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Silica-bonded chiral stationary phases with structurally simple π-donor chiral selectors for high-performance liquid chromatography

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ABSTRACT

Seven new chiral stationary phases obtained from (*S*)-phenylalanine derivatives, (*R*)-Mosher's acid and (*S*)-naproxen were prepared and evaluated. The racemic substances used to test them contained either π-acidic or π-basic sites. The best results were observed when the chiral entity bonded to γ-aminopropylsilica gel was 3,5-dimethylanilido-, 3,5-dimethylbenzoyl- or 3,5-dimethoxybenzoyl-(*S*)-phenylalanine and -(*S*)-naproxen.

INTRODUCTION

Although silica gel bonded to optically active compounds has a relatively limited scope of application, it constitutes an important kind of stationary phase for the resolution of racemic compounds by high-performance liquid chromatography (HPLC) [1]. The main advantage of such stationary phases is their ease of preparation when compared with macromolecular supports such as proteins, polysaccharides or synthetic polymers whose range of application is wider than that of silica-bonded chiral stationary phases [2].

Many of the chiral molecules used for bonding on silica gel have either π-donor or π-acceptor radicals. Chiral entities described in π-acceptor stationary phases are almost always 3,5-dinitrobenzoyl derivatives of amino acids. However, π-donor stationary phases have several kinds of chiral entities, most of which bear a naphthyl radical [3]. This structural diversity on π-donor chiral entities shows that a suitable family of π-donor chiral selectors has not yet been found.

New silica-bonded stationary phases with the naphthylethylamine group, either isolated or associated with amino acids, as chiral entity have recently been described, with a relatively wide range of application [4,5]. However, the general use of chiral stationary phases having π-donor character is only recommended for the resolution of racemic compounds bearing a 3,5-dinitrobenzoyl group.

In this context, we considered the utility of

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searching for new π-donor chiral selectors, taking into account the good performances of stationary phases with a naphthyl or a 3,5-disubstituted phenyl radical [3,6]. According to the literature, the performances of π-donor stationary phases are not improved if the structure of the chiral entity becomes more complex, so we chose easily accessible, structurally simple molecules.

In a previous paper [7] we showed that the coexistence of two different chiral centres on the same silica gel can prevent the resolution of certain racemic compounds. Therefore, we utilized optically active molecules with only one asymmetric centre to be bonded on γ-aminopropylsilanized silica gel.

We describe the preparation of seven new chiral stationary phases, six of which have a π-donor character. These stationary phases were obtained by covalently bonding either optically active acids or (*S*)-phenylalanine derivatives on γ-aminopropylsilanized silica gel. The structures of all of them are given in Figs. 1 and 2.

Chiral silica bonded phases were tested with several racemic compounds, also used in our previous study [7] (Fig. 3).

EXPERIMENTAL

NMR spectra were measured using a Bruker AC200 spectrometer. Tetramethylsilane (TMS) was used as the internal standard with chemical shifts measured in ppm. Rotatory power was measured with a Perkin-Elmer Model 241 polarimeter. Elemental analyses were performed by the Service Central de Microanalyse du CNRS (Vernaison,

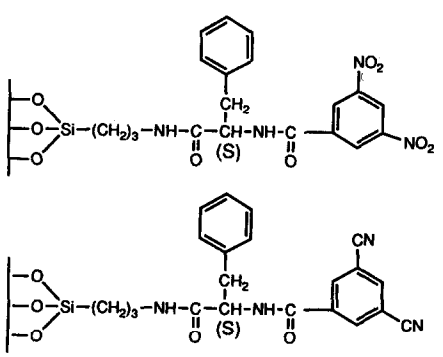


Fig. 1. Structures of chiral stationary phases with a π-acceptor character.

