and 1170 cm.$^{-1}$ (sulfonate),[15] no hydroxyl; n.m.r. signals at 5.30 diffuse triplet (1 proton, 1 H, $J \sim 3$ c.p.s.), 3.90 s (2 protons, $CH_2OSO_2CH_2$), 2.92 s (3 protons, mesylate), 0.98, 0.84, and 0.82 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{21}H_{36}O_3S$: C, 68.42; H, 9.84; S, 8.70. Found: C, 69.06; H, 9.59; S, 8.63.

B. *Via* **Diol 10.**—A solution of 8.37 g. of lactone **5** in 300 ml. of anhydrous ether was added to a swirled suspension of 6.0 g. of lithium aluminum hydride in 400 ml. of anhydrous ether and the mixture was refluxed for 3 hr. The excess reagent was decomposed in the usual way, the aqueous layer was extracted with ether, and the extracts were combined with the original ether layer, washed with water, dried, and evaporated to furnish 8.3 g. of diol **10**, which crystallized from acetone as colorless needles: m.p. 176–179° (the analytical sample had m.p. 182–183°); infrared bands at 3300–3400 and 1080 cm.$^{-1}$ (hydroxyl); n.m.r. signals at 3.80 s (2 protons, OH, removed on exchange with D_2O), 3.68, 3.16 (AB quartet, 2 protons, CH_2OH, $J_{AB} = 11$ c.p.s.), 0.87, 0.87, and 0.78 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{20}H_{36}O_2$: C, 77.86; H, 11.76. Found: C, 77.86; H, 11.61.

Acetylation of 4.0 g. of diol **10** with acetic anhydride–pyridine for 2 hr. at 80° gave, after the usual working up, 4.5 g. (quantitative) of monoacetate **11** which crystallized from aqueous methanol as colorless flat needles: m.p. 101–102°; infrared bands at 3600, 1040 (OH), 1735, 1715, and 1280–1250 cm.$^{-1}$ (acetate). The infrared spectrum in carbon tetrachloride showed only one carbonyl band at 1740 cm.$^{-1}$. N.m.r. signals occurred at 4.67, 3.98 (AB quartet, 2 protons, CH_2OAc, $J_{AB} = 11$ c.p.s.), 2.01 s (3 protons, acetate), 0.93, 0.85, and 0.83 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.61; H, 10.89.

A solution of 3.0 g. of **11** in 100 ml. of pyridine was cooled to 0° and treated slowly with 11 ml. of thionyl chloride. After addition was complete the ice bath was removed and the mixture was kept at 25° for 4 hr., then poured onto ice, and extracted three times with ether. The combined extracts were washed well with water, twice with 1 *N* hydrochloric acid, and again with water, dried, and evaporated to give 2.6 g. (92%) of acetate **8**, identical (infrared and n.m.r.) with the compound described in A.

Alcohol 12.—A solution of 1.4 g. of acetate **8** in 60 ml. of acetic acid and 3 drops of 61% perchloric acid was shaken under hydrogen at 20 p.s.i.g. pressure in the presence of platinum catalyst (from 0.2 g. of platinum oxide) for 22 hr. at room temperature. The catalyst was removed by filtration through Celite and the filtrate was diluted with water, saturated with salt, and extracted twice with ether. The combined ether extracts were washed successively with water, 2 *N* aqueous sodium hydroxide, and water, dried, and evaporated to give 1.3 g. of crude acetate **13**: infrared bands ($CHCl_3$) at 1735 cm.$^{-1}$ (acetate); n.m.r. signals at 4.31, 3.94 (AB quartet, 2 protons, CH_2OAc, $J_{AB} = 11$ c.p.s.), 2.06 s (3 protons, acetate), 0.96, 0.86, and 0.68 p.p.m. (methyl singlets), no olefinic resonances.

