Fatty Acids: Part 26.[1]
Partial Synthesis of C_{18} Mono- and Dimethyl Furanoid Fatty Esters

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ABSTRACT

Dimethylene interrupted dioxo derivatives of 10, 13-epoxy-11-methylocadeca-10, 12-dienoate (from latex) and 9 (10), 12 (13)-epoxyoctadeca-9 (10), 11 (12)-dienoates (from linoleate) were successfully methylated at the methylene carbons located between the two oxo groups using methyl iodide and KOH in DMSO. The resulting dimethyldioxo derivatives were cyclodehydrated to furnish methyl 10, 13-epoxy-11, 12-dimethyloctadeca-10, 12-dienoate and a mixture of methyl 9(10), 12(13)-epoxy-10(11), 11(12)-dimethyloctadeca-9(10), 11(12)-dienoate. Similarly, methylation at C-11 of methyl 12-oxo-octadec-*cis*-9-enoate (from methyl ricinoleate) gave methyl 9, 12-epoxy, 11-methyloctadeca-9, 11-dienoate on cyclodehydration.

INTRODUCTION

Furanoid fatty acids isolated from the lipid extracts of fish have all been found to contain a methyl group at the 3-position of the furan system and in some cases at the 4-position as well (2-5). The furanoid fatty acid isolated from the latex of the rubber tree (*Hevea brasiliensis*), however, is a single C_{18} isomer with a methyl group exclusively at the 3-position of the furan ring (6).

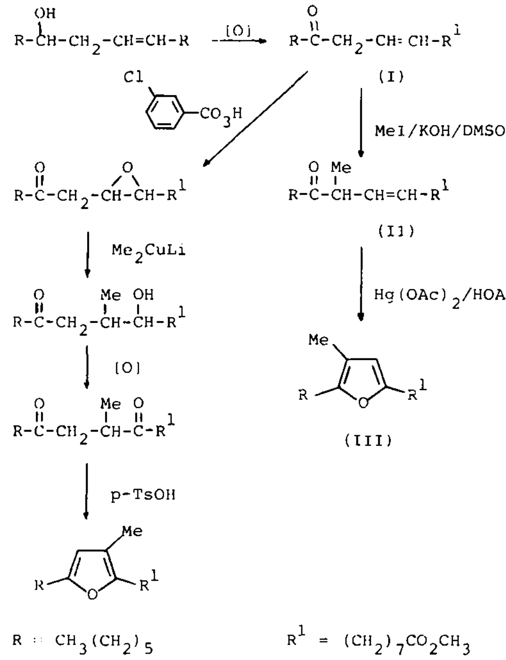
This paper reports the results of the preparation of mono and dimethyl furanoid fatty esters from methyl linoleate and ricinoleate, and a pure dimethyl C_{18} isomer from the furanoid ester obtained from the latex of the rubber plant. (Monomethyl and dimethyl furanoid refer to furanoid esters containing a methyl substituent at the 3- or 4-position and both 3,4-positions of the furan ring, respectively.)

Schlenk et al. (7) have prepared a naturally occurring mono- and a dimethyl C_{20} furanoid ester by total synthesis. Lie Ken Jie and Sinha (8) have demonstrated the ease of chain extension of the C_{18} furanoid ester to its C_{20} homologue. Our aim has been to obtain by partial synthesis similar compounds from more readily available starting material.

RESULTS AND DISCUSSION

Linoleic, ricinoleic and several other naturally occurring fatty acids have been shown to be readily convertible to furanoid ester derivatives (9, 10). Lie Ken Jie and Lam (9) succeeded in producing a C_{18} monomethyl furanoid ester from methyl ricinoleate as summarized in Scheme 1.

In view of the fact that the 3- and 4-positions of the furan system of furanoid esters are difficult to substitute by direct methylation, our efforts were concentrated on the methylation of the dioxostearate derivatives which could readily be obtained through acid methanolysis of the respective furanoid ester (11) or by introducing the methyl group(s) at an intermediate stage prior to furan formation. Johnstone et al. (12) reported the use of a mixture of methyl iodide, potassium hydroxide and dimethyl sulfoxide to effect methylation of acidic methylene groups. Thus, our treatment of a dimethylene interruped dioxostearate isomer with the same reagent (MeI/KOH/DMSO) permitted selective methylation of the more acidic methylene carbons located between the oxo functions. Methyl 9, 12-dioxostearate gave 75% methyl 10, 11-dimethyl-9, 12-dioxostearate after 48 hr of reaction with MeI/KOH/DMSO. However, this reaction period produced also a trace ($\sim$5%) of a trimethylated fatty ester as shown by the gas liquid chromatography (GLC) and mass spectrometry (MS) analyses. The attempt to increase the yield of dimethyl derivatives by manipulating reaction time and reactant concentration was also further accompanied by a substantial increase of trimethylation at C-2 (Scheme 2).



