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Uniform copper nanoparticles as an inexpensive and efficient catalyst for synthesis of novel β-carbonyl-1, 2, 3-triazoles in water medium

Hadi Esmaeili-Shahri[1] · Hossein Eshghi[2] · Jalil Lari[1] · Seyyed Amin Rounaghi[3] · Effat Esmaeili-Shahri[1]

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Abstract

Copper nanoparticles as an efficient, inexpensive catalyst were prepared via ball milling for synthesis of β-carbonyl 1, 2, 3-triazoles from azido alcohol by click reaction in water. An extensive range of raw materials such as sodium azide, phenacyl bromide, epichlorohydrin, and terminal alkynes were used. Complete reduction of CuO in presence of $NaBH_4$ was done via ball milling with a ball-to-powder weight ratio of 50:1 under air atmosphere at room temperature. The final copper nanoparticles (Cu NPs) were characterized by SEM, EDX, XRD and FT-IR. The Cu NPs catalyzed one-pot three component synthesis of β-carbonyl 1, 2, 3-triazoles at room temperature with short reaction time and high product yields. The catalyst could be easily recovered and reused in several successive runs.

Keywords Click chemistry · Copper nanoparticles · β-carbonyl-1, 2, 3-triazoles · Green solvent

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✉ Hossein Eshghi
heshghi@um.ac.ir

[1] Department of Chemistry, Faculty of Science, Payame Noor University, PO Box 19395-3697, Tehran, Iran

[2] Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran

[3] Department of Materials Engineering, Birjand University of Technology, 9719866981 Birjand, Iran

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Introduction

The growing demand for novel pharmaceuticals has led researchers to use facile, high-yield and biologically oriented synthetic methods. In recent years, the advent of click chemistry has propelled the field of synthetic methodologies [1–4]. The Huisgen reaction is a common click reaction, which proceeds via a thermal 1, 3-dipolar cycloaddition reaction of azides and alkynes. The Huisgen reaction was promoted by using copper-based catalysts in azide-alkyne cycloaddition (CuAAC) reaction for production of a wide range of five-membered heterocycles [5–10]. 1, 2, 3-Triazoles are a significant class of heterocyclic compounds with an extensive range of industrial use such as optical brighteners, solar cells, herbicides and fungicides. Additionally, the 1, 2, 3-triazole family is found in new synthetic drugs for many diseases, such as cancer and HIV (Fig. 1) [8–14]. Substitution on the 1, 2, 3-triazole ring, such as carbonyl groups, increases the efficiency of these structures.

The placement of substrates in 1, 4-disubstituted 1, 2, 3-triazole rings also affects the pharmaceutical and biological activity of these substances. It is very important to make 1, 2, 3-triazoles from available low-cost raw materials. Based on research literature, reaction of sodium azide, terminal alkenes, and alpha halo ketones was used for synthesis of 1, 4-disubstituted 1, 2, 3-triazoles [2–4, 6, 7, 12, 15, 16].

Heterogeneous catalysts with recyclable properties are widely used in chemical synthesis [2–4, 12]. An important branch of heterogeneous catalysts is metallic nanocatalysts that provide the high surface-to-volume ratios for catalytic performances [11, 12].

The possibility of producing nanocatalysts on large scales is a key point [2–4]. From among heterogeneous catalysts, heterogeneous copper catalysts are very important in the synthesis of heterocyclic compounds, because of minimized product contamination and high purity of the product in copper catalyzed processes. Copper nanostructure catalyzes 1, 4-disubstituted 1, 2, 3-triazole and 1, 5-disubstituted 1, 2, 3-triazole cyclization reaction in short reaction time and high yields [2–4, 6, 12, 18]. Representatively, 1, 2, 3-triazoles have been synthesized in metal-free and azide-free conditions [19–27].

In this work, Cu nanoparticles (Cu NPs) were prepared via ball milling, and after full characterization were used for the synthesis of novel β-carbonyl -l, 2, 3-triazoles and triazole azido alcohols. Cu NPs have very useful properties, such as heterogeneity, possibility of being produced on a large scale and reusability without any structural changes.

The first step in realization of this goal was the synthesis of the different terminal alkynes via reaction of phenol and its derivatives with propargyl bromide (Scheme 1a). Then, novel β-carbonyl -l, 2, 3-triazoles were synthesized via Cu NPs catalyzed cyclization reaction of sodium azide, terminal alkynes and halo ketones in water at room temperature (Scheme 1b). The performance of this catalytic system in producing nearly pure products at high yield was excellent.

In the following, a multi-stage synthesis was planned by using the same catalyst (Cu NPs) for the synthesis of triazole azido alcohol to design drugs. This

