A new environmentally friendly method for the synthesis of calix(4)pyrroles over molecular sieve catalysts

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Abstract

MCM-41 was found to be the most effective heterogeneous catalyst for the synthesis of calix(4)pyrrole. Various metal ion substituted MCM-41 samples were synthesized and were used to improve the yields of calix(4)pyrrole. Co-MCM-41 was found to give maximum yields. The effects of varying Si/Al ratio in MCM-41, molar ratio of various reactants, and the role of solvent towards this macrocyclization reaction have been studied.
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1. Introduction

Calix(4)pyrroles exhibit exceptional chemical and physical properties that have suggested a vast number of potential applications in host–guest chemistry [1–4]. The chelating capabilities of these calixpyrroles have been the subject of intensive research aimed at gaining both understanding and control on guest recognition and binding [5,6]. Recently, Sessler and coworkers [7–9] reported that calix(4)pyrroles are effective and selective receptors for anions and neutral guest species. They find novel applications as coordination complexes, catalytic materials, nano-sponges, molecular machines, nanoentities and semi conducting materials [10]. Selective synthesis of these calix(4)pyrroles in high yields by an environmentally clean process is of topical interest, so as to meet the increasing demand of reducing the pollution hazards caused by the usage of homogeneous acid catalysts. Heterogeneous catalytic synthesis is known to be one of the most effective ways to control the selectivity to calix(4)pyrrole with high yield and it has the potential to be scaled-up at relatively low cost. Properly functionalized and structurally ordered mesoporous materials, such as MCM-type silicas and alumina [11–15], with tunable pore size distributions have attracted much attention for their potential applications as new catalytic scaffolds to direct and orient the conformation of desired products [16–21]. For example, recent interest in synthesis of calix(4)pyrroles over Al-MCM-41 [22–24] catalysts has highlighted the future application of these materials for the synthesis of macrocycles.

In this work, we basically aim to investigate the effect of pore size, role of different transition metal ions during the synthesis of calix(4)pyrroles over MCM-41 catalysts. Here, we have intensively investigated the effect of transition metal ions including Mn-, V-, Cr-, Fe- and Co-incorporated MCM-41 for the synthesis of macrocycles. Among other parameters studied are the effect of solvent, molar ratio between the reactants and also Si/Al ratio of Al-MCM-41 catalyst.

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2. Experimental

2.1. Catalyst preparation

Al-MCM-41 has been synthesized according to reported literature [25]. Metal ions have been isomorphously substituted into the framework. The metal precursors for Ti, V are titanium isopropoxide, vanadylacetylacetonate, respectively and the corresponding metal nitrates for remaining metal ions. The method of synthesis is similar to that of Al-MCM-41 [26–28], except that the metal precursor is dissolved in NaOH and aluminum isopropoxide solution before adding TEAOH. The molar composition used was $0.5MXOY/0.5Al_2O_3/31.0SiO_2/2.2(surfactant)_2/3.16(TEA)_2O/1.89 Na_2O/615H_2O$.

Al-MCM-41 with different Si/Al ratios has been synthesized by varying the Si/Al ratio from 0 to 45 during its synthesis. The catalysts of HZSM-5, Hβ, TS-1 have been obtained from Conteka (Sweden), HY from PQ Corporation (USA) and HX from Aldrich (USA). The reactants pyrrole, acetone, methylethyl ketone, methylisobutylketone, 1,3-diphenyl acetone, ethylacetoacetate are obtained from Aldrich (USA).

2.2. Catalyst characterization

The BET surface areas were determined by single point method using pulse Chemisorb 2700 (Micromeretics, USA). NH_3-TPD studies are carried out using AutoChem 2910 (Micromeritics, USA) instrument.

