



Nanoporous metal-organic framework $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ as an efficient heterogeneous catalyst for one-pot facile synthesis of 1,2,3-triazole derivatives in ethanol: Evaluating antimicrobial activity of the novel derivatives

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KEYWORDS

Triazoles;
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Abstract. Solvent-free ball-milling synthesized porous metal-organic framework $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ (BDC: benzene-1,4-dicarboxylic acid, DABCO: 1,4-diazabicyclo [2.2.2]octane) has been proved to be a practical catalyst for facile and convenient synthesis of 1,2,3-triazole derivatives via multicomponent reaction of terminal alkynes, benzyl or alkyl halides, and sodium azide in ethanol. Avoidance of usage and handling of hazardous organic azides, using ethanol as an easily available solvent, and simple preparation and recycling of the catalyst make this procedure a truly scale-up-able one. The high loading of copper ions in the catalyst leads to efficient catalytic activity and hence, its low-weight usage in reaction. The catalyst was recycled and reused several times without significant loss of its activity. Furthermore, novel derivatives were examined to investigate their potential antimicrobial activity via microdilution method.

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1. Introduction

1,2,3-triazoles are 5-membered heterocyclic compounds that are present in many biologically active compounds such as anti-bacteria [1], anti-fungal [2], anti-cancer [3], and anti-HIV [4] drugs. They are also used in dyes [5], corrosion inhibitors [6], and anti-oxidants [7] and applied as organic synthesis intermediates. The uncatalyzed reaction of Alkynes and Azides Cycloaddition (AAC) (Huisgen cycloaddition) is thermodynamically

disfavored and proceeds slowly by producing poor yields of 1,4- and 1,5-regioisomers [8]. In 2002, Sharpless et al. first discovered the regioselective synthesis of 1,2,3-triazoles catalyzed by Cu (I). The dramatic changes in the regioselective synthesis of triazoles, including short reaction time and high yield of products, marked the new concept of click chemistry in science [9]. The copper used in AAC reaction can be obtained from three sources, including Cu (I) salts (along with bases and/or ligands), Cu (II) salts with a reducing agent (usually sodium ascorbate), and metallic copper [10].

In many of the reported click reactions, acetylenic compound reacts with organic azides [11,12]. From the point of view of safety, some of these organic azides

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have explosive nature and are not favorable [13]. To solve this problem, in-situ reaction of organic halides and sodium azide in the same pot with acetylenic substrate is strongly recommended. Many reported click reactions have been performed by employing homogeneous catalysts involving copper [14–17]. However, use of homogeneous copper complexes brings its own problems, especially in pharmaceutical industry, in which removing even trace amounts of heavy metals from the end products is necessary [18]. To overcome this difficulty, heterogenizing the homogeneous catalyst is a worthwhile effort [19,20]. For this purpose, many solid materials have been used as solid supports, including alumina [21], mesoporous silica [22], magnetic nanoparticles [23], magnetic starch [24], protein scaffolds [25], hydroxyapatite [26], etc. In many cases, tedious preparation procedures, inefficient copper loading, catalyst leaching, and low thermal stability of catalyst are problematic. On the other hand, along with the mentioned problems, there are some substantial disadvantages such as the difficulty of accessibility to active sites and diffusion of reaction materials into the pores of the supported backbone, which often lead to reduction in reaction rate.

Metal-Organic Frameworks (MOFs) are considered as a multi-purpose supramolecular platform to develop heterogeneous catalysts [27], especially in organic reactions. Their high surface area, low density, and maneuverable designing make them highly interested catalysts in chemistry reactions [28]. MOFs can be produced by electrochemical, mechanochemical, sonochemical, solvothermal, and microwave-assisted methods [29]. Ball milling technique has several advantages over other methods, such as short reaction time, being solvent-free, quantitative yields, and high atom efficiency. Herein, we wish to report a straightforward procedure for synthesis of 1,2,3-triazole derivatives via one-pot multicomponent reaction of an acetylenic compound, an organic halide, and sodium azide catalyzed by ball-milling prepared $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ as a low-leaching, high-loading, clean, and recyclable catalyst in ethanol.

