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FATTY ACIDS, PART 17.*

THE SYNTHESIS AND CHROMATOGRAPHIC AND SPECTROSCOPIC PROPERTIES OF THE CYCLOPROPANE ESTERS DERIVED FROM ALL THE METHYL OCTADECENOATES (Δ^2-Δ^{17}).

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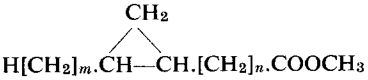
All the *cis* octadecenoic esters have been converted to cyclopropane compounds by reaction with zinc–copper couple and di-iodomethane. Their gas–liquid chromatographic behaviour on four liquid phases is described. Six isomers (2,3 -; 3,4 -; 4,5 -; 15,16 -; 16,17 -; and 17,18 -) have distinctive nuclear magnetic resonance spectra and two (2,3 - and 17,18 -) have distinctive infra red spectra.

Discussion

In continuance of our study of series of closely related long-chain acids[1–4]) we report the preparation and properties of the methyl esters of sixteen cyclopropane acids.



$$H[CH_2]_m.\overset{CH_2}{CH\text{—}CH}.[CH_2]_n.COOCH_3$$

$m + n = 15;\quad n = 0 — 15$

Cyclopropane acids are present in a wide range of bacterial[5]), protozoan[6]), and plant species[7,8]) but only a few compounds have been fully identified because of difficulties of isolation and of structure determination. These include one C_{17}[9]), one C_{18} (dihydromalvalic), and two C_{19} (lactobacillic and dihydrosterculic) acids in addition to acids of higher molecular weight with one or two cyclopropane systems[10,11]). The analysis and identification of these acids has recently attracted interest[12–14]) and we considered it worthwhile to prepare and examine a complete series of cyclopropane compounds.

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The standard method of preparing stereochemically pure cyclopropanes is by the reaction of methylene iodide and a zinc–copper couple with an olefin[15,16]) and we have applied this method to the methyl *cis*-octadecenoates[1]). The cyclopropane esters were purified by preparative silver ion thin-layer chromatography. Only three of these esters (the 6,7-; 9,10-; and 11,12- isomers) have been synthesised previously[14,16]).

Gas–liquid chromatography

Retention data for the cyclopropane esters on four different stationary phases are quoted as carbon numbers[17]) or equivalent chain lengths[18]) in table 1.

The stationary phases used were Apiezon L (capillary column), neopentylglycol succinate (capillary column), diethyleneglycol succinate (packed column), and polyethyleneglycol adipate (packed column). The carbon numbers on all four phases show similar changes: starting with the 2,3-isomer the value declines to the 5,6- ester, is fairly constant until the 11,12-compound, then rises at increasing rate to the 17,18- isomer. Similar values quoted for a series of branched methyl octadecanoates[19]) have recently been discussed[20]). Our carbon numbers resemble those of the olefinic esters from which they were prepared. This is shown in table 2 where the differences in carbon number between olefinic and cyclopropane esters are listed. These show remarkable similarity for polar and non-polar phases for most isomers.

With the capillary NPGS column (efficiency ~15000 theoretical plates)

TABLE 1

Carbon numbers of methyl *cis*-methyleneoctadecanoates

Isomer	NPGS	DEGS	PEGA	ApL
2,3	19.38	19.64	19.55	18.98
3,4	19.32	19.62	19.50	18.85
4,5	19.30	19.58	19.46	18.84
5,6	19.20	19.51	19.36	18.76
6,7	19.20	19.55	19.37	18.76
7,8	19.18	19.52	19.35	18.75
8,9	19.15	19.51	19.37	18.73
9,10	19.24	19.55	19.37	18.73
10,11	19.25	19.55	19.40	18.78
11,12	19.25	19.58	19.44	18.78
12,13	19.29	19.65	19.48	18.80
13,14	19.41	19.71	19.56	18.85
14,15	19.45	19.82	19.65	18.96
15,16	19.50	19.94	19.80	19.02
16,17	19.80	20.30	20.19	19.22
17,18	20.04	20.54	20.38	19.38

TABLE 2

Difference in carbon number between methyl octadecenoates[4]) and cyclopropane esters derived from them