2.3. Catalytic reaction

Catalytic reactions were carried out according to the following procedure. Pyrrole (7.2 mmol) and suitable ketone in 1:1 molar ratio are mixed in 20 ml dichloromethane (DCM) taken in a 100 ml round bottom flask. To this reaction mixture, 0.5 g of the calcined and dried catalyst is added. After the catalyst was added, the reaction was started by immersing the flask into oil bath preheated at the reaction tempera-

ture. The reaction was carried out under vigorous stirring condition for duration of 10 h. The catalyst is then separated by filtration and washed thoroughly with 100 ml of dichloromethane (DCM) in around five equal installments (20 ml × 5 times). Then the solvent is removed under reduced pressure to give a viscous residue. The products **1a**, **1b** and **1c** (Table 1) are fractionated by column chromatography using silica (100–200 mesh size) with *n*-hexane as eluent. They are characterized by (^{1}H and ^{13}C) NMR, FTIR, CHNS (EI, HR). Mass spectrometry and quantification has been done by using HPLC. The detailed characterization by mass spectrometry is reported elsewhere [29].

3. Results and discussion

3.1. Effect of zeolite structure on synthesis of calix(4)pyrrole (**1a**)

Equimolar ratio of pyrrole and acetone are refluxed over various zeolite and mesoporous molecular sieves. The cyclic tetramer, viz., meso-octamethyl calix(4)pyrrole, **1a** has been formed with substantial yields over Al-MCM-41 and HZSM-5 (Si/Al = 30) catalysts. The formation on Al-MCM-41 can be attributed for its mesoporous nature (pore size ∼ 30 Å) but HZSM-5, with smaller pore size of 5.6 Å, is found to promote both dimer **1b** and cyclic tetramer **1a** as shown in Fig. 1. To understand the formation of the macrocycles over Al-MCM-41 and HZSM-5 catalysts, we poisoned the surfaces of both catalysts by chemical vapor deposition (CVD) of Ph_2SiCl_2 [30] and tetraethoxysilane (TEOS) [31], respectively, to get Al-MCM-41-P and HZSM-5-P. Then the macrocyclization was performed on both these catalysts. As expected, there was no **1a** formation over poisoned HZSM-5-P where as the yields of **1a** over Al-MCM-41-P did not have much effect, as shown in Fig. 1. From this, it clearly indicates that in case of HZSM-5, macrocyclization is taking place on external surface of the catalyst whereas Al-MCM-41, the macrocyclization is taking place inside the mesopores. The mesoporous nature can be

Table 1
Effect of metal ion substitution in M-MCM-41 on the synthesis of meso-octamethyl calix(4)pyrrole

M-MCM-41	S_{BET} (m^2 g^{-1})	NH$_3$ uptake (mmol g^{-1})	Conversion of pyrrole (%)	Yield of product (wt%)		
				Calix(4)pyrrole (**1a**)	Dimer (**1b**)	Others[a]
Al	912.2	0.442	92.4	67.5	3.1	21.8
Ti	878.8	–	97.7	51.1	28.2	18.4
Cr	844.6	0.417	99.2	42.7	42.6	13.9
Mn	868.2	0.312	99.3	47.6	37.9	13.8
Fe	838.1	0.276	99.7	45.5	31.9	22.2
Co	951.6	0.598	100	95.6	1.7	2.7
Ni	846.2	0.160	99.9	36.9	50.3	12.7
Cu	856.9	–	99.4	30.1	49.8	19.5
Zn	842.1	0.165	99.1	33.4	14.4	51.3
Zr	–	0.343	99.6	45.7	39.6	14.3
Nb	–	–	99.8	46.3	35.9	17.6

Pyrrole:acetone = 1:1 (mole ratio); solvent: DCM (20 ml); reaction time: 20 h; catalyst weight: 0.5 g.
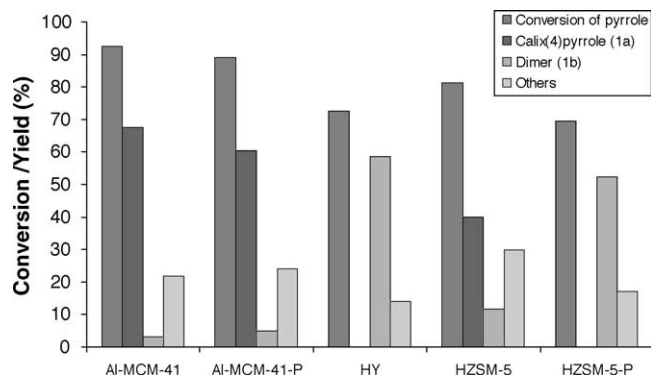[a] Others: linear trimer **1c** and tetramer **1d**, respectively.

