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Shahla Vaysipour, Zahra Rafiee, Masoud Nasr-Esfahani

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Synthesis and characterization of copper (II)-poly(acrylic acid)/M-MCM-41 nanocomposite as a novel mesoporous solid acid catalyst for the one-pot synthesis of polyhydroquinoline derivatives

Shahla Vaysipour, Zahra Rafiee* and Masoud Nasr-Esfahani

Department of Chemistry, Faculty of Science, Yasouj University, Yasouj, 75918-74831, Iran

* Corresponding author: E-mail address: z.rafiee@yu.ac.ir; Tel: +98-74-33223048

Synthesis and characterization of copper (II)-poly(acrylic acid)/M-MCM-41 nanocomposite as a novel mesoporous solid acid catalyst for one-pot synthesis of polyhydroquinoline derivatives

Shahla Vaysipour, Zahra Rafiee* and Masoud Nasr-Esfahani

A novel, green and recoverable nanocomposite was designed, synthesized and fully characterized. The resulting nanocomposite have successfully used as a catalyst for the condensation of various aromatic aldehydes, dimedone, β -ketoester and ammonium acetate under mild and solvent free conditions to yield polyhydroquinoline derivatives in good to excellent yields.



Abstract

In this study, a novel mesoporous silica nanocomposite (MSNC) based on poly(acrylic acid) and amine-functionalized MCM-41 mesoporous silica as amplification agents was constructed via an ultrasonic-assisted method as a straightforward, fast, eco-friendly and it is denoted as M-MCM-41. Then Cu (II) was immobilized on PAA/M-MCM-41 surface and the novel heterogeneous reusable catalyst was fully characterized using appropriate techniques such as Fourier transform infrared (FT-IR), X-ray diffraction (XRD), energy dispersive spectroscopy (EDS), field emission scanning electron microscopy (FE-SEM), thermogravimetry analysis (TGA) and N₂ adsorption-desorption. The resulting catalyst was successfully used for the condensation of various aromatic aldehydes, dimedone, β-ketoester and ammonium acetate under solvent-free and mild conditions to yield polyhydroquinoline derivatives in good to excellent yields. Also, the experimental evidence was demonstrated that Cu (II)-PAA/M-MCM-41 nanocomposite could act as a recoverable and reusable nanocatalyst without a meaningful drop in the yield and the reaction time at least four times.

Keywords: Nanocomposite, Mesoporous silica nanoparticles, MCM-41, Poly(acrylic acid) (PAA), Copper (II), Polyhydroquinoline (PHQ)

1. Introduction

Nanomaterials are especially of interest due to their distinct electronic, optical, magnetic and catalytic properties [1,2]. The nanocomposites (NC)s with an organic polymer matrix filled with organic or inorganic fillers are important members of NC materials which offer a higher surface to volume ratio in collation to the pure polymer [3-5]. The polymeric NCs (PNC)s incorporate the favorable properties of inorganic and organic ingredients, such as high thermal stability, mechanical, electrical, biocidal and flexibility, to obtain new materials with considerably improved physical and/or chemical properties [6-9]. Despite the diverse possibility of nanofiller candidates, an important stage before use is the examination of their features such as composition, morphologies, geometries, sizes, and porosities. Nanofiller components have been categorized according to the pore diameter as micro-(2 < nm), meso-(2-50 nm), and macroporous (> 50 nm) which play a basic role on the physicochemical properties of NCs [10,11]. Among the wide range of materials, mesoporous silica nanoparticles (MSNs) with different pore sizes and structures including hexagonal MCM-41 [12-15], cubic MCM-48 [16,17], hexagonal SBA-15 [18,19], wormhole framework MSU-J [20-22], two-dimensional, hexagonally ordered MSU-H [23], and mesocellular silica foam MSU-F silicas [24] are suitable candidates for the preparation of PNCs.

