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# Facile synthesis of spiro thiazolidinone via cyclic ketones, amines and thioglycolic acid by MCM-41-Schiff base-$CuSO_4{\cdot}5H_2O$

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## Abstract

Mesoporous MCM-41-supported Schiff base and $CuSO_4{\cdot}5H_2O$ (MCM-41@Schiff base-$CuSO_4{\cdot}5H_2O$) catalyzed one-pot three-component condensation of cyclic ketones, amines and thioglycolic acid in toluene. And a series of corresponding spiro thiazolidinone derivatives were obtained in high yields (up to 97%). The synthesized catalyst was characterized via FT-IR, XRD, SEM, TEM and EDS and can be easily recovered by centrifugation and reused at 10 times without any change in catalytic activity. Moreover, the scale-up experiment also demonstrated the practicability of the catalytic system on the condensation. The possible mechanisms pave the way to investigation on the reactions of other cyclic ketones with thioglycolic acid.

**Keywords** Heterogeneous · MCM-41 · Schiff base · Thiazole · Condensation

## Introduction

Thiazole is key structural subunits in heterocyclic chemistry and is present in many natural products, pharmaceuticals, polymers and agrochemicals [1]. Because of the significant medicinal value and physiological activity, such as anti-inflammatory [2], antitumoral [3], antiviral [4] and antibacterial activity [5], thiazole-containing derivatives have attracted many chemical and medical researchers' interest. And recently, thiazole derivatives have also a wide range of applications in functional materials [6–8]. Many different catalytic methods are available to synthesize thiazolidinone

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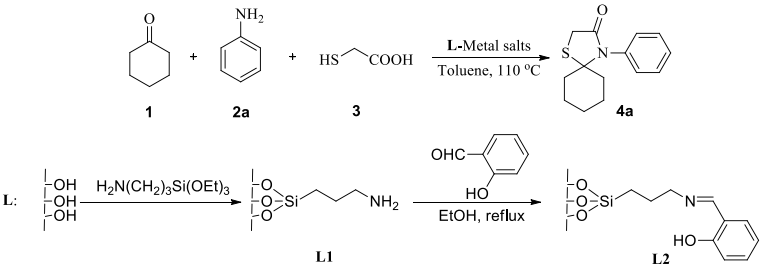
derivatives, among which the main catalysts to the synthesis are metal complexes[9], ionic liquids [10–13], DCC [14, 15], organic acids [16–18] and enzymes [19, 20] and magnetic materials [21]. However, most of these catalysts are homogeneous catalysts that are difficult to separate and reuse, environmentally unfriendly and waste control. Recently, the development of heterogeneous catalysts [10, 22] for the recycling and catalytic life has become an important research field for economic and environmental [23]. And, to further address the idea of high activity, recyclability and reusability, organic functional groups have emerged as the ordered mesoporous siliceous material support because of their high active site to catalysis. Thus, designing and searching for a highly effective and recyclable catalytic system is still strongly interesting and desirable. Up to now, only two catalytic examples of cyclization reaction with cycloketimines and mercaptoacetic acid have been reported. One is $HClO_4$–$SiO_2$ system reported by Chakraborti's group [24], and the other is MCM-41@Schiff base-metal complex system reported by our group [25]. And to the best of our knowledge, all of the examples focus on aromatic aldehydes. Herein, we reported our efforts on the development of the catalytic cyclization reaction of spiro thiazolidinone with cycloketone, aromatic amines and mercaptoacetic acid by MCM-41@Schiff base-$CuSO_4{\cdot}5H_2O$ (Scheme 1).

## Results and discussion

The amine-functionalized MCM-41 and Schiff base-supported MCM-41 were prepared according to the procedure shown in Scheme 1. Amine-functionalized MCM-41 was achieved by MCM-41 and 3-(triethoxysilyl)propan-1-amine in ethanol [26]. Then, salicylaldehyde was added to suspension of MCM-41@$NH_2$ in ethanol. The mixture was filtered, and the residue was washed by dichloromethane and ether. MCM-41@Schiff base was dried under vacuum. The catalysts were characterized by SEM, TEM and FT-IR.

The FT-IR spectra of MCM-41, MCM-41@$NH_2$ (**L1**), MCM-41@Schiff base (**L2**) and **L2**-$CuSO_4{\cdot}5H_2O$ are shown in Fig. 1. The observation of prominent peaks at 1085 $cm^{-1}$ and 799 $cm^{-1}$ in FT-IR spectrum of these catalysts was related to the Si–O–Si band. In the FT-IR spectrum of MCM-41@$NH_2$ (**L1**), new absorption peaks appeared at around 1500 $cm^{-1}$ and 1250 $cm^{-1}$ that were corresponding to




