Journal of Chromatography, 211 (1981) 274–279
Elsevier Scientific Publishing Company, Amsterdam — Printed in The Netherlands

CHROM. 13,787

Note

Gas chromatographic separation of some enantiomers on optically active copper(II) complexes

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(Received March 9th, 1981)

Schurig[1] accomplished the first gas chromatographic (GC) resolution of a chiral olefin on an optically active rhodium(I) complex in 1977. In principle, such complexation gas chromatography[2] should be applicable to all conceivable ligand–metal interactions. Indeed some enantiomers of epoxy compound were resolved[3,4] on optically active nickel(II) or europium(III) complexes. Recently we have found that α-hydroxy carboxylic acid ester enantiomers could be resolved on copper(II) complexes of optically active Schiff's bases[5,6]. In the present paper we wish to report the first direct separation of some chiral amino alcohols, amines, amino acid esters and alcohols by GC on optically active copper(II) complexes.

EXPERIMENTAL

Chemicals

1-Dimethyl, 1-diethyl and 1-dibutylamino-2-propanol were purchased from Wako (Osaka, Japan). Their O-trimethylsilyl (TMS) and O-acetyl (Ac) derivatives were prepared by silylation with hexamethyldisilazane and trimethylchlorosilane in pyridine, and by acylation with acetic anhydride in pyridine, respectively. 3-(2,2,2-Trifluoroethoxy)- and 3-methoxy-1-*tert.*-butylamino-2-propanol were prepared from 3-chloro-1-*tert.*-butylamino-2-propanol by treatment with 2,2,2-trifluoroethanol or methanol in alkaline solution. The 3-chloro-1-*tert.*-butylamino-2-propanol was derived by aminolysis with *tert.*-butylamine from epichlorohydrin. Amino acid isopropyl esters were prepared from the corresponding amino acids by esterification in an acidic isopropanol. 2-Ethylpiperidine, 1-phenylethylamine, tetrahydrofurfuryl alcohol and α-phenylpropargyl alcohol were purchased from Tokyo Kasei (Tokyo, Japan) and 4-hydroxy-3-methyl-2-(2-propenyl)-2-cyclopenten-1-one (allethrolone) was provided by Dr. Itaya of our laboratory.

The binuclear copper(II) complexes of N-salicyliden-(*R*)-2-amino-1,1-bis(5-*tert.*-butyl-2-octyloxyphenyl)-propan-1-ol (R-1648-Cu) and N-salicyliden-(*S*)-2-amino-1,1-diphenylpropan-1-ol (S-1600-Cu) were prepared by Dr. Nagase as described previously[7].

0021-9673/81/0000–0000/$02.50

Gas chromatography

The experiments were carried out with a Shimadzu Model GC-7A gas chromatograph equipped with a flame ionization detector.

Glass capillary columns (40 m or 20 m × 0.25 mm I.D.) coated with the mixture of R-1648-Cu and silicone OV-101 (1:1) or the mixture of S-1600-Cu and Ucon oil 50-HB-5100 (1:1) were used. Packed columns (2 m × 3 mm I.D.) filled with Chromosorb W AW DMCS (80–100 mesh) coated with 6% of the mixture of R-1648-Cu and silicone OV-101 (5:1) were also used.

RESULTS AND DISCUSSION

The results of the GC separation of amino alcohol, amine, amino acid ester and alcohol enantiomers are summarized in Table I.

Racemic amino alcohols were resolved into their antipodes with good separation factors. A typical chromatogram is shown in Fig. 1. As these optically active copper(II) complexes show high selectivity for amino alcohols, their enantiomers can be also separated on a packed column as shown in Fig. 2. The mass spectra obtained from two separated peaks were identical and consistent with the standard spectrum of the racemic compound.

Hitherto, racemic amino alcohols were resolved generally in the form of N-acyl-O-ester derivatives using amino acid or amine derivatives as the chiral stationary phases[8,9]. It is notable that amino alcohols were separated without any pretreatment such as acylation. It was shown that nitrogen-attached and oxygen-attached hydrogen are not always necessary for the separation of these amino alcohol enantiomers.

