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FATTY ACIDS, PART 27*

THE FORMATION OF 1,4-EPOXIDES FROM METHYL LINOLEATE AND RELATED ESTERS BY REACTION WITH TOLUENE-*p*-SULPHONIC ACID AND AN APPROPRIATE SOLVENT

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When heated with toluene-*p*-sulphonic acid in the presence of methanol or dioxan, methyl linoleate gives mainly isomeric methyl octadecadienoates (~ 22 %) and 1,4-epoxides (tetrahydrofurans, ~ 44 %). These last are methyl *cis*- and *trans*-9,12 and 10,13-epoxystearates along with lesser amounts of the 8,11 and 11,14 isomers. Similar products result from other non-conjugated octadecadienoates and from hydroxy- and methoxyoctadecenoates. The structures of the 1,4-epoxides are based on chromatographic, spectroscopic, and chemical evidence. A mixture of the *cis* and *trans* 9,12-epoxides is prepared by an unambiguous synthesis.

Discussion

We recently reported our intention of studying the properties of long-chain polyenoic acids and our hope that some of these reactions might be accompanied by cyclisation to furnish compounds with a carbocyclic system incorporated into the long-chain acid$^{1)}$. The present paper reports further attempts to achieve this end which, though unsuccessful, led to long-chain compounds with a heterocyclic system (mainly 2,5-disubstituted tetrahydrofurans). These compounds may also be described as 1,4-epoxides and we prefer this nomenclature because it emphasises their relationship to the common long-chain acids.

Carbocyclisation of polyenoic acids such as linoleic and linolenic occurs in a number of reactions (particularly thermal polymerisation, alkali isomerisation, and autoxidation) which have been extensively studied$^{2)}$. Monocyclic compounds related to cyclohexane, cyclohexene, and benzene have been identified, as have a few bicyclic systems.

The changes which occur in unsaturated acids under strongly acidic con-

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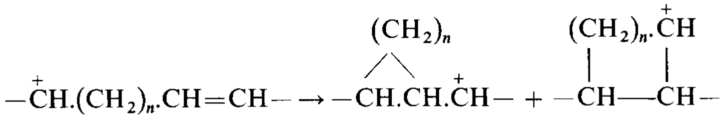
ditions have been studied extensively by Ansell and his colleagues[3,4]), and by Showell *et al.*[5,6]). They have shown that monoenoic acids give rise to γ or δ lactones and/or cyclopentenones and cyclohexenones as major products. In the few polyenoic acids which have been examined at least one of the double bonds is fairly close to the carboxyl group. This does not apply to the systems which we are reporting here.

It is known that carbonium ions of type (**1**) may undergo cyclisation to



$$-\overset{+}{C}H.(CH_2)_n.CH{=}CH- \longrightarrow -\overset{(CH_2)_n}{\overset{\wedge}{CH.CH}}.\overset{+}{C}H- \;+\; -\overset{(CH_2)_n.\overset{+}{C}H}{CH \text{——} CH}-$$

(**1**) (**2**) (**3**)

carbonium ions (**2**) and/or (**3**) and we hoped that protonation of methyl linoleate which gives (**1**,$n=1$ or 2) might produce cyclised products derived from (**2**) and/or (**3**).

Reaction of methyl linoleate

When methyl linoleate is treated at 100 °C with toluene-*p*-sulphonic acid in the presence of enough methanol (or dioxan) to make the mixture homogeneous the product is a mixture of esters, most of which are more polar than linoleate. Six fractions were isolated by preparative TLC and these have been shown to be: isomeric methyl octadecadienoates (A, 22%), both conjugated and non-congujated; 1,5-epoxy esters (B, 4%); 1,4-epoxy esters (C, 44%); unsutarated hydroxy esters (D, 10%); methyl toluene-*p*-sulphonate (E, 15%); and highly polar (possibly polymeric) material (F, 5%).

The chromatographic and spectroscopic properties of fraction A showed it to be a complex mixture of esters. Further separation by silver ion TLC gave four fractions (A1–A4) which were examined by chromatography and spectroscopy and submitted to von Rudloff oxidation. In addition to the following conclusions, fractions A1 and A2 contained isomeric octadecenoates probably arising from the oleate (2%) present in the linoleate used in this reaction.

A1 (~7%) mainly non-conjugated dienes containing some conjugated (*t*, *t*) isomers

A2 (~4%) mainly non-conjugated dienes containing some conjugated (*t*, *t* and *c*, *t*) isomers,

A3 (~3%) mainly non-conjugated dienes (*t*, *t* and *c*, *t*),

A4 (~8%) mainly unchanged linoleate.

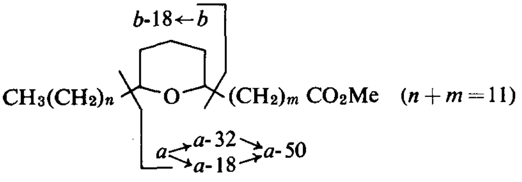
Fraction B was difficult to purify and was always contaminated with fractions A and C. Analysis of one sample (95% pure) indicated the presence of a third oxygen atom. Its mass spectrum showed many similarities to that of fraction C but B and C differed in their chromatographic behaviour on both TLC and GLC [cf. ref. 7], and we consider fraction B to be mainly 1,5-epoxy esters. The expected 9,13-epoxide appears to be accompanied by appreciable amounts of the 8,12 and 10,14 isomers (see table 1).

