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Enantiomer separation of pyrethroid insecticides by high-performance liquid chromatography with chiral stationary phases

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ABSTRACT

The separation of enantiomers of pyrethroid insecticide esters by high-performance liquid chromatography was studied using some recently developed chiral stationary phases. Improved resolution was obtained for compounds with a variety of acid and alcohol moieties containing one to three chiral centres.

INTRODUCTION

As the individual isomers of chiral pyrethroid insecticide esters have widely differing biological activities, it is important to be able to determine the amount of each enantiomer. High-performance liquid chromatography (HPLC) with chiral stationary phases is a very useful technique for the analysis of these enantiomers, because it is a rapid, non-destructive technique in which there is little chance of epimerization during the course of analysis.

Many attempts have been made to apply HPLC with chiral stationary phases to the direct separation of pyrethroid enantiomers. Okamoto *et al.*[1] resolved the isomers of phenothrin on a chiral polymer column. Chapman[2] and Papadopoulou-Mourkidou[3] separated isomers of pyrethroids based on α-cyano-3-phenoxybenzyl alcohol, and Doi *et al.*[4] obtained separations of pyrethroids with no α-cyano group in the alcohol moiety using Pirkle-type columns[5,6]. Cayley and Simpson[7] made a more systematic study of the separation of pyrethroid isomers with a covalently bonded Pirkle-type stationary phase. Useful separation were reported for various pyrethroids, but unfortunately the separations of many compounds were incomplete.

Recently, we have developed[8,9] urea-derivative chiral stationary phases derived from (*S*)-1-(α-naphthyl)ethylamine with (*S*)-valine and (*S*)-*tert*.-leucine chemically bonded to 3-aminopropylsilanized silica (I and II), which are efficient for the separation of racemic ester compounds. We have also developed[10] a modified Pirkle-type column with (*R*)-N-(3,5-dinitrobenzoyl)-1-naphthylglycine ionically bonded to 3-aminopropylsilanized silica (III), and found that this phase could resolve some ester racemates.

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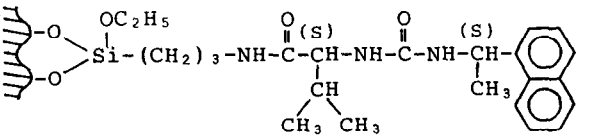
I



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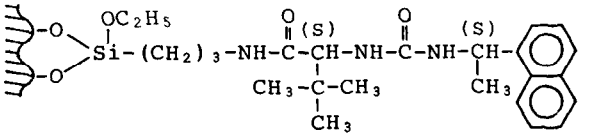

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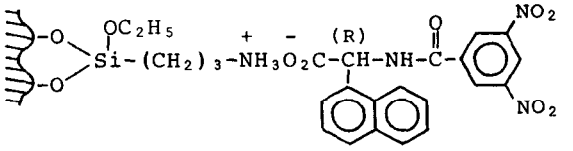

TABLE I

PYRETHROIDS USED

Common name	*Systematic name*	*Isomers*	*Total number of isomers*
Terallethrin	(*RS*)-3-Allyl-2-methyl-4-oxocyclopent-2-enyl 2,2,3,3-tetramethylcyclopropanecarboxylate	(α*RS*)	2
Fenpropathrin	(*RS*)-α-Cyano-3-phenoxybenzyl 2,2,3,3-tetramethylcyclopropanecarboxylate	(α*RS*)	2
Resmethrin	5-Benzyl-3-furylmethyl (1*RS*)-*cis,trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)-cyclopropanecarboxylate	(1*RS*)*cis,trans*	4
Permethrin	3-Phenoxybenzyl (1*RS*)-*cis,trans*-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropanecarboxylate	(1*RS*)*cis,trans*	4
Phenothrin	3-Phenoxybenzyl (1*RS*)-*cis,trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate	(1*RS*)*cis,trans*	4
Tetramethrin	3,4,5,6-Tetrahydrophthalimidomethyl (1*RS*)-*cis,trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate	(1*RS*)*cis,trans*	4
Fenvalerate	(*RS*)-α-Cyano-3-phenoxybenzyl (*RS*)-2-(4-chlorophenyl)-3-methylbutyrate	(α*RS*)(*RS*)	4
Cypermethrin	(*RS*)-α-Cyano-3-phenoxybenzyl (1*RS*)-*cis,trans*-3-(2,2-dichlorovinyl-2,2-dimethylcyclopropanecarboxylate	(α*RS*) (1*RS*)*cis, trans*	8
Allethrin	(*RS*)-3-Allyl-2-methyl-4-oxocyclopent-2-enyl (1*RS*)-*cis,trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate	(α*RS*)(1*RS*)*cis,trans*	8
Bioallethrin	(*RS*)-3-Allyl-2-methyl-4-oxocyclopent-2-enyl (1*R*)-*trans*-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate	(α*RS*)(1*R*)*trans*	2

