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Lewis acid-containing mesoporous molecular sieves as solid efficient catalysts for solvent-free Mukaiyama-type aldol condensation

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Abstract

The activity of the titanium mesoporous molecular sieve Ti-MCM-41 and amorphous Ti-silicate materials for carbon–carbon bond formation in the Mukaiyama aldol-type reaction between benzaldehyde and methyl trimethylsilyl dimethylketene acetal was studied and the reaction network established. Only tetrahedral $\mathrm{Ti^{IV}}$ is catalytically active, where $\mathrm{Ti^{VI}}$ and highly dispersed TiO_2 are not active or only slightly active for the Mukaiyama reaction and have no effect on selectivity. Whereas in Ti-zeolites only a some of the active sites are accessible to reactants, all of them are accessible in Ti-MCM-41. The structured Ti-MCM-41 offers a clear catalytic advantage over amorphous Ti-silicalites. Water has a negative effect on catalytic activity and selectivity, and catalyst preactivation and hydrophobicity play an important role in the final catalytic behavior. The influence of different solvents on conversion was explored.

Keywords: Lewis acid catalyst; Mukaiyama reaction; Aldol-type condensation; Heterogeneous catalysis; Mesoporous molecular sieves; Ti-MCM-41

1. Introduction

Developing active and selective solid catalysts for the formation of new carbon–carbon bonds is a matter of considerable interest. Brønsted solid acids are used commercially to catalyze reactions such as alkylation, dimerization, acylations, etc. [1–4]. Meanwhile, solid bases such as alkaline-substituted zeolites, alkaline-earth oxides [5,6], hydrotalcites [7–11], and ALPONs [12,13] have been used successfully for nucleophillic reactions involving carbanion-type species for the formation of new carbon–carbon bonds through aryl-ring side-chain alkylation, Knoevenagel and aldol condensations, and Michael additions, among others. Finally, Lewis acids are also largely used as catalysts for alkylation, polymerization, Friedel–Crafts, and acylation, but also for aldol-type condensations and related reactions [14]. For instance, Lewis acids derived from Ti, Sn, Zn, Al, and rare earths, among others, have been used within stoichiometric or catalytic amounts for the preparation of crossed aldols by the reaction of silyl enol ethers or silyl ketene acetals with aldehydes and ketones, known as the Mukaiyama aldol condensations or Mukaiyama-type aldol condensation [15–19]. Some heterogeneous catalysts, such as clays, acid polymers, amorphous silica–alumina, and metal zeolites (ZSM-5 and Beta), have been reported to be active for this reaction [20–25]. Especially relevant for us was the work of Kumar et al. [26–28], who found that TS-1 and Ti-Beta were oxophilic Lewis catalysts able to carry out the Mukaiyama reaction in the absence of H_2O. The similarity in the activities of TS-1 and Ti-Beta led the authors to speculate that the reaction was mainly occurring on the external surface of the zeolite, and, consequently, it may very well be that only a fraction of the potential active sites was accessible to reactants. If this is the case, it seems to us that MCM-41 mesoporous materials could be better catalysts than metal zeolites for the Mukaiyama reactions, provided the metal Lewis acid site in the mesoporous metal silicate is tetrahedrally coordinated and isolated on the walls. Thus, in the present work we show that well-prepared

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Ti-MCM-41 catalysts [29] are more active than the corresponding ZSM-5 and Beta zeolites for the Mukaiyama reaction between benzaldehyde (**1**) and methyl trimethylsilyl dimethylketene acetal (**2**), while giving very high selectivity for the desired condensation product (**3a**, **3b**). We show the effect of catalyst activation and its hydrophobicity on activity. The reaction has been studied with various solvents and under solvent-free conditions. Finally, the influence of water and the hydrophobicity of the catalyst on activity and selectivity is also presented.

2. Experimental

2.1. Materials

Samples of Ti-zeolites and Ti-MCM-41 were prepared in the following way. TS-1 zeolite was synthesized by a method based on the wetness impregnation of an amorphous SiO_2–TiO_2 solid with a solution of tetrapropylammonium hydroxide [30], Ti-Beta zeolite was obtained in fluoride media with a previously reported procedure [31], and Ti-MCM-41 catalysts were prepared from a gel with the following molar composition [29]: SiO_2:x $Ti(OEt)_4$:0.12 CTABr:0.26 TMAOH:24.3 H_2O, where x is varied between 0 and 0.08. CTABr and TMAOH correspond to cetyltrimethylammonium bromide (from Aldrich) and tetramethylammonium hydroxide (from Aldrich), respectively. The silica source was Aerosil-200, from Degussa, and $Ti(OEt)_4$ was supplied by Alpha Products.

2.2. Surface silylation

Typically surface silylation was performed as follows [32]. One gram of calcined Ti-MCM-41 was autogassed at 300 °C for 2 h. Then 10 g of solution containing 1.34 g of hexamethyldisilazane (obtained from ABCR GmbH & Co) in toluene was added under nitrogen on the dehydrated Ti-MCM-41. The resulting mixture was refluxed under an inert atmosphere at 120 °C for 2 h. Then the silylated sample was filtrated and washed with 250 ml of toluene.

2.3. Ti grafting MCM-41 sample

Ti/MCM-41 grafted samples were obtained with a previously described procedure [33], with the use of titanocene dichloride as a source of titanium and triethylamine to activate the surface silanols of the MCM-41 sample.

2.4. Characterization of materials

2.4.1. IR spectroscopy

Experiments were carried out in a Nicolet FT-IR 710 spectrometer, and the samples were heated at 400 °C and 10^{-4} Torr.

2.4.2. UV–vis spectroscopy

All of the analysis was carried out in a Varian Cary 5 with barium sulfate as an internal standard.

2.4.3. Raman spectroscopy

Raman spectra were collected with a Renishaw inVia Raman spectrometer equipped with a Leica DMLM microscope and a 514-nm Ar^+ ion laser as an excitation source. A ×50 objective of 0.37-mm optical length was used to focus the depolarized laser beam on a spot of about 2 µm in diameter, with a laser power at the sample of 2.0 mW. The Raman scattering was collected with a CCD array detector, in the 50–2000 cm^{-1} spectral region with a resolution of 2 cm^{-1}. Each reported spectrum is the average of 20 scans with an exposure time of 10 s each.

