Geometric Configuration and Etherification Reactions of Some Naturally Occurring 9-Hydroxy-10,12- and 13-Hydroxy-9,11-octadecadienoic Acids[1a]

R. G. POWELL, C. R. SMITH, JR., AND I. A. WOLFF

Northern Regional Research Laboratory,[1b] Peoria, Illinois 61604

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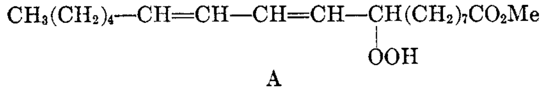
The hydroxy acids in *Xeranthemum annuum* seed oil are shown to be 9-hydroxy-*trans*-10,*cis*-12-octadecadienoic and 13-hydroxy-*cis*-9,*trans*-11-octadecadienoic acids. Their geometric configurations were established by partial reduction of the corresponding methyl esters (**1** and **2**) with diimide, and subsequent oxidative cleavage of the isolated *cis*-monoene products. Hydrazine in the presence of oxygen proved unsuitable as a diimide source for reduction of **1** and **2**, but potassium azodicarboxylate was used successfully for this purpose. The acid-catalyzed etherification reactions of these conjugated dienols (**1** and **2**), as well as of their allylic reduction products (**4** and **11**), were explored.

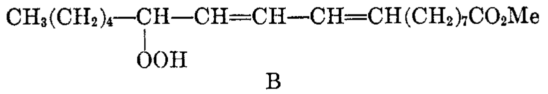
The seed glycerides of a number of plants contain conjugated dienols—long-chain acids with a hydroxyl group α to a conjugated diene grouping. The first of these to be characterized, dimorphecolic (9-hydroxy-*trans*-10,*trans*-12-octadecadienoic) acid, was shown to be a major constituent (66.5%) of *Dimorphotheca sinuata* seed oil.[2]

Other conjugated hydroxydienoic acids were soon found in other seed oils, mainly in the plant family *Compositae*. Morris and co-workers obtained evidence for the occurrence of two of these, separable by thin layer chromatography (tlc) and presumably isomeric with dimorphecolic acid, in several seed oils.[3] They found that both had a *cis,trans* configuration of double bonds, rather than *trans,trans* as in dimorphecolic acid, and suggested that they had structures analogous to the hydroperoxides (A + B) obtained from methyl linoleate *via* lipoxidase oxidation[4] or autoxidation.[5] The structural relationship of dimorphecolic acid to these hydroperoxides was also pointed out by Smith and co-workers.[2a]



$CH_3(CH_2)_4-CH=CH-CH=CH-\underset{\text{OOH}}{CH}(CH_2)_7CO_2Me$

A



$CH_3(CH_2)_4-\underset{\text{OOH}}{CH}-CH=CH-CH=CH(CH_2)_7CO_2Me$

B

cis,trans-Conjugated dienols have been isolated from a few seed oils. Both the 9 and 13 isomers were found in oils of *Tragopogon porrifolius*[6] and *Tagetes erecta*.[7] In contrast, *Calendula officinalis* seed oil contains only the 9 isomer,[8] and *Coriaria nepalensis* affords only the 13 isomer (coriolic acid).[9] These and some structurally related conjugated dienols also occur as metabolites associated with prostaglandin E_1.[10]

From time to time, it has been postulated both that the *cis,trans*-conjugated hydroperoxides derived from linoleate[4a,5a,11] and that the *cis,trans*-conjugated dienols found as constituents of seed glycerides[3,8,12] have the oxygen function situated α to a *trans* rather than to a *cis* bond. No direct experimental evidence to support these predictions had been reported prior to a recent communication by Tallent and co-workers.[9] By applying nuclear magnetic resonance (nmr) spin-decoupling techniques, these workers deduced the geometric configuration of the individual double bonds of coriolic acid and thus showed that it is 13-hydroxy-*cis*-9,*trans*-11-octadecadienoic acid.

Dimorphecolic acid,[7,13] coriolic acid,[9] and the *cis,trans*-dienol from *Calendula officinalis*[8] seed oil are all optically active, and all have the D configuration. Hydroperoxides obtained by lipoxidase-catalyzed oxidation of sodium linoleate are optically active;[11] as expected, those resulting from autoxidation are not.[11]

In this paper, we describe the determination of geometric configuration of the conjugated dienols of *Xeranthemum annuum* seed oil by an adaptation of the diimide reduction method. Some previously unexplored reactions of these dienols, and of their reduction products and related compounds, will also be presented. The isolation of the hydroxy acids of *Xeranthemum annuum* seed oil and the characterization of other unusual components of this oil were reported previously.[14]

Structures and Geometric Configurations.—A concentrate of hydroxy acid methyl esters[14] from *Xeranthemum annuum* seed oil was resolved by countercurrent distribution. Figure 1 summarizes the results after 600, 2670, and 5400 transfers. Nearly pure fractions of hydroxy esters **1** and **2** were obtained after combining material isolated from the appropriate tubes[15] indicated by the shaded areas. Both esters had infrared maxima at 10.18 and 10.54 (*cis,trans*-conjugated di-

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[1] (a) Presented at the 153rd Meeting of the American Chemical Society, Miami Beach, Fla., April 1967, Abstracts of Papers, p 197–O. (b) This is a laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

[2] (a) C. R. Smith, T. L. Wilson, E. H. Melvin, and I. A. Wolff, *J. Am. Chem. Soc.*, **82**, 1417 (1960); (b) R. G. Binder, T. H. Applewhite, M. J. Diamond, and L. A. Goldblatt, *J. Am. Oil Chemists' Soc.*, **41**, 108 (1964).

