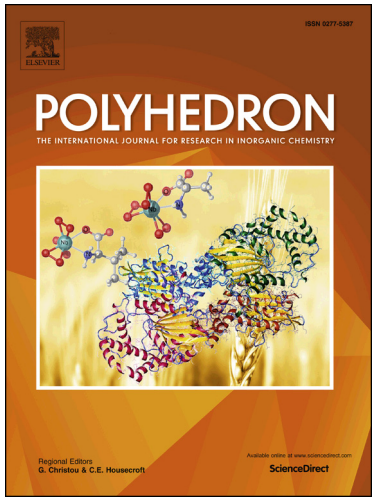

Copper Supported on Functionalized MCM-41 as a Novel and a Powerful Heterogeneous Nanocatalyst for the Synthesis of Benzothiazoles

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PII: S0277-5387(18)30723-X
DOI: https://doi.org/10.1016/j.poly.2018.11.005
Reference: POLY 13552

To appear in: *Polyhedron*

Received Date: 19 May 2018
Revised Date: 30 October 2018
Accepted Date: 3 November 2018

Please cite this article as: N. Noroozi Pesyan, H. Batmani, F. Havasi, Copper Supported on Functionalized MCM-41 as a Novel and a Powerful Heterogeneous Nanocatalyst for the Synthesis of Benzothiazoles, *Polyhedron* (2018), doi: https://doi.org/10.1016/j.poly.2018.11.005

Copper Supported on Functionalized MCM-41 as a Novel and a Powerful Heterogeneous Nanocatalyst for the Synthesis of Benzothiazoles

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Abstract

A new functionalized mesoporous catalyst (Cu(II)-Glycerol/MCM-41) has been synthesized as a highly efficient heterogeneous nanocatalyst for the synthesis of benzothiazoles derivatives. Powder XRD, TGA, TEM, SEM, EDX, BET, FT-IR and ICP-OES techniques are employed to characterize the prepared nanocatalyst. These one-pot reactions were carried out under green and mild reaction conditions in EtOH as a green solvent and the catalyst can be reused up to 5 consecutive cycles without significant change in its catalytic activity.

Keywords: mesoporous silica, copper, benzothiazoles, green reaction conditions.

1. Introduction

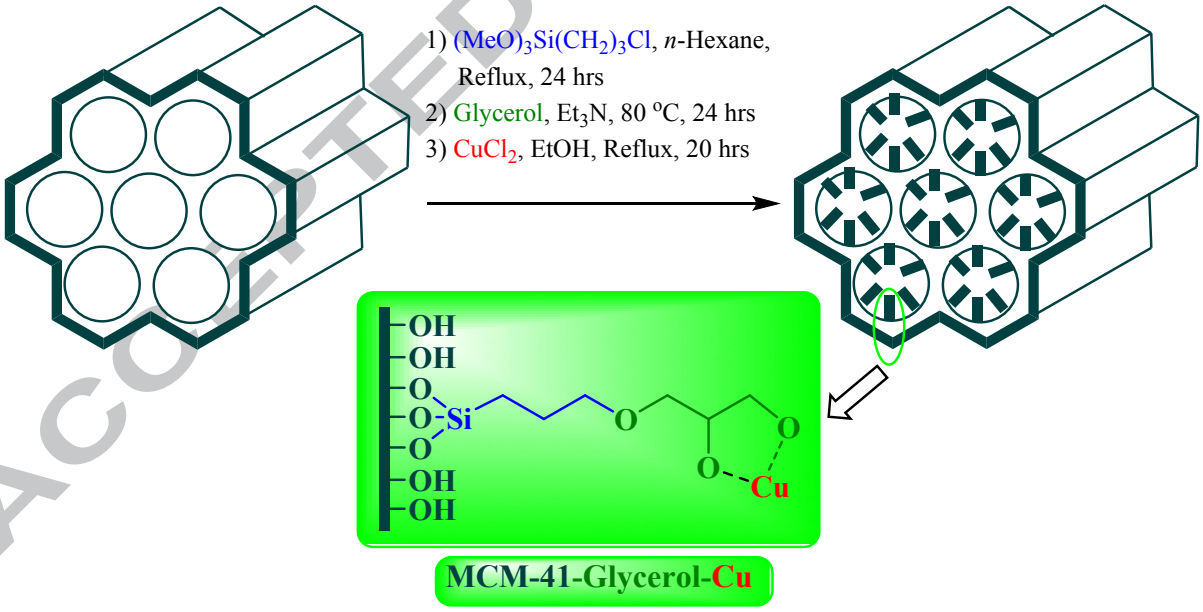
Benzothiazols are a most important scaffold of heteroaromatic compounds in organic chemistry [1], and its derivatives due to their building blocks in biological and therapeutic activities are vital core structures used to create drugs, for instance antiviral [2], antiulcer [3], antioxidant, antibacterial [4], anti-diabetes [5], anticancer [6], enzyme inhibition [7]. Further, benzothiazole rings are found in a myriad of natural products, for example vitamin B12 [8] and also organic functional materials such as fluorescent dyes [9].

According to previous literatures, several approaches for the formation of benzothiazole formatives have been reported [10] such as synthesis of 2-aryl(alkyl)benzothiazoles from 2-

aminothiophenol and aldehydes in air/DMSO oxidant system [11], using iron phthalocyanine as a catalyst [12] and one of them is the condensation of 2-aminothiophenol with carbonyl compounds [13].

However, these procedures, suffer from drawbacks or harsh reaction conditions such as high temperature, use of toxic reagents, air-sensitive, strong acid catalysts, low yields and etc. These factors stimulate chemists to search and develop a more effective and environmentally friendly process [14]. In the past few decades, the use of heterogeneous catalysts as a reusable, economic and green catalyst has attracted a much attentions in academic and industrial purposes [15].

In continuation of our studies, on functionalizing nanoparticles with variant derivatives for catalysis applications, we would like to report a facile procedure for the synthesis of benzothiazoles drivatives from aminothiophenol and various aldehydes catalyzed by a novel heterogeneous nanocatalyst (Cu(II)-Glycerol/MCM-41) as a highly efficient and reusable nanocatalyst under mild conditions in green solvent (EtOH) at 25 °C. Scheme 1 shows the details of the supported catalyst preparation procedure.



