enoic, heptadecanoic, eicosenoic and tetracosanoic acids; all but pentadecenoic acid (1.6% by area) were less than 1%. The fatty acids with an odd number of carbon atoms, viz. 9:0, 11:0, 13:0, 13:1, 15:1 and 17:0, were found in small quantities amounting to 2.2% in total.

The protein content of all the defatted seed meals ranged from 21.3-37.5% by weight (Table I), which is lower than that of usual oilseed meals, but adequate enough to be useful as a cattle and poultry feed. The protein from leucaena is of high nutritional value and compares well with the nutritive value of alfalfa (12). However, leucaena is toxic to nonruminants when the levels of mimosine reach ca. 10% in the diet. New, low mimosine varieties are now in an advanced stage of development (12).

The mineral composition of the defatted meals were comparable with our earlier reports on *Acacia* (3) and *Bauhinia* (4).

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♣Oxidative Cyclization of 1-Octadecanol and Hydroxy Fatty Esters with Lead Tetraacetate

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ABSTRACT

Oxidative cyclization of methyl 2-hydroxyoctadecanoate, methyl 10-hydroxyundecanoate and 1-octadecanol produced a good yield of the corresponding tetrahydrofuran (THF) derivatives characterized successively as methyl 2,5-epoxyoctadecanoate, methyl 7,10-epoxyundecanoate and 1,4-epoxyoctadecane. The structure of these cyclic derivatives have been established by elemental analyses and spectral studies.

INTRODUCTION

Lead tetraacetate (LTA) oxidation of monohydric alcohols bearing a carbon hydrogen bond in the γ-position represents a valuable synthetic route to tetrahydrofuran derivatives. The fact that cyclization proceeds via hydrogen abstraction at an unactivated position (γ-carbon hydrogen bond) places this transformation among a class of highly useful reactions for controlled functionalization of remote intramolecular position. This reaction has received attention primarily in short-chain alcohols. Abbot and Gunstone (1) have reported the formation of 1,4- and 1,5-epoxides from long-chain hydroxy esters with LTA and with silver oxide/bromine and mercuric oxide/iodine. Continuing our work (2) on the synthesis of fatty acid derivatives with LTA, an attempt has been made to prepare long-chain heterocyclic derivatives of potential physiological interest. The present paper describes the synthesis of THF derivatives from 1-octadecanol and the fatty esters containing a hydroxy group at the penultimate carbon and in close proximity to the ester function, using benzene, dimethyl formamide (DMF) and dimethyl sulphoxide (DMSO) to study the solvent effect.

EXPERIMENTAL PROCEDURES

Infrared (IR) spectra were obtained with a Perkin-Elmer 621 Spectrophotometer (liquid films). Nuclear magnetic resonance (NMR) spectra were obtained on a Varian A60 spectrometer. Chemical shifts were observed in ppm with tetramethylsilane as the internal standard. The abbreviations s, t, m and br denote singlet, triplet, multiplet and broad. Mass spectra were recorded on a JEOL JMS-D300 spectrometer at 70 eV. Column and thin layer chromatography (TLC) were carried out by standard procedures using light petroleum and diethyl ether as the developing solvent.

MATERIALS AND METHODS

2-Hydroxyoctadecanoic acid was prepared from α-brominated product (3) by hydrolysis, as described by Sweet and Estes (4). 10-Hydroxyundecanoic acid was obtained by solvomercuration demercuration (5) of 10-undecenoic acid. 1-Octadecanol was prepared by a lithium aluminium hydride reduction of stearic acid by the procedure of Gunstone and Inglis (6).

Acids were converted to methyl esters using methanolic sulphuric acid (0.25 M) and LTA was freshly prepared (7).

