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FATTY ACIDS, PART 21*

THE REARRANGEMENT OF METHYL 12, 13-EPOXYOLEATE BY BORON TRIFLUORIDE WITH FORMATION OF CYCLOPROPANE ESTERS

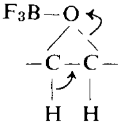
H B S CONACHER† and F D GUNSTONE

Department of Chemistry, The University of St Andrews, Purdie Building
St Andrews Scotland

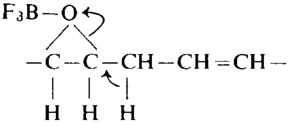
Treated with boron trifluoride etherate in dioxan solution, methyl 12,13-epoxyoleate gives the 12- and 13-oxo-oleates as major products These are accompanied by cyclopropane compounds (8–11 %) which are mainly the *cis* and *trans* isomers of methyl 9,10-methylene-12-oxo-heptadecanoate [1-(7′-carbomethoxyheptyl), 2-(2′-oxoheptyl)cyclopropane] In benzene solution the cyclopropanes are formed in higher yield (38 %) The structure of long-chain cyclopropane esters can be determined by oxidation with chromic acid

Introduction

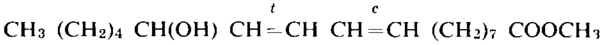
Methyl 9,10-epoxystearate gives methyl 9- and 10-oxostearates in high yield when treated with boron trifluoride etherate in boiling dioxan [1]) Reaction probably occurs through the enolic form of these ketones which would arise through the changes shown in (**1**) We hoped that a similar reaction on methyl vernolate (12,13-epoxy-oleate) might involve the hydrogen atom of the activated methylene group at C(11) and furnish methyl coriolate (**3**) through the changes shown in (**2**)



(**1**)



(**2**)



$$CH_3\,(CH_2)_4\,CH(OH)\,\overset{t}{CH{=}CH}\,\overset{c}{CH{=}CH}\,(CH_2)_7\,COOCH_3$$

(**3**)

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* Part 20, Chem Phys Lipids 3 (1969) 191–202

† Present address Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Canada

Interest in this epoxide rearrangement arises from its possible biological significance [2,3])

Results and Discussion

The reaction between methyl vernolate and boron trifluoride etherate has been studied under three sets of conditions

(U) boron trifluoride etherate (1 5 mole) in boiling dioxan for three hours,
(V) boron trifluoride etherate (0 5 mole) in cold dioxan overnight,
(W) boron trifluoride etherate (0 5 mole) in cold benzene for half an hour

The reaction product, after isolation, is readily separated into one major component (B) and three minor components (A, C and D) by chromatography The products identified in each experiment are set out in table 1

TABLE 1

Reaction products (% wt) from methyl vernolate and boron trifluoride etherate

	U[†]	V[†]	W[†]
non-oxygenated esters (A)	10	2	6
oxo-esters (B)	70	84	65
13-oxocyclopropane (*trans*)*	10	6	13
13-oxocyclopropane (*cis*)*		1	13
9-oxocyclopropane (*cis* and *trans*)		1	8
13-oxo 9*c*	18	20	23
13-oxo 9*t*	-	2	8
12-oxo 9*c*	28	51	–
12-oxo 10*t*	14	–	-
ether	-	3	
fluorohydrins (C)	10	9	19
dihydroxy esters (D)	10	5	10

* Since these are strictly derivatives of heptadecanoic acid they should be 12-oxo derivatives but are here referred to as 13-oxocyclopropanes to emphasise that the oxygen function is still attached to what was originally C(13)

[†] Reaction conditions (see experimental)

Fraction D This is the most polar fraction and is mainly methyl 12,13-dihydroxyoleate It shows a strong O—H stretching band in its infra-red spectrum (3595 cm^{-1}) and is oxidised, under von Rudloff conditions, to nonanedioic acid before hydrogenation and to dodecanedioic acid after hydrogenation

Fraction C This minor component may contain fluorohydrins It showed two major peaks when run on a DEGS column (27 6 and 27 9) but only poorly defined peaks on an ApL column It has the polarity expected of a monohydroxy compound (TLC) and shows O—H (3595 cm^{-1}) and C—F

(1070 cm^{-1}) stretching bands in its infra-red spectrum Compounds of this type were recognised in the earlier study of methyl expoxystearate [1]) When treated again with boron trifluoride etherate (condition U) this fraction was converted to a complex mixture of products including some which resembled the products obtained originally from epoxyoleate

Fraction A This proved to be a complex mixture of esters which probably do not contain any additional oxygen The ultra-violet spectrum indicated the presence of conjugated trienes and oxidative degradation gave octanedioic and nonanedioic acids Its behaviour on GLC and silver ion TLC showed it to contain several polyunsaturated esters Some of these might result from dehydration of esters like coriolic (**3**) but it has not been possible to identify any individual components Additional information is given in the Experimental Section

