Accepted Manuscript

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S0926-860X(15)30067-3
http://dx.doi.org/doi:10.1016/j.apcata.2015.07.015
APCATA 15462
Applied Catalysis A: General
16-4-2015
5-7-2015
6-7-2015

Please cite this article as: Mahnaz Tavassoli, Amir Landarani-Isfahani, Majid Moghadam, Shahram Tangestaninejad, Valliolah Mirkhani, Iraj Mohammadpoor-Baltork, Polystyrene-supported ionic liquid copper complex: A reusable catalyst for one-pot three-component click reaction, Applied Catalysis A, General http://dx.doi.org/10.1016/j.apcata.2015.07.015

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Polystyrene-supported ionic liquid copper complex: A reusable catalyst for one-pot three-component click reaction

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Highlights

■ A copper complex was attached to chloromethylated polystyrene > A heterogeneous catalyst was prepared > The catalyst was used for click reaction of alkynes and arylhalide > The catalyst was reusable Abstract- Copper(II) complex of 1,2-*bis*(4-pyridylthio)ethane immobilized on polystyrene was a used as a highly stable, active, reusable and green catalyst for click synthesis of 1,2,3-triazoles *via* one-pot three-component reaction of organic halides, sodium azide and alkynes. The catalyst was characterized by FT-IR spectroscopy, thermogravimetric analysis, elemental analysis, field emission scanning electron microscopy, energy dispersive X-ray, transmissiondiversity of organic halides or α-bromoketones and alkyl/aryl terminal alkynes, and excellent yields of the products were obtained using 0.2 mol% of catalyst. This catalytic system also showed excellent activity in the synthesis of bis-1,4-disubsitituted 1,2,3-triazoles. Moreover, the catalyst could be recycled and reused for seven cycles without any decrease in its catalytic activity.

Keywords: Copper complex; Click reaction; Polystyrene; Triazole; Ionic liquid.

1. Introduction

The use of transition metal complexes as catalyst has rapidly increased in recent years because of their ability to catalyze a wide range of chemical transformations [1]. Among them, Cu(II) complexes have long been found as effective catalysts in a variety of organic synthesis [2]. Due to their low cost, high

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activity and selectivity, these complexes have also found numerous industrial such as dehydrogenation of alcohols [3], methanol synthesis [4], production of hydrogen in fuel cells [5].

In last decade, the copper complexes have attracted much attention in click chemistry. Click chemistry, first introduced by the groups of Meldal [6] and Sharpless [7], describes a new concept for conducting organic reactions. Based upon the premise, organic synthesis should take advantages such as being modular, stereospecific, high-yielding and involving simple and green protocols [8]. Preparation of 1,2,3-triazoles by copper-catalysed alkyne-azide cycloaddition (CuAAC) has emerged as a prominent "*Click*" chemistry [9-11]. 1,2,3-Triazoles have received considerable attention in synthetic organic chemistry due to their numerous biological and pharmaceutical activities such as anti-HIV [12-14], antibacterial [15-17], and antiallergic [18] properties.

The typical procedure for synthesis of 1,2,3-triazoles is Huisgen [3+2] cycloaddition of organic azides and terminal alkynes in the presence of copper catalysts [19]. However, the early Huisgen cycloaddition process required a strong electron-withdrawing substituent on either azide or alkyne and high temperature for a prolonged period of time, and often afforded a mixture of 1,4-and 1,5disubstituted isomers. [20, 21] During the past decades, alternative copper-catalysed processes have represented a significant advance in regioselective synthesis of 1,2,3-triazoles [22-25]. In the first report of this reaction, the active Cu(I) species (CuI, CuBr) were directly formed from Cu(I) salts in the presence of ligands [26]. Because of the instability of Cu(I) salts, Cu(I) was prepared *in situ via* reduction of different Cu(II) salts (CuCl₂,CuBr₂ or CuSO₄) [27-30] with ascorbate or by comproportion of Cu(0) nano size clusters and Cu(II) [31, 32]. Nevertheless, the preparation of copper immobilized on supports such silica [33], Zeolite [34] and magnetic nanoparticles have become increasingly more profitable from easy recovery and economical viewpoints [35].

