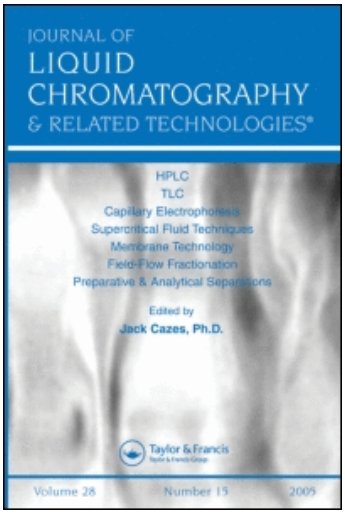

Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

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Online publication date: 26 April 2000

To cite this Article Kontrec, Darko , Vinković, Vladimir and Šunjić, Vitomir(2000) 'PREPARATION AND EVALUATION OF THE CHIRAL STATIONARY PHASES BASED ON N-4-(2,5,6-TRICHLORO-1,3-DICYANO)-PHENYL DERIVATIVES OF L-α-AMINO ACIDS', Journal of Liquid Chromatography & Related Technologies, 23: 8, 1203 — 1215
To link to this Article: DOI: 10.1081/JLC-100100409
URL: http://dx.doi.org/10.1081/JLC-100100409

J. LIQ. CHROM. & REL. TECHNOL., 23(8), 1203–1215 (2000)

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ABSTRACT

Regioselective functionalization of 2,4,5,6-tetrachloro-1,3-dicyanobenzene (TCDCB) by nucleophilic substitution of the chlorine atom at C(4) for N-L-α-amino acid residue enables preparation of new chiral selectors (**1**-**5**). Their binding to aminopropyl silica gel afforded new brush-type chiral stationary phases (**CSP-1**–**CSP-4**). Chiral stationary phases **CSP-5** and **CSP-6** that comprise dipeptide units L-Ala-L-Pro and L-Ala-L-Ala, respectively, were obtained by the solid-state coupling of C(4) substituted derivatives of 2,5,6-trichloro-1,3-dicyanobenzenes **4** and **5** to γ-L-alanylaminopropyl silica gel. Best resolution for some of 23 test racemates was achieved with **CSP-4** and **CSP-6**. This study reveals hydrogen bonding via a sterically exposed amide group and a π–π type interaction via an π-acid persubstituted benzene ring in these CSPs as the main contribution to chiral recognition.

INTRODUCTION

Chiral stationary phases (CSPs) based on various derivatives of α-amino acids are repeatedly reported in the literature as effective in the resolution of

some racemic analytes. Such CSPs usually comprise N-(3,5-dinitrobenzoyl) derivatives of α-amino acids (DNB-AA),[1-5] some other amides of α-amino acids,[6-8] and also N- and O-functionalized α-amino acids and peptides.[9-15]

The use of 2,4,5,6-tetrachloro-1,3-dicyanobenzene (TCDCB) as moderately π-deficient but highly polarized N-aryl unit in these CSPs was prompted by our recent observation, based on the analysis of the UV and CD spectra of its chiral derivatives with (*R*)-1-phenylethylamine (*R*-PEA), that its amino derivatives, possess highly polar (push-pull type) structures.[16] Their π-acid properties change to weak and strong π-basic properties with a number of the amino groups that can regioselectively substitute the chlorine atoms. Although *R*-PEA derivatives of TCDCB did not exhibit chiral recognition of some test racemates, more π-basic (*R*)-naphthylethylamine (*R*-NEA) derivatives proved valuable as chiral selectors in some HPLC columns.[17] Continuing the project of preparation of chiral stationary phases that contain derivatives of TCDCB as one of the crucial units, we prepared chiral selectors **1**–**5**, then bound them to silica to obtain chiral stationary phases **CSP-1**–**CSP-6**, and tested these novel CSPs for resolution of 23 racemic analytes in the HPLC mode.

EXPERIMENTAL

Chemicals

The reagents were supplied as follows: 2,4,5,6-tetrachloro-1,3-dicyanobenzene by Caffaro S.p.A. (Italy); L-phenylalanine, L-alanine, N-Boc-L-alanine, L-asparagine monohydra e, and 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ) by Sigma-Aldrich (Aldrich Chimica, Milano, Italy); L-α-phenylglycine, L-proline, and trifluoroacetic acid by Fluka (Buchs, Switzerland); sodium carbonate, sodium sulfate, hydrochloric acid, and potassium hydroxide by Kemika (Zagreb, Croatia); Nucleosil 100-5 NH_2 (5 μm) by Macherey-Nagel (Düren, Germany).

