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FATTY ACIDS

I. SYNTHESIS OF ALL THE METHYL UNDECYNOATES AND THE METHYL *cis*-UNDECENOATES AND A STUDY OF THEIR GAS–LIQUID CHROMATOGRAPHIC PROPERTIES

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SUMMARY

All the methyl *n*-undecynoates and *cis*-undecenoates have been synthesised and the gas–liquid chromatographic behaviour of both series of isomers was studied on polar (DEGS and Silar 10C) and non-polar (Apiezon L) stationary phases. The possibility of identification and separation of these isomers is discussed.

INTRODUCTION

A systematic study of the unsaturated C_{18} fatty acids was initiated by Gunstone and Ismail[1]. This study revealed some very unusual and characteristic properties of positional isomers of unsaturated fatty esters on gas–liquid (GLC) and thin-layer chromatography (TLC) and proton magnetic resonance spectroscopy[2–4]. Biochemical studies of these isomers have also been conducted and have produced some very interesting results[5–7].

Scholfield and Dutton[8] and Ackman and Hooper[9] made extensive use of GLC data to predict the equivalent chain length and to identify poly-unsaturated long-chain methyl esters, mainly by applying the additivity of retention times for ethylenic functions in aliphatic fatty acids.

A new polar stationary phase, Silar 10C (a dicyanopropyl silicone), is said[10] to give high separation factors for fatty acid methyl esters by their degree of unsaturation. We decided to synthesise the acetylenic and *cis*-ethylenic C_{11} acids and to study their behaviour on this new polar phase.

All undecynoic acids were readily prepared by well established methods[1–4]. Difficulty was encountered in the oxidation of undec-3-ynol into undec-3-ynoic acid, as this preparation resulted in a mixture of the Δ^{3a} and Δ^{4a} isomers.

GAS–LIQUID CHROMATOGRAPHY

The equivalent chain lengths (ECL) of all acetylenic and *cis*-ethylenic C_{11}

TABLE I

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL AND MIXTURES OF UNSATURATED C_{11} METHYL ESTERS ON APL

Isomer	*ECL*	*A1**	*A2**	*A3**	*A4**	*A5***	*A6****	*A7****	*A8****	*A9*§	*Isomer*	*ECL*	*B1**	*B2***	*B3***	*B4***	*B5***	*B6****
Δ^{2a}	11,61	—	—		—	—	—	—	—	—	Δ^{2c}	10,98	—	10,93	—	—	—	—
Δ^{3a}	11,17		—	—	—	11,17	—	11,17	—	—	Δ^{3c}	10,87	—	—	—	—	—	—
Δ^{4a}	11,02		—	—	—	—		—	—	—	Δ^{4c}	10,76	—	—	—	—	—	—
Δ^{5a}	11,02		—	11,05	—	—	—	11,07	11,08	—	Δ^{5c}	10,75	10,73	10,75	—	—	—	10,81
Δ^{6a}	11,05		—	—	—		—	—	—	—	Δ^{6c}	10,79	—	—	—	—	10,80	—
Δ^{7a}	11,07	—	11,10	—	—	—	—		—	11,15	Δ^{7c}	10,83	—	—	—	10,85	—	—
Δ^{8a}	11,14	—		—	11,13		11,17	—	11,18	11,15	Δ^{8c}	10,89	—	—	10,89	—	—	—
Δ^{9a}	11,52	11,53	11,52	11,52	11,50	11,50	—	—	—	—	Δ^{9c}	11,10	11,08	—	11,07	11,15	11,09	—
Δ^{10a}	11,00	11,00	—	—	—	—	11,05	—	—	—	Δ^{10c}	10,89	—	—	—	—	—	10,91

* Base-line separation.
** Twin peak separation.
*** Shoulder separation.
§ No separation.

