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PREPARATION OF ALL STEREOISOMERS OF ^{14}C-LABELLED 3-(2,2-DICHLOROETHENYL)- AND 3-(2,2-DIBROMOETHENYL)-2,2-DIMETHYLCYCLOPROPANECARBOXYLIC ACIDS

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SUMMARY

The four ^{14}C-labelled stereoisomers of both 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid and 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylic acid, the improtant acid components of various potent insecticidal pyrethroids, were prepared efficiently from [1-^{14}C]chrysanthemic acid (5) for use in comparative metabolic studies. α-Bromo-β-naphthyl *d,l-cis,trans*-[1-^{14}C]chrysanthemate (6) was oxidized with osmium tetroxide-sodium periodate to give the formyl ester (7) in 78% yield. Wittig reaction of 7 with dichloromethylenetris(dimethylamino)phosphorane at -75 - -70 °C afforded the dichlorovinylated ester (8) quantitatively. Optical resolution of 8 by preparative HPLC using a chiral-phase column led to the four stereoisomers (8a - 8d) with optical purities more than 99%. Hydrolyses of the esters (8a - 8d) yielded the corresponding optically active 3-(2,2-dichloroethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic acids (1a - 1d) quantitatively. Similarly, Wittig reaction of the formyl ester (7) with dibromomethylenetris(dimethylamino)phosphorane, followed by optical resolution and hydrolysis, gave four optically active 3-(2,2-dibromoethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic acids (2a - 2d) in considerably high yields.

Key Words: 3-(2,2-Dichloroethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic Acid, 3-(2,2-Dibromoethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic Acid, [1-^{14}C]Chrysanthemic Acid, Insecticidal Pyrethroids, Optically Active

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INTRODUCTION

Two dihalovinyl analogues of chrysanthemic acid, 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid (DCV acid) and 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylic acid (DBV acid), are important acid components of several potent synthetic pyrethroids such as permethrin, cypermethrin and deltamethrin, which provide high insecticidal activities together with adequate photostabilities and moderate mammalian toxicities[1],[2]. Both of the acids possess two chiral carbons in their molecules, giving four possible stereoisomers, i.e., *(1R)-cis*, *(1S)-cis*, *(1R)-trans* and *(1S)-trans* isomers. Recently, it has become known that some optically active pyrethroids show different metabolism in animals depending upon stereochemistry of the acid moieties[3],[4]. Therefore, in order to clarify the precise metabolism of the pyrethroids related with these dihalovinyl acids, it was required to prepare radioactive DCV and DBV acids in optically active form as the key intermediates for the syntheses of the pyrethroidal esters. In this paper, we describe a convenient method for the syntheses of all stereoisomers of both acids labelled with carbon-14 at the C-1 position of the cyclopropane ring.

RESULTS AND DISCUSSION

In planning, we had to address two major tasks: (i) ^{14}C-labelling of DCV and DBV acids; and (ii) efficient separation of the individual four stereoisomers of labelled DCV and DBV acids. Synthetic methods for the large-scale preparation of non-radioactive DCV and DBV acids have been reported. These are mainly classified into two types of reactions: carbene addition[5],[6],[7] and cyclization of halo carbonyl compounds[8],[9]. These methods are, however, impractical for the present labelling work because of their tedious processes and predicted low yields especially in small-scale preparation.

As illustrated in Fig. 1, one plausible retrosynthetic analysis of DCV and DBV acids would require a formyl ester (VII), which we hoped would afford dihalovinylated esters (VIII and IX) by applying the Wittig reaction[10],[11]. A key intermediate VII could be derived from cyclopropane-labelled chrysanthemic acid (V) through esterification and oxidation according to our previous method[12],[13].

