mol wt 412.50). The intensity data were measured on a Hilger-Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). A crystal measuring approximately 0.15 × 0.20 × 0.8 mm was used for data collection; the data were corrected for absorption (μ = 17.1 cm^{-1}). A total of 1502 reflections were measured for $\theta < 57°$, of which 1452 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure[30] and was refined by full-matrix least-squares methods. In the final refinement, anisotropic thermal parameters were used for the heavier atoms, and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure-factor calculations, but their parameters were not refined. The presence of sulfur permitted determination of the absolute configuration which is shown in Figure 1. Both enantiomers were refined. The final weighted R values were 0.0452 for the configuration illustrated and 0.0490 for its antipode, thus conclusively establishing the absolute configuration of **1e**. The final difference map had no peaks greater than ±0.3 Å^{-3}.

(30) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A* **1971**, *27*, 368.

Registry No. **1a**, 72229-33-5; **1b**, 72229-34-6; **1c**, 38456-39-2; **1d**, 72229-35-7; **1e**, 72229-36-8; **1f**, 72229-37-9; **1g**, 72229-38-0; **1h**, 72229-39-1; mollisorin B, 72258-24-3.

Supplementary Material Available: Final atomic parameters (Table IV), anisotropic thermal parameters (Table V), bond lengths (Table VI), bond angles (Table VII), and selected torsion angles (Table VIII) of **1e** (6 pages). Ordering information is given on any current masthead page.

Sesquiterpene Lactones of *Hymenoxys insignis*. X-ray Analyses of Hymenograndin and Hymenosignin[1]

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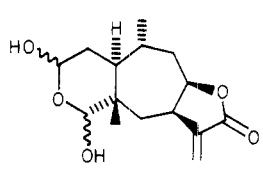
Hymenoxys insignis yielded the new guaianolide hymenosignin (**2**) and the new helenanolide acetylhymenograndin (**3b**). The structures were established by physical methods. These included X-ray analyses of **2** and hymenograndin (**3a**), whose previously postulated stereochemistry at C-2 and C-3 was found to require revision. Conformations of the various compounds and their bearings on the CD curves of substances related to **3a,b** are discussed, and a suggestion is made to account for the co-occurrence of hymenosignin and acetylhymenograndin.

Several *Hymenoxys* species are important livestock poisons.[2] Their toxicity and mutagenic activity is due primarily to the secohelenanolide hymenovin (**1**) which is



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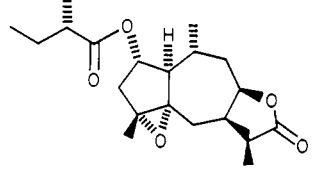
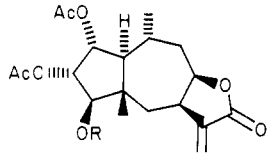


2



3a, R = H
b, R = Ac

a mixture of hemiacetal epimers derived from a hypothetical hydrated seco dialdehyde.[3-5] Various related dilactones[6,7] and helenanolides[11-13] are other typical constituents of the genus. In the present paper we report isolation and structure determination of a new guaianolide, **2**, and a new helenanolide, **3b**, from the Mexican species *Hymenoxys insignis* (Gray ex Wats) Cockll. and comment on the possible significance of their co-occurrence. Hy-

(1) Work at The Florida State University was supported in part by a grant from the U.S. Public Health Service (CA-13121) through the National Cancer Institute.

(2) Kingsbury, J. M. "Poisonous Plants of the United States and Canada"; Prentice Hall: Englewood Cliffs, NJ, 1964.

(3) Ivie, G. W.; Witzel, D. A.; Herz, W.; Kannan, R.; Norman, J. D.; Rushing, D. D.; Johnson, J. H.; Rowe, L. D.; Veech, J. A. *J. Agric. Food Chem.* **1975**, *23*, 841.

(4) Ivie, G. W.; Witzel, D. A.; Herz, W.; Sharma, R. P.; Johnson, A. E. *J. Agric. Food Chem.* **1976**, *24*, 681.