All solvents were pro analysis grade, purchased from J.T. Baker (Deventer, Holland).

TLC was performed on Merck's (Darmstadt, Germany) DC-alufolien with Kieselgel 60_{254}.

Racemates used for columns evaluation were purchased from Sigma-Aldrich: trans-stilbenoxide (TR-1), benzoine (TR-2), benzoine methyl ether (TR-3), flavanone (TR-4), Tröger base (TR-5), warfarin (TR-6), 1,1'-bis-2-naphthol (TR-7), and 1-(9-anthryl)-2,2,2-trifluoro-1-ethanol (TR-8). The other racemates were prepared in our laboratory: ethyl-7-chloro-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepine-3-carboxylate (TR-9), ethyl-7-chloro-1,3-

dimethyl- 2-oxo-5- phenyl-2,3- dihydro-1H- 1,4-benzodiazepine-3- carboxylate (TR-10), N^1(1-phenylethyl)-2,2-dimethylpropanamide (TR-11), N^1-(1-phenylethyl)benzamide (TR-12), N^1-(1-phenylethyl)-1-naphthamide (TR-13), N^1-phenyl-2-(4-isobutylphenyl)propanamide (TR-14), N^1-(1-phenylethyl)-3,5-dinitrobenzamide (TR-15), and all 8 isopropyl esters of N-3,5-dinitrobenzoyl derivatives of amino acids (TR-16–TR-23).

Apparatus

IR spectra were obtained for KBr pellets, on a Perkin Elmer M 137 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-GEM 300 for $CDCl_3$ solutions, if not stated otherwise; shifts are given in ppm downfield from TMS as an internal standard. Elemental analyses were done in Central Analytical Service (CAS) at Ruđer Bošković Institute.

Chromatography was performed with a Knauer WellChrom Maxi-Star K-1000 pump (Knauer GmbH, Berlin, Germany) using a Knauer HPLC 6-port-valves injector with a 20 μL loop. Detection was achieved at 254 nm with a Knauer WellChrom K-2500 detector. Integration of the chromatograms was made with the BDS software package (Barspec Ltd., Rehovot, Israel). The following parameters were measured:

k_1': capacity factor of the first eluted enantiomer, $(t_1-t_0)/t_0$;

k_2': capacity factor of the second eluted enantiomer, $(t_2-t_0)/t_0$;

α: selectivity factor, $\alpha = k_2'/ k_1'$;

R_S: resolution factor, $R_S = 2(t_2-t_1)/(w_1+w_2)$; w is the base width of the peaks.

The packing of HPLC columns purchased from Max Stevenson (Berlin, Germany) was performed by a slurry technique using Knauer pneumatic HPLC-pump. n-Hexane, 2-propanol and other solvents used for HPLC chromatography were analytical grade from J. T. Baker, and redistilled before using to obtain HPLC quality.

Preparation of Stationary Phases

Preparation of the Compounds 1–5, General Procedure

To the solution of TCDCB in MeOH was added warm solution of the L-amino acid and Na_2CO_3 in H_2O. Molar ratio of TCDCB:L-AA:Na_2CO_3 was 1:2:2. The reaction mixture was heated under reflux for 90 min, filtered, and

the filtrate extracted with dichloromethane. The aqueous layer was acidified with 1 M aq. HCl and the product separated as described for any particular compound.

N-2,5,6-Trichloro-1,3-Dicyanophenyl-L-Phenylalanine (1)