In this paper we present some improved results obtained for the separation of pyrethroid isomers by HPLC with the chiral stationary phases I–III.

EXPERIMENTAL

Chiral stationary phases I–III were prepared by the method described previously[8,9]. Stainless-steel columns (250 × 4 mm I.D.) were slurry packed with these phases using a conventional technique[11]. These columns are available from Sumika Chemical Analysis Service (Osaka, Japan), as SUMICHIRAL OA-4000, OA-4600 and OA-2500I respectively. SUMICHIRAL OA-2000 [(*R*)-N-(3,5-dinotrobenzoyl)phenylglycine chemically bonded to 3-aminopropylsilanized silica] and SUMICHIRAL OA-4700 [urea derivative derived from (*R*)-1-(α-naphthyl)ethylamine with (*S*)-*tert.*-

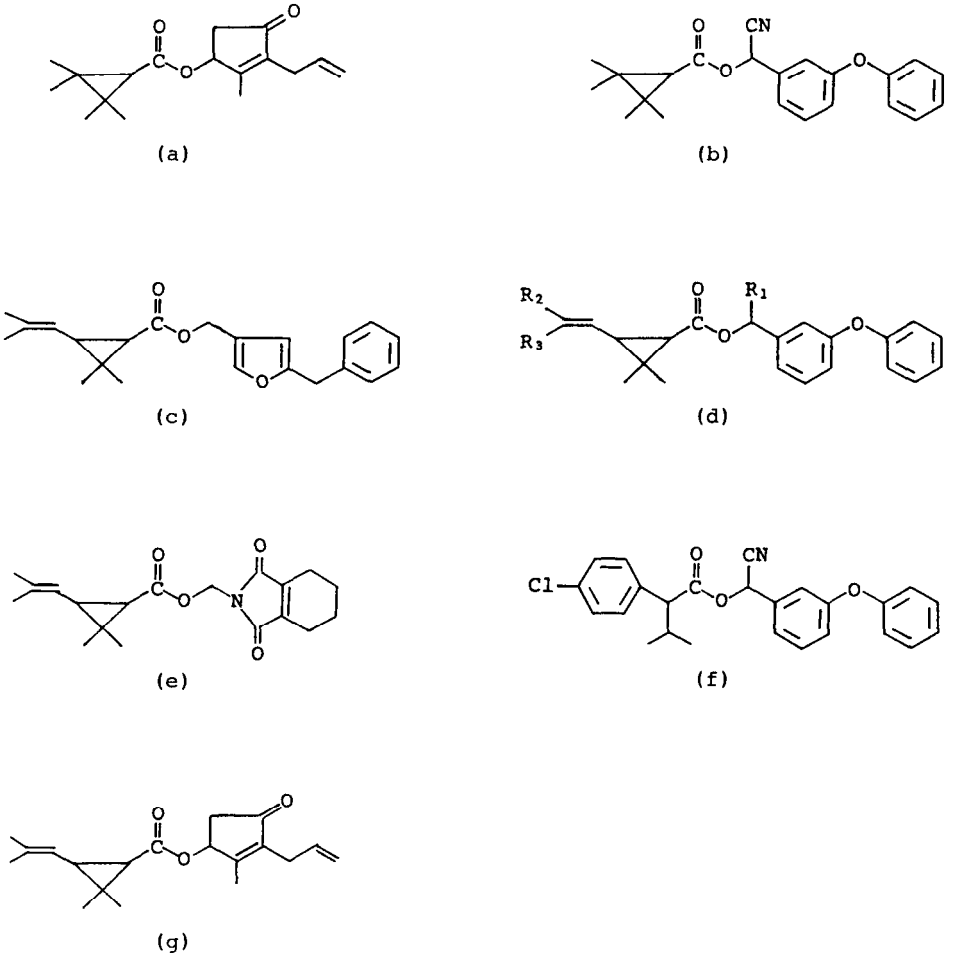

Fig. 1. Structures of pyrethroids: (a) terallethrin; (b) fenpropathrin; (c) resmethrin; (d) $R_1 = H$, $R_2 = R_3 = Cl$, permethrin; $R_1 = H$, $R_2 = R_3 = CH_3$, phenothrin; $R_1 = CN$, $R_2 = R_3 = Cl$, cypermethrin; (e) tetramethrin; (f) fenvalerate; (g) allethrin and bioallethrin.

leucine chemically bonded to 3-aminopropylsilanized silica] columns were also used for the separation of fenvalerate and cypermethrin isomers, respectively. The experiments were carried out using a Waters Assoc. Model 510 high-performance liquid chromatograph equipped with a variable-wavelength ultraviolet detector operated at 230 nm.

The common and chemical names of the pyrethroid insecticides used are summarized in Table I and their structures are shown in Fig. 1. We have adopted the names as given by Cayley and Simpson[7]. These compounds were kindly provided by Sumitomo Chemical (Osaka, Japan). All other chemicals were purchased from Wako (Osaka, Japan).

TABLE II

HPLC ENANTIOMER SEPARATION OF PYRETHROID INSECTICIDES

