Improved Preparation of 9,10,12,13-Tetrahydroxystearic Acids from *anti-cis,cis*-9,10,12,13-Diepoxystearic Acid[1]

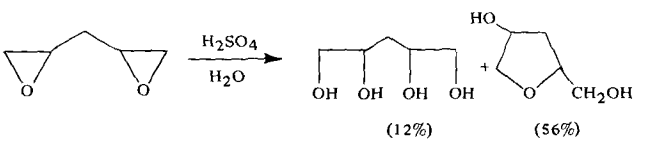
MOHAMMED A. KHUDDUS, YUTAKA USUI, and **DANIEL SWERN,** Fels Research Institute and Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122
Pennsylvania 19122

ABSTRACT

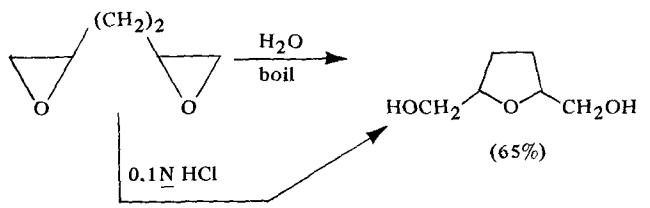
A mixture of isomeric 9,10,12,13-tetrahydroxystearic acids (*threo,threo,threo* and *threo,erythro,threo*) can be prepared from *anti-cis,cis*-9,10,12,13-diepoxystearic acid in over 80% yield by way of the intermediate di(hydroxy-alkoxysulfonium) salts and in ca. 68% yield by way of the intermediate di(hydroxy-formate) esters obtained by acid-catalyzed epoxide ring opening with dimethyl sulfoxide and formic acid, respectively. Mechanisms and stereochemistry of formation of the two isomers are discussed. Factors that influence the formation of cyclic products in competition with tetrahydroxystearic acids also are described. The key to the greatly improved yield of tetrahydroxystearic acids over prior literature procedures is avoiding water during ring opening of the protonated epoxide, as even small quantities of water cause marked reduction in yields of tetrahydroxystearic acids.

INTRODUCTION

The stereospecific conversion of monoepoxides to 1,2-dihydroxy compounds in high yields by acid-catalyzed hydrolysis is well documented. In contrast, diepoxides, in which the oxirane groups are separated by one or two carbon atoms, give low yields of tetrols; the major products are 5- or 6-membered ring ethers. Paul and Tchelitcheff (1), for example, studied the aqueous acid (H_2SO_4) hydrolysis of diepoxypentane and reported the formation of a dihydroxytetrahydrofuran as the major product (56%) and 1,2,4,5-tetrahydroxypentane as the minor product (12%).

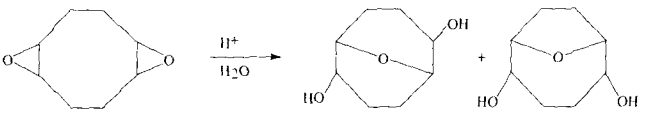


Wood and Wiggins (2) observed that hydrolysis of 1,2,5,6-diepoxyhexane with boiling water yields a tetrahydrofuran derivative as the major product (65%) but *none* of the expected tetrahydroxyhexane. Similar results were obtained by Ross (3) using 0.1N HCl.



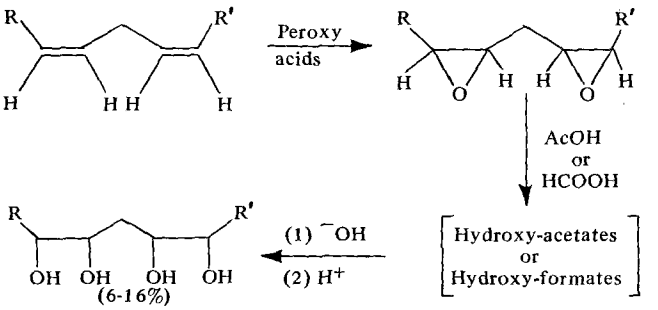
Cope and coworkers (4) showed that 1,2,5,6-diepoxycyclooctane gives bicyclic ethers in 100% yield on treatment with aqueous sulfuric acid but no tetrols.