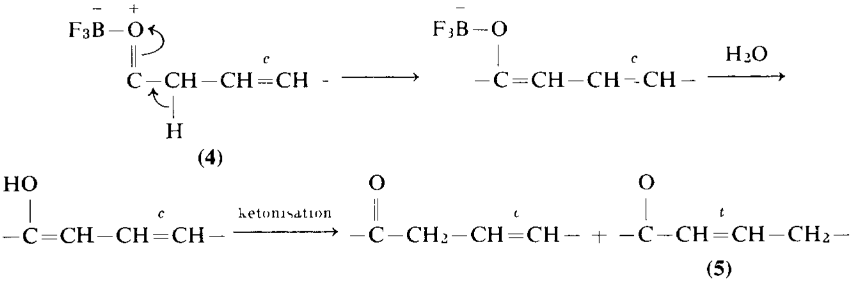
Fraction B It was expected that this major component would be a mixture of methyl 12- and 13-oxo-oleates but, although these were present, several other oxo esters were separated and identified The amounts of these varied with the experimental conditions though minor components shown as absent in experiment U (table 1) may have been overlooked in our early studies Separation was effected mainly by silver ion chromatography but saturated and unsaturated esters were sometimes separated after the latter had reacted with mercuric acetate

Methyl 12-oxo-octadec-trans-10-enoate

This product is only formed under the vigorous reaction condition (U) Its ultra-violet spectrum (λ_{max} at 225 mμ, $E^{1\%}_{1\,cm}$/480) showed the presence of an $\alpha\beta$-unsaturated ketone and the infra-red spectrum revealed a *trans* double band (970 cm^{-1}) conjugated with a ketone (1670 and 1685 cm^{-1}) It was oxidised to decanedioic acid and reduced to an oxostraeate which must have been 12-oxostearate since it gave hendecanedioic and dodecanedioic acids when oxidised with chromic acid We then showed that under these reaction conditions (U) an authentic sample of methyl 12-oxo-oleate (**4**) (another product of this reaction) was partially isomerised ($\sim 30\%$) to the conjugated *trans* isomer (**5**) Methyl 9-oxo-octadec-12-enoate (with the same enone unit as 13-oxo-oleate) was not changed under these conditions Isomerisation probably occurs through the enolised ketone as shown on p 206

Methyl 12- and 13-oxo-oleates

These were not separated from one another and were first identified in admixture with about 10% of the cyclopropane esters to be described later This mixture showed no significant ultra-violet adsorption but the infra-red spectrum indicated carbonyl stretching at the usual positions (1710 and


(4)

(5)

1735 cm^{-1}) and gave no significant evidence of *trans* unsaturation Oxidative fission gave nonanedioic acid as the only dibasic acid along with (presumably) methyl 4-oxononanoate from the 13-oxo ester Hydrogenation gave a mixture of oxostearates * When these were oxidised with chromic acid three major dibasic acids (hendecanedioic, dodecanedioic, and tridecanedioic) were accompanied by small amounts of heptanedioic, octanedioic and nonanedioic acids now known to result from the cyclopropane esters which contaminated this sample To determine the relative proportions of the 12- and 13-oxostearates the oxo esters were converted to oximes, rearranged to amides, and hydrolysed to various products including dodecanedioic acid from 12-oxostearate and tridecanedioic acid from 13-oxostearate[4]) When rearrangement is carried out in dioxan the 12-oxo-oleate and 13-oxo-oleate represent 70 and 30% of the mixture in the benzene reaction 12-oxo-oleate is not formed

Careful separation by silver ion TLC gave a component which resembled the above oxo-oleates in most of its properties but was separated from them This is believed to be methyl 13-oxo-octadec-*trans*-9-enoate Its infra-red spectrum has absorption bands at 1710 and 970 cm^{-1} and von Rudloff oxidation gives nonanedioic acid and (presumably) 4-oxononanoic acid

Cyclopropane esters

The identification of the saturated oxo esters present in Fraction B was facilitated by the discovery that these compounds are obtained in larger amounts when the rearrangement is conducted in benzene (W) and by their characteristic NMR spectra These esters were shown to be mainly the *cis* and *trans* isomers of methyl 9,10-methylene-12-oxoheptadecanoate (**6**) on the basis of the evidence presented below Methyl 11,12-methylene-9-oxoheptadecanoate (**7**) may also be present as a minor component and the

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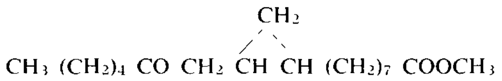
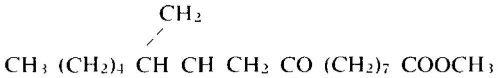
* The cyclopropane esters which accompanied these oxo-oleates were unaffected by both these reactions

evidence for this is discussed later.



$$CH_3(CH_2)_4\,CO\,CH_2\,\overset{CH_2}{CH\;CH}\,(CH_2)_7\,COOCH_3$$

(**6**)



$$CH_3(CH_2)_4\,\overset{CH_2}{CH\;CH}\,CH_2\,CO\,(CH_2)_7\,COOCH_3$$

(**7**)

(i) This mixture behaved like oxo and epoxy esters on thin layers of silica and as saturated esters of this type on silver ion plates. Its saturated nature was confirmed by the fact that it was unchanged after oxidation and after catalytic hydrogenation.

(ii) Gas liquid chromatography showed the presence of two components (table 5) which were only separated on the GLC/MS.

(iii) Significant infra-red absorption bands were observed at 1710 (oxo), 1735 (ester), and 1020 and 3050 cm^{-1} (cyclopropane[5])).

(iv) The NMR spectrum confirmed the absence of olefinic protons and displayed complex signals in the 9.5-10.3 τ region equivalent to four protons and consistent with a mixture of *cis* and *trans* cyclopropanes[6]).