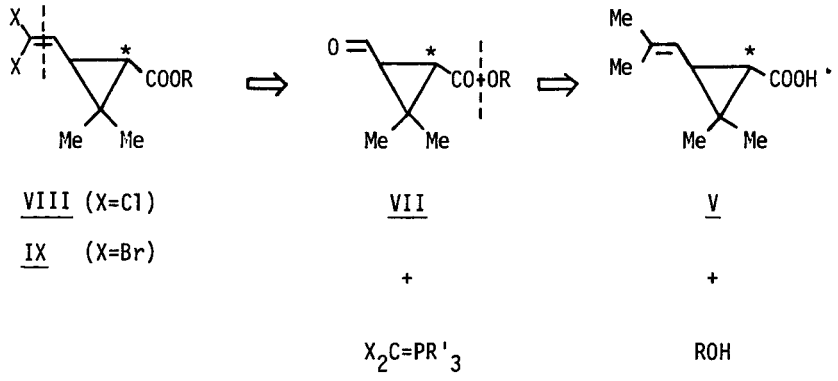

Fig. 1 A plausible retrosynthetic analysis of the dihalovinyl analogues of chrysanthemic acid for the cyclopropane-labelling

In the design of the reaction sequence, selection of a protecting group for the carboxyl group in V was a matter of great significance to us, since we expected that the dihalovinylated esters VIII and IX, the products of the Wittig reaction, could be directly separated into the corresponding four stereoisomers on HPLC with a chiral-phase column. After several trials, it was found that a good separation of α-bromo-β-naphthyl esters of DCV and DBV acids was provided by HPLC using a chiral-phase column, γ-[*(R)*-N-(3,5-dinitrobenzoyl)phenylglycyl]-aminopropyl silica[14], as shown in the experimental section (Table 3). From this finding, we selected α-bromo-β-naphthol for protection of the carboxyl group and designed the reaction sequence shown in Fig. 2.

[1-^{14}C]Chrysanthemic acid (5) was synthesized by applying our previous method[15]. Thus, [2-^{14}C]glycine (4) prepared from potassium [^{14}C]cyanide (3) in three steps according to the method of Ehrensvärd[16] was esterified, diazotized and condensed with 2,5-dimethyl-2,4-hexadiene in the presence of copper catalyst to give ethyl [1-^{14}C]chrysanthemate. Hydrolysis of the ester afforded the acid 5, being a 2:3 mixture of the *cis* and *trans* isomers, in 25% yield from 3.

The acid 5 was chlorinated with oxalyl chloride and subsequently esterified with α-bromo-β-naphthol in the presence of pyridine to give α-bromo-β-naphthyl

