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Remarkable acceleration of cyanosilylation by the mesoporous Al-MCM-41 catalyst†

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The presence of the heterogeneous mesoporous Al-MCM-41 catalyst remarkably accelerated the cyanosilylation of various aldehydes and ketones with trialkylsilyl cyanide, giving the corresponding cyanohydrin silyl ethers in quantitative yields under mild reaction conditions.

The development of efficient heterogeneous catalysts for the production of fine and speciality chemicals has been a very active area of research because heterogeneous catalysts have the advantage in terms of catalyst separation, handling, and recycling.[1] Solid catalysts also allow the design of continuous flow processes. Ordered mesoporous materials are very attractive as solid catalysts for fine chemicals synthesis often involving bulky reactants and products due to their large pore openings and high surface areas.[2] For instance, aluminium substituted mesoporous silicas show acid catalysis for numerous fine chemicals syntheses, including the aldol reaction,[3] Friedel–Crafts reaction,[4] Diels–Alder reaction,[5] acetalization,[6] and esterification.[7] However, the acidic properties of mesoporous aluminosilicates are close to that of conventional amorphous silica–alumina and there are few examples of the reactions in which mesoporous aluminosilicates exhibit much higher catalytic activities than amorphous silica–alumina.[8] Herein, we report the great advantage of Al-MCM-41 over amorphous silica–alumina or zeolites as a catalyst for cyanosilylation.

The cyanosilylation of carbonyl compounds with trialkylsilyl cyanide is an important reaction in organic synthesis for producing cyanohydrin derivatives, which can be transformed into a variety of building blocks, including α-hydroxy acids, α-hydroxy ketones, and β-amino alcohols.[9] Lewis acids,[10] Lewis bases,[11] *N*-heterocyclic carbenes,[12] and organic or inorganic salts[13] homogeneously catalyze this reaction. Although several heterogeneous catalysts have been reported,[14] the catalytic activities are lower than homogeneous catalysts. Moreover, heterogeneous catalytic reactions suffer from substrate limitations; the yields of the cyanohydrin products from aliphatic aldehydes and ketones are unsatisfactory.

We initially used benzaldehyde as a model substrate to investigate the effect of mesoporous catalysts on the cyanosilylation with trimethylsilyl cyanide (TMSCN). Prior to the reaction, the catalysts were pretreated *in vacuo* at 120 °C for 1 h. Fig. 1 shows the progress of the reactions with time. When mesoporous aluminosilicate (Al-MCM-41, Si/Al = 20) was used as the catalyst, the reaction rapidly proceeded even at 0 °C to quantitatively yield the desired cyanohydrin trimethylsilyl ether in 5 min (Fig. 1; Table 1, entry 1). In contrast, aluminium-free mesoporous silica (MCM-41) and the prepared amorphous SiO_2–Al_2O_3 with the same Si/Al ratio as Al-MCM-41 barely catalyzed the reaction (Fig. 1; Table 1, entries 2 and 3). Furthermore, two types of commercially available amorphous SiO_2–Al_2O_3 (Si/Al = 5 and 2) were inactive (Table 1, entries 4 and 5).[15] These results indicate that both the ordered mesoporous structure and the presence of aluminium in silicates are indispensable for promoting the reaction. It is remarkable that Al-MCM-41 is much more active than amorphous SiO_2–Al_2O_3 in acid-catalyzed reactions. Note that the pseudo-first order rate constant of Al-MCM-41 normalized to the surface area is about two thousand times larger than that of SiO_2–Al_2O_3 (Si/Al = 20). Zeolite catalysts such as H-Y and H-ZSM-5 were ineffective for the reaction (Table 1, entries 6 and 7), possibly due to their small pore sizes. For comparison, Fig. 1 also includes the result of Et_3N, a good homogeneous catalyst for this reaction.[11a] The catalytic activity per weight of Al-MCM-41 was about 600 times higher than that of Et_3N (Table 1, entry

