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A new Cu-anchored mesoporous organosilica material for facile C-S coupling reactions under microwave irradiation

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Graphical Abstract



Cu-grafted functionalized SBA-15 material has been synthesized via post-synthesis functionalization of SBA-15 and it showed excellent catalytic activity for the synthesis of thioether derivatives via one-pot three component C-S coupling reactions.

Research Highlights

- Synthesis of Cu-anchored 2D-hexagonally ordered functionalized mesoporous silica.
- 3-(2-Aminoethylamino)propyl-dimethoxymethyl grafted SBA-15 showing D² species in ²⁹Si NMR.
- One-pot three-component C-S cross-coupling reactions for the synthesis of thioethers.
- Microwave assisted heating for fast and convenient C-S coupling reactions.

ABSTRACT

We report a new ordered Cu-anchored 2D-hexagonal mesoporous imine functionalized organosilica material Cu-MPIOS. This Cu-anchored mesoporous material has been synthesized via post synthetic functionalization of SBA-15 with 3-(2-aminoethylamino)propyl-dimethoxymethylsilane followed by Schiff-base condensation with 2-thiophene carboxaldehyde.

Cu(I) has been grafted finally over Schiff-base functionalized mesoporous material through chemical impregnation to obtain Cu-MPIOS. The materials are characterized thoroughly using various techniques like powder X-ray diffraction, N₂ adsorption/desorption analysis, FTIR, UV-visible spectroscopy, HR-TEM, FE-SEM, ¹³C cross-polarization magic angle spinning NMR, TGA/DTA, EPR, AAS and CHN chemical analysis. High Brunauer-Emmett-Teller (BET) surface area and the presence of very large size mesopores (8.1 nm) in Cu-MPIOS has motivated us to explore its catalytic activity in one-pot three-component C-S cross coupling reaction by varying different aryl halides in the aqueous medium under microwave assisted heating conditions. This heterogeneous Cu-catalyst shows high catalytic performance as well as good recycling efficiency in this C-S coupling reaction, suggesting its future potential for the synthesis of value added thioether derivatives.

Keywords: C-S coupling; functionalized mesoporous silica; D² type silica species; Cu-grafting; microwave heating.

1. Introduction

Organically functionalized mesoporous materials have attracted huge attention in the recent times due to their versatile utility in various demanding applications such as acid/base catalysis [1-4], bi-functional/dehydration catalysis [5,6], gas storage [7], sensing [8], adsorption [9], light harvesting [10] and so on. A wide range of transition metal complexes can be grafted at the surface of these functionalized mesoporous materials to explore their catalytic applications [11-14]. Compared with their homogeneous counterpart these supported heterogeneous catalysts are more demanding due to their ease of separation through simple filtration technique, non-leaching behavior of the reactive metal ions/species, quite less moisture sensitivity and good recycling efficiency. Organically functionalized mesoporous material have high BET surface area together with a large pore diameter and bearing suitable functional group with donor site(s), that can bind with metal-ion via strong coordination bond or chelation. This can lower the possibility of leaching of the metal ions from the catalyst surface during the liquid phase reaction. Thus,

among several insoluble solid catalysts known today, organically functionalized mesoporous materials provide greater accessibility of the reagent molecule towards the active site, high chemical as well as mechanical stability, recycling efficiency and higher turn-over numbers.

The C-S, C-C and C-N cross-coupling reactions are indispensable tool in synthetic organic chemistry for the production of several important biological and pharmaceutical compounds [15-18]. These compounds are widely used for the treatment of Alzheimer's disease [19], Parkinson's disease [20], inflammation, asthma and also for cancer etc. Among numerous cross-coupling reactions, transition metal-mediated C(aryl)–S bond formation reaction is a much less studied reaction than corresponding C-N and C-O bond formations due to the more favorable parallel oxidative S-S coupling reaction [21] and the simultaneous deactivation of the metal catalyst through the coordination with a sulfur heteroatom. Usually the C-S bond formation has severe drawback due to the use of foul smelling thiols as well as volatility during reaction, leading to environmental pollution and health safety matter. Several heterogeneous catalysts bearing active metals like Pd [22,23], Co [24], Ni [25-27], and Cu [28-31] are reported for the C-S cross-coupling reactions. Due to high cost of palladium complexes like acetate, phosphine and organophosphorous ligands, as well as high moisture sensitivity, their use in cross coupling reactions are not so advantageous. On the other hand, Ni and Co containing catalysts are associated with the problem of toxicity in the systems. Among various transition metals, copper salts/complexes present a readily available and very cheap source for the homogeneous catalysts. But the problems arising due to the homogeneity of such catalyst over a heterogeneous support, leaching from the catalyst surface and air sensitivity of the catalysts have inspired us to find alternative pathway in designing Cu-anchored functionalized mesoporous material.

