RSC Advances

TOC Graphical Abstract

Efficient synthesis of 1,4-disubstituted 1,2,3-triazoles using Cu(II)-PBS-HPMO as heterogeneous catalyst
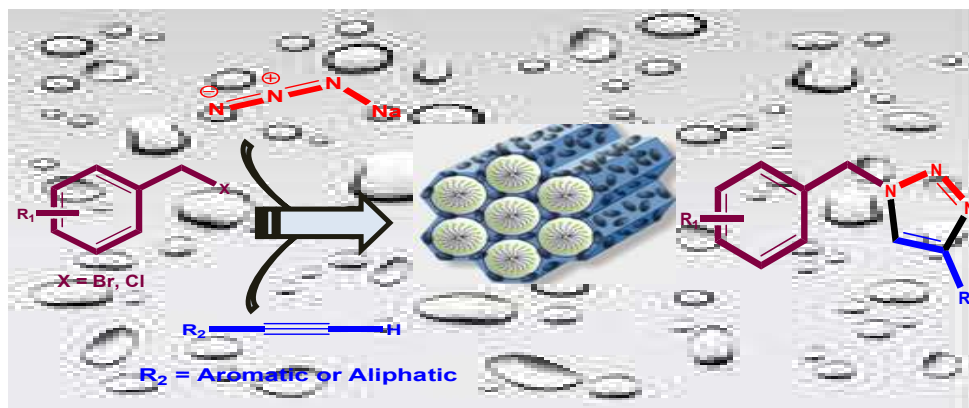
PAPER

Cu(II) PBS-bridged PMOs catalyzed one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles in water through click chemistry

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Abstract   A series of PBS-HPMO and Cu(II)-PBS-HPMO were synthesized from self-assembly of 1,2-bis(triethoxysilyl)ethane and porphyrin bridged silsesquioxane (PBS). These synthesized PBS-HPMO and Cu(II)-PBS-HPMO were characterized using different spectroscopic and non-spectroscopic techniques, namely, XRD, FT-IR, nitrogen adsorption-desorption isotherms, UV-visible, EPR, *etc*. Among these, the porphyrin bridged PMOs, specifically Cu(II)-PBS-HPMO, has been found to be the proficient catalyst for
10 multicomponent reaction of benzyl halides with sodium azide and terminal alkynes. This catalyst allowed for high regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles through one-step and atom economic tandem reaction as well as water as the solvent. No additional base or ligand or reducing agent is required. Not only benzyl halides, hetero benzyl halides have also been achieved in remarkable yields and in a completely regioselective manner. A series of structurally diverse 1,2,3-triazoles were also prepared in good to excellent yields from easily accessible starting materials by employing this protocol. Additionally, this process is purely heterogeneous
15 and the cascade reactions were performed in water and the efficient catalyst recyclability makes such synthesis a truly green process.

1 Introduction

In the context of green chemistry, the search for alternative safer, cleaner, and ecofriendly technologies are playing vital role in synthetic organic chemistry. With this objective, chemists are
20 facing one of the major challenges to develop organic chemical processes using new catalysts and catalytic systems, which diminish the waste and shrinkage the generation of hazardous substances, *etc*. Catalysis, in particular, heterogeneous catalysis is one of the fundamental aspects of ecological chemistry. On the
25 other hand, multicomponent reactions (MCRs) have proved to be very prominent and effective bond-forming tools in synthetic organic chemistry along with medicinal and combinatorial chemistry, in recent years. MCRs are convergent chemical synthesis processes, where three or more starting materials in a
30 single synthetic operation without any isolation of any intermediate are involved. These approaches have multiple advantages such as the elimination of complicated purification

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operations, use of the readily available starting materials and permit savings on solvents as well as reagents. In addition, MCRs are the most potent tools for the creation of intricate structures in a single step.[1,2] Hence, we have been working on MCRs
50 employing a new class of ecofriendly heterogeneous catalysts that are easy to prepare, handle, and recyclable.

Since 2001, the click reaction of azides and terminal alkynes has received prominent admiration, which was pioneered by Sharpless and co-investigators.[3] Huisgen 1,3-dipolar azide–
55 alkyne cycloaddition[4] has been recognized as one of the most noteworthy synthetic tools because of the expedient and reliable assembly of 1,2,3-triazole moieties, which exhibit an ample spectrum of biological activities and often found as vital nucleus of biologically active molecules.[5] Also, cycloaddition of azides
60 with alkynes has emerged as an archetypical example of "click chemistry", and a key step in the first series of click backbone amide linkers.[6] The obtained 1,2,3-triazole scaffolds possess interesting properties and led to a substantial growth in click chemistry research. The wide scope of azide-alkyne cycloaddition
65 is firmly demonstrated by its use in numerous areas of life and material sciences, including drug discovery,[7] bioconjugation chemisrty,[8] supramolecular chemistry,[9] solid phase reaction,[10] DNA labelling,[11] drug-like molecules with significant biological properties comprising anti-HIV activity[12] and antimicrobial
70 activity against Gram positive bacteria, assembly of glycoclusters[13] and glycodendrimers,[14] stationary phases for functionalized HPLC column,[15] *etc*.