Fig. 1. Effect of catalyst structure on the formation of calix(4)pyrrle **1a**.

seen by a representative TEM picture given in Fig. 2, which confirms the hexagonal structure where straight channels parallel to each other with no branching, except possibility at the particle edges, where some channels bend to form a bundle. The channel diameter is found to be uniformly 30 Å and is favoring **1a** formation.

We also performed the macrocyclization over HY, where significant quantity of linear dimer **1b** is formed with no cyclic **1a** formation (Fig. 1). Since the molecular size of **1a** (∼ 13.1 Å) is lower that that of supercage of HY (∼13.4 Å), **1a** formation in the super cages of HY zeolite is expected. After the reaction, the catalyst without washing has been subjected to solid-state NMR studies (^{1}H and ^{13}C NMR) and compared the generated data with liquid state NMR of **1a**. These studies confirmed that cyclic tetramer is not formed in supercages of HY zeolite. SAPO-5 with ∼7.3 Å pore size and mild acidity contributed to lower levels of conversion. Formation of calix(4)pyrrole **1a** has also been investigated employing mordenite and montmorillonite. Low conversion of pyrrole with negligible amounts of **1a** and **1b** is observed due to their low acidic nature.

Thus, Al-MCM-41 is found to be better catalyst for the synthesis of calix(4)pyrroles. Various transition metal ions
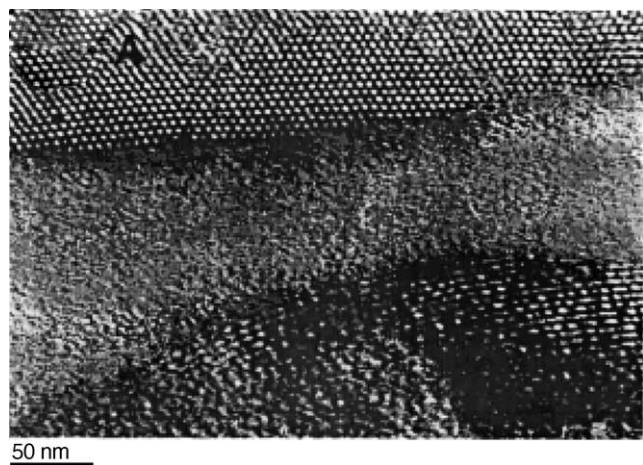

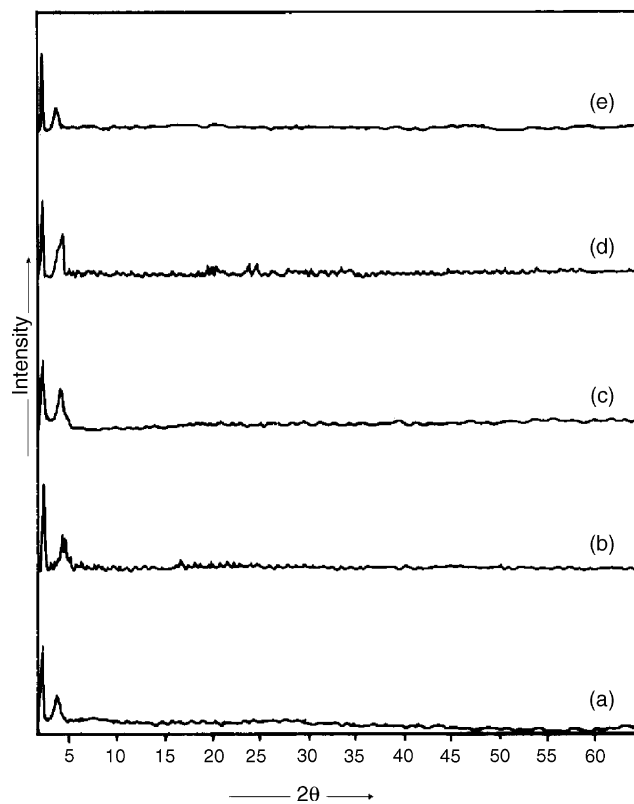Fig. 2. Transmission electron micrograph (TEM) of MCM-41 showing its hexagonal pore structure.

