Tetrahedron Letters 54 (2013) 2164–2170

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A new application of rhodanine as a green sulfur transferring agent for a clean functional group interconversion of amide to thioamide using reusable MCM-41 mesoporous silica

Suman Ray [a], Asim Bhaumik [b], Arghya Dutta [b], Ray J. Butcher [c], Chhanda Mukhopadhyay [a,*]

[a] Department of Chemistry, University of Calcutta, 92 APC Road, Kolkata 700009, India
[b] Department of Materials Science, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700 032, India
[c] Department of Chemistry, Howard University, Washington, DC 20059, USA

ARTICLE INFO

Article history:
Received 19 December 2012
Revised 13 February 2013
Accepted 14 February 2013
Available online 22 February 2013

Keywords:
Thioamide
Rhodanine
MCM-41
Green synthesis
Reusable catalyst

ABSTRACT

A novel thionation protocol for amide compounds, with the system rhodanine/secondary amine has been discovered. Clean and efficient synthesis of a variety of thioamides can be achieved through this simple and convenient method using MCM-41 mesoporous silica as an acid catalyst. For this purpose we have synthesized MCM-41 silica and characterized by using an array of sophisticated analytical techniques like BET, HR TEM, EDX, XRD, 29Si MAS NMR and FTIR. This reaction is therefore a very neat example of a functional group interconversion.

Multidrug resistance (MDR) often emerges in the treatment of cancer following exposure of the patient to chemotherapeutic agents.[1a] *P*-glycoprotein (*P*-gp, also known as MDR1)[1b,c] is one such protein associated with MDR in cancer chemotherapy. In more recent work, it was demonstrated that essentially single-atom changes, that is, interchanging amide to thioamide functionality in rosamine/rhodamine structures gave high inhibitor property to *P*-gp.[1a,d] Thioamide drugs, ethionamide (ETH), prothionamide (PTH), thiacetazone (TAZ) and isoxyl (ISO) (Fig. 1), have been widely used for many years in the treatment of mycobacterial infections.[1e–i] Thioamides[1j–o] are also essential building blocks for a variety of chemically and pharmaceutically relevant compounds, such as thiazolines, betaines, mesoionic rhodanines, etc.[1p–r,2–4] The most exploited route for the synthesis of thioamides involves the nucleophilic attack of some suitable sulfur-containing agent on the carbon atom of C=O bond leading to the substitution of oxygen by the sulfur.[5] To effect this transformation, Lawesson's reagent[6] and P_4S_{10}, either alone or with additives,[7] are the reagents of choice. Many other useful reagents such as H_2S,[8] CS_2,[9] R_2PSX,[10] $(Et_2Al)_2S$,[11] NaSH,[12] TMS_2S,[13] elemental sulfur,[14] aq ammonium sulfide,[15] SiS_2,[16] HMDST,[17] etc. have also been reported. However, the uses of these reagents suffer from serious environmental and operational issues.[5] Therefore, the development of novel synthetic strategies for thionation is of paramount interest.

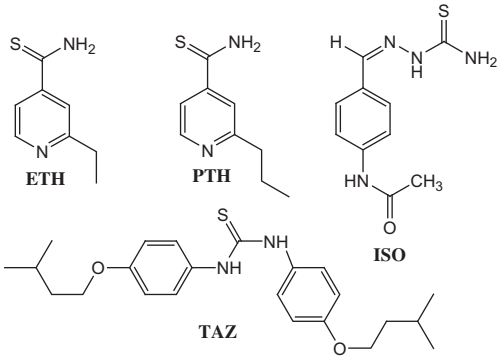


Figure 1. Some thioamide containing drug molecules.

The use of heterogeneous catalysts in chemical processes would simplify catalyst removal and minimize the amount of waste formed. However, a substantial decrease in the activity is frequently observed due to the heterogeneous nature of the materials in reaction media.[18,19] Open framework MCM-41 mesoporous molecular sieves with high surface areas and large pore sizes and pore volumes, favouring an easy accessibility of the organic functions within the insoluble solid, appear attractive for their

* Corresponding author.
E-mail address: cmukhop@yahoo.co.in (C. Mukhopadhyay).

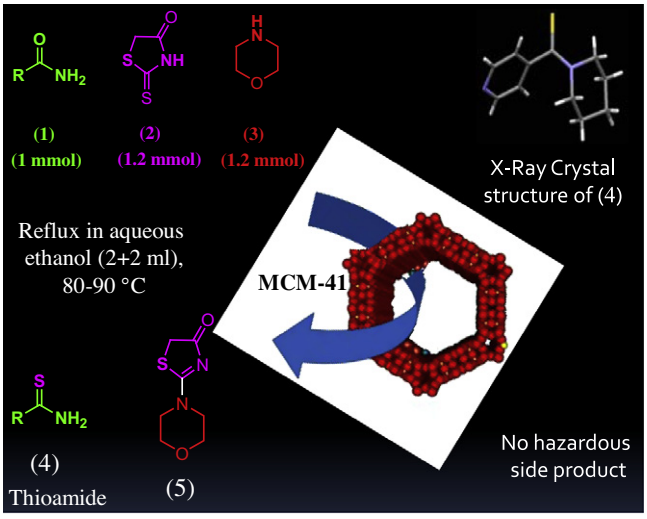
0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.02.045

development and uses as insoluble solid catalyst. MCM-41 displays a very large specific surface area of approximately 1000 $m^2 g^{-1}$. This property makes MCM-41 very interesting to be used as a heterogeneous catalyst.

