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MCM-41 type molecular sieves as catalysts for the Friedel–Crafts acylation of 2-methoxynaphthalene

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Abstract

Molecular sieves of the MCM-41 type were studied as catalysts for the Friedel–Crafts acylation of 2-methoxynaphthalene in the liquid phase. When MCM-41 in the H^+ form is used as Brønsted-acid catalyst, acylation with acetic anhydride gives substitution predominantly at the 1-position. Increased reaction temperatures lead to a slight decrease of selectivity to acylation at the 1-position. The regenerability of H-MCM-41 is found to be excellent. For the acylation of 2-methoxynaphthalene with acetyl chloride Zn-MCM-41 was studied as a Lewis-acid catalyst, but both selectivity and regenerability are less favourable than in the case of the H-MCM-41 catalysed acylation of with acid anhydride.

Keywords: Friedel–Crafts acylation; 2-Methoxynaphthalene; Acylation ; Acid anhydride; MCM-41

1. Introduction

The synthesis of aromatic ketones is an important process in several areas of the fine chemicals industry. Many synthetic fragrances of the musk type contain an acetyl group, while the synthesis of various pharmaceuticals also involves an aromatic acylation step. A major drawback of the conventional Lewis-acid metal chloride catalysts for Friedel–Crafts acylation is that they are non-regenerable and must be used in more than stoichiometric amounts. The hydrolysis of the complexes formed between the aromatic ketone products and the catalysts results in highly corrosive waste streams, the disposal of which leads to environmental problems.

In recent years considerable attention has been paid to the potential of zeolites to act as heterogeneous and re-usable catalysts in many organic reactions [1]. In 1986 Chiche et al. reported on the acylation of toluene by various carboxylic acids over lanthanide-exchanged zeolites, particularly CeY, at 180°C in an autoclave reactor [2]. Zeolite catalysed Friedel–Crafts acylations in the liquid phase have also been reported with acyl chlorides [3,4] or acid anhydrides [5,6] as acylating reagents, over various zeolites such as LaY, HY and H-Beta [5].

Due to the limitations of their pore size, the access to these zeolites is restricted to molecules with kinetic diameters up to 8 Å. The mesoporous molecular sieve MCM-41, an aluminosilicate type material, possesses a hexagonal arrangement of uniformly sized, unidimensional mesopores with diameters which can be systematically varied from 20–80 Å [7] and should therefore be an interesting catalyst for conver-

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sions involving larger molecules. Recently, H-MCM-41 with pore diameter of about 40 Å proved to be an interesting catalyst in the direct Fries acylation [8] and in the tetrahydropyranylation of alcohols and phenols [9].

In this study the catalytic activity of MCM-41 type molecular sieves for the Friedel–Crafts acylation is reported. As an aromatic substrate 2-methoxynaphthalene was chosen. Acylation of 2-methoxynaphthalene at the 6-position is of particular interest because of the production of the anti-inflammatory Naproxen. MCM-41 in the H form was studied as a Brønsted-acid catalyst for acylation with acetic anhydride, isobutyric anhydride and benzoic anhydride. For the acylation with acetyl chloride, the Lewis acid form Zn-MCM-41 was used.

Acylation of 2-methoxynaphthalene generally occurs at the kinetically controlled 1-position [5], as shown in Fig. 1. However, migration of the acyl group from the 1-position to the 6-position [10] and protiodeacylation [11] of the acyl group at the 1-position may eventually result in the formation of the thermodynamically most stable 6-acylated product. Minor amounts of the 8-acylated 2-methoxynaphthalene have also been detected under Friedel–Crafts conditions [12]. It may be noted that the 1-, 6- and 8-positions are electronically activated by the 2-methoxy group.

