Vigorous drying at 140° resulted in loss of solvent of crystallization.

Anal. Calcd. for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.47; H, 6.83.

Tetrahydroalantolactone (IV).—A mixture of 0.2 g. of III, 0.5 ml. of ethanedithiol and 0.5 ml. of boron trifluoride etherate was allowed to stand overnight, diluted with water, and extracted with ether. The ether extracts were washed, dried, and concentrated; yield 0.24 g. of thioketal, m.p. 160°, which recrystallization from benzene–petroleum ether raised to 165–166°.

Anal. Calcd. for $C_{17}H_{26}O_2S_2$: C, 62.82; H, 8.05; S, 19.6. Found: C, 62.56; H, 8.03; S, 19.6.

A solution of 0.25 g. of the thioketal in 25 ml. of ethanol was mixed with 1 teaspoonful of Raney nickel and refluxed with stirring for 25 hr. On working up in the usual manner, there was obtained after recrystallization 0.05 g. of tetrahydroalantolactone, m.p. 142°, undepressed on admixture of an authentic sample of m.p. 142°, infrared spectra superimposable.

Lithium Aluminum Hydride Reduction of Tetrahydropinnatifidin.—Reduction of 1 g. of III with 0.5 g. of lithium aluminum hydride in anhydrous ether by the Soxhlet method, decomposition of excess hydride with water and dilute sulfuric acid, washing and drying of the ether layer yielded on concentration 0.8 g. of IX, m.p. 190°. Recrystallization from benzene–methanol raised the m.p. to 191–192°, $[\alpha]^{25}D$ +25.8° (95% ethanol, *c*, 0.946).

Anal. Calcd. for $C_{15}H_{28}O_3$: C, 70.27; H, 11.01. Found: C, 70.05; H, 11.00.

Constituents of *Helenium* Species. XII. Sesquiterpene Lactones of Some Southwestern Species[1,2]

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Tenulin, isotenulin, helenalin, neohelenalin, mexicanin E, and two new sesquiterpene lactones linifolin A and linifolin B were isolated in a study of six not previously investigated *Helenium* species. Structures for the new compounds are proposed.

The genus *Helenium* is rich in sesquiterpene lactones. Helenalin (I)[3] and tenulin (II),[4] the main constituents of *H. autumnale* L.[5] and *H. amarum* (Raf.) H. Rock,[6] respectively, also have been isolated from the Southwestern species *H. microcephalum* DC.,[8] *H. elegans* DC.,[5,9] and *H. mexicanum* H.B.K.[10] and from some members of the vernal-flowering Southeastern section *Leptopoda*.[7,11,12] A series of new sesquiterpene lactones has been obtained from Southeastern species,[2,11,12] from *H. mexicanum* H.B.K.[3,10,13] and from *H. bigelovii* Gray.[15] We now wish to report the results of an investigation of six Southwestern species which have not been examined previously. The remaining member of the section *Leptopoda* has also been studied.

All Southwestern species contained relatively large amounts of a sesquiterpene lactone fraction, but the yields of crystalline substances were generally small. *Helenium arizonicum* Blake afforded isotenulin (III).[16] *H. laciniatum* Gray yielded helenalin. *H. scorzoneraefolium* (DC.) Gray gave an isomer of helenalin, m.p. 149–150°; the amount isolated was too small to permit further investigation. *H. Bloomquistii* Rock[17] yielded tenulin.

Extraction of *H. linifolium* Rydb. and extensive chromatography furnished tenulin and two previously undescribed substances of formula $C_{17}H_{20}O_5$ which were named linifolin A and linifolin B. Linifolin A, m.p. 195–198°, $[\alpha]^{25}D$ +30°, was assigned structure IV on the basis of the following evidence.

The ultraviolet spectrum, λ_{max} 215 and 320–325 mμ (ε12,300 and 43) was similar to that of helenalin[4] and many of its congeners, the absorption being due to superposition of the cyclopentenone chromophore (infrared bands at 1710 and 1595 cm.$^{-1}$) and the α, β-unsaturated lactone (infrared bands at 1755—double strength, combination of γ-lactone and acetate—and 1660 cm.$^{-1}$). The presence of the

(1) Supported in part by a grant from the U.S. Public Health Service (RG-5814).

