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Polystyrene resin-supported CuI-cryptand 22 complex: a highly efficient and reusable catalyst for three-component synthesis of 1,4-disubstituted 1,2,3-triazoles under aerobic conditions in water

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Polystyrene resin-supported copper(I) iodide-cryptand-22 complex (PS–C22–CuI) was synthesized and characterized by FT-IR, EDX, SEM, XPS, and TG-DTA analysis. This complex was found to be a highly active and robust heterogeneous catalyst for either three-component reaction of organic halides, sodium azide, and terminal alkynes, or the reaction of organic azides and alkynes to form 1,4-disubstituted 1,2,3-triazoles in good to excellent yields at room temperature, using water as the green solvent. The catalyst can be not only easily isolated from the final product by filtration but also reused without significant loss of catalytic activity.

1. Introduction

1,2,3-Triazoles have recently received a considerable amount of interest in organic synthesis and industry. They have been used in combinatorial chemistry, pharmaceuticals (drug discovery),[1] optical brighteners,[2] dyes,[3] agrochemicals,[4] the synthesis of macromolecular architectures,[5] and biologically active agents.[6] The 1,2,3-triazole core is a key structural motif in many bioactive compounds, exhibiting a wide range of activities, such as anti-HIV,[7] anti-microbial,[8] anti-allergic,[9] and anti-convulsant.[10]

The Huisgen 1,3-dipolar cycloaddition reaction between a terminal alkyne and an azide to generate substituted 1,2,3-triazoles is one of the most extensively studied click reactions to date. The formation of triazoles in 'click chemistry' has represented definitive advances: high yield and selectivity, optimal atom economy, the possibility of the application of solvents like water, and gentle reaction conditions. Usually, 1,4-disubstituted 1,2,3-triazoles are formed by stepwise cycloaddition of azides and terminal alkynes in the presence of copper catalysts.[11] When the reaction is performed with a ruthenium catalyst, the 1,5-adduct is preferred instead.[12] In homogeneous regiospecific alkyne-azide cycloaddition (AAC) reactions, the catalyst can be introduced as either a Cu(I) salt, or in situ reduction of Cu(II).[11,13–16] On the other hand, heterogeneous catalytic systems can have advantages, such as more surface area resulting higher loading of the active sites, simpler isolation of the reaction products and recycling of the catalyst systems by filtration.[17,18] Cu(I) AAC catalysts have been immobilized onto various supports, such as zeolites,[19] polymers,[20] silica-supported *N*-heterocyclic carbene,[21] activated charcoal,[22] alumina,[23] and titanium dioxide.[24] However, heterogeneous catalysts immobilized with Cu(I) species frequently suffer from its inherent thermodynamic instability, which results in its easy oxidation to Cu(II) and/or disproportionation to Cu(0) and Cu(II). Moreover, the use of copper(I) iodide has been avoided in many cases, because the in situ formed copper(I) acetylides derived from CuI undergo homocoupling upon exposure to air, yielding side products (Glaser coupling);[25] besides, the copper(I) acetylides are formed with extremely high reactivity and explosive nature in open air.[26,27] Consequently, using Cu(I) catalysts requires an inert atmosphere and anhydrous solvents. Nevertheless, nitrogen- or phosphorus-based ligands are known to protect the metal center from oxidation and disproportionation. The use of these ligands usually causes an enhancement of cuprous–catalytic activity.[17] Very recently, as part of our attempts to identify a robust and easily prepared system to catalyze carbon–carbon and carbon-heteroatom bond-forming reactions of terminal alkynes, we demonstrated that the complexes of Pd(II) and Cu(I) with the commercially available diazacrown ether, 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (Kryptofix® 22 or

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cryptand-22) operate as active homogeneous catalysts under aerobic conditions.[28–30] We thought that the flexible macrocyclic and chelating effect of such *N*- and *O*-containing ligand may assist in stabilizing the reactive palladium and copper intermediates. In an effort to find an efficient catalyst for Cu(I) AAC reaction, here, we introduce the heterogeneous, recyclable, heat- and air-stable Cu(I) complex (PS–C22–CuI).

The utilization of multi-component reactions (MCRs) to synthesize novel chemicals, drug-like scaffolds, and natural product compounds has pervaded in organic transformations.[31,32] This is due to the fact that these products can be prepared directly in a single step and diversity can be achieved simply by varying the reaction substrates.[33]

Due to their versatile processing capabilities and ease of separation and recycling, polymer-supported catalysts offer many advantages for industrial applications. These catalysts can prevent the contamination of the ligand residue in the products. Chloromethylated polystyrene is one of the most widely studied heterogeneous supports, because it is sufficiently flexible with good catalytic activity. Polymer-supported ligands, such as 1-nitroso-2-naphthol,[34] ethylenediamine,[35] *N*-heterocyclic carbenes,[36] 2-aminophenanthroline,[37] anthranilic acid,[38] and macrocyclic Schiff base[39] that can form effective complexes with transition metals (Pd, Zn, Cd) have been utilized in the Sonogashira, Heck and Suzuki cross-coupling reactions.

We now wish to report a new reusable and efficient heterogeneous polystyrene resin-supported copper(I) iodide cryptand-22 complex (PS–C22–CuI) for the synthesis of 1,4-disubstituted 1,2,3-triazoles either from organic azides and terminal alkynes or from organic halides, sodium azide, and terminal alkynes in water at room temperature.