(5) (a) Kim, H. L.; Rowe, L. D.; Camp, B. J. *Res. Commun. Chem. Pathol. Pharmacol.* **1975**, *11*, 647. (b) Pettersen, R. C.; Kim, H. L. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1399.

(6) Herz, W.; Aota, K.; Holub, M.; Samek, Z. *J. Org. Chem.* **1970**, *35*, 2611.

(7) Hymenovin, one of whose components has been named hymenoxon,[5] is easily converted[8] to the dilactones psilotropin (floribundin) and greenein which were isolated earlier[6] from several *Hymenoxys* species. The dilactones may therefore be artifacts. One of us has suggested[3,9] that the elusive "vermeeric acid" which is responsible for the toxicity of the South African *Geigeria* species may be the C-8 epimer of hymenovin and is converted upon extraction to the dilactone vermeerin.[6,10] The latter has been found in some toxic *Hymenoxys* species as well.[6]

(8) (a) Hill, D. W.; Kim, H. L.; Martin, C. L.; Camp, B. J. *J. Agric. Food Chem.* **1977**, *25*, 1304. (b) Hill, D. W.; Camp, B. J. *Ibid.* **1979**, *27*, 882.

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(10) Anderson, L. A. P.; de Kock, W. T.; Pachler, K. G.; Brink, C. V.; D. M. *Tetrahedron* **1967**, *23*, 4153.

(11) Ortega, A.; Romo de Vivar, A.; Romo, J. *Can. J. Chem.* **1968**, *46*, 1358. The name odoratin applied originally to the helenanolide isolated by these workers was subsequently changed to hymenoratin: Romo, J.; Romo de Vivar, A.; Aguilar, M. *Bol. Inst. Quim. Univ. Nac. Auton. Mex.* **1969**, *21*, 66.

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Table I. ^{1}H NMR Spectra[a,g]

	2	2[b]	2[c]	3a	3a[b]	3b	6
H-1	*d*	1.88 d	*d*	*d*	1.05 dd	1.65 dd	1.77 t
H-2	4.79 d, br	4.68 d, br	4.97 d, br	4.92 m	4.80 dd	5.02 t	5.00 dd
H-3a	2.21 dd	1.78 m	2.27 d, br	4.92 m	4.94 dd	5.32 dd	5.27 dd
H-3b	1.97 m	1.78 m	2.05 d, br				
H-4				3.71 d	3.43 d	5.14 d	4.97 d
H-6a	1.90 dd	*d*	2.05 m	1.53 dd	1.71 dd	1.74 dd	1.59 dd
H-6b	1.57 dd	1.22 dd	1.64 d, br	*d*	0.99 dd	1.48 dd	*d*
H-7	2.90 m	2.00 m	2.88 m	3.16 m	2.13 m	3.26 m	2.68 m
H-8	4.70 dt	3.90 dt	4.72 dt	4.76 ddd	4.00 ddd	4.78 ddd	4.72 m
H-9a	1.97 m	1.5 m	1.9 m	2.14 m	1.53 m	*d*	*d*
H-9b	1.63 m	1.5 m	1.9 m	1.81 dd, br	1.36 dd, br	1.83 dd, br	*d*
H-10	*d*	1.69 m	*d*	*d*	*d*	*d*	*d*
H-11	2.90 m	2.13 m	3.00 m				*d*
H-13	1.15 d[e]	0.83 d[e]	1.11 d[e]		6.16 d	6.26 d	1.05 d[e]
				5.61 d	4.91 d	5.59 d	
H-14[e]	1.16 d	0.89 d	1.14 d	1.08 d	0.74 d	1.08 d	1.09 d
H-15[e]	1.40	0.97	1.39	0.97	0.53	1.03	1.04
H-2′	2.32 m	2.27 m	2.42 m	2.08[f]	1.73[f]	2.13[f]	2.10[f]
H-3a′	1.68 m	1.39 m		2.08[f]	1.62[f]	2.06[f]	2.04[f]
H-3b′	1.46 m					2.03[f]	2.00[f]
H-4′[e]	0.90[f]	0.85	0.90[f]				
H-5′[e]	1.11 d	1.08 d	1.16 d				