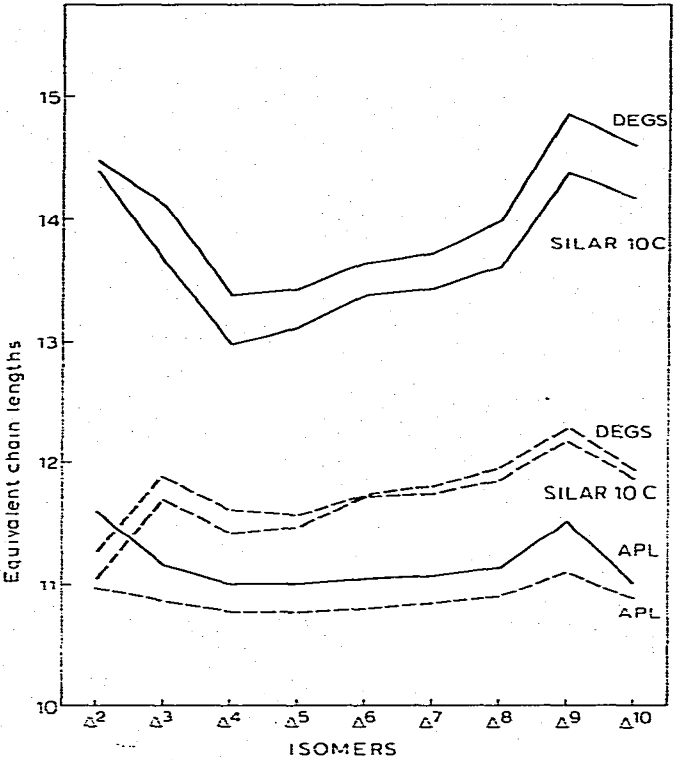

Fig. 1. Equivalent chain lengths of acetylenic (———) and *cis*-ethylenic (- - - -) C_{11} esters on different stationary phases.

esters on Apiezon L (APL), diethylene glycol succinate polyester (DEGS) and Silar 10C are compared in Fig. 1 and actual values recorded in Tables I–III.

Methyl undecynoates

These isomers gave ECL values ranging from 11.00 to 11.17 on the non-polar APL column, except for Δ^{2a} (11.52) and Δ^{9a} (11.61), for which the values were significantly higher. Three isomers, namely Δ^{4a}, Δ^{5a} and Δ^{10a}, had retention times almost identical with that of the saturated C_{11} ester.

On polar stationary phases, the ECL values were found to be in the range 13.38–14.87 on DEGS and 12.99–14.39 on Silar 10C. On both phases the Δ^{4a} isomer gave the lowest and the Δ^{9a} isomer the highest ECL value. Values were also markedly increased when the triple bond was close to the carbomethoxy end, as in the Δ^{2a} and Δ^{3a} isomers.

When the chromatographic behaviour of mixtures of these isomers was examined on polar and non-polar stationary phases (Tables I–III), it was possible to describe the degree of separation as base-line, twin peak or shoulder. The results are summarised in Table IV.

TABLE II

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL AND MIXTURES OF UNSATURATED C_{11} METHYL ESTERS ON DEGS

Isomer	*ECL*	*E1**	*E2**	*E3***	*E4***	*E5****	*Isomer*	*ECL*	*F1**	*F2***	*F3****	*F4****
Δ^{2a}	14,49	—	14,41	—	14,41		Δ^{2c}	11,28		11,25	—	
Δ^{3a}	14,12	14,11	—		14,11		Δ^{3c}	11,88		11,84	11,86	
Δ^{4a}	13,38	—				13,39	Δ^{4c}	11,62			11,59	
Δ^{5a}	13,43	13,41					Δ^{5c}	11,58	11,60			11,63
Δ^{6a}	13,64			13,61		13,62	Δ^{6c}	11,73				
Δ^{7a}	13,72	—	13,71				Δ^{7c}	11,81				11,83
Δ^{8a}	13,99	—		13,98			Δ^{8c}	11,95				
Δ^{9a}	14,87	—					Δ^{9c}	12,29	12,30			
Δ^{10a}	14,60	—					Δ^{10c}	11,93				

* Base-line separation.
** Twin peak separation.
*** Shoulder separation.

TABLE III

EQUIVALENT CHAIN LENGTHS OF INDIVIDUAL AND MIXTURES OF UNSATURATED C_{11} METHYL ESTERS ON SILAR 10C

Isomer	*ECL*	*C1**	*C2**	*C3***	*C4***	*C5****	*Isomer*	*ECL*	*D1**	*D2**	*D3***	*D4***	*D5***	*D6***	*D7***	*D8***
Δ^{2a}	14,39						Δ^{2c}	11,03					11,03			
Δ^{3a}	13,65						Δ^{3c}	11,70								
Δ^{4a}	12,99						Δ^{4c}	11,44			11,45					11,42
Δ^{5a}	13,12		13,10		13,13		Δ^{5c}	11,48	11,48			11,45	11,48		11,48	
Δ^{6a}	13,38			13,35	13,40		Δ^{6c}	11,73		11,70		11,71			11,70	11,70
Δ^{7a}	13,45		13,48			13,48	Δ^{7c}	11,77			11,76					
Δ^{8a}	13,61	13,67		13,65		13,61	Δ^{8c}	11,86								
Δ^{9a}	14,38						Δ^{9c}	12,19	12,17	12,21				12,17		
Δ^{10a}	14,18	14,19					Δ^{10c}	11,88						11,86	—	—

* Base-line separation.
** Twin peak separation.
*** Shoulder separation.

