Note

Gas Chromatographic Separation of Optical Isomers of Chrysanthemic Acid on an Optically Active Stationary Phase

Naobumi Ôi, Masao HORIBA
and Hajimu KITAHARAInstitute for Biological Science,
Sumitomo Chemical Co., Ltd.,
4-2-1, Takatsukasa, Takarazuka,
Hyogo 665, Japan

Received November 25, 1980

Chrysanthemic acid which is a very important compound as the acid moiety of various insecticidal pyrethroids (allethrin, tetramethrin, resmethrin, phenothrin, etc.) has four isomeric forms: (+)-*trans*, (–)-*trans*, (+)-*cis* and (–)-*cis*. As well known optical isomers of these pyrethroidal esters have different toxicities for insects, depending upon the configuration of the chrysanthemoyl group

in the molecule, it is important to analyze the ratio of optical isomers of chrysanthemic acid.

Generally, the optical purity of enantiomeric compounds can be determined by forming derivatives with optically active reagents and analyzing the resulting mixture of diastereoisomers by gas chromatography.¹⁾ In the case of chrysanthemic acid, all four isomers were separated in the form of esters with (+)-2- or (–)-2-octanol²⁾ and also in the form of amides with (+)- α -methylbenzylamine.³⁾ However, it is desirable to separate the four optical isomers directly with an optically active stationary phase, because for the above methods the optical purity of the derivative-forming reagent should be 100%, and if not, it is necessary to correct the obtained values according to the optical purity of chiral reagents.

We have recently accomplished the direct gas chromatographic separation of α -alkylphenylacetic acid enantiomers in the form of isopropylamide using *N,N'*-[2,4-(6-ethoxy-1,3,5-triazine)diyl] bis(L-valyl-L-valyl-L-valine isopropyl ester) (OA-300) as a chiral stationary phase.⁴⁾ In this paper a similar method is described for chrysanthemic acid in which various optically inactive amines are used as the derivative-forming reagent.

The results of the gas chromatographic separation of optical isomers of chrysanthemic acid amides are given in Table I. All four optical isomers of chrysanthemic acid

TABLE I. GAS CHROMATOGRAPHIC SEPARATION OF OPTICAL ISOMERS OF CHRYSANTHEMIC ACID AS THEIR AMIDE DERIVATIVES^a

$\begin{array}{c} \text{(CH}_3\text{)}_2\text{C} \\ =\text{CH}-\text{CH}-\text{CH}-\text{CONHR} \\ \quad \quad \quad \diagup \quad \diagdown \\ \quad \quad \quad \text{C} \\ \quad \quad \quad \diagdown \quad \diagup \\ \text{CH}_3 \quad \text{CH}_3 \end{array}$	<i>cis</i> Isomer			<i>trans</i> Isomer		
	Retention time (min) ^b			Retention time (min) ^b		
	(+)	(–)	$\alpha((-)/(+))$	(+)	(–)	$\alpha((-)/(+))$
R = <i>i</i> -C ₃ H ₇	4.71	4.80	1.019	5.80	5.80	1.000
<i>n</i> -C ₃ H ₇	7.58	7.72	1.018	9.60	9.60	1.000
<i>i</i> -C ₄ H ₉	3.10	3.10	1.000	3.42	3.50	1.023
<i>i</i> -C ₄ H ₉	8.62	8.78	1.019	10.70	10.82	1.011
<i>n</i> -C ₄ H ₉	10.90	11.11	1.010	14.20	14.20	1.000
<i>n</i> -C ₆ H ₁₃	23.75	24.20	1.019	31.20	31.20	1.000
<i>cyclo</i> -C ₆ H ₁₁	27.84	28.40	1.020	34.45	35.00	1.016
–C(CH ₃) ₂ CH ₂ C(CH ₃) ₃	9.46	9.60	1.015	10.44	10.70	1.025
<i>n</i> -C ₈ H ₁₇	50.70	51.70	1.020	66.60	67.10	1.008
–	105.4	106.9	1.014	125.0	129.7	1.038
–CH ₂ (CH ₂) ₁₀ CH ₃	225.3	229.8	1.020	298.9	301.3	1.008
–	79.30	80.40	1.014	108.6	108.6	1.000
–CH ₂ –	79.40	80.70	1.016	111.1	112.2	1.010
–C(CH ₃) ₂ –	49.00	49.91	1.019	61.00	62.10	1.018

^a Chromatographed on a glass capillary column (40 m × 0.25 mm i.d.) coated with OA-300; column temperature, 180°C; carrier gas, helium at 0.57 ml/min.

^b Time from solvent peak.

were separated in the form of cyclohexyl-, 1,1,3,3-tetramethylbutyl-, 1-adamantyl- and α -dimethylbenzyl-amides with separation factors ranging from 1.014 to 1.020 for *cis*-isomers and from 1.016 to 1.038 for *trans*-isomers. A typical chromatogram is shown in Fig. 1. The other racemic amides of chrysanthemic acid were resolved into their antipodes as only *cis*- or *trans*-isomers. This is the first gas chromatographic separation of enantiomers of cyclopropanecarboxylic acid. Peak identification was done by chromatographing some mixtures of chrysanthemic acid amide enantiomers of known configurations. The (+)-isomer eluted prior to the (–)-isomer with both *cis*-

and *trans*-isomers.

This study enabled us to develop a new analytical method for the determination of optical isomers of chrysanthemic acid. These results will be reported elsewhere.

EXPERIMENTAL

Gas chromatography was carried out with a Shimadzu GC-7A gas chromatograph equipped with a flame ionization detector. Chromatographic conditions are given in Table I. A thermostable optically active stationary phase, OA-300, was prepared as described previously.⁵⁾ The optical isomers of chrysanthemic acid and α -dimethylbenzylamine were prepared in our laboratory. Propyl-, isopropyl-, butyl-, isobutyl-, *t*-butyl-, hexyl-, cyclohexyl-, octyl-, 1,1,3,3-tetramethylbutyl-, lauryl-, 1-adamantyl- and benzyl-amine, and aniline were purchased from Wako Pure Chemical Co., Ltd. Chrysanthemic acid was converted into amides by treatment with the corresponding amines in the presence of *N,N'*-dicyclohexylcarbodiimide in toluene.

REFERENCES

- 1) E. Gil-Av and D. Nurok, *Advan. Chromatogr.*, **10**, 99 (1974).
- 2) A. Murano, *Agric. Biol. Chem.*, **36**, 2203 (1972).
- 3) F. E. Rickett, *Analyst*, **98**, 687 (1973).
- 4) N. Ôi, M. Horiba and H. Kitahara, *Bunseki Kagaku*, **28**, 607 (1979).
- 5) N. Ôi, O. Hiroaki and H. Shimada, *Bunseki Kagaku*, **28**, 125 (1979).

FIG. 1. Gas Chromatogram of Enantiomeric Chrysanthemic Acid 1,1,3,3-Tetramethylbutylamide.

(1), (+)-*cis*; (2), (–)-*cis*; (3), (+)-*trans*; (4), (–)-*trans*. GC conditions: same as in Table I except that the column length was 60 m.