**Scheme 1** Synthesis of thiazolidinone and the ligands

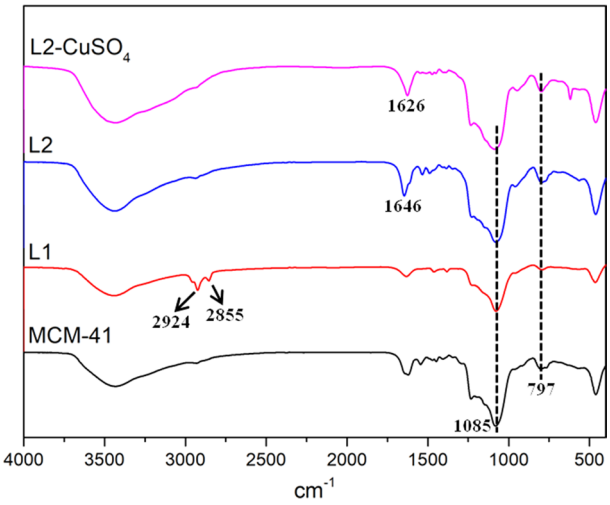



**Fig. 1** IR patterns of MCM-41, amine-functionalized MCM-41 **L1**, MCM-41@Schiff base **L2** and **L2**-$CuSO_4{\cdot}5H_2O$

$NH_2$ symmetric bending vibration and N–H bending vibration [27]. The characteristic peaks at 2924 $cm^{-1}$ and 2855 $cm^{-1}$ were corresponding to vibration of C-H stretching vibration peaks. The free ligand, MCM-41@Schiff base (**L2**), exhibits a C=N asymmetric bending vibration at 1646 $cm^{-1}$ [28, 29]. Besides, compared with the spectrum of **L2,** the absorption shift of C=N band in **L2**-$CuSO_4{\cdot}5H_2O$ structure moves to lower frequency, which considers that the C=N bond was successfully coordinated with copper ion.

The low-angle XRD patterns and wide-angle XRD patterns of MCM-41, MCM-41@$NH_2$ (**L1**), MCM-41@Schiff base (**L2**) and **L2**-$CuSO_4{\cdot}5H_2O$ are outlined in Fig. 2, respectively. In the low-angle XRD patterns, the MCM-41 shows three

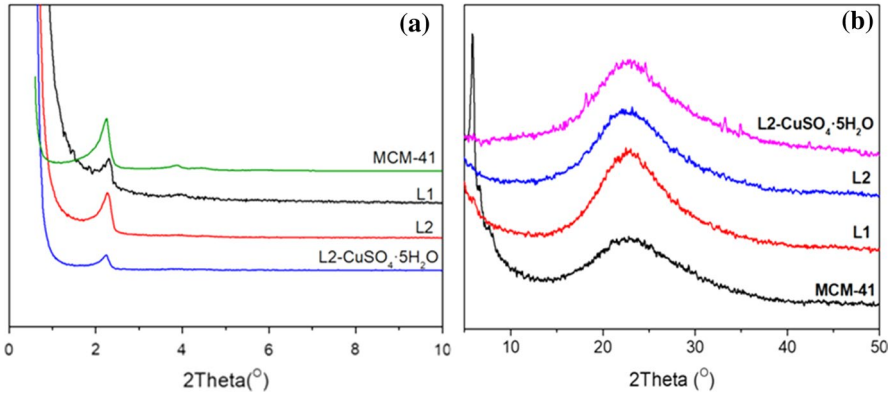
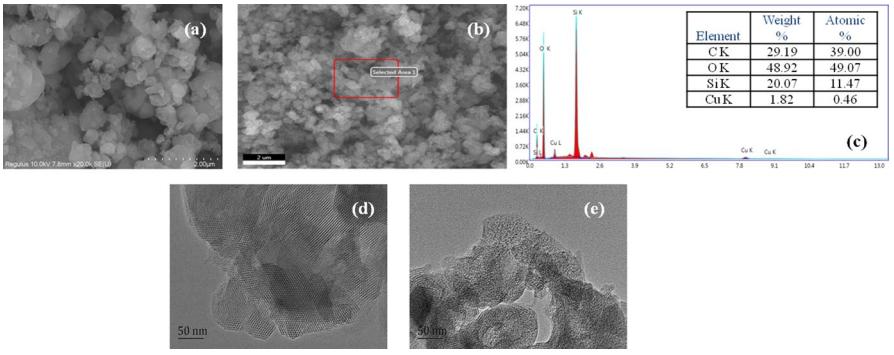



**Fig. 2** Low-angle XRD patterns of ligands (**a**) and wide-angle XRD patterns of ligands (**b**)

diffraction peaks at 2$\theta$ 2.2°, 3.8° and 4.4°, attributed to 100, 110 and 200 reflection planes, respectively. The X-ray diffraction pattern of the **L1**, **L2** and **L2**-$CuSO_4{\cdot}5H_2O$ reveals 2D hexagonally structured pores at low angles, and the diffraction pattern is not observed at high angle because of the amorphous nature of the hole wall [30]. In the wide-angle XRD patterns, there is a wide and intense peak (2$\theta$ = 23°) of amorphous silica. These results demonstrated that hexagonally ordered mesostructures of **L1**, **L2** and **L2**-$CuSO_4{\cdot}5H_2O$ remained unchanged after modifying, compared with MCM-41. And, there is no diffraction peak of metal phase in XRD pattern of **L2**-$CuSO_4{\cdot}5H_2O$. Combined with the FT-IR spectra analysis, we think that the loaded copper salt is highly dispersed and its structure size is lower than the size limit of detection [31].