Reaction of Methyl 2-Hydroxyoctadecanoate (*1a*) with LTA

The hydroxy ester (1 g, 3.1 mmol) in benzene (20 mL) and LTA (1.37 g, 3.1 mmol + 10% excess) were refluxed for 3 hr. When a starch iodide test showed complete consumption of tetravalent lead, dry ether (20 mL) was added to the reaction mixture. After keeping the mixtures for 1-2 hr at 5 C, lead diacetate was removed by filtration and was subsequently washed twice with benzene to extract the

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reaction product. The combined filtrates were diluted with ether, washed successively with 5% aqueous sodium bicarbonate and water and then dried. The removal of solvent yielded a brown viscous oil that on analytical TLC showed a major spot along with *1*a.

The major compound (*2*a, 55.4%) was purified by silica gel column chromatography eluting with petroleum ether/ether (98:2, v/v).

Reaction of Methyl 10-Hydroxyundecanoate (*1*b) with LTA

A mixture of methyl 10-hydroxyundecanoate (1 g, 4.6 mmol), LTA (2.03 g, 4.6 mmol + 10% excess) and benzene (20 mL) was refluxed and worked up as described earlier to yield an oily yellowish liquid. This product showed a distinct spot on TLC along with the spot of unreacted ester. Purification by column chromatography as usual gave the product (2b, 51%), which was judged pure by TLC.

Reaction of 1-Octadecanol (*1*c) with LTA

1-Octadecanol (1 g, 3.7 mmol) taken in benzene (20 mL) was refluxed with LTA (1.63 g, 3.7 mmol + 10% excess) with frequent interruptions in heating. After 3 hr, a brownish viscous oil was produced. TLC showed 3 spots, one distinct major spot and a very faint spot, possibly for 1,5-epoxide, along with the starting material. Silica gel column chromatographic separation gave only one TLC homogeneous product (*2*c, 59%).

RESULTS AND DISCUSSION

The procedure of Micovic et al. (8) for oxidative cyclization of hydroxy compounds was followed in the present investigation.

Reaction of methyl 2-hydroxyoctadecanoate (*1*a) with an equimolar quantity of LTA in benzene resulted in the formation of methyl 2,5-epoxyoctadecanoate (*2*a, Scheme 1) as a pleasant smelling liquid. Increasing the amount of LTA to 1.5-2.0 mol per mol of hydroxy ester did not appreciably increase the yield.

The IR spectrum of *2*a showed the expected (9) bands at 1750 ($COOCH_3$) and 1260, 1190, 1160 and 1020 cm^{-1} (C—O). The disappearance of the band at 3420 cm^{-1} indicated the participation of hydroxy function in oxidative cyclization. Its NMR spectrum was more informative about the assigned structure. In addition to the familiar signals of fatty esters, 2 characteristic signals were observed at 3.90 ppm and 4.37 ppm ascribable to ring protons adjacent to ether function. The signal at 3.90 ppm is attributed to the proton on the fatty acid chain side. The signal for the other equivalent ring alpha proton appeared farther down the spectrum at 4.37 ppm, because the adjacent ester carbonyl group removed the shielding effect. This indicated the presence of a THF ring in close proximity to the ester function.

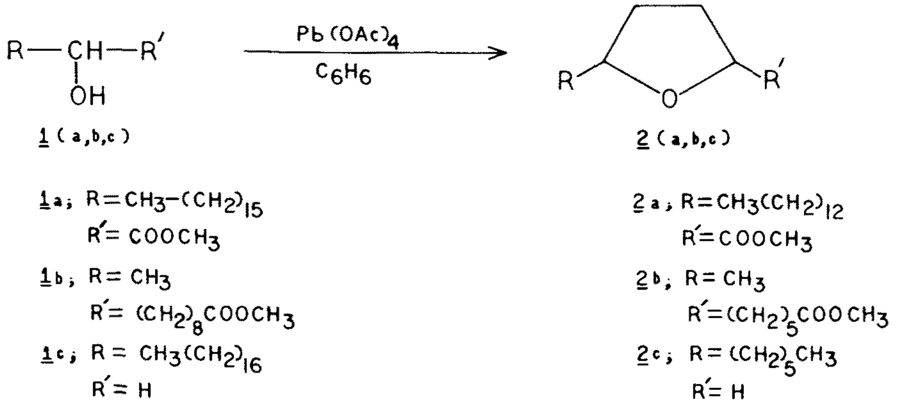
Confirmation of the structure *2*a as a 2,5-epoxy (THF) derivative was obtained from the mass spectral (MS) analysis. In addition to the molecular ion peak at 312 (3, $M^{+\cdot}$), other significant peaks included 253 (5, b), 235 (1.2, b-18), 225 (100, d), 211 (5, b-42), 129 (11, a), 102 (2, c), 101 (17, a-28), 97 (37, a-32) and 87 (10, a-42). These ions are considered to arise from the cleavage indicated in Scheme 2.