[3] L. J. Morris, R. T. Holman, and K. Fontell, *ibid.*, **37**, 323 (1960).

[4] (a) A. L. Tappel in "The Enzymes," Vol. VIII, 2nd ed, P. D. Boyer *et al.*, Ed., Academic Press Inc., New York, N. Y., 1963, p 275; (b) M. Hamberg and B. Samuelsson, *Biochem. Biophys. Res. Commun.*, **21**, 531 (1965); (c) A. Dolev, W. K. Rohwedder, and H. J. Dutton, *Lipids*, **2**, 28 (1967).

[5] (a) H. H. Sephton and D. A. Sutton, *J. Am. Oil Chemists' Soc.*, **33**, 263 (1956), and references cited therein; (b) O. S. Privett and M. L. Blank, *ibid.*, **39**, 465 (1962), and references cited therein.

[6] M. J. Chisholm and C. Y. Hopkins, *Can. J. Chem.*, **38**, 2500 (1960).

[7] C. Y. Hopkins and M. J. Chisholm, *ibid.*, **43**, 3160 (1965).

[8] R. C. Badami and L. J. Morris, *J. Am. Oil Chemists' Soc.*, **42**, 1119 (1965).

[9] W. H. Tallent, J. Harris, I. A. Wolff, and R. E. Lundin, *Tetrahedron Letters*, 4329 (1966).

[10] (a) M. Hamberg and B. Samuelsson, *J. Am. Chem. Soc.*, **88**, 2349 (1966); (b) D. H. Nugteren, R. K. Beerthuis, and D. A. Van Dorp, *Rec. Trav. Chim.*, **85**, 405 (1966).

[11] O. S. Privett, C. Nickell, W. O. Lundberg, and P. D. Boyer, *J. Am. Oil Chemists' Soc.*, **32**, 505 (1955).

[12] F. D. Gunstone, *Chem. Ind.* (London), 1033 (1965).

[13] T. H. Applewhite, R. G. Binder, and W. Gaffield, *Chem. Commun.*, 255 (1965).

[14] R. G. Powell, C. R. Smith, and I. A. Wolff, *Lipids*, **2**, 172 (1967).

[15] Tube number indicates the total number of tubes through which the material had progressed.

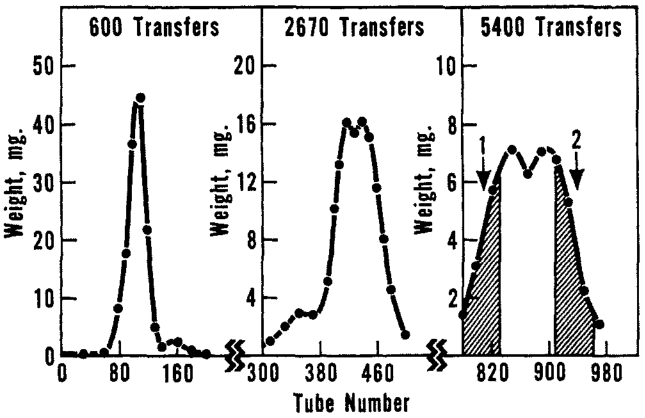

Figure 1.—Countercurrent distribution of *Xeranthemum annuum* hydroxy acid methyl ester concentrate.

ene[16]) and at 2.76 μ (hydroxyl). In addition, esters **1** and **2** each had a single maximum in the ultraviolet at 234 mμ (*cis,trans*-conjugated diene) and both showed some optical activity. Oxidative cleavage with permanganate–periodate placed the hydroxyl and conjugated diene groupings of both between C-9 and C-13 on normal 18-carbon chains.

Partial diimide reduction[17a] has been applied successfully to the determination of double-bond geometry in other conjugated aliphatic systems[17b] and seemed an obvious approach to the configurational problem of the conjugated dienols. However, the hydroxyl group proved to be a complicating factor. When **1** was treated with a methanolic solution of hydrazine in the presence of air under the same conditions used by previous workers,[17b] a nitrogen-containing by-product was formed in considerable amount. We circumvented this difficulty by substituting potassium azodicarboxylate[18] as the diimide source. In all our reductions of *cis,trans*-dienols, *cis*-monoene predominated over *trans*-monoene products in a ratio of nearly 2:1. In this respect, our results resembled those of Mikolajczak and co-workers,[17b] who observed that the *trans* double bond of a *cis,trans*-conjugated diene is reduced somewhat faster than is the *cis* double bond. Partial diimide reduction of **1** with potassium azodicarboxylate afforded a mixture of four compounds (see Scheme I) which were resolved by preparative tlc on silver nitrate impregnated silica. These four compounds were, in order of increasing R_f (see Figure 2), a *cis*-monoene (**3**), starting material **1**, a *trans*-monoene (**4**), and a saturated ester (**5**), mp 49.5–50.0°. Oxidative cleavage products of *cis*-monoene **3** were converted into methyl esters and examined by gas–liquid partition chromatography (glpc). Two major components were found, methyl hexanoate (**6**) and an ester γ-lactone (presumably **7**). These results placed the *cis* double bond of both **1** and **3** at the 12,13 position, and their hydroxyl group at C-9.