Furthermore, in heterocyclic chemistry, the triazole moiety treated as a robust keystone in complex molecular architectures.[16]
75 Recently, several groups have reported triazole moieties acting as donors in metal complexes including applications in catalysis[17]

such as the tris-(triazole) ligands,[18] as well as very proficient catalysts for the azide-alkyne cycloaddition reaction. Also, (triazolylmethyl) phosphines and tetradentate bis(triazolylamines) for Pd-catalyzed allylic alkylation reactions[19] and Mn-catalyzed epoxidation reactions,[20] respectively. Additionally, 1,2,3-triazole scaffolds are smart linking units due to the capability of hydrogen bonding and stable to metabolic degradation, which is responsible for binding the biomolecular targets and can improve the solubility of the compounds. They display a number of chemotherapeutic properties along with significant anticonvulsant properties.[21]

Cu(I) catalyzed cycloaddition of azides with alkynes has gained gigantic attention began with the focal discovery by Sharpless and co-workers[3,22] as well as Meldal *et al.*[23] independently, in which copper(I) catalysts showed a dramatic rate acceleration of up to 10^7 times.[24] Generally, the sources of copper(I) include oxidation of copper metal turnings,[25] direct addition of cuprous salts (CuI, CuBr) with methyl(phenyl)sulfane,[26] iminopyridine,[27] mono- (or) polydentate nitrogen ligands,[18,28] *N*-heterocyclic copper carbene complexes,[22b] and comproportionation of copper(0)/copper(II), usually limited to special applications (e.g., biological systems).[29] Recently, the copper catalysts immobilized on various supports have been explored for the Huisgen cyclization of azides to alkynes namely, amine-bound silica,[30] and superparamagnetic mesoporous silica,[31] a ligand-bound organic polymer,[32] activated charcoal,[33] a polysaccharide,[34] zeolites,[35] hydrotalcite,[36] AlO(OH),[37] *etc.* Conversely, most of these catalysts with CuI species often less advised due to their thermodynamic instability, the formation of alkyne-alkyne coupling product, and other undesired by-products. Subsequently, many of these reports involved homogeneous in nature, an inert atmosphere as well as anhydrous solvents.[36a]

Periodic mesoporous organosilicas (PMOs) have gained significant attention due to their large surface area and structural diversity of the organosilica frameworks. PMOs are an innovative type of organic–inorganic hybrid materials, synthesized from up to 100% organic-bridged alkoxysilane precursors (R–[Si(OR')$_3$]$_n$, n ≥ 2, R = organic group, R' = -CH$_3$, -C$_2$H$_5$, *etc.*), in which these organic groups were densely and covalently embedded within the silica framework.[38] Moreover, in PMOs the organic groups are not only distributed uniformly inside the framework but also not affected the pore, which is more favorable for the guest molecule diffusion.[39] PMOs with dissimilar bridging organic groups could be potentially applied in various fields, namely, adsorption, catalysis, drug delivery, metal ion detection, optics, *etc.*[40] Specifically, PMOs are well suited for use as catalysts because of numerous advantages they offer, including easy accessibility, rapid diffusion, and favorable mass transfer for substrates into and out of the mesopores.[41] Hence, PMOs are most promising candidates for heterogeneous catalysis along with good reusability owing to strong covalent attachment of the catalytic active metal centres at the mesopore surface.[42]

We herein report synthesis of a series of PBS-HPMO as well as Cu(II)-PBS-HPMO as novel catalysts and the original use for the synthesis of 1,4-disubstituted 1,2,3-triazoles as MCR with readily available starting materials and water as the solvent. To the best of our knowledge, very few instances, Cu(II) (as Cu(II)-hydrotalcite, Cu(II) acetate *etc.*) was used for the regioselective synthesis of 1,4-disubstituted 1,2,3-triazoles.[36] It is worth mentioning here that the Cu(II)-PBS-HPMO has been employed for the first time in the field of azide-alkyne cycloaddition MCR and reached with high product yield.

2 Experimental section

2.1 Reagents and materials

All chemicals for synthesis of materials and catalytic activity testing were purchased from Sigma-Aldrich Corporation, St. Louis, MO (U.S.A.) and directly used without further purification.

2.2 Synthesis of tetrakis(4-carboxyphenyl)porphyrin (TCPP)[43]

Pyrrole (10 mmol) and 4-carboxybenzaldehyde (10 mmol) were added to reagent grade propionic acid (100 mL). The mixture was refluxed for 1 h, resulting crude product was allowed to cool down to room temperature and then methanol (100 mL) was added and continued to be chilled in an ice bath with stirring. Then after, the resultant solid was removed by filtration and thoroughly washed with methanol and hot water and then the porphyrin was purified. The observed atomic ratio of C/N was 12.35. Theoretical atomic ratio of C/N for {C$_{48}$H$_{30}$N$_4$O$_8$} is 12. The spectral data are as follows: ^{1}H NMR (d$_6$-DMSO): 8.85 ppm (s, 8H), 8.39-8.33 ppm (m, 16 H). m/z 791 ([M + H]$^+$ calcd. for 790.77). FT-IR spectrum: 1299 cm^{-1}(C-O stretch of carboxylic acid), 1693 cm^{-1} (C=O in carboxylic acid), 2500 cm^{-1}~3300 cm^{-1} (Broad, (-OH) in acid).