	ECL(DEGS)	ECL(ApL)
fraction B	20.0	17.8
fraction C	21.34, 12.66	18.60

As the major product of this reaction, fraction C attracted most attention. Spectroscopic and degradative evidence suggested that it was a mixture of 1,4-epoxides and this was confirmed by an independent synthesis of methyl 9,12-epoxystearates. Fraction C gave a single peak on ApL columns (ECL 18.60) but a double peak on DEGS columns (21.34 and 21.66). We have not been able to separate the compounds responsible for these two peaks and consider them to arise from the *cis* and *trans* epoxides. The NMR spectrum showed no unusual features apart from a broad band underneath the sharp singlet at 6.4 τ produced by the $COOCH_3$ protons. This broad signal was more clearly observed in the spectrum of the free acid. The absence of olefinic protons was also confirmed. Combustion analysis showed the presence of a third oxygen atom. The compound was unaffected by catalytic hydrogenation, by reduction with sodium borohydride, or by reaction with hexamethyldisi-

TABLE 1

Mass spectrum of fraction B



	8,12-	9,13-	10,14-
b	169(33)	155(100)	141(51)
b-18	151(15)	137(46)	123(36)
a	227(8)	241(18)	255(9)
a-18	209(33)*	223(30)*	237(9)
a-32	195(13)	209(33)*	223(30)*
a-50	177(8)	191(12)	205(5)

The above figures are *m/e* values and intensity of peak relative to the base peak (=100).

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* Peaks produced from more than one isomer.

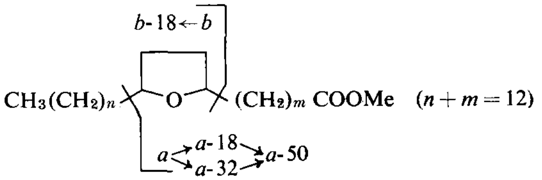
lazane and trimethylchlorosilane. This evidence suggests a saturated ether which must be cyclic and tetrahydrofurans (1,4-epoxides) or tetrahydropyrans (1,5-epoxides) seem most likely.

Attempts to determine the position of these units in the aliphatic chain by oxidation with chromium trioxide in acetic acid under various conditions[8]) were not successful. Many products (30–50) were obtained and though some of these were identified the results were not of diagnostic value. Spectroscopic and chromatographic examination indicated the presence of monobasic acids (C_5–C_7), dibasic acids (C_8–C_{11}), unidentified oxo-esters, γ-lactones, and (possibly) oxygenated C_{18} esters.

The mass spectrum was more informative, especially after methyl 9,12-epoxystearate had been synthesised and its mass spectrum interpreted. Details given in table 2 indicate the presence of the 9,12- and 10,13-epoxides as major products accompanied by the 8,11- and 11,14-isomers.

TABLE 2

Mass spectrum of fraction C and of methyl 9,12-epoxystearate



	8,11	9,12	10,13	11,14	synthetic 9,12
b	169(16)	155(98)	141(100)	127(16)	155(100)
b-18	151(6)	137(27)	123(42)	109(18)	137(38)
a	213(7)	227(78)	241(84)	255(8)	227(94)
a-18	195(49)*	209(58)*	223(15)*	237(1)	209(11)
a-32	181(5)	195(49)*	209(58)*	225(15)*	195(59)
a-50	163(6)	177(11)	191(8)	205(1)	177(14)

The above figures are m/e values and intensity of peaks relative to the base peak (=100).

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* Peaks produced from more than one isomer.

The remaining fractions were not completely identified. Fraction D probably contains methyl hydroxyoctadecenoates and fraction E is mainly methyl toluene-*p*-sulphonate. The final fraction is mainly polymeric.

Influence of reaction conditions

When the reaction was conducted for a shorter time (12 hr of 6 hr) fraction A was somewhat larger and fraction C somewhat smaller. More significantly in the 12 hr reaction product fraction C consisted of 1,4-epoxides (74%) accompanied by *cis* (10%) and *trans* (16%) isomers of methyl methoxyoctadecenoate. The possibility that these compounds are intermediates in the formation of 1,4-epoxides is discussed below.

Solvent effects were also examined. With benzene, cyclohexane, diglyme, or nitrobenzene, ether-insoluble intractable products resulted. In dioxan solution the product resembled that obtained with methanol except that it was present in acidic form and had to be methylated prior to investigation.

In methanol solution cyclic ethers were best obtained (~40%) at reaction temperatures between 95 and 105 °C. At lower temperatures more linoleate survived the reaction; at higher temperatures there was more of the highly-polar product (120 °C) or more tarry material (140 °C upwards).

With more methanol or less acid there was less epoxide and more unreacted linoleate; with less solvent or more acid intractable tars resulted.

Reactions with other esters

Reaction with toluene-*p*-sulphonic acid and methanol for 12 hr has been examined for some other esters. Conjugated octadecadienoates (9*c*,11*t* and 10*t*,12*c* dienes obtained by alkali-isomerisation of methyl linoleate) gave no cyclic ethers and extensive polymerisation occurred. Methyl ricinstearolate also behaved differently from the other esters and gave only very polar products.