2. Experimental

2.1. MCM-41

Mesoporous MCM-41 materials were prepared according to a modification of example 11 of Ref. [13]. Cetyltrimethylammonium chloride (25% in water) was used instead of the hydroxide. The as-synthesised materials were liberated from the template by calcination in air at 540°C for 2 days. H-MCM-41 was prepared by ion-exchange of the calcined MCM-41 (Si/Al = 17.5) in a 1 M NH_4NO_3 solution in water, at 60°C for 12 h. The resulting NH_4-MCM-41 was converted to the active H-MCM-41 by calcination in air at 450°C. For the preparation of Zn-MCM-41 the calcined MCM-41 (Si/Al = 21.7) was ion-exchanged in aqueous 0.3 M $Zn(NO_3)_2$ at 60°C. Prior to use the Zn-MCM-41 was activated at 450°C in air. The atomic Al:Zn ratio was 1:0.37. All MCM-41 samples were characterised by X-ray powder diffraction, the results of which were in agreement with literature data [7]. Si/Al ratios and the degree of ion exchange were determined by ICP–AES/AAS analysis. Pore volume and BET areas were determined by nitrogen physisorption experiments on a Quantachrome Autosorb 6 instrument. The samples were outgassed for 16 h under vacuum at 350°C prior to use. The results are summarised in Table 1.

2.2. Chemicals

All chemicals were used without further purification as received from Aldrich or Janssen Chimica.

2.3. Reaction procedure

All reactions were carried out in a thermostatted liquid phase reactor equipped with a stirrer and a reflux condenser. A typical reaction

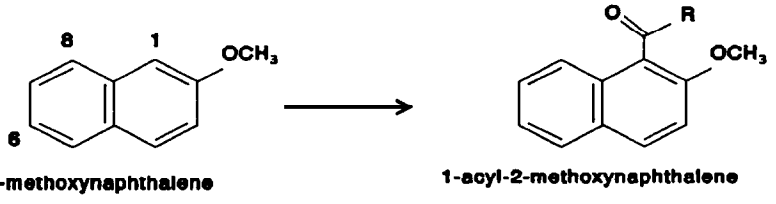


Fig. 1. Acylation of 2-methoxynaphthalene by acid anhydride or acyl chloride at the 1-position.

Table 1
Characterisation of MCM-41 materials

	Degree of ion-exchange (%)	Si/Al	BET area (m^2/g)	Pore volume (cm^3/g)
H-MCM-41	100	17.5	1075	0.95
Zn-MCM-41	74	21.7	795	0.6

run was as follows: 7.90 g 2-methoxynaphthalene (50 mmol), 2.55 g acetic anhydride (25 mmol) (or 0.94 g acetyl chloride, 12 mmol) were stirred in 50 ml chlorobenzene together with 1 g nitrobenzene as internal standard. To this solution 0.8 g activated H-MCM-41 (or 0.8 g Zn-MCM-41) was added. Samples were taken periodically and analysed by gas chromatography on a CP Sil 5 CB column and on a VG 70SE mass spectrometer using 70 eV as ionisation energy.

2.4. Synthesis of 6-acetyl-2-methoxynaphthalene (6-AC-2MN) and 1-benzoyl-2-methoxynaphthalene (1-BZ-2MN)

Authentic samples of the model products 6-AC-2MN and 1-BZ-2MN were synthesised by classical methods [14,15] as reference compounds for identification of the H-MCM-41 and Zn-MCM-41 catalysed acylation reactions. Equimolar amounts of the corresponding acyl chloride were reacted with 2-methoxynaphthalene in the presence of $AlCl_3$ (1 mol per mol acyl chloride) as catalyst in nitrobenzene. The crude products were purified by steam distillation and by column chromatography on Silica Gel 60 with ethyl acetate/hexane (1:15) as eluent. The identity of 6-AC-2-MN was confirmed by ^1H NMR spectroscopy. The identity of 1-BZ-2MN was confirmed by ^1H NMR correlation spectroscopy (COSY), ^{13}C NMR spectroscopy, heteronuclear ($^{13}C-^1H$) correlation spectroscopy (HETCOR) and by the attached proton test technique (ATP). All NMR experiments were performed on a Varian 400 MHz spectrometer.