2.5. Catalytic reaction

The Mukaiyama reaction between benzaldehyde (**1**) and methyl trimethylsilyl dimethylketene acetal (**2**) was carried out in a two-necked glass batch reactor under a N_2 atmosphere. Before the reaction, the calcined catalyst was activated in vacuum overnight at 250 °C. Benzaldehyde (106 mg; 1 mmol) was placed in another flask, together with 280 mg of methyl trimethylsilyl dimethylketene acetal (1.5 mmol) and 170 mg of n-dodecane (1 mmol) as an internal standard, and 2 ml of anhydrous dichloromethane. The reaction mixture was stirred for a few minutes at ambient temperature (20–25 °C), and an aliquot was analyzed and considered the time zero value. The reaction solution was added to the preactivated catalyst, and the mixture was stirred magnetically for 24 h at the reflux temperature of the solvent (40 °C). Six aliquots of 25 µl were withdrawn at different reaction times and subsequently analyzed by gas chromatography with a 5% phenylsilicone column (ZB-5) 25 m in length.

3. Results and discussion

3.1. Thermally catalyzed reaction

When silyl ketene acetal (**2**) is reacted with benzaldehyde (**1**) at the reflux temperature of CH_2Cl_2 (40 °C) in a 1.5:1 mol ratio in the absence of any catalyst, some thermal conversion occurs, and a 6% yield of the corresponding β-hydroxy ester (**3a**, **3b**) is formed after 24 h (Table 1), indicating that the homogeneous reaction is slow at this temperature. When the reaction occurs in the presence of well-crystallized pure silica MCM-41 with a BET surface area of 858 $m^2\ g^{-1}$ (Table 2), under the same reaction conditions, the yield of the condensation product increases to 20% (Table 1). The result suggests that the silanol groups, in spite of their low acidity, are able to catalyze the reaction, and/or the large adsorption capacity of the MCM-41 sample (concentration effect) produces an increase in the reaction rate of the

Table 1
Silanol reactivity for the Mukaiyama-aldol type reaction[a]

Catalyst	Conversion of (**1**) (mol%)	Selectivity (mol%)		Yield of (**3a**, **3b**) (mol%)
		(**3a**, **3b**)	Others	
None	8	75	25	6
Aerosil	9	89	11	8
Silica gel (GE0050)	13	92	8	12
MCM-41	20	95	5	19

[a] Reaction conditions: 1 mmol PhCHO, 1.5 mmol silyl ketene acetal, 2 ml CH_2Cl_2, 0.025 g catalyst activated (250 °C, vacuum, overnight), 24 h, at reflux temperature of the solvent.

Table 2
Physical properties of some mesoporous molecular sieves[a]

Catalyst	TiO_2 (wt%)	BET area ($m^2\,g^{-1}$)	Total pore volume ($cc\,g^{-1}$)	Pore size (Å)
MCM-41	0	858	1.08	39.6
Ti-MCM-41 (0.4)	0.4	872	1.01	39.0
Ti-MCM-41 (0.7)	0.7	920	0.99	39.6
Ti-MCM-41 (1.0)	1.0	950	1.02	39.2
Ti-MCM-41 (2.3)	2.3	900	0.96	39.2
Ti-MCM-41 (2.7)	2.7	1065	1.01	39.5
Ti-MCM-41 (4.4)	4.4	915	0.98	39.0
Ti-MCM-41 (5.0)	5.0	956	0.97	39.2
Ti-MCM-41 (8.7)	8.7	926	0.98	39.3
Ti-MCM-41 (11.6)	11.6	833	1.02	39.0
2Ti/MCM-41[b]	2.8	912	1.03	40.2
5Ti/MCM-41[b]	5.1	1020	1.06	39.5

[a] All materials synthesized in ITQ.

[b] Titanium incorporated to the mesoporous molecular sieve via grafting following the procedure described in the synthesis of the materials.

bimolecular Mukaiyama condensation reaction. We have analyzed these hypotheses by carrying out the reaction in the presence of Aerosil-200 (Degussa; BET = 200 $m^2\,g^{-1}$; Table 3) with external and accessible sylanol groups, and with amorphous silica GE0050 (Scharlau) with a relatively large BET surface area (500 $m^2\,g^{-1}$). The results obtained (Table 1) show a lower activity for the aerosil or the amorphous silica than for the MCM-41 material, despite the fact that the number of silanols in the amorphous silicas is not that different from that of MCM-41 (Fig. 1). This suggests that the higher activity of MCM-41 should be better related to the concentration effect achieved with the very high surface area ordered silica. Our observation agrees with the fact that pure silica MCM-41 is active in catalyzing the condensation of silyl ketene acetals with aldehydes [34].

3.2. *Lewis acid catalysis: reaction network*

The activity of the pure silica MCM-41 strongly increased when a Lewis acid such as Ti was incorporated at the walls during the synthesis. Indeed, the UV–visible spectrum of the Ti-MCM-41 catalyst shows a charge transfer band at ~210 nm (Fig. 2), which is indicative of the presence of tetrahedrally coordinated Ti. This Ti^{IV} can act as a Lewis acid, and it is known that homogeneous and heterogeneous Lewis acids can catalyze the Mukaiyama-aldol reaction of silyl ketene acetals with carbonyl compounds [28,35].

Table 3
Physical properties of some micropore catalysts

Catalyst	Si/Ti	TiO_2 (wt%)	BET area ($m^2\,g^{-1}$)
Aerosil 200	0	0	200
Silica gel (Ge0050)	0	0	500
Ti-SAM (ENI)	36	3.2	798
TS-1[a]	50	2.6	–
Ti-Beta[a]	56	2.3	455

[a] Zeolites synthesized in the ITQ following the procedure described in the experimental part.

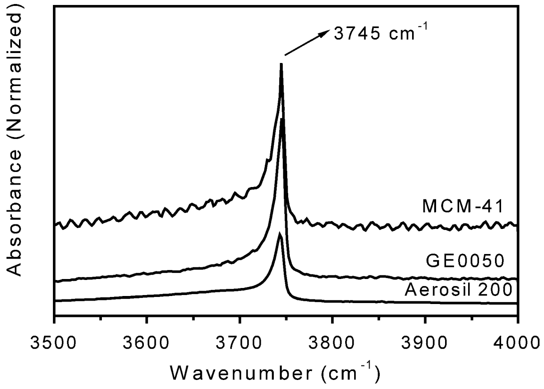


Fig. 1. IR spectra of different pure siliceous molecular sieves.