However, long reaction times, high temperature, formation of homocoupling products of alkynes (Glaser coupling) and the use of large amounts of copper are the limitations and drawbacks of many of the previously reported methods [36, 37]. Therefore, the development of a reusable, eco-friendly and

more convenient catalyst for the regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles is still in demand.

Accordingly, various procedures for the preparation of 1,4-disubstituted 1,2,3-triazoles through the *in situ* generation of organic azides have been developed. [38, 39] But, only a few reports are available dealing with the synthesis of bis-1,4-disubstituted 1,2,3-triazoles [40].

Ionic liquids are able to dissolve and stabilize copper salts for regioselective click reaction [41]. But they have some disadvantages such as difficulties in reusability of catalyst and product isolation, which make them economically and environmentally unfavorable. Thus, the ionic liquid supported species can solve this serious drawback [42].

Polystyrene as a solid support has gained substantial popularity, due to its low cost, ready availability, chemical inertness, and facile functionalization [43].

These results in combination with our efforts on the development of efficient copper catalysts for organic transformations [44-46], prompted us to report a green, convenient and regioselective method for synthesis of mono- and *bis*-1,4-disubstituted 1,2,3-triazoles in the presence of Cu(II) immobilized on polystyrene supported ionic liquid as a reusable catalyst (Scheme 1).



Scheme 1.Click reaction catalysed by Cu(II)-PsIL

2. Experimental Section

2.1. General Remarks

The chemicals were purchased from Fluka and Merck chemical companies. FT-IR spectra were recorded on a JASCO 6300D spectrophotometer. ¹H and ¹³C NMR (400 and 100 MHz) spectra were recorded on a Bruker Avance 400 MHz spectrometer using CDCl₃ as solvent. Elemental analysis was performed on a LECO CHNS-932 analyzer. Thermogravimetric analysis (TGA) was carried out on a Mettler TG50 instrument under air flow at a uniform heating rate of 10 °Cmin⁻¹ in the range 30-600 °C. The scanning electron micrographs were taken on a Hitachi S-4700 field emission-scanning electron microscope (FE-SEM). The transmission electron microscopy (TEM) was carried out on a Philips CM10 transmission electron microscope operating at 100 kV. The copper content of the catalyst was determined by a Jarrell-Ash 1100 ICP analysis. The CV measurements were carried out on Autolab Potentiostat/Galvanostat101 instrument controlled by Nova 1.8 Software (Eco Chemie, Utrecht, the Netherlands).

2.2. Synthesis of 1,2-bis(4-pyridylthio)ethane, (1)

A mixture of 4-bromopyridinium chloride (5.1 mmol, 1 g), 1,2-ethanedithiol (0.3 mL, 3.5 mmol) and sodium hydroxide (7.7 mmol, 0.3 g) in 10 mL of DMF was stirred at 80 °C for 24 h. The reaction progress was monitored by TLC (eluent diethyl ether/ methanol, 2:1). The mixture was diluted with water and EtOAc. The aqueous layer was extracted, and evaporated under reduced pressure. Then, residue was purified by recrystallization from ethanol to afford the pure product.

2.3. Immobilization of 1,2-bis(4-pyridylthio)ethane on polystyrene, (2)

In a round-bottomed flask equipped with a condenser and a magnetic stirrer bar, a mixture of chloromethylated polystyrene (1), (1 g) and 1,2-*bis*(pyridylthio)ethane, (0.1 g, 0.4 mmol) in DMF (10 mL) was stirred at 80 °C for 24 h. Then, the reaction mixture was filtered and the resulting solid washed with ethanol (2×20 mL) and dried in a vacuum oven at 50 °C.

2.4. Synthesis of polystyrene supported ionic liquid (PsIL), (3)

To a slurry of polystyrene-bound 1,2-*bis*(4-pyridylthio)ethane (2) (1 g) in toluene (10 mL) was added methyl iodide (5 ml) and stirred at room temperature for 6 h. Then, the mixture was filtered; the precipitate was washed with ethanol (2×20 mL) and dried in a vacuum oven at 50 °C.

