SHORT COMMUNICATIONS

Stereospecific Synthesis of *cis* and *trans* Fatty Esters

ABSTRACT

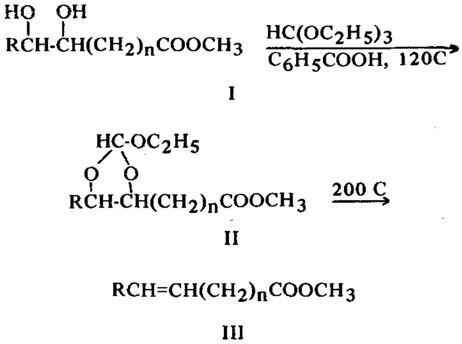
The *erythro* and *threo* isomers of methyl 9,10-dihydroxyoctadecanoate and the *threo* isomer of methyl 12,13-dihydroxy-*cis*-9-octadecenoate were converted into methyl *cis*- and *trans*-9-octadecenoate and methyl *cis*-9,*trans*-12-octadecadienoate, respectively, by reaction of the dihydroxy ester with triethyl orthoformate to give the 2-ethoxy-1,3-dioxolane which was thermally decomposed to the unsaturated ester.

INTRODUCTION

1,2-Diols have been converted stereospecifically into alkenes via dibromides (1), benzylidene acetals (2), cyclic thiocarbonates (3-7), dimesylates (8), and by direct reaction with phosphonium iodide in acetic acid (9). Gunstone and Jacobsberg (10) have successfully applied two of these reactions to the fatty acid field. They were able to convert methyl *threo*-12,13-dimesyloxyoleate to methyl *cis*-9,*trans*-12-octadecadienoate in 58% conversion (80% yield after allowing for unreacted dimesylate). Yield is not given, however, on the preparation of the dimesylate. The 9*c*,12*t*-18:2 ester was also obtained from methyl *threo*-12,13-dihydroxyoleate through the cyclic thiocarbonate but no yields are given for this route.

RESULTS AND DISCUSSION

We have successfully applied a reaction first described by Crank and Eastwood (11) and Josan and Eastwood (12) which is convenient and simple to carry out, uses readily available reagents, and gives better than 80% conversion of the diol to the desired alkene. In this reaction, the dihydroxy ester, I, is heated slowly with triethyl orthoformate and an acid catalyst to form ethanol and the 2-ethoxy-1,3-dioxolane, II. This product may be isolated, if desired, by distillation from a basic solution. However, for preparing the alkene, it is only necessary to heat the unisolated intermediate slowly to about 200 C, at which point it decomposes to ethanol, CO_2, and the unsaturated ester, III.



$$\overset{\text{HO}}{\text{RCH}}\text{-}\overset{\text{OH}}{\text{CH}}(\text{CH}_2)_n\text{COOCH}_3 \xrightarrow[\text{C}_6\text{H}_5\text{COOH, 120C}]{\text{HC(OC}_2\text{H}_5)_3}$$

I

$$\text{RCH-CH(CH}_2)_n\text{COOCH}_3 \xrightarrow{200\text{ C}}$$

II

$$\text{RCH=CH(CH}_2)_n\text{COOCH}_3$$

III

We have applied this reaction to the stereospecific conversion of methyl *erythro*- and *threo*-9,10-dihydroxystearates into methyl oleate and elaidate, respectively, and methyl *threo*-12,13-dihydroxy-*cis*-9-octadecenoate into methyl *cis*-9,*trans*-12-octadecadienoate.

Silver ion thin layer chromatography (Ag-TLC) and gas liquid chromatography (GLC) on OV275 were used for *cis-trans* separation and identification. Retention times for the several isomers were determined with authentic samples and compared well with the results obtained.

^{13}C nuclear magnetic resonance (NMR) spectroscopy also served to demonstrate the identity and purity of the products. The chemical shift is about $\delta 27.3$ for carbon atoms alpha to a *cis* double bond and about $\delta 32.7$ for carbon atoms alpha to a *trans* double bond. The oleate prepared here showed a peak at $\delta 27.23$ and none at $\delta 32.7$, while the elaidate showed a peak at $\delta 32.69$ and none at $\delta 27.23$. Analyses of weighed mixtures indicated that less than 4% of one isomer could be detected in a mixture with the other isomer.

In the 9,12-diene, the pertinent chemical shifts were C8 $\delta 27.25$; C11, $\delta 30.55$; C14, $\delta 32.70$. The chemical shift for a methylene group between two double bonds is $\delta 25.75$ if both are *cis*, $\delta 35.70$ if both are *trans*, and $\delta 30.55$ if one double bond is *cis* and the other is *trans* (13). Thus, this diene is 9-*cis*,12-*trans*.

EXPERIMENTAL PROCEDURE

Gas liquid chromatography was conducted on a Packard 7400 series gas chromatograph with a flame ionization detector. The glass column (4 mm x 20 ft) was packed with 15% OV275 on 100/120 mesh Gas Chrom P-AW-DMCS and operated at 200 with a flow of 35 ml/min of He at a pressure of 37 psi.

Thin layer chromatography was carried out on Precoated TLC Silica Gel 60 F254 plates (E. Merck) impregnated with silver nitrate, and developed in 100% benzene.

^{13}C NMR spectroscopy was conducted on a Bruker WH 90 Fourier Transform NMR spectrometer operating at 22.63 MHz.

Methyl *trans*-9-Octadecenoate

threo-9,10-Dihydroxystearic acid (mp 94 C) was converted with methanol and sulfuric acid to the methyl ester in 95% yield. In a small distillation apparatus were placed methyl *threo*-9,10-dihydroxystearate (0.8 g, 0.0024 mole), triethyl orthoformate (0.8 g), and benzoic acid (0.03 g). The pot was heated slowly in an oil bath to 120 C and the theoretical amount of ethanol was collected. The pot was then heated slowly to 210 C and all volatile material was collected. After cooling to room temperature, the pot contents were passed through a column (15 mm ID) packed with silica gel (5 g). The first 50 ml of petroleum ether eluate contained 0.68 g (0.0023 mole, 95% yield) of methyl elaidate. This material gave one spot on Ag-TLC and showed about 4% of ethyl benzoate and no methyl oleate on GLC.

Methyl *cis*-9,*trans*-12-Octadecadienoate

Vernonia anthelmintica seed oil was acetolyzed, saponified, and esterified as described by Gunstone (14). The mixture of *Vernonia* methyl esters was separated on a silica gel chromatographic column into a nonhydroxy fatty ester fraction (21%) (PE:EE-90:10) and methyl *threo*-12,13-dihydroxy-*cis*-9-octadecenoate (79%) (PE:EE-50:50). This dihydroxy ester (3.8 g, 0.0115 mole) was placed in the pot of a small distillation apparatus together with triethyl orthoformate (1.8 g, 0.0122 mole) and benzoic acid (0.05 g). The pot was heated slowly in an oil bath to 120 C and kept at this temperature for 0.5 hr while distillate was collected. The temperature was then raised slowly to 210 C and all volatile material was collected. The pot contents were passed through a column (15 mm ID) containing silica gel (8 g). The first 100 ml of petroleum ether eluate contained 2.77 g (82%) yield) of methyl *cis*-9,*trans*-12-octadecadienoate. GLC showed the presence of about 1.5% ethyl benzoate and no methyl linoleate. Ag-TLC showed one spot which ran a little ahead of methyl linoleate and a little behind methyl oleate.

HENRY RAKOFF
EDWARD A. EMKEN
Northern Regional Research Center
ARS, USDA
Peoria, IL 61604

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