Quantum Yield Determination.—A solution was prepared by dissolution of 0.130 g of acetophenone and 0.062 g of chlorobenzene[15] in enough tetramethylallene to make the total volume 10 cc. Two tubes, each containing 3.4 cc of the solution, were irradiated in a merry-go-round apparatus for periods of 4 and 6 hr using solution filters containing $NiSO_4$–$CoSO_4$ and potassium acid phthalate to isolate the 3130-Å group of lines. Samples containing 3.4 cc of a mixture of 1,3-cyclohexadiene (1.312 g), benzophenone (0.916 g), and hexadecane[15] (0.1395 g) in 50.0 cc of benzene were irradiated in parallel with the reaction samples. The product mixtures were analyzed by vapor chromatography and the quantum yield for disappearance of acetophenone was calculated on the assumption that the quantum yield for dimerization of cyclohexadiene is 0.88 under the specified conditions.[16] The measured value of the quantum yield was 0.58 after 4 hr and 0.60 after 6 hr.

(15) Internal standard for vapor chromatographic analysis.
(16) G. F. Vesley, unpublished study.

Registry No.—**1**, 16717-87-6; **2**, 16717-86-5; **3**, 16717-88-7; **4**, 14315-05-0; **5**, 14315-03-8; **6**, 14315-04-9; **7**, 16717-92-3; **8**, 16717-93-4; **9**, 16717-94-5; **10**, 16717-95-6; **11**, 16717-96-7; **12**, 16717-97-8; **13**, 16717-98-9; **14**, 16718-04-0; **15**, 14315-02-7; **16**, 16718-00-6; **17**, 2570-82-3; **18**, 14315-08-3; **19**, 14315-07-2.

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Sesquiterpene Lactones of *Helenium alternifolium* (Spreng.) Cabrera. Structures of Brevilin A, Linifolin A, and Alternilin[1,2]

WERNER HERZ, CHARLES M. GAST,[3] AND P. S. SUBRAMANIAM

Department of Chemistry, Florida State University, Tallahassee, Florida 32306

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Helenium alternifolium (Spreng.) Cabrera from near Tucuman, Argentina, furnished primarily tenulin and smaller amounts of brevilin A, previously isolated from *H. brevifolium* (Nutt.) A. Wood, linifolin A, previously isolated from *H. linifolium* Rybd., and 6,3′-dimethoxy-5,7,4′-flavone. A collection of *H. alternifolium* from near La Plata, Argentina, afforded the new sesquiterpene lactone alternilin as the sole crystallizable constituent. Structures of brevilin A, linifolin A, and alternilin have been established.

Since our last summary[4] of work on constituents of *Helenium* species, the complete stereochemistry of mexicanin A,[5] thurberilin,[6] and tetrahydrobigelovin[6] has been established and the relative configuration of bromomexicanin E[7] has been determined. A new guaianolide, virginolide, has been extracted from *H. virginicum* Blake,[1] a structure has been deduced for mexicanin H[8] and previously known lactones have been isolated from *H. plantagineum* (DC.) MacBride.[9] In the present paper we wish to report our work on the Argentinian species *H. alternifolium* (Spreng.) Cabrera which allowed us to determine the structure of two previously isolated pseudoguaianolides, brevilin A[10] and linifolin A,[11] and that of a new congener, alternilin.

Examination of *H. alternifolium* collections from near Tucuman, Argentina, furnished 6,3′-dimethoxy-5,7,4′-trihydroxyflavone[12] and tenulin[13] as the principal sesquiterpene lactone constituent. Smaller quantities of other lactones were also isolated. One of the minor lactones was identified as linifolin A, $C_{17}H_{20}O_5$, mp 201–203°,[11,14] previously isolated from *H. linifolium* Rydb., to which we had assigned[11] a gross structure stereoisomeric with that of acetylhelenalin (**2**) (Chart I),[13b,15] balduilin (**3**),[13b,16] and bigelovin (**4**).[17,18] Because hydrogenation of linifolin A afforded, in our hands,[11] a tetrahydro derivative of mp 149–150° which differed from acetyltetrahydrohelenalin (**6**), acetyldihydromexicanin C (11-epiacetyltetrahydrohelenalin), tetrahydrobalduilin (**7**), 11-epitetrahydrobalduilin, tetrahydrobigelovin (**8**), and dihydroisotenulin (**9**) and, because of a subsequent report[19] that hydrogenation of the fourth possible *trans*-fused isomer acetylmexicanin I (**5b**) afforded a substance of mp 109° which was presumably 11-epidihydroisotenulin (**10**), we were forced to conclude[11] that linifolin A differed from compounds **2**–**5** in configuration at one or more of the asymmetric centers at C-1, C-5, C-7, and C-10 and suggested[5] that, because of the inversion of the Cotton effect during hydrogenation, linifolin A might belong to the 1-*epi* series.