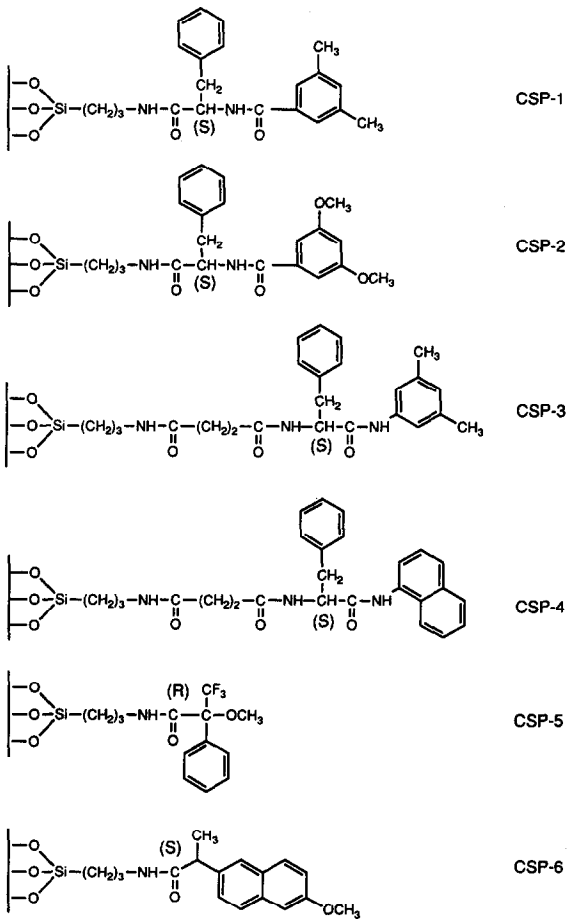


Fig. 2. Structures of chiral stationary phases with a π-donor character.

France). The chromatographic experiments were carried out on an HP 1090 liquid chromatograph (Hewlett-Packard, Palo Alto, CA, USA) equipped with a PU 4020 UV detector (Philips, Cambridge, UK). The chiral stationary phases were packed into stainless-steel tubes (100 × 4.6 mm I.D.) by the slurry method according to Coq *et al.* [8]. The volume of sample injected was 5 μl, the flow-rate of the pump was 1 ml/min, the detection wavelength was 254 nm and the mobile phases consisted of various mixtures of *n*-heptane, chloroform and methanol.

Chemicals and reagents

Compounds **1–3** (Fig. 3) were obtained by treating the methyl ester of each amino acid with 3,5-dinitrobenzoyl chloride. Compound **6** was prepared

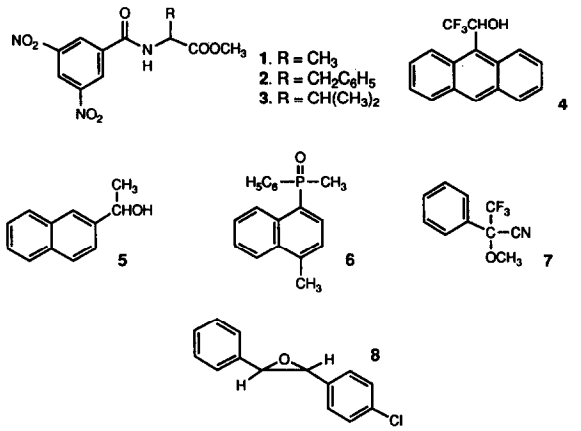


Fig. 3. Structures of test compounds.

by the method described previously [9]. All were identified by their ^{1}H NMR spectra and elemental analysis. Compounds **4**, **5**, **7** and **8** were purchased from Aldrich.

*(S) - tert. - Butoxycarbonylphenylalanyl - 3,5 - di - methylanilide (**9**) and (S)-tert.-butoxycarbonyl-phenylalanyl-1-naphthylamide (**10**) (Fig. 4).* To a solution of 3.6 g (13.6 mmol) of L-N-Boc-phenylalanine and 14.0 mmol of the appropriate amine in 50 ml of tetrahydrofuran (THF), a solution of 3.46 g (14.0 mmol) of 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ) in 30 ml of THF was added. The mixture was allowed to react overnight at room temperature, then the solution was evaporated. The residue was diluted with dichloromethane and washed with 1% orthophosphoric acid, 0.2 *M* potassium hydroxide and distilled water. After drying over sodium sulphate, the solution was evaporated and the residual solid collected.