[a] Run at 270 MHz in $CDCl_3$ unless specified otherwise. Shifts in parts per million downfield from Me_4Si. Unmarked signals are singlets. [b] In C_6D_6. [c] In C_5D_5N. [d] Obscured. [e] Three-proton intensity. [f] Acetate. [g] *J*'s [proton,proton = *J* (Hz)] in **2**: 1,10 = 10; 1,2 = 2; 2,3a = 6.5; 2,3b < 1; 3a,3b = 15; 6a,7 = 5; 6b,7 = 2.5; 7,8 = 8,9a = 5; 7,11 = 6; 6,9b = 9; 10,14 = 11,13 = 2′,5′ = 3′,4′ = 7. In **3a**: 1,10 = 12; 1,2 = 10; 2,3 = 9; 3,4 = 7; 6a,6b = 13; 6a,7 = 7, 4; 6b,7 = 15; 7,8 = 8; 7,13 = 2.5, 2; 8,9a = 12; 8,9b = 3; 9a,9b = 14; 9b,10 < 1; 10,14 = 7. In **3b**: 1,10 = 10; 1,2 = 2,3 = 9; 7,13 = 2.8, 2; otherwise as in **3a**. In **6**: 1,10 = 1,2 = 9.5; 2,3 = 8; 11,13 = 10,14 = 7.

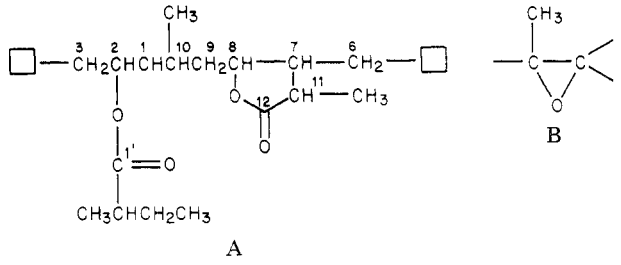
Table II. ^{13}C NMR Spectra[a]

	2	3a	3b	5	6
C-1	54.81 d	50.84 d	51.08 d[b]	51.62 d	49.95 d
C-2	77.27 d[c]	76.88 d[c]	76.37 d	59.22 d[c]	77.30 d
C-3	39.08 t[b]	76.18 d[c]	72.02 d[b]	61.67 d[c]	72.15 d[b]
C-4	69.67[d]	80.62 d[b]	79.93 d	75.61 d[d]	80.27 d
C-5	67.96[d]	41.78	41.40	58.64	40.96
C-6	24.51 t[e]	39.38 t	39.14 t[b]	75.18 d[d]	34.86 t[b]
C-7	39.60 d[f]	38.15 d	39.13 d[b]	45.16 d	37.94 d[b]
C-8	77.44 d[c]	72.63 d	71.93 d[b]	73.49 d	72.57 d
C-9	35.93 t[e]	34.89 t[b]	34.35 t	34.34 t	29.52 t
C-10	29.80 d	28.89 d	28.79 d	25.99 d	29.52 d
C-11	38.89 d[f]	139.45	138.94	136.33	37.94 d[b]
C-12	178.02	171.15	171.04	169.24	178.02
C-13	10.35 q	123.02 t	123.34 t	126.14 t	10.25 q
C-14	20.81 q	17.64 q	18.41 q	16.92 q	18.52 q
C-15	15.34 q[b]	20.18 q	20.20 q	19.88 q	20.49 q
C-1′	176.31	169.82	169.67		170.86
C-2′	41.62 d[b]	169.63	169.47		169.61
C-3′	26.67 t	20.64 q	169.26		169.61
C-4′	11.52 q	20.56 q	20.94 q		20.49 q
C-5′	16.40 q		20.52 q		20.49 q
			20.52 q		20.49 q

[a] Run in $CDCl_3$ at 67.9 MHz. Unmarked signals are singlets. [b] Assignments based on single-frequency off-resonance decoupling. [c,d,e] Assignments interchangeable. [f] Assignments interchangeable but made by SFORD.

menovin was absent.[14] Stereochemistries were established by X-ray analysis of **2** and of hymenograndin whose previously assigned stereochemistry[13] was found to require revision to **3a**.