2.3 Synthesis of porphyrin bridged silsesquioxane (PBS)

A mixture of TCPP (1 mmol), 3-aminopropyltriethoxysilane (4 mmol) and dicyclohexyl carbodiimide (4 mmol), THF (50 ml) were stirred at 80 °C for 12 h under nitrogen atmosphere. The mixture was allowed to cool down to room temperature. The reaction mixture was filtered off and washed with THF and petroleum ether in several times.[43b] The observed C/N was 9.82, and the theoretical atomic ratio of C/N for {C$_{84}$H$_{114}$N$_8$O$_{16}$Si$_4$} is 10.5. The spectral data are as follows: ^{13}C CPTOSS NMR: 10.46, 22.0, 31.12 and 42.02 ppm (C in propyl groups of silane and terminal CH$_3$ of ethoxy group), 116, 127,134 and 143 ppm (aromatic & pyrrolytic C) and 173 ppm (C=O in amide) FT-IR spectrum: 950 cm^{-1} ~ 1250 cm^{-1} (Si-O-C), 1664 cm^{-1} (C=O in amide), 1528, 3276 cm^{-1} (N-H bonds of aromatic).

2.4 PBS bridged hybrid periodic mesoporous organosilica (PBS-HPMO)

A series of PBS-HPMO were prepared by taking various molar percentages of PBS precursors. In this, the hexadecyltrimethylammonium bromide (CTAB, 0.47 g) was added to distilled water (8.85 g) / NH$_3$H$_2$O (4.45 g), and the mixture was vigorously stirred to get clear solution (Table 1). Then, PBS and 1,2-bis(triethoxysilyl)ethane (BTEE) were added to the CTAB solution according to the desired ratio and the mixture was stirred for 24 h at room temperature. The resulting

precipitate was collected by filtration, extracted with ethanol/HCl solution and dried at 60 °C.

Table 1 Parameters for hybrid mesoporous organosilica synthesis using PBS and BTEE.

Catalyst	CTAB (g)	PBS (g)	BTEE (g)	Ammonia water /H_2O
PBS-HPMO-1	0.47	0.02	0.9	4.45/8.85
PBS-HPMO-2	0.47	0.08	0.9	4.45/8.85

2.5 Metalation of PBS-HPMO with copper

PBS-HPMOs (0.5 g) and copper acetate monohydrate (0.25 g) were added to methanol (30 mL), and the mixture was stirred for 12 h at 80 °C. The resulting precipitate was collected by filtration, washed with methanol and water in several times, and dried at 60 °C (Scheme 1). The synthesized Cu-PBS-HPMOs were characterized by UV–Vis spectroscopy and electron paramagnetic resonance (EPR) spectroscopy.
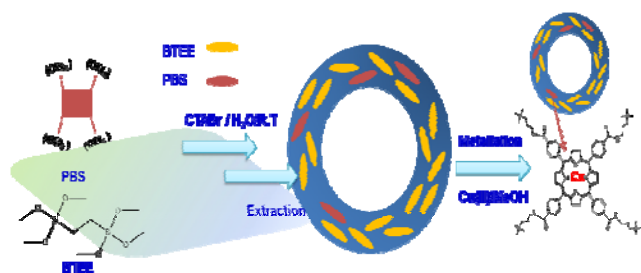
Scheme 1 Typical synthetic route of Cu(II)-PBS-HPMOs.

2.6 Characterization techniques

The X-ray diffraction (XRD) patterns were recorded on a Rigaku Multiflex diffractometer with a monochromated high-intensity Cu Kα radiation (λ = 1.54 Å). Scanning was performed under the ambient conditions over the 2θ range of 0.7 - 5 ^{0} at a rate of 0.5 ^{0}/min (40 kV, 30 mA). Solid-state NMR spectra were collected through a DSX Bruker NMR 600 MHz. The N_2 adsorption-desorption isotherms and pore size distribution were achieved by using a Micromeritics tristar apparatus at liquid N_2 temperature. The specific surface area is obtained from nitrogen adsorption isotherm by using the BET equation. Pore diameter was calculated by using the Barrett-Joyner-Halenda (BJH) method using the desorption branch of the adsorption-desorption isotherms. Cu(II)-PBS-PMOs were analysed and characterized by UV-visible and EPR spectroscopy by using Solidspec-3700 and JEOL FA200 instruments, respectively. FT-IR spectra were attained in KBr pellets with VERTEX 80V FT-IR vacuum spectromete.