Fig. 3. Powder XRD pattern of calcined (a) Al-MCM-41; (b) Fe-MCM-41; (c) Co-MCM-41; (d) Ni-MCM-41 and (e) Cu-MCM-41.

were substituted hydrothermally in the framework of MCM-41 and their catalytic activity has been studied towards this macrocyclization reaction.

3.2. Macrocylization over several metal ion-containing MCM-41

Table 1 shows the catalytic role of several metal ion-containing MCM-41 towards the macrocylization of calix(4)pyrroles **1a**, from pyrrole and acetone in DCM solvent. All samples of M-MCM-41 were characterized by XRD and the patterns show all four different characteristic peaks of mesoporous materials with hexagonal arrangement of their channels Fig. 3. This indicates that all the prepared catalysts have a structure comparable to that of Si-MCM-41 [32] suggesting that the mesoporous structure was retained after the introduction of each metal ion.

When acetone and pyrrole are condensed in dichloromethane in presence of Co-MCM-41, calix(4)pyrrole **1a** yield up to 95% has been obtained as compared to 67.5% yield in the case of Al-MCM-41, as was reported to be effective for the macrocyclization in a previous study [24]. The enhanced yield has been attributed to cobalt ion behaving as a template between pyrrole rings for directing the reacting groups to the correct position for cyclization reaction. This cation, however showed no tendency to form complexes which could isolate with **1a**. It has been demonstrated that when cobalt exists on

the surface of silica, the multiple silanol bonds to a cobalt atom contract the pore wall, which results in the decrease of the pore size [33]. But, our results of increase in surface area (951.6 m^2 g^{-1}) and high acidity (0.598 mmol g^{-1}) of Co-MCM-41 suggest that cobalt was successfully incorporated into the silica framework thus favoring the formation of **1a**. Because the incorporation of cobalt increases the pore size about 0.1 nm in comparison to siliceous MCM-41. This may be due to the differences in the bond lengths between the cations and oxygen. The Co−O bond length is longer in comparison to that of Si−O. On the basis of this rationale the increase of pore size suggests that cobalt is incorporated in the silica framework so that the longer Co−O bond leads to an increase of the pore size [34] which favours more to the formation of **1a** with high yield and selectivity.

Generally, heterogeneous catalysts often suffer extensively from leaching of active metal species during reactions and eventually lose their catalytic activity. To our surprise, CoMCM-41, catalysts maintained their high catalytic activity even after four recycling and reuse of the catalysts Fig. 4. Here, experiments of macrocyclization were carried out, where the catalyst was filtered and the mother liquor was allowed to react further. But after the catalyst was removed, no further reaction was observed and no traces of Co ions were observed in the mother liquor when analyzed by ICP–MS. Further, the reaction was carried out three to four times over the same catalyst, where the catalyst was activated for 2 h and got approximately similar yields repetitively.
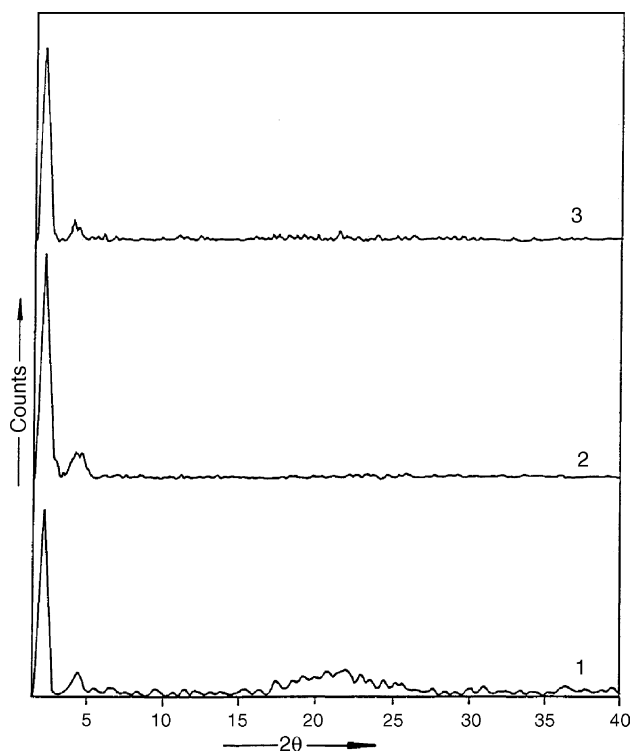