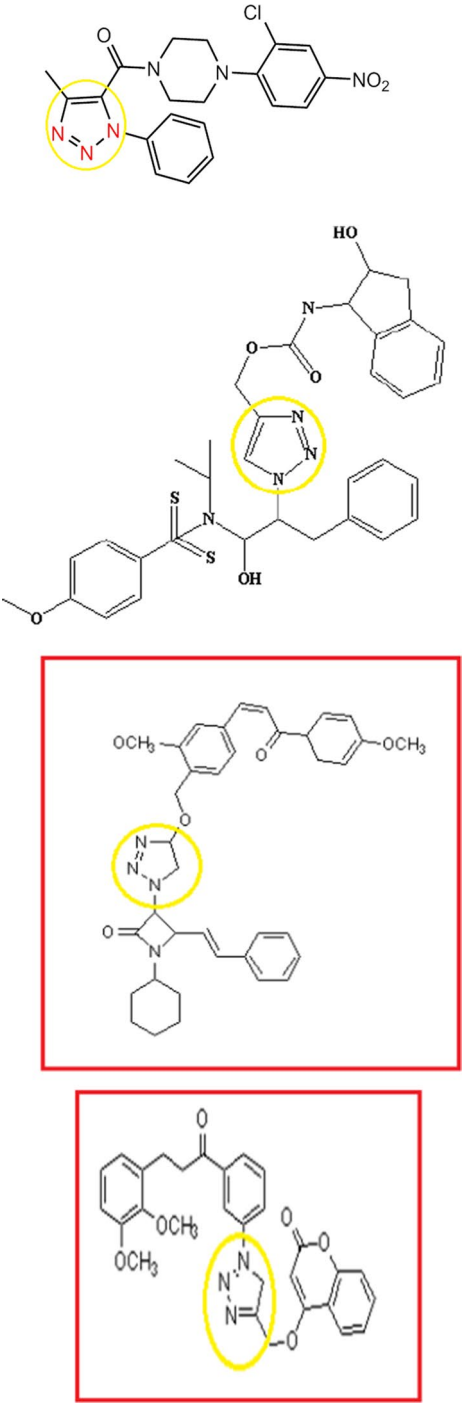
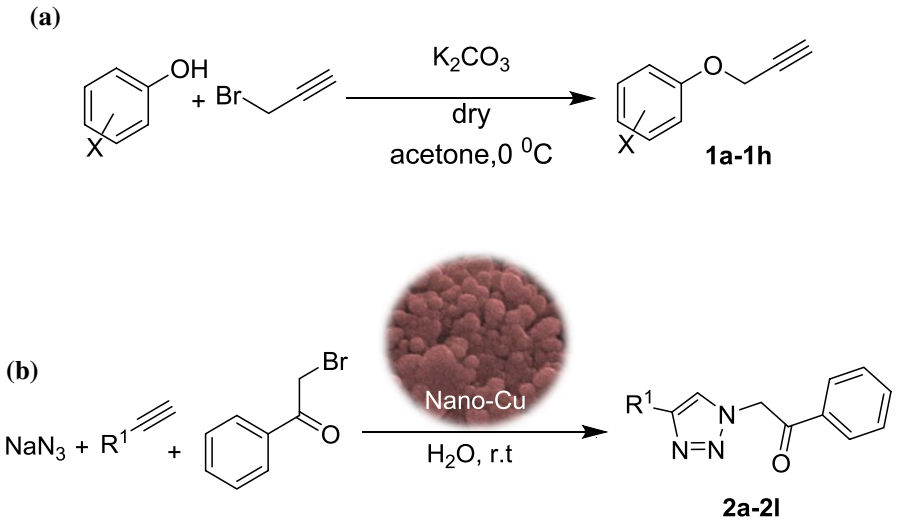


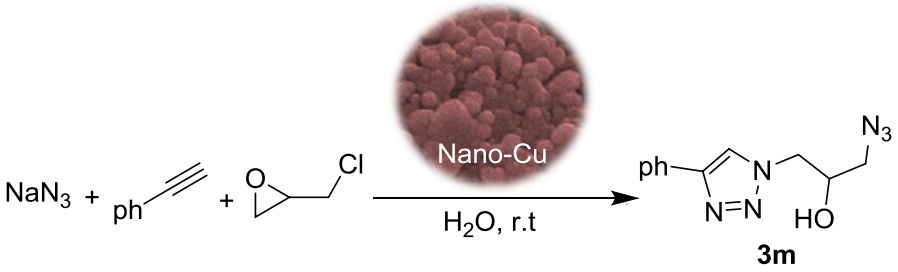
Fig. 1 Some derivatives of 1, 2, 3-triazole with a biological application



Scheme 1 **a** The synthesis of terminal alkynes of phenol. **b** Multicomponent synthesis of β-carbonyl -1, 2, 3-triazoles from halo ketone

azidotriazole alcohol was synthesized through the simplest raw materials, such as sodium azide alkyne and α-halocton (as well as in some cases instead of α-halate ketone, epichlorohydrin). We intend to react with triazole azido alcohol with nitrile to make important polycyclic compounds. At this stage, the same catalyst (Cu NPs) is used, but because there were no facilities for product purification, work on this part is still in progress [17, 30, 31] (Scheme 2).

In order to increase the scope of work, the reaction was carried out with ethyl-2-bromoacetate and 1-chloropropan-2-one as another alkylating agents, which did not produce significant results due to instability of these reagents in water. We are also reminded that our previous work was devoted to this reaction with epoxides in the presence of different catalyst [2].



Scheme 2 Multicomponent synthesis of triazole azido alcohol from epichlorohydrin

Experimental

Instruments and reagents

All reagents were purchased from Merck and Sigma-Aldrich Company and used in the same situation without purification. Electrothermal Type 9100 was used to measure the melting point. By using DMSO-d_6 or $CDCl_3$ as a deuterat solvent, the ^1H and ^{13}C NMR spectra were obtained on a Bruker DRX 300 MHz Avance spectrometer at 300 and 75 MHz. Chemical shifts are presented in ppm downfield from TMS as internal standard; coupling constants *J* are given in Hertz. Microstructure, phase characterization of the catalyst were recorded using a Philips X'Pert X-ray diffractometer (XRD) with Cu Kα radiation ($\lambda = 0.154056$ nm), and the diffraction data were collected over a 2θ range of 5–95° with a step width of 0.02°. FT-IR spectra were prepared at room temperature by a Thermo Nicolet Avatar 370 infrared spectrometer, using KBr pellets (USA). Using a Tescan Mira 3 scanning electron microscope (SEM) that operated at 20 kV, the powder morphology was studied and elemental contained were curtained by using an Ansamx EDS instrument with 15.00 eV resolution.