The remaining esters (see table 3) gave results similar to those obtained with methyl linoleate. Cyclic ethers are formed from geometrical isomers of linoleate and from appropriate hydroxy and methoxy octadecenoates.

Mechanism

In this reaction methyl linoleate gives mainly isomeric octadecadienoates and isomeric epoxyoctadecanoates. The presence of the isomeric dienes is

TABLE 3

Products of 12-hr reaction with toluene-*p*-sulphonic acid and methanol

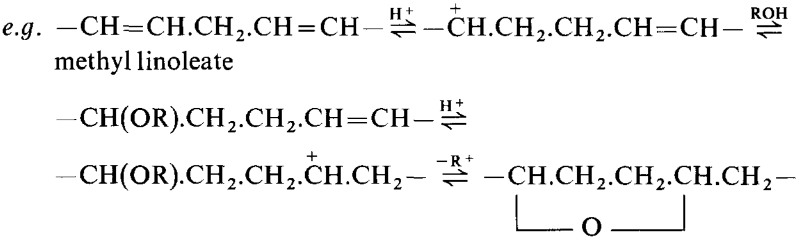
	TLC fractions (wt %)			
methyl ester	A	B	C	D+E+F
18:2(9*c*,12*c*)	36	3	41	20
18:2(9*c*,12*t* + 9*t*,12*c*)	24	4	35	37
18:2(9*t*,12*t*)	21	4	34	41
12-OH 18:1(9*c*)	13	3	30	54
12-OH 18:1(9*t*)	16	4	29	51
12-OMe 18:1(9*c*)	12	5	32	51
9-OH 18:1(12*c*)	14	4	31	51

readily explained in terms of protonation and deprotonation giving rise to conjugated and non-conjugated dienes with *trans* unsaturation. In the simplified scheme shown below it is assumed that every protonation–deprotonation sequence yields a *trans* olefin; in fact, both *cis* and *trans* isomers may be formed.

$$9c{,}12c \xrightarrow{H^+} \text{carbonium ion} \xrightarrow{-H^+} \begin{cases} 9c{,}13t + 9c{,}12t + 9c{,}11t \\ 8t{,}12c + 9t{,}12c + 10t{,}12c \end{cases}$$

These dienes can react again producing isomers with two *trans* double bonds, isomers with double bonds even further apart, and methylene interrupted dienes other than those of the 9,12 series. Conjugated dienes, in particular, are likely to be involved in polymerisation processes.

The cyclic ethers are mainly the *cis* and *trans* 9,12– and 10,13– epoxides along with some of the 8,11 and 11,14 isomers. The additional oxygen atom may come from the solvent (methanol or dioxan) and/or from the acid (toluene-*p*-sulphonic) and we have little evidence to decide between these possibilities. The observation that 12-methoxyoleate gave less cyclic ether than the octadecadienoates might suggest that reaction occurs at least in part through a tosylate; the necessity of having an oxygen-containing solvent suggests that it is involved in the reaction. Shepherd and Showell[6]) have shown that acid-catalysed double bond migration in oleic acid occurs through the reversible formation of an acyloxy derivative.



e.g. $-CH{=}CH.CH_2.CH{=}CH- \overset{H^+}{\rightleftharpoons} -\overset{+}{C}H.CH_2.CH_2.CH{=}CH- \overset{ROH}{\rightleftharpoons}$

methyl linoleate

$-CH(OR).CH_2.CH_2.CH{=}CH- \overset{H^+}{\rightleftharpoons}$

$-CH(OR).CH_2.CH_2.\overset{+}{C}H.CH_2- \overset{-R^+}{\rightleftharpoons} -\underbrace{CH.CH_2.CH_2.CH}_{O}.CH_2-$

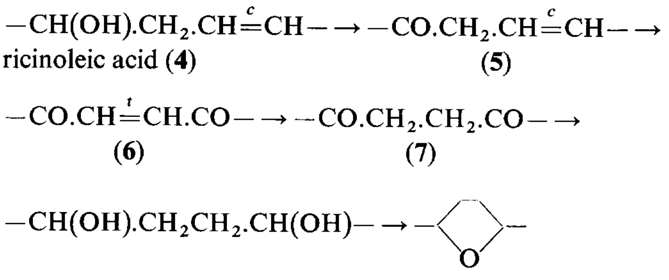
10,13 epoxide

[R = Me or Ts].

Consistent with this mechanism we have now discovered several other reactions of methyl ricinoleate and of methyl 9-hydroxyoctadec-*cis*-12-enoate and their derivatives in which 1,4-epoxides are formed, sometimes in quite high yield[9]).

