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Spherical MCM-41 as support material in enantioselective HPLC

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Abstract

Spherical MCM-41 particles covalently linked with (*R*)-naphthylethylamine as selector are reported as a new chiral stationary phase for HPLC and show excellent resolution and efficiency in combination with low inlet pressures. © 2001 Elsevier Science Ltd. All rights reserved.

The field of catalysis has already benefited from the discovery of the mesoporous, semi-crystalline M41S materials. Their unique pore structure—characterized by a uniform pore diameter, a large pore volume and high surface area—in addition to high thermal stability and mild acidity also make these materials excellent candidates for use in chromatography. Several research groups already showed the beneficial effects of unfunctionalized MCM-41 in the field of gas chromatography, size exclusion chromatography and normal-phase HPLC.[1–3] We previously reported the first preparation of MCM-41 and MCM-48 based enantioselective stationary phases (CSPs) and their use in enantioselective HPLC.[4] They combined high retention and separation factors with relatively short analysis times and low inlet pressures. Aiming at a further improvement of enantioselective chromatographic separations, a new CSP is reported here based on spherical MCM-41 particles (MCM-41 (SPH)). These beads with regular shape and narrow particle and pore size distribution are expected to be beneficial for use as chromatographic support from a diffusional point of view.

MCM-41 (SPH) was obtained following a literature procedure,[5] which is a modification of Stöber's synthesis of monodisperse silica spheres.[6] In 50 g of deionized water, 2.5 g of *n*-hexadecyltrimethylammonium bromide (HDTMABr) was dissolved. To this surfactant solution, 13.2 g of an ammonia solution (32 wt% in water) and 60 g of ethanol were added. The solution was stirred for 15 minutes (250 rpm) and 4.7 g of tetraethoxysilane (TEOS) was added. The resulting synthesis gel, having a molar composition of 1TEOS:0.3HDTMABr:11NH_3:

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$144H_2O:58EtOH$, was stirred for 2 hours at room temperature. The white precipitate was filtered, washed with water and ethanol and dried overnight at 333 K. Calcination of the material was performed at 823 K for 5 hours at a heating rate of 1 K per minute. Scanning electron microscopy (Fig. 1(a)) confirms the expected particle morphology. The particles approach a perfect spherical shape and their size ranges from 0.2 to 1 μm. This is in contrast with MCM-41 synthesized by classical, well-established methods.[7,8] Following these methods, agglomerates of curved hexagonal rods with dimensions between 5 and 15 μm are normally obtained, as shown in Fig. 1(b). A fractionation procedure was applied to both MCM-41 samples by subjecting the particles to repeated sedimentation in isopropanol. SEM pictures of the starting, decanted and remaining phase showed that this treatment was clearly beneficial for the MCM-41 prepared following the classical method: the amorphous silica was mainly removed from the sample and a much more homogeneous MCM-41 sample could be obtained. On the other hand, an identical particle size distribution was observed for the spherical MCM-41, indicating no beneficial effect of fractionation for this material. The XRD pattern of MCM-41 (SPH) shows several Bragg peaks at low angles, typical for MCM-41 materials (Fig. 2). The

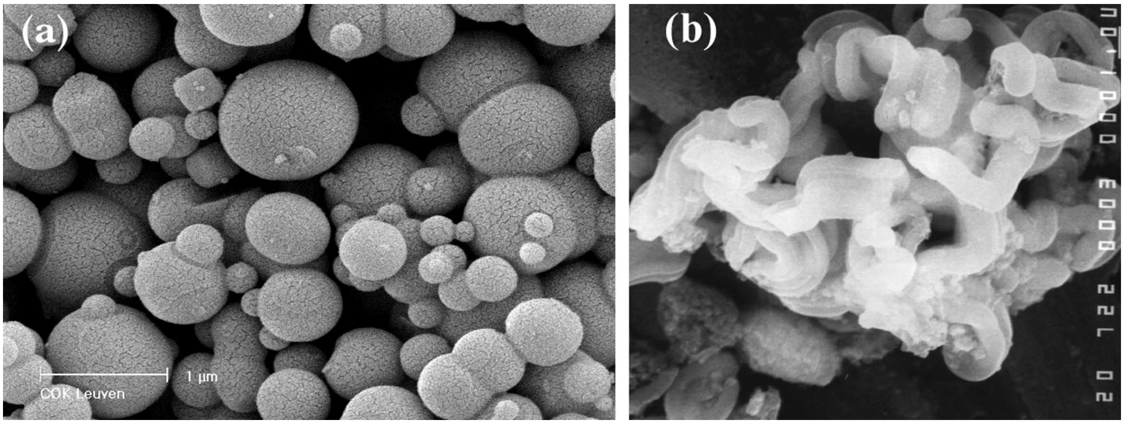

Figure 1. Scanning electron micrograph of calcined (a) MCM-41 (SPH) and (b) MCM-41 resulting from a classical synthesis procedure