Scheme 1. Details of process for the Synthesis of Cu(II)-Glycerol/MCM-41

2. Results and discussion

2.1. Characterization of the nanocatalyst

The structure of nanocatalyst was characterized by Fourier transform infrared spectroscopy, thermogravimetry, inductively coupled plasma-optical emission spectrometry, scanning electron microscopy, Energy dispersive X-ray, X-ray powder diffraction and Brunauer-Emmet-Teller techniques.

Figure 1 displays scanning electron microscopy (SEM images) of the synthesized nanocatalyst. These images reveal spherical structure and confirm that the catalyst was formed of uniform nanometer-sized particles, and the morphology of Cu(II)-Glycerol/MCM-41 (Figure 1b), is similar to the particle form of MCM-41 (Figure 1a), also can be seen that the size of the nanoparticle is 80 nm.

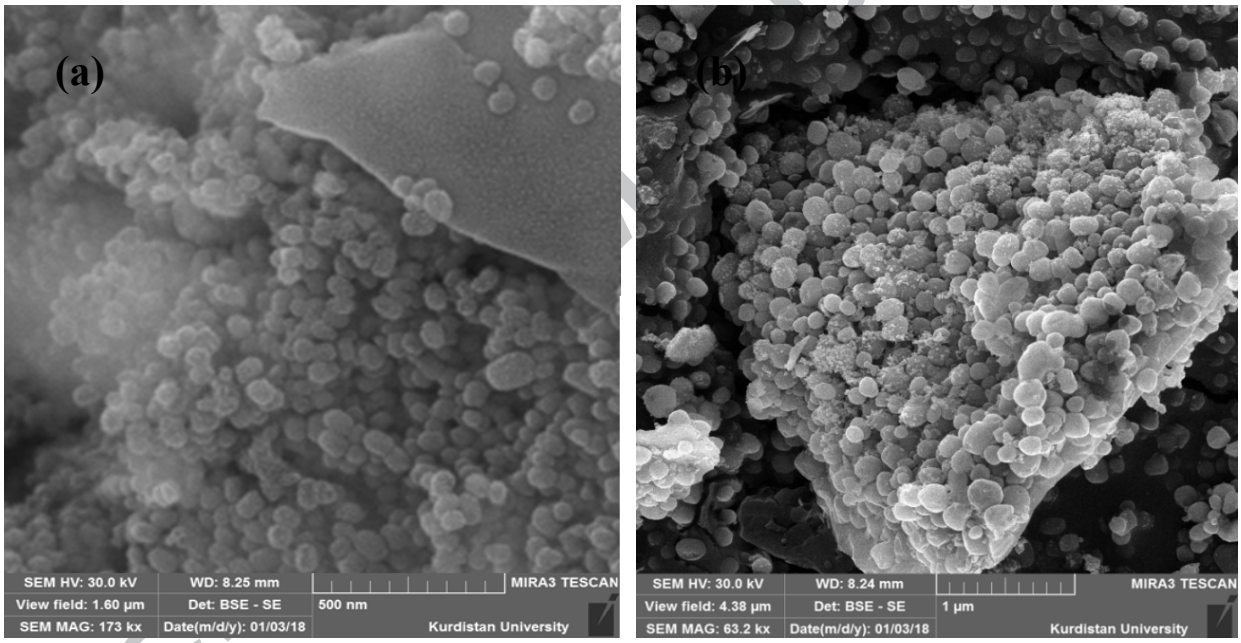


Figure 1. SEM of the synthesized MCM-41 (a) and Cu(II)-Glycerol/MCM-41 (b)

Figure 2 reveals the FT-IR spectra obtained for (curve a) MCM-41, (curve b) CPTMS/MCM-41, (curve c) Glycerol/MCM-41 and (curve d) Cu(II)-Glycerol/MCM-41. Curve (a) shows the spectrum of MCM-41 and signals appeared at 1075-800 and 450 cm^{-1} are corresponding to Si-O and Si-O-Si stretching vibration respectively. Curve (b) exhibit absorption band at 2930 cm^{-1} which is mainly due to C–H stretching. The signals in the spectral region of 3400 and 1230 cm^{-1} can be assigned to O–H and C–O stretching vibrations of glycerol (Figure 2c).

As shown in Figure 2d, the curve displayed successful coordination of Cu within the channels of mesoporous.