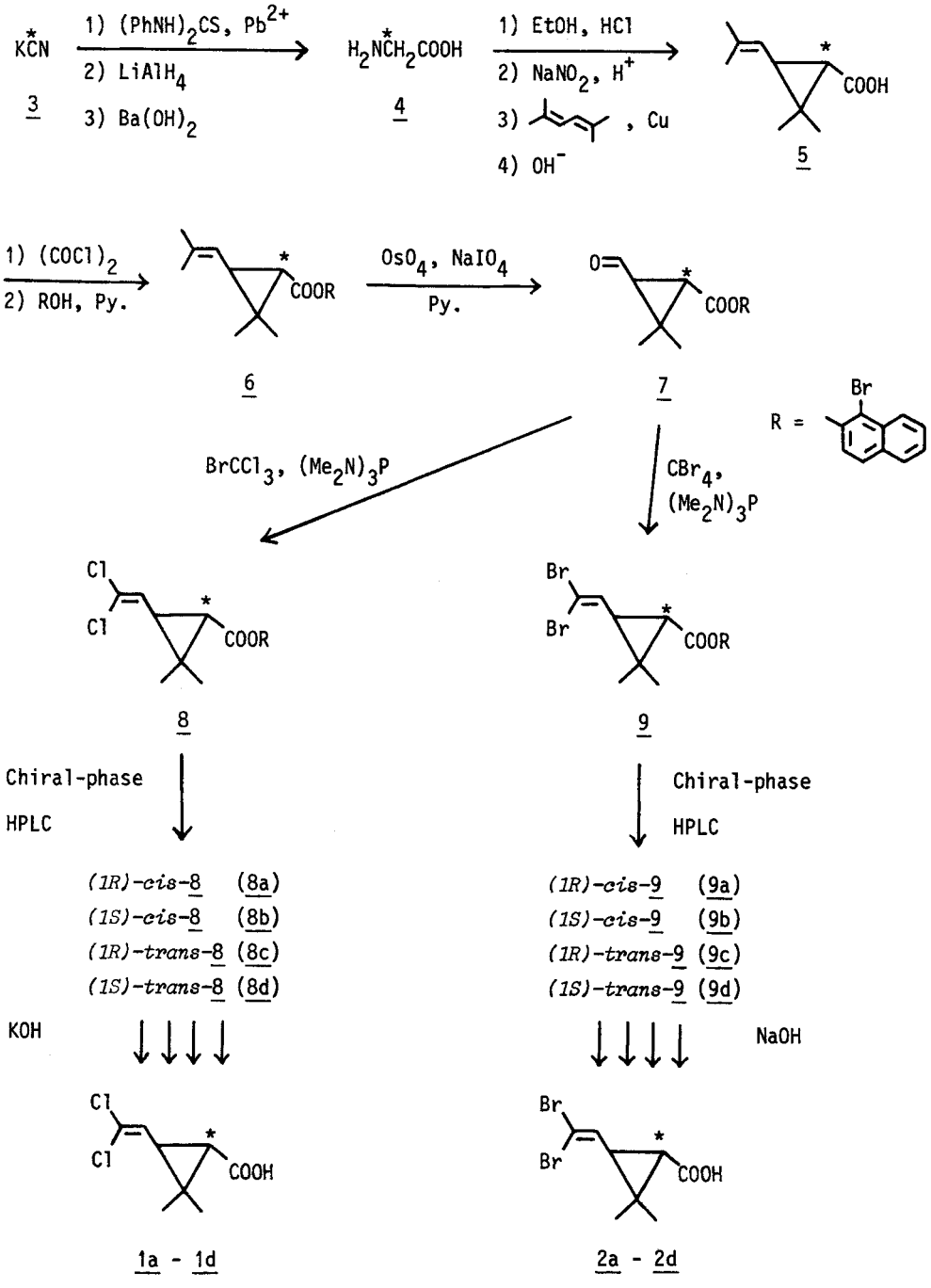

Fig. 2 Scheme for the preparation of all stereoisomers of 3-(2,2-dichloroethenyl)- and 3-(2,2-dibromoethenyl)-2,2-dimethyl-[1-^{14}C]cyclopropanecarboxylic acids

[1-^{14}C]*chrysanthemate* (6) quantitatively. Oxidation of the olefinic side chain of 6 was carried out by treatment with an excess amount of sodium periodate and a catalytic amount of osmium tetroxide[12],[13] in the presence of pyridine[17] to afford α-bromo-β-naphthyl 2-formyl-3,3-dimethyl[1-^{14}C]cyclopropanecarboxylate (7) in 78% yield after purification by column chromatography.

Initial attempts involving the conventional Wittig reaction of 7 with dichloromethylenetriphenylphosphorane[12],[18] resulted in a poor yield of the desired dichlorovinyl product. The unsuccessful results appeared to be based on the bulkiness of the bromonaphthyl group in 7. Therefore, dichloromethylene-tris(dimethylamino)phosphorane prepared from bromotrichloromethane (BTCM) and hexamethylphosphoroustriamide (HMP) was selected as an alternative relatively small Wittig reagent, and tried in the reaction. According to Salmond's method[19], the *trans* formyl ester (*t*-7) was readily converted into the corresponding dichlorovinylated ester (*trans*-8) in a good yield (about 85%). Under the same condition, the *cis* formyl ester (*c*-7), however, gave a poor yield of the *cis* dichlorovinylated ester (*c*-8) (less than 10%). In order to improve the yield of the *cis* isomer (*c*-8), we studied the effects of molar ratios of reagents vs. the formyl ester (*c*-7), methods and reaction temperatures. The representative results of a number of runs under various conditions are summarized in Table 1.

The yield of the *cis* dichlorovinylated ester (*c*-8) was markedly dependent upon the molar ratios of the reagents and methods used. The use of the excess of HMP (a molar ratio of HMP/MTCM more than 2.0) resulted in unfavorable effects on the yield. Method B was obviously superior to Method A (Salmond's method). These results suggested that the formyl ester suffered some decomposition directly with unreacted HMP before undergoing the Wittig reaction. Reaction temperature was found to be another key factor of this reaction. Lower temperature (-75 - -70 °C) was more favorable than -20 - -15 °C probably due to protection from decomposition of the phosphorane intermediate.