A mixture of the above oil in 60 ml. of methanol and 10 ml. of 2 *N* aqueous sodium hydroxide was heated on a steam bath for 1 hr., then diluted with water, and extracted thrice with ether. The combined extracts were washed successively with water, 1 *N* hydrochloric acid, and water, dried, and evaporated to yield 0.9 g. (73% from **8**) of alcohol **12** which crystallized from aqueous methanol as colorless needles: m.p. 114–115°; infrared bands at 3400 and 1040 cm.$^{-1}$ (OH); n.m.r. signals at 3.83, 3.51 (AB quartet, 2 protons, CH_2OH, $J_{AB} = 11$ c.p.s.), 0.96, 0.86, and 0.68 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{20}H_{36}O$: C, 82.12; H, 12.40. Found: C, 82.50; H, 12.57.

The alcohol **12** was further characterized as its mesylate **14** which crystallized from methanol as colorless plates: m.p. 149.5–150°; infrared bands at 1350 and 1180 cm.$^{-1}$ (sulfonate), no hydroxyl or carbonyl absorption; n.m.r. signals at 4.60, 4.06 (AB quartet, 2 protons $CH_2OSO_2CH_3$, $J_{AB} = 9$ c.p.s.), 2.99 s (3 protons, mesylate), 1.01, 0.84, and 0.68 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{21}H_{38}O_3S$: C, 68.05; H, 10.34; S, 8.65. Found: C, 68.26; H, 9.93; S, 8.34.

13-*epi*-Tetrahydrorimuic Acid 15.—A solution of 0.1 g. of alcohol **12** in 30 ml. of acetone was stirred at 25° with 1.0 ml. of Jones reagent for 1 hr. and then diluted with water. The precipitate was collected, washed well with water, and crystallized from aqueous acetone to give acid **15**: m.p. 192–193°; $[\alpha]D$ −13° (*c* 1.27) (lit.[12] m.p. 190°, $[\alpha]D$ −15°); infrared bands at 2650–2800 and 1700 cm.$^{-1}$ (carboxylic acid); n.m.r. signals at 1.23, 0.88, and 0.67 p.p.m. (methyl singlets); the carboxylic acid proton was superimposed on the methylene envelope.

13-*epi*-Rimuane 2.—Deaerated Jones reagent was added dropwise to a stirred solution of 0.8 g. of alcohol **12** in 60 ml. of acetone at 0° under nitrogen. When a brown color persisted, the mixture was diluted with water and extracted twice with ether. The combined extracts were washed, dried, and evaporated to yield crude aldehyde **16** as an oil: infrared bands ($CHCl_3$) at 2750 and 1725 cm.$^{-1}$ (aldehyde).

A mixture of this crude aldehyde, 70 ml. of diethylene glycol, 9 ml. of hydrazine hydrate, and 9 g. of potassium hydroxide was heated under reflux for 6.5 hr., then cooled, diluted with water, and extracted thrice with hexane. The combined extracts were washed twice with 1 *N* hydrochloric acid and twice with water, dried, and evaporated to furnish 0.58 g. of an oil which was taken up in hexane and chromatographed on 40 g. of alumina prepared in hexane. Elution with that solvent gave a colorless mobile oil which solidified on cooling and crystallized from methanol at −10° as colorless needles of 13-*epi*-rimuane **2** (yield 0.275 g., 36%): m.p. 52–53°; $[\alpha]D$ −21°; infrared bands (CCl_4) at 1385 and 1365 cm.$^{-1}$ (*gem*-dimethyl); n.m.r. signals at 0.83, 0.83, 0.79, and 0.66 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{20}H_{36}$: C, 86.88; H, 13.12. Found: C, 86.62; H, 13.03.

Continued elution with hexane and ether afforded 0.2 g. of the azine **17** which crystallized from acetone as colorless needles: m.p. 220–221°; infrared bands at 1640 cm.$^{-1}$ (C=N); n.m.r. signals at 8.14 s (1 proton, C*H*=N—), 1.17, 0.87, and 0.70 p.p.m. (methyl singlets).

Anal. Calcd. for $C_{40}H_{68}N_2$: N, 4.85. Found: N, 4.76.

(15) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co. Ltd., London, 1956, p. 300.

Arbiglovin. A New Guaianolide From *Artemisia bigelovii* Gray[1]

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In continuation of our study of American *Artemisia* species,[2] we have carried out a systematic search for sesquiterpene lactones in *Artemisia bigelovii* Gray. This resulted in the isolation of a new guaianolide, $C_{15}H_{18}O_3$, m.p. 201–203°, $[\alpha]D$ +199°, which we have called arbiglovin.

