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FATTY ACIDS, PART XVI*: THE SYNTHESIS OF ALL ISOMERIC C_{18} FURAN-CONTAINING FATTY ACIDS

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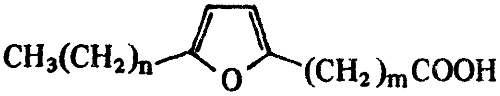
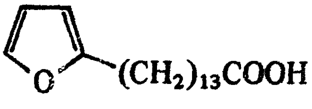
The synthesis of all isomeric C_{18} furan-containing fatty acids from furan, furfural or methyl octadecadiynoate is described.

I. Introduction

Morris et al. [1] reported the first isolation of 9,12-epoxyoctadeca-9,11-dienoic acid from the seed oil of *Exocarpus cupressiformis* Labil. Recently Glass [2,3] and Gunstone et al. [4] described the occurrence of several similar long chain furan-containing fatty acids in fish oils. The precise role of such compounds in nature is still unknown, but mounting interest in the chemistry and biochemistry of these rare lipid molecules prompted the need for a systematic study of the physical, chemical and biological properties of complete series of isomeric furan acids. We chose to study the C_{18} furan acid isomers (1–14) for two main reasons: (a) one of the 14 possible isomers, viz. 9,12-epoxyoctadeca-9,11-dienoic acid (8), in this series is naturally occurring and (b) C_{18} fatty acids have been most extensively studied in the past.



	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)
m =	0	1	2	3	4	5	6	7	8	9	10	11	12
n =	12	11	10	9	8	7	6	5	4	3	2	1	0



(14)

The first total synthesis of a C_{18} furan acid, (8), was reported by Elix and Sargent [5], while we described the preparation of (7) from synthetic 7,11-octadecadienoic acid [6]. Partial synthesis of (8) from natural linoleic acid [7] and from ricinoleic acid [8,9] were also reported.

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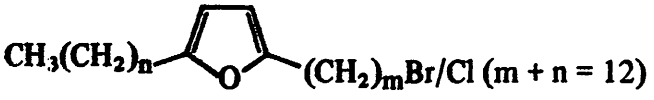
* Fatty Acids, Part XV, J. Chromatog., 136 (1977) 178

II. Results and Discussion

Furan and furfural were readily accessible starting material for this work. Alkylation of furan at its relatively more reactive 2- or 5-position of the ring was achieved by initial treatment of furan with a molar equivalent of butyl lithium to form the 2-lithio furan derivative, which was condensed with 1-bromoalkane of the required chain length [10]. The resulting 2-alkylfuran was similarly alkylated at the 5-position of the ring using ω-dibromoalkanes [11] or ω-iodochloroalkanes to give the corresponding furan-containing C_{17} halide (15). Conversion of the latter to the cyano derivative followed by alkali hydrolysis gave the required C_{18} furan acid.

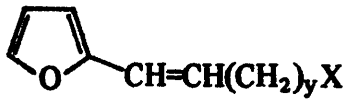


(15)

It is noteworthy to point out that the sodium salts of C_{18} furan acids are only *sparingly* soluble in water and form a distinct layer at the interface of water and diethyl ether, unless a large quantity of water is added. Potassium salts of these acids are *very soluble* in diethyl ether, possessing a property contrary to that exhibited by the potassium salts of long chain fatty acids.

Compounds (5, 6, 7, 8, 10 and 11) were prepared by this method with an average overall yield of 35% based on the amount of furan used.

Furfural has an aldehyde group at the 2-position of the furan ring and thus presents a ready site for chain extension via the Wittig reaction. Coupling of the triphenylphosphonium salt of the required 1-bromoalkane or methyl ω-bromoalkanoate to furfural in the presence of a strong base (NaH or NaOEt) in dimethylsulphoxide (DMSO) gives mainly the *cis*-alkenylated furan derivative (16).



(16)

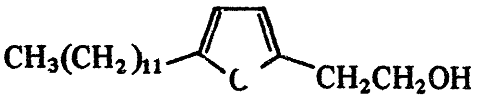
(X = CH_3 or $COOCH_3$)
(y = number of methylene groups)

Catalytic hydrogenation of (16) over Lindlar catalyst [12] at atmospheric pressure or palladium on charcoal at approx. 40 lb/inch^3 gave the corresponding 2-alkylfuran or methyl ω-(2′-furyl)-alkanoate. The use of Lindlar catalyst was preferred over palladium on charcoal as the latter tends to cause over-hydrogenation at high pressure resulting in the production of undesired tetrahydrofuryl derivaties.

