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Axially dissymmetric bianthracene-based chiral stationary phase for the high-performance liquid chromatographic separation of enantiomers

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Abstract

Enantiomerically pure (a*R*)-1,1′-bianthracene-2,2′-dicarboxylic acid is prepared and bonded to a 3-aminopropylsilanized silica via an amide linkage to afford a novel chiral stationary phase (CSP 2) for high-performance liquid chromatographic separation of enantiomers. The performance of CSP 2 is compared with that of the previously prepared binaphthalene-based CSP (CSP 1), which was obtained by bonding axially dissymmetric (a*S*)-1,1′-binaphthalene-2,2′-dicarboxylic acid to the silica. As is expected from the chiral discrimination mechanism proposed for CSP 1, in which simultaneous π-donor–acceptor interaction and dipole-stacking interaction between the CSP and the analytes play a critical role for the separation of enantiomers, CSP 2 shows a greatly improved performance as compared with CSP 1 in the separation of a wide range of enantiomeric amino acids, amines, alcohols and carboxylic acids as the 3,5-dinitrophenyl derivatives.

1. Introduction

It is well known that the chiral discrimination ability of a selector molecule mostly determines the performance of a so-called "brush-type" chiral stationary phase (CSP) for the high-performance liquid chromatographic (HPLC) separation of enantiomers [1–3]. In this context, introduction of an axially dissymmetric 1,1′-binaphthalene skeleton into the CSP is of potential interest, considering the fact that the remarkable chiral-discriminating ability of the atropisomeric 1,1′-binaphthalenes has been the subject of intense studies in the last two decades; highly efficient asymmetric syntheses and/or chiral recognitions have been achieved by the use of this class of optically active molecules [4,5]. In fact, Sogah et al. [6] succeeded as early as 1975 in a complete resolution of amine and amino ester salts by a chiral binaphthalene-crown ether bonded to silica gel, though subsequent applications of atropisomeric biaryls to the CSPs have been quite limited [7–10].

We have previously reported the preparation of a CSP for the HPLC separation of enantiomers by bonding axially disymmetric (a*S*)-1,1′-binaphthalene-2,2′-dicarboxylic acid [(a*S*)-**1**] to a 3-aminopropylsilanized silica gel via an amide linkage (CSP 1) (Fig. 1), which efficiently discriminates a wide variety of enantiomeric C-

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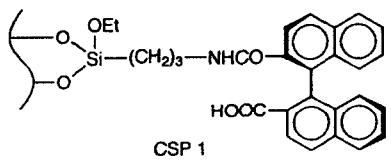
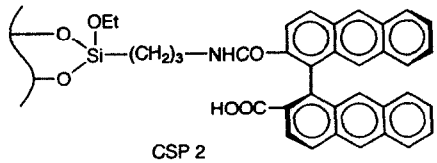


CSP 1



CSP 2

Fig. 1. Axially disymmetric binaphthalene- (CSP 1) and bianthracene-based CSP (CSP 2).

centrochiral analytes as the 3,5-dinitrophenyl derivatives as well as axially chiral 1,1′-biaryls bearing polar substituents on the 2,2′-positions [11]. A simplified chiral discrimination model depicted in Fig. 2 nicely explains the relevant chromatographic behaviours of 3,5-dinitrophenylcarbamates derived from enantiomeric alcohols. It has been supposed that only the approach of the analyte from the upper side of the horizontal naphthalene plane is stereo-differentiating, because it allows π-donor–acceptor interaction between the π-basic naphthalene plane of the CSP and the π-acidic 3,5-dinitrophenyl ring of the analyte to cooperate with

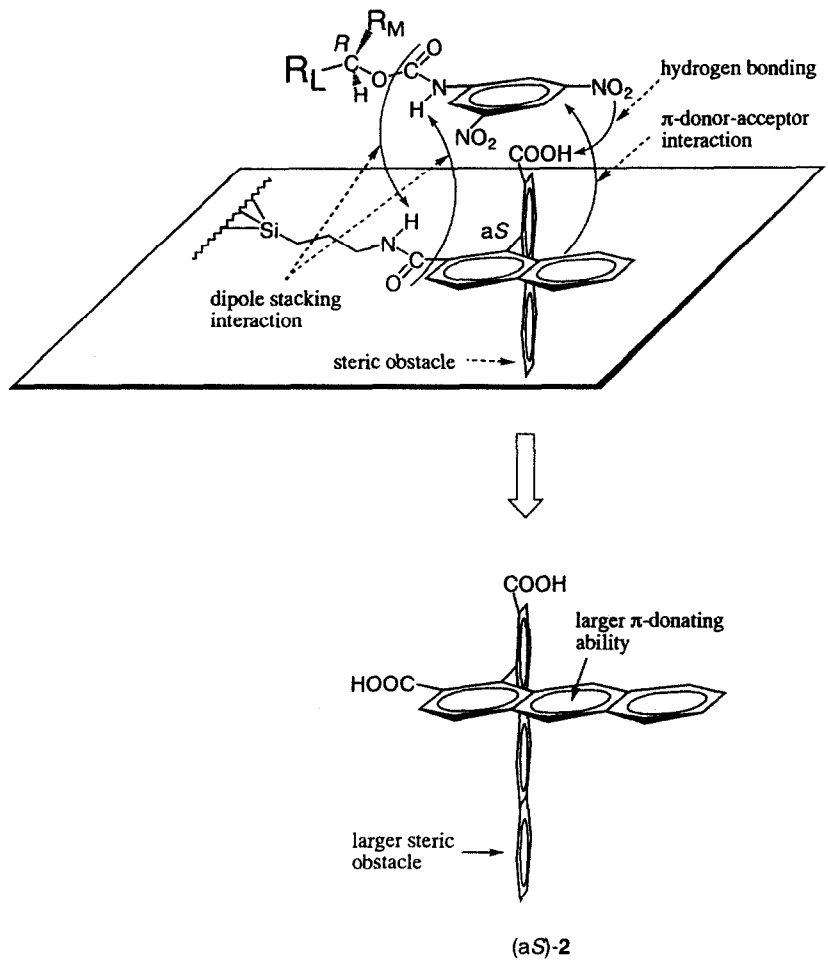


Fig. 2. Chiral discrimination model for binaphthalene-based selector of CSP 1 and an extension to bianthracene-based selector.