When 3,5-dimethylaniline was used, recrystallization from toluene–heptane gave 3.8 g (76%) of a white solid, m.p. 142°C. ^{1}H NMR (200 MHz): δ (C^2HCl_3) 1.41 (s, 9H, *tert.*-butyl), 2.21 (s, 6H, CH_3Ar[a]), 3.13 (m, 2H, CH_2Ar'), 4.61 (m, 1H, CH), 5.55 (d, 1H, N*H*CH), 6.71 (s, 1H, C^4H), 7.03 (s, 2H, C^2H and C^6H), 7.26 (s, 5H, Ar'H), 8.36 (m, 1H, NHAr). ^{13}C NMR (50.3 MHz): δ (C^2HCl_3) 21.2 (CH_3Ar), 28.2 [$(CH_3)_3$], 38.6 (CH_2), 56.7 (CH), 80.4, (Cq = quaternary carbon atom), 117.8 (C^2H and C^6H), 126.0 and 126.9 (C^4H and $C^{4'}H$), 128.6 and 129.3 ($C^{2',6'}H$ and $C^{3',5'}H$), 136.7 and 137.2 (C^1 and $C^{1'}$), 138.4 ($C^{3,5}$), 155.8 (OCON), 169.7 (CON). $[\alpha]_D^{23} = -13.7°$ (*c* = 1.4, chloroform). Analysis: calculated for $C_{22}H_{28}N_2O_3$, C 71.71, H 7.66, N 7.60; found, C 71.79, H 7.56, N 7.46%.

When 1-naphthylamine was used, recrystalliza-

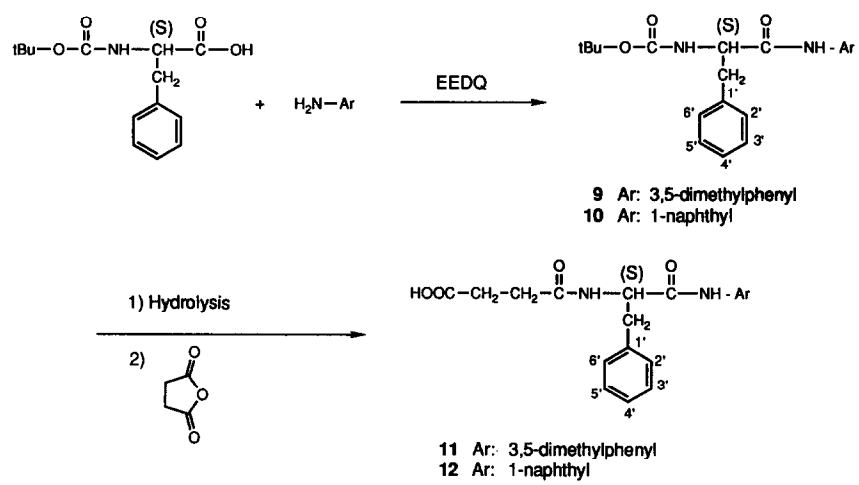


Fig. 4. Scheme for the preparation of **11** and **12**. tBu = *tert.*-Bu

[a] Ar and Ar' refer to the formulae in Figs. 4 and 5. Ar represents the disubstituted phenyl radical, symbolized by Ar and numbered 1, 2 .... and also the naphthyl radical of compounds 10 and 12. Ar' represents the phenyl radical C_5H_6 the positions of which are numbered 1', 2', etc.

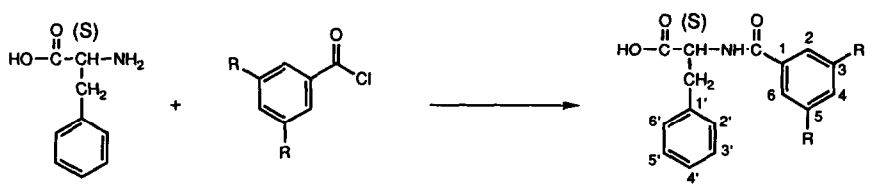
tion from toluene gave 5 g (94.5%) of a white solid, m.p. 139°C. ^{1}H NMR (200 MHz): δ (C^2HCl_3) 1.46 (s, 9H, *tert.*-butyl), 3.24 (d, 2H, CH_2Ar'), 4.68 (m, 1H, CH), 5.39 (m, 1H, N*H*CH), 7.3–7.9 (m, 12H, ArH and Ar'H), 8.44 (m, 1H, NHAr). ^{13}C NMR (50.3 MHz): δ (C^2HCl_3) 27.7 [$(CH_3)_3$], 37.5 (CH_2), 56.2 (CH), 80.0 (Cq *tert.*-butyl), 120–136 (CH and Cq aromatic), 155.3 (OCON), 169.6 (CON). $[\alpha]_D^{23} = -33.6°$ (c = 1.5, chloroform). Analysis: calculated for $C_{24}H_{26}N_2O_3$, C 73.82, H 6.71, N 7.17; found, C 73.64, H 6.91, N 7.05%.