The synthesis of Cu NPs from CuO

At the start of construction operations, CuO (2.43 g) was combined with $NaBH_4$ (0.57 g) to create a CuO/$NaBH_4$ molar ratio of 2 [2–4]. The above mixture was placed in a hardened steel vial filled with steel balls (10 mm diameter), and a weight ratio of 50:1 was used between ball-to-powder. The 70-min milling procedure was operated with a rotating speed of 250 rpm in ambient atmosphere at high energy. Before using the catalyst for synthesis, purification was done, and the mixture was cleaned with distilled water/methanol (3:1) (2 × 10 mL) to remove $NaBH_4$ and boron oxides [2–4].

The synthesis of terminal alkynes (1a–1h)

K_2CO_3 (10 mmol) 1.38 g and phenols (10 mmol) in dry acetone (15 mL) at 0 °C were stirred, then propargyl bromide 1.19 g (10 mmol) was added to this mixture. The mixture was allowed to reach room temperature. Under these conditions, it was stirred for 17 h. After evaporation of the solvent, the product was extracted with ethyl acetate (3 × 10 mL). The organic phase was washed with water, cold NaOH (5%) and saturated brine and finally dried with anhydrous $MgSO_4$. The organic phase was evaporated, and terminal alkynes 1a–1h were obtained in 85–60% yield [18].

General procedure for the synthesis of β-carbonyl 1, 2, 3-triazoles (2a–2l)

The terminal alkynes (1.0 mmol), phenacyl bromide 0.199 g (1.0 mmol), sodium azide 0.078 g (1.2 mmol) and Cu NPs (0.01 g) were stirred in water (5 mL) as a

solvent. Progress of the reaction was monitored using TLC in n-hexane/ethyl acetate (4:1). After completion of the reaction, to separate the heterogeneous catalyst, the total reaction mixture was centrifuged. In this way the catalyst was separated from the mixture. The upper phase was diluted with H_2O (5 mL), and extracted with ethyl acetate (3 × 10 mL). Saturated brine was used twice for washing the organic phase and this phase was dried with anhydrous $MgSO_4$. β-carbonyl-1, 2, 3-triazoles were obtained after the solvent evaporation in vacuum. Although the obtained β-carbonyl-1, 2, 3-triazoles are almost pure, in order to increase their purity, column chromatography from a silica gel column and ethyl acetate-hexane as eluent was used. Finally, the used heterogeneous catalyst was washed with methanol three times and dried in room temperature.

Spectral data of representative compounds

2.5a Phenyl-2-(4-phenyl-1,2,3 triazol-1-yl)ethanone (*2a*)[18, 28, 29, 35, 41]: Light yellow solid, yield: 75%, $C_{16}H_{13}N_3O$, M.p.: 143 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.05 (d, 2H, Ar, J = 6 Hz), 7.99 (s, 1H, CH), 7.90 (d, 1H, Ar, J = 6 Hz), 7.71 (t, 1H, Ar, J = 6 Hz), 7.58 (t, 2H, Ar, J = 8.5 Hz), 7.47 (t, 2H, Ar, J = 8.5 Hz), 7.38 (t, 2H, Ar, J = 8.5 Hz), 5.92 (s, 2H, CH_2) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.3, 134.6, 133.9, 132.5, 130.49, 129.2, 128.8, 128.4, 128.2, 125.8, 121.5, 99.96, 55.51 ppm.

2.5b 2-(4-Hydroxymethyl-1,2,3 triazol-1-yl)-1-phenyl-ethanone (*2b*)[18, 37–39]: Light yellow solid, yield: 72%, $C_{11}H_{11}N_3O_2$, M.p.: 106 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (dd, 2H, Ar, J_1 = 8.4 Hz, J_2 = 1.5 Hz), 7.74 (s, 1H, CH), 7.71 (td, 1H, Ar, J_1 = 7.5 Hz, J_2 = 1.5 Hz), 7.59 (t, 2H, Ar, J = 7.5 Hz), 5.90 (s, 2H, CH_2), 4.89 (s, 2H, CH_2), 2.40 (b, 1H, OH) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.2, 134.7, 133.9, 129.2, 128.1, 123.5, 56.76, 55.44 ppm. FT-IR (KBr): ν_{max}: 3306, 1691 and 1229 cm^{-1}.

2.5c 2-(4-(phenoxy methyl)-1H-1,2,3-triazol-1-yl)-1-phenyl-ethanone (2c)[40]: Dark green solid, yield: 68%; $C_{17}H_{15}N_3O_2$, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.03 (d, 2H, Ar, J = 7.5 Hz), 7.82 (s, 1H, CH), 7.70 (t, 1H, Ar, J = 7.5 Hz), 7.57 (t, 2H, Ar, J = 7.5 Hz), 7.33 (t, 2H, Ar, J = 7.8 Hz), 7.05–6.98 (m, 3H, Ar), 5.88 (s, 2H, CH_2), 5.28 (s, 2H, CH_2) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.2, 158.2, 144.5, 139.4, 134.7, 133.9, 129.2, 128.1, 127.4, 127.1, 125.8, 124.6, 123.5, 116.8, 115.9, 56.7, 55.4 ppm.

2.5d 2-(4-((4-chlorophenoxy)methyl)-1H-1,2,3-triazol-1-yl)-1-phenylethanone (2d): Dark solid; yield: 61%; $C_{17}H_{14}N_3O_2Cl$, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.02 (d, 2H, Ar, J = 7.8 Hz), 7.83 (s, 1H, CH), 7.70 (t, 1H, Ar, J = 7.2 Hz), 7.56 (t, 2H, Ar, J = 7.8 Hz), 7.27 (d, 2H, Ar, J = 8.7 Hz), 6.95 (d, 2H, Ar, J = 8.7 Hz), 5.89 (s, 2H, CH_2), 5.23 (s, 2H, CH_2) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.2, 156.8, 155.2, 139.4, 134.7, 134.0, 133.8, 129.3, 128.5, 128.0, 127.8, 127.3, 126.1, 124.6, 116.8, 115.9, 62.1, 55.5 ppm.

