Journal of Chromatography, 115 (1975) 559–570
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CHROM. 8542

FATTY ACIDS

V. SYNTHESIS OF ALL THE DIMETHYLENE-INTERRUPTED METHYL OCTADECADIYNOATES AND A STUDY OF THEIR GAS–LIQUID CHROMATOGRAPHIC PROPERTIES[*]

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(Received June 17th, 1975)

SUMMARY

All the dimethylene-interrupted methyl octadecadiynoates have been synthesised and the gas–liquid chromatographic behaviour of these isomers was studied on polar [Carbowax 20M, FFAP, DEGA, DEGS and Silar 10C (recently renamed as Apolar 10C)], semi-polar (XE-60) and non-polar (SE-30, OV-101 and Apiezon L) stationary phases. The possibility of identification and separation of these isomers is discussed. The $\Delta^{3a,7a}$ isomer was found to decompose on most polar phases and the $\Delta^{2a,6a}$ isomer could not be eluted from the Carbowax 20M phase.

INTRODUCTION

Christie and Holman synthesised the complete series of methylene-interrupted *cis,cis*-octadecadienoic acids[2] and studied the physical[2–4] and some biological[5] properties of these isomers in detail. The occurrence in nature of several dimethylene-interrupted octadecadienoic acid isomers[6–11] led us to prepare the complete series of the 1,5-diacetylenic C_{18} acids to study their physical, chemical, and biological properties.

All dimethylene-interrupted octadecadiynoic acids were readily synthesised by well established methods[12]. Fig. 1 outlines the various synthesis routes. Of the possible twelve isomers only four ($\Delta^{6a,10a}$, $\Delta^{7a,11a}$, $\Delta^{8a,12a}$ and $\Delta^{11a,15a}$) were previously synthesised[12–14].

EXPERIMENTAL AND RESULTS

Gas–liquid chromatography

The gas–liquid chromatographic (GLC) results were obtained under the con-

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[*] For Part III, see ref. 1.