The different catalysts were characterized by SEM as illustrated in Fig. 3a, b. It was observed that the porous spherical structure exhibited no significant alterations after the immobilization. The elemental composition of **L2**-$CuSO_4{\cdot}5H_2O$ was illustrated by the energy-dispersive X-ray spectroscopy (EDS), and confirmed the presence of C, O, Si and Cu elements (Fig. 3c). The TEM images of the MCM-41 and **L2**-$CuSO_4{\cdot}5H_2O$ catalyst show that the immobilized catalyst **L2**-$CuSO_4{\cdot}5H_2O$ maintained hexagonally ordered mesostructures (Fig. 3e).

The activity of the catalysts as described above was tested in the model reaction of cyclohexanone, aniline and thioglycolic acid in toluene at 110 °C. The results are shown in Table 1. The reaction occurred smoothly in the presence of 0.005 g MCM-41, MCM-41@$NH_2$ (**L1**) and MCM-41@Schiff base (**L2**), affording the corresponding products in 38%, 45% and 60% (Table 1, entries 1, 3 and 4). At the same time, a comparative experiment was performed. When the model reaction was catalyzed by $SiO_2$ leading to low yield, 4-phenyl-1-thia-4-azaspiro[4.5]decan-3-one (**4a**) has been reported (Table 1, entry 2). Compared with MCM-41, the reaction would greatly be facilitated by the pores [32]. And then, the metal salts were added in the reaction system, because Schiff base-metal salt shows high catalytic activity in the catalysis field. The copper salt-supported MCM-41@Schiff base was found that the efficiency superior to other metal salts in the catalytic experiments. And the co-catalytic effect of $CuSO_4{\cdot}5H_2O$ and **L2** was better than that of other copper salts (Table 1, entries




| Element | Weight % | Atomic % |
|---|---|---|
| CK | 29.19 | 39.00 |
| OK | 48.92 | 49.07 |
| SiK | 20.07 | 11.47 |
| CuK | 1.82 | 0.46 |

**Fig. 3** SEM images of MCM-41 (**a**) and **L2**-$CuSO_4{\cdot}5H_2O$ (**b**), EDS image of **L2**-$CuSO_4{\cdot}5H_2O$ (**c**), TEM images of MCM-41 (**d**) and **L2**-$CuSO_4{\cdot}5H_2O$ (**e**)

**Table 1** Optimization of the reaction conditions

| Entry | Catalyst | Solvent | Time (h) | Yield (%) [a] |
|---|---|---|---|---|
| 1 | MCM-41 | Toluene | 10 | 38 |
| 2 | $SiO_2$ | Toluene | 10 | 11 |
| 3 | **L1** | Toluene | 10 | 45 |
| 4 | **L2** | Toluene | 10 | 60 |
| 5 | **L2**-$Cu(NO_3)_2{\cdot}3H_2O$ | Toluene | 10 | 79 |
| 6 | **L2**-$CuSO_4{\cdot}5H_2O$ | Toluene | 10 | 93 |
| 7 | **L2**-$Cu(AcO)_2{\cdot}H_2O$ | Toluene | 10 | 77 |
| 8 | **L2**-$CuCl_2{\cdot}2H_2O$ | Toluene | 10 | 70 |
| 9 | **L2**-CuCl | Toluene | 10 | 84 |
| 10 | $CuSO_4{\cdot}5H_2O$ | Toluene | 10 | 50 |
| 11 | **L2**-$CuSO_4{\cdot}5H_2O$ | $H_2O$ | 10 | 10 |
| 12 | **L2**-$CuSO_4{\cdot}5H_2O$ | EtOH | 10 | 85 |
| 13 | **L2**-$CuSO_4{\cdot}5H_2O$ | $CH_3CN$ | 10 | Trace |
| 14 | **L2**-$CuSO_4{\cdot}5H_2O$ | $CH_3COCH_3$ | 10 | Trace |
| 15 | **L2**-$CuSO_4{\cdot}5H_2O$ | $CH_2Cl_2$ | 10 | Trace |
| 16 | **L2**-$CuSO_4{\cdot}5H_2O$ | THF | 10 | Trace |
| 17[b] | **L2**-$CuSO_4{\cdot}5H_2O$ | Toluene | 10 | 76/83 |
| 18[c] | **L2**-$CuSO_4{\cdot}5H_2O$ | Toluene | 10 | 78/85 |
| 19[d] | **L2**-$CuSO_4{\cdot}5H_2O$ | Toluene | 10 | 79/93 |
| 20 | **L2**-$CuSO_4{\cdot}5H_2O$ | – | 10 | 79 |
| 21 | **L2**-$CuSO_4{\cdot}5H_2O$ | Toluene | 8/12 | 80/94 |
| 22[e] | **L2**-$CuSO_4{\cdot}5H_2O$ | Toluene | 10 | 94 |

Reaction conditions (unless noted otherwise): cyclohexanone (0.1 mmol), aniline (0.1 mmol), thioglycolic acid (0.12 mmol), **L** (0.005 g) and metal salt (5 mol%) in toluene (0.5 mL) at 110 °C 10 h