2. Experimental

2.1. Materials and instruments

For the preparation and characterization of the Cu-MOF, all the starting materials and the instruments were used as previously described elsewhere [30]. Acetylenic compounds, aryl/alkyl halides, sodium azide, sodium ascorbate, and solvents were purchased from Merck or Aldrich and used as received.

^1H NMR and ^{13}C NMR were recorded by a Bruker Avance DRX-500 instrument using deuterated dimethyl sulfoxide (d_6 -DMSO) and tetramethylsilane (TMS).

2.2. General procedure for preparation of $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$

Cu-MOF was prepared based on the previously described method [30]. In the 10 mmol scale, a mixture of $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$, H_2BDC , and DABCO with a molar ratio of 2:2:1 was used and 2.57 g of the pure catalyst was obtained, which corresponded to 91% isolated yield.

2.3. General procedure for reaction of terminal alkynes, aryl/alkyl halide, and sodium azide

In a 20-mL round-bottom flask, to a mixture of alkyne (1 mmol), halide (1 mmol), NaN_3 (1.2 mmol), 20 mol% Na-ascorbate (0.039 g), and 20 mg $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$, 2 mL ethanol was added. The reaction mixture was heated up to 60°C and stirred for an appropriate time, as indicated in Table 1. The reaction progress was monitored by TLC or GC. After reaction completion, the obtained colloidal particles were filtered and added to hot ethyl acetate. The second filtration removed the catalyst. Then, the solvent was evaporated under reduced pressure and the solid crude was recrystallized from n-hexane: EtOAc to afford the pure solid products. The structures of all products were determined based on their physical and/or spectral data compared with the data in the literature.

2.4. Antimicrobial activity

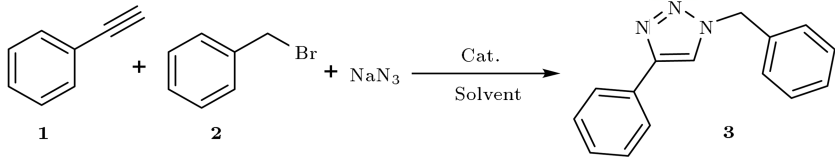
The new synthesized compounds were examined for their antimicrobial activity against two bacteria, namely *Staphylococcus aureus* ATCC 25923 and *Escherichia coli* ATCC 25922, and *C. albicans* ATCC 10231 as fungi by microdilution method. Microdilution susceptibility assay was performed using the NCCLS method to determine the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC). Cefixime was used as the standard in order to control antibacterial sensitivity and Nystatin as antifungal standard agent.

3. Results and discussion

3.1. Catalyst characterization

Ball milling reaction of 1,4-benzenedicarboxylic acid, DABCO, and copper (II) acetate at room temperature within 2 hours resulted in the formation of $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ as a green powder in a solvent-free manner [30] (Scheme 1). The catalyst was characterized by Powder X-Ray Diffraction (PXRD), SEM, TEM, BET, ICP, and FT-IR.

In FT-IR spectroscopy, the peak at 1620 cm^{-1} was assigned to COO asymmetric stretching mode and the peaks at 1564, 1506, 1151, and 1015 cm^{-1} were related to phenyl modes [31]. As it is obvious in Figure

Table 1. Optimization of reaction conditions in the reaction model^a.