2. Results and discussion

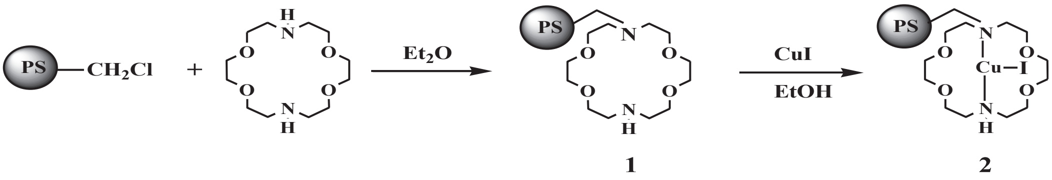
2.1. Synthesis and characterization of PS–C22–CuI catalyst

First, polymer-bound C22 (PS–C22) **1** was easily prepared by treating chloromethylated polystyrene (containing 6.2 wt % of Cl per gram of resin, 1.75 mmol/g Cl) with an appropriate amount of cryptand-22 in Et_2O at room temperature for 24 h (Scheme 1); the PS–C22 ligand was characterized by elemental analysis. The nitrogen content of this resin was 1.95% (1.39 mmol/g), indicating that only 40% of all the chlorine atoms were replaced by amine groups. The presence of the C22 ligand on the polystyrene was also confirmed by FT-IR spectra with disappearance of the C–Cl peak at 1263[35] cm^{-1} (due to $-CH_2Cl$ groups) of the starting polymer and appearance of a sharp band around 3457 cm^{-1} due to the N–H vibrations (Fig. 1a–b). Then, C22-functionalized polystyrene resin-supported CuI (PS–C22–CuI) complex **2** was prepared by the treatment of the resulting PS–C22 with a solution of copper(I) iodide in refluxing EtOH for 24 h (Scheme 1). This catalyst was characterized by FT-IR, EDX, SEM, XPS, and TG-DTA. FT-IR spectrum of the complex **2** showed a υ_{N-H} stretch at 3446 cm^{-1}, a lower frequency than that observed for the free ligand in PS–C22 (3457 cm^{-1}), indicating a coordination between the cryptand nitrogen atoms and the Cu(I) ion (Fig. 1c). The SEM images of the polymer-anchored ligand (PS–C22) and its copper(I) complex clearly show the morphological change, which occurred on the surface of the polymer matrix after loading of the metal (Fig. 2). EDX data also supports the metal attachment on the surface of polymer matrix with energy bands of 8.04, 8.90 KeV (K lines) and 0.93 KeV (L line) (Fig. 3). Moreover, the copper loading of polymer-anchored Cu(I) complex, as determined by inductively coupled plasma (ICP) was obtained to be 1.1% (0.17 mmol/g). The X-ray diffraction (XRD) pattern of the catalyst did not show any significant peak for the metal due to the low copper loading weight or the small crystal domains.[40] Further evidence for the attachment of C22 and metal on to the polymeric support is confirmed by X-ray photoelectron spectroscopy (XPS) of the complex (Fig. 4). The peaks at 282.2, 399.7, and 530.9 eV are attributed to C, N, and O, atoms, respectively; $Cu2p_{3/2}$ and $2p_{1/2}$ peaks appeared at 931.6 and 952.7 eV, respectively (inset).[18,41] Thermogravimetric-differential thermal analysis (TG-DTA) showed that the polymer-anchored Cu(I) complex was stable up to 428 °C (Fig. 5).

2.2. Catalytic performance of PS–C22–CuI catalyst for the synthesis of triazoles from organic azides and terminal alkynes

Our initial investigation was focused on the catalytic activity of C22-functionalized polystyrene resin-supported Cu(I) complex **2** in the Cu AAC synthesis of triazoles. Therefore, we chose benzyl azide and phenylacetylene as model substrates, and examined their reaction in the presence of PS–C22–CuI complex (0.2 mol %) under various aerobic conditions (Table 1, entries 1–14). The reaction rates were markedly dependent on the solvent and the catalyst loading. When solvents, such as DMSO, DMF, EtOH, ^{t}BuOH, and even solvent-less condition were used, moderate to good yields of the cyclization products were obtained (Table 1, entries 1–5). When organic/aqueous mixed solvents were used, a slight boost in the product yields was observed (Table 1, entries 6–7). Finally, to our delight, the reaction showed a good compatibility when water was used as the solvent. Then, different catalyst loadings between 0.1 and 0.5 mol % were investigated for the reaction (Table 1, entries 9–12). Among the various catalyst loadings, 0.3 mol % of the catalyst was found to be the best (Table 1, entry 10). To find out if the in situ formation of PS–C22/CuI in the reaction vessel would drive the reaction, the reaction was also performed in the presence of CuI (0.3 mol %) and PS–C22 (40 mg); stirring the reaction mixture for 10 h under the same reaction conditions produced the corresponding product in 18% yield (Table 1, entry 13). Also, the above cycloaddition reaction was performed using CuI (0.003 mmol, 0.3 mol %) and C22 ligand (0.006 mmol, 0.6 mol %); the corresponding triazole was obtained in 23% yield under the same reaction conditions (Table 1, entry14). Therefore, we decided to use H_2O as solvent and 0.3 mol % PS–C22–CuI catalyst as the optimal conditions in further studies.

To examine the scope of the Huisgen [3+2] cycloaddition of alkynes and organic azides, a variety of terminal alkynes reacted with organic azides smoothly and generated the corresponding



Scheme 1. Preparation of the PS–C22–CuI.