[1]Presented in part at the AOCS Meeting, Ottawa, September 1972.



The formation of cyclic ethers from the diepoxides is explained by a mechanism involving solvolytic opening of one of the oxirane groups in the first step, followed by nucleophilic substitution on the second oxirane group by one of the hydroxyl groups. Craig and coworkers (5), on the other hand, reported that 1,2,4,5-diepoxycyclohexane gives the expected tetrols in quantitative yield on acid hydrolysis. In this case, intramolecular cyclization should be difficult, because of the strained rings that would be formed.

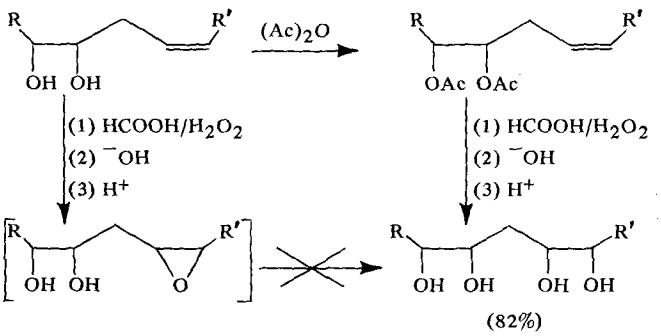
Among long chain diepoxides, the acid-catalyzed hydrolysis of 9,10,12,13-diepoxystearic acid derived from linoleic acid has long been of continuing interest to lipid chemists (6-9). Yields of 9,10,12,13-tetrahydroxystearic acids (THSA) of only 6-16% have been obtained from linoleic acid on reaction with hydrogen peroxide and acetic (6) or formic acid (7-9) followed by hydrolysis (Scheme 1). The cyclic 5-membered or 6-membered cyclic ethers were presumed to be the major product(s), even though it was not possible to isolate, separate, and characterize them at the time.



(Linoleic acid: R = Me[CH_2]$_4$⁻, R' = [CH_2]$_7$⁻COOH.)

Scheme 1.

In contrast, Bharucha and Gunstone (10) obtained high yields (82%) of tetrahydroxystearic acids from 12,13-dihydroxy-Δ^9-*cis*-octadecenoic acid by first acetylating the hydroxyl groups prior to epoxidation and then hydrating the oxirane ring with simultaneous removal of the acetate groups (Scheme 2).



(R = Me[CH_2]$_4$⁻, R' = -[CH_2]$_7$COOH).

Scheme 2.

When the dihydroxyoctadecenoic acid was epoxidized prior to acetylation, however, and the oxirane group then was hydrated, only cyclic ethers were formed. The reason for the failure to obtain tetrols in the latter case seems obvious, i.e., free hydroxyl groups are undesirable and assist cyclization. Two isomers of THSA were isolated by Bharucha and Gunstone; they had mp of 147.5-148.5 C and 121-122 C. Configurational assignments for the isolated THSA were not made, but later Wood et al. (11) obtained the same isomers by potassium permanganate oxidation of *trans,trans*-linoleic acid. The higher mp isomer was assigned the *threo,threo,threo*-configuration (TTT-THSA) and the lower mp isomer the *threo,erythro,threo*-configuration (TET-THSA), based upon information obtained from synthetic ratios, gas liquid chromatography (GLC), relative complexation with arsenite as shown by thin layer chromatography (TLC), and mp.

Previous workers were not concerned with the stereochemistry of the starting material (9,10,12,13-diepoxystearic acid) and of the resulting products (9,10,12,13-tetrahydroxystearic acid[s]) nor with their configurational interrelationships. The reasons for cyclization in competition with the formation of tetrahydroxystearic acid(s) generally were ignored. This investigation was undertaken to attempt to clarify some of these unresolved problems.

