Pergamon

Tetrahedron Letters 43 (2002) 9073–9075

TETRAHEDRON
LETTERS

Self-aldol condensation of unmodified aldehydes catalysed by secondary-amine immobilised in FSM-16 silica

Ken-ichi Shimizu,[a,*] Eidai Hayashi,[a] Takuro Inokuchi,[b] Tatsuya Kodama,[b] Hisahiro Hagiwara[a] and Yoshie Kitayama[b]

[a]*Graduate School of Science and Technology, Niigata University, Ikarashi-2, Niigata 950-2181, Japan*
[b]*Department of Chemistry and Chemical Engineering, Faculty of Engineering, Niigata University, Ikarashi-2, Niigata 950-2181, Japan*

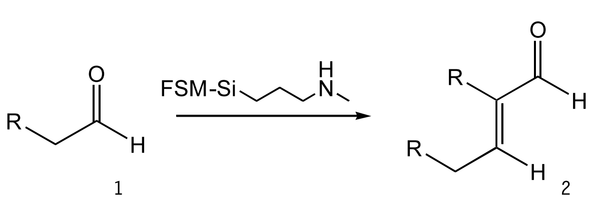
Received 2 September 2002; revised 7 October 2002; accepted 11 October 2002

Abstract—Self-aldol condensation of unmodified aldehydes was catalysed effectively by *N*-metlyl-3-aminopropylated FSM-16 mesoporous silica, whose activity was higher than that of homogeneous amine catalyst. © 2002 Elsevier Science Ltd. All rights reserved.

Heterogeneous catalysts for the synthesis of fine chemicals have attracted considerable attention from both environmental and economical points of view, because they offer several advantages in organic synthesis, e.g. simplification of reaction procedures, easy separation of products, repeated use, and so on.[1] Mesoporous silicas represent ideal inorganic supports for immobilised catalysts due to their high surface area and large pore size.[1a,2] For example, novel heterogeneous basic catalysts in which amines are covalently anchored to mesoporous silicas have been reported to be effective.[2] We have recently reported that the secondary-amine immobilised FSM-16 mesoporous silica acts as an efficient heterogeneous catalyst for 1,4-conjugate addition of unmodified aldehydes to vinylketones which cannot be catalysed by ordinary oxidic solid bases.[3]

Nucleophilic reactions of unmodified aldehydes are difficult to control affording a mixture of complicated products often because of higher reactivity of formyl groups under either basic or acidic reaction condition. In order to solve such problems, aldehydes were transformed once to their stable synthones which were then reacted with electrophiles.[4] After the reaction, the products were transformed back to aldehydes. In the case of self-aldol condensation of unmodified aldehydes leading to α,β-unsaturated aldehydes (enals), there have been several examples employing aqueous sodium hydroxide,[5a] 2,4,6-trimethylphenoxymagnesium bromide,[5b] boric acid,[5c] electrolysis[5d] or pyrrolidine/benzoic acid.[5e] Since enals are versatile intermediates for organic synthesis, efforts to explore novel catalytic system for this reaction are still continuing. For example, it was recently found by Hagiwara et al. that diethylaminotrimethylsilane catalysed the aldol condensation of unmodified aldehydes, though a large amount of the catalysts (50 mol%) were required.[6] In order to improve the catalytic performance of this reaction, we have attempted immobilisation of the amine catalyst to provide a recyclable and efficient solid catalyst. We delineate herein that self-aldol condensation of unmodified aldehydes is catalysed by secondary-amine grafted on FSM-16 (Scheme 1). The catalytic behaviour of this material as well as the recycling characteristics is presented to exemplify the effectiveness of this catalytic system.

Pure silica FSM-16 (881 m^2 g^{-1}) was prepared from kanemite according to the method previously described.[7] The aminopropyl groups were anchored on



Scheme 1.

Keywords: aldehydes; aldol reactions; amine catalyst; mesoporous silica.

* Corresponding author. Tel.: +81-25-262-6777; fax: +81-25-262-7010; e-mail: kshimizu@eng.niigata-u.ac.jp

PII: S0040-4039(02)02313-4

FSM-16 silica by the post-modification method[2b,8] using 3-aminopropyltriethoxysilane, *N*-methyl-3-aminopropyltriethoxysilane and *N*,*N*-dimethyl-3-aminopropyltriethoxysilane to give three catalysts abbreviated as NH_2–FSM, NHMe–FSM and NMe_2–FSM, respectively. For comparison, *N*-methyl-3-aminopropylated amorphous silica (NHMe–SiO_2) was also prepared by using commercial silica gel (Cabosil, 200 $m^2\ g^{-1}$) as a support. Nitrogen contents of NH_2–FSM, NHMe–FSM, NMe_2–FSM and NHMe–SiO_2 were 0.75, 0.74, 0.52 and 0.76 mmol g^{-1}, respectively. ^{13}C MAS NMR spectra showed the presence of aminopropyl groups anchored on FSM-16, and analyses using XRD and N_2 adsorption showed the preservations of the high surface area and long-range ordered structure of the mesoporous support.[3]