Rhodanine is an interesting organic molecule with potential biological activities.[20–24] However, the application of this molecule in organic synthesis was limited in the 3-component reaction with aldehyde and amine[25–28] until recently. We have reported for the first time the reaction of rhodanine with ketones and secondary amine with the aid of re-usable heterogeneous silica-pyridine based catalyst.[29] Inspired by these foregoing discussion and given our interest and experience in heterogeneous catalysis,[28–32] we herein report a novel and convenient approach for thionation of amides, with rhodanine/secondary amine in the presence of MCM-41 mesoporous silica as a heterogeneous '*E*' catalyst (Eco-friendly, Efficient and Economic) (Scheme 1).

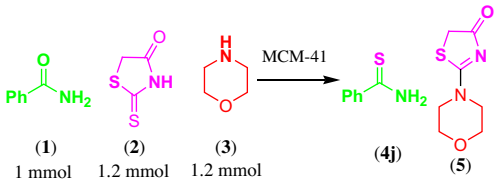
A survey of the literature revealed that no attempt has been made so far to investigate the general applicability of this potential thionating agent. Hence, we set out to explore the ability of rhodanine/secondary amine for thionation. In order to ascertain the feasibility of this transformation benzamide was selected as a model substrate, and conversion to its thio analogue was studied under a variety of conditions. Several common solvents, viz. DCE, DCM, toluene, THF, EtOH, MeOH and water were tested (Table 1). Though the yields of the reaction increased in polar-protic solvent than aprotic and non polar solvent, the reaction was not satisfactory in water (Table 1, entry 8), possibly due to less homogeneity of the reaction mixture. Therefore aqueous-ethanol (1:1 v/v) came out as a best choice of solvent. Similarly, temperature appears to play a significant role because there was only 50% thioamide formation after stirring the reaction mixture at 50–60 °C for 8 h (Table 1, entry 10) in aqueous ethanol instead of 89% yield at 80–90 °C (Table 1, entry 9).

When the reaction was performed using a stoichiometric amount (1.0 equiv) of rhodanine, the yield of **4j** was slightly reduced (74%) than when 1.2 equiv of rhodanine was used (89%). With the optimal reaction conditions in hand, we extended our synthetic protocol to examine its generality and substrate scope (Table 2). A wide range of primary, secondary and tertiary thioamides were readily synthesized from the corresponding amides. In addition to the amides, ketones could also be converted into the corresponding thioketones with this present reaction protocol (Table 2, entries **4u** and **4v**). It is worthy to mention that a single crystal structure of thioamide was scarcely reported in most of



Scheme 1. Thionation of amide using reusable MCM-41.

Table 1
Optimization of reaction conditions for the one-pot synthesis of thioamide **4j**[a]



Entry	Solvent (4 ml)	Temp	Time (h)	Yield[b] (%)
1	DCM	25–30	36	15
2	DCE	80–85	36	25
3	Toluene	90–100	12	40
4	Acetone	50–55	14	38
5	THF	60–65	16	31
6	MeOH	60–65	10	45
7	EtOH	75–80	10	85
8	H_2O	90–100	11	65
9	EtOH/H_2O (2 + 2 ml)	75–80	8	89
10	EtOH/H_2O (2 + 2 ml)	50	8	50

[a] Reagents and condition: Benzamide (1 mmol), rhodanine (1.2 mmol), morpholine (1.2 mmol), 40 mg MCM-41 different solvents, different temperature, different time, reflux.
[b] Isolated yields.

the earlier work where the structure determination mainly relied on NMR spectroscopy. The conversion of C=O to C=S can be realized from the ^{13}C NMR spectra as the amide carbonyl peak at around δ 160–170 ppm shifted to δ 190–210 ppm in the product, indicating the presence of a thioamide. Gratifyingly, we confirmed the structure of an unknown compound (**4a**) unambiguously through an X-ray single crystal analysis (CCDC 914935) (Fig. 2).

Another intriguing observation is that 10% conversion to thioamide was achieved only with rhodanine without any secondary amine additive, instead of 89% with equimolar quantity of rhodanine and secondary amine. This observation clearly established that amines have some role in transferring sulfur from rhodanine to amide. Again the starting materials were mostly unaffected without MCM-41. Therefore the attenuated acidity of MCM-41 was crucial for this transformation. Good to excellent conversion was also achieved with different weak and strong homogeneous acids like AcOH, HCl, H_2SO_4 etc. However, they required repeated work-up, neutralization of strong acids and extensive chromatographic purification. Ultimately the isolated yields were very low. Therefore, the reactions were performed employing MCM-41 as the right choice of catalyst and was demonstrated to be the key for rendering the reaction clean and obtained good to excellent yields. We have also used different types of other commonly used acid catalysts, mainly heterogeneous catalysts to make the work-up easier like TiO_2, SiO_2 NP, commercially available macroporous silica etc. However MCM-41 due to its very large surface area reproduced better performance than the others. On the basis of the results obtained above, a plausible reaction scenario for this reaction is outlined in Scheme 2. The key findings of high significance of MCM-41 described in this work are three-fold. Firstly the attack of secondary amine (**3**) on C=S of rhodanine (**2**) is an acid catalysed reaction[27–29] and in this present work MCM-41 performs efficiently as an acid catalyst to afford an in situ intermediate (**6**). Secondly the silanol groups present on the surface of MCM-41 coordinate with the oxygen atom of amide carbonyl which in turn increases its electrophicity[28–30] and attack of –SH of intermediate (**6**) becomes easier affording another in situ intermediate (**7**). Subsequent water elimination from (**7**) is also greatly assisted by MCM-41 to give the target compound (**4**). The third high significance of MCM-41 is its easy separation by filtration and no additional work up procedure like neutralization of strong acid or

Table 2
Synthesis of thioamide[a]