2.5e 1-phenyl-2-(4-((o-tolyloxy) methyl)-1H-1,2,3-triazol-1-yl)ethanone (2e): Black oily compound; yield: 74%; $C_{18}H_{17}N_3O_2$, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, 2H, Ar, J = 7.5 Hz), 7.81 (s, 1H, CH), 7.71 (t, 1H, Ar, J_1 = 7.5 Hz), 7.58 (t, 2H, Ar, J = 6 Hz), 7.20 (dd, 2H, Ar, J_1 = 9 Hz, J_2 = 9 Hz), 7.05 (d, 1H, Ar),

5.88 (s, 2H, CH_2), 5.30 (s, 2H, CH_2), 2.29 (3H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.2, 158.2, 144.7, 138.6, 134.6, 133.9, 129.3, 129.3, 129.2, 128.1, 124.7, 122.1, 115.7, 112.4, 111.6, 61.9, 55.44, 21.5 ppm; FT-IR (KBr): ν_{max}: 3096, 1702, 1496, 1226 cm^{-1}. Molecular Weight: 307.0.

2.5f 1-phenyl-2-(4-((m-tolyloxy)methyl)-1H-1,2,3-triazol-1-yl)ethanone (2f)[36]: Yellow crystal clear; yield: 84%; $C_{18}H_{17}N_3O_2$, ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 8.04$ (d, 2H, Ar, $J = 9$ Hz), 7.81 (s, 1H, CH), 7.71 (t, 1H, Ar, $J = 6$ Hz), 7.57 (t, 2H, Ar, $J = 9$ Hz), 7.21 (t, 1H, Ar, $J = 9$ Hz), 6.85 (m, 3H, Ar), 5.87 (s, 2H, CH_2), 5.27 (s, 2H, CH_2), 2.36 (3H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 75.6 MHz): $\delta = 190.2$, 156.4, 145.0, 134.6, 133.9, 130.9, 130.7, 129.2, 129.1, 128.1, 127.0, 126.7, 124.4, 120.9, 114.9, 62.3, 55.49, 16.2 ppm; FT-IR (KBr): ν_{max}: 3141, 1702, 1595, 1223 cm^{-1}. Molecular Weight: 307.0.

2.5g 1-phenyl-2-(4-((p-tolyloxy)methyl)-1H-1,2,3-triazol-1-yl)ethanone (2g): White crystal clear; yield: 77%; $C_{18}H_{17}N_3O_2$, M.p.: 136 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.02 (d, 2H, Ar, $J = 7.5$ Hz), 7.80 (s, 1H, CH), 7.70 (t, 1H, Ar, $J = 7.5$ Hz), 7.56 (t, 2H, Ar, $J = 7.8$ Hz), 7.11 (d, 2H, Ar, $J = 8.4$ Hz), 6.92 (d, 2H, Ar, $J = 8.4$ Hz), 5.86 (s, 2H, CH_2), 5.24 (s, 2H, CH_2), 2.31 (3H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.2, 156.1, 144.8, 134.6, 133.9, 130.5, 130.0, 129.2, 129.1, 128.1, 127.0, 126.7, 124.6, 120.8, 114.7, 62.1, 55.4, 20.5 ppm. Molecular Weight: 307.0.

2.5h 2-(4-((4-nitrophenoxy)methyl)-1H-1,2,3-triazol-1-yl)-1-phenylethanone (2h): Orange oily compound; yield: 60%; $C_{17}H_{14}N_4O_4$, M.p.: 115 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, 2H, Ar, $J = 7$ Hz), 7.88 (s, 1H, CH), 7.71 (t, 1H, Ar, $J = 7.2$ Hz), 7.53 (t, 2H, Ar, $J = 7.8$ Hz), 7.14-7.079 (m, 4H, Ar), 5.40 (s, 2H, CH_2), 4.50 (s, 2H, CH_2) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.2, 165.7, 142.2, 141.3, 134.4, 134.2, 133.9, 133.2, 129.0, 128.6, 127.1, 125.9, 122.9, 116.1, 115.2, 62.7, 55.71 ppm, FT-IR (KBr): ν_{max}: 3261, 1697, 1592, 1510 and 1341 cm^{-1}.

2.5k 4-((1-(2-oxo-2-phenylethyl)-1H-1,2,3-triazol-4-yl)methoxy)benzonitrile (2k): Light yellow crystal; yield: 62%; $C_{18}H_{14}N_4O_2$. M.p.: 138 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.0 (d, 2H, Ar, $J = 7.2$ Hz), 7.87 (s, 1H, CH), 7.68 (t, 1H, Ar, $J = 9$ Hz), 7.64–7.52 (m, 4H, Ar), 7.11–7.05 (m, 2H, Ar), 5.92 (s, 2H, CH_2), 5.32 (s, 2H, CH_2) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): 190.1, 161.4, 143.3, 134.7, 134.0, 133.9, 133.7, 129.2, 129.0, 128.5, 128.1, 127.9, 125.1, 119.1, 115.6, 104.5, 62.3, 55.9 ppm. FT-IR (KBr): ν_{max}: 3141, 2227, 1696, 1608 and 1228 cm^{-1}.

2.5l 2-(4-((2-chloro-5-methylphenoxy)methyl)-1H-1,2,3-triazol-1-yl)-1-phenylethanone (2l): White must blanket crystal; yield: 70%; $C_{18}H_{16}N_3O_2Cl$, M.p.: 113.5 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, 2H, Ar, $J = 9$ Hz), 7.87 (s, 1H, CH), 7.68 (t, 1H, Ar, $J = 6$ Hz), 7.54 (t, 2H, Ar, $J = 6$ Hz), 7.23 (d, 2H, Ar, $J = 9$ Hz), 6.94 (s, 1H, Ar), 6.75 (d, 2H, Ar, $J = 6$ Hz), 5.88 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 2.34 (3H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 190.2, 153.4, 138.1, 134.6, 133.8, 129.8, 129.1, 129.0, 128.1, 124.9, 124.7, 122.8, 119.9, 119.8, 115.2, 62.3, 55.59, 21.36 ppm.