Based on these data, the best condition of Entry 6 was chosen for the synthesis of the *cis,trans* dichlorovinylated ester (8). BTCM was allowed to react with HMP in CH_2Cl_2 at -75 - -70 °C for 45 min to prepare the phosphorane,

Table 1 Optimization of the Wittig dichlorovinylation of the *cis* formyl ester (*c*-7)

Entry No.	Molar ratios			Methods*1)	Reaction temp.[°C]	Yields of *c*-8 [%]*2)
	c-7	BTCM	HMP			
1	1.0	1.2	2.7	A	-20 - -15	6
2	1.0	2.0	5.0	A	-20 - -15	5
3	1.0	2.0	3.4	A	-20 - -15	18
4	1.0	2.0	3.4	B	-20 - -15	67
5	1.0	1.3	2.2	B	-75 - -70	56
6	1.0	2.0	3.4	B	-75 - -70	99

*1) A: HMP was added to a mixture of the formyl ester (*c*-7) and BTCM (Salmond's method).

B: The formyl ester was added to the phosphorane prepared from BTCM and HMP.

*2) Isolated yields based on *c*-7.

to which was added a solution of 7 in the same solvent by taking 40 min to keep the temperature around -70 °C. The mixture was stirred at the same temperature for an additional 30 min, and then quenched with 5% HCl. After column chromatography, a 33:67 mixture of the *cis,trans* dichlorovinylated ester (8) was obtained in 98% yield.

The ester 8 was optically resolved by preparative HPLC using a chiral-phase column described above to give the four stereoisomers (8a - 8d) with optical purities more than 99% in nearly theoretical yields. Each optically active ester (8a - 8d) was hydrolyzed with diluted alkaline solution in aqueous alcohol to afford the corresponding [1-^{14}C]DCV acid (1a - 1d) quantitatively. Their yields and optical purities are summarized in Table 2.

Similarly, Wittig reaction of the formyl ester 7 (*cis/trans* = 36/64) with dibromomethylenetris(dimethylamino)phosphorane, which was prepared from carbon

Table 2 Optically active 3-(2,2-dichloroethenyl)- and 3-(2,2-dibromoethenyl)-2,2-dimethyl-[1-^{14}C]cyclopropanecarboxylic acids ([1-^{14}C]DCV and [1-^{14}C]DBV acids)

Stereoisomers	[1-^{14}C]DCV acids (1a - 1d)				[1-^{14}C]DBV acids (2a - 2d)			
		Radiochem. yields [%] *1)	Optical purities [%] *2)	Optical rotations $[\alpha]_D$ *3)		Radiochem. yields [%] *1)	Optical purities [%] *2)	Optical rotations $[\alpha]_D$ *4)
(1R)-cis	1a	9.2	100	+ 28°	2a	11.4	100	+ 16°
(1S)-cis	1b	9.9	99.7	- 27°	2b	11.2	100	- 16°
(1R)-trans	1c	22.5	100	+ 35°	2c	20.6	99.1	+ 38°
(1S)-trans	1d	24.3	99.2	- 36°	2d	19.3	100	- 41°

*1) From [1-^{14}C]chrysanthemic acid (5).

*2) Determined by chiral-phase HPLC of the α-bromo-β-naphthyl esters (8a - 8d, 9a - 9d).

*3) Measured in chloroform (c = 1.0) at 23 °C.

*4) Measured in chloroform (c = 2.0) at 23 °C.

tetrabromide and HMP, gave the dibromovinyl product 9 (*cis/trans* = 34/66) in a quantitative yield. Optical resolution of 9 by the same HPLC method followed by hydrolyses of the four stereoisomers (9a - 9d) afforded optically active [1-^{14}C]DBV acids (2a - 2d) in considerably high yields. Their yields and optical purities are also summarized in Table 2.

All ^{14}C-labelled compounds prepared in this work were identical chemically in every respect with the unlabelled authentic materials.

EXPERIMENTAL

Radio thin-layer chromatography (RTLC) was carried out on a Silica Gel 60 F_{254} plate (Merck), and the radioactivity on the plate was measured with a Thin Layer Chromatogram Scanner (Aloka, Japan).