TABLE IV

SEPARATION OF MIXTURES OF METHYL UNDECYNOATES

Degree of separation	*Difference in ECL values*		
	APL	*DEGS*	*Silar 10C*
Base-line	≥0.38 (A1–4)*	≥0.69 (E1–2)	≥0.33 (C1–2)
Twin peak	0.35 (A5)	≥0.35 (E3–4)	≥0.23 (C3–4)
Shoulder	≥0.12 (A6–8)	0.26 (E5)	0.16 (C5)
No separation	0.07 (A9)	—	—

* Samples.

Methyl cis-undecenoates

These ethylenic isomers gave ECL values which were smaller than 11.00 on APL, with the exception of Δ^{9c} (11.10). There was little difference in the retention times among these isomers, although it was possible to recognize that Δ^{4c} had the lowest ECL value in the series. On polar phases, the ECL values ranged from 11.28 to 12.29 on DEGS and 11.03 to 12.19 on Silar 10C. Both sets of ECL values gave an almost parallel plot except in the case where the double bond was located between C_6 and C_7, as Δ^{6c} isomer had identical ECL values on DEGS and Silar 10C. Relatively high values were obtained for Δ^{3c} and Δ^{9c}, while Δ^{4c} again gave the lowest ECL value.

The behaviour of mixtures of these isomers on polar and non-polar stationary phases is given in Table V.

TABLE V

SEPARATION OF MIXTURES OF METHYL *cis*-UNDECENOATES

Degree of separation	*Difference in ECL values*		
	APL	*DEGS*	*Silar 10C*
Base-line	0.45 (B1)*	0.71 (F1)	≥0.46 (D1–2)
Twin peak	≥0.21 (B2–5)	0.60 (F2)	≥0.25 (D3–8)
Shoulder	0.14 (B6)	≥0.23 (F3–4)	—

* Samples.

SYNTHESIS AND PROPERTIES

Methyl undec-2-ynoate (Δ^{2a})

1-Decyne (19 g, 0.138 mole) in anhydrous diethyl ether (50 ml) was added to ethyl magnesium bromide (prepared from 4.8 g of magnesium, 22 g of ethyl bromide and 200 ml of diethyl ether) at 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 sulphuric acid (2 *M*, 100 ml) was added and the acidic fraction isolated in the usual way. Distillation gave undec-2-ynoic acid (9.4 g, 37.5% yield, b.p. 116–120°/0.2 mm; ref. 11: 103°/0.3 mm).

Undec-2-ynoic acid (5 g) was refluxed with 14% boron trifluoride–methanol complex (10 ml) and anhydrous methanol (50 ml) for 20 min. The solution was diluted with water and extracted with light petroleum (b.p. 60–80°). The crude methyl undecynoate (5.5 g) was purified by preparative silver ion TLC. Cleavage oxidation[12] of the methyl *cis*-undec-2-enoate gave nonanoic acid as the only monobasic acid.

Methyl undec-3-ynoate (Δ^{3a})

Undec-3-ynol. 1-Nonyne (25 g, 0.20 mole) in anhydrous diethyl ether (100 ml) was added to ethyl magnesium bromide (prepared from 9.6 g of magnesium, 44 g of ethyl bromide and 400 ml of diethyl ether) and refluxed for 1 h. The suspension was cooled and gaseous ethylene oxide (30 g) was flushed through the reaction vessel over a 1-h period and the reaction mixture left overnight, during which time it formed a semi-solid mixture. The ethereal mixture was then heated to reflux and the ether gradually replaced by benzene (250 ml) until the distillation temperature reached 60°. Cold dilute sulphuric acid (2 *M*, 500 ml) was added and the mixture extracted with diethyl ether. Distillation gave undec-3-ynol (19.5 g, 58% yield, b.p. 54–62°/0.25 mm).