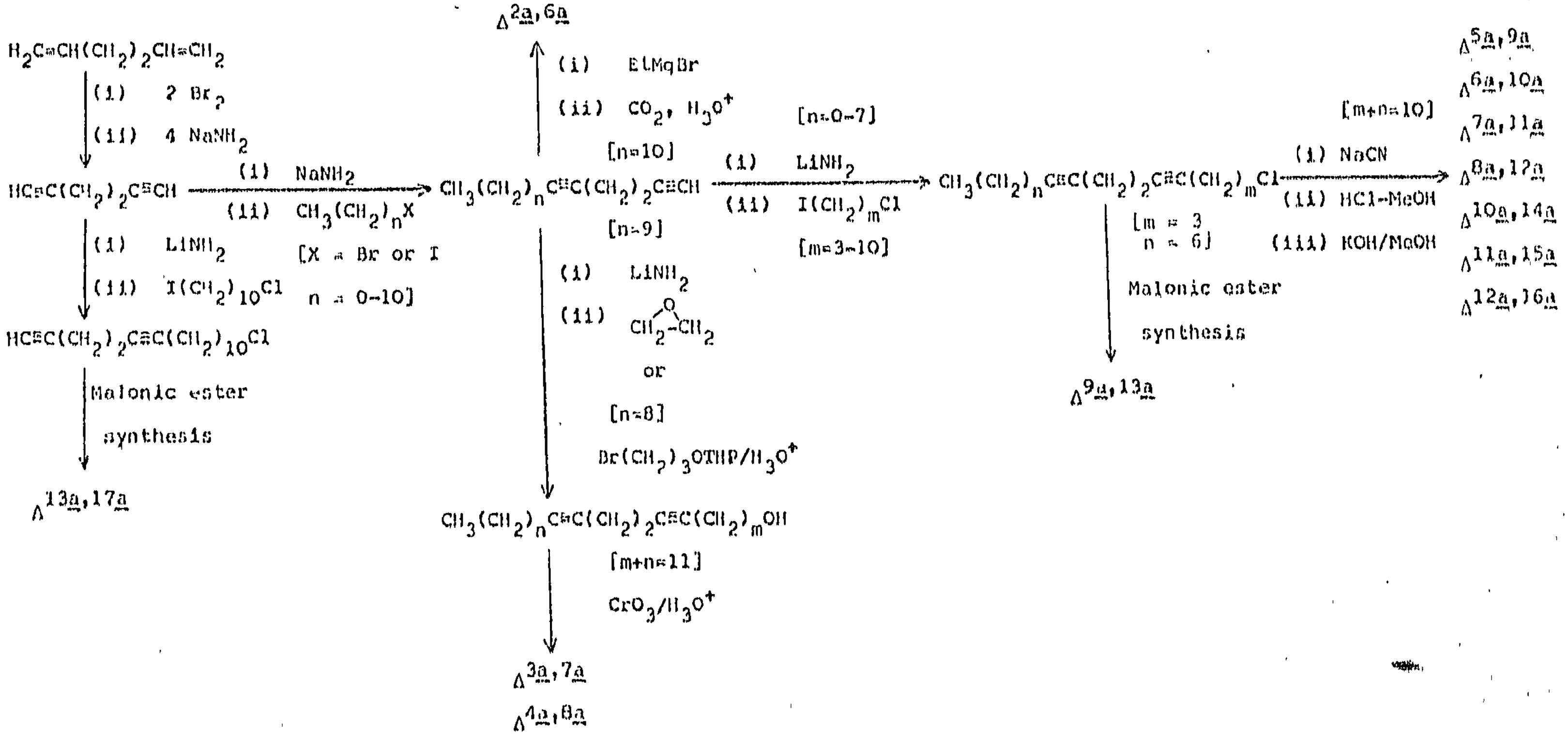

Fig. 1. Scheme of the various routes for the synthesis of dimethylene-interrupted octadecadiynoic acids.

TABLE I

CONDITIONS FOR GLC

Column length, 2 m.

Stationary phase	*Temperature (°C)*	*Carrier gas (nitrogen) flow-rate (ml/min)*	*Internal diameter (mm)*
10% DEGA	190	150	6.2
20% DEGS	190	50	3.1
10% FFAP	205	50	3.1
10% Carbowax 20M	205	50	3.1
10% Silar 10C*	190	60	6.2
20% XE-60	190	125	6.2
3% SE-30	205	50	3.1
1.5% OV-101	200	50	3.1
5% Apiezon L (APL)	220	150	6.2

* Recently renamed as Apolar 10C (ref. 15).

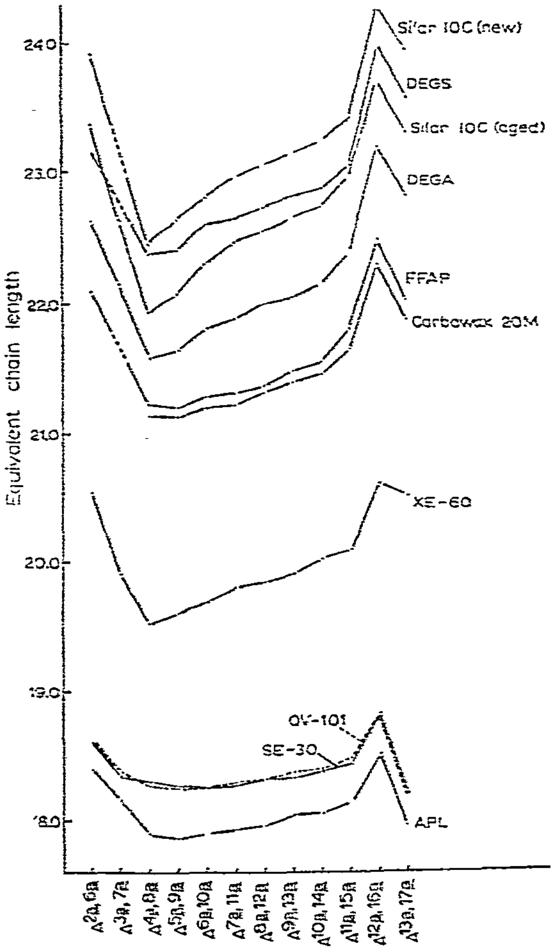

Fig. 2. Equivalent chain length of diacetylenic C_{18} methyl esters on different stationary phases.

TABLE II

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS AND THEIR MIXTURES ON APL

Isomer	*ECL*	*A1**	*A2**	*A3***	*A4****	*A5****
$\Delta^{2c,6c}$	18.40	—	18.40	—	—	—
$\Delta^{3c,7c}$	18.16	—	—	—	—	—
$\Delta^{4c,8c}$	17.90	—	—	—	17.95	—
$\Delta^{5c,9c}$	17.87	—	—	—	—	17.92
$\Delta^{6c,10c}$	17.90	17.90	—	—	—	—
$\Delta^{7c,11c}$	17.93	—	—	17.92	—	—
$\Delta^{8c,12c}$	17.96	—	—	—	—	17.92
$\Delta^{9c,13c}$	18.03	—	18.03	—	—	—
$\Delta^{10c,14c}$	18.05	—	—	—	17.95	—
$\Delta^{11c,15c}$	18.14	—	—	18.15	—	—
$\Delta^{12c,16c}$	18.51	18.50	—	—	—	—
$\Delta^{13c,17c}$	17.96	—	—	—	—	—

* Baseline separation.
** Twin peak separation.
*** No separation.

ditions given in Table I on a Pye 104 or Varian 940 chromatograph equipped with a flame ionization detector.

