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Note

(*R*)-N-(3,5-Dinitrobenzoyl)-1-naphthylglycine as a chiral stationary phase for the separation of enantiomers by high-performance liquid chromatography

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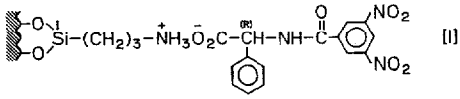
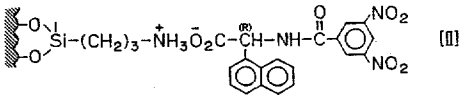
In 1981 Pirkle and Finn[1] developed the chiral stationary phase I, consisting of (*R*)-N-(3,5-dinitrobenzoyl)phenylglycine ionically bonded to γ-aminopropyl silanized silica, which offers superior performance for the separation of arylalkylcarbinols by high-performance liquid chromatography (HPLC). Soon it was clear that this phase can also separate enantiomers of various compounds[2]. This phase contains a dinitrobenzoyl group, which acts as a π-acceptor, and it was found that the combination of the π–π donor–acceptor interaction with diastereomeric hydrogen bonding is very effective for chiral recognition.

On the other hand, we have developed some π-donor type chiral phases consisting of (*S*)- or (*R*)-1-(α-naphthyl)ethylamine and showed that the naphthyl group attached to the asymmetric carbon atom plays effective role in chiral recognition[3–5].

In this work, we prepared a chiral stationary phase II consisting of (*R*)-N-(3,5-dinitrobenzoyl)-1-naphthylglycine ionically bonded to γ-aminopropyl silanized silica, which contains both a dinitrobenzoyl group and a naphthyl group attached to an asymmetric carbon atom, and its chromatographic properties were investigated.



[I]



[II]

EXPERIMENTAL

Preparation of stationary phase II

(*R,S*)-1-Naphthylglycine methyl ester was synthesized from 1-naphthylaceto-

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nitrile (Wako, Osaka, Japan) according to the procedure described by Baumgarten *et al.*[6]. (*R,S*)-N-(3,5-Dinitrobenzoyl)-1-naphthylglycine methyl ester was prepared from (*R,S*)-1-naphthylglycine methyl ester by reaction with 3,5-dinitrobenzoyl chloride in dry tetrahydrofuran at room temperature. (*R,S*)-N-(3,5-Dinitrobenzoyl)-1-naphthylglycine was isolated by the subsequent acid hydrolysis of (*R,S*)-N-(3,5-dinitrobenzoyl)-1-naphthylglycine methyl ester. (*R*)-N-(3,5-Dinitrobenzoyl)-1-naphthylglycine (m.p. 138.3°C) was obtained from the racemic compound by HPLC separation with a SUMIPAX OA-4000 chiral column (250 × 8 mm I.D.) (Sumitomo Chemical, Osaka, Japan). Elemental analysis: calculated for $C_{19}H_{13}N_3O_7$, C 57.73, H 3.31, N 10.63; found, C 56.81, H 3.71, N 10.18%. NMR (acetone-d_6): δ 6.58 (d, 1H), 7.40–8.30 (m, 8H), 9.00–9.14 (m, 3H). IR (potassium bromide): 3400–3080, 1725 (vs), 1650 (vs), 1530 (vs), 1340 (vs), 1180, 1075, 915, 780, 720 cm^{-1}. High-resolution mass spectrum: calculated for $C_{19}H_{13}N_3O_7$, 395.0752; found, 395.0728. Treatment of γ-aminopropyl silanized silica (LiChrosorb NH_2, 5 μm; E. Merck, Darmstadt, F.R.G.) with (*R*)-N-(3,5-dinitrobenzoyl)-1-naphthylglycine affords ionically bonded chiral stationary phase II.

Liquid chromatography

The experiments were carried out using a Shimadzu LC-5A high-performance liquid chromatograph equipped with a UVD-2 ultraviolet detector (254 nm). A stainless-steel column (250 × 4 mm I.D.) was slurry packed with stationary phase II using a conventional technique. The column packed with stationary phase I was represented by SUMIPAX OA-2000I (250 × 4 mm I.D.) (Sumitomo Chemical). The chromatographic conditions are given in Table I. The solutes and solvents were of analytical-reagent grade. Some compounds were provided by Sumitomo Chemical. The structures of the components used are shown in Fig. 1.

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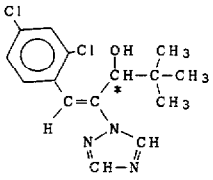

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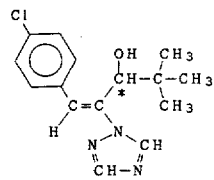
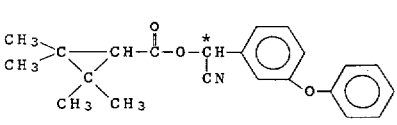


Fenpropathrin



Terallethrin

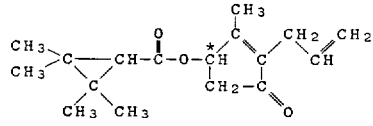


Fig. 1. Structures of compounds used (see Table I).

