methosulfate was reacted with diethyl lithiophosphonate. Diethyl 3,5-dimethylpyridine-2-phosphonate was obtained in 54% yield by distillation: bp 107° (0.03 mm); nmr (neat) δ 1.33 (t, 6, J = 7 Hz, CH_3CH_2O), 2.32 (s, 3, CH_3Ar at C_5), 2.63 (s, 3, CH_3Ar at C_3), 4.25 (quintet, 4, J = 7 Hz, CH_3CH_2O), 7.52 (d, 1, ArH at C_4), 8.45 (s, 1, ArH at C_6).

Anal. Calcd for $C_{11}H_{18}NO_3P$: C, 54.32; H, 7.41; N, 5.76; P, 12.76. Found: C, 54.17; H, 7.35; N, 5.47; P, 12.88.

3,5-Dimethylpyridine-2-phosphonic Acid.—Hydrolysis of diethyl 3,5-dimethylpyridine-2-phosphonate (3 g) as described in previous examples yielded, after crystallization from aqueous ethanol, 3,5-dimethylpyridine-2-phosphonic acid, 1.2 g (54%), mp >300°.

Anal. Calcd for $C_7H_{10}NO_3P$: C, 44.92; H, 5.35; N, 7.49; P, 16.58; mol wt, 187. Found: C, 44.16; H, 5.62; N, 7.60; P, 16.62; mol wt, 186 (KOH titration).

Diethyl 3,4-Dimethylpyridine-2-phosphonate (19) and diethyl 4,5-Dimethylpyridine-2-phosphonate (20).—The procedure described for diethyl pyridine-2-phosphonate (**12**) was used. Distillation gave a mixture of **19** and **20** (47.5%): bp 125–126° (0.05 mm); nmr (neat) δ 1.33 (t, 6, J = 7 Hz, CH_3CH_2O), 2.30 (s, 15/4, CH_3Ar at C_4 and CH_3Ar at C_4 in **20**), 2.59 (s, 9/4, CH_3-Ar at C_3 in **19**), 4.27 (quintet, 4, J = 7 Hz, CH_3CH_2O), 7.30 (d, 3/4, ArH at C_5 in **19**), 7.76 (d, 1/4, ArH at C_3 in **20**), 8.50 (d, 1, ArH at C_6). From both ArH and $ArCH_3$ ratio of **19** to **20** is 3:1.

Anal.[28] Calcd for $C_{11}H_{18}NO_3P\cdot 1/2H_2O$ (mixture of **19** and **20**): C, 52.38; H, 7.54; N, 5.56; P, 12.30. Found: C, 52.82, 52.75; H, 7.56, 7.86; N, 5.59; P, 12.69.

Diethyl 2,6-Dimethylpyridine-4-phosphonate (24).—*n*-Butyllithium (23% in hexane) (87 ml, 0.2 mol) was added dropwise during 1.25 hr at −5–0° to diethyl phosphonate (60 g, 0.45 mol). To the resulting diethyl lithiophosphonate was added solid *N*-methoxy 2,6-dimethylpyridinium methosulfate [from 2,6-dimethylpyridine *N*-oxide (24.6 g, 0.2 mol) and dimethylsulfate (25.2 g, 0.2 mol)] portionwise during 2 hr at 5–15°. The mixture was stirred at room temperature overnight and heated at 70° for 2 hr. After cooling, water (150 ml) was added and the organic portion extracted into chloroform (three 100-ml portions). The basic portion was obtained by extraction of the chloroform solution with 3 *N* hydrochloric acid, basification, reextraction with chloroform, and evaporation. Distillation of the residue gave 2,6-dimethylpyridine [10 g (47%), bp 59–61° (70 mm)], and two further fractions [(a) bp 70–95° (0.2 mm) (0.7 g), and (b) bp 95–98° (0.2 mm) (13.5 g)]. Glc analysis indicated fraction a to consist of 2,6-dimethylpyridine (0.1 g), 2,6-dimethylpyridine *N*-oxide (0.5 g), and diethyl 2,6-dimethylpyridine-4-phosphonate (0.1 g) and fraction b to consist of 2,6-dimethylpyridine *N*-oxide (0.6 g) and diethyl 2,6-dimethylpyridine-4-phosphonate (12.6 g). The yield of phosphonate is 24% and the yield of *N*-oxide is 6%. Redistillation of fraction b gave pure phosphonate (**24**): bp 105° (0.2 mm); nmr (neat) δ 1.32 (t, 6, J = 7 Hz, CH_3CH_2O), 2.55 (s, 6, CH_3Ar), 4.20 (quintet, 4, J = 7 Hz, CH_3CH_2O), 7.44 (d, 2, J = 13.5 Hz, ArH).