We started from TCDCB (4.0 g; 15.0 mmol), L-phenylalanine (4.97 g; 30.0 mmol), Na_2CO_3 (3.18 g; 30.0 mmol), MeOH (100 mL), H_2O (100 mL), CH_2Cl_2 (2 x 100 mL) and 1 M HCl (50 mL). The acidic solution was extracted with CH_2Cl_2 (2 x 50 mL), organic extracts were washed with a solvent mixture water–MeOH (2:1) and filtered. After drying over Na_2SO_4, the solvent was evaporated to dryness, leaving 4.60 g (77%) of **1**, yellow, slightly colored oil. IR (KBr): 3350, 2220, 1730, 1575, 1510, 1460, 1450, 1430, 1380, 1350, 1260, 1210, 1110, 1080, 1035, 920, 849, 750, 740, and 700 cm^{-1}. ^1H NMR: 3.37 (2 H, d, J = 5.3 Hz), 5.51-5.57 (1 H, m), 6.01 (1 H, d, J = 8.7 Hz), 7.15-7.24 (2 H, m), 7.28-7.35 (2 H, m), and 8.45 (1 H, s). ^{13}C NMR: 38.48, 56.58, 95.53, 104.42, 112.56, 113.74, 120.23, 128.00, 128.96, 129.23, 133.41, 139.84, 141.77, 148.43, and 174.99. Anal. calcd. for $C_{17}H_{10}N_3O_2Cl_3$ (394.62): C 51.73, H 2.55, and N 10.65%. Found: C 51.84, H 2.74, and N 10.72%.

N-2,5,6-Trichloro-1,3-Dicyanophenyl-L-α-Phenylglycine (2)

We started from TCDCB (4.0 g; 15.0 mmol), L-α-phenylglycine (4.55 g; 30.0 mmol), Na_2CO_3 (3.18 g; 30.0 mmol), MeOH (100 mL), H_2O (100 mL), CH_2Cl_2 (2 x 50 mL) and 1 M HCl (50 mL). The acidic solution was stored in a refrigerator overnight and the precipitated solid separated by vacuum filtration. The product was washed with water, dried in vacuum desiccator over KOH and crystallized from EtOH, affording 1.40 g (25%) of pure **2**, white powder. IR (KBr): 3500, 3320, 2220, 1715, 1570, 1500, 1450, 1380, 1310, 1290, 1260, 1210, 1180, 1120, 1070, 1040, 1000, 960, 910, 860, 760, 720, and 690 cm^{-1}. ^1H NMR (acetone-d_6): 5.56 (2H, bs), 6.22 (1 H, d, J = 7.0 Hz), and 7.35-7.50 (5 H, m). ^{13}C NMR: 59.89, 97.25, 104.66, 113.12, 114.19, 121.17, 127.94, 129.32, 129.48, 136.48, 139.69, 141.58, 148.98, and 171.41. Anal. calcd. for: $C_{16}H_8N_3O_2Cl_3$ (380.60): C 50.48, H 2.11, and N 11.04%. Found: C 50.53, H 2.36, and N 10.86%.

N-2,5,6-Trichloro-1,3-Dicyanophenyl-L-Asparagine (3)

We started from TCDCB (5.0 g; 18.8 mmol), L-asparagine monohydrate (5.64 g; 37.6 mmol), Na_2CO_3 (3.98 g; 37.6 mmol), MeOH (100 mL), H_2O (100 mL), CH_2Cl_2 (2 x 100 mL), and 1 M HCl (50 mL). The acidic solution was extracted with CH_2Cl_2 (2 x 100 mL), organic layer washed with water, and then solution evaporated to the half of volume. By the storing in the refrigerator the product was precipitated, separated by vacuum filtration, and washed with cooled CH_2Cl_2. After drying in vacuum desiccator over KOH, 2.51 g (37%) of

3 as a white powder was obtained. IR (KBr): 3480, 3360, 3320, 2900, 2500, 2220, 1730, 1650, 1570, 1500, 1400, 1320, 1200, 1120, 850, 810, and 750 cm^{-1}. ^{1}H NMR (DMF-d_7): 3.10-3.45 (2H, m), 5.55-5.75 (1H, m), 7.50 (1H, s), 8.11 (1H, s), and 8.50 (1H, d, J = 8.6 Hz,). ^{13}C NMR (DMF-d_7): 35.67, 53.95, 94.64, 102.06, 113.28, 114.28, 119.57, 138.55, 141.30, 149.99, 171.75, and 172.79. Anal. calcd. for $C_{12}H_7N_4O_3Cl_3$ (361.56): C 38.96, H 1.95, and N 15.49%. Found: C 39.92, H 2.12, and N 15.41%.

