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Cu-grafted functionalized mesoporous SBA-15: a novel heterogeneous catalyst for facile one-pot three component C-S cross-coupling reaction of aryl halides in water

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Abstract

A highly ordered 2D-hexagonal Cu-grafted functionalized mesoporous SBA-15 (Cu-PIF-SBA-15) has been designed through post-synthetic modification of mesoporous SBA-15. Surface functionalization technique has been employed to synthesize –NH_2 functionalized mesoporous SBA-15 material. Schiff-base condensation of this –NH_2 functionalized SBA-15 with phloroglucinol-dialdehyde leads to the formation of PIF-SBA-15. Reaction of PIF-SBA-15 with $Cu(OAc)_2.H_2O$ in ethanol under reflux leads to the formation of Cu-PIF-SBA-15 catalyst. This Cu-PIF-SBA-15 catalyst exhibits excellent catalytic activity in one-pot three component C-S coupling reaction for a diverse range of aryl halides (bromide and chloride) with thiourea and benzyl bromide in aqueous medium to offer aryl alkyl thioether in very good yields. Due to strong binding ability of the imine-N and phenolic-OH functional groups present in the phloroglucinol-diimine moiety of the framework, the anchored Cu(II) could not leach out from the surface of the mesoporous catalyst during the course of reaction and it has been observed that six repetitive reaction cycles not could cause any appreciable loss in the catalytic activity of this material.

Keywords: Aryl alkyl thioethers; Cu-catalyzed C-S coupling reaction; one-pot three component couplings; thioetherification; functionalized mesoporous silica.

Introduction

Catalytic methods involving the C-S bond formation reactions have been emerged as most versatile and powerful tool for the synthesis of value added thioethers.[1,2] Among thioethers the diaryl sulfides are of great significance due to their broad spectrum of therapeutic activities and they can be employed for diverse clinical applications in the treatment of cancer,[3] HIV, Alzheimer's[4] and Parkinson's diseases.[5] C-C, C-O, C-N cross coupling reactions can be effectively mediated by using various types of transition metal catalysts.[6,7] However, metal catalyzed *S*-arylation has been comparatively less explored than *N*-arylation and *O*-arylation because of the associated oxidative S-S homocoupling reaction and deactivation of metal catalysts by sulfur containing compounds. Various transition metals including Pd,[8] Fe,[9] Co,[10] Ni[11] and Cu[12] catalysts have been employed for *S*-arylation reactions. Among them the copper catalysts have been considered as the most effective and attractive in the *S*-arylation of aryl halides with thiols due to their high abundance and environmentally benign reaction conditions with minimum waste and health hazard to the environment. Usually, C-S coupling reactions suffers from the severe drawbacks including direct use of volatile and foul-smelling thiols, which could lead to strict environmental and safety problems, and thus place a ceiling on any scale up operation. Moreover, most of the C-S bond formation reactions are performed in the presence of toxic, flammable, expensive, non recyclable organic solvents and their disposal has been regarded as a key issue for the sustainable development of catalytic process in chemical industry.

To make the catalytic processes green and sustainable considerable efforts have been devoted to carry out the C-S coupling reactions under solvent-free conditions or in ionic liquid[13] or by using water as a reaction medium.[14-16] Water as a reaction medium also provides greater chemoselectivity compared with the other organic solvents.[17] In order to overcome the problems of the handling of thiols, various novel odorless protocols for making the C-S bond have been developed by the researchers. One-pot Michael addition reactions *via* an odorless process involving *in-situ* generation of S-alkylisothiouronium salts in water[18] and one-pot thioetherification of aryl halides using thiourea[19] (free from the foul smell of thiols) are worthy to mention here. The organic compounds such as 3-[bis(alkylthio)methylene]pentane-2,4-diones,[20] dialkyl disulfides,[21] 4,4-bis(alkylthio)but-3-en-2-ones[22] have been rigorously employed as thiol equivalent precursors for this purpose. But the shortcomings associated with these odorless protocols include use of homogeneous catalysts, strong alkaline medium and long reaction time. As a result these catalytic methods for C-S coupling or *S*-arylation reaction lacks in the recycling efficiency of the catalyst.

Recently, heterogeneous catalysts are hugely acknowledged for the sustainable development of any catalytic process due to their easy recovery, recycling as well as minimization of undesired toxic wastes[23] and *E*-factor.[24] The problems usually connected with the homogeneous catalysts can be easily overcome by heterogenisation of homogeneous counterpart onto insoluble inorganic or organic solid support in which active components are strongly immobilized.[25] Among several approaches of immobilization on the insoluble solid matrices organically functionalized mesoporous materials can be regarded as the most promising one in the catalysis research area due to their huge surface area, high adsorption capacity, tunable pore size distribution, high hydrothermal and mechanical stability.[26-28] The periodicity of nanoscale pores in these organically functionalized mesoporous materials could favor the easy accessibility of the catalytic sites and possible diffusion of the solvent and reactants within the insoluble solid matrix.[29] Mesoporous materials could be functionalized through several organic reactions in such a way so that the organic functional groups offer a crucial role to anchor the catalytic active sites (metal/metal oxide nanoparticles,[30,31] metal complexes[12]) covalently at the surface of the pores with the preservation of porous host structure. Recently, we have developed Cu(II)-anchored furfural imine-functionalized mesoporous silica, which exhibited excellent catalytic activity for conducting one-pot thioetherification in aqueous medium.[32]

Herein, we design a new Cu-containing phloroglucinol-diimine functionalized mesoporous SBA-15 catalyst *via* covalent grafting of Cu(II) at the surface of mesopores and the material has been employed in the one-pot, odorless C-S coupling reaction of aryl halides (bromide and chloride) using thiourea and benzyl bromide in aqueous medium in the presence of K_2CO_3 base at 100 ^{O}C. At first, amine functionalized mesoporous SBA-15 has been synthesized by the surface functionalization of calcined SBA-15 with 3-aminopropyl-triethoxysilane. This amine functionalized SBA-15 undergoes Schiff-base condensation reaction with phloroglucinol-dialdehyde to offer PIF-SBA-15 material, which on treatment of $Cu(OAc)_2.H_2O$ in absolute ethanol leads to the formation of novel Cu-PIF-SBA-15 mesoporous catalyst. This Cu-PIF-SBA-15 catalyst has been thoroughly characterized by using powder XRD, HR TEM, FE SEM, N_2 sorption, FT IR, ICP-AES, AAS and EXAFS experimental tools.

Experimental section

Synthesis of 3-aminopropyl functionalized SBA-15. Pure silica SBA-15 was synthesized by following the reported procedure as described before.[33] 0.1 g calcined SBA-15 was dispersed in 15 ml $CHCl_3$. Then 0.18 g of 3-aminopropyltriethoxysilane (3-APTES) was added dropwise into the dispersed $CHCl_3$ solution and the resulting mixture was allowed to stir at room temperature under N_2 atmosphere for about 12 h. The resulting white solid was isolated by filtration followed by washing with chloroform and dichloromethane and finally dried in air. The white colored solid was designated as -NH_2-SBA-15.

Synthesis of phloroglucinol-diimine functionalized mesoporous SBA-15 (PIF-SBA-15). Phloroglucinol-dialdehyde was prepared by following the procedure as described before.[34] Light red colored phloroglucinol-dialdehyde (0.0008 mol, 0.145g) was dissolved in 5 ml methanol by simple stirring at room temperature. 3-APTES functionalized SBA-15 material (-NH_2-SBA-15) was also dispersed into 15 ml methanol under continuous stirring condition. Then previously prepared phloroglucinol-dialdehyde solution was added dropwise into the amine functionalized methanol solution. After complete addition of aldehyde solution the resulting reaction mixture was kept under refluxing condition for about 10 h at 333 K. The color change of the reaction mixture from colorless to deep red was observed and no further color change took place on further reflux. The reaction mixture was cooled at room temperature and the final red product was collected through filtration, washed repeatedly with hot methanol to remove the unreacted dialdehyde. The red colored material was dried in air and was designated as PIF-SBA-15.