(v) The mass spectrum showed a molecular ion peak of *m/e* 310 and fragmentation consistent with a carbonyl in the position shown in (**6**). The two components of this mixture gave identical spectra. Further details are discussed later.

(vi) Reduced by sodium borohydride, the mixed oxo esters gave two compounds with the chromatographic and spectroscopic properties (absorption bands at 3595, 3050, 1735, and 1020 cm^{-1}) expected of a hydroxy ester.

(vii) Desoxo esters were prepared by reduction of the tosylhydrazones. These had the infra-red spectrum (1020 and 3050 cm^{-1}), NMR spectrum, and retention behaviour on DEGS and ApL columns expected of cyclopropane esters[6, 8]).

(viii) Oxidation of the oxo esters by chromic acid gave nonanedioic, octanedioic, and heptanedioic acids along with hexanoic and pentanoic acids (table 2). The desoxo esters gave the same dibasic acids along with octanoic, heptanoic, and hexanoic acids. The value of this observation, which fixes the position of the cyclopropane ring is discussed later.

(ix) At one stage the rearrangement product was thought to have structure (**10**). This compound was synthesised but differed from both components of the ester mixture in its GLC behaviour, infra-red spectrum, NMR spectrum, and mass spectrum and in the products of chromic acid oxidation.

(x) Finally compound (**12**), a homologue of (**6**), was synthesised in its *cis* form and in a mixture of *cis* and *trans* forms. Allowing for the homologous

TABLE 2

Products of chromic acid oxidation of cyclopropane esters

methyl esters	esters of dibasic acids (area %)					esters of monobasic acids					
	C_{10}	C_9	C_8	C_7	C_6	C_{10}	C_9	C_8	C_7	C_6	C_5
authentic samples											
cis-8,9-methyleneoctadecanoate			61	24	15	+	+	+			
cis-9,10-methyleneoctadecanoate		56	27	17			+	+	+		
cis-10,11-methyleneoctadecanoate	49	28	23					+	+	+	
10,11-methylene-12-oxoheptadecanoate	+	+	+								
cis-9,10-methylene-12-oxo-octadecanoate		57	34	9					+		
desoxo ester from above		60	24	16			+	+	+		
rearrangement products											
9,10-methylene-12-oxoheptadecanoate		55	30	15						+	
desoxo ester from above		57	25	18							

relation between (**6**) and (**12**), they agreed in their infra-red spectra, NMR spectra, mass spectra, GLC behaviour, and in the products of chromic acid oxidation

Other cyclopropane esters

In a careful study of Fraction B a subfraction was obtained from one reaction product (W) which had similar chromatographic, NMR, and infra-red properties to the mixed oxo cyclopropane esters just discussed but was separated from these in a very slight but real manner on silver ion TLC This may be the 11,12-methylene-9-oxo ester and the mass spectrum of this component supports this view (see below)

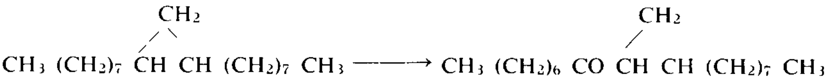
The 'ether' components

Another mixed component isolated from Fraction B had carbon numbers of 22 3 and 23 2 (DEGS) and 18 5 and 19 5 (ApL) The infra-red spectrum showed no carbonyl group other than ester and no *trans* unsaturation It had peaks at 1055 and 1215 cm^{-1}, possibly indicative of ethers Following Goldsmith⁹) who isolated several cyclic ethers in the reaction of gerianiolene epoxide with born trifluoride, it is possigle that some saturated cyclic ethers have been formed in this rearrangement

Chromic acid oxidation of cyclopropane esters

This reaction was sufficiently useful in the determination of structure to merit futher comment Using authentic samples⁶) we found that oxidation consistently furnished three dibasic acids and three monobasic acids Since these are easily recognised by GLC the structure of the cyclopropane ester is readily determined Our results on authentic compounds and on compounds isolated in our rearrangement studies are summarised in table 2

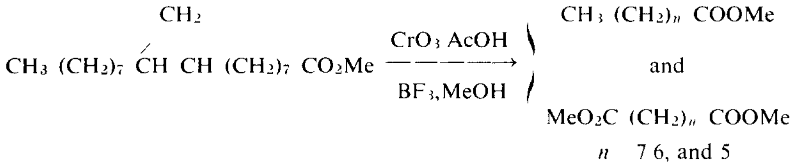
Prome and Asselineau¹⁰) have since described the chromic acid oxidation of the long-chain cyclopropane (**8**) They claim that the major product (**9**), which they later examined by mass spectroscopy as means of a structure determination,¹¹) was accompanied by three monobasic acids [nonanoic (12%) octanoic (5%), and heptanoic (3%)]



$$CH_3(CH_2)_7\overset{CH_2}{CH\,CH}(CH_2)_7CH_3 \longrightarrow CH_3(CH_2)_6CO\overset{CH_2}{CH\,CH}(CH_2)_7CH_3$$

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

This suggests that we are examining secondary oxidation products, nevertheless the procedure is a valuable method of determining the position of a cyclopropane ring in a long-chain ester For example