(2) Previous paper, W. Herz, R. B. Mitra, K. Rabindran, and N. Viswanathan, *J. Org. Chem.*, **27**, 4041 (1962).

(3) W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *J. Am. Chem. Soc.*, in press.

(4) W. Herz, W. A. Rohde, K. Rabindran, P. Jayaraman, and N. Viswanathan, *ibid.*, **84**, 3851 (1962).

(5) E. P. Clark, *ibid.*, **58**, 1982 (1936).

(6) E. P. Clark, *ibid.*, **61**, 1836 (1939); **62**, 597 (1940). This is the prior designation for the more commonly employed *H. tenuifolium* Nutt.[7]

(7) H. F. L. Rock, *Rhodora*, **59**, 101, 128, 168, 203 (1957).

(8) R. Adams and W. Herz, *J. Am. Chem. Soc.*, **71**, 2546 (1949).

(9) The possible conspecificity of *H. montanum* Nutt., *H. quadridentatum* Labill., and *H. badium* (Gray) Greene, also investigated by Clark,[8] with one of the aforementioned species is now being studied by Dr. H. F. L. Rock (private communication). *H. macrocephalum* mentioned by Clark is undoubtedly a misprint for *H. microcephalum*, since no such species is recorded in the botanical literature.

(10) A. Romo de Vivar and J. Romo, *Chem. Ind.* (London), 882 (1959); *Ciencia* (Mex.), **21**, (1), 33 (1961).

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

(12) W. Herz, P. Jayaraman, and H. Watanabe, *ibid.*, **82**, 2276 (1960).

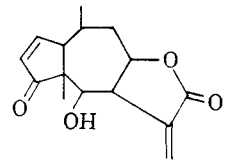
(13) This includes the interesting norsesquiterpene lactone mexicanin E[14] (*vide infra*).

(14) A. Romo de Vivar and J. Romo, *J. Am. Chem. Soc.*, **83**, 2326 (1961).

(15) Private communication from Professor T. A. Geissman University of California at Los Angeles.

(16) Presumably this is not an artifact resulting from isomerization of tenulin during the isolation procedure, since other species (*vide infra*) yielded tenulin and no isotenulin.

(17) This is a new species (private communication from Dr. Rock) whose description has not yet been published.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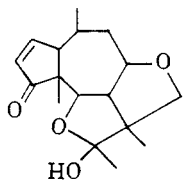
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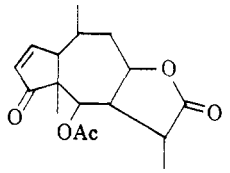
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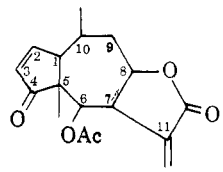
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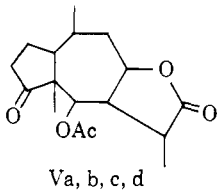
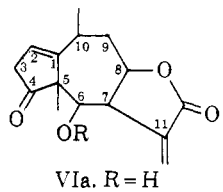
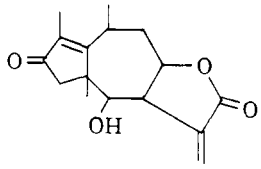

Va, b, c, d


VIa. R = H
b. R = Ac


VII

exocyclic methylene group was demonstrated by ozonolysis. Catalytic hydrogenation confirmed the presence of two double bonds and led to tetrahydrolinifolin A, m.p. 149–150°.

Because a cyclopentenone nucleus was present, it was logical to assume that linifolin A had the carbon skeleton of helenalin and tenulin. This was confirmed by a comparison of the n.m.r. spectrum with the n.m.r. spectra of helenalin acetate and balduilin,[3] which also established the lactone ring orientation.[4]

