to remove the inorganic salts the ether solution was analyzed by glpc (column C, 64°, 120 ml/min) was found to contain essentially only one volatile compound. This compound was later collected by preparative glpc (column B, 73°) and was shown to be identical to ethyl butyrate by comparison of glpc retention times and infrared spectra. The actual yield of ethyl butyrate (**12**) in the ether solution was determined to be 225 mg (39% from **11**) by glpc (column C, 64°, 120 ml/min) using mesitylene as an internal standard. A second yield determination was made by glpc on the residual liquid (1.20 g) remaining after the ether was distilled off through a Vigreux column at atmospheric pressure. The overall yield was found to be 35%.

**Reduction of Ethyl Cinnamate.**—Reduction[15] of 880 mg (5.00 mmol) of ethyl cinnamate with 114 mg (0.016 g-atom) of lithium gave 983 mg of a viscous yellow liquid which contained only one volatile compound as shown by glpc (column B, 121°, 150 ml/min). This compound was found to be identical with ethyl hydrocinnamate (**14**) by comparison of infrared and nmr spectra. The actual yield of the ester was determined to be 18% by glpc (column B, 121°, 150 ml/min) using ethyl phenylacetate as an internal standard. A second reduction by the same procedure except that 128 mg of lithium was used gave a 16% yield of ethyl hydrocinnamate.

**Reduction of *trans*-Cinnamic Acid.**—A solution of 740 mg (5.0 mmol) of *trans*-cinnamic acid in 26 ml of ether was added with stirring to a solution of 148 mg (0.021 g-atom) of lithium in 82 ml of anhydrous ammonia under argon. The solution was stirred for 15 min at the liquid ammonia boiling point and was then cooled 5 min with powdered Dry Ice before quenching with 7.5 g of ammonium chloride. After addition of 60 ml of ether and evaporation of the ammonia, the reaction mixture was acidified with 10% concentrated hydrochloric acid. The ether extract was washed with water, dried with sodium sulfate, and evaporated to give 743 mg of a viscous oil. Glpc analysis (column C, 142°, 120 ml/min) of the oil revealed that only hydrocinnamic acid was present and that the actual yield of the acid was 65%. Crystallization of the oil in petroleum ether (bp 30–60°) and recrystallization from the same solvent gave 390 mg (52%) of hydrocinnamic acid, mp 46–48° (lit.[16] mp 48°). The infrared spectrum was identical with that of authentic hydrocinnamic acid.

**Registry No.**—2-Carbethoxycyclohexanone methoxymethyl enol ether, 25096-42-8; 2-carbethoxycyclopentanone methoxymethyl enol ether, 25096-43-9; 2-carbethoxy-4-*t*-butylcyclohexanone methoxymethyl enol ether, 25096-44-0; ethyl benzoylacetate methoxymethyl enol ether, 25096-45-1; ethyl 2-*n*-butylacetoacetate methoxymethyl enol ether, 25095-46-2; ethyl acetoacetate methoxymethyl enol ether, 25096-47-3; *cis*-**8**, 25096-48-4; *trans*-**8**, 25096-49-5.

**Acknowledgments.**—We thank the National Science Foundation for support in the form of a traineeship to J. E. S. and the National Institutes of Health for financial assistance.

(16) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," Wiley, New York, N.Y., 1964, p 312.

# Isolation and Structure of Two New Germacranolides[1] from *Polymnia uvedalia* (L.) L.

WERNER HERZ AND S. V. BHAT

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

*Received February 13, 1970*

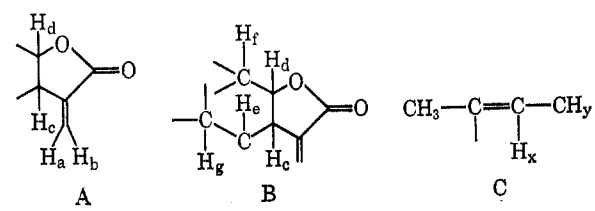
Examination of several collections of *Polymnia uvedalia* (L.) L. yielded varying quantities of two new highly oxygenated germacranolides uvedalin (**1a**) and polydalin (**1d**) which were correlated. Experiments and spectroscopic studies which led to the determination of their structure are described. *P. laevigata* Beadle gave the eudesmanolide ivalin. The flavone artemetin was isolated from *P. canadensis L.*, which contained only small amounts of sesquiterpene lactones.

As part of our general study of subtribe *Melampodiinae*, tribe *Heliantheae*, family *Compositae*,[2] we have investigated North American representatives of the genus *Polymnia* which is endemic to the Western Hemisphere.[3] The isolation and structure determination of two new highly oxygenated germacranolides from *Polymnia uvedalia* (L.) L. is reported herewith.

Collections of *P. uvedalia* from Rabun County, Ga., Leon County, Fla., and W. Va. furnished two crystalline sesquiterpene lactones whose relative yield varied somewhat with location[4] and which were named uvedalin and polydalin.

Uvedalin (**1a**), $C_{23}H_{28}O_9$, mp 131–3°, $[\alpha]D$ +12.8°, was a conjugated γ-lactone (ir bands at 1765 and 1665 $cm^{-1}$, with strong uv end absorption). The nmr spectrum (Table I) exhibited the typical two doublets ($H_a$ and $H_b$) of partial structure A whose presence was confirmed by facile formation of a pyrazoline (**2a**) and by controlled sodium borohydride reduction to a dihydro derivative **3a** in whose nmr spectrum the signals of $H_a$ and $H_b$ were replaced by a new methyl doublet. Spin-decoupling experiments involving $H_a$ and $H_b$ established the location of the $H_c$ multiplet at 2.8 ppm; this in turn was coupled to two doublets of doublets at 5.00 and 6.55 ppm, one of which represented the $H_d$ resonance.

The other doublet of doublets was tentatively assigned to hydrogen ($H_e$) under one of three ester functions whose presence was indicated by the consump-




(1) Supported in part by grants from the National Science Foundation (GB-6413) and the U. S. Public Health Service (RG-05814).

(2) The original impetus for these studies is given by W. Herz, S. V. Bhat, and A. L. Hall, *J. Org. Chem.*, **35**, 1110 (1970).

(3) The most recent review of this genus is by J. R. Wells, *Brittonia*, **17**, 144 (1965).

(4) Although the three previously described[3,5] varieties of *P. uvedalia* are no longer recognized,[6] the variation in lactone content might be due to the existence of separate chemical races. Material from both West Virginia and Georgia would have keyed out as var. *uvedalia* although differing consistently in lactone content, while material from Florida, which chemically resembled the collection from Georgia, would have been assigned to var. *floridana*.[3] This problem is receiving further attention from Dr. J. R. Wells.

(5) S. F. Blake, *Rhodora*, **19**, 46 (1917).

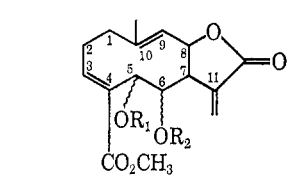
(6) J. R. Wells, *ibid.*, **71**, 786 (1969). We are indebted to Dr. Wells for authenticating the collections and for valuable correspondence.