Because of the very limited geographical distribution of *H. insignis* only small amounts of the new compounds were available, and we were forced to rely entirely on physical methods for structure elucidation. Extensive spin-decoupling experiments on the less polar crystalline substance **2** which we have called hymenosignin, $C_{20}H_{30}O_5$ (high-resolution mass spectrum), in various solvents to permit separation and irradiation of superimposed signals (Table I) resulted in deduction of partial structure A which was



A B

also in harmony with the ^{13}C NMR spectrum (Table II). The frequencies of H-2 and H-8 (numbering as in final formula) were such that they had to represent hydrogens

(14) The extraction was carried out under conditions[3] which allow isolation of hymenovin without rearrangement. Thus the absence of reports concerning the toxicity of *H. insignis* is not necessarily due to the very limited geographical distribution of this species.

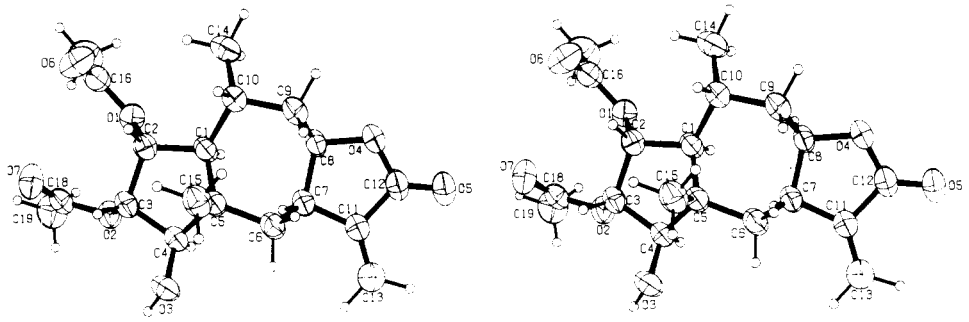


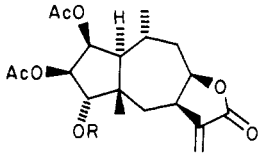
Figure 1. Stereoscopic view of hymenosignin (**2**).

under two oxygens associated with two ester carbonyls (two singlets at 178 and 176 ppm). One of the two esters was a γ-lactone (IR band at 1765 cm^{-1}); this required joining C-12 to C-11 and, therefore, attachment of the 2-butyl residue of the second ester (IR band at 1720 cm^{-1}) to C-1′. The remaining three carbons and one oxygen of the empirical formula were represented by partial structure B (methyl singlet at 1.41 ppm, two carbon singlets near 70 and 68 ppm) whose combination with A led to the biogenetically plausible gross structure of **2**, that of a guaianolide which is unusual in being unfunctionalized on C-10.

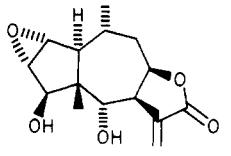
Because the stereochemistry of hymenosignin could not be deduced unambiguously from the NMR data, recourse was had to X-ray crystallography. Crystal data are listed in the Experimental Section. Figure 1 is a stereoscopic drawing of the molecule which in view of the absolute configuration of other lactones from *Hymenoxys* and related species is also believed to represent the absolute configuration, although it was not possible to deduce this from the X-ray data. H-1, the ester function on C-2, the 4,5-epoxide, and the C-10 methyl group are all α, the lactone ring is fused cis, and the C-11 methyl group is β. The cycloheptane ring is a slightly distorted boat with a C(7)–C(8)–C(1)–C(10) central plane and C(1)–C(5)–C(6)–C(7) and C(8)–C(9)–C(10) outer planes; the lactone ring is slightly puckered but approximates an envelope with C-7 as the flap. Tables V–IX, listing final atomic and final anisotropic thermal parameters, bond lengths, bond angles, and selected torsion angles, are available as supplementary material.