The preparation of methyl *cis*- and *trans*-9,12-epoxyoctadecanoates

A mixture of methyl *cis*-and *trans*-9,12-epoxyoctadecanoates was prepared by an un ambiguous route based on the work of Nichols and Schipper[10]) and of Kouhoupt[11]).



$$-CH(OH).CH_2.CH\overset{c}{=}CH-\rightarrow -CO.CH_2.CH\overset{c}{=}CH-\rightarrow$$

ricinoleic acid (**4**) (**5**)

$$-CO.CH\overset{t}{=}CH.CO-\rightarrow -CO.CH_2.CH_2.CO-\rightarrow$$

(**6**) (**7**)

$$-CH(OH).CH_2CH_2.CH(OH)-\rightarrow$$

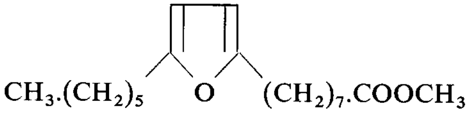
(**8**) (**9**)

Ricinoleic acid (**4**) was oxidised, first to 12-oxo-oleic acid (**5**) and then to 9,12-dioxo-octadec-*trans*-10-enoic acid (**6**). This was reduced catalytically to (**7**) and then by sodium borohydride to 9,12-dihydroxystearic acid (**8**). When this was boiled with methanolic sulphuric acid, esterification and cyclodehydration occurred and cyclic ethers were isolated in good yield (78%). Since this cyclisation is unlikely to give a 1,5-epoxide, the two peaks observed in gas liquid chromatography on DEGS columns are considered to arise from the *cis* and *trans* isomers of the product.

The infra-red spectrum, NMR spectrum, and mass spectrum (table 2) of this product were identical with the spectra of the cyclic ether obtained from methyl linoleate (fraction C) except for those peaks in the mass spectrum which come from isomeric 1,4-epoxides.

The mass spectra of (**6**), (**7**), and the dimethyl ether of (**8**) are summarised in table 4. The *m/e* values of the larger peaks are listed and these are explained on the basis of accepted fragmentation patterns for long-chain oxo and methoxy esters.

The cyclodehydration of 9,12-dioxostearic acid (**7**) which occurred during methylation of the acid with methanolic boron trifluoride, gave a long-chain furanoid ester (**10**) which is of interest because it has been reported to occur naturally[12]). A more involved synthesis of (**10**) has already been reported[13]).



(**10**)

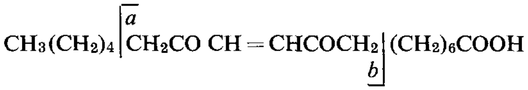
Our product appears to have the same spectroscopic properties as the natural and synthetic samples already described.

The unsaturated dioxo acid (**6**) was reduced to 9,12-dihydroxyoctadec-*trans*-10-enoic acid but attempts to cyclodehydrate this gave a complex mixture with no evidence of a dihydrofuran derivative. It is known that *cis* ene diols are readily converted to dihydrofurans[14]) and our failure to achieve

TABLE 4

Mass spectra of some oxygenated C_{18} acids

9,12-*Dioxo-octadec*-trans-10-*enoic acid*

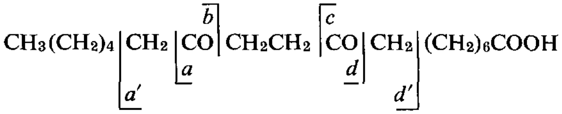


$$\mathrm{CH_3(CH_2)_4}\,\overset{a}{\big|}\,\mathrm{CH_2CO\;CH{=}CHCOCH_2}\,\underset{b}{\big|}\,\mathrm{(CH_2)_6COOH}$$

Major peaks: 310(20,M^+), 240(3,*a*), 209(12,?), 197(17,*a*-43), 182(6,*b*), 179(11,?), 167(6,*b*-15), 154(15,?), 139(100,*b*-43), 112(92,*c*)

Fragments *a* and *b* result from McClafferty rearrangement and both readily lose 43 mass units (CH_3CO). Fragment *c* (112) is the central unit remaining after McClafferty rearrangements as in *a* and *b*, i.e. $CH_3COCH{:}CHCOCH_3$.

9,12-*Dioxostearic acid*

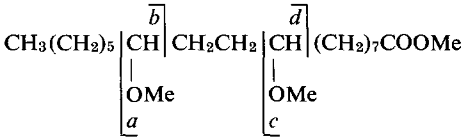


$$\mathrm{CH_3(CH_2)_4}\,\underset{a'}{\big|}\,\mathrm{CH_2}\,\underset{a}{\big|}\,\mathrm{CO}\,\overset{b}{\big|}\,\mathrm{CH_2CH_2}\,\overset{c}{\big|}\,\mathrm{CO}\,\underset{d}{\big|}\,\mathrm{CH_2}\,\underset{d'}{\big|}\,\mathrm{(CH_2)_6COOH}$$

Major peaks: 312(12,M^+), 242(43,*a*′), 227(5,*a*), 224(34,*a*′-18), 209(29,*a*-18), 199(12,*a*-28) 185(11,199-14), 184(74,*d*′), 181(37,?), 171(44,*c*) 169(50,*d*), 153(12,*c*-18), 141(49,*d*-28), 127(38,141-14), 114(100,*e*), 113(74,*b*)

Fragments *a*, *b*, *c*, and *d* result from α-cleavage; *a*′ and *d*′ from β-cleavage accompanied by McClafferty rearrangement. Fragments *a*, *a*′, and *c* each lose 18 mass units (H_2O) whilst *a* and *d* lose 28 mass units (CO) followed by 14 mass units (CH_2). Fragment *e* (114) is the central unit remaining after McClafferty rearrangements as in *a*′ and *d*′, i.e. $CH_3COCH_2CH_2COCH_3$.