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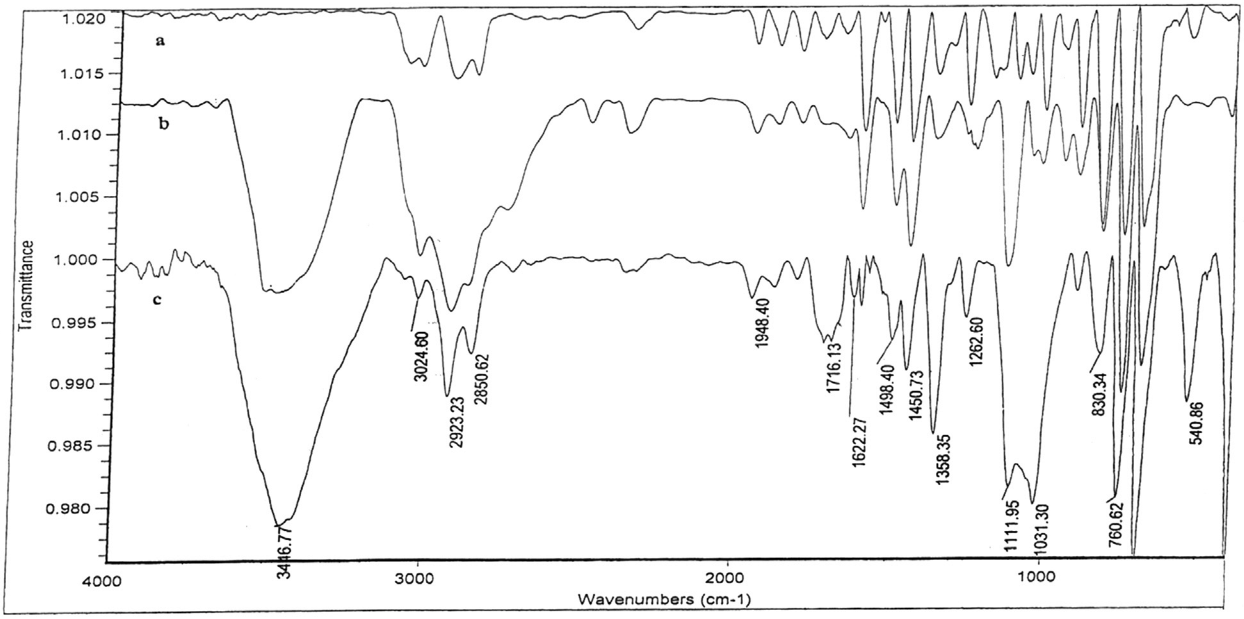

Fig. 1. FT-IR spectra of (a) chloromethylated polystyrene, (b) polymer-supported C22 (PS–C22), and (c) PS–C22–CuI complex.

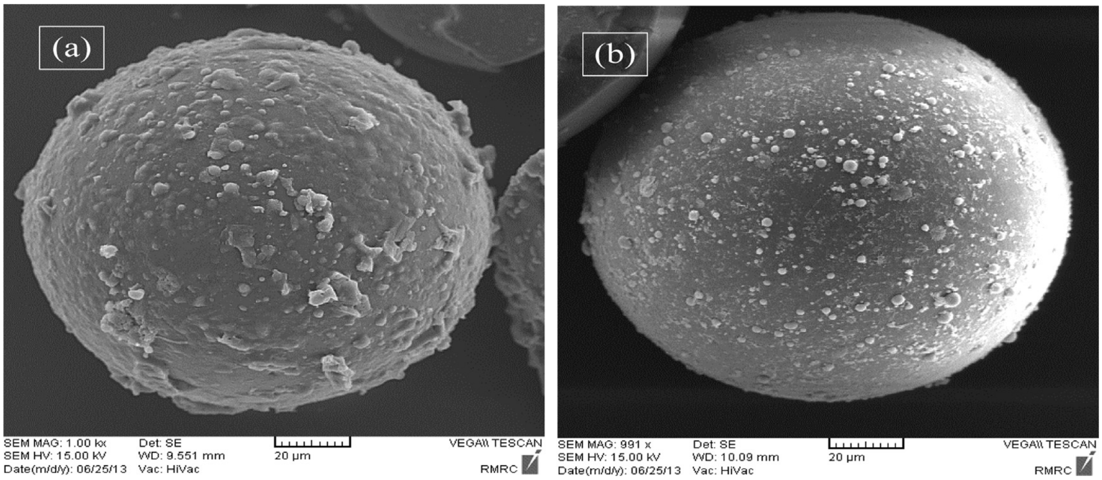

Fig. 2. SEM images of the PS–C22 ligand (a), and the PS–C22–CuI (b).

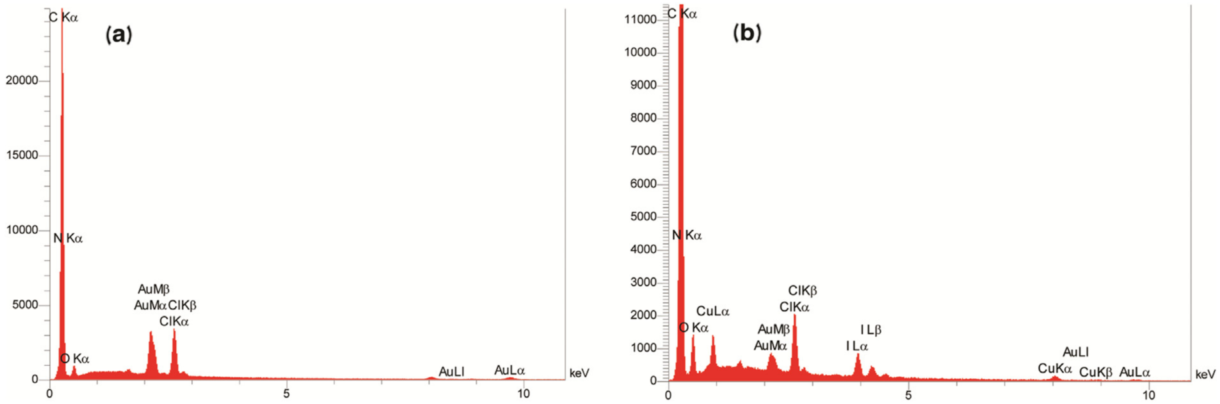

Fig. 3. EDX spectra of PS–C22 (a) and PS–C22–CuI complex (b).