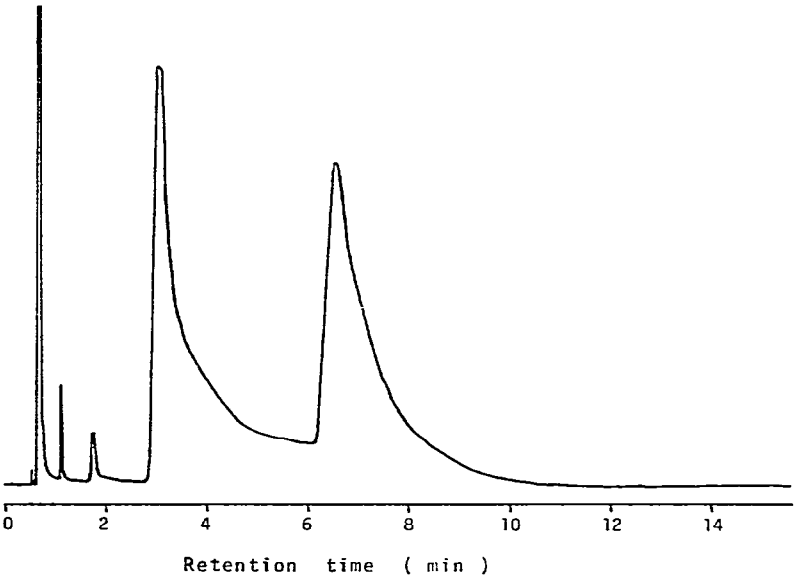

Fig. 1. Gas chromatogram of racemic 1-dimethylamino-2-propanol. Column: glass capillary (20 m × 0.25 mm I.D.) coated with a mixture of R-1648-Cu and silicone OV-101 (1:1). Temperature: 60° C. Carrier gas (helium) flow-rate: 1.2 ml/min.

TABLE I

GAS CHROMATOGRAPHIC SEPARATION OF AMINO ALCOHOL, AMINE, AMINO ACID ESTER AND ALCOHOL ENANTIOMERS

Glass capillary columns, 20 m × 0.25 mm I.D. Carrier gas, helium at a flow-rate of 1.2 ml/min.

Compound				*Stationary phase*							
				R-1648-Cu + Silicone OV-101 (1:1)				*S-1600-Cu + Ucon oil 50-HB-5100 (1:1)*			
				Temp. (°C)	*Retention time* (min)*		α**	*Temp. (°C)*	*Retention time* (min)*		α**
					First peak	*Second peak*			*First peak*	*Second peak*	
Amino alcohols $Y\text{-}CH(OX)\text{-}CH_2\text{-}N(R_2)\text{-}R_1$											
X	R_1	R_2	*Y*								
H	CH_3	CH_3	CH_3	20	2.38	5.94	2.496	60	2.63	4.88	1.856
TMS	CH_3	CH_3	CH_3	60	1.76	2.09	1.188				
Ac	CH_3	CH_3	CH_3	60	2.79		1.000				
H	C_2H_5	C_2H_5	CH_3	60	2.89	3.91	1.353	60	3.28	3.50	1.067
TMS	C_2H_5	C_2H_5	CH_3	60	5.24	5.64	1.076				
Ac	C_2H_5	C_2H_5	CH_3	60	7.13		1.000				
H	$n\text{-}C_4H_9$	$n\text{-}C_4H_9$	CH_3	60	42.76	46.59	1.097	60	32.20		1.032
TMS	$n\text{-}C_4H_9$	$n\text{-}C_4H_9$	CH_3	60	72.61	74.16	1.021				
Ac	$n\text{-}C_4H_9$	$n\text{-}C_4H_9$	CH_3	60	97.66		1.000				
H	$t\text{-}C_4H_9$	H	OCH_2CF_3	85	70.91(−)	107.56 (+)	1.528	80	50.80(+)	71.80 (−)	1.413
H	$t\text{-}C_4H_9$	H	OCH_3	85	75.65	114.25	1.510	100	41.28	50.24	1.217

Amines								
2-Ethylpiperidine	60	37.39	43.45	1.162	60	60.00	78.40	1.307
1-Phenylethylamine	80	35.84	37.33	1.042	120	10.40	11.00	1.058
Amino acid isopropyl esters								
Alanine***	70	96.0(D)	111.6(L)	1.160	80	25.87	28.52	1.102
α-Aminobutyric acid***	70	74.6	91.6	1.230				
Valine***	70	91.6(D)	105.2(L)	1.150				
Alcohols								
Tetrahydrofurfuryl alcohol	60	3.58	3.84	1.072				
Allethrolone	85	135.12	136.72	1.012	120	68.19	69.26	1.010
α-Phenylpropargyl alcohol	80	23.06	25.59	1.110				

* Measured from solvent peak.