Radio high performance liquid chromatography (RHPLC) was conducted at ambient temperature on a LC-3A high performance liquid chromatograph (Shimadzu, Co., Ltd., Japan) equipped with a SPD-2A UV-detector (Shimadzu, 254 nm) and a RLC-551 Radioanalyzer (Aloka). A stainless steel column (25 cm x 4 mm ID) packed with γ-[*(R)*-N-(3,5-dinitrobenzoyl)phenylglycyl]aminopropyl silica (Sumipax OA-2000, Sumika Chemical Analysis Service, Ltd., Japan; 10 μm) was used for the analyses of optically active α-bromo-β-naphthyl 3-(2,2-dichloroethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylates (8a - 8d) and 3-(2,2-dibromoethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylates (9a - 9d). Operating condition: mobile phase n-hexane/1,2-dichloroethane = 20/1 (v/v), flow rate 1.0 ml/min. Their retention times are shown in Table 3.

Optical rotations of 3-(2,2-dichloroethenyl)- and 3-(2,2-dibromoethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic acids ([1-^{14}C]DCV and [1-^{14}C]DBV acids) (1a - 1d and 2a - 2d) were measured in chloroform at 23 °C with a Model 241 Polarimeter (Perkin-Elmer).

d,l-cis,trans-[1-^{14}C]Chrysanthemic acid (5) -- The acid 5 was synthesized according to the method described in our previous papers[15]. Thus, potassium [^{14}C]-cyanide (3) (289 mCi, 22.0 mCi/mmol, 13.1 mmol) was condensed with 1,3-diphenyl-

Table 3 Retention times of the four stereoisomers of α-bromo-β-naphthyl 3-(2,2-dichloroethenyl)- and 3-(2,2-dibromoethenyl)-2,2-dimethyl-[1-^{14}C]cyclopropanecarboxylates (8 and 9) on the chiral-phase HPLC

Stereoisomers	Retention times [min]	
	8	9
(1R)-cis	14.1 (8a)	11.9 (9a)
(1S)-cis	15.7 (8b)	13.2 (9b)
(1R)-trans	21.3 (8c)	18.2 (9c)
(1S)-trans	23.2 (8d)	19.8 (9d)

2-thiourea in the presence of basic lead carbonate to give 1-[^{14}C]cyano-N,N'-diphenylformamidine, which was reduced with lithium aluminium hydride and subsequently hydrolyzed with barium hydroxide to afford [2-^{14}C]glycine (4) (107 mCi). Esterification of 4 with ethanol-hydrogen chloride followed by diazotization with sodium nitrite-sulfuric acid and subsequent condensation with 2,5-dimethyl-2,4-hexadiene in the presence of copper catalyst gave ethyl [1-^{14}C]chrysanthemate. Hydrolysis of the ester led to the acid 5 (71.0 mCi); the purity 99% (*cis/trans* = 2/3) on RTLC [isopropyl acetate saturated with 10% aq. ammonia/methanol = 3/1 (v/v), R_f 0.24 (*cis*) and 0.17 (*trans*)].

α-Bromo-β-naphthyl [1-^{14}C]chrysanthemate (6) -- A mixture of [1-^{14}C]chrysanthemic acid (5) (71.0 mCi, 3.23 mmol) and oxalyl chloride (2.00 ml, 2.98 g, 23.4 mmol) in anhydrous n-pentane (10 ml) was stirred at room temperature for 1 hr and evaporated to give a yellow oil of [1-^{14}C]chrysanthemoyl chloride, which was dissolved in anhydrous petroleum benzine (10 ml). To the solution of the acid chloride was added a solution of α-bromo-β-naphthol (714 mg, 3.35 mmol) and pyridine (0.500 ml, 489 mg, 6.18 mmol) in anhydrous toluene (8 ml), and the mixture was stirred at room temperature for 2 hr. After dilution with 5% hydrochloric acid, the mixture was extracted with ether. The extract was washed with 5% sodium hydroxide, water and brine, successively, and dried

(Na_2SO_4). Evaporation of the solvent gave the ester 6 (71.0 mCi); the purity 98% on RTLC [benzene, R_f 0.55; n-hexane/ethyl acetate = 20/1 (v/v), R_f 0.34].