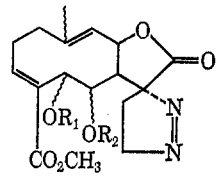
TABLE I

NMR SPECTRA OF UVEDALIN, POLYDALIN AND DERIVATIVES[a]

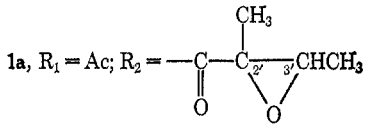
| Compd | H-3 | H-5 | H-6 | H-7 | H-8[b] | H-9[b] | H-13 | H-3′ | Me C-10 | Me C-2′ | Me C-3′ | $CO_2Me$ | AC |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1a** | 6.92 (m) | 5.33 (d, 8.4) | 6.55 (dd, 8.4, 1.4) | 2.8 (m) | | | 5.61 (d, 3)<br>6.12 (d, 3.5) | 2.99 (q, 5.4) | 1.96 (br) | 1.44 | 1.14 (d, 5.4) | 3.72 | 1.96 |
| **1b** | 6.98 (m) | 5.38 (d, 8.4) | 6.61 (dd, 8.4, 1.4) | 2.8 (m) | | | 5.74 (d, 3)<br>6.22 (d, 3.5) | 4.16 (q, 6.5) | 1.98 (br) | 1.29 | 1.49 (d, 6.5) | 3.80 | 1.98 |
| **1c** | 7.05 (m) | 5.41 (d, 8.4) | 6.64 (dd, 8.4, 1.4) | 2.8 (m) | 5.11 (dd) | 4.93 (dd) | 5.73 (d, 3)<br>6.27 (d, 3.5) | 3.8 (q) | 2.00 (br) | 1.22 | 1.20 (d, 8.5) | 3.81 | 2.00 |
| **1d** | 7.03 (m) | 5.36 (d, 8.4) | 6.60 (dd, 8.4, 1.4) | 2.8 (m) | | | 5.74 (d, 3)<br>6.26 (d, 3.5) | | 2.00 (br) | 1.50 | 2.19 | 3.81 | 2.00 |
| **3a** | 7.01 (m) | 5.39 (d, 8.4) | 6.25 (dd, 8.4, 1.4) | 2.8 (m) | | | 1.26 (d,[c] 6.5) | 3.08 (q, 5.4) | 1.97 (br) | 1.53 | 1.30 (d, 5.4) | 3.80 | 1.97 |
| **3c** | 7.05 (m) | 5.43 (d, 8.4) | 6.26 (dd, 8.4, 1.4) | 2.8 (m) | | | 1.29 (d,[c] 6.6) | | 1.99 (br) | 2.47 | | 3.83 | 1.99 |
| **3d** | 6.81 (m) | 3.85 (d, 8.0) | 4.37 (d, br 8.0) | 2.6 (m) | 5.03 (dd) | 4.74 (d, br) | 1.15 (d,[c] 7.0) | | 1.83 (d, 1.0) | | | 3.73 | |
| **3e** | 7.00 (m) | 5.36 (d, 8.4) | 6.15 (dd, 8.4, 1.4) | 2.7 (m) | 4.95 (dd, 8.5, 10.3) | 4.77 (d, br, 10.3) | 1.27 (d,[c] 6.5) | | | | | 3.80 | 2.12<br>1.99 |
| **3f** | 7.01 (m) | 5.29 (d[e]) | 5.18 (d, br[e]) | 2.8 (m) | 4.96 (dd) | 4.87 (d, br) | 1.22 (d,[c] 7.0) | | 1.93 (d, 1.2) | | | 3.88 | 2.08 |
| **3g** | 6.90 (m) | 4.00 (d, 9) | 4.86[c] | 2.3 (m) | | | 1.35 (d,[c] 5.5) | | 1.90 (br) | 1.25[d] | | 3.77 | |
| **4a** | 6.75 (dd, 4.5, 11.5) | 5.96 (d, 8.4) | 6.15 (d, 8.4) | | 5.00 (m) | | 1.10 (d,[c] 6.5) | 3.03 (q, 5.4) | 1.00 | 1.46 | 1.27 (d, 5.4) | 3.80 | 2.00 |
| **5a** | 7.14 (dd, 7.0, 10.2) | 5.90 (d, 8.4) | 6.73 (dd, 8.4, 1.4) | 3.0 (m) | 4.24 (t, br, 9.4) | 2.70 (d, br, 9.4) | 5.84 (3)<br>6.23 (d, 3.5) | 3.04 (q, 5.4) | 1.70 | 1.47 | 1.20 (d, 5.4) | 3.74 | 2.06 |
| **6a** | 7.16 (dd, 7.0, 10.2) | 5.98 (d, 8.4) | 6.32 (dd, 8.4, 1.4) | 2.1 (m) | 4.22 (t, br, 9.4) | 2.60 (d, br, 9.4) | 1.30 (d,[c] 6.5) | 3.08 (q, 5.4) | 1.70 | 1.52 | 1.31 (d, 5.4) | 3.84 | 2.05 |
| **7a** | | 5.43[e] | 5.43[e] | | 5.00 (m) | | 1.16 (d, 6.5) | 3.05 (q, 5.4) | 1.00 | 1.50 | 1.31 (d, 5.4) | 3.73 | 2.04 |
| **8** | 6.87 (m) | 5.20 (m) | | 2.8 (m) | | | 1.35 (d, 7.0) | | 1.80 (d, 0.5) | | | | |
| **9a** | 7.08 (d, br) | 5.00 (d, 8.4) | 5.95 (dd, 8.4, 1.4) | 2.7 (m) | | | 3.08[g] | 3.12 (q, 5.4) | 1.94 (br) | 1.54 | 1.32 (d, 5.4) | 3.80 | 2.04 |

[a] Spectra were run in $CDCl_3$ on a Varian A-60 nmr spectrometer using TMS as internal standard. Chemical shifts are in parts per million. Signals are denoted in the usual way: d, doublet; t, triplet; q, quartet; m, multiplet; c, complex signal whose center is given; br, somewhat broadened singlet. Unmarked signals are singlets. Figures in parentheses are line separations in hertz. Signals in first eight columns correspond to one proton unless otherwise specified; signals in last five columns correspond to three protons. [b] Generally the overlapping AB part of ABX system centered in the region of 4.9–5 ppm, with $H_A$ ($\alpha$ H-8) at lower field and $H_B$ (H-9) at higher field. For chemical shifts and coupling constants in case of **1a**, see Table II. [c] Three protons. [d] Two methyls of acetonide. [e] Superimposed signals. [f] AB system centered near 5.4 ppm. [g] Two protons.