N-2,5,6-Trichloro-1,3-Dicyanophenyl-L-Alanine (4)

We started from TCDCB (5.0 g; 18.8 mmol), L-alanine (3.35 g; 37.6 mmol), Na_2CO_3 (3.98 g; 37.6 mmol), MeOH (100 mL), H_2O (100 mL), CH_2Cl_2 (2 x 100 mL) and 1 M HCl (50 mL). Product **4** was isolated as described for **1**; obtained was 4.12 g (68%) of **4**, slightly yellow oil. IR (KBr): 3320, 2220, 1740, 1570, 1500, 1450, 1420, 1290, 1200, 1150, 990, 910, 850, 800, 730, and 650 cm^{-1}. ^{1}H NMR: 1.72 (3H, d, J = 6.6 Hz), 5.21-5.25 (1H, m), 6.39 (1H, d, J = 7.9 Hz), and 9.20 (1H, s). ^{13}C NMR: 19.38, 51.55, 94.87, 103.85, 112.39, 113.42, 119.92, 139.62, 141.71, 148.14, and 175.91. Anal. calcd. for $C_{11}H_6N_3O_2Cl_3$ (318.53): C 41.47, H 1.89, and N 13.19%. Found: C 41.52, H 1.82, and N 13.21%.

N-2,5,6-Trichloro-1,3-Dicyanophenyl-L-Proline (5)

We started from TCDCB (5.0 g; 18.8 mmol), L-proline (4.32 g; 37.6 mmol), Na_2CO_3 (3.98 g; 37.6 mmol), MeOH (100 mL), H_2O (100 mL), CH_2Cl_2 (2 x 100 mL) and 1 M HCl (50 mL). Product **5** was isolated as described for **1**; 6.40 g (98%) of **5**, yellow oil was obtained. IR (KBr): 2970, 2920, 2880, 2220, 1720, 1550, 1500, 1440, 1380, 1350, 1300, 1250, 1210, 1170, 1130, 1100, 1060, 1030, 920, 750, 740, and 720 cm^{-1}. ^{1}H NMR: 1.17-1.39 (2H, m), 1.93-2.08 (2H, m), 2.14-2.27 (1H, m), 2.52-2.64 (1H, m), 3.32-3.38 (1H, m), and 8.80 (1H, s). ^{13}C NMR: 25.15, 30.12, 53.20, 61.67, 104.10, 109.02, 112.37, 113.37, 128.16, 140.53, 141.65, 152.75, and 176.56. Anal. calcd. for $C_{13}H_8N_3O_2Cl_3$ (344.57): C 45.31, H 2.34, and N 12.19%. Found: C 45.62, H 2.41 and N 12.46%.

Preparation of Chiral Stationary Phases CSP-1–CSP-4, General Procedure

A mixture of silica gel Nucleosil 100-5 NH_2 (2.0 g; 1.36% N and 3.49% C), chiral selector **1**–**4** (1.6 mmol), and EEDQ (1.6 mmol) in dichloromethane (10.0 mL), was stirred overnight at ambient temperature. The modified silica gel was collected on G-4 filter, washed with MeOH, and dried at 70°C for 4 h. **CSP-1**. Yield 2.13 g; Anal. C 8.32, H 1.21, N 1.69%. The % of N reveals that 1.0 g of the stationary phase contains 0.078 mmol of chiral selector **1**. **CSP-2**. Yield 2.15 g; Anal. C 8.08, H 1.05, N 1.66%. The % of N reveals that 1.0 g of the stationary phase contains 0.069 mmol of chiral selector **2**. **CSP-3** Yield 2.18 g; Anal. C 8.95, H 1.43, N 1.78%. The % of N reveals that 1.0 g of the

stationary phase contains 0.074 mmol of chiral selector **3**. **CSP-4** Yield 2.19 g; Anal. C 8.83, H 1.38, N 1.71%. The % of N reveals that 1.0 g of the stationary phase contains 0.083 mmol of chiral selector **4**.

Preparation of Chiral Stationary Phase CSP-5

Suspension of N-Boc-L-alanine (0.44 g, 2.34 mmol), EEDQ (0.58 g, 2.34 mmol), Nucleosil 100-5 NH_2 and dry THF (10 mL) was stirred for 18 h at ambient temperature. γ-L-alanylaminopropyl silica gel was collected on G-4 filter, washed with MeOH, and dried at 70°C for 4 h. This material was suspended in CF_3COOH (10 mL), and after 15 min stirring H_2O (20 mL) was added. Solid material was collected on G-4 filter, washed with 2 M Na_2CO_3, then water. This product was dried at 70°C for 4 h and added to the stirred solution of the compound **5** (0.75 g, 2.34 mmol) and EEDQ (0.58 g, 2.34 mmol) in dry THF (10 mL), and stirring continued for 18 h at ambient temperature. Work-up as above afforded 1.67 g of **CSP-5**. Anal. C 6.02, H 1.37, and N 1.76%. The % of N reveals that 1.0 g of the chiral stationary phase contains 0.071 mmol of bonded chiral selector.