SCHEME 1. Preparation of monomethyl furanoid ester from methyl ricinoleate.

Methylation of the dioxo derivative obtained from the latex furanoid ester furnished 78% of dimethyl furanoid ester (Scheme 3). Similarly, methylation by the same procedure of oxidized methyl ricinoleate gave predominantly methyl 11-methyl-12-oxooctadec-9-*cis*-enoate. The presence of a double bond at C-9 favored alkylation at C-11. The latter was converted to the corresponding monomethyl furanoid ester by treatment with mercuric acetate in glacial acetic acid (Scheme 1).

METHODS

Analytical (AR) grade solvents were used for the present work and, where required, solvents were dried and distilled before use. Column and thin layer chromatography (TLC) were carried out by the standard procedure. Generally, petroleum ether (40-60 C) with increasing amount of diethyl ether was used as eluent for column chromatography. Details of spectroscopic methods are described in Part 5 (13). Mass spectra were run at 70 eV and the data are presented in the order: m/z, source of fragment, intensity

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[1] For part 25, see reference 1.

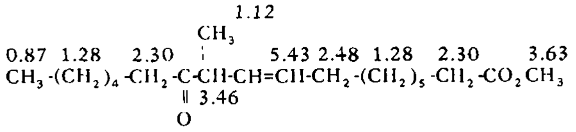
relative to base peak = 100. ^1H Nuclear magnetic resonance (NMR) studies were carried out on a JEOL FX90 model (90 MHz) instrument.

Preparation of Monomethyl Furanoid Ester from Methyl Ricinoleate (Scheme 1)

Methyl 12-oxo-octadec-9-*cis*-enoate (**I**) was prepared by the method of Gunstone et al. (14).

A mixture of powdered KOH (1.12 g, 0.02 M) and DMSO (2 mL) was stirred at 20 C for 10 min. Methyl 12-oxooctadec-9-*cis*-enoate (**I**, 1.45 g, 0.005 M) was added, followed by methyl iodide (1.42 mL, 0.01 M), and the reaction mixture was further stirred for 1 hr. Water (50 mL) was added and the reaction mixture extracted with diethyl ether (3 × 20 mL). The combined ether extract was thoroughly washed with water, dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (25 g sillica gel) to give TLC pure compound **II** (69% yield).

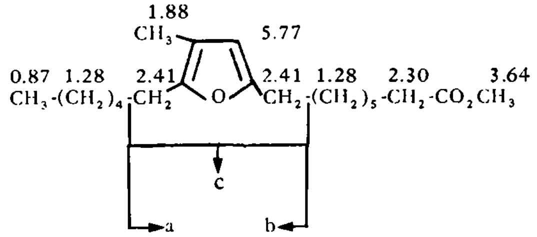
IR (cm^{-1}): 1740 (νC=O), ester); 1710 (νC=O, Oxo). NMR (δ):



$$\overset{0.87}{\mathrm{CH_3}}\text{-}\overset{1.28}{\mathrm{(CH_2)_4}}\text{-}\overset{2.30}{\mathrm{CH_2}}\text{-}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\text{-}\overset{\overset{1.12}{\mathrm{CH_3}}}{\underset{3.46}{\mathrm{CH}}}\text{-}\overset{5.43}{\mathrm{CH{=}CH}}\text{-}\overset{2.48}{\mathrm{CH_2}}\text{-}\overset{1.28}{\mathrm{(CH_2)_5}}\text{-}\overset{2.30}{\mathrm{CH_2}}\text{-}\overset{3.63}{\mathrm{CO_2CH_3}}\qquad \mathbf{(II)}$$

Methyl 12-oxo-11-methyloctadec-9-*cis*-enoate (**II**) was converted to methyl 9, 12-epoxy-11-methyloctadeca-10, 12-dienoate (**III**, 50% yield) using mercuric acetate and glacial acetic acid (9).