Equivalent chain length (ECL) values were calculated from the distances between the solvent front and the peak of the other eluted components. Saturated methyl esters (C_{15}, C_{16}, C_{18}, C_{19}, C_{20}, C_{22}) were used as internal standards.

The ECL values of all diacetylenic esters are compared in Fig. 2 and actual values are recorded in Tables II–X.

Methyl octadecadiynoates. The lowest ECL values of these isomers were

TABLE III

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS AND THEIR MIXTURES ON SE-30

Isomer	*ECL*	*B1**	*B2***	*B3***	*B4****	*B5*§
$\Delta^{2c,6c}$	18.61	—	18.63	—	—	—
$\Delta^{3c,7c}$	18.35	—	—	—	—	—
$\Delta^{4c,8c}$	18.30	—	—	—	—	—
$\Delta^{5c,9c}$	18.27	—	18.25	—	—	—
$\Delta^{6c,10c}$	18.26	—	—	18.26	—	18.32
$\Delta^{7c,11c}$	18.27	—	—	—	18.28	—
$\Delta^{8c,12c}$	18.32	—	—	—	—	—
$\Delta^{9c,13c}$	18.33	—	—	—	—	18.32
$\Delta^{10c,14c}$	18.38	—	—	—	18.37	—
$\Delta^{11c,15c}$	18.44	—	—	18.45	—	—
$\Delta^{12c,16c}$	18.82	18.81	—	—	—	—
$\Delta^{13c,17c}$	18.20	18.21	—	—	—	—

* Baseline separation.
** Twin peak separation.
*** Shoulder separation.
§ No separation.

ABLE IV

QUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS ND THEIR MIXTURES ON OV-101

somer	*ECL*	*C1**	*C2***	*C3***	*C4****	*C5*§
^{2a,6a}	18.63	—	18.63	18.58	—	—
^{3a,7a}	18.38	—	—	—	—	—
^{4a,8a}	18.27	—	—	—	—	—
^{5a,9a}	18.25	—	18.25	—	—	—
^{6a,10a}	18.25	—	—	—	—	—
^{7a,11a}	18.29	18.29	—	—	—	—
^{8a,12a}	18.32	—	—	—	—	—
^{9a,13a}	18.37	—	—	18.37	—	18.44
^{10a,14a}	18.40	—	—	—	18.39	—
^{11a,15a}	18.48	—	—	—	—	18.44
^{12a,16a}	18.82	18.84	—	—	—	—
^{13a,17a}	18.21	—	—	—	18.31	—

* Baseline separation.
** Twin peak separation.
*** Shoulder separation.
§ No separation.

recorded on the non-polar APL phase with values ranging from 17.87–18.51, while on OV-101 and SE-30 phases these isomers gave almost identical retention behaviours and ECL values ranged from 18.25–18.82 and from 18.26–18.82, respectively. On all three mentioned non-polar phases, the $\Delta^{2a,6a}$ and $\Delta^{12a,16a}$ isomers exhibited the highest while the $\Delta^{4a,8a}$–$\Delta^{7a,11a}$ isomers gave the lowest ECL values (with nearly identical ECL values on OV-101 and SE-30).

On the semi-polar XE-60 phase, the ECL values were in the range 19.52–20.61 with $\Delta^{2a,6a}$, $\Delta^{12a,16a}$ and $\Delta^{13a,17a}$ isomers exhibiting nearly identical ECL values. The

TABLE V

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS AND THEIR MIXTURES ON XE-60

Isomer	*ECL*	*D1**	*D2***	*D3***	*D4****
^{2a,6a}	20.55	—	—	—	—
^{3a,7a}	19.90	—	—	—	—
^{4a,8a}	19.52	19.53	—	—	—
^{a,9a}	19.60	—	19.61	—	—
^{a,10a}	19.67	—	—	—	19.79
^{a,11a}	19.80	—	—	19.82	—
^{a,12a}	19.83	—	—	—	19.79
^{a,13a}	19.90	—	19.88	—	—
^{2a,14a}	20.01	20.00	—	19.99	—
^{1a,15a}	20.09	—	—	—	—
^{2a,16a}	20.61	—	—	—	—
^{3a,17a}	20.51	—	—	—	—

* Baseline separation.
** Twin peak separation.
*** No separation.