The physical constants of the freshly isolated linifolin A from *H. alternifolium*, however, coincided so closely with those reported for acetylmexicanin I (**5b**)[9,19] that a direct comparison was called for. Acetylation of samples of mexicanin I supplied by Dr. Romo de Vivar or isolated from *Helenium autumnale* L.[20] gave material

(1) Constituents of Helenium Species. XXI. Previous paper: W. Herz and P. S. Santhanam, *J. Org. Chem.*, **32**, 507 (1967).
(2) Supported in part by a grant from the U. S. Public Health Service (GM-05814).
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(4) W. Herz and M. V. Lakshmikantham, *Tetrahedron*, **21**, 1711 (1965).
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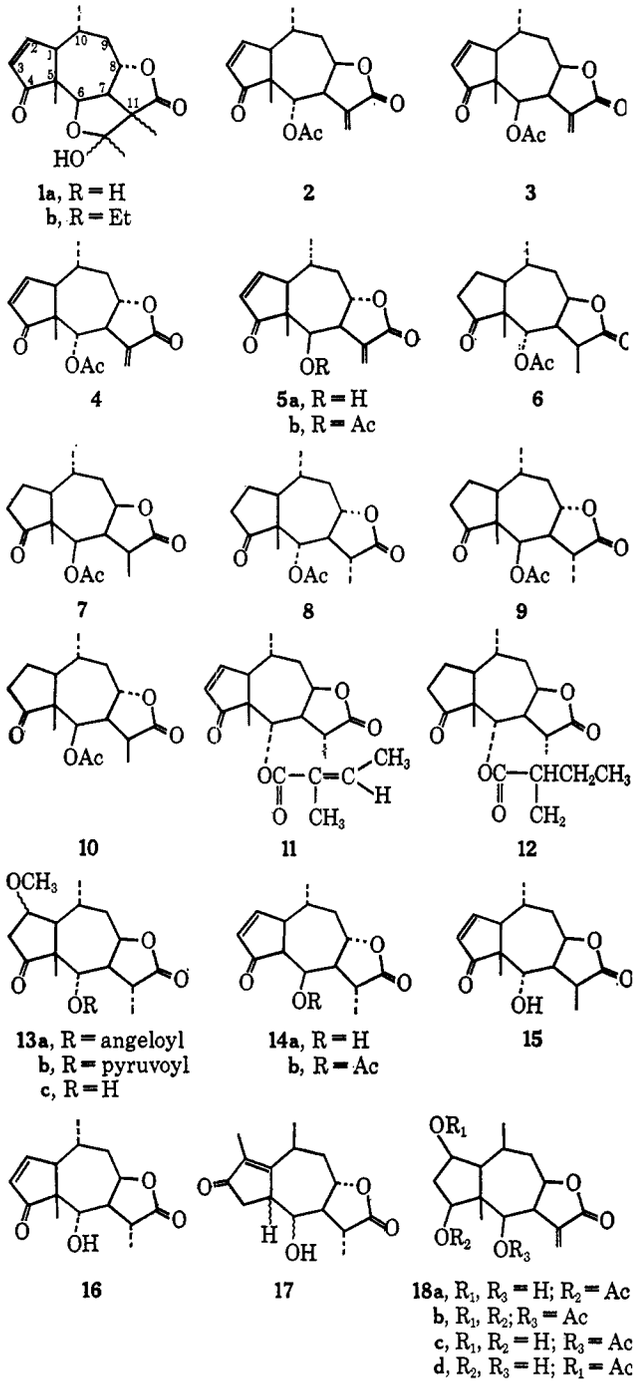
(6) A. Romo de Vivar, L. Rodriguez-Hahn, J. Romo, M. V. Lakshmikantham, R. N. Mirrington, J. Kagan, and W. Herz, *ibid.*, **22**, 3279 (1966).
(7) C. N. Caughlan, Mazhar-ul-Haque, and M. T. Emerson, *Chem. Commun.*, 151 (1966).
(8) J. Romo, A. Romo de Vivar, and P. Joseph-Nathan, *Tetrahedron Lett.*, 1029 (1966).
(9) M. Silva, *J. Pharm. Sci.*, **56**, 922 (1967).
(10) W. Herz, R. B. Mitra, K. Rabindran, and W. A. Rohde, *J. Amer. Chem. Soc.*, **81**, 1481 (1959).
(11) W. Herz, *J. Org. Chem.*, **27**, 4043 (1962).
(12) J. W. ApSimon, N. B. Haynes, K. Y. Sim, and W. B. Whalley, *J. Chem. Soc.*, 3788 (1963).
(13) (a) W. Herz, W. A. Rohde, K. Rabindran, P. Jayaraman, and N. Viswanathan, *J. Amer. Chem. Soc.*, **84**, 3857 (1962); (b) W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *Tetrahedron*, **19**, 1359 (1963).
(14) The melting point was slightly higher than that reported earlier,[11] but the compound was identical in all respects (nmr and ir spectra, tlc) with the sample from *H. linifolium*.
(15) W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *J. Amer. Chem. Soc.*, **85**, 19 (1963).
(16) W. Herz, R. B. Mitra, and P. Jayaraman, *ibid.*, **81**, 6061 (1959).
(17) B. A. Parker and T. A. Geissman, *J. Org. Chem.*, **27**, 4127 (1962).
(18) W. Herz and M. V. Lakshmikantham, *Tetrahedron*, **21**, 1711 (1965).
(19) E. Dominguez and J. Romo, *ibid.*, **19**, 1415 (1963).
(20) P. S. Subramaniam, unpublished work.