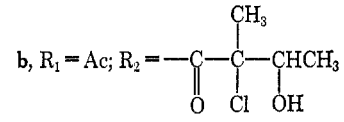




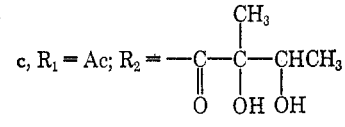
**2a**



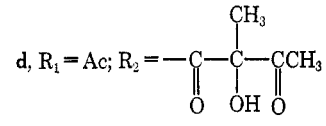
**1a**, $R_1$ = Ac; $R_2$ = —C(=O)—C(CH$_3$)(2′)—(3′)CHCH$_3$ (epoxide)



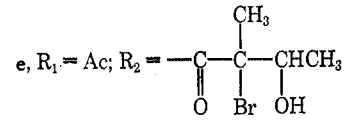
**b**, $R_1$ = Ac; $R_2$ = —C(=O)—C(CH$_3$)(Cl)—CH(OH)CH$_3$



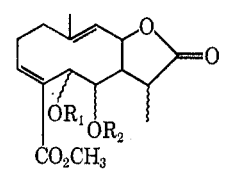
**c**, $R_1$ = Ac; $R_2$ = —C(=O)—C(CH$_3$)(OH)—CH(OH)CH$_3$

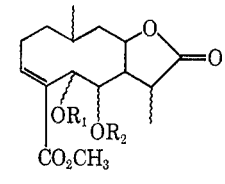


**d**, $R_1$ = Ac; $R_2$ = —C(=O)—C(CH$_3$)(OH)—C(=O)CH$_3$

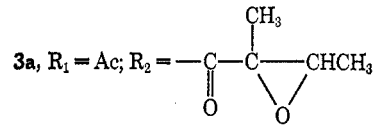


**e**, $R_1$ = Ac; $R_2$ = —C(=O)—C(CH$_3$)(Br)—CH(OH)CH$_3$

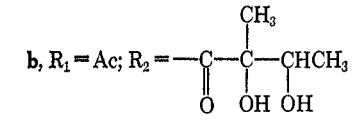




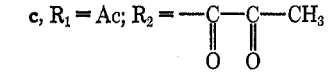
**4a**



**3a**, $R_1$ = Ac; $R_2$ = —C(=O)—C(CH$_3$)(2′)—(3′)CHCH$_3$ (epoxide)



**b**, $R_1$ = Ac; $R_2$ = —C(=O)—C(CH$_3$)(OH)—CH(OH)CH$_3$

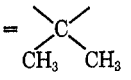


**c**, $R_1$ = Ac; $R_2$ = —C(=O)—C(=O)—CH$_3$

**d**, $R_1$, $R_2$ = H

**e**, $R_1$, $R_2$ = Ac

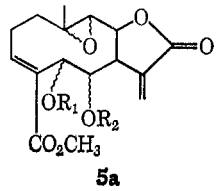
**f**, $R_1$ = Ac; $R_2$ = H

**g**, $R_1$, $R_2$ = 

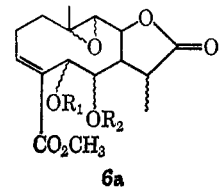
tion of 3.9 equiv of alkali on hydrolysis and by ir bands at 1740, 1725, and 1710 cm$^{-1}$. The multiplicity of $H_d$ and $H_e$ permitted further expansion to B.

The presence, in the nmr spectra of uvedalin and all of its derivatives, of a sharp three-proton singlet near 2 ppm suggested that one of the ester groups was an acetate.[7] A second ester function was probably associated with a carbomethoxy group (three-proton signal near 3.8 ppm which disappeared on basic hydrolysis). Lastly, if uvedalin were a sesquiterpene lactone as seemed likely, its empirical formula required a five-carbon acid as the third ester component.

Catalytic hydrogenation of **1a** with Pd–C yielded tetrahydrouvedalin (**4a**). The transformation of **1a** to **4a** involved, in addition to reduction of the exocyclic methylene group, saturation of the system C (ir band at 1675 cm$^{-1}$) as evidenced by disappearance from the nmr spectrum of a narrowly split vinyl methyl resonance and its replacement by a new methyl doublet. The vinyl proton associated with this system ($H_x$) had its signal at 4.85 ppm, broadened by coupling to the vinyl methyl group and coupled in turn (ABX system) to some other proton ($H_y$). Further evidence for C was the conversion of **1a** and **3a** to epoxides **5a** and **6a**.



**5a**



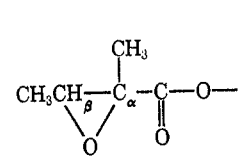
**6a**

In the nmr spectra of these substances the methyl signal appeared as a sharp singlet and the resonance of the vinyl proton ($H_x$) had moved upfield to near 2.7 ppm.

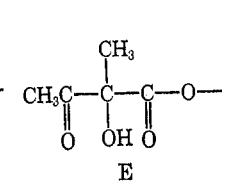
(7) A negative iodoform test ruled out the possibility that this was a methyl ketone signal.

Treatment of uvedalin with hydrochloric acid in dioxane resulted in addition of the elements of hydrogen chloride. In the nmr spectrum the conversion of **1a** to the product **1b** was attended by the shift of a one-proton quartet from 2.99 to 4.16, the shift of a methyl doublet from 1.14 to 1.49, the shift of a methyl singlet from 1.44 to 1.29, and the appearance of an –OH resonance at 3.27 ppm (disappears on deuterium exchange, ir band at 3525 cm$^{-1}$). That the new hydroxyl group was tertiary was indicated by the nmr spectrum and the failure of **1b** to undergo oxidation with Jones reagent. These observations could be accommodated by assuming the presence of D as the five-carbon ester side chain. This was conclusively established by hydrolysis experiments to be described subsequently and by double resonance experiments which showed that the methyl doublet at 1.14 ppm ($H_\gamma$) was coupled to the quartet at 2.99 ppm ($H_\beta$).

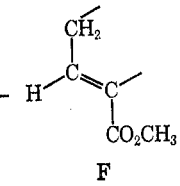
Uvedalin on treatment with sulfuric acid in aqueous acetone gave a diol **1c**. Jones oxidation of this substance followed by separation of two isomers gave pure **1d**, identical in all respects with natural polydalin $C_{23}H_{28}O_{10}$, mp 181–183°, $[\alpha]_D$ +8.4°. The spectral changes were consonant with the conclusion that polydalin differed from uvedalin only in containing the side chain E instead of D.



D



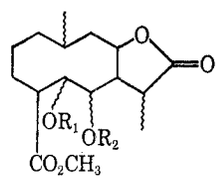
E



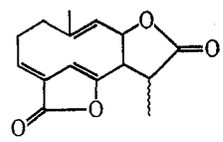
F

The foregoing evidence in favor of partial structures A, C, and D and the presence of an acetate function accounted for seven of the nine oxygen atoms present in

**1a**. Since the uv spectra of **3a** and **4a** still showed strong end absorption, thus indicating the presence in uvedalin of a second chromophore (ir bands in **1a** at 1710 and 1625, in **3a** at 1720 and 1630, in **4a** at 1720 and 1645 $cm^{-1}$), it was deduced that the carbomethoxy group which accounted for the remaining two oxygen atoms was conjugated and associated with the signal of a low field proton near 7 ppm whose chemical shift required it to be vinylic and attached to the $\beta$ position. In support of this hypothesis, hydrogenation of **1a** with platinum oxide furnished a hexahydro derivative **7a**



**7a**

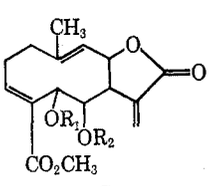


**8**

which was transparent in the uv. The conversion of **1a** to **7a** was accompanied by disappearance of the 7-ppm signal in the nmr, the disappearance of the remaining double-bond frequency, and the shift of the 1710 band to 1740 $cm^{-1}$ in the ir.