The ultraviolet spectrum of arbiglovin (**1**), λ_{max} 227 mμ (ϵ_{max} 19,500), indicated the presence of conjugation, the chromophore of a disubstituted α,β-unsaturated ketone being superimposed on that of a conjugated lactone. This was supported by the infrared spectrum which exhibited strong bands at 1705 and 1625 cm.$^{-1}$ reminiscent of β-alkyl-substituted cyclopentenones.[2] The remaining two oxygens were presumably present as a γ-lactone (infrared band at 1770 cm.$^{-1}$) conjugated with a methylene group (shoulder near 1660 cm.$^{-1}$).

The presence of an exocyclic methylene group conjugated with a lactone was shown chemically by ozonolysis (formation of formaldehyde) and preparation of a pyrazoline. The presence of two double bonds

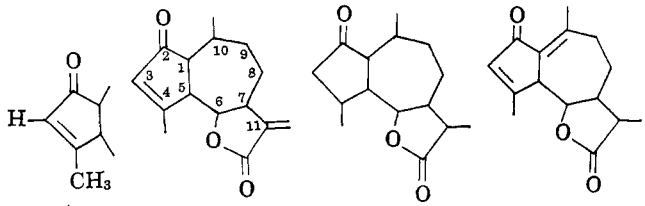
(1) Supported in part by a grant from the Mallinckrodt Chemical Works.

(2) Previous paper: W. Herz and K. Ueda, *J. Am. Chem. Soc.*, **83**, 139 (1961).

was confirmed by microhydrogenation. The product, tetrahydroarbiglovin (2), exhibited strong infrared bands at 1780 (γ-lactone) and 1745 cm.$^{-1}$ (cyclopentanone), the cyclopentanone carbonyl being flanked by a methylene group (positive Zimmermann test, infrared band at 1425 cm.$^{-1}$).

The n.m.r. spectra of arbiglovin and tetrahydroarbiglovin verified these conclusions. Arbiglovin had two low-field doublets at 6.20 and 5.53 p.p.m. (J = 3.5 c.p.s.) characteristic of a methylene group conjugated with a lactone.[3,4] Those were absent in the n.m.r. spectrum of 2. A vinyl proton resonance at 6.00 p.p.m., somewhat broadened by allylic coupling to a methyl group at 2.27 p.p.m. (J = 1 c.p.s.) was found in the n.m.r. spectrum of 1, but not of 2, the chemical shifts and appearance of these signals being typical of partial structure A.[2] Arbiglovin also exhibited a methyl doublet at 0.75 p.p.m. and a doublet of doublets (J_1 = 10 c.p.s., J_2 = 9 c.p.s.) at 4.33 p.p.m. The chemical shift of the latter is characteristic of hydrogen on carbon carrying lactone oxygen which, because of the multiplicity, must be spin-coupled to two adjacent hydrogens.

Tetrahydroarbiglovin had a doublet at 1.23 p.p.m. (J = 7 c.p.s.), which was ascribed to the methyl group α to a carbonyl group, and two other methyl doublets at 0.89 and 0.98 p.p.m. This indicated that two new methyl groups had been formed by hydrogenation of the exocyclic methylene and the vinylic methyl group.



A 1 2 3a, b

A tentative and biogenetically plausible structure for arbiglovin based on these data would be 1. If this were correct, tetrahydroarbiglovin would be 2, identical or stereoisomeric with tetrahydroachillin from achillin (3a), a constituent of *Achillea lanulosa* Nutt.,[5] or tetrahydroleucodin from leucodin (3b), which has been isolated from *Artemisia leucodes* Schenck[6,7] and identified[5] as desacetoxymatricarin. A direct comparison of tetrahydroleucodin[8] with tetrahydroarbiglovin established their identity, thus confirming the structure postulated for arbiglovin.

Extraction of *Artemisia canadensis* Michx., which has not been studied previously, did not furnish crystalline sesquiterpene lactones.