Synthesis of Cu-PIF-SBA-15. 1 g of the light red colored PIF-SBA-15 was suspended in 20 ml absolute ethanol under stirring condition. Then 0.2 g of $Cu(OAc)_2.H_2O$ was added into the ethanol solution and was refluxed for about 12 h at 363 K. The color of the mesoporous material was changed into brown color. The reaction mixture was cooled at room temperature and the resulting mesoporous material was filtered through suction with thoroughly washing with ethanol. The isolated brown colored mesoporous solid was designated as Cu-PIF-SBA-15 catalyst. The outline for the preparation of this Cu-PIF-SBA-15 catalyst is shown in Scheme 1.

General procedure for one-pot three component C-S coupling reaction over Cu-PIF-SBA-15. An oven-dried round bottomed flask equipped with magnetic stirring bar was charged with K_2CO_3 (552 mg, 4 mmol), thiourea (91 mg, 1.2 mmol), aryl halide (1 mmol), benzyl bromide (188 mg, 1.1 mmol) and Cu-PIF-SBA-15 (25 mg) in 5 ml water. Then the resulting mixture was refluxed in a preheated oil bath at 373 K under aerobic condition for the appropriate reaction time. Progress of the reaction was monitored by TLC. After a period of time the reaction was stopped and the reaction mixture was cooled at room temperature. Cu-catalyst was collected by filtration. Then the catalyst was washed repeatedly with water to remove the unreacted base and thiourea. Then the filtrate was extracted with EtOAc. The combined organic layer was washed with water and brine solution. Then the combined organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness to deliver the desired aryl alkyl thioethers as colorless oil. The isolated crude product was characterized by ^1H and ^{13}C NMR. The one pot C-S coupling reaction of aryl halide by using thiourea and benzyl bromide catalyzed by Cu-PIF-SBA-15 catalyst using H_2O as a solvent is depicted in the Scheme 2.

Results and discussion

The small angle X-ray powder diffraction patterns for the PIF-SBA-15 and Cu-PIF-SBA-15 samples are shown in the plots a and b of Figure 1. As seen from the figure that PIF-SBA-15 material displays three characteristic diffraction peaks in the 2θ region of 0.9 to 2.0 and these can be attributed for the 100 (strong), 110 (weak) and 200 (weak) reflections corresponding to the 2D-hexagonal mesostructure (Figure 1a). Decrease in the intensities of the peaks for the 110 and

200 planes for Cu-PIF-SBA-15 could be attributed to the grafting of Cu(II) complexes at the surface of the imine functionalized mesoporous SBA-15 material, which causes the lowering of local order (Figure 1b).[35] Whereas an increase in the *d*-spacing associated with the grafting of Cu(II) complexes in Cu-PIF-SBA-15 material (Figure 1b) could be responsible for the small shift in the XRD pattern. N_2 adsorption/desorption isotherms for the Cu-PIF-SBA-15 catalyst has been given in the Figure 2. The material presents typical type IV isotherm with a very large H2 type hysteresis loop in the 0.5 to 0.8 relative pressure of N_2. Mesopores with ordered arrangement can be established from this isotherm and the large hysteresis loop, which is the special feature for the large tubular pores of SBA-15. The BET surface area for Cu-PIF-SBA-15 material is 208 m^2g^{-1}. The pore size distribution of the material has been shown in the inset of Figure 2. The pore size distribution has been calculated by employing non-local density functional theory (NLDFT) method, which suggests that large mesopores having dimensions *ca.* 6.3 nm are uniformly distributed throughout the material. Pore volume of this material is 0.209 ccg^{-1}. This pore volume is large enough to allow diffusion of bulky organic molecules throughout the mesoporous channel and helps them to interact with each other for performing this one-pot three component coupling reaction.[27]

TEM images of the Cu-PIF-SBA-15 catalyst are shown in the Figure 3. Figure 3A also suggests that the large mesopores having dimensions ca. 6-7 nm are arranged regularly in a honey-comb like hexagonal array throughout the material. Information regarding channel directions, which are parallel to the thickness of the plate and the 110 reflection planes in the sample is noticeable from the TEM image (Figure 3B, perpendicular to the pore axis). The Fast Fourier Transform (FFT) pattern of a selected area of the sample (inset of the Figure 3B) reveals the 2D-hexagonal arrangement of the large mesopores.[36] The black colored spots observed in the

TEM images (Figures 3A and 3B) are the Cu-nanoclusters, which could be formed due to the coordination of phenolic–OH group and imine-nitrogen atoms with Cu^{2+}. The TEM image of the blank mesoporous SBA-15 without Cu has been shown in the Figure 3D. From this image it is quite evident that the pores having dimension 6-7 nm are not blocked with the copper. No black colored spots are found at the surface of the pores for this blank mesoporous SBA-15 material devoid of copper (Figure 3D). EPR spectra for the Cu-PIF-SBA-15 material (Figure 4) displayed four splitting features (m_I= -3/2, -1/2, +1/2, +3/2) in the low-field region for the parallel component, which are generated due to the hyperfine coupling between the unpaired electron and the nuclear spin of copper (I=3/2). But the signal for the perpendicular component ($g_\perp$= 2.07) remains un-resolved. From this EPR spectrum we can conclude that Cu^{2+} cations present in the sample assume axial symmetry. Another two important parameters $g_\parallel$= 2.26 and $A_\parallel$= 165G can be calculated from this EPR spectrum, which suggests the significant tetrahedral distortion of square planar complex around the Cu(II) ion.[37] In a planar bonding $g_\parallel$ decreases and $A_\parallel$ increases in the order of CuO_4>CuO_3N>CuO_2N_2>CuN_4. Here in our EPR spectrum for Cu-PIF-SBA-15 catalyst $g_\parallel$ and $A_\parallel$ values are 2.26 and 165G, respectively. Thus from the $A_\parallel$ and $g_\parallel$ values it can be concluded that tetrahedrally distorted Cu(II) discrete units are present in Cu-PIF-SBA-15.[38]

FT IR spectrum for phloroglucinol-diimine functionalized SBA-15 (PIF-SBA-15, Figure 5a) shows the peak at 1649 cm^{-1}, which can be attributed to the C=N bond stretching frequency of the imine bond. IR spectrum of Cu-PIF-SBA-15 material (Figure 5b) displays the peak for the C=N stretching frequency at *ca.*1631 cm^{-1}, which has been shifted to higher wavenumber, indicating that C=N bond is coordinated to Cu(II) through the lone pair of electron of nitrogen of Schiff-base ligand. The two strong absorption bands centered at 1564 cm^{-1} and 1456 cm^{-1} is attributed to the asymmetric and symmetric vibrations, respectively, of the bridging acetate ions.[39] This result clearly signifies that Cu has been covalently grafted into the mesopores channel of the PIF-SBA-15 material *via* coordination with imine N and O donors of phloroglucinol-diimine Schiff-base ligand. The two Cu atoms are linked together by bridging acetate ions.

Extended X-ray absorption fine structure (EXAFS spectrum) of Cu-PIF-SBA-15 (Figure 6A) catalyst illustrates very small pre-edge peaks due to 1s→3d transition at 8999.2 eV, corresponding to the oxidation state of Cu as ~+2. To get a more quantitative insight, the experimentally obtained $\chi(R)$ versus R spectra of the Cu-PIF-SBA-15 sample has been fitted with theoretically generated spectra (Figure 6B). To start with, the experimental spectrum the known crystallographic structure of CuO has been used to generate the theoretical $\chi(R)$ versus R spectrum of the sample. Catalyst environment and the co-ordination number of Cu in the Cu-PIF-SBA-15 catalyst are given in Table 1. A Cu-O first shell at a distance of 1.95 Å and having a coordination number of 4, a second Cu-O shell at a distance of 2.78 Å and having a coordination number of 2 and a third Cu-Cu shell at distance of 2.90 Å and having coordination of 4 have been considered as a reference to provide the theoretical spectrum of the sample upto a distance of 4 Å from the central Cu atom. Subsequently, the theoretically generated $\chi(R)$ versus R spectrum has been fitted with the experimentally obtained spectrum with the bond distance (R), coordination number (N) and the Debye-Waller factor (σ^2, representing the thermal and structural disorders) as fitting parameters. The experimentally obtained $\chi(R)$ versus R spectra of the catalyst Cu-PIF-SBA-15 catalyst was subsequently been fitted the best-fit curves in Figure 6B. Further, the best fit parameters have been given in Table 1. This EXAFS analysis data (Table

1) of the Cu-PIF-SBA-15 catalyst clearly proves that the Cu-O coordination takes places in the Cu-complex grafted with the SBA-15 material.