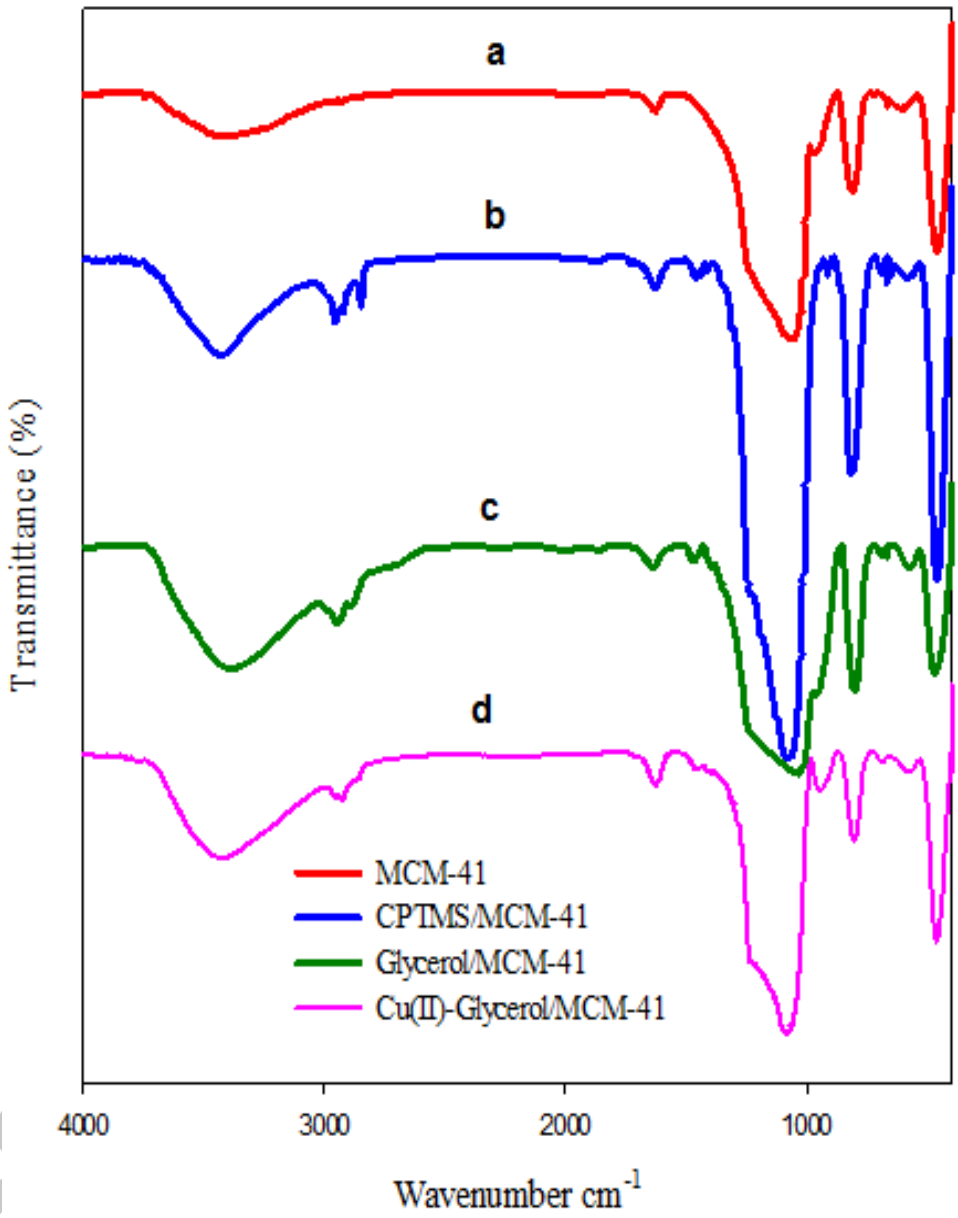


Figure 2. FT-IR spectra of, (a) MCM-41, (b) CPTMS/MCM-41, (c) Glycerol/MCM-41 and (d) Cu(II)-Glycerol/MCM-41

The small angle powder diffraction (XRD) patterns of both MCM-41 and Cu(II)-Glycerol/MCM-41 are displayed in Figure 3. The XRD patterns of the nano particles show three well-resolved peaks indicative of the (100), (110) and (200) diffractions. The intensity

peaks of MCM-41 after functionalization became weak. This result indicates that the organic compounds and Cu are located inside the channels of the mesoporous structure.

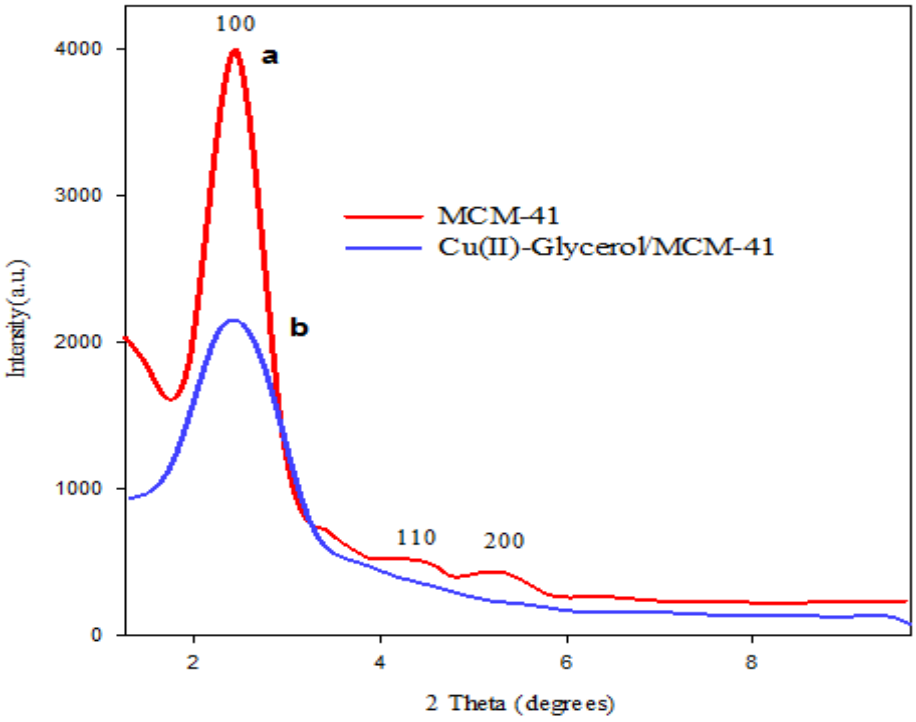


Figure 3. Low-angle powder XRD pattern of (a) MCM-41 and (b) Cu(II)-Glycerol/MCM-41

The EDX (Energy dispersive X-ray) data evidently shows the presence of Si, C, O, Cl, and Cu in functionalized mesoporous MCM-41 (Figure 4).