A more polar noncrystalline substance from *H. insignis*, $C_{21}H_{28}O_8$ (high-resolution mass spectrum), was a triacetate (methyl singlets at 2.13, 2.06, and 2.03 ppm) in which the three ester functions were attached to methinyl carbons (^1H and ^{13}C NMR spectra, Tables I and II). The substance also incorporated an α-methylene-γ-lactone function because it exhibited narrowly split doublets at 6.26 and 5.60 ppm (H-13) coupled to a one-proton multiplet at 3.26 ppm (H-7); the latter was in turn coupled to a multiplet at 4.78 ppm (H-8). Since no other centers of unsaturation were present (^{13}C NMR spectrum), the substance was bicyclic and, because of the presence of a methyl singlet and a methyl doublet, either an alantolide or a pseudoguaianolide; if it was the latter, it was probably of the helenanolide subclass. Spin decoupling then established the entire sequence of carbon atoms shown in formula **3b**, where the quaternary carbon atom carrying the methyl group had to be inserted between C-1, C-4, and C-6 to account for the multiplicities in the ^1H NMR spectrum.

Formula **3b**, devoid of stereochemistry, represents the gross structure of the acetate of hymenograndin, a constituent of *H. grandiflora*,[13] and, in fact, acetylation of hymenograndin produced material identical in all respects with the substance from *H. insignis*. ^1H NMR and ^{13}C NMR spectra of hymenograndin are included in Tables I and II for comparison. Now in our work on hymenograndin preference was given to **4a** over **3a** on the basis



4a, R = H
b, R = Ac



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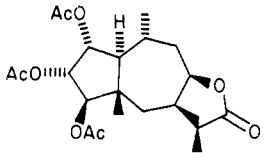


6

of a comparison between calculated and observed lanthanide-induced shifts. While the differences between the two sets of values calculated for **3a** and **4a** were, on the whole, not great, the observed shift of the signal of the C-5 methyl group, in proximity to the hydroxyl group on C-4, was reasonably close to that predicted for **4a**, while being vastly different from the value predicted for **3a**. Because the present study provided an incentive for checking the reliability of such predictions, an X-ray analysis of hymenograndin was undertaken.

Crystal data for hymenograndin are listed in the Experimental Section. Figure 2 is a stereoscopic drawing of hymenograndin which shows that formula **3a** rather than **4a** is correct and that an error, presumably due to inadequate assessment of conformational distortions, had entered into our earlier calculations. Interestingly enough, Figure 1 also indicates that the observed values for $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ (12, 10, and 9 Hz) accord more satisfactorily with **3a**, where the dihedral angles involving H-1 and H-2, H-2 and H-3, and H-3 and H-4 are −160, 5.1, and 144.8°, respectively, than with **4a** although this was not apparent from the Dreiding model.

Tables X–XIV listing final atomic and final anisotropic thermal parameters, bond lengths, bond angles, and selected torsion angles of hymenograndin are available as supplementary material. The cycloheptane ring is a boat, as proposed earlier,[13] with a central plane encompassing C(5)–C(6)–C(9)–C(10) and outer planes C(6)–C(7)–C(8)–C(9) and C(5)–C(1)–C(10). The cyclopentane ring is an envelope with C(5) as the flap. The γ-lactone ring is nearly flat, the sum of the internal torsion angles (Table XIV) being only 26°. The sign of the very small C=C—C=O torsion angle (ω_2 of Table III) is positive if the absolute configuration of hymenograndin is as depicted in Figure 1, as seems highly likely, is not paired with the sign of ω_3,[15]

(15) McPhail, A. T.; Sim, G. A. *Tetrahedron* **1973**, *29*, 1751.

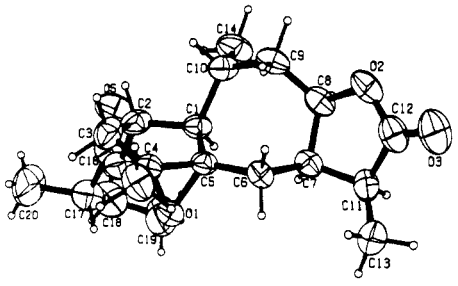


Figure 2. Stereoscopic view of hymenograndin (**3a**).