EXPERIMENTAL PROCEDURES

Preparation of *anti-cis,cis*-9,10,12,13-Diepoxystearic Acid

Linoleic acid (112 g, 0.40 mol) was placed in a 2-l three-neck flask immersed in an ice bath. Peroxyacetic acid (1000 g of 1 M in an acetic acid solution), in which sodium acetate (8.2 g, 0.1 mol) had been dissolved, was added for 30 min with efficient stirring, while maintaining reaction temperature at 10-15 C during the addition and for an additional 4 hr. The reaction mixture was poured into ice-water (3 liter), and the white precipitate was filtered with suction, washed with several liters of cold water, and dried under vacuum. The crude product was dissolved in warm methanol (250 ml), and the solution was cooled overnight at 0 C. The crystals were filtered, washed with a small quantity of cold methanol, and dried under vacuum to yield moderately pure *anti-cis,cis*-9,10,12,13-diepoxystearic acid, mp 76-79 C (12). Recrystallization from ethanol (150 ml) yielded the pure compound (30 g), mp 79-80 C (lit [7] 77.8-78.2 C). (*syn-cis,cis*-9,10,12,13-Diepoxystearic acid also is formed, but it is retained in the mother liquors.)

Preparation of 9,10,12,13-THSA—Dimethyl Sulfoxide Methods

Method A: from preformed di(alkoxysulfonium) salts: Dry dimethyl sulfoxide (DMSO) (2.5 ml, 0.0307 mol) and 2,4,6-trinitrobenzensulfonic acid (TNBSA) (1.802 g, 0.00615 mol) were heated and stirred at 60 C to obtain a thick yellow solution. The reaction mixture was cooled to room temperature and a solution of *anti-cis,cis*-9,10,12,13-diepoxystearic acid (0.9578 g, 0.00307 mol) in DMSO (1.5 ml) was added dropwise with stirring over 10 min, followed by stirring for an additional 15 min. The thick yellow solution then was poured into a mixture of ethyl acetate (100 ml) and ether (200 ml) and stirred for 30 min. The upper solvent layer was decanted and the residual oily insoluble material (di[alkoxysulfonium] salts) was stirred with aqueous $NaHCO_3$ solution (38 ml containing 0.78 g $NaHCO_3$, 0.0092 mol) for 17-20 hr until a homogeneous solution was obtained. The solution then was acidified with 10% hydrochloric acid (6 ml) to pH 2 causing the 9,10,12,13-tetrahydroxystearic acids to precipitate. The precipitate was filtered, washed thoroughly with water (200 ml) to remove excess HCl and TNBSA, and dried. The precipitate then was stirred with cold ether (100 ml) for 5 min and refiltered, and the insoluble fraction was washed with cold ether to give 0.52-0.62 g insoluble white solid; 50-60% yield, mp 125-140 C. GLC analysis (described later) showed this product to be a mixture of *threo*-9,10-*threo*-10,12-*threo*-12,13-tetrahydroxystearic acid (TTT-THSA) and *threo*-9,10-*erythro*-10,12-*threo*-12,13-tetrahydroxystearic acid (TET-THSA) in a ratio of ca. 2:1.

Method B: in situ hydrolysis of di(alkoxysulfonium) salts: Dry DMSO (2.5 ml, 0.0307 mol) and TNBSA (1.802 g, 0.00615 mol) were heated and stirred at 60 C to obtain a thick yellow solution. The reaction mixture was cooled to room temperature, and a solution of *anti-cis,cis*-9,10,12,13-diepoxystearic acid (0.9578 g, 0.00308 mol) in DMSO (1.5 ml) was added dropwise with stirring over 10 min, followed by stirring for an additional 15 min. The thick yellow solution was poured into water (30 ml) (the reaction flask was rinsed with an additional 10 ml of water); then an aqueous $NaHCO_3$ solution was added (0.78 g $NaHCO_3$, 0.00923 mol, in 10 ml water). An additional volume of water (50 ml) was added to bring the total volume to 100 ml. The heterogeneous system (pH 8) was stirred at room temperature for 2 hr, and the resulting homogeneous yellow solution was acidified with 10% HCl (6 ml) to pH 2. The precipitated tetrahydroxystearic acids were filtered and washed with cold water (200 ml) until free of HCl and TNBSA. The vacuum-dried precipitate then was stirred with ether (100 ml) for 5 min and filtered. The insoluble fraction was washed with cold ether to give 0.57-0.62 g insoluble white solid; 55-60% yield, mp 125-141.5 C. GLC analysis showed this product to be a mixture of TTT-THSA and TET-THSA in a ratio of ca. 2:1. The in situ method just described is the preferred procedure.