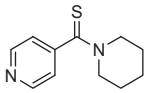
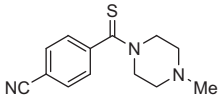
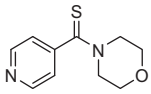
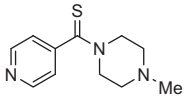
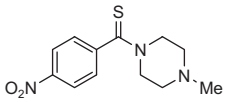
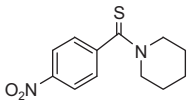
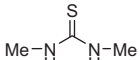
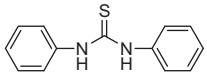
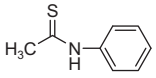
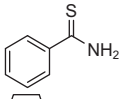
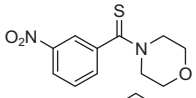
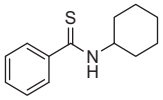
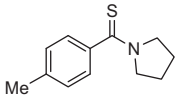
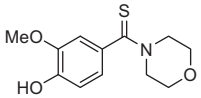
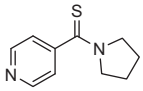
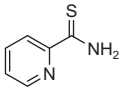
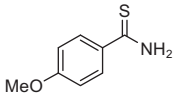
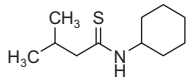
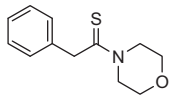
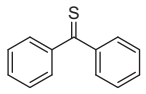
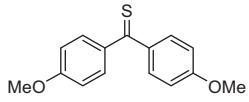
Entry	Product	Time (h)	Yield[b] (%)	Ref.
4a		9	89	–
4b		9	73	–
4c		8	81	–
4d		12	71	–
4e		8	76	–
4f		7	89	1j
4g		14	68	1l
4h		15	65	1m
4i		8	70	1k
4j		8	89	1k
4k		8	75	5
4l		7	82	1j
4m		13	72	1j
4n		10	79	1j
4o		11	73	1j
4p		9	83	–
4q		9	81	5
4r		11	78	1n

Table 2 (*continued*)

Entry	Product	Time (h)	Yield[b] (%)	Ref.
4s		7	61	1n
4t		7	89	1o
4u		10	82	5
4v		12	77	5

[a] Reagents and condition: Different corresponding amides (1 mmol), rhodanine (1.2 mmol), morpholine (1.2 mmol), 40 mg MCM41 aqueous ethanol (2 + 2 ml), different time, reflux at 80–90 °C.
[b] Isolated yields.

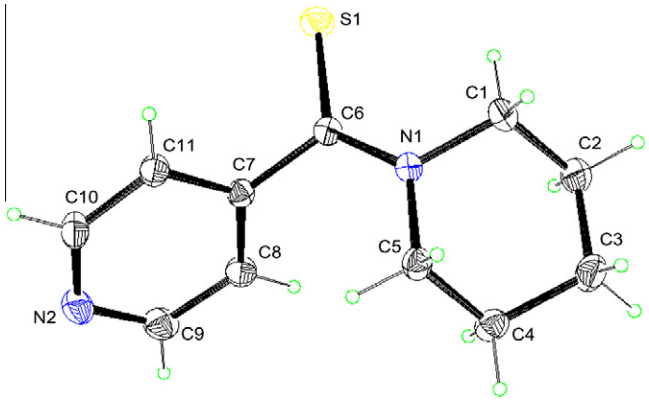
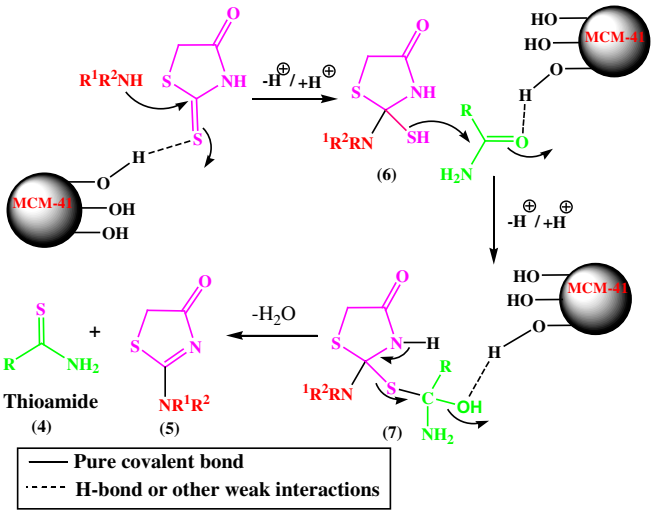
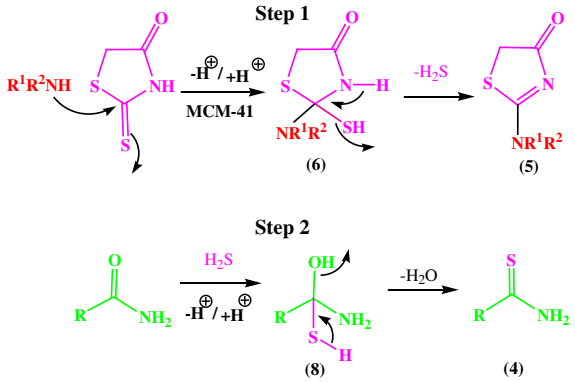


Figure 2. ORTEP diagram of **4a** (CCDC 914935).



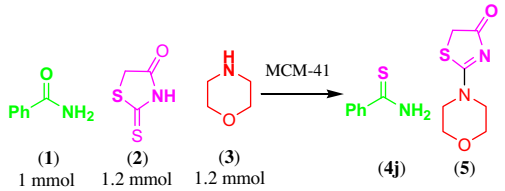
Scheme 2. Plausible mechanism for thioamide formation.

bases is required. Ultimately the reaction is very clean with very high isolated yield. It is also worth mentioning that after transferring sulfur to amide rhodanine is converted into 2-aminothiazolidinone (**5**). The thiazolidinone nucleus is known as wonder nucleus because it gives out different derivatives with all different types of



Scheme 3. Another possibility leading to thioamide (**4**).