TABLE VI

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS AND THEIR MIXTURES ON CARBOWAX 20M

Isomer	*ECL*	*E1**	*E2***	*E3***	*E4****	*E5*§
$\Delta^{2a,6a}$	—	—	—	—	—	—
$\Delta^{3a,7a}$	—	—	—	—	—	—
$\Delta^{4a,8a}$	21.13	—	—	—	—	21.15
$\Delta^{5a,9a}$	21.10	21.09	—	21.09	—	—
$\Delta^{6a,10a}$	21.19	—	—	—	21.19	—
$\Delta^{7a,11a}$	21.21	—	21.21	—	—	—
$\Delta^{8a,12a}$	21.31	—	—	—	—	21.15
$\Delta^{9a,13a}$	21.39	—	—	21.35	21.35	—
$\Delta^{10a,14a}$	21.44	—	—	—	—	—
$\Delta^{11a,15a}$	21.64	21.63	21.63	—	—	—
$\Delta^{12a,16a}$	22.28	—	—	—	—	—
$\Delta^{13a,17a}$	21.86	—	—	—	—	—

* Baseline separation.
** Twin peak separation.
*** Shoulder separation.
§ No separation.

$\Delta^{4a,8a}$ isomer gave the lowest ECL value of all isomers and there was a significant and gradual increase in the ECL values by the remaining isomers as the unsaturated centres moved nearer to the terminal end of the carbon chain.

On the polar stationary phases, the ECL values were lowest on Carbowax 20M, ranging from 21.10–22.28, and highest on Silar 10C phase (Note: a newly packed column) with an ECL value ranging from 22.44–24.29. The DEGS phase was found to be more polar than DEGA with ECL values ranging from 22.37–23.98 and

TABLE VII

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS AND THEIR MIXTURES ON FFAP

Isomer	*ECL*	*F1**	*F2***	*F3***	*F4****	*F5*§
$\Delta^{2a,6a}$	22.09	—	—	—	—	—
$\Delta^{3a,7a}$	—	—	—	—	—	—
$\Delta^{4a,8a}$	21.22	—	—	—	—	21.29
$\Delta^{5a,9a}$	21.19	—	—	—	21.19	—
$\Delta^{6a,10a}$	21.28	—	—	21.29	—	—
$\Delta^{7a,11a}$	21.31	—	—	—	—	21.29
$\Delta^{8a,12a}$	21.36	—	—	—	21.35	—
$\Delta^{9a,13a}$	21.47	—	21.49	—	—	—
$\Delta^{10a,14a}$	21.54	—	—	21.54	—	—
$\Delta^{11a,15a}$	21.79	21.78	21.79	—	—	—
$\Delta^{12a,16a}$	22.47	22.47	—	—	—	—
$\Delta^{13a,17a}$	22.01	—	—	—	—	—

* Baseline separation.
** Twin peak separation.
*** Shoulder separation.
§ No separation.

TABLE VIII

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS AND THEIR MIXTURES ON DEGA

Isomer	ECL	G1*	G2**	G3***	G4§
$\Delta^{2a,6a}$	22.62	—	—	—	—
$\Delta^{3a,7a}$	22.14	—	—	—	—
$\Delta^{4a,8a}$	21.59	21.60	—	21.67	—
$\Delta^{5a,9a}$	21.64	—	21.66	—	—
$\Delta^{6a,10a}$	21.80	—	—	21.79	—
$\Delta^{7a,11a}$	21.87	—	—	—	21.91
$\Delta^{8a,12a}$	21.98	—	21.97	—	21.91
$\Delta^{9a,13a}$	22.03	22.03	—	—	—
$\Delta^{10a,14a}$	22.13	—	—	—	—
$\Delta^{11a,15a}$	22.37	—	—	—	—
$\Delta^{12a,16a}$	23.19	—	—	—	—
$\Delta^{13a,17a}$	22.81	—	—	—	—

* Baseline separation.
** Twin peak separation.
*** Shoulder separation.
§ No separation.

from 21.59–23.19, respectively. The ECL values of these isomers ranged from 21.19–22.47 on the FFAP phase.