2.5. Immobilization of Cu(II) triflate on PsIL, (Cu(II)-PsIL), (4)

A mixture of Cu(OTf)₂ (15 mg) and PsIL, (3), (1 g) in ethanol (10 mL) was refluxed for 24 h. The reaction mixture was filtered; the solid material was washed with ethanol (2×20 mL) and then dried in a vacuum oven at 40 °C to afford the Cu-PsIL catalyst.

2.6. Electrochemical studies

The cyclic voltammograms (CVs) were recorded at 25 °C using a three-electrode assembly including, an Ag/AgCl (3 M KCl) reference electrode, a large area Pt plate as the counter electrode (70 times larger than that of the working electrode), and the modified glassy carbon electrode (GCE) disk as the working. Toward the study of electrochemical behavior of Cu(II)-PSIL, the catalyst was casted on the GCE surface. CVs were recorded in acetate buffer electrolyte (pH= 5) at a potential scan rate of 10 mVs⁻¹.

2.7. General procedure for synthesis of 1,2,3-triazoles by the reaction of benzyl bromides, alkynes and sodium azide

A mixture of Cu(II)-PsIL (0.2 mol%, 10 mg) and sodium ascorbate (5 mg) in PEG-400 (2 mL) was allowed to stirrer for 2 min and then, benzyl bromide (1 mmol), sodium azide (1.2 mmol) and alkyl/phenyl acetylene were added to mixture. The reaction mixture was stirred at 65 °C and its progress was monitored by TLC (eluent diethyl ether/ethyl acetate, 2:1). After completion of the reaction, water and ethyl acetate were added; the catalyst was separated by filtration and washed with acetone and water, and dried under vacuum. The organic layer was separated and dried over Na₂SO₄. The products were purified by recrystallization from *n*-hexane/EtOAc.

2.8. General procedure for synthesis of 1,2,3-triazoles from α -bromo ketones, alkynes and sodium azide

A mixture of Cu(II)-PsIL (0.2 mol%, 10 mg) and sodium ascorbate (5 mg) in PEG-400 (2 mL) was allowed to stirrer for 2 min and then α -bromo ketones (1 mmol), sodium azide (1.2 mmol) and alkyl/phenyl acetylene were added to mixture. The reaction mixture was stirred at 65 °C. After completion of the reaction (as monitored by TLC, elutent diethyl ether/ethyl acetate, 1:1), water and ethyl acetate was added to mixture and catalyst was filtered and washed with acetone and water. The organic layer was dried over Na₂SO₄. If necessary, purification of product was performed by recrystallization from *n*-hexane/EtOAc.

2.9. General procedure synthesis of bis 1,2,3-triazoles

A mixture of Cu(II)-PsIL (0.4 mol%, 20 mg) and sodium ascorbate (10 mg) in PEG-400 (3 mL) was allowed to stirrer for 2 min and then 1,4 /1,2-*bis*(bromomethyl)benzene (1 mmol), sodium azide (2.4 mmol) and alkyl/phenyl acetylene were added to mixture. The reaction mixture was stirred at 65 °C. The reaction progress was monitored by TLC. The workup of the desired product was as described above.

3. Results and Discussion

3.1. Synthesis and characterization of Cu(II)-PsIL-

The preparation route for catalyst is shown in Scheme 2. The ligand, 1,2-*bis*(4-pyridylthio)ethane (**A**) was prepared by the reaction of 4-bromopyridinium chloride with 1,2-ethandithiol. Reaction of this ligand with chloromethylated polystyrene, PS, afforded the supported ligand, **B**. Then, **B** was reacted with methyl iodide in to prepare the polystyrene supported ionic liquid (PsIL). These processes were monitored by elemental analysis, FT-IR and thermogravimetric analysis (TGA). The nitrogen content of the PsIL, measured by CHNS analysis, showed a value of about 1.5%. Based on this value, the amount of IL supported on the polystyrene is about 0.53 mmolg⁻¹.



Scheme 2. The preparation route for catalyst

The FT-IR spectrum of the PsIL showed characteristic band of pyridinium ring at 1645 cm⁻¹ (C=N). In addition, the characteristic band at 1160 cm⁻¹ (C-S) was observed, while the FT-IR spectrum of polystyrene showed no band in this region (Fig. 1).