Linifolin A exhibited the vinyl proton signals characteristic of the cyclopentenone chromophore[4,18]—two doublets of doublets at 7.51 (H_2, $J_{H_1H_2} = 2$, $J_{H_1H_3} = 6$) and 6.01 p.p.m. (H_3, $J_{H_1H_3} = 3$), and the two methylene doublets at 6.16 and 5.60 p.p.m. ($J = 4$). Methyl singlets appeared at 1.21 (C-5) and 2.02 p.p.m. (acetate) and the C-10 methyl doublets at 1.26 p.p.m. ($J = 6$). The chemical shift of H_6-doublet at 5.85 p.p.m. ($J = 4.5$) indicated that the acetate was located at C-6. The appearance of the lactone ether hydrogen (signal centered at 4.86 p.p.m., two large, $J = 10$, and one smaller, $J = 3$, spin couplings) confirmed lactone ring closure to C-8.[3,4]

Tetrahydrolinifolin A (Va) is different from three other compounds—acetyltetrahydrohelenalin (Vb), tetrahydrobalduilin (Vc), and dihydroisotenulin (Vd)—which have the same gross structure and common stereochemistry at C-1, C-5, C-7 and C-10, but differ at C-6 and/or C-8.[19]

Linifolin B, m.p. 149–151°, had the conjugated lactone group of linifolin A (ozonolysis, infrared band at 1660 cm.$^{-1}$, two n.m.r. doublets at 6.19 and 5.75 p.p.m., $J = 3$), but the second double bond indicated by the analysis was not conjugated with the cyclopentanone carbonyl (infrared maximum of triple intensity at 1755 cm.$^{-1}$, weak ultraviolet absorption at 280 mμ, high absorption at 205–210 mμ). The presence of two double bonds was confirmed by hydrogenation. The n.m.r. spectrum indicated that the relationship between IV and linifolin B (VIb) is that existing between helenalin (I) and mexicanin A (VIa).[3] In analogy with the n.m.r. spectra of VIa[3] and similar compounds of the parthenin series,[18] VIb exhibited a vinyl proton triplet at 6.05 p.p.m. ($J = 1.5$) due to H_2. The two protons at C-3 appeared as two doublets at 2.94 and 3.04 p.p.m. ($J = 1.5$). H_8 was the usual complex triplet centered at 4.61 p.p.m. and H_6 was a poorly resolved doublet at 4.41 p.p.m. Methyl signals were found at 1.02 (C-5-methyl), 1.31 (doublet, $J = 7$, C-10 methyl) and 2.12 p.p.m. (acetate).

H. ooclinium Gray[20] yielded neohelenalin (VII)[3] and a small amount of a crystalline substance $C_{14}H_{16}O_3$, m.p. 91.5–92.5°, which in spite of its somewhate lower melting point was identified as mexicanin E[14] by direct comparison.[21]

A future communication will deal with the structure of this interesting norsesquiterpene lactone.

Only a small quantity of the relatively rare *H. Drummondii* Rock[7] was available. The sesquiterpene lactone content was small and no crystalline substances could be isolated.

Experimental[22]

The general procedure used for isolating the sesquiterpene lactone fraction (referred to as crude gum) has been described previously.[11]

H. Arizonicum **Blake.**—This species was collected on July 5, 1960, in Coconino County, Arizona. Extraction of 1350 g. of whole ground plant furnished 89 g. of crude gum which did not solidify. A solution of 71 g. of the gum in benzene–chloroform (1:2) was chromatographed over 450 g. of alumina (eluent benzene–chloroform 2:1, 150-ml. fractions). Fractions 6–16 crystallized on stirring with acetone–diisopropyl ether; yield 2.6 g. of isotenulin after one crystallization. The mother liquors were combined with fractions 3–5, dissolved in benzene, and allowed to

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

(19) W. Herz, R. B. Mitra, and P. Jayaraman, *ibid.*, **81**, 6061 (1959).

(20) This previously recognized species may be reduced to subspecies or variety rank (private communication from Dr. Rock).

(21) We wish to thank Dr. J. Romo for an authentic sample.

(22) Melting points are uncorrected. Analyses by Dr. F. Pascher, Bonn, Germany. Infrared spectra were taken on a Perkin-Elmer Infracord instrument. N.m.r. spectra were taken on a Varian HR-60 spectrometer by Mr. Fred Boerwinkle in deuteriochloroform solution with tetramethylsilane serving as internal standard. Funds for the purchase of the n.m.r. spectrometer were provided by the Institute of Molecular Biophysics of the Florida State University. Ultraviolet spectra were run in 95% ethanol solution on a Cary Model 14 spectrophotometer.

evaporate to 50 ml. at room temperature. Filtration yielded an additional 1.3 g. of isotenulin, total yield 3.9 g. (0.3%), identified by comparison with an authentic sample. Further elution of the column with more polar solvents failed to yield crystalline material.