Method B: in situ hydrolysis of di(alkoxysulfonium) salts—role of water in initial reaction: Method B was repeated but with 1 ml of water added to the original DMSO-TNBSA mixture before addition of the diepoxystearic acid. After the ether washings, the ether-insoluble portion (THSA) weighed only 0.345 g (33% yield, mp 125-140 C).

Method C: use of the preformed salt of DMSO and trinitrobenzenesulfonic acid (anhydrous conditions): The crystalline salt of DMSO and TNBSA (composition 2 DMSO·1 TNBSA) (2.761 g, 0.00615 mol), the preparation of which is described below, was dissolved in dry DMSO (4 ml). A solution of 9,10,12,13-diepoxystearic acid (0.95 g, 0.00307 mol) in 1.5 ml of dry DMSO then was added dropwise with stirring over 10 min followed by stirring for an additional 15 min to obtain a thick homogeneous solution. The solution was poured into water (30 ml) (the reaction flask was rinsed with an additional 10 ml water); aqueous $NaHCO_3$ (0.7783 g, 0.00923 mol in 10 ml water) was added. Then the volume was brought to 100 ml by addition of water. Stirring at room temperature for 2 hr gave a homogeneous solution (the sticky oily layer disappeared during this period). The solution was acidified to pH 2 with 10% HCl (6 ml), and the precipitated THSA were filtered and washed thoroughly with water (200 ml) to free them from HCl and TNBSA. The vacuum dried precipitate was stirred with ether (100 ml) for 5 min and filtered, and the insoluble precipitate was washed with ether to give 0.887 g insoluble THSA (83% yield, mp 120-140 C). This product was shown to be a mixture of TTT-THSA and TET-THSA in a ratio ca. 2:1 (GLC). Pure TTT, mp 147-148.5 C (lit [10,11] 148 C) was isolated by crystallization of the crude material from isopropanol. From the isopropanol filtrate, TET, mp 121-122 C, contaminated with ca. 10% TTT as an impurity, was obtained by evaporation. Pure TET could not be isolated; it always was contaminated with small quantities of TTT. Recrystallization of the crude THSA from hot acetone also gives pure TTT-THSA but not pure TET-THSA.

Preparation of crystalline salt of dimethyl sulfoxide and 2,4,6-trinitrobenzenesulfonic acid ([DMSO]$_2$H$^+$TNBSA$^-$). TNBSA (3.6 g, 0.0123 mol) was dissolved in DMSO (5 ml, 0.0615 mol) at 60 C. The thick yellow solution was cooled to room temperature, then poured into an excess of ethyl acetate (100-200 ml), and stirred for 20 min at room temperature. The crystalline salt ([DMSO]$_2$H$^+$TNBSA$^-$) that precipitated was filtered and washed with cold ethyl acetate followed by cold ether. The crude salt weighed 4.6 g (83% yield), mp 100-105 C. The salt was dissolved in acetone and precipitated by the addition of ether. The yield of purified salt was 75%; mp 112-114 C. The NMR (CD_3NO_2) spectrum shows three singlets at δ 2.97 (12H); 8.54 (2H); and 10.25 (1H).

Analysis: Calculated for $C_{10}H_{15}N_3O_{11}S_3$: C, 26.72; H, 3.34; N, 9.35; S, 21.38; neutral equivalent 449. Found: C, 26.98; H, 3.49; N, 9.56; S, 21.47; neutral equivalent 454.

Formic acid method: Formic acid (30 ml, 97%) was cooled to 7-10 C and *anti-cis,cis*-9,10,12,13-diepoxystearic acid (1.57 g, 0.005 mol) was added with stirring, which was continued for 20 min at 10 C. The reaction mixture was poured into 300 ml water, and sufficient (10-15%) aqueous sodium hydroxide was added dropwise to make the solution basic. After stirring at room temperature for 1 hr, the solution, now homogeneous, was acidified with concentrated hydrochloric acid and cooled in an ice bath for several hours. The white crystalline precipitate was filtered, washed with ether, and dried to yield crude THSA (1.4 g, mp 119-143 C).