Isomer	NPGS	DEGS	ApL
2,3	1.31	1.32	1.00
3,4	0.90	0.88	0.98
4,5	1.16	1.16	1.12
5,6	1.07	1.17	1.10
6,7	1.06	1.10	1.11
7,8	1.04	1.07	1.11
8,9	1.03	1.06	1.09
9,10	1.10	1.06	1.10
10,11	1.06	1.02	1.12
11,12	1.02	1.00	1.10
12,13	1.02	1.03	1.07
13,14	1.09	0.95	1.05
14,15	1.05	0.96	1.10
15,16	1.04	0.93	1.13
16,17	1.05	0.92	1.08
17,18	1.55	1.63	1.49
Range*	1.02–1.16	0.92–1.17	1.05–1.13
Average*	1.06	1.03	1.10

* Excluding 2,3–; 3,4–; and 17,18– isomers.

isomers differing in carbon number by 0.06 were well separated; the ApL column (~40000 theoretical plates) separated isomers differing in carbon number by 0.04. It is thus possible to distinguish between the 9,10- and 11,12- isomers which may frequently occur together.

Nuclear magnetic resonance spectroscopy

The interpretation of the NMR spectra of *cis*-1,2- disubstituted cyclopropanes has been the subject of some controversy, now apparently settled[21]). The spectrum of the ester (I) ($n = m = 7$) is characterised by a multiplet at 10.3 τ (1 proton) assigned to the proton H*b* *cis* to the two alkyl substituents, and a broad band at 9.4 τ (3 protons) arising from the signals of the H*a*, H*c*, and H*d* protons. The chemical shifts for these and other protons in all the isomeric cyclopropane esters are listed in table 3. The 5,6- to 14,15- methylene isomers have spectra very similar to one another but the remaining six isomers have characteristic features which allow them to be distinguished from each other

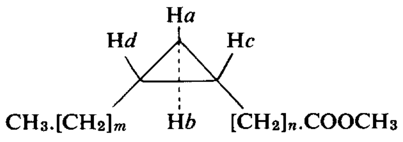

TABLE 3

Principal features in the NMR spectra of isomeric methyl *cis*-methyleneoctadecanoates [chemical shifts are expressed in p.p.m. down field from internal tetramethylsilane ($\tau = 10$). Figures in brackets denote the number of protons]

Isomer	$—OCH_3$	α-CH_2	$—(CH_2)_n—$	$—CH_3$	Cyclopropane protons			
					H*c*	H*d*	H*a*	H*b*
2,3	6.42 (3)	—	8.73	9.09 (3)	7.97	8.36 (2)		9.47 (1)
3,4	6.40	7.76 (2)	8.72	9.11	8.22	~9.1		10.14
4,5	6.39	7.64	8.73	9.11	8.27	9.35		10.23
5,6	6.40	7.72	8.73	9.11	9.38 (3)			10.30
6,7	6.41	7.73	8.73	9.11	9.40			10.31
7,8	6.40	7.73	8.73	9.10	9.40			10.30
8.9	6.40	7.75	8.71	9.10	9.40			10.31
9,10	6.40	7.75	8.69	9.10	9.40			10.31
10,11	6.41	7.77	8.69	9.11	9.40			10.31
11,12	6.41	7.77	8.70	9.11	9.40			10.31
12,13	6.40	7.77	8.70	9.09	9.40			10.31
13,14	6.40	7.77	8.71	9.09	9.41			10.31
14,15	6.41	7.77	8.73	9.07	9.41			10.31
15,16	6.41	7.77	8.72	8.97	9.40			10.30
16,17	6.41	7.77	8.73	9.02	9.40			10.35
17,18	6.41	7.78	8.73	—	8.29 (1)	9.07 (2)		9.60 (2)

The protons attached to C(2), α to the $COOCH_3$ group, usually exhibit a triplet at about 7.77 τ, but these are affected by the near presence of the cyclopropane group. In the 2,3- isomer this group is part of the cyclopropane system, in the 3,4- isomer the C(2) protons give a doublet at 7.76 τ, and in the 4,5- isomer a triplet at 7.64 τ.

The cyclopropane ring can also affect the signal caused by protons in the ω-methyl group which is normally a distinct triplet at about 9.1 τ. This becomes a poorly defined triplet at 8.97 τ in the 15,16- isomer, a doublet at 9.02 τ in the 16,17- isomer, and is absent from the 17,18- isomer.