2.5. Deacylation experiments

Deacylation experiments were run as follows: To 0.25 g 1-BZ-2MN or 6-AC-2MN and 0.25 g nitrobenzene (internal standard) in 25 ml chlorobenzene, 0.20 g activated H-MCM-41 was added. Samples were taken periodically and analysed by GC on a CP Sil 5 CB column.

3. Results and discussion

3.1. Acylation of 2-methoxynaphthalene with acid anhydrides catalysed by H-MCM-41

The results of the H-MCM-41 catalysed acylation of 2-methoxynaphthalene with acid anhydrides are presented in Table 2. Conversions are given with respect to the anhydride, taking into account that the acid left does not acylate the substrate. The selectivity for the 1-acylated products at moderate temperatures was very high, amounting to practically 100% at up to 100°C. Acylation with the more bulky isobutyric anhydride at low temperatures resulted in a small amount of the 6-acylated product, probably due to steric reasons. Steric hindrance to acylation is in the order 1- > 8- > 6-position. Increasing the reaction temperature resulted in higher conversions, accompanied by formation of small amounts of the 6- and 8-acylated side products. At higher temperatures the reversibility of the acylation at the 1-position plays a role in the distribution of the products [5,11]. The acyl group at the 1-position is subject to protiodeacylation. Since this phenomenon is not involved in the thermodynamically more stable and the sterically unhindered 6-, or less hindered 8-substituted aromatic ketones, high reaction temperatures lead to a decrease in the selectivity for the 1-position. This explanation is supported by the deacylation experiments carried out with 1-BZ-2MN and 6-AC-2MN. Fig. 2 illustrates the instability of 1-BZ-2MN at 132°C in chlorobenzene in the presence of H-MCM-41. After 24 h 91% of the 1-BZ-2MN was deacy-

lated to 2-methoxynaphthalene and benzoic acid. The 2-methoxynaphthalene was readily desorbed from the molecular sieve and thus to be detected by GC. The amount of benzoic acid detected in the reaction mixture was lower than to be expected from the degree of deacylation; acylation of the MCM-41 surface might be a factor. However, re-acylation of 2-methoxynaphthalene with the chemisorbed benzoyl groups was not observed. At 70°C 1-BZ-2MN proved to be stable, with no deacylation being observed. At 132°C 6-AC-2MN did not show any deacylation in chlorobenzene in the presence of H-MCM-41, illustrating the thermodynamic stability of the 6-substituted 2MN. It may be noted that the stability of 6-AC-2MN also is preserved in the presence of both the acylating agent and H-MCM-41. As a result of the relatively low acidity of H-MCM-41, the decrease of selectivity for the 1-position was low, compared with the acetylation catalysed by

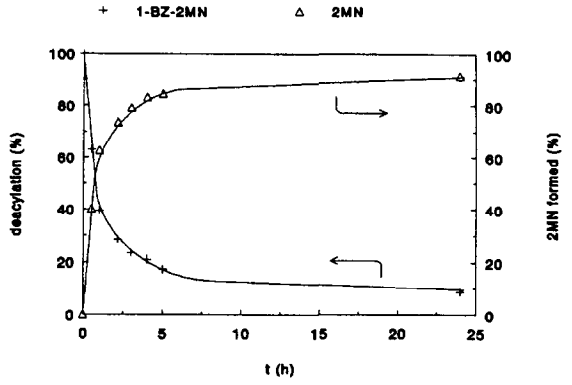
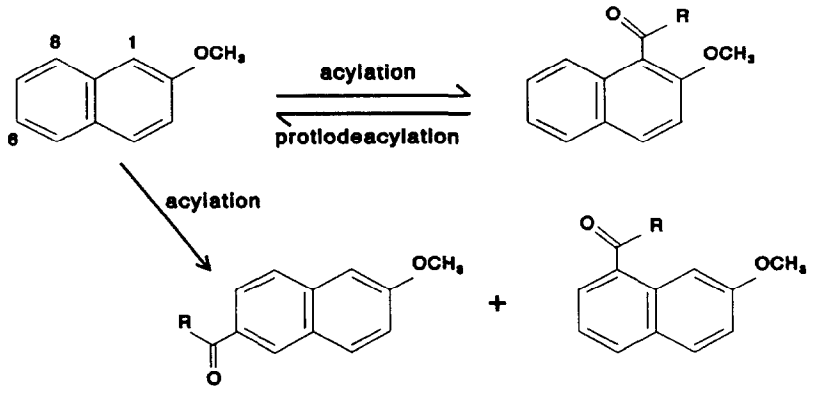


