Knoevenagel and aldol condensations catalysed by a new diamino-functionalised mesoporous material

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Abstract

Knoevenagel and aldol condensations have been reported by a new diamino-functionalised MCM-41 catalyst synthesised by condensation of the trimethoxysilylpropylethylenediamine on MCM-41. This solid base catalyst is found to be very efficient with reusability for a number of times with consistent activity. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

Current interest is focused on the development of environmentally friendly solid catalysts for clean processes in fine chemical industries. Knoevenagel and aldol condensations are ubiquitous reactions in organic chemistry right from the syntheses of small molecules to the elegant intermediates of anti-hypertensive drugs and calcium antagonists [1,2]. It is generally catalysed by weak bases like primary, secondary, tertiary amines, ammonium or ammonium salts [3–6] under homogeneous conditions. Later, inorganic solids and solid-supported reagents, such as anionic resins [7], KF [8], magnesium and aluminium oxides [9–11], zeolites [12], hydrotalcites [13], amino group immobilised on silica gel [14], clays [15], alkali and alkaline earth carbonates [16], were used because they provided operational simplicity and higher selectivity with the possibility of reusability. Solid basic catalysts are receiving increased attention in the recent past as they facilitate a variety of organic reactions that take place via carbanionic intermediates. A new family of mesoporous materials discovered recently [17,18] ushered a new era of supports with conceivable industrial application in the fine chemicals synthesis due to their tuneable larger pore sizes 30 Å. Recently, condensation reactions catalysed by alkali metal ion-exchanged mesoporous material MCM-41

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MCM-41 + (CH₃O)₃Si(CH₂)₃NH⌢NH₂ ⟶ O—Si—(CH₂)₃—NH⌢NH₂

diamino-functionalised
mesoporous material
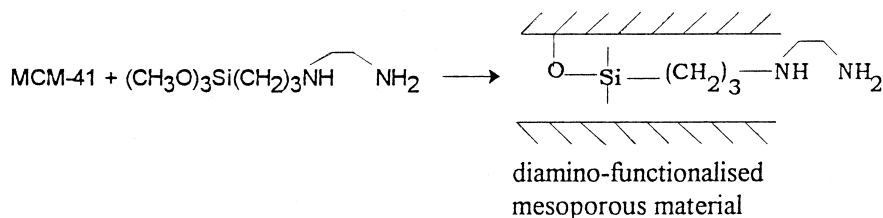
Scheme 1.

were reported using high temperatures, 150°C and longer reaction times, 3–7 h [19]. Macquarrie and Jackson [20,21] and Lasperas et al. [22] used monoaminopropyl-functionalised MCM for the Knoevenagel condensations of aldehydes and ketones with ethyl cyanoacetate. Relatively high yields were obtained at higher temperatures (80–110°C) on prolonged reaction times. The former introduced aminopropyl (trimethoxy) silane along with template *n*-dodecylamine during the synthesis of MCM and obtained monoamine grafted onto the lattice of the solid on subsequent removal of template, while Lasperas et al. [22] anchored the monoamino moiety on MCM-41 directly through silanation process.

Herein, we report the preparation of diamino-functionalised mesoporous material by anchoring 3-trimethoxysilylpropylethylenediamine moiety on calcined MCM-41 (Scheme 1) and its successful application in both aldol and Knoevenagel condensation reactions under very mild conditions. Incidentally, this is the first report of the use of organofunctionalised MCM catalyst for the aldol condensation reaction. These catalysts show very high activities and can be reused several times.

2. Experimental

2.1. Preparation of the catalyst

The present catalyst was prepared in two steps: first preparation of the mesoporous material [23] (pure silica MCM-41, BET surface area = 1086 m^2/g) followed by reaction of the calcined solid (at 550°C for 4 h) with 3-trimethoxysilylpropylethylenediamine in dry toluene under similar conditions as reported earlier [15]. After functionalisation, the BET surface area was 590 m^2/g.

2.2. Knoevenagel condensation

In a typical procedure, 0.02 g catalyst and 0.392 g (2 mmol) of 3,4,5-trimethoxybenzaldehyde were taken in dry toluene (5 ml). To this solution, 0.125 ml (2 mmol) of malanonitrile was added and the mixture was stirred at 50°C for 15 min. The reaction was monitored by TLC. After completion of reaction, the catalyst was filtered; the filtrate was concentrated and purified by column chromatography (hexane:ethylacetate) on silica gel (yield = 357 mg, 91%). The product was then analysed by IR

R₁\ ⟍=O + H₂C⟨CN/Y ──Catalyst──▶ R₁\C=C⟨CN/Y + H₂O
R₂/   R₂/
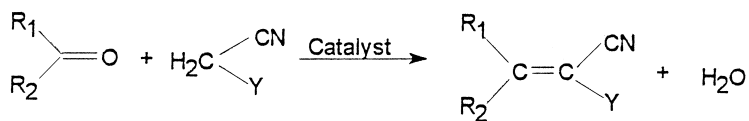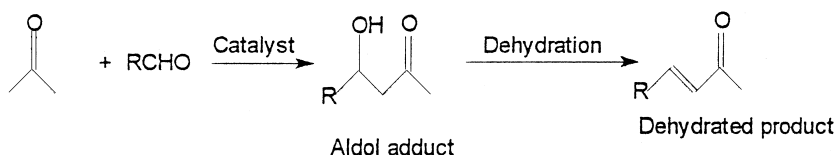
Scheme 2.