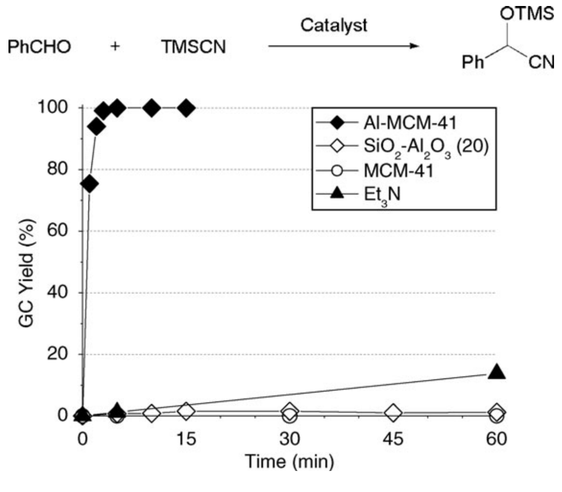

Fig. 1 Time course of cyanosilylation. Reaction conditions: benzaldehyde (1 mmol), TMSCN (5 mmol), catalyst (5 mg), CH_2Cl_2 (10 mL), 0 °C.

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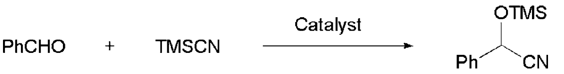
Table 1 Cyanosilylation of benzaldehyde with TMSCN by various catalysts[a]

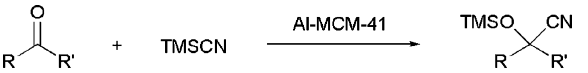


Entry	Catalyst[b]	Solvent	Time/min	Yield[c] (%)	k[d]/min^{-1}
1	Al-MCM-41	CH_2Cl_2	5	100	1.6
2	MCM-41	CH_2Cl_2	60	0	—
3	SiO_2–Al_2O_3 (20)	CH_2Cl_2	60	1	1.3×10^{-4}
4	SiO_2–Al_2O_3 (5)	CH_2Cl_2	60	2	1.7×10^{-4}
5	SiO_2–Al_2O_3 (2)	CH_2Cl_2	60	4	1.7×10^{-3}
6	H-Y	CH_2Cl_2	60	4	6.7×10^{-4}
7	H-ZSM-5	CH_2Cl_2	60	0	—
8	γ-Al_2O_3	CH_2Cl_2	60	10	1.5×10^{-3}
9	Et_3N[e]	CH_2Cl_2	60	14	2.7×10^{-3}
10	Al-MCM-41	Toluene	15	100	4.9×10^{-1}
11	Al-MCM-41	DMF	15	30	5.0×10^{-2}
12	Al-MCM-41	CH_3CN	15	3	2.3×10^{-3}
13	Al-MCM-41	THF	15	1	5.0×10^{-4}

[a] Reaction conditions: benzaldehyde (1 mmol), TMSCN (5 mmol), catalyst (5 mg), solvent (10 mL), 0 °C. [b] Figures in parentheses are the molar ratio of Si/Al. [c] Each yield was determined by GC using phenanthrene as an internal standard. [d] Pseudo-first order rate constant. [e] Et_3N (5 mg) corresponds to 5 mol%.

9). The rate of cyanosilylation catalyzed by Al-MCM-41 greatly depended on the type of solvent, but the most suitable solvent was CH_2Cl_2. Additionally, toluene was a good solvent, but a slightly longer reaction time was required (Table 1, entry 10). On the other hand, the reaction in polar solvents such as DMF[16] and CH_3CN was slow, and the reaction did not proceed in THF (Table 1, entries 11–13). A similar trend has been reported for the Sn-montmorillonite catalyzed cyanosilylation.[14a]

Table 2 Cyanosilylation of various carbonyl compounds with TMSCN catalyzed by Al-MCM-41[a]



Entry	Substrate	Time/min	Yield[b] (%)
1	PhCHO	1	100 (99)[c]
2[d]	PhCHO	1	96
3	4-MeC_6H_4CHO	1	100
4	2,4,6-$Me_3C_6H_2CHO$	1	99
5	4-$MeOC_6H_4CHO$	1	100
6	4-BrC_6H_4CHO	1	100
7	4-$CF_3C_6H_4CHO$	1	99
8	2-Naphthaldehyde	1	100
9	$PhCH_2CH_2CHO$	1	99
10	*c*-$C_6H_{11}CHO$	1	100
11	*t*-BuCHO	1	94
12	Acetophenone	5	90
13	Acetophenone	60	99 (98)[e]
14	Benzylacetone	5	100 (99)[e]
15	Cyclohexanone	5	100