IR (cm^{-1}): 3100 (νC-H, furan); 1745 (νC=O, ester); 1580, 1640 (νC=C, furan), and 1020 (ring breathing). NMR (δ):



(III)

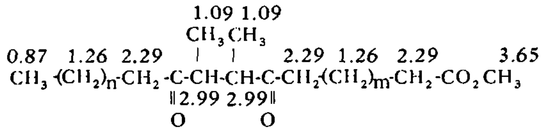
MS (70 eV): 322 (M^+, 44), 251 (a, 100); 179 (b, 73); 109 (c+1, 53).

Preparation of Dimethyl Furanoid Ester from Methyl Linoleate (Scheme 2)

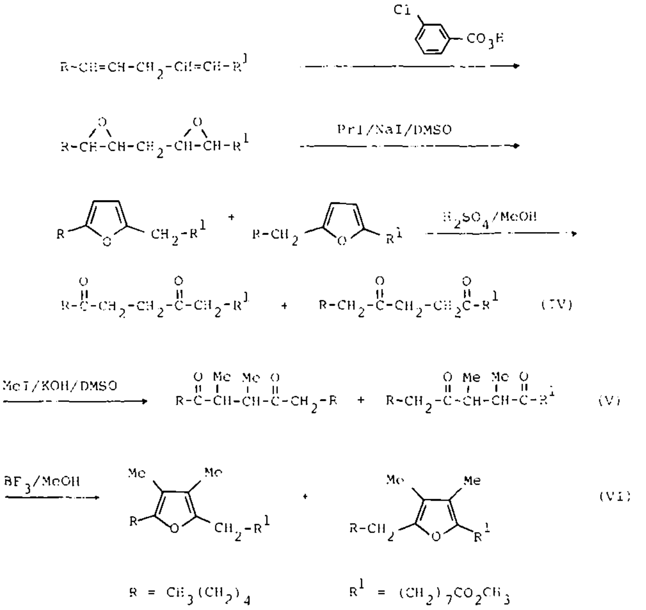
A mixture of 9 (10), 12 (13)-epoxyoctadeca-9 (10), 11 (12)-dienoate was prepared from methyl linoleate (9). Acid methanolysis (H_2SO_4/MeOH) of the latter (11) gave the corresponding mixture of dimethylene interrupted C_{18} dioxo derivatives (**IV**) in 42% yield based on the amount of methyl linoleate used.

Treatment of the dioxostearates (**IV**, 0.97 g, 0.003 M) with KOH (1.0 g, 0.018 M) and methyl iodide (1.7 mL, 0.012 M) in DMSO (2 mL) at 60 C for 48 hr gave after column chromatographic purification of the extract a mixture of dimethyl dioxostearates (**V**) in 74% yield.

IR (cm^{-1}): 1740 (νC=O, ester), 1710 (νC=O, Oxo). NMR (δ).



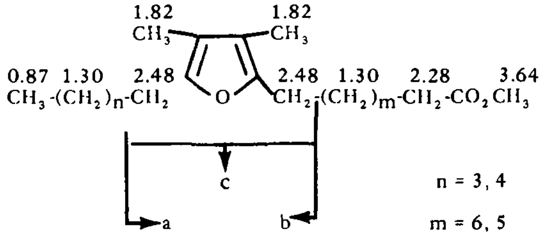
$$\overset{0.87}{\mathrm{CH_3}}\text{-}\overset{1.26}{\mathrm{(CH_2)_n}}\text{-}\overset{2.29}{\mathrm{CH_2}}\text{-}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\text{-}\overset{\overset{1.09}{\mathrm{CH_3}}}{\underset{2.99}{\mathrm{CH}}}\text{-}\overset{\overset{1.09}{\mathrm{CH_3}}}{\underset{2.99}{\mathrm{CH}}}\text{-}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\text{-}\overset{2.29}{\mathrm{CH_2}}\text{-}\overset{1.26}{\mathrm{(CH_2)_m}}\text{-}\overset{2.29}{\mathrm{CH_2}}\text{-}\overset{3.65}{\mathrm{CO_2CH_3}}\qquad \mathbf{(V)}$$



SCHEME 2. Preparation of dimethyl furanoid esters from methyl linoleate.

Subsequent treatment of the dimethyl dioxostearate (**V**) with BF_3/MeOH (11) furnished a mixture of methyl 9 (10), 12 (13)-epoxy-10 (11), 11 (12)-dimethyloctadeca-9 (10), 11 (12)-dienoate (**VI**). The product (78% yield) was purified by chromatography (20 g silica gel), but gas liquid chromatographic analysis (DEGS) indicated 50% purity only (ECL = 22.0).