H. laciniatum **Gray.**—Extraction of 2250 g. of ground whole plant, collected near Peon, Sonora, Mexico, on July 9, 1960, furnished 50 g. of crude gum which could not be crystallized or chromatographed satisfactorily. The gum dissolved slowly on stirring with benzene and allowing to stand. Crystals began to separate. They were filtered, washed with a little benzene, and recrystallized from benzene–petroleum ether (b.p. 35–60°), wt. 1.1 g. of material melting at 159–161.5°. An additional recrystallization raised the m.p. to 164–166°. The product was identified as helenalin by comparison with an authentic sample. No other crystalline fractions could be isolated.

H. Scorzoneraefolium (**DC.**) **Gray.**—Ground whole plant, wt. 700 g., collected on July 25, 1960, near El Zarco and Las Cruces, Federal District, Mexico, yielded only 2.4 g. of crude gum. Trituration with petroleum ether did not induce crystallization, but the petroleum ether decantate deposited crystals which were identical with material obtained by chromatographing the gum (solvent benzene) over 40 g. of alumina, collecting the benzene–chloroform (1:1) eluate and recrystallizing the latter from acetone–diisopropyl ether, yield 0.04 g., m.p. 149–150°, infrared bands at 3600 (hydroxyl), 1750 (lactone), 1650 (double bond conjugated with lactone), 1700, and 1590 cm.$^{-1}$ (cyclopentenone).

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92; O, 24.40. Found: C, 68.51; H, 6.83; O, 24.15.

H. Bloomquistii **Rock.**—This previously undescribed species was collected on July 31, 1960, near Barraganes, Chihuahua, Mexico. Ground whole plant, wt. 2.5 kg., yielded 34 g. of crude gum, 16 g. of which was taken up in 25 ml. of chloroform and 15 ml. of ether and chromatographed over 150 ml. of alumina. The following fractions were collected: Seven 100 ml. fractions of benzene–chloroform (1:2) five 100-ml. fractions of chloroform and eight 100-ml. fractions of chloroform–methanol (49:1). Fractions 3–10 were dissolved in acetone and diluted with diisopropyl ether to incipient cloudiness. The cloudiness was discharged by adding some acetone and the solutions were allowed to stand at room temperature. There precipitated 1.3 g. of crystalline material, m.p. 185–192°, identified as tenulin by comparison with authentic material.

H. Linifolium **Rydb.**—Ground whole plant, wt. 1.8 kg., collected in April, 1961, in Southeastern Texas, yielded 98 g. of crude gum. An 82-g. portion was dissolved in 75 ml. of chloroform and 60 ml. of benzene and chromatographed over 450 g. of alumina. The following fractions were collected: Eleven 100-ml. fractions of benzene–chloroform (1:1), eleven 100-ml. fractions of chloroform, six 500-ml. fractions of chloroform–methanol (49:1), and two 500-ml. fractions of chloroform–methanol (9:1). Fractions 8–20 were taken up in benzene and filtered from undissolved material. The solid was washed with a little benzene and recrystallized from acetone–diisopropyl ether, yield 1.9 g., 187–190°, identified as tenulin by comparison with authentic material.

Fractions 1–7 were dissolved in 50 ml. of benzene and rechromatographed over 150 g. of alumina. Benzene (seventeen 100 ml. fractions) eluted solid material, wt. 7.5 g., which was a mixture of linifolin A and linifolin B. Chloroform (fifteen 100-ml. fractions) eluted gums which were combined with the filtrate from tenulin (fractions 8–20 of the first chromatogram), concentrated to 50 ml. and rechromatographed over 125 g. of alumina. Benzene (sixteen 100-ml. fractions) eluted an additional 5.5 g. of crystalline linifolin A–linifolin B mixture, chloroform eluted gums which could not be induced to crystallize.