the dipole-stacking interaction between the two amide linkages of the CSP and analyte to determine the stability of the adsorbates by virtue of the stereochemistry of the alcohol moieties (Fig. 2). Thus, 3,5-dinitrophenylcarbamates from (*R*)-alcohols are more retained than those from (*S*)-counterparts on CSP 1 bearing (a*S*)-binaphthalene axis. Validity of the chiral discrimination model has been substantiated by ^{1}H NMR studies of a solubilized model compound of the CSP and analytes as well as the elution behaviours of a wide range of structurally related analytes on CSP 1 [12].

The model strongly tempted us to replace the binaphthalene moiety of CSP 1 by a bianthracene skeleton, because the anthracene nuclei should not only be a far better π-donor but also make a bulkier steric hinge to suppress the non-stereoselective approach of the analytes to the CSP than the naphthalene rings (Fig. 2). Soundness of the hypothesis has partially been proved in a preliminary communication in which the separations of the 3,5-dinitrophenyl-derivatized alcohols were significantly improved by the use of a bianthracene-based CSP (CSP 2) (Fig. 1) [13]. Herein we report the full details of the preparation and performance of CSP 2, showing that it exhibits a greatly improved chiral selectivity as compared with CSP 1 and discriminates a variety of analytes which include amino acids, amines, alcohols and carboxylic acids as the 3,5-dinitrophenyl derivatives and biaryls bearing polar substituents on the 2,2′-positions.

2. Experimental

2.1. General

LC was performed using a Shimadzu LC-6A or a JASCO Trirotor-III apparatus equipped with a Shimadzu SPD-6A or a JASCO Uvidec-100-III ultraviolet detector (254 nm), respectively. A stainless-steel column (250 mm × 4.6 mm I.D.) was slurry packed with the packing material described below using conventional techniques.

IR spectra were measured on a Shimadzu IR-460 grating spectrophotometer. Optical rotations were recorded on a Union PM-101 automatic digital polarimeter in a 1-cm cell. Melting points were measured on a Yamato MP-21 apparatus and are uncorrected. Microanalyses were carried out in the Microanalytical Laboratory of the Institute for Chemical Reaction Science, Tohoku University.

2.2. Materials

The preparation of 3-aminopropylsilanized silica gel (Tosoh silica gel base, spherical 5-μm particles, microsphere diameter, 100 Å) (found: C, 8.10; H, 2.07; N, 1.42%; calculated: 1.01 mmol–NH_2/g gel based on N) was described before [11]. Reagent-grade commercial materials were used as purchased unless otherwise noted. A sample of 2,2′-dimethyl-1,1′-bianthraquinone (**3**) was generously provided by Mitsui Toatsu Chemicals. Solvents used for HPLC were distilled before use.

2.3. Preparation of enantiomerically pure (aR)-1,1′-bianthracene-2,2′-dicarboxylic acid [(aR)-2]

The preparation of enantiomerically pure (a*R*)-**2** was performed according to the procedures reported by Bell and Waring [14] with a slight modification.

2,2′-Bis(dibromomethyl)-1,1′-bianthraquinone (4)

Crude bianthraquinone **3** was purified by the method of Ulich and Waldron [15]. A 15.0-g amount of crude **3** was dissolved in concentrated H_2SO_4 (45 ml), to which 13 ml of nitrobenzene were added. To the mechanically stirred solution 15 ml of water were slowly added. During the addition, the temperature of the mixture raised to ca. 100°C. After standing overnight at room temperature, the mixture was filtered and the precipitate was washed with 80% H_2SO_4, and the remaining nitrobenzene was removed by steam distillation. The mixture was filtered and the solid was washed with water and dried in vacuo to give a purified sample, 13.5 g; m.p. > 310°C.

Bromination of **3** was carried out in a 300-ml four-necked flask fitted with a mechanical stirrer, a reflux condenser topped with a gas-absorption trap, a thermometer and a dropping funnel. To a mechanically stirred solution of the purified **3** (12.0 g, 27.2 mmol) in nitrobenzene (75 ml) kept at higher than 170°C was added dropwise a bromine solution (26 g) in nitrobenzene (25 ml) during 6 h, and then the reaction was continued for another 2 h. After the reaction mixture had been cooled to ambient temperature, the resulting yellow precipitate was recovered by filtration, washed with nitrobenzene and then with diethyl ether and dried in vacuo to give bis(dibromomethyl)bianthraquinone **4**, 15.8 g (77% yield), m.p. > 300°C; IR (KBr) (cm^{-1}), 3100, 1670, 1580, 1500, 1320, 1280, 990, 930, 714, 638.