*Succinyl (S)-phenylalanyl-3,5-dimethylanilide (**11**).* A 2-g (5.4-mmol) amount of **9** was dissolved in glacial acetic acid (36 ml) and cooled in an ice-bath. Hydrogen chloride was passed through for 40 min and the solution was left to stand at room temperature for 3 h. The solvent was removed *in vacuo* and the residual solid was washed in diethyl ether. The solid was dissolved in pyridine (25 ml) and succinic anhydride (2.7 g, 27 mmol) was added. After stirring for 24 h at room temperature, the mixture was evaporated and the residue treated with 5% orthophosphoric acid and distilled water. Recrystallization from ethanol–water gave 1.7 g (84%) of a white solid, m.p. 178°C. ^{1}H NMR (200 MHz): δ {[$^2H_6$]dimethyl sulphoxide (DMSO-d_6)} 1.83 (s, 6H, CH_3Ar), 2.00–2.12 (m, 4H, CH_2CH_2), 2.56–2.75 (AB zone of ABX system, 2H, CH_2Ar'), 4.35 (m, 1H, CH), 6.27 (m, 1H, NHAr), 6.73–6.84 (m, 8H, ArH and Ar'H), 7.40 (d, 1H, N*H*CH), 8.91 (s, 1H, COOH). ^{13}C NMR (50.3 MHz): δ (DMSO-d_6) 19.9 (CH_3Ar), 28.1 and 29.2 (CH_2CH_2), 36.5 (CH_2Ar'), 53.5 (CH), 116.4 (C^2H and C^6H), 124.1 and 125.1 (C^4H and $C^{4'}H$), 126.8 and 127.9 ($C^{2',6'}H$ and $C^{3',5'}H$), 136.1 and 136.8 (C^1 and $C^{1'}$), 136.6 (C^3 and C^5), 168.4, 170.5 and 173.1 (CO). $[\alpha]_D^{23} = -18.5°$ (c = 1.3, pyridine). Analysis: calculated for $C_{21}H_{24}N_2O_4$, C 68.46, H 6.56, N 7.60; found, C 68.80, H 6.72, N 7.58%.

*Succinyl (S)-phenylalanyl-1-naphthylamide (**12**).* Analogously to **11**, **12** was obtained from **10** (2 g, 5.12 mmol). Recrystallization from ethanol–water gave 1.7 g (85%) of a white solid, m.p. 170°C. ^{1}H NMR (200 MHz): δ (DMSO-d_6) 2.44 (m, 4H, CH_2CH_2), 2.88–3.30 (AB zone of ABX system, 2H, CH_2Ar'), 4.87 (m, 1H, CH), 7.18–8.04 (m, 12H, ArH and Ar'H), 8.43 (d, 1H, N*H*CH), 10.0 (s, 1H, NHAr), 11.6–12.4 (ba, 1H, COOH). ^{13}C NMR (50.3 MHz): δ (DMSO-d_6) 29.0 and 29.8 (CH_2CH_2), 37.7 (CH_2Ar), 54.6 (CH), 122–130 (CH aromatic), 127.9, 133.1, 133.5 and 137.6 (Cq aromatic), 170.7, 171.2 and 173.8 (CO). $[\alpha]_D^{23}$ −23.7° (c = 1.4, pyridine). Analysis: calculated for $C_{23}H_{22}N_2O_4$, C 70.76, H 5.68, N 7.17; found, C 70.68, H 5.95, N 7.01%.

3,5-Dicyanobenzoic acid. 3,5-Dicyanotoluene (5 g, 35 mmol) was dissolved in 30 ml of acetic acid and 5 ml of concentrated sulphuric acid and cooled in an ice-bath. Chromic oxide (9 g, 90 mmol) dissolved in 90 ml of acetic acid was added while stirring. The solution was stirred at room temperature for 14 h and poured on ice. The resulting solid was filtered and dissolved in aqueous sodium carbonate solution. The solution was filtered and acidified with hydrochloric acid. The solid was collected by filtration and washed with water. Recrystallization from water gave 1.5 g (25%) of a white solid, m.p. 228°C. ^{1}H NMR (200 MHz): δ (C^2HCl_3–DMSO-d_6) 7.74 (d, 1H, C^4H), 7.81 (d, 2H, C^2H and C^6H). ^{13}C NMR (50.3 MHz): δ (C^2HCl_3–DMSO-d_6) 112.4 and 114.7 (CN and $C^{3,5}$), 132.3 (C^1), 135.2 ($C^{2,6}H$), 137.5 (C^4H), 162.7 (COOH). Analysis: calculated for $C_9H_4N_2O_2$, C 62.80, H 2.34, N 16.27; found, C, 62.27, H 2.36, N 16.27%.