Methyl 9,12-dimethoxystearate



$$\mathrm{CH_3(CH_2)_5}\,\underset{a}{\big|}\,\underset{\mathrm{OMe}}{\mathrm{CH}}\,\overset{b}{\big|}\,\mathrm{CH_2CH_2}\,\underset{c}{\big|}\,\underset{\mathrm{OMe}}{\mathrm{CH}}\,\overset{d}{\big|}\,\mathrm{(CH_2)_7COOMe}$$

Major peaks: 173(10,*a*), 241(44,*a*-32), 209(6,*a*-64), 201(100,*c* and *d*), 169(72,*c*-32 and *d*-32), 137(16,*c*-64 and *d*-64), 127(72,*b*), 95(30,*b*-32)

Fragments *a*, *b*, *c*, and *d* result from α-cleavage and each can subsequently lose 32 or 64 mass units[21].

this is readily explained in terms of the shape of the molecule with its *trans* double bond.

Experimental

Solvents

Ether and benzene, after drying over anhydrous calcium chloride, were decanted and stored over sodium wire. Dioxan was distilled from calcium hydride and kept over sodium wire. Carbon disulphide was stored in the dark over calcium chloride and pyridine was distilled from potassium hydroxide pellets. Petroleum refers to petroleum ether (b.p. 40–60 °C).

Thin layer chromatography (TLC)

Analytical TLC was carried out on glass plates (20 × 5 cm) layered with silica gel G (0.25 mm) or with the same adsorbent containing silver nitrate (15%). For preparative purposes larger plates (20 × 20 cm) and thicker layers (1 mm) were employed. Binary mixtures of ether and petroleum were used as developing solvents. Symbols such as PE40 indicate the percentage (by volume) of the second component in the mixture. Analytical plates were rendered visual by spraying with phosphomolybdic acid and heating in an oven (~110 °C) for 10 min. Preparative plates were sprayed with a 0.2% methanolic solution of 2,7-dichlorofluorescein and then viewed under ultraviolet light. Separated products were recovered in 85–95% yield) from preparative plates by slurrying the adsorbent with ether.

Gas liquid chromatography (GLC)

A Pye 104 chromatograph with nitrogen as carrier gas and ApL (3%) or DEGS (20%) as stationary phase was employed throughout this investigation. Retention times are quoted as ECL's15). Peak areas, calculated from peak height and from the width at half height, are quoted as composition (% wt) without correction. Some ECL's are collected in table 5.

Spectroscopic data

Infra-red spectra were recorded on a Perkin-Elmer Infracord 237 using solutions (1%) in carbon disulphide or carbon tetrachloride in liquid cells (1 mm path length) with sodium chloride windows. Some samples were examined on thin films in sodium chloride cells.

Ultra-violet spectra were measured on methanolic solutions in 1 cm quartz cells with a Unicam SP800 spectrophotometer.

A Perkin-Elmer R10 spectrometer (60 MHz) was used to record NMR spectra of carbon tetrachloride solutions (10%) with tetramethylsilane as internal standard.

Mass spectra were recorded on an AEI MS9'02 instrument. Values of *m/e* (tables 1, 2, and 4) are expressed as a percentage of the base peak selected from *m/e* values >70.

General chemical procedures

Preparation of trimethylsilyl ethers. A pyridine (1 ml) solution of the hydroxy ester (~5 mg) was shaken for 30 sec with hexamethyldisilazane

TABLE 5

ECL's of some methyl esters

Ester	DEGS	ApL
ricinoleate	25.8	–
ricinelaidate	25.8	–
ricinstearolate	28.4	–
12-methoxyoleate	21.7	18.6
9-hydroxyoctadec-*cis*-12-enoate	26.2	–
18:2 (9*c*,12*t* and 9*t*,12*c*)	19.4	17.6
18:2 (9*c*,11*t* and 10*t*,12*c*)	20.4	19.1
9,12-dihydroxystearate (TMSi ethers)	19.75*	20.22*
9,12-dihydroxyoctadec-*trans*-10-enoate (TMSi ethers)	20.0	20.2
9,12-dimethoxystearate	24.0	19.9
9,12-epoxystearates	21.34, 21.66*	18.60*
9,12-epoxyoctadec-9,11-dienoate	21.3	18.0

* ECL's quoted to two decimal places are the mean of several observations.

(0.2 ml) and trimethylchlorosilane (0.1 ml). After standing for a further 5 minutes, the pyridine was removed *in vacuo* and the residue mixed with ether (0.3 ml) for GLC examination.

Methylation. (a) On a small scale (<2 g) acids were methylated by refluxing for 15 minutes with methanolic boron trifluoride (14%, 1 part by volume) diluted with methanol (4 parts by volume). After reaction, the mixture was added to saturated salt solution and extracted with ether.

(b) Large scale esterifications were effected with methanolic sulphuric acid solution (2.5%) at room temperature overnight or by refluxing for one hour.

(c) Hydroxy esters (60 mg) were converted to methoxy esters by refluxing with dry silver oxide (50 mg) and methyl iodide (1.5 ml) for 2–3 hr. The mixture was diluted with ether, filtered, and the product purified by preparative TLC.

Von Rudloff oxidation. This was carried out as described by Tulloch and Craig[16]).