Preparation of Chiral Stationary Phase CSP-6

Starting from Nucleosil 100-5 NH_2, N-Boc-L-Ala (0.425 g, 2.23 mmol), and EEDQ (0. 55 g, 2.23 mmol) γ-L-alanylaminopropyl silica gel was prepared as described for **CSP-5**. This product was coupled with compound **4** (0.71 g, 2.23 mmol) in the presence of EEDQ (0.55 g, 2.23 mmol) as described for **CSP-5**, to afford 1.73 g of **CSP-6**. Anal. C 5.41, H 1.31 and N 1.94%. The % of N reveals that 1.0 g of the stationary phase contains 0.103 mmol of bonded chiral selector.

RESULTS AND DISCUSSION

Chiral selectors **1**–**5** were prepared by regioselective nucleophilic substitution of C(4) chlorine by the amino group of L-α-amino acids L-alanine, L-phenylalanine, L-phenylglycine, L-asparagine, and L-proline, used as sodium salts in aqueous methanol, Figure 1. Binding of chiral selectors **1**–**4** to the terminal amino group of Nucleosil 100-5 NH_2, effected by EEDQ in dichloromethane, afforded **CSP-1**–**CSP-4**, Figure 1. Both synthetic steps are simple and proceed amenable to any scale-up; the loading of silica gel was determined from the elemental analysis.

CSP-1–**CSP-4** were tested in HPLC columns on the resolution of 23 test racemates (TR-1–TR-23), Figure 2. The results are presented in Tables 1 and 2, only effected resolutions are presented.