Reduction of **2** in an identical manner also gave four products (see Scheme II). Resolution of these as before (see Figure 2) yielded a *cis*-monoene (**10**), starting material **2**, a *trans*-monoene (**11**), and a saturated ester (**12**), mp 52.0–52.5°. Oxidative cleavage of *cis*-monoene **10** gave, after work-up of the products as indicated, methyl nonanedioate (**13**) and a γ-lactone, presumably **14**. These results placed a *cis* bond at the 9,10 position in **2** and in **10** and the hydroxyl at C-13. Thus the complete structures of the conjugated dienols derived from *Xeranthemum annuum* seed oil are 9-hydroxy-*trans*-10,*cis*-12-octadecadienoic (**1**) and 13-hydroxy-*cis*-9,*trans*-11-octadecadienoic acids (**2**). Further confirmation for structures **1** and **2** was provided by comparison of their 60-Mc nmr spectra with that of methyl coriolate, particularly the portions in which vinyl protons exhibit complex splitting.

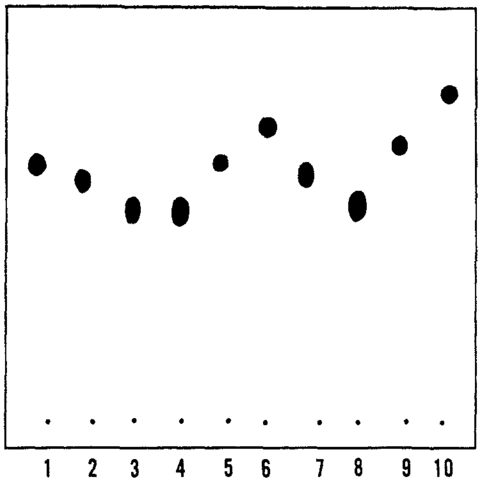

Figure 2.—Thin layer chromatography of some reference methyl esters and products from diimide reductions of **1** and **2** (25% silver nitrate–silica gel G; developed with hexane–ether, 3:2): (1) 9-hydroxy-*trans*-10,*trans*-12-octadecadienoate (**17**); (2) 9-hydroxy-*trans*-10,*cis*-12-octadecadienoate (**1**); (3) 9-hydroxy-*cis*-12-octadecenoate (**3**); (4) authentic **3** from *Strophanthus*; (5) 9-hydroxy-*trans*-10-octadecenoate (**4**); (6) 9-hydroxyoctadecanoate (**5**); (7) 13-hydroxy-*cis*-9,*trans*-11-octadecadienoate (**2**); (8) 13-hydroxy-*cis*-9-octadecenoate (**10**); (9) 13-hydroxy-*trans*-11-octadecenoate (**11**); and (10) 13-hydroxyoctadecanoate (**12**). The tlc plate was sprayed with 50% sulfuric acid and heated. Spots were reproduced by tracing.

Both of the *Xeranthemum* dienols (**1** and **2**) exhibited very slight but nevertheless measurable optical activity. The observed rotations were of the same sign expected for the pure D isomers,[8,9,13] but were of considerably lesser magnitude. Badami and Morris[8] found a significant discrepancy in the magnitude of rotation of two samples of methyl (+)-9-hydroxy-10,-12-octadecadienoate isolated from different batches of *Calendula officinalis* seed. They speculated that racemization may have occurred during storage of one sample. It appears that **1** and **2** isolated from *Xeranthemum* seed are partial racemates. Whether they were biosynthesized thus or were partially racemized at some stage, we cannot say at present. If there was racemization by some unknown mechanism, there must have been practically no stereomutation of double bonds, since our results indicated that **1** and **2** were essentially pure geometric isomers.

Etherification Reactions.—In previous papers,[19] we made certain observations concerning the reactivity of conjugated enynols under mildly acidic conditions and drew comparisons with the behavior of conjugated