The Vilsmeier formylation reaction (phosphorus oxychloride in dimethylformamide (DMF)) of the 2-alkylfuran or methyl ω-(2′-furfuryl)-alkanoate provided an aldehyde function at the 5-position of the furan ring [13,14]. Similar chain extension by Wittig reaction, followed by hydrogenation of the resulting intermediate, furnished the required C_{18} furan ester. Compounds (3, 4, 9, 12, 13 and 14) were produced by this method with an average overall yield of 16% based on the amount of furfural used.

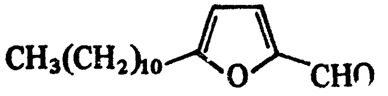
The hydration procedure of synthetic dimethylene interrupted methyl octadecadiynoates, followed by the acid catalysed cyclodehydration of the intermediate methyl 1,4-dioxostearates to the C_{18} furan esters was described in an earlier publication [6]. Compound (**2**) was prepared by this method. The overall yield for this reaction was 4% based on the amount of methyl octadecadiynoate used.

The three general methods presented above did not provide every isomer in the series. For compound (**1**) the insertion of the carboxyl group was achieved by carbonation of the 5-lithio-derivative of 2-tridecylfuran [10]. Our attempt to synthesise (**2**) from its corresponding 1-hydroxy derivative (**17**) failed, as the latter was readily oxidised with rupture of the furan ring.



(17)

In the production of (**3**), the intermediate (**18**) was chain extended by 2 carbon atoms by the method described by Rajagopalan and Raman [15] using malonic acid in the presence of an organic base.



(18)

From the synthesis of (**13**), 2-methylfuran was prepared from furfural by the Huang-Minlon reduction [16]. The routes of all the C_{18} furan acids are summarised in schemes 1 and 2.

III. Experimental

Petroleum refers to light petroleum of b.p. 60–80°C. ^1H-Nmr spectra were measured on a Hitachi Perkin Elmer 20A spectrometer at 60 MHz, using carbon tetrachloride as solvent with tetramethylsilane as internal standard. Infrared spectra were recorded on a Perkin-Elmer 577 spectrophotometer. Mass spectra were recorded on a Hitachi RMS-4 mass spectrometer at 70 eV with a source pressure at 10^{-6} Torr and an inlet temperature of 150–180°C. Melting points (uncorrected) were recorded on a Reichert Thermovart apparatus. Microanalyses were performed by the Australian Microanalytical Service, Division of Applied Chemistry, CSIRO, Melbourne, Australia.

The microanalyses, melting points and mass spectral data of the isomers are summarised in tables 1 and 2.

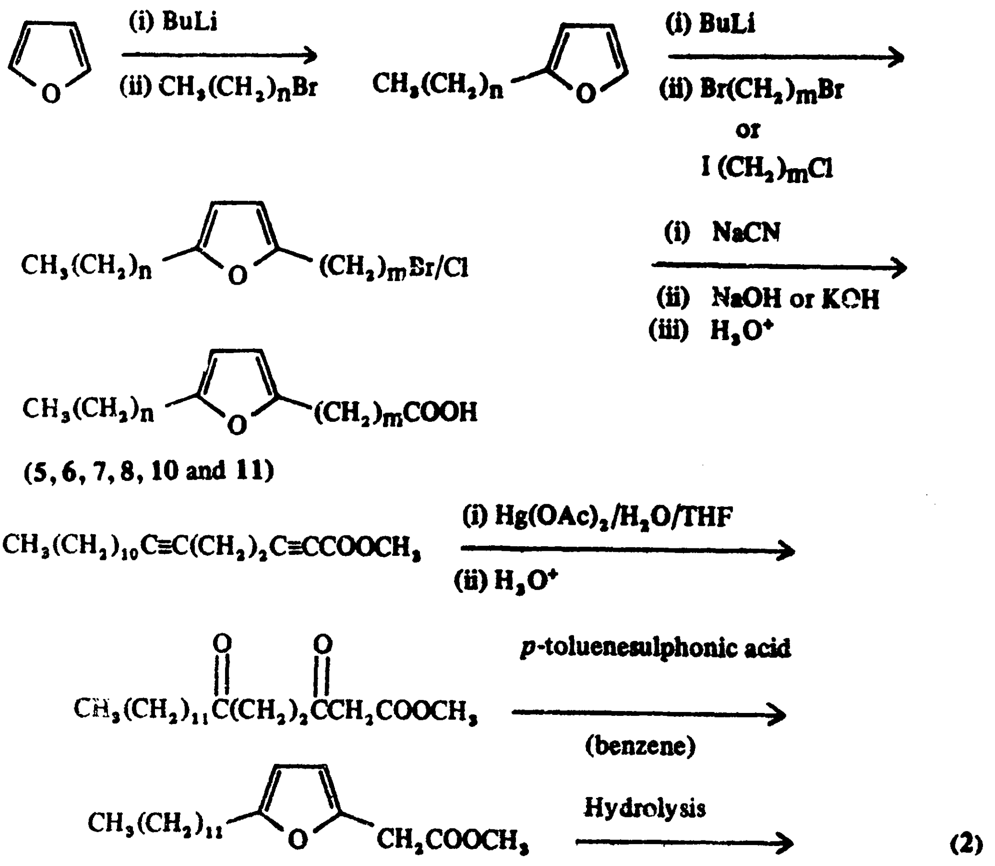
A. 2,5-Epoxyoctadeca-2,4-dienoic acid (1)