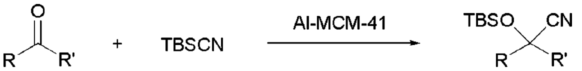
[a] Reaction conditions: substrate (1 mmol), TMSCN (1.2 mmol), Al-MCM-41 (5 mg), CH_2Cl_2 (2 mL), room temperature. [b] Each yield was determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. [c] Isolated yield of the corresponding cyanohydrin formed by desilylating the cyanohydrin trimethylsilyl ether *via* acidic hydrolysis. [d] Recovered catalyst was used. [e] Isolated yield after silica gel column chromatography.

The Al-MCM-41 catalyzed cyanosilylation smoothly proceeded using a slight excess (1.2 equiv.) of TMSCN at room temperature (Table 2, entry 1). After the run, the catalyst was thoroughly removed by filtration, and a new reaction was performed by adding benzaldehyde and TMSCN to the resulting filtrate. However, an increase in the yield was not observed, which indicates that Al-MCM-41 works as a heterogeneous catalyst. In addition, the recovered catalyst could be reused without a significant loss in the yield (Table 2, entry 2). The Al-MCM-41 catalyzed cyanosilylation was applicable to a wide range of carbonyl compounds. Aromatic aldehydes substituted with an electron-donating group or an electron-withdrawing group and aliphatic aldehydes were uniformly transformed into the corresponding cyanohydrin trimethylsilyl ether in quantitative yields and an extremely short reaction time (1 min) (Table 2, entries 3–11). Excellent yields for the desired adducts were obtained for sterically hindered aldehydes such as mesitaldehyde and pivalaldehyde (Table 2, entries 4 and 11). The Al-MCM-41 catalyst was also effective for the cyanosilylation of aromatic, aliphatic, and alicyclic ketones to yield the corresponding cyanohydrin silyl ether quantitatively, but a slightly longer reaction time was necessary (Table 2, entries 12–15). It is noteworthy that benzylacetone, a less reactive aliphatic ketone,[14b,14c] completely afforded the desired product in 5 min. Furthermore, we have found that the Al-MCM-41 catalyst is effective for the cyanosilylation with a bulky silyl cyanide like *tert*-butyldimethylsilyl cyanide (TBSCN) (Table 3). Although the reaction with TBSCN was slower compared to the reaction with TMSCN, the corresponding cyanohydrin TBS ethers were given in high yields.

Finally, we performed the continuous cyanosilylation of benzaldehyde with TMSCN using a fixed-bed flow reactor in order to demonstrate the merit of Al-MCM-41 as a heterogeneous catalyst. The desired cyanohydrin trimethylsilyl ether was constantly produced with yields larger than 98% for at least 24 h (Fig. 2). No significant changes in the structure of Al-MCM-41 were detected by XRD before and after the reaction, whereas the surface area and the pore volume had slightly decreased after the reaction. The total productivity of the experiment was equivalent to 120 gram per day per gram-catalyst.

In summary, we have demonstrated that Al-MCM-41 is a highly active heterogeneous catalyst for the cyanosilylation of carbonyl compounds. Using a very small amount of Al-MCM-41, various cyanohydrin silyl ethers are quantitatively and

Table 3 Cyanosilylation of various carbonyl compounds with TBSCN catalyzed by Al-MCM-41[a]



Entry	Substrate	Time/min	Yield[b] (%)
1	PhCHO	10	97
2	$PhCH_2CH_2CHO$	30	83
3	Benzylacetone	120	97

[a] Reaction conditions: substrate (1 mmol), TBSCN (1.2 mmol), Al-MCM-41 (5 mg), CH_2Cl_2 (2 mL), room temperature. (TBS = *t*-$BuMe_2Si$). [b] Isolated yield after silica gel chromatography.