1,1'-Bianthraquinone-2,2'-dicarboxylic acid (5)

In a 300-ml three-necked flask equipped with a mechanical stirrer, a reflux condenser and a thermometer, were placed concentrated H_2SO_4 (120 ml), anhydrous boric acid (18 g) and **4** (15.0 g, 19.8 mmol). The mixture was stirred at 120–130°C for 5 h. The cooled mixture was slowly added to an ice–water (250 ml), and a brown precipitate was recovered by filtration, washed with water and dried in vacuo to give 2,2'-bisformyl-1,1'-bianthraquinone. This material was used without further purification for the next step by dissolving in hot acetic acid (90 ml). To the stirred solution kept at 60°C was added portion wise CrO_3 (15.0 g, 0.15 mol) during 1 h. The mixture was heated at reflux for 5 h, and then poured into water (300 ml). The precipitated crude diacid **5** was worked up as usual, which included filtration, washing with water free from chromium ions, dissolving in NaOH solution, decoloration with Norite, hot filtration and regeneration of the free acid by addition of concentrated HCl solution. The resulting precipitate was filtered and dried in vacuo to give 4.95 g of **5** (yield 50%), m.p. > 300°C (browned at 285–290°C); IR (KBr) (cm^{-1}), 3600–2500 (br), 1700, 1690, 1580, 1300, 1260, 970, 930, 860, 790, 710. Analysis: found, C 71.43, H 2.96%; calculated for $C_{30}H_{14}O_8$, C 71.72, H 2.81%.

Racemic 1,1'-bianthracene-2,2'-dicarboxylic acid (2)

To a 500-ml two-necked round-bottomed flask equipped with a mechanical stirrer and a reflux condenser, were placed zinc dust (10 g, 150 mg-atom) and 2 *M* HCl (20 ml). After the mixture was stirred for several minutes, the inside of the flask was purged with nitrogen and supernatant liquid was removed by decantation. The zinc was further washed with 1 *M* NaOH (20 ml) and the liquid was again removed by decantation. To the residue were added **5** (4.50 g, 8.96 mmol) and 28% ammonium hydroxide solution (130 ml). The mixture was heated under gentle reflux for 4 h. During the time course the red reaction mixture turned to yellow. At this point, another 180 ml of water were added and reflux was continued for 0.5 h. The mixture was filtered hot. Addition of concentrated HCl to the filtrate caused precipitation of yellow gel. This was filtered, washed with water and dried in vacuo. The dry material was crushed in a mortar and crystallized twice from glacial acetic acid to give **2** as a hairy yellow precipitate, 3.60 g (yield 91%); m.p. 300–305°C. Crystallization from *o*-dichlorobenzene gave pure **2** as yellow prisms, m.p. 305–307°C; IR (KBr) (cm^{-1}), 3600–2500 (br), 1690, 1340, 890, 740, 475. Analysis: found, C 81.43, H 4.10; calculated for $C_{30}H_{18}O_4$, C 81.68, H 4.32.

Optical resolution of racemic 2

Racemic **2** (3.0 g, 6.8 mmol) was suspended in 120 ml of ethanol and heated at reflux. To the mixture were added 5.0 g of quinidine (15.4 mmol) at once. The suspension disappeared at one time, but soon precipitation began. The mixture was refluxed for another 0.5 h and cooled to room temperature. The precipitate was filtered and again suspended in 50 ml of ethanol and refluxed for 0.5 h. The cool mixture was filtered and dried in vacuo to give a sample of (a*R*)-**2**-quinidine salt, 3.20 g (yield 45%); $[\alpha]_{546}^{25}$ −516° (*c* 0.52, $CHCl_3$). The salt was boiled in 80 ml of 1% NaOH solution for 1 h and filtered. The filtrate was made acidic by addition of 6 *M* HCl, and the resulting precipitate was taken into ethyl acetate. Evaporation of the solvent gave

(a*R*)-**2** as a yellow powder, 1.23 g [yield 86%, based on (a*R*)-**2**]; m.p. 257–259°C (acetic acid) (lit. [14], m.p. 253–255°C), $[\alpha]_{546}^{26}$ −457° (*c* 0.80, acetone) {lit. [14], $[\alpha]_{546}^{26}$ −440° (*c* 0.80, acetone)}. A sample of the optically active diacid was treated with diazomethane to give the dimethyl ester, the enantiomeric homogeneity of which was confirmed by HPLC on N-(3,5-dinitrobenzoyl)phenylglycine-based CSP (Pirkle column).

2.4. Preparation of the CSPs

Binaphthalene-based CSP 1 was that used in the previous studies, which was prepared by bonding (a*S*)-1,1′-binaphthalene-2,2′-dicarboxylic acid to the above mentioned 3-aminopropylsilanized silica gel; 0.47 mmol binaphthalene unit/g gel [11].

Bianthracene-based CSP 2

A mixture of the 3-aminopropylsilanized silica gel (3.00 g), (a*R*)-**2** (0.92 g, 2.08 mmol) and N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) (1.03 g) in DMF (30 ml) was irradiated with ultrasound under a nitrogen atmosphere in the water-bath of an ultrasound laboratory cleaner (35 W, 41 kHz) which was maintained at 20°C. After 8 h irradiation, the modified silica gel was filtered, washed successively with tetrahydrofuran, methanol, acetone and diethyl ether, and dried in vacuo to give 3.44 g of CSP 2. Analysis: found, C 16.67, H 1.81%, N 1.51%; calculated, 0.29 mmol bianthracene unit/g gel based on C.

2.5. Preparation of the derivatized enantiomeric analytes

Alcohols (R^1R^2CH–OH) used for derivatization to **8l**, **m**, **n**, **u**, **v**, **y** and **z** were prepared according to the general procedure by using the Grignard method from alkyl bromide (R^1–Br) and aldehyde (R^2–CHO) [16] and those [$R^1R^2CH(CH_2)_n$–OH] to **10a–c** were prepared by the reduction of the corresponding carboxylic acids [$R^1R^2CH(CH_2)_{n-1}$–COOH] with $LiAlH_4$ [12]. Carboxylic acids (R^1R^2CH–COOH) used for derivatization to **11d–h**, **j**, **m–p** and **12a** were prepared via the carboxylation of the corresponding Grignard reagents by treatment with dry ice according to the conventional methods [12]. Parent carboxylic acids **11c** [17] and **11l** [18] were resolved to optically active forms by use of quinine and (*S*)-(+)-phenylethylamine, respectively, for the determination of the elution orders. Binaphthol (**13b**) [19] and biaryl carboxylic acid derivatives (**13c–i**) [20,21] were prepared by the literature procedure. Other samples used were of commercial origin.