1. 2-Tridec-1'-enylfuran

A mixture of 1-bromododecane (43.7 g, 0.175 mol), triphenylphosphine (46 g,

Table 1

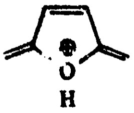
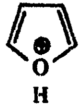
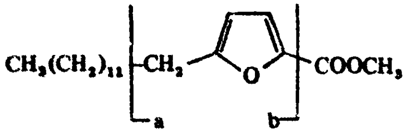
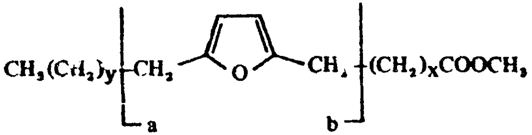
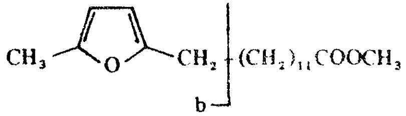
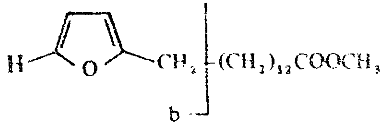
Isomer	Melting point °C (uncorrected)	$(C_{18}H_{30}O_3$: C=73.43, H=10.27% Found	
		C%	H%
(1)	80.0–81.0	73.15	10.22
(2)	53.0–54.0	70.43	10.05
(3)	53.5–54.5	73.45	10.28
(4)	36.0–36.5	73.49	10.52
(5)	47.0–48.0	73.20	10.24
(6)	44.0–45.0	73.23	9.94
(7)	35.0–36.0	72.99	10.42
(8)	20.0–21.0	72.98	10.12
(9)	31.0–31.5	73.21	10.24
(10)	42.5–43.5	73.08	10.44
(11)	42.5–43.5	73.01	10.16
(12)	45.5–46.0	72.88	10.43
(13)	62.0–63.0	73.79	10.40
(14)	59.5–60.0	73.49	10.06



Scheme 1

Table 2

Mass spectral analysis of all C_{18} furan ester isomers. Values quoted in brackets refer to intensity of fragment relative to the base peak = 100. Those marked with an asterisk may result from more than one fragment.

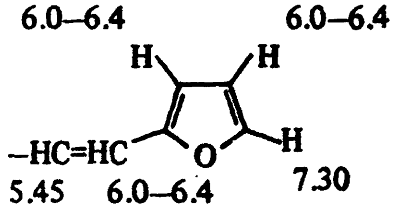
Isomer	Fragment	M 308	M-31 277	a	b	 c 107	 H d 95	 e 81	 H f 69
(1)		(100)	(7)	139(100)	249(62)	–	–	(46)	(13)
									
(2) [x = 0, y = 10]		(100)	–	153(36)	249(63)	(26)	(51)	(12)	(9)
(3) [x = 1, y = 9]		(100)	–	167(63)	235(61)	(24)	(36)	(11)	(12)
(4) [x = 2, y = 8]		(85)	(23)	181(64)	221(41)	(100)	(33)	(9)	(3)
(5) [x = 3, y = 7]		(100)	(27)	195(61)	207(100)	(46)	(56)	(23)	(5)
(6) [x = 4, y = 6]		(70)	(17)	209(35)	193(100)	(36)	(67)	(22)	(6)
(7) [x = 5, y = 5]		(69)	(14)	223(28)	179(100)	(20)	(38)	(11)	(6)
(8) [x = 6, y = 4]		(37)	(23)	237(20)	165(100)	(30)	(66)	(24)	(9)
(9) [x = 7, y = 3]		(47)	(10)	251(19)	151(100)	(19)	(47)	(17)	(18)
(10) [x = 8, y = 2]		(33)	(8)	265(12)	137(100)	(14)	(39)	(13)	(7)
(11) [x = 9, y = 1]		(100)	(20)	279(33)	123(44)	(17)	(22)	(16)	(8)
(12) [x = 10, y = 0]		(100)	(24)	293(9)	109(80)	–	(55)	(30)	(13)
(13)		(18)	(4)	–	95(100)	–	–	(7)	(13)
(14)		(34)	(16)	–	81(100)*	–	–	(100)*	(35)

0.175 mol) and benzene (100 ml) was refluxed for 2d. Evaporation of the solvent under reduced pressure gave the phosphonium salt as a viscous oil, which was washed with anhydrous diethyl ether and dried under vacuum.