Preparation of long-chain esters

Methyl ricinstearolate and methyl linoleate (containing 2.5% of methyl oleate as the only impurity) were available.

Methyl Ricinoleate. Castor oil (12 g) was neutralised by percolation with chloroform (300 ml) through a column of alumina. The neutral oil (10 g) was converted to methyl esters (9.1 g) by refluxing for 30 min with dry methanolic sodium methoxide (0.5% 50 ml). The mixture was then poured into water (100 ml), saturated with sodium chloride, and extracted with ether (2 × 50 ml). The mixed esters were chromatographed on a column of silica gel (200 g) using 200 ml portions of P, PE5, PE10, PE20, PE40, and PE60 as eluting solvents. The eluate was collected in 100 ml fractions and examined by TLC. Methyl ricinoleate (7.3 g), eluted mainly by PE40, was adjudged pure on the basis of TLC (PE40) and GLC (DEGS) examination.

*Methyl 9-hydroxyoctadec-*cis*-12-enoate.* This ester (740 mg) was isolated similarly from a concentrate (850 mg) previously obtained from *Strophanthus courmontii* seed oil[17]).

Methyl ricinelaidate. Ricinstearolic acid (500 mg), dissolved in dry tetrahydrofuran (20 ml), was added to liquid ammonia (~200 ml). Small pieces of lithium were added until a blue colour was obtained and the mixture was stirred for 90 min with the addition of lithium as required to maintain the blue colour. Water (2 ml) was then added and after the ammonia had evaporated the residue was acidified with hydrochloric acid (2 *M*) and extracted with ether (2 × 30 ml). After methylation the product showed strong infra-red absorption at 970 cm^{-1} and had a higher R_f value than methyl ricinoleate on a silver ion TLC plate (PE40).

Methyl 12-methoxyoleate. This was prepared from methyl ricinoleate by reaction with silver oxide and methyl iodide (see above) and purified by preparative TLC (PE25).

Stereomutation of methyl linoteate[18]). Nitric acid (6 *M*, 16 ml) was added to an ether solution (50 ml) of methyl linoleate (2 g) followed by sodium nitrate solution (2 *M*, 24 ml). After shaking for 20 minutes the organic product (2.4 g) was chromatographed (silica gel G, PE5) and the methyl octadecadienoates (1.2 g) were separated by preparative silver ion TLC into the 9*t*,12*t*, (480 mg, 48%), 9*c*,12*t* and 9*t*,12*c* (310 mg, 31%) and 9*c*,12*c* isomers (110 mg 11%).

Alkali-isomerisation of methyl linoleate[19]). Methyl linoleate (750 mg) was heated for 4 hr at 95 °C with a solution of potassium t-butoxide in t-butanol (5%, 75 ml). The solvent was then distilled off and the residue acidified (2 *M* hydrochloric acid) and extracted with ether (2 × 40 ml). After methylation, the product (680 mg) was separated by preparative silver ion TLC (PE30) to give the mixed 9*c*,11*t* and 10*t*,12*c* dienoates (610 mg).

*The reaction of methyl linoleate with toluene-*p*-sulphonic acid.*

Methyl linoleate (1 g, 3.4 mmole), toluene-*p*-sulphonic acid (5 g, 26 mmole) and dry methanol (2 ml) were heated in an oil bath at 100 °C for 18 hr. The reaction mixture was diluted with water (50 ml) and the ether extracts (2 × 40 ml) were washed with sodium bicarbonate solution (5%, 30 ml) and with water (2 × 30 ml). The product (0.92 g) was a dark brown oil with ECL's of 18.6, 19.4, 19.9, 21.4, 21.7 and 22.3 (DEGS) and 17.6, 17.8, and 18.6 (ApL). TLC (PE25) showed the presence of six components (A–F in order of increasing polarity which were separated by preparative TLC.

Fraction A (22%) showed ECL's of 18.6, 19.5, 20.6 and 21.1 on DEGS and 17.6 (80%) and 18.1 and 18.6 on ApL. The infra-red spectrum contained significant peaks at 990, 970 and 950 cm^{-1} and the ultra-violet spectrum had absorption maxima at 223($E^{1\%}_{1\,cm}$ 117), and 231 nm($E^{1\%}_{1\,cm}$ 115). Hydrogenation gave only methyl stearate whilst von Rudloff oxidation gave several dibasic (C_6–C_{11}) and monobasic (C_5–C_9) acids. The fraction was subdivided by preparative silver ion TLC (PE25).

Subfraction A1 (32%, ECL on DEGS: 18.5, 19.1, 19.3, 19.6, 20.0, and 21.1) had infra-red bands at 990 and 970 cm^{-1}. Subfraction A2 (20%, 18.5, 19.3, 19.9, 20.5, and 21.1) had infra-red bands at 990, 970 and 950 cm^{-1}. These samples were not oxidised since they contained methyl octadecenoates arising from the methyl oleate present as an impurity in the methyl linoleate. The third subfraction (12%, 19.1, 19.3) showed an infra-red band at 970 cm^{-1} and gave C_6–C_{11} dibasic acids and C_5–C_8 monobasic acids when oxidised. The final fraction (37%, 19.4) gave azelaic and hexanoic acids (along with only traces of suberic and heptanoic) when oxidised.