Derivatization of these samples was according to the procedure described before [11,12].

3. Results and discussion

Chiral selector molecule (a*R*)-**2** was prepared starting from bianthraquinone **3** according to the method reported by Bell and Warning [14] (Fig. 3). Oxidation of the methyl substituents of **3** via bis(dibromomethyl) derivative **4** to dicarboxylic acid **5** followed by quinone-carbonyl reduction by zinc dust gave racemic acid **2**. Optical resolution of this material with quinidine gave an (a*R*)-**2**-quinidine salt as the less soluble precipitate. After acidic workup to remove the base, two recrystallizations from acetic acid gave essentially enantiopure (a*R*)-**2** as evidenced by HPLC analysis of the methyl ester on a Pirkle column. The atropisomeric (a*R*)-**2** was bonded to a 3-aminopropylsilanized silica via an amide linkage in dimethyl formamide with the aid of EEDQ under ultrasonic irradiation at 20°C to give the bianthracene-modified silica gel. This was slurry packed into a 250 × 4.6 mm I.D. stainless-steel column using conventional packing techniques to give CSP 2 bearing the chiral selector of opposite axial chirality as compared to CSP 1 (Fig. 1).

Enantiomeric samples were amino acids as the N-3,5-dinitrobenzoyl butyl esters (**6**), amines as the 3,5-dinitrophenylureas (**7**), alcohols as the 3,5-dinitrophenylcarbamates (**8–10**), carboxylic acids as the 3,5-dinitroanilides (**11** and **12**), 1,1′-bi-2-naphthols (**13a**, **b**) and biarylcarboxylic acids as the N-butylamides (**13c–i**) as summarized in

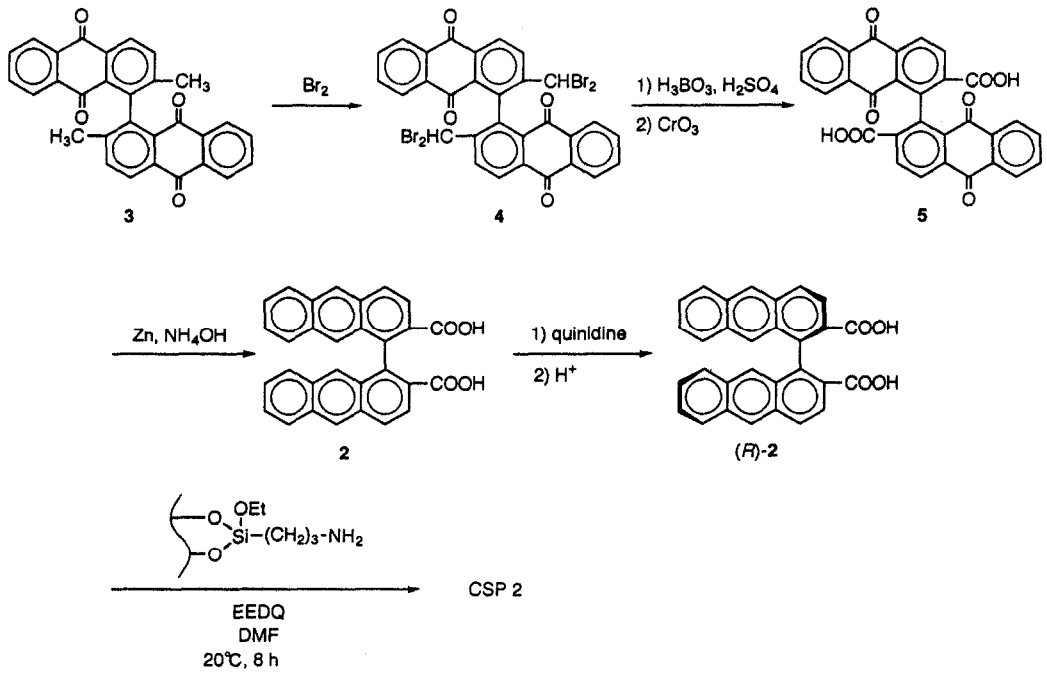


Fig. 3. Preparation of (a*R*)-**2** and CSP 2. DMF = Dimethylformamide.

Fig. 4. They were eluted on CSP 2 with an alcohol–hexane mixture, the composition of which was varied to adjust the capacity factor, k', in a comparable range. The results of the chromatographic resolution of these analytes are summarized in Table 1. A number of analytes could be resolved on CSP 2, and in favorable cases separation factors (α) greater than 3 were attained as seen for **8w**, **11k** and **q**. For comparison, also included in Table 1 are the results of the elution of the same samples on the binaphthalene-based CSP 1, some of which came from previous work [11,12]. Fig. 5 shows the resolutions of representative analytes on CSPs 1 and 2, illustrating the good performances of these CSPs.

Where chiral resolutions were attainable, the elution orders of each analyte were reversed from CSP 1 to CSP 2, which was consistent with the inverted axial configuration of the chiral selector molecules bonded to the silica support (Fig. 1). Thus, CSP 2 bearing (a*R*)-bianthracene axis retained more strongly the (*S*)-enantiomers of the derivatized amino acids, amines and alcohols. This implies that similar chiral discrimination mechanisms are operative in these two phases, as supposed by the postulated mechanistic picture (Fig. 2). Generally speaking, CSP 2 showed considerably better separations than CSP 1 in terms of α values, although there were some cases where the latter showed almost equal or slightly superior separations to those obtained by the former. Considering the eluent compositions utilized, CSP 2 retained all the analytes examined more strongly than CSP 1. It seems that an increased π-donor–acceptor interaction plays a particularly important role for retention by incorporation of the bianthracene moiety in place of the binaphthalene residue (see below).