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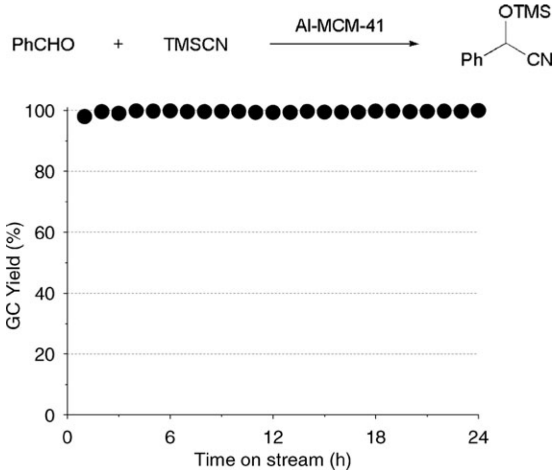

Fig. 2 Cyanohydrin trimethylsilyl ether yield during a continuous flow reaction. Reaction conditions: benzaldehyde (6.7 wt%) and TMSCN (1.05 equiv.) in CH_2Cl_2, Al-MCM-41 (100 mg, loaded in a 4 mm I.D. × 30 mm Pyrex glass tube), flow rate (3.8 g h^{-1}), room temperature.

quickly obtained from a wide range of aldehydes and ketones under mild reaction conditions. This report clearly exhibits the promising abilities of mesoporous aluminosilicates as catalysts in organic synthesis, especially for fine chemicals synthesis. The active sites over the Al-MCM-41 catalyst are presently unclear, but the effective combination of both the activation of carbonyl compounds by the acid sites arising from H/Al-MCM-41 and the activation of trialkylsilyl cyanide by the base sites possibly based on Na/Al-MCM-41 may be responsible for the excellent catalytic activity. Further studies to elucidate the acceleration mechanism of the Al-MCM-41 catalyst for cyanation are currently under way.

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Notes and references

1 (*a*) *Fine Chemicals Through Heterogeneous Catalysis*, ed. R. A. Sheldon and H. van Bekkum, Wiley-VCH, Weinheim, 2001; (*b*) *Special issue: Recoverable Catalysts and Reagents*, ed. J. A. Gladysz, *Chem. Rev.*, 2002, **102**, 3215; (*c*) A. Corma and H. Garcia, *Chem. Rev.*, 2003, **103**, 4307.

2 (*a*) A. Corma, *Chem. Rev.*, 1997, **97**, 2373; (*b*) D. T. On, D. Desplantier-Giscard, C. Danumah and S. Kaliaguine, *Appl. Catal., A*, 2003, **253**, 545; (*c*) A. Taguchi and F. Schüth, *Microporous Mesoporous Mater.*, 2005, **77**, 1.

3 M. J. Climent, A. Corma, H. Garcia, R. Guil-Lopez, S. Iborra and V. Fornés, *J. Catal.*, 2001, **197**, 385.

4 E. Armengol, M. L. Cano, A. Corma, H. García and M. T. Navarro, *J. Chem. Soc., Chem. Commun.*, 1995, 519.

5 (*a*) M. Onaka and R. Yamasaki, *Chem. Lett.*, 1998, **27**, 259; (*b*) T. Kugita, S. K. Jana, T. Owada, N. Hashimoto, M. Onaka and S. Namba, *Appl. Catal., A*, 2003, **245**, 353.

6 (*a*) B. R. Jermy and A. Pandurangan, *J. Mol. Catal. A: Chem.*, 2006, **256**, 184; (*b*) M. W. C. Robinson and A. E. Graham, *Tetrahedron Lett.*, 2007, **48**, 4247.

7 S. Ajaikumar and A. Pandurangan, *J. Mol. Catal. A: Chem.*, 2007, **266**, 1.

8 (*a*) R. Mokaya and W. Jones, *J. Catal.*, 1997, **172**, 211; (*b*) N. Katada, H. Fujinaga, Y. Nakamura, K. Okumura, K. Nishigaki and M. Niwa, *Catal. Lett.*, 2002, **80**, 47; (*c*) M. Onaka, N. Hashimoto, Y. Kitabata and R. Yamasaki, *Appl. Catal., A*, 2003, **241**, 307.