Table 1 shows the results of the aldol condensation of *n*-hexanal by various catalysts.[9] The reaction of *n*-hexanal in the presence of catalytic amount of the amine immobilised catalysts gave enal **2** with moderate to high yield (entries 1–4). By using 5 mol% of NHMe–FSM, the enal **2** was obtained as a single isomer[10] in 83% isolated yield.[11]The activity of amine-free FSM-16 silica was very low (3% yield after 20 h), confirming that anchored amino groups were the catalytic species of immobilised catalysts. The activity was dependent strongly on the type of amines supported. The order of the activity was classified by the order of amino groups, secondary>primary>tertiary (entries 1–3), which may suggest the intervention of enamine pathway.[6] It should be noted that amine immobilised catalysts exhibited higher activity than conventional solid bases such as MgO and hydrotalcite.

Table 1. Self-aldol condensation of *n*-hexanal by various solid catalysts[a]

Entry	Catalysts ([N]/mol%)[b]	*t* (h)	Conversion (%)[c]	**2** Yield (%)[d]
1	NHMe–FSM (5)	2	97	85 (83)
2	NH_2–FSM (5)	20	86	70
3	NMe_2–FSM (5)	20	60	43
4	NHMe–SiO_2 (5)	20	96	69
5	1st reuse (5)[e]	2	97	81
6	2nd reuse (5)[e]	2	94	83
7	3rd reuse (5)[e]	2	90	77
8	MgO[f,g]	20	56	26
9	Hydrotalcite[f,h]	24	22	11

[a] Reactions were conducted with *n*-hexanal (1 mmol) in toluene (5 mL) at reflux temperature under N_2.

[b] Amount of the catalyst tested.

[c] Conversion of *n*-hexanal determined by GC using *o*-xylene as internal standard.

[d] GC yield. Isolated yield is shown in a parenthesis.

[e] Reuse of NHMe–FSM after entry 1.

[f] The catalyst loading was 0.1 g. Prior to the reaction, catalysts were calcined at 500°C for 1 h.

[g] MgO (JRC–MGO-1) was supplied from the Catalysis Society of Japan.

[h] Mg–Al hydrotalcite ($Mg_6Al_2(OH)_{16}CO_3{\cdot}4H_2O$) was supplied from Kyowa Chemical Industry Co., Ltd.

To exclude the possible leaching of any active catalytic species in solution, the model reaction was examined for self-aldol condensation of *n*-hexanal employing NHMe–FSM catalyst. When the solid catalyst was removed at an early stage of the reaction ($t = 10$ min, 40% yield), the reaction did not proceed further. This result proves heterogeneous catalytic activity of NHMe–FSM and no contribution from homogenous catalysis. The catalyst can be easily separated from the reaction mixture by simple filtration and can be recycled. The catalyst removed by filtration showed a decrease in the catalytic activity (60% yield after 2 h). However, the activity was recovered (entries 5–7) comparable to that observed for the first run (entry 1), when the filtered catalyst was simply dispersed in dilute aqueous solution of K_2CO_3 (2 mM) for 5 min, followed by washing with distilled water and subsequent drying at 373 K.[12] By this treatment, the catalyst was reusable for all the three cycles in the repeated runs without a marked loss of the activity.

The profiles of the reaction catalysed by NHMe–FSM, NHMe–SiO_2 were shown in Fig. 1 together with that of a homogeneous secondary-amine catalyst, *N*-methyl-3-propylamine. The catalysts based on mesoporous silica showed higher activity than that on amorphous silica; the initial rate of the former catalyst was 2.2 times higher than the latter catalyst. It is noteworthy that NHMe–FSM exhibited much higher activity than the homogenous amine catalyst in terms of both the initial rate and the yield. We believe, at present, that the higher activity of NHMe–FSM catalyst than its homogenous counterpart as well as secondary-amine supported on amorphous silica, is due to the enrichment of the reactants inside the well ordered pores of mesoporous silica.

Representative examples of the self-aldol condensation of several aldehydes with NHMe–FSM catalyst are summarised in Table 2. In all cases, the reaction pro-

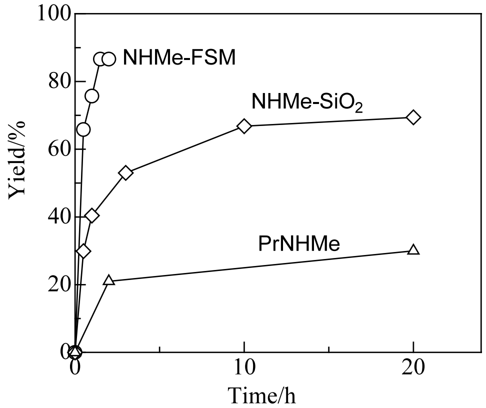


Figure 1. Plot of GC yield of **2** versus time for self-aldol condensation of *n*-hexanal with (○) NHMe–FSM (5 mol%), (◇) NHMe–SiO_2 (5 mol%) and (△) *N*-methyl-3-propylamine (10 mol%).