(3) W. Herz, H. Watanabe, M. Miyazaki, and Y. Kishida, *J. Am. Chem. Soc.*, **84**, 2601 (1962).

(4) W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *ibid.*, **85**, 19 (1963).

(5) E. H. White and R. E. K. Winter, *Tetrahedron Letters*, 137 (1963).

(6) K. S. Rybalko and P. S. Massagetov, *Med. Prom. SSSR*, **15**, No. 11, 25 (1961); *Chem. Abstr.*, **56**, 15608 (1962).

(7) M. Holub and V. Herout, *Collection Czech. Chem. Commun.*, **27**, 2980 (1962).

(8) We are grateful to Dr. P. T. Kondratenko, Director of the All-Union Research Institute of Medicinal and Aromatic Plants, Moscow, U.S.S.R., for a generous sample of leucodin which allowed us to carry out this comparison.

Experimental Section[9]

Isolation of Arbiglovin.—Above-ground parts of *Artemisia bigelovii* Gray, collected by Mr. Robert Barr 10 miles north of Show Low, Navajo County, Ariz., on July 24, 1962 (Barr No. 62-429), 0.95 kg., were ground and extracted with hot chloroform for 3 days. Solvent was removed at reduced pressure and the residue was dissolved in 400 ml. of ethanol, warmed to about 50°, and treated with a hot solution of 10 g. of lead acetate and 3 ml. of acetic acid in 250 ml. of water. The mixture was allowed to stand overnight. The supernatant liquid was filtered, concentrated *in vacuo*, and extracted thoroughly with chloroform. The chloroform extract was washed, dried, and evaporated, and the residual gum, 15 g., was chromatographed over 150 g. of Mallinckrodt 100 mesh silicic acid. The material eluted with benzene was rechromatographed over silicic acid. Benzene–chloroform (3:1) eluted solid material which was recrystallized twice from acetone–hexane. The colorless needles of arbiglovin melted at 201–203°, $[\alpha]^{25.5}D$ 199°, yield 0.9 g. (0.1%).

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.20; H, 7.37. Found: C, 73.50; H, 7.56.

The pyrazoline was prepared by mixing a solution of 0.1 g. of 1 in 8 ml. of dry tetrahydrofuran with 10 ml. of an ethereal solution of diazomethane. After 3 days in the refrigerator, the solvents were removed and the residue was recrystallized from chloroform–cyclohexane, m.p. 164–167°.

Anal. Calcd. for $C_{16}H_{20}N_2O_3$: C, 66.64; H, 6.99; N, 9.72; O, 16.65. Found: C, 66.51; H, 7.07; N, 9.94; O, 16.55.

A solution of 0.1 g. of 1 in 10 ml. of acetic acid was ionized for 30 min. at 0°, diluted with water, and steam distilled into a chilled saturated aqueous solution of dimedone. After standing, there precipitated 31 mg. of the dimedone derivative of formaldehyde, m.p. 183–185°.

Tetrahydroarbiglovin (2).—A suspension of 0.1 g. of platinum oxide in 50 ml. of ethanol was saturated with hydrogen and mixed with 0.2 g. of arbiglovin, and the hydrogenation was continued at atmospheric pressure. Hydrogen absorption stopped after consumption of 2 mole equiv. of hydrogen. Solvent was evaporated at reduced pressure and the residue was chromatographed over 15 g. of silicic acid. Elution with benzene gave a small amount of gum; elution with benzene afforded a viscous oil which solidified after trituration with hexane. Crystallization from acetone–hexane gave white needles, m.p. 148–150° (with previous sintering at 142°). The melting point improved to 154–155°, yield 0.035 g., after filtration through a column of alumina and three crystallizations from acetone–hexane: lit.[10] m.p. for tetrahydroleucodin 158–159°, lit.[5] m.p. for tetrahydroachillin 146–147°. However, the infrared spectrum differed from the infrared spectrum of tetrahydroachillin supplied by Professor E. H. White to whom we express our thanks.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86; O, 19.17. Found: C, 71.93; H, 9.00; O, 19.37.