FE-SEM images of Cu-PIF-SBA-15 are shown in the Figure 7. From the Figures 7A and 7B it is definitely observed that Cu nanoclusters (having dimensions *ca* 0.22-0.3 μm) are formed due to the coordination of imine-N atoms and O atoms of phenolic–OH groups and these are dispersed homogeneously throughout the surface of the material. The SEM images reveal that the Cu-nanoclusters are attached onto the surface of the functionalized silica and they form an isolated irregular cluster island with a wide size distribution. The image further revealed that the white contrasts observed throughout the specimen are the locally populated Cu-nanoclusters. Actually these Cu nanoclusters are strongly anchored with the organic ligands which are viewed from the upper surface of the catalyst. The physical phenomena involve for the generation and stabilization of Cu-nanoclusters are the (i) interaction at the surface and (ii) diffusion of nanoclusters at the surface. These Cu-nanoclusters are generated due to the interaction of the surface functional groups with the metal ions. Now these already generated Cu-nanoclusters along with the other Cu-coordinated sites undergo diffusion to develop larger cluster island at the surface.[40] As a result catalytically active Cu-nanoclusters are more exposed at the surface of the catalyst,[41] which facilitates the interact with the organic reactants readily in the one-pot three component C-S coupling reaction.

Catalysis:

Cu-PIF-SBA-15 mesoporous heterogeneous catalyst has been employed in a series of one-pot C-S coupling reaction of different aryl halides with thiourea and benzyl bromide in aqueous medium under aerobic conditions (Scheme 2). We have performed a control experiment to make sure that the catalytic activity originates from the grafted Cu-sites into the mesoporous channel of the Cu-PIF-SBA-15 catalyst (Table 2). The one-pot C-S coupling reaction of 4-bromoanisole, thiourea and benzyl bromide was taken as a representative case to carry out this control experiment. At first the reaction was performed in absence of any catalyst (Table 2, entry 1) in aqueous medium at 100 ^{o}C. However, no product formation was observed in this case. We have also carried out this three-component coupling reaction by using SBA-15, SBA-15-NH_2 and PIF-SBA-15 (Table 2, entries 2, 3 and 4) as the catalysts at 100 ^{o}C in H_2O. But in these cases also no reaction takes place and the starting components remain unreacted. Triggered by these unsatisfied results, the reaction was carried out by using homogeneous phase $Cu(OAc)_2.H_2O$ as catalyst (Table 2, entry 5). In this case product yield was 42%. This result clearly proves that the catalytic activity generates from the Cu-sites. But due to homogenous nature of the $Cu(OAc)_2.H_2O$ it cannot be reused and recycled for further times. Homogeneous part of the catalyst with a loading 0.14 mmol g^{-1} takes 15 h to carry out the reaction with the corresponding product yield 42%. But when this homogeneous part of the catalyst is grafted in the imine functionalized mesoporous SBA-15 material with a loading 0.164 mmol g^{-1}, then the rate of the catalytic reaction is drastically increased. Loading is increased in about 0.02 mmol g^{-1} in our catalyst compared with the homogeneous counterpart. So from this result we can conclude that the rate of the catalytic reaction has been increased with the increase of loading of copper by little bit amount for our Cu-PIF-SBA-15 catalyst compared with the homogeneous counterpart of the catalyst. Then the reaction was performed using Cu-nanoparticles grafted SBA-15 (Table 2, entry 6) under same reaction condition. In this case yield of the product has been increased a little. But when this one-pot coupling reaction was carried out in the presence of Cu-PIF-SBA-15 catalyst (Table 2, entry 7) then the yield significantly increased upto 79%. This experimental result proves that the surface area and mesoporocity offer a decisive role for performing one-pot three component C-S coupling reaction for preparation of different substituted thioethers. Large surface area allows the diffusion of organic molecules into the mesoporous channel of functionalized SBA-15 material and helps them to interact with the Cu-nanoclusters grafted at the surface. That is why the rate of this C-S coupling reaction is quite high than the other conventional catalysts.

Effect of reaction temperature. Temperature plays a crucial role in the catalytic activity of Cu-PIF-SBA-15 for this C-S coupling reaction in aqueous medium considering the reaction of 4-bromoanisole, thiourea and benzyl bromide as a representative case (Table 3). Table 3 further revealed that no reaction occurred at 25 °C while conversion increased steadily up to 100 °C with no further benefit above this temperature.

Effect of solvent. In order to optimize the best solvent needed for this reaction, we have carried out this one-pot C-S coupling reaction in various solvent under aerobic condition over Cu-PIF-SBA-15 as catalyst. The one-pot aryl sulfur coupling reaction of 4-bromoanisole, thiourea and benzyl bromide in the presence of K_2CO_3 base has been considered as the representative case. The results are listed in the Table 4. All the reactions have been performed under refluxing condition considering the different solvents. Only reaction in DMF has been conducted at 110 ^{o}C. For the solvent like THF poor yield of product is obtained. But with the addition of polar protic solvent in THF yield increased upto 10%. As the lack of solvation on the nucleophile (here thiolate ion) increases the rate of substitution reaction. When EtOH (polar protic) was used as solvent then the thiolate ion gets solvated through solvation and hence 40% product yield was obtained. When polar aprotic solvents like DMF and CH_3CN are used then 50% and 45% yield of products are obtained, respectively. Here yield has been increased a little bit amount compared with the polar protic solvent EtOH due to presence of naked thiolate nucleophile. But surprisingly in water 79% yield of product was obtained, which may be due to the good solubility of thiourea and potassium carbonate in water. Thus, for this one-pot thioetherification reaction by using Cu-PIF-SBA-15 catalyst water can be regarded as the best solvent.

One-pot three component C-S coupling reaction under optimized condition (water as reaction medium and 100 ^{o}C reaction temperature) was performed by considering various aromatic halides (bromide and chloride) with benzyl bromide and thiourea (Table 5). The times (h) taken to carry out the reaction for different compounds are given in the Table 5. The results of Table 5 suggest that reaction takes 10-12 h for completion for all bromo- and chloro-arenes and the respective turn over numbers (TONs) are moderately high *ca* 171-193. ^{1}H and ^{13}C NMR results are listed in the supporting information (ESI). Cu content in the fresh Cu-PIF-SBA-15 catalyst was 0.164 mmol g^{-1} as measured by ICP-AES analysis. Electron donating (Table 5, entries 1, 5 and 9) and electron withdrawing (Table 5, entries 2, 4, 6, 7, 10, 11, 12, 13 and 14) functional groups attached with the aryl chlorides and bromides underwent one-pot *S*-arylation reaction very smoothly. The *meta*-substituted bromo- and chloro-arenes (Table 5, entries 9 and 14) participated in the aryl sulfur coupling reaction without any complexity. Thus the nature and position of the functional groups attached with the aryl bromides and chlorides do not play significant role for this reaction. Heterocyclic bromide likes 4-bromopyrazole (Table 5, entry 8) became compatible for this reaction. Several sensitive functional groups such as -Cl, -Br, -NO_2 attached with the aromatic ring took part in the reaction with equal efficiency (Table 5, entries 9-14).

Reusability of the catalyst. In order to check reusability of the Cu-PIF-SBA-15 catalyst, the one-pot C-S coupling reaction of 4-bromoanisole, thiourea and benzyl bromide under optimized reaction conditions was carried out. After the completion of the reaction, catalyst was recovered from the reaction mixture by employing simple separation technique. Then the catalyst was washed with copious amount of water to remove excess base and thiourea. Then catalyst was again washed with ethyl acetate followed by with diethyl ether to remove excess organic reactants. Then the recovered catalyst was dried in air and activated in an oven at 75 ^{o}C for about 6 h. The Cu-PIF-SBA-15 catalyst had the potential of efficient recycling for further six additional reaction cycles without significant loss of catalytic activity establishing the recycling and reusability of the catalyst. Only very little drop in the product yield in each catalytic cycle is observed. It is quite evident from the Table 6 that the TON of the catalyst is retained from fresh to the 6th reaction cycles, suggesting high catalytic efficiency of Cu-PIF-SBA-15.