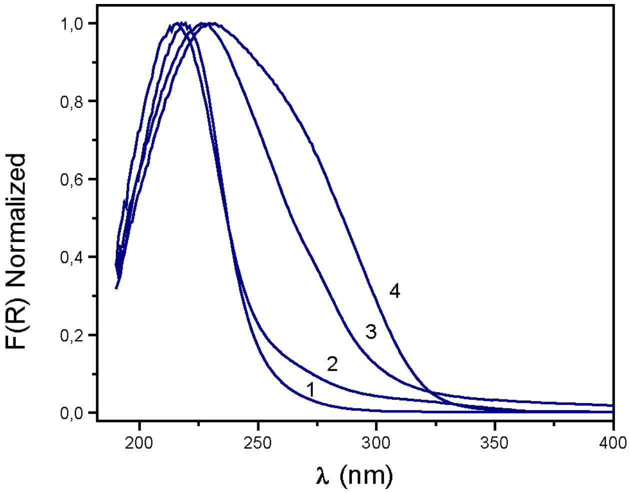
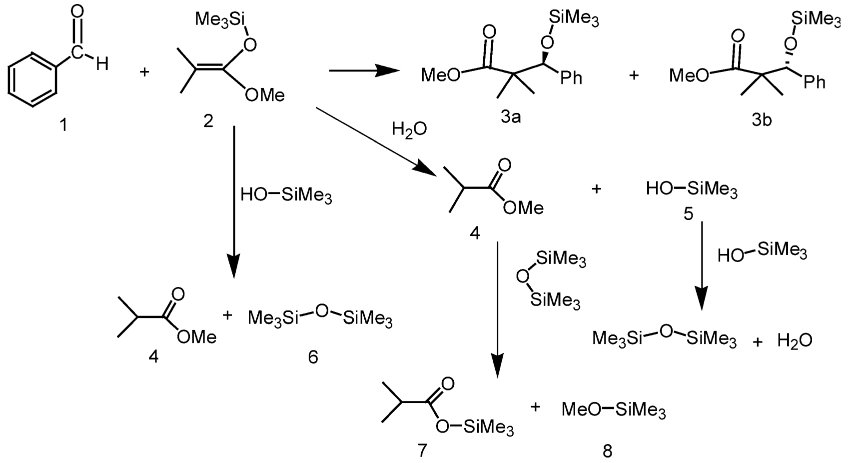


Fig. 2. UV–vis spectra of titanium containing catalysts: (1) TS-1, (2) Ti-Beta, (3) Ti-MCM-41 (2.7), (4) Ti-SAM (ENI).

The products obtained during the reaction of silyl ketene acetal (**2**) with benzaldehyde (**1**) in the presence of Ti-MCM-41 were methyl 2,2-dimethyl-3-phenyl-3-(trimethylsilyloxy)propanoic acid methyl ester (**3a**, **3b**), 2-methyl-propanoic acid methyl ester (**4**), 2-methyl-propanoic acid trimethylsilyl ester (**7**), trimethylhydroxysilane (**5**), and hexamethyldisiloxane (**6**). When the yields of the different products were plotted versus total conversion (Fig. 3), it was possible to see that in addition to the very main aldol condensation product, minor amounts of 2-methyl-propanoic acid methyl ester



Scheme 1. Reaction network for Mukaiyama's reaction between benzaldehyde and methyl trimethylsilyl dimethylketene acetal on Ti-molecular sieves.

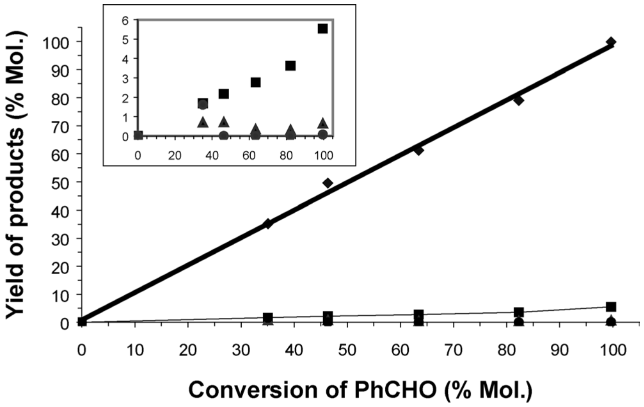


Fig. 3. Yield of products vs conversion of benzaldehyde for the Mukaiyama aldol-type reaction. Reaction conditions: 1 mmol PhCHO, 1.5 mmol silyl ketene acetal, 2 ml CH_2Cl_2, 0.025 g activated catalyst (at 250 °C, in vacuum, overnight) at reflux temperature of the solvent during 24 h. (◆) Methyl-2,2-dimethyl-3-phenyl-3-(trimethylsilyloxy)propanoic acid methyl ester (**3a**, **3b**), (■) hexamethyldisiloxane (**6**), (▲) 2-methyl-propanoic acid trimethylsilyl ester (**7**), (●) 2-methyl-propanoic acid methyl ester (**4**).

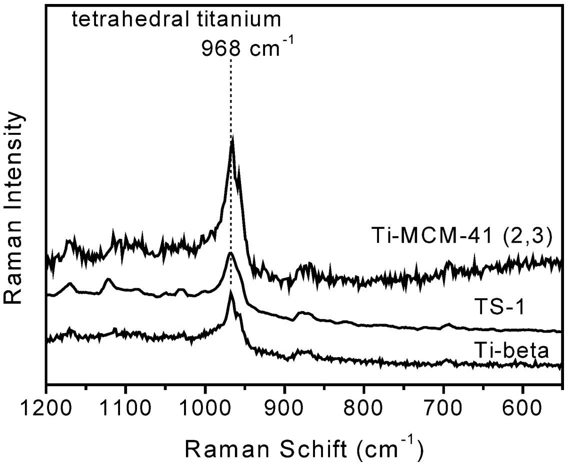


Fig. 4. Raman spectra of titanium containing catalysts.

(**4**) and trimethylhydroxysilane (**5**) were also formed as primary products, from the hydrolysis of the silyl ketene acetal by H_2O present with the reactants or by H_2O remaining adsorbed on the solid, despite the fact that the sample was preactivated in vacuum (10^{-1} Torr) at 250 °C. In addition to the hydrolysis products, 2-methyl-propanoic acid trimethylsilyl ester (**7**), and trimethylmethoxysilane (**8**) were observed as secondary products, and hexamethyldisiloxane (**6**) was a primary plus secondary product, and their formation can occur through the reaction network presented in Scheme 1.

Nevertheless, it should be noted that in all experiments carried out with Ti-MCM-41, selectivity for the β-hydroxyester (aldol) was always above 95%.

