# The use of M41S materials in chiral HPLC

**Carla Thoelen, Kris Van de Walle, Ivo F. J. Vankelecom and Pierre A. Jacobs***

*Katholieke Universiteit Leuven, Faculty of Agricultural and Applied Biological Sciences, Centre for Surface Chemistry and Catalysis, Kardinaal Mercierlaan 92, B-3001 Heverlee, Leuven, Belgium.*
*E-mail: pierre.jacobs@agr.kuleuven.ac.be*

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**Siliceous MCM-41 and MCM-48, covalently linked with the chiral selector (*R*)-naphthylethylamine, have been evaluated as supports in chiral HPLC and show for several racemates higher separation factors than for a stationary phase based on amorphous silica.**

Since the discovery of MCM-41 and MCM-48 in 1992, much research has been reported on their use in the field of catalysis, where their mesoporosity is beneficial for the conversion of large substrates.[1–3] These mesoporous molecular sieves are characterized by a high specific surface area in combination with highly ordered pores. These pores are one-dimensional in the case of MCM-41 in contrast to the three-dimensional network of MCM-48. Furthermore, the pore size of these materials can be tuned between 15 and 100 Å. In the domain of heterogeneous chiral catalysis, an extensively growing research area owing to the increasing demand for enantiomerically pure products, these mesoporous materials provide interesting supports for the development of new chiral catalysts.[4,5] Recently, in chromatographic separation techniques such as GC and HPLC, the use of non-functionalized MCM-41 has also been reported.[6,7] In chiral HPLC however, M41S materials were, up till now, not investigated in terms of their performance as supports in spite of their numerous advantages.

In this study, three chiral stationary phases (CSPs) with (*R*)-naphthylethylamine [(*R*)-NEA] as chiral selector were synthesized starting from amorphous silica, Si-MCM-41 and Si-MCM-48, respectively. MCM-41 and MCM-48 were prepared following a hydrothermal synthesis procedure.[8] They were characterized by XRD, SEM and sorption measurements. In both cases, the BET area appeared to be *ca.* 1000 m$^2$ g$^{-1}$. The particle sizes of the resulting MCM-41 and MCM-48 are 5–15 μm and 0.1–0.5 μm, respectively. After silylation of the pore walls with aminopropyltriethoxysilane, these materials as well as Lichrosorb-NH$_2$ (Merck, 10 μm particle size), a reference for amorphous silica, were coupled with (*R*)-NEA (Fig. 1). This was done using succinic acid as a spacer molecule, according to the literature procedure.[9]

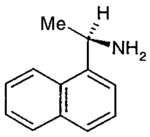

**Fig. 1** Chiral selector used: (*R*)-naphthylethylamine.

Thermogravimetric analysis (TGA) revealed the amount of chiral selector on the supports: 0.06, 0.24 and 0.23 mmol (*R*)-NEA per gram of Lichrosorb-NH$_2$, MCM-41 and MCM-48, respectively. With the same technique, these functionalized materials were found to be thermally stable up to 130 °C. Moreover, because the selector is linked covalently, the materials are stable in all common solvents.

In order to compare the performance of the MCM-41 based CSP with the performance of the phase based on amorphous silica, two manually packed columns (10 cm) were tested in chiral HPLC experiments (Table 1) for their chiral recognition ability towards three racemates (Fig. 2). The higher separation factors achieved with MCM-41 as support are very promising. The resolution and efficiency, however, are quite poor, but can be improved by applying the slurry packing technique. Therefore in the following step, a slurry packed column of MCM-41 was tested on the same racemates (Table 2) and the study was extended to MCM-48, for which the three-dimensional pore structure might further improve the chromatographic separation.

The chiral stationary phase based on MCM-41 is characterized by 3–4 fold higher retention factors for the tested racemates than that based on amorphous silica. This is in accordance with their difference in specific area (Lichrosorb-NH$_2$: 300 m$^2$ g$^{-1}$, MCM-41: 1000 m$^2$ g$^{-1}$), leading to a higher coverage with chiral selector. This also explains the excellent separation factors achieved. An augmentation of the separation factor by 40% was obtained for DNB–NEA by using the column based on MCM-41 instead of that based on amorphous silica.

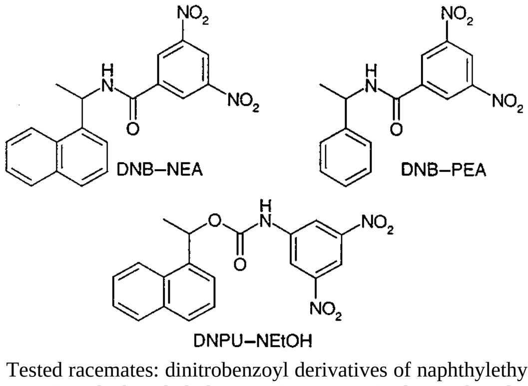

**Fig. 2** Tested racemates: dinitrobenzoyl derivatives of naphthylethylamine (DNB–NEA) and phenylethylamine (DNB–PEA), dinitrophenylurethane derivative of naphthylethanol (DNPU–NEtOH).