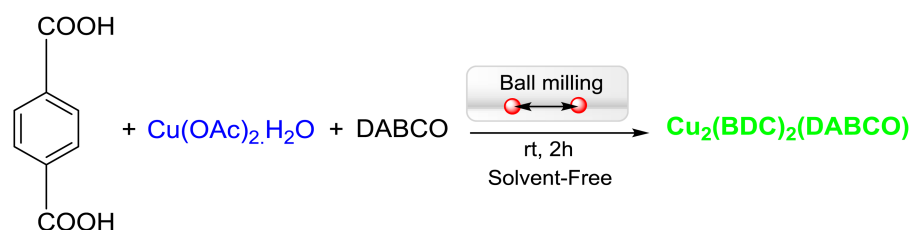
Entry	Cat.	Cat. amount (mg)	Sodium ascorbate (%mol)	Solvent	Temp. (°C)	Time	Yield (%) ^b
1	-	-	-	EtOH	rt	12 h	NR
2	-	-	-	EtOH	60	12 h	trace
3	Cu-MOF	20 mg	-	EtOH	60	1 h	68 ^c
4	Cu-MOF	20 mg	5	EtOH	60	1 h	81
5	Cu-MOF	20 mg	10	EtOH	60	45 min	85
6	Cu-MOF	20 mg^d	20	EtOH	60	45 min	98
7	Cu-MOF	10 mg	20	EtOH	60	45 min	88
8	Cu-MOF	30 mg	20	EtOH	60	45 min	98
9	Cu-MOF	20 mg	20	EtOH	rt	3 h	83
10	Cu-MOF	20 mg	20	DMF	60	2 h	7
11	Cu-MOF	20 mg	20	CH ₃ CN	60	2 h	20
12	Cu-MOF	20 mg	20	CH ₂ Cl ₂	reflux	2 h	trace
13	Cu-MOF	20 mg	20	THF	reflux	2 h	10
14	Cu-MOF	20 mg	20	neat	60	5 h	10

^a Phenylacetylene (1 mmol), sodium azide (1.2 mmol), benzyl bromide (1 mmol), sodium ascorbate (20 mol%, 0.039 g), solvent (2 mL).

^b Isolated yield.

^c The homocoupling product has been formed as by-product.

^d Corresponds to 7 mmol%.

**Scheme 1.** Synthesis of Cu₂(BDC)₂(DABCO) by ball-milling.

1, 2 θ peaks in XRD pattern have striking resemblance with the reported values in the literature [32].

The BET technique was adopted to evaluate porosity and surface area of ball-milling prepared Cu₂(BDC)₂(DABCO). The BET surface area of 1012 m²/g, obtained by ball-milling method, was considerably higher than the sonochemically prepared report by morsali et al. (499 m²/g) [32]. The mesoporousness of the catalyst was demonstrated by N₂ adsorption-desorption diagrams; the hysteric loop

from BJH desorption dV/dlog(D) pore volume diagram is shown in Figure 2 (pore diameter of 3.9 nm).

SEM and TEM images of the prepared Cu₂(BDC)₂(DABCO) are represented in Figures 3 and 4, which confirm nanoscale size and homogenous distribution of catalyst particles.

Additionally, the Cu content of Cu₂(BDC)₂(DABCO) was measured as 23 wt.% by inductively coupled plasma (ICP) technique.

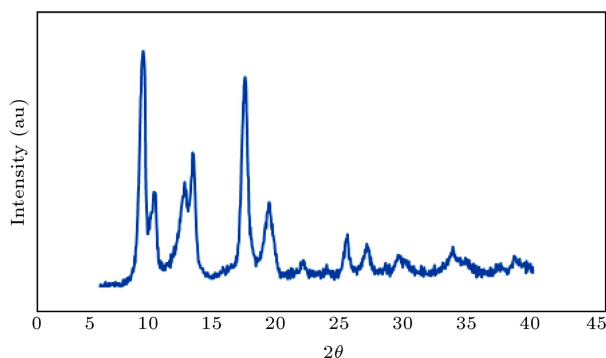


Figure 1. XRD pattern of ball-milling prepared nano $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$.

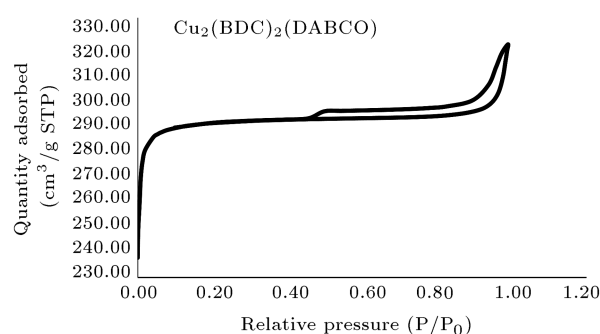


Figure 2. The N_2 adsorption-desorption isotherms of the nanoporous $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$.