Table III. Lactone Ring Torsion Angles (deg) of 3a

C(8)-O(4)-C(12)-C(11)	ω_1	-6.6
C(13)-C(11)-C(12)-O(5)	ω_2	1.5
C(11)-C(7)-C(8)-O(4)	ω_3	-5.3
C(6)-C(7)-C(8)-C(9)	ω_4	-3.3

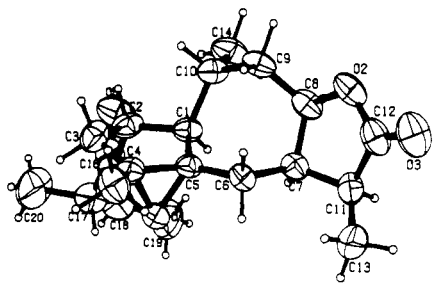
Table IV. Cyclopentane Ring Torsion Angles of 3a, 5, and 6

	3a	5[a]	6[b]
C(5)-C(1)-C(12)-C(3)	-32.1	-27.3	-16.5
C(1)-C(2)-C(3)-C(4)	6.3	9.7	-13.4
C(2)-C(3)-C(4)-C(5)	22.1	24.5	39.4
C(3)-C(4)-C(5)-C(1)	-41.3	-39.6	-48.1
C(4)-C(5)-C(1)-C(2)	44.8	41	39.3

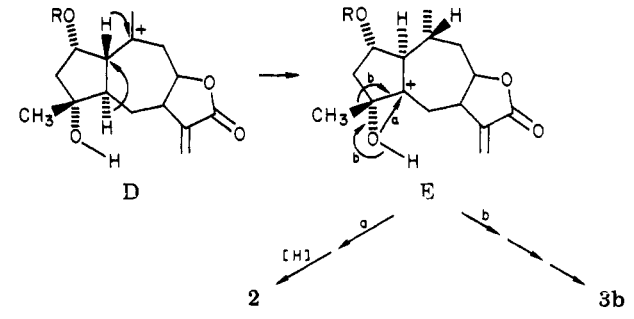
[a] Taken from ref 19c. [b] Taken from ref 5b.

a situation encountered in only two other sesquiterpene lactones,[16,17] and does not correspond to the sign of the (negative) Cotton effect associated with the n,π^* transition of the α,β-unsaturated lactone.[13] Thus hymenograndin appears to be another exception to the generalization[18] that chirality of the lactone chromophone (ω_2) determines the sign of the Cotton effect. However, it has been suggested recently[17] that the sign of ω_3 which is negative for **3a** and paired with ω_4 may provide a better correlation with lactone CD.

Conformation and torsion angles of **3a**, including those of the five-membered ring, are essentially identical with those of autumnolide (**5**)[19a,b] for which an X-ray analysis has been reported[19c] and which exhibits a negative lactone Cotton effect just like **3a** and **3b** (see Experimental Section). On the other hand there are some surprising differences between **3a** and hymenolane (**6**) obtained from *H. odorata*, an 11,13-dihydro derivative of acetylhymenograndin (**3b**), whose structure was also solved by X-ray crystallography.[5b] $NaBH_4$ reduction of **3b** yielded hymenolane, thus providing a chemical correlation between the two substances. While saturation of the 11,13 double bond could easily account for the observed minor differences in the torsion angles of the cycloheptane ring, the alteration in the internal torsion angles of the cyclopentane ring on acetylation of the 4-hydroxyl shown in Table IV is more difficult to explain. The ^1H and ^{13}C NMR spectra of hymenolane are included in Tables I and II; the diamagnetic shift of its H-4 resonance relative to that of H-4 of **3b** is noteworthy. In the ^{13}C NMR spectrum the greater shielding of its C-6 relative to the C-6 of **3a** and **3b** can

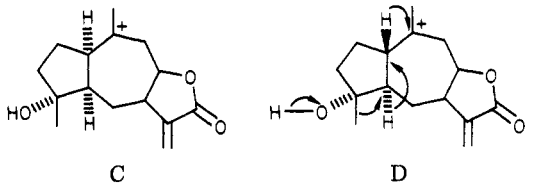


Scheme I



be attributed to the steric effect of the newly introduced methyl group on C-11, but the equally pronounced effect on C-9 was not anticipated.