Sodium hydride (60% dispersion in oil, 6.5 g, 0.162 mol) was washed with *n*-pentane, dried under vacuum and dissolved in DMSO (50 ml) at 75°C. The phosphonium salt was dissolved in warm DMSO (100 ml) and added to the sodium hydride solution under nitrogen. The reaction mixture was stirred for a further 1 hr, which resulted into a red coloured suspension.

Furfural (15.4 g, 0.16 mol) in DMSO (50 ml) was added to the reaction mixture and stirred for 12 hr. Water (250 ml) was then added and the reaction mixture extracted with diethyl ether. The solvent was replaced by petroleum and the white precipitate (viz. triphenylphosphonium oxide) was removed by filtration. Chromatographic separation of the crude product yielded pure 1-(2′-furyl)-tridec-1-ene (10.3 g, 26%). The infrared spectrum shows aromatic C–H and C=C stretchings at 3120 and 1583, 1492 cm^{-1} respectively.

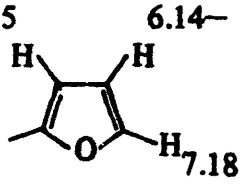
^{1}H-NMR δ (CCl_4):



2. 2-Tridecylfuran

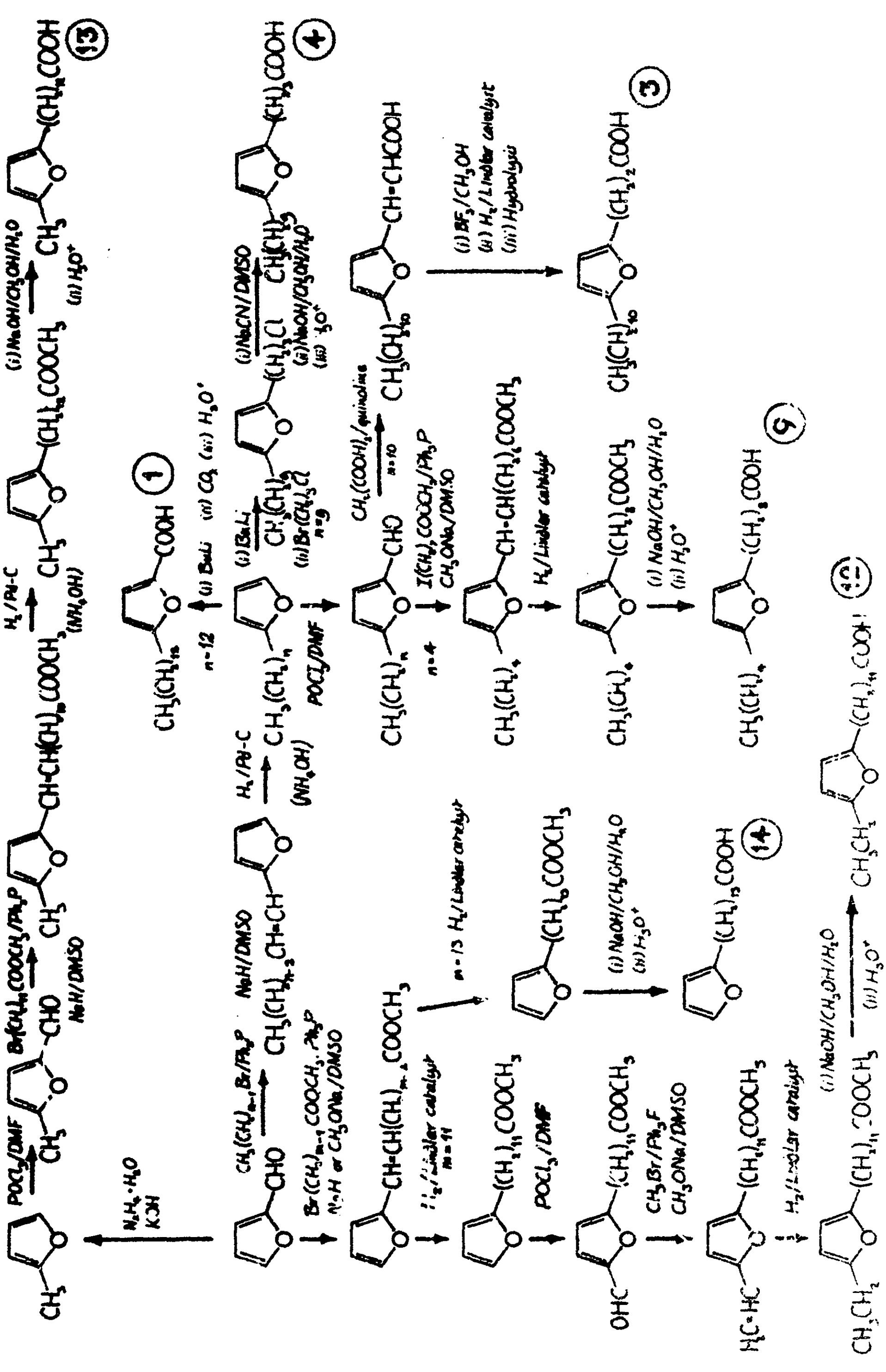
A mixture of 1-(2′-furyl)-tridec-1-ene (7.7 g, 0.031 mol), ethyl acetate (20 ml), ethanol (10 ml), ammonium hydroxide (2 M, 1 ml) and 10% palladium on charcoal (100 mg) was agitated under excess hydrogen at 38 lb/inch^2 pressure for 2 hr. Isolation of the reaction product gave 2-tridecylfuran (6.8 g, 88%, purity 99% by GLC).