α-Bromo-β-naphthyl 2-formyl-3,3-dimethyl[1-^{14}C]cyclopropanecarboxylate (7) -- A mixture of α-bromo-β-naphthyl [1-^{14}C]chrysanthemate (6) (71.0 mCi, 3.23 mmol), osmium tetroxide (10 mg), sodium periodate (1.49 g, 6.98 mmol) and pyridine (2.0 ml) in dioxane-water (4/1 v/v, 28 ml) was heated at 50 - 55 °C for 1 hr under nitrogen stream. After cooling, the mixture was diluted with 5% hydrochloric acid (150 ml) and extracted with ether. The extract was washed with 5% hydrochloric acid, 5% sodium carbonate, 5% sodium thiosulfate, water and brine, successively. After drying over anhydrous sodium sulfate, the solvent was evaporated to give an oily residue, which was chromatographed on silica gel with benzene. Evaporation of the main fraction afforded the formyl ester 7 (55.3 mCi); the purity 99% on RTLC [benzene, R_f 0.12 (*cis*) and 0.16 (*trans*); n-hexane/ethyl acetate = 20/1 (v/v), R_f 0.11].

α-Bromo-β-naphthyl 3-(2,2-dichloroethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylate (8) -- To a stirring mixture of hexamethylphosphoroustriamide (1.30 g, 7.96 mmol) in anhydrous dichloromethane (45 ml) was added dropwise a solution of bromotrichloromethane (928 mg, 4.68 mmol) in the same solvent (45 ml) at -75 - -70 °C (in a dry ice-acetone bath) during 35 min under dry nitrogen, and the mixture was stirred at -70 °C for a further 10 min to prepare a solution of dichloromethylenetris(dimethylamino)phosphorane. To the solution of the phosphorane was added dropwise a solution of the formyl ester 7 (51.6 mCi, 2.34 mmol) in anhydrous dichloromethane (45 ml) to keep the temperature at -75 - -70 °C during the addition (about 40 min). After complete addition of 7, the mixture was stirred at the same temperature for an additional 30 min and then diluted with 5% hydrochloric acid. The organic layer was separated, washed with water and brine, dried (Na_2SO_4) and evaporated to give a brown oil, which was chromatographed on silica gel with benzene. The main fraction was evaporated to afford pale yellow crystals of the dichlorovinylated ester 8 (50.7 mCi); the purity more than 99% on both RHPLC (*cis*/*trans* = 32.8/67.2) and RTLC [benzene,

R_f 0.58 (*cis*) and 0.54 (*trans*); n-hexane/ethyl acetate = 20/1 (v/v), R_f 0.28 (*cis*) and 0.25 (*trans*)].

Optical resolution of α-bromo-β-naphthyl 3-(2,2-dichloroethenyl)-2,2-dimethyl-[1-^{14}C]cyclopropanecarboxylate (8) by chiral-phase HPLC -- The dichlorovinylated ester 8 (50.7 mCi, 954 mg, 2.30 mmol) was dissolved in chloroform (2.2 ml) and injected portionwise (70 µl) into the preparative HPLC [Sumipax OA-2000 column (10 µm, 8 mm ID x 50 cm x 2); n-hexane/1,2-dichloroethane (20/1 v/v) as the solvent with a flow rate of 4.0 ml/min; monitored by UV absorbance at 254 nm]. The fractions containing the *(1R)-cis* isomer (8a) (retention time 28.7 min), the *(1S)-cis* isomer (8b) (retention time 32.2 min), the *(1R)-trans* isomer (8c) (retention time 38.1 min) and the *(1S)-trans* isomer (8d) (retention time 42.9 min) were collected individually and evaporated to dryness to give 8a (6.96 mCi, optical purity 100%), 8b (6.83 mCi, optical purity 99.7%), 8c (15.7 mCi, optical purity 100%) and 8d (16.1 mCi, optical purity 99.2%), respectively.