Leaching Test. Leaching test was performed to understand the nature of the Cu-PIF-SBA-15 catalyst. After the reaction was over, the catalyst was separated by filtration. Then 30 wt% of nitric acid was added to the filtrate, and the resulting solution was adjusted to 5 wt% nitric acid solution. Now Cu content in the filtrate solution was determined by using Atomic absorption spectrometric (AAS) analysis. Atomic absorption spectrometric analysis of the liquid phase suggested absence of Cu in the filtrate and it remains completely colorless. Further, the ICP-AES analysis for the reused catalyst confirms that no leaching of Cu takes place during the course of reaction. Cu content has been marginally reduced to 0.159 mmol g^{-1} after the sixth catalytic reaction cycle (this decrease is within the experimental error of the ICP-AES chemical analysis). These experimental results clearly signify that no leaching of Cu occurred during the course of the reaction and Cu-nanoclusters are covalently grafted with the organic functional groups in the mesoporous silica. Thus, Cu-PIF-SBA-15 catalyzed C-S coupling reactions are purely heterogeneous in nature.

Hot filtration Test. Hot filtration test was carried out under optimized condition considering 4-bromo anisole as the representative case. After 6 h of the reaction it has been realized that only *ca.* 50% conversion was achieved, confirmed by GC and ^{1}H NMR analysis. Then the C-S coupling reaction was again continued with this filtrate for another 6 h under the similar reaction conditions. But no further increase in product conversion after another 6 h reaction time was observed. This experimental result clearly proves that Cu complex nanoclusters are covalently anchored with the organic functional groups in the mesopore surface of functionalized SBA-15 material. No further increase in product conversion beyond 50% has been observed. This further suggested no leaching of Cu during the course of reaction and heterogeneous nature of the catalyst. AAS analysis for the Cu content in used Cu-PIF-SBA-15 catalyst revealed 1.05 wt% Cu, which is a close agreement with the Cu loading of the fresh catalyst estimated independently from the ICP-AES analysis.

Plausible reaction pathway. One-pot three component C-S coupling reaction proceeds *via in situ* formation of *S*-alkylisothiouronium salt.[19] The plausible reaction pathway catalyzed by Cu-PIF-SBA-15 catalyst for the development of aryl alkyl thioether has been shown in the Figure 8. At the first step, thiourea reacts with benzyl bromide in the presence of K_2CO_3 base to produce *S*-alkylisothiouronium salt. This *S*-alkylisothiouronium salt has been hydrolyzed with base to generate thiolate ions and urea. Pyrolysis of urea upon heat treatment of the reaction mixture takes place to offer CO_2 (g) and ammonia. Generated thiolate ions are the synthetic equivalent of thiols. Aryl halide in undergoes oxidative addition reaction with the Cu(II)-complex grafted into the mesoporous wall of phloroglucinol-diimine functionalized SBA-15 material to afford an intermediate (**A**). Then in situ generated thiol moiety takes part into the nucleophilic addition reaction with the intermediate (**A**) to produce an aryl organocopper sulfide intermediate (**B**). This intermediate **B** on reductive elimination provided cross coupled aryl alkyl thioether.

Characterization of the reused catalyst: Reused catalyst was further characterized by small angle powder XRD pattern, TEM and SEM analyses in order to investigate any further noticeable change occurs in the catalyst after the catalysis. Small angle powder X-ray diffraction pattern of the reused catalyst (Figure 1c) displays the characteristic mesophase of the Cu-PIF-SBA-15 catalyst. Only a little decrease in the intensity of peak for the reused catalyst in the XRD pattern is observed, which may be due to the blocking of some mesopores by organic molecules during the course of reaction. From this XRD pattern we can conclude that the 2D-hexagonal mesophase of the Cu-PIF-SBA-15 catalyst has been preserved after the catalysis. A little shift in the powder XRD pattern of reused catalyst occurs (Figure 1c). After several repetitive reaction cycles the expansion in pore-wall for the reused catalyst could occur due to the hydrolysis of silica species present at the catalyst surface. As a result *d*-spacing for the reused catalyst is increased. This increase in the *d*-spacing is responsible for the shift in the peak position for the reused catalyst. TEM image (Figure 3C) of the reused catalyst suggests that the 2D-hexagonal mesostructure of the Cu-PIF-SBA-15 material has been retained and there is no obvious change in uniform distribution of Cu-nanoclusters throughout the material after the catalysis. SEM images of the reused Cu-PIF-SBA-15 catalyst (Figures 7C and 7D) further suggest us that there is no change in the morphology and size of the Cu-grafted sites during the catalysis. The above results imply that the catalyst was very stable during the catalysis and could sustain these conditions.

Conclusions

In conclusion, we have developed a novel Cu(II)-grafted phloroglucinol-diimine functionalized mesoporous SBA-15 material by using post grafting technique. Surface functionalization, Schiff-base condensation followed by Cu(II) impregnation resulted this Cu-grafted phloroglucinol-diimine functionalized mesoporous SBA-15. This novel mesoporous catalyst Cu-PIF-SBA-15 has been employed to carry out an efficient, one-pot, odorless C-S coupling reaction of aryl halides (bromides and chlorides) using thiourea and benzyl bromide in aqueous medium in the presence of K_2CO_3 base at 100 ^{o}C. This novel protocol is free from foul-smelling thiols for preparation of C-S bond is easy, clean, inexpensive, practical and environmentally benign. This catalyst showed negligible leaching of Cu, and can be reused for six repetitive reaction cycles without significant loss of any catalytic activity. Thus, growing demand of environmentally benign synthesis could be achieved over Cu-PIF-SBA-15 in this C-S coupling reactions using water as the reaction medium.

Supporting Information

Characterization techniques, Preparation of Cu-nanoparticles supported over SBA-15, ^{1}H and ^{13}C NMR chemical shifts for different coupling products are available in the Supporting Information. This information is available free of charge via the Internet at http://pubs.acs.org/.

Acknowledgements

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Table 1 Best-fit parameters of the bond distance, coordination number and the Debye-Waller factors for the Cu-PIF-SBA-15 catalyst.

	Cu-O1	**Cu-O2**	**Cu-Cu**
R (Å)	1.97	2.71	3.37
N	2.5	0.9	1.5
σ^2	0.005	0.005	0.005

Table 2 Screening of different catalysts for one-pot three component C-S coupling reaction[a]

Entry	**Catalyst**	**Time (h)**	**Yield[b](%)**
1	No catalyst	15	0.0
2	SBA-15	15	0.0
3	SBA-15-NH_2	15	0.0
4	PIF-SBA-15	15	0.0
5	$Cu(OAc)_2.H_2O$[c]	15	42.0
6	Cu nanoparticles supported over SBA-15	15	50.0
7	Cu-PIF-SBA-15[d]	12	79.0

[a]Reaction conditions: 4-bromoanisole (1 mmol, 187 mg), benzyl bromide (1.1 mmol, 188 mg), thiourea (1.2 mmol, 91 mg), K_2CO_3 (4 mmol, 552 mg), solvent (H_2O, 5 ml), temperature (100 ^oC) Cu-PIF-SBA-15 Catalyst (25 mg). [b]Isolated yield of product, [c]Cu loading 0.14 mmol g^{-1}. [d] Cu loading in Cu-PIF-SBA-15 catalyst 0.164 mmol g^{-1}.