^{1}H-NMR δ (CCl_4):



3. 2,5-Epoxyoctadeca-2,4-dienoic acid

n-Butyl lithium (15% in *n*-hexane, 4 ml) was added to a cooled (–20°C) solution of 2-tridecylfuran (1.56 g, 6.26 mmol) in anhydrous diethyl ether (50 ml) under nitrogen and the mixture stirred for 10 min. The reaction mixture was allowed to warm to room temperature and then refluxed for a further 4 hr. Solid carbon dioxide (10 g) was added to the cooled reaction mixture at –20°C and stirred for 12 hr. The ethereal extract furnished crude 2,5-epoxyoctadeca-2,4-dienoic acid, which on recrystallization from petroleum furnished pure 2,5-epoxyoctadeca-2,4-dienoic acid (1.0 g, 54%).


POCl$_3$/DMF
Br(CH$_2$)$_{14}$COOCH$_3$/Ph$_3$P
NaH/DMSO
H$_2$/Pd-C
(NH$_4$OH)
(i) NaOH/CH$_3$OH/H$_2$O
(ii) H$_3$O$^+$
13
N$_2$H$_4$·H$_2$O
KOH
n=12
(i) BuLi (ii) CO$_2$ (iii) H$_3$O$^+$
1
CH$_3$(CH$_2$)$_{n-1}$Br/Ph$_3$P
NaH/DMSO
(i) BuLi
(ii) Br(CH$_2$)$_3$Cl
n=9
(i) NaCN/DMSO
(ii) NaOH/CH$_3$OH/H$_2$O
(iii) H$_3$O$^+$
4
Br(CH$_2$)$_{m-1}$COOCH$_3$; Ph$_3$P
NaH or CH$_3$ONa/DMSO
POCl$_3$/DMF
n=4
I(CH$_2$)$_7$COOCH$_3$/Ph$_3$P
CH$_3$ONa/DMSO
CH$_2$(COOH)$_2$/quinoline
n=10
(i) BF$_3$/CH$_3$OH
(ii) H$_2$/Lindlar catalyst
(iii) Hydrolysis
3
H$_2$/Lindlar catalyst
m=11
m=13 H$_2$/Lindlar catalyst
H$_2$/Lindlar catalyst
(i) NaOH/CH$_3$OH/H$_2$O
(ii) H$_3$O$^+$
9
POCl$_3$/DMF
(i) NaOH/CH$_3$OH/H$_2$O
(ii) H$_3$O$^+$
14
CH$_3$Br/Ph$_3$P
CH$_3$ONa/DMSO
H$_2$/Lindlar catalyst
(i) NaOH/CH$_3$OH/H$_2$O
(ii) H$_3$O$^+$
12

Scheme 2.

B. 3,6-Epoxyoctadeca-3,5-dienoic acid (2)

A mixture of methyl 2,6-octadecadiynoate (1.0 g, 3.45 mmol), mercury (II) acetate (2.0 g, 6.28 mmol), THF (25 ml) and water (25 ml) was stirred at room temperature for 4 days. Dilute hydrochloric acid (2 M, 50 ml) was added and the resulting mixture stirred for a further 1 hr. The ethereal extract furnished crude methyl 3,6-dioxostearate (0.80 g).

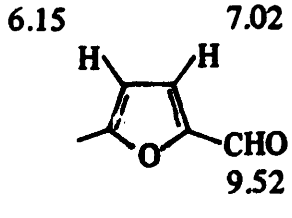
The crude methyl dioxostearate was refluxed for 12 hr with *p*-toluenesulphonic acid (0.3 g) in benzene (100 ml) using a Dean and Stark water separator. Silicic acid chromatographic separation of the product gave pure methyl 3,6-epoxyoctadeca-3,5-dienoate. Hydrolysis of the latter gave the corresponding acid (0.04 g, 4%).