Undec-3-ynoic acid. Chromic acid (15 ml) (prepared from 13.4 g of chromium trioxide and 10 ml of concentrated sulphuric acid, diluted to 50 ml with water) was added to a cooled solution of undec-3-ynol (4 g, 0.024 mole) in acetone (100 ml) and stirred for 30 min. The acidic fraction was isolated in the usual way, esterified and purified by preparative TLC (1.1 g, 23.4% yield). However, GLC analysis on 20% DEGS showed that this was contaminated with 23% of methyl undec-4-ynoate.

Oxidation of the semi-hydrogenated product gave octanoic and heptanoic acids in a ratio of about 4:1 and some propanedioic and butanedioic acids. Final purification of methyl undec-3-ynoate was achieved by preparative GLC on a 20% DEGS column.

Methyl undec-4-ynoate (Δ^{4a})

Undec-4-ynol. Pent-4-ynol (25.2 g, 0.30 mole) in anhydrous tetrahydrofuran (THF) (100 ml) was added to a suspension of lithium amide (prepared from 5.6 g of lithium, 1 g of iron(III) nitrate and 2 l of ammonia solution) and stirred for 1½ h. 1-Bromohexane (66 g, 0.40 mole) in THF (100 ml) was added and the mixture stirred overnight. Distillation of the ethereal extract gave undec-4-ynol (32.4 g, 64% yield, b.p. 70–84°/0.01 mm: ref. 13: 135–140°/20 mm).

Undec-4-ynoic acid. Undec-4-ynol (4.8 g) gave crude undec-4-ynoic acid (3 g, 51% yield) by chromic acid oxidation as described in the preparation of undec-3-ynoic acid. The crude acid was esterified and purification by silica column chromatography gave pure methyl undec-4-ynoate (2.8 g, 47.6% yield).

Cleavage oxidation of the *cis*-undec-4-enoic acid gave heptanoic and butanedioic acids only.

Methyl undec-5-ynoate (Δ^{5a})

1-Chlorodec-4-yne. 1-Bromopentane (75 g, 0.496 mole) in THF (125 ml) was added to a suspension of lithium acetylide (prepared from 7.0 g of lithium, 2 l of ammonia solution and acetylene) prepared by the titration procedure[14]. Lithium amide (prepared from 7 g of lithium, 2 g of iron(III) nitrate and 1.5 l of ammonia solution) was carefully added to the reaction mixture and stirred for a further 1 h. 1-Bromo-3-chloropropane (96.0 g, 0.61 mole) in THF (150 ml) was added and the reaction mixture was stirred overnight. The ethereal extract could not be distilled beyond

52°/12 mm owing to excessive foaming. However, GLC analysis indicated the presence of 80% of 1-chlorodec-4-yne (57.8 g) in the product. No further purification of this product was attempted, but the reaction was carried through to the next stage instead.

1-Cyanodec-4-yne. Impure 1-chlorodec-4-yne (55.8 g) was heated at 120–130° for 3 h with sodium cyanide (19.6 g, 0.40 mole) in dimethyl sulphoxide (125 ml). The mixture was cooled, diluted with water (500 ml) and extracted with light petroleum (b.p. 60–80°). Removal of the solvent under reduced pressure gave a crude nitrile (44.8 g).

Methyl undec-5-ynoate. The crude nitrile (44.8 g) was left in a solution of 25% (w/w) hydrogen chloride in methanol (600 ml) for 72 h. The methanolic solution was diluted with ice–water (1.5 l) and extracted with light petroleum (b.p. 60–80°). Distillation through a 50-cm Vigreux column gave methyl undec-5-ynoate (45.0 g, b.p. 97–99°/1.2 mm; ref. 15: 118–122°/0.15 mm for acid). However, this sample contained 24.5% of a chloroalkene, which was removed by silver ion TLC.

Cleavage oxidation of the *cis*-undec-5-enoic acid gave only hexanoic and pentanedioic acids.

Methyl undec-6-, -7- and -8-ynoates (Δ^{6a}, Δ^{7a}, Δ^{8a})

The corresponding 1-chlorodecyne intermediates were prepared in a similar manner to undec-5-ynoate by appropriate chain extension methods. These chlorides were converted into the cyano derivatives and then treated with hydrogen chloride–methanol. All methyl esters obtained by this procedure were contaminated with small amounts of chloroalkenes. However, these isomers were initially purified by fractional distillation and then by silver ion TLC. Yields are given in Table VI.