Anal. Calcd for $C_{11}H_{18}NO_3P$: C, 54.32; H, 7.41; N, 5.76; P, 12.76. Found: N, 5.61; P, 12.88.

2,6-Dimethylpyridine-4-phosphonic Acid.—Diethyl 2,6-dimethylpyridine-4-phosphonate (**24**) (4 g) was heated under reflux with 18% HCl (50 ml) for 5 hr. Evaporation of the aqueous acid, trituration with ethanol, and recrystallization from aqueous ethanol yielded pure 2,6-dimethylpyridine-4-phosphonic acid, 2 g (65%), mp >300°.

Anal. Calcd for $C_7H_{10}NO_3P$: C, 44.92; H, 5.35; N, 7.49; P, 16.58. Found: C, 44.48; H, 5.42; N, 7.33; P, 16.40.

Registry No.—**12**, 23081-78-9; **12** (picrate), 26384-80-5; **17**, 26384-81-6; **18**, 26384-83-8; **19**, 26384-82-7; **20**, 26384-84-9; **24**, 26384-85-0; pyridine-2-phosphonic acid, 26384-86-1; diethyl 6-methylpyridine-2-phosphonate, 26384-87-2; 6-methyl-2-phosphonic acid, 26384-88-3; diethyl 4-methylpyridine-2-phosphonate, 26384-89-4; 4-methylpyridine-2-phosphonic acid, 26384-90-7; 3-methylpyridine-2-phosphonic acid, 26384-91-8; diethyl-3,5-dimethylpyridine-2-phosphonate, 26384-92-9; 3,5-dimethylpyridine-2-phosphonic acid, 26384-93-0; 2,6-dimethylpyridine-4-phosphonic acid, 26394-19-4.

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New Pseudoguaianolides from *Hymenoxys* Species. A New Type of Lactone Closure[1,2]

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Hymenoxys linearifolia Hook. afforded the flavone hymenoxin and two new pseudoguaianolides, linearifolin A and B, whose structure and stereochemistry has been inferred. Linearifolin B contains a δ-lactone ring closed to C-9 of the pseudoguaiane skeleton. *H. acaulis* (Pursh) K. F. Parker yielded 3,3′-dimethoxy-4′,5,7-trihydroxyflavone and the previously known pseudoguaianolide fastigilin C whose stereochemistry is discussed. *H. subintegra* Cockll. gave the modified pseudoguaianolide psilotropin and *H. rusbyi* (Gray) Cockll. psilotropin, the pseudoguaianolide glucoside paucin and the flavone pectolinarigenin.

In an earlier paper[3] we reported the isolation and structure determination of sesquiterpene dilactones and lactone glycosides from several *Hymenoxys* species. We now describe the results of our examinations of *H. linearifolia* Hook., *H. acaulis* (Pursh) K. F. Parker, *H. subintegra* Cockll., and *H. rusbyi* (Gray) Cockll.

Extraction of *H. linearifolia* Hook. yielded the flavone hymenoxin (5,7-dihydroxy-3′,4′,6,8-tetramethoxyflavone) previously isolated[4] from *H. scaposa* DC and two new isomeric sesquiterpene lactones which we have named linearifolin A and B.