3.3. *Accessibility of Ti-sites in MCM-41*

It was said before that mesoporous Ti-molecular sieves could offer diffusional advantages with respect to Ti-zeolites. In order to check this, two highly crystalline Ti-zeolite samples (TS-1 and Ti-Beta) were prepared. UV–visible spectroscopy (Fig. 2) shows a well-defined adsorption band at ~210 nm, which can be associated with tetrahedrally coordinated framework titanium [36]. It should be pointed out that extraframework TiO_2 was not detected by Raman spectroscopy in Ti-MCM-41 or in the two Ti-zeolites (Fig. 4). When the activity of Ti-MCM-41 was compared with that of TS-1 and Ti-Beta (Table 4 and Fig. 5), the former was much more active, as judged from the turnover frequency (TOF), which we calculated by dividing the initial rate by the moles of Ti in the catalyst, which made it 4 times larger.

The above results support the hypothesis that probably not all of the Ti sites in the zeolites but only those close to the external surface are able to react [26,28], whereas in the case of Ti-MCM-41 the larger pore diameter allows a better diffusivity of the reactants, which can reach the Ti sites located at the pore walls. Nevertheless, the above observations do not guarantee that all of the Ti sites in Ti-MCM-41 are accessible through the pores, since some Ti^{IV} could be buried within the walls, making it inaccessible to reactants. Thus, in order to clarify this point, we prepared a sample of Ti on MCM-41 (2Ti/MCM-41) by anchoring Ti to the walls of a

Table 4
Activity of different titanium silicates for the Mukaiyama-aldol type reaction of benzaldehyde and methyl trimethylsilyl dimethylketene acetal[a]

Catalyst	TiO_2 (wt%)	Conversion of (**1**) (mol%)	Selectivity to the products (mol%)		Yield (**3a**, **3b**) (mol%)	TON at 5 h	TOF (h^{-1})
			(**3a**, **3b**)	Others			
TS-1[b]	2.6	6	83	17	5	4	1
Ti-Beta[b]	2.3	37	100	0	37	37	7
Ti-MCM-41 (2.3)	2.3	77	100	0	77	48	10
2Ti/MCM-41[c]	2.8	72	99	1	71	61	12
5Ti/MCM-41[c]	5.1	99	99	1	98	29	6
Ti-SAM (ENI)[b]	3.2	64	98	2	63	17	3

[a] Reaction conditions: 1 mmol PhCHO, 1.5 mmol silyl ketene acetal, 2 ml CH_2Cl_2, 0.025 g of activated catalyst (at 250 °C, in vacuum, overnight) at reflux temperature of the solvent during 24 h.

[b] With 2 h of activation.

[c] With Ti/MCM-41 grafted.

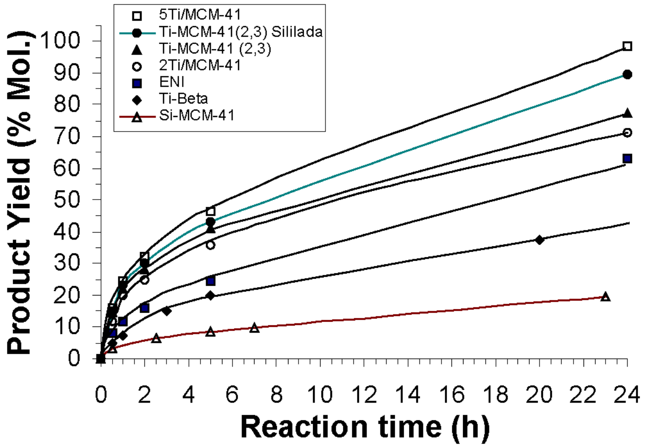
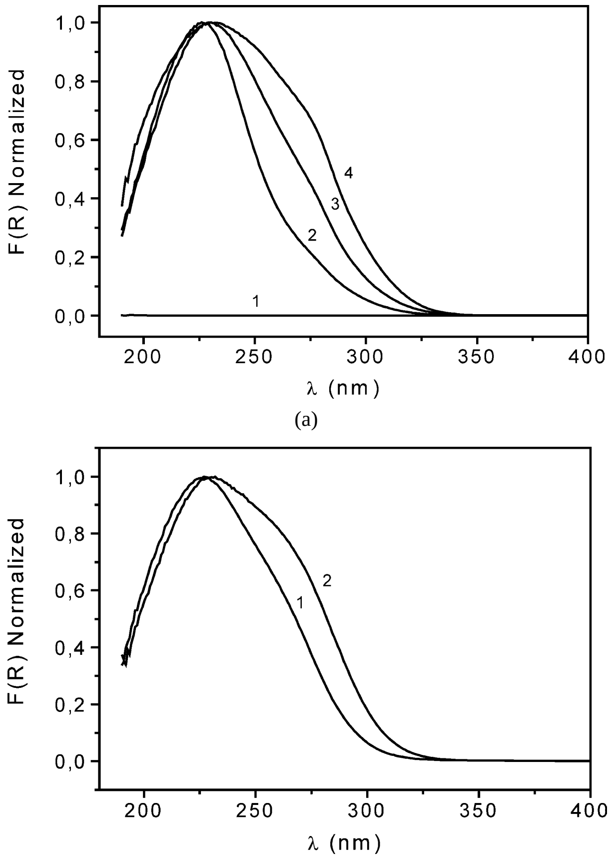


Fig. 5. Yield of the condensation product vs reaction time for Mukaiyama reaction of PhCHO and silyl ketene acetal over titanium mesoporous molecular sieves. Reaction conditions: 1 mmol PhCHO, 1.5 mmol silyl ketene acetal, 2 ml of CH_2Cl_2, 0.025 g of activated catalyst (at 250 °C, in vacuum, overnight) at reflux temperature of the solvent (40 °C) during 24 h.



(a)

(b)

Fig. 6. UV–vis spectra for Ti-MCM-41 samples with different amount of TiO_2. (a) Titanium incorporated to the mesoporous molecular sieve via synthesis: (1) MCM-41, (2) Ti-MCM-41 (2.3), (3) Ti-MCM-41 (5.0), (4) Ti-MCM-41 (11.6); (b) titanium incorporated via grafting: (1) 2Ti/MCM-41, (2) 5Ti/MCM-41.

pure silica sample of MCM-41 [33]. Note that spectroscopic characterization shows that in this sample the Ti atoms are also tetrahedrally coordinated (Fig. 6b). The aldol condensation activity of 2Ti/MCM-41, per atom of Ti, per hour (i.e., TOF), is very close to that of the Ti-MCM-41 (2.3) (see Table 4 and Fig. 5), indicating that most, if not all, of Ti sites in Ti-MCM-41 are accessible through the pores.