Greater interest attaches to the changes in the signals from the cyclopropane system. For most isomers there is a multiplet at 10.3 τ (proton H*b*) and a broad band at 9.4 τ (protons H*a*, H*c*, and H*d*). For the three isomers with the cyclopropane ring closest to the ester group the signal for H*b* is moved downfield to 10.23 τ (4,5- isomer) 10.14 τ (3,4- isomer), and 9.47 τ (2,3- isomer). In these isomers the signal normally at 9.4 τ moves to 9.35 (4,5- isomer), ~ 9.1 (3,4- isomer), and 8.36 τ (2,3- isomer) and arises from two protons only (H*a* and H*d*). The remaining proton (H*c*) produces a signal at 8.27 (4,5-), 8.22 (3,4-), and 7.97 τ (2,3- isomer). These three isomers are clearly distinguished from the remainder and from one another. As expected, the 17,18- isomer also differs from the rest with signals at 8.29 (H*c*), 9.07 (H*a* and H*d*), and 9.60 τ (two H*b* protons).

Infra red spectroscopy

1,2- Disubstituted cyclopropanes give characteristic absorption bands at 1020 and 3050 cm^{-1}. These are present in the 4,5- to 15,16- isomers we have examined but are shifted slightly in the other isomers. They appear at 1025 and 3055 in the 3,4- isomer, 1026 and 3048 in the 16,17- isomer, and 1010 and 3065 cm^{-1} in the 17,18- isomer. In the 2,3- isomer there is an absorption band at 1078 cm^{-1}, the second band is no longer apparent, and the ester carbonyl frequency is shifted from 1735 cm^{-1} to 1725 cm^{-1}.

Experimental

Synthesis

The zinc–copper couple was prepared as previously described by one of us[16]). In a typical procedure a solution of di-iodomethane (4 ml) and the mono-enoic ester (0.5 g) in anhydrous ether (10 ml) was added to the zinc–copper couple (2 g). in anhydrous ether (10 ml) and refluxed overnight. The mixture was then poured into cold hydrochloric acid (1 N) and the ethereal extract washed with water. After removal of ether and of di-iodomethane under vacuum (100°/0.2 mm Hg) the cyclopropane ester was separated from unchanged olefinic ester by preparative TLC on layers of silica gel (0.6 mm) impreganted with silver nitrate (15%). These were developed with ether–petrol mixtures (10: 90). The yield was generally 70–80% but a little lower with the 2,3- (40%) and 3,4- (60%) isomers. Alternate samples were subject to combustion analysis.

	C	H
Calc. for $C_{20}H_{38}O_2$	77.36%	12.33%
3,4- isomer	77.42	12.52
5,6- isomer	77.70	12.36
7,8- isomer	77.69	12.15
9,10- isomer	77.39	12.26
12,13- isomer	77.51	12.25
14,15- isomer	77.43	12.10

Gas–liquid chromatography

The following columns were used:

NPGS, 50 m × ¼ mm internal diameter capillary column, operating temperature 190°, inlet pressure 20 p.s.i.

ApL, 50 mm × ¼ mm internal diameter capillary column, operating temperature 220°, inlet pressure 25 p.s.i.

DEGS, 5 foot × ¼ inch column packed with DEGS (20%) on Gas Chrom Z (70–80 mesh), operating temperature 180°, inlet pressure 50 p.s.i.

PEGA, 5 foot × ¼ inch column packed with PEGA (15%) on Gas Chrom Z (70–80 mesh) operating temperature 190°, inlet pressure 50 p.s.i.

The capillary columns were used with a Perkin–Elmer F11 chromatograph and the packed columns with a Pye 104 chromatograph. Both instruments were fitted with flame ionisation detectors. The carrier gas was nitrogen.

Carbon numbers were calculated from distances between the solvent front and the peak of eluted esters. Saturated C_{14}, C_{16}, and C_{18} esters were used as internal standards.

Nuclear magnetic resonance

NMR spectra were obtained with 15% solutions of esters in carbon tetrachloride using a Perkin–Elmer R-10 spectrometer operating at 60 Mc/s. Chemical shifts were measured in p.p.m. downfield from internal tetramethyl-silane ($\tau = 10$).

Infra red spectrometry

Spectra were obtained on 1% carbon disulphide solutions in 1 mm cells with a Perkin–Elmer 621 spectrophotometer.

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