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MCM-41-TBD as a new, efficient, supported heterogeneous catalyst for the synthesis of thioureas

Roberto Ballini,[a,*] Giovanna Bosica,[a] Dennis Fiorini,[a] Raimondo Maggi,[b,*] Paolo Righi,[c]
Giovanni Sartori[b] and Raffaella Sartorio[b]

[a] *Dipartimento di Scienze Chimiche dell'Università, Via S. Agostino 1, 62032 Camerino (MC), Italy*
[b] *Dipartimento di Chimica Organica e Industriale dell'Università, Parco Area delle Scienze 17A, 43100 Parma, Italy*
[c] *Dipartimento di Chimica Organica 'A. Mangini' dell'Università, V. le Risorgimento 4, 40136 Bologna, Italy*

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Abstract—The preparation of thioureas, by reaction of carbon disulfide with primary amines, can be efficiently catalyzed, under heterogeneous conditions, by MCM-TBD as a new and reusable catalyst. © 2002 Elsevier Science Ltd. All rights reserved.

The manufacture of fine chemicals for preparation of pharmaceuticals, agrochemicals and new materials represents an ever expanding area of interest. Unfortunately, as clearly stated in recent reviews and reports, the classical synthetic routes to fine chemicals and pharmaceuticals are responsible for the production of large amounts of pollutant by-products.[1] This drawback can be partly overcome by replacing stoichiometric processes with cleaner catalytic alternatives.[2]

Moreover, a further step toward environmentally friendly synthetic routes is represented by the application of solid and reusable catalysts[3] and by the development of solventless processes.[4]

The synergic combination of these strategies with the atom-economy approach opens new important perspectives for the modern development of eco-efficient large-scale synthetic processes.[5]

One particular promising area of research which can combine the advantages of the homogeneous catalysis with the best properties of the heterogeneous materials is the immobilization of catalytically active organic compounds on inorganic solid supports, resulting in the production of hybrid organic–inorganic catalysts, which are safely handled and stored and can be easily recovered by filtration at the end of the reaction and reused for many cycles.[6]

Different heterogeneous basic catalysts were thus prepared and utilized to promote fundamental reactions of synthetic interest such as aldol condensation,[7] epoxidation[8] and glyceride formation.[9] In this context Jacobs et al. recently reported the preparation of a novel, heterogeneous and strongly basic catalyst, in which 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) is covalently bonded to the surface of the mesoporous MCM-41 silica. This hybrid organic–inorganic material was claimed to efficiently promote some fundamental base-catalysed C–C forming reactions such as the Knoevenagel condensation and the Michael addition.[10]

In the course of our continuing investigation on using heterogeneous catalysts for fine chemicals preparation, we found that the above hybrid organic–inorganic material here called MCM-41-TBD efficiently catalyses the reaction of amines with carbon sulfide affording *N*,*N*′-disubstituted thioureas in good yield and selectivity. This reaction was examined since, over the last few years, thiourea moiety has been of interest as a structural modification to molecules designed as receptor antagonists, as natural product mimics, or as synthetic intermediates to amides or guanidines.[11] The hybrid organic–inorganic material MCM-41-TBD was selected as the base catalyst in the present study being easily synthesised from commercially available reagents by using simple experimental methodologies. Here we show results of a detailed study of the reaction.

TBD is a strong guanidine base (p$K_b = 25$)[12] widely utilised as acid scavenger and homogeneous catalyst, i.e. for transesterification reactions.

Keywords: thioureas; supported bases; heterogeneous catalysis; 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD).

* Corresponding authors. Fax: +39-0737-402297; e-mail: roberto.ballini@unicam.it

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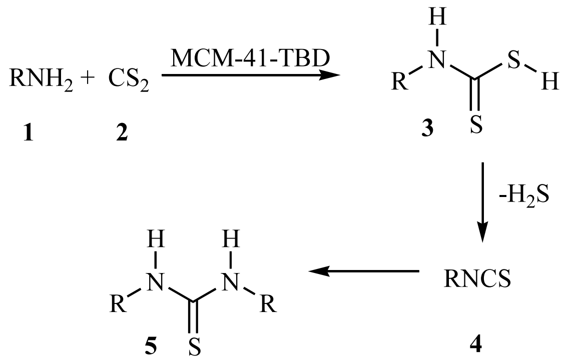
The heterogeneous catalyst MCM-41-TBD was prepared by slightly modifying the methodology described by Jacobs et al.[10] Thus, TBD was previously linked to 3-trimethoxysilylpropoxymethyloxirane by nucleophilic addition to the epoxide moiety. The resulting compound was then anchored to the *meso*-porous MCM-41 silica[13] by reaction of the trimethoxysilyl group with the surface silanols. The loading of the supported TBD was 0.97 mmol/g.