Another important point about mesoporous molecular sieve catalysts is the potential catalytic benefit of the very regular pores present in these materials, compared with fully amorphous mesoporous materials. In the case of the Mukaiyama condensation with solid titanium catalysts, we have also carried out the reaction with an amorphous mesoporous Ti-catalyst (SAM) [37]. Characterization of Ti sites in this sample (Fig. 2) shows that they are tetrahedrally coordinated. Activity results (Table 4) indicate that Ti-MCM-41 is more active than the amorphous material, showing the benefit of the regular pore dimensions in MCM-41. The reason for this can be related with a better structure of the Ti in Ti-MCM-41 due to the presence of the surfactant, or to the presence of bottlenecks at the pores in the case of the amorphous material that can limit the accessibility of the reactants to some Ti sites.

3.4. *Influence of Ti site concentration (Ti-MCM-41) on reactivity*

We have attempted to maximize the number of Ti Lewis active sites by introducing further amounts of Ti during the

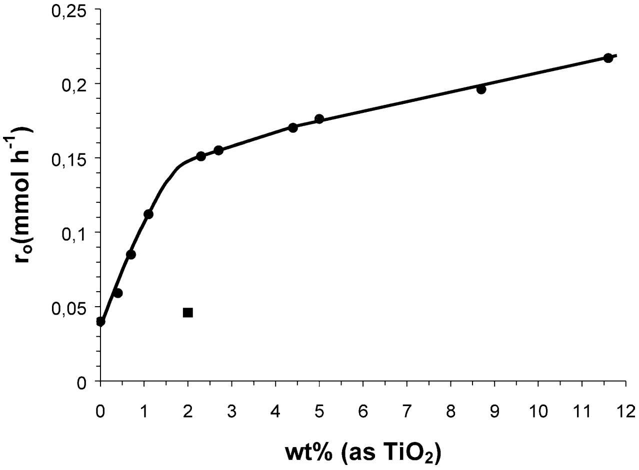


Fig. 7. Initial rate (r_0) vs wt% of TiO_2 for Mukaiyama reaction of PhCHO and silyl ketene acetal over titanium mesoporous molecular sieves. Reaction conditions: 1 mmol PhCHO, 1.5 mmol silyl ketene acetal, 2 ml of CH_2Cl_2, 0.025 g of activated catalyst (at 250 °C, in vacuum, overnight) at reflux temperature of the solvent during 24 h. (●) Ti-MCM-41 samples with different wt% of titanium (as TiO_2); (■) Si-MCM-41 with impregnated titanium.

synthesis of the titanosilicate mesoporous molecular sieve. If all of the Ti atoms were in the form of isolated and tetrahedrally coordinated sites, then the activity should be directly proportional to the Ti content. Thus, if we plot initial reaction rate versus Ti content in Ti-MCM-41 samples, we can see (Fig. 7) that when the Ti concentration increases above 1–2% not all Ti atoms are in the form of active sites for the Mukaiyama condensation. A detailed characterization of the different catalysts by UV–visible and Raman spectroscopy (Figs. 6 and 8) shows that for Ti-MCM-41 samples with Ti contents larger than ~1–2 wt%, in addition to the ~210-nm UV band associated with Ti^{IV}, absorption bands at ~270 and ~320 nm appear, indicating the presence of Ti–O–Ti pairs and even TiO_2. When the Ti content increases further, the relative intensity of the higher frequency bands increases. Raman spectroscopy confirms the presence of extraframework TiO_2 (bands at 450 and 610 cm^{-1} assigned to rutile clusters and four bands at 144, 397, 518, 641 cm^{-1} assigned to anatase particles) [38,39] in the samples with larger Ti content. Our results indicate that octahedrally coordinated Ti and TiO_2, even if highly dispersed (in several samples TiO_2 was not detected by XRD, but only by Raman and UV spectroscopies), are not catalytically active, or at least they are much less active than isolated Ti^{IV} for the Mukaiyama condensation between benzaldehyde and silyl ketene acetals. Results from Table 5 show, however, that the presence of extraframework titanium does not affect the selectivity of the catalyst. To further confirm this, 2 wt% Ti (in the form of TiO_2) was impregnated on pure silica MCM-41 and, after calcination at 500 °C, was tested under the same reaction conditions as described above. The activity result is given in Fig. 7, confirming that extraframework TiO_2 has very low activity.

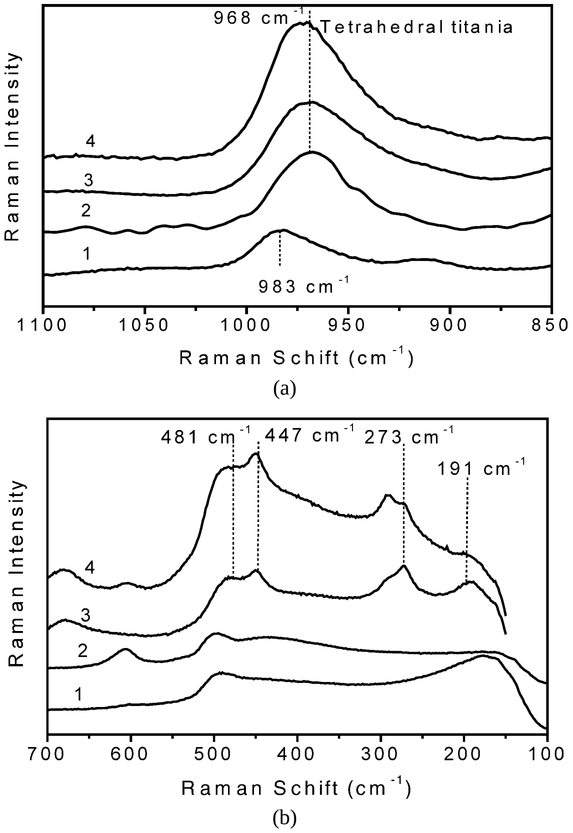


Fig. 8. Raman spectra of titanium containing mesoporous molecular sieves. (a) Region of the spectra where appears characteristic tetrahedral band for titania: (1) MCM-41, (2) Ti-MCM-41 (2.3), (3) Ti-MCM-41 (5.0), (4) Ti-MCM-41 (11.6); (b) bands assigned to octahedral titania: (1) MCM-41, (2) Ti-MCM-41 (2.3), (3) Ti-MCM-41 (5.0), (4) Ti-MCM-41 (11.6).

Table 5
Influence of the titanium incorporation into MCM-41 on the activity and selectivity for the Mukaiyama reaction[a]

TiO_2 (wt%)	Conversion of (**1**) (mol%)	Selectivity (mol%)
2.3	26	100
5.0	63	100
11.6	70	100
2.3[b]	65	100
5.0[b]	81	100
11.6[b]	82	100

[a] Reaction conditions: 2 mmol PhCHO, 3 mmol silyl ketene acetal, 2 ml CH_2Cl_2, 0.035 g of Ti-MCM-41 activated (250 °C, vacuum, 2 h), 7 h of reaction at reflux temperature of the solvent.