A portion of the crude product (1 g) was stirred with ether (50 ml) at room temperature to remove oily products and filtered. By this treatment, 0.14 g (14%) of an ether-soluble liquid and 0.86 g (86%) of an ether-insoluble solid (mp 126.0-145.0 C) were obtained. GLC analysis showed the latter product to be a mixture of 10% TET-THSA and 90% TTT-THSA.

A portion of the ether-insoluble solid (0.579 g) was dissolved in 6 ml hot isopropanol and cooled to 5 C. The precipitate was filtered and washed with 2 ml cold isopropanol to yield 0.437 g white crystals, mp 147.0-148.5 C, which consisted almost exclusively of TTT-THSA containing a trace of TET-THSA. Further recrystallization from ethanol at 5 C gave pure (GLC) TTT-THSA, mp 148.0-148.5 C.

Analysis: Calculated for $C_{18}H_{36}O_6$: C, 62.07; H, 10.34; O, 27.59; neutral equivalent 348.5. Found: C, 62.04; H, 10.47; O, 27.49; neutral equivalent 348.2.

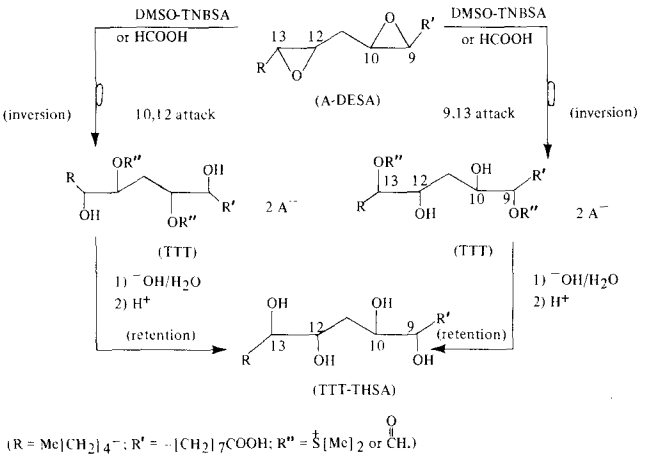
The filtrate from the isopropanol crystallization of the ether-insoluble solid was evaporated to dryness in a rotary vacuum evaporator. The residue was washed with a few ml of ether, and the resulting white crystals were filtered and dried to yield 0.064 g product, mp 118.0-120.0 C, which consisted of 75% TET-THSA and 25% TTT-THSA. The total yield of mixed THSA from the diepoxystearic acid was 69% before crystallization and 60% after crystallization.

If 88% formic acid was used instead of 97% formic acid, the yield of THSA was reduced to 50-55% and correspondingly larger amounts of ether-soluble oily byproducts were produced.

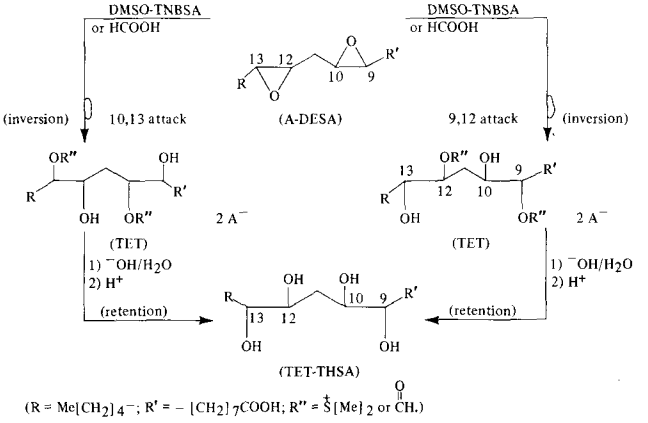
GLC analysis of 9,10,12,13-tetrahydroxystearic acids: First, methyl esters of the crude mixed (as well as pure) THSA were prepared by reaction with diazomethane in 10% MeOH-ether solution, according to the procedure of Schlenk and Gellerman (13). Tetratrifluoroacetates of the methyl esters then were prepared by reaction of the methyl esters with excess trifluoroacetic anhydride at room temperature for 24 hr, according to the procedure of Wood et al. (11). Excess trifluoroacetic anhydride was evaporated in a N_2 stream (hood). The residue was dissolved in CCl_4 and analyzed by GLC (Varian Aerograph Model A90-D3 gas chromatograph equipped with a thermal conductivity detector). Analyses were carried out on a 5 ft x 1/4 in. O.D. stainless steel column packed with 20% methylsilicone polymer (SE-30) coated on 60-80 mesh, Chromosorb W operating at 220 C; helium was the carrier gas. Retention times for the methyl esters of the tetratrifluoroacetates of TET and TTT under the conditions used were 33 and 44.5 min, respectively, at 220 C. Peak enhancements were observed at precisely these retention times with authentic compounds.