Elution orders of isomers were established by the injection of the pure isomers individually. Mobile phase: (A) hexane–1,2-dichloroethane–ethanol (500:30:0.15); (B) hexane–1,2-dichloroethane–ethanol (500:10:0.05); (C) hexane–1,2-dichloroethane (500:1). A flow-rate of 1.0 ml/min was typically used for the 250 × 4 mm I.D. column at room temperature. An injection volume of 1 μl (1 mg/ml) was typically used. k'_1, k'_2 = Capacity factors of first- and second-eluted isomer; α = separation factor (k'_2/k'_1).

Compound	*Isomers*	*Phase*	*Mobile phase*	k'_1/k'_2	α
Terallethrin	$\alpha S/\alpha R$	I	A	5.32/ 6.19	1.16
Fenpropathrin	$\alpha R/\alpha S$	II	B	3.00/ 3.77	1.26
Resmethrin	(1*R*)*cis*/(1*S*)*cis*	III	C	9.79/10.53	1.08
	(1*R*)*trans*/(1*S*)*trans*			11.43/12.05	1.05
Permethrin	(1*R*)*cis*/(1*S*)*cis*	III	C	8.20/ 9.24	1.13
	(1*R*)*trans*/(1*S*)*trans*			14.69/15.25	1.04
Phenothrin	(1*R*)*cis*/(1*S*)*cis*	III	C	4.98/ 5.42	1.09
	(1*R*)*trans*/(1*S*)*trans*			6.13/ 6.49	1.06
Tetramethrin	(1*R*)*cis*/(1*S*)*cis*	III	A	22.32/24.10	1.08
	(1*R*)*trans*/(1*S*)*trans*			25.98/26.87	1.03
Fenvalerate	(αR) (*S*)/(αS) (*R*)	III	A	7.77/11.25	1.45
	(αS) (*S*)/(αR) (*R*)			10.05/13.42	1.34
	(αR) (*S*)/(αS) (*R*)	OA-2000	A	7.55/ 8.35	1.11
	(αS) (*S*)/(αR) (*R*)			8.98/10.42	1.16
Cypermethrin	(αR) (1*R*)*cis*/(αS) (1*S*)*cis*	II	B	4.91/ 6.16	1.25
	(αR) (1*S*)*cis*/(αS) (1*R*)*cis*			6.51/ 6.91	1.06
	(αR) (1*R*)*trans*/(αS) (1*S*)*trans*			7.50/ 9.17	1.22
	(αR) (1*S*)*trans*/(αS) (1*R*)*trans*			9.-17/9.96	1.09
	(αR) (1*R*)*cis*/(αS)(1*S*)*cis*	OA-4700	B	4.76/ 5.05	1.06
	(αR) (1*S*)*cis*/(αS) (1*R*)*cis*			6.04/ 6.27	1.04
	(αR) (1*R*)*trans*/(αS)(1*S*)*trans*			7.10/ 7.47	1.05
	(αR) (1*S*)*trans*/(αS) (1*R*)*trans*			8.55/ 8.78	1.03
	(αR) (1*R*)*cis*/(αS) (1*S*)*cis*	II+	B	4.03/ 4.59	1.14
	(αR) (1*S*)*cis*/(αS) (1*R*)*cis*	OA-4700		5.23/ 5.47	1.05
	(αR) (1*R*)*trans*/(αS) (1*S*)(1*R*)*trans*			6.06/ 6.80	1.12
	(αR) (1*S*)*trans*/(αS) (1*R*)*trans*			7.42/ 7.79	1.05
Allethrin	(αS) (1*R*)*cis*/(αR) (1*S*)*cis*	II	A	4.54/ 5.87	1.29
	(αS) (1*S*)*cis*/(αR) (1*R*)*cis*			4.87/ 5.52	1.13
	(αS) (1*R*)*trans*/(αR) (1*S*)*trans*			5.05/ 6.14	1.28
	(αS) (1*S*)*trans*/(αR) (1*R*)*trans*			5.28/ 6.14	1.16