Scheme 3.

and ^{1}H NMR. The catalyst was washed with the solvent and used for recycling.

2.3. Aldol reaction

In a typical procedure, 0.2 g catalyst and 0.106 ml (1 mmol) of benzaldehyde were taken in acetone (5 ml) and heated at 50°C. The reaction was monitored by TLC and the work-up was carried out in the same manner as in Knoevenagel reaction. The product was then analysed by IR and ^{1}H NMR.

3. Results and discussion

The efficacy of this catalyst as a base (0.3 mmol/g of loading) was tested towards two important model organic reactions—Knoevenagel condensation (Scheme 2) and aldol reaction (Scheme 3).

The Knoevenagel condensation of various aldehydes and ketones were carried out with (a) malononitrile and (b) ethyl cyanoacetate as the active methylene compounds. In all the reactions except cinnamaldehyde and acetophenone, the conversions are total in toluene with exclusive formation of dehydrated products (Table 1). In the condensation of cinnamaldehyde with ethyl cyanoacetate, when toluene was used as the solvent, the yield was only 30%. However, changing the solvent from toluene to DMF produced the trisubstituted olefin in 57% yield at room temperature and in 75% yield at 60–70°C. The solvent effect established here is in conso-

Table 1
Knoevenagel condensation by diamino-functionalised mesoporous material

Entry	R_1	R_2	Y	Solvent	Yield[a] (%)
1	Ph	H	CN	Toluene	99
2	Ph	H	CO_2Et	Toluene	100
3	Ph CH=CH	H	CN	Toluene	99
4	Ph CH=CH	H	CO_2Et	DMF	75[b]
5	$(OMe)_3 C_6H_2$	H	CN	Toluene	100 (91[c])
6	$(OMe)_3 C_6H_2$	H	CO_2Et	Toluene	85
7	C_4H_3O	H	CN	Toluene	100
8	C_4H_3O	H	CO_2Et	Toluene	100
9	$MeOC_6H_4$	H	CN	Toluene	100
10	$MeOC_6H_4$	H	CO_2Et	Toluene	89 (85[c])
11	$PhCH_2CH_2$	Me	CN	Toluene	100
12	$PhCH_2CH_2$	Me	CO_2Et	Toluene	30
13	Ph	Me	CN	DMF	75
14	p-NO_2-C_6H_4	H	CN	Toluene	100
15	p-NO_2-C_6H_4	H	CO_2Et	Toluene	100
16	cC_5H_{10}		CN	Toluene	95
17	cC_5H_{10}		CO_2Et	Toluene	81
18	Ph	H	CN	Toluene	0[d]

[a] NMR yields based on the aldehyde.
[b] At 60–70°C, 57% at R.T.
[c] Isolated yield.
[d] Using unfunctionalised mesoporous material.

Table 2
Aldol condensation by diamino-functionalised mesoporous material

Entry	Nucleophile	Electrophile	Time (h)	conv.[a] (%)	selectivity[a] (%)	
					Aldol adduct	Dehydrated product
1	Me_2CO	4-Cl-PhCHO	9	84	69	31
2	Me_2CO	PhCHO	3	79	52	48
3	Me_2CO	2-$MeOC_6H_4CHO$	9	81	47	53
4	Me_2CO	4-$MeOC_6H_4CHO$	9	68	16	84
5	Me_2CO	3,4,5-$(MeO)_3C_6H_2CHO$	9	86	34	66
6	Me_2CO	4-NO_2-PhCHO	1	100	15	85
7	Me_2CO	4-CH_3-PhCHO	9	75	33	67
8	Me_2CO		9	100	34	66
9	Me_2CO		9	100	40	60
10	Me_2CO		6	70	9	91

[a] NMR yields based on the aldehyde.

nance with the results reported by others [24,25] in Knoevenagel reaction.

It is very interesting to note that the turn-over frequency (TOF) of the reactions displayed manifold excess than the one reported recently with in situ introduced monoaminopropyl (trimethoxy) silane during the synthesis of MCM [20,21]. For example, the TOF^{h-1} of the reactions of aromatic aldehyde, benzaldehyde and aliphatic ketone, cyclohexanone with ethyl cyanoacetate is 1330. The activity of the used catalyst is consistent for five recycles amounting to 1700 TON. The identical reactivity shown by both aliphatic and aromatic carbonyl compounds with ethyl cyanoacetate is in contrast to the earlier reports. Moreover, both the *p*-nitrobenzaldehyde and *p*-anisaldehyde gave high yield with malononitrile and ethyl cyanoacetate indicating that the rate of the reaction is independent of the substituent in the aromatic ring.