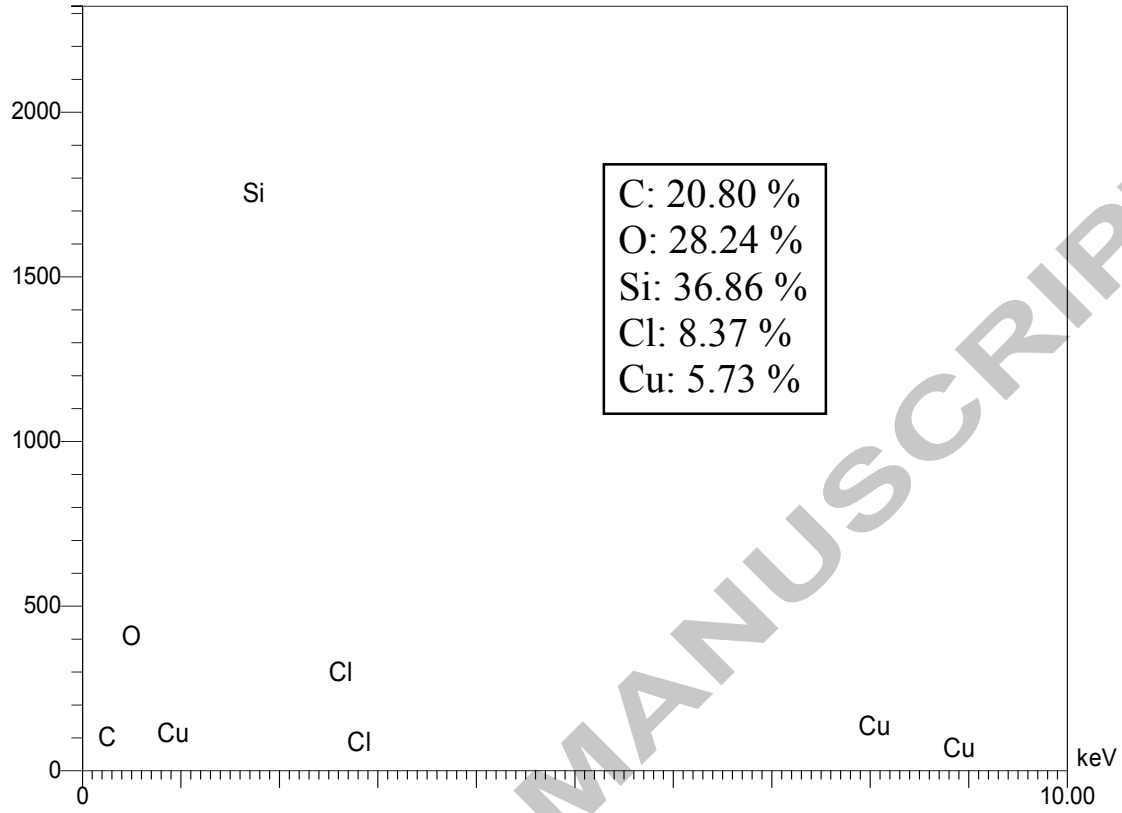


Figure 4. The EDX spectrum of Cu(II)-Glycerol/MCM-41

N_2 adsorption-desorption isotherms of the prepared MCM-41 and Cu(II)-Glycerol/MCM-41 are reported in Figure 5. After incorporation substance in the framework of MCM-41, the original surface area (S_{BET}) of 1000 m^2/g and total pore volume (V_{total}) of 1.3 cm^3/g were reduced to 600 and 0.7, respectively [16]. Moreover, the wall diameter of 1.1 nm was increased to 2.9 nm. These results confirm the successful anchored of the Cu on the surface of mesochannels.

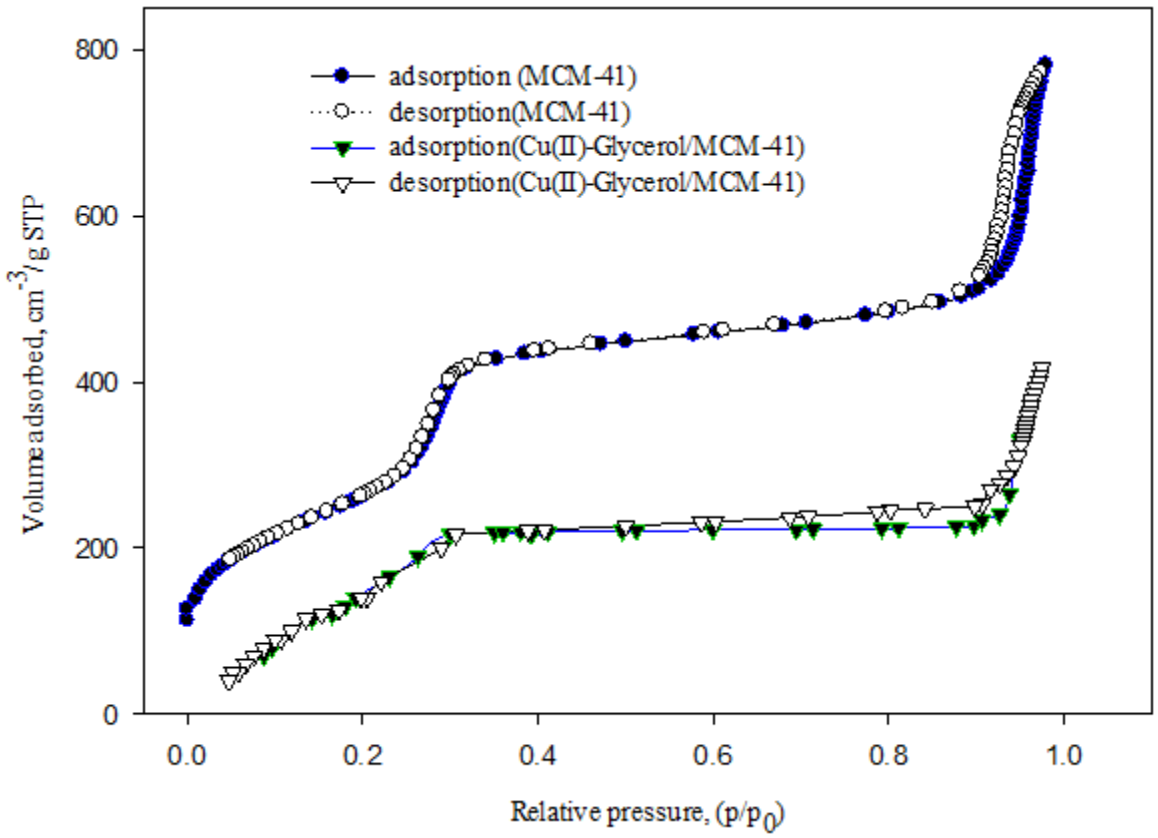


Figure 5. N_2 adsorption–desorption isotherms for, (a) MCM-41 and (b) Cu(II)-Glycerol/MCM-41

Figure 6 is indicative of the thermal gravimetric analysis (TGA) curves of (a) MCM-41, (b) CPTMS/MCM-41, (c) Glycerol/MCM-41 and (d) Cu(II)-Glycerol/MCM-41 which shows a weight loss due to the decomposition upon heating. The small amount of weight loss below 200 degrees Celsius is attributed to the removal of solvent molecules. The weight loss within range of 200-800 degrees Celsius is associated with the decomposition of organic functional groups located inside framework. The TGA diagrams confirmed the formation of Cu complex.