**Table 1** Chromatographic performance of manually packed Lichrosorb-NH$_2$ and Si-MCM-41 based CSPs[a]

| | Lichrosorb-NH$_2$ (manually packed) | | | | | Si-MCM-41 (manually packed) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Component | $k_S$ | $k_R$ | $\alpha$ | $N$ | $R_s$ | $k_S$ | $k_R$ | $\alpha$ | $N$ | $R_s$ |
| DNB–NEA | 1.36 | 2.96 | 2.18 | 447 | 2.68 | 4.50 | 13.78 | 3.06 | 74 | 1.88 |
| DNB–PEA | 1.37 | 2.10 | 1.53 | 429 | 1.38 | 4.41 | 8.28 | 1.88 | 58 | 0.92 |
| DNPU–NEtOH | 1.21 | 1.41 | 1.17 | —[b] | —[b] | 3.30 | 3.97 | 1.20 | —[b] | —[b] |

[a] Mobile phase: *n*-hexane–1,2-dichloroethane–ethanol (40:12:3), flow rate: 0.6 ml min$^{-1}$, UV detection (254 nm), $k$ = retention factor, $\alpha$ = separation factor, $N$ = plate number, $R_s$ = resolution. [b] Peak width determination was impossible owing to poor peak resolution.

**Table 2** Chromatographic performance of slurry packed Si-MCM-41 and Si-MCM-48 based CSPs[a]

| | Si-MCM-41 (slurry packed) | | | | | Si-MCM-48 (slurry packed) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Component | $k_S$ | $k_R$ | $\alpha$ | $N$ | $R_s$ | $k_S$ | $k_R$ | $\alpha$ | $N$ | $R_s$ |
| DNB–NEA | 3.31 | 10.44 | 3.16 | 136 | 2.50 | 3.48 | 9.11 | 2.62 | 605 | 4.7 |
| DNB–PEA | 3.34 | 6.47 | 1.93 | 117 | 1.32 | 3.47 | 5.92 | 1.71 | 680 | 2.76 |
| DNPU–NEtOH | 2.51 | 3.16 | 1.26 | —[b] | —[b] | 2.46 | 3.02 | 1.23 | 667 | 0.94 |

[a] Mobile phase: *n*-hexane–1,2-dichloroethane–ethanol (40:12:3), flow rate: 0.6 ml min$^{-1}$, UV detection (254 nm), $k$ = retention factor, $\alpha$ = separation factor, $N$ = plate number, $R_s$ = resolution. [b] Peak width determination was impossible owing to poor peak resolution.

The resolution and particularly the efficiency are poor owing to the large peak widths. Peak tailing prevents accurate determination of the peak widths. Nevertheless, MCM-41 seems to be a promising support material because of the high separation factors in combination with a good analysis time ($<30$ min for the strongest retained component) and very acceptable inlet pressures (100 bar). Moreover, the mobile phase used was optimized for the amorphous silica CSP, so probably further improvements can be made for the column based on MCM-41 by changing the composition of the mobile phase.

By using slurry packed columns of MCM-41 and MCM-48 based CSPs, band broadening, which is disadvantageous to the efficiency, can be reduced owing to the formation of a more uniformly packed bed. Comparing Tables 1 and 2, both the resolution and the efficiency of the separation with MCM-41 are clearly improved by use of this packing method; the efficiency of the column was doubled. The use of MCM-48 as support leads to further improvement with the efficiencies increasing by a factor of six, owing to a faster mass transfer through the three-dimensional pore system. Separations performed on this material show very good resolution and efficiency, and only slightly lower separation factors (the separation factor decreases by $<20\%$ compared to the use of MCM-41 as support). Band broadening is substantially reduced and peak symmetry is improved. The nature of the pore system together with the smaller particle dimensions and the narrower particle size distribution can account for the successful separation with MCM-48. On both columns, based on either MCM-41 or MCM-48, a whole range of racemates are currently being tested. No loss of chromatographic performance was observed with time illustrating the stability of the materials towards repeated cycles of guest exchange.

In conclusion, the first utilization of M41S materials as supports in chiral HPLC is reported. Both MCM-41 and MCM-48 show high retention and separation factors for the tested racemates and are very promising for liquid chromatography. These results, in combination with good analysis times and very acceptable inlet pressures, make these HPLC columns successful analytical instruments. Excellent resolution and efficiency could be achieved with MCM-48. Columns based on MCM-41 show good resolution, but the efficiency should be further improved by a better control of the particle size distribution. The influence of pore size and selector loading on chromatographic performance is under current investigation for both M41S materials.

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