*N-Acyl-(S)-phenylalanines (**13–16**) (Fig. 5).* (*S*)-Phenylalanine (4.13 g, 25 mmol) was dissolved in 45 ml of 1 *M* sodium hydroxide solution and



13 R: NO_2 **15** R: CH_3
14 R: CN **16** R: OCH_3

Fig. 5. Scheme for the preparation of **13–16**.

cooled in an ice-bath. The appropriate acyl chloride (25 mmol), obtained by treating the corresponding acid with thionyl chloride, and 50 ml of 1 *M* sodium hydroxide solution were added simultaneously, with magnetic stirring, over a period of 20 min. The solution was stirred at room temperature for 90 min and acidified with concentrated hydrochloric acid (pH 2–3). The resulting solid was collected by filtration and washed with water. Recrystallization from ethanol yielded the corresponding N-acylphenylalanine.

N-(3,5-Dinitrobenzoyl)-(*S*)-phenylalanine (**13**) was described previously [10].

N-(3,5-Dicyanobenzoyl)-(*S*)-phenylalanine (**14**) could not crystallized, so it was dissolved in methanol and boiled with charcoal, filtered and evaporated; yield 42%, m.p. 110°C. ^{1}H NMR (200 MHz): δ (C^2HCl_3–DMSO-d_6) 2.60–3.05 (m, 2H, CH_2), 4.47 (m, 1H, CH), 6.85 (s, 5H, phenyl), 7.73 (s, 1H, C^4H), 8.10 (s, 2H, C^2H and C^6H), 8.50 (d, 1H, NH). ^{13}C NMR (50.3 MHz): δ (C^2HCl_3–DMSO-d_6) 36.1 (CH_2), 53.5 (CH), 112.7 (C^3 and C^5), 115.4 (CN), 125.6 ($C^{4'}H$), 127.3 and 128.1 ($C^{2',6'}H$ and $C^{3',5'}H$), 129.8 ($C^{1'}$), 134.5 ($C^{2,6}H$), 135.4 (C^1), 136.3 (C^4H), 162.0 (CONH), 172.0 (COOH). $[\alpha]_D^{23} = -32.9°$ (c = 1,3, pyridine). Analysis: calculated for $C_{18}H_{13}N_3O_3 . H_2O$, C 64.10, H 4.48, N 12.46; found, C 64.19, H 4.41, N 12.63%.

N-(3,5-Dimethylbenzoyl)-(*S*)-phenylalanine (**15**) was obtained in 86% yield, m.p. 139°C. $[\alpha]_D^{23} = -31.5°$ (c = 1.4, pyridine). ^{1}H NMR (200 MHz): δ ($CDCl_3$) 2.33 (s, 6H, CH_3), 3.32 (m, 2H, CH_2), 5.09 (m, 1H, CH), 6.61 (d, 1H, NH), 7.14–7.31 (m, 8H, ArH), 8.65 (bb, 1H, COOH). ^{13}C NMR (50.3 MHz): δ (C^2HCl_3) 21.1 (CH_3), 37.2 (CH_2), 55.5 (CH), 124.7 ($C^{2,6}H$), 127.2 ($C^{4'}$), 128.6 and 129.4 ($C^{2',6'}H$ and $C^{3',5'}H$), 133.2 and 135.5 (C^1 and $C^{1'}$), 133.3 (C^4H), 138.3 ($C^{3,5}$), 168.1 (CONH), 175.0 (COOH). Analysis: calculated for $C_{18}H_{19}NO_3$, C 72.72, H 6.40, N 4.71; found, C 72.99, H 6.30, N 4.74%.