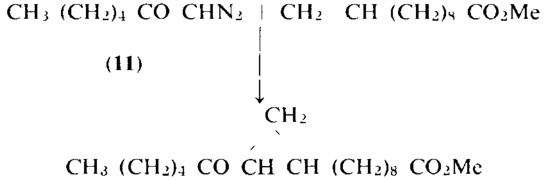


$$CH_3(CH_2)_7\overset{CH_2}{CH\;CH}(CH_2)_7CO_2Me \xrightarrow[BF_3,MeOH]{CrO_3\,AcOH} \left\{\begin{array}{c} CH_3(CH_2)_nCOOMe \\ \text{and} \\ MeO_2C(CH_2)_nCOOMe \end{array}\right.$$

n 7 6, and 5

Synthesis of methyl 10,11-methylene-12-oxoheptadecanoate [1-(8'-carbomethoxyoctyl),2-(hexanoyl)cyclopropane]

This compound (**10**) was prepared following the procedure recently described by Lefort *et al*[12]) by the reaction of the diazoketone (**11**) with methyl hendecenoate



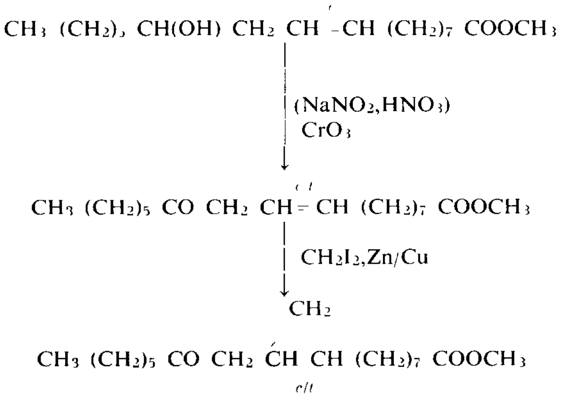
$$\begin{array}{c} CH_3(CH_2)_4CO\,CHN_2 + CH_2\;CH(CH_2)_8CO_2Me \\ \textbf{(11)} \quad \downarrow \\ CH_3(CH_2)_4CO\overset{CH_2}{CH\;CH}(CH_2)_8CO_2Me \end{array}$$

(**10**)

The product, with its oxo group conjugated to the cyclopropane unit, differs in its chromatographic and spectroscopic properties from the isomeric non-conjugated compound (**6**) isolated from our rearrangement reaction

Synthesis of methyl cis- *and* trans-*9,10-methylene-12-oxo-octadecanoates [1-(7'-carbomethoxyheptyl),2-(2'-oxo-octyl)cyclopropane]*

These homologues of the rearrangement product (**6**) were readily prepared by the Simmonds-Smith reaction[6]) on methyl 12-oxo-oleate prepared from methyl ricinoleate and also on a mixture of the *cis* and *trans* isomers prepared from the mixed methyl esters of castor oil which had been partially isomerised



$$\begin{array}{c} CH_3(CH_2)_5CH(OH)CH_2\overset{c}{CH{=}CH}(CH_2)_7COOCH_3 \\ \downarrow \scriptstyle (NaNO_2,HNO_3)\;CrO_3 \\ CH_3(CH_2)_5CO\,CH_2\overset{c\,t}{CH{=}CH}(CH_2)_7COOCH_3 \\ \downarrow \scriptstyle CH_2I_2,Zn/Cu \\ CH_3(CH_2)_5CO\,CH_2\underset{c/t}{\overset{CH_2}{CH\;CH}}(CH_2)_7COOCH_3 \end{array}$$

(**12**)

Mass spectra of the oxo cyclopropane esters

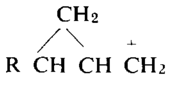
In addition to the peaks normally associated with long-chain esters, many of the major peaks in these spectra can be interpreted in terms of the expected cleavage γ or β to the carbonyl group There is also some evidence of peaks arising from the cyclopropylmethylene cation (**13**) and form the rearrangement shown in (**14**)→(**15**) followed by allylic cleavage (See table 3)

TABLE 3

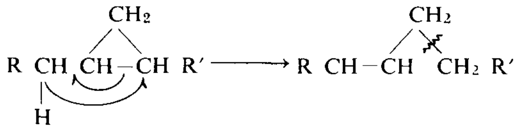
Mass spectra of some oxo cyclopropane esters
(*m/e* values and percentage of base peak)

	A*		B*		C*		D*	
molecular ion	324		310		310		310	
base peak	113		99		97		99	
α-cleavage to the C=O grp	113	(100)	99	(100)	153	(37)	99	(100)
	239	(2)	239	(1)	185	(68)	239	(9)
	207	(4)	207	(3)	153	(37)	207	(16)
β-cleavage to the C=O grp	128	(3)	114	(3)	168	(42)	254	(9)
	254	(6)	254	(3)	200	(5)	222	(11)
	222	(2)	222	(2)	168	(42)		
β-cleavage to cyclopropane (**13**)	181	(5)	167	(5)	125	(97)	153	(16)
	239	(2)	239	(1)	253	(5)		
	207	(4)	207	(3)	221	(3)		
allylic cleavage after	141	(20)	127	(16)	213	(5)	197	(4)
rearrangement (**14**→**15**)	153	(24)	139	(21)	181	(58)	165	(18)
					225	(18)		
					193	(5)		

* A (**11**, synthetic) methyl 9,10-methylene-12-oxo-octadecanoate
* B (**6**, rearrangement product) methyl 9,10-methylene-12-oxoheptadecanoate
* C (**7**, rearrangement product) methyl 11,12,-methylene-9-oxoheptadecanoate
* D (**10** synthetic) methyl 10,11-methylene-12-oxoheptadecanoate