The $\Delta^{3a,7a}$ isomer decomposed when injected onto all polar stationary phases except DEGA. A series of components was eluted and the largest peak eluted from Carbowax gave an ECL value of 19.76, FFAP (20.72), DEGS (20.64), and Silar 10C (20.78). Moreover, the $\Delta^{2a,6a}$ isomer could not be eluted from the Carbowax 20M column. All polar columns used in this work were newly packed and it is noteworthy

TABLE IX

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS AND THEIR MIXTURES ON DEGS

Isomer	ECL	H1*	H2**	H3***	H4***	H5§
$\Delta^{2a,6a}$	23.18	23.26	—	—	—	—
$\Delta^{3a,7a}$	—	—	—	—	—	—
$\Delta^{4a,8a}$	22.37	22.36	—	—	—	—
$\Delta^{5a,9a}$	22.40	—	—	—	22.48	22.59
$\Delta^{6a,10a}$	22.59	—	22.58	—	—	—
$\Delta^{7a,11a}$	22.63	—	—	—	—	22.59
$\Delta^{8a,12a}$	22.72	—	—	—	22.75	-
$\Delta^{9a,13a}$	22.80	—	—	—	—	—
$\Delta^{10a,14a}$	22.86	—	—	—	—	—
$\Delta^{11a,15a}$	23.05	—	23.14	—	—	—
$\Delta^{12a,16a}$	23.98	—	—	23.93	—	—
$\Delta^{13a,17a}$	23.59	—	—	23.63	—	—

* Baseline separation.
** Twin peak separation.
*** Shoulder separation.
§ No separation.

TABLE X

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL DIACETYLENIC C_{18} METHYL ESTERS AND THEIR MIXTURES ON SILAR 10C

Isomer	*Newly packed column*						*Aged column*					
	ECL	*I1**	*I2***	*I3***	*I4****	*I5****	*ECL*	*J1**	*J2***	*J3***	*J4****	*J5****
$\Delta^{2a,6a}$	23.92	—	—	—	—	—	23.38	—	—	—	—	—
$\Delta^{3a,7a}$	—	—	—	—	—	—	22.61	—	—	—	—	—
$\Delta^{4a,8a}$	22.44	—	—	—	22.46	—	21.93	21.93	—	—	—	—
$\Delta^{5a,9a}$	22.62	—	—	—	22.46	—	22.06	—	22.06	—	—	—
$\Delta^{6a,10a}$	22.79	—	22.79	22.89	—	—	22.29	—	—	—	—	—
$\Delta^{7a,11a}$	22.95	22.95	—	—	—	—	22.45	22.46	—	22.44	22.52	—
$\Delta^{8a,12a}$	23.05	—	—	23.05	—	23.10	22.53	—	22.53	—	—	—
$\Delta^{9a,13a}$	23.14	—	23.14	—	—	—	22.63	—	—	—	22.52	—
$\Delta^{10a,14a}$	23.24	—	—	—	—	23.10	22.72	—	—	22.64	—	22.81
$\Delta^{11a,15a}$	23.43	23.43	—	—	—	—	22.96	—	—	—	—	22.81
$\Delta^{12a,16a}$	24.29	—	—	—	—	—	23.70	—	—	—	—	—
$\Delta^{13a,17a}$	23.95	—	—	—	—	—	23.31	—	—	—	—	—

* Baseline separation.
** Twin peak separation.
*** No separation.

to point out that, when the $\Delta^{3a,7a}$ isomer was injected onto an aged (in constant use for about one year) Silar 10C column, this isomer did not show any signs of decomposition. All isomers were subsequently re-run on the aged Silar 10C column (Table X) and the corresponding ECL value of each individual isomer was on an average 0.53 fractional chain length (FCL) lower than that observed on the newly packed Silar 10C column. Nevertheless, the two sets of data produced a coherent parallel plot. No immediate explanation could be given for this unexpected behaviour of the $\Delta^{3a,7a}$ isomer. From the above observation it seems that $\Delta^{2a,6a}$ and $\Delta^{3a,7a}$ isomers are very labile compounds; they seem to polymerise on contact with the polar groups of the stationary phases at high temperatures (190–205°) or isomerise into less polar substances. A separate study has now been designed to investigate further this unusual behaviour and to determine the nature of this deviation.