In a preliminary experiment the reaction of benzylamine selected as the model reagent with an excess of CS_2 (Scheme 1, R = Bn) was carried out in the presence of MCM-41-TBD catalyst (molar ratio benzylamine/TBD = 10, determined on the basis of loading value). Thus, a mixture of **1a** (3 mmol, 0.32 g), carbon disulfide **2** (50 mmol, 3.8 g) utilised as solvent reagent and MCM-41-TBD (0.3 g) was reacted in a small autoclave equipped with a magnetic stirring, at 90°C. After 15 h, the thiourea **5a** was easily recovered in 68% yield by removing the excess of CS_2 (N_2), dissolving the final product in methanol, removing the catalyst by filtration, and adding water until the precipitation was complete (Scheme 1).

Surprisingly the commercially available cross-linked polystyrene-bound TBD, commonly utilised as an acid scavenger, was much less active as basic catalyst in the same model reaction being **5a** obtained in 25% yield. This result is probably due to the low polarity of CS_2 [$E_T(30) = 32.8$ Kcal mol^{-1}][14] which limits the swelling extent of the material and consequently hampers the access of reactants to the active sites.



Scheme 1.

Table 1.

Entry	R	**5** yield [select.] (%)
a	PhCH	68 [94]
b	$CH_3(CH_2)_4$	84 [95]
c	$CH_3(CH_2)_7$	91 [93]
d	*c*-C_6H_{11}	90 [98]
e	Ph	72 [98]
f	4-$CH_3OC_6H_4$	84 [97]
g	4-ClC_6H_4	57 [96]
h	(*R*)-Ph(CH_3)CH	91 [95]
i	$CH_3CH_2NH(CH_2)_2$	72 [91]

The procedure could be efficiently applied to both aromatic and aliphatic primary amines. Secondary amines such as, for example, *N*-methylaniline and dibutylamine, were quantitatively recovered unchanged from the final reaction mixture because of the prevented production of the isothiocyanate intermediate **4**. However, when the secondary amine contains an additional primary amino group, the cyclic thiourea could be obtained in 72% yield (Table 1, entry i).

Moreover, the use of this heterogeneous catalyst makes product isolation easier and gives clean reaction.

Finally, we faced the problem of the catalyst recycling: at the end of the model reaction with amine **1a** the MCM-41-TBD was filtered on Büchner funnel, washed with THF, dried under vacuum and reused. The catalyst could be utilized with similar results for two further cycles (reaction: 68%; first recycle: 66%; second recycle: 63%).

In conclusion, we have reported the use of a solid base easily prepared by anchoring the guanidine TBD to mesoporous silica MCM-41 as efficient and reusable catalyst for the preparation of thioureas from primary amines and carbon disulfide.

Preparation of MCM-41-TBD is as follows: TBD 87.2 mmol, 1 g) was added to a solution of 3-trimethoxysilylpropoxymethyloxirane (5.9 mmol, 1.3 ml) in dry DMF (10 ml) and the stirring was continued for 15 h at rt. Then, the solution was poured into a flask containing dry toluene (50 ml) and MCM-41 previously heated at 300°C for 15 h (3.5 g). The resulting slurry was refluxed for 1 h and then the produced methanol was distilled out. This operation was repeated three times. After cooling, the so prepared supported catalyst was filtered on Büchner and washed with toluene (100 ml), methylene chloride (200 ml) and methanol (100 ml) and then treated for 24 h in a Soxhlet apparatus using a 1/1 diethyl ether/methylene chloride mixture. Finally the solid was dried under vacuum for 2 h.

General procedure for the preparation of thioureas (3) is as follow: the selected amine (3 mmol), CS_2 (50 mmol, 3.8 g, 3 ml), and MCM-TBD (0.3 g) were heated in a small autoclave at 90°C. After 15 h the reaction mixture was cooled to rt, the excess of carbon disulfide was then removed by a stream of nitrogen, and hot methanol (50 ml) was added in order to dissolve the crude product, so that the catalyst can be removed by filtration. After cooling the thiourea was crystallized by addition of water. The pure product was isolated by filtration and, when necessary, recrystallised from methanol.

All the products gave mps and spectral data consistent with the reported ones.

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