(**13**)



(**14**) (**15**)

Related isomerisations and mechanism

We have confirmed the earlier observation[1]) that saturated epoxy esters give equal amounts of the two possible oxo esters as major rearrangement products With methyl 9,10-epoxyoctadec-12-ynoate also there was no evidence of cyclised products but the unsaturated centre had a considerable influence on the relative amounts of the 9-oxo (5%) and 10-oxo (95%) esters formed These are the results of reactions occurring in dioxan solution in benzene solution oxo esters seem not to be formed

The rearrangement of methyl vernolate is also affected considerably by a change of solvent from dioxan to benzene In particular (i) the yield of cyclopropane ester is much lower in dioxan (8–10%) than in benzene (34%), (ii) the cyclopropane is mainly *trans* in the dioxan reaction, in benzene it is equally *cis* and *trans*, and (iii) in dioxan solution the total yield of "12-oxo" esters* is slightly greater than the total yield of "13-oxo" esters† (see table 4) whereas in benzene solution no ' 12-oxo ' esters are obtained

TABLE 4

Effect of solvents on the yield of 12-oxo and ' 13-oxo' esters* during epoxide rearrangement

ester	solvent	Fraction B %	12-oxo esters* %	13-oxo esters* %
12,13-epoxyoleate	benzene	65	–	100
12,13-epoxyoleate	dioxan	84	60	40
12,13-epoxystearate	dioxan	81	50	50
9,10-epoxyoctadec-12-ynoate†	dioxan	89	95†	5†

* See footnote to table 1

† This ester actually gave 10-oxo(95 %) and 9-oxo(5 %) esters but these are represented in the equivalent 12-oxo 13-oxo ratio

Our views on the mechanism of this reaction are summarised in Scheme 1 The catalyst reacts with the epoxide to furnish the oxonium ion (**16**) which has potential carbonium ion character (**17** and **18**) The first of these is the source of the 12-oxo-oleate which reacts further under vigorous conditions to give the conjugated enone ester Carbonium ion (**18**) is a homoallylic cation and such ions are now known to be capable of behaving as highly stabilised cyclopropylmethylene ions (**19**)[13 17]) This undergoes rearrangement to (**20**), perhaps through a non-classical carbonium ion, and then yields the oxo cyclopropane esters (**6**) Carbonium ion (**18**) gives methyl 13-oxo-oleate and stereomutation of the double bond probably results from the resonance of (**18**) and (**19**) The 9-oxocyclopropane esters (**7**) may be formed through a cyclic ether such as (**21**)

With saturated epoxides rearrangement occurs only in the more polar solvent (dioxan) when the two carbonium ions (like **17** and **18**) are solvent-

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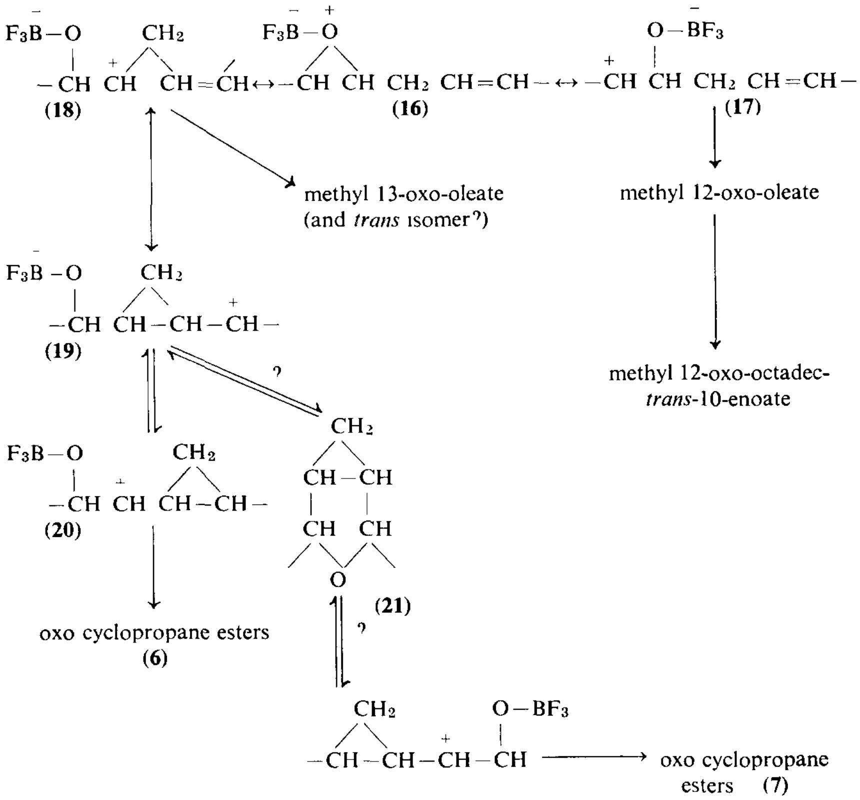
* See footnote to table 1

SCHEME I

The rearrangement of methyl vernolate under the influence of boron trifluoride



stabilised and reaction occurs equally through each of them With epoxy oleate all the ions (**17**)–(**20**) are formed and in the presence of dioxan lead to similar total amounts of "12- and 13-oxo" esters* with a slight advantage to the "12-oxo" compounds [illegible] We have no satisfactory explanation of the very uneven distribution of products with the acetylencic epoxide