2.7 Synthesis of 1,4-disubstituted 1,2,3-triazoles

All chemicals employed in this study were commercially available and used without further purification. A mixture of benzyl halide (1 mmol), sodium azide (1.2 mmol), terminal alkyne (1.1 mmol) and catalytic amount of Cu(II)-PBS-HPMO-2 (10 mg) in water (1.5 mL) were stirred at 100 ^{0}C for an appropriate time. After completion of the reaction, as confirmed by thin layer chromatography (TLC), the reaction mixture was filtered off and washed with ethyl acetate (3×5 mL). The combined layers were dried over anhydrous Na_2SO_4, concentrated in vacuum and purified by column chromatography on 60-120 mesh silica gel using ethyl acetate and hexane as the eluent (1:9) to afford the pure 1,4-disubstituted 1,2,3-triazoles. All products were identified by comparing their spectral data with the literature. Additionally, the solid catalyst was conveniently separated by centrifugation from the reaction mixture and examined its activity in the subsequent experiments.

3 Results and discussion

The low-angle powder XRD patterns of the synthesized PBS-HPMO-n and Cu(II)-PBS-HPMO-n catalysts are presented in Fig. 1. As shown in Fig. 1, the well-resolved diffraction peaks at 2θ = 1.4–2 reflect the (100) planes of ordered and textural uniformity of MCM-41 type mesoporous materials. The N_2 adsorption-desorption isotherms of PBS-HPMO-n are shown in Fig. 2. The isotherms can be classified as type IV isotherms, which are corresponding to the presence of ordered mesoporous material.[41,43] The textural properties including surface area, pore diameter, *etc*. are shown in Table 2. As the PBS content increases, the pore diameter curve shifts from 2.25 to 2.40 nm. The tendency of mesopore shrinkage with increasing PBS loading is also revealed by the changes in the surface area and total pore volume.
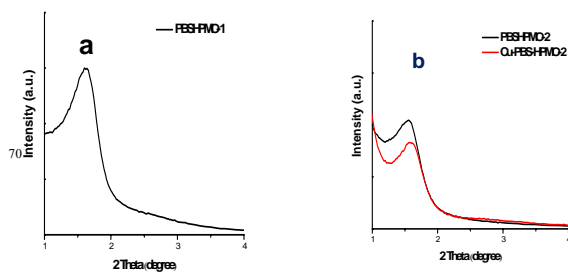

Fig. 1 Powder XRD patterns of PBS-HPMO-1 (a), PBS-HPMO-2 and Cu-PBS-HPMO-2 (b).
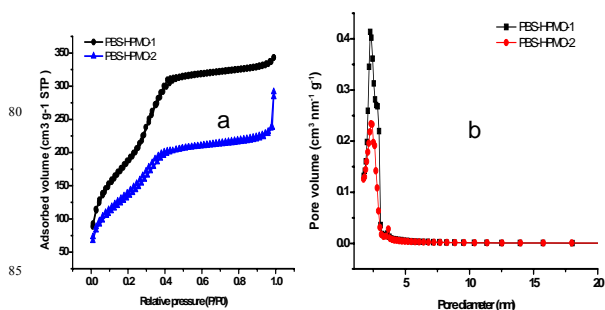

Fig. 2 Nitrogen adsorption-desorption isotherms (a) and pore size distribution (b) of PBS HPMO-n.

Table 2 The textural properties of synthesized PBS-HPMO-n.

| Catalyst	BTE (mmol)	PBS (mmol)	BET surface area (m^2/g)	Pore diameter (nm)	Total pore volume $(cm^3\,g^{-1})$	PBS amount *
PBS-HPMO-1	2.5	0.01	706	2.25	0.53	0.01 mmol
PBS-HPMO-2	2.5	0.04	477	2.40	0.43	0.03 mmol

*Calculated by TGA analysis

From UV-vis spectroscopy, the spectra of the PBS-HPMO-1 and PBS-HPMO-2 have shown one Soret band at 419 and 418.5 nm along with four Q bands at 516, 555, 597, 660 and 517, 553, 594, 647 nm, respectively. Also, Cu(II)-PBS-HPMO-1 and Cu(II)-PBS-HPMO-2 exhibited Soret bands at 410 and 409 nm and accompanied with Q bands in the range of 541 and 541, 581 nm, respectively (Fig. 3). These obtained results revealed that the synthesized catalysts are having the PBS unit in the bridged mesoporous organosilica (Table 3). Additionally, the change in the Q band region (fewer bands) on metalation is because of changed symmetry to the free-base porphyrin.[44]
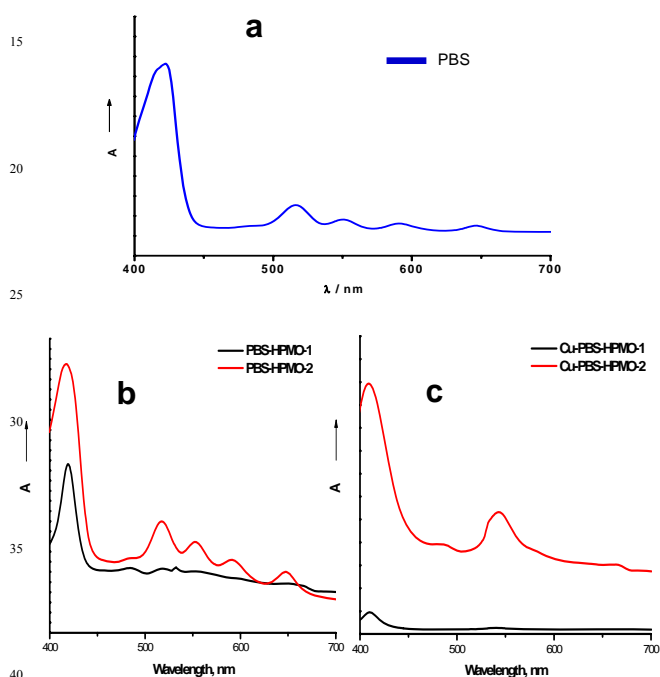
Fig. 3 UV-vis spectra of PBS (a) and PBS-PMO-n (b), and Cu-PBS-PMO-n (c).