Herein, we report the synthesis of a new Cu-grafted organically functionalized mesoporous SBA-15 material via post-synthetic stepwise functionalizations of the parent pure silica SBA-15 material with 3-(2-aminoethylamino)propyldimethoxymethylsilane, 2-thiophene carboxaldehyde and copper chloride dehydrate, respectively. After amine functionalization over SBA-15 using 3-(2-aminoethylamino)-propyldimethoxymethylsilane, the MPAOS material (mesoporous amine functionalized organosilica) is subjected to Schiff base condensation reaction with 2-thiophene carboxaldehyde in anhydrous DMF under nitrogen atmosphere offering

MPIOS, which on treatment with CuCl₂.2H₂O at refluxing condition in ethanol resulted Cugrafted mesoporous catalyst Cu-MPIOS. This Cu-MPIOS material showed high catalytic efficiency in one pot C-S coupling reaction of benzyl bromide, thiourea and 4-bromoanisole in the presence of a mild base in aqueous medium under microwave assisted heating conditions and it also displayed good recycling efficiency. Use of microwave heating over conventional batch reactions has drastically reduced 10-12 h reactions to few minutes under the present reactions conditions over Cu-MPIOS catalyst.

2. Experimental

2.1. Material

P123 (Poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol), TEOS (tetraethyl orthosilicate) and 3-(2-aminoethylamino)propyldimethoxymethylsilane (M=206.36 g/mol) were purchased from Sigma Aldrich (India), 2-thiophene carboxaldehyde (M=112.15 g/mol) and copper chloride dihydrate (M=134.45 g/mol) were obtained also from Sigma Aldrich. The organic solvents were used as received.

2.2. Instrumentation

Nitrogen adsorption/desorption isotherms were obtained by using a Quantachrome Autosorb 1-C surface area analyzer at 77 K. Prior to gas adsorption, samples were degassed for 10-12 h at 453 K under high vacuum. NLDFT pore size distributions were determined from the sorption isotherm using the N₂ adsorption at 77 K on silica cylindrical pore model. Powder X-ray diffraction patterns were recorded on a Bruker D8 Advance SWAX diffractometer operated at 40 kV voltage and 40 mA current. The instrument has been calibrated with a standard silicon sample, using Ni-filtered Cu Ka (λ =0.15406 nm) radiation. FT-IR spectra of the functionalized mesoporous materials were recorded by using a Nicolet MAGNA-FT IR 750 spectrometer Series II. The UV-visible spectra of the material was recorded using UV 2401PC with an integrating sphere attachment where BaSO₄ was used as the background standard. For TEM analysis, 10 mg material was dispersed into dry ethanol by 5-10 minutes sonication. Then one drop of the

dispersed solution was dropped onto the carbon coated copper grid and dried before TEM analysis. To analyze the morphology and particle size of the samples JEOL JEM 6700 field emission scanning electron microscope (FE SEM) was used. Solid state ¹³C CP MAS NMR spectrum of the sample was obtained on a Bruker Advance 500 MHz NMR spectrometer using a 4 nm MAS probe under static condition (spinning rate 5000 Hz, with side band suppression). The copper content of the samples was determined by Shimadzu AA-6300 atomic absorption spectrophotometer (AAS). The EPR (electron paramagnetic resonance) spectrum was recorded for the solid sample at room temperature using a JESFA200ESR spectrometer (JEOL). Thermogravimetric analysis (TGA) and differential thermal analysis (DTA) of the sample were performed in a TGA instrument thermal analyzer TA-SDTQ-600 under air flow. The carbon, hydrogen and nitrogen (CHN) contents were determined in a Vario EL III elemental analyzer.