C. 4,7-Epoxyoctadeca-4,6-dienoic acid (3)

1. 5-Undecyl-2-furfural

Phosphorous oxychloride (12.3 g, 0.08 mol) was added dropwise to DMF (20 g) at 0°C. The solution was stirred for 1 hr at 0°C and a solution of 2-undecylfuran (17 g, 0.077 mol) in DMF (20 ml) was slowly added. The reaction mixture was stirred at this temperature for 1 hr and maintained at 20°C for a further 1.5 hr. The reaction mixture was poured into ice water (100 g) and solid sodium carbonate (20 g) was added to the aqueous mixture and left at room temperature for 12 hr. Extraction of the reaction mixture with diethyl ether gave crude 5-undecyl-2-furfural (15 g, 78%), which was used without further purification.

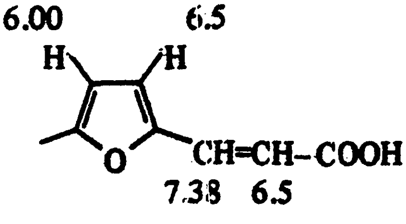
^{1}H-NMR δ (CCl_4):



2. 4,7-Epoxyoctadeca-2,4,6-trienoic acid

A mixture of crude 5-undecyl-2-furfural (5 g, 0.02 mol), malonic acid (2.6 g, 0.025 mol, dried at 120°C for 30 hr), piperidine (0.1 ml) and pyridine (25 ml) was heated at 100°C for 2.5 hr and then refluxed for a further 15 min. The cooled reaction mixture was poured into ice cold dilute hydrochloric acid (2 M, 50 ml). The precipitate was filtered, washed with cold water and recrystallised from methanol-water to give pure 4,7-epoxyoctadeca-2,4,6-trienoic acid (2.5 g, 42%, m.p. 100–101°C; C, 73.93; H, 9.65. Found: C, 73.26; H, 9.76.).

^{1}H-NMR δ (CCl_4):



3. 4,7-Epoxyoctadeca-4,6-dienoic acid

Hydrogenation of methyl 4,7-epoxyoctadeca-2,4,6-trienoate at atmospheric pressure in the presence of Lindlar catalyst in ethyl acetate gave pure methyl 4,7-epoxyoctadeca-4,6-dienoate. Hydrolysis of the ester gave on recrystallisation of the acid fraction pure 4,7-epoxyoctadeca-4,6-dienoic acid (90%), based on the amount of methyl 4,7-epoxyoctadeca-2,4,6-trienoate.

D. 5,8-Epoxyoctadeca-5,7-dienoic acid (4)

1. 1-Chloro-4,7-epoxyheptadeca-4,6-diene

The solvent of a solution of *n*-butyl lithium (20 ml, 15% w/w in *n*-hexane) was replaced by anhydrous THF at −20°C under nitrogen. 2-Decylfuran (5.5 g, 0.026 mol) in THF (50 ml) was added dropwise and the resulting yellow solution was stirred at −20°C for 4 hr. 1-Bromo-3-chloropropane (12.5 g, 0.08 mol) in THF (30 ml) was then added to the reaction mixture, stirred at −20°C for 2 hr and allowed to remain at room temperature for 12 hr. Water (50 ml) was added to the reaction mixture and the ethereal extract gave crude 1-chloro-4,7-epoxyheptadeca-4,6-diene (5.5 g, 75%).

2. 1-Cyano-4,7-epoxyheptadeca-4,6-diene

A mixture of crude 1-chloro-4,7-epoxyheptadeca-4,6-diene (5.5 g, 0.019 mol), sodium cyanide (1.5 g, 0.031 mol) and DMSO (30 ml) was heated at 120°C for 3 hr. Water (100 ml) was added to the reaction mixture and the ethereal extract furnished crude 1-cyano-4,7-epoxyheptadeca-4,6-diene (4.4 g, 84%). The infrared spectrum shows aromatic C–H and C=C stretchings at 3100 and 1600, 1570 cm^{-1} respectively and C≡N stretching at 2250 cm^{-1}.

3. 5,8-Epoxyoctadeca-5,7-dienoic acid

A mixture of crude 1-cyano-4,7-epoxyheptadeca-4,6-diene (2.43 g, 0.009 mol), sodium hydroxide (6.4 g), methanol (20 ml) and water (20 ml) was refluxed for 48 hr. Water (150 ml) was added to the reaction mixture and isolation of the acidic fraction gave after recrystallisation from petroleum pure 5,8-epoxyoctadeca-5,7-dienoic acid (1.25 g, 48%; 16% based on the amount of 2-decylfuran used).