The importance of the presence of a π-accepting site in the analytes was discussed in detail in a previous paper for chiral recognition on CSP 1 [12]. It was shown that the 3,5-dinitrophenyl moiety is especially advantageous not only for electronic reasons but also because of steric arrangement of the nitro groups which seemingly enables hydrogen bonding to the 2′-carboxyl function of the binaphthalene selector (Fig. 2)

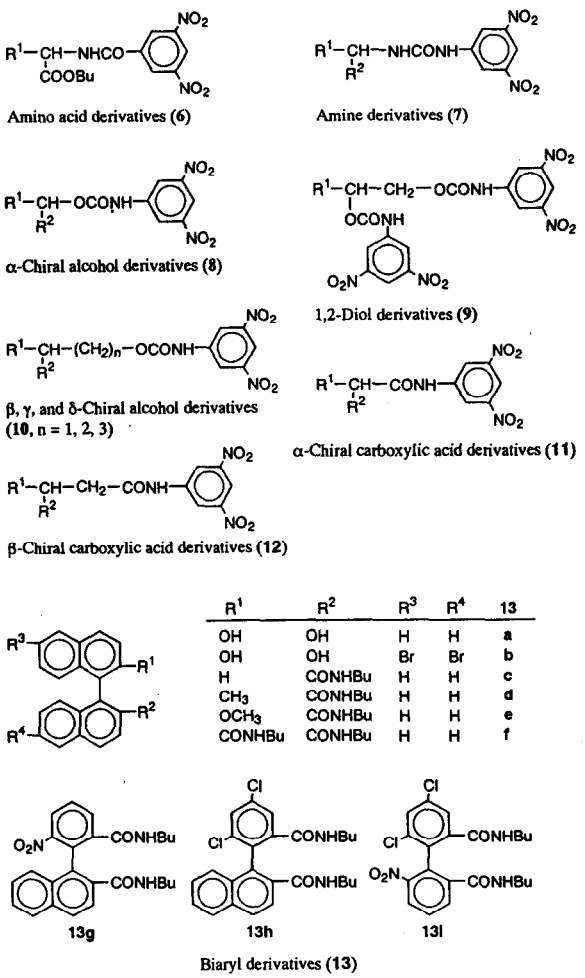


Fig. 4. Structures of enantiomers (see also Table 1).

[12]. Steric hindrance caused by *ortho* substituents on the aryl moieties was detrimental to chiral recognition on CSP 1. Similar situations also hold for CSP 2 as exemplified by Table 2 which compares the separations of ten carbamates prepared from 1-phenylethanol and ten amides from 2-phenylpropionic acid.

Close inspection of the data in Table 1 permits several comments on the chromatographic behaviours of the respective analytes on CSPs 1 and 2, although it should be noted that a wide spectrum of the analytes does not always allow a consistent clear-cut explanation by the proposed chiral discrimination model alone. Among the eleven analytes of derivatized amino acids **6** and amines **7** examined, three samples (**6b**, **c** and **7a**) did not separate on CSP 1, but did separate with baseline resolution on CSP 2. Somewhat bothering is the behaviour of the derivatized phenylglycine **6d**. It was separated on CSP 1 but not on CSP 2. Only in this case, however, the elution order was reversed, i.e. the (*R*)-enantiomer eluted first on CSP 1 bearing (a*S*)-binaphthalene axis. As suggested previously [11], CSP 1 might recognize the phenyl substituent directly attached to the chiral centre being bulkier than the COOBu group. This situation may change by incorporation of the bianthracene moiety where enhanced π-donor–acceptor interactions of the CSP and the analyte may lead to too much spurious interactions which retain the analyte **6d** strongly as evidenced by the large k' value without distinguishing between the enantiomers.

As for aliphatic 2-alkanol carbamates (**8a–g**), derivatized 2-butanol separated on CSP 2, that is, the CSP discriminated the methyl from the ethyl unit. On both CSPs, the selectivity α increased but retention k' decreased with the increase of the alkyl chain length. This seems to show that the selectivity mainly depends on the difference of the bulk between the two alkyl substituents attached to the carbinyl carbon, while steric hindrance rather than the hydrophobic attractive force is operative between the CSPs and the alkyl chains of the analytes on the normal mode elution. In accordance with these assumptions, the selectivity of octanol derivatives (**8e**, **i** and **j**) decreased as the hydroxy group approached to the centre of the alkyl chain, while the retentions were kept within a rather comparable range. Both CSPs discriminated structural differences of the two alkyl substituents of the same carbon numbers as exemplified by **8l** and **8n**.

Although relative steric bulkiness of alkyl and alkenyl moiety is controversial ([22], see also [23]), CSP 1 seems to recognize vinyl to be bulkier than ethyl as judged by the separability of **8p** but not **8a** on CSP 1. This seems to imply that an unsaturated substituent in the vicinity of the chiral centre of the analyte causes electronic repulsion against the CSP, resulting in a bulkier exclusion volume than the Van der Waals radius.