A similar reaction of methyl 10-hydroxyundecanoate (*1*b) with LTA in the final stage yielded a liquid that was characterized as methyl 7,10-epoxyundecanoate (*2*b, Scheme 1). In the IR spectrum, besides an absorption at 1740 cm^{-1} ($COOCH_3$), other characteristic THF ring C—O stretching bands of moderate intensity were observed at 1240, 1190, 1160, 1095 and 1010 cm^{-1}. The hydroxyl had disappeared from the product (*2*b). Its NMR spectrum contained a multiplet (3H) at 1.20 ppm for the terminal methyl protons. The appearance of these protons farther down the spectrum can be attributed to the presence of a THF ring at the penultimate. The chemical shifts for the 2-ring protons to the ether oxygen were the same (3.90 ppm) in this case.

The 7,10-epoxide fragmented on MS in a similar way, giving a molecular ion peak at 214 (6, $M^{+\cdot}$). The base peak at 85 results from cleavage b and other significant peaks 199 (54, a), 172 (6, c), 171 (6, a-28), 167 (17, a-32), 157 (8, a-42), 67 (22, b-18), 57 (40, b-28) and 43 (85, b-42) arise from the fragmentation shown in Scheme 3.

Likewise, on treating 1-octadecanol (*1*c) with LTA, the above procedure furnished the product (*2*c) of oxidative cyclization. The resulting THF derivative was characterized as 1,4-epoxyoctadecane (*2*c, Scheme 1). Its IR spectrum showed the absence of a hydroxyl band (3350 cm^{-1}) as observed in earlier products. However, the spectrum displayed other bands at 1230, 1060 and 1040 cm^{-1} characteristic of C—O. Its NMR spectrum exhibited the structure revealing a diagnostic 3-proton multiplet at 3.80 ppm for proton α to the ether oxygen. Further, the signal for 4 equivalent ring protons were observed farther down the spectrum at 1.80 ppm as a multiplet confirmed the presence of a THF ring.

The 1,4-epoxide (*2*c) resulting from the cyclization of 1-octadecanol had the expected (10) MS with a molecular ion peak at 268 (0.9 $M^{+\cdot}$). (All MS values quoted are m/z and figures in parentheses denote the intensity relative to the base peak = 100 along with source of the ions.) An intense peak at 71 (a > 100) showed the presence of a