General procedure for the synthesis of triazole azido alcohol (3 m)

Phenyl acetylene (1 mmol) 1.2 g, NaN_3 (4 mmol) 0.268 g and epichlorohydrin (2 mmol) was stirred in water (8.0 mL) in the presence of the Cu NPs (0.01 g) at room temperature for 5 h. After completion of the reaction (monitored by TLC) the mixture was diluted with ethyl acetate (5 mL). In the following, the Cu NPs catalyst was separated by centrifuging. Then 5 mL water was added to the reaction mixture and extracted with EtOAc (3×10 mL). By saturated brine, organic phases was washed and dried with anhydrous $MgSO_4$. Solvent was evaporated in vacuum and triazole azido alcohol was obtained in 45% yield. The column chromatography from silica gel column and ethyl acetate-hexane as eluent was used to increase purity of products.

2.6a 1-azido-3-(4-phenyl-1H-1,2,3-triazol-1-yl)propan-2-ol (*3m*) [10, 30]: $C_{11}H_{12}N_6O$, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.67 (d, 2H, Ar, $J = 12.9$ Hz), 7.60 (s, 1H, CH), 7.71 (m, 3H, Ar, $J = 7.2$ Hz),4.83 (b, 1H, OH), 4.21 (m, 2H, CH_2), 3.69 (m, 1H, CH), 3.39 (m, 2H) ppm.

Results and discussion

Characterization of catalyst

Based on our previously reported method for synthesis of Cu nanostructures (NSs), [2–4] the molar ratio of $CuO/NaBH_4$ is an important factor in crystalline structure of obtained Cu nanoparticles. With a $CuO/NaBH_4$ molar ratio of 4, the ratio of Cu NPs to CuO and Cu_2O NSs was low [2–4]. Therefore, a modified method was used for the synthesis of Cu NPs. In this modified method, the molar ratio of $CuO/NaBH_4$ was 2. The Cu NPs were synthesized via ball mill reduction with very high purity, which was further investigated with SEM, EDS, FT-IR and XRD analyses.

As shown in Fig. 2a, SEM image of catalyst revealed that Cu nanoparticles are spherical. The particles of the catalyst are in the size of the nanoparticles. Also, the EDS result indicated that the elemental composition of the catalyst is Cu and O, which can be attributed to the existence of CuO nanoparticles (Fig. 2b).

The peaks at 567 cm^{-1} and 621 cm^{-1} in the FT-IR spectrum of the catalyst can be attributed to the stretching vibrations of a Cu–O bond. Also, the peak located at 721 cm^{-1} was attributed to Cu_2O species, which were produced from surface oxidation of Cu NPs. Specified peaks appeared in the range of 1008–1333 cm^{-1} related to the combination of B and O, which are unwittingly produced in the production process [32, 33] (Fig. 3).

The crystalline structure of catalyst was studied with XRD analysis, as shown in Fig. 4. It is clear that CuO was reduced to Cu NPs. Characteristic diffraction peaks of Cu nanoparticle were observed in the XRD pattern.[2–4, 35] Weak peaks at 2θ 36.5°, 39° and 2θ 36.5° in XRD pattern are related to CuO, Cu_2O, respectively [2–4, 34, 35]. The appearance of these compounds is probably due to the surface oxidation of the sample. Also, no diffraction peaks were observed for boron species in

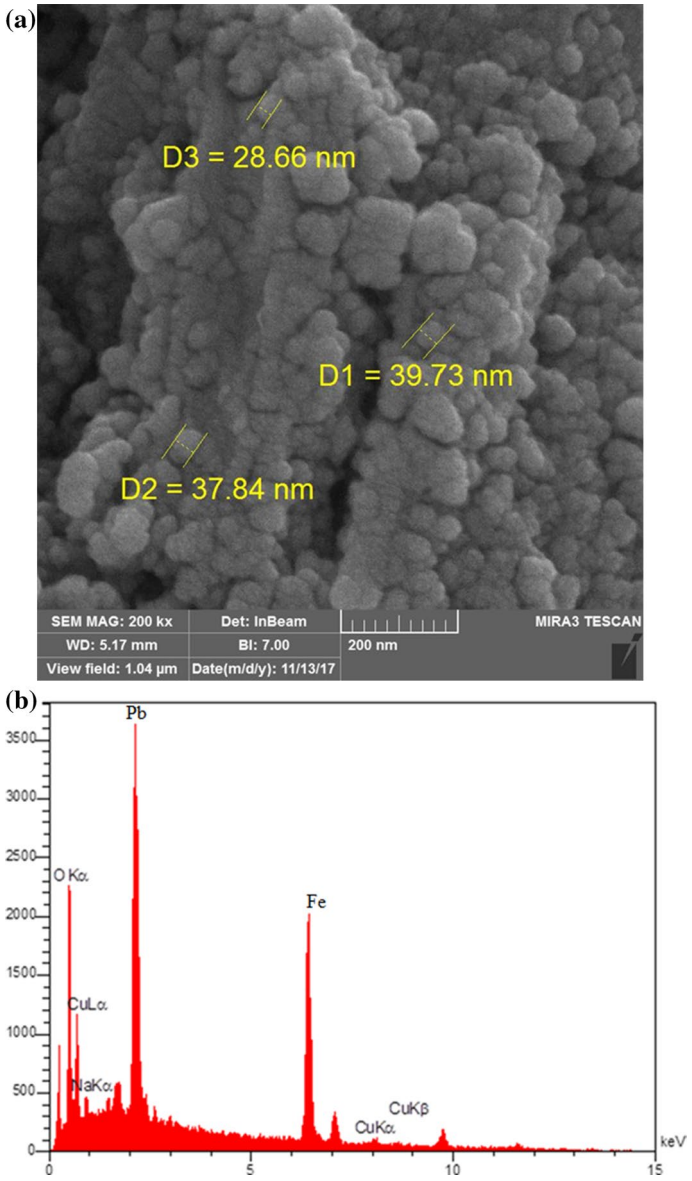


Fig. 2 **a** SEM image of synthesized Cu nanocatalyst, **b** EDS analysis of synthesized Cu nanocatalyst