Tetrahydroarbiglovin was also obtained by hydrogenation of arbiglovin with platinum oxide in ethyl acetate at 2 atm. An attempted isomerization of 2 with anhydrous potassium carbonate in methanol resulted in conversion to a gummy hydroxy acid, presumably by opening of the lactone ring, which could not be lactonized by heating with acetic anhydride in pyridine.

Tetrahydroleucodin (3b).—A solution of 0.15 g. of leucodin[8] in 100 ml. of methanol was shaken with 92 mg. of platinum oxide at a hydrogen pressure of 32 p.s.i. for 4 hr. The solution was filtered and concentrated and the residue was chromatographed over 20 g. of silicic acid. Elution with benzene–chloroform and recrystallization from acetone–hexane afforded tetrahydroleucodin, m.p. 155–157°, m.m.p. with tetrahydroarbiglovin (2) 154–156°, infrared spectra superimposable, indistinguishable from 2 by thin layer chromatography.

Extraction of *Artemisia canadensis* Michx.—Ground leaves, 1350 g., of *Artemisia canadensis* Michx.,[11] collected by Dr. B. H. Braun in Boulder Canyon, Colo., on Aug. 30, 1960, were ex-

(9) Melting points and boiling points are uncorrected. Analyses were by Dr. F. Pascher, Bonn, Germany. Rotations and infrared spectra were run in chloroform solution, n.m.r. spectra in deuteriochloroform, and ultraviolet spectra in 95% ethanol.

(10) K. S. Rybalko, *Zh. Obshch. Khim.*, **33** (8), 2734 (1963).

(11) This is sometimes considered a subspecies of *Artemisia campestris* L. For a discussion of this point and possible synonyms, see H. M. Hall and F. E. Clements, "The Phylogenetic Method in Taxonomy," No. 326, Carnegie Institution, Washington, D. C., 1923.

tracted with chloroform and worked up in the usual fashion. The residual gum, 19.2 g. was chromatographed over 160 g. of silicic acid. The column was eluted with benzene, benzene–chloroform, chloroform, and chloroform–methanol, but none of the eluates furnished crystalline material.

Optical Rotatory Dispersion and Absolute Configuration. VI. Structure and Absolute Configuration of Helenynolic Acid[1]

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Helenynolic acid, a new hydroxy acid containing the vinylacetylene chromophore, was recently isolated from the seed oil of *Helichrysum bracteatum* and was shown[3] by oxidative degradation, spectral properties, and lithium aluminum hydride reduction to have the structure 9-hydroxy-*trans*-10-octadecen-12-ynoic acid (Ia). It is thus closely related to 8-hydroxyximenynic acid (II), 8-hydroxyisanic acid (III), and 8-hydroxybolekic acid (IV), all of which occur in natural fats and oils and possess the normal C_{18} skeleton.[4]

$CH_3(CH_2)_4C{\equiv}CCH{=}CHCH(OH)(CH_2)_7COOR$
Ia, R = H
b, R = CH_3

$CH_3(CH_2)_5CH{=}CHC{\equiv}CCH(OH)(CH_2)_6COOH$
II

$CH_2{=}CH(CH_2)_4(C{\equiv}C)_2CH(OH)(CH_2)_6COOH$
III

$CH_2{=}CH(CH_2)_2CH{=}CH(C{\equiv}C)_2CH(OH)(CH_2)_6COOH$
IV

The absolute configuration of the asymmetric carbon atom in I is of considerable interest in view of current work[4] on the biogenesis of the C_{18} acetylenic acids in plants.

The rotatory dispersion curve of methyl helenynolate (Figure 1) shows two closely spaced positive Cotton effects, with peaks at 232 and 243 mμ, superimposed on a strong positive background. This is in excellent agreement with its vinylacetylene chromophore [λ_{max} 228 and 238 mμ (ϵ 17,400 and 14,300, respectively)].