Fig. 4. Powder XRD pattern of Co-MCM-41 (1) uncalcined; (2) calcined and (3) regenerated.

Table 2
Solvent effects on synthesis of meso-octamethyl calix(4)pyrrole (**1a**)

Entry	Solvent	Conversion of pyrrole (%)	Yield of product (wt%)		
			Calix(4)pyrrole (**1a**)	Dimer (**1b**)	Others[a]
1	DCM	92.4	67.5	3.1	21.8
2	CHCl$_3$	99.5	45.7	28.3	25.4
3	CCl$_4$	95.1	53.2	16.3	25.6
4	Methanol	97.3	33.4	50.9	12.9
5	Ethanol	96.6	28.3	39.2	29.1
6	Acetonitrile	97.8	84.1	1.7	11.9
7	Acetone	100	83.7	1.3	15.0

Pyrrole:acetone = 1:1 (mole ratio); catalyst: Al-MCM-41; reaction time: 20 h; catalyst weight = 0.5 g.
[a] Others include trimer **1c** and tetramer **1d**, respectively.

On the other metal ion, viz., Cr, Mn, Fe, Ni and Cu, substituted MCM-41 catalysts, the overall conversions of pyrrole is (Table 2) found to exceed 90%. However, the yields of **1a** varied from 30% (Cu-MCM-41) to a maximum of 47.6% (Mn-MCM-41). The decrease in yields is attributed to low acidity and low surface of M-MCM-41 as compared to Al-MCM-41. The Ni-MCM-41 has provided a maximum dimer **1b** yield (50.3%), which indicates its least acidity (0.160 mmol g^{-1}) which seems to be adequate for dimer formation and which does not promote further macrocyclization towards tetramer formation.

3.3. Effect of solvent

A synergy exists between the molecular sieves and solvents employed for the synthesis of macromolecules. The molecular sieve itself can be viewed as the second solvent, which can selectively extracts the substrate molecules from the bulk solvent depending upon their size and hydrophobic nature. Our investigations have shown that non-polar chlorinated solvents, viz., CHCl$_3$, CH$_2$Cl$_2$ and CCl$_4$, which are hydrophobic in nature, promote the formation of **1a** as compared to hydrophilic polar solvents. The aprotic solvents like acetone and acetonitrile favors **1a** formation in comparison to the protic solvents like methanol and ethanol as shown in Table 2.

Table 3
Reactant molar ratio variation on the synthesis of meso-octamethyl calix(4)pyrrole (**1a**)

Entry	Pyrrole:acetone	Conversion of pyrrole (%)	Yield of product (wt%)		
			Calix(4)pyrrole (**1a**)	Dimer (**1b**)	Others[a]
1	1:1	92.4	67.5	3.1	21.8
2	1:1.5	100	82.3	5.8	11.9
3	1:∞	100	88.4	3.0	8.6

Solvent = DCM (20 ml); reaction time: 20 h; catalyst: Al-MCM-41; catalyst weight = 0.5 g.
[a] Others include trimer **1c** and tetramer **1d**, respectively.