Table 3 Effect of reaction temperature (^{o}C) for one-pot three component C-S coupling reaction[a]

Entry	**Temperature (^{o}C)**	**Yield[b] (%)**
1	25	No reaction
2	40	5
3	60	30
4	80	60
5	100	79

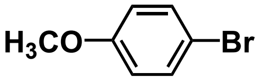
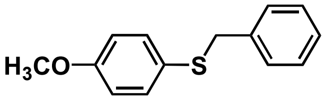
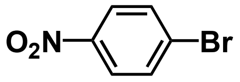
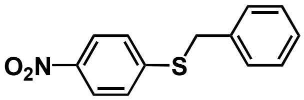
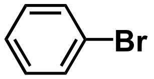
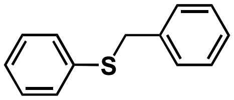
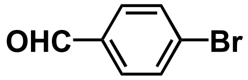
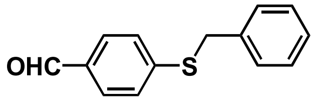
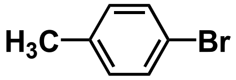
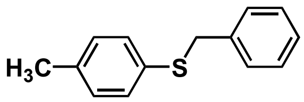
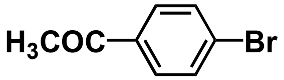
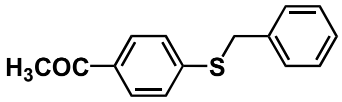
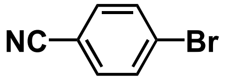
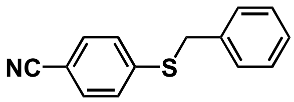
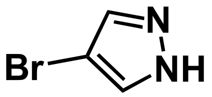
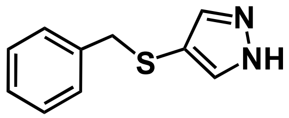
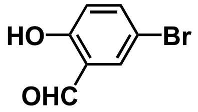
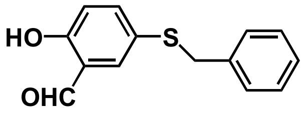
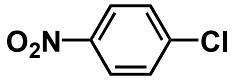
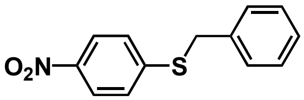
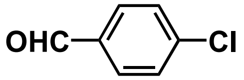
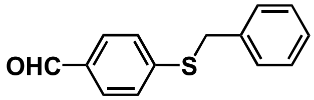
[a] Reaction conditions same as that given in Table 2. All the reactions were performed for 12 h.

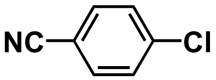
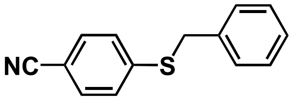
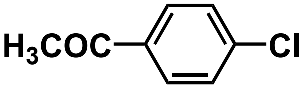
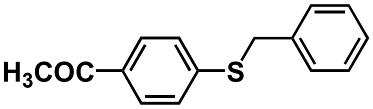
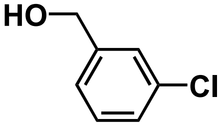
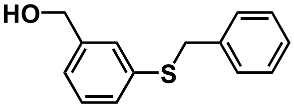
Table 4 Variation of different solvents for one-pot three component C-S copuling reaction[a]

Solvent	**Yield (%)**
THF[b]	5
THF: H_2O (1:1)[c]	10
EtOH[d]	40
DMF[e]	50
CH_3CN[f]	45
H_2O[g]	79

[a]Reaction conditions same as that given in Table 2, [b]65 °C, [c]65 °C, [d]90 °C, [e]110 °C, [f]80 °C, [g]100 °C. All the reactions were performed for 12 h; Cu loading in Cu-PIF-SBA-15 catalyst 0.164 mmol g^{-1}.

Table 5 One-pot three component C-S coupling reaction of different haloarenes catalyzed by Cu-PIF-SBA-15 catalyst under optimized reaction condition[a]

Entry	Aryl Halides	Time (h)	Product	Yield (%)	TON[b]
1		12		79	193
2		10		78	191
3		12		75	183
4		10		75	183
5		12		78	191
6		12		76	185
7		10		75	183
8		12		78	191
9		12		78	191
10		12		75	183
11		12		72	175

12		12		75	183
13		12		70	171
14		12		70	171

[a]Reaction conditions is same as that given in Table 2.; [b]Turn over number (TON) = moles of substrate converted per mole of active site; Cu loading in Cu-PIF-SBA-15 = 0.164 mmol g^{-1}.

Table 6 Recycling potential of mesoporous Cu-PIF-SBA-15 catalyst in C-S coupling reactions

No. of cycles	Fresh	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6
Yield (%)	79	79	79	77	77	75	74
Time (h)	12	12	12	12	12	12	12
TON	193	193	193	187	187	183	180

Caption for figures

Figure 1	Small angle powder XRD pattern of PIF-SBA-15 catalyst (a), Cu-PIF-SBA-15 (b) and reused catalyst after sixth catalytic cycle (c).
Figure 2	N_2 adsorption/desorption isotherm of the phloroglucinol-diimine functionalized Cu-grafted mesoporous catalyst Cu-PIF-SBA-15. Pore size distributions estimated through NLDFT method is shown in the inset.
Figure 3	HR TEM images (A, parallel to pore axis), (B, perpendicular to pore axis) of Cu-PIF-SBA-15; TEM image of reused catalyst after sixth (C) catalytic cycles and TEM image of blank silica SBA-15 without Cu (D). Fast Fourier Transform (FFT) pattern is shown in the inset of Figure B.
Figure 4	EPR spectrum of Cu-PIF-SBA-15 catalyst.
Figure 5	FTIR spectra of PIF-SBA-15 (a) and Cu-PIF-SBA-15 (b).
Figure 6	EXAFS analysis data of Cu-PIF-SBA-15 (A) and radial distribution function ($\chi(R)$ versus R) around Cu atom (without phase-shift correction) for the Cu-PIF-SBA-15 catalyst as obtained from the experimental $\mu(E)$ versus E spectra.
Figure 7	FE-SEM images of Cu-PIF-SBA-15 catalyst (a, b and c) and reused catalyst after first cycle (d).
Figure 8	Plausible reaction pathway for one-pot three component C-S coupling reaction catalyzed by Cu-PIF-SBA-15 catalyst.

Caption for Schemes

Scheme 1	Synthesis of Cu-PIF-SBA-15 catalyst.
Scheme 2	One-pot three component C-S coupling catalytic reaction over Cu-PIF-SBA-15 catalyst.

Figure 1 [Mondal *et. al*]

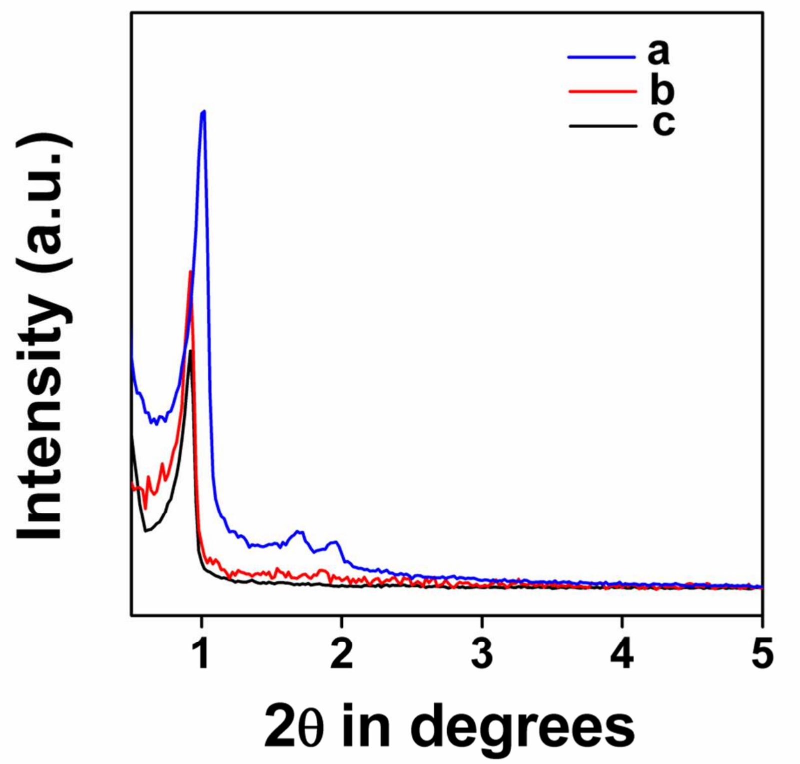


Figure 2 [Mondal *et. al*]