SCHEME 1

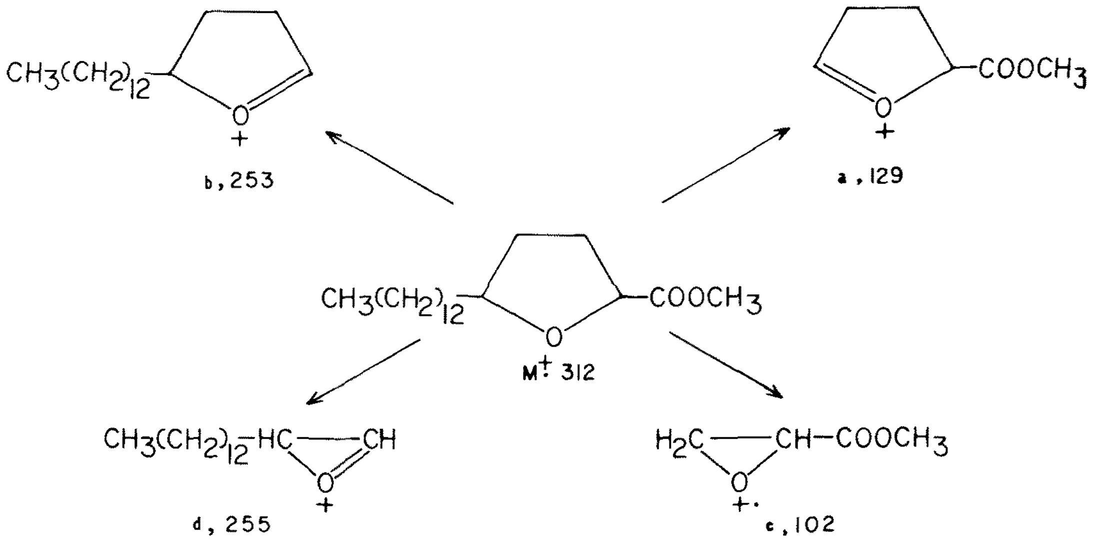
THF ring. Other significant peaks at 57 (94, a-14), 55 (100, a-16) and 43 (a-28>100) dominated the spectrum, possibly because of fragmentation of the ring after α-cleavage. Other major peaks were observed at 267 (3.3, b), 70 (55, a-1), 69 (79, 70-1), 68 (33, 69-1), 56 (47, 57-1) and 44 (5.6, c) as shown in Scheme 4.

The 1,4-epoxides synthesized from the reaction of alcohol and hydroxy fatty esters with LTA in the presence of benzene were found to be identical in all respects (spectral data, elemental analysis, TLC and Co-TLC) with the 1,4-epoxides obtained in presence of DMF and DMSO.

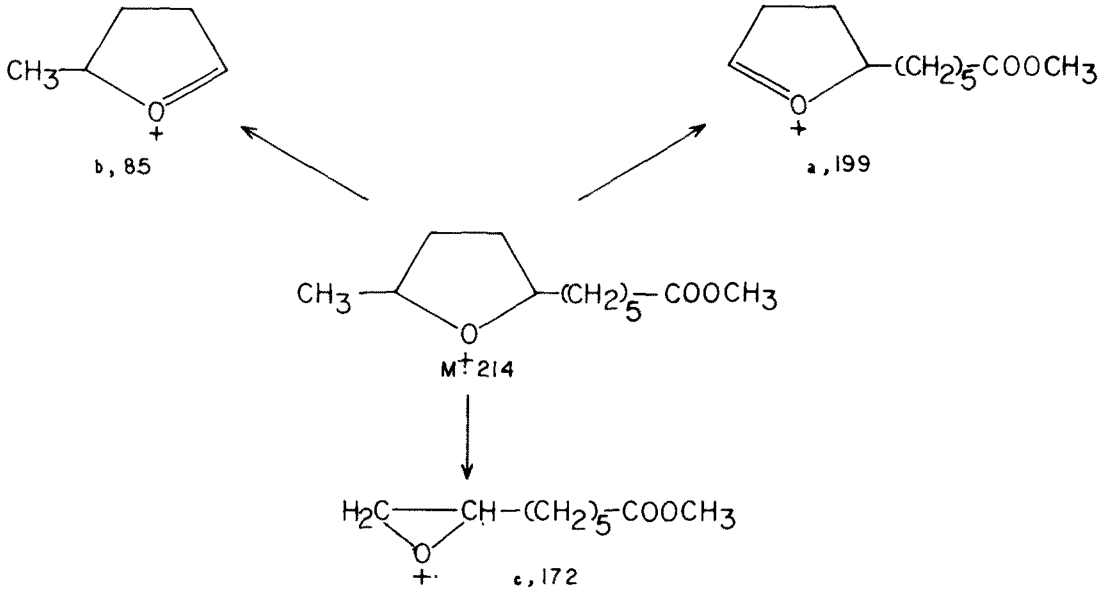
The boiling point, polarity and nature of the solvent affect the yield of 1,4-epoxides by ca. 8% in the sequence, benzene > DMF > DMSO, which may be rationalized as follows.