Table 2. Self-aldol condensation of various aldehydes with NHMe–FSM[a]

Entry	Aldehydes	[N] (mol%)[b]	*t* (h)	**2** Yield (%)[c]
1	*n*-Propanal	5	1	83
2	*n*-Butanal	5	2	84
3	*n*-Octanal	10	2	93
4	*n*-Decanal	10	2	56
5	$Ph(CH_2)_2CHO$	10	8	44

[a] Reactions were conducted with aldehydes (1 mmol) in toluene (5 mL) at reflux temperature under N_2.

[b] Amount of the catalyst tested.

[c] Yield determined by GC using *o*-xylene as internal standard.

ceeded smoothly in the presence of a catalytic amount of NHMe–FSM to afford enals **2** in high yields. However, with this catalyst, the self-aldol condensation of 2-butenal or 2-methylpropionaldehyde did not proceed.

In summary, we have demonstrated that the secondary-amine immobilised FSM-16 mesoporous silica acts as an effective heterogeneous catalyst in the self-aldol condensation of unmodified aldehydes. The present system is a new heterogeneous catalysis for an environmentally friendly C–C bond forming reaction because the catalyst is easily separated by simple filtration and is reusable without apparent decrease of the activity.

References

1. (a) *Fine Chemicals through Heterogeneous Catalysis*; Sheldon, R. A.; van Bekkum, H., Eds.; Wiley–VHC: Weinheim, 2001; (b) Izumi, Y.; Urabe, K.; Onaka, M. *Zeolite, Clay, and Heteropoly Acid in Organic Reactions*; Kodansha–VCH, 1992.
2. (a) Price, P. M.; Clark, J. H.; Macquarrie, D. J. *J. Chem. Soc., Dalton Trans.* **2000**, 101; (b) Burunel, D. *Microporous Mesoporous Mater.* **1999**, *27*, 329; (c) Rao, Y. V. S.; Vos, D. E. D.; Jacobs, P. A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2661; (d) Rodriguez, I.; Iborra, S.; Corma, A.; Rey, F.; Jorda, J. L. *Chem. Commun.* **1999**, 593; (e) Demicheli, G.; Maggi, R.; Mazzacani, A.; Righi, P.; Sartori, G.; Bigi, F. *Tetrahedron Lett.* **2001**, *42*, 2401.
3. Shimizu, K.; Suzuki, H.; Hayashi, E.; Kodama, T.; Tsuchiya, Y.; Hagiwara, H.; Kitayama, Y. *Chem. Commun.* **2002**, 1068.
4. (a) Stork, G.; Brizzolara, A.; Landesman, H.; Szmuskovics, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207; (b) Brown, M. *J. Org. Chem.* **1968**, *33*, 162; (c) Duhamel, P.; Hennequin, L.; Poirier, J. M.; Travel, G. *Tetrahedron* **1986**, *42*, 4777.
5. (a) Haussermann, M. *Helv. Chim. Acta* **1951**, *34*, 1482; (b) Casnati, G.; Pochini, A.; Salerno, G.; Ungaro, R. *Tetrahedron Lett.* **1974**, *15*, 959; (c) Offenhauer, R. D.; Nelsen, S. F. *J. Org. Chem.* **1968**, *33*, 774; (d) Shono, T.; Kashimura, S.; Ishizaki, K. *Electrochim. Acta* **1984**, *29*, 603; (e) Ishikawa, T.; Uedo, E.; Okada, S.; Saito, S. *Synthesis* **1999**, 450.
6. Hagiwara, H.; Ono, H.; Komatsubara, N.; Hoshi, T.; Suzuki, T.; Ando, M. *Tetrahedron Lett.* **1999**, *40*, 6627.
7. Inagaki, S.; Fukushima, Y.; Kuroda, K. *J. Chem. Soc., Chem. Commun.* **1993**, 680.
8. Typically, 2.0 g of the FSM-16 sample was evacuated at 150°C and then toluene (20 mL) containing *N*-methyl-3-aminopropyl(triethoxy)silane (2 mmol) was introduced. The mixture was heated at reflux temperature for 3 h and the solid was filtered off, washed with toluene and acetone and dried at 100°C overnight.
9. Before the reaction, the catalyst was dried in air at 150°C for 1 h. The reaction was carried out by stirring the reaction mixture containing aldehyde (1 mmol) in dry toluene (5 mL) at reflux temperature under nitrogen atmosphere. Progress of the reaction was monitored by GC analyses of aliquots using *o*-xylene as an internal standard.
10. The geometry of the products from *n*-hexanal, *n*-decanal and hydrocinnamaldehyde was determined to be *E* from NOE enhancements between aldehydic and olefinic protons.
11. The yield was lower than the conversion of *n*-hexanal. This may be due to the oligomerisation or the adsorption of aldehydes on the catalyst.
12. This observation may be explained as follows. The organic acids, present as impurities in aldehydes or produced during the reaction, neutralised the amine catalysts. The organic acids were removed by the treatment with dilute aqueous K_2CO_3 solution.