Spin-decoupling experiments at 90 MHz[8] eventually permitted expansion of partial structure B to G. Irradiation at the frequency of H-6 ($H_e$ of B) affected the signal of H-7 ($H_c$) and collapsed the doublet of H-5 ($H_f$ or $H_g$) at 5.4 ppm to a sharp singlet. Conversely, irradiation at the frequency of H-5 collapsed the H-6 resonance but indicated no observable allylic coupling of H-5 to the low field vinyl signal near 7 ppm (H-3). Irradiation of H-3 affected signals in the methylene region, hence the grouping F was present.

Since the signals of H-8 ($H_d$) and H-9 ($H_f$ or $H_g$) overlapped in the nmr spectrum of **1a** the 90 MHz nmr spectrum of **6a** was studied. Irradiation of the H-7 multiplet ($H_c$) at 2.1 ppm collapsed a doublet of doublets at 6.3 (H-6 = $H_e$) to a doublet and converted the triplet of H-8 at 4.14 ppm ($H_d$) to a doublet. In turn, irradiation of H-8 simplified the signal of H-7 and collapsed a doublet at 2.57 ppm to a singlet. Since this doublet originated in proton $H_x$ of partial formula C (*vide supra*), $H_y$ of C was identified as $H_d$ of B. If it is borne in mind that H-5 (now identified as $H_g$ of B) is only coupled to one proton, *i.e.*, H-6, and that the empirical formula requires the presence of an additional methylene group, only one combination of B, C, and the methylene group is possible, *i.e.*, that represented by G. This formula also explains the observation that H-9 of **1a** is not only coupled vicinally to H-8 ($J$ = 10.3 Hz) and allylically to the C-10 methyl group ($J \sim 0.6$ Hz), but that there exists another allylic coupling ($J$ = 0.8 Hz) to one of the protons on C-1.



G

The problem of assigning the acetate and $\alpha$-methyl-$\alpha,\beta$-epoxybutyrate groups to C-5 and C-6 remained and was solved in the following manner. After attempts at selective hydrolysis of **1a**, **1d**, **4a**, or **5a** had resulted in complex mixtures or remained unsuccessful, it was reasoned that in accord with previous experience[9] selective hydrolysis of a pyruvate function in the presence of an acetate might be achieved. Hence, tetrahydropolydalin (**3b**)[10] was converted by periodate oxidation to the pyruvate **3c** which had relevant nmr signals at 5.43 (d, H-5) and 6.26 (dd, H-6).

Treatment of **3c** with potassium carbonate at room temperature for 2.5 hr effected complete hydrolysis to the diol **3d** (H-5 signal at 3.85, H-6 signal at 4.37 ppm) which gave a positive periodate test for the presence of a vicinal glycol function and was further characterized as the diacetate **3e** (H-5 signal at 5.36, H-6 signal at 6.15 ppm). However, when exposure of **3c** to sodium bicarbonate was limited to 15 min, selective hydrolysis occurred with formation of the monoacetate **3f**. In the nmr spectrum of this substance the signals of H-5 and H-6 were superimposed near 5.3 ppm which clearly demonstrated that hydrogen on carbon carrying the acetate function of uvedalin or polydalin was responsible for the doublet near 5.3 ppm and identical with H-5. Hence the gross structures of uvedalin and polydalin were those shown in formulas **1a** and **1d**.

Hydrolysis of **3c** by refluxing methanolic potassium carbonate for 3 hr followed by acidification resulted in a dilactone whose formulation as **8** was in keeping with the spectroscopic evidence [uv maximum at 249 nm; ir bands at 1778, 1760, 1655, and 1650 (sh); for nmr spectrum see Table I]. Its formation established the presence of a carbomethoxy group chemically and proved that its location was $\gamma$ to the oxygen function on C-6.

As concerns stereochemistry, it is assumed that the absolute configuration of the C-11 side chain is $\beta$ as in all other sesquiterpene lactones of established stereochemistry. An attempt to distinguish between *cis* and *trans* stereochemistry of the 9,10 double bond on the basis NOE's was not satisfactory.[11] Moreover, although it was possible to convert **3d** to an acetonide **3g**, inspection of molecular models showed that this information and knowledge of coupling constants obtained by inspection of Table I and from spin-decoupling experiments was not sufficient to determine the stereochemistry at C-5 and C-6.[14]

On the other hand, the strongly negative Cotton effect exhibited by **1a** ($\lambda_{max}$ 225 nm, $\theta$ −1810) suggested *cis* fusion of the $\gamma$-lactone ring, if a recently formulated empirical rule relating to the sign of the lactone Cotton effect to the nature of the lactone ring

(8) We are grateful to the National Science Foundation for a grant which permitted purchase of a Bruker 90-MHz nmr spectrometer.

(9) W. Herz and M. V. Lakshmikantham, *Tetrahedron*, 1711 (1965).

(10) Treatment of **1d** with sodium borohydride reduced not only the exocyclic double bond conjugated with the lactone, but also the keto group of the side chain. The resulting gummy material was apparently a mixture of C-3′ epimers (nmr spectrum).

(11) Although NOE's involving H-9 or H-1 and the C-10 methyl group have been used successfully for this purpose,[12,13] no useful results could be obtained in the present instance, apparently due to sample difficulties.

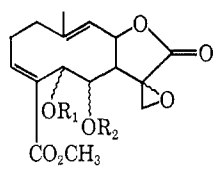
(12) W. Herz, P. S. Subramaniam, P. S. Santhanam, K. Aota, and A. L. Hall, *J. Org. Chem.*, **35**, 1453 (1970).

(13) K. Takeda, I. Horibe, M. Teraoka, and H. Minato, *Chem. Commun.*, 940 (1968); *J. Chem. Soc. C*, 1491 (1969).

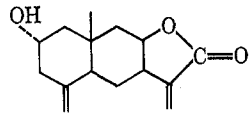
(14) Unfortunately it was not possible to determine unambiguously $J_{6,7}$ in **3g** which might have aided in establishing the relative stereochemistry at these centers.

junction[15] were applicable. From the molecular model of uvedalin with H-8 $\alpha$ formation of a pyrazoline would then be predicted to occur predominantly by attack of diazomethane from the $\alpha$ side, regardless of the configuration at C-5 or C-6. The resulting pyrazoline **2a** would be expected to display a curve of negative sign.[16] This was indeed observed ($\lambda_{max}$ 316 nm, $\theta$ −4900).