The lowering of yield in polar solvents could be explained by the high reflux temperature of DMF (153 C) and DMSO (189 C) apparently required for oxidation. In the presence of polar solvents, the reaction gives a high yield of carbonyl compounds (11). The important factor (12) involving the lowering of the yield of 1,4-epoxy derivatives may be that the heterolytic cleavage of the O—Pb bond in the alkoxy lead triacetate (type a) with the elimination of an α-proton is favored in polar solvents (Scheme 5). Finally, the least formation of 1,4-epoxide in LTA-DMSO can be accounted for by its hygroscopic nature.

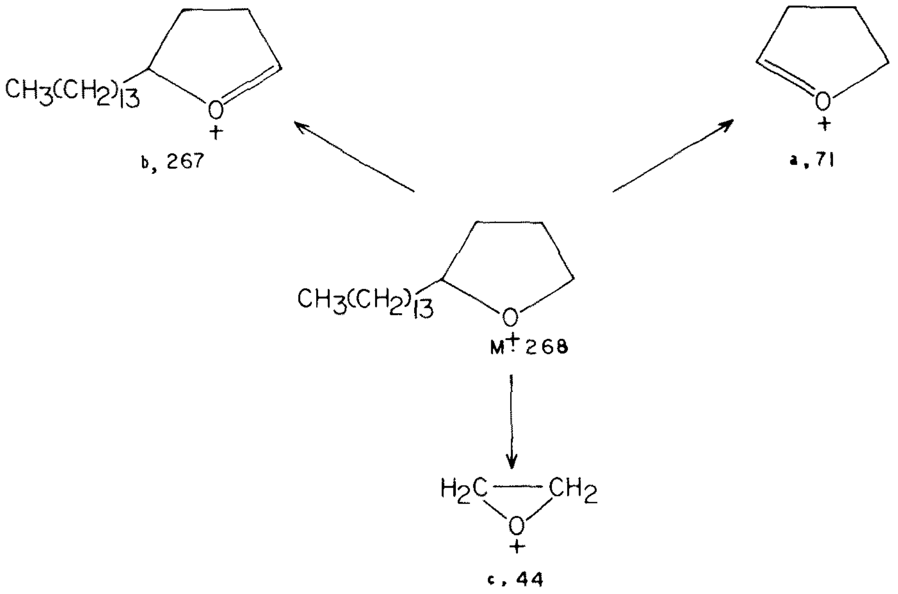
A comparative study of the 2 well-known methods used for the preparation of 1,4-epoxides reveals some advantages of the LTA method over the oxymercuration-demercuration (OM-DM) technique (10). The LTA method is one step and mild, and involves a free-radical process. On the other hand, the OM-DM method has been reported to be a 2-step reaction and proceeds through a mercurinium ion. The wide applicability of LTA reagent may also be explained in terms of the involvement of a hydroxy grouping located at any position in the chain. Contrary to it, the OM-DM method is restricted to the hydroxyolefinic function being positioned appropriately.



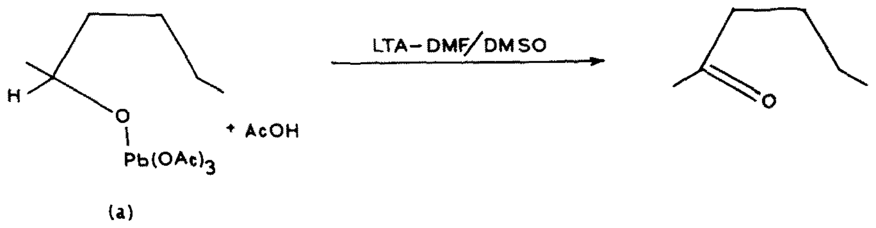
SCHEME 2



SCHEME 3



SCHEME 4



SCHEME 5

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