Table 3
Optimization of sulfur transferring agent



Entry	Sulfur sources	Conversion[b] (%)	Yield[c] (%)
1	Rhodanine	95	89
2	P_4S_{10}	93	71
3	Na_2S	25	15
4	$(NH_4)_2S$	30	22
5	NaHS	29	20
6	$PSCl_3$	76	50
7	CS_2	55	41

[a]Reagents and condition: Benzamide (1 mmol), different sulfur sources (1.2 mmol), 40 mg MCM-41, aqueous-ethanol (2 + 2 ml), 80–90 °C, 8 h reflux.
[b] Percentage was calculated from ^{1}H NMR spectra (300 MHz).
[c] Isolated yields.

biological activities.[33] Thiazolidin-4-one ring systems are of considerable interest as they are a core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities.[34a–e] 2-Imino-thiazolidin-4-ones have been found to have potent anti-inflammatory,[35a–c] antiviral activities[35a,d] and antifungal activity.[34b] Therefore, in our case the by product 2-aminothiazolidinone (**5**) is also a biologically beneficial compound and therefore does not cause any detrimental effect to the environment rendering the transformation green.

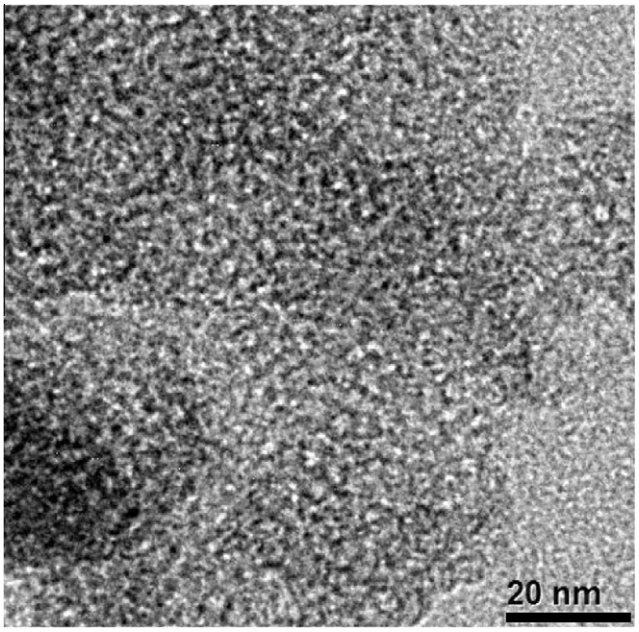


Figure 4. A representative HRTEM image of MCM-41.

Another possibility might be the secondary amines first attack rhodanine expelling H_2S as shown in step 1 in Scheme 3. Then a concomitant attack of H_2S on amide and subsequent loss of water might be proposed. If it would be so then a large amount of H_2S would be released in the environment and a large excess of rhodanine would be required. Since the present reaction was not carried out in a sealed vessel and only a stoichiometric amount of (1.0 equiv) rhodanine could afford as high as 74% thiomide (**4j**), it might be proposed that loss of H_2S in the environment is largely prevented. Therefore, the expulsion of H_2S is not the valid proposition rather the attack of –SH of intermediate (**6**) is a more acceptable proposed mechanism.

We were also interested to know whether the reaction is possible with H_2S gas or not. Therefore, when benzamide was heated at 80–90 °C in the presence of an equivalent amount of Na_2S which in turn produces H_2S with water afforded only 15% conversion to thioamide and a large amount of H_2S was released into environment (Table 3). Other sulfur transferring agents were also tested for this transformation; however rhodanine/amine system was superior in terms of cleaner reaction, higher isolated yields and environment compatibility.

Effect of different secondary amines on the yield of thioamide was also studied. It was observed that all the cyclic secondary amines afforded more or less same yields of **4j**, albeit the reaction

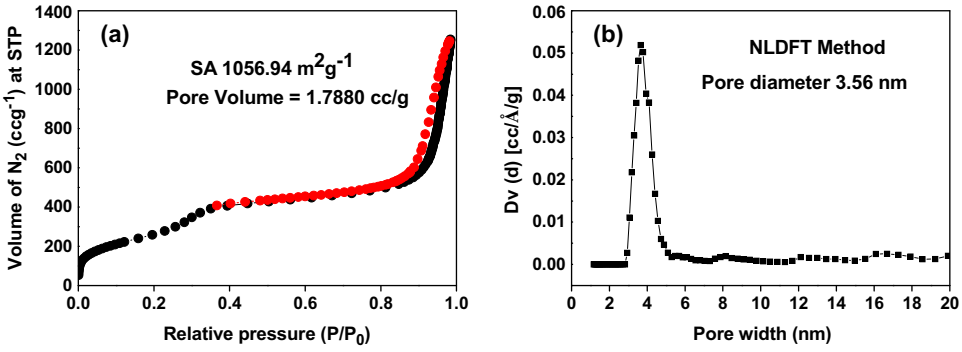


Figure 3. (a) N_2 sorption isotherm and (b) NLDFT pore size distribution of MCM-41.