N-(3,5-Dimethoxybenzoyl)-(*S*)-phenylalanine (**16**) was obtained in 80% yield, m.p. 146°C. ^{1}H NMR (200 MHz): δ (C^2HCl_3–DMSO-d_6) 2.74 (m, 2H, CH_2), 3.34 (s, 6H, CH_3O), 4.36 (m, 1H, CH), 6.10 (d, 1H, C^4H), 6.50 (d, 2H, C^2H and C^6H), 6.82 (m, 5H, phenyl), 7.83 (d, 1H, NH). ^{13}C NMR (50.3 MHz): δ (C^2HCl_3–DMSO-d_6) 35.7 (CH_2), 52.9 (CH), 54.0 (CH_3O), 102.1 (C^4H), 104.0 ($C^{2,6}H$), 125.5 ($C^{4'}H$), 126.9 and 127.8 ($C^{2',6'}H$ and $C^{3',5'}H$), 134.7 and 135.8 (C^1 and $C^{1'}$), 159.1 ($C^{3,5}$), 165.5 (CONH), 170.4 (COOH). $[\alpha]_D^{23} = -30.8°$ (c = 1.3, pyridine). Analysis: calculated for $C_{18}H_{19}NO_5$, C 65.65, H 5.81, N 4.25; found, C 65.60, H 5.75, N 4.06%.

Chiral stationary phases

All chiral stationary phases were obtained from the appropriate chiral acidic compound according to the procedure described previously [7]. Elemental analyses are given in Table I.

RESULTS AND DISCUSSION

Chromatographic behaviour of stationary phases

Chromatographic results are given in Table II. We have also included results obtained from two π-acceptor stationary phases bearing N-(3,5-dinitrobenzoyl)-(*S*)-phenylalanine or N-(3,5-dicyanobenzoyl)-(*S*)-phenylalanine as chiral selectors (CSP-A1 and CSP-A2, respectively). CSP-A1 has already been described [10] and the corresponding results come from ref. 7. CSP-A2 was prepared in order to compare the efficacy of the 3,5-dicyanobenzoyl radical with that of the 3,5-dinitrobenzoyl radical, both being π-acceptors. Although the chromatographic behaviours of these two stationary phases are similar, the performance of CSP-A1 is better than that of CSP-A2. This is a new illustration of the efficacy of the 3,5-dinitrobenzoyl radical in the resolution of racemic compounds by means of silica-bonded chiral stationary phases, either when belonging to the chiral selector in the stationary phase or being borne by the racemic compound [7].

Enantiomers of racemic test compounds, except **5** and **6**, and to a lesser extent **4**, are well resolved by four of the six π-donor stationary phases, *viz.*, CSP-1, CSP-2, CSP-3 and CSP-6, whose chiral entities are 3,5-dimethylbenzoyl-(*S*)-phenylalanine, 3,5-dimethoxybenzoyl-(*S*)-phenylalanine, (*S*)-phenylalanyl-3,5-dimethylanilide and (*S*)-naproxen, respectively. The choice of chiral entities constituted by a substituted phenyl radical with electron-donating groups seems to be correct. On the other hand, with respect to the naphthyl group, our results are not conclusive. Although CSP-6 [(*S*)-naproxen] gives good results, like those of chiral sta-

TABLE I

ELEMENTAL ANALYSES OF CHIRAL STATIONARY PHASES

Chiral stationary phase	Elemental analysis (%)			Ratio of carbon atoms per nitrogen atom		Bonded chiral moieties per gram of stationary phase[a] (mmol)	
	C	H	N	Analytical	Theoretical[a]	From %C	From %N
CSP-A1	10.93	1.76	2.69	4.74	4.75	0.48	0.48
CSP-A2	9.45	1.45	2.28	4.84	4.75	0.41	0.41
CSP-1	11.54	1.48	1.74	7.74	10.50	0.46	0.62
CSP-2	13.69	1.93	2.00	7.99	10.50	0.54	0.71
CSP-3	12.99	1.95	2.16	7.01	8.00	0.45	0.51
CSP-4	12.28	1.87	1.67	8.58	8.67	0.39	0.40
CSP-5	7.56	1.16	1.02	8.65	13.00	0.48	0.73
CSP-6	9.42	1.56	1.04	10.57	17.00	0.46	0.74

[a] Calculations made with regard to organic moiety structures in each stationary phase. The remaining free NH_2 groups were not considered.