RESULTS AND DISCUSSION

Anhydrous DMSO reacts cleanly and rapidly with *anti-cis,cis*-9,10,12,13-diepoxystearic acid at room temperature in the presence of the anhydrous salt of 2,4,6-trinitrobenzenesulfonic acid (TNBSA) with DMSO ([DMSO]$_2$TNBSA) (14) to give di(hydroxy-alkoxysulfonium) salts (Schemes 3 and 4) as the principal products. Upon aqueous basic hydrolysis, the salts are converted to a 2:1 mixture of *threo,threo,threo-* (TTT) and *threo,erythro,threo-* (TET) tetrahydroxystearic acids (THSA) in over 80% yield, Repetition of the reaction with anhydrous DMSO as solvent, but using TNBSA·3 H_2O as the acid catalyst, causes a substantial reduction in yield to 50-60%. When a small quantity of water is added to the reaction mixture of diepoxystearic acid-DMSO-TNBSA·3 H_2O, yields drop even further to 33%. From these experiments, it is clear that water interferes with the desired conversion of the diepoxy acid to THSA.



Scheme 3.



Scheme 4.

A similar trend (yield reduction with increased water content) also is observed in the formic acid method of conversion of the diepoxy acid to THSA (Schemes 3 and 4). Thus, when the diepoxystearic acid is treated with 97% formic acid followed by basic hydrolysis, TTT-THSA and

TET-THSA are obtained in 60-68% yield (TTT:TET, 9:1). When 88% formic acid is used, the yield drops to 50-55%. It seems clear now that earlier workers, unaware of the importance of the role of water, could not have obtained higher yields of THSA, because the diepoxystearic acids, prepared from linoleic acid, were treated with dilute *aqueous* formic or acetic acids in the initial ring opening step (6-9).

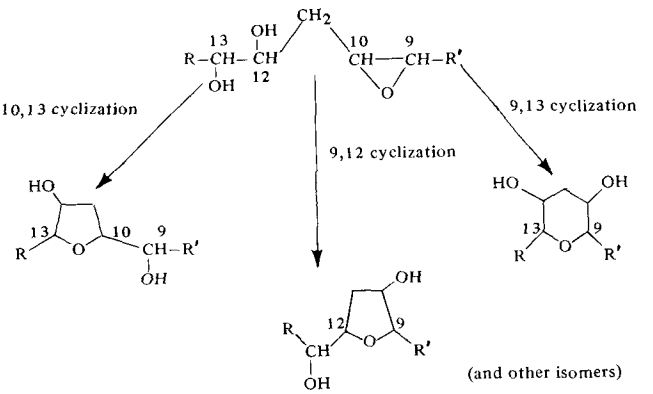
Mechanisms and stereochemistry: Nucleophilic attack by DMSO or formic acid (Schemes 3 and 4) on protonated *anti-cis,cis*-9,10,12,13-diepoxystearic acid (A-DESA) can occur by four different pathways to give two (and only two) isomeric di(hydroxy-alkoxysulfonium) salts or di(hydroxy-formates), respectively: (a) attack on the two most widely separated oxirane carbon atoms (9,13) with *trans* ring opening (inversion), (b) attack on the two closest oxirane carbon atoms (10,12) with *trans* ring opening (inversion), (c) attack on oxirane carbon atom (10) and oxirane carbon atom (13) with *trans* ring opening (inversion), and (d) attack on oxirane carbon atom (12) and oxirane carbon atom (9) with *trans* ring opening (inversion).