[b] Reaction made with 0.075 g of catalyst.

In conclusion, higher conversions with very high selectivity for the Mukaiyama reaction can be obtained with Ti-MCM-41 catalysts containing large amounts (11.6 wt% TiO_2) of Ti. In this case only a part of the Ti, that is, isolated framework Ti^{IV}, is active, whereas the extraframework TiO_2 has little if any effect on reactivity. With this Ti-MCM-41 sample, the activity per weight of titanosilicate is 4 times higher than for the most active Ti-Beta catalyst at the reflux temperature of CH_2Cl_2 (40 °C).

Table 6
Effect of the catalyst activation for the Mukaiyama reaction[a]

Ti-MCM-41 activation	CH_2Cl_2 (ml)	Time (h)	Conversion of (**1**) (mol%)	Selectivity (mol%)		Hydrolysis product yield (mol%)		
				(**3a**, **3b**)	Others	(**6**)	(**4**)	(**7**)
Yes	1	14	83	99	1	3	8	4
No	1	23	67	100	0	3	22	3
Yes	0.25	4	84	99	1	3	7	1
No	0.25	4	78	99	1	0	1	1
Yes	0.5	5	57	99	1	2	13	2
No	0.5	5	49	100	0	2	18	3

[a] Reaction conditions: 0.02 g of Ti-MCM-41 (2.3 wt% TiO_2), 1 mmol of PhCHO, 1.5 mmol of silyl ketene acetal, toluene as solvent, reaction made in flask microreactors (2 ml) hermetically closed at 100 °C. Activation of the Ti-MCM-41 samples at 250 °C, in vacuum (10^{-1} mmHg) overnight.

Table 7
Effect of the use of 4A molecular sieves in the Mukaiyama reaction[a]

Ti-MCM-41 (g)	Molecular sieves 4A	Time (h)	Conversion of (**1**) (mol%)	Selectivity (mol%)		Hydrolysis product yield (mol%)		
				(**3a**, **3b**)	Others	(**6**)	(**4**)	(**7**)
0.035	Yes	21.5	69	100	0	4	7	1
0.040	No	21.5	50	100	0	5	9	1
0.100	Yes	22	96	98	2	0	0	0
0.100	No	23	60	100	0	7	11	0

[a] Reaction conditions: Ti-MCM-41 (2.3 wt% TiO_2) activated (at 250 °C, in vacuum, 2 h), 2 mmol of PhCHO, 3 mmol of silyl ketene acetal, 2 ml of anhydrous CH_2Cl_2 at reflux temperature of the solvent.

Table 8
Effect of the silylation of Ti-MCM-41 (2.3 wt% TiO_2) on the catalytic activity of the Mukaiyama reaction[a]

C (wt%)	$Si(Me)_3/SiO_2$	Conversion of (**1**) (mol%)	Selectivity (mol%)		Hydrolysis product yield (mol%)		
			(**3a**, **3b**)	Others	(**6**)	(**4**)	(**7**)
0	0	77	100	0	0	0	0
7.89	0.16	90	100	0	1	0	0

[a] Reaction conditions: 0.025 g of Ti-MCM-41 (2.3 wt% TiO_2) activated (at 250 °C, in vacuum, 2 h), 1 mmol of PhCHO, 1.5 mmol of silyl ketene acetal, 2 ml of CH_2Cl_2, at reflux temperature of the solvent during 24 h.

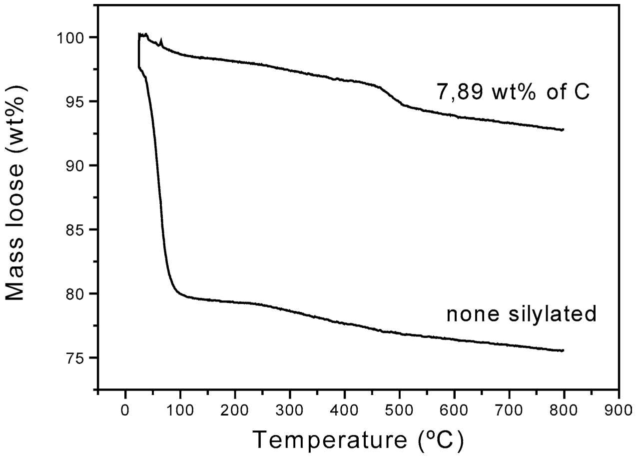
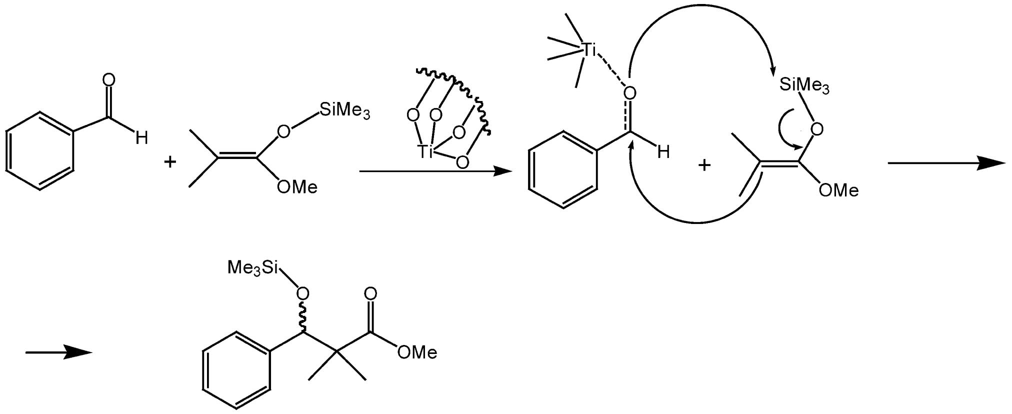


Fig. 9. Thermogavimetric analysis (TG) of titanium containing mesoporous molecular sieves with different silylation degree.

3.5. *Effect of catalyst activation and postsynthesis treatment*

We have seen before that the most important competing reaction was the hydrolysis of the silyl ketene acetals, due to residual amounts of water remaining adsorbed on the catalyst, and/or present in the benzaldehyde, silyl ketene acetal, and solvent. It has also been claimed [26–28,40] that water poisons Ti Lewis acid sites, decreasing the activity of Ti-zeolites. We have confirmed this in the case of Ti-MCM-41, by performing the experiments with a sample exposed to the open atmosphere, without heating under vacuum before use, and with a catalyst sample previously activated in situ at 250 °C under a vacuum of 10^{-1} Torr for 2 h. The results from Table 6 show that water removal by catalyst activation has a positive effect on conversion. Further removal of the water present in reactants and solvent by means of a 4A molecular sieve further increases the activity of the catalyst (Table 7).