2.3. Synthesis of mesoporous amine functionalized organosilica (MPAOS)

Following a reported literature procedure SBA-15 material has been synthesized [32,33] and calcined to make it template-free. Then 600 mg of calcined SBA-15 was dispersed in 50 mL cleaned round bottom flask containing dry toluene (25 mL). Then 619 mg (3 mmol) of 3-(2-aminoethylamino)propyl dimethoxymethylsilane was added to the previous solution drop by drop. The resulting solution mixture was allowed to reflux for 24 h under N₂ atmosphere at 120-130 °C temperature. The light cream colored solid was collected using filtration and thoroughly washed with toluene, dichloromethane and methanol. The solid product was dried in air for one day and designated as MPAOS.

2.4. Synthesis of mesoporous imine functionalized organosilica (MPIOS)

At first 300 mg of MPAOS material was suspended in 100 mL two neck round bottom flask containing anhydrous DMF (25 mL). Previously, the flask was purged with nitrogen gas to make inert atmosphere and then 408 mg (3 mmol) of 2-thiophenecarboxaldehyde was gradually added to the former solution mixture under continuous stirring condition using a syringe via

rubber septa. Then the reaction mixture was allowed to reflux for 12 h under inert atmosphere at 130-140 °C temperature. Initially, the colour change was noticed from light cream to light brown but further colour change has not been observed during reflux. The resulting solid was collected by simple filtration technique and washed with ethanol to remove unreacted thiophene compound. The light brown colored product was dried in air and designated as MPIOS.

2.5. Synthesis of Cu anchored MPIOS (Cu-MPIOS)

200 mg of imine functionalized SBA-15 (MPIOS) was dispersed in 25 mL absolute ethanol in 50 mL round bottom flask. 150 mg of CuCl₂.H₂O was added to the former solution during continuous stirring condition. Then the solution mixture was refluxed for 12 h under N₂ atmosphere at 80-85 °C temperature. The reaction mixture was cooled down to room temperature and finally the brown coloured solid product was isolated by filtration. Then it was washed thoroughly with ethanol, distilled water to get rid of unreacted CuCl₂.H₂O from the material surface and dried in air, named as Cu-MPIOS.

2.6. C-S coupling reaction over Cu-MPIOS

For a typical experiment, C-S cross coupling reaction has been performed under microwave irradiation by changing substrate, solvent and temperature in the presence of catalyst. 20 mg catalyst and above mentioned three different reactant components were taken in 10 ml MW glass vial containing 5 mL H₂O. We have performed the coupling reaction using 4-bromoanisole (1.1 mmol, 188 mg); thiourea (1.2 mmol, 91 mg); and benzyl bromide (1 mmol, 187 mg) in the presence of the Cu-catalyst. A small magnetic needle was inserted in the sealed glass vial to make homogeneous mixture during progression of reaction (15 min). Then the loaded tube was placed in the microwave reactor pre-set at desired temperature. After completion of reaction the glass tube was cooled down to room temperature and transferred the solution to a separating funnel. The product was extracted using ethyl acetate and washed thoroughly with deionised water. Finally the oily pale yellow colored product was obtained after solvent evaporation using rotary evaporator, and characterized through ¹H and ¹³C NMR analyses using CDCl₃ as solvent.

3. Results and Discussion

3.1. Nanostructure and porosity

The small angle powder X-ray diffraction patterns of MPAOS, MPIOS and Cu-MPIOS are shown in Figure 1. From the figure it is noticed that the above mentioned three materials show three peaks due to distinct planes i.e. 100, 110 and 200 of the 2D-hexagonal mesophase [34,35]. The MPIOS material exhibits three diffraction peaks at 20 value of 0.92 (strong), 1.59 (weak) and 1.83° (weak) whereas Cu-MPIOS displayed peaks at 0.99, 1.68 and 1.94° , respectively. On the other hand decrease in *d*-spacing value of 0.6 nm (from 9.5 to 8.9 nm) and small shift of peak position towards higher 20 value indicates the grafting of Cu-sites at the surface of the imine functionalized mesoporous silica framework. Further, several sharp peaks have appeared in the wide angle PXRD pattern of Cu-MPIOS as shown in Figure S1, suggested crystalline nature of Cu-MPIOS after grafting of Cu.