[a]Isolated yield

[b]Use 3 mol%/10 mol% $CuSO_4{\cdot}5H_2O$

[c]Use 0.0025/0.0100 g **L2**

[d]0.3 mL/1.0 mL toluene

[e]The complex of **L2**-$CuSO_4{\cdot}5H_2O$ was pre-prepared

5–9). After solvent screening, toluene proved to be the best choice for the reaction (Table 1, entry 6). The reaction was also monitored with different ratios of **L2** and $CuSO_4{\cdot}5H_2O$, and the results showed that 0.0050 g **L2**/5 mol% $CuSO_4{\cdot}5H_2O$ of catalyst was the best ratio for the catalytic reaction (Table 1, entries 17 and 18). In the subsequent investigation of the solvent consumption of the system, the yield of the reaction decreased with the decrease in the amount of solvent, even in the solvent-free condition (Table 1, entries 19 and 20). Moreover, shortening the reaction time resulted in a lower yield, and prolonging reaction time could not improve the yield (94% yield), either. Finally, compared with the catalyst prepared in situ, the same result was obtained with the pre-prepared complex of **L2**-$CuSO_4{\cdot}5H_2O$ (Table 1, entry 22).

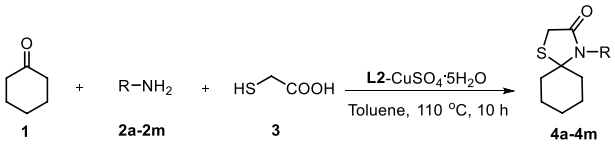
**Table 2** Substrate scope for the condensation reaction

| Entry | R | Product | Yield (%)[a] | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $C_6H_5$ | **4a** | 93 | 63 [24] |
| 2 | *p*-$FC_6H_4$ | **4b** | 82 | 70 [33] |
| 3 | *p*-$ClC_6H_4$ | **4c** | 85 | 71 [34] |
| 4 | *p*-$BrC_6H_4$ | **4d** | 93 | 72 [35] |
| 5 | *p*-$CH_3C_6H_4$ | **4e** | 95 | 68 [36] |
| 6 | *p*-$CH_3OC_6H_4$ | **4f** | 93 | 77 [37] |
| 7 | *m*-$FC_6H_4$ | **4g** | 95 | – |
| 8 | *m*-$ClC_6H_4$ | **4h** | 92 | [38] |
| 9 | *m*-$BrC_6H_4$ | **4i** | 97 | – |
| 10 | *m*-$CH_3OC_6H_4$ | **4j** | – | – |
| 11 | *m*-$CH_3C_6H_4$ | **4k** | – | – |
| 12 | *o*-$CH_3OC_6H_4$ | **4l** | 90 | – |
| 13 | $C_6H_5CH_2$ | **4m** | 96 | – |

Reaction conditions (unless noted otherwise): cyclohexanone (0.1 mmol), aniline (0.1 mmol), thioglycolic acid (0.12 mmol), **L2** (0.005 g) and $CuSO_4{\cdot}5H_2O$ (5 mol%) in toluene (0.5 mL) at 110 °C 10 h

[a]Isolated yield

[b]Yield of reference



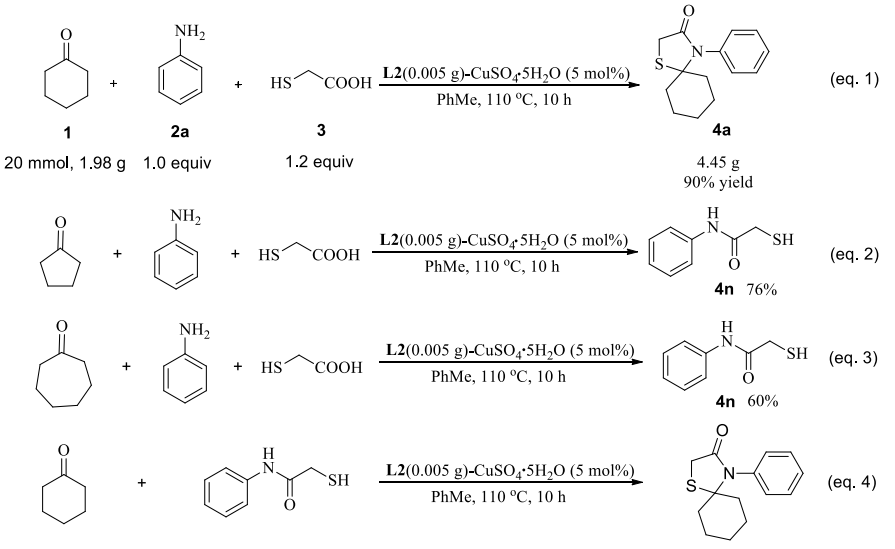

**Scheme 2** The cyclization of cyclohexanone, aniline and thioglycolic

Under the optimized conditions, an investigation of the substrate scope of this reaction of the scope of cyclohexanone, amines and thioglycolic acid was examined (Table 2). Compound **4a** with no substituents in the phenyl ring of amine was high active, 93% yield. The best compounds were obtained when withdrawing substituents (F, Cl and Br) and donating substituents ($CH_3$ and $OCH_3$) were introduced in para position of the amines (**4b–f**). Halogen substituents in meta position are well tolerated, and > 90% yields were obtained (**4 g–i**). However, in comparison with entries 7–9, none of the desired product was obtained when *meta*-methoxy and *meta*-methyl aniline were used in this reaction. We thought the electronic effect is the main reason, because only at the *meta* position lower the *ortho* and *para* electron-donating groups on the increasing electron density. Benzylamine can also be used as a substrate with the current catalytic system, the corresponding product **4 m** was obtained in 96% yield (Table 2, entry 13) (Scheme 2).