Linearifolin A, $C_{20}H_{24}O_6$, mp 187–188°, $[\alpha]_D$ −90.0°, exhibited uv absorption at 218 nm (ε 22,500), the high intensity suggesting the presence of at least two chromophores. The ir spectrum indicated the presence of an α,β-unsaturated γ-lactone (1765, 1649 cm^{-1}), a hydroxyl group (3665, 3415 cm^{-1}), an α,β-unsaturated cyclopentenone (1711, 1580 cm^{-1}) of the type found in helenalin[5] and ambrosin,[6] and an unsaturated conju-

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

(2) Previous paper on Sesquiterpene Lactones: H. Yoshioka, A. Higo, T. J. Mabry, W. Herz, and G. Anderson, *Phytochem.*, in press.

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

(4) M. B. Thomas and T. J. Mabry, *ibid.*, **32**, 3254 (1967).

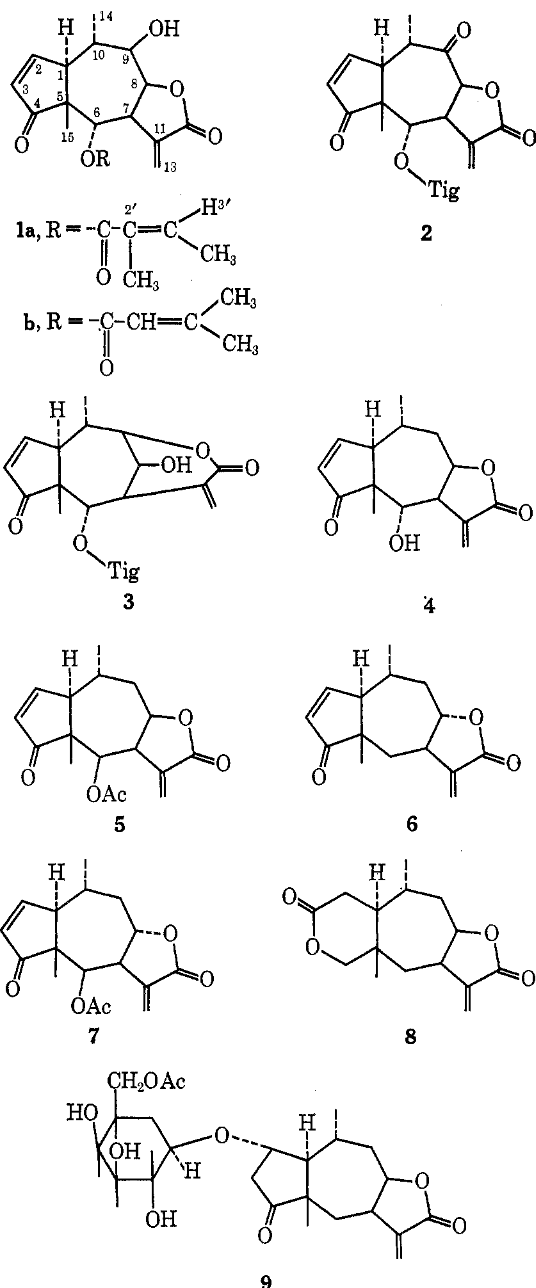
(5) W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *J. Amer. Chem. Soc.*, **85**, 19 (1963).

(6) W. Herz, H. Watanabe, M. Miyazaki, and Y. Kishida, *ibid.*, **84**, 2601 (1962).

gated ester (1720, 1270 cm^{-1}) which, because of the analytical values, was probably an angelate, tiglate or senecioate.

The nmr spectrum of linearifolin A showed the low field doublets of doublets at 7.78 ($J_1 = 5.9$, $J_2 = 1.7$ Hz) and 6.09 ppm ($J_1 = 5.9$, $J_2 = 3$ Hz) characteristic of the unsubstituted α,β-unsaturated cyclopentenone found in helenalin[5] and ambrosin,[6] the usual narrowly split doublets at 6.25 ($J = 2.5$ Hz) and 6.44 ppm ($J = 2.6$ Hz) due to the conjugated methylene group of these compounds, and the signals of a tigloyl group[7] (complex vinyl quartet at 6.61, vinyl methyl multiplets at 1.79 and 1.73 ppm).