Table 4
Si/Al ratio variation effects in Al-MCM-41 on synthesis of meso-octamethyl calix(4)pyrrole (**1a**)

Entry	Al-MCM-41 (Si/Al)	Conversion of pyrrole (%)	Yield of product (wt%)		
			Calix(4)pyrrole (**1a**)	Dimer (**1b**)	Others[a]
1	15	92.4	67.5	3.1	21.8
2	30	98.7	43.7	16.8	38.2
3	45	97.2	35.3	18.4	43.4
4	0	99.4	1.8	94.8	2.8

Reaction time: 20 h; catalyst weight: 0.5 g; solvent = DCM (20 ml), molar ratio: 1:1; reaction time = 20 h.

[a] Others include trimer **1c** and tetramer **1d**, respectively.

3.4. Effect of reactant molar ratio

The effect of molar ratio of pyrrole to acetone has been studied in 1:1 to 1:∞ range. It has been observed that by increasing the molar ratio of pyrrole to ketone, the yield of **1a** increased from 67.5 to 88.3% with simultaneous increase in conversion of pyrrole from 92.8 to 100% (Table 3). At lower stoichiometric ratio of pyrrole and acetone, other products like linear dimmer **1b**, trimer **1c** and tetramer **1d** formation is favoured. But as the molar ratio is increased, the formation of other products has shown a declining trend favoring the formation more cyclic tetramer **1a**.

3.5. The effect of Si/Al ratio in Al-MCM-41

We also report the effect of Al substitution in the framework of MCM-41 on the macrocyclization towards calix(4)pyrrole **1a**. This study is believed to be of great interest because, from a practical point of view, the potential application of MCM-41 is very likely to involve the presence of aluminum in the materials generally improves the acidity and ion exchange capability which is crucial for the acid catalysis. An increase in Al content in the framework of MCM-41 enhances the acidity and has accordingly a strong effect on macrocyclization, viz., enhanced yield of **1a** as shown in Table 4. It is interesting to note that Si/Al ratio has no significant influence on conversion of pyrrole. Which clearly indicates that the framework acidity is quite adequate for condensation of pyrrole and acetone to corresponding dimer **1b** (viz., 94.8%) (entry 4, Table 4) and is not sufficient for further cyclization to tetramer as negligible amounts of calix(4)pyrrole **1a** only formed. By decreasing the Si/Al from 45 to 15, the other products including trimer **1c** and linear tetramer **1d** further reacts with pyrrole to the corresponding calix(4)pyrrole **1a**, respectively.

4. Conclusions

Al-MCM-41 is found to be the most effective catalyst for the macrocyclization reactions and the yield of macrocycles could be drastically improved by incorporating Co ion iso-

morphously in the framework. Further, substitution of such small amount in the framework made the catalyst more resistant towards leaching in comparison to various impregnated catalysts. Shape selectivity and acidity were found to be the crucial parameters for this macrocyclization reaction.