Fig. 2. Deacylation of 1-BZ-2MN at 132°C in chlorobenzene in the presence of H-MCM-41.

Table 2
Acylation of 2-methoxynaphthalene by acid anhydrides in various solvents catalysed by H-MCM-41 (24 h reaction time)

Acetic anhydride					
Solvent	*T*	Selectivity to (%)			Conversion
	(°C)	1-AC-2-MN	6-AC-2MN	8-AC-2-MN	(%)
chlorobenzene	30	100	–	–	7.4
	46	100	–	–	10.6
	70	100	–	–	14.9
	100	97	2	1	40.7
	132	95	4	1	57.1
nitrobenzene	70	98	2	0	19.5
	132	94	5	1	59.3
carbon disulfide	46	100	–	–	12.2
Isobutyric anhydride					
Solvent	*T*	Selectivity to (%)			Conversion
	(°C)	1-IB-2-MN	6-IB-2MN	8-IB-2-MN	(%)
chlorobenzene	70	97	3	–	7.3
	100	95	5	–	16.7
	132	71	7	–	31.2 [a]
Benzoic anhydride					
Solvent	*T*	Selectivity to (%)			Conversion
	(°C)	1-BZ-2-MN	6-BZ-2MN	8-BZ-2-MN	(%)
chlorobenzene	70	100	–	–	2.8
	100	98	1	1	16.7
	132	96	1.5	2.5	50
nitrobenzene	132	97	1	2	44.1

[a] Small amounts of di-acylated 2-methoxynaphthalene and of an ester of isobutyric acid and 2-methoxynaphthalene were observed in the reaction mixture.



Scheme 1. Acylation of 2-methoxynaphthalene catalysed by H-MCM-41.

Hβ, USY or ZSM-12, described earlier by Harvey et al. [5]. No consecutive isomerisation was found, which may be of practical relevance. These findings may be summarised by the reaction path presented in Scheme 1, for the acylation of 2-methoxynaphthalene.

The catalytic activity of H-MCM-41 for acylation of 2-methoxynaphthalene is clearly presented in Table 3 which shows turnover numbers (TON) of 10–20 for the catalytic sites in H-MCM-41, assuming each H^+ to represent an active site. This assumption was supported by a reaction that was run under the same conditions with MCM-41 in the Na form. The conversion of 2-MN to 1-AC-2MN was then found to be $< 1\%$, illustrating the importance of the protonic sites in H-MCM-41 on activity. Blank experiments run without H-MCM-41 under the same conditions did not show any conversion of 2-methoxynaphthalene.

The conversions in the above described reactions are with respect to the anhydrides, taking into account that the acid left does not acylate.

Table 3
Turnover numbers of the catalytic sites in H-MCM-41 in the acylation of 2-methoxynaphthalene in chlorobenzene at 132°C

Acylating reagent	TON
acetic anhydride	19.8
isobutyric anhydride	10.8
benzoic anhydride	17.3

Since 2-methoxynaphthalene is the more expensive compound, specially in the case of the acylation by acetic anhydride, it is of interest to increase the conversion of 2-methoxynaphthalene by using an excess of acetic anhydride. In Table 4 are presented the results of the reaction of 2-methoxynaphthalene with acetic anhydride in chlorobenzene at 100°C. Also included is an experiment in which acetic anhydride (30 ml) was used as solvent. As can be seen, it is indeed possible to increase the amount of acylated 2-methoxynaphthalene. A slight decrease of selectivity for the acylation at the 1-position was observed for the reaction in acetic anhydride as solvent. However, it must be noted that in this case also small amounts of unidentified high molecular weight products were formed and that