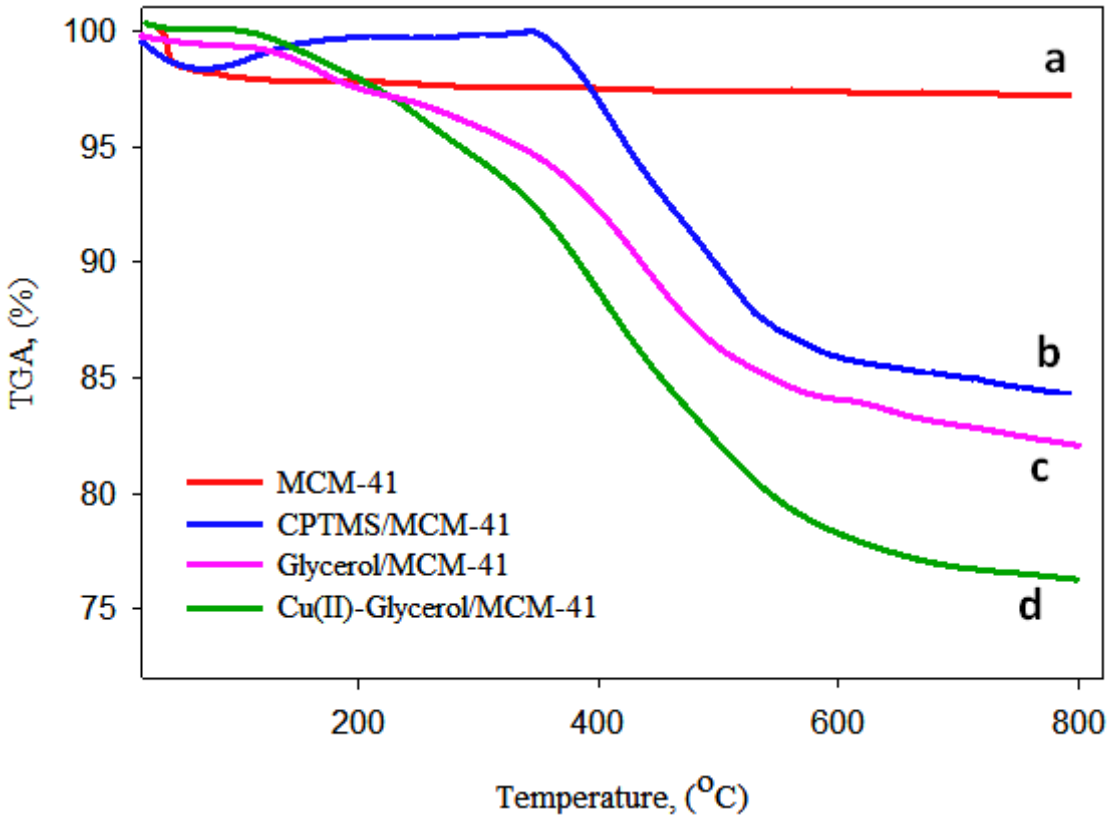


Figure 6. TGA thermograms of (a) MCM-41, (b) CPTMS/MCM-41, (c) Glycerol/MCM-41 and (d) Cu(II)-Glycerol/MCM-41

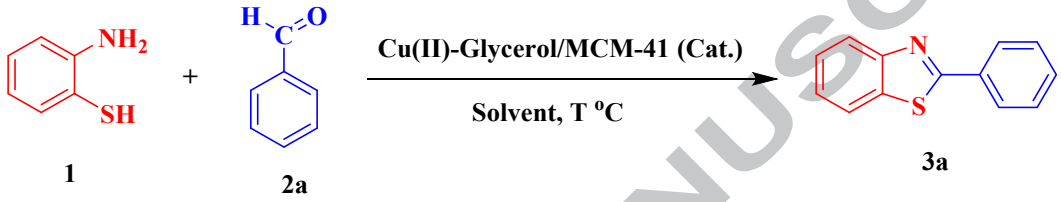
Determination of the loading exact amount of copper into the mesoporous silica MCM-41 was carried out ICP–OES analysis. The Cu content of the nanocatalyst was 4.5 %.

2.2. Application of Cu(II)-Glycerol/MCM-41 complex for the synthesis of benzothiazoles

After characterization of the nanocatalyst structure, we investigated the catalytic activity of Cu(II)-Glycerol/MCM-41 complex as a new and recyclable nanocatalyst for the synthesis of benzothiazoles. The parameters such as catalyst amount, reaction temperature and kind of solvent were optimized initially in the reaction of *o*-aminothiophenol with benzaldehyde as a test model (Table 1). In the first step, various amounts of the nanocatalyst was tested. Control experiments confirmed that no desired product was obtained in the absence of a Cu(II)-Glycerol-MCM-41 (Table 1, entry 1) and the best result was obtained in the presence 7 mg of nanocatalyst (Table 1, entry 2). As it can be seen from Table 1, different solvents including

CH_3CN, CH_2Cl_2, MeOH, EtOH, PEG and EtOAc were tested (Table 1, entries 3-8). And the EtOH is more effective for this reaction (Table 1, entry 2). The effect of the temperature was also examined, that the best result for the reaction was room temperature (Table 1, entry 2). It was found that 7 mg of Cu(II)-Glycerol-MCM-41 in EtOH at 25 degrees Celsius is the best conditions for the synthesis of benzothiazoles.

Table 1. Optimization of reaction conditions



1 **2a** **3a**

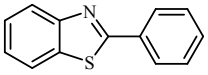
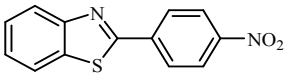
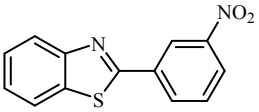
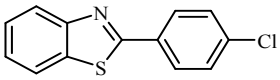
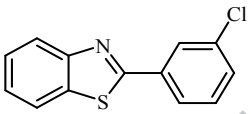
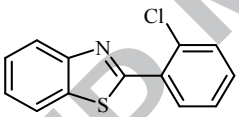
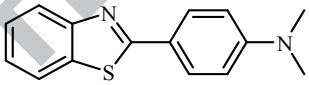
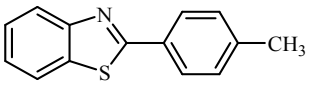
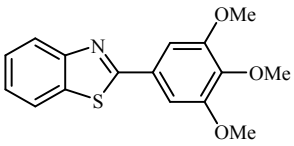
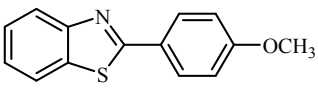
Entry	Cat. (mg)	Solvent	Temp (°C)	Time (h)	Yield (%)[a]
1	0	EtOH	rt	5	-
2	**7**	**EtOH**	**rt**	**3**	**98**
3	5	EtOH	rt	5	65
4	7	PEG	60	3	65
5	7	EtOAc	60	5	40
6	7	CH_2Cl_2	rt	6	65
7	7	MeOH	rt	3.5	80
8	7	CH_3CN	rt	3	60

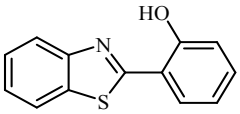
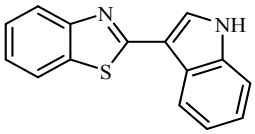
Reaction conditions: *o*-aminothiophenol (1.0 mmol), benzaldehyde (1.0 mmol), [a]Isolated yields provided.