Table 3 UV-vis absorption bands of synthesized catalysts.

Catalyst	Soret band (nm)	Q bands (nm)
PBS-HPMO-1	419	516, 555, 597, 660
PBS-HPMO-2	418.5	517, 553, 594, 647
Cu PBS-HPMO-1	410	541
CuPBS-HPMO-2	409	541, 581

The typical FT-IR spectra of synthesized PBS-HPMO-n and Cu(II)-PBS-HPMO-n catalysts are presented in Fig. 4. The FT-IR spectra displayed a strong absorbance in the range of 1200-1000 cm^{-1} that reveal the stretching of the Si-O-Si bond and the bands related to Si–O–C and Si–C are overlapped with the strong absorption bands of the Si–O–Si vibration modes in this region.[45] All samples also showed bands at 1644 cm^{-1} and 3443 cm^{-1} which are due to PBS moiety.
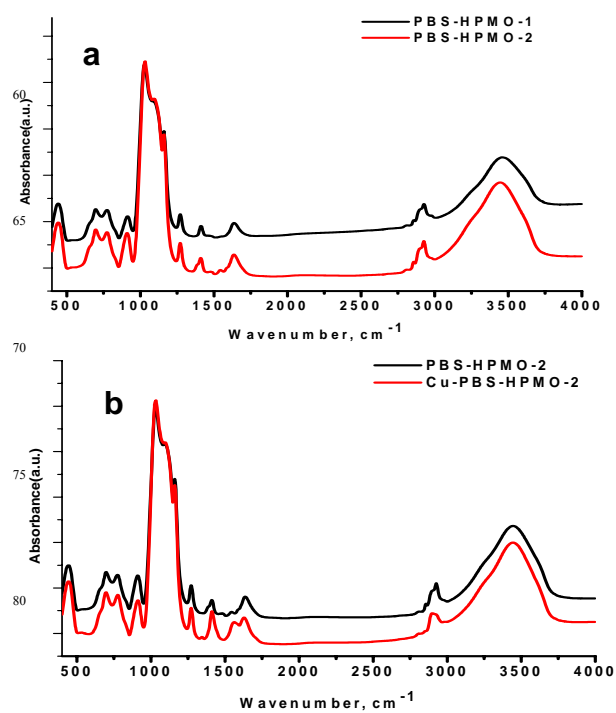
Fig. 4 FT-IR spectra of PBS-PMO-n (a) and Cu-PBS-PMO-n (b).

Synthesized PBS-HPMOs and Cu(II)-PBS-HPMOs were characterized by means of EPR spectroscopy to confirm the presence of Cu(II) ions inside the PBS-HPMOs after metalation (Fig. 5). From Fig. 5, the EPR spectrum reveals the presence of Cu(II) ions in the synthesized materials and Cu(II)-PBS-HPMO-2 sample exhibits high a intensity of signal than the Cu(II)-PBS-HPMO-1 due to smaller amount of Cu(II) ions inside the porphyrin bridged PMO. The EPR spectrum of Cu(II)-PBS-HPMO-2 containing adsorbed Cu(II) ions has shown the g parameters at $g_{||}$~2.20 and $g_{\perp}$~2.06, which indicates that the Cu(II) ions are linked to nitrogen ligands in the PBS. Solid state ^{29}Si NMR experiments often afford expedient information regarding the chemical environment around the Si nuclei with

organic functional moieties presence in the hybrid matrices. From ^{29}Si NMR spectra, the down field chemical shifts at -64 and -57 ppm resembles different Si states (T^2 and T^3) such as T^2 [SiR(OH)(OSi)$_2$] and T^3 [SiR(OSi)$_3$] and were shown in Fig. 6, where R is the PBS moiety and BTEE. All characterization techniques revealed the formation of PBS-HPMOs and Cu(II)-PBS-HPMOs materials.
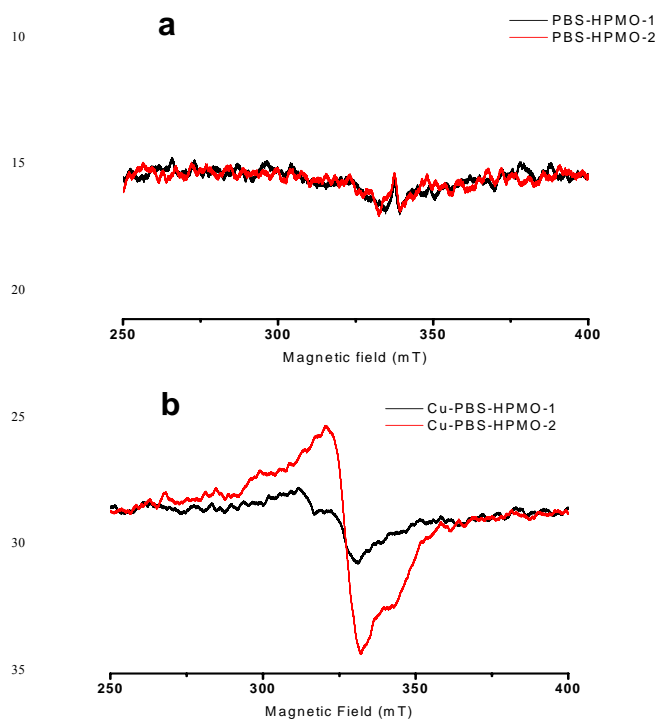