Table 1
Separation of enantiomers on CSP 1 and CSP 2

No.	R^1	R^2	CSP 1			CSP 2		
			Eluent	k'_1	α	Eluent	k'_1	α
Amino acid derivatives (6)								
6a	CH_3 (Ala)		A	4.58 (*S*)	1.13[a]	C	6.79 (*R*)	1.76
6b	Iso-C_3H_7 (Val)		A	2.64	1.00[a]	C	3.45 (*R*)	1.31
6c	Iso-C_4H_9 (Leu)		A	2.71	1.00[a]	C	3.46 (*R*)	1.63
6d	Ph (PhGly)		A	4.27 (*R*)	1.15[a]	C	9.18	1.00
6e	CH_2Ph (Phe)		A	5.20 (*S*)	1.14[a]	C	10.31 (*R*)	1.67
Amine derivatives (7)								
7a	CH_3	Iso-C_3H_7	D	5.59	1.00	E	6.69	1.17
7b	CH_3	*n*-C_6H_{13}	D	4.45	1.16[b]	E	5.60	1.46
7c	CH_3	Ph	E	4.48 (*S*)	1.30[b]	G	6.61 (*R*)	1.73
7d	CH_3	1-Naphthyl	E	5.47 (*S*)	1.24[b]	G	8.56 (*R*)	1.53
7e	CH_3	$(CH_2)_2Ph$	E	3.86	1.10	G	5.20	1.18
7f	Ph	CH_2Ph	E	6.77	1.11	G	13.40	1.06
α-Chiral alcohol derivatives (8)								
8a	CH_3	C_2H_5	A	5.36	1.00	C	4.26	1.13
8b	CH_3	*n*-C_3H_7	A	4.78 (*S*)	1.08	C	3.86 (*R*)	1.20
8c	CH_3	*n*-C_4H_9	A	4.38	1.15	C	3.48	1.31
8d	CH_3	*n*-C_5H_{11}	A	4.11	1.19	C	3.36	1.46
8e	CH_3	*n*-C_6H_{13}	A	3.93 (*S*)	1.21[a]	C	3.19 (*R*)	1.56
8f	CH_3	*n*-C_7H_{15}	A	3.76	1.22	C	3.10	1.66
8g	CH_3	*n*-C_8H_{17}	A	3.68	1.24	C	3.01	1.72
8h	C_2H_5	*n*-C_3H_7	A	4.27	1.09	C	3.94	1.05
8i	C_2H_5	*n*-C_5H_{11}	A	3.50	1.23	C	3.54	1.23
8j	*n*-C_3H_7	*n*-C_4H_9	A	3.64	1.08	C	3.47	1.15
8k	*n*-C_3H_7	*n*-C_5H_{11}	A	3.73	1.04	C	3.47	1.13
8l	*n*-C_3H_7	Iso-C_3H_7	A	3.81	1.10	C	3.65	1.05
8m	*n*-C_4H_9	Iso-C_3H_7	A	3.50	1.23	C	3.47	1.27
8n	*n*-C_4H_9	Iso-C_4H_9	A	3.60	1.22	C	3.37	1.27
8o	*trans*-2-Methylcyclohexanol		A	6.19	1.07	C	4.27	1.19
8p	CH_3	$CH=CH_2$	A	5.90	1.08	C	5.56	1.12
8q	2-Cyclohexene-1-ol		A	3.84	1.00	C	6.16	1.10
8r	CH_3	Ph	B	3.86 (*S*)	1.54[a]	E	3.93 (*R*)	2.31
8s	C_2H_5	Ph	B	3.44	1.53[a]	E	3.95	2.21
8t	*n*-C_3H_7	Ph	B	3.33	1.43[a]	E	3.82	2.04
8u	Iso-C_3H_7	Ph	B	3.56	1.56	E	3.74	2.16
8v	Cyclo-C_6H_{12}	Ph	B	4.08 (*S*)	1.38	E	4.17 (*R*)	1.99
8w	CH_3	2-Naphthyl	B	5.62	1.55	E	5.25	3.10
8x	Ph	2-Naphthyl	B	12.12	1.04	E	16.95	1.28
8y	CH_3	CH_2Ph	B	4.74 (*S*)	1.17	E	3.45 (*R*)	1.59
8z	C_2H_5	CH_2Ph	B	4.18	1.18	E	3.44	1.49
8α	α-Tetralol		B	3.84	1.00	E	4.27	1.04
8β	β-Tetralol		B	5.28	1.08	E	4.18	1.05