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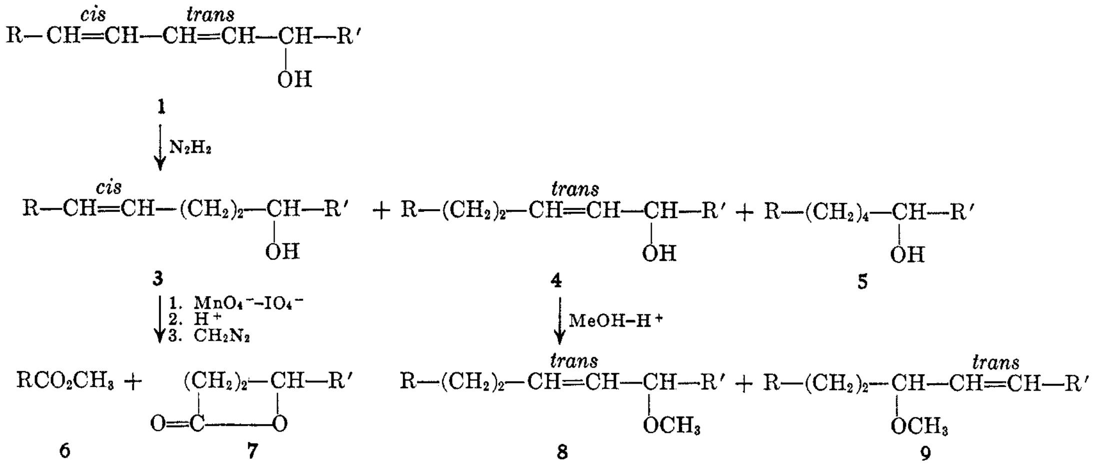
(16) J. R. Chipault and J. M. Hawkins, *J. Am. Oil Chemists' Soc.*, **36**, 535 (1959).

(17) (a) For reviews, *cf.* S. Hünig, H. R. Müller, and W. Thier, *Angew. Chem. Intern. Ed. Engl.*, **4**, 271 (1965); C. E. Miller, *J. Chem. Educ.*, **42**, 254 (1965); (b) K. L. Mikolajczak, M. O. Bagby, R. B. Bates, and I. A. Wolff, *J. Org. Chem.*, **30**, 2983 (1965), and references cited therein.

(18) J. W. Hamersma and E. I. Snyder, *ibid.*, **30**, 3985 (1965).

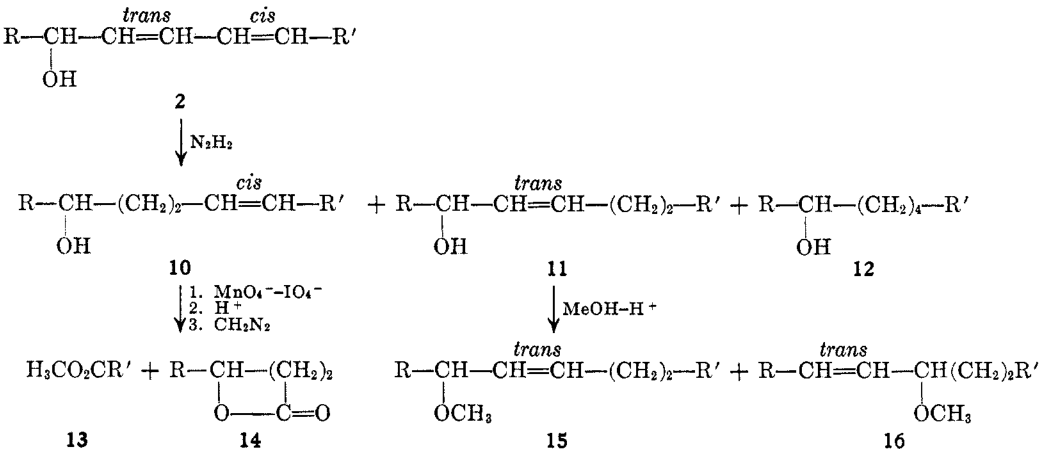
(19) (a) R. G. Powell, C. R. Smith, C. A. Glass, and I. A. Wolff, *ibid.*, **30**, 610 (1965); (b) R. G. Powell, C. R. Smith, C. A. Glass, and I. A. Wolff, *ibid.*, **31**, 528 (1966).

SCHEME I



$R = CH_3(CH_2)_4$-
$R' = -(CH_2)_7CO_2CH_3$

SCHEME II



$R = CH_3(CH_2)_4$-
$R' = -(CH_2)_7CO_2CH_3$

dienols. Since compounds **1** and **2** had been provided by our isolation work and compounds **4** and **11** had been made available by diimide reduction of **1** and **2**, it seemed desirable to extend our studies on the etherification reactions of α,β-unsaturated alcohols. We suggested[19a] that, when solvolyzed in 0.1 N methanolic sulfuric acid, a conjugated dienol such as methyl dimorphecolate (**17**) would undergo reversible etherification much more rapidly than dehydration. We now have verification of this hypothesis. Rapid etherification of **17** was effected simply by dissolving it in 0.1 N acidic methanol at room temperature. After reaction periods as short as 30 min, no starting material or conjugated triene was detected in the products. However, two new spots of nearly equal intensity appeared which were attributed to *trans,trans*-methyl ether (**18**) and its *trans,trans* rearrangement product (**19**) on the basis of their infrared spectra and tlc migration characteristics (see Scheme III).