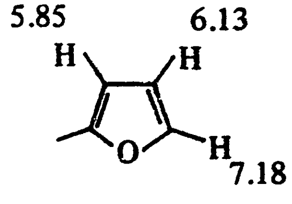
The synthesis of compounds **5**, **6**, **7**, **8**, **10** and **11** is represented by the method described for 8,11-epoxyoctadeca-8,10-dienoic acid.

E. 8,11-Epoxyoctadeca-8,10-dienoic acid (7)

1. 2-Heptylfuran

The solvent of a hexane solution of *n*-butyl lithium (1.6 M, 80 ml) was replaced by THF (40 ml) and kept under nitrogen. Furan (8.8 g, 0.13 mol) in THF (20 ml) was added dropwise into the cooled solution of *n*-butyl lithium and stirred at −20°C for 4 hr. 1-Bromoheptane (17.9 g, 0.1 mol) in THF (20 ml) was then added dropwise into the solution, stirred at −20°C for 2 hr and at room temperature for 12 hr. Water was added and isolation gave crude 2-heptyl furan (16 g, 96%), which was used without further purification.

^1H-NMR δ (CCl_4):



2. 1-Bromo-7,10-epoxyheptadeca-7,9-diene

2-Heptylfuran (16 g, 0.096 mol) was added dropwise to a THF solution of butyl lithium (from 80 ml, 1.6 M in hexane) at −20°C under nitrogen and the reaction mixture stirred at −20°C for 4 hr. 1,6-Dibromohexane (73.2 g, 0.3 mol) in THF (30 ml) was added into the solution and stirred at −20°C for 2 hr and at room temperature for a further 12 hr. Water (100 ml) was added and the ethereal extract gave a mixture of unreacted 1,6-dibromohexane and 1-bromo-7,10-epoxyheptadeca-7,9-diene. The volatile dibromohexane was distilled off at 60°C/0.1 mm and the residue was mainly composed of 1-bromo-7,10-epoxyheptadeca-7,9-diene (29.2 g).

3. 1-Cyano-7,10-epoxyheptadeca-7,9-diene

Crude 1-bromo-7,10-epoxheptadeca-7,9-diene (20 g, approx. 0.06 mol) was added dropwise into a solution of sodium cyanide (7.4 g, 0.15 mol) in DMSO (50 ml). The solution was stirred at 80°C for 2 hr. The reaction mixture was poured into ice water and the ethereal extract gave crude 1-cyano-7,10-epoxyheptadeca-7,9-diene (14.6 g, 98%).

4. 8,11-Epoxyoctadeca-8,10-dienoic acid

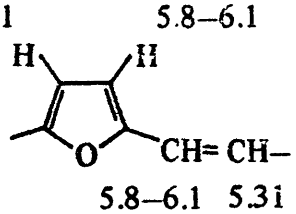
A mixture of 1-cyano-7,10-epoxyheptadeca-7,9-diene (10 g, 0.04 mol), potassium hydroxide (20 g), water (50 ml) and ethanol (50 ml) was refluxed for 48 hr. Water (200 ml) was added and the product was extracted with diethyl ether. The ethereal extract (containing the potassium salt) was shaken with excess dilute HCl, washed with brine and evaporation of the solvent gave after recrystallisation from petroleum pure 8,11-epoxyoctadeca-8,10-dienoic (3.75 g, 12.7% based on the amount of 2-heptylfuran used).

F. 10,13-Epoxyoctadeca-10,12-dienoic acid (9)

1. Methyl 10,13-epoxyoctadeca-8,10,12-trienoate

A mixture of pure sodium methoxide (3 g, 0.055 mol), 8-carbomethoxyoctyltriphenylphosphonium bromide (29 g, 0.058 mol) and DMF (50 ml) was stirred for 2 hr at 20°C under nitrogen. Anhydrous diethyl ether (70 ml) was syringed into the solution and the mixture refluxed for 1 hr. Crude 5-pentyl-2-furfural (5 g, 0.030 mol) [prepared for 2-pentylfuran by Vilsmeier formylation method] in anhydrous diethyl ether (50 ml) was added, to the cooled reaction mixture, which was stirred for a further 12 hr. Column chromatographic separation of the product gave pure methyl 10,13-epoxyoctadeca-8,10,12-trienoate (5.4 g, 59%; 49% based on the amount of 2-pentylfuran used).

^{1}H-NMR δ (CCl_4):



2. 10,13-epoxyoctadeca-10,12-dienoic acid

Methyl 10,13-epoxyoctadeca-8,10,12-trienoate (1.02 g, 0.003 mol) was hydrogenated over Lindlar catalyst (0.2 g) in ethyl acetate at atmospheric pressure to give methyl 10,13-epoxyoctadeca-10,12-dienoate (0.77 g, 75%). Hydrolysis of the latter furnished pure 10,13-epoxyoctadeca-10,12-dienoic acid (0.63 g, 86%).