TABLE VI

YIELDS AND BOILING POINTS OF 1-CHLORODECYNES AND METHYL UNDECYNOATES

Compound	*Yield (%)*	*B.p.*
1-Chlorodec-5-yne	46.5	119–120°/22 mm (ref. 16: 78–80° 2 mm)
1-Chlorodec-6-yne	23.0	124–128°/25 mm
1-Chlorodec-7-yne	55.0	120–122°/20 mm
Methyl undec-6-ynoate		97.0–97.5°/0.7 mm
Methyl undec-7-ynoate		98.0–99.0°/0.8 mm
Methyl undec-8-ynoate		104–105°/1.0 mm

Cleavage oxidation of the *cis*-undecenoic acids gave only the corresponding monobasic and dibasic acids.

Methyl undec-9-ynoate (Δ^{9a})

Undec-9-ynoic acid. Bromine (41.6 g, 0.26 mole) was carefully added to undec-10-enoic acid (47 g, 0.255 mole) in carbon tetrachloride (200 ml). The solvent was removed under reduced pressure and the dibromo-acid was then added to a concentrated solution of potassium hydroxide (135 g in 40 ml of water) contained in an 800-ml beaker. The mixture was slowly heated to 160° and then placed in a pre-heated oven at 190° for 1 h. The reaction mixture was acidified, extracted with diethyl ether and distillation gave crude undec-9-ynoic acid (32 g, 68.9% yield, b.p. 120–130°/0.05 mm). The acid was recrystallised from *n*-hexane to give pure undec-9-ynoic acid (21 g, 45.2% yield, m.p. 58°: ref. 17: m.p. 58–59°, 61°).

Undec-9-ynoic acid (9 g) was esterified and purified by preparative silver ion TLC. Oxidation cleavage of the *cis*-undecenoic acid gave only nonanedioic acid.

Methyl undec-10-ynoate (Δ^{10a})

Undec-10-ynoic acid. Bromine (30.4 g, 0.19 mole) was added to undec-10-enoic acid (30 g, 0.16 mole) in carbon tetrachloride (400 ml). The solvent was removed under reduced pressure and the crude dibromoundecanoic acid in anhydrous diethyl ether (150 ml) was then added to a suspension of sodamide in liquid ammonia (prepared from 13.8 g of sodium, 2 g of iron(III) nitrate and 2 l of ammonia) and stirred overnight. Water (400 ml) was added and the aqueous solution acidified with dilute hydrochloric acid (5 *M*, 500 ml) and extracted with diethyl ether. Distillation gave undec-10-ynoic acid (22 g, 74.7% yield, b.p. 116–120°/0.06 mm, m.p. 43°; ref. 18: b.p. 124–130°/3 mm, m.p. 42.5–43°).

Esterification of undec-10-ynoic acid (2 g) with boron trifluoride–methanol complex (3 ml) and anhydrous methanol (20 ml) gave pure methyl undec-10-ynoate (1.8 g, 85% yield). Oxidation of the *cis*-undec-10-enoic acid gave only decanedioic acid.

Semi-hydrogenation

A mixture of methyl undecynoate (0.5 g), Lindlar catalyst[19] (0.1 g), quinoline (0.2 g) and ethyl acetate (25 ml) was shaken in an atmosphere of hydrogen. The rate of hydrogen absorption decreased markedly after the theoretical amount (57.1 ml) had been absorbed (3–5 min). The mixture was filtered and the filtrate washed with dilute hydrochloric acid and with water and dried over anhydrous sodium sulphate. GLC analysis indicated 98–99% conversion into the methyl *cis*-undecenoate. Infrared analysis gave no absorption peak at 965 cm^{-1}, thus indicating the absence of *trans*-isomers.

Gas–liquid chromatography

GLC results were obtained under the conditions given in Table VII on a Pye 104 chromatograph equipped with a flame ionization detector.

TABLE VII

CONDITIONS FOR GLC

Stationary phase	*Column length (m)*	*Temperature (°C)*	*Carrier gas and flow-rate (ml/min)*
5% APL	2	175	N_2, 40
20% DEGS	2	190	N_2, 50
10% Silar 10C	2	125	N_2, 45

ECL values were calculated from distances between the solvent front and the peak of the other eluted components. Saturated methyl esters were used as internal standards: C_8, C_{10} and C_{12} (on APL) and C_{10}, C_{12} and C_{14} (on DEGS and Silar 10C) for the acetylenic esters, and C_8, C_{10} and C_{12} for the *cis*-undecenoates.

CONCLUSION

The polar phase Silar 10C was more efficient than DEGS in the separation of isomeric unsaturated methyl esters. On all phases, the equivalent chain length was very reproducible and possible identification of the isomer could be achieved by studying the ECL values on the three phases.

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