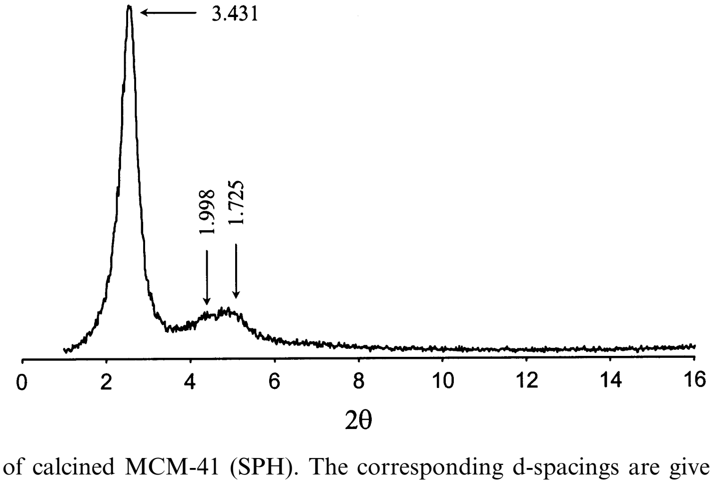

Figure 2. XRD pattern of calcined MCM-41 (SPH). The corresponding d-spacings are given for each peak (in nm)

lattice parameter (a) equals 4.0 nm ($a=2d_{100}/\surd 3$). From nitrogen sorption measurements, a specific surface area of 955 m^2/g was obtained and a pore diameter of 2.4 nm. These values were determined using the Brunauer–Emmett–Teller and the Barrett–Joyner–Halenda (from desorption data) method, respectively. In Fig. 3, a transmission electron micrograph visualizes the pores in a spherical MCM-41 particle.

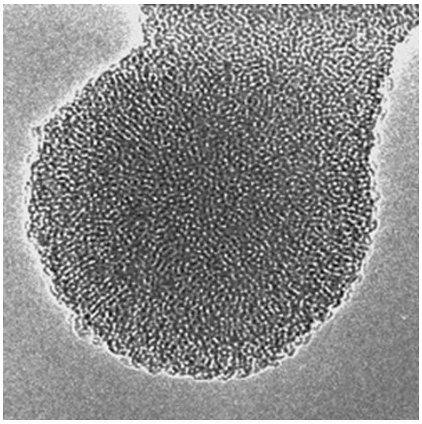

Figure 3. Transmission electron micrograph of calcined MCM-41 (SPH)

According to a literature procedure for the derivatization of silica stationary phases,[9] MCM-41 (SPH) was functionalized with (*R*)-α-(1-naphthyl)ethylamine after being silylated with γ-aminopropyltriethoxysilane (APTS), according to a literature procedure for the silylation of amorphous silica gels.[10] After pretreatment under vacuum at 298 K for 24 hours, 3 g of the M41S material was refluxed under nitrogen in 100 ml of a 5 wt% solution of APTS in dry toluene for 12 hours. The silylated product was filtered, Soxhlet extracted with dichloromethane and dried under vacuum at 423 K for 24 hours. To a suspension of 1 g of amine-functionalized silica in 30 ml of water, 2 g of succinic anhydride was added with swirling. The pH of the solution was maintained at 4.0 with 2N NaOH. The slurry was stirred at room temperature for 5 hours. The silica was collected by filtration, washed with water, methanol and diethyl ether (Et_2O), and dried in air at 333 K. To 1 g of this modified silica in 30 ml of dry tetrahydrofuran (THF), 1.25 g of 1,1′-carbonyldiimidazole was added at 273 K and stirred at this temperature for 3 hours. The chiral selector (*R*)-α-(1-napthyl)ethylamine (1.25 g) was added subsequently and the mixture was further stirred at room temperature for another 5 hours. The modified silica was collected by filtration, thoroughly washed with THF, methanol and Et_2O, and dried in air at 333 K overnight.

The coverage with chiral selector, determined by means of thermogravimetric analysis, equaled 0.31 mmol/g. After packing the resulting material, the column of 10 cm length was tested at 35°C in the chromatographic separation of racemic mixtures of dinitrobenzoyl derivatives of naphthylethylamine and phenylethylamine, abbreviated as DNB-NEA and DNB-PEA, respectively (Table 1).

Table 1
Chromatographic performance of the CSPs based on MCM-41 (SPH) and MCM-41 (prepared following a classical procedure)[a]

	MCM-41 (SPH)								
Component	t_{rS}	t_{rR}	w_{bS}	w_{bR}	k_S	k_R	α	N	R_s
DNB-PEA	7.88	11.44	1.09	1.68	2.99	4.79	1.60	830	2.56
DNB-NEA	8.06	16.44	1.37	3.29	3.04	7.25	2.38	554	3.60
	MCM-41 (prepared following a classical procedure and fractionated)								
Component	t_{rS}	t_{rR}	w_{bS}	w_{bR}	k_S	k_R	α	N	R_s
DNB-PEA	10.65	16.92	2.42	4.25	3.68	6.44	1.75	308	1.88
DNB-NEA	11.18	25.46	2.54	6.34	4.24	10.93	2.58	311	3.22

[a] Mobile phase: *n*-hexane/1,2-dichloroethane/ethanol (40:12:3), flow rate: 0.6 ml/min, UV detection (254 nm), t_r = retention time in minutes, w_b = peak width at base in minutes, k = retention factor, α = separation factor, N = plate number, R_s = resolution.