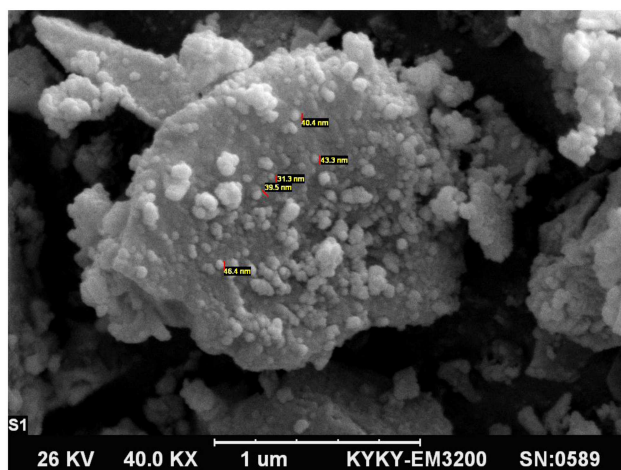


Figure 3. SEM photographs of $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$.

3.2. Optimization of reaction conditions

To find the optimized reaction conditions, reaction of phenyl acetylene, benzyl bromide, and sodium azide was chosen as the reaction model. As it is shown in Table 1 (entries 1 and 2), in the absence of the catalyst, no product was formed after 12 h at room temperature (entry 1). By warming the reaction content up to 60°C , only trace amount of the product was formed (entry 2). By employing $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ as catalyst in 10, 20, and 30 mg loading at 60°C in ethanol (entries 3-

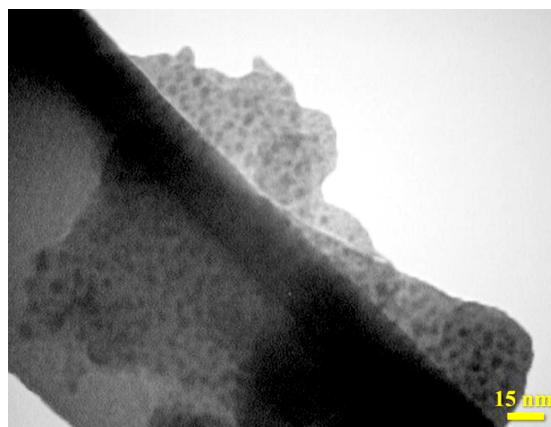


Figure 4. TEM images of $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$.

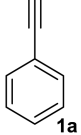
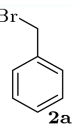
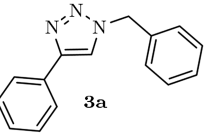
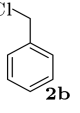
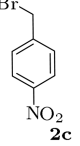
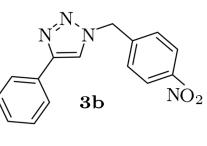
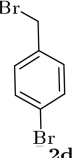
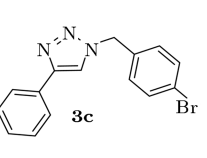
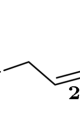
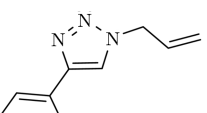
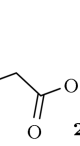
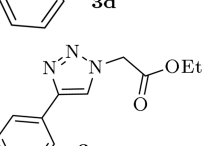
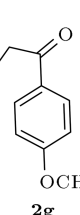
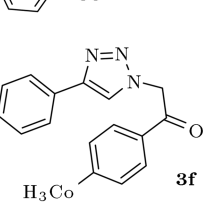
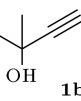
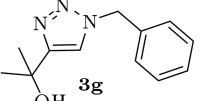
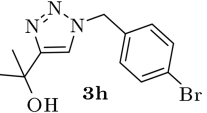
8), the desired product was formed in high to excellent yields, depending on the amount of the used sodium ascorbate. In the absence of sodium ascorbate (entry 3), homocoupling of phenyl acetylene occurred as side reaction, but by adding sodium ascorbate in 5, 10 and 20 mol%, only triazole product was formed. The best result was obtained when using 20 mg (7 mmol%) of Cu-MOF along with 20 mol% of sodium ascorbate (entry 6). Further increase in the catalyst did not change the yield, considerably (entry 6 versus 8). By comparing entry 6 with 9, we realized the importance of heating the reaction up to 60°C in contrast to room temperature. Other solvents were examined in the reaction model, but as it is apparent in Table 1 (entries 10-13), no other solvents surpassed the ethanol medium. Furthermore, in neat reaction condition, after 5 h, only 10% of the product was formed (entry 14).