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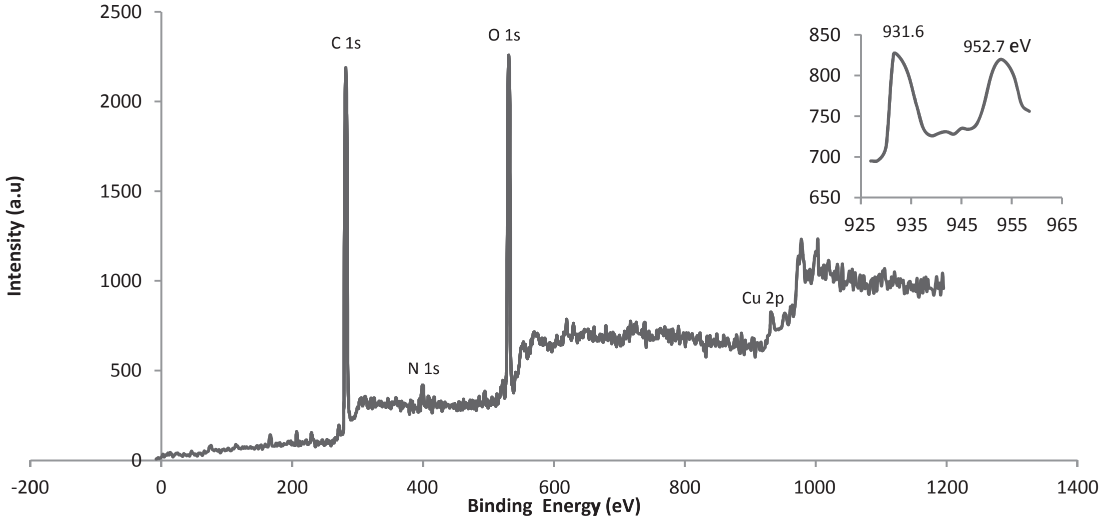

Fig. 4. XPS spectrum of PS–C22–CuI with expansion (inset).

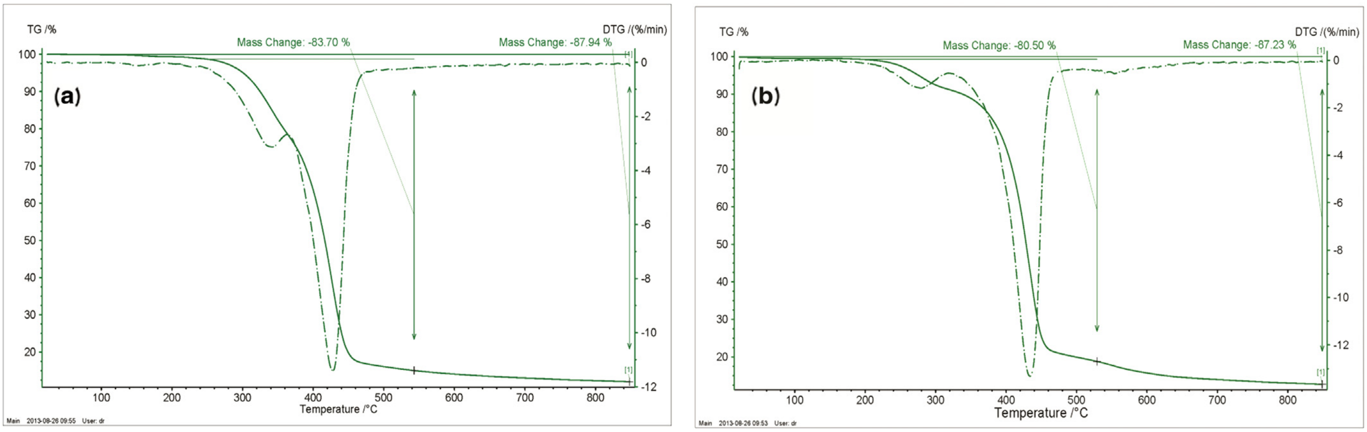

Fig. 5. TG-TDA curves of PS–C22 (a) and PS–C22–CuI complex (b).

1,4-disubstituted-1,2,3-triazoles in high to excellent yields (Table 2). The results indicated that primary, secondary, and tertiary aliphatic as well as the traditional benzylic azides coupled with aromatic and aliphatic alkynes to generate a range of triazoles. Generally, the more electron-rich azides reacted with the highest efficiency [benzyl (entries 1, 3, 11, 13, 16) ≥1° alkyl (entries 6 and 14) >2° alkyl (entry 4) >3° alkyl (entries 5 and 15)]. The exceptions in this trend are phenacyl azides (Table 2, entries 7 and 8). Among alkynes, phenylacetylene reacted slightly better than other terminal alkynes. The system also proved robust toward alcohol-substituted alkyne, propargyl alcohol (Table 2, entry 9).

2.3. Catalytic one-pot three-component synthesis of triazoles

To further improve the utility and user friendliness of PS–C22–CuI-catalyzed synthesis of triazoles, we developed its practical one-pot three-component variant described herein. The azides are generated in situ from corresponding halides, whereupon they are captured by copper(I) acetylides forming the corresponding 1,4-disubstituted 1,2,3-triazoles.