TABLE I

HPLC SEPARATION OF ENANTIOMERS ON CHIRAL STATIONARY PHASES

The separation factor of the enantiomers, α, is the ratio of the capacity factors; k_1' is the capacity factor for the initially eluted enantiomer. Mobile phase: (A) hexane–ethanol (300:1); (B) hexane–1,2-dichloroethane–ethanol (400:40:1); (C) hexane–1,2-dichloroethane–ethanol (100:20:1); (D) hexane–1,2-dichloroethane–ethanol (500:20:0.1); (E) hexane–1,2-dichloroethane–ethanol (500:30:0.15); (F) hexane–1,2-dichloroethane–ethanol (500:15:1); (G) hexane–ethanol (100:1). A flow-rate of 1.0 ml/min was used for the 250 × 4 mm I.D. column at room temperature.

Compound	*Phase I*				*Phase II*			
	α	k_1'	*First eluted enantiomer*	*Mobile phase*	α	k_1'	*First eluted enantiomer*	*Mobile phase*
1-Phenylethanol	1.03	6.59	(−)-	A	1.06	6.10	(−)-	A
1-(α-Naphthyl)ethanol	1.03	8.28	(−)-	B	1.10	8.80	(−)-	B
Benzoin	1.04	3.10	(+)-	C	1.12	3.01	(+)-	C
S-3308*	1.00	4.56		C	1.14	3.87	(*R*)-	C
S-3307*	1.00	5.57		C	1.09	5.75	(*R*)-	C
Fenpropathrin*	1.04	5.66	(*R*)-	D	1.09	5.98	(*R*)-	D
Terallethrin*	1.00	7.39		E	1.13	9.68	(+)-	E
1-Phenylethylamine**	1.13	4.26	(+)-	F	1.41	3.81	(+)-	F
2-(4-Chlorophenyl)isovaleric acid***	1.04	4.50	(+)	G	1.30	3.88	(+)-	G

* Structures as in Fig. 1.

** Resolved as N-acetyl derivative.

*** Resolved as isopropylamide derivative.

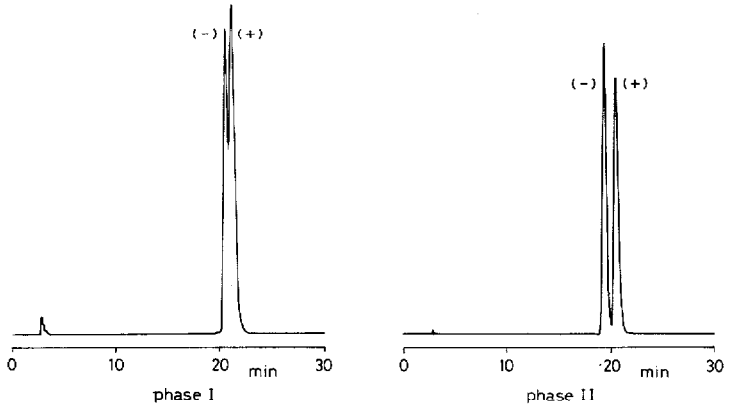


Fig. 2. Separation of the enantiomers of racemic 1-phenylethanol on chiral stationary phases I and II. Chromatographic conditions as in Table I.

RESULTS AND DISCUSSION

The chiral stationary phase II is a modification of phase I. In order to investigate the effect of the replacement of the phenyl group in phase I by a 1-naphthyl group, the retention and enantioselectivity of several racemates were measured under identical conditions on both chiral phases. The results of these measurements are given in Table I.

The capacity factors for these solutes do not differ greatly, but the enantioselectivity differs significantly on the two phases. All of the racemates in Table I show larger α values on phase II than on phase I. It is emphasized that phase II can resolve well some alcohol and ester racemates that can hardly be resolved in phase I. Typical chromatograms are shown in Figs. 2 and 3. These results clearly show that the

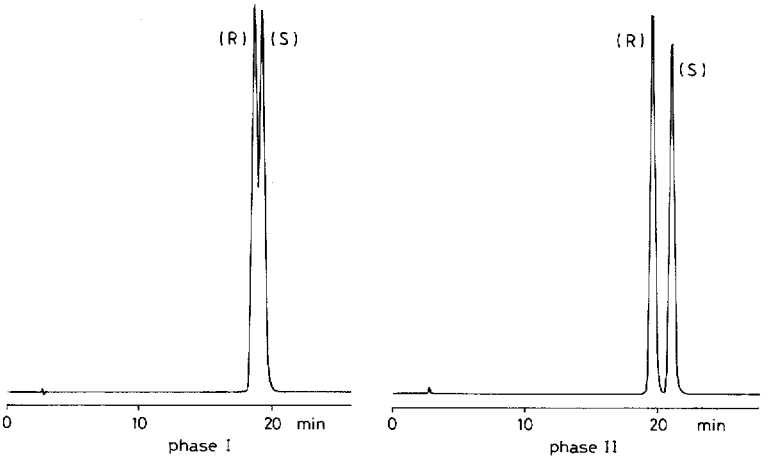


Fig. 3. Separation of the enantiomers of racemic fenpropathrin on chiral stationary phases I and II. Chromatographic conditions as in Table I.

naphthyl group in phase II plays a much more effective role in chiral recognition than the phenyl group in phase I.

The enantiomeric solution orders of these solutes, including aromatic alcohols, esters and amides, are identical on phase I and II. This result suggests but does not prove that a similar chiral recognition mechanism is operating on both phases. Various interactions, such as hydrogen bonding, π–π donor–acceptor interactions, dipole–dipole stacking and Van der Waals interactions seem to contribute for to the enantiomer separation, as demonstrated by many workers[7].

Prikle's original stationary phase I is very well known and widely used, and the modified chiral stationary phase II, which has excellent enantioselectivity, is very promising for the separation of enantiomers of a wide range of classes of compounds.

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