With these results in hand, to study the utility and generality of this approach, the catalytic activity of Cu(II)-Glycerol-MCM-41 was further explored for wide variety of substituted benzaldehydes, and the outcomes are listed in Table 2.

Table 2. Reaction of *o*-aminothiophenol with different benzaldehydes in EtOH at room temperature

Entry	Product (**3**) [a]	Time (h)	Yield (%)[b]

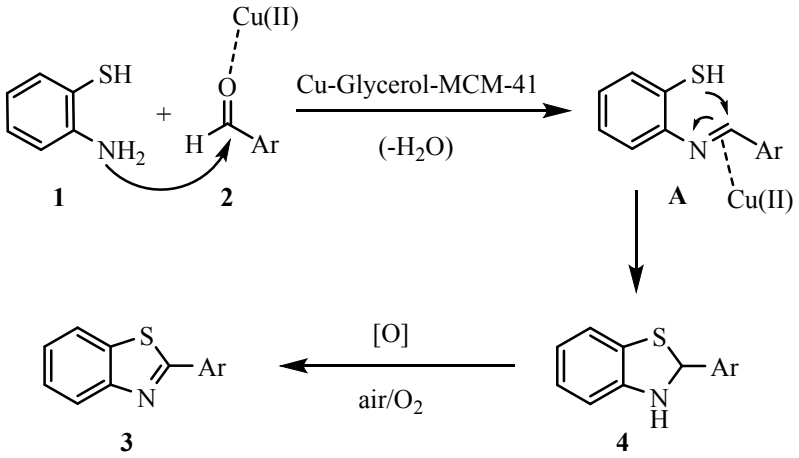
1	 **a**	3	98 [11,17]
2	 **b**	2	97 [17]
3	 **c**	2.5	96 [11,17]
4	 **d**	2.5	96 [11,17]
5	 **e**	3	94 [17]
6	 **f**	3.5	92 [11,17]
7	 **g**	4	95 [17]
8	 **h**	3.8	92 [11,17]
9	 **i**	5	88 [17]
10	 **j**	4	89 [11,17]

11	 **k**	4.5	87 [17]
12	 **l**	4.5	84 [17]

[a] The products were identified and characterized by comparison of their physical and spectral data with those of authentic samples. [b] Yields refer to those purified products.

The results revealed that the reaction worked excellent for a wide range of substituted benzaldehyde and the reaction was quite general. The results showed that benzaldehyde with electron-withdrawing groups such as 4-nitrobenzaldehyde reacted quickly than the benzaldehyde with the electron-donating substituents such as 4-methylbenzaldehyde (Table 2, entries 2 and 8). The sterically hindrance of the substituted benzaldehyde significantly influenced the catalytic efficiency. For instance, the sterically hindered *o*-chlorobenzaldehyde furnished the target product in lower yield and longer reaction times than *p*-chlorobenzaldehydes (Table 2, entries 6 and 4). One of the important aspects of this method is the successful reaction of indole-3-carboxaldehyde as model compounds for heteroaldehyde with *o*-aminothiophenol to give the target products in high yields (Table 2, entry 12).

According to the previous literatures, a proposed mechanism is shown in Scheme 2. Firstly, 2-aminothiophenol (**1**) reacts with benzaldehyde (**2a**) to form an imine intermediate **A** [12,18]. Then the intermediate cyclizes to heterocycle **4a**. Upon formation, ready oxidation of **4a** gives the desired 2-arylbenzothiazoles [17-19].



Scheme 2. Proposed mechanism for the synthesis of benzothiazoles in the presence of Cu(II)-Glycerol-MCM-41

3. Experimental

3.1. Materials and apparatus

All reagents and solvents emploied in this work were obtained from Sigma-Aldrich, Fluka, and Merck chemical companies and utilized without any purification. Proton nuclear magnetic resonance (400 MHz) and carbon nuclear magnetic resonance (100 MHz) spectra were measured with BRUKER NMR-Spectrometer. The FT-IR analyses were carried out with Nexus 670 FT-IR spectrometer. TLC (Thin layer chromatography) analysis was applied over Merck silica gel SIL G/UV_{254} plates. The content of Cu was measured by ICP-OES (Model: VISTA-PRO, Varian, Australia). The catalyst pore volume, Surface area and average pore size were determined with nitrogen adsorption–desorption isotherms at liquid N_2 temperature. The crystalline structure of synthesized samples were recorded by XRD using a Co radiation source under the conditions of 40 kV and wavelength λ = 1.78897 Å. TGA of the samples were performed on a Shimadzu DTG-60 apparatus. SEM measurements were performed with FESEM-TESCAN MIRA3. Finally, the catalyst component measurement was carried out by the EDX using a FESEM-TESCAN MIRA3.

3.2. Preparation of Cu (II)-Glycerol/MCM-41

The solution containing 480 ml distilled water, 1.0 cetyltrimethylammonium bromide (CTAB) and 3.5 ml NaOH (2 M) was stirred at 80 °C. Next, 5 ml of TEOS was added drop-wise into the solution and the obtained mixture was refluxed under continuous stirring for 2 hrs. The resulted mesoporous Si-MCM-41 was filtered and washed by distilled water and dried in an oven at 70 °C followed by calcination at 550 °C for 5 hrs with a ramp 2 °C min^{-1}. The obtained MCM-41 nanoparticles (4.8 g) with 3-chloropropyltrimethoxysilane (CPTMS, 5.0 g) was added to *n*-hexane (96 ml). The reaction mixture was stirred under refluxing and argon atmosphere for 24 hrs. Then, the prepared nanoparticles (CPTMS/MCM-41) was filtered, washed with *n*-hexane and dried under vacuum. Subsequently, (1 g) of CPTMS/MCM-41 was added onto the solution of (50 ml) Glycerol and (2 mL) Et_3N, and then the reaction mixture was stirred at 80 °C for 24hrs. Then, the product (Glycerol/MCM-41) was filtered and washed by dry ethanol and dried in vacuum oven at 60 °C. In the final step to a solution of (3 g) Glycerol-MCM-41 in (50 ml) ethanol was added 1 g of $CuCl_2$ and stirred under reflux for 20 hrs. The Cu(II)-Glycerol-MCM-41 was then collected by filtration and washed with ethanol and dried in vacuum at 60 °C .