We initially carried out the standard three-component click reaction of benzyl bromide and sodium azide with phenylacetylene in water to investigate the role of solvents and the catalyst loading using PS–C22–CuI as heterogeneous catalyst (Table 1, entries 15–21). It was found that water is the suitable solvent, which gives the best result for the one-pot three-component click reaction in the presence of 0.6 mol % of PS–C22–CuI catalyst (Table 1, entry 18). Under these optimized reaction conditions, the generality and scope of this one-pot three-component protocol was explored, using various alkyl halides (benzylic, primary, secondary, and tertiary) and terminal alkynes (aliphatic and aromatic). The results are summarized in Table 2. As shown in Table 2, a range of structurally diverse alkyl halides (chlorides, bromides, and iodides), such as benzylic, primary, secondary, and tertiary, as well as phenacyl halides were examined and coupled with different terminal alkynes. In most cases, the three-component reaction proceeded smoothly in water to give the corresponding 1,2,3-triazoles in good to high yields, and only 1,4-regioisomers were detected as the products. However, in some cases, the one-pot reaction gave lower yields than those expected (Table 2, entries 4–6 and 14–16). This was attributed to lower miscibility of the substrates in water at room temperature; therefore, when DMSO/H_2O (1:2) was used as solvent in the reactions, a significant boost in product yields was observed.

A comparative study of the reaction conditions and results for copper-catalyzed reactions of: (i) benzyl azide with phenylacetylene, and (ii) benzyl bromide, phenylacetylene, and sodium azide using other methods and those reported in this work is given in Table 3, which clearly demonstrates the advantages of the present methodology.

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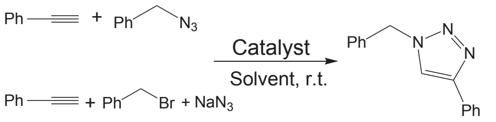
Table 1
Influence of different reaction parameters on the PS—C22—CuI-catalyzed click reaction



Entry	Catalyst	Mol % of Cu	Solvent	Yield (%)[c]
1	**2**[a]	0.2	—	58
2	**2**[a]	0.2	DMSO	78
3	**2**[a]	0.2	DMF	68
4	**2**[a]	0.2	^{t}BuOH	69
5	**2**[a]	0.2	EtOH	71
6	**2**[a]	0.2	H_2O/DMSO (2:1)	83
7	**2**[a]	0.2	H_2O/DMF (2:1)	75
8	**2**[a]	0.2	H_2O	84
9	**2**[a]	0.1	H_2O	73
10	**2**[a]	**0.3**	**H_2O**	**99**
11	**2**[a]	0.4	H_2O	99
12	**2**[a]	0.5	H_2O	99
13	**1**/CuI[a]	0.3	H_2O	18
14	C22/CuI[a]	0.3	H_2O	23
15	**2**[b]	0.2	H_2O	56
16	**2**[b]	0.4	H_2O	63
17	**2**[b]	0.5	H_2O	86
18	**2**[b]	**0.6**	**H_2O**	**99**
19	**2**[b]	0.8	H_2O	99
20	**2**[b]	0.6	H_2O/DMSO (2:1)	99
21	**2**[b]	0.6	H_2O/DMF (2:1)	81

Two results in bold values signify the best optimized conditions in the two experiments, (two- and three-components).

[a] Azide—alkyne reaction conditions: benzyl azide (1 mmol), phenylacetylene (1 mmol) and catalyst in solvent (3 mL) at room temperature for 10 h in air.

[b] Three-component reaction conditions: benzyl bromide (1 mmol), NaN_3 1.1. mmol), phenyacetylene (1 mmol) and catalyst in solvent (3 mL) at room temperature for 15 h in air.

[c] Isolated yields.

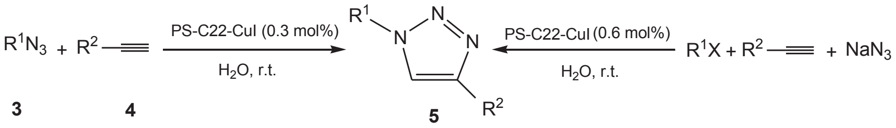
Table 3
Comparison of the reaction conditions and results for the copper-catalyzed click reaction

Entry	Catalyst (mol %)	Condition	Time/temp. (°C)	Yield (%)	Ref.
1	Cu/CR11 (12)[a] Cu/CR20 (7)[a]	Neat/NEt_3 Neat	4 h, 70 4 h, 70	98 93	46
2	ZnO—CuO (3)[a]	H_2O/^{t}BuOH (2:1) Ultrasonic	10 min, r.t.	100	47
3	CuO—CeO_2[b]	Amberlite-supported azide/EtOH	65 min, reflux	91	48
4	$CuSO_4\cdot 5H_2O$ (10)[a] $CuSO_4\cdot 5H_2O$ (10)[b]	H_2O/N_2H_4 H_2O/N_2H_4	45 min, r.t. 4 h, r.t., then 1 h 100	95 81	43
5	Cu NP/C (0.5)[b]	H_2O	3 h, 70	98	40
6	Cu/Al_2O_3 (10)[b]	Ball-milling/neat	1 h, r.t.	96	41
7	CuI (15)[b]	[bmim][BF_4]/H_2O/L-Proline/Na_2CO_3	4 h, r.t.	97	49
8	PS-—C22—CuI (0.3)[a] PS—C22—CuI (0.6)[b]	H_2O H_2O	10 h, r.t. 15 h, r.t.	99 99	This work

[a] Reaction of benzyl azide with phenylacetylene.

[b] Three-component reaction of the benzyl bromide, phenylacetylene and NaN_3.