The co-occurrence of a helenanolide and a 1,5-cis-fused guaianolide in the same plant extract seems to have only one precedent.[20,21] In accordance with a previously enunciated biogenetic scheme[22] one could postulate that **2** and **3b** arise by cyclization of separate *trans,trans*- and *cis,trans*-1(10),4-germacradiene precursors or their 4,5-epoxide analogues to C and D, respectively, with D undergoing further transformation to a helenanolide (arrows).[23] However, the unusual absence of unsaturation and hydroxylation or epoxidation involving C-10 of **2** and the α-orientation of the C-10 methyl group suggest the possibility of a later branch point resembling E in the biogenesis of the lactones of *H. insignis* (Scheme I). Stabilization of the charge in a cation E by the hydroxyl oxygen would lead to hymenosignin (**2**), whereas methyl migration, oxidation, acetylation, and reduction would lead



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to acetylhymenograndin (**3b**).

Experimental Section

Isolation of 2 and 3b. Aerial parts of *Hymenoxys insignis* (Gray ex Wats) Cockll. were collected on August 2, 1975, on a mountainside above Cerro Potosi, north of Galeana, Nueva Leon, Mexico (Bierner No. 51358, on deposit in the herbarium in the University of Tennessee), dried, ground, and extracted with acetone in a Soxhlet apparatus. To avoid possible rearrangement of labile sesquiterpene lactones, we spotted the crude extract, 11.3 g, on several preparative TLC plates coated with silica gel (60 GF: 254–366, EM reagent, 2 mm thickness) and developed by using the solvent system MeOH–$CHCl_3$ (1:49). Examination under UV light showed five bands, none of which contained hymenovin. Fraction I contained waxy material which included sitosterol. Fraction II (1.65 g) on further purification with the same solvent system yielded a fraction (0.27 g) whose IR spectrum exhibited a γ-lactone band. Preparative TLC of this material (EtOAc–hexane) gave two bands which upon extraction yielded 31 mg of hymenosignin (R_f 0.3) and 46 mg of acetylhymenograndin (R_f 0.2). Fraction III contained no lactones and is still being investigated. TLC examination of fractions IV and V indicated the presence of a complex mixture of flavonoids.

Hymenosignin (**2**) was recrystallized from benzene–hexane: mp 111–113 °C; $[\alpha]_D$ +10.8° (*c* 0.014 75, $CHCl_3$); IR ($CHCl_3$) 1765, 1720, 1175, 1090, 1020 cm^{-1}. The molecular ion was extremely weak but could be detected by chemical ionization mass spectrometry and was measured by the peak-matching procedure.

Anal. Calcd for $C_{20}H_{30}O_5$: mol wt 350.2093. Found: mol wt (mass spectrometry) 350.2093.

Significant peaks in the low-resolution mass spectrum appeared at *m/e* 248 ($M^+ - C_5H_{10}O_2$), 233 ($M^+ - C_5H_{10}O_2 - CH_3$), 205, 203, 175, 148 (base peak), 135, 122, 118, 85 (C_5H_9O).

Acetylhymenograndin (**3b**) was a colorless gum which had the following: IR ($CHCl_3$) 1752, 1740 (br), 1260, 1230 cm^{-1}; UV (MeOH) λ_{max} 212 nm (ε 7850); $[\alpha]_D$ +60° (*c* 0.0160, $CHCl_3$); CD (MeOH) $[\theta]_{249}$ −5250, $[\theta]_{212}$ +33 500 (last reading).

Anal. Calcd for $C_{21}H_{28}O_8$: mol wt 408.1789. Found: mol wt (mass spectrometry) 408.1789.

Other significant peaks in the high-resolution mass spectrum appeared at *m/e* (relative intensity) 348 ($C_{19}H_{24}O_6$, 7.3), 306 ($C_{17}H_{22}O_5$, 36.4), 264 ($C_{15}H_{20}O_4$, 24.5), 246 ($C_{15}H_{18}O_3$, 71.6).

Acetylation of hymenograndin (**3a**) in the manner described earlier[13] gave a substance identical in all respects (TLC, IR, NMR at 270 MHz) with **3b**. To 200 mg of this material in 5 mL of MeOH was added with stirring and cooling in an ice bath 20 mg of $NaBH_4$ over a period of 30 min. After an additional 24 h at room temperature the precipitated product, 180 mg, was filtered and recrystallized from EtOAc. The product was identical in all respects (melting point, TLC, NMR at 270 MHz) with authentic hymenolane (**6**).