RESULTS AND DISCUSSION

The chromatographic results are summarized in Table II.

The chiral stationary phases I–III are all efficient for the enantiomer separation of pyrethroid insecticide esters, but the enantioselectivities differ for the individual compounds. Hence a good choice of the stationary phase is important for practical analysis. It is also important to use a suitable mobile phase for the efficient separation of isomers, because the polarity of the mobile phase sensitively affects the capacity factors (k') and the separation factors (α) of solutes.

The two isomers of terallethrin and fenpropathrin, which contain one asymmetric carbon atom in the alcohol moiety, were completely separated with the phases I and II. Typical chromatogram are shown in Figs. 2 and 3.

Resmethrin, permethrin, phenothrin and tetramethrin, which contain two asymmetric carbon atoms in the acid moiety, were resolved into their four isomers with phase III. A typical example of a chromatogram is shown in Fig. 4. Separations of these compounds were comparable to those achieved by Doi *et al.*[4] using a Pirkle-type column.

A useful separation of the four isomers of fenvalerate, each of which contain one asymmetric carbon atom in the alcohol and acid moiety, was obtained by Cayley *et al.*[7] and Papadopoulou-Mourkidou[3] using a Pirkle-type phase. We achieved a better separation with phase III than that with SUMICHIRAL OA-2000 Pirkle-type

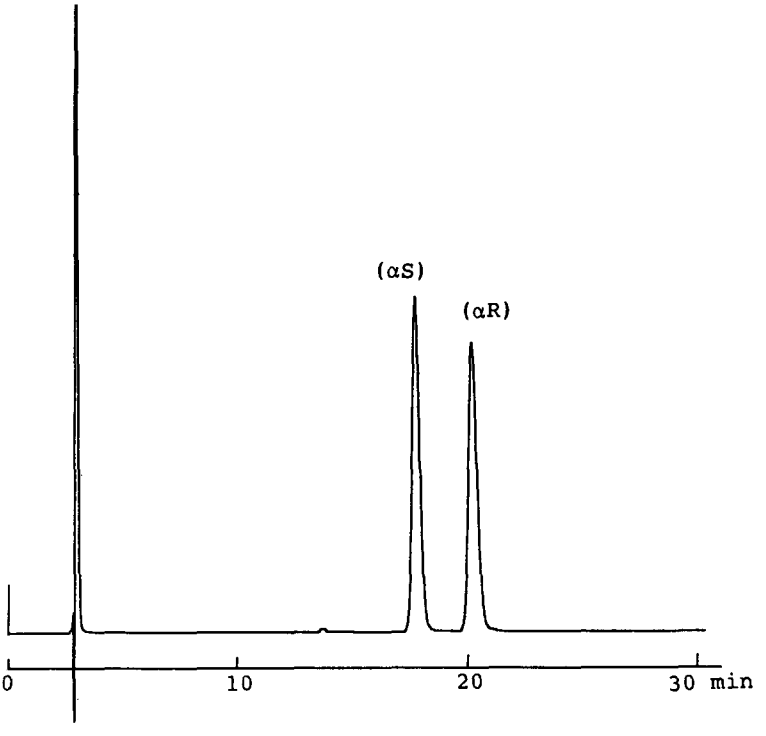

Fig. 2. Separation of terallethrin isomers with phase I. Chromatographic conditions as in Table II.