Because of the further presence in the nmr spectrum of a methyl singlet and a methyl doublet, it seemed reasonable to postulate for linearifolin A the pseudoguaianolide structure **1a** (devoid of stereochemistry) where attachment of the tigloyl side chain to C-6 (with H-6 being accounted for by a somewhat broadened



(7) R. R. Frazer, *Can. J. Chem.*, **38**, 549 (1960).

singlet at 5.29 ppm) and lactone ring closure to C-8 (with H-8 being tentatively identified as a doublet of doublets at 5.02 ppm) was based on analogy to the substitution patterns found in other pseudoguaianolides of *Helenium*, *Gaillardia*, and *Hymenoxys* species.[3,8]

Linearifolin A also contained a secondary hydroxyl group whose presence was indicated by the infrared spectrum and by a second nmr signal near 3.7 ppm superimposed on a resonance provisionally attributed to H-7. Attachment of the hydroxyl to C-9 of the provisional formula was necessitated by the multiplicity of the H-8 signal (doublet of doublets), a deduction which was corroborated by examination of the nmr spectrum of a substance **2** produced by oxidation of linearifolin A. In the nmr spectrum of **2**, the resonance attributed to H-8 of linearifolin A had undergone the expected downfield shift and simplification to a doublet; furthermore, the multiplet near 3.7 ppm had been reduced to one-proton intensity.

Detailed analyses of the nmr spectra of **1a** and **2**, which are presented in Table I,[9] and are based on identification of every proton by double resonance techniques, confirmed the carbon skeleton and oxygenation pattern postulated for linearifolin A. Identification of the H-7 resonance in **1a** and **2** was achieved in the usual[10] way by irradiating at frequencies corresponding to those of H-13a and H-13b. Conversely, in the case of **2**, irradiation at 3.7 ppm collapsed not only the H-13a and H-13b doublets, but also the broad singlet at 5.66 ppm (clearly due to H-6 because it had not undergone simplification during the conversion of **1a** to **2**) and the slightly broadened doublet of H-8 at 5.56. All other signals remained unaltered, thus leading to partial structure A for **2**.

In the case of **1a**, irradiation at 3.7 ppm (H-7 and H-9 superimposed) also affected a multiplet at 2.30, identifiable as H-10 because it was coupled to the methyl doublet at 1.41 ppm. Such mutual coupling could also be demonstrated in **2** between the methyl doublet and a multiplet at 2.7 ppm. H-10 was further coupled to a multiplet found at 3.09 in **1a** and at 3.43 ppm in **2**. This multiplet was coupled vicinally to the β-hydrogen atom of the α,β-unsaturated cyclopentenone system and allylically to the α hydrogen. The above observations allowed expansion of A to B which requires attachment of the quaternary methyl group to C-5, as in **1**.

We defer consideration of the direction of the lactone ring closure and the stereochemistry until we have dealt with linearifolin B. This neutral substance $C_{20}H_{24}O_6$, mp 214–215°, $[\alpha]_D$ −104°, which was isolated only in small quantity, possessed the cyclopentenone chromophore of linearifolin A (nmr signals at 7.63 and 6.08 ppm, see Table I), its tigloyl side chain (nmr signals at 6.66, vinyl proton, 1.86 and 1.72, vinyl methyls), its secondary (doublet at 1.48 coupled to one-proton H-10 multiplet[11] at 2.4 ppm) and tertiary methyl group (singlet at 1.03 ppm), and a hydroxyl group (ir spectrum). However, except for the H-6 resonance, which was now a narrowly split doublet at 5.27 and was identified through its being coupled to H-7 at 3.53 ppm, the

(8) See, for example, W. Herz, P. S. Subramaniam, and N. Dennis, *J. Org. Chem.*, **34**, 2915 (1969).

(9) The 90-mHz Bruker nmr spectrometer used in this work was purchased with the aid of a grant from the National Science Foundation.

(10) W. Herz, S. Rajappa, S. K. Roy, J. J. Schmid, and R. N. Mirrington, *Tetrahedron*, **22**, 1907 (1966).

(11) The numbering system used here anticipates the structure which was deduced eventually.