IR (cm^{-1}): 1740 (νC=O, ester), 1580, 1670 (νC=C, furan ring). NMR (δ):



(VI)

n = 3, 4

m = 6, 5

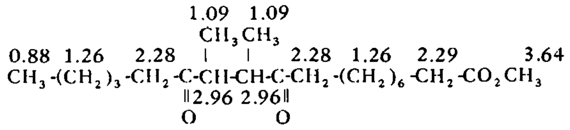
MS (70 eV): 336 (M^+, 55); 279, 293 (a, 100, 85); 179, 193 (b, 44, 34); 123 (c+1, 53); 305 (M-31, 22).

Preparation of Dimethyl Furanoid Ester from Latex Furanoid Ester (Scheme 3)

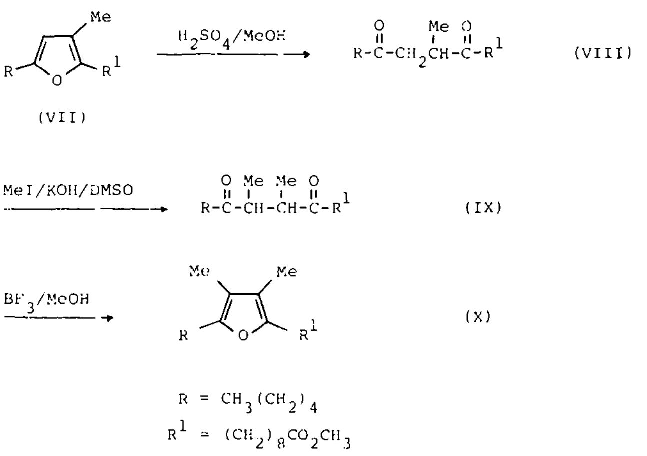
Methyl 10, 13-epoxy-11-methyloctadeca-10, 12-dienoate (**VII**) was isolated from the latex of the rubber plant (*Hevea brasiliensis*) (6), and converted to methyl 10, 13-dioxo-11-methylstearate (**VIII**, 39% yield) using 10% H_2SO_4 in methanol (11).

A mixture of dioxostearate (**VIII**, 0.85 g, 0.0025 M), KOH (0.84 g, 0.015 M), DMSO (2 mL) and methyl iodide (1.42 mL, 0.01 M) was stirred at 60 C for 40 hr. The product (**IX**, 65% yield) was isolated and purified by column chromatography (sillica gel, 20 g).

IR (cm^{-1}): 1740 (νC=O, ester); 1710 (νC=O, Oxo). NMR (δ):



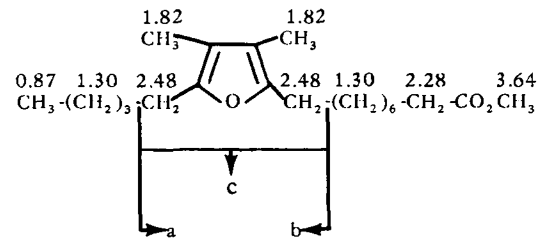
$$\overset{0.88}{\mathrm{CH_3}}\text{-}\overset{1.26}{\mathrm{(CH_2)_3}}\text{-}\overset{2.28}{\mathrm{CH_2}}\text{-}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\text{-}\overset{\overset{1.09}{\mathrm{CH_3}}}{\underset{2.96}{\mathrm{CH}}}\text{-}\overset{\overset{1.09}{\mathrm{CH_3}}}{\underset{2.96}{\mathrm{CH}}}\text{-}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\text{-}\overset{2.28}{\mathrm{CH_2}}\text{-}\overset{1.26}{\mathrm{(CH_2)_6}}\text{-}\overset{2.29}{\mathrm{CH_2}}\text{-}\overset{3.64}{\mathrm{CO_2CH_3}}\qquad \mathbf{(IX)}$$



SCHEME 3. Methylation of latex furanoid ester.

Methyl 10, 13-dioxo-11, 12-dimethylstearate (**IX**) was refluxed with BF_3 in MeOH (11), which gave on purification methyl 10, 13-epoxy-11, 12-dimethyloctadeca-10, 12-dienoate (**X**, 89%). GLC analysis (DEGS) indicated 68% purity only (ECL = 22.05).

IR (cm^{-1}): 1740 (νC=O, ester); 1580, 1640 (νC=C, furan), and 1010 (ring breathing). NMR (δ):



(X)

MS (70 eV): 336 (M^+, 59%); 279 (a, 100); 179 (b, 43); 305 (M-31, 18); 123 (c+1, 49).

ACKNOWLEDGMENTS

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