The thermal decomposition behaviour of polystyrene supported ionic liquid (PsIL) was also compared with chloromethylated polystyrene (Ps) by thermogravimetric analysis (TGA). As can be seen in Fig. 2, the curves show main weight loss from 350 to 450 °C, attributed to the main chain pyrolysis, commencing at about 350 °C with the evolution of aromatics from the degradation of the styrene. However, the weight loss curve of PsIL shows two steps. The second step from 450 to 550 °C is

attributed to the degradation of ionic liquid unit. These results clearly indicate that the ionic liquid or ligand have been covalently linked to polystyrene.

After preparation and characterization of PsIL, copper was immobilized on the polystyrene *via* complexation of copper(II) triflate with ligand to produce the polystyrene supported ionic liquid copper complex, Cu(II)-PsIL, (Scheme 2). The copper content of this catalyst, measured by ICP analysis, was obtained to be 0.2 mmol per gram of Cu(II)-PsIL.

The SEM images of the polystyrene and the Cu(II)-PsIL catalyst showed that the surface morphology of the two samples is different. The surface of the catalyst is rough due to the presence of ionic liquid ligand (Fig. 3). EDX analysis confirmed the presence of copper in the catalyst (Fig. 3c). The EDX analysis clearly showed the presence of chloride and iodide ions in the catalyst matrix.

As a further indication for the presence of iodide and chloride ions, the supported complex was used as an ion exchange resin in a column through which aqueous NaNO₃ solution was passed. After elution with H_2O , the eluate was analyzed for its halide ions content by the potentiometric titration. As can be seen in Fig. 4, the titration curve has two equivalence points for iodide and chloride which shows values about 0.59 and 0.53 mmolg⁻¹ for iodide and chloride ion, respectively. On the other hand, the amount of iodide ions clearly shows that all nitrogen pyridines have been quaternerized.

The Cu(II)-PsIL catalyst was also characterized by TEM (Fig. 5). The dark regions or black spots in the photograph demonstrate the copper species while the colourless parts belong to polystyrene, this is due to the higher electron density of copper compared to polystyrene supported ionic liquid.

3.2. Cyclic voltammetry of Cu(II)-PsIL

The redox behavior of Cu species with different oxidation states could be studied *via* some electrochemical techniques such as cyclic voltammetry (CV). According to the ability of ligand to stabilize the certain oxidation states of the metal, the distinct peaks are observed [47]. In the case of Cu, the two anodic peaks could be attributed to the conversion of Cu(0) to Cu (I) and Cu (I) to Cu (II) [47]. Fig. 6 represents the CVs of the Cu(II)-PSIL casted GCE in acetate buffer (0.1 M, pH= 5) solution before and after the treatment with sodium ascorbate as a reducing agent. The voltammogram in Fig. 6a

depicts the electrochemical behavior of Cu(II)-PSIL in its non-reduced form. The first anodic peak at approximate potential of -0.07 V, could be attributed to the conversion of Cu(0) to Cu(I) [48]. The second peak positioned at approximate potential of 0.21 V was also resulted from the conversion of Cu species to Cu(II) on GCE surface [49]. In reverse direction, the cathodic peak at -0.04 V was belonged to the reduction of Cu species [49]. The voltammogram in Fig. 6b belongs to the catalyst after reduction with sodium ascorbate. To obtain this species, the catalyst was stirred with sodium ascorbate for 30 min and then filtered. As can be seen, the peak corresponds to Cu(II) has been disappeared and only the peak attributed to the conversion of Cu(0) to Cu(I) presents. These observations clearly confirm the oxidation state of the copper species and also the reduction of Cu(II) to Cu(I) in the presence of sodium ascorbate.

3. 2. Investigation of catalytic activity of Cu(II)-PsIL in the synthesis of 1,2,3-triazole derivatives

First, the copper complex using CuCl₂ as the copper source was prepared and its catalytic activity was investigated in the model reaction. In this case only 15% of the corresponding triazole was produced. To increase the electron-deficiency of the copper centre, we decided to use the copper triflate as copper source. In the presence of triflates the interaction of copper centre and phenylacetylene will be increased. Therefore, the catalytic activity of Cu(II)-PsIL catalyst was investigated in click reaction. In this manner, the three-component reaction between phenyl acetylene (1 mmol), 4-bromobenzyl bromide (1 mmol) and sodium azide (1.2 mmol) in the presence of Cu(II)-PsIL was chosen as model reaction. The reaction conditions such as sodium ascorbate, amount of catalyst, the type of solvent and temperaturewere optimized and a summary of the optimization results is provided in Table 1.