In the benzene solution the rearrangement of saturated (and acetylenic) epoxides to ketones does not occur and olefinic epoxide gives derivatives of "13-oxostearate" [illegible] only This suggests that in the absence of a polar solvent carbonium ion (**17**) becomes unimportant and reaction occurs only through that carbonium ion (**18**) which is stabilised through the resonance possibilities of homo-allylic cations

Although long-chain cyclopropane acids occur naturally this is the

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* See footnote to table I

first report of their formation by interaction of an appropriately placed double bond and an ionic centre produced during a reaction There are many reactions of acids such as ricinoleic or linoleic or linolenic during which homoallylic cations may be formed and the formation of cyclopropanes during such reactions may be more general than is yet realised Already there is evidence that cyclopropanes can be formed in high yield from appropriate derivatives of ricinoleic acid 18 19)

Experimental

General

All solvents were dried and distilled before use Petroleum refers to the fraction boiling between 40 and 60

TLC was carried out with thin layers of silica (0 3 mm for analytical purposes and 1 mm for preparative purposes) When required, silver nitrate (15%) was incorporated into the silica layer The developing solvent was ether mixed with benzene or petroleum and these mixtures are indicated by symbols such as PE30 indicating a 70 30 mixture of petroleum and ether

A Pye 104 was used for GLC It was fitted with a column (5′ × ¼″) packed with Gas Chrom Z (70–80 mesh) coated with diethylene glycol succinate (DEGS, 20%) or with Apiezon L (ApL, 5%) and normally operated at 190 or 210 respectively A list of carbon numbers (equivalent chain lengths) observed during this investigation is given in table 5

TABLE 5

Carbon numbers (equivalent chain lengths) of methyl esters used in this investigation

methyl esters	DEGS	ApL
cis-12,13-epoxystearate	24 0	19 3
cis-12,13-epoxyoleate	24 6	19 1
cis-9,10-epoxyoctadec-12-ynoate	26 0	19 1
12-oxostearate	24 9	19 4
12-oxo-oleate	25 3	19 1
12-oxo-octadec-*trans*-10-enoate	26 8	19 9
4-oxononanoate	15 2	10 3
cis-9 10-methylene-12-oxoheptadecanoate	25 6	19 2
trans-9,10-methylene-12-oxoheptadecanoate	24 8	18 8
cis-9,10-methylene-12-hydroxyheptadecanoate	26 4	–
trans-9,10-methylene-12-hydroxyheptadecanoate	25 7	-
cis-9,10-methyleneheptadecanoate	18 6	17 8
trans-9 10-methyleneheptadecanoate	18 0	17 4
10,11-methylene-12-oxoheptadecanoate	25 2	19 1
10,11-methylene-12-hydroxyheptadecanoate	25 7	-
cis-9,10-methylene-12-oxo-octadecanoate	26 6	20 2
trans-9,10-methylene-12-oxo-octadecanoate	25 8	19 8

Infra-red spectra were run on Perkin Elmer spectrophotometers (137, 237, or 621) using thin films in sodium chloride discs or solutions in carbon disulphide (1%) in 1 mm pathlength cells Ultra-violet spectra were recorded in methanol solution with a Unicam SP 800 spectrophotometer A Perkin Elmer R10 spectrometer (60 Mc/sec) was used to record NMR spectra on 15% solutions in carbon tetrachloride

Methylation was carried out with boron-trifluoride/methanol20) and von Rudloff oxidation as recommended by Tulloch and Craig 21)

The chromic acid oxidation of saturated long-chain esters containing hydroxy, oxo or cyclopropane groups was based on the procedure of Smith *et al* 22) Hydrogenated ester (15 mg) in acetic acid solution (2 ml) was stirred at room temperature for two hours with a solution of chromium trioxide (120 mg) in acetic acid (2 ml) After dilution with water (25 ml), excess of oxidant was destroyed with sulphur dioxide, and the oxidation products extracted with petroleum (2 × 10 ml) These were usually methylated and examined by GLC The results of some of these oxidations are collected together in table 2

The structure and composition of mixed oxo esters was determined by the following procedure based on Cobern *et al* 4) Hydrogenated oxo ester (60 mg) was refluxed with hydroxylamine hydrochloride (50 mg) and fused sodium acetate (60 mg) in water/ethanol (1 4, 3 ml) After four hours the mixture was diluted with water (2 ml), extracted with ether (2 × 25 ml), and the recovered oximes (60 mg) heated at 110 for two hours with concentrated sulphuric acid (2 ml) After careful addition of water (2 ml), through the condenser to the cooled amide solution, the mixture was refluxed for two hours Dibasic acids were extracted from the acidic reaction mixture, methylated and examined by GLC

Catalytic hydrogenation was effected with 10% palladium charcoal at atmospheric pressure Methanol was generally used as solvent

Preparation of epoxy and oxo esters used in this investigation

Methyl *cis*-12,13-epoxystearate was prepared from synthetic methyl octadec-*cis*-12-enoate (350 mg, 1 2 m mole) by reaction overnight at room temperature with an ethereal solution of mono-perphthalic acid (5 ml, 2 2 mole) The epoxy ester (320 mg) was purified by preparative TLC Methyl oleate was converted to methyl *cis*-9,10-epoxystearate in the same way