Autumnolide (**5**) was available from earlier work;[19a] CD (MeOH) $[\theta]_{249}$ −5250, $[\theta]$ 33 500 (last reading).

X-ray Analysis of 3a. Single crystals of hymenograndin were prepared by slow crystallization from MeOH. They belonged to space group $P2_12_12_1$, with a = 9.623 (3) Å, b = 11.135 (2) Å, c = 18.343 (4) Å, and d_{calcd} = 1.238 g cm^{-3} for Z = 4 ($C_{19}H_{26}O_7$, mol wt 366.41). The intensity data were collected on a Hilger–Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). A crystal measuring approximately 0.15 × 0.20 × 0.6 mm was used for data collection; the data were not corrected for absorption (μ = 7.9 cm^{-1}). A total of 1540 reflections were measured for $\theta < 57°$ of which 1452 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple solution procedure[24] and was refined by full-matrix least-squares methods. In the final refinement, anisotropic thermal parameters were used for the heavier atoms, and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were used in the structure-factor calculations, but their parameters were not refined. The final discrepancy indices were R = 0.034 and R_w = 0.042 for the 1452 observed reflections. The final difference map had no peaks greater than ±0.2 $Å^{-3}$.

X-ray Analysis of 2. Single crystals of **2** were prepared by slow crystallization from benzene–hexane. They belonged to space group $P2_12_12_1$, with a = 10.248 (3) Å, b = 10.699 (5) Å, c = 18.220 (5) Å, and d_{calcd} = 1.165 g cm^{-3} for Z = 4 ($C_{20}H_{30}O_5$, mol wt 350.46). The procedure used was the same as described in the previous paragraph: crystal of approximately 0.25 × 0.5 × 0.6 mm, no absorption correction (μ = 6.8 cm^{-1}), 1562 reflections of which 1383 were considered observed. The final discrepancy indices were R = 0.069 and R_w = 0.086 for the 1383 observed reflections. The final difference map had no peaks greater than ±0.3 $Å^{-3}$.

Acknowledgment. We wish to thank Dr. H. L. Kim for a sample of hymenolane.

Registry No. **2**, 72264-71-2; **3a**, 51292-55-8; **3b**, 72264-72-3; **5**, 20505-32-2; **6**, 62121-29-3.

Supplementary Material Available: Final atomic parameters (Table V), anisotropic thermal parameters (Table VI), bond lengths (Table VII), bond angles (Table VIII), and selected torsion angles (Table IX) for **2** and Tables X–XIV listing the same parameters, respectively, for **3a** (10 pages). Ordering information is given on any current masthead page.

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Thiophene Systems. 3. Synthesis of Thieno[3,4-*b*][1,5]benzoxazepin-10-one and Thieno[3,4-*b*][1,5]benzothiazepin-10-one[1,2]

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In an intensive investigation of novel tricyclic systems, several synthetic routes were attempted to prepare the title compounds. Condensation of either *o*-aminophenol (**5**) or *o*-aminobenzenethiol (**6**) with keto ester **4** gave **7** or **8**, respectively, the products of undesired reaction orientation. In an alternative approach, acid chloride **13** condensed with **5** to give amide **14** which gave title lactam **1** by the action of polyphosphoric acid. Other attempted methods for closing **14** to **1** were less efficient. Reaction of **13** with **6** gave bis-acyl derivative **17** or benzothiazole **18**, depending on reaction conditions. Reaction of disulfide **19** with **13** gave bis-amide **20** which was cleaved to mercaptan **21** with sodium borohydride. Title lactam **2** as well as **18** formed when **21** was treated with polyphosphoric acid. Both **1** and **2** were selectively chlorinated at the 3-position to give **23** and **24**, respectively.

As part of a continuing effort to develop novel tricyclic systems, the syntheses of thieno[3,4-*b*][1,5]benzoxazepin-10-one (**1**) and thieno[3,4-*b*][1,5]benzothiazepin-10-one (**2**) and their derivatives were subjects of intensive investiga-

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