3.3. General procedure for the synthesis of benzothiazoles

In a 25-mL, round-bottom flask, a mixture of *o*-aminothiophenol (1.0 mmol), aldehyde (1.0 mmol) and Cu(II)-Glycerol-MCM-41 (7 mg) in EtOH (3 mL) was stirred magnetically at room temperature for the appropriate time (Table 1). After completion of the reaction, as indicated by TLC, the reaction mixture was filtered to isolate the nanocatalyst and the crude product (filtrate) was purified by column chromatography on silica gel or recrystallization in toluene to give the desired products.

4. Reusability of heterogeneous catalyst

The reusability of the nanocatalyst supported on mesoporous was investigated in the synthesis of benzothiazole under the optimized conditions. For this study, we used the benzaldehyde in the reaction with *o*-aminothiophenol for the synthesis of benzothiazole **3a**. After completion of each run, isolation of the Cu(II)-Glycerol-MCM-41 was easily performed by centrifugation process. The solid catalyst was extensively rinsed with EtOH and ethyl acetate to remove residual product and dried in an oven at 80 degrees Celsius and then used directly in the next run without changing the reaction conditions. The data showed that this

nanocatalyst can be reused in five successive reactions without any decrease in the catalytic efficiency (Figure 7). Also the nature of the recovered catalyst was investigated using XRD pattern (Figure 8), EDX (Table 3) and TEM (Figure 9). According to EDS measurements the amount of Cu was determined for unreacted catalyst (5.73%) and after fifth run (2.64%). Figure 9 show the TEM image of representative region of Cu(II)-Glycerol-MCM-41 and highly ordered hexagonal arrangement of pores can be clearly observed after five recycles of Cu(II)-Glycerol-MCM-41. These results for the recovered catalyst indicate that the catalyst can be recycled five time successfully without any significant change in its structure or mesoporosity in silicate parent.

To examine leaching of copper in reaction mixture and heterogeneity of described catalyst, we performed hot filtration for the synthesis of benzothiazoles derivatives from the reaction of *o*-aminothiophenol and benzaldehyde. In this experiment, we obtained the yield of product in half time of the reaction that it was 55%. Then, the reaction was repeated and in half time of the reaction, the catalyst separated and allowed the filtrate to react further. We found that, after this hot filtration, no further reaction was observed. The yield of reaction in this stage was 55% that confirmed the leaching of copper is little.

