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Note

Gas chromatographic separation of chrysanthemic acid ester enantiomers on a novel chiral stationary phase

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Although the direct gas chromatographic separation of optical isomers on chiral stationary phases has already been achieved for various compounds, many stationary phases are often not suitable for the separation of enantiomers of nitrogen-free compounds, such as carboxylic acid esters. König and co-workers[1,2] have succeeded in separating the enantiomers of the trifluoroacetylated esters of 2-hydroxycarboxylic acids, and we[3] have achieved the separation of enantiomers of unacetylated esters of 2-hydroxycarboxylic acids, but the separation of alkylcarboxylic acid ester enantiomers has never been reported.

Recently we[4,5] have found that enantiomers of chrysanthemic acid ethyl esters can be partially resolved using some N-acyl derivatives of (*R*)- or (*S*)-1-(α-naphthyl)ethylamine, which contain two asymmetric carbon atoms attached to both nitrogen and carbon atoms of the amide group.

In this paper we report that a novel amide phase derived from (1*R*,3*R*)-*trans*-chrysanthemic acid with (*S*)-mandelic acid (*R*)-1-(α-naphthyl)ethylamide shows excellent stereoselectivity for chrysanthemic acid ester and 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid ester enantiomers.

EXPERIMENTAL

Synthesis of O-(1R,3R)-trans-chrysanthemoyl-(S)-mandelic acid (R)-1-(α-naphthyl)-ethylamide stationary phase

The stationary phase was obtained from (*S*)-mandelic acid (*R*)-1-(α-naphthyl)ethylamide (prepared as described previously[5]) (0.002 mol) by reaction with (1*R*,3*R*)-*trans*-chrysanthemoyl chloride (0.0027 mol) in dry dioxane (10 ml) in the presence of pyridine (0.003 mol) at 100°C for 2 h. After removal of the solvent under reduced pressure, the residue was dissolved in ethyl acetate and the solution was washed successively with 1 *N* hydrochloric acid, saturated sodium hydrogen carbonate solution and water.

After drying over sodium sulphate, the crude product was purified by column chromatography on silica gel. The fraction eluted with chloroform was the desired compound, as demonstrated by NMR and mass spectrometry. Elemental analysis: found, C 78.6, H 7.4, N 3.0%; calculated for $C_{30}H_{33}NO_3$, C 79.1, H 7.3, N 3.1% $[\alpha]_D^{20}$: + 34° (c = 0.30% in chloroform). M.p.: 53–55°C.

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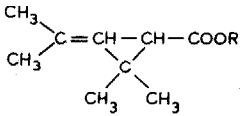
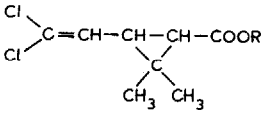
TABLE I

GAS CHROMATOGRAPHIC SEPARATION OF ENANTIOMERS

Chromatography on 40 m × 0.25 mm I.D. glass capillary columns coated with O-(1*R*,3*R*)-*trans*-chrysanthemoyl-(*S*)-mandelic acid (*R*)-1-(α-naphthyl)ethylamide. Carrier gas: helium at 0.7–0.8 ml/min.