Among MSNs, MCM-41 as a hexagonal arrangement of unidimensional pore channels has been attracted a great deal of attention over nearly two decades ago due to

its unique properties such as biocompatibility, abundant surface silanol groups (Si-OH), extremely large surface area (700-1500 m²g⁻¹), tunable pore size (varying from 1.5 to 10 nm), thermal and chemical stability for recyclability and relatively hydrophobic nature, favourable surface for further functionalization [3,5,25-27]. Four types of silanol groups exist on the surface of mesoporous MCM-41: 1) Terminal silanol groups (isolated or free silanol); 2) Geminal silanol groups; 3) Ethereal silanol groups (siloxane) and 4) Vicinal silanol groups (hydrogen-bonded) [28]. Notwithstanding these desirable properties, MCM-41 in pure silica form has low inherent acidity and indicates weak hydrogen bonding sites which decreases its performance in the fields of catalysis [29]. Also, surface modification of mesoporous silica nanoparticles as nanofillers by an organic-inorganic compound as a connecting agent is a general path to increase a strong interfacial interaction between the nanofillers and polymer and to enhance the scattering of the nanofillers in a polymer matrix [3,30,31].

Among different polymers that are being studied, poly(acrylic acid) (PAA) has received considerable attention. PAA is a water-soluble polymer, non-toxic, hydrophilic, biocompatible superabsorbent and is the simplest synthetic poly(carboxylic acid). PAA is selected as a host polymer in this research due to its charming properties such as excellent stability in acidic and basic, biodegradable, permeability and high ability to attach with a variety of metal ions in solution [32-34].

Polyhydroquinoline (PHQ) derivatives are an important class of organic *N*-heterocyclic compounds and have been attracted considerable attention due to their key role in pharmacological and biological activities [35].

In view of the therapeutic importance of PHQ derivatives, organic chemists have explored several procedures for the synthesis of these compounds. General method for the synthesis of PHQ derivatives is multi-component reaction of aldehydes, β-dicarbonyl compounds, active methylene compounds and ammonium acetate using various catalysts such as ceric ammonium nitrate (CAN) [36], FSM-16-SO₃H [37], [pyridine-SO₃H]Cl [38], polymer [39], MCM-41 [40], Ni-nanoparticle (NP) [41], ionic liquids [42], *p*-TSA [43], BINOL-phosphoric acid derivatives [44], montmorillonite K-10 [45], TiO₂ NPs [46], SnO₂ NPs [47], HClO₄-SiO₂ [48], Fe₃O₄@B-MCM-41 [49], MCM-41-OBF₂ [50], silica-bonded imidazolium-sulfonic acid chloride [51], SBA-15/SO₃H [52], IL-HSO₄@SBA-15 [53] and MCM-41@Serine@Cu(II) [54].

However, there is a need to find new catalysts and green methods to minimize the drawbacks of existing methods such as use of toxic organic solvents, prolonged reaction times, poor yields, difficulty in catalysts recovery, excess reagents and harsh reaction conditions. In recent years with the development of green chemical technology, the copper heterogeneous catalysts have been widely used for organic synthesis under solvent-free conditions because of their chemical, economic, and environmental aspects [54]. Solid catalysts due to lack of corrosiveness, safety, and ability to reduce the amount of waste isolation are harmless to the environment. Therefore many reactions in organic chemistry are performed in the presence of solid catalysts.

In this paper, the preparation and characterization of Cu(PAA) complex grafted over the modified surface MCM-41 using 3-aminopropyltriethyoxysilane (Cu(II)-PAA/M-MCM-41) as a novel acid nanocatalyst (Scheme 1) were reported and the applicability of this catalyst for the synthesis of new PHQ derivatives at 80 °C under solvent-free conditions was studied (Scheme 2).

2. Experimental

2.1. Methods and materials

All chemicals and reagents in this study were purchased from Merck and Aldrich chemical companies. The reaction progress and the purity determination of the compounds were monitored by thin-layer chromatography (TLC). Melting points were determined using an Electrothermal KSB1N capillary apparatus and uncorrected. Fourier transform infrared (FT-IR) spectra were recorded with a JASCO FT-IR/680 plus spectrometer in the scanning range of 4000-400 cm⁻¹ using KBr pellet. ¹H NMR and ¹³C NMR spectra were obtained with Bruker 400 and 100 MHz instrument spectrometer on the solution in DMSO-d₆ or CDCl₃. The X-ray diffraction (XRD) data were conducted on a Panalytical X' Pert Pro X diffractometer equipped with Cu K_{α} radiation (λ =0.1542 nm) at 40 kV and 40 mA. The elements in the sample were probed by energy dispersive spectroscopy (EDS) using the TESCAN Vega model instrument. The particle size and surface morphology of catalyst were examined by carrying out field emission scanning electron microscopy (FE-SEM) using a SIGMA VP model from ZEISS Company. Thermogravimetric analysis (TGA) of the samples was performed on an STA 6000 instrument (Perkin Elmer, America) between 30 and 800 °C at a heating rate of 20 °C/min under a nitrogen atmosphere. N2 adsorptiondesorption isotherms were obtained on a BELSORP-mini II-REOTERM japan instrument. The surface area was determined based on BET analyses. Pore size

distribution was derived from the desorption branches of the isotherms based on the BJH model, and the total pore volume was calculated using BJH analyses.