When the model reaction was carried out in the absence of sodium ascorbate and catalyst at 65 °C; no product was formed under these conditions (Table 1, entry 1). In order to check the ability iodide ions in the reduction of Cu(II) to Cu(I), the model reaction was carried out in the presence of Cu(II)-PsIL (0.2 mol%) and in the absence of sodium ascorbate, in which only a trace amount of the desired product was obtained (Table 1, entry 2). For further investigation on effect of iodide ions on catalyst activity, the model reaction was performed in the presence of NaI instead of sodium ascorbate for

reducing of Cu(II) to Cu(I) (Table 1, entry 16). But, the result showed that the trace amount of the corresponding triazole was produced.

While, in the presence of Cu(II)-PsIL (0.2 mol%) and in the absence of sodium ascorbate, only a trace amount of the desired product was obtained (Table 1, entry 2). These results show that the Cu(II) species have low ability in catalysing this reaction. When, the same reaction was performed in the presence of Cu(II)-PsIL (0.2 mol%) and sodium ascorbate (5 mg), the highest yield was obtained. Then, the effect of different solvents was studied in the model reaction (Table 1, entries 3-11). It was found that, the solubility of sodium azide is an efficient parameter on the yield of the desired product. In aprotic polar and nonpolar solvents, the reaction gives very low yield probably because of poor solubility of sodium azide; while, in polar protic solvents, higher yield of the corresponding triazole was obtained (70%). Among the solvents examined, PEG-400 was found to be the best reaction medium. The effects of amount of the catalyst and temperature were also investigated; on increasing them, the yield of the desired product did not increase further (Table 1, entries 12 and 14), but the yield decreased on lowering these parameters (Table 1, entries 13 and 15).

Consequently, from the observations summarized in Table 1, we concluded that 0.2 mol% of the catalyst and 5 mg sodium ascorbate in PEG-400 at 65 $^{\circ}$ C, are the most appropriate reaction conditions for this transformation.

Using the optimized reaction conditions, the scope and applicability of the copper catalysed synthesis of 1,4-disubstituted 1,2,3-triazoles by the reaction of different alkynes and substituted benzyl bromides was explored. As can be seen in Table 2, both aromatic and aliphatic terminal acetylenes gave the corresponding triazoles in excellent yields, high purity, and excellent regioselectivity, in which only 1,4-regioisomeric products were formed. However, aryl alkynes required shorter reaction times compared to their aliphatic counterparts. It was also found that the benzyl bromides containing electron-donating and electron-withdrawing substituents reacted efficiently to afford the desired products in high yields.

Encouraged by the obtained results with benzyl bromides, the potential of this catalytic system in the synthesis of 1,4-disubstituted 1,2,3-triazoles using α -bromo ketones was also investigated. A variety of structurally divergent α -bromo ketones having different functional groups on the aromatic ring were reacted with terminal alkynes and sodium azide in thepresence of Cu(II)-PsIL/sodium ascorbate to generate the corresponding β -keto-1,2,3-triazoles in 87-98% yields at 65 °C within 10-25 min (Table 3, entries 1-5). Moreover, hetereocyclic α -bromo ketone such as 2-(bromoacetyl)furan participated well in this reaction under similar conditions to afford the desired product in 90% yield after 25 min (Table 3, entry 6).

In order to further widen the applicability of this catalytic system and due to the various applications of *bis*-triazoles in the field of coordination chemistry [50, 51], and as precursors for ionic liquids [52,53], the preparation of *bis*-triazoles was also studied. The results are summarized in Table 4. As the data demonstrate, the "*bis-click*" reaction of 1,2-*bis*(bromomethyl)benzene or 1,4-*bis*(bromomethyl)benzene with terminal alkynes and sodium azide was performed efficiently in the presence of Cu(II)-PsIL catalyst at 65 °C and the corresponding *bis*-1,2,3-triazoles were obtained in high yields.