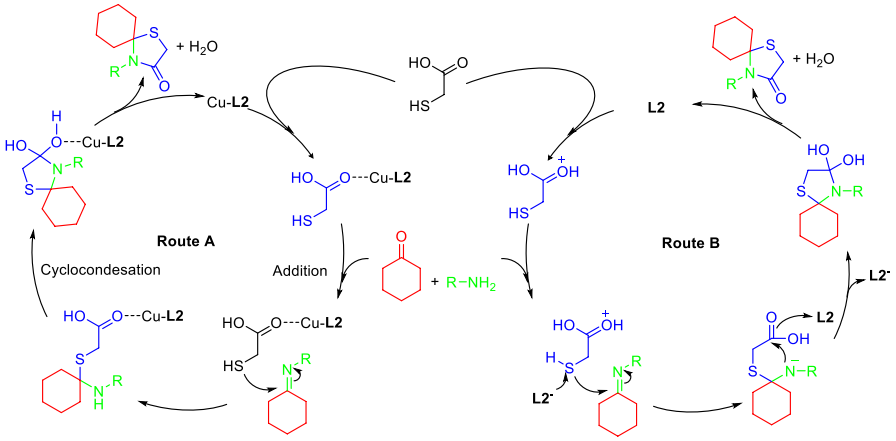
We then examined the synthetic utility of the catalyst system, a scaled-up reaction of cyclohexanone, aniline and thioglycolic acid by using the **L2**-$CuSO_4{\cdot}5H_2O$ was

performed. As shown in Scheme 3, by treatment of the starting materials (20 mmol), a good yield (90%) was still afforded (Scheme 3, Eq. 1). Subsequently, under the optimized conditions, the three-component reaction of cyclopentanone (and cycloheptanone), aniline and thioglycolic acid was investigated. Disappointingly, the spiro thiazolidinone derivatives could not be detected with the cyclopentanone and cycloheptanone, and the ring opening of 2-mercapto-N-phenylacetamide **4n** was produced (Scheme 3, Eqs. 2 and 3). And then, the experiment of cyclohexanone and **4n** was performed (Scheme 3, Eq. 4). What is more, Chakraborti et al. [24] introduced the main amide product **4n** formed by condensation of open-chain ketone (such as acetophenone) is obtained. We think that the steric distortion of cyclopentanone and cycloheptanone may be responsible for the increase in steric resistance. Unfortunately, the target product **4a** was not observed. According to our previous works [25], plausible reaction mechanisms are explained in Scheme 4. In the first step, the thioglycolic acid is activated by the Lewis acid catalyst **L2**-$CuSO_4{\cdot}5H_2O$ to start the addition reaction of *N*-cyclohexylideneaniline that is synthesized by cyclohexanone and aniline. An intramolecular cyclocondensation is then promoted by the Cu thioglycolic acid and aniline of the intermediate. Finally, the **L2**-Cu-spiro thiazolidinone is converted to the product by the loss of $H_2O$ (Route A). Additionally, **L2** has some catalytic activity to this reaction. The cyclization reaction may proceed via phenolic hydroxyl group of **L2** to enhance nucleophilicity of mercapto group of thioglycolic acid, which causes thioglycolic acid facile addition on the imino. Subsequently, the cyclocondensation product of 4-thiazolidinone is formed in successive steps (Route B) [20].

Under optimized conditions, as a heterogeneous catalyst, the recyclability of MCM-41@Schiff base-$CuSO_4{\cdot}5H_2O$ was examined in the cyclization reaction




**Scheme 3** Scaled-up version and condensation of other cyclic ketones




**Scheme 4** Proposed catalytic mechanism

(Fig. 4). Following the completion of reaction, the catalyst was recovered by centrifugation and dried, and then the amount of substrates was determined according to the amount of recovered catalyst for the next cycle. It was found that the catalyst was able to perform the reaction for ten runs without significant effect on the yield. The spiro thiazolidinone **4a** was still obtained with 90% yield after the tenth recycle. In addition, the recovered catalyst was characterized by FT-IR, which was consistent with the spectrum of the original catalyst. In the "hot filtration" test, the separated organic phase was used as catalyst for the reactions, but no product was observed.