Fig. 5 EPR spectra of PBS-PMO-n (a) and Cu-PBS-PMO-n (b).
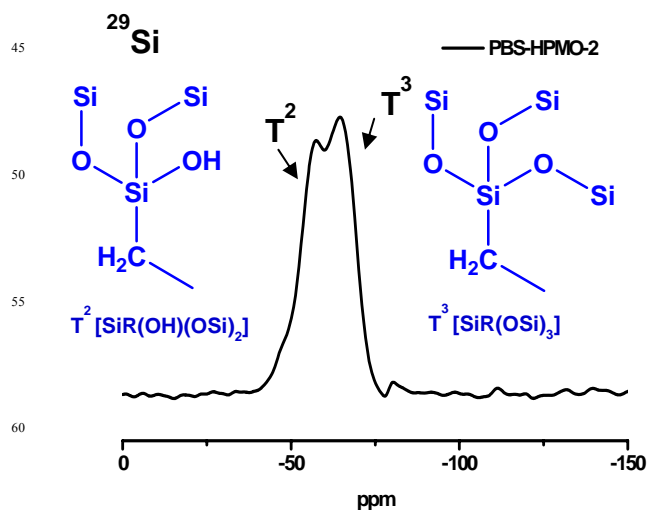

Fig. 6 Solid state ^{29}Si NMR spectra of PBS-HPMO-2.

As part of our on-going research, we have been working on porphyrin bridged PMOs having a regular porous structure, large surface area and tunable surface properties, which play vital role in the field of catalysis and are preferable for specific and selective catalysis. Very recently, we have successfully employed PMO catalysts for Baeyer-Villiger oxidation reaction with cyclic ketones as the starting materials.[41] Now, we wish to extend our work to MCRs by using these PMOs. We report herein a novel Cu(II)-PBS bridged PMOs for MCRs with readily available starting materials such as benzyl halides, sodium azide, and terminal alkynes for the synthesis of 1,4-disubstituted 1,2,3-triazoles (Scheme 2). The MCR consists one-pot, two-step synthesis of 1,4-disubstituted 1,2,3-triazoles proceed by click reaction through the formation of benzyl azides from sodium azide and benzyl halides. In click chemistry, the formation of organic azide [R–N$_3$] is the crucial step, and these azides made a fleeting appearance in organic synthesis. The benzyl azides are formed easily with in short reaction times and confirmed by the observation of the characteristic azido stretching frequency at ~2100 cm^{-1}.[36b] Remarkably, the construction of heterocyclic frameworks having nitrogen atom is playing vital role in organic synthesis as well as medicinal chemistry because of their existence in many natural products and biologically active molecules.[46]
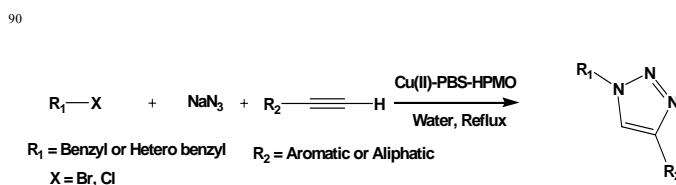
Scheme 2 Synthesis of 1,4-disubstituted 1,2,3-triazoles with different benzyl halides, sodium azide and various terminal alkynes by using Cu(II)-PBS-HPMO-2 catalyst.

In order to find out the best catalytic system suited for the synthesis of 1,4-disubstituted 1,2,3-triazoles, we examined typical reaction parameters. For instance, benzyl bromide (1 mmol), sodium azide (1.2 mmol), and phenylacetylene (1.1 mmol) were used as model substrates with a series of synthesized PBS-HPMO, Cu(II)-PBS-HPMO catalysts in various solvents. These results are illustrated in Table 4. The preliminary results revealed that Cu(II)-PBS-HPMO-2 catalyst exhibits promising catalytic activity in the presence of water under reflux conditions with enhanced regioselectivity towards the desired 1,4-disubstituted 1,2,3-triazole product (Table 4, Entry 4). The Cu(II)-PBS-HPMO-1 also showed good catalytic activity in comparison to copper free PBS-HPMO catalyst (Table 4, Entry 3). Nevertheless, the yields were lower than that of the Cu(II)-PBS-HPMO-2 catalyst. The Cu^{II} species present in the frame works of PMOs exhibited remarkable activity in the absence of inert atmosphere and without addition of any sacrificial ligands and additives. Trace amounts of products including some by-products and longer reaction times were noted in the absence of the catalyst (Table 4, Entry 5), and also we observed different spots in the TLC in the presence of catalyst under room temperature conditions (Table 4, Entry 7).

