Journal of Chromatography, 208 (1981) 404–408
Elsevier Scientific Publishing Company, Amsterdam — Printed in The Netherlands

CHROM 13,574

Note

Direct separation of some alcohol enantiomers by gas chromatography with amino acid derivatives as chiral stationary phases

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(Received December 9th, 1980)

It is well known that gas chromatography with optically active stationary phases is an elegant method for the direct separation of various chiral compounds. For example, the enantiomers of amino acids[1,2], amines[3,4] and carboxylic acids[5,6] are resolved with amino acid or amine derivatives, and the enantiomers of olefins[7] and epoxy compounds[8] are resolved with optically active metal complexes.

However, alcohol enantiomers have never been resolved. Karagounis and Lippold[9] claimed the separation of racemic 2-butanol on diethyl *d*-tartrate, but their results could not be reproduced by Goldberg and Ross[10]. Berrod *et al.*[11] studied the behaviour of chiral alcohols by gas chromatography on chiral phases. They detected the start of resolution by measuring the optical activity of trapped fractions corresponding to the ascent and to the descent of the peak. However, the separation was insufficient to observe graphically the commencement of resolution.

Recently we have accomplished the first direct separation of some chiral alcohols by gas chromatography on an amino acid derivative[12]. The details of this separation are given in this paper.

EXPERIMENTAL

Chemicals

(±)- and (+)-1-phenylethanol (I), (±)-1-phenyl-2-propyn-1-ol (III), (±)-1-(α-naphthyl)ethanol (IV), (±) and (+)-pantoyl lactone (V) are commercially available. (±)-1-Phenyl-2,2,2-trifluoroethanol (II) was prepared by the action of ethanolic sodium borohydride on 2,2,2-trifluoroacetophenone. (±)- and (+)-4-hydroxy-3-methyl-2-(2-propenyl)-2-cyclopenten-1-one (allethrolone, VI) and (±)-4-hydroxy-3-methyl-2-(2-propynyl)-2-cyclopenten-1-one (propargyllone, VII) were provided by Dr. Itaya of our laboratory.

The optically active stationary phases N,N′-[2,4-(6-ethoxy-1,3,5-triazine)diyl]bis(L-valyl-L-valine isopropyl ester) (OA-200), N,N′-[2,4-(6-ethoxy-1,3,5-triazine)diyl]bis(L-valyl-L-valyl-L-valine isopropyl ester) (OA-300) and N,N′,N″-[2,4,6-(1,3,5-triazine)triyl]tris(N$^{\alpha}$-lauroyl-L-lysine *tert.*-butylamide) (OA-400) were prepared as described previously[13–15].

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Gas chromatography

The experiments were carried out with a Shimadzu Model GC-7A gas chromatograph equipped with a flame-ionization detector. Glass capillary columns of length 30, 40 or 95 m and I.D. 0.25 mm coated with the optically active stationary phases were used. The carrier gas was helium. GC–mass spectrometric measurements were performed on a Shimadzu Model LKB-9000 instrument.

RESULTS AND DISCUSSION

The GC results are summarized in Table I. Seven chiral alcohols were resolved into their antipodes with separation factors of 1.012–1.071 on amino acid derivatives as optically active stationary phases. A typical chromatogram is shown in Fig. 1. The mass spectra obtained from two separated peaks were identical, as shown in Fig 2.

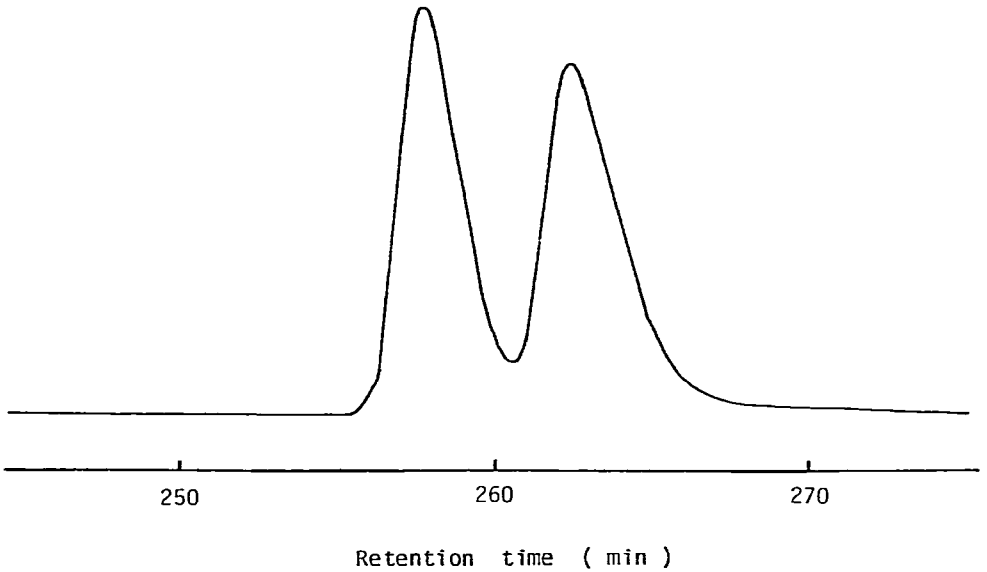

Fig 1 Gas chromatogram of racemic 1-phenyl-2,2,2-trifluoroethanol Glass capillary column (95 m × 0 25 mm I D) coated with OA-400, column temperature, 100°C, carrier gas, helium at 0 43 ml/min