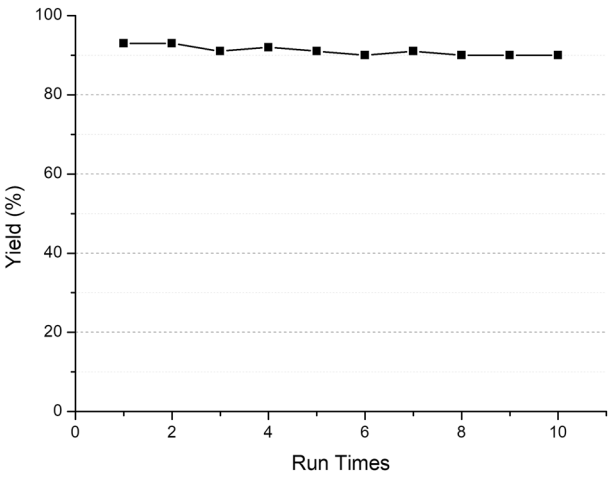



**Fig. 4** Catalyst recycling studies

## Experimental

All chemicals and mesoporous materials were purchased from Adamas-Beta and used without further purification. The purity of compounds was checked by thin-layer chromatography (TLC) using ethyl acetate/petroleum ether(v/v) as an eluent, and FT-IR spectrum was recorded on Bruker Equinox 55 FT-IR spectrophotometer as KBr discs. The $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded on an INOVA-400 spectrometer operating at 400 MHz for $^{1}H$ and 100 MHz for $^{13}C$ in $DCl_3$ using TMS as an internal standard. The prepared ligands were characterized by FT-IR, XRD, SEM and TEM.

### Typical procedure for synthesis of thiazolidinone derivatives

A mixture of **L2** (0.005 g) and $CuSO_4{\cdot}5H_2O$ (5 mol%) in toluene (0.5 mL) was stirred at room temperature for 0.5 h. Then, cyclohexanone (0.0098 g, 0.10 mmol), aromatic amine (0.0093 g, 0.10 mmol) and thioglycolic acid (0.014 g, 0.12 mmol) were added and stirred at reflux for 10 h. The process was monitored by TLC. The reaction mixture was purified by column chromatography on silica gel using petroleum ether/ethyl acetate to give the product **4a**.

### Physical and spectroscopic data for 4a–4m

#### 4-Phenyl-1-thia-4-azaspiro[4.5]decan-3-one 4a

Yellow solid, 90% yield, m.p: 169 °C. $^{1}H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.50–7.39 (m, 3H), 7.20–7.12 (m, 2H), 3.69 (s, 2H), 2.03–1.96 (m, 2H), 1.77–1.54 (m, 8H).

#### 4-(4-Fluorophenyl)-1-thia-4-azaspiro[4.5]decan-3-one 4b

White solid, 82% yield, m.p: 170–171 °C. $^{1}H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.15 (d, $J = 1.5$ Hz, 2H), 7.13 (s, 2H), 3.67 (s, 2H), 1.97 (d, $J = 8.2$ Hz, 2H), 1.79–1.54 (m, 8H).

#### 4-(4-Chlorophenyl)-1-thia-4-azaspiro[4.5]decan-3-one 4c

White solid, 85% yield, m.p: 180 °C. $^{1}H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.45–7.41 (m, 2H), 7.12–7.08 (m, 2H), 3.67 (s, 2H), 1.97 (d, $J = 8.3$ Hz, 2H), 1.83–1.57 (m, 8H).

**4-(4-Bromophenyl)-1-thia-4-azaspiro[4.5]decan-3-one 4d**

White solid, 93% yield, m.p: 184–185 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.63–7.54 (m, 2H), 7.06–7.01 (m, 2H), 3.67 (s, 2H), 1.97 (d, $J$ = 8.3 Hz, 2H), 1.82–1.49 (m, 8H).

**4-p-Tolyl-1-thia-4-azaspiro[4.5]decan-3-one 4e**

Yellow solid, 95% yield, m.p: 189 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.24 (d, $J$ = 0.6 Hz, 2H), 7.05–7.01 (m, 2H), 3.67 (s, 2H), 2.38 (s, 3H), 1.97 (d, $J$ = 10.3 Hz, 2H), 1.75–1.53 (m, 8H).

**4-(4-Methoxyphenyl)-1-thia-4-azaspiro[4.5]decan-3-one 4f**

Yellow solid, 93% yield, m.p: 144–145 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.09–7.05 (m, 2H), 6.96 (d, $J$ = 9.0 Hz, 2H), 3.83 (s, 3H), 3.67 (s, 2H), 1.96 (d, $J$ = 10.6 Hz, 2H), 1.80–1.57 (m, 8H).

**4-(3-Fluorophenyl)-1-thia-4-azaspiro[4.5]decan-3-one 4g**

White solid, 95% yield, m.p: 156–157 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.53–7.47 (m, 1H), 7.28 (dd, $J$ = 8.2, 1.8 Hz, 1H), 7.18–7.14 (m, 1H), 6.84 (tdd, $J$ = 8.3, 2.5, 0.9 Hz, 1H), 3.52 (s, 2H), 2.20–2.05 (m, 5H), 1.70–1.57 (m, 5H). $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 172.5, 162.3, 144.4, 130.7, 123.6, 116.3, 109.8, 74.1, 43.4, 39.1, 25.6, 24.9. Analysis calc. for $C_{14}H_{16}FNOS$ (265.09): C, 63.37; H, 6.08; N, 5.28. Found: C, 63.21; H, 6.03; N, 5.43.