The nitrogen adsorption-desorption isotherm of Cu-MPIOS material is shown in Figure 2. It exhibits the typical type IV isotherm with a large H1 type hysteresis loop in the range of 0.6 to 0.82 relative pressure of nitrogen, suggesting mesoporosity of the material [36,37]. As shown in Figure 2, the material displayed hysteresis loop in the high pressure region with sharp adsoption and desorption branches indicative of the presence of uniform large pore size. The pore size distribution has been estimated applying Non Local Density Functional Theory (NLDFT), as shown in the inset of Figure 2. It is clearly seen from the pore size distribution plot that there is one sharp peak at 8.1 nm. The BET (Brunauer-Emmett-Teller) surface area of Cu-MPIOS material was found to be 306 m²g⁻¹ and the pore volume was estimated to be 0.6216 g cc⁻¹. The De Boer statistical thickness (*t*-plot) indicates that surface area of Cu-MPIOS sample is obtained only due to mesoporosity as the microporous contribution to the surface area is nil.

3.2. Spectroscopic analysis

The FTIR spectra of three materials MPAOS, MPIOS and Cu-MPIOS have been shown in Figure 3. In plot 3a, the peak appearing at 1575 cm⁻¹ is due to strong in-plane $-NH_2$ scissoring. The broad peak arising at 3404 cm⁻¹ is for -NH stretching frequency. The peak at 2940 cm⁻¹ and 2869 cm⁻¹ could be assigned due to the presence of $-CH_3$ and $-CH_2$ groups in two plots. In plot

3b, the peak at 1634 cm⁻¹ can be attributed to the formation of imine bond (–C=N) via Schiff base condensation reaction, which has been shifted towards higher wavenumber region at 1656 cm⁻¹ indicating the proper coordination of copper through lone pair electron of ligand containing atoms. The Si-C stretching vibration appears at 800 cm⁻¹ for three samples. The C-N stretching vibration peak at 1000-1200 cm⁻¹ is merged with the stretching frequency of Si-O-Si in the range of 1130-1000 cm⁻¹ and that of Si-CH₂-Si in the range of 1250–1200 cm⁻¹ [38,39]. The other two absorption bands at 1547 and 1442 cm⁻¹ could be attributed to the asymmetric and symmetric vibration of bridging Cl atom, also suggest that Cu has been grafted to the material surface via coordination bond.

To identify the different types of silicon species in the material the solid state 29 Si CP/MAS NMR spectroscopic analysis has been carried out. As seen from the Figure 4, it is noticed that the Q bands appear in the region of -93 ppm to -120 ppm. Apart from the Q³ and Q⁴ signals, presence of new single signal at -19.5 ppm is designated as D^2 silicon [D^2 = $Si(OSi)2R_1R_2],$ proper grafting of suggesting the 3-(2aminoethylamino)propyldimethoxymethylsilane to the SBA-15 material [40,41]. On the other hand the absence of signal at -12 ppm chemical shift confirms the absence of further silanols on silica framework. This result suggested the grafting of $R_1R_2Si(O_2)$ moieties in between two Q^3 Si units. On the other hand, the ¹³C CP MAS NMR spectrum [42,43] of Cu-MPIOS material has been demonstrated in figure 4b where the more intense peak at 3 ppm and other two peaks in the region of 18 to 26 ppm designate the presence of -CH₃ and -CH₂ groups in organic moiety. The three carbons adjacent to nitrogen atom are appeared in the region of 41 to 48 ppm whereas for aromatic carbon the peaks are observed in 126 ppm to 148 ppm region. The peak at 168 ppm is attributed to the presence of imine group in Cu-MPIOS material.

The UV-visible spectra of three materials have been represented in Figure S2. As seen from figure S2a, the absorption bands were observed due to $n \rightarrow \pi^*$ transition of nitrogen lone pair and another transition $\sigma \rightarrow \sigma^*$ for presence of aliphatic group in the 3-(2-Aminoethylamino)propyldimethoxymethylsilane functionalized material. Figure S2b shows fully different spectrum with increased intensity absorption band due to additional $\pi \rightarrow \pi^*$ transition of imine functionalized material [44]. So, UV-visible spectra confirm the presence of chromophoric group in the moiety. Figure S2c presents the spectrum for the Cu grafted material which shows

very slight change in the absorption region compared to the parent material suggesting proper grafting of Cu to MPIOS, retaining the organic framework.

3.3. Electron Paramagnetic Resonance

To know the significant changes in coordination environment of metal (copper) centre, EPR (electron paramagnetic resonance) analysis has been carried out at room temperature using freshly prepared copper grafted solid catalyst. As shown in Figure 5 the EPR spectrum of Cu-MPIOS exhibits a rhombic structure corresponding to g values of $g_x=2.4$, $g_y=2.15$ and $g_z=2.01$. The differing value of all the g factors suggest that structure is not typical tetrahedral and may be caused due to the presence of a Cu–Cl…Cu non-bonding interaction resulting in a pentacoordinated quasi-square pyramidal structure of the material [45,46]. The presence of chlorine atom in EDAX also supports the proposed framework composition.