Encouraged by these results, the scope of the reaction was extended to other substrates. As it is shown in Table 2, acetylenic compounds bearing electron withdrawing as well as electron donating groups (e.g., phenylacetylene, 4-methoxyphenylacetylene, 3-phenyl-1-propyne, and 1-nitro-4-(prop-2-yn-1-yloxy)benzene) led to the formation of triazoles in high to excellent yields with acceptable reaction times. Propargyl alcohol and 1,1-dimethylpropargyl alcohol were also converted to the corresponding products in good yields. On the other hand, some benzyl or alkyl bromide/chloride was chosen as a halide reactant. In all cases, chloride substrates required longer reaction times than bromide ones did, which was reasonable due to better effect of living group of bromide ion than that of chloride (compare, for example Table 2, entries 1 and 2). These results indicate that the catalytic systems can readily be applied to the three-component click synthesis of 1,4-disubstituted-1,2,3-triazoles.

3.3. Hot filtration test

In order to investigate catalyst leaching, a hot filtration test was carried out. For this purpose, the reaction of phenyl acetylene, benzyl bromide, and sodium azide

Table 2. Huisgen 1,3-dipolar cycloaddition catalyzed by $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ in ethanol.^a

Entry	Substrate 1	Halide 2	Product 3	Time	Yield (%) ^b	M.p. (°C) [Ref.]
1				45 min	98	128-130 (128-130) [33]
2	1a		3a	1 h	95	128-130 (128-130) [33]
3	1a			45 min	95	156-158 (156-157) [34]
4	1a			1 h	95	151-152 (151-152) [34]
5	1a			1 h	90	50-52 (56-57) [35]
6	1a			1.5 h	88	98-100 (97-99) [36]
7	1a			1.5 h	90	152-154 (155-157) [37]
8		2a		1 h	92	76-77 (76-77) [38]
9	1b	2b	3g	1.5 h	90	76-77 (76-77) [38]
10	1b	2d		1.5 h	92	115-117 (115-117) [39]

^a Reaction condition: Alkyne (1 mmol), alkyl halide (1 mmol), NaN_3 (1.2 mmol), sodium ascorbate (20 mol%), $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ (20 mg), solvent (EtOH, 2 mL), 60°C.

^b Isolated yield.

Table 2. Huisgen 1,3-dipolar cycloaddition catalyzed by $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ in ethanol^a (continued).

Entry	Substrate 1	Halide 2	Product 3	Time	Yield (%) ^b	M.p. (°C) [Ref.]
11		2a		1.5 h	93	73-75 (74-77) [40]
12	1c	2b	3i	2 h	90	73-75 (74-77) [40]
13		2a		1.5 h	90	100-102 (100-101) [41]
14	1d	2b	3j	1.5 h	87	100-102 (100-101) [41]
15	1d	2c		1 h	90	152-154 [present Work]
16	1d			1 h	92	80-82 [present Work]
17		2a		1.5 h	92	141-143 (142-145) [42]
18	1e	2b	3m	1.5 h	89	141-143 (142-145) [42]

^a Reaction condition: Alkyne (1 mmol), alkyl halide (1 mmol), NaN_3 (1.2 mmol), sodium ascorbate (20 mol%), $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ (20 mg), solvent (EtOH, 2 mL), 60°C.