After selection of the most efficient catalyst, we further screened with different solvents to adjust the reaction conditions.

Amongst all the solvents, the reaction proceeded well in water, which was found to be the most appropriate solvent for synthesis of desired 1,4-disubstituted 1,2,3-triazoles with excellent yields. The enriched product yields are partly due to the hydrophobic
5 nature of the organic reactants, since their repulsion from water

Table 4 Optimization of the reaction conditions for the synthesis of 1,4-disubstituted 1,2,3-triazoles.[a]

Entry	Catalyst	Solvent	Temp. (^{0}C)	Time (h)	Yield (%)[b]
1	PBS-HPMO-1	Water	100	7	45
2	PBS-HPMO-2	Water	100	7	60
3	Cu-PBS-HPMO-1	Water	100	4	81
4	Cu-PBS-HPMO-2	Water	100	3.5	96
5	-	Water	100	10	-[c]
6	Cu-PBS-HPMO-2	-	100	6	72
7	Cu-PBS-HPMO-2	Water	RT	10	-[d]
8	Cu-PBS-HPMO-2	Toluene	110	3.5	27
9	Cu-PBS-HPMO-2	Methanol	65	3.5	70
10	Cu-PBS-HPMO-2	DCM	40	3.5	15
11	Cu-PBS-HPMO-2	DMF	120	3.5	65
12	Cu-PBS-HPMO-2	Benzene	80	3.5	32
13	Cu-PBS-HPMO-2	THF	65	3.5	64
14	Cu-PBS-HPMO-2	Acetonitrile	80	3.5	73

[a] Reagents and reaction conditions: benzyl bromide (1 mmol), sodium azide (1.2 mmol), phenylacetylene (1.1 mmol), catalyst (10 mg), and solvent 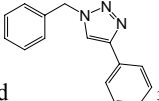(1.5 mL); unless otherwise mentioned. [b] Yields of isolated products. [c] Without catalyst. [d] Undesired products including starting materials.
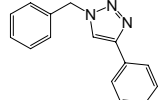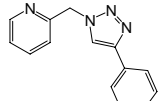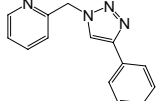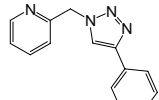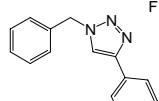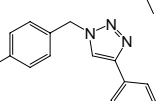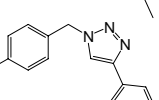
10 would enhance the number of collisions between the organic molecules and increases their ground-state energies, leading to an increase in the reaction rate.[47] In recent years, water has been considered as an excellent reaction medium in synthetic organic chemistry with many promising advantages. Moreover, we have
15 observed that several reactions frequently progress optimally in

pure water. Although, the rate acceleration is trivial, the use of water as the only reaction medium has additional benefits such as ease of product isolation and safety, thanks to its high heat capacity and unique redox stability.[48] The nonpolar solvents such
20 as toluene and benzene are not suitable for the title reaction of 1,2,3-triazoles with this catalyst (Table 4, Entries 8 and 12). The polar solvents namely, methanol, DMF, THF, and acetonitrile furnished the products in moderate yields (Table 4, Entries 9,11,13 and 14). However, DCM yielded very low in comparison
25 to other solvents (Table 4, Entry 10). This is probably due to interference of the solvents with the surface active sites of the catalysts. Interestingly, good yields were observed under solvent-free conditions (Table 4, Entry 6).

With this optimized reaction conditions (catalyst, solvent,
30 temperature, and additive-free) in hand, we sought to extend our studies through a variety of benzyl halides with sodium azide followed by [3+2] cycloaddition with dissimilar terminal alkynes

Table 5 Synthesis of 1,4-disubstituted 1,2,3-triazoles from
35 halides, sodium azide, and various benzyl terminal alkynes.[a]

Entry	Halide	Alkyne	Product	Time (h)	Yield (%)[b]
1				4	93
2				3.5	96
3				5	89
4				6	91
5				6	81
6				4	93
7				4	94
8				6	86

Continued.....

Entry	Halide	Alkyne	Product	Time (h)	Yield (%)[b]
9	MeO-benzyl bromide	phenylacetylene	MeO-benzyl triazole, 4-phenyl	4.5	92
10	benzyl bromide	4-fluorophenylacetylene	benzyl triazole, 4-(4-fluorophenyl)	4	90
11	benzyl bromide	1-Octyne	benzyl triazole, 4-(CH₂)₅	7	86
12	O₂N-benzyl bromide	4-methylphenylacetylene	O₂N-benzyl triazole, 4-tolyl	7.5	82
13	O₂N-benzyl bromide	4-fluorophenylacetylene	O₂N-benzyl triazole, 4-(4-fluorophenyl)	9	79
14	Br-benzyl bromide	4-methylphenylacetylene	Br-benzyl triazole, 4-tolyl	6	88
15	Br-benzyl bromide	4-fluorophenylacetylene	Br-benzyl triazole, 4-(4-fluorophenyl)	7	85
16	MeO-benzyl bromide	1-Octyne	MeO-benzyl triazole, 4-(CH₂)₅	6	83

Continued......