Compared to most of the previously reported methods, the yield with the Cu(II)-PsIL catalyst is higher, the reaction time is shorter and the turn over frequency (TOF) is higher, indicating the efficiency of this method (Table 5).

3.3. Recycling of the Cu(II)-PsIL catalyst

The recycling and reusability of a catalyst are key roles in economical and environmental aspects. Therefore, the reusability of Cu(II)-PsIL was examined in the reaction of 4-bromobenzyl bromide with phenyl acetylene and in the presence of sodium azide under the optimized conditions. After completion of reaction, the mixture was first cooled to room temperature, diluted with water and ethyl acetate and the catalyst was separated by simple filtration and reused. The results showed that the catalyst could be reused seven consecutive times without significant loss of its catalytic activity (Fig. 7). The amount of copper leached

was determined by ICP which indicated that only a trace amount of copper (less than 2%) was leached in the first run.

4. Conclusions

In conclusion, we demonstrated a novel and eco-friendly strategy for regioselective synthesis of 1,4disubstituted-1,2,3-triazoles *via* one pot three-component reaction of substituted benzyl bromides, sodium azide and terminal alkyne in the presences of catalytic amounts of Cu(II) immobilized on polystyrene supported ionic liquid (Cu(II)-PsIL). This method is appropriate to both aromatic/aliphatic acetylenes and benzyl bromide/ α -bromo ketones, and generates a diverse range of triazoles in excellent yields. This catalytic system was also used efficiently for the synthesis of *bis*1,4-disubstituted-1,2,3triazoles. Ease of recovery and reuse of the catalyst, short reaction times, wide scope and simple workup procedure make this method a valid contribution to the existing methodologies.

Acknowledgments. The authors are grateful to the Research Council of the University of Isfahan for financial support of this work.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/.

Abbreviations:

<xps:span class=deft>Ps, Polystyrene; PsIL, Polystyrene supported ionic liquid; Cu(II)</xps:span>
<xps:span class=defd>PsIL, Polystyrene supported ionic liquid copper complex.</xps:span>

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Fig. 1. The FT-IR spectrum of: (a) chloromethylatedpolystyrene and (b) polystyrene-supported ionic liquid (PsIL).

Fig. 2. Thermogram of: (a) chloromethylatedpolystyrene (Ps), (b) polystyrene supported ionic liquid (PsIL).

Fig. **3.** SEM image of: (a) chloromethylated polystyrene, (b) Cu(II)-PsIL and (c) SEM-EDX spectrum of Cu(II)-PsIL.

Fig. 4. Potentiometric titration curve for iodide and chloride ions.

Fig. 5. TEM image of Cu(II)-PsIL.

Fig. 6. CVs of Cu(II)-PSIL modified GCE a) before and b)after treatment with sodium ascorbate in 0.1 M acetate buffer (pH= 5) and scan rate of 10 mVs^{-1} .

Fig. 7. Reusability of the Cu(II)-PsIL catalyst in the 1,4-disubstituted 1,2,3-triazole of benzyl bromide, phenyl acetylene and sodium azide.



Fig. 1. FT-IR spectrum of: (a) chloromethylated polystyrene and (b) polystyrene-supported ionic liquid (PsIL)



Fig. 2. Thermogram of: (a) chloromethylated polystyrene (Ps), (b) polystyrene supported ionic liquid (PsIL)



Fig. 3. SEM image of: (a) chloromethylated polystyrene, (b) Cu(II)-PsIL and (c) SEM-EDX spectrum of Cu(II)-PsIL



Fig. 4. Potentiometric titration curve for iodide and chloride ions



Fig. 5.TEM image of Cu(II)-PsIL



Fig. 6. CVs of Cu(II)-PSIL modified GCE a) before and b)after treatment with sodium ascorbate in 0.1





Fig. 7. Reusability of the Cu(II)-PsIL catalyst in the synthesis of 1,4-disubstituted 1,2,3-triazole from benzyl bromide, phenyl acetylene and sodium azide

Table 1. Optimization of conditions in the reaction of 4-bromobenzyl bromide with phenylacetylene