2.2. Preparation of MCM-41

MCM-41 mesoporous compound was synthesized according to the procedure described in literature [55]. Succinctly, 2.4 g of cetyltrimethylammonium bromide (CTAB) as a surfactant template was dissolved in 120 mL of deionized water and stirred until a solution was formed. Then, 10 mL of ammonia was added dropwise with vigorous stirring for 5 min. After that, 10 mL of tetraethylorthosilicate (TEOS) as a source of silicon for the preparation of the mesoporous material was added into the solution to form a gel composition (supersaturated solution). This solution was stirred for 72 h under reflux conditions and N₂ atmosphere, and then the mixture was allowed to cool to room temperature. The solid product was separated by filtration, washed with deionized water and ethanol. The obtained white solid was dried in an oven at 70°C for 12 h. The final step involved calcinating the sample at 550 °C for 12 h to remove the organic template.

2.3. Preparation of amino-functionalized MCM-41 (M-MCM-41)

MCM-41 was functionalized with 3-aminopropyltriethoxysilane (3-APTES) (a silane coupling agent) as follows: MCM-41 (0.6 g) was dispersed in 30 mL of anhydrous toluene by sonicating for 45 min at room temperature, and then 3-APTES (4.42 mmol) was added to the mixture under reflux with stirring under an argon atmosphere for 24 h. The white solid MCM-41-(SiCH₂CH₂CH₂NH₂)_x was collected and washed three

times with ethanol and deionized water to remove unreacted 3-APTES, and dried in an oven at 80°C for 24 h [31].

2.4. Synthesis of polyacrylic acid (PAA)

A solution of 2 mmol of acrylic acid (AA) in dry CHCl₃ (40 mL) was added to 10 mmol of ethylene glycol dimethacrylate (EGDMA) and 0.05 g of azobisisobutyronitrile (AIBN) as an initiator. After complete addition, the reaction mixture was stirred under reflux conditions at 60°C for 24 h under a N₂ atmosphere. PAA was precipitated by pouring into 20 mL of methanol. The obtained product was filtered, washed successively with methanol and dried overnight at 40 °C [56].

2.5. Preparation of PAA/M-MCM-41 NC

For the fabrication of PAA/M-MCM-41 NC using a green and rapid method, 3.0 g of PAA was added to 30 mL of double distilled water at 87 °C and stirred for at least 30 min until a clear solution of PAA was obtained. Simultaneous, 0.06 g of M-MCM-41 was added to 10 mL of the same solvent and sonicated for 1 h. Then, M-MCM-41 solution was added to the polymer matrix solution to obtain a clear suspension, and the suspension refluxed for 4 h at 80 °C followed by sonication for 40 min. In the final step, the resulting clean homogeneous solution was poured onto a glass plate, and the solvent was evaporated in an oven at 30 °C for 24 h.

2.6. Preparation of Cu(II)-PAA/M-MCM-41 NC

In the last step, for the synthesis of Cu(II)-PAA/M-MCM-41 NC, 1 g of PAA/M-MCM-41 and 0.604 g of Cu(NO₃)₂.3H₂O were mixed in 30 mL of ethanol under reflux

conditions for 24 h under an argon atmosphere. The resulting catalyst was filtered, washed with ethanol and dried in a vacuum to obtain the heterogenized complex (Cu(II)-PAA/M-MCM-41) as a novel nanocatalyst.

2.7. General procedure for the synthesis of polyhydroquinoline derivatives via Hantzsch reaction

To a test tube containing a mixture of aromatic aldehydes (1 mmol), dimedone (1 mmol, 0.14 g), ethyl (or methyl) acetoacetate (1 mmol) and ammonium acetate (1.5 mmol, 0.11 g) was added Cu(II)-PAA/M-MCM-41 (0.02 g) as a catalyst. Then, the reaction mixture was stirred at 80 °C under solvent-free conditions. The progress of the reactions was monitored by TLC (ethyl acetate/n-hexane, 1:4). After the completion of the reaction, the resulting mixture was cooled to room temperature and then cold water was added. The obtained solid was collected by filtration and purified by recrystallization from hot ethanol to afford the pure product. In this study, the catalyst was recycled and reused five times without significant loss of its catalytic activity.