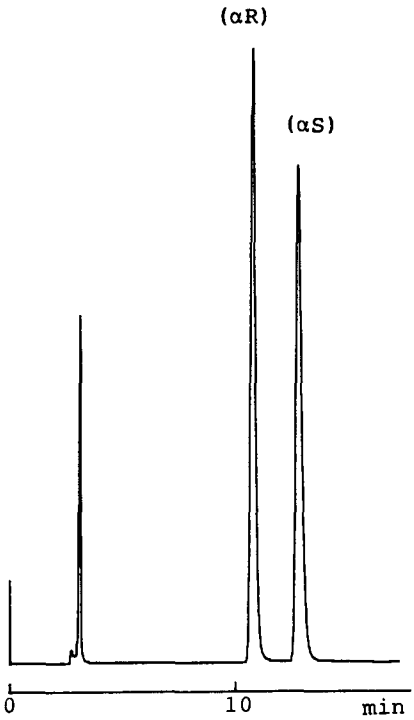

Fig. 3. Separation of fenpropathrin isomers with phase II. Chromatographic conditions as in Table II.

phase, as shown in Fig. 5. It is interesting that the elution orders of the four isomers are different on these two phases: (α*R*)(*S*), (α*S*)(*R*), (α*S*)(*S*), (α*R*)(*R*) on SUMICHIRAL OA-2000 and (α*R*)(*S*), (α*S*)(*S*), (α*S*)(*R*), (α*R*)(*R*) on the phase III. This result may be due to the large difference in enantioselectivity between the two phases. The separation factors for two enantiomer pairs (α*R*)(*S*) and (α*S*)(*R*) and (α*S*)(*S*) and (α*R*)(*R*), were 1.11 and 1.16, respectively, on SUMICHIRAL OA-2000 and 1.45 and 1.34, respectively, on the phase III.

The separation of the eight isomers of cypermethrin, which contain one chiral centre in the alcohol moiety and two chiral centres in the acid moiety, was difficult using a Prikle-type column[2,7]. The separation with phases I–III was also incomplete.

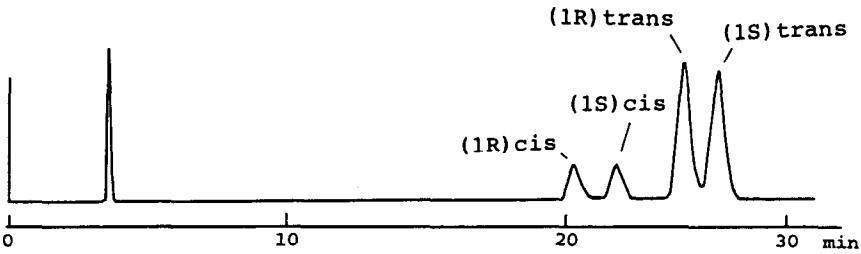

Fig. 4. Separation of phenothrin isomers with phase III. Chromatographic conditions as in Table II.

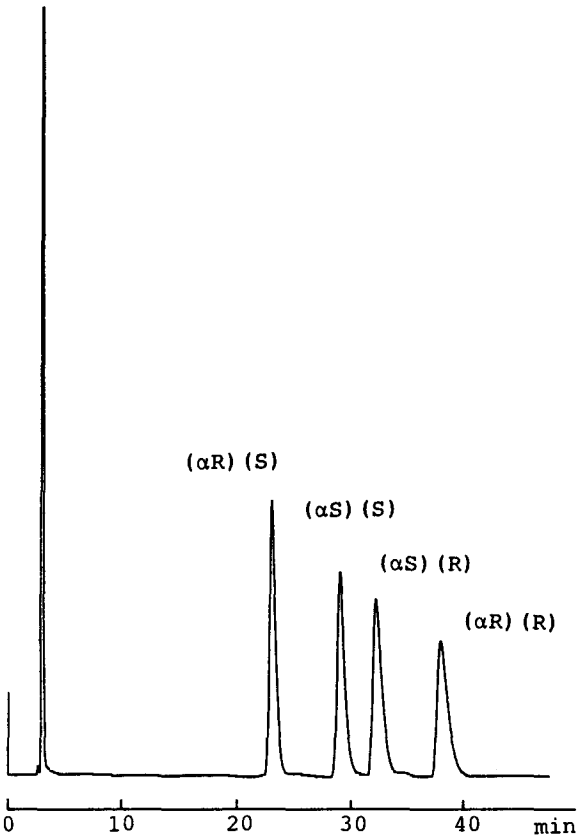

Fig. 5. Separation of fenvalerate isomers with phase III. Chromatographic conditions as in Table II.