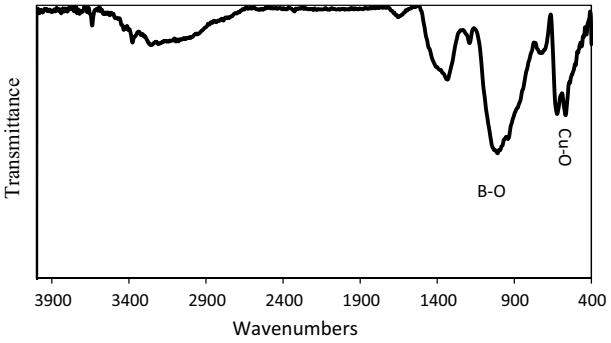
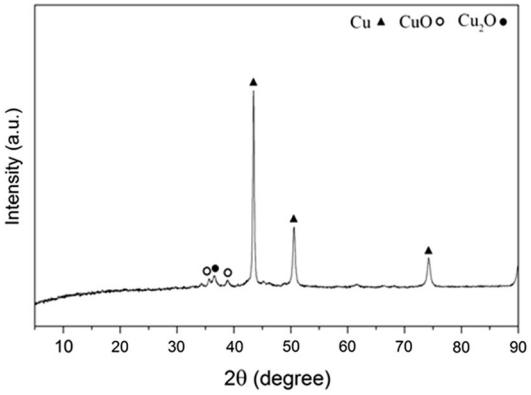


Fig. 3 FT- IR spectrum of synthesized Cu nanocatalyst

Fig. 4 XRD pattern of synthesized Cu nanocatalyst



the XRD spectrum of catalyst, which indicates the non-crystalline structure of these compounds and purity of catalyst.

Catalytic activity of Cu nanocatalyst in synthesis of β-carbonyl-1, 2, 3-triazoles with different terminal alkynes

At the beginning, the desired terminal alkynes were synthesized from reaction of phenol derivatives and propargyl bromide in high yields (Table 1). In continuation, reaction of sodium azide, phenyl acetylene and phenacylbromide (2-bromo-1-phenylethanone) was selected as a model reaction. In toluene as a solvent at room temperature without any catalyst no cyclic products were obtained even after 36 h (Table 2, entry 1). In the presence of a catalyst, different solvents were tested for model reaction (Table 2, entries 4–7). It was concluded that the polar solvents were more effective in this reaction. By increasing the catalyst amount from 0.01 to 0.1 g, no significant increase was observed in the reaction yield. Also, different temperatures (25, 50, 75 °C) were tested for model reaction with 0.01 g of catalyst. Based on these results, 0.01 g of catalyst in water and room temperature was selected as optimized reaction condition.

Table 1 The synthesis of terminal alkynes (1a–h)

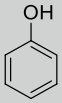
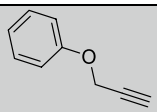
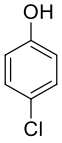
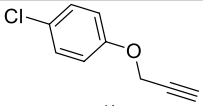
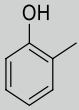
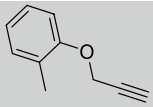
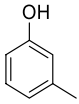
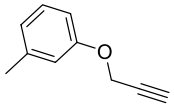
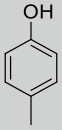
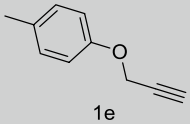
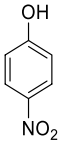
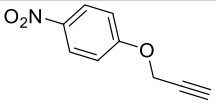
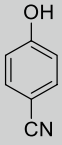
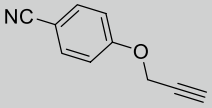
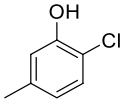
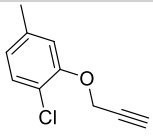
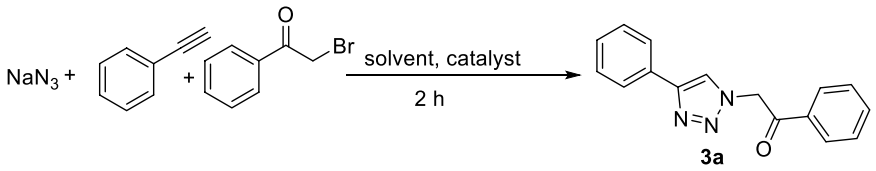
	Phenol	Products	Yield%
1		 1a	**75**
4		 1b	**60**
5		 1c	**82**
6		 1d	**85**
7		 1e	**80**
8		 1f	**65**
9		 1g	**60**
10		 1h	**74**

Table 2 Optimization of the reaction condition



Entry	Solvent	Temperature (°C)	Catalyst loading (g)	Yield (%)
1	Toluene	25	0	0
2	DMF	25	0.010	65
3	Ethanol	25	0.010	63
4	Water	25	0.010	80
5	Water	25	0.020	81
6	Water	25	0.025	80
7	Water	25	0.100	82

Subsequently, different types of terminal alkynes with electron-withdrawing group and electron-donating groups have been used in described conditions in the click reaction. All products with high yields and purity were obtained (Table 3).