Next, we explored the efficacy of the catalyst towards aldol reaction (Scheme 3), which is usually carried out by soluble bases, such as sodium hydroxide or alkali metal alkoxides [26,27]. The results of the reaction of various aldehydes with acetone are presented in Table 2. The reaction of *p*-chlorobenzaldehyde (entry no. 1) affords aldol predominantly, while the dehydrated α,β-unsaturated compound is a minor product (Table 2).

When benzaldehyde or *o*-anisaldehyde are used in the reaction, the aldol and the dehydrated products are formed in equal proportions (entries 2 and 3). On the other hand, the reaction of all the other substituted aldehydes yields the dehydrated product as the major one. In all the cases, the overall conversion is very high. The activity of the catalyst for five recycles is consistent (Table 2).

4. Conclusion

Thus, the reactions described here (Tables 1 and 2) have a broad scope, since the catalyst can be easily filtered off and reused for several

cycles without any further reactivation. The reused catalyst gave identical yields with consistent rates compared with the results obtained by the fresh catalyst. The present catalyst is an interesting candidate for commercial exploitation. This new solid base catalyst developed by us becomes a practical alternative to soluble bases in view of the following advantages: (a) high catalyst activity under mild reaction conditions; (b) easy separation of the catalyst after the reaction; and (c) reusability of the catalyst for several times.

Acknowledgements

References

[1] G. Marciniak, A. Delgado, G. Leclerc, J. Velly, N. Decker, J. Schwartz, J. Med. Chem. 32 (1989) 1402.
[2] D. Enders, S. Muller, A.S. Demir, Tetrahedron Lett. 29 (1988) 6437.
[3] E. Knoevenagel, Chem. Ber. 27 (1894) 2345.
[4] G. Jones, Org. React. 15 (1967) 204.
[5] L.F. Tietze, U. Beifuss, in: B.M. Trost (Ed.), Comprehensive Organic Synthesis, Pergamon, Oxford, 1991.
[6] J. March, Advanced Organic Chemistry, 4th edn., Chichester, 1992.
[7] W. Richardhein, J. Melvin, J. Org. Chem. 26 (1961) 4874.
[8] L. Rand, D. Haidukewych, R.J. Dolinski, J. Org. Chem. 31 (1966) 1272.
[9] H. Moison, F. Texier-Boullet, A. Foucaud, Tetrahedron 43 (1987) 537.
[10] J. Muzart, Synthesis (1982) 60.
[11] F. Texier-Boullet, A. Foucaud, Tetrahedron Lett. 23 (1982) 4927.
[12] A. Corma, V. Fornes, R.M. Martin-Aranda, A. Garcia, J. Primo, Appl. Catal. 59 (1990) 237.
[13] A. Corma, V. Fornes, R.M. Martin-Aranda, F. Rey, J. Catal. 134 (1992) 58.
[14] E. Angeletti, C. Canepa, G. Martinetti, P. Venturello, J. Chem. Soc., Perkin Trans. 1 (1989) 105.
[15] Y.V. Subba Rao, B.M. Choudary, Synth. Commun. 21 (1991) 1163.
[16] M.A. Aramendia, V. Borau, C. Jimenez, J.M. Marinas, F.J. Romero, Chem. Lett. (1995) 279.
[17] J.S. Beck, J.C. Vartuli, W.J. Roth, M.E. Leonowicz, C.T. Kresge, K.D. Schmitt, C.T.-W. Chu, D.H. Olson, E.W. Shep-

pard, S.B. McCullen, J.B. Higgins, J.L. Schlenker, J. Am. Chem. Soc. 114 (1992) 10834.

[18] C.T. Kresge, M.E. Leonowicz, W.J. Roth, J.C. Vartuli, J.S. Beck, Nature 359 (1992) 710.

[19] K.R. Kloetstra, H. van Bekkum, J. Chem. Soc., Chem. Commun. (1995) 1005.

[20] D.J. Macquarrie, D.B. Jackson, J. Chem. Soc., Chem. Commun. (1997) 1781.

[21] D.J. Macquarrie, J. Chem. Soc., Chem. Commun. (1996) 1961.

[22] M. Lasperas, T. Llorett, L. Chaves, I. Rodriguez, A. Cauvel, D. Brunel, Stud. Surf. Sci. Catal. 108 (1997) 75.

[23] A. Tuel, S. Gontier, Chem. Mater. 8 (1996) 114.

[24] P. Laszlo, Acc. Chem. Res. 19 (1986) 121.

[25] P.W. Lednor, R. de Ruiter, J. Chem. Soc., Chem. Commun. (1991) 1625.

[26] A.T. Nielsen, W.T. Houlihan, Org. React. 16 (1968) 1.

[27] C.H. Heathcock, in: B.M. Trost (Ed.), Comprehensive Organic Synthesis, Pergamon, Oxford, 1991.