CHART I



identical in all respects with linifolin A. Since mexicanin I has been correlated[19] with tenulin, the formula of linifolin A is therefore **5b**. However, repetition of the earlier[11] hydrogenation of linifolin A again furnished a substance of mp 152–154°, $[\alpha]D$ +17.40, identical with the sample of mp 149–150° previously prepared by us[11] from linifolin A and not the material of mp 109°, $[\alpha]D$ +48°, reported by the Mexican workers. We are unable to account for this discrepancy in the physical properties of what must be 11-epidihydroisotenulin.

The second minor lactone melted sharply but variably in the range 116–127° and was identified by direct comparison as brevilin A, a substance previously[21] isolated in very low yield from *H. brevifolium* (Nutt.) A. Wood, although the empirical formula assigned earlier to brevilin A now requires correction to $C_{20}H_{26}O_5$.

The presence of an α,β-unsaturated α,β-unsubstituted cyclopentenone moiety, deduced earlier on the basis of the infrared and ultraviolet spectra, was corroborated by the nmr spectrum which exhibited the usual[13,15] doublets of doublets at 7.75 and 6.00 ppm. However, the presence of one methyl singlet at 1.01 (presumably that of C-5 methyl) and two methyl doublets at 1.50 and 1.20 ppm (C-10 and C-11 methyl) indicated that the lactone group was saturated as in tenulin[13] rather than unsaturated as in helenalin or isohelenalin.[15] The second conjugated double bond (infrared band at 1650 cm^{-1}) was therefore placed in an unsaturated side chain. The latter, already suggested by the empirical formula, was identified as an angeloyl group, because of a broad signal at 6 ppm and two characteristic vinyl methyl multiplets at 1.86 and 1.70 ppm.[4]

Catalytic hydrogenation of brevilin A (**11**) yielded a noncrystalline tetrahydro derivative (**12**) whose infrared and nmr spectra reflected changes resulting from saturation of a cyclopentenone chromophore and an angeloyl side chain. Attempts to hydrolyze **11** or **12** in an effort to confirm the direction of lactone ring closure and point of attachment of the ester function (C-6 rather than C-8)[22] were either unsuccessful or required drastic conditions leading to mixtures of desangeloyl derivatives. However, the fortuitous discovery that **13a** was formed from **11** on treatment with methanol–potassium bicarbonate appeared to afford a means of protecting the cyclopentenone function during oxidative removal of the side chain in the manner previously[4] adopted for thurberilin. Ozonolysis of **13a** furnished acetaldehyde and a pyruvate **13b** which it was expected would be cleaved under milder conditions than those required for the hydrolysis of **11**. Simultaneous elimination of the methoxy group under the influence of base was envisioned as a distinct possibility, a reaction which it was hoped would permit the direct correlation of brevilin A with one of the known epimers of desacetylisotenulin (**14a**). In fact a detailed analysis of chemical shifts and coupling constants in the nmr spectra of brevilin A derivatives indicated that brevilin belonged to either the dihydrohelenalin (**15**) or mexicanin C (**16**) series, but was not a derivative of balduilin (**3**), bigelovin (**4**), or isotenulin (**14b**).

Hydrolysis of **13b** with potassium carbonate in boiling methanol afforded as the only crystalline component of a complex mixture a new α,β-unsaturated keto lactone whose ultraviolet (λ_{max} 238 and 302 mμ, ϵ 15,700 and 110) and nmr spectra were consonant with formula **17** (exclusive of stereochemistry). This would be the result of a "neo" rearrangement of the proximate hydrolysis and elimination product.[23] Since **17** clearly differed from dihydroneohelenalin[13b] which is formed in low yield from dihydrohelenalin (**15**) on treatment with methanolic potassium carbonate and has the same gross

(21) W. Herz, R. B. Mitra, K. Rabindran, and W. A. Rohde, *J. Amer. Chem. Soc.*, **81**, 1481 (1959).

(22) Nmr signals of H-6 and H-8 were found at 5.45 br (width at half-height, $w^{1/2}$ = 3) and 4.74 tbr (5.5) ppm. Since in pseudoguaianolides containing oxygen substituents at C-6 and C-8 the signal of hydrogen under lactone oxygen generally appears at higher field than that of hydrogen under ester oxygen, this observation clearly pointed to **11** (devoid of stereochemistry) as the correct structure of brevilin A, particularly since no pseudoguaianolides with a lactone ring oriented toward C-6 have so far been found in *Helenium* and related species.

(23) The mechanism of this rearrangement in the tenulin series is discussed in reference 13a.