Table 4
Variation of the amount of acetic anhydride in the acylation of 2-methoxynaphthalene (50 mmol) catalysed by H-MCM-41 in chlorobenzene (50 ml) at 100°C (24 h reaction time)

Acetic anhydride (mmol)	Product distribution (%)			Acylated 2MN (mmol)
	1-AC-2MN	6-AC-2MN	8-AC-2MN	
25	97	2	1	10.2
50	97	2	1	12.7
100	97	2	1	15.6
320 [a]	96	3	1	42.3

[a] Acetic anhydride (30 ml) was used as solvent instead of chlorobenzene. A blank reaction, without H-MCM-41, did not show any conversion.

Table 5
Regenerability of H-MCM-41 in the acylation of 2-methoxynaphthalene with acetic anhydride at 100°C

Cycle	Selectivity to (%)			Conversion
	1-AC-2-MN	6-AC-2MN	8-AC-2-MN	(%)
1	97	2	1	40.7
2	97	2	1	38.3
3	97	2	1	37.8

the catalyst rapidly turned into a dark material, being indicative of heavy coke formation compared with reactions using chlorobenzene as solvent.

The excellent regenerability of H-MCM-41 is shown in Table 5. After each reaction cycle the H-MCM-41 was separated from the reaction mixture by filtration, washed, dried and reactivated for 2 days at 450°C. No loss of activity or selectivity could be detected after three reaction cycles. From Table 2 it can be seen that the choice of solvent does not have a substantial effect on the conversion or selectivity, which is in contrast to the classical homogeneous acylation. In the classical acylation reaction there is an effect of the solvent on the distribution of isomers formed, depending on the ability of the solvent to form a complex with the acylating agent [10,16]. In carbon disulfide predominantly acylation at the 1-position is observed, as contrasted with the reaction in nitrobenzene where the 6-position is acylated [10]. Apparently, in the present case the environment in which the reaction takes place is dominated by the internal pore structure of the molecular sieve rather than the solvent.

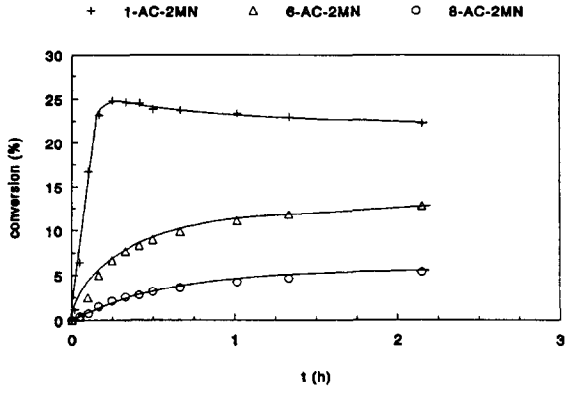


Fig. 3. Acylation of 2-methoxynaphthalene with acetyl chloride catalysed by Zn-MCM-41 in chlorobenzene at 132°C.

3.2. Acylation of 2-methoxynaphthalene with acetyl chloride catalysed by Zn-MCM-41

Table 6 presents the results of the acylation of 2-methoxynaphthalene with acetyl chloride, catalysed by the Lewis acid Zn-MCM-41. Conversions are given with respect to the acetyl chloride. Acetyl chloride was proved to be much less active as acylating agent in the presence of the Brønsted-acid catalyst H-MCM-41 than in the presence of the Lewis-acid catalyst Zn-MCM-41. Therefore, the investigation into the acylation with acetyl chloride was restricted to the catalysis by Zn-MCM-41. As can be seen in

