 2 Regioselectivity in azide attack to epoxides

TABLE 3 Comparison of efficiency of various catalysts in synthesis of **3a**

Entry	Catalyst	Yield (%)	Time (h)	Temperature (°C)	Ref.
1	Fe_2O_3	81	5	100	16
2	ZnO	Trace	24	100	16
3	Meso-tetra(2-chlorophenyl)porphyrin cu@MWCNT[a]	95	0.8	r.t.	14
4	Meso-tetra(2-chlorophenyl)porphyrin-cu	82	2	r.t.	14
5	Cu(II)–azide complex [cu(H_2L)(N_3)]·CH_3OH	91	8	r.t.	17
6	(Cu/Cu_2O) nanostructure	75	2	r.t.	This work

[a]MWCNT, multi-walled carbon nanotubes.

stretching of Cu—O, whereas that at 629 cm^{-1} is attributed to Cu_2O.[29,30] Also, the characteristic peaks at 1045 and weak peaks at 1397–1605 cm^{-1} in the spectrum correspond to B—O vibrations.[32]

The reaction of sodium azide, phenylacetylene and styrene oxide was chosen as a model reaction. In the absence of catalyst, no cyclic product was obtained in toluene as a solvent after 48 h stirring at room temperature (Table 1). Then, we focused on the use of the nanocopper catalyst in various solvents. The results showed that the reaction was effective in polar solvents and water was selected as the main solvent for the synthesis of triazoles.

Then, the model reaction was carried out in the presence of 5, 10 and 15 mg of catalyst. Also, 10 mg of catalyst was used at 25, 50 and 75 °C. Although 50 and 75 °C led to good yields, preferably the reaction was performed at room temperature (Table 1, entries 1–4 and 6). Thus, the optimized reaction conditions were 10 mg of nanocatalysts in water at room temperature for 2 h.

Under these conditions, the click reaction was extended to a variety of epoxides. The results are presented in Table 2. We examined the reactions with several epoxides to produce regioselective products with good yields.

The use of aliphatic epoxides yields a single regioisomer through preferential attack at more hindered terminal carbon atom. Regioselectivity is decreased in the case of aromatic epoxides but also gives more substituted regioisomers **3a**–**3 l** in good yields. Epoxide activated by the nanocopper catalyst is effective in azide attack to more hindered terminal carbon atom of epoxide. This eventually leads to the production of more substituted regioisomers **3a**–**3 l** (Scheme 2).

To investigate catalyst recyclability, the reaction of phenylacetylene, styrene oxide and sodium azide as model reaction was examined. For this purpose, after completion of the reaction, the mixture was centrifuged in a test tube and was then decanted to separate the heterogeneous catalyst. The heterogeneous catalyst was washed several times with methanol and dried at room temperature for 20 min. The nanocatalyst was reused three times without much change in yields with the three runs giving yields of 75, 73 and 70%, respectively.

Then, the performances of various catalysts in the model reaction (styrene oxide, sodium azide and phenylacetylene in a 1:1:1 molar ratio) were compared (Table 3). Cu/Cu_2O NSs as a catalyst was used in water without using any toxic co-catalyst at room temperature, in contrast to some nanoparticles or nanohybrids which catalyse the same reaction at high temperature or in the presence of a co-catalyst.

4 | CONCLUSIONS

We have developed a simple and useful method for the synthesis of β-hydroxy-1,4-disubstituted 1,2,3-triazoles via a three-component reaction of epoxide, sodium azide and alkyne with Cu/Cu_2O NSs as a catalyst in water, without using any toxic co-catalyst or solvent at ambient temperature. This protocol can be used to produce a diverse range of single regioisomer products. Some of these β-hydroxy-1,4-disubstituted 1,2,3-triazoles have been synthesized for the first time. The Cu/Cu_2O NSs can be easily recycled and reused without significant loss of catalytic activity. Also the ball milling approach that was used in the preparation of the Cu/Cu_2O NSs is a simple method and provides the nanocatalyst through a solid-state reaction.

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How to cite this article: Esmaeili-Shahri H, Eshghi H, Lari J, Rounaghi SA. Click approach to the three-component synthesis of novel β-hydroxy-1,2,3-triazoles catalysed by new (cu/Cu_2O) nanostructure as a ligand-free, green and regioselective nanocatalyst in water. *Appl Organometal Chem*. 2017;e3947. https://doi.org/10.1002/aoc.3947