3.4. X-ray photoelectron spectroscopy

The XPS spectrum of Cu-MPIOS catalyst is given in Figure 6. The two binding energy values 935 eV and 955 eV corresponding to Cu 2p core splitting into Cu $2p_{3/2}$ and Cu $2p_{1/2}$ components, respectively. The absence of satellite peak at 944 eV ruling out the presence of +2 oxidation state of copper instead of +1 [47,48]. Although we used a Cu²⁺ precursor in the reaction, the conversion of Cu⁺² to Cu⁺¹ during the synthesis could be attributed due to the presence of organic thiols in the reaction medium and this has been well documented in the literature [49,50]. From the XPS result, the valance state of Cu species in the Cu-MPIOS material is found to be +1.

3.5. Microscopic structure analysis

The FEG-TEM images of Cu-MPIOS material has been shown in Figure 7. In most of the specimen, the regularly arranged ordered hexagonal pores, is perpendicular to the pore axis with a dimension of ~7.8 nm are noticed, suggesting the mesoporous material. The Fast Fourier Transform (FFT) pattern is shown in the inset of Figure 7a, indicating highly ordered hexagonal

array of the material. The figure 7b displays the channel like structure which is parallel to the pore axis. The FE-SEM images of the CU-MPIOS material has been demonstrated in Figure 8 at two different magnifications (22,000 and 7,000). The hexagonal cluster type of morphology was observed for this material.

3.6. Thermal stability and CHN analysis

In order to investigate the thermal stability of Cu-MPIOS material, thermal gravimetric analysis has been carried out at 10 °C temperature ramp under air flow from 25 °C to 800 °C temperature range. The TGA/DTA profile has been given in Figure S3. The first decrease in weight loss up to 79 °C, correspond to adsorbed water molecule in the porous framework. The second weight loss at 300 °C is attributed to cleavage of organic functionalized part of the framework. Thermal analysis data suggested high thermal stability of Cu grafted organic functionalized mesoporous silica material. CHN analysis data revealed carbon, hydrogen and nitrogen content in Cu-MPIOS sample where C= 18.47 %, H= 5.83 %, N= 4.85 %, respectively.

3.7. Catalysis

As a heterogeneous catalyst Cu-MPIOS has been used for one pot three component C-S cross coupling reaction using different aromatic halide with thiourea and benzyl bromide in microwave heating condition at 140°C in water medium. The resulting yield and turn over numbers of the products are summarized in Table. 1. As seen from the table the yield of the product thioethers varies from 65-81%. Benzyl phenyl sulfide, benzyl 4-methoxyphenyl sulfide and benzyl 4-cyanophenyl sulfide are very demanding pharmaceutically and these are formed in very good yield over this Cu-grafted functionalized mesoporous material. The observed turn over numbers (TONs) are very high and it was in the range of 186-232 for different ortho- meta- and para- substituted aromatic halides. We didn't observe significant change in the C-S coupling product yields in ortho-, meta- or and para-substitution in the aromatic halide as well as chloride or bromide as halide group for these

reactions (Table 1). However, no thioether product was obtained when the reaction was carried out in the absence of catalyst using similar conditions.

3.7.1. Dependence of temperature in C-S coupling reaction

As temperature plays a crucial role for catalysis, the reaction was carried out with varying reaction temperature using 4-bromoanisole, thiourea and benzyl bromide as model system. The conversion of the starting material to product was studied using thin layer chromatography and it was found that with increasing temperature up to 140 °C maximum conversion was obtained, but further increase in temperature does not affect the intensity of product spot significantly. Figure 9 represents the dependence of product yield on different temperature.

3.7.2. Solvent dependence

To optimize the best solvent for this one-pot three-component thioesterification reaction, we have used four different solvents EtOH, CH₃CN, H₂O and DMF. After completion of reaction it is noticed that the yield is more in aqueous medium due to high solubility of thiolate ion in water than other organic solvents. The dependence of C-S product yield on various solvents is shown in Figure 10. As seen from this bar diagram that under the optimized reaction conditions at 140 °C temperature and microwave assisted heating the C-S coupling product yield is highest (81%). Since the reaction involved ionic pathway via tholate anions [51], polar protic solvents with higher dielectric constant favored the reaction. Polar aprotic property of DMF and CH₃CN could be responsible for lower yield of the respective coupling products. On the other hand, higher solubility of thiourea and potassium carbonate in water together with its higher dielectric could be responsible for higher yield of the C-S coupling products in water.