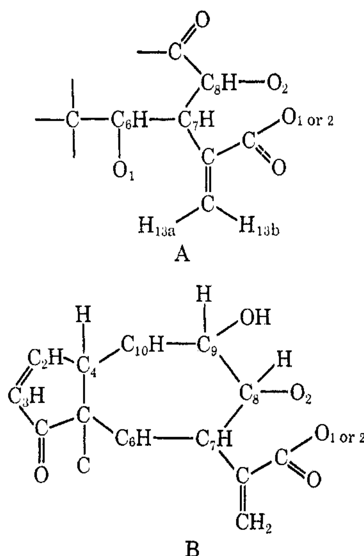
TABLE I[a]

NMR SPECTRA OF LINEARIFOLIN DERIVATIVES[a]

	1a		1b[b]		6[b]		3	
H-1	3.09 ddd[c]	$J_{1,2} = 1.7$[c]	3.08 ddd	$J_{1,2} = 2.0$	3.43 c	$J_{1,2} = 2.0$	3.15 ddd	$J_{1,2} = 1.8$
H-2	7.78 dd	$J_{2,3} = 5.9$	7.75 dd	$J_{2,3} = 6.0$	7.69 dd	$J_{2,3} = 6.0$	7.63 dd	$J_{2,3} = 5.8$
H-3	6.09 dd	$J_{1,3} = 3.0$	6.08 dd	$J_{1,3} = 3.0$	6.28 dd	$J_{1,3} = 2.5$	6.08 dd	$J_{1,3} = 2.9$
H-6	5.29 br[d]	$J_{6,7} = 1.3 \pm 0.3$[d]	5.28 br	$W_{1/2} = 3$	5.66 br	$J_{6,7} = 1.1$	5.27 d	$J_{6,7} = 3.7$
H-7	3.68 c[e]	$J_{7,8} = 6.0$[f]	3.68 c	$J_{7,8} = 8.1$	3.71 c	$J_{7,8} = 8.2$	3.53 m	$W_{1/2} = 8.7$
H-8	5.02 dd br	$J_{8,9} = 2.1$	4.99 dd br	$J_{8,9} = 2.5$	5.56 d br	$J_{8,10} = 0.8$	4.39 m	$W_{1/2} = 6$
H-9	3.65 c[g]	$J_{9,10} = 10.4 \pm 0.6$[h]	3.65 c				4.73 br	$W_{1/2} = 4$
H-10	2.30 c	$J_{1,10} = 10.7$	2.30 c	$J_{1,10} \sim 10.5$	2.71 c	$J_{1,10} = 13.2$	2.38 c	$J_{1,10} = 12.6$
H-13a	6.25 d	$J_{7,13a} = 2.4$	6.27 d	$J_{7,13a} = 2.4$	5.88 d	$J_{7,13a} = 3.3$	6.09 br	$J_{7,13a} < 0.5$
H-13b	6.44 d	$J_{7,13b} = 2.6$	6.46 d	$J_{7,13b} = 2.6$	6.36 d	$J_{7,13b} = 3.8$	6.68 br	$J_{7,13b} = 0.9$
H-14	1.41 d[i]	$J_{10,14} = 6.5$	1.39 d[i]	$J_{10,14} = 6.5$	1.50 d[i]	$J_{10,14} = 8.2$	1.48 d[i]	$J_{10,14} = 7.2$
H-15	0.98[i]		0.98[i]		0.87[i]	$J_{6,15} < 0.5$	1.03[i]	
H-3′	6.68	$J_{3',3'\text{-Me}} = 7 \pm 0.5$	5.52 m[j]		6.66 c		6.66 c	$J_{3',3'\text{-Me}} = 7 \pm 0.5$
2′-Me	1.75 m[i]	$J_{2'\text{-Me},3'\text{-Me}} \sim 1.0$			1.74 m[i]		1.72 m[i]	$J_{2'\text{-Me},3'\text{-Me}} \sim 1.0$
3′-Me	1.79 m[i]	$J_{3',2'\text{-Me}} \sim 1.5$	1.87 d[i]	$J_{2',3'\text{-Me}} = 1.4$	1.76 m[i]		1.80 m[i]	$J_{3',2'\text{-Me}} \sim 1.5$
			2.14 d[i]	$J_{2',3'\text{-Me}} = 1.2$				