**4-(3-Chlorophenyl)-1-thia-4-azaspiro[4.5]decan-3-one 4h**

White solid, 92% yield, m.p: 180 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.64 (t, $J$ = 2.0 Hz, 1H), 7.39–7.37 (m, 1H), 7.28 (s, 1H), 7.13–7.10(m, 1H), 3.52 (s, 2H), 2.19–2.06 (m, 5H), 1.74–1.56 (m, 5H). $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 172.7, 149.8, 135.3, 130.7, 128.7, 126.9, 120.8, 68.4, 43.4, 39.8, 25.3, 24.9. Analysis calc. for $C_{14}H_{16}FNOS$ (265.09): C, 59.67; H, 5.72; N, 4.97. Found: C, 59.60; H, 5.91; N, 4.85.

**4-(3-Bromophenyl)-1-thia-4-azaspiro[4.5]decan-3-one 4i**

White solid, 97% yield, m.p: 182–183 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.58–7.54 (m, 1H), 7.36–7.31 (m, 2H), 7.12–7.09 (m, 1H), 3.67 (s, 2H), 2.01–1.95 (m, 2H), 1.84–1.58 (m, 8H). $^{13}$C NMR (100 MHz, CDCl3) $\delta$ 171.9, 143.9, 130.1, 127.5, 126.9, 123.5, 121.1, 69.2, 43.5, 39.8, 26.0, 24.2. Analysis calc. for $C_{14}H_{16}BrNOS$ (325.01): C, 51.54; H, 4.94; N, 4.29. Found: C, 51.41; H, 4.87; N, 4.55.

**4-(2-Methoxyphenyl)-1-thia-4-azaspiro[4.5]decan-3-one 4l** Yellow solid, 90% yield, m.p: 169–170 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.35 (dd, $J$ = 8.0, 1.6 Hz,

1H), 7.08–7.06 (m, 1H), 6.99–6.94 (m, 1H), 6.89 (dd, $J = 8.1$, 1.3 Hz, 1H), 3.89 (s, 3H), 3.53 (s, 2H), 2.21–2.16 (m, 2H), 2.12–1.75 (m, 3H), 1.75–1.50 (m, 5H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.0, 163.4, 129.1, 128.8, 122.5, 116.1, 112.9, 68.1, 56.4, 39.2, 25.8, 24.5. Analysis calc. for $C_{15}H_{19}NO_2S$ (277.11): C, 64.95; H, 6.90; N, 5.05. Found: C, 64.87; H, 6.92; N, 5.15.

**4-Benzyl-1-thia-4-azaspiro[4.5]decan-3-one 4m** White solid, 96% yield, m.p: 249–250 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34–7.27 (m, 4H), 7.25–7.21 (m, 1H), 4.58 (s, 2H), 3.63 (s, 2H), 1.81–1.52 (m, 10H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.8, 137.5, 129.2, 128.9, 127.2, 64.0, 47.4, 36.1, 35.9, 33.1, 25.6, 24.6. Analysis calc. for $C_{15}H_{19}NOS$ (261.12): C, 68.93; H, 7.33; N, 5.36. Found: C, 68.72; H, 7.50; N, 5.33.

**2-Mercapto-*N*-phenylacetamide 4n** White solid, m.p: 159–160 °C. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.41 (s, 1H), 7.61 (d, $J = 7.6$ Hz, 2H), 7.35 (t, $J = 8.0$ Hz, 2H), 7.16 (d, $J = 7.4$ Hz, 1H), 3.66 (d, $J = 9.0$ Hz, 2H), 2.30 (s, 1H).

## Conclusion

In summary, MCM-41-Schiff base-$CuSO_4{\cdot}5H_2O$ has been synthesized and was characterized using various spectroscopic techniques. Its catalytic activity as heterogeneous catalyst for the cyclocondensation of spiro thiazolidinone derivatives through a three-component one-pot synthesis has been described. The corresponding products were obtained in good yields (up to 97%). The reaction could be amplified to gram scales under the optimized conditions without loss of yield. What is more, the catalyst showed a good level of recyclability (90% yield was afforded after ten cycles of reaction). Finally, comparative investigations of thioglycolic acid and other cyclic ketones and the proposed reaction of by-product and cyclohexanone confirm the mechanism might be operating in the intermediate of imine. In our group, further applications of the ordered mesoporous siliceous material to other reactions are ongoing.

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## References

1. B. Eftekhari-Sis, M. Zirak, A. Akbari, Chem. Rev. **113**, 2958 (2013)
2. Z.Q. Li, X.Z. Li, M.B. Su, L.X. Gao, Y.B. Zhou, B.C. Yuan, X.L. Lyu, Z.Q. Yan, C.J. Hu, H. Zhang, C. Luo, Z. Chen, J. Li, Y.J. Zhao, J. Med. Chem. **63**, 4388 (2020)