Table 2
PS—C22—CuI-catalyzed synthesis of 1,2,3-triazoles[a]



Entry	R^1	X	R^2	Product	Yield (%)[b]	
					Two component	Three component/time (h)
1	$PhCH_2$	Br	Ph	**5a**[17]	99	99/15
2	$PhCH_2$	Cl	Ph	**5a**[17]	—	98/15
3	p-$NO_2C_6H_4CH_2$	Br	Ph	**5b**[44]	98	96/16
4	Cyclohexyl	Br	Ph	**5c**[17]	88	57 (84)[c]/20
5	1-Adamantyl	Br	Ph	**5d**[11]	81	45 (78)[c]/20
6	n-C_8H_{17}	I	Ph	**5e**[44]	97	62 (93)[c]/21
7	$PhCOCH_2$	Cl	Ph	**5f**[42]	86	82/17
8	p-$BrC_6H_4COCH_2$	Br	Ph	**5g**[42]	82	81/17
9	$PhCH_2$	Br	CH_2OH	**5h**[43]	78	73/20
10	$PhCH_2$	Cl	CH_2OH	**5h**[43]	—	68/20
11	$PhCH_2$	Br	CO_2CH_3	**5i**[44]	93	85/17
12	$PhCH_2$	Cl	CO_2CH_3	**5i**[44]	—	83/17
13	p-$NO_2C_6H_4CH_2$	Br	CO_2CH_3	**5j**[44]	97	91/17
14	n-C_8H_{17}	I	CO_2CH_3	**5k**[44]	93	61 (91)[c]/21
15	1-Adamantyl	Br	CO_2CH_3	**5l**[45]	78	56 (73)[c]/21
16	$PhCH_2$	Br	n-C_4H_9	**5m**[41]	92	61 (84)[c]/20

[a] Two component reaction conditions: organic azide (1 mmol), alkyne (1 mmol), PS—C22—CuI (0.3 mol %), H_2O (3 mL) at room temperature for 10 h under aerial atmosphere; Three-component reaction conditions: Alkyl halide (1 mmol), NaN_3 (1.1 mmol), alkyne (1 mmol), catalyst (0.6 mol %), H_2O (3 mL) at room temperature.

[b] Isolated yields.

[c] At room temperature for 20 h, using DMSO/H_2O (1:2 v/v, 3 mL).

2.4. Recycling of the catalyst

The recyclability of heterogeneous catalysts is a very important issue, especially for commercial applications. Thus, the feasibility of repeated use of PS—C22—CuI was also examined for the two methods of synthesizing triazoles, using the reaction of benzyl azide with phenylacetylene (0.3 mol % of the catalyst), and one-pot three-component reaction from benzyl bromide, phenylacetylene, and sodium azide (0.6 mol % of catalyst). In both methods, the catalyst was separated from the reaction mixture by filtration after each experiment, then washed with water and ethyl acetate, and air-dried carefully before being used in subsequent runs. As shown in Fig 6, it was found that while the product (**5a**) yield, which was prepared by benzyl azide decreased slightly over four recycling runs, a sharp fall in yield ending up in 71%, was observed when one-pot three-component reaction was followed (Fig. 6).

3. Conclusion

We have demonstrated that the polystyrene-anchored cryptand-22 copper(I) iodide, PS—C22—CuI, complex is a highly efficient and reusable catalyst for the alkyne-azide cycloaddition (AAC)

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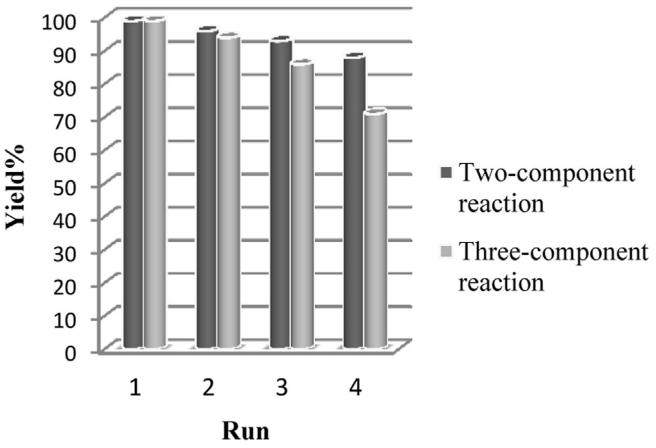

Fig. 6. Recycling activity of the PS–C22–CuI catalyst.

reactions in water at room temperature. This heterogeneous catalyst can be used for either the Huisgen [3+2] cycloaddition of alkynes and organic azides or one-pot three-component synthesis of 1,4-disubstituted 1,2,3-triazoles from alkynes, sodium azide, and alkyl halides at room temperature in water. The catalyst is easily separated and can be recycled for four runs. Simple preparation of the complex, oxygen insensitivity, low catalyst loading, and excellent catalytic performance in aqueous media make it a good heterogeneous system and a useful alternative to other heterogeneous copper catalysts.

4. Experimental section

All chemicals were commercial reagent grades and purchased from Merck and Aldrich. Chloromethylated polystyrene (CM PS) resin cross-linked with 1% DVB (70–90 mesh, 1.5–2.0 mmol/g of Cl) was purchased from Aldrich. XPS (X-ray photoelectron spectroscopy) data was recorded with 8025-BesTec twin anode XR3E2 X-ray source system. Thermogravimetric-diffraction thermal analysis (TG-DTA) was carried out using a thermal gravimetric analysis instrument (NETZSCH TG 209 F1 Iris) with a heating rate of 10 °C min^{-1}. XRD patterns were recorded by an Xpert MPD, X-ray diffractometer using Cu Kα radiation. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded using a Bruker AQS-300 Avance spectrometer. The scanning electron microscopy (SEM) images were obtained using a scanning electron microscope VEGA\\\\TESCAN-LMU. FT-IR spectra were recorded on ABB Bomem model FTLA 2000 instrument. The Cu content of the complex was determined using inductively coupled plasma (ICP, Varian vista-mpx), and surface morphology of the catalyst was analyzed using Energy-dispersive-X-ray (VEGA, TESCAN-LMU) equipped with EDX facility. Micro analytical data was collected by a Perkin–Elmer, USA, 2400C elemental analyzer.