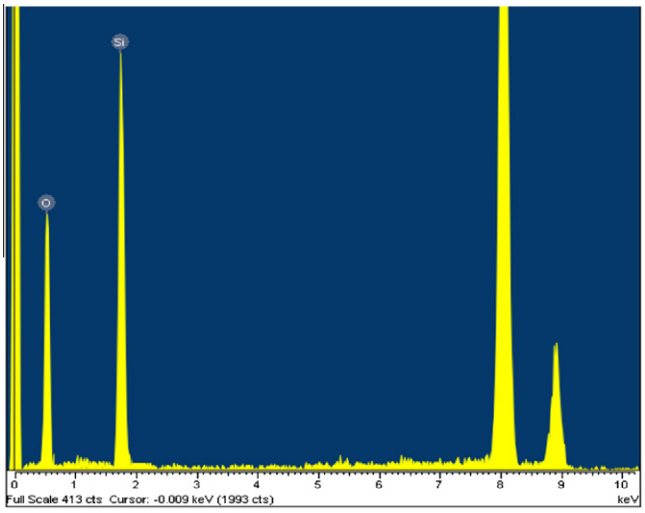


Figure 5. EDS analysis of PSNP.

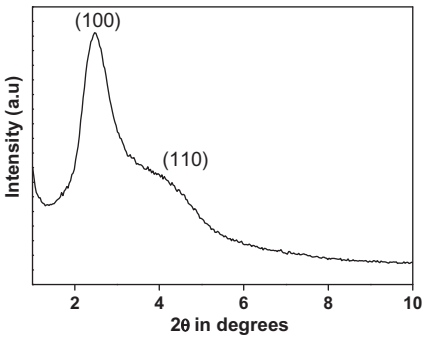


Figure 7. Small angel XRD pattern of MCM-41.

was successful with dimethyl and diethyl amine in very poor yield. Diallyl amine and the aromatic primary amines were totally unproductive. Considerably better yield was obtained with cyclohexyl amine. Therefore cyclic secondary amines were the obvious choice and thus we selected morpholine as an effective additive with rhodanine.

N_2 adsorption isotherm of the sample is recorded. The irreversible type IV adsorption isotherms of MCM-41 with H1 hysteresis loop defined by IUPAC are observed, that is a typical feature of mesoporous materials (Fig. 3, panel a).[36,37]

The Brunnauer–Emmett–Teller surface area of the material obtained by using N_2 adsorption–desorption isotherm was found out to be quite high 1057 $m^2\,g^{-1}$. Pore volume is also very high (1.79 cc g^{-1}). Pore size distribution (PSD) plot employing the non local density functional theory (NLDFT) suggested a narrow distribution with peak pore dimension of ca. 3.56 nm (Panel b). Sharp increase in N_2 uptake at high P/P_0 suggested the presence of interparticle mesopores.

TEM image analysis of the catalyst revealed that the MCM-41 material is composed of uniform ca. 25–30 nm size mostly spherical particles. HRTEM image shows an ordered arrangement of mesopores. Dimension of the pores is of ca. 3.2 nm (Fig. 4).

The chemical characterization for the MCM-41 was carried out by EDS analysis. The results of chemical analysis revealed that four elements –C, O, Si and Cu, existed in MCM-41 (Fig. 5). C and Cu peaks come from the carbon coated copper grid used for TEM and EDS analyses. EDS chemical analysis confirmed that the expected MCM-41 silica have successfully developed in this study.[38]

The 29Si MAS NMR spectral pattern for MCM-41 is shown in Figure 6, panel a. This pattern is quite broad like amorphous mesoporous silica. Three major peaks in this sample at −100.5, −103.0 and −113.9 ppm were observed. These peaks have been assigned to tetrahedral Q^2, Q^3 and Q^4 silica species, respectively where $Q^n = Si(OSi)_n(OH)_{4-n}$, $n = 2–4$. High Q^4 percentage indicated highly condensed network.[39] Such a high Q^4 concentration is of paramount importance for the catalytic activity of silica based catalyst, since reduction of surface silanols introduces high hydrophobicity (and thus more affinity towards organic substrates).[39]

The chemical structure of MCM-41 was studied using FT-IR spectroscopy (Fig. 6, panel b). In the IR spectra of the MCM-41 a strong and broad band in the range of 3500–3400 cm^{-1} corresponds to the hydrogen bonded Si–OH groups and adsorbed water, another broad band at 1638 cm^{-1} is also due to O–H vibration of adsorbed water.[29] The sharp features around 1092 cm^{-1} and the absorption peak at 467 cm^{-1} are assigned to asymmetric stretching and bending vibration of Si–O–Si. The observed results agree with previously published results in the literatures[29] and this confirmed the similarity in structural characteristics of the developed MCM-41 by the present method.

Characterization of MCM-41 with X-ray diffraction yields a diffractogram with a limited number of reflections, all situated at low angles. The MCM-41 material is highly ordered; showing two strong diffractions for the 100, 110 planes at 2θ equal to 2.5°, 4.3° corresponding to 3D-hexagonal mesophase (Fig. 7).[39,40] The reflection for 200 plane is not well resolved. These sharp signals indicated the long-range order of the uniform hexagonal mesoporous structure, which is the extraordinary characteristic of MCM-41 present in this present sample.

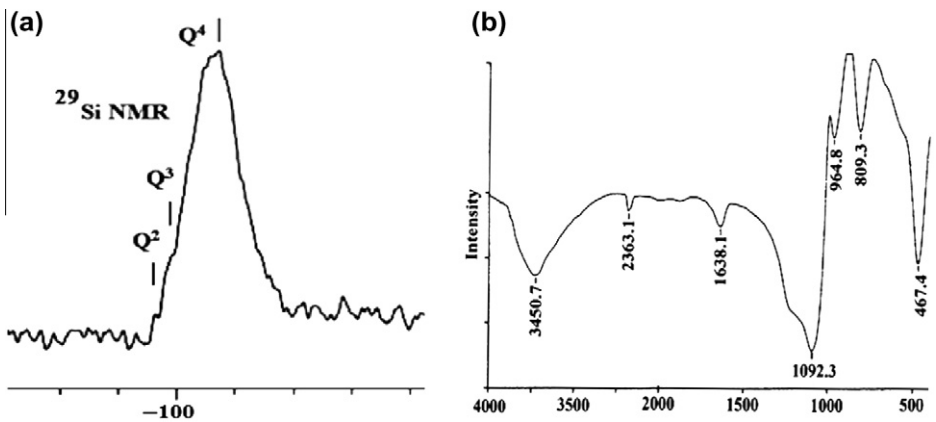


Figure 6. (a) 29 Si MAS NMR spectra and (b) IR analysis of MCM-41.