Ethyl-4-(3-ethoxy-4-hydroxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-

hexahydroquinoline-3-carboxylate (5i)

M.P: 198-200°C; **IR** (**KBr**) υ (cm⁻¹) = 3448 and 3283 (OH and NH stretching vibration), 3077 (=C-H stretching vibration, sp²), 2964 (C-H stretching vibration, sp³), 1689 (C=O ester stretching vibration), 1613 (C=O ketone stretching vibration), 1489 (C=C, Ar, stretching vibration), 1269 (C-O, ether, stretching vibration), 1214 (C-O, ester, stretching vibration); ¹H **NMR (400 MHz, DMSO-d₆)** δ (**ppm):** 0.89 (s, 3H), 1.02 (s, 3H), 1.17 (t, *J*=12 Hz, 3H), 1.30 (t, *J*=7.2 Hz, 3H), 2.01 (d, *J*=8 Hz, 1H), 2.18 (d, *J*=8.2 Hz, 1H), 2.27 (s, 3H), 2.29 (d, *J*=5.6 Hz, 1H), 2.42 (d, *J*=8.6 Hz, 1H), 3.86-3.95 (q, 2H), 3.96-4.07 (q, 2H), 4.75 (s. 1H), 6.50 (dd, *J*₁=1.0 Hz, *J*₂=0.8 Hz, 1H), 6.59 (d, *J*=4 Hz, 1H), 6.70 (d, *J*=1.0 Hz, 1H), 8.56 (s, NH), 9.03 (s, OH); ¹³C NMR (100 MHz, DMSO-d₆) δ (ppm): 14.7, 15.3, 18.7, 26.8, 29.7, 32.6, 35.4, 50.8, 59.4, 64.2, 104.5, 110.7, 113.9, 115.5, 120.1, 139.4, 144.9, 145.3, 146.2, 149.7, 167.5, 194.8

3. Results and discussion

3.1. Preparation of Cu(II)-PAA/M-MCM-41 NC

The schematic pathway for the fabrication of Cu(II)-PAA/M-MCM-41 NC is depicted in Scheme 1. Due to mesoporous silica MCM-41 physicochemical properties with hexagonal order arrays, this compound was selected as a nanofiller. Recently, it has aroused great research interest because of its significant advantages including the hydrophilicity of its surface, good thermal stability, degradability, high surface area, large pore volume, easy handling and low cost of manufacture as well as good chemical and mechanical stability. The most prominent feature of mesoporous MCM-41 is its ability to grafting with other active sites of molecules due to the abundance of active hydroxyl groups on the internal and external surfaces of its 3D framework. First, MCM-41 NPs were prepared through a sol-gel method in a basic solution by CTAB as a template. Then, MCM-41 surface was modified by 3-APTES under ultrasonic irradiation to improve the dispersibility of M-MCM-41 in water as a solvent. The alkoxy groups of the silane coupling agent react readily with the abundant hydroxyl groups on the surface of MCM-41. Hence, it can be used as a good filler for the preparation of the NC based on PAA. The possible interaction between carbonyl and

hydroxyl groups of the polymer moiety and -OH and -NH₂ groups on the surface of the functionalized mesoporous silica may efficiently interact by hydrogen bonding [57]. Finally, the reaction of PAA/M-MCM-41 with Cu(NO₃)₂.3H₂O in ethanol under reflux conditions for 24 h lead to the production of new catalyst, Cu(II)-PAA/M-MCM-41 NC using immobilization of copper (II) on the surface of MCM-41 mesoporous and PAA by coordination bonding through hydroxyl and carbonyl groups interaction.

3.2. Characterization of catalyst

Cu(II)-PAA/M-MCM-41 NC was fully characterized by a variety of techniques such as FT-IR, XRD, EDX, FE-SEM, TGA, and BET.