Rapid conversion into a mixture of methoxy derivatives occurred when *cis,trans*-dienol **2** was allowed to react under identical conditions. After reaction for 30 min, only methyl ethers were observable by infrared and tlc analyses. However, 41% of the original *cis,trans* configuration remained in these products as estimated by the method of Chipault and Hawkins.[16] The analyses clearly demonstrated the presence of three products, presumably a mixture of methyl ethers **18** and **20** and a small amount of **19**. When the reaction was allowed to proceed for longer periods, conversion of the remaining *cis,trans* conjugation into *trans,trans* conjugation occurred at a slower rate[20] (see Experimental Section). The tlc spot attributed to **20** gradually disappeared, leaving only two spots of equal intensity attributed to **18** and **19**. Reflux of a mixture of *trans,trans* ethers (**18** and **19**) for 1.5 hr then gave all *trans*-conjugated triene as the major product.[21]

Partial retention of *cis,trans* configuration after essentially complete etherification of **2** is quite significant and recalls work concerning preservation of geometry in allylic carbonium ions.[22,23] Our results may be rationalized as follows (refer to Scheme III). In acidic methanol **2** gives delocalized carbonium ion **2a**

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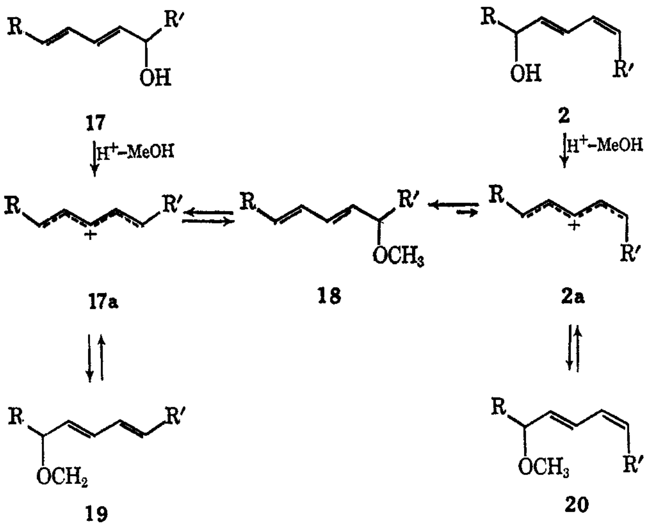
[20] When Braude, *et al.*, carried out the anionotropic rearrangement of phenylpropenylcarbinol in aqueous ethanol, they observed that some ethyl ether was formed both before and after rearrangement and that the parent alcohol was rearranged faster than the corresponding ether [*cf.* E. A. Braude, E. R. H. Jones, and E. S. Stern, *J. Chem. Soc.*, 396 (1946)].

[21] Hopkins and Chisholm[7] found that, when dimorphecolic acid is dehydrated with boiling acetic acid, a 1:1 mixture of all-*trans*-8,10,12- and all-*trans*-9,11,13-octadecatrienoic acid results. This observed formation of both possible positional isomers fits in with our proposed mechanistic scheme.

[22] (a) W. G. Young, S. H. Sharman, and S. Winstein, *J. Am. Chem. Soc.*, **82**, 1376 (1960), and references therein; (b) W. G. Young and J. S. Franklin, *ibid.*, **88**, 785 (1966); (c) H. L. Goering and R. R. Josephson, *ibid.*, **84**, 2779 (1962), and references therein.

[23] J. H. Brewster and H. O. Bayer, *J. Org. Chem.*, **29**, 105 (1964).

SCHEME III



R = $CH_3(CH_2)_4$–
R′ = $-(CH_2)_7CO_2CH_3$

which reacts, with nearly equal probability, to give unrearranged *cis,trans* ether **20** or its *trans,trans* "allylic" rearrangement product, **18**. Equilibration of **18** and **20** then gives a slow conversion of **20** into thermodynamically more stable *trans,trans* products **18** and **19**. Etherification of **17** proceeds *via* pentadienyl carbonium ion **17a** which yields only *trans,trans* ethers **18** and **19**. As **17** gave no observable *cis,trans* products, we can assume that **2a** and **17a** are distinct species with significant rotational barriers and that **17a** does not isomerize to **2a**. Since **2** initially yields a mixture containing considerable *cis,trans* product, we can also assume that ion **2a** does not readily isomerize directly to **17a**. In any event, the conversion of **2a** into **18** and **20** is certainly much faster than the direct *cis,trans* → *trans,trans* isomerization of **2a**.

Upon treatment with refluxing 0.1 *N* acidic methanol, *trans*-monoene **4** was converted into a mixture of two compounds in approximately equal amounts. These were markedly less polar than **4** and were resolvable by tlc. An infrared spectrum of the reaction product differed from that of **4** primarily in that the 2.76-μ (OH) peak had been replaced by a broad band (9.18 μ) characteristic of a methoxyl group. Consequently, these two compounds were considered to be **8** (the methyl ether of **4**) and its allylic rearrangement product, **9**. *trans*-Monoene **11** similarly yielded methyl ether **15** and its allylic rearrangement product, **16**.