9 (*a*) R. J. H. Gregory, *Chem. Rev.*, 1999, **99**, 3649; (*b*) J.-M. Brunel and I. P. Holmes, *Angew. Chem., Int. Ed.*, 2004, **43**, 2752; (*c*) F.-X. Chen and X. Feng, *Synlett*, 2005, 892; (*d*) T. R. J. Achard, L. A. Clutterbuck and M. North, *Synlett*, 2005, 1828.

10 (*a*) D. A. Evans, L. K. Truesdale and G. L. Carroll, *J. Chem. Soc., Chem. Commun.*, 1973, 55; (*b*) D. A. Evans and L. K. Truesdale, *Tetrahedron Lett.*, 1973, **14**, 4929; (*c*) K. Iwanami, M. Aoyagi and T. Oriyama, *Tetrahedron Lett.*, 2005, **46**, 7487; (*d*) K. Iwanami, M. Aoyagi and T. Oriyama, *Tetrahedron Lett.*, 2006, **47**, 4741.

11 (*a*) S. Kobayashi, Y. Tsuchiya and T. Mukaiyama, *Chem. Lett.*, 1991, **20**, 537; (*b*) L. Wang, X. Huang, J. Jiang, X. Liu and X. Feng, *Tetrahedron Lett.*, 2006, **47**, 1581; (*c*) S. E. Denmark and W. Chung, *J. Org. Chem.*, 2006, **71**, 4002.

12 (*a*) Y. Fukuda, Y. Maeda, S. Ishii, K. Kondo and T. Aoyama, *Synthesis*, 2006, 589; (*b*) J. J. Song, F. Gallou, J. T. Reeves, Z. Tan, N. K. Yee and C. H. Senanayake, *J. Org. Chem.*, 2006, **71**, 1273.

13 (*a*) X. Liu, B. Qin, X. Zhou, B. He and X. Feng, *J. Am. Chem. Soc.*, 2005, **127**, 12224; (*b*) N. Kurono, M. Yamaguchi, K. Suzuki and T. Ohkuma, *J. Org. Chem.*, 2005, **70**, 6530.

14 (*a*) K. Higuchi, M. Onaka and Y. Izumi, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 2016; (*b*) M. L. Kantam, P. Sreekanth and P. L. Santhi, *Green Chem.*, 2000, **2**, 47; (*c*) B. Karimi and L. Ma'Mani, *Org. Lett.*, 2004, **6**, 4813; (*d*) S. Huh, H.-T. Chen, J. W. Wiench, M. Pruski and V. S.-Y. Lin, *Angew. Chem., Int. Ed.*, 2005, **44**, 1826; (*e*) K. Yamaguchi, T. Imago, Y. Ogasawara, J. Kasai, M. Kotani and N. Mizuno, *Adv. Synth. Catal.*, 2006, **348**, 1516.

15 The catalytic activity of amorphous SiO_2–Al_2O_3 (Si/Al = 5 and 2) greatly depended on the temperature of the pretreatment. When the catalysts were pretreated *in vacuo* at 300 °C for 3 h, the pseudo-first order rate constant increased from 1.7×10^{-4} (*in vacuo* at 120 °C for 1 h) to 8.0×10^{-3} min^{-1} for SiO_2–Al_2O_3 (Si/Al = 5) and from 1.7×10^{-3} to 7.6×10^{-3} min^{-1} for SiO_2–Al_2O_3 (Si/Al = 2). On the other hand, the influence of the pretreatment on the catalytic activity of Al-MCM-41, MCM-41, amorphous SiO_2–Al_2O_3 (Si/Al = 20), and zeolites (H-Y and H-ZSM-5) was small.

16 Recentry, Olah *et al.* reported that DMF itself highly promotes the cyanosilylation of aldehydes with TMSCN at room temperature (G. K. S. Prakash, H. Vaghoo, C. Panja, V. Surampudi, R. Kultyshev, T. Mathew and G. A. Olah, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 3026). In our examination, when benzaldehyde (1 mmol) was treated with TMSCN (5 mmol) in DMF (10 mL) at 0 °C without the Al-MCM-41 catalyst, the desired product was obtained in 12% yield in 15 min.

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