^b Isolated yield.

was chosen in the described optimized reaction condition. For full investigation, we prepared two reaction pots at the same condition. After 20 min (half time of reaction), the catalyst was hot filtrated from both solutions. The rest of the mixture was stirred in one reaction pot (pot no. 1) for another 25 min, while the

other pot (pot no. 2) was worked up, which yielded 45% of the desired triazole. After another 25 min, the reaction in pot 1 was worked up and no further triazole production was observed. The same protocol was applied to the reaction of propargyl alcohol as acetylenic substrate with benzyl chloride and sodium

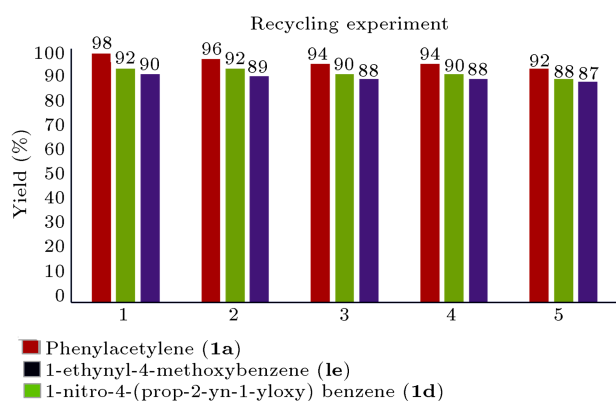


Figure 5. Recycling experiments on the reaction model and reactions with substrates with EDG and EWG substituents.

azide. Two reaction pots with the same materials were prepared and after 1 h, the catalyst was filtered from both reactions. One of the reactions (pot no. 1) was worked up, while the second one was stirred for further 1 h. The yield of both reactions was 49%, while the reaction for 2 h in the presence of the catalyst afforded 90% of the desired product (Table 2, entry 12). To secure this result, the solution in pot no. 1 was investigated by atomic absorption spectroscopy, which showed no copper ion in the reaction medium. The results demonstrated well heterogeneity of the catalyst.

3.4. Catalyst reusability

The reusability of the catalyst was investigated in further runs of the reaction model (phenyl acetylene, benzyl bromide, sodium azide) with 1-ethynyl-4-methoxybenzene and 1-nitro-4-(prop-2-yn-1-yloxy)benzene as representatives having electron donating (EDG) and electron withdrawing (EWG) groups, respectively. After each run, the recovered catalyst was washed with hot methanol several times and then, dried in a vacuum oven. The recovered catalyst was used for subsequent reaction runs without significant loss of activity (Figure 5). The XRD patterns after recovery cycles showed structural stability of catalyst in reaction medium (Figure 6).

3.5. Comparison with other studies

To show the merit of the present work for synthesis of 1,2,3-triazole derivatives, a comparison with the related literature using other catalysts was performed, the results of which are tabulated in Table 3. As it is shown, in some cases, inert atmosphere was needed (Table 3, entries 10 and 11), but in our method, the reaction was carried out in ethanol under normal atmospheric condition. Furthermore, all the compared studies required longer reaction times to complete the reaction model (up to 48 h), while our methodology needed only 45 minutes.

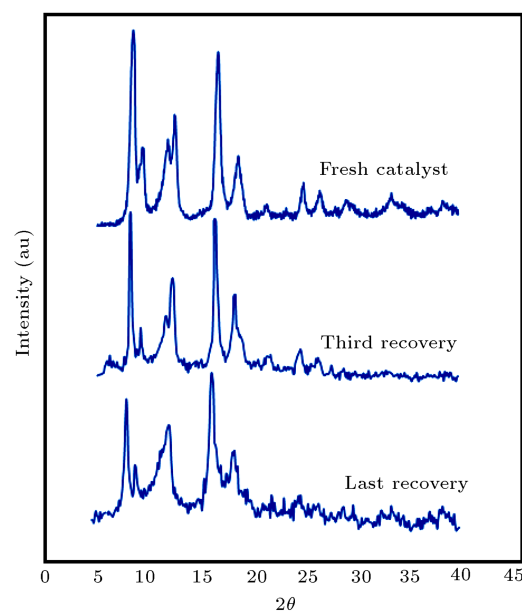
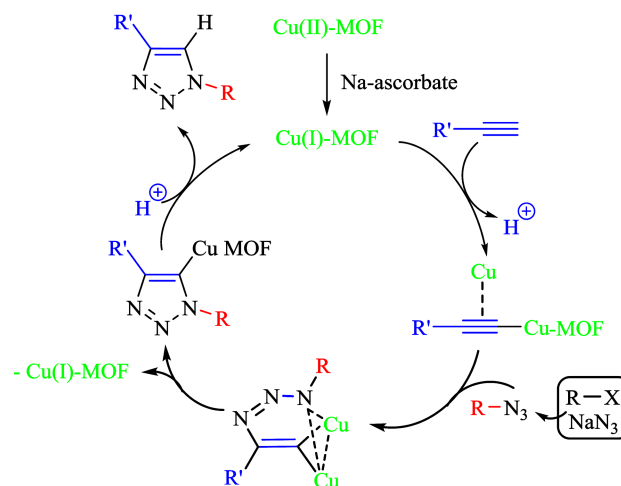