*Polymnia laevigata Beadle* furnished considerable quantities of ivalin (**10**), a eudesmanolide previously




**9a**




**10**

isolated only from certain *Iva* species.[17,18] *Polymnia canadensis L.* contained a small amount of a sesquiterpene lactone mixture; the only substance isolated in crystalline form was artemetin (5-hydroxy-3,4′,5′,6,7-pentamethoxyflavone).[19] The implications of these findings will be discussed elsewhere.

## Experimental Section[20]

**Extraction of *Polymnia uvedalia*.** (**A**).—Dried and ground leaves of *Polymnia uvedalia* (L.) L., wt 4.5 kg, collected by Dr. J. R. Wells on Aug 26, 1966, in Calhoun Co., W. Va., 3.1 miles from the Gilmer-Calhoun Co. line (voucher specimen on deposit in herbarium of the Cranbrook Institute of Science, Bloomfield Hills, Mich.) was extracted with chloroform and worked up in the usual manner.[16] The crude gum, wt 34 g, was chromatographed over 1.1 kg of silicic acid (Mallinckrodt, 100 mesh), 1000-ml fractions being collected in the following order: 1–6 (benzene), 7–18 (benzene–chloroform, 4:1), 19–32 (benzene–chloroform, 1:1), 33–52 (benzene–chloroform, 1:4), 53–62 (chloroform), 63–71 (chloroform–ether, 19:1), 72–77 (chloroform–methanol, 19:1), 78–80 (chloroform–methanol, 9:1). Fractions 23–32 eluted a gum which showed a major spot on tlc. Rechromatography over 300 g of silicic acid gave 8.0 g of crude uvedalin on elution with benzene–chloroform (1:1) which on recrystallization from ethyl acetate–hexane gave 4.5 g of pure material. Fractions 50–55 gave a gum showing a major spot. Rechromatography over 100 g of silicic acid gave 1.58 g of crude polydalin in the chloroform fractions. Recrystallization from ethyl acetate gave 0.6 g of pure material. Fractions 59–71 eluted a gum which showed two major overlapping spots on tlc. The lactones responsible for the spots could not be separated satisfactorily and polymerized rapidly. All other fractions gave gums showing several spots. Repetition of the extraction with *P. uvedalia* collected at the same spot on Aug 1, 1969, gave approximately the same results.

(**B**).—Ground *P. uvedalia*, collected by Mr. R. Lazor on July 12, 1969, in Leon County, Fla. (Lazor No. 3744 on deposit in herbarium of Florida State University), wt 10.9 kg, was extracted in the usual manner. The crude gum, wt 35 g, was chromatographed over 1 kg of silicic acid, 800-ml fractions being collected in the following order: 1–10 (benzene), 11–20 (benzene–chloroform 2:1), 21–30 (benzene–chloroform 1:2), 31–50 (chloroform), 51–60 (chloroform–methanol 19:1), 61–74 (chloroform–methanol 9:1). Fractions 21–24 contained several spots one of which corresponded to uvedalin. Fractions 32–35 eluted semicrystalline material which yielded 2.5 g of pure polydalin. Fractions 61–63 gave a gum showing a major spot. This was recrystallized from ethanol and gave 2.1 g of a crystalline saturated alicyclic alcohol, mp 275–278°. All other fractions were gums showing several spots.

(**C**).—Extraction of 2.8 kg of *P. uvedalia*, collected by Mr. R. Lazor on Aug 11 in Rabun County, Ga. (Lazor No. 3783), in the usual manner gave 10 g of crude gum which on chromatography, as described in section B, afforded 2.5 g of crude polydalin and in the earlier fractions a spot corresponding to uvedalin.

Uvedalin (**1a**): mp 131–133°; $[\alpha]^{24}D$ +12.8° (*c* 4.69); ir bands at 1765, 1740, 1725, 1710, 1665, and 1625 cm$^{-1}$; uv $\lambda_{max}$ 210 nm ($\epsilon$ 14,300); CD curve (1 cm cell) $\lambda_{max}$ 255 nm ($\theta$ −1810). The 90-MHz nmr spectrum and all coupling constants determined by double irradiation are listed in Table II.[21]

TABLE II

90-MHz SPECTRUM OF UVEDALIN

| | Ppm | Hz |
|---|---|---|
| H-1a,b | 2.1–2.8 (c) | $J_{1a,9}$ = 0.8[a] |
| H-2a,b | 2.1–2.8 (c) | $J_{2a,3}$ = 7.6, $J_{2b,3}$ = 9.6 |
| H-3 | 6.99 (c) | |
| H-5 | 5.40 (d) | $J_{5,6}$ = 8.4 |
| H-6 | 6.64 (dd) | $J_{6,7}$ = 1.4 |
| H-7 | 2.77 (m) | $J_{7,8}$ = 8.4 |
| H-8 | 5.10 (dd) | $J_{8,9}$ = 10.3 |
| H-9 | 4.96 (dbr) | $J_{9,C\text{-}10\ Me} \sim 0.6$ |
| C-10 Me | 2.01 | |
| H-13$_{cisoid}$ | 5.71 (d) | $J_{7,13\text{-}cis}$ = 3.1 |
| H-13$_{transoid}$ | 6.25 (d) | $J_{7,13\text{-}trans}$ = 3.4 |
| C-2′ Me | 1.46 | |
| C-3′ Me | 1.19 (d) | $J_{3',3'\text{-}Me}$ = 5.4 |
| H-3′ | 3.01 (q) | |
| Acetate | 2.01 | |

[a] Values of all coupling constants were confirmed by double irradiation or INDOR experiments.

*Anal.* Calcd for $C_{23}H_{28}O_9$: C, 61.60; H, 6.29; O, 32.11. Found: C, 61.36; H, 6.31; O, 32.15.

Pure polydalin (**1d**) melted at 181–183° and had $[\alpha]^{21}D$ +8.4° (*c* 5.36); ir bands at 1765, 1735, 1725, 1710, 1670, and 1628 cm$^{-1}$; uv end absorption ($\epsilon$ 27, 100 at 202 nm), CD curve (1 cm cell) $\lambda_{max}$ 253, 310 nm ($\theta$ − 1740, −694); positive iodoform test.

*Anal.* Calcd for $C_{23}H_{28}O_{10}$: C, 59.48; H, 6.08; O, 34.45. Found: C, 59.50; H, 5.98; O, 34.97.

**Reactions of 1a.** (**A**).—A solution of 100 mg of **1a** in 2 ml of methanol and 2 ml of 1 *N* sodium hydroxide was heated on the water bath for 15 min, evaporated to dryness at reduced pressure and the residue titrated with 0.1 *N* hydrochloric acid. This indicated that 3.9 mol equiv of base had been consumed.

(**B**).—A solution of 100 mg of **1a** in 20 ml of ether was allowed to stand with 5 ml of ethereal diazomethane at 5° for 3 days. The pyrazoline **2a** which had separated was recrystallized from ethyl acetate: yield 95 mg, mp 166–168° dec, CD curve $\lambda_{max}$ 316 nm ($\theta$ −4900).

*Anal.* Calcd for $C_{24}H_{30}N_2O_9$: C, 58.77; H, 6.16; N, 5.71. Found: C, 59.29; H, 6.30; N, 5.78.