Fig. 1 shows the FT-IR spectra of pristine MCM-41 (a), M-MCM-41 (b), neat PAA (c), PAA/M-MCM-41 NC (d) and Cu(II)-PAA/M-MCM-41 NC (e). The absorption band around 3500 cm⁻¹ observed in all spectra is related to both the O-H stretching of the surface silanol groups and the hydrogen-bonded adsorbed water molecules. The absorption bands observed at 1083 and 807 cm⁻¹ are characteristics of the Si-O-Si asymmetric and symmetric stretching vibrations and the band at 458 cm⁻¹ can be assigned to the Si-O-Si bending mode (Fig.1a). For M-MCM-41, new bands were observed that is attributed to the organic moiety of the attached silane coupling agent (Fig. 1b). The broad peak at about 3400 cm⁻¹ region is attributed to both the hydroxyl and amine groups present on the surface of MCM-41 as well as surface silanols. A new band around 2938 cm⁻¹ is assigned to the C-H stretching vibration of methylene of the propyl group and a weak peak at 689 cm⁻¹ is attributed to the Si-C stretching vibrations which is absent in the spectrum of pristine MCM-41. Fig. 1c and 1d show the FT-IR spectra of neat PAA and PAA/M-MCM-41 NC, respectively. Neat PAA shows a broad absorption band

around 3600-3300 cm⁻¹ due to the presence of -OH groups of acid. The absorption peaks around 2986 and 2953 cm⁻¹ corresponded to the sp³ C-H stretching vibrations of alkyl groups in PAA. The absorption band around 1700 cm⁻¹ is attributed to the stretching vibration of the carbonyl group of carboxylic acid, and also, the occurrence of the peak at 1158 cm⁻¹ is attributed to C-O stretching vibration of PAA. The peak at 1454 cm⁻¹ is assigned to CH₂ bending. The FT-IR spectrum of NC (Fig. 1d) is also exhibited the presence of both the polymer and modified filler. The linkage of M-MCM-41 with PAA caused scarce changes in the intensities of absorption bands of neat PAA as well as the addition of new absorption bands in the range of 800-400 cm⁻¹ owing to the Si-C stretching and Si-O-Si bending as mentioned above (Fig. 1c). The intensity of the broad band around 3600-3000 cm⁻¹ is decreased after adsorption of Cu(II) (Fig. 1 e). It may be due to the interaction of copper with hydroxyl, amines and carbonyl groups. A significant decrease is observed in the relative intensity of the characteristic band for C-O located at 1073 cm⁻¹, denoting the formation of the O-Cu band. It may be as an outcome of the formation of a complex between Cu(II) bonded to PAA/M-MCM-41 NC surface and weakening of Cu-N and Cu-O bonds.

XRD patterns of the MCM-41 (a), M-MCM-41 (b) and Cu(II)-PAA/M-MCM-41 (c) in the range of $0 < 2\theta < 10$ are presented in Figure 2. The XRD pattern of MCM-41 shows three peaks assigned to 100, 110, and 200 reflections which are attributed to the ordered 2D-hexagonal structure (Fig. 2a). XRD pattern of M-MCM-41 shows that the intensities of these peaks decreased. Pore filling of MCM-41 by 3-APTES can be the probable reason for the reduction of peaks intensity (Fig. 2b). In the XRD pattern of Cu(II)-PAA/M-MCM-41 NC (Fig. 2c), the 100 diffraction peak of the M-MCM-41 can still be observed in the polymer matrix NC but with less intensity, as well as the disappearance of the signals at higher angles.

This phenomenon may be due to decreased pore size as well as the increase of wall thickness. Nevertheless, the XRD results showed that the mesoporous hexagonal channels were still present after modification.

Surface morphology of Cu(II)-PAA/M-MCM-41 NC was investigated via FE-SEM analysis. As can be seen, the NC is formed in small particle size and approximately uniform (Fig.3).

The EDX analysis of the NC is shown in Figure 4. The EDX spectrum of the NC has all bands related to the elements that exist in the NC structure (Si, O, N, C, and Cu). The strong band related to the C atom at the spectrum confirms that polymer grafted successfully on the mesoporous silica (M-MCM-41) surface.