G. 13,16-Epoxyoctadeca-13,15-dienoic acid (12)

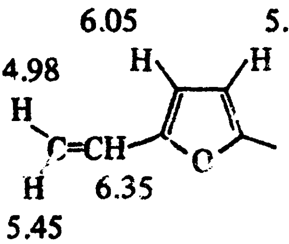
1. Methyl 13,16-epoxyhexadeca-13,15-dienoate

Reaction of furfural (38.4 g, 0.40 mol) with the triphenylphosphonium salt of methyl 11-bromoundecanoate (180 g, 0.33 mol) in the presence of sodium hydride (20 g, 60% dispersion, 0.58 mol) in DMSO (200 ml) gave methyl 13,16-epoxyhexadeca-11,13,15-trienoate (11 g, 12.1%). Hydrogenation of the latter over Lindlar catalyst furnished methyl 13,16-epoxyhexadeca-13,15-dienoate (10.5 g, 94%). The infrared spectrum shows aromatic C–H and C=C stretchings at 3120 and 1595, 1508 cm^{-1} respectively, and C=O stretching at 1740 cm^{-1}.

2. 13,16-Epoxyoctadeca-13,15-dienoic acid

Formylation of methyl 13,16-epoxyhexadeca-13,15-dienoate (10 g, 0.036 mol) with phosphorus oxychloride (6 g, 0.039 mol) in DMF (9 g, 0.125 mol) gave methyl 13,16-epoxy-16-formyl-hexadeca-13,15-dienoate (10 g, 90%). Reaction of the latter with the triphenyl phosphonium salt of bromomethane (9.5 g, 0.027 mol) in the presence of sodium methoxide (1.34 g, 0.025 mol) in DMSO (200 ml) gave methyl 13,16-epoxyoctadeca-13,15,17-trienoate (4.3 g, 39%).

^{1}H-NMR δ (CCl_4):



Hydrogenation of the latter over Lindlar catalyst furnished methyl 13,16-epoxyoctadeca-13,15-dienoate (4.2 g; 97%). Pure 13,16-epoxyoctadeca-13,15-dienoic acid (3.6 g, 90%) was obtained on hydrolysis.

*H. 14,17-Epoxyoctadeca-14,16-dienoic acid (***13***)*

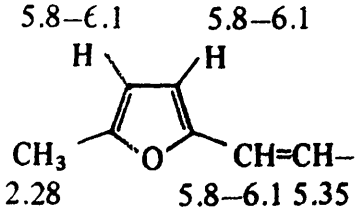
1. 2-Methyl furan

Hydrazine hydrate (70 ml) was added dropwise to furfural (48 g, 0.505 mol) in diethylene glycol (300 ml) and the reaction mixture stirred at 20°C for 1.5 hr Potassium hydroxide (95 g) was added and the yellow reaction mixture heated at 40°C for 0.5 hr. 2-Methyl furan (23 g, 57%, b.p. 60–70°) was directly distilled from the reaction mixture.

2. Methyl 14,17-epoxyoctadeca-12,14,16-trienoate

2-Methyl furan was formylated (70%) and reaction of the resulting 5-methyl-2-furfural with the triphenyl phosphonium salt of methyl 12-bromododecanoate in DMSO gave methyl 14,17-epoxyoctadeca-12,14,16-trienoate (4%).

^{1}H-NMR δ (CCl_4):

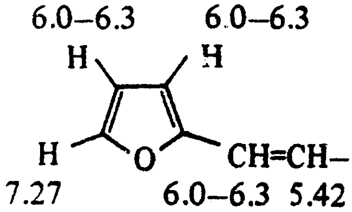


Hydrogenation of the latter in the presence of palladium on charcoal in ethanol and trace amount of ammonium hydroxide at 36 lb/inch^2 for 1 hr gave methyl 14,17-epoxyoctadeca-14,16-dienoate. Hydrolysis of this ester yielded pure 14,17-epoxyoctadeca-14,16-dienoic acid (63%) on recrystallisation from petroleum.

*I. 15,18-Epoxyoctadeca-15,17-dienoic acid (***14***)*

Reaction between furfural (7.2 g, 0.075 mol) and the triphenylphosphonium salt of methyl 13-bromotridecanoate (43 g, 0.076 mol) in sodium hydride (1.8 g, 0.075 mol) in DMSO (250 ml) gave methyl 15,18-epoxyoctadeca-13,15,17-trienoate (3.28 g, 14%).

^{1}H-NMR δ (CCl_4):



Hydrogenation of the latter over Lindlar catalyst gave methyl 15,18-epoxyoctadeca-15,17-dienoate. Hydrolysis of the ester furnished 15,18-epoxyoctadeca-15,17-dienoic acid (2.9 g, 91%).

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