Table 6
Acylation of 2-methoxynaphthalene by acetyl chloride in various solvents catalysed by Zn-MCM-41 (24 h reaction time)

Solvent	T	Selectivity to (%)			Conversion
	(°C)	1-AC-2-MN	6-AC-2MN	8-AC-2-MN	(%)
chlorobenzene	46	93	4	3	25.1
	100	48	28	24	35.5
	132	45	37	18	40.4
nitrobenzene	46	74	18	8	22.4
	180	1	81	18	28.4
1,2-dichloroethane	81	63	26	11	39.6
carbon disulfide	46	97	2	1	39.6
hexane	46	100	–	–	14.9
	69	89	7	4	34.3

Table 7
Regenerability of Zn-MCM-41 in the acylation of 2-methoxynaphthalene with acetyl chloride at 100°C

Cycle	Selectivity to (%)			Conversion	Degree of
	1-AC-2-MN	6-AC-2MN	8-AC-2-MN	(%)	Zn-exchange (%)
1	48	28	24	35.5	74
2	63	22	15	42.9	67
3	75	15	10	46.7	58

Table 5, the highest selectivity for acylation at the 1-position was obtained at lower temperatures (46°C). At higher temperatures the selectivity for 1-AC-2MN decreased rapidly. In nitrobenzene at a reaction temperature of 180°C it was even found that only a negligible amount of 1-AC-2MN was formed, whereas the selectivity for 6-AC-2MN was 81%. Compared with the Brønsted-acid catalysed acylation of 2MN (Table 2), the Zn-MCM-41 catalyst gave lower selectivity to 1-AC-2MN at low temperatures and the decrease of selectivity for acylation at the 1-position with increasing temperature was greater. In the case of Zn-MCM-41 catalysed acylation the low selectivity at higher reaction temperatures is most probably due to deacylation of the sterically hindered 1-AC-2MN. This is clearly illustrated in Fig. 3, which represents the acylation of 2MN with acetyl chloride catalysed by Zn-MCM-41 in nitrobenzene at 132°C. It can be seen that the conversion to 1-AC-2MN rapidly reaches a maximum of 25% after 15 min, after which the amount of 1-AC-2MN eventually declines to 18% after 24 h, accompanied by an increasing conversion to 6-AC-2MN of 15% after 24 h. Zn^{2+} interacts directly with the carbonyl function, which might lead to an easier de-acylation of the sterically hindered 1-AC-2-MN than is the case in the protiodeacylation of 1-AC-2MN by H-MCM-41.

The regenerability of Zn-MCM-41 for the acylation of 2-methoxynaphthalene with acetyl chloride in chlorobenzene at a reaction temperature of 100°C is shown in Table 7. No loss of activity could be observed. However, the distribution of acylated products changes substantially after each reaction cycle. In the third reaction cycle the amount of the kinetically most easily formed 1-AC-2MN is higher than in the first cycle. ICP/AAS analysis of the used zeolites shows that during a reaction Zn-MCM-41 undergoes zinc loss by leaching. Whereas the degree of Zn^{2+} at the commencement of the first cycle was 74%, at the commencement of the third cycle this had fallen to 58%.

4. Conclusion

The mildly acidic H-MCM-41 is a suitable Brønsted-acid catalyst for the Friedel–Crafts acylation of 2-methoxynaphthalene, using anhydrides as acylating reagents, representing a chlorine free acylation route. At temperatures up to 100°C the selectivity to the 1-acylated product is practically 100%. At higher temperatures the sterically hindered 1-acylated product becomes subject to protiodeacylation, resulting in small amounts of the thermodynamically favoured and sterically less hindered 6- and 8-acylated products. The regenerability of the solid catalyst is excellent. The use of the Lewis acid Zn-MCM-41 as catalyst for the Friedel–Crafts acylation of 2-methoxynaphthalene seems less favourable, because of the lower selectivity and the leaching of Zn^{2+} ions from the molecular sieve. However, at high reaction temperatures the selectivity for the 6-acylated product becomes very high.

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