Thermogravimetric analysis (TGA) of MCM-41, M-MCM-41, and Cu(II)-PAA/M-MCM-41 NC is presented in Figure 5. TGA of MCM-41 indicated two steps of weight loss. The weight loss is 1.99% in the first step from 25°C to 200 °C that is related to loss of moisture inside the MCM-41 channels and in the second step in the range of 450-900 °C, the weight loss (3.19%) is mainly due to water loss formed by the density of silanol groups (Fig. 5a). The thermogram of functionalized MCM-41 (MCM-41-n Pr-NH₂) showed a three-step weight loss at temperatures ranging from 25 to 900 °C (Fig. 5b). The first region at temperatures between 25 °C and 200 °C corresponds to the removal of physisorption water held in the pores. The weight losses in the second and third steps are chiefly due to the decomposition of the organic propyl amino fragments on the surface of the synthesized mesoporous silica MCM-41 NPs. The TGA thermogram of the Cu(II)-PAA/M-MCM-41 NC was provided in Fig. 5c. As can be seen from Fig. 5c, the thermal analysis identified three separate weight loss regions on the TG curve. The first decomposition stage at 25-150 °C probably corresponded to the removal of

water or silane coupling agent that had been physically absorbed on the surface of the M-MCM-41. The TGA results showed that the most weight loss was occurred at about 200-350 °C, that can be associated to the decomposition of functional groups of PAA and the final weight loss step begins around 400 °C and ends about 800 °C is due to the decomposition/combustion of organic ligand present in the NC. Overall, these results show that by introducing M-MCM-41 as a nanofiller into PAA, the thermal stability of NC has been dramatically improved; this improvement could be due to good interaction between the polymer matrix and mesoporous materials as well as the inherently good thermal stability of the mesoporous MCM-41. Noteworthy, due to the catalyst stability of up to 200 °C, this new NC can be used in organic reactions.

The N₂ adsorption-desorption isotherm of Cu (II)-PAA/M-MCM-41 NC is shown in Figure 6. N₂ sorption measurements have been applied to determine the physical properties including surface area, pore size distribution, and pore volume. Type IV isotherm is recognizable for MCM-41 with H1 hysteresis loop. On modifying MCM-41 with APTES, the surface area of MCM-41 reduced from 986.16 to 694.98 m²/g and the pore size decreased from 3.56 to 3.3 nm [58]. On Cu (II)-PAA/M-MCM-41, a further reduction in the surface area from 694.98 to 101.5 m²/g and pore size from 3.3 to 1.22 nm was observed. Moreover, the results presented in Table 1 show that the pore volume Cu (II)-PAA/M-MCM-41 is 0.114 cm³/g. The reduction of BET surface area, volume and pore size of Cu(II)-PAA/M-MCM-41 NC clearly is related to pore entrance blocking.

3.3. Study of Cu(II)-PAA/M-MCM-41 NC catalytic activity through the synthesis of polyhydroquinoline derivatives

After approving of the presented catalyst using the aforementioned technical skills, the catalytic application of Cu(II)-PAA/M-MCM-41 NC was investigated in the synthesis of several polyhydroquinoline derivatives. Initially, the reaction conditions were optimized with the model reaction of benzaldehyde (1), dimedone (2), ethyl acetoacetate (3) and ammonium acetate (4). The effect of various solvents, temperature and amount of catalyst was studied to obtain optimal conditions and the results were summarized in Table 2.

To optimize the required catalyst amount, different amounts of the nanocatalyst were applied and according to the obtained results (Table 2, entries 1-6), 0.02 g of the catalyst was chosen as the best amount with the highest yield in the model reaction. Moreover, this reaction was performed in the absence of nanocatalyst. The product was obtained only in trace amounts even after an extended time. Therefore, the presence of the catalyst was essential for the completion of the reaction. Increasing the number of acidic active sites by increasing the amount of catalyst resulted in decrease of concentration of reactants at the active sites and finally a decline in yield (Table 2, entries 5 and 6) [59].

The effect of solvent and temperature was investigated by performing the model reaction in the presence of 0.02 g of catalyst in various solvents and temperatures (Table 2, entries 7-16). The reaction was carried out in the presence of various solvents like ethanol, methanol, chloroform, water and acetonitrile and also under solvent-free conditions. The polar solvents such as EtOH and MeOH were found to be better solvents than the non-polar solvents. The low efficiencies in non-polar solvents may be due to the poor solubility of the reactants in these solvents and low catalyst dispersion. The yields were better under solvent-free conditions than solvents (Entries 1-11). It is also important to note that increasing the

temperature improves the yields of the reaction (Entries 12-16). The best result was at 80 °C under solvent-free conditions (Entry 4).