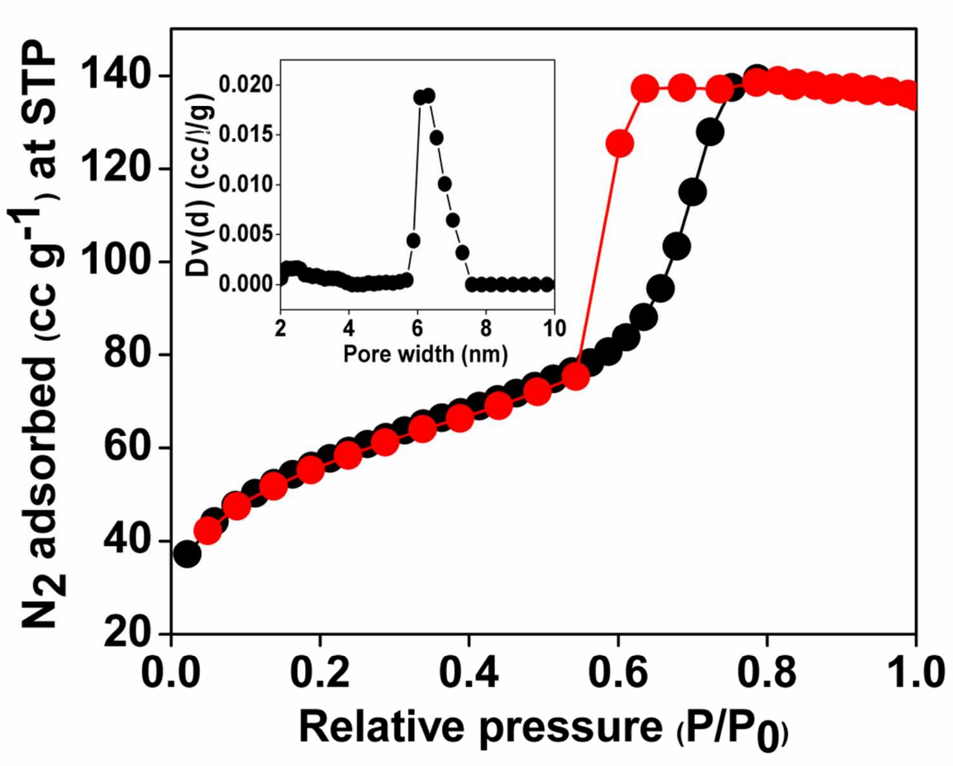


Figure 3 [Mondal *et. al*]

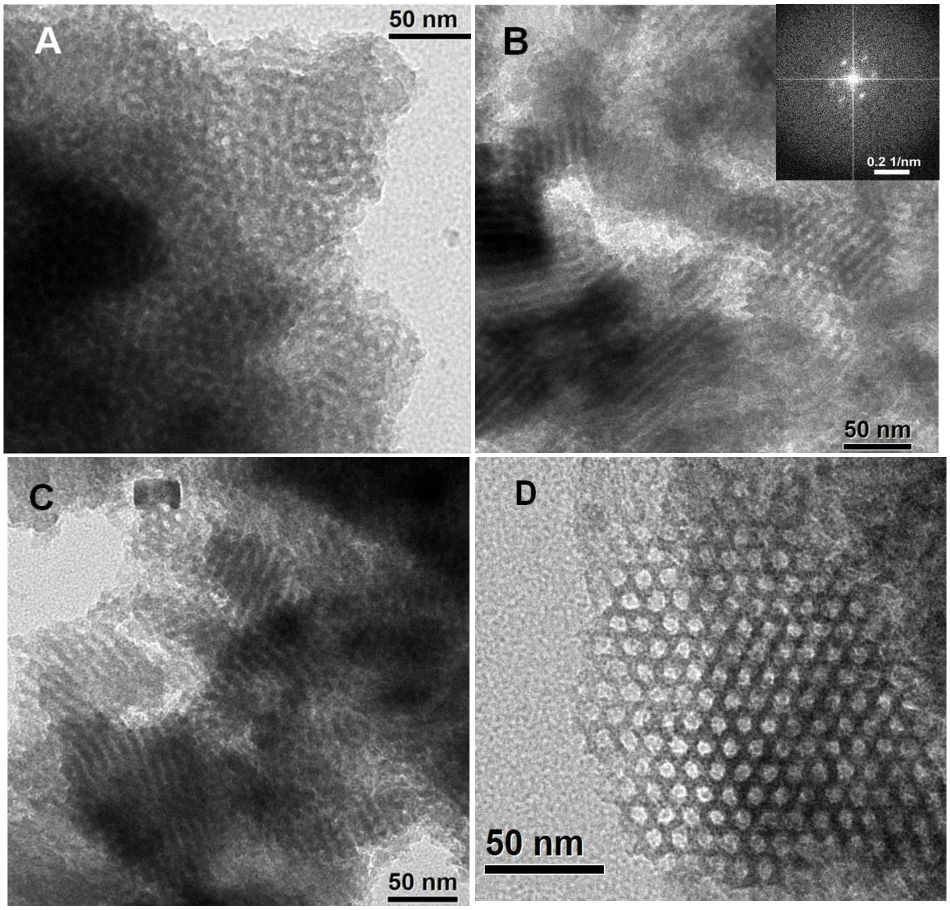


Figure 4 [Mondal *et. al*]

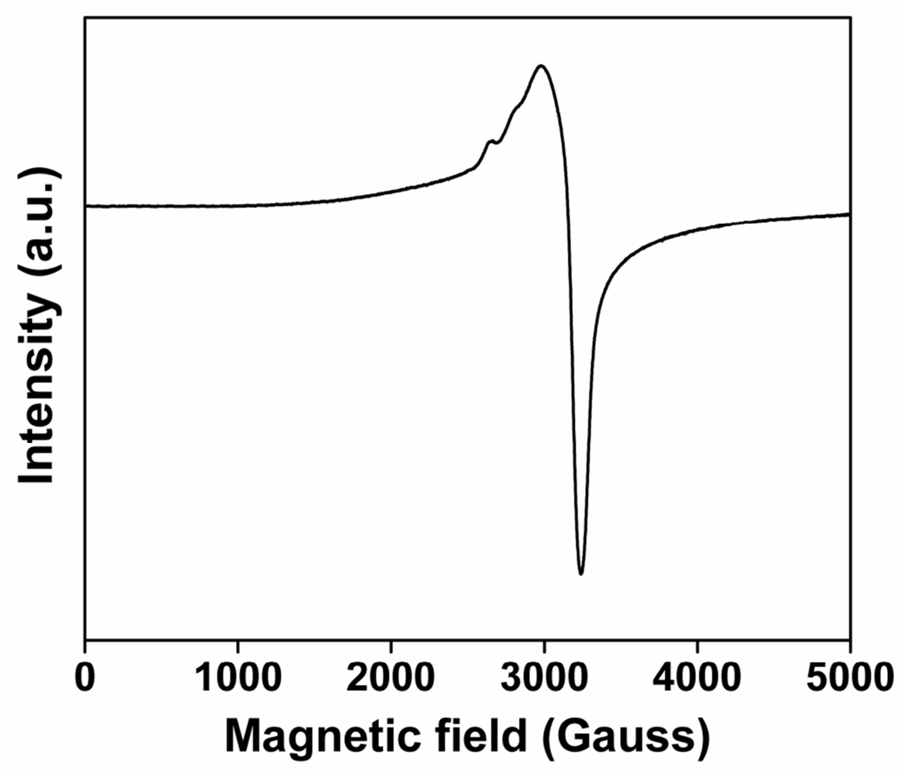


Figure 5 [Mondal *et. al*]