Optically active 3-(2,2-dichloroethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic acids ([1-^{14}C]DCV acids) (1a - 1d) -- A mixture of the *(1R)-cis* ester (8a) (6.96 mCi, 0.316 mmol), 15% potassium hydroxide (0.56 ml) and methanol (1.46 ml) was stirred at room temperature overnight. After dilution with water, the mixture was washed with ether. The aqueous layer separated was acidified with hydrochloric acid and extracted with ether. The ethereal solution was extracted with saturated sodium bicarbonate solution. The bicarbonate solution was carefully acidified and re-extracted with ether. The extract was washed with water and brine, dried (Na_2SO_4) and evaporated to give *(1R)-cis*-3-(2,2-dichloroethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic acid (*(1R)-cis*-[1-^{14}C]DCV acid) (1a) (6.08 mCi); the purity 98% on RTLC [isopropyl acetate saturated with 10% aq. ammonia/methanol = 3/1 (v/v), R_f 0.28 (*cis*) and 0.23 (*trans*); chloroform/methanol/acetic acid = 100/5/1 (v/v/v), R_f 0.47 (*cis*) and 0.43 (*trans*)], $[\alpha]_D$ + 28° (c = 1.00). In the same manner as desribed above, other optically active esters, 8b (6.83 mCi), 8c (15.7 mCi) and 8d (16.1 mCi), were also converted into the corresponding [1-^{14}C]DCV acids, 1b (6.57 mCi, $[\alpha]_D$ - 27°), 1c (14.9 mCi, $[\alpha]_D$ + 35°) and 1d (16.0 mCi, $[\alpha]_D$ - 36°), respectively.

α-Bromo-β-naphthyl 3-(2,2-dibromoethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylate (9) -- To a stirring mixture of hexamethylphosphoroustriamide (626 mg, 3.84 mmol) in anhydrous dichloromethane (25 ml) was added dropwise a solution of carbon tetrabromide (747 mg, 2.27 mmol) in the same solvent (25 ml) at -75 - -70 °C during 20 min, and the mixture was stirred around -70 °C for a further 10 min under dry nitrogen. To the mixture was added dropwise a solution of α-bromo-β-naphthyl 2-formyl-3,3-dimethyl[1-^{14}C]cyclopropanecarboxylate (7) (27.2 mCi, 24.0 mCi/mmol, 1.13 mmol; *cis/trans* = 36/64 on RTLC) in anhydrous dichloromethane (25 ml) to keep the temperature at -75 - -70 °C (during 25 min), and the mixture was stirred at the same temperature for an additional 30 min. After dilution with 5% hydrochloric acid, the organic layer was separated, washed with water and brine, dried (Na_2SO_4) and evaporated to give a residue, which was chromatograghed on silica gel with benzene. The main fraction was evaporated to afford colorless crystals of the dibromovinylated ester 9 (26.9 mCi); the purity more than 99% on both RHPLC (*cis/trans* = 34.3/65.7) and RTLC [benzene, R_f 0.59].

Optical resolution of α-bromo-β-naphthyl 3-(2,2-dibromoethenyl)-2,2-dimethyl-[1-^{14}C]cyclopropanecarboxylate (9) by chiral-phase HPLC -- A solution of the dibromovinylated ester 9 (26.9 mCi, 564 mg, 1.12 mmol) in chloroform (2.8 ml) was injected portionwise (75 μl) into the preparative HPLC [Sumipax OA-2000 column (10 μm, 8 mm ID x 50 cm x 2); n-hexane/1,2-dichloroethane (20/1 v/v) as the solvent with a flow rate of 4.0 ml/min; monitored by UV absorbance at 254 nm]. The fractions containing the *(1R)-cis* isomer (9a) (retention time 19.8 min), the *(1S)-cis* isomer (9b) (retention time 21.8 min), the *(1R)-trans* isomer (9c) (retention time 28.7 min) and the *(1S)-trans* isomer (9d) (retention time 31.8 min) were collected individually and evaporated to give 9a (4.65 mCi, optical purity 100%), 9b (4.02 mCi, optical purity 100%), 9c (7.78 mCi, optical purity 99.1%) and 9d (7.68 mCi, optical purity 100%), respectively.