Fraction B (4%, found: C,73.0; H,12.1; calc. for $C_{19}H_{36}0_3$:C,73.0; H,11.6%. ECL's 20.0 on DEGS and 17.8 on ApL.) There was no evidence of unsaturation from either the infra-red or NMR spectra. Some features of the mass spectrum are given in table 1.

Fraction C (44%, found: C,73.3; H,11.8; calc. for $C_{19}H_{36}0_3$:C,73.0; H,11.6%. ECL's 21.34 and 21.66 on DEGS and 18.60 on ApL.) The infra-red spectrum showed a peak at 1110 cm^{-1} (ether absorption). In the NMR spectrum of the methyl ester there was a broad signal under the singlet at 6.4 τ. This was also evident (equivalent to two protons) in the spectrum of the free acid. Some features of the mass spectrum are given in table 2.

Fraction D (10%) had ECL's of 22.3 and 26.3 (DEGS) which became 22.3 and 19.4 after silylation. The infra-red spectrum showed significant bands at 3480 and 970 cm^{-1}.

Fraction E (15%) *and F* (4%) did not give GLC peaks under normal operating conditions. Fraction E had a NMR spectrum similar to that of methyl toluene-*p*-sulphonate with diagnostic signals at 2.2–2.8 τ (aromatic protons), 7.6 τ (CH_3Ar), and 6.4 τ (methyl ester).

In a similar reaction carried out for only 12 hr the same six fractions were isolated: A,32%; B,5%; C,35%; D,9%; E,15%; and F,4%. These showed similar properties to those already described except that the NMR spectrum of fraction C showed an additional signal at 6.7 τ ($\sim$1 proton). Preparative silver ion TLC gave three subfractions. The largest of these, (Ca, 74%) was identical with the product isolated in the previous experiment. The second fraction (Cb, 16%) showed infra-red absorption at 2820 cm^{-1}(OCH_3) and

970 cm^{-1} (*trans* double band). Von Rudloff oxidation gave monobasic (C_6 and C_7) and dibasic (C_8–C_{10}) acids along with other compounds of ECL (as methyl esters) 10.8, 11.8, and 23.4 (DEGS) and 9.2, 10.2, 11.2, 14.8, 15.8, 15.9 (ApL). The final fraction (Cc,10%) had a similar infra-red spectrum to Cb but much weaker absorption at 970 cm^{-1}. Oxidation of Cc gave similar products to Cb but nonanedioic acid and the product of ECL 11.7 (DEGS) predominated.

In a reaction conducted for 6 hr, fraction C (24%) contained less of this new product, The NMR signal at 6.7 τ was very small.

*The reaction of other esters with toluene-*p*-sulphonic acid*

Several esters (300 mg, table 3) related to methyl linoleate were heated at 100 °C for 12 hr with toluene-*p*-sulphonic acid (1.5 g) and methanol (0.6 ml). Each reaction product was separated by TLC and examined by GLC as described for methyl linoleate. Apart from methyl ricinstearolate and the conjugated octadecadienoates the other esters gave products with ECL's similar to those observed in the methyl linoleate reaction. The product from methyl ricinstearolate showed two very polar spots on TLC (PE25) but gave no GLC peaks. The conjugated dienoates gave three bands on TLC: A(20%), ECL 20.5 (DEGS) and 18.1 (ApL), infra-red absorption at 990 and 950 cm^{-1} (*c,t*-dienes); B(33%), no peaks on GLC; and C(47%), no peaks on GLC.

The synthesis of methyl cis- *and* trans-*9,12-epoxystearates*

*9,12-Dioxo-octadec-*trans*-10-enoic acid. (a) From castor acids via 12-oxo-oleic acid.* Castor oil (55 g) was refluxed for one hour with potassium hydroxide (16 g) dissolved in water (80 ml) and methanol (80 ml) and the mixed acids (51 g) were recovered in the usual way. An oxidising solution of sodium dichromate dihydrate (32.5 g) in water (40 ml), acetic acid (300 ml), and concentrated sulphuric acid (17.5 ml) was quickly added to a vigorously stirred solution of castor acids (50 g) in acetic acid (500 ml). After only 30 sec iced-water (1 l) was added and the mixture filtered. The wet precipitate was taken up in petroleum (800 ml), the solution dried over sodium sulphate, and then cooled to −25 °C to furnish 12-oxo-oleic acid [23 g, 55%, m.p. 37.5–39 °C, lit. 40 °C[10])]. This acid showed significant infra-red absorption bands at 3010 and 1710 cm^{-1}, NMR signals at 4.4–4.6 and 6.9–7.0 τ, and was oxidised to nonanedioic acid and octan-2-one.

Further oxidation of 12-oxo-oleic acid (20 g) was effected with sodium dichromate dihydrate (32 g) in water (160 ml), acetic acid (160 ml), and concentrated sulphuric acid (16 ml) by stirring for one hour at 40–45 °C. After addition of iced-water (800 ml) and filtration, the product was crystallised from aqueous ethanol (90%, 200 ml) to give 9,12-dioxo-octadec-*trans*-10-

enoic acid [10.3 g 48%, m.p. 111–112 °C, lit. 112–113 °C[10])], found: C,69.7; H,9.6; calc for $C_{18}H_{30}0_4$: C,69.7; H,9.7%]. The acid had significant infra-red absorption band at 1685 and 1000 cm^{-1} and an absorption band in the ultraviolet at 232 nm ($\varepsilon = 13\ 250$) [lit.[20]) 228 nm, ε max 16 000]. Oxidation gave nonanedioic and heptanoic acids. (For details of the mass spectrum see table 4.)