Di(hydroxy-alkoxysulfonium) salts and di(hydroxy-formate) esters obtained by the pathways of Scheme 3 yield TTT-THSA exclusively upon hydrolysis. The comparable intermediates obtained by the pathways of Scheme 4 yield TET-THSA. In connection with the hydrolysis of the sulfonium salts reported here, water attacks exclusively on sulfur, with retention. Such exclusive attack on sulfur in other alkoxysulfonium salts is well documented in literature (15-20). Further evidence for exclusive attack on sulfur comes from our own detailed work on the conversion of 1,2-epoxycyclohexane to *trans*-1,2-cyclohexanediol (21) and the stereospecific conversion of *cis*- and *trans*-9,10-epoxystearic acid to *threo*- and *erythro*-9,10-dihydroxystearic acids, respectively (14). In the hydrolysis of purely aliphatic primary and secondary alkoxysulfonium salts, attack by water on carbon is not found (22). Attack on carbon occurs only with the more reactive systems, such as tertiary, benzylic, and allylic alkoxysulfonium salts (22). In the case of the formate esters, hydrolysis occurs by attack of water on the carbonyl atom of the ester, rather than on the alkyl carbon atom of the aliphatic chain; thus, retention occurs in these cases also in the hydrolysis step. It is not clear at this time why the DMSO process gives a 2:1 ratio of TTT:TET and the formic acid a 9:1 ratio.

Role of water: In attempting to assess the role of water in the acid-catalyzed hydrolysis of *anti-cis,cis*-9,10,12,13-diepoxystearic acid to THSA, it is reasonable to assume that water attacks one of the protonated oxirane groups in the ring opening step to give 12,13-dihydroxy-9,10-epoxystearic acid or 9,10-dihydroxy-12,13-epoxystearic acid as intermediates. Either of the intermediates then can undergo facile intramolecular nucleophilic attack by one of the hydroxyl groups on the remaining protonated oxirane group to yield five- or six-membered cyclic ethers instead of THSA, as illustrated in Scheme 5, for one of the intermediates only.

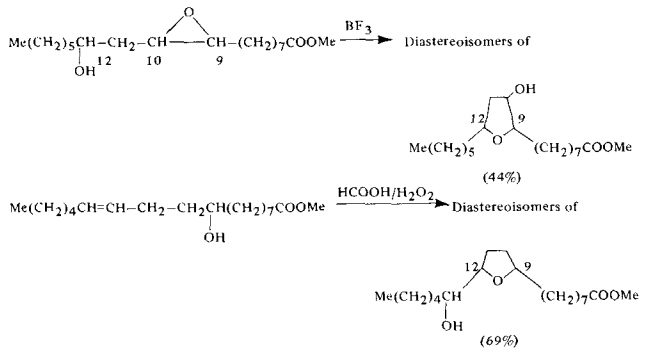
Evidence for the hypothesis concerning the role of water is based upon the work of Bharucha and Gunstone (10) who, as noted earlier, treated 12,13-dihydroxy-Δ^9-*cis*-octadecenoic acid with $HCOOH/H_2O_2$, followed by hydrolysis and acidification, and obtained cyclic ethers predominantly, *not tetrahydroxystearic acids*, presumably via 12,13-dihydroxy-9,10-epoxystearic acid as an intermediate (Scheme 2). In contrast, when 12,13-dihydroxy-Δ^9-*cis*-octadecenoic acid first is acetylated and then subjected to similar treatment (peroxyformic acid oxidation and hydrolysis), 9,10,12,13-THSA (mp 147.5-148.5 and 121-122 C) are obtained in 82% yield.

Additional evidence for intramolecular acid-catalyzed cyclization of dihydroxy epoxides, in which the functional groups are separated by one or two carbon atoms, comes from Abbot and Gunstone's more recent work (Scheme 6) (23).



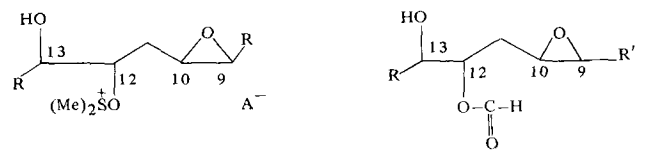
$R = CH_3(CH_2)_4^-$; $R' = -(CH_2)_7COOH$

Scheme 5.