For the recyclability study of the catalyst, phenacyl bromide, phenyl acetylene, and sodium azide were selected as model reaction. For this purpose, at the end of the reaction, heterogeneous catalyst was separated by centrifuging. The heterogeneous catalyst was washed three times with methanol and dried at room temperature for 2 h. Without an extreme change in yields, the catalyst was reused for three times with 85, 75, and 70% of yields for runs 1-3, respectively.

The performance of the catalyst was compared with other catalytic systems. Various catalysts have been used in the synthesis of triazoles. Some of these catalysts produce 1, 4-disubstituted 1, 2, 3-triazoles and some other 1, 5-disubstituted 1, 2, 3-triazoles. Different catalysts were compared in terms of efficiency and type of substitution product in reaction model (phenacyl bromide, sodium azide and phenyl acetylene in a 1:1:1 molar ratio). Cu NPs (this work), were used in the absence of any toxic co-catalyst which promote the reaction at room temperature in water as a green solvent. The different catalysts (efficiency and type of substitution product in synthesis of β- carbonyl 1, 2, 3-triazole) was compared with the other same research (Table 4).

For the chemical structure study of products, the ^{1}H- NMR NOESY spectrum was obtained from product 2 g. The NOESY effects between both methylene hydrogen and triazole proton confirm the 1, 4-disubstituted-1, 2, 3-triazole product in comparison with 1,5-disubstituted 1,2,3-triazole (Figs. 5, 6).

Table 3 Synthesis of β-carbonyl - 1, 2, 3-triazoles

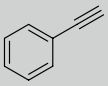
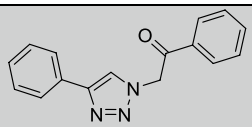
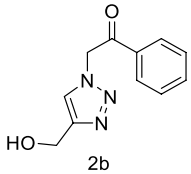
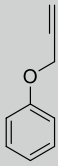
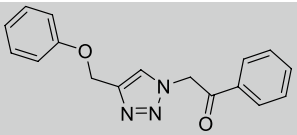
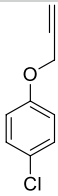
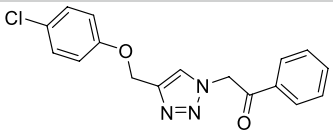
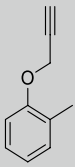
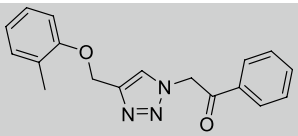
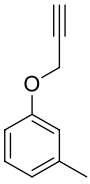
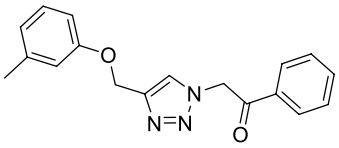
	Alkyne	Products	Yield %
1		 2a	75
2		 2b	72
3		 2c	68
4		 2d	61
5		 2e	74
6		 2f	84

Table 3 (continued)

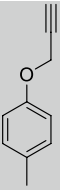
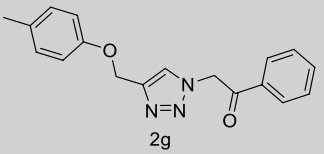
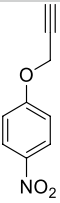
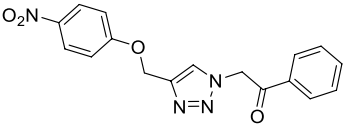
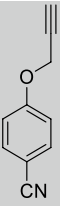
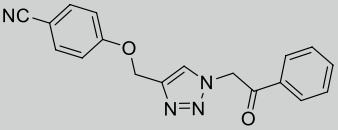
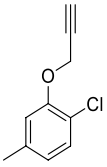
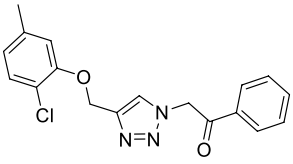
7		 2g	77
8		 2h	60
9		 2k	62
10		 2l	70

Table 4 Comparison of different catalysts (efficiency and type of substitution product in synthesis of β-carbonyl 1, 2, 3-triazoles) (3a)

Entry	Catalyst	Yield (%)	Time (h)	Temperature(°C)	References
1	Cu(I)-Catalyzed	87	24	100	[34]
2	$Cp^*RuCl(PPh_3)_2$	–	0.8	r.t	[36]
3	$[Cp^*RuCl_2]_2$	–	2	r.t	[36]
4	Cp_2Ni/Xantphos	83	8	r.t	[35]
5	Cu nanoparticle	75	2	r.t	This work

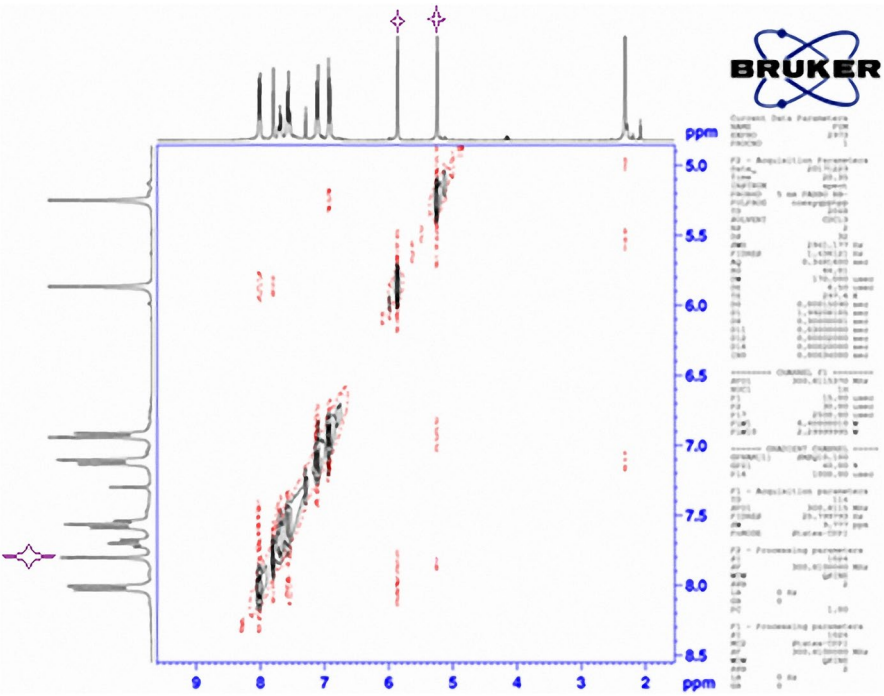


Fig. 5 ^{1}H- NMR NOESY spectrum 1,4-Disubstituted-1,2,3-triazoles (2g)