3.7.3. Catalyst variation

To prove that the catalytic activity generates from the grafted Cu sites into mesoporous channel of Cu-MPIOS, a control experiment has been furnished taking 4-bromoanisole, thiourea, and benzyl bromide for one pot C-S coupling reaction as a reference. It has been observed no product formation occurs when the reaction is performed in absence of any catalyst in the aqueous medium. In addition to that MPAOS, MPIOS are used as catalyst for these three component coupling reaction at the aforesaid temperature in water medium. In that case the concentrations of the reacting components remain unchanged after the reaction. Hence, no product was yielded. Owing to this limitation same reaction was carried forward with homogeneous phase CuCl₂, 2H₂O shows a moderate yield of 46%, proving that the catalytic activity originates from the Cu sites. Although in ability to reuse and recycle the catalyst due to their homogeneous nature is a drawback. Cu-MPIOS catalyst based one pot reaction surprisingly depicts a high yield of maximum 81%. This deviation surely suggested the distinctive role of mesoporosity and surface area of the catalyst for C-S coupling reaction for the synthesis of different substituted thioether. Due to the large surface area, the organic molecule can easily be diffused through the mesoporous channel of functionalized silica material and interact with the Cu mediated sites. Table 2 represents the % yield of thioether products utilizing various catalysts.

3.7.4. Reusability test

To check the reusability behavior of Cu grafted imine functionalized SBA-15 catalyst (Cu-MPIOS), successive one-pot C–S coupling reactions have been carried out under same optimized conditions. After completion of reaction the catalyst has been recovered from the reaction mixture by simple filtration and washed thoroughly with deionized water to get rid of the excess K_2CO_3 base and highly soluble thiourea. Then it was washed with ethyl acetate to remove trace amount of organic reactant molecules. To reuse the catalyst for same coupling reaction, it was dried in oven at 75°C temperature for 2 h. No fresh catalyst was added to compensate any loss of the catalyst during recollection. The recycling efficiency has been plotted

in Figure 11. From this plot it is noticed that after completion of five reaction cycles the product yield decreases about 8%. Thus, very little decrease in the product yield after each reaction cycle proofs the high reusable behavior of the mesoporous Cu-catalyst.

3.7.5. Leaching test

A hot filtration test [52] has been conducted for the coupling reaction between 4bromoanisole, thiourea, and benzyl bromide as a representative reaction to demonstrate the possibility of the leaching of copper into the catalytic mixture during a reaction. After 8 min of reaction under microwave conditions the reaction mixture was filtered under hot conditions and with the filtrate, reaction was again continued for another 8 min under same conditions. It was found that there was no gain in the product yield in the second phase of the reaction in comparison to the first (46.8 and 46.6% yield for before and after hot filtration tests, successively). Further, AAS analysis of the filtrate could not detect the presence of Cu in the solution. This result suggests almost no leaching of Cu-species during the entire course of reaction and the catalyst is heterogeneous in nature.

3.7.6. Possible reaction mechanism

The possible reaction pathway in the one-pot three-component C-S coupling over Cu-MPIOS catalyst is supposed to proceed via generation of (S)-alkylisothiouronium salt via reaction between thiourea and benzyl bromide in the presence of a base. Then the salt was hydrolysed to thiolate ion and urea in basic medium where decomposition of urea during reaction produces ammonia and CO₂. Generation of ammonia used to maintain basicity of the reaction medium. The aryl halide can undergo the oxidative addition reaction with Cu-anchored mesoporous material, which could be the intermediate step of this catalytic cycle. In the meantime the generated thiolate ion can attack to the intermediate complex to form aryl organocopper sulfide intermediate via nuclophilic addition reaction. This is followed by the formation of the cross C-S coupled product aryl alkyl thioether via reductive elimination reaction. Although Jiang et al has reported the CuCl-catalyzed C-S cross-coupling reactions between alkenes and aromatic compounds for the synthesis of a wide range of thioethers with a

comparable yield [53], the catalysts recovery from the reaction mixture is a practical problem there. Among the Cu(I) based heterogeneous catalytic systems, Cu₂O powder has been employed in the reaction between thiol and aryl iodides to obtain the thioethers [54], but the use of large amount of KOH base in the reaction is not environment friendly and probably cause leaching of Cu(I) to the reaction mixture. Thus, the new Cu-grafted functionalized mesoporous material reported here is beneficial over the existing catalytic systems for the C-S cross-coupling reactions and the reaction proceeds very smoothly within only 20 min reaction time under microwave assisted heating conditions.