Scheme 6.

In the acid-catalyzed hydration of diepoxides, in which the oxirane groups are separated by one or two carbon atoms, we have assumed that one oxirane group is opened first to yield a dihydroxy-epoxide intermediate followed by intramolecular cyclization by one of the hydroxyl groups to give cyclic ethers. Similar stepwise ring opening also must be predicted in the ring opening of A-DESA by dry DMSO and 97% HCOOH to give mono(hydroxy-alkoxysulfonium) salts and mono(hydroxy-formate) esters, respectively, as the first intermediates:



Mono(hydroxy-alkoxysulfonium) salt Mono(hydroxy-formate)ester

(Other possible isomers are not shown)

In these intermediates there is only one hydroxyl group instead of two, as in literature. Furthermore, the single hydroxyl group may not be as available for cyclization, as it may be bonded partially to the adjacent positive sulfur or carbon atom of the carbonyl group (electrophilic centers). This may explain why we are able to obtain excellent yields of THSA and very little by-product cyclic ether when water is absent or present in low concentrations. The improved hydration method yields only two isomeric THSA, mp 147-148 and 121-122 C, which have properties similar to those reported by Wood and coworkers (11). These isomers (as methyl esters of their tetratrifluoroacetates) are separated readily and analyzed by GLC. Recrystallization of the original crude mixture of THSA from hot acetone or

isopropanol provides pure TTT, mp 147-148 C, but pure TET could not be isolated from the crude tetrol reaction mixture. It always was contaminated with a small amount (ca. 10%) of TTT; the mixture melts at 121-122 C.

ACKNOWLEDGMENT

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REFERENCES

1. Paul, R., and S. Tchelitcheff, Compt. Rend. 239:1504 (1954).
2. Wood, D.J.C., and L.F. Wiggins, Nature 164:402 (1949).
3. Ross, W.C.J., J. Chem. Soc. 2257 (1950).
4. Cope, A.C., B.S. Fisher, W. Funke, J.M. McIntosh and M.A. McKervy, J. Org. Chem. 34:2231 (1969).
5. Craig, T.W., G.R. Harvey and G.A. Berchtold, Ibid. 32:3743 (1967).
6. Green, T.G., and T.P. Hilditch, Biochem. J. 29:1552 (1935).
7. Swern, D., and G.B. Dickel, J. Amer. Chem. Soc. 76:1957 (1954).
8. McKay, A.F., N. Levitin and R.N. Jones, Ibid. 76:2383 (1954).
9. McKay, A.F., and A.R. Bader, J. Org. Chem. 13:75 (1948).
10. Bharucha, K.E., and F.D. Gunstone, J. Chem. Soc. 1611 (1956).
11. Wood, R., E.L. Bever and F. Snyder, Lipids 1:399 (1966).
12. Maerker, G., E.T. Haeberer and S.F. Herb, JAOCS 43:505 (1966).
13. Schlenk, H., and J. Gellerman, Anal. Chem. 32:1412 (1960).
14. Khuddus, M.A., and D. Swern, Tetrahedron Lett. 411 (1971).
15. Leonard, N.J., and C.R. Johnson, J. Amer. Chem. Soc. 84:3701 (1962).
16. Johnson, C.R., Ibid. 85:1020 (1963).
17. Buck, K.W., A.B. Foster, A.R. Perry and J.M. Webber, Chem. Commun. 433 (1965).
18. Hogeveen, H., G. Maccagneni and F. Montanari, J. Chem. Soc. (C) 1585 (1966).
19. Cinquini, M., S. Colonna and F. Montanari, Ibid. (C) 1213 (1967).
20. Cinquini, M., S. Colonna and F. Montanari, Ibid. (C) 572 (1970).
21. Khuddus, M.A., Ph.D. Thesis, November 1972, Temple University, Philadelphia, Pa.
22. Khuddus, M.A., and D. Swern, J. Amer. Chem. Soc., In press.
23. Abott, G.G., and F.D. Gunstone, Chem. Phys. Lipids 7:290 (1971).

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