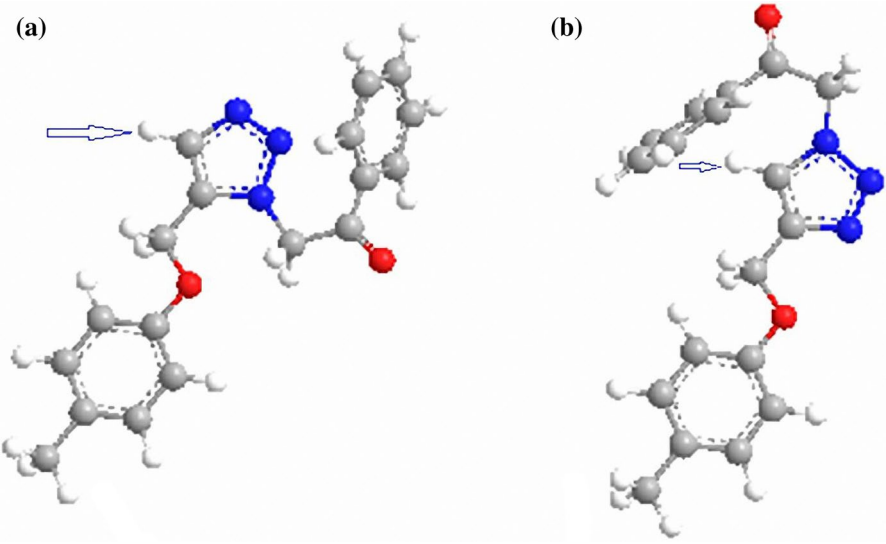
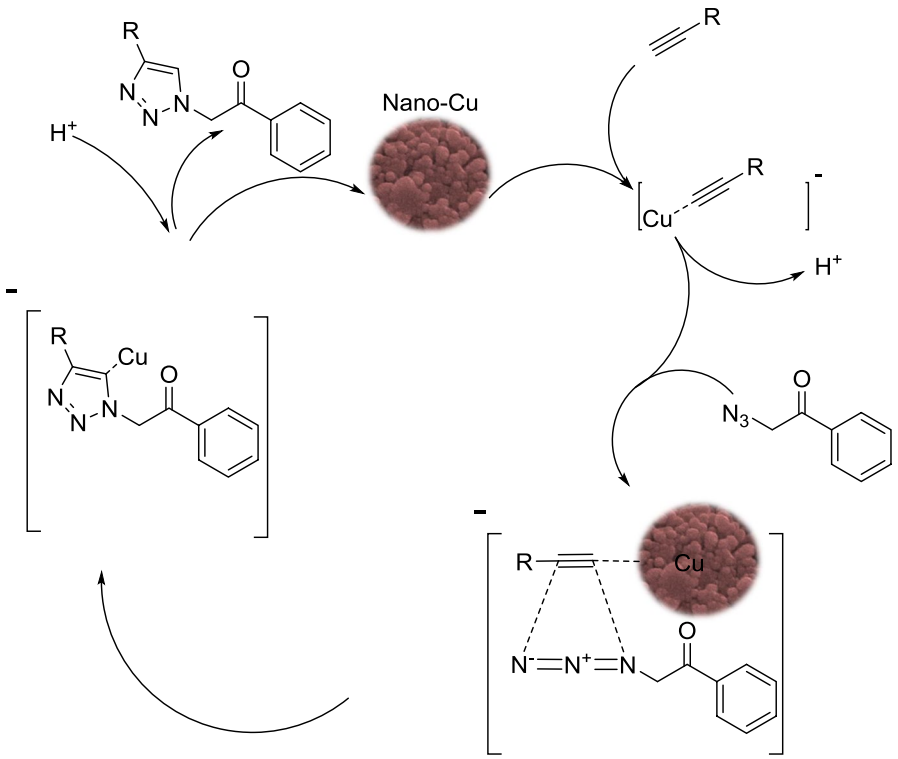


Fig. 6 1,5-disubstituted-1,2,3-triazoles (**a**) 1,4-Disubstituted-1,2,3-triazoles (**b**)



Scheme 3 Suggested mechanism

Finally, we suggested a mechanism which Cu (I) in the surface of Cu nanoparticles is responsible for this click reaction as outlined in Scheme 3 [9].

Conclusion

We have presented a simple and effective method for synthesis of β-carbonyl-1, 2, 3-triazoles through a multicomponent reaction of terminal alkyne, sodium azide and phenacyl bromide (or epichlorohydrin). The Cu NPs were synthesized as a recyclable catalyst for room temperature synthesis of triazoles in water, without using any toxic solvent or co-catalysts. This protocol can be applied to provide a wide range of β-carbonyl-1, 2, 3-triazoles with high purity. Some of these β-carbonyl-1, 2, 3-triazoles are new, and for the first time have been reported. Also, this protocol can be used for production of triazole azido alcohol, as they are very useful precursor in the synthesis of pharmaceutical derivatives. In addition, simplicity in catalyst preparation and its reusability without significant change in catalytic activity are the advantages of this method.

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