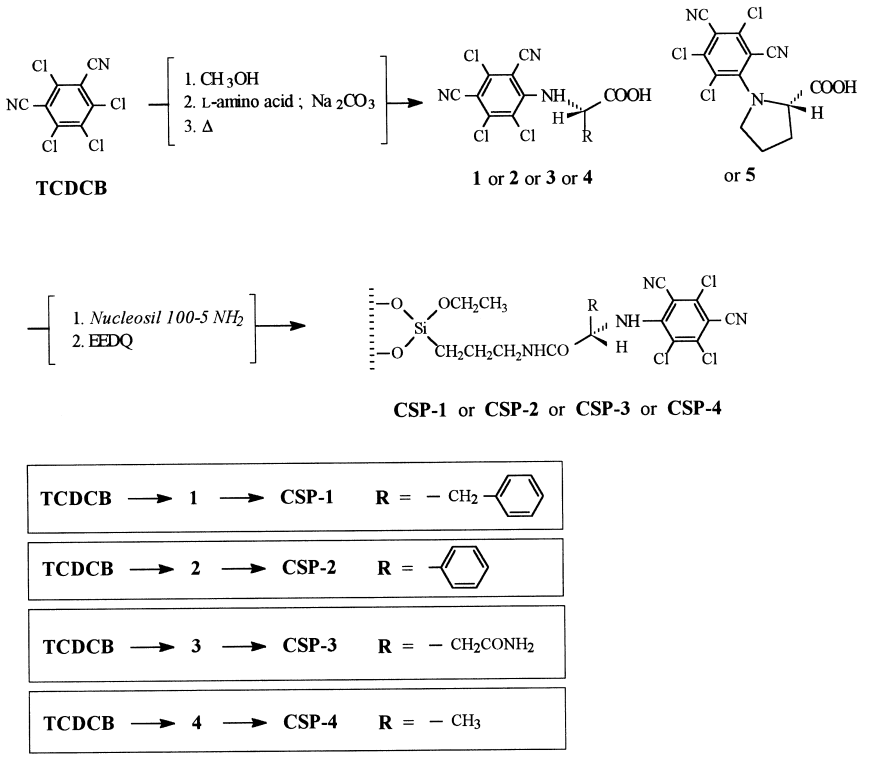

Figure 1. Scheme of the preparation of **CSP-1-CSP-4.**

CSP-1, incorporating L-Phe exhibited only insufficient resolution of isopropylesters of DNB-AA's. With both eluent systems (A or B) only $R_S \geq 0.6$ was achieved, and the highest α was between 1.04–1.07. These results revealed the absence of any rigid enough molecular cleft effective in enantiorecognition. There is presumably only weak contribution of the amide group to hydrogen bonding, whereas π-acid and π-basic contribution compensate. **CSP-2**, incorporating L-PhGly exhibited acceptable resolution for 1,4-benzodiazepine TR-9 ($R_S = 1.17$, $\alpha = 1.51$), and low resolution of TR-10 and TR-13. It is worth noting that N(1)-H 1,4-benzodiazepine TR-9 is much more effectively resolved than its N(1)-Me congener TR-10, revealing the importance of the hydrogen bond-donor group in the analyte. All three compounds are π-basic, indicating contribution of a donor-acceptor interaction with persubstituted benzene unit within CSP. The absence of any remarkable resolution with **CSP-3** reveals that

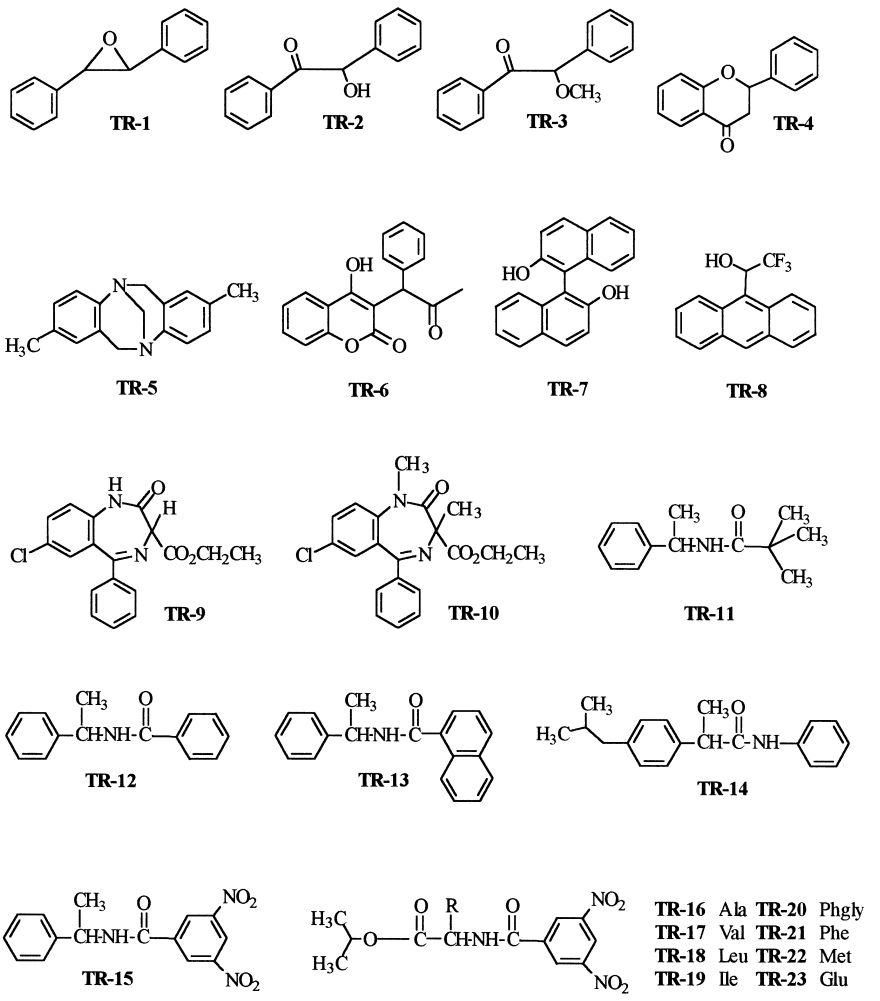

Figure 2. Racemic compounds used for evaluation of HPLC columns.

terminal $CONH_2$ group rises strong, non-selective, and non-productive interactions with test racemates. **CSP-4** proved the most efficient of all, herewith, reported chiral phases. It has resolved the largest number of racemates, some of them with suitable efficacy, Table 1. It presumably acts as both hydrogen bonding donor and π-acceptor, since the most effectively resolved is N(1)-H 1,4-benzodiazepine TR-9, and its N(1)-Me congener TR-10 only poorly.