Methyl *cis*-9,10-epoxyoctadec-12-ynoate was prepared from the crepenynic acid present in *Afzelia cuanzensis* seed oil23) by epoxidation of the mixed methyl esters and isolation of the required epoxide by TLC 24)

Methyl *cis*-12,13-epoxyoleate (vernolate) was isolated from *Vernonia* *anthelmintica* seed oil. The oil (20 g) was neutralised by percolation through a short column of alumina (4 × 1″, 100–200 mesh, Type H, P. Spence and Sons Ltd.) using chloroform as solvent. The neutralised oil (16.9 g) was shaken overnight with dry methanolic sodium methoxide (220 ml. 0.02 *N*) poured into water (750 ml), acidified to *p*H4 with sulphuric acid (0.1 *N*), and immediately extracted with ether (3 × 250 ml) to give Vernonia esters (13.4 g). These (7.2 g) were chromatographed on a column of silica (250 g, Whatman SG31) and eluted with petroleum containing increasing proportions of ether. Methyl vernolate (2.9 g), eluted predominantly with PE20, was over 98% pure (TLC and GLC) and contained only traces of methyl oleate and linoleate.

Methyl 12-oxo-oleate was prepared by oxidation of castor oil methyl esters by chromic acid 25).

Isomerisation of epoxy esters with boron trifluoride etherate

(U) Methyl vernolate (350 mg, 1.1 m mole) was refluxed for three hours in anhydrous dioxan (20 ml) with boron trifluoride etherate (0.25 ml, 2.0 m mole) and the product (345 mg) recovered by ether extraction after dilution with water. Methyl 12-oxo-oleate (30 mg) treated similarly gave a mixture (28 mg) of starting material (70%) and methyl 12-oxo-oxtadec-*trans*-10-enoate (30%).

(V) Methyl vernolate (2.0 g, 6.5 m mole) was stirred at room temperature overnight in anhydrous dioxan (100 ml) with boron trifluoride etherate (0.4 ml, 3.2 m mole) to give the rearrangement product (1.98 g).

(W) Methyl vernolate (1.14 g. 3.7 m mole) reacted in anhydrous benzene (50 ml) with boron trifluoride etherate (0.25 ml, 2.0 m mole) for half an hour at room temperature and gave 1.09 g of product. In boiling benzene an intractable product was obtained.

Separation procedures

(a) The reaction product (0.3–1.0 g) was first chromatographed on silica gel (100–200 g Whatman SG31) with petroleum containing increasing amounts of ether. Eluted material was monitored by TLC (PE30) and combined to give four major components. Fraction A (2–10%) eluted with PE10, Fraction B (64–84%, PE20–PE40), Fraction C (9–19%, PE40–PE80), and Fraction D (5–13%, PE60-ether). The recovery of material was generally greater than 95%.

(b) Since methyl 12-oxo-oleate autoxidises very rapidly on silver ion TLC this method of separation was suitable only when this ester was not formed (reaction in benzene) or could be sacrificed. In a typical example Fraction B (90 mg from experiment W) was separated by preparative silver ion TLC into three fractions. B1, 36 mg, carbon numbers on DEGS 24.8 (50%) and

25 6(50%), B1a, 19 mg, 24 8(34%), 25 3(48%), and 25 6(18%), B2, 29 mg, 25 3(100%)

(c) Component B3 (methyl 12-oxo-octadec-*trans*-10-enoate), which was only formed under reaction conditions U, was separated from two other components (B1 and B2) by silver ion TLC (PE25) when it ran with B1 ahead of B2, followed by TLC (PE10) when it ran behind B1

(d) The saturated components of Fraction B (100 mg from experiment V) were recovered after reaction overnight with a stock solution (2 ml) made by dissolving mercuric oxide (1 4 g) in a mixture of methanol (25 ml) acetic acid (0 3 ml), and water (1 ml) 26) The solvent was removed below 30 and the residue extracted with ether and recovered by preparative TLC Silver ion TLC of the unreacted esters (15 mg) gave B1, 10 mg, carbon numbers on DEGS 22 7(7%), 24 8(80%), and 25 6(13%) B1a 1 mg, and B2, 2 mg On a larger scale 72 mg of B1 was recovered from 900 mg of Fraction B

Products obtained from reaction with methyl vernolate

Most of the results obtained by using general methods already detailed have been given in the Discussion Further results are given in the tables and only additional information is given here

Fraction A The ultra-violet spectrum contained peaks at 233, 257, 267, and 277 mμ and the infra-red spectrum showed significant absorption at 945, 970, and 980 cm^{-1} After hydrogenation, it showed the same GLC behaviour as methyl stearate Attempts to separate the components of this fraction by silver ion TLC and to examine them by partial hydrazine reduction were unsuccessful GLC on DEGS and ApL columns gave several peaks and the following tentative conclusions were made about the composition of Fraction A (from Experiment W) esters with a conjugated diene and an isolated double bond (15%), carbon numbers 21 2 and 21 7 (DEGS) and 18 0 and 18 4 (ApL), esters with a conjugated triene (28%), 23 2 and 23 7 (DEGS) and 19 2 and 19 5 (ApL) unidentified esters (57%) 23 2 and 23 7 (DEGS) and 18 4 and 18 8 (ApL)