**Dihydrouvedalin (3a).**—To a solution of 0.228 g of **1a** in 10 ml of methanol was added with stirring 0.190 g of sodium borohydride in 5 ml of methanol at 0°. Stirring was continued for 1 hr, the solution was acidified, evaporated at reduced pressure, diluted with 10 ml of water, and extracted with chloroform. The washed and dried extract was evaporated and the residue was repeatedly recrystallized from ethyl acetate–hexane. Pure **3a**: yield 0.09 g; mp 183–186°; $[\alpha]^{20}D$ −35.2° (*c* 2.98); ir bands 1780, 1760, 1735, 1720, 1675, and 1630 cm$^{-1}$; $\lambda_{max}$ 206 nm ($\epsilon$ 11,300).

*Anal.* Calcd for $C_{23}H_{30}O_9$: C, 61.32; H, 6.71; O, 31.96. Found: C, 61.75; H, 6.26; O, 31.73.

**Tetrahydrouvedalin (4a).**—A solution of 0.147 g of **1a** in 25 ml of ethyl acetate was reduced at atmospheric pressure with prereduced 10% Pd-C. Hydrogen uptake ceased after absorption of 2 mol equiv of hydrogen. The product was recrystallized

(15) T. G. Waddell, W. Stöcklin, and T. Geissman, *Tetrahedron Lett.*, 1313 (1969).

(16) G. Snatzke, *Riechst, Aromen, Körperpflegem.*, **19**, 98 (1969); M. Suchy, L. Dolejs, V. Herout, F. Sorm, G. Snatzke, and J. Himmelreich, *Collect. Czech. Chem. Commun.*, **34**, 229 (1969).

(17) W. Herz and G. Högenauer, *J. Org. Chem.*, **27**, 905 (1962).

(18) W. Herz, H. Chikamatsu, N. Viswanathan, and V. Sudarsanam, *ibid.*, **32**, 682 (1967).

(19) Y. Mazur and A. Meisels, *Bull. Res. Counc. Isr.*, **5A**, 67 (1955); Z. Cekan and V. Herout, *Collect Czech. Chem. Commun.*, **21**, 79 (1956).

(20) Experimental conditions specified in ref 2 apply.

(21) Chemical shifts differed slightly from the values obtained at 60 MHz (Table I) owing to small calibration errors. The spin-decoupling experiments were carried out by Mr. A. L. Hall.

from ethyl acetate–hexane. Pure **4a**, yield 0.085 g, had mp 185–187°; ir bands at 1775, 1760, 1740, 1720, and 1645 $cm^{-1}$; uv $\lambda_{max}$ 205 nm ($\epsilon$ 10, 100).

*Anal.* Calcd for $C_{23}H_{32}O_9$: C, 61.05; H, 7.13; O, 31.82. Found: C, 60.93; H, 6.95; O, 32.08.

**Uvedalin Epoxide (5a).**—A solution of 100 mg of **1a** in 4 ml of dry chloroform was allowed to stand with 100 mg of *m*-chloroperbenzoic acid overnight at 0°. The reaction mixture was washed in the usual fashion, dried and evaporated and the residue recrystallized from acetone–petroleum ether. The pure product, yield 54 mg, had mp 218–220°; ir bands at 1765, 1755, 1732, 1715, 1665, and 1632 $cm^{-1}$.

*Anal.* Calcd for $C_{23}H_{28}O_{10}$: C, 59.48; H, 6.08; O, 34.45. Found: C, 59.21; H, 61.31; O, 34.32.

An isomeric epoxide **9a** was prepared as follows. A mixture of 0.3 g of **1a**, 10 ml of tetrahydrofuran, 2.1 g of potassium carbonate, and 2.5 ml of water was stirred overnight. The solvents were removed *in vacuo* and 5 ml of water was added. Unreacted **1a**, wt 0.21 g, was recovered by extraction with chloroform. The aqueous layer was acidified and extracted with chloroform. The washed and dried extract was evaporated and the residue was recrystallized from ethyl acetate–hexane to yield 60 mg of **9a** which had mp 158–161° (depressed on admixture of **5a**); $[\alpha]^{24}D$ +11.5° (*c* 4.36); ir bands at 1795, 1755, 1740, 1720, 1670, and 1630 $cm^{-1}$.

*Anal.* Calcd for $C_{23}H_{28}O_{10}$: C, 59.48; H, 6.08; O, 34.45. Found: C, 59.12; H, 6.24; O, 34.62.

**Dihydrouvedalin Epoxide (6a).**—Epoxidation of 0.1 g of **3a** with *m*-chloroperbenzoic acid in the manner described in the previous section gave after recrystallization from acetone–petroleum ether, 86 mg of **6a** which had mp 213–215°, $[\alpha]^{25}D$ −73.6° (*c* 1.97).

*Anal.* Calcd for $C_{23}H_{30}O_{10}$: C, 59.22; H, 6.48. Found: C, 59.20; H, 6.38.

**Preparation of 1b and 1e.**—A solution of 0.33 g of **1a**, 4 ml of dioxan and 0.5 ml of dilute (1:1) HCl was kept overnight with stirring, evaporated at reduced pressure, diluted with water and extracted with chloroform. The washed and dried extracts were evaporated. The residue was purified by preparative tlc and recrystallized from ethyl acetate–hexane. There was obtained 0.23 g of **1b** which had mp 177–179°; ir bands at 3525, 1765, 1750, 1735, 1710, 1670, and 1628 $cm^{-1}$; uv end absorption ($\epsilon$ 22,400 at 203 nm).

*Anal.* Calcd for $C_{23}H_{29}O_9Cl$: C, 57.03; H, 6.32; Cl, 7.33. Found: C, 57.46; H, 6.04; Cl, 7.55.

Reaction of 0.1 g of uvedalin with 0.2 ml of dilute HBr (1:1) in the same manner gave, after recrystallization from ethyl acetate, 60 mg of **1e** which had mp 174–176°; ir bands at 3522, 1763, 1750, 1732, 1715, 1668, and 1628 $cm^{-1}$.

*Anal.* Calcd for $C_{23}H_{29}O_9Br$: C, 52.17; H, 5.48; Br, 15.10. Found: C, 52.53; H, 5.73; Br, 15.04.

**Conversion of Uvedalin to Polydalin.**—A solution of 0.15 g of **1a** in 5 ml of acetone and 1 ml of water containing 4 drops of concentrated sulfuric acid was kept at room temperature for 24 hr, evaporated at reduced pressure and extracted with chloroform. The washed and dried extract was evaporated and the residue was chromatographed over silica gel to give 0.12 g of starting material and 0.03 g of **1c** as a gum which had ir bands at 3540 (broad), 1765, 1745, 1735, 1718, 1670, and 1628 $cm^{-1}$.