Table 1

Parameters Obtained for Entioselective Chromatography for Some of Racemic Analytes on the Columns Filled with CSP-1-CSP-3

CSP	Mobile Phase	Analyte	k'_1	α	Rs
CSP-1	A	TR-17	2.04	1.07	0.51
	A	TR-19	1.91	1.06	0.24
	A	TR-20	2.66	1.05	0.22
	A	TR-21	2.80	1.07	0.21
	A	TR-22	2.66	1.04	0.21
CSP-2	A	TR-5	2.99	1.08	0.72
	B	TR-5	2.64	1.04	0.72
	A	TR-9	7.03	1.51	1.17
	A	TR-10	2.03	1.10	0.35
	B	TR-10	4.42	1.08	0.28
	B	TR-12	14.47	1.09	0.28
	B	TR-13	29.73	1.12	0.94
	B	TR-14	4.24	1.08	0.74
CSP-3	A	TR-5	1.31	1.07	0.69
	A	TR-7	3.23	1.04	0.53
	B	TR-7	4.84	1.04	0.78
	A	TR-16	3.81	1.03	0.21
	A	TR-19	2.83	1.01	0.18
	B	TR-19	1.88	1.05	0.84
	A	TR-21	4.22	1.03	0.22

A: n-Hexane/2-propanol (9:1); B: n-hexane/dichloromethane/methanol (100:30:1).

Relative efficacy of this CSP in resolution of isopropylesters of DNB-AA's TR-17, TR-19-TR-22 revealed, as the most important contribution, hydrogen bonding by the amide group near to the chiral center, already reported for structurally related CSPs based on N-cyanuric acid derivatives of α-amino acid.[18]

In order to improve hydrogen bonding interactions we prepared TCDCB derivatives of dipeptides L-Ala-L-Pro and L-Ala-L-Ala. Synthetically, the approach to **CSP-5** and **CSP-6** is simple and appealing since it is convergent and comprises separate preparation of chiral selectors **4** and **5**, then their binding to the solid support, previously modified by coupling of terminal L-Ala carboxy group to *Nucleosil 100-5 NH_2*, Fig. 3.

Table 2

Parameters Obtained for Entioselective Chromatography for Some of Racemic Analytes on the Column Filled with CSP-4

CSP	Mobile Phase	Analyte	k'_1	α	Rs
CSP-4	A	TR-7	2.53	1.07	0.52
	B	TR-7	3.54	1.07	1.02
	A	TR-8	1.62	1.08	0.58
	B	TR-8	2.90	1.05	0.49
	A	TR-9	9.51	1.17	1.24
	B	TR-9	13.69	1.08	1.07
	B	TR-10	1.17	1.08	0.32
	A	TR-14	2.77	1.06	0.82
	A	TR-15	2.17	1.05	0.31
	B	TR-16	3.41	1.04	0.61
	A	TR-17	1.97	1.07	0.64
	B	TR-17	2.11	1.06	0.81
	A	TR-19	1.10	1.09	0.63
	B	TR-19	1.95	1.08	1.05
	A	TR-20	1.78	1.05	0.48
	B	TR-20	3.02	1.04	0.62
	A	TR-21	1.91	1.05	0.66
	B	TR-21	2.90	1.06	0.87
	A	TR-22	2.51	1.02	0.18
	B	TR-22	3.78	1.05	0.86

A: n-Hexane/2-propanol (9:1); B: n-hexane/dichloromethane/methanol (100:30:1).

Table 3

Parameters Obtained for Enantioselective Chromatography of Racemic Analytes TR-16-TR-23 on the Columns Filled with CSP-5-CSP-6

CSP	Analyte	k'_1	α	Rs
CSP-5	TR-20	3.33	1.08	0.60
CSP-6	TR-16	3.21	1.07	0.75
	TR-17	2.62	1.11	0.94
	TR-18	2.30	1.06	0.66
	TR-19	2.44	1.11	0.93
	TR-20	3.57	1.08	0.84
	TR-21	5.20	1.15	0.98
	TR-22	4.41	1.08	0.89
	TR-23	3.76	1.05	0.63

Mobile phase: n-hexane/2-propanol (9:1).