Comparing these chromatographic data with the performance of the column based on MCM-41 resulting from the classical synthesis procedure, MCM-41 (SPH) is clearly superior as support. Both retention times and peak widths are strongly reduced. In addition, excellent resolutions and efficiencies are obtained. In comparison with the non-fractionated MCM-41

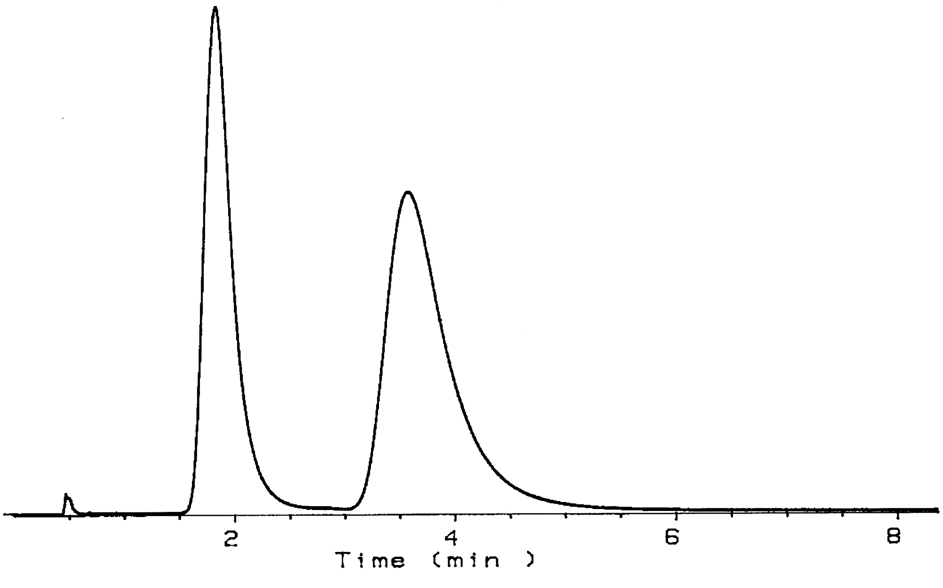

Figure 4. Separation of DNB-NEA at a flow rate of 2.4 ml/min using the enantioselective HPLC column based on MCM-41 (SPH)

reported earlier,[4] the improvement of resolution and efficiency is even more pronounced. Almost identical retention times and peak widths are noticed compared with MCM-48 supports,[4] though slightly lower separation factors and resolution. The inlet pressures on the other hand are four times lower for MCM-41 (SPH). This is extremely important if higher flow rates are envisaged in view of shorter analyses times. Even at a flow rate of 2.4 ml/min, peak separations at base are still achieved together with acceptable inlet pressures (Fig. 4).

Taking all these aspects into account, MCM-41 (SPH) appears to be the best support material for the system under study. This can be attributed to the homogeneously packed bed which results from the uniform particle shape and the narrow particle size distribution.

In conclusion, a new enantioselective HPLC column based on spherical MCM-41 particles as support is reported. Among the members of the M41S family, this material is clearly superior as support in enantioselective HPLC. Excellent resolution and efficiency could be achieved for the tested racemates. Moreover, the HPLC column is characterized by a good performance at low inlet pressures, even when high flow rates are used.

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References

1. Raimondo, M.; Perez, G.; Sinibaldi, M.; De Stefanis, A.; Tomlinson, A. A. G. *Chem. Commun.* **1997**, 1343–1344.
2. Kurganov, A.; Unger, K.; Issaeva, T. *J. Chromatogr. A* **1996**, *753*, 177–190.
3. Grün, M.; Kurganov, A. A.; Schacht, S.; Schüth, F.; Unger, K. K. *J. Chromatogr. A* **1996**, *740*, 1–9.
4. Thoelen, C.; Van de Walle, K.; Vankelecom, I. F. J.; Jacobs, P. A. *Chem. Commun.* **1999**, 1841–1842.
5. Grün, M.; Lauer, I.; Unger, K. K. *Adv. Mater.* **1997**, *9*, 254–257.
6. Stöber, W.; Fink, A.; Bohn, E. *J. Colloid Interface Sci.* **1968**, *26*, 62–69.
7. Cheng, C.-F.; Park, D. H.; Klinowski, J. *J. Chem. Soc., Faraday Trans.* **1997**, *93*, 193–197.
8. Franke, O.; Rathousky, J.; Schulz-Ekloff, G.; Stárek, J.; Zukal, A. *Stud. Surf. Sci. Catal.* **1994**, *84*, 77–84.
9. Ôi, N.; Nagase, M.; Doi, T. *J. Chromatogr.* **1983**, *257*, 111–117.
10. Caravajal, G. S.; Leyden, D. E.; Quinting, G. R.; Maciel, G. E. *Anal. Chem.* **1988**, *60*, 1776–1786.