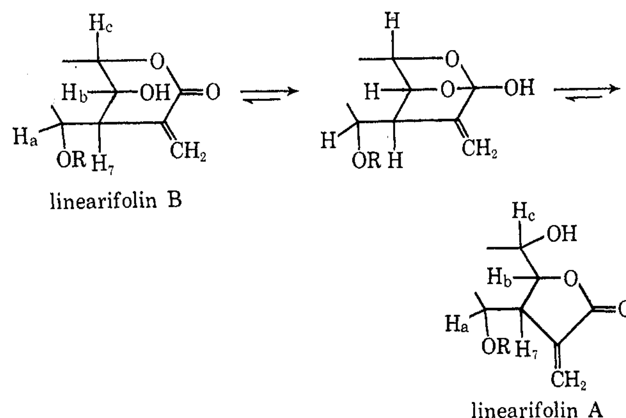
[a] Run at 90 MHz in $CDCl_3$ solution on a Bruker nmr spectrometer, using tetramethylsilane as an internal standard. Multiplicities are indicated by the usual symbols: d, doublet; m, multiplet; c, complex multiplet whose center is given; br, broadened singlet. Unmarked signals are singlets. Coupling constants are accurate to within <0.2 Hz unless specified otherwise. [b] Line positions and J's taken directly from primary spectrum. Decoupling was used to identify signals and J's, not to measure them. [c] Obtained when either H-2 or H-3 was decoupled. [d] $W_{1/2} = 2.7$ Hz, apparently due to long range coupling to H-15. $J_{6,7}$ measured on lines assigned to H-7 which were perturbed on irradiation of H-6. [e] Calculated line position based on coupling constants and observation of individual lines of H-7 during decoupling of H-10. [f] Taken directly from primary spectrum. Assignment of large coupling (6.0) to H-7 is based on INDOR spectrum of H-7 which could arise only from H-8. [g] Calculated line position based on coupling constants and on observation of lines of H-9 during decoupling involving protons coupled to H-7. [h] Measured on H-10 when H-14 was irradiated. H-10 then collapsed to an apparent triplet ($J_{9,10} \cong J_{1,10}$). [i] Three protons. [j] H-2′ of senecioyl side chain.

nmr spectrum of linearifolin B differed significantly in the 3.5–6.5-ppm region from that of linearifolin A. The



signals of the exocyclic methylene group were slightly broadened (by coupling to H-7) singlets, an observation which immediately excluded a structure similar to **1** with the lactone closed to C-6 or C-8.[12] This was also apparent from the ir spectrum which exhibited a strong asymmetrical band centered at 1715 cm^{-1} (superposition of cyclopentenone, ester, and probably one additional carbonyl group), but no absorption characteristic of the usual γ-lactone function. Neither of the two other signals in the 3.5–6.5-ppm region, at 4.73 (slightly broadened singlet) and 4.39 ppm (broad singlet or narrowly split multiplet), although clearly assignable to hydrogen on carbon carrying oxygen, was demonstrably and unambiguously spin coupled to the other, to H-7 or to H-10.[15] Attempts to oxidize linearifolin B in order to simplify the nmr spectrum and to identify the proton under the hydroxyl group resulted in recovery of a complex mixture; acetylation produced a mixture of at least two acetates (tlc analysis).[16]

A fortuitous discovery finally led to the structure elucidation of linearifolin B. An nmr tube containing a pyridine-d_5–$CDCl_3$ solution of linearifolin B was allowed to stand at room temperature for 5 weeks until the solvent had evaporated. Redetermination of the nmr spectrum of the residue indicated that a considerable portion of linearifolin B had been converted to linearifolin A; this was confirmed by isolation of linearifolin A from the reaction mixture. Since pyridine alone did not seem to effect conversion of linearifolin B to linearifolin A, we attribute the observed transformation to the catalytic influence of a weak acid, possibly pyridinium chloride formed on prolonged standing of the solution, on the potential equilibrium illustrated below.