TABLE I

SELECTED NMR SIGNALS[a]

Compound	H-2	H-4	H-6	H-8
Flexuosin A	4.16 c	3.81 dbr (4.5)	5.98 d (4)	4.61 td (10.5, 3)
Diacetylflexuosin A	5.0 tbr (9)	4.78 dbr (4)	5.88 d (3.5)	4.68 td (11, 3)
Alternilin	4.9 c	3.78 dbr	4.88 d (3.5)	4.68 tc (11)

[a] Multiplicites are expressed by the usual symbols d doublet, t triplet, br broadened singlet, c complex signal whose center is given. Line separations are given in parentheses.

structure **17**, it seemed likely that the immediate precursor of **17** was **16**, *i.e.*, mexicanin C.

Hydrolysis of **13b** with methanolic potassium carbonate at room temperature furnished again a complex mixture in which the presence of mexicanin C could be demonstrated by thin layer chromatography and spectrophotometrically, although the substance could not be isolated in pure form. However, since compounds of the mexicanin C series appear to possess the more stable configuration at C-11,[24] this observation does not necessarily exclude the possibility that brevilin A possesses the opposite configuration at C-11 although, for the reasons stated above, we conclude tentatively that brevilin A is angeloylmexicanin C (**11**).

A fourth lactone isolated in very small quantity possessed analytical values and spectroscopic properties consonant with **1b**, possibly the result of a reaction between tenulin and ethanol during the isolation process rather than a naturally occurring substance. Efforts to prepare this compound from tenulin and ethanol in the presence of catalytic amounts of acid failed. However, a similar substance is formed on treatment of tenulin with ethylene glycol.[25]

Examination of a single *H. alternifolium* collection from near La Plata, Argentina, furnished no tenulin, linifolin A, or brevilin A, but gave as the sole crystallizable component a small quantity of a new sesquiterpene lactone which we have named alternilin. Alternilin, $C_{17}H_4O_{26}$, mp 193–195°, $[\alpha]^{25}D$ +11.20, exhibited infrared bands (see Experimental Section) which indicated the presence of two hydroxyl groups, an α,β-unsaturated γ-lactone, and an ester function. The empirical formula suggested that the ester function was an acetate, a hypothesis which was verified by the nmr spectrum which had a doublet at 4.88 and a methyl singlet at 1.96 ppm. The spectrum also revealed the presence of an exocyclic methylene group (doublets at 6.15 and 5.55 ppm) conjugated with a lactone (complex triplet at 4.58 ppm), two secondary hydroxyl groups (multiplet at 4.9, broadened doublet at 3.78 ppm), a methyl singlet, and a methyl doublet.

Acetylation of alternilin afforded diacetylflexuosin A (**18b**) of known gross structure and uncertain configuration.[26] Since flexuosin A is **18c**,[26] alternilin must be **18a** or **18d**. A comparison of the nmr spectra of **18b**, **18c**, and alternilin (Table I) clearly showed that alternilin had structure **18d**. Thus the broadened doublet associated with H-4 exhibits the same chemical shift in the spectra of flexuosin A and alternilin; hence C-4 of alternilin carries a free hydroxyl group as well. However, alternilin displays the sharp doublet associated with H-6 more than 1 ppm upfield from the H-6 doublets of flexuosin A and its diacetate; hence C-6 of alternilin carries a hydroxyl group. Conversely, the H-2 multiplets of alternilin and **18c** are found considerably downfield from the H-2 multiplet of flexuosin A; hence C-2 of alternilin carries an acetoxyl group.

(24) Tetrahydrohelenalin is isomerized[6] to dihydromexicanin C on treatment with potassium carbonate.

(25) E. P. Clark, *J. Amer. Chem. Soc.*, **62**, 1254 (1940).

(26) W. Herz, Y. Kishida, and M. W. Lakshmikantham, *Tetrahedron*, **20**, 979 (1964).

Experimental Section[27]

Extraction of *Helenium alternifolium* (Spreng.) Cabrera. A.— Above ground plant material collected by Mr. P. R. Legname near Los Puestos, Department of Leales, Tucuman province, Argentina, on Oct 20, 1965, in the flowering stage was ground, extracted with chloroform, and worked up in the usual manner. This resulted in 66.2 g of gum which was dissolved in benzene and placed on a chromatographic column containing 1.1 kg of silicic acid (Mallinckrodt, 100 mesh). On standing, crystalline material separated from solvent at the top of the column. It was scooped out, recrystallized from benzene, and identified as tenulin, yield 6.4 g, by melting point, mixture melting point, infrared spectrum, and tlc. The remaining material was chromatographed in the usual way, 2-l. fractions being collected. Fractions 1–9 (benzene), 10–19 (benzene–chloroform 4:1), 20–29 (benzene–chloroform, 3:1), 30–39 (benzene–chloroform, 2:1), 40–49 (benzene–chloroform 1:1), 50–59 (benzene–chloroform, 1:2), and 60–69 (benzene–chloroform, 1:2) gave practically nothing or gums which were mixtures of several constituents (tlc). Fractions 70–80 (benzene–chloroform, 1:4) solidified on standing. Recrystallization from ether–hexane furnished 2.51 g of brevilin A: λ_{max} 223 and 320 mμ (ϵ 15,000); ir bands at 1775 (γ-lactone), 1710 (cyclopentenone and conjugated ester carbonyl), 1650 (double bond of side chain), and 1585 cm^{-1} (double bond of cyclopentenone); nmr signals at 7.75 dd (6, 1.5, H-2), 6.00 dd (6, 2.5, H-3), 6 c (vinyl proton of side chain), 5.45 br ($w^{1/2}$ = 3, H-6), 4.74 tbr (5.5, H-8), 1.86 dq and 1.70 m (vinyl methyls of side chain), 1.50 d (6.5, C-11 methyl), 1.20 d (6.5, C-10 methyl), and 1.01 ppm (C-5 methyl); $[\alpha]D$ −264° (*c* 1.00); ORD curve ϕ_{400} −1380°, ϕ_{352} −7260°, ϕ_{328} 0, ϕ_{298} −6050°, ϕ_{272} 0, ϕ_{250} −11,600° (last reading). The melting point was variable in the range 116–127°, the last being that of the analytical sample, but all samples had infrared spectra superimposable on and tlc behavior identical with that of the sample of brevilin A, mp 116–117°, previously isolated from *H. brevifolium* (Nutt.) A. Wood.

Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.57; O, 23.09. Found: C, 69.28; H, 7.24; O, 23.14.

Fractions 81–84 (chloroform) remained gummy, but fractions 85–87 solidified on standing. Recrystallization from methanol–water and then from acetone–isopropyl ether furnished 0.4 g of linifolin A: melting point and mixture melting point with authentic material[10] and with acetylmexicanin I[28] 201–203°; infrared spectra superimposable; nmr signals at 7.54 dd (6' 2, H-2), 6.01 dd (6, 3, H-3), 6.17 d (3) and 5.60 d (3.5, exocyclic methylene group), 5.84 d (4.5, H-6), 4.75 d (10, 3, H-8), 3.4 c (H-7), 2.02 (acetate methyl), 1.25 d (7, C-10 methyl), and 1.21 ppm (C-5 methyl). Fractions 88–91 (chloroform), 92–99 (chloroform–methanol, 99:1), 100–108 (chloroform–ether, 19:1), and 109–128 (chloroform containing increasing quantities of methanol) were mixtures (tlc). The mother liquors of fractions 85–87 were combined with fractions 88–94 and rechromato-

(27) Melting points are uncorrected. Analyses were by Dr. F. Pascher, Bonn, Germany. Ultraviolet spectra were run in 95% ethanol, infrared spectra in chloroform, rotations in chloroform, and nmr spectra in deuteriochloroform unless otherwise specified. Petroleum ether was the fraction boiling at 30–60°. ORD curves were run by Mr. Babu Rao in 95% ethanol on a JASCO Model ORD-UV 5 spectropolarimeter.

(28) We wish to thank Dr. A. Romo de Vivar for supplying an authentic sample of this compound.

graphed over silicic acid. Benzene–chloroform eluted solid material. Three recrystallizations from ethyl acetate–hexane gave 0.2 g of 6,3′-dimethoxy-5,7,4′,trihydroxyflavone: mp and mmp[29] 225–227° (lit.[12] mp 227–228°); nmr signals (DMSO-d_6) at 13.45 (5-OH), 10.33 very diffuse (7-OH and 4′-OH), 7.70 dd (9, 2) and 7.08 d (9, AB system of H-4′ and H-5′), 7.70 d (2, H-2′), 7.02 (H-8), 6.75 (H-3), 3.98, and 3.87 ppm (two methoxyls). Methylation of 40 mg of the flavone with methyl iodide and potassium carbonate in acetone followed by recrystallization from ethyl acetate–hexane furnished 28 mg of 5,6,7,3′,4′-pentamethoxyflavone, mp 169–1718 (lit.[30] melting points variously reported in the range 169–1798). Comparison with an authentic specimen kindly supplied by Professor T. A. Geissman established identity.

Fractions 97–103 which contained the same constituents (tlc) were combined and rechromatographed. This resulted in the isolation of additional quantities of the above flavone and more tenulin.

B.—A second collection of *H. alternifolium* (2.7 kg) by Mr. Legname at Los Puestos on Dec 10, 1966, on extraction with chloroform and work-up in the usual manner yielded 52 g of gum which was chromatographed over 1.2 kg of silicic acid, 1-l. fractions being collected. Fractions 1–9 (benzene), 10–18 (benzene–chloroform, 4:1) and 19–25 (benzene–chloroform, 3:2) eluted practically nothing. Fractions 26–29 (benzene–chloroform, 3:2) eluted a gum which solidified on standing. Rechromatography over 120 g of silicic acid (eluents benzene–chloroform, 3:2 and 1:1) and crystallization from ether–petroleum ether afforded 2.4 g of brevilin A, mp 125–127°. Fractions 30–38 (benzene–chloroform, 3:2) eluted gums which partially solidified on standing; tlc showed this to be a mixture of two main components contaminated with several other lower R_f impurities. Rechromatography over 48 g of silicic acid followed by crystallization from acetone–isopropyl ether of the solid fractions eluted with chloroform yielded 0.65 g of linifolin A, mp and mmp 201–203°.