Experimental Section

Infrared spectra were determined with Infracord Model 137 or Model 337 spectrophotometers[24] on 1% carbon disulfide solutions. Ultraviolet spectra were determined with a Beckman DK-2A far-ultraviolet spectrophotometer. Melting points were determined with a Fisher-Johns block and are uncorrected. Optical rotatory dispersion (ORD) was determined by means of a Cary Model 60 recording spectropolarimeter. Nmr spectra were determined with a Varian A-60 spectrometer on deuteriochloroform solutions containing 1% tetramethylsilane. Glpc analyses were carried out as described by Miwa, *et al.*[25] Tlc analyses utilized silica gel G or 25% silver nitrate impregnated silica gel G plates and appropriate solvent systems.[26] Countercurrent distribution utilized a 200-tube Craig-Post apparatus and an acetonitrile–hexane solvent system.[27]

Preliminary Characterization of the *Xeranthemum* Hydroxy Ester Concentrate.—Isolation of a hydroxy ester concentrate, λ_{max}^{hexane} 234 mμ ($E_{1\,cm}^{1\%}$ 822), was described previously.[14] The fraction (2.1 g) was further concentrated by chromatography on a silica gel column with hexane–ethyl ether (4:1) as the eluting solvent. This procedure afforded 1.6 g of hydroxy esters, λ_{max}^{hexane} 234 mμ (ε 25,000). An infrared spectrum showed hydroxyl (2.76 μ) and *cis,trans*-conjugated diene (10.18 and 10.54 μ). Tlc analyses of the mixture on silica gel G plates[26] gave two spots judged to be of equal intensity. Permanganate–periodate cleavage of a portion of this hydroxy ester concentrate by the procedure of von Rudloff[28] and glpc analyses of the products, as methyl esters,[25] gave hexanoic and nonanedioic acids as the only significant cleavage products.

Countercurrent Distribution of *Xeranthemum* Hydroxy Esters.—The concentrate of *cis,trans*-hydroxy esters (1.6 g) was dissolved in 40 ml of lower phase (acetonitrile) and 40 ml of upper phase (hexane) and then placed in the first tube of a 200-tube countercurrent distribution apparatus. The remaining tubes were all filled (40 ml of both upper and lower phase in each) and the instrument was set for automatic recycle operation. After 600, 2670, and 5400 transfers, weight curves were plotted as is shown in Figure 1. Contents of tubes containing minor "shoulders" that became apparent in the weight curves (tube-140–180, after 600 transfers; tubes 300–380, after 2670 transfers) were removed from the instrument and replaced with fresh solvent. After 5400 transfers, 177 mg of a single ester (**1**) resulted from the combined contents of tubes[15] 780–830: λ_{max}^{hexane} 234 mμ (ε 26,700). A second ester (**2**), 196 mg, was obtained from the combined contents of tubes 910–960: λ_{max}^{hexane} 234 mμ (ε 27,000). Infrared and nmr spectra of **1** and **2** were nearly identical and did not readily distinguish **1** from **2**, or either of these from known methyl 13-hydroxy-*cis*-9,*trans*-12-octadecadienoate.[9] ORD of **1** showed a plain positive curve from 600 to 400 mμ, $[\alpha]_{400}$ +1.5° (*c* 1.6, hexane); similar measurements on **2** gave a plain negative curve, $[\alpha]_{400}$ −0.5° (*c* 1.6 hexane).

Partial Diimide Reduction of 1.—Our first attempts at partial reduction of dienols utilized hydrazine in the presence of air as a diimide source.[17b] Significant nitrogen incorporation was observed in the crude products, verified by microanalysis and by a band in the infrared at 5.96 μ (possibly C=N). These by-products were not examined further. Potassium azodicarboxylate[18] gave no nitrogen-containing products when used as the diimide source in our work.

A 0.14-g (4.5 × 10^{-4} mole) portion of **1** was placed in a 50-ml flask, along with 2.37 g (1.2 × 10^{-2} mole) of potassium azodicarboxylate and 8.7 ml (2.7 × 10^{-1} mole) of absolue methanol.[18] To this mixture was slowly added dropwise and with continuous stirring a 1:1:1 mixture of methanol, acetic acid, and water. After addition of 3 ml of this mixture (2 hr), the yellow color characteristic of the azodicarboxylate was no longer evident. At this point, 25 ml of water was added and the reaction products were isolated by repeated hexane extraction. The combined hexane extracts were dried over sodium sulfate and yielded 127 mg of products. Tlc analysis on 25% silver nitrate impregnated silica gel G[26] showed four distinct spots. The four products were separated on preparative (1 mm) tlc plates with ethyl ether–hexane (3:2) as the developing solvent. These products were, in order of increasing R_f (Figure 2), as follows: **3**, 26 mg, a *cis*-monoene having an infrared maximum at 2.75 μ (OH); **1**, 23 mg, unreacted starting material; **4**, 13 mg, a *trans*-monoene with infrared maxima at 2.76 (OH) and at 10.35 μ (isolated *trans* C=C); and **5**, 48 mg, a hydroxyoctadecanoate, mp 49.5–50.0°, with an infrared maximum at 2.75 μ (OH).[29] Infrared spectra and tlc-migration characteristics of **3** and of known

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[24] The mention of firm names or trade products does not imply that they are endorsed or recommended by the U. S. Department of Agriculture over other firms or similar products not mentioned.

[25] T. K. Miwa, K. L. Mikolajczak, F. R. Earle, and I. A. Wolff, *Anal. Chem.*, **32**, 1739 (1960).

[26] L. J. Morris and D. M. Wharry, *J. Chromatog.*, **20**, 27 (1965).

[27] C. R. Scholfield, J. Nowakowska, and H. J. Dutton, *J. Am. Oil Chemists' Soc.*, **37**, 27 (1960).