4. Conclusions

Cu-anchored ordered 2D hexagonal imine functionalized mesoporous organosilica material has been synthesized via post synthetic functionalization of SBA-15 with 3-(2-aminoethylamino)propyl-dimethoxymethylsilane followed by Schiff-base condensation reaction with 2-thiophene carboxaldehyde and Cu(II) impregnation. This Cu-grafted mesoporous material showed excellent catalytic activity and recycling efficiency in the one-pot three-component C-S cross coupling reaction of aryl halides, thiourea and benzylbromide in aqueous medium under microwave assisted heating conditions. Very efficient and environment friendly rout for the synthesis of these medicinal compounds via C-S coupling reaction over Cu-grafted functionalized mesoporous material may motivate the researchers to explore its catalytic potential for the synthesis of a wide range of value added coupling products.

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Figure 1. The small angle powder XRD pattern of MPAOS (a), MPIOS (b) and Cu-MPIOS (c).



Figure 2. The N_2 adsorption/desorption isotherm of the Cu anchored mesoporous imine functionalized organosilica catalyst Cu-MPIOS. The pore size distributions plot, determined by the NLDFT (Non Local Density Functional Theory) method is shown in the inset.



Figure 3. The FTIR spectra for three different materials (a) MPAOS, (b) MPIOS and (c) Cu-MPIOS.



Figure 4. ²⁹Si MAS NMR (a) and ¹³C CP MAS NMR (b) spectra of Cu-MPIOS material, recorded on a Bruker Advance 500 MHz NMR spectrometer.



Figure 5. The EPR spectrum of Cu-MPIOS sample.



Figure 6. The XPS data of Cu-MPIOS material.



Figure 7. The FEG-TEM images of Cu-MPIOS material (a) perpendicular to the pore axis, (b) parallel to the pore axis. The FFT pattern is shown in the inset of figure 8a.



Figure 8. The FE-SEM images of Cu-MPIOS material at high (left) and low (right) magnification.



Figure 9. Dependence of product yield on reaction temperature for 4-bromoanisole as a model example.



Figure 10. Dependence of C-S coupling product yield (mol%) by varying different solvents.



Figure 11. Recycling efficiency of Cu-MPIOS material up to fifth reaction cycle.



Scheme 1. Schematic representation for the formation of Cu-MPIOS material.



Scheme 2. Schematic illustration for one component C-S coupling reaction over Cu-MPIOS material.

Entry	Aryl halide	Time (min)	Product	Yield (%)	TON
1	Br	15	s S	77	221.2
2	H ₃ CO Br	15	H ₃ CO	81	232.7
3	H ₃ C Br	15	H ₃ C	79	227.0
4	OHC	15	онс	75	215.5
5	O ₂ N Br	15	O ₂ N S	76	218.3
6	ОНС	15	онс	73	209.7
7	H ₃ C	15	H ₃ C	76	218.3
8	NC	15	NC	78	224.1
9	HO	15	HO	74	212.6

Table 1. One pot three component C-S coupling reactions in microwave assisted heating conditions under optimized reaction conditions over the Cu-MPIOS material.



^aReaction was performed using 1 mmol 4-bromoanisole, 1.2 mmol thiourea and 1.1 mmol benzyl bromide over 20 mg catalyst at same reaction temperature 140 °C, for 10 min.

^bTON (Turn over number) is the no. of moles of substrate converted divided by mole of active site present in the catalyst.

Table 2. Dependence of product yield on various catalysts at 140 °C temperature using 4bromoanisole, thiourea and benzyl bromide as model system

	Catalyst name	Time (min)	Temperature (°C)	Product yield (%)
1.	SBA-15	20	140	0
2.	MPAOS	20	140	0
3.	MPIOS	20	140	0
4.	Cu-MPIOS	15	140	81
5.	CuCl ₂ , 2H ₂ O	20	140	46