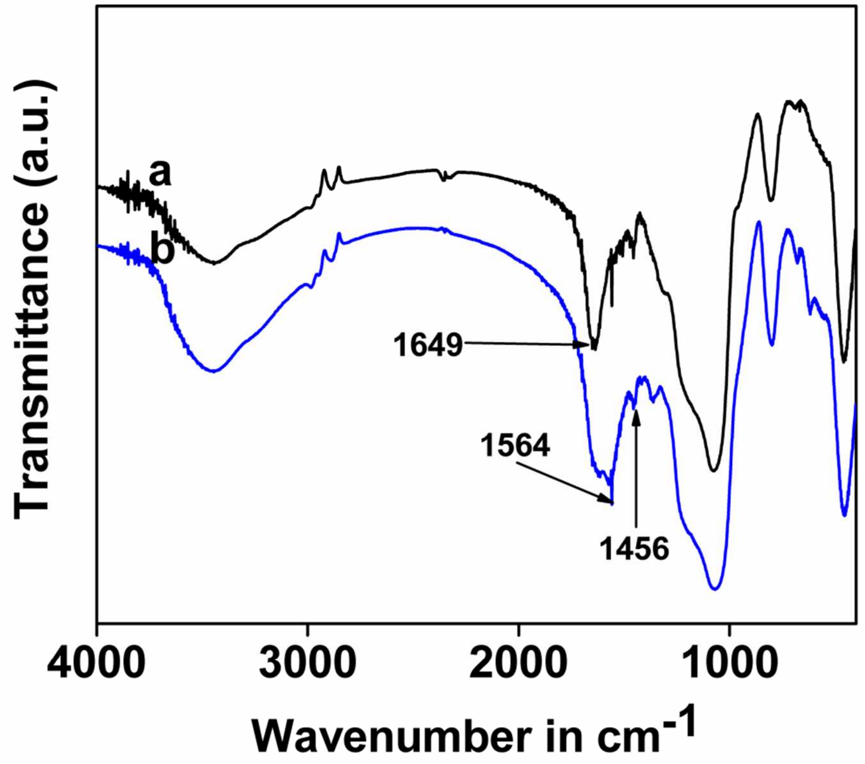


Figure 6 [Mondal *et. al*]

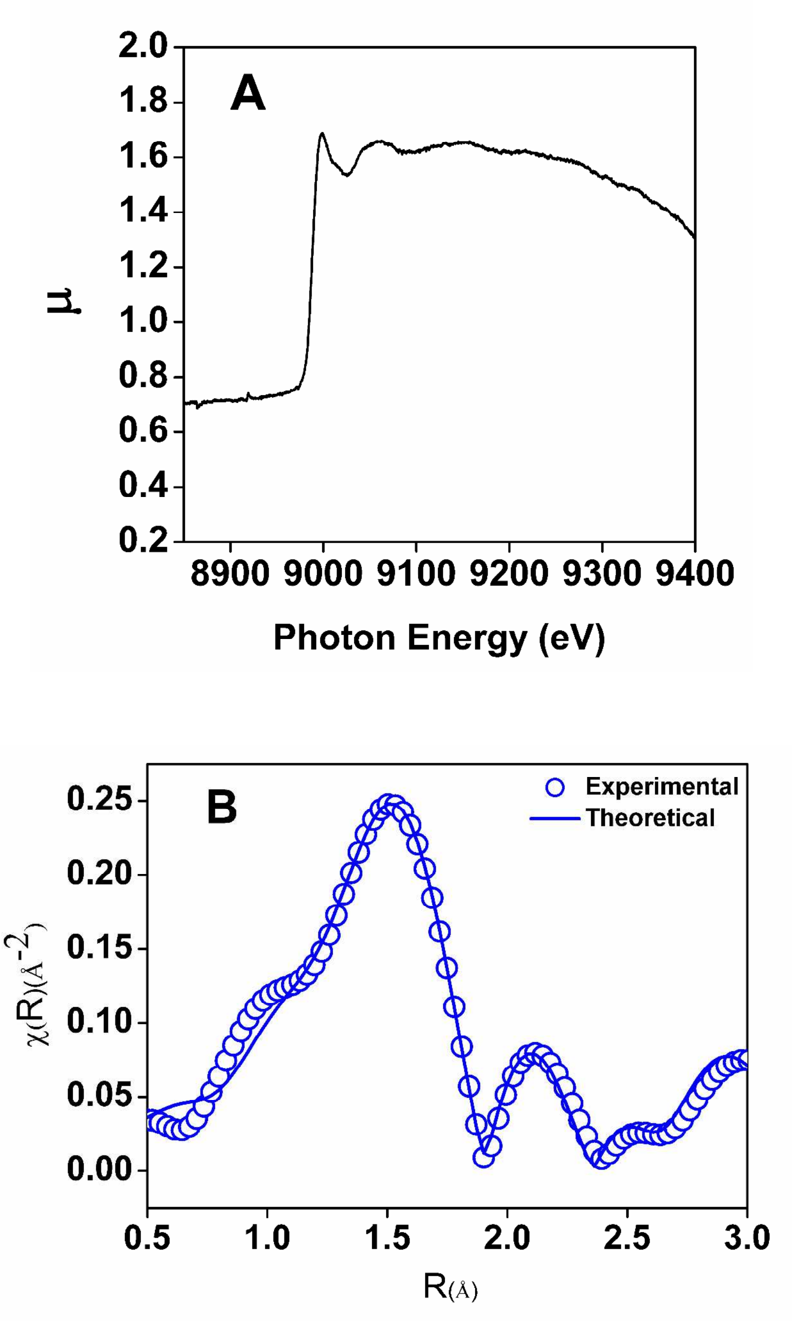


Figure 7 [Mondal *et. al*]