Table 1 *(continued)*

No.	R^1	R^2	CSP 1			CSP 2		
			Eluent	k'_1	α	Eluent	k'_1	α
1,2-Diol derivatives (9)								
9a	CH_3		E	9.34	1.00	G	13.94	1.04
9b	C_2H_5		E	7.87	1.06	G	12.04	1.27
9c	n-C_4H_9		E	6.21	1.24	G	10.84	1.55
9d	n-C_6H_{13}		E	5.38 (*R*)	1.31	G	10.20 (*S*)	1.80
9e	Ph		F	4.02 (*R*)	1.45	G	18.15 (*S*)	2.73
9f	*trans*-Cyclohexane-1,2-diol		E	6.43	1.00	G	8.63	1.20
β, γ and δ-Chiral alcohol derivatives (10)								
10a	CH_3	Ph ($n=1$)	B	5.05 (*R*)	1.09[b]	E	3.99 (*S*)	1.13
10b	CH_3	Ph ($n=2$)	B	5.23	1.00[b]	E	4.35 (*R*)	1.15
10c	CH_3	Ph ($n=3$)	B	4.99	1.00[b]	E	4.57 (*R*)	1.03
α-Chiral carboxylic acid derivatives (11)								
11a	CH_3	C_2H_5	A	12.33	1.08[b]	E	4.80	1.03
11b	CH_3	n-C_3H_7	A	9.73	1.09	E	4.04	1.04
11c	CH_3	n-C_4H_9	A	8.97 (*R*)	1.27[b]	E	3.71 (*S*)	1.21
11d	CH_3	n-C_5H_{11}	A	8.49	1.31	E	3.49	1.32
11e	CH_3	n-C_6H_{13}	A	7.93	1.37[b]	E	3.65	1.44
11f	CH_3	n-C_7H_{15}	A	7.60	1.37	E	3.14	1.54
11g	CH_3	n-C_8H_{17}	A	7.38	1.39	E	3.06	1.64
11h	C_2H_5	n-C_3H_7	A	9.36	1.00	E	3.27	1.03
11i	C_2H_5	n-C_4H_9	A	8.51	1.25	E	2.90	1.27
11j	C_2H_5	n-C_5H_{11}	A	8.04	1.29	E	2.75	1.40
11k	CH_3	Ph	B	7.57 (*R*)	1.63[b]	F	4.67 (*S*)	3.38
11l	C_2H_5	Ph	B	7.26(*R*)	1.46[b]	F	4.74 (*S*)	2.86
11m	n-C_3H_7	Ph	B	7.02	1.47[b]	F	4.34	2.76
11n	Iso-C_3H_7	Ph	B	7.28	1.34	F	4.27	2.65
11o	n-C_4H_9	Ph	B	8.03	1.19	F	4.76	2.30
11p	Cyclo-C_6H_{12}	Ph	B	8.67	1.17	F	5.11	2.38
11q	CH_3	5-OMe-(2-Naphthyl)	C	8.56	1.72	F	8.38	3.04
β-Chiral carboxylic acid derivatives (12)								
12a	CH_3	Ph ($n=1$)	B	7.82 (*R*)	1.50[b]	F	5.09 (*S*)	2.61
Biaryl derivatives (13)								
13a			B	3.41 (*S*)	1.09[a]	C	4.07 (*R*)	1.31
13b			B	5.86	1.24	C	6.38	1.81
13c			A	2.22	1.00[a]	B	2.04	1.00
13d			A	1.46	1.00[a]	B	1.39	1.00
13e			A	3.06 (*S*)	1.09[a]	B	2.80 (*R*)	1.12
13f			B	5.41 (*S*)	1.38[a]	B	5.09 (*R*)	1.47
13g			B	4.58 (*R*)	1.21[a]	B	5.12 (*S*)	1.34
13h			B	3.25	1.26[a]	B	3.18	1.29
13i			B	3.24 (*S*)	1.13[a]	B	3.43 (*R*)	1.18

For structures, see Fig. 4. Mobile phases: hexane–2-propanol, (A) 90:10, (B) 85:15 and (C) 80:20; hexane–ethanol, (D) 90:10, (E) 80:20 and (F) 70:30; and (G) hexane–ethanol–methanol (70:20:10). Flow-rate: 1 ml/min. k'_1 = Capacity factor for the initially eluted enantiomer. The configuration of the initially eluted enantiomer is indicated in parentheses. The separation factor, α, is the ratio of the capacity factors of the enantiomers.

[a] Data from Ref. 11.

[b] Data from Ref. 12.

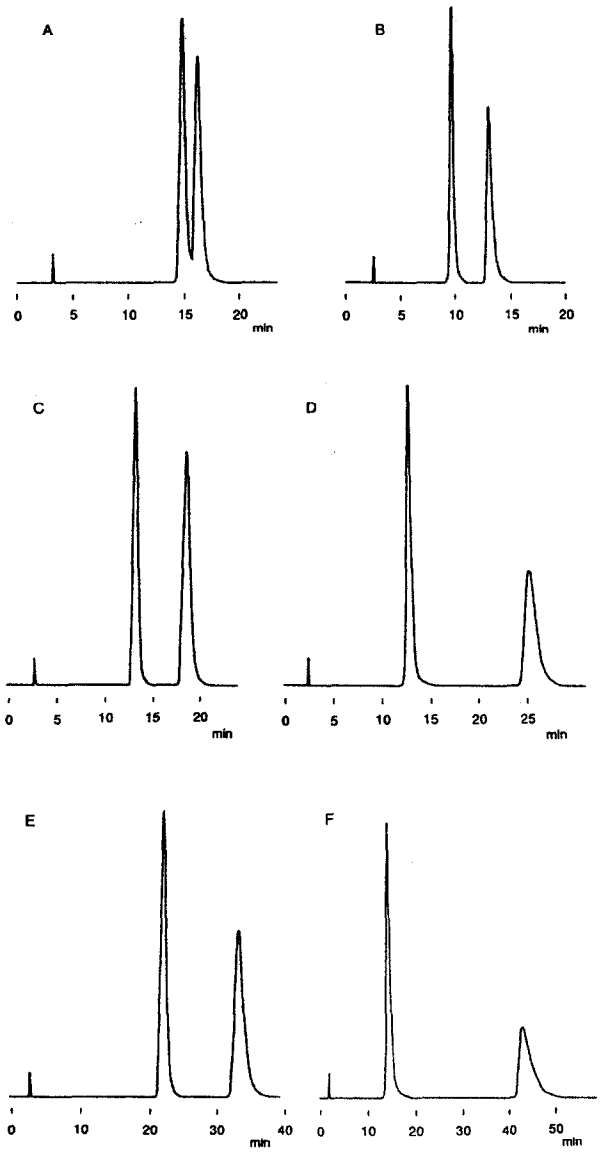


Fig. 5. Chromatographic separation of enantiomers. Separation of N-3,5-dinitrobenzoyl butyl ester of alanine (**6a**) on CSP 1 (A) and CSP 2 (B); separation of 3,5-dinitrophenylcarbamate of 1-phenylpropanol (**8s**) on CSP 1 (C) and CSP 2 (D); separation of 3,5-dinitroanilide of 2-phenylpropionic acid (**11k**) on CSP1 (E) and CSP 2 (F). Conditions as in Table 1.