Since water has a negative effect on catalyst activity, we decided to prepare hydrophobic Ti-MCM-41 samples with a postsynthesis silylation treatment. This was done with a hexamethyldisilazane treatment, following the procedure given in the Experimental section [32,41]. TG results from Fig. 9 indicate that silylation of the sample causes the total amount of adsorbed water and the water desorption temperature to decrease. Then, when the conversions of silylated and nonsilylated samples are compared (Table 8), we can see that



Scheme 2. A possible mechanism for Mukaiyama's reaction between benzaldehyde and methyl trimethylsilyl dimethylketene acetal on Ti-molecular sieves.

Table 9
Influence of the solvent in the Mukaiyama reaction[a]

Solvent	Conversion of (**1**) (mol%)	Selectivity (mol%)		Hydrolysis product yield (mol%)	
		(**3a**, **3b**)	Others	(**6**)	(**4**)
CH_2Cl_2[b]	90	100	0	5	15
CH_3CN	85	100	0	8	24
Toluene	54	100	0	4	13
$CHCl_3$	35	100	0	19	39
Dioxane	7	100	0	2	8
THF	4	100	0	3	32

[a] Reaction conditions: 1 mmol PhCHO, 1.5 mmol silyl ketene acetal, 2 ml of solvent, 0.02 g of Ti-MCM-41 (2.7 wt% TiO_2) activated (at 250 °C, in vacuum, overnight), at 50 °C during 22 h of reaction.

[b] At reflux temperature of the solvent (40 °C).

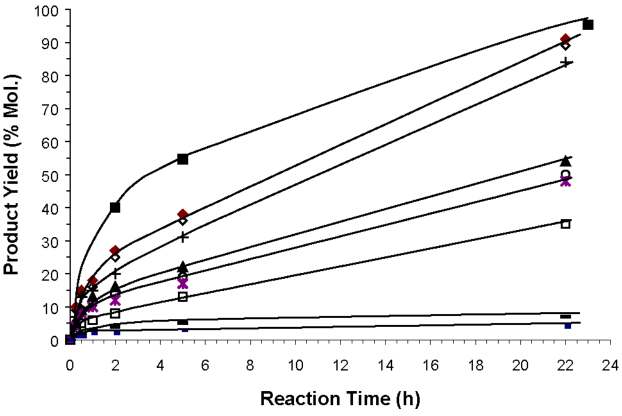


Fig. 10. Yield of the product vs reaction time for Mukaiyama-type reaction using different solvents. Reaction conditions: 1 mmol PhCHO, 1.5 mmol silyl ketene acetal, 2 ml of solvent, 0.020 g of activated Ti-MCM-41(2.7) (at 250 °C, in vacuum, overnight) at reflux temperature of the solvent (40 °C) during 22 h. (■) with no solvent, (◇) with anhydrous CH_2Cl_2, (◆) repeated experiment with dry CH_2Cl_2, (+) with CH_3CN, (▲) with toluene, (○) with dry $CHCl_3$ (4A molecular sieves), (⋇) with dry $CHCl_3$, (□) with not dry $CHCl_3$, (–) with dioxane, (-) with THF.

silylation increases the activity of the catalyst by decreasing the coordination of H_2O with Ti sites.

3.6. *Effect of the solvent*

Mukaiyama's condensations are usually carried out in the presence of solvents [18,41], and in the case of solid catalysts different organic solvents have been used [25,28,34,42,43]. In the case of Ti molecular sieves, a plausible mechanism for the Mukaiyama reaction (see Scheme 2) involves a polarized transition state, and therefore it is not unreasonable to think that the polarity of the solvent can have an effect on the stabilization of the transition state. Then a series of solvents with different polarities have been used; the results are given in Table 9.

Results from Fig. 10 clearly show that when the reaction is carried out in THF and dioxane, the reaction proceeds very slowly. This is probably due to a strong adsorption of the solvent through the oxygen atoms to the Ti sites of

Table 10
Solvent free Mukaiyama aldol-type reaction over Ti-MCM-41 (2.3 wt% TiO_2)[a]

Solvent	Temperature (°C)	Ti-MCM-41 (g)	Time (h)	Conversion of (**1**) (mol%)	Selectivity (mol%)	Hydrolysis product yield (mol%)		
						(**6**)	(**4**)	(**7**)
Yes	100	0.100	5	51	100	0	2	5
No	100	0.100	5	79	100	0	0	1
Yes	100	0.035	24	54	100	4	6	0
No	100	0.035	7	93	100	0	0	0
Yes[b]	40	0.035	21	50	100	5	9	0
No	40	0.035	7	70	99	0	0	0

[a] Reaction conditions: Ti-MCM-41 (2.3 wt% TiO_2) activated (at 250 °C, in vacuum, 2 h), 2 mmol of PhCHO, 3 mmol of silyl ketene acetal, 2 ml of toluene.

[b] With 2 ml of CH_2Cl_2.

Table 11
Solvent free Mukaiyama aldol-type reaction over titanium containing mesoporous molecular sieves[a]

Solvent	TiO_2 (wt%)	Conversion of (**1**) (mol%)	Selectivity (mol%)	Hydrolysis product yield (mol%)		
				(**6**)	(**4**)	(**7**)
Yes	2.3	36	100	0	0	0
No	2.3	78	100	1	0	0
Yes	5.0	37	100	1	10	1
No	5.0	82	100	1	0	0
Yes	11.6	53	100	2	11	1
No	11.6	77	100	0	2	0

[a] Reaction conditions: 0.025 g of activated Ti-MCM-41 (at 250 °C, in vacuum, overnight), 1 mmol of PhCHO, 1.5 mmol of silyl ketene acetal, 2 ml of CH_2Cl_2, at reflux temperature of the solvent during 5 h.

the catalyst. Furthermore, the large difference in activity observed when the reaction is performed in CH_2Cl_2 and $CHCl_3$ is remarkable. In principle, and from the point of view of polarity, we did not expect the large differences observed. Nevertheless, duplication of the experiments confirms the observation. However, to a first approximation, since the water content in $CHCl_3$ is larger than in CH_2Cl_2 and water has a negative effect on conversion, this may influence the difference in activity observed. After the $CHCl_3$ solvent is dried with the use of a dehydrated A zeolite, an improvement in conversion occurs. However, there is still a large conversion difference with respect to CH_2Cl_2. We have no explanation for this observation at this point.