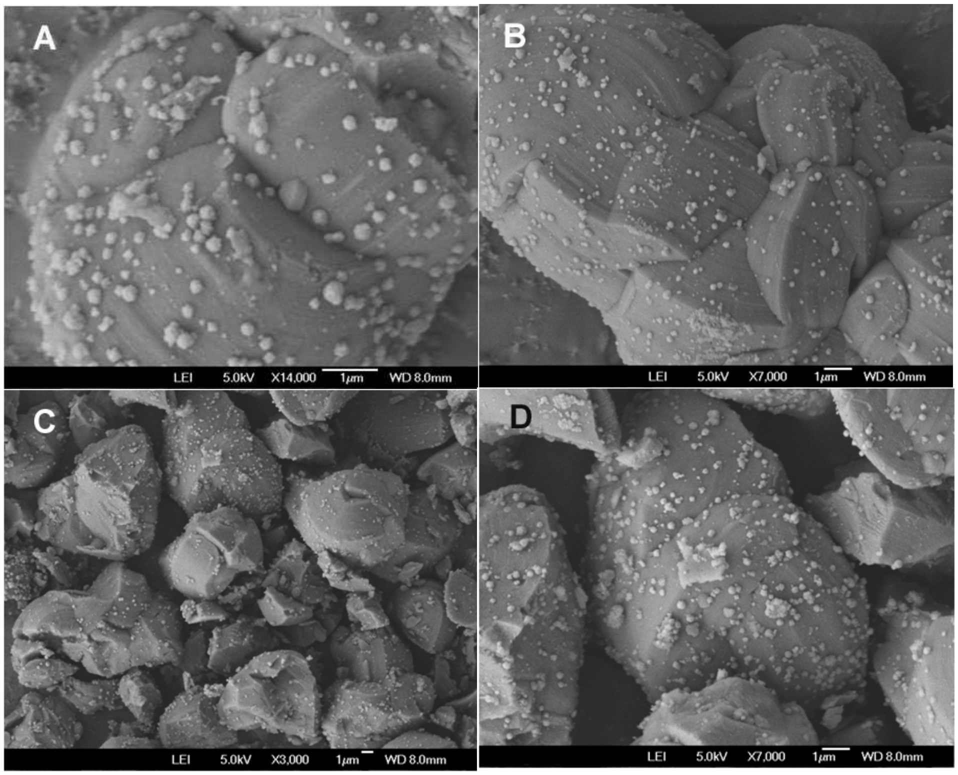
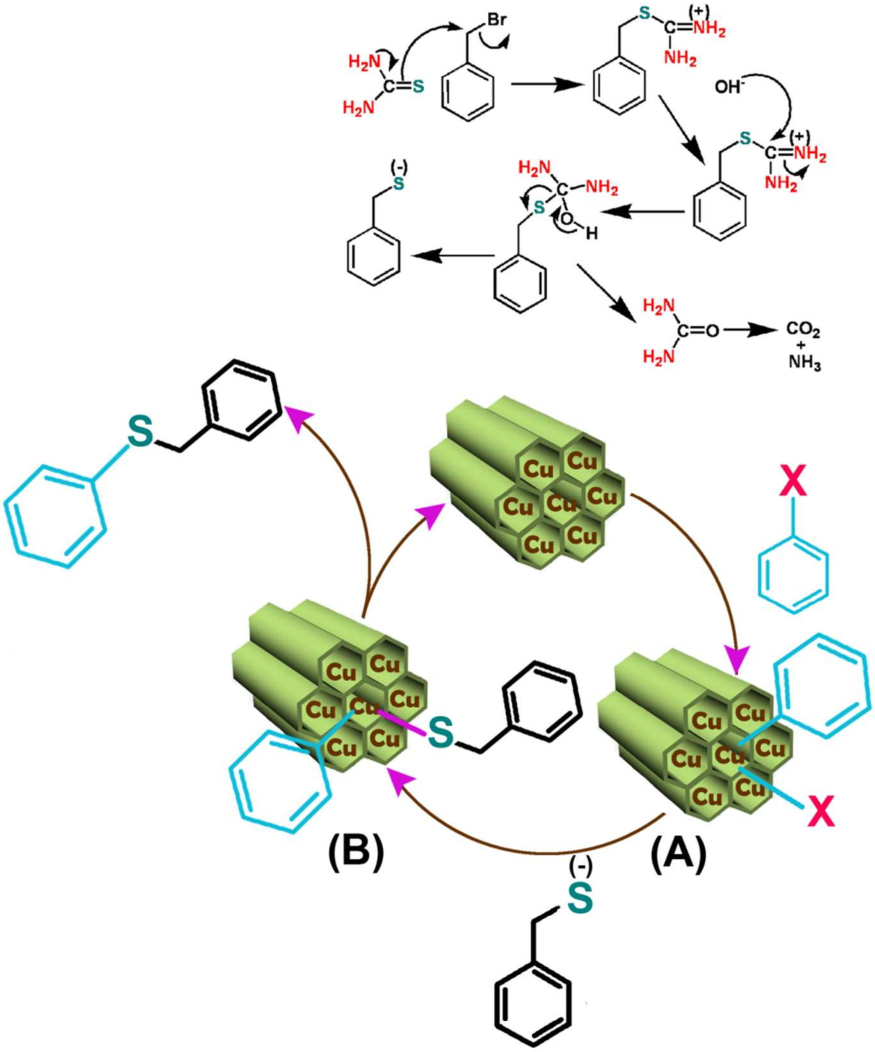
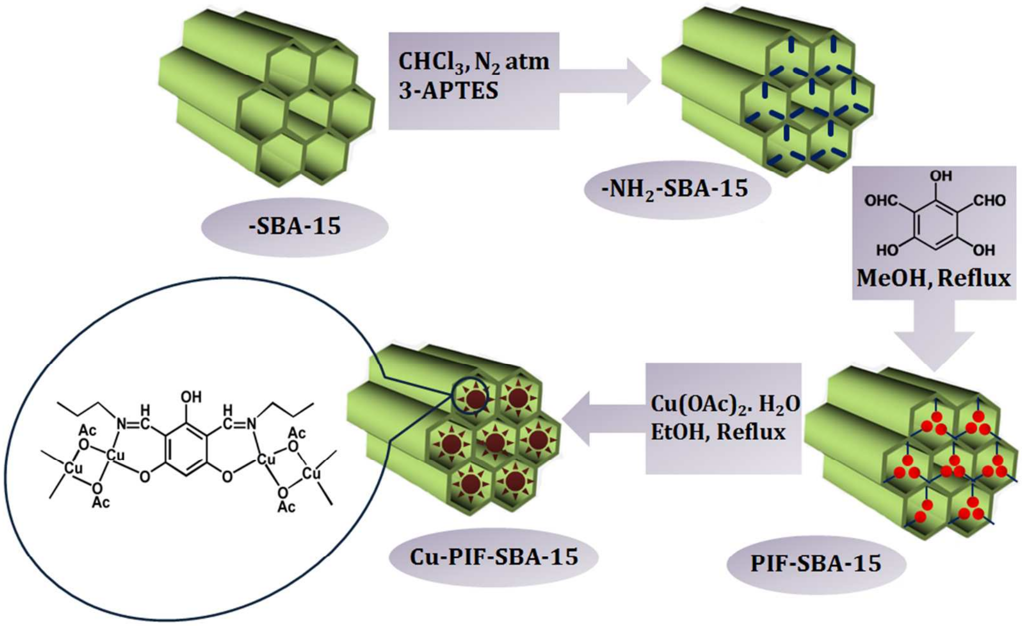


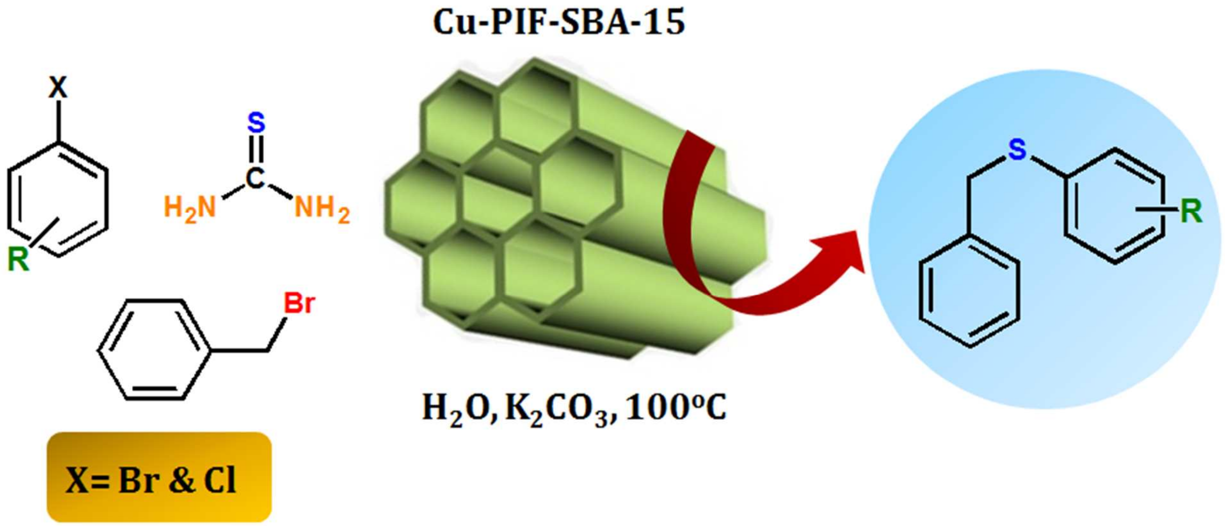
Figure 8 [Mondal *et. al*]



Scheme 1 [Mondal *et. al*]



Scheme 2 [Mondal *et. al*]



Cu-grafted functionalized mesoporous SBA-15: a novel heterogeneous catalyst for facile one-pot three component C-S cross-coupling reaction of aryl halides in water

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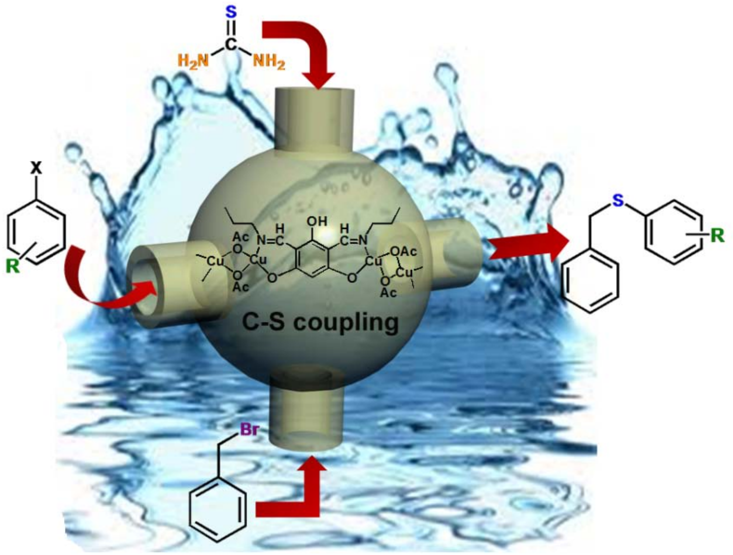

Highly ordered 2D-hexagonal Cu-grafted functionalized mesoporous SBA-15 has been synthesized through post-synthetic modification of mesoporous SBA-15. The material showed excellent catalytic activity in one-pot three component C-S coupling reaction of diverse range of aryl halides with thiourea and benzyl bromide in aqueous medium.