4.1. Preparation of the polymer-anchored PS–C22–CuI (2)

In a 100 mL round-bottom flask equipped with a magnetic stirrer bar, chloromethylated polystyrene resin (2 g, almost 1.75 mmol/g of Cl) was allowed to swell in diethyl ether (40 mL) for 24 h; then cryptand-22 (0.65 g, 2.5 mmol) was added to the flask and stirred for 72 h at room temperature. The polymer beads were filtered and the residue was washed sequentially with diethyl ether (4×40 mL), and then dried in an oven to obtain the polymer-supported cryptand-22 (**1**).

Then, the C22-functionalized polymer (**1**) was swollen in EtOH (50 mL) for 1 h; then, CuI (0.42 g, 2.2 mmol) was added and the mixture was heated at reflux in that solvent for 24 h in N_2 atmosphere. The product formed was filtered off, washed with EtOH (3×30 mL) and finally dried in vacuum at 50 °C for 24 h.

4.2. General procedure for [3+2] cycloaddition of terminal alkynes and organic azides

In a 10 mL round-bottom flask, catalyst **2** (20 mg, containing 0.3 mol % of Cu), terminal alkyne (1.0 mmol), organic azide (1.0 mmol), and water (3 mL) were added. The mixture was stirred at room temperature for 10 h under aerial conditions. Then EtOAc (5 mL) was added to the mixture, filtered and washed with water (2×3 mL) and EtOAc (2×3 mL); the organic layer was separated, dried ($MgSO_4$), and concentrated in vacuum to give the crude product, which was almost pure.

4.3. General procedure for the one-pot 3-component synthesis of azides

Alkyne (1 mmol), sodium azide (1.1 mmol), organic halide (1 mmol), and water (3 mL) were placed together in a 10 mL round-bottom flask. PS–C22–CuI (40 mg, containing 0.6 mol % of Cu) was then added to the above solution. The suspension was magnetically stirred for 10 h at room temperature. After completion of the reaction as followed by TLC, EtOAc (5 mL) was added to the mixture, filtered, and washed with water (2×3 mL) and EtOAc (2×3 mL). The organic phase was separated, dried ($MgSO_4$), and concentrated in vacuum to give the crude product that was further purified by recrystallization with ethanol/water (3:1 v/v). In the case of triazole **5h**, after completion of the reaction, water was evaporated and EtOAc (5 mL) was added. The mixture was filtered to separate the catalyst and the filtrate was concentrated under vacuum to obtain the desired product, which was almost pure.

All compounds were characterized by IR, ^{1}H and ^{13}C NMR spectroscopy.

*4.3.1. 1-Benzyl-4-phenyl-1H-1,2,3-triazole (**5a**).*[17] White solid; mp 129–130 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.81 (d, J=8.5 Hz, 2H), 7.69 (s, 1H), 7.28–7.42 (m, 8H), 5.54 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=148.2, 134.7, 130.5, 129.2, 128.84, 128.77, 128.2, 128.1, 125.7, 119.7, 54.2; Calculated for $C_{15}H_{13}N_3$ C=76.57%, H=5.57%, N=17.86%: Found C=76.48%, H=5.42%, N=17.86%.

*4.3.2. 1-(4-Nitrobenzyl)-4-phenyl-1H-1,2,3-triazole (**5b**).*[44] White solid; mp 158–161 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.25 (d, J=8.7 Hz, 2H), 7.82 (d, J=7.5 Hz, 2H), 7.76 (s, 1H), 7.33–7.47 (m, 5H), 5.71 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=148.7, 148.1, 141.7, 130.1, 128.9, 128.54, 128.5, 125.7, 124.4, 119.7, 53.2; Calculated for $C_{15}H_{12}N_4O_2$ C=64.28%, H=4.32%, N=19.99%: Found C=64.37%, H=4.28%, N=19.92%.

*4.3.3. 1-Cyclohexyl-4-phenyl-1H-1,2,3-triazole (**5c**).*[17] White solid; mp 104–106 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.83 (d, J=8.1 Hz, 2H), 7.77 (s, 1H), 7.42 (t, J=7.3 Hz, 2H), 7.27–7.35 (m, 1H), 4.45–4.55 (m, 1H), 2.26 (d, J=7.6 Hz, 2H), 1.97 (d, J=6.0 Hz, 2H), 1.77–1.82 (m, 3H), 1.32–1.52 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=147.3, 130.9, 128.8, 127.9, 125.6, 117.3, 60.1, 33.6, 25.20, 25.16; Calculated for $C_{14}H_{17}N_3$ C=73.98%, H=7.53%, N=18.45%: Found C=73.82%, H=7.49%, N=18.43%.

*4.3.4. 1-Adamantyl-4-phenyl-1H-1,2,3-triazole (**5d**).*[11] White solid; mp 218–222 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.80 (d, J=8.2 Hz, 2H), 7.67 (s, 1H), 7.40 (t, J=8.0 Hz, 2H), 7.27–7.33 (m, 1H), 2.36 (s, 6H), 2.10 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=148.3, 130.5, 128.2, 128.1, 125.7, 119.5, 66.9, 49.3, 35.5, 32.6; Calculated for

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$C_{18}H_{21}N_3$ C=77.37%, H=7.58%, N=15.05%: Found C=77.21%, H=7.45%, N=14.97%.

4.3.5. 1-Octyl-4-phenyl-1H-1,2,3-triazole (***5e***).[44] White solid; mp 74–78 °C; ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.84 (d, J=8.3 Hz, 2H), 7.75 (s, 1H), 7.43 (t, J=7.2 Hz, 2H), 7.30–7.36 (m, 1H), 4.39 (t, J=7.3 Hz, 2H), 1.94 (quin, J=7.0 Hz, 2H), 1.26–1.34 (m, 10H), 0.88 (t, J=5.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=147.7, 130.7, 128.8, 128.1, 125.7, 119.4, 50.4, 31.7, 30.4, 29.1, 28.97, 26.5, 22.6, 14.1; Calculated for $C_{16}H_{23}N_3$ C=74.65%, H=9.01%, N=16.34%: Found C=74.87%, H=8.92%, N=16.33%.