[28] E. von Rudloff, *Can. J. Chem.*, **34**, 1413 (1956).

[29] Reported[9,30,31] melting points of methyl hydroxyoctadecanoates: racemic 9-hydroxy, 50.3–50.6°; 9D-hydroxy, 53.0–53.5°; racemic 13-hydroxy, 53.3–53.5; 13D-hydroxy, 56–57°.

[30] S. Bergström, G. Aulin-Erdtman, B. Rolander, E. Stenhagen, and S. Östling, *Acta Chem. Scand.*, **6**, 1157 (1952).

[31] G. J. Schroepfer and K. Bloch, *J. Biol. Chem.*, **240**, 54 (1965).

methyl 9-hydroxy-*cis*-12-octadecenoate from *Strophanthus*[32] were identical.

Anal. Calcd for $C_{19}H_{38}O_3$: C, 72.56; H, 12.18. Found: C, 72.93; H, 12.43.

Partial Diimide Reduction of Known Methyl 13-Hydroxy-*cis*-9,*trans*-11-octadecadienoate.—A 0.14-g (4.5×10^{-4} mole) portion of **2** was placed in a 50-ml flask, along with 2.25 g (1.2×10^{-2} mole) of potassium azodicarboxylate and 8.3 ml (2.6×10^{-1} mole) of absolute methanol. The reduction was carried out and products (0.13 g) were recovered as was described previously for **1**. Tlc analyses of this material gave four spots and these were separated preparatively as before. These were, in order of increasing R_f (Figure 2), as follows: **10**, 26 mg, a *cis*-monoene with an infrared maximum at 2.75 μ (OH); **2**, 29 mg, unreacted starting material; **11**, 13 mg, a *trans*-monoene having infrared maxima at 2.76 (OH) and 10.35 μ (isolated *trans*); and **12**, 42 mg, a hydroxyoctadecanoate, mp 52.0–52.5°, with an infrared maximum at 2.75 μ (OH).[29] Reduction of known methyl 13D-hydroxy-*cis*-9,*trans*-11-octadecadienoate[9] and work-up in the same manner gave products with infrared spectra and tlc characteristics identical with those of **10**, **11**, and **12**. In this instance, however, the fully saturated product had a melting point, 54.5–55.0°, more in agreement with the expected methyl 13D-hydroxyoctadecanoate.[9]

Anal. Calcd for $C_{19}H_{38}O_3$: C, 72.56; H, 12.18. Found: C, 72.92; H, 12.21.

Oxidative Cleavage of *cis*-Monoenes 3 and 10.—A 25-mg sample of *cis*-monoene **3** was cleaved oxidatively by the procedure of von Rudloff.[28] The solvent was removed with a rotary evaporator, the solid alkaline residue was acidified with concentrated hydrochloric acid, and the cleavage products were recovered by repeated extractions with ether. The combined ether extracts were dried over sodium sulfate; removal of the solvent afforded 18 mg of solid products. Glpc analyses of this material showed hexanoic acid as the only monobasic acid present. Methyl esters were then prepared by using an ethereal solution of diazomethane. An infrared spectrum showed, in addition to the expected methyl ester carbonyl, a strong band at 5.64 μ characteristic of γ-lactones. Glpc analyses of the methyl esters gave methyl hexanoate and a product (70%) having equivalent chain lengths[25] of 16.76 on Apiezon L and 25.20 on Resoflex-446. These values were attributed to an ester γ-lactone (**7**). A small amount of dimethyl nonanedioate (**13**) was also present, undoubtedly owing to an impurity of **10** in the sample of **3** which was cleaved.

Oxidative cleavage of **10** (22 mg) was carried out in an identical manner and yielded 23 mg of free acid products. Methyl esters were prepared as before and the presence of a strong band at 5.64 μ *in the infrared spectrum* again indicated the presence of a γ-lactone. Glpc analyses indicated dimethyl nonanedioate (**13**) (55%) and presumably a C-9 γ-lactone (**14**) (40%) with equivalent chain lengths of 10.8 on Apiezon L and 15.5 on Resoflex-446.

Reaction of *trans*-Monoenes 4 and 11 in 0.1 *N* Acidic Methanol.—A 9-mg sample of **4** was refluxed for 1.5 hr with 5 ml of 0.1 *N* sulfuric acid in methanol. The mixture was then diluted with 15 ml of water and extracted with ether, and the combined ether extracts were dried over sodium sulfate. In the infrared, the isolated products (8 mg) indicated retention of the isolated *trans* band (10.35 μ), loss of the hydroxyl band (2.76 μ), and a new band at 9.18 μ characteristic of a methoxyl group. Only two products were observable by tlc analysis on ordinary silica G (hexane–ether, 4:1). These gave spots of equal intensity having R_f values of 0.56 (**8**) and 0.61 (**9**).[33]

A sample of **11** (11 mg) was etherified in an identical fashion except that 0.1 *N* hydrochloric acid was used. Recovery as before gave 9 mg of products. These also showed retention of the isolated *trans* C=C band (10.35 μ), loss of the hydroxyl band (2.76 μ), and a new band at 9.18 μ (OCH_3). Tlc analysis revealed two products with R_f values of 0.61 (**16**) and 0.62 (**15**).