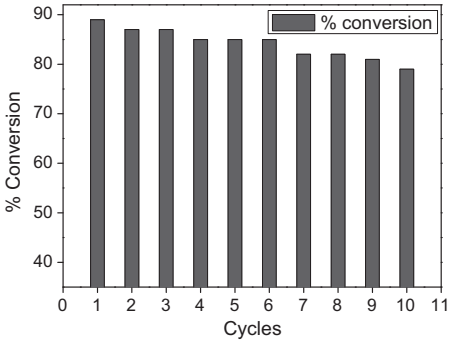


Figure 8. Recycling of MCM-41 catalyst for the reaction forming **4a**.

The reactions were carried out using different amounts of the catalyst and the optimum amount (40 mg) has been determined (optimization table is given in Supplementary data) Determination of this optimum amount to achieve maximum yield was very essential to establish the efficacy and broaden the applicability of the proposed process. For this purpose the reaction forming **4j** was chosen as a test reaction.

In the presence of MCM-41 (preheated at 100 °C for 4 h) the reaction between benzamide, rhodanine and morpholine occurred with 89% yield of **4j**. The same reaction in the presence of MCM-41 after having it exposed to ambient atmosphere for 10 days produced a similar observation. Obviously, there was no deteriorating effect of heat, aerial oxygen or moisture towards activity of the catalyst which also provided evidence that the catalyst had the potential of efficient recycling. The recycled catalyst could be used at least ten times with almost same efficiency as that of the first run without any further treatment (Fig. 8). Detailed characterization of the catalyst after 5th run showed that it was unaffected under the condition of the reaction. The XRD pattern of the recovered catalyst showed sharp peaks at 2.6° and 4.4° corresponding to 3D-hexagonal mesophase indicating that the mesoporous structure of MCM-41 still remained intact after recycling.

It is the first report of the use of rhodanine as the potential thionating agent for amide and MCM-41 is being used for thionation purpose also for the first time. Moreover, the entire process was highly atom-efficient. So the present protocol minimizes the dispersal of the harmful chemicals in the environment and maximizes the use of renewable resources. In this light, this highly efficient catalytic process[41] can also be considered as a green technology. The unprecedented catalytic performance demonstrated by MCM-41 holds a significant promise for the achievement of novel catalyst systems. The new catalytic procedures for the thionation of amide fulfil the triple bottom-line philosophy of green chemistry and are important addition to the toolbox of medicinal chemists. The spectral and analytical data[42] of one representative compound (**4a**) is provided in the main manuscript.

Acknowledgments

We acknowledge UGC for financial support (F. No. 37-398/2009 (S.R.) dated 11-01-2010), CSIR for fellowship (S.R.) and NMR Research Centre, IISc, Bangalore-560012 for the solid state Si-29 MAS NMR spectrum.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.02.045.