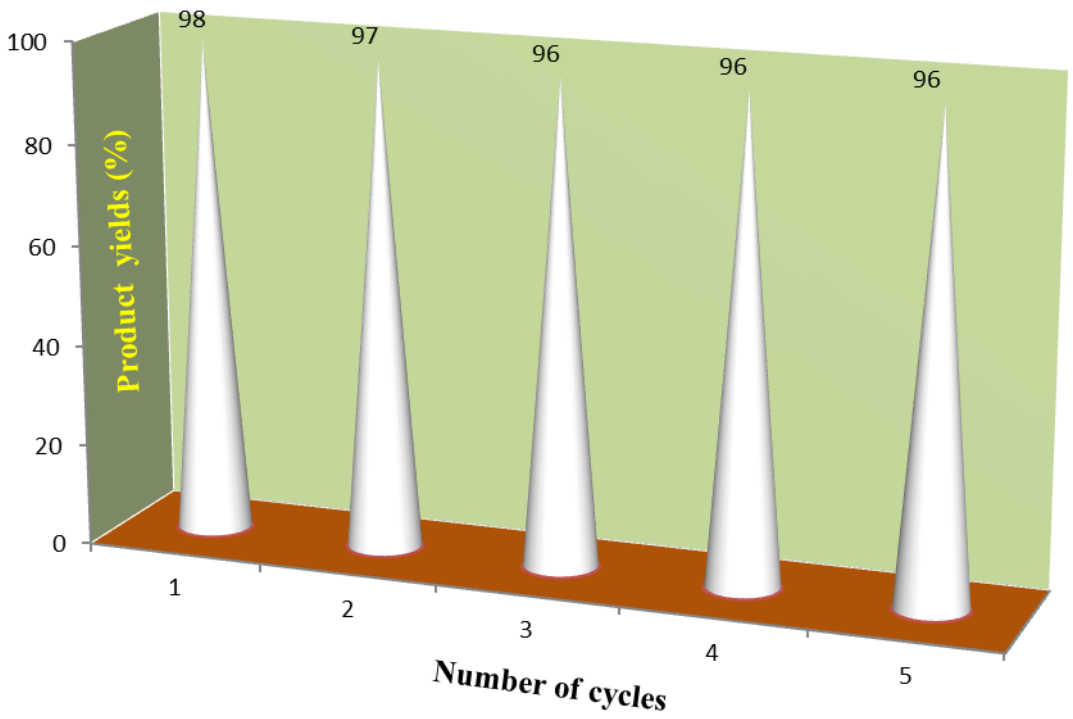


Figure 7. Reusability of the Cu (II)-Glycerol-MCM-41 nanocatalyst

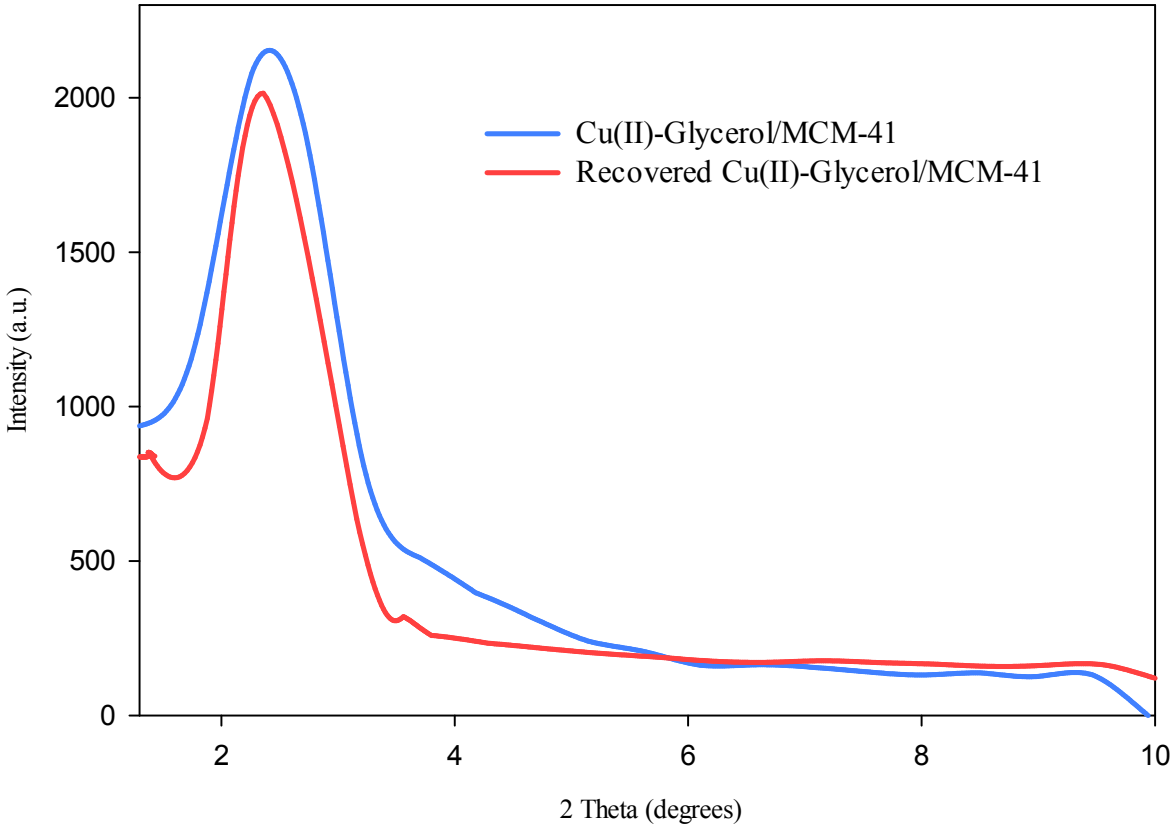


Figure 8. XRD pattern of recovered Cu (II)-Glycerol/MCM-41 nanocatalyst

Table 3. EDX data of recovered Cu (II)-Glycerol-MCM-41 nanocatalyst

Elt	Line	Int	W%	A%
C	Ka	6.4	27.76	41.17
O	Ka	47.0	31.85	35.46
Si	Ka	212.0	27.78	17.62
Cl	Ka	43.5	9.96	5.01
Cu	La	5.7	2.64	0.74
			100.00	100.00

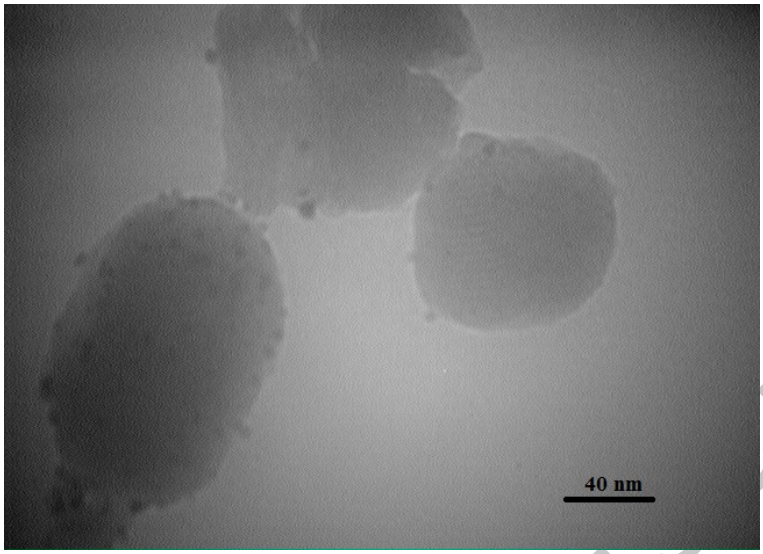


Figure 9. TEM image of recovered Cu (II)-Glycerol-MCM-41 nanocatalyst

5. CONCLUSION

In conclusion, we have demonstrated a novel type of recoverable nanostructure that was synthesized by supporting of Cu complex on MCM-41 nanoparticles (Cu(II)-Glycerol-MCM-41) and characterized by variant techniques such as SEM, BET, XRD, TGA, EDX, FT-IR and ICP-OES. The Cu-complex (Cu(II)-Glycerol/MCM-41) very effectively catalyzed the formation of benzothiazoles from *o*-aminothiophenol and aldehydes. The significant advantages of this catalytic procedure are: easy and inexpensive preparation, high reusability and high air or moisture stability of nanocatalyst, green solvent, eco-friendly, room temperature, easy workup, high functional group acceptability, short reaction times, excellent reaction yield and simple purification methods.

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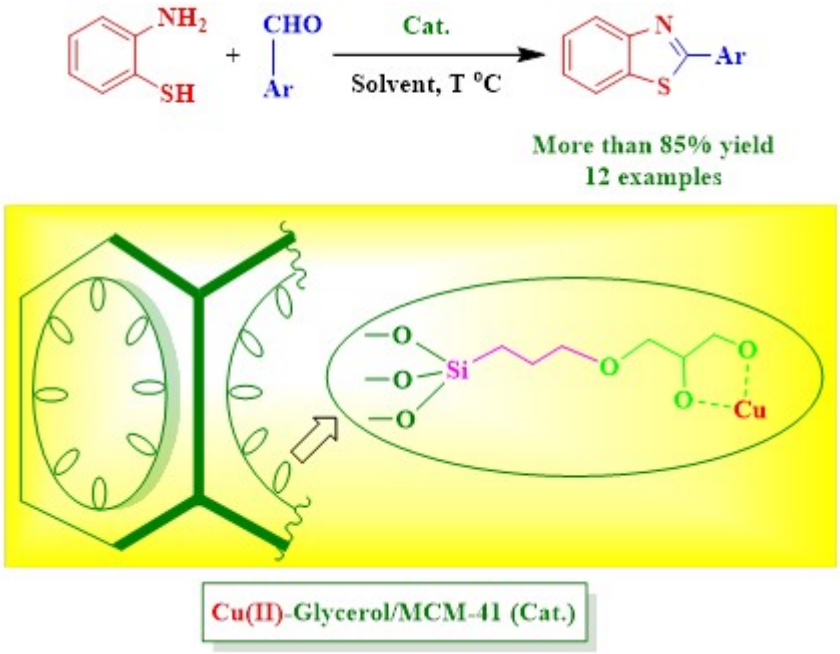

Graphical Abstract

Copper Supported on Functionalized MCM-41 as a Novel and a Powerful Heterogeneous Nanocatalyst for the Synthesis of Benzothiazoles

Hana Batmani[a], Forugh Havasi[b] and Nader Noroozi Pesyan[a]*

NH2
SH
CHO
Ar
Cat.
Solvent, T °C
N
S
Ar
More than 85% yield
12 examples
Si
O
Cu
Cu(II)-Glycerol/MCM-41 (Cat.)