Fractions 39–49 (benzene–chloroform, 1:1) eluted a yellow solid. Three recrystallizations from ethyl acetate–hexane gave 0.18 g of 6,3′-dimethoxy-5,7,4′-trihydroxyflavone, mp and mmp 225–227°.

Fractions 50–58 (benzene–chloroform, 1:1) eluted semisolid material. Repeated rechromatography over three 60-g portions silicic acid gave in the benzene–chloroform (1:1) fractions 2.48 g of tenulin and 0.12 g of a new lactone: mp 185–187°; $[\alpha]^{25}D$ +22.2 (*c* 1.0); λ_{max} 228 mμ (ε 7420); infrared bands at 1775 (γ-lactone), 1709, and 1582 cm^{-1} (cyclopentenone) (the spectrum differing from that of tenulin chiefly in the absence of an –OH stretching frequency and in the fingerprint region near 1150 and 780 cm^{-1}); nmr signals at 7.70 dd (6, 2, H-2), 6.20 dd (d, 2.5, H-3), 5.24 tc (11, H-8), 4.54 d (6, H-6), 3.72 m (AB part of ABX_3 multiplet, CH_3CH_2O), 1.51, 1.30, 1.30 (C-5 methyl, C-11 methyl, and acetal methyl), 1.28 br (CH_3CH_2O), and 1.12 d (7, C-10 methyl).

Anal. Calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84; O, 23.92. Found: C, 68.60; H, 7.80; O, 23.64.

Fractions 59–80 (benzene–chloroform, 1:1) and 81–95 (benzene–chloroform, 2:3) were almost pure tenulin, yield 7.5 g. Fractions 96–108 (benzene–chloroform, 1:4) and 109–118 (chloroform) eluted additional quantities of impure tenulin. Further elution with ethereal and methanolic chloroform eluted polar gums which showed several spots on tlc.

C.—A collection of 0.5 kg of *H. alternifolium* collected by Dr. A. L. Cabrera in the vicinity of La Plata, Buenos Aires Province, Argentina, during the 1964–1965 growing season, was extracted and worked up in the usual way. The crude gum (25 g) was dissolved in benzene and chromatographed over 0.5 kg of silicic acid. Fractions 1–25 (400-ml portions of benzene and benzene–chloroform, 4:1) gave waxy material; fractions 26–45 (500- and 600-ml portions of benzene–chloroform, 3:1 and 2:1), fractions 46–54 (1-l. portions of benzene–chloroform, 1:1), 55–64 (1-l. portions of benzene–chloroform, 1:2), 65–74 (benzene–chloroform, 3:1), 75–84 (benzene–chloroform, 4:1), and 85–94 (benzene–chloroform, 4:1) gave small amounts of gummy mixtures (tlc) which did not yield homogeneous material when fractions containing identical spots were combined and rechromatographed. Fraction 95–105 (chloroform–methanol, 99:1) and 106–111 (chloroform–methanol, 19:1) furnished larger amounts of gum. Fraction 108 crystallized on standing. Recrystallization from chloroform afforded alternilin: mp 193–195°; $[\alpha]^{25}D$ +11.2 (*c* 1.02); infrared bands at 36,000 (sharp, double strength, two –OH), 1770 (γ-lactone), 1740 (acetate), and 1660 cm^{-1} (conjugated double bond); nmr signals (deuterioacetone and D_2O) at 6.15 d (3.5) and 5.55 d (3.5, exocyclic methylene group), 4.9 m (H-2), 4.88 d (3.5, H-6), 4.58 tc (11, H-8), 3.78 dbr (4, H-4), 3.07 c (H-7), 1.96 (acetate methyl), 1.00 d (6, C-10 methyl), and 0.90 ppm (C-5 methyl).

Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46; O, 29.59. Found: C, 62.95; H, 758; O, 29.73.

Rechromatography of fractions 107–111 which also contained alternilin (tlc) afforded in the benzene–chloroform (1:1) eluate additional quantities of alternilin, total yield 0.65 g. No other sesquiterpene lactones could be identified.

Acetylation of 0.1 g of alternilin with pyridine–acetic anhydride and work-up in the usual manner furnished a viscous gum which gradually crystallized when allowed to stand with a small amount of chloroform. Recrystallization gave diacetylflexuosin, A, mp 128–130°, identical with authentic material. The nmr spectrum exhibited signals at 6.24 d (3.5) and 5.40 d (3.5, exocyclic methylene group), 5.88 d (3.5, H-6), 5.0 tbr (9, H-2), 4.78 dbr (4, H-4), 4.58 tc (11, H-8), 3.18 c (H-7), 2.5 c (H-2), 2.13, 2.03, 2.01 (three acetate methyls), 1.07 d (6, C-10 methyl), and 0.88 ppm (C-5 methyl). The assignments were confirmed by spin decoupling experiments carried out by J. J. Schmid. Irradiation at 3.07 ppm collapsed the doublets at 6.24, 5.88, and 5.40 to singlets and affected the multiplet at 4.58. Irradiation at 4.58 ppm simplified the 3.07 multiplet to a broad triplet (J = 4). Irradiation at 4.87 and 4.50 ppm affected a complex signal near 2.5; conversely irradiation at 2.5 ppm simplified the signals at 5.0 and at 4.78 ppm.