After establishing the optimal conditions, in order to verification of applicability and efficiency of this catalyst, we were studied the synthesis of a variety of substituted polyhydroquinoline (5a-5p) in the presence of Cu(II)-PAA/M-MCM-41 NC as a heterogeneous and recoverable catalyst using different aromatic aldehydes bearing both electron-donating and electron-withdrawing substituents under the determined conditions. The afforded results showed that in all instances the corresponding polyhydroquinoline derivatives were obtained in good to excellent yields in suitable time (Table 3, entries 1-16). The reaction of aromatic aldehydes having electron-withdrawing groups was rather faster than electrondonating groups. To show the advantage of the present study, we collated the catalytic activity of Cu(II)-PAA/M-MCM-41 in the synthesis of polyhydroquinoline derivatives with other catalysts. As shown in Table 4, Cu(II)-PAA/M-MCM-41 NC is better than and/or comparable with most of the previous studies in terms of applied solvent, reaction time, temperature and catalyst amount due to good surface area, high reactivity and excellent stability. These findings considerably confirm the high efficiency of the present catalyst in the synthesis of polyhydroquinoline derivatives.

A proposed mechanism pathway for the synthesis of polyhydroquinoline derivatives is portrayed in Scheme 3. Initially, dimedone is converted to its active enol form using Cu (II)-PAA/M-MCM-41 and reacted to the activated aldehyde by the catalyst for the formation of the corresponding Knoevenagel intermediate I. On the other hand, the insitu generated NH₃ from ammonium acetate reacts with activated β -ketoester to yield the corresponding intermediate II. Then, the reaction between these two intermediates

generates intermediate III. Tautomerization of intermediate III leads to the formation of intermediate IV. Afterward, the intramolecular nucleophilic attack of the amino group to the activated carbonyl group leads to intermediate V. At the end of the removal of the water molecule of this intermediate leads to the production of polyhydroquinoline derivatives 5a-5p [54,60].

According to the green chemistry viewpoint, recoverability and recycling of the catalyst is an important issue in modern catalysis researches. The reusability of Cu(II)-PAA/M-MCM-41 was investigated after the completion of the reaction for the one-pot, four-component reaction of benzaldehyde, dimedone, ethyl acetoacetate and ammonium acetate. Cu(II)-PAA/M-MCM-41 NC was successfully recycled by filtration and washed with MeOH, and dried in 100 °C for the next run without a considerable decrease in its catalytic activity. It was found that the catalyst can be recovered and reused in five reaction cycles with only a slight decrease in the reaction yield (Fig. 7).

4. Conclusions

In summary, in this research for the first time the preparation of a novel and efficient heterogeneous catalyst was reported. Applicability of the catalyst Cu(II)-PAA/M-MCM-41 was tested for the synthesis of polyhydroquinoline derivatives by condensation of dimedone, β -ketoester, ammonium acetate as a source of nitrogen and a range of aromatic aldehydes in the absence of solvent. The encouraging points of this study are eco-friendly and mild reaction conditions, easy separation and reusability of the catalyst, short reaction time with high product yields, and easy work-up.

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Caption for Schemes

Scheme 1. Schematic illustration for the fabrication of Cu (II)-PAA/M-MCM-41 NC.

Scheme 2. Synthesis of polyhydroquinoline derivatives using a one-pot, four-component reaction in the presence of Cu(II)-PAA/M-MCM-41 NC.

Scheme 3. Suggested mechanism for the synthesis of polyhydroquinoline derivatives using Cu(II)-PAA/M-MCM-41 NC.

Legend for the Figures

Figure 1. The FT-IR spectra of pristine MCM-41 (a), M-MCM-41 (b), neat PAA (c),

PAA/M-MCM-41 NC (d) and Cu(II)-PAA/M-MCM-41 NC (e).

Figure 2. XRD patterns of MCM-41 (a), M-MCM-41 (b) and Cu(II)-PAA/M-MCM-41(c).

Figure 3. The FE-SEM image of Cu(II)-PAA/M-MCM-41 NC.

Figure 4. Energy-dispersive X-ray spectroscopy (EDS) spectrum of Cu(II)-PAA/M-MCM-41 NC.

Figure 5. TGA thermograms of MCM-41 (a), M-MCM-41 (b) and Cu(II)-PAA/M-MCM-41 (c).

Figure 6. Nitrogen adsorption-desorption isotherms of Cu(II)-PAA/M-MCM-41 NC.

Figure 7. Reusability of the NC catalyst in the reaction of benzaldehyde, dimedone, ethyl acetoacetate and ammonium acetate.