It should be pointed out that the reaction can be carried out with good activity and selectivity without solvent (Tables 10 and 11), and we see no benefit to using any of the above solvents for the Mukaiyama-type condensation reaction with solid catalysts, where the adsorption properties have been controlled by direct synthesis or by postsynthesis treatment, as in the present case.

4. Conclusions

We have demonstrated that well-prepared Ti-MCM-41 is a better solid catalyst for the Mukaiyama-aldol condensation than Ti-zeolites, because of the lower diffusional restriction for reactants and the possibility of introducing isolated Ti^{IV} sites on the walls. The presence of water reduces the catalytic activity and produces the hydrolysis of the silyl ketene acetal. This problem can be minimized by preactivation of the catalyst in situ, by drying of the solvent and, particular, if the catalyst is made more hydrophobic by silylation. A series of solvents has been studied, and the presence of solvent does not improve the catalytic performance. Silylated Ti-MCM-41 can be recycled without any loss in activity or selectivity.

References

[1] H. Yamamoto, A. Hasegawa, K. Ishihara, Angew. Chem. Int. Ed. 40 (2001) 4077.
[2] S. Kobayashi, K. Manabe, S. Limura, Chem. Commun. (2002) 94.
[3] A. Corma, J. Catal. 216 (2003) 298.
[4] S. Kobayashi, Y. Mori, K. Manabe, Tetrahedron 57 (2001) 2537.
[5] A. Hosomi, T. Nakagawa, K. Miura, J. Am. Chem. Soc. 124 (2002) 536.
[6] M.A. Aramendia, V. Borau, C. Jiménez, J.M. Marinas, J.R. Ruiz, F.J. Urbano, Appl. Catal. A 255 (2003) 301.
[7] L.M. Parker, N.B. Milestone, R. Newman, Ind. Eng. Chem. Res. 34 (1995) 1196.
[8] M.A. Drezdon, Inorg. Chem. 27 (1998) 4628.
[9] D. Tichit, B. Coq, CatTech 7 (2003) 206.
[10] M.J. Climent, A. Corma, S. Iborra, K. Epping, A. Velty, J. Catal. 225 (2004) 316.
[11] A. Corma, S. Iborra, M. Mifsud, M. Renz, M. Susarte, Adv. Synth. Catal. 346 (2004) 257.
[12] S. Delsarte, M. Florea, P. Grange, Silicates Industriels 69 (2004) 69.
[13] M.J. Climent, A. Corma, H. García, R. Guil-López, S. Iborra, V. Fornés, J. Catal. 197 (2001) 385.
[14] A. Corma, H. García, Chem. Rev. 103 (2003) 4307.
[15] T. Mukaiyama, K. Manno, K. Narasaka, J. Am. Chem. Soc. 96 (1974) 7503.
[16] Y. Yamamoto, K. Maruyama, K. Matsumoto, J. Am. Chem. Soc. 105 (1983) 6963.
[17] T. Mukaiyama, Angew. Chem. Int. Ed. 16 (1997) 817.
[18] E.M. Carreira, Comprehensive Asymetric Catálisis I–III 3 (1997) 997, chap. 29.1.
[19] M. Lemaire, D. Rechavi, Chem. Rev. 102 (2002) 3467.
[20] S. Kobayashi, Eur. J. Org. Chem. 1 (1999) 15.
[21] L. Teck-Peng, L. Xu-Ran, Tetrahedron 55 (1999) 10789.
[22] C.R. Brindaban, S. Manika, B. Sanjay, Tetrahedron Lett. 34 (1993) 1989.
[23] M.T. Reetz, D. Giebel, Angew. Chem. Int. Ed. 39 (2000) 2498.
[24] H. Matsuhashi, M. Tanaka, H. Nakamura, K. Arata, Appl. Catal. A 208 (2001) 1.
[25] D.L. Gin, W.J. Zhou, W. Gu, Chem. Mater. 13 (2001) 1949.
[26] M. Sasidharan, R. Kumar, J. Catal. 220 (2003) 326.
[27] R. Kumar, M. Sasidharan, Catal. Lett. 38 (1996) 251.
[28] R. Kumar, P. Vincent, K.V. Srinivasan, V.N. Raju, M. Sasidharan, Chem. Commun. (1996) 129.
[29] T. Blasco, A. Corma, M.T. Navarro, J. Pérez-Pariente, J. Catal. 156 (1995) 65.
[30] D.P. Serrano, M.A. Uguina, G. Ovejero, R. Van Grieken, M. Camacho, Micropor. Mater. 4 (1995) 273.
[31] T. Blasco, M.A. Camblor, A. Corma, P. Esteve, J.M. Guil, A. Martinez, J.A. Perdigón-Melón, S. Valencia, J. Phys. Chem. B 102 (1998) 75.
[32] A. Corma, J.L. Jordá, M.T. Navarro, J. Pérez-Pariente, F. Rey, J. Tsuji, Stud. Surf. Sci. Catal. 129 (2000) 169.
[33] J.M. Thomas, G. Sankar, F. Rey, T. Maschmeyer, Nature 378 (1995) 159.
[34] M. Iwamoto, H. Ishitani, Tetrahedron Lett. 44 (2003) 299.
[35] R. Mahrwald, Chem. Rev. 99 (1999) 1095.
[36] E. Gianotti, A. Frache, S. Coluccia, J.M. Thomas, T. Maschmeyer, L. Marchese, J. Mol. Catal. A: Chem. 204–205 (2003) 483.
[37] G. Bellusi, L. Zambelli, A. Corma, M.E. Domine, Eur. Patent Appl. 1403358 (2004), to EniTecnologie.
[38] S. Bordiga, A. Damin, F. Bonino, G. Ricchiardi, C. Lamberti, A. Zecchina, Angew. Chem. Int. Ed. 41 (2002) 4734.
[39] R. Hoppe, A. Ortlam, J. Rathousky, G. Schulz-Ekloff, A. Zukal, Micropor. Mater. 8 (1997) 267.
[40] H. Yamamoto, M. Kaneeda, S. Nakamura, K. Ishihara, J. Am. Chem. Soc. 118 (1996) 12854.
[41] A. Corma, M.E. Domine, J.A. Gaona, J.L. Jorda, M.T. Navarro, F. Rey, J. Pérez-Pariente, J. Tsuji, B. McCulloch, L.T. Nemeth, Chem. Commun. (1998) 2211.
[42] S. Kobayashi, K. Manabe, Y. Mori, Angew. Chem. Int. Ed. 40 (2001) 2816.
[43] S. Kobayashi, S. Nagayama, J. Am. Chem. Soc. 120 (1998) 2985.