A solution of 0.02 g of **1c** in 4 ml of acetone and a few drops of Jones reagent was stirred for 0.5 hr at 0°. Excess reagent was destroyed by addition of methanol and the solvents were removed *in vacuo*. The residue was extracted with chloroform. The washed and dried extract was evaporated and the residue (two spots on tlc) was subjected to preparative tlc. The more polar fraction was recrystallized from ethyl acetate–hexane to give 8 mg of material, mp 180–182°, identical in all respects (mixture melting point, ir, and nmr) with naturally occurring polydalin (**1d**).

*Anal.* Calcd for $C_{23}H_{28}O_{10}$: C, 59.48; H, 6.08; O, 34.45. Found: C, 59.30; H, 6.02; O, 34.59.

**Hexahydrouvedalin (7a).**—A solution of 0.403 g of **1a** in 25 ml of acetic acid was reduced overnight at atmospheric pressure with prereduced platinum oxide catalyst until hydrogen absorption ceased (2.9 mol equiv). The product, wt 0.40 g, was a gum which could not be crystallized and had $[\alpha]^{25}D$ +15.0° (*c* 5.0); ir bands at 1775, 1760, and 1740 $cm^{-1}$; weak uv end absorption ($\epsilon$ 360 at 203 nm).

**Tetrahydropolydalin (3b).**—A solution of 0.386 g of **1d** in 25 ml of methanol was reduced with 0.354 g of sodium borohydride in the manner described earlier for **1a**. The product, purified by preparative tlc, was a gum which could not be crystallized and had ir bands at 3520, 1772, 1732, 1715, 1670, and 1630 $cm^{-1}$.

**Preparation of 3c.**—A mixture of 0.51 g of **3b**, 20 ml of methanol, 10 ml of water and 0.319 g of sodium metaperiodate was stirred at room temperature for 4.5 hr, evaporated *in vacuo*, diluted with water and extracted with chloroform. The washed and dried extract was evaporated and the residue was recrystallized three times from ethyl acetate–hexane to give 0.21 g of pure **3c**: mp 195–197°; $[\alpha]^{23}D$ −41.7 (*c* 1.2); ir bands at 1770, 1765, 1740, 1720, 1672, and 1630 $cm^{-1}$; uv $\lambda_{max}$ 220 nm ($\epsilon$ 9100), end absorption $\epsilon$ 16, 600 at 200 nm.

*Anal.* Calcd for $C_{21}H_{26}O_9$: C, 59.71; H, 6.20; O, 34.09. Found: C, 60.12; H, 6.01; O, 33.80.

**Hydrolysis of 3c.** (**A**).—A solution of 0.03 g of **3c** and 0.03 g of $NaHCO_3$ in 10 ml of 80% aqueous methanol was stirred in a nitrogen atmosphere for 15 min, acidified, evaporated *in vacuo*, diluted with 5 ml of water and extracted with chloroform. The washed and dried extract was evaporated and the residue purified by preparative tlc. The product **3f**, wt 0.0287, was a gum which cound not be crystallized and had ir bands at 3400, 1765, 1730, 1710, 1670, and 1622 $cm^{-1}$.

*Anal.* Calcd for $C_{18}H_{24}O_7$: C, 61.35; H, 6.86; O, 31.78. Found: C, 60.97; H, 7.15; O, 31.74.

(**B**).—Repetition of the above experiment with 0.15 g of **3c** and 0.15 g of potassium carbonate for 2.5 hr gave, after the usual work-up, a solid which was recrystallized from ethyl acetate–hexane. The product **3d**, wt 76 mg, had mp 168–170°; ir bands at 3520, 3360, 1765, 1690, 1670, and 1628 $cm^{-1}$; uv $\lambda_{max}$ (220 nm) ($\epsilon$ 7100) and end absorption ($\epsilon$ 14, 400 at 202 nm).

*Anal.* Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15: O, 30.93. Found: C, 62.35; H, 6.88; O, 30.91.

Acetylation of 50 mg of **3d** in the usual fashion (acetic anhydride pyridine) and recrystallization of the product from ethyl acetate–hexane furnished 45 mg of diacetate **3e**: mp 204–206°; $[\alpha]^{24}D$ −40.6°; ir bands at 1775, 1745, 1735, 1720, 1670, and 1630 $cm^{-1}$.

*Anal.* Calcd for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64; O, 32.45. Found: C, 60.68; H, 6.55; O, 32.69.

The acetonide **3g** was prepared from **3d** by the anhydrous cupric sulfate–acetone method and had mp 176–178° after recrystallization from ethyl acetate (end absorption $\epsilon$ 20,000 at 203 nm). It was not analyzed, but the nmr spectrum (Table I) verified its structure.

(**C**).—The previous experiment was repeated by refluxing 0.03 g of **3c** and 0.03 g of potassium carbonate in 10 ml of aqueous methanol for 3 hr. After acidification, the usual work-up gave a residue which was recrystallized from ethyl acetate to give **8**: mp 246–248°; ir bands at 1778, 1760, 1655, and 1650 $cm^{-1}$; uv $\lambda_{max}$ 249 nm ($\epsilon$ 6200) and end absorption ($\epsilon$ 2000 at 201 nm).

*Anal.* Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.22; O, 24.59. Found: C, 69.38; H, 6.59; O, 24.45.

**Extraction of *Polymnia laevigata*.**—Dried and ground leaves of *P. laevigata* Beadle, wt 3.6 kg, collected by Dr. J. R. Wells on July 1, 1967, 2 miles southeast of Monteagle, Tenn., and in July 1966 3.5 miles southeast of Monteagle (voucher on deposit in Cranbrook Institute of Science), were extracted with chloroform in the usual fashion. The crude gum, wt 36 g, was chromatographed over 350 g of silicic acid, 1000-ml fractions being collected in the following order: fractions 1–30 benzene, 31–45 benzene–chloroform (1:1), 46–64 chloroform, 65–70 chloroform–ether (9:1), 71–76 chloroform–methanol (9:1), 77–79 chloroform–methanol (1:1). Fractions 38–54 gave 15 g of solid which was recrystallized from ethyl acetate to give 10.5 g of pure ivalin, mp 130–132°, identified by comparison with authentic material.[18] The other fractions contained gummy mixtures (tlc) which could not be separated satisfactorily by rechromatography. **1a** and **1d** were absent.

**Extraction of *Polymnia canadensis*.**—Dried and ground leaves of *P. canadensis* L., wt 3.3 kg, collected by Dr. J. R. Wells in Aug 1966 and July 1967 in a ravine along a limestone talus slope at the junction of Hayden Run Road and Scioto River, Franklin County, Ohio (vouchers on deposit at Cranbrook Institute of Science), was extracted in the usual fashion with chloroform. The crude gum, wt 15 g, was chromatographed over 400 g of silicic acid, 500 ml fractions being collected in the following order: fractions 1–6 benzene, 7–15 benzene–chloroform (2:1), 16–24 benzene–chloroform (1:2), 25–30 chloroform, 31–35 chloroform–methanol (19:1), 36–40 chloroform–methanol (9:1). Fractions 22–23 which were semicrystalline were recrystallized

repeatedly from ethanol to give 18 mg of pure artemetin: mp 162–163°; mol wt (by mass spectrometry) 388; nmr signals 7.22 (d) and 6.97 (d) ($J$ = 9.2, H-6′ and H-5′ respectively), 7.70 (H-2′), 6.48 (H-8), 3.96, 3.94, 3.92, and 3.88 ppm (4 methoxyls); and gave the color reaction previously reported for artemetin. The mixture melting point with an authentic sample[22] was not depressed. The methyl ether had mp 156–157°, mixture melting point with an authentic sample[22] undepressed. All other fractions were gums showing several spots. Repetition of the extraction with plant material collected in July 1969 at the same location gave the same results.