R	*Enantiomer*								
		Column temperature (°C)	*Retention time* (min)*		α**	*Column temperature (°C)*	*Retention time* (min)*		α**
			1st peak	*2nd peak*			*1st peak*	*2nd peak*	
CH_3	*Cis*	100	–	–	–	100	31.83	32.67	1.026
	Trans		9.91	10.12	1.021		41.07	42.10	1.025
C_2H_5	*Cis*	100	14.31	14.41	1.007	100	44.96	46.04	1.024
	Trans		14.61	14.87	1.018		59.14	60.54	1.024
n-C_3H_7	*Cis*	100	–	–	–	100	74.56	76.49	1.026
	Trans		25.42	25.97	1.022		98.89	101.4	1.025
iso-C_3H_7	*Cis*	100	14.68	14.83	1.010	100	44.30	44.94	1.014
	Trans		15.26	15.55	1.019		59.00	60.20	1.020
n-C_4H_9	*Cis*	100	42.06	42.86	1.019	100	128.8	131.9	1.024
	Trans		43.97	44.92	1.022		173.4	177.5	1.024
tert.-C_4H_9	*Cis*	100	13.53	13.53	1.000	100	44.48	44.48	1.000
	Trans		14.19	14.37	1.013		58.08	58.88	1.014
n-C_6H_{13}	*Cis*	100	142.4	145.6	1.022	120	118.2	120.6	1.020
	Trans		150.2	153.3	1.021		155.3	158.4	1.020
cyclo-C_6H_{11}	*Cis*	100	210.7	214.2	1.017	120	173.8	176.5	1.016
	Trans		221.3	226.9	1.025		228.1	233.3	1.023
n-C_8H_{17}	*Cis*	120	130.5	132.1	1.012	150	79.63	80.69	1.013
	Trans		140.2	142.5	1.016		100.7	102.0	1.013

* Measured from solvent peak.

** Separation factor calculated from 2nd peak/1st peak retention time ratio.

Gas chromatography

The experiments were carried out with a Shimadzu GC-7A gas chromatograph equipped with a flame-ionization detector. The glass capillary columns (40 m × 0.25 mm I.D.) were coated with a 5% solution of the stationary phase in chloroform.

RESULTS AND DISCUSSION

The gas chromatographic results are given in Table I. Various alkyl esters of racemic chrysanthemic acid and 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid can be resolved in this stationary phase. In particular *n*-butyl, *n*-hexyl and cyclohexyl ester enantiomers of chrysanthemic acid and methyl, ethyl and *n*-propyl ester enantiomers of 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid were separated with sufficient separation factors for the determination of enantiomers of both *cis* and *trans* isomers. Typical chromatograms are shown in Figs. 1 and 2.

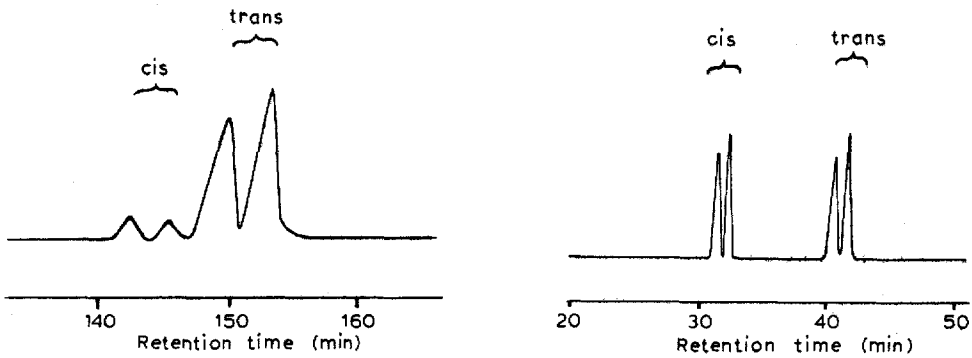


Fig. 1. Gas chromatogram of racemic chrysanthemic acid *n*-hexyl ester. Glass capillary column (40 m × 0.25 mm I.D.) coated with O-(1*R*,3*R*)-*trans*-chrysanthemoyl-(*S*)-mandelic acid (*R*)-1-(α-naphthyl)ethylamide. Temperature, 100°C; carrier gas, helium at 0.7 ml/min.

Fig. 2. Gas chromatogram of racemic 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid methyl ester. Conditions as in Fig. 1.

It is interesting that this stationary phase, which contains three asymmetric carbon atoms, shows excellent enantioselectivity for these carboxylic acid ester enantiomers in comparison with that of N-(1*R*,3*R*)-*trans*-chrysanthemoyl (*R*)-1-(α-naphthyl)ethylamine[4] or O-lauroyl-(*S*)-mandelic acid (*R*)-1-(α-naphthyl)ethylamide, which contain two asymmetric centres.

We suggest this stationary phase could be useful for the separation of optical isomers of other carboxylic acid esters.

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