References and notes

1. Orchard, A.; Schamerhorn, G. A.; Calitree, B. D.; Sawada, G. A.; Loo, T. W.; Claire Bartlett, M.; Clarke, D. M.; Detty, M. R. *Bioorg. Med. Chem.* **2012**, *20*, 4290; (b) Gottesman, M. M.; Fojo, T.; Bates, S. E. *Nat. Rev. Cancer* **2002**, *2*, 48; (c) Szakacs, G.; Paterson, J. K.; Ludwig, J. A.; Booth-Genthe, C.; Gottesman, M. M. *Nat. Rev. Drug Disc.* **2006**, *5*, 219; (d) Gannon, M. K.; Holt, J. J.; Bennett, S. M.; Wetzel, B. R.; Loo, T. W.; Bartlett, M. C.; Clarke, D. M.; Sawada, G. A.; Higgins, J. W.; Tombline, G.; Raub, T. J.; Detty, M. R. *J. Med. Chem.* **2009**, *52*, 3328; (e) Wang, F.; Langley, R.; Gulten, G.; Dover, L. G.; Besra, G. S.; Jacobs, W. R., Jr.; Sacchettini, J. C. *J. Exp. Med.* **2007**, *204*, 73; (f) Fajardo, T. T.; Guinto, R. S.; Cellona, R. V.; Abalos, R. M.; Dela Cruz, E. C.; Gelber, R. H. *Am. J. Trop. Med. Hyg.* **2006**, *74*, 457; (g) Yajko, D. M.; Nassos, P. S.; Hadley, W. K. *Antimicrob. Agents Chemother.* **1987**, *31*, 117; (h) Crofton, J.; Chaulet, P.; Maher, D.; Grosset, J.; Harris, W.; Norman, H.; Iseman, M.; Watt, B. *Guidelines for the Management of Multidrug-Resistant Tuberculosis*; World Health Organization: Geneva, Switzerland, 1997; (i) Nishida, C. R.; Ortiz de Montellano, P. R. *Chem. Biol. Interact.* **2011**, *192*, 21; (j) Zbruyev, O. I.; Stiasni, N.; Kappe, C. O. *J. Comb. Chem.* **2003**, *5*, 145; (k) Kaleta, Z.; Makowski, B. T.; Soos, T.; Dembinski, R. *Org. Lett.* **2006**, *8*, 1625; (l) Abai, M.; Holbrey, J. D.; Rogersz, R. D.; Srinivasan, G. *New J. Chem.* **2010**, *34*, 1981; (m) Bowmaker, G. A.; Chaichit, N.; Hanna, J. V.; Pakawatchai, C.; Skeltone, B. W.; White, A. H. *Dalton Trans.* **2009**, 8308; (n) Pathare, S. P.; Chaudhari, P. S.; Akamanchi, K. G. *Appl. Catal., A: Gen.* **2012**, *425–426*, 125; (o) Nguyen, T. B.; Ermolenko, L.; Al-Mourabit, A. *Org. Lett.* **2012**, *14*, 4274; (p) Wipf, P.; Venkatraman, S. *J. Org. Chem.* **1996**, *61*, 8004; (q) Attanasi, O. A.; Berretta, S.; Crescentini, L. D.; Favi, G.; Filippone, P.; Giorgi, G.; Lillini, S.; Mantellini, F. *Tetrahedron Lett.* **2007**, *48*, 2449; (r) Attanasi, O. A.; Crescentini, L. D.; Favi, G.; Filippone, P.; Giorgi, G.; Mantellini, F.; Perrulli, F. R.; Spinelli, D. *Tetrahedron Lett.* **2008**, *49*, 3837.
2. Padwa, A.; Beall, L. S.; Heidelbaugh, T. M.; Bing, L.; Sheehan, S. M. *J. Org. Chem.* **2000**, *65*, 2684.
3. McManus, S. P.; Lee, K. Y.; Pittman, C. U. *J. Org. Chem.* **1974**, *39*, 3041.
4. (a) Jagodzinski, T. S. *Chem. Rev.* **2003**, *103*, 197; (b) Prokopcova, H.; Kappe, C. O. *J. Org. Chem.* **2007**, *72*, 4440.
5. Pathak, U.; Pandey, L. K.; Tank, R. *J. Org. Chem.* **2008**, *73*, 2890.
6. (a) Jesberger, M.; Davis, T. P.; Barner, L. *Synthesis* **2003**, 1929; (b) Cava, M. P.; Levinson, M. I. *Tetrahedron* **1985**, *41*, 5061.
7. (a) Hurd, R. N.; DeLaMater, G. *Chem. Rev.* **1961**, *61*, 45; (b) Brillon, D. *Sulfur Rep.* **1992**, *12*, 297.
8. (a) Asquith, R. S.; Hammick, D. Ll; Williams, P. L. *J. Chem. Soc.* **1948**, 1181; (b) Fournier, C.; Paquer, D.; Vazeux, M. *Bull. Soc. Chim. Fr.* **1975**, 2753.
9. Zong, Z.-M.; Peng, Y.-L.; Liu, Z.-G.; Zhou, S.-L.; Wu, L.; Wang, X.-H.; Wei, X.-Y.; Lee, C. W. *Korean J. Chem. Eng.* **2003**, *20*, 235.
10. (a) Oae, S.; Nakanishi, A.; Tsujimoto, N. *Chem. Ind.* **1972**, 575; (b) Pedersen, B. S.; Lawesson, S. O. *Bull. Soc. Chim. Belg.* **1977**, *86*, 693.
11. Ishii, Y.; Hirabayashi, T.; Imaeda, H.; Ito, Jpn, K. Patent 4,0441, 1974; *Chem. Abstr.* **1975**, *82*, 156074f.
12. Bodine, J. J.; Kaloustian, M. K. *Synth. Commun.* **1982**, *12*, 787.
13. Smith, D. C.; Lee, S. W.; Fuchs, P. L. *J. Org. Chem.* **1994**, *59*, 348.
14. (a) Pedersen, B. S.; Scheibye, S.; Nilsson, N. H.; Lawesson, S. O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 223; (b) Yang, C. O.; Rotstein, D. M.; Labadie, S. S.; Walker, K. A. M. *Synlett* **1995**, 655.
15. Charette, A. B.; Grenon, M. *J. Org. Chem.* **2003**, *68*, 5792.
16. (a) Dean, F. M.; Goodchild, J.; Hill, A. W. *J. Chem. Soc.* **1969**, 2192; (b) Dean, F. M.; Goodchild, J.; Hill, A. W.; Moore, S.; Zahman, A. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1335.
17. Degl'Innocenti, A.; Capperucci, A.; Castagnoli, G.; Malesci, I. *Synlett* **2005**, 1965.
18. Leadbeater, N. E.; Marco, M. *Chem. Rev.* **2002**, *102*, 3217.
19. Rafiee, E.; Eavani, S. *Green Chem.* **2011**, *13*, 2116.
20. Lee, C. L.; Sim, M. M. *Tetrahedron Lett.* **2000**, *41*, 5729.
21. (a) Troutman, H. D.; Long, L. M. *J. Am. Chem. Soc.* **1948**, *70*, 3436; (b) Mishra, S.; Srivastava, S. K.; Srivastava, S. D. *Indian J. Chem., Sect. B* **1997**, *36*, 826.
22. Foye, W. O.; Tovivich, P. J. *Pharm. Sci.* **1977**, *66*, 1607.
23. Sudo, K.; Matsumoto, Y.; Matsushima, M.; Fujiwara, M.; Konno, K.; Shimotohno, K.; Shigeta, S.; Yokota, T. *Biochem. Biophy. Res. Commun.* **1997**, *238*, 643.
24. Ohishi, Y.; Mukai, T.; Nagahara, M.; Yajima, M.; Kajikawa, N.; Miyahara, K.; Takano, T. *Chem. Pharm. Bull.* **1990**, *38*, 1911.
25. (a) Pulici, M.; Quartieri, F. *Tetrahedron Lett.* **2005**, *46*, 2387; (b) Kandeel, K. A.; Youssef, A. M.; El-Bestawy, H. M.; Omar, M. T. *J. Chem. Res., Synop.* **2003**, *11*, 682.
26. Bourahla, K.; Derdour, A.; Rahmouni, M.; Carreaux, F.; Bazureau, J. P. *Tetrahedron Lett.* **2007**, *48*, 5785.
27. Anderluh, M.; Jukic, M.; Petric, R. *Tetrahedron* **2009**, *65*, 344.
28. Mukhopadhyay, C.; Ray, S. *Tetrahedron Lett.* **2011**, *52*, 6431.
29. Mukhopadhyay, C.; Ray, S. *Tetrahedron* **2011**, *67*, 7936.
30. Mukhopadhyay, C.; Ray, S. *Catal. Commun.* **2011**, *12*, 1496.
31. Das, P.; Butcher, R. J.; Mukhopadhyay, C. *Green Chem.* **2012**, *14*, 1376.
32. Mukhopadhyay, C.; Rana, S. *Catal. Commun.* **2009**, *11*, 285.
33. Abhinit, M.; Ghodke, M.; Pratima, N. A. *Int. J. Pharm. Pharm. Sci.* **2009**, *1*, 47.
34. (a) Mulwad, V. V.; Mir, A. A.; Parmar, H. T. *Indian J. Chem.* **2009**, *48B*, 137; (b) Chavan, A. A.; Pai, N. R. *Arkivoc* **2007**, *xvi*, 148; (c) Vigorita, M. G.; Ottana, R.; Monforte, F.; Maccari, R.; Trovato, A.; Monforte, M. T.; Taviano, M. F. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2791.