Linifolin A. A. Preparation from Mexicanin I.—Acetylation of mexicanin I[31] from *H. mexicanum* H. B. K. or *H. autumnale* L.[20] Torr. in the usual way gave material of mp 201–203 and 202–204° indistinguishable from linifolin A.

B. Hydrogenation to Tetrahydrolinifolin A (11-Epidihydroisotenulin).—The hydrogenation of linifolin A was repeated under the conditions reported by Herz[10] and by Dominguez and Romo.[18] In both instances the product had mp 152–150° and was identical with the substance of mp 149–150° previously obtained:[10] infrared spectra superimposable; tlc behavior identical; $[\alpha]^{25}D$ +17.4° (*c* 1.01); nmr signals at 5.78 d (2.5, H-6), 4.73 m (H-8), 2.08 (acetate), 1.19 and 1.09 d (7, C-10 and C-11 methyls), and 0.88 ppm (C-5 methyl).

Reactions of Brevilin A. A. Catalytic Hydrogenation.—A solution of 0.2 g of brevilin A in ethanol was reduced with palladium–charcoal catalyst at a hydrogen pressure of 15 lb/in.^{2} Removal of ethanol *in vacuo* resulted in a gum which could not be induced to crystallize but was identified as tetrahydrobrevilin A (12) through its nmr spectrum which had signals at 5.25 br ($w^{1/2}$ = 3, H-6), 5.70 tbr (6, H-8), 1.42 d (6.5), 1.05 d (6.5), 1.04 d (6.5, three methyl doublets), and 0.80 ppm (C-5 methyl). The methyl triplet of the side chain was submerged in the methyl and methylene envelope. The substance had infrared bands (neat) at 177° and 1740 cm^{-1}, but exhibited no bands characteristic of double bonds.

B. Attempted Hydrolysis.—A solution of 0.2 g of brevilin A was refluxed for 1 hr with a methanol–water solution containing 0.2 g of potassium carbonate, cooled, salted out with sodium chloride, and extracted with ether. The ether extract was extracted with base, but only a trace of acid appeared to have been formed. The neutral fraction could not be induced to crystallize. Its nmr spectrum indicated that hydrolysis had not taken place, but that the starting material had been epimerized, presumably at C-11. Signals appeared at 7.60 dd (6, 2) and 6.07 dd (6, 3, exocyclic methylene group), 6 c (vinyl proton of side chain), 5.38 br, 4.87 c (H-8), 3 c (H-7), 1.87 dq, and 1.70 m (vinyl methyls of side chain), 1.48 d (6.5) and 1.30 d (6.5, C-11, and C-10 methyls), and 1.25 ppm (C-5 methyl).

In a modification of the above experiment, a solution of 0.15 g of brevilin A in methanol was mixed with water containing

(29) We wish to thank Professor W. B. Whalley for supplying an authentic sample.

(30) J. Gripenberg in "The Chemistry of Flavonoid Compounds," T. A. Geissman, Ed., The Macmillan Co., New York, N. Y., 1962, p 426; N. Morita, *Chem. Pharm. Bull.* (Tokyo), **8**, 59, 66 (1960); L. J. Swift, *J. Food Sci.*, **29**, 766 (1964).

(31) We wish to thank Dr. A. Romo de Vivar for supplying an authentic sample.

0.15 g of sodium bicarbonate in such a way that both substances remained in solution and was allowed to stand overnight.

This resulted in the formation of large needles of 2-methoxy-2,3-dihydrobrevilin A (**13a**) which were filtered and recrystallized from methanol–water. The product (0.08 g) had mp 203–205°; infrared bands at 1780 (γ-lactone), 1750 (cyclopentanone), 1720, and 1645 cm^{-1} (conjugated ester); nmr signals at 6.00 qbr (vinyl proton of side chain), 5.35 br ($w^{1/2}$ = 3, H-6), 4.69 tbr (6, H-8), 3.90 tbr (4, H-2), 3.20 (methoxy), 1.90 dg and 1.72 m (vinyl methyls of side chain), 1.50 d (6.5, C-11 methyl), 1.12 d (6.5, C-10 methyl), and 1.05 ppm (C-5 methyl); ORD curve ϕ_{400} 258°, ϕ_{318} 3620°, ϕ_{310} 3290 (shoulder), ϕ_{296} 0, ϕ_{278} −3100, ϕ_{250} −2010 (last reading). More material could be obtained from the mother liquor.

Anal. Calcd for $C_{21}H_{30}O_6$: C, 66.65; H, 7.99; O, 25.36. Found: C, 66.49; H, 7.69; O, 26.08.