TABLE XI

SEPARATION OF MIXTURES OF METHYL OCTADECADIYNOATES

Stationary phase	*Degree of separation (Difference in ECL)*			
	Baseline	*Twin peak*	*Shoulder*	*No separation*
APL	$\geqslant$0.37 (A1–2)	0.21 (A3)	—	$\leqslant$0.15 (A4–5)
SE-30	0.60 (B1)	$\geqslant$0.18 (B2–3)	0.11 (B4)	0.07 (B5)
OV-101	0.53 (C1)	$\geqslant$0.26 (C2–3)	0.19 (C4)	0.11 (C5)
XE-60	0.49 (D1)	$\geqslant$0.19 (D2–3)	—	0.16 (D4)
Carbowax 20M	0.54 (E1)	$\geqslant$0.29 (E2–3)	0.20 (E4)	0.18 (E5)
FFAP	0.68 (F1)	$\geqslant$0.26 (F2–3)	0.17 (F4)	0.09 (F5)
DEGA	0.44 (G1)	0.34 (G2)	0.21 (G3)	0.11 (G4)
DEGS	0.81 (H1)	0.46 (H2)	$\geqslant$0.32 (H3–4)	0.23 (H5)
Silar 10C (new)	0.48 (I1)	$\geqslant$0.26 (I2–3)	—	$\leqslant$0.19 (I4–5)
Silar 10C (aged)	0.52 (J1)	$\geqslant$0.27 (J2–3)	—	$\leqslant$0.24 (J4–5)

Mixtures of these isomers were also examined on all available stationary phases including the aged Silar 10C column (Tables II–X) and it is possible to describe the degree of separation as baseline, twin peak or shoulder. The results are summarized in Table XI. On the non-polar stationary phases the efficiency of separation of the isomers on SE-30 was almost identical to that of OV-101, but better than on APL phase. The Silar 10C phase was superior in separating these isomers to any of the other polar stationary phases. On all phases, the ECL value was very reproducible, as demonstrated by the examination of mixtures of these isomers.

Synthesis and properties

Methyl 2,6-octadecadiynoate ($\Delta^{2a,6a}$)

1,5-Heptadecadiyne. Bromine (165 g, 1.03 mole) was slowly added to a mixture of 1,5-hexadiene (41 g, 0.5 mole) in diethyl ether (150 ml) at 0–5°. The solvent and any excess bromine were removed under reduced pressure and the crude 1,2,5,6-tetrabromohexane in tetrahydrofuran (THF) (150 ml) was then added to a sodium amide suspension in liquid ammonia (prepared from 64 g of sodium, 2 g of iron(III) nitrate and 2.5 l of liquid ammonia) and stirred for 1.5 h. 1-Bromoundecane (110 g, 0.5 mole) in THF (100 ml) was then added and the reaction mixture stirred overnight. Distillation of the ethereal extract gave 1,5-heptadecadiyne (10.5 g, 10.4% yield, b.p. 88–94°/0.05 mm Hg).

Methyl 2,6-octadecadiynoate. 1,5-Heptadecadiyne (10.1 g, 0.1 mole) in anhydrous diethyl ether (30 ml) was added to ethylmagnesium iodide (prepared from 2.4 g of magnesium, 15.5 g of ethyl iodide and 150 ml of diethyl ether) at 0–5° and refluxed for 1 h. The suspension was then cooled to 0–5° and dry carbon dioxide gas was flushed through the reaction flask. An exothermic reaction ensued and the passage of carbon dioxide gas was stopped when the temperature dropped to 5°. Dilute hydrochloric acid (5 *M*, 100 ml) was added and the acidic fraction isolated in the usual way. Re-crystallisation of the crude acid from *n*-hexane gave pure 2,6-octadecadiynoic acid [6.3 g, 55% yield, m.p. 64–64.5°; anal.: C = 77.95%, H = 10.24% (calcd. C = 78.21%, H = 10.21%*)]. The acid (2.2 g, 0.008 mole) was refluxed with 14% boron trifluoride–methanol complex (10 ml) and anhydrous methanol (30 ml) for 20 min. The solution was diluted with water and extracted with *n*-hexane (three times 30 ml). Pure methyl 2,6-octadecadiynoate (1.5 g, 65% yield) was obtained.

Methyl 3,7- and 4,8-octadecadiynoates ($\Delta^{3a,7a}$, $\Delta^{4a,8a}$)

The corresponding 1,5-hexadecadiyne (7% yield, b.p. 86–90°/0.05 mm Hg) and 1, pentadecadiyne (13% yield, b.p. 63–65°/0.02 mm Hg) intermediates were prepared in a manner similar to 1,5-heptadecadiyne by appropriate chain-extension methods.