TABLE II

CAPACITY FACTORS, k'_1, OF FIRST-ELUTED ENANTIOMER AND SELECTIVITY FACTORS, α, IN THE COLUMNS TESTED

Chiral stationary phase	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**	
	k'_1	α	k'_1	α	k'_1	α	k'_1	α	k'_1	α	k'_1	α	k'_1	α	k'_1	α
CSP-A1	1.84 (*R*)[a]	1.19	1.27 (*R*)	1.21	1.03 (*R*)	1.22	2.18 (*S*)	1.19	8.10	1.06	19.17	1.13	0.35	1.27	0.52	1.60
CSP-A2	2.15 (*R*)	1.13	1.38 (*R*)	1.18	1.22 (*R*)	1.13	1.79	1.03	6.28	1.00	16.81	1.05	0.31	1.00	0.63	1.43
CSP-1	2.02 (*R*)	1.63	0.90 (*R*)	1.90	0.62 (*R*)	1.81	2.91	1.00	2.73	1.00	1.64	1.00	0.19	14.86	0.14	1.50
CSP-2	1.66 (*R*)	2.29	0.75 (*R*)	2.21	0.56 (*R*)	2.00	2.06	1.00	2.12	1.00	0.39	1.00	0.18	23.00	0.04	3.33
CSP-3	1.90 (*R*)	2.32	0.91 (*R*)	2.10	0.65 (*R*)	2.47	1.50	1.00	2.48	1.00	2.33	1.00	0.14	3.55	0.14	1.70
CSP-4	2.86 (*R*)	1.13	1.51 (*R*)	1.17	1.15 (*R*)	1.19	1.54	1.00	4.37	1.00	7.45	1.00	0.20	1.00	0.20	1.80
CSP-5	0.72	1.00	0.31	1.00	0.26	1.00	0.85	1.00	3.26	1.06	2.16	1.00	0.24	2.17	0.10	1.50
CSP-6	5.53 (*S*)	1.34	2.37 (*R*)	1.51	1.37 (*S*)	1.51	2.10	1.03	6.00	1.00	5.93	1.00	0.26	4.20	0.22	1.50
Mobile phase chloroform + 0.5% methanol–heptane	70:30		70:30		70:30		70:30		25:75		50:50		10:90		25:75	

[a] Absolute configuration of first-eluted enantiomer.

tionary phases with a naphthylethylamine group [7,11], CSP-4, with a 1-naphthylamido group, shows mediocre performance.

The elution order of enantiomers is the same on all stationary phases in which (*S*)-phenylalanine is the chiral moiety in the chiral selector. However, the radical responsible for π–π interaction is bonded to the acidic group of (*S*)-phenylalanine in CSP-3 and CSP-4 and to the amino group in CSP-1 and CSP-2. Hence, the order of elution of enantiomers does not seem to be affected by the direction of fixing of the π-donor or π-acceptor groups on the amino acid. This observation is not in accordance with the three-point attachment recognition model in which the π-π interaction is the most important [12].

As we have already shown [7], the resolution of **7** is in general particularly good. The behaviour of this compound led us to prepare CSP-5 in which (*R*)-Mosher's acid is the chiral entity. We hypothesized that a certain reciprocity could be applied to the chiral recognition in this chiral moiety, but the performance of CSP-5 is the worst of the group of stationary phases tested.

Importance of the classification of stationary phases as π-donors and π-acceptors

As expected, π-acceptor racemic compounds, 3,5-dinitrobenzoyl derivatives of methyl esters of amino acids (compounds **1–3**), are well resolved by all the new stationary phases (except CSP-5). On the other hand, their ability to resolve **4**, **5** and **6**, which are π-donors, is obviously limited. However, this must be qualified, given that such compounds are poorly resolved by CSP-A1 and especially CSP-A2, which are π-acceptors. In general, however, racemic compounds bearing a 3,5-dinitrobenzoyl group are well resolved by either π-acceptor or π-donor chiral stationary phases.

The foregoing would seem to indicate that the classification of π-donor and π-acceptor chiral silica-bonded stationary phases is not sufficiently justified if it refers to the nature of the principal solute–stationary phase interactions in the enantiomeric recognition. More probably the whole chiral moiety should be taken into account instead of individual interactions, in the search for a hypothetical chiral recognition mechanism. However, this classification is convenient to distinguish two fairly different kinds of HPLC chiral stationary phases: those with a 3,5-dinitrobenzoyl radical (π-acceptors) and those without (π-donors).

CONCLUSIONS

Of the seven chiral stationary phases described here, four gave good results in the resolution of racemic compounds possessing either π-acidic or π-basic sites. This study has shown that chiral entities with a relatively simple structure can give efficient chiral stationary phases.

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