Ozonolysis of 13a.—A solution of 0.15 g of the preceding compound in ethyl acetate was ozonized at −45° for 30 min. The reaction mixture was steam distilled into a solution of dinitrophenylhydrazine. This resulted in the precipitation of acetaldehyde 2,4-dinitrophenylhydrazone, mp and mmp 146–147°. The flask residue was extracted with ether. The ether extract was dried and evaporated and the residual gum was recrystallized from ether–hexane and ether. The product (**13b**) was formed in 60% yield and melted at 172–174°, $[\alpha]^{25}D$ 22°. It had infrared bands at 1780 (γ-lactone), 1750 (ester), and 1740 cm^{-1} (α-ketone); nmr signals at 5.30 br ($w^{1/2}$ = 3, H-6), 4.68 tbr (6, H-8), 3.90 rbr (4, H-2), 3.20 (methoxyl), 2.33 (methyl ketone), 1.40 d (7, C-11 methyl), 1.10 d (7, C-10 methyl), and 1.03 ppm (C-5 methyl).

Anal. Calcd for $C_{19}H_{26}O_7$: C, 62-28; H, 7.15, O, 30.57. Found: C, 61.90; H, 7.34; O, 30.58.

Hydrolysis of 13b. A.—A solution of 0.3 g of the preceding compound in methanol–water containing 0.3 g of potassium carbonate was allowed to stand overnight and then acidified with dilute hydrochloric acid, diluted with water, and extracted with chloroform. The extract was dried and evaporated *in vacuo*. The residue could not be induced to crystallize. Its nmr spectrum (DMSO-d_6) showed the presence of a mixture and indicated that elimination of the methoxyl group to regenerate a cyclopentenone function had taken place. This was also evident from the infrared spectrum which exhibited bands at 3580 and 3400 (bonded and nonbonded hydroxyl), 1760 (γ-lactone), 1700, and 1585 cm^{-1} (cyclopentenone) and, in the finger print region, all bands characteristic of mexicanin C (as well as others). An extra absorption at 1630 cm^{-1} was provisionally ascribed to the presence of the $\Delta^{1,2}$ isomer.

Direct comparison with the nmr spectra of mexicanin C[32] and dihydrohelenalin[33] in DMSO-d_6 demonstrated that all signals characteristic of mexicanin C were present, that dihydrohelenalin was absent, and that another α,β-unsaturated cyclopentenone, possibly the C-1 epimer of mexicanin C, was a second contaminant. Thin layer chromatography in three solvent systems confirmed the presence of mexicanin C and of two other substances. However, attempts to isolate pure mexicanin C by preparative thin layer chromatography of the mixture were not successful.

In a second experiment, 0.108 g of **13b**, 0.12 g of potassium carbonate, 5 ml of methanol, and 1.6 ml of water were stirred at room temperature for the somewhat longer period of 24 hr. The usual work-up yielded a gummy residue which showed at least four spots on tlc. Preparative tlc resolved the mixture into two main bands. The lower R_f band showed two major spots which on being recrystallized from acetone–isopropyl ether gave 2 mg of **17** (*vide infra*). The higher R_f band showed two major spots whose R_f values corresponded to those of mexicanin C and dihydrohelenalin.

B.—A mixture of 0.12 g of **13b**, 0.12 g of potassium carbonate, 2 ml of water, and 6 ml of methanol was refluxed on the steam bath for 1 hr. The solvents were evaporated *in vacuo*, the residual gum was mixed with ice water, acidified with concentrated hydrochloric acid and extracted thoroughly with chloroform. The combined extracts were washed, dried, and evaporated and the residual gum was recrystallized from acetone–isopropyl ether. There was obtained 15 mg of **17** in the form of colorless needles which sintered near 270° and melted at 282–285° with decomposition. The substance had infrared bands (Nujol) at 3380, 1770 (γ-lactone), 1680, and 1625 cm^{-1} (cyclopentenone); λ_{max} 238 and 302 mμ (ϵ_{max} 15,700 and 110); nmr signals at 5.0 m (H-8), 3.9 m (H-6), 1.65 d (J = 2, a vinyl methyl), and 1.18 d ppm (7, six protons, C-10 and C-11 methyl). It differed from dihydroneohelenalin in ir and nmr spectrum. The mixture melting point with dihydroneohelenalin was depressed.

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63; O, 24.21. Found C, 67.76; 7.71; O, 24.26.

Examination of the mother liquors by tlc revealed a spot which corresponded to mexicanin C but no dihydrohelenalin.

Registry No.—Brevilin A, 16503-32-5; linifolin A, 5988-99-8; alternilin, 16434-63-2; **12**, 16434-64-3; **13a**, 16434-65-4; **13b**, 16434-66-5; **17**, 16452-39-4.

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(32) We wish to thank Dr. A. Romo de Vivar for an authentic sample of this compound.

(33) The nmr spectrum of this compound has not been recorded previously. It exhibited signals at 7.74 dd (6, 1.4, H-2), 5.96 dd (6, 3, H-3), 5.13 d (5, -OH), 4.8 tbr (6, H-8), 4.08 c ($w^{1/2}$ = 3, H-6), 1.18 d (5, C-10 and C-11 methyl), and 0.78 ppm (C-5 methyl).