However, the chromatogram obtained with phase II (Fig. 6a) shows that the enantioselectivity of this phase is essentially sufficient for the separation of four enantiomer pairs, and the adjacent peaks of two diastereomeric isomers [(α*S*)(1*S*)*trans* and (α*R*)-(1*S*)*trans*] unfortunately overlap. We have found that the combination of two chiral stationary phases, phase II and SUMICHIRAL OA-4700, afforded a sufficient separation of the eight isomers of cypermethrin as shown in Fig. 6b. The good selectivity of SUMICHIRAL OA-4700 for the diastereomeric isomers may contribute to the successul separation of the eight isomers.

Cayley and Simpson[7] indicated that a mixture of the eight isomers of allethrin, which has a chiral alcohol moiety with no α-cyano group, was only partially resolved using a Pirkle-type column. However, an efficient separation of allethrin into eight isomers was acomplished with phase II, as shown in Fig. 7a. The chromatogram of bioallethrin (Fig. 7b) clearly shows that this compound consists of the (α*S*)(1*R*)*trans* and (α*R*)(1*R*)*trans* diastereomeric pair.

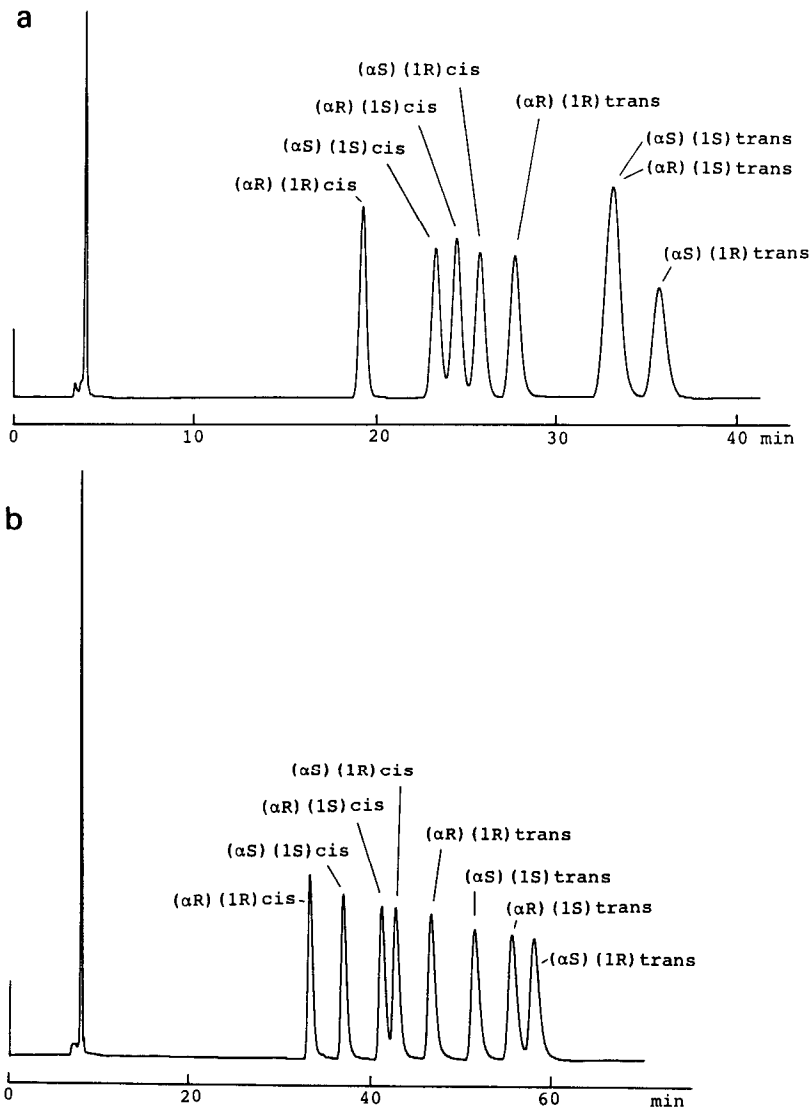

Fig. 6. Separation of cypermethrin isomers: (a) with phase II; (b) with phase II and SUMICHIRAL OA-4700 in series. Chromatographic conditions as in Table II.