(12) The magnitude of $J_{7,13}$ in guaianolides, pseudoguaianolides, germacranolides, and eudesmanolides depends on the stereochemistry of the lactone ring[3,10] and the nature of the carbon skeleton,[13,14] both factors influencing the dihedral angle between H-7 and H-13. For the purpose of the present discussion it is sufficient to state that a value of $J_{7,13} < 1$ is incompatible with the structure of a normally constituted pseudoguaianolide.

(13) Z. Samek, *Tetrahedron Lett.*, 671 (1970).

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

(15) The complexity of the H-7 and H-10 signals made it difficult to ascertain positively the effect, if any, produced on them by irradiating near 4.43 and 4.73 ppm. Conversely any effects on the signals at 2.4 and 3.15 ppm produced by irradiating near 4.43 and 4.73 ppm were at best questionable.

(16) That these compounds represented acetyllinearifolin A and acetyllinearifolin B became apparent subsequently.

The ir spectra of linearifolin A and linearifolin B and the shifts in the frequencies of H_b and H_c are consonant with this interpretation. H_a, the only one of the three protons H_a, H_b, and H_c not significantly affected by the conversion, must be associated with the ester side chain. Since it is spin coupled only to H-7 it must be identified as H-6. Expressions **1a** for linearifolin A and **3** for linearifolin B (exclusive of stereochemistry) then follow.

Formula **1a** differs from that previously[10] derived for fastigilin C (**1b**) only in the nature of the ester side chain at C-6. The similarity of chemical shifts and coupling constants between fastigilin C and compounds of the helenalin series has already been commented upon and led to the conclusion[10] that fastigilin C possesses the stereochemistry of helenalin (**4**),[17-19] at C-1, C-5, C-6, C-7, C-8, and C-10 although the stereochemistry at C-9 was left undefined. The isolation of fastigilin C from *Hymenoxys acaulis*, which is described in the Experimental Section, now permitted a detailed comparison of fastigilin C and linearifolin A. This led to the stereochemistry depicted in **1a**, **1b**, and **3**.

The data of Table I demonstrate the almost perfect coincidence of the nmr signals of linearifolin A and fastigilin C when the signals of the different ester side chains are disregarded. Hence it can be deduced that the stereochemistry of **1a** and **1b** is the same at all centers, including that at C-9.

The CD curves of linearifolin A, fastigilin C, and helenalin are listed in Table II, together with those of

TABLE II

CD CURVES OF SOME PSEUDOGUAIANOLIDES[a]

	Ketone —Cotton effect—		Lactone —Cotton effect—	
	λ_{max} (nm)	$[\theta]$	λ_{max}	$[\theta]$
Linearifolin A (**1a**)	322	−4640	264	−2070
Fastigilin C (**1b**)	322	−6080	264	−4030
Helenalin (**4**)	320	−7470		−4590[b]
Balduilin (**5**)	320	−7880	258	−3940
Aromaticin (**6**)	322	−4102	258	+1860
Linifolin A (**7**)	326	−4420	262	+803

[a] Determined on a Jasco ORD/UV-5 recording spectrometer in methanol solution. [b] Not a maximum. Ellepticity measured at 255 nm.

certain other pseudoguaianolides of established absolute configuration. The similarities in sign and magnitude of ketone Cotton effects indicate that **1a** and **1b** possess the same trans-fused pseudoguaianolide ring system (H-1 α, C-5 methyl β) as helenalin, balduilin, and their congeners. With H-1 α, the large value of $J_{1,10}$ evident from Table I which is characteristic of trans-diaxial coupling then requires that the C-10 methyl group of **1a** and **1b** be α, as in all other pseudoguaianolides from *Helenium*, *Gaillardia*, and *Hymenoxys* species. Construction of models, taking into account the coupling constants listed in Table I, then leads to the stereochemistry depicted in **1a**, **1b**, and **3**.

Additional evidence for the cis stereochemistry of the γ-lactone ring fusion in linearifolin A and fastigilin C is provided by the following. (1) On the basis of the generalization[3,13] that $J_{7,13\ trans} \geqslant 3$