3,7-Octadecadiyn-1-ol. 1,5-Hexadecadiyne (15.5 g, 0.07 mole) in THF (50 ml) was added to a suspension of lithium amide (prepared from 7 g of lithium, 1 g of iron(III) nitrate and 2 l of liquid ammonia) and stirred for 1 h. Excess ethylene oxide (8 g, 2.0 moles) was added to the suspension and the mixture was stirred for 48 h under reflux. The crude octadecadiynol was purified by silica column chromatography (4. g, 18% yield).

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* The value in parentheses is the same for all isomers.

4,8-Octadecadiyn-1-ol. 1,5-Pentadecadiyne (26.8 g, 0.13 mole) in THF (50 ml) was added to a suspension of lithium amide (prepared from 7 g of lithium, 1 g of iron(III) nitrate and 2 l of ammonia) and stirred for 1.5 h. 3-Bromotetrahydropyranyl propanol (22 g, 0.098 mole) in THF (50 ml) was then added and the reaction mixture was stirred overnight. The ethereal extract was shaken with dilute sulphuric acid (0.2 *M*, 100 ml) and the pure octadecadiynol isolated by column chromatography (10 g, 29% yield).

Methyl 3,7- and 4,8-octadecadiynoates. Both octadecadiynoic acids were obtained by chromic acid oxidation. Chromic acid (prepared from 2.25 g of chromium trioxide, 1.7 ml of concentrated H_2SO_4 and diluted to 8 ml with water) was added to 3,7-octadecadiyn-1-ol (4.5 g, 0.017 mole) in acetone (50 ml) at 0–5°. The mixture was then stirred for 30 min at room temperature, diluted with water and extracted with diethyl ether. The acidic fraction was isolated and on re-crystallisation gave pure 3,7-octadecadiynoic acid (1.4 g, 33% yield, m.p. 93–94°; anal.: C = 78.20%, H = 10.09%).

4,8-Octadecadiynoic acid (4.0 g, 38% yield, m.p. 95–95.5; anal.: C = 78.15%, H = 10.31%) was similarly obtained. Esterification of the acids gave pure methyl octadecadiynoates.

Methyl 5,9-octadecadiynoate ($\Delta^{5a,9a}$)

1,5-Tetradecadiyne. 1,5-Tetradecadiyne (27.4 g, 38% yield, b.p. 68–70°/0.05 mm Hg, lit. 124–128°/13 mm Hg[16]) was prepared in a similar manner as described for 1,5-heptadecadiyne by appropriate chain-extension procedure.

1-Chloro-4,8-heptadecadiyne. 1,5-Tetradecadiyne (27.4 g, 0.14 mole) in THF (50 ml) was added to a suspension of lithium amide (prepared from 1.4 g of lithium, 0.5 g of iron(III) nitrate and 2 l of ammonia) and stirred for 1 h. 1-Bromo-3-chloropropane (39 g, 0.2 mole) in THF (40 ml) was then added and the mixture stirred overnight. The ethereal extract was distilled until the temperature reached 80°/0.05 mm Hg. The crude chloroheptadecadiyne was percolated (*n*-hexane as eluent) through a silica gel column (30 g) to give a light yellow coloured 85% pure 1-chloro-4,8-heptadecadiyne (35 g, 94% yield).

Methyl 5,9-octadecadiynoate. 1-Chloro-4,8-heptadecadiyne (35 g, 0.13 mole) was heated at 120° in dimethyl sulphoxide (100 ml) in the presence of sodium cyanide (9 g, 0.18 mole) for 3 h. The isolated cyano derivative was left in 25% (w/w) of hydrogen chloride–methanol (400 ml) for 20 h. The reaction mixture was poured into ice (500 g) and extracted with light petroleum (b.p. 60–80°). The crude ester was subsequently percolated through a silica gel (20 g, *n*-hexane as eluent) column and then refluxed with sodium hydroxide (12 g, 0.3 mole) in methanol (600 ml) for 1 h. The acidic fraction was isolated and re-crystallisation from *n*-hexane gave pure octadecadiynoic acid (9.2 g, 31%, m.p. 51–51.5°, anal.: C = 78.48%, H = 10.27%). The acid was converted to its methyl ester using boron trifluoride–methanol complex.