Figure 6. XRD patterns of fresh catalyst vs. recycled catalyst.



Scheme 2. Proposed reaction mechanism.

3.6. Proposed reaction mechanism

Based on the previous studies [54], a reasonable mechanism was proposed engaging two copper atoms (Scheme 2). As it is shown, the first copper atom coordinated the triple bond and afterwards, the acetylenic hydrogen was replaced with the second copper atom resulting in the formation of copper acetylide. This was followed by coordination with the in situ prepared organic azide. Subsequently, azide-alkyne 1,3-dipolar cycloaddition was formed to give the desired triazole product. Release of Cu-MOF ensured the initiation of another similar mechanism cycle.

3.7. Microbial studies

The new synthesized compounds (**3k** and **3l**) were screened in vitro for their antibacterial activity

Table 3. The comparison of $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ with reported catalysts in the synthesis of **3a**.

Entry	Catalyst	Catalyst loading	Time (h)	Temp. ($^{\circ}\text{C}$)	Reaction condition	Yield (%)	Ref.
1	CuSO_4 /sodium ascorbate	5 mol%	24	20	water; <i>t</i> -butyl alcohol	98	[43]
2	LS-Cu/sodium ascorbate ^a	5 mol%	8	80	Ethanol	96	[44]
3	Cellulose supported Cu(II) complex/sodium ascorbate	0.05 mol%	3	70	H_2O	95	[45]
4	MNP@PIL Cu/sodium ascorbate ^b	4 mg	2.5	50	H_2O	95	[46]
5	Tris(triazolyl)methanol-Cu(I)	0.25 mol%	8	40	Water	99	[47]
6	Cu-CPSIL ^c	1.0 mol%	48	20	Water	98	[10]
7	Silica-Immobilized NHC-Cu(I) ^d	0.5 mol% Cu	6	80	Water	98	[48]
8	HMS-DP-Cu(II) ^e	5 mol%	8	80	Ethanol	98	[49]
9	Porous copper	5 mol%	29	55	Water	96	[50]
10	CuI/1-benzyl-3-picolybenzimidazole iodide	CuI (0.01 mmol),	24	20	Water, inert atmosphere	95	[51]
11	CuI-zeolite	20 mg	15	90	Water, inert atmosphere	90	[52]
12	Cu-TPA ^f ; triethylamine	10 mol%	8	90	<i>N,N</i> -dimethyl-formamide	85	[53]
13	$\text{Cu}_2(\text{BDC})_2(\text{DABCO})$	20 mg	45 min	60	Ethanol	98	This Work

^a LS: Lignosulfonate.^b Copper sulfate in layered poly (imidazole-imidazolium) coated magnetic nanoparticles.^c Cross-linked polymeric ionic liquid material-supported copper.^d N-heterocyclic Carbene (NHC) ligands.^e 2-butoxy-3,4-dihydropyrans as dual anchoring reagents.^f Copper-exchanged phosphotungstic acid.**Table 4.** Antibacterial and antifungal activities of compounds **3k** and **3l**.