This electronic effect may be more operative in CSP 2 than in CSP 1; separations of alkyl aryl carbinol derivatives (**8r–w**) were greatly improved by changing CSP 1 to CSP 2. Conformational preferences of 6-membered cyclic systems may obscure the difference of the effective steric bulk of the relevant moieties attached to the carbinyl carbons to result in inferior separability of cyclohexenol derivatives (**8q**, α and β) [24].

Several 1,2-diols were converted into the bis(3,5-dinitrophenylcarbamate)s (**9**) and proved to separate well on CSP 2, although the separation of **9a** was not complete even on CSP 2. This means that the presence of an extra dinitrophenylcarbamate moiety at the terminus of an alkyl chain did not disturb the chiral recognition of alcohol derivatives. It should also be noted that CSP 1 discriminated at best the β-chiral centre of a homologous alcohol, while CSP 2 could recognize a chiral centre even at the γ-position (compare **10a** with **b**).

Carboxylic acids as the 3,5-dinitroanilides (**11**) also showed elution behaviours similar to those of the corresponding derivatized alcohols (**8**), except that the first-eluting enantiomers of the former belonged to the dissimilar stereochemistry of the latter enantiomers as fully discussed in a previous paper [12]. Good separations of α-aryl-substituted carboxylic acid derivatives are also noticeable, and derivatized naproxen (**11q**), an important non-steroidal anti-inflammatory agent, attained an α value as high as 3.04.

It is of particular interest to note that in case of the 3,5-dinitrophenyl derivatized analytes (**8–12**), CSP 2 required about twice the amount of the 2-propanol or ethanol content in the hexane-based eluent system to obtain retentions comparable to those obtained by CSP 1, suggesting a significantly enhanced π-donor–acceptor interaction between the anthracene donor and the 3,5-dinitrophenyl acceptor. On the other hand, in case of the biaryl analytes **13**, the retentions on CSP 2 did not so much increase as compared to those on CSP 1. Furthermore, the selectivity was not so much improved by changing from CSP 1 to 2. This is in good accordance with the chiral discrimination model (Fig. 6) which is based on that proposed for the separation of biaryl analytes **13** on CSP 1, where chiral discrimination and retention occur mainly via the hydrogen bonding interactions between the two sets of the 2,2′-substituents of the CSP and the

Table 2
Separation of carbamates of 1-phenylethanol and amides of 2-phenylpropionic acid on CSP 2

R	$PhCH(CH_3)$–OCONH–R			$PhCH(CH_3)$–CONH–R		
	Eluent	k'_1	α	Eluent	k'_1	α
3,5-$(NO_2)_2$–C_6H_3	C	10.36 (*R*)	2.80	E	7.64 (*S*)	3.30
2,4-$(NO_2)_2$–C_6H_3	C	4.26	1.00	E	3.14 (*S*)	1.09
p-NO_2–C_6H_4	C	3.19 (*R*)	1.31	E	2.37 (*S*)	1.48
3,5-Cl_2–C_6H_3	C	1.14 (*R*)	1.37	E	1.03 (*S*)	1.51
2,4-Cl_2–C_6H_3	C	0.52	1.00	E	0.69	1.00
p-Cl–C_6H_4	C	1.16 (*R*)	1.18	E	1.07 (*S*)	1.20
C_6H_5	C	1.14	1.00	E	0.91 (*S*)	1.09
p-CH_3–C_6H_4	C	1.06	1.00	E	1.04 (*S*)	1.09
p-OCH_3–C_6H_4	C	1.91	1.00	E	1.61 (*S*)	1.09
Iso-C_3H_7	C	0.42	1.00	E	0.85	1.00

Mobile phases: (C) hexane–2-propanol (80:20) and (E) hexane–ethanol (80:20). See Table 1 for HPLC conditions.

analyte, mostly irrespective of the backbone binaphthalene skeleton. Thus, biaryls bearing only one such polar substituent (**13c** and **d**) did not separate on both CSPs.

4. Conclusions

Highly efficient CSPs were prepared by bonding atropisomeric 1,1′-binaphthalene- and 1,1′-bianthracene-2,2′-dicarboxylic acid to 3-aminopropylsilanised silica (CSP 1 and 2, respectively),

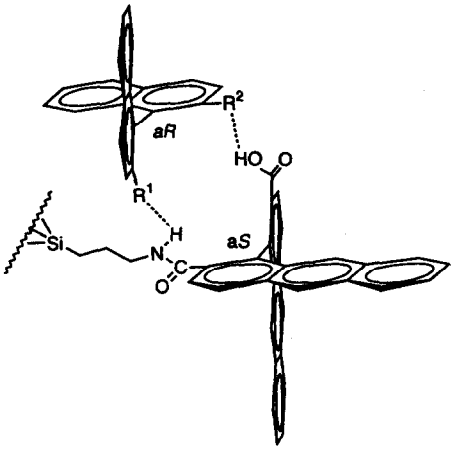


Fig. 6. Chiral discrimination model of biaryl analytes on CSP 2.

which can discriminate a wide range of amino acids, amines, alcohols and carboxylic acids as the 3,5-dinitrophenyl derivatives as well as biaryls bearing polar substituents on the 2,2′-positions. CSP 2 shows a similar elution order for an enantiomeric pair but greatly improved selectivity as compared to that of CSP 1, which is in good accordance with the proposed chiral recognition mechanism for CSP 1 (Fig. 2). These CSPs were quite stable under the experimental conditions used for the data accumulation during more than a year operation. Taking into account the ready availability of chiral selector molecule 1,1′-binaphthalene-2,2′-dicarboxylic acid **1** in both enantiomeric forms [25,26], the binaphthalene-based CSPs should be very useful for practical separation of a variety of 3,5-dinitrophenyl-derivatized enantiomers.

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