Optically active 3-(2,2-dibromoethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic acids ([1-^{14}C]DBV acids) (2a - 2d) -- A mixture of the *(1R)-cis* ester (9a) (4.65 mCi, 0.194 mmol), 35% sodium hydroxide (0.10 ml) and ethanol (1.9 ml) was stirred at room temperature overnight. After addition of water (0.9 ml), the mixture was stirred at the same temperature for further 5 hr to complete the hydrolysis. The mixture was then diluted with water and washed with ether. The aqueous layer obtained was acidified with hydrochloric acid and extracted with ether. The extract was washed with water and brine, dried over anhydrous sodium sulfate and evaporated to give a residue, which was chromatographed on silica gel with chloroform/acetone/acetic acid (400/40/1 v/v/v). The main fraction was evaporated to dryness to afford *(1R)-cis*-3-(2,2-dibromoethenyl)-2,2-dimethyl[1-^{14}C]cyclopropanecarboxylic acid (*(1R)-cis*-[1-^{14}C]DBV acid) (2a); the purity 99% on RTLC [chloroform/methanol/acetic acid = 100/5/1 (v/v/v), R_f 0.41 (*cis*) and 0.36 (*trans*)], $[\alpha]_D$ + 16° (c = 2.00). In the same manner as described above, other optically active esters, 9b (4.02 mCi), 9c (7.78 mCi) and 9d (7.68 mCi), were also converted into the corresponding [1-^{14}C]DBV acids, 2b (3.95 mCi, $[\alpha]_D$ - 16°), 2c (7.24 mCi, $[\alpha]_D$ + 38°) and 2d (6.76 mCi, $[\alpha]_D$ - 41°), respectively.

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REFERENCES

1. Elliott M. and Janes N.F. - Chem. Soc. Rev. 7: 473 (1978).
2. Elliott M., Farnham A.W., Janes N.F., Needham P.H., Pulman D.A. and Stevenson J.H. - Nature 246: 169 (1973) & 248: 710 (1974).
3. Miyamoto J., Beynon K.I., Roberts T.R., Hemingway R.J. and Swaine H. - Pure and Applied Chemistry 53: 1697 (1981).

4. (a) Kaneko H., Matsuo M. and Miyamoto J. - Toxicol. Appl. Pharmacol. 83: 148 (1986).
(b) Miyamoto J., Kaneko H. and Okuno Y. - Xenobiotic Conjugation Chemistry (ACS Symposium Series 299): 268 (1986).
5. Farkas J., Kourim P. and Sorm F. - (a) Chem. Iisty 52: 688 (1958); (b) Coll. Czech. Chem. Comm. 24: 2230 (1959).
6. Burt P.E., Elliott M., Farnham A.W., Janes N.F., Needham P.H. and Pulman D. A. - Pestic. Sci. 5: 791 (1974).
7. Aratani T. - (a) Jap. Patent 54-73758 (1979); (b) J. Syn. Org. Chem. Jap. 43: 1134 (1985).
8. (a) Kondo K., Matsui K., Negishi A. and Takahatake Y. - Jap. Patent 51-63145 (1976).
(b) Mori F., Ohmura Y., Nishida T. and Itoi K. - Jap. Patent 51-41324 (1976).
9. House H.O. - Modern Synthetic Reactions (2nd Edition), W.A. Benjamin, Inc., Menlo Park, California, U.S.A. (1972).
10. Elliott M., Farnham A.W., janes N.F., Needham P.H. and Pulman D.A. - Nature 244: 456 (1973).
11. Elliott M., Janes N.F. and Pulman D.A. - U.S. Patent No. 4024163 (1977).
12. Nakatsuka I., Shono F. and Yoshitake A. - J. Label. Comp. Radiopharm. 13: 561 (1977).
13. Kanamaru H., Yoshitake A. and Nakatsuka I. - Radioisotopes 35: 242 (1986).
14. Oh-i N., Doi T., Nara T. and Inda Y. - Jap. Patent 59-116544 (1984).
15. Kanamaru H., Kamada T., Yoshitake A. and Nakatsuka I. - Radioisotopes 35: 103 & 169 (1986).
16. Ehrensvärd G. and Stjernholn R. - Acta Chem. Scand. 3: 971 (1949).
17. Criegee R., Marchand B. and Wannowius H. - Ann. Chem. 550: 99 (1942).
18. Elliott M., Janes N.F., Pulman D.A., Gaughan L.C., Unai T. and Casida J.E. - J. Agric. Food Chem. 24: 270 (1976).
19. Salmond W.G. - Tetrahedron Lett. 1977: 1239.