Novel compound	Bacterial strains				Fungal strain	
	<i>S. aureus</i>		<i>E. coli</i>		<i>C. albicans</i>	
	ATCC 25923	ATCC 25923	ATCC 25922	ATCC 25922	ATCC 10231	ATCC 10231
	MIC ^a ($\mu\text{g}/\text{mL}$)	MBC ^b ($\mu\text{g}/\text{mL}$)	MIC ($\mu\text{g}/\text{mL}$)	MBC ($\mu\text{g}/\text{mL}$)	MIC ($\mu\text{g}/\text{mL}$)	MBC ($\mu\text{g}/\text{mL}$)
3k ^c	128	> 128	256	> 256	64	64
3l ^d	256	> 256	256	> 256	128	128
Cefixime	0.5	2	0.12	0.5	–	–
Nystatin	–	–	–	–	16	64

^a Minimum inhibitory concentrations; ^b Minimum bactericidal concentrations;^c 1-(4-Nitrobenzyl)-4-((4-nitrophenoxy)methyl)-1H-1,2,3-triazole; ^d 1-Allyl-4-((4-nitrophenoxy)methyl)-1H-1,2,3-triazole.

against gram-positive (*Staphylococcus aureus*) and gram-negative (*Escherichia coli*) bacteria, and *Candida albicans* as fungi. The results were compared with standard drugs Cefixime and Nystatin that are given in the Table 4. Both of the compounds showed moderate activity against bacteria and relatively good activity against *C. albicans*. Meanwhile, from the biological viewpoint, **3k** was better than **3l**.

4. Conclusion

A mild, efficient, and recoverable catalytic system was developed for three-component reaction of terminal alkynes, benzyl or aryl halides, and sodium azide in ethanol. We found that various starting materials could exclusively produce 1,4-disubstituted-1,2,3-triazole regioisomers in high to excellent yields.

Negligible catalyst leaching approved by hot-filtration test, its reusability, and the straightforward ball-milling procedure for the formation of $\text{Cu}_2(\text{BDC})_2(\text{DABCO})$ are some exceptional advantages of the explained methodology. Also, the new compounds showed moderate to good biological activity.

Spectral data of the new compounds

1-(4-Nitrobenzyl)-4-((4-nitrophenoxy)methyl)-1H-1,2,3-triazole (3k)

White solid; yield 90%, mp: 152-154. IR (KBr): 634 (m), 729 (m), 844 (m), 1000 (m), 1107 (s), 1259 (s), 1330 (s), 1346 (s), 1498 (s), 1517 (m), 1595 (s), 3110 (w). ^1H NMR (500 MHz, DMSO): $\delta = 5.34$ (s, 2H), 5.82 (s, 2H), 7.27 ($J = 9.5$ Hz, d, 2H), 7.55 ($J = 8.5$ Hz, d, 2H), 8.22 ($J = 9.5$ Hz, d, 2H), 8.25 ($J = 8.5$ Hz, d, 2H), 8.42 (s, 1H). ^{13}C NMR (125 MHz, DMSO): $\delta = 51.7, 61.5, 115.0, 123.6, 125.2, 125.5, 128.8, 140.7, 141.9, 143.0, 146.9, 162.9$. Anal. Calcd for $\text{C}_{16}\text{H}_{13}\text{N}_5\text{O}_5$ (355.30): C, 54.09; H, 3.69; N, 19.71. Found: C, 53.92; H, 3.65; N, 19.57. $[\text{M}+\text{H}]^+$: Calc.: 356.0982, Meas.: 356.0982.

1-Allyl-4-((4-nitrophenoxy)methyl)-1H-1,2,3-triazole (3l)

Pale yellow solid; yield 92%, mp: 80-82. IR (KBr): 638 (m), 750 (m), 850 (m), 1010 (m), 1110 (m), 1263 (s), 1340 (s), 1512 (s), 1593 (s), 3132 (w). ^1H NMR (500 MHz, DMSO): $\delta = 5.04$ ($J = 6$ Hz, d, 2H), 5.24 (m, 4H), 6.06 (m, 1H), 7.27 ($J = 9.5$ Hz, d, 2H), 8.22 (s, 1H), 8.25 ($J = 9.5$ Hz, d, 2H). ^{13}C NMR (125 MHz, DMSO): $\delta = 52.6, 62.7, 116.2, 119.7, 125.8, 126.7, 133.5, 141.9, 142.7, 164.1$. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_3$ (260.25): C, 55.38; H, 4.65; N, 21.53. Found: C, 55.53; H, 4.61; N, 20.97. $[\text{M}+\text{H}]^+$: Calc.: 261.0989, Meas.: 261.0982.

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