(22) W. Herz, *J. Org. Chem.*, **26**, 3014 (1961).

**Registry No.**—**1a**, 24694-79-9; **1b**, 24694-80-2; **1c**, 24694-81-3; **1d**, 24728-11-8; **1e**, 24694-82-4; **2a**, 24728-12-9; **3a**, 24728-13-0; **3b**, 24806-56-2; **3c**, 24694-83-5; **3d**, 24694-84-6; **3e**, 24694-85-7; **3f**, 24694-86-8; **3g**, 24728-14-1; **4a**, 24694-87-9; **5a**, 24694-88-0; **6a**, 24694-89-1; **7a**, 24694-90-4; **8**, 24694-91-5; **9a**, 24694-92-6; artemetin, 479-90-3.

# Sesquiterpene Lactones and Lactone Glycosides from *Hymenoxys* Species[1,2]

WERNER HERZ[3] AND K. AOTA

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

M. HOLUB[4] AND Z. SAMEK

*Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Praha 6, Czechoslovakia*

*Received February 17, 1970*

A group of interesting sesquiterpene dilactones has been isolated from some *Hymenoxys* species. Floribundin (**3**) and vermeerin (**2**), the latter previously found in South African *Geigeria* species, were isolated from the southwestern U. S. stock poison *H. richardsonii* and the South American *H. anthemoides*. *H. anthemoides* also yielded anthemoidin and themoidin which are dihydro derivatives of **2** and **3**, respectively. *H. greenei* gave **3** and the dilactone greenein (**6**). Separate collections of *H. odorata* afforded either a lactone glucoside hymenoxynin (**14a**) or the pseudoguaianolide glucoside paucin (**13a**) and a lactone lactal hymenolide (**8a**) which could be correlated with hymenoxynin and floribundin. Structures, stereochemistry, and conformations for all compounds were derived by chemical methods and extensive application of nmr techniques.

As a consequence of the discovery of a group of biogenetically "abnormal" sesquiterpene lactones, the so-called pseudoguaianolides, in some *Helenium* species,[5] the genera *Helenium* and *Gaillardia*, the latter adjoining *Helenium* in the taxonomic scheme of *Compositae* (tribe *Helenieae*, subtribe *Heleniinae*), have received careful scrutiny.[6,7] In general, elaboration of pseudoguaianolides seems characteristic of these two genera, although some exceptions have been noted.[6,8]

While *Helenieae* is thought by many to be a rather artificial assemblage not deserving of tribal status,[11] certain natural subdivisions exist. For example, it is generally agreed that the genus *Hymenoxys* is closely allied to *Helenium* and *Gaillardia*. Accordingly, chemical examination of *Hymenoxys* species appeared to be of interest. Knowledge of their sesquiterpene lactone content could conceivably contribute to a better understanding of phylogenetic relationships within the group. Moreover several representatives such as *Hymenoxys odorata* DC. and *H. richardsonii* (Hook) Ckll. var. *floribunda* (pingue bitterweed) are well-known stock poisons of the American southwest;[12] it seemed possible that sesquiterpene lactones might be responsible for their activity. We have therefore embarked on a study of this genus. In the following we report the results of our initial study of four *Hymenoxys* species. Work on other species is continuing.[13]

## Results

Table I lists species included in the present investigation and the crystalline sesquiterpene lactones isolated

(1) Supported in part by a grant from the U. S. Public Health Service (GM-05814).

(2) Previous paper on Sesquiterpene Lactones: W. Herz and S. V. Bhat, *J. Org. Chem.*, **35**, 2605 (1970).

(3) To whom correspondence should be addressed.

(4) On leave of absence at Florida State University, 1967–1968.

(5) W. Herz, W. A. Rohde, K. Rabindran, P. Jayaraman, and N. Viswanathan, *J. Amer. Chem. Soc.*, **84**, 3857 (1962); W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *ibid.*, **85**, 19 (1963).

(6) For reviews of work through 1966, see W. Herz, "Pseudoguaianolides in *Compositae*, Recent Advances in Phytochemistry," T. J. Mabry, R. E. Alston, and V. C. Runeckles, Ed., Appleton-Century-Croft, New York, N. Y., 1968, p 220; J. Romo and A. Romo de Vivar, "The Pseudoguaianolides, Progress in the Chemistry of Natural Products," L. Zechmeister, Ed. Springer Verlag, Vienna, Vol. 25, 1967, p 90.

(7) For the most recent paper on *Helenium* species, see W. Herz, P. S. Subramaniam, and N. Dennis, *J. Org. Chem.*, **34**, 2915 (1969).

(8) To these exceptions must now be added pulchellins B, C, E, and F from Western races of *G. pulchella* Foug. Recent work[9] has shown these sesquiterpene lactones to be eudesmanolides rather than pseudoguaianolides as originally supposed.[10]

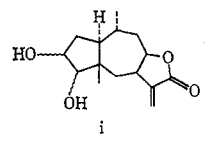
(9) H. Yoshioka, N. Dennis, W. Herz, and T. J. Mabry, *J. Org. Chem.*, **35**, 627 (1970).

(10) W. Herz and S. Inayama, *Tetrahedron*, **20**, 341 (1964); W. Herz and S. K. Roy, *Phytochemistry*, **6**, 661 (1969).

(11) A. Cronquist, *Amer. Midl. Natur.*, **53**, 478 (1955); O. Solbrig, *J. Arnold Arboretum*, **44**, 436 (1963).

(12) J. M. Kingsbury, "Poisonous Plants of the United States and Canada," Prentice-Hall, Englewood Cliffs, N. J., 1964.

(13) While our work was in progress, two other groups reported on constituents of certain *Hymenoxys* species. Thomas and Mabry[14] isolated a number of flavonoids from *H. scaposa* DC. whereas Romo and coworkers[15] obtained a new pseudoguaianolide odoratin (i) from a San Luis Potosi




i

collection of *H. odorata*. Because we encountered different sesquiterpene lactones in collections of *H. odorata* from two separate localities (*vide infra*, Table I), the difference between the results reported by the Mexican workers and by us is not particularly surprising. Moreover, odoratin appears to be a possible precursor of the substances isolated by us (*vide infra*).

(14) M. B. Thomas and T. J. Mabry, *J. Org. Chem.*, **32**, 3254 (1967); *Tetrahedron*, 3675 (1968); *Phytochemistry*, **7**, 787 (1968).

(15) A. Ortega, A. Romo de Vivar, and J. Romo, *Can. J. Chem.*, **46**, 1538 (1968).