References

[1] P.A. Gale, J.L. Sessler, V. Kral, Chem. Commun. (1998) 1.
[2] D. Jacoby, C. Floriani, A. ChiesiVilla, C. Rizzoli, J. Chem. Soc. Chem. Commun. (1991) 220.
[3] D. Jacoby, C. Floriani, A. ChiesiVilla, C. Rizzoli, J. Chem. Soc. Chem. Commun. (1991) 790.
[4] T.G. Levitskaia, M. Marquez, J.L. Sessler, J.A. Shriver, T. Vercouter, B.A. Moyer, Chem. Commun. 17 (2003) 2248.
[5] F.P. Schmidtchen, Org. Lett. 4 (2002) 431.
[6] H. Miyaji, W. Sato, J.L. Sessler, Angew. Chem. Int. Ed. 39 (2000) 1777.
[7] P.A. Gale, J.L. Sessler, V. Kral, V. Lynch, J. Am. Chem. Soc. 118 (1996) 5140.
[8] P.A. Gale, P. Anzenbacher Jr., J.L. Sessler, Coord. Chem. Rev. 222 (2001) 57.
[9] J.L. Sessler, P.A. Gale, in: K.M. Kadish, K.M. Smith, R. Guilard (Eds.), Porphyrin Hand Book, vol. 6, Calixpyrroles: Novel Anion and Neutral Substrate Receptors, Academic Press, San Diego, CA, 1999, p. 257.
[10] C.L. Ratson, J.L. Atwood, P.J. Nicholas, I.B.N. Sudria, Chem. Commun. (1996) 2615.
[11] J.S. Beck, C. Vartuli, W.J. Roth, M.E. Leonowicz, C.T. Kresge, K.D. Schmitt, C.t.-W. Chu, D.H. Olson, E.W. Sheppard, S.B. McCullen, J.B. Higgins, J.L. Schlenker, J. Am. Chem. Soc. 114 (1992) 10834.
[12] (a) A. Corma, Chem. Rev. 97 (1997) 2373;
(b) A. Sayari, Chem. Mater. 8 (1996) 1840.
[13] T. Maschmeyer, F. Rey, G. Shankar, J.M. Thomas, Nature 378 (1995) 159.
[14] R.A. Sheldon, Curr. Opin. Solid State Mater. Sci. 1 (1996) 101.
[15] N. Igarashi, K.A. Koyano, Y. Tanaka, S. Nakata, K. Hashimoto, T. Tatsumi, Microporous Mesoporous Mater. 59 (2003) 43.
[16] D.E. De Vos, M. Dams, B.F. Sels, P.A. Jacobs, Chem. Rev. 102 (2002) 3615.
[17] P. Selvam, S.K. Bhatia, C.G. Sonwane, Ind. Eng. Chem. Res. 40 (2001) 3237.
[18] M. Ziolek, I. Nowak, B. Kilos, I. Sobczak, P. Decyk, M. Trejda, J.C. Volta, J. Phys. Chem. Solids 65 (2004) 571.
[19] V. Hulea, F. Fajula, J. Catal. 225 (2004) 213.
[20] D. 20, G. Bruhviler, Calzaferri, Microporous Mesoporous Mater. 72 (2004) 1.
[21] S.K. Jana, T. Kugita, S. Namba, Appl. Catal. A 266 (2004) 245.
[22] M. Radha Kishan, N. Srinivas, K.V. Raghavan, S.J. Kulkarni, J.A.R.P. Sarma, M. Vairamani, Chem. Commun. (2001) 2226.
[23] K.V. Raghavan, S.J. Kulkarni, M. Radha Kishan, N. Srinivas, USA patent, no. US6605194 dated 12.08.2003.
[24] M. Radha Kishan, N. Srinivas, S.J. Kulkarni, M. Rama Krishna Prasad, K.V. Raghavan, Stud. Surf. Sci. Catal. 135 (2001), 28-O-04.
[25] A. Ortlam, J. Rathousky, G. Schulz-Ekloff, G. Zukal, Microporous Mater. 6 (1996) 171.
[26] A. Tuel, Microporous Mesoporous Mater. 27 (1999) 151.

[27] A.J.J. Arnold, J.P.M. Niederer, T.E.W. Nießen, W.F. Hölderich, Microporous Mesoporous Mater. 28 (1999) 353.

[28] S. Suvanto, J. Hukkamäki, T.T. Pakkanen, T.A. Pakkanen, Langmuir 16 (2000) 4109.

[29] S. Prabhakar, M. Radha Kishan, S.P. Mirza, K.V. Raghavan, M. Vairamani, Rapid Commun. Mass Spectrom. 18 (2004) 2077.

[30] B.F.G. Johnson, S.A. Raynor, D.S. Shephard, T. Mashmeyer, J.M. Thomas, G. Sankar, S. Bromley, R. Oldroyd, L. Gladden, M.D. Mantle, Chem. Commun. (1999) 1167.

[31] R.W. Weber, K.P. Moller, C.T.O'. Conner, Microporous Mesoporous Mater. 35 (2000) 533.

[32] J.L. Blin, C. Otjacques, G. Herrier, B.L. Su, Int. J. Inorg. Mater. 3 (2001) 75–86.

[33] M. Morey, H. Davidson, H. Eckert, G. Stucky, Chem. Mater. 8 (1996) 486.

[34] S. Lim, D. Ciuparu, C. Pak, F. Dobek, Y. Chen, D. Harding, L. Pfefferle, G. Haller, J. Phys. Chem. B 107 (2003) 11048.