Reaction of *trans,trans*-Dienol 17 in 0.1 *N* Acidic Methanol.—A 46-mg sample of **17** was placed in a 50-ml flask along with 10 ml of 0.1 *N* hydrochloric acid in methanol. The flask was flushed with nitrogen, stoppered, and allowed to stand at 27°. At intervals of 5, 15, 30, 60, 120, and 240 min, 1.5-ml aliquots were removed from the reaction mixture. Each aliquot was immediately added to 10 ml of 5% sodium bicarbonate solution. In each case, reaction products were recovered by ether extraction and then subjected to tlc analysis on silica G (hexane–ether 4:1). After 5 min of reaction, tlc analysis demonstrated that most of the starting material **17**, R_f 0.11, had been converted into a nearly equal mixture of two new products (**18**, R_f 0.53, and **19**, R_f 0.59). No starting material or products other than **18** and **19** were detectable after 30 min and no further changes in composition were noted up to 240 min. The crude products, **18** and **19**, showed retention of the 10.12-μ (*trans,trans*-diene) band and loss of the 2.75-μ (OH) band and possessed a new broad maxima in the 8.9–9.2-μ (OCH_3) region of the infrared. No *cis,trans* peaks were detected. A later experiment in which 0.1 *N* sulfuric was substituted for 0.1 *N* hydrochloric acid gave identical results.

A 23-mg portion of the crude methyl ethers **18** and **19** and 5 ml of 0.1 *N* methanolic sulfuric acid were then refluxed for 1.5 hr. The products (19 mg) were recovered by ether extraction. Tlc analysis indicated conjugated triene as a major product, although at least three other spots were apparent. The presence of a strong band at 10.06 μ in the infrared and maxima at 258, 268, and 279 mμ in the ultraviolet [λ_{max}^{hexane} 268 mμ (ε 14,600)] confirmed that conjugated triene was present in the product mixture.

Reaction of *cis,trans*-Dienol 2 in 0.1 *N* Acidic Methanol.—A 90-mg portion of **2** was placed in a 50-ml flask along with 9 ml of 0.1 *N* methanolic sulfuric acid. The flask was flushed with nitrogen, stoppered, and allowed to stand at 27°. After periods of 3, 6, 10, 20, 60, and 120 min, 1.3-ml aliquots were removed and these were immediately added to 10-ml solutions of 5% sodium bicarbonate. The products were recovered by ether extraction and examined as before. After 3 min of reaction, tlc analysis showed **2** (R_f 0.17) and spots attributed to methyl ethers **18** (R_f 0.53) and **20** (R_f 0.60). After 30 min starting material was no longer evident and no further changes were apparent up to 120 min. The fractions were then examined on 25% silver nitrate impregnated silica G (hexane–ether, 4:1).[34] The mixture of **18** and **19** obtained from **17** migrated together under these conditions (R_f 0.51). Reaction products from **2** initially (3 min) had equally intense spots of R_f 0.43 and 0.51. The spot having R_f 0.43 slowly disappeared until only a trace remained after 120 min and the predominant spot had R_f 0.51. The spot of R_f 0.43 was attributed to **20**. Quantitative infrared analyses for remaining *cis,trans* conjugation[15] were corrected to allow for 18% *trans,trans* isomers in the sample of **2** used in this experiment and are summarized as follows [time, min (%)]: 0 (100), 3 (81), 6 (73), 10 (59), 20 (45), 30 (41), 60 (36), and 120 (20). Thus 41% of the initial *cis,trans* diene of **2** remained after 30 min of reaction and none of this could be attributed to remaining **2**. The etherification products had lost the 2.75-μ (OH) band and possessed a new, rather broad, band in the 8.9–9.3-μ (OCH_3) region.

Registry No.—**1**, 10075-07-7; **2**, 10075-08-8; **3**, 6084-83-9; **4**, 10075-09-9; **5**, 2447-53-2; **10**, 10127-46-5; **11**, 10127-47-6; **12**, 2540-76-3; methyl 13D-hydroxyoctadecanoate, 10075-10-2; 9-hydroxy-*trans*-10,*cis*-12-octadecadienoic acid, 10075-11-3; 13-hydroxy-*cis*-9,*trans*-11-octadecadienoic acid, 10075-12-4.

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(32) F. D. Gunstone., *J. Chem Soc.*, 1274 (1952).

(33) On unimpregnated silica, Morris and Wharry[26] have demonstrated that R_f values of oxygenated fatty acids are dependent primarily on the position of the oxygen function and that double bonds have little or no effect on R_f. By analogy with the hydroxystearates, R_f values of methoxy derivatives should increase in the following order: C-9 < C-11 < C-13. Resolution of isomeric methoxyoctadecadienoates by tlc has been reported [*cf.* M. J. Diamond, R. E. Knowles, R. G. Binder, and L. A. Goldblatt, *J. Am. Oil Chemists' Soc.*, **41**, 430 (1964)].

(34) On silver nitrate impregnated silica R_f is primarily dependent on the number and type of unsaturated bonds present. The *cis,trans*-conjugated dienes are retarded relatively more than their *trans,trans* isomers.[26]