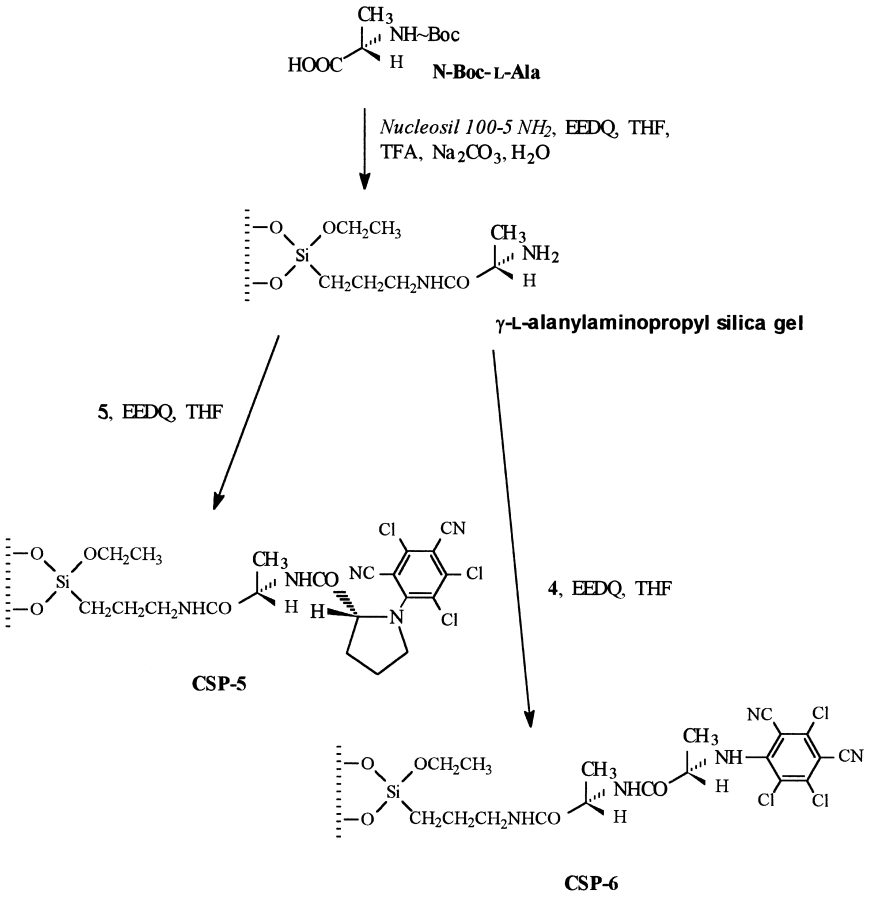

Figure 3. Scheme of the preparation of **CSP-5** and **CSP-6**.

Interestingly, **CSP-6** proved notably more effective then **CSP-5**, presumably because of too crowded situation around the L-Pro-amide bond and near to π-acidic persubstituted benzene; this situation offers not enough space for creation of a chiral hole to bind the enantiomers of an analyte. **CSP-6** instead resolves all tested isopropylesters of DNB-AAs, TR-16–TR-23, some of them with high efficacy, Table 3.

CONCLUSION

In conclusion, resolution by novel **CSP-1**–**CSP-6** revealed limited contribution of π-acidic persubstituted benzene ring to chiral recognition, and rele-

vant contribution of hydrogen bonding via amido group. Besides, the exposure and the distance between amido group and persubstituted benzene ring seem to be important elements of recognition, in view of the best results obtained with **CSP-4** and **CSP-6**, incorporating L-Ala residues. Hydrogen bonding by additional amido group, distant from chiral center in **CSP-3**, also lowers resolution ability. Two amido groups in the structure of **CSP-5** and **CSP-6**, particularly a proline moiety in **CSP-6**, reduce the conformational mobility of chiral selectors. Of the two CSPs containing dipeptides as chiral selector, those with L-Ala-L-Ala unit (**CSP-6**) proved superior to that containing conformationally rigid L-Ala-L-Pro units (**CSP-5**). Best resolutions were obtained with **CSP-4**, where unfavorable (compensating) π-π interactions of the aromatic ring in the amino acid residues of **CSP-1** and **CSP-2**, and persubstituted aromatic rings are absent. The work is in progress towards preparation of the CSPs that a comprise rigid chemical selector with π-basic derivatives of TCDCB and π-acidic auxiliary.

ACKNOWLEDGMENTS

This work was supported by POLYtech S.c.r.l. (Area di Ricerca, Trieste, Italy) within the joint project on development of new enantioseparation processes. Valuable technical advice by Dr. Ahmed Aced, Iris Technologies Inc., is acknowledged.

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Received September 7, 1999 Author's Revisions December 3, 1999
Accepted October 8, 1999 Manuscript 5181