Sample	$\frac{S_{BET}}{(m^2/g)}$	Pore diameter by BJH method (nm)	Pore volume (cm ³ /g)	
Cu(II)-PAA/M- MCM-41	101.5 1.22		0.114	

Table 2

Optimization of the amount of catalyst, solvent and the reaction temperature for the synthesis of polyhydroquinolines.

Entry	Catalyst	Solvent ^a	Temperature	Time	Yield ^b
	(g)		(°C) (min)		(%)
1	-	-	80 190		35
2	0.01	-	80 35		75
3	0.015	-	80	80 30	
4	0.02	-	80	25	94
5	0.025	-	80	25	92
6	0.03	-	80	25	86
7	0.02	CHCl ₃	60	60 120	
8	0.02	CH ₃ CN	80 90		63
9	0.02	MeOH	65 55		90
10	0.02	EtOH	80	45	90
11	0.02	H ₂ O	100 70		78
12	0.02		r.t	95	70
13	0.02		60 40		82
14	0.02	-	70	30	89
15	0.02	-	90	22	90
16	0.02	-	100	27	92

^a Solvent volume = 5 mL ^b Isolated yield.

Table 3

Preparation of polyhydroquinolines **5a-p** in the presence of Cu(II)-PAA/M-MCM-41 NC.^a



Entry	Ar	Product	R	Time (min)	Yield ^b (%)	Mp ^c (°C)
1	C ₆ H ₅	5a	OEt	25	94	203-205
2	4-Cl C ₆ H ₄	5b	OEt	20	96	242-244
3	4-CN C ₆ H ₄	5c	OEt	28	85	141-144
4	4-OMe C ₆ H ₄	5d	OEt	34	87	255-257
5	2,4-Cl C ₆ H ₃	5e	OEt	24	92	242-244
6	4-Br C ₆ H ₄	5f	OEt	28	90	252-254
7	4-Me C ₆ H ₄	5g	OEt	30	89	260-263
8	$4-NO_2 C_6H_4$	5h	OEt	40	92	243-245
9	3-OEt-4-OH C ₆ H ₃	5i	OEt	30	88	198-200
10	3-OMe-4-OH	5j	OEt	31	86	206-209
11	$2-\text{Cl }C_6\text{H}_4$	5k	OEt	28	93	209-212
12	3-OH C ₆ H ₄	51	OEt	33	91	220-222
13	C ₆ H ₅	5m	OMe	30	95	210-212
14	4-Cl C ₆ H ₄	5n	OMe	27	93	219-222
15	2,4-Cl C ₆ H ₃	50	OMe	26	90	252-255
16	4-Me C_6H_4	5p	OMe	36	89	270-274

^aReaction conditions: aldehyde = 1 mmol; dimedone =1 mmol; ethyl (or methyl) acetoacetate = 1 mmol; ammonium acetate = 1.5 mmol; Cu(II)-PAA/M-MCM-41 = 0.02 g. ^bIsolated yield.

^cMelting points are uncorrected.

Table 4

The comparative study of the activity of Cu(II)-PAA/M-MCM-41 NC with other catalysts for the synthesis of compound 5a.

Entry	Catalyst	Conditions	Time (min)	Yield (%)	Ref.
1	TiO ₂ NPs	EtOH, 80 °C, 10	105	92	[46]
•		mol% of catalyst	10	- -	
2	Co ₃ O ₄ -CNTs	EtOH, reflux, 30	40	95	[60]
2		mg of catalyst	20	02	[07]
3	FSM-16-SO ₃ H	EtOH/reflux, 40	30	93	[37]
1	EarO @P MCM 41	FtOU/roflux 50	40	00	[40]
4	1°C3O4@D-INICINI-41	mg of catalyst	40	90	[49]
5	MCM-41-OBF ₂	EtOH reflux	50	91	[50]
5		EtOH, ultrasonic.	50		[30]
6	SBA-15/SO ₃ H	70 mg of catalyst	25	92	[52]
		EtOH/80 °C, 50			
7	MCM-41@Serine@Cu	mg of catalyst	210	91	[54]
	(II)	Solvent-free, 90			
8	MCM-41	°C, 1 mol% of	15	90	[40]
		catalyst			
9	HClO ₄ -SiO ₂	Solvent-free, 90	8	95	[48]
		°C, 50 mg of			
10	Cu (II)-PAA/M-MCM-	catalyst	25	94	This Work
	41	Solvent-free, 80			
		°C, 20 mg of			
		catalyst			



