(b) *Directly from castor acids.* A vigorously stirred solution of castor acids (50 g) in acetic acid (550 ml) was oxidised by quick addition of a solution of sodium dichromate dihydrate (36.5 g) in water (45 ml), acetic acid (325 ml), and concentrated sulphuric acid (20 ml). When the temperature had fallen from 54 to 47 °C more oxidising agent [sodium dichromate dihydrate (41 g), water (200 ml), acetic acid (100 ml), and concentrated sulphuric acid (20 ml)] was added and the mixture stirred at 40–45 °C for one hour. The dioxo acid was precipitated with iced water (1.5 l) and recrystallised from 90% aqueous ethanol 9.7 g, 22%, m.p. 111–112 °C).

9,12-Dioxostearic acid. The unsaturated dioxo acid (2.3 g) was hydrogenated at atmospheric pressure (10% Pd/C, 0.4g; methanol (50 ml), 1 hr). When filtered and cooled to −30 °C the solution gave crystals of 9,12-dioxostearic acid [1.8 g, 78%, m.p. 95 °C; lit. 96–96.5 °C[10]) found: C,69.0; H,10.6; calc. for $C_{18}H_{32}0_4$: C,69.2; H,10.3%]. The acid had an infra-red absorption band at 1700 cm^{-1} and was oxidised by chromic anhydride to hexanoic, heptanoic, octanedioic, and nonanedioic acids. For details of the mass spectrum see table 4.

9,12-Dihydroxystearic acid. The saturated dioxo acid (1 g) and sodium borohydride (1 g) were stirred in dry methanol (50 ml) for 30 min at room temperature. The reaction mixture was then acidified and extracted to give 9,12-dihydroxystearic acid [0.96 g, 95%, m.p. 109–118 °C, lit. 80–82 °C and 119–121 °C for the two isomeric forms of this acid [10]) found: C,68.2; H,11.7; calc for $C_{18}H_{36}0_4$: C,68.3; H,11.5%]. The acid showed infra-red absorption at ~3300 and 1700 cm^{-1}. It was converted to its methyl ester by reaction with boron trifluoride and methanol and to methyl 9,12-dimethoxystearate by reaction with silver oxide and methyl iodide. For details of the mass spectrum see table 4.

Methyl 9,12-epoxystearates. The dihydroxy acid (0.91 g) was refluxed for 6 hr with methanolic sulphuric acid (7.5%, 100 ml). The crude product (0.84 g) separated by preparative TLC (PE25), gave methyl 9,12-dihydroxystearate (22%) and methyl 9,12-epoxystearate (78%, found: C,73.0; H,11.6; calc. for $C_{19}H_{36}0_3$: C,73.0; H,11.6%). The infra-red spectrum of the 1,4-epoxide had an absorption hand at 1110 cm^{-1} and the NMR spectrum showed a broad signal at 6.4 τ arising from protons α to an ether oxygen. This isomeric mixture could not be distinguished chromatographically from the product obtained from methyl linoleate (fraction C) and from some related esters.

Methyl 9,12-epoxyoctadeca-9,11-dienoate [methyl 8-(5-hexyl-2-furyl) octanoate]

9,12-Dioxostearic acid (400 mg) was refluxed for 20 minutes with methanolic boron trifluoride (14%, 4 ml) and more methanol (20 ml). The product (380 mg) was separated by preparative TLC (PE25) and the furan derivative (196 mg, 50%) isolated as the least polar fraction. It had the same polarity on TLC as the synthetic 9,12-epoxystearates. It has an ultra-violet absorption band at 222 nm, $\varepsilon=9840$ [lit.[13]) 222 nm, $\varepsilon=10\,200$] and showed diagnostic absorption in its infra-red spectrum at 3105, 1570, and 1020 cm^{-1}. Its NMR spectrum contained a singlet (2H) at 4.28 τ.

Attempted cyclisation of 9,12-dihydroxyoctadec-trans-*10-enoic acid*

The unsaturated 9,12-dioxo acid (1 g) was reduced with sodium borohydride (1.2 g) in methanol solution (100 ml) during 30 min to 9,12-dihydroxyoctadec-*trans*-10-enoic acid (0.96 g, 95%, m.p. 90–95 °C; found: C,68.5; H,11.2; calc for $C_{18}H_{34}O_4$:C,68.8; H,10.9%). Its infra-red spectrum showed characteristic bands at 3260, 3340, 1700 and 970 cm^{-1}. Von Rudloff oxidation gave heptanoic and nonanedioic acids.

This dihydroxy acid (100 mg), boiled for 5 hr with methanolic sulphuric acid (7.5%, 10 ml), gave a product (100 mg, ECL's of 23.0 and 23.7 DEGS) which showed characteristic triene absorption (~10%) in its ultra-violet spectrum [λ max and ε:258(3970), 268(5260), and 278 nm(4130)]. TLC and the NMR spectrum indicated a complex mixture of compounds.

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