Entry	Catalyst Amount	Solvent	T [°C]	Time	Yield
	[mol%]			[min]	[%] ^a
1	-	PEG-400	65	15	_
2^{b}	0.2	PEG-400	65	15	Trace
3	0.2	Methanol	65	15	70
4	0.2	Toluene	65	30	40
5	0.2	H ₂ O	65	15	78
6	0.2	Ethanol	65	15	72
7	0.2	DMF	65	25	65
8	0.2	PEG-400/H ₂ O (1:1)	65	15	89
9	0.2	Ethanol/ $H_2O(1:1)$	65	15	75
10	0.2	PEG-400	65	15	99
11	0.2	Acetonitrile	65	30	38
12	0.3	PEG-400	65	15	99
13	0.1	PEG-400	65	30	71
14	0.2	PEG-400	85	15	99
15	0.2	PEG-400	45	30	73
16 ^c	0.2	PEG-400	65	30	Trace

^aIsolated yield.

^bWithout sodium ascorbate.

^cThe reaction was performed in the presence of sodium iodide instead of sodium ascorbate.

Table 2. Three-component synthesis of 1,4-disubstituted 1,2,3-triazoles from benzyl bromides catalyzed by Cu(II)-PsIL.



Entry	Benzyl bromide	R	Product	Time [min]	Yield [%] ^a
1	Br	Ph	Ph N=N, N-	15	99
2	-Br O ₂ N	Ph	Br Ph N=N Ph	15	95
3	Br	Ph	NO ₂ N=N Ph	12	99
4	Br	C ₆ H ₁₃		15	94
5	Br	C ₆ H ₁₃	N=N, N	20	95
6	O ₂ N Br	C ₆ H ₁₃	Br N=N, N N Oc	23	97
7	Br	C ₅ H ₁₁		20	93
8	Br	C ₅ H ₁₁	N=N, N	22	94
9	-Br O ₂ N	C ₅ H ₁₁	Br	23	98
			NO ₂		

^aIsolated yield.

Table 3. Three-component synthesis of 1,4-disubstituted 1,2,3-triazoles from α -bromo ketones catalyzed by Cu(II)-PsIL.

	Ar Br +	R-== +	+ NaN ₃ $\xrightarrow{Cu(II)-PsIL(0.2 \text{ mol}\%)}$ Sodium ascorbate (5 mg) PEG-400, 65 °C R N^{-N}		N O O Ar
Entry	α-Bromoketones	R	Product	Time [min]	Yield[%] ^a
1	Br	Ph	N≈ ^N o Br	10	98
2	O ₂ N Br	Ph		12	87
3	F Br	Ph	N = N N O	10	97
4	O Br OMe	C ₅ H ₁₁	N=N N O O O Me	10	96
5	O Br	C ₅ H ₁₁	N ^N N O	25	92
6	O Br	Ph	N=N N O	15	90

^aIsolated yield.

Table 4. Three-component synthesis of 1,4-disubstituted 1,2,3-triazoles from 1,2-*bis*(bromomethyl) and 1,4-*bis*(bromomethyl)benzene catalyzed by Cu(II)-PsIL.^a





^aReaction conditions: Organic halide (1 mmol), alkyne (2 mmol), sodium azide (2.4 mmol), Cu(II)-PsIL (0.4 mol%), sodium ascorbate (10 mg) in PEG-400 (3 ml) at 65 °C. ^bIsolated yield.

Table 5. Comparison of conventional protocols used for 1,4-disubstituted 1,2,3-triazoles.

Br	Br + Ph \rightarrow + NaN	3 [Cu]	$\rightarrow Ph$	Br	
Catalyst	Conditions	Time [min]	Yield [%] ^a	TOF	Ref.
Cu(II)-PsIL	PEG-400, 65 °C	15	99	1980	This work
Cu(II)-TD@nSiO ₂ ^b	Ethanol/H ₂ O (2:1), r.t	17	99	1166	[45]
CuFe ₂ O ₄	H ₂ O, 70 °C	180	93	6.2	[51]
Nano copper (I)	Ethanol, reflux	60	92	92	[52]
P ₄ VPy-CuI ^c	H ₂ O, reflux	20	89	215	[53]

^aIsolated yield.

^bCopper immobilized on nanosilica triazine dendrimer.

^cCopper iodide nanoparticles on poly(4-vinyl pyridine).