Methyl 6,10-, 7,11-, 8,12-, 10,14-, 11,15- and 12,16-octadecadiynoates ($\Delta^{6a,10a}$, $\Delta^{7a,11a}$, $\Delta^{8a,12a}$, $\Delta^{10a,14a}$, $\Delta^{11a,15a}$, $\Delta^{12a,16a}$)

The corresponding 1,5-alkadiyne (see Table XII) and 1-chloroheptadecadiyne intermediates were prepared in a similar manner to 5,9-octadecadiynoate by appropriate chain-extension methods. The C_{17} chlorides were converted into the cyano derivative and then treated with hydrogen chloride–methanol. The resulting methyl

ABLE XII

HYSICAL PROPERTIES OF 1,5-ALKADIYNES, $CH_3(CH_2)_nC\equiv C(CH_2)_2C\equiv CH$

B.p. (°C)/mm Hg	*Lit. b.p. (°C)/mm Hg*	*Ref.*	*% yield*
57–59/0.1	118–124/16	12	33
81–83/4.0	100/20	13	30
69–72/4.0	94–96/16	12	24
	76–78/10	17	
75–76/35	62/19	18	30
75–77/52	50–55/22	14	37
	67–68/50	19	
125–135/760	67–68/100	19	20

ester was then hydrolysed to the acid and the latter purified by re-crystallisation from *n*-hexane.

Methyl 9,13- and 13,17-octadecadiynoates ($\Delta^{9a,13a}$, $\Delta^{13a,17a}$)

1,5-Decadiyne (43% yield, b.p. 76–82°/15 mm Hg, 90% pure) and 16-chloro-5.9-hexadecadiyne (83% yield) were obtained by appropriate chain-extension methods from 1,5-hexadiyne.

Methyl 9,13-octadecadiynoate. 16-Chloro-5,9-hexadecadiyne (38.1 g, 0.15 mole) was refluxed in the presence of sodium iodide (15 g, 0.1 mole) and sodium diethyl malonate (prepared from 2.27 g of sodium, 16 g of diethyl malonate and anhydrous ethanol 150 ml) for 16 h. The malonic ester derivative was isolated and hydrolysed with potassium hydroxide (27 g, 0.75 mole) in ethanol (275 ml) to the corresponding diacid (29.9 g). The crude diacid derivative (12.5 g) was refluxed with sulphuric acid (0.25 *M*, 250 ml) in dimethyl sulphoxide (250 ml) for 24 h. The hydrolysis product was isolated and esterified. Methyl 9,13-octadecadiynoate was isolated by silica gel column chromatography (5 g, 34% yield). Pure 9,13-octadecadienoic acid was ob-

TABLE XIII

MELTING POINTS OF ALL DIMETHYLENE-INTERRUPTED OCTADECADIYNOIC ACIDS

Isomer	*M.p.** *(°C)*	*M.p. lit. (°C)*	*Ref.*	*Microanalysis***	
				C (%)	*H (%)*
$\Delta^{2a,6a}$	64–64.5			77.95	10.24
$\Delta^{3a,7a}$	93–94			78.20	10.09
$\Delta^{4a,8a}$	95–95.5			78.15	10.31
$\Delta^{5a,9a}$	51–51.5			78.48	10.27
$\Delta^{6a,10a}$	57–57.5	56.5–57	20	78.50	10.40
$\Delta^{7a,11a}$	48–48.5	48–48.5	13	78.39	10.45
$\Delta^{8a,12a}$	53–53.5	52.5–53	20	78.42	10.42
$\Delta^{9a,13a}$	53.5–54.5			78.32	10.08
$\Delta^{10a,14a}$	61–62			78.43	10.42
$\Delta^{11a,15a}$	75–76	76–77.1	14	77.85	10.10
$\Delta^{12a,16a}$	78–79			78.32	10.33
$\Delta^{13a,17a}$	62–62.5			77.86	10.76

* Uncorrected.

** Calculated; C = 78.21%, H = 10.21%.

tained by re-crystallisation from *n*-hexane (m.p. 53.5–54.5°; anal.: $C = 78.32\%$ $H = 10.08\%$).

Methyl 13,17-octadecadiynoate. 16-Chloro-1,5-hexadecadiyne (46% yield) was prepared by appropriate chain extension from 1,5-hexadiyne. Extension of the chloro-hexadecadiyne by malonic ester synthesis gave pure 13,17-octadecadiynoic acid (m.p. 62–62.5°, 6% yield; anal.: $C = 77.86\%$, $H = 10.76\%$).

Melting points of all octadecadiynoic acids are summarized in Table XIII.

Purity check

Small portions (10 mg–3 g) of the methyl octadecadiynoate isomers were partially hydrogenated over Lindlar catalyst[21] and cleavage oxidation[22] of the methy *cis,cis*-octadecadienoates (25 mg) gave the corresponding mono- and/or dicarboxylic acid moities only.

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