Entry	Halide	Alkyne	Product	Time (h)	Yield (%)[b]
17	O₂N-benzyl bromide	phenylacetylene	O₂N-benzyl triazole, 4-phenyl	8	81
18	Br-benzyl bromide	phenylacetylene	Br-benzyl triazole, 4-phenyl	5.5	86
19	4-methylbenzyl bromide	4-fluorophenylacetylene	4-methylbenzyl triazole, 4-(4-fluorophenyl)	7	86
20	4-methylbenzyl bromide	phenylacetylene	4-methylbenzyl triazole, 4-phenyl	5	91
21	4-methylbenzyl bromide	4-methylphenylacetylene	4-methylbenzyl triazole, 4-tolyl	6	90
22	O₂N-benzyl bromide	1-Octyne	O₂N-benzyl triazole, 4-(CH₂)₅	10	82
23	Br-benzyl bromide	1-Octyne	Br-benzyl triazole, 4-(CH₂)₅	9	84

[a] Reagents and reaction conditions: Halide (1 mmol), sodium azide (1.2 mmol), terminal alkyne (1.1 mmol), catalyst (10 mg), and solvent (1.5 mL). [b] Yields of isolated products.

by using novel Cu(II) catalyzed process, and the results are exemplified in Table 5. Likewise, reactions of most of the substrates with several benzyl halides and terminal alkynes bearing electron neutral and -donating as well as electron-withdrawing groups were accomplished smoothly and the corresponding 1,2,3- triazoles are attained in good to excellent yields. The benzyl halides generated moderate to excellent yields with aliphatic to aromatic terminal alkynes, respectively. Interestingly, the hetero benzyl halide namely, 2-picolyl chloride exhibited excellent yield with diverse terminal alkynes (Table 5, Entries 3-5). The benzyl halides offered good yields with aromatic terminal alkynes, however lower yields were notified with aliphatic terminal alkynes (Table 5). The benzyl halide having strong withdrawing group (-NO₂) has delivered moderate yields after taking long time (Table 5, Entries 13, 17, 22). We have conducted this reaction on a large scale (with benzyl bromide (10 mmol), sodium azide and phenylacetylene as the model reaction) to further advance the industrial utility of the catalytic formulations; remarkably, we found significant regioselectivity and high yields of the desired products.
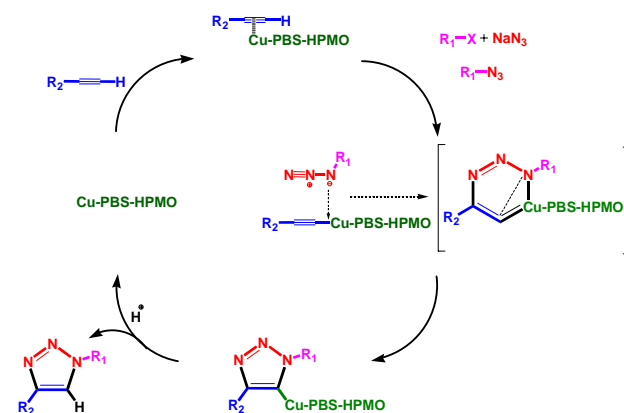
Scheme 3 Plausible reaction mechanism for 1,4-disubstituted 1,2,3-triazole formation with Cu(II)-PBS-HPMO catalyst.

By analogy with our investigation and earlier reports, the plausible mechanistic pathways for the synthesis of 1,4-disubstituted 1,2,3-triazoles with Cu(II)-PBS-HPMO catalyst are shown in Scheme 3. The one-pot multicomponent click reaction involves first the formation of in-situ generated organic azide with in short reaction time with the increased polarity marginally by benzyl substitution of the azide.[29] The role of the Cu species in the porphyrin bridged PMOs is to facilitate the formation of the CuII–acetylide complex and the activation of the azide function towards nucleophilic attack by reducing the electron density of the alkyne. Eventually, the porphyrinatocopper catalyst regenerated by protonolysis of the intermediate to afford the corresponding 1,2,3-triazoles. Interestingly, the used Cu(II)-PBS-HPMO catalyst did not exhibit any significant loss of product yield, and the catalyst could be recycled successively for five runs.

4   Conclusions

In summary, an efficient, straightforward, and atom-economical one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles is reported for the first time using Cu(II)-PBS-HPMO as heterogeneous catalyst. This simple and environmentally benign catalysis ensures under mild conditions without any reducing agents and additives. This protocol involved both benzyl halides and hetero benzyl halides, afforded great yields with terminal alkynes (aromatic and aliphatic). In addition, the Cu(II)-PBS-HPMO shown reusability with consistent activity for at least five cycles, indicates as green catalyst. Moreover, it has the potential for large scale applications.

Acknowledgements

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