Reduction of the oxo group in Fraction B1 7) (Methyl *cis* and *trans*-9,10-methylene-12-oxo-heptadecanoate) This mixture (17 mg) was refluxed with tosylhydrazine (27 mg) in methanol containing concentrated sulphuric acid (6 ml, 1%) and the recovered tosylhydrazone (32 mg) refluxed overnight with sodium borohydride (100 mg) in methanol (10 ml) The desoxo esters (5 mg after TLC, PE20) were oxidised with chromic acid (table 2)

Isomerisation of methyl 12,13-epoxystearate

In cold dioxan (V), methyl 12 13-epoxystearate (125 mg) gave a product (120 mg) which was separated by preparative TLC (PE30) into Fractions B

(81%), C(10%), and D(8%) The major fraction (carbon number 24 9 (DEGS) and 19 4 (ApL), infra-red absorption bands at 1710 and 1735 cm^{-1}) gave dodecanedioic (51%) and tridecanedioic (49%) when submitted to oximation and Beckmann rearrangement

Fraction C showed O—H(3595 cm^{-1}) and C—F(1070 cm^{-1}) absorption in its infra-red spectrum and a single peak on GLC (27 5, DEGS) Fraction D showed O—H absorption (3595 cm^{-1}) in its infra-red spectrum

Isomerisation in benzene solution gave an intractable product which did not seem to contain any oxo-esters

Methyl 9,10-epoxystearate gave corresponding results both in dioxan and in benzene solution

Isomerisation of methyl 9,10-epoxyoctadec-12-ynoate

In cold dioxan (V), this acetylenic epoxide (100 mg) gave a product (100 mg) separated by preparative TLC (PE30) into Fractions B (89%) C (8%), and D (3%)

The major component showed oxo absorption (1720 cm^{-1}) in its infra-red spectrum After hydrogenation [carbon numbers 24 9 (DEGS) and 19 4 (ApL)] oximation, and Beckmann rearrangement, nonanedioic (5%) and decanedioic (95%) acids were obtained The oxo ester was reduced by sodium borohydride (carbon number of trimethylsilyl ether 21 4 on DEGS) and then hydrogenated (carbon number of trimethylsilyl ether 19 8 on DEGS)

Isomerisation in benzene gave polymeric material (TLC) and no identifiable components (GLC)

Synthesis of methyl 10,11-methylene-12-oxoheptadecanoate

Hexanoyl chloride (2 8 g 0 021 mole) in anhydrous ether (50 ml) was added gradually to a stirred dry ethereal solution of diazomethane (250 ml, 0 067 mole) Ether and excess of diazomethane were removed under nitrogen and the residue extracted with dry petroleum (100 ml), gave the diazoketone (2 8 g)

Methyl hendecenoate (7 0 g, 0 035 mole) in cyclohexane (15 ml distilled from sodium wire) containing anhydrous copper sulphate (1 5 g, heated to 200 for four hours immediately before use) was stirred at 87–90 during the dropwise addition over four hours of a solution of diazoketone (2 8 g, 0 020 mole) and methyl hendecenoate (3 0 g, 0 015 mole) in cyclohexane (15 ml) After cooling, filtering, and removing cyclohexane, the residue (13 0 g) gave the oxo cyclopropane ester by preparative TLC (PE20)

The synthetic ester showed only small signals around 9 5 τ in its NMR spectrum and had infra-red bands at 1685, 1730, 1030, and 3070 cm^{-1}

After reduction with sodium borohydride it furnished a hydroxy ester with infra-red bands at 3595, 1020, and 3050 cm^{-1} and distinctive cyclopropane signals at 9.55–9.75 τ in its NMR spectrum.

Synthesis of methyl 9,10-methylene-12-oxo-octadecanoates

Zinc dust (2.0 g) was added to vigorously stirred, nearly boiling acetic acid. After one minute cupric acetate monohydrate (0.4 g) was added and the mixture stirred for two minutes until the blue colour disappeared. The hot supernatant liquid was decanted and the residue washed with acetic acid (5 × 20 ml) and ether (5 × 20 ml).

Di-iodomethane (4 ml) and methyl 12-oxo-oleate (215 mg) were added to the zinc/copper couple suspended in ether (10 ml), and the solution refluxed overnight. The ether was then decanted and washed with cold dilute hydrochloric acid (1 *N*, 3 × 10 ml) and water (3 × 10 ml). After removal of ether and excess of di-iodomethane, the cyclopropane ester (150 mg) was isolated by preparative silver ion TLC (PE25).

A mixture of *cis* and *trans* cyclopropane esters was prepared in the same way starting with methyl *cis*- and *trans*-12-oxo-octadec-9-enoates. These oxo esters were themselves prepared by oxidation of castor oil methyl esters (2.16 g) which had been vigorously stirred for fifteen minutes with a mixture of nitric acid (2 ml, 50%) and sodium nitrite solution (1 ml, 15%).

Both the *cis* and the *trans* isomers have infra-red absorption bands at 1710, 1735, 1020, and 3050 cm^{-1}. In the NMR spectrum the *cis* cyclopropane has a signal at 10.2 τ and the *cis trans* mixture has signals at 9.7 and 10.2 τ. The two samples have identical mass spectra.

By reduction of the tosylhydrazones the mixed *cis trans* oxo esters were converted to their desoxo derivatives.

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