Hydrogenation of methyl helenynolate with 10% palladium on charcoal in methanol gave a saturated ester, m.p. 51°, identified as methyl 9-D-hydroxyoctadecanoate by comparison with a sample prepared by the action of diazomethane on synthetic 9-D-hydroxyoctadecanoic acid.[5] The identity of the natural

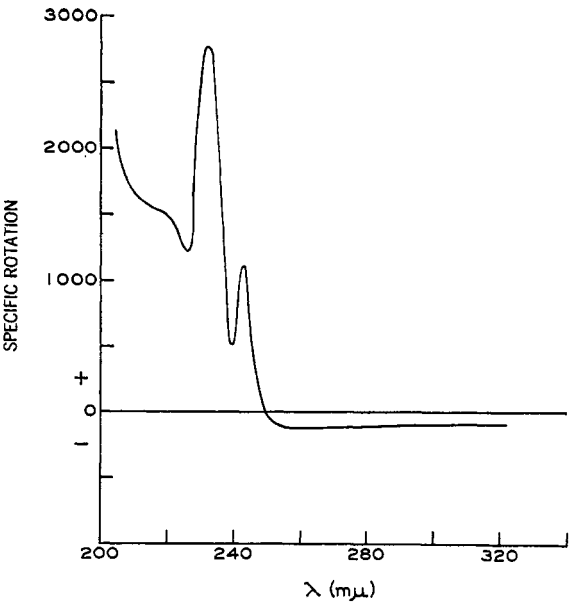

Figure 1.—Rotatory dispersion curve of (−)-methyl helenynolate.

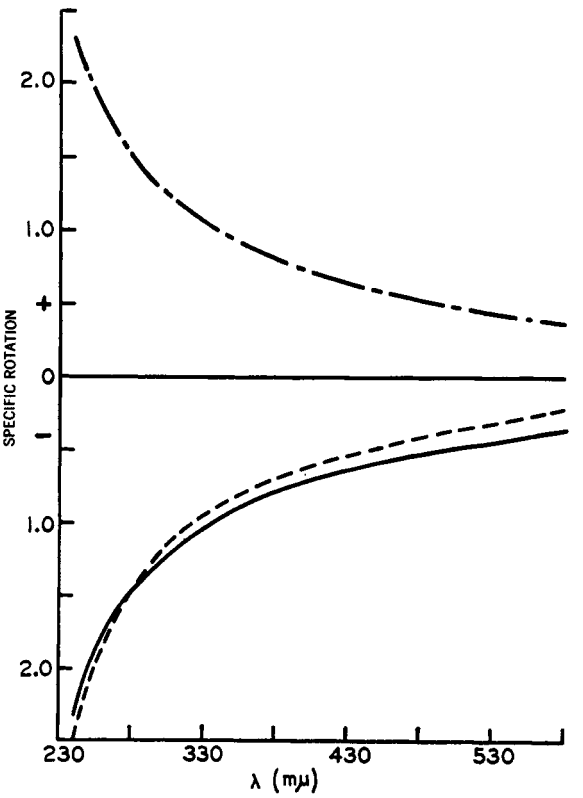

Figure 2.—Rotatory dispersion curves of (−)-methyl 12-D-hydroxyoctadecanoate (———), (+)-methyl 12-L-hydroxyoctadecanoate (—·—·), and (−)-methyl 9-D-hydroxyoctadecanoate (———).

and the synthetic samples by mixture melting point, infrared spectrum, and gas chromatographic retention time offers conclusive proof of the correct location of the 9-hydroxy group in I.

The two samples of the ester also gave the same rotatory dispersion curve (Figure 2), closely similar to that (Figure 2) of (−)-methyl 12-D-hydroxyoctadecanoate, obtained from D-(+)-methyl ricinoleate by catalytic hydrogenation. Since both ricinoleic acid and its hydrogenation product (−)-12-hydroxyoctadecanoic

(1) Supported (in part) by Research Grant HE-5881 from the National Institutes of Health, U. S. Public Health Service.

(2) A laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(3) R. G. Powell, C. R. Smith, Jr., C. A. Glass, and I. A. Wolff, *J. Org. Chem.*, **30**, 610 (1965).

(4) For review, see J. D. Bu'Lock, *Progr. Org. Chem.*, **6**, 86 (1964).

(5) C. D. Baker and F. D. Gunstone, *J. Chem. Soc.*, 759 (1963). We are indebted to Professor Gunstone for a sample of synthetic 9-D-hydroxyoctadecanoic acid.