Extensive fractional crystallization of the linifolin A–linifolin B mixture (total wt. 13 g.) from acetone–petroleum ether (b.p. 60–90°) yielded, as the less soluble component, needles of linifolin A, m.p. 195–198°, $[\alpha]^{26}D$ +33° ($CHCl_3$, *c*, 0.36).

Anal. Calcd. for $C_{17}H_{20}O_5$: C, 67.09; H, 6.22; O, 26.29. Found: C, 67.12; H, 6.54; O, 26.41.

The more soluble component was linifolin B, needles from benzene–petroleum ether, m.p. 149–151°. It was clearly distinguishable from linifolin A by its infrared spectrum which served as a criterion of purity when the mother liquors were worked up.

Anal. Calcd. for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62; O, 26.29. Found: C, 66.98; H, 7.31; O, 25.88.

A solution of 0.1 g. of linifolin A in 20 ml. of chloroform was ozonized at −70° and steam distilled into a solution of dimedone, yield 0.045 g. (45%) of formaldehyde–dimedone derivative, m.p. 118–189°. Ozonolysis of 0.1 g. of linifolin B gave 0.039 g. (39%) of the formaldehyde–dimedone derivative.

A solution of 0.1 g. of linifolin A in 20. ml. of ethanol was reduced with 0.01 g. of prereduced platinum oxide in a semimicro hydrogenator, uptake 18.5 ml., calculated for two double bonds 16.5 ml.[23] The residue was recrystallized from acetone–diisopropyl ether, m.p. 149–150°, depression to 128–131° on admixture of dihydroisotenulin, infrared band at 1755–1750 cm.$^{-1}$ (strong, combination of γ-lactone, acetate, and cyclopentanone).

Anal. Calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84; O, 25.95. Found: C, 66.37; H, 7.87; O, 26.03.

Hydrogenation of 0.1 g. of linifolin B consumed 2 mole-equivalents of hydrogen, but the product (strong infrared band at 1755 cm.$^{-1}$) could not be induced to crystallize even after chromatography.

Anal. Calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84; O, 25.95. Found: C, 66.00; H, 8.01; O, 25.68.

H. Ooclinium **Gray.**—This was collected near La Zarca, Durango, Mexico, on July 29, 1960. The finely ground plant, wt. 2.85 kg., yielded 135 g. of gum which could not be induced to crystallize. A 28 g. portion was dissolved in 35 ml. of chloroform and 50 ml. of benzene and chromatographed over 400 g. of alumina. The following fractions were collected: Seven 150-ml. fractions of benzene, five 100-ml. fractions of benzene–chloroform (1:1), twenty 100-ml. fractions of chloroform, and 2 l. of chloroform–methanol (19:1). Fraction 3 crystallized on stirring with petroleum ether. Two crystallizations from benzene–petroleum ether yielded an analytical sample of mexicanin E, m.p. 91.5–92.5°, wt. 0.19 g., λ_{max} 214 and 314 mμ (ε 38,000 and 75), infrared bands at 1760 and 1660 (conjugated lactone) and 1700 and 1590 cm.$^{-1}$ (cyclopentenone). Direct comparison with an authentic sample of m.p. 94–97° established identity (infrared spectra and n.m.r. spectra superimposable, mixed m.p. 94–97°).

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94; O, 20.67. Found: C, 72.14; H, 7.11; O, 20.78.

The chloroform eluates on stirring with a small amount of benzene yielded a gummy solid which was filtered and washed with a little acetone. Two recrystallizations from acetone–petroleum ether (b.p. 60–90°) furnished 1.15 g. of crystalline material, m.p. 218–221°, shown to be identical with neohelenalin by comparison with authentic material.

H. Drummondii **Rock.**—This material was collected in April, 1961, in East Texas. Extraction of 500 g. of ground whole plant furnished only 1 g. of crude gum which did not yield crystalline material after chromatography over alumina.

Acknowledgment.—We wish to express our particular thanks to Dr. H. F. L. Rock of the Department of Biology, Vanderbilt University, for collecting the material used in this study. Thanks are also due to Dr. P. Jayaraman for help with some of the characterizations.

(23) This experiment was carried out by Dr. P. Jayaraman.