** Separation factor calculated by second peak/first peak.

*** Chromatographed on 40 m × 0.25 mm I.D. glass capillary column using helium at a flow-rate of 0.7 ml/min.

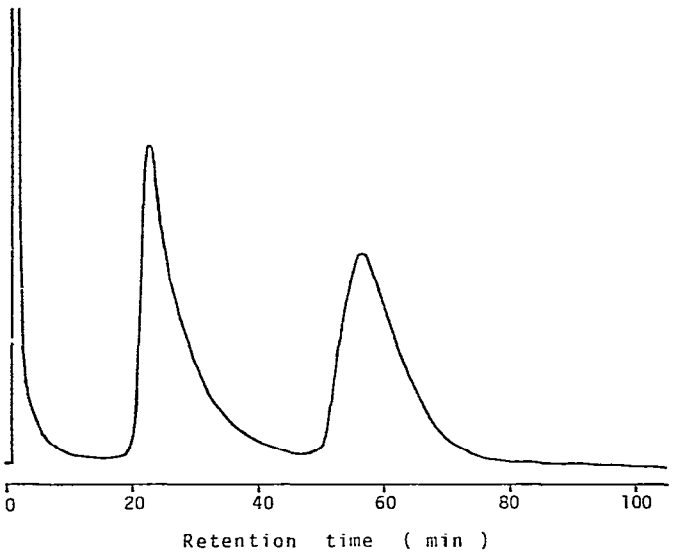

Fig. 2. Gas chromatogram of racemic 1-dimethylamino-2-propanol. Column: glass (2 m × 3 mm I.D.) packed with 80–100 mesh Chromosorb W AW DMCS coated with 6% of a mixture of R-1648-Cu and silicone OV-101 (5:1). Temperature: 60°C. Carrier gas (helium) flow-rate: 40 ml/min.

However, the free hydroxy group should be effective for the enantiomeric separation because separation factors apparently decreased when the hydroxy group was trimethylsilanized, and no separation was observed when the hydroxy group was acylated.

It is also worth noting that some racemic amines and amino acid esters could be directly separated without N-acylation although the peak shape accompanied by tailing was rather broad. An example of this is shown in Fig. 3. Moreover, it is

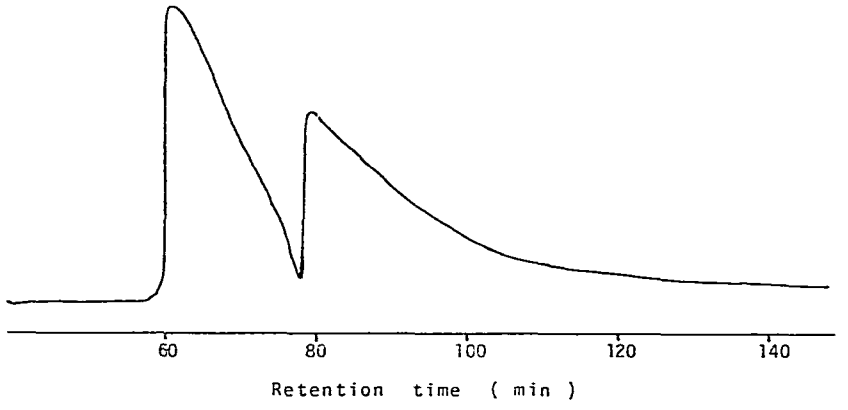

Fig. 3. Gas chromatogram of racemic 2-ethylpiperidine. Column: glass capillary (20 m × 0.25 mm I.D.) coated with a mixture of S-1600-Cu and Ucon oil 50-HB-5100 (1:1). Temperature: 60°C. Carrier gas (helium) flow-rate: 1.2 ml/min.

interesting that some chiral alcohols were resolved into their antipodes although no baseline separation had been obtained.

We consider that these results on optically active copper complexes give new light for complexation GC.

ACKNOWLEDGEMENTS

The authors thank Dr. Nagase, Dr. Aratani and Mr. Yoneyoshi for gifts of the optically active copper complexes used in this work.

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