Hitherto, all racemic compounds for the direct GC resolution with amino acid derivatives as chiral stationary phases were limited to enantiomers which involved NH groups linked to the asymmetric carbon atom or its neighbouring atom. In order to separate alcohol enantiomers, it was necessary to convert them into diastereomeric esters by use of chiral acids. Recently, we found that some α-hydroxycarboxylic acid esters could be resolved on OA-300 or OA-400 if α-hydroxy groups were not acylated[16], and moreover α-hydroxycarboxylic acid esters, such as di-*l*-menthyl (+)-tartrate, were effective as chiral stationary phases for the resolution of enantiomers of amino acids, amines and carboxylic acids[17]. These results apparently indicated that OH groups linked to the asymmetric carbon atom could contribute to the formation of diastereomeric complexes for the separation of enantiomers and suggested that it would be possible to resolve some chiral alcohols.

TABLE I
GAS CHROMATOGRAPHIC SEPARATION OF ALCOHOL ENANTIOMERS

No.	*Compound*	*Stationary phase*	*Column length (m)*	*He flow-rate (ml/min)*	*Column temperature (°C)*	*Retention time* (min)*		*Separation factor, α (2nd/1st)*
						First peak	*Second peak*	
I	1-Phenylethanol	OA-400	95	0.43	100	121 23 [*S* (−)]	123.20 [*R* (+)]	1 016
II	1-Phenyl-2,2,2-trifluoroethanol	OA-400	95	0 43	100	257 60	262 30	1 018
III	1-Phenyl-2-propyn-1-ol	OA-400	40	0 5	100	124 70	126 20	1.012
IV	1-(α-Naphthyl)ethanol	OA-300	40	0 7	160	48.33	49.00	1.014
V	Pantoyl lactone	OA-400	40	0 5	100	82.00 [*S* (+)]	87.80 [*R* (−)]	1.071
VI	Allethrolone	OA-300	40	0.7	160	33.94 [*S* (+)]	34.41 [*R* (−)]	1 014
VII	Propargyllone	OA-200	30	1.1	130	66 93	71 06	1 062

* Measured from solvent peak.

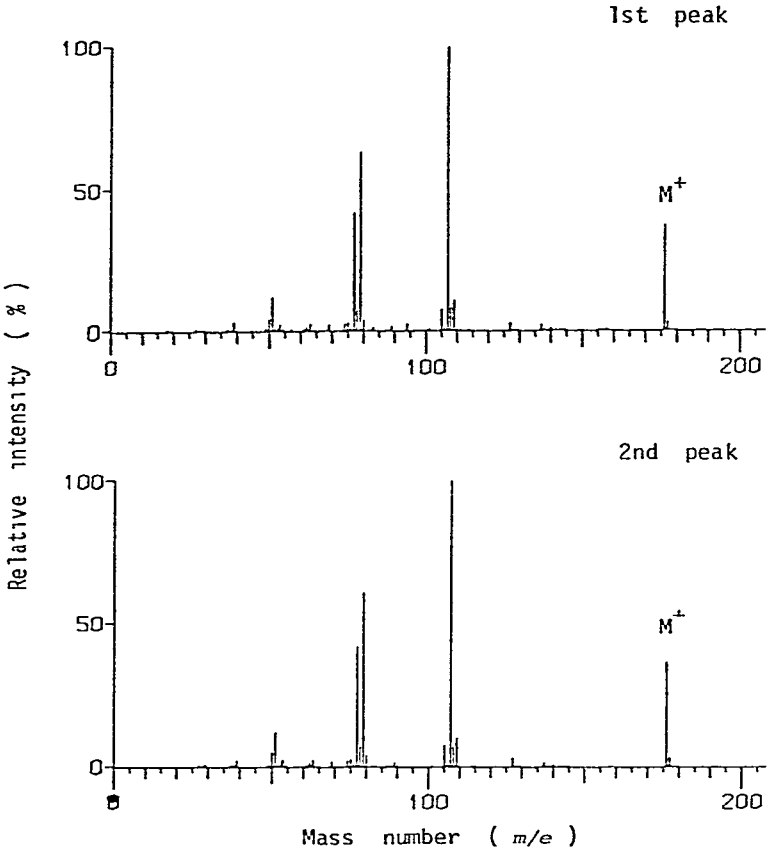

Fig. 2. Mass spectra of racemic 1-phenyl-2,2,2-trifluoroethanol Inlet system, GC with a glass capillary column as described in Fig 1, chamber temperature, 250°C; electron energy, 70 eV.

We have now accomplished the direct separation of alcohol enantiomers with amino acid derivatives, and such separations may be useful for the determination of the optical purity of chiral alcohols without any pre-treatment.

Although the order of emergence was only assigned as (I), (V) and (VI) in this study, it is clear that (*S*)-isomers are consistently eluted prior to (*R*)-isomers with these three chiral alcohols. The same order was also found with α-hydroxycarboxylic acid ester enantiomers, as reported previously[16]. We consider that the above correlation for enantiomers of alcohols and related compounds which possess an OH group linked to the asymmetric carbon atom throw new light on chiral solute–solvent interactions.

ACKNOWLEDGEMENT

The authors thank Dr. N. Itaya for gifts of the samples used in this work.

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