4.3.6. 1-Phenyl-2-(4-phenyl-1H-1,2,3-triazol-1yl)-1-ethanone (***5f***).[42] Pale yellow solid; mp 144–146 °C; IR (KBr): υ=1700 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.81 (d, J=8.2 Hz, 2H), 7.67 (s, 1H), 7.37–7.43 (m, 5H), 7.27–7.34 (m, 3H), 5.58 (s, 2H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=196.8, 148.2, 137.6, 134.7, 132.5, 130.1, 129.2, 128.8, 128.3, 128.1, 125.7, 54.2; Calculated for $C_{16}H_{13}N_3O$ C=72.99%, H=4.98%, N=15.96%: Found C=73.16%, H=4.87%, N=15.85%.

4.3.7. 1-(4-Bromophenyl)-2-(4-phenyl-1H-1,2,3-triazol-1yl)-1-ethanone (***5g***).[42] Pale yellow solid; mp 179–181 °C; IR (KBr): υ=1696 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ=8.21 (d, J=8.6 Hz, 2H), 7.81 (d, J=8.6 Hz, 2H), 7.76 (s, 1H), 7.40–7.47 (m, 4H), 7.35–7.37 (m, 1H), 5.76 (s, 2H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=196.8, 148.0, 141.8, 137.6, 132.4, 130.1, 128.9, 128.5, 128.4, 128.3, 125.7, 53.2; Calculated for $C_{16}H_{12}BrN_3O$ C=56.16%, H=3.53%, N=12.28%: Found C=55.94%, H=3.46%, N=12.27%.

4.3.8. (1-Benzyl-1H-1,2,3-triazol-4-yl)methanol (***5h***).[43] White solid; mp 74–77 °C; IR (KBr): υ=3263 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.46 (s, 1H), 7.31–7.40 (m, 3H), 7.24–7.27 (m, 2H), 5.49 (s, 2H), 4.74 (s, 2H), 3.37 (brs, 1H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=134.5, 129.1, 128.8, 128.1, 121.8, 56.3, 54.2; Calculated for $C_{10}H_{11}N_3O$ C=63.48%, H=5.86%, N=22.21%: Found C=63.73%, H=5.72%, N=22.17%.

4.3.9. 1-Benzyl-4-methoxycarbonyl-1,2,3-triazole (***5i***).[44] White solid; mp 104–105 °C; IR (KBr): υ=1721 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.99 (s, 1H), 7.34–7.36 (m, 3H), 7.25–7.27 (m, 2H), 5.55 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=161.1, 140.2, 133.7, 129.3, 129.1, 128.3, 127.5, 54.4, 52.2; Calculated for $C_{11}H_{11}N_3O_2$ C=60.82%, H=5.10%, N=19.34%: Found C=60.98%, H=5.02%, N=19.27%.

4.3.10. 1-(4-Nitrobenzyl)-4-methoxycarbonyl-1,2,3-triazole (***5j***).[44] Pale yellow solid; mp 188–190 °C; IR (KBr): υ=1721 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ=8.96 (s, 1H), 8.23 (d, J=8.6 Hz, 2H), 7.55 (d, J=8.6 Hz, 2H), 5.84 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ=160.5, 147.3, 142.8, 138.9, 129.8, 129.2, 123.99, 52.2, 51.9; Calculated for $C_{11}H_{10}N_4O_4$ C=50.38%, H=3.84%, N=21.37%: Found C=50.90%, H=3.64%, N=21.37%.

4.3.11. 1-Octyl-4-methoxycarbonyl-1,2,3-triazole (***5k***).[44] White solid; mp 76–78 °C; IR (KBr): υ=1730 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ=8.08 (s, 1H), 4.40 (t, J=7.3 Hz, 2H), 3.95 (s, 3H), 1.92 (quin, J=6.9 Hz, 2H), 1.24–1.30 (m, 10H), 0.86 (t, J=6.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=161.3, 139.9, 127.3, 52.2, 50.7, 31.6, 30.1, 28.9, 28.8, 26.3, 22.6, 14.0; Calculated for $C_{12}H_{21}N_3O_2$ C=60.23%, H=8.84%, N=17.56%: Found C=60.52%, H=8.69%, N=17.52%.

4.3.12. 1-Adamantyl-4-methoxycarbonyl-1,2,3-triazole (***5l***).[45] White solid; mp 100–103 °C; IR (KBr): υ=1727 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.98 (s, 1H), 3.91 (s, 3H), 2.34 (s, 6H), 2.08 (s, 3H), 1.71 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=161.1, 140.3, 127.4, 66.9, 52.2, 49.3, 35.4, 32.6; Calculated for $C_{14}H_{19}N_3O_2$ C=64.35%, H=7.33%, N=16.08%: Found C=64.58%, H=7.12%, N=15.84%.

4.3.13. 1-Benzyl-4-butyl-1,2,3-triazole (***5m***).[41] White solid; mp 61–64 °C; ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.31–7.36 (m, 3H), 7.20–7.23 (m, 3H), 5.45 (s, 2H), 2.66 (t, J=7.6 Hz, 2H), 1.60 (quin, J=7.3 Hz, 2H), 1.33 (sext, J=7.4 Hz, 2H), 0.88 (t, J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=148.9, 135.0, 129.0, 128.5, 127.9, 120.6, 53.9, 31.5, 25.4, 22.3, 13.8; Calculated for $C_{13}H_{17}N_3$ C=72.52%, H=7.96%, N=19.52%: Found C=72.35%, H=7.83%, N=19.38%.

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Supplementary data

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