35. (a) Blanchet, J.; Zhu, J. *Tetrahedron Lett.* **2004**, *45*, 4449; (b) Unangst, P. C.; Connor, D. T.; Cetenko, W. A.; Sorenson, R. J.; Kostlan, C. R.; Sircar, J. C.; Wright, C. D.; Schrier, D. J.; Dyer, R. D. *J. Med. Chem.* **1994**, *37*, 322; (c) Johnson, A. R.; Marletta, M. A.; Dyer, R. D. *Biochemistry* **2001**, *40*, 7736; (d) Harnden, M. R.; Bailey, S.; Boyd, M. R.; Taylor, D. R.; Wright, N. D. *J. Med. Chem.* **1978**, *21*, 82–87.
36. (a) Chandra, D.; Jena, B. K.; Raj, C. R.; Bhaumik, A. *Chem. Mater.* **2007**, *19*, 6290; (b) Modak, A.; Mondal, J.; Aswal, V. K.; Bhaumik, A. *J. Mater. Chem.* **2010**, *20*, 8099.
37. Garcia-Cuello, V. S.; Giraldo, L.; Moreno-Piraján, J. C. *Catal. Lett.* **2011**, *141*, 1659.
38. Nair, R.; Yoshida, Y.; Maekawa, T.; Sakthi Kumar, D. *Prog. Nat. Sci.: Mater. Int.* **2012**, *22*, 193.
39. Samanta, S.; Laha, S. C.; Mal, N. K.; Bhaumik, A. *J. Mol. Catal. A: Chem.* **2004**, *222*, 235.
40. (a) Soni, K.; Rana, B. S.; Sinha, A. K.; Bhaumik, A.; Nandi, M.; Kumar, M.; Dhar, G. M. *Appl. Catal., B: Environ.* **2009**, *90*, 55; (b) Samanta, S.; Mal, N. K.; Bhaumik, A. *J. Mol. Catal. A: Chem.* **2005**, *236*, 7.
41. *General synthetic procedure for preparation of thioamide (**4**)*: In a typical reaction a solution of amide (1 mmol), rhodanine (1.2 mmol) and Morpholine (1.2 mmol) in EtOH/water (2 + 2 ml) were refluxed at 80–90 °C till completion using 40 mg of MCM-41 catalyst. The completion of the reaction was indicated by the disappearance of the starting material in thin layer chromatography. After completion of the reaction the solvent was evaporated in a rotary evaporator and the crude product was taken in dichloromethane and filtered to separate the products as filtrate from the catalyst (residue). Then the crude product was purified by silica gel column chromatography where the compound (**5**) came out from the column with 25%EtOAc/75% petroleum ether, but thioamide (**4**) came out with 65%EtOAc/35% petroleum ether making their separation easy. The thioamides (**4**) were characterized by IR, ^{1}H NMR, ^{13}C NMR, CHN and X-ray single crystal analysis.
42. *(Piperidin-1-yl)(pyridin-4-yl)methanethione (**4a**)*: Yellow solid, mp 160–162 °C (DCM/EtOAc 1:1); IR ν_{max} (KBr) 3435, 3013, 2938, 2859, 1586, 1494, 1448, 1286 and 1246 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.54 (2H, d, J = 4.5 Hz), 7.19 (2H, d, J = 4.8 Hz), 4.22 (2H, br s), 3.39 (2H, t, J = 5.1 Hz), 1.64 (4H, br s), 1.48 (2H, s); ^{13}C NMR (75 MHz, DMSO-d_6) δ: 195.3, 150.4, 149.8, 119.6, 53.1, 49.9, 26.7, 25.2, 23.8; Anal. Calcd for $C_{11}H_{14}N_2S$: C, 64.04; H, 6.84; N, 13.58%. Found C, 64.24; H, 6.91; N, 13.41%.