CONCLUSION

It was found that chiral stationary phases I–III are very efficient for the enantiomer separation of pyrethroid insecticides. HPLC with these chiral phases is very promising for the enantiomer analysis of technical preparations, formulations and residues of various pyrethroid esters.

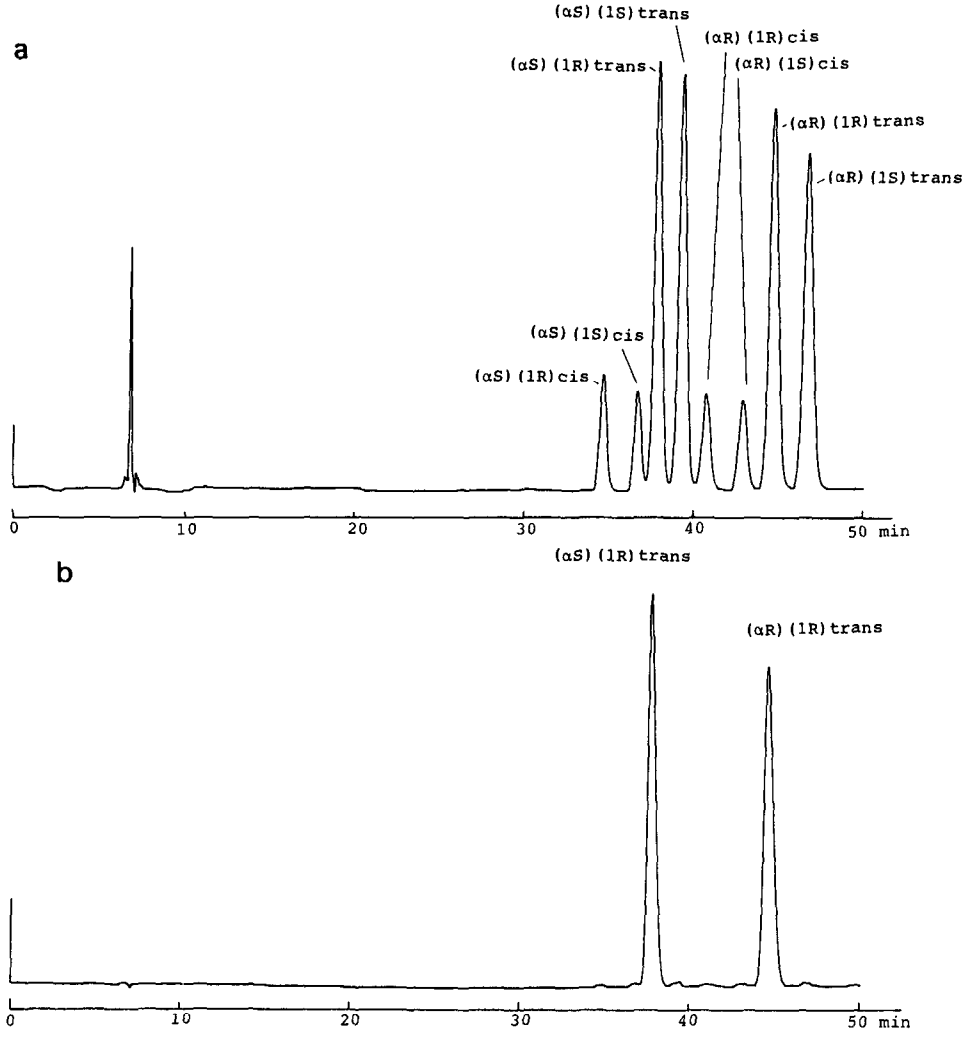

Fig. 7. Separation of (a) allethrin and (b) bioallethrin isomers with phase II. Chromatographic conditions as in Table II.

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