3. S.D. Shen, M. Hadley, K. Ustinova, J. Pavlicek, T. Knox, S. Noonepalle, M.T. Tavares, C.A. Zimprich, G.P. Zhang, M.B. Robers, C. Bařinka, A.P. Kozikowski, A. Villagra, J. Med. Chem. **62**, 8557 (2019)
4. S. Sinha, S.L. Manju, M. Doble, ACS Med. Chem. Lett. **10**, 1415 (2019)
5. E.S.H. El-Tamany, S.Z. Sowellim, A.A. Hamed, A.S. Radwan, Res. Chem. Intermed. **41**, 2675 (2015)
6. L. Zhang, W.Y. Deng, B.Q. Wu, L. Ye, X.F. Sun, Z.F. Wang, K. Gao, H.B. Wu, C.H. Duan, F. Huang, Y. Cao, ACS Appl. Mater. Int. **12**, 753 (2020)
7. K. Dölling, H. Zaschke, H. Schubert, J. Prakt. Chem. **321**, 643 (1979)
8. L.L. Zhang, X.J. Liu, S.S. Lu, J. Liu, S.L. Zhong, Y.B. Wei, T. Bing, N. Zhang, D.H. Shangguan, ACS Appl. Bio. Mater. **3**, 2643 (2020)
9. A. Ahlawat, P. Khatkar, V. Singh, S. Asija, Res. Chem. Intermed. **44**, 4415 (2018)
10. N. Azgomi, M. Mokhtary, J. Mol. Catal. A Chem. **398**, 58 (2015)
11. A. Daghlavi, E. Kowsari, M. Abdouss, M.H. Ghasemi, E. Asadi, Res. Chem. Intermed. **46**, 3593 (2020)
12. A.K. Yadav, M. Kumar, T. Yadav, R. Jain, Tetrahedron Lett. **50**, 5031 (2009)
13. L.D. Khillare, M.R. Bhosle, A.R. Deshmukh, R.A. Mane, Res. Chem. Intermed. **41**, 8955 (2015)
14. T. Srivastava, W. Haq, S.B. Katti, Tetrahedra **58**, 7619 (2002)
15. Z. Turgut, C. Yolacan, F. Aydogan, E. Bagdatli, N. Ocal, Molecules **12**, 2151 (2007)
16. M. Singh, M. Saquib, S.B. Singh, S. Singh, P. Ankit, S. Fatma, J. Singh, Tetrahedron Lett. **55**, 6175 (2014)
17. M.A. Chaudhari, J.B. Gujar, D.S. Kawade, P.V. Shinde, M.S. Shingare, Res. Chem. Intermed. **41**, 10027 (2015)
18. H. Mohammadi, H.R. Shaterian, Res. Chem. Intermed. **46**, 1109 (2020)
19. H. Zheng, Y.J. Mei, K. Du, Q.Y. Shi, P.F. Zhang, Catal. Lett. **143**, 298 (2013)
20. U.R. Pratap, D.V. Jawale, M.R. Bhosle, R.A. Mane, Tetrahedron Lett. **52**, 1689 (2011)
21. L. Shiri, A. Ghorbani-Choghamarani, M. Kazemi, Res. Chem. Intermed. **43**, 2707 (2017)
22. N. Foroughifar, S. Ebrahimi, Chin. Chem. Lett. **24**, 389 (2013)
23. J.S.M. Lee, A.I. Cooper, Chem. Rev. **120**, 2171 (2020)
24. D. Kumar, M. Sonawane, B. Pujala, V.K. Jain, S. Bhagat, A.K. Chakraborti, Green Chem. **15**, 2872 (2013)
25. H.X. Pang, Y.H. Hui, K. Fan, X.J. Xing, Y. Wu, J.H. Yang, W. Shi, Z.F. Xie, Chin. Chem. Lett. **27**, 335 (2016)
26. C.C. Wang, S.L. Xie, Z.F. Xie, Y.H. Hui, Chin. J. Org. Chem. **33**, 2391 (2013)
27. E.M. Flefel, W.A. Ei-Sayed, A.M. Mohamed, W.I. Ei-Sofany, H.M. Awad, Molecules **22**, 170 (2017)
28. N. Amirmahami, N.O. Mahmovdi, M. Malakootian, A. Pardakhty, N. Seyedi, Res. Chem. Intermed. **46**, 4595 (2020)
29. M. Nikoorazm, A. Ghorbani-Choghamarani, H. Mahdavi, S.M. Esmaeili, Micropor. Mesopor. Mat. **211**, 174 (2015)
30. M. Nikoorazm, A. Ghorbani-choghamarani, N. Noori, Res. Chem. Intermed. **42**, 4621 (2016)
31. S. Karthikeyan, M.P. Pachamuthu, M.A. Isaacs, S. Kumar, A.F. Lee, G. Sekaran, Appl. Catal. B Environ. **199**, 323 (2016)
32. K. Fan, Y.H. Hui, X.M. Hu, W. Shi, H.X. Pang, Z.F. Xie, New J. Chem. **39**, 5916 (2015)
33. Y.H. Wu, Y.P. Jin, J.L. Cao, P. Yilihan, Y.J. Wen, J.X. Zhou, J. Ind. Eng. Chem. **20**, 2792 (2014)
34. D. Kaminskyy, D. Khyluk, O. Vasylenko, R. Lesyk, Tetrahedron Lett. **53**, 557 (2012)
35. E.M. Flefel, H.H. Sayed, A.I. Hashem, E.A. Shalaby, W. Ei-Sofany, F.M.E. Abdel-Megeid, Med. Chem. Res. **23**, 2515 (2014)
36. D.V. Kaminśkyi, Farmatsevtichnii Zhurnal (Kiev, Ukraine) **6**, 36 (2010)
37. A.K. Chakraborti, Indian Pat. Appl., **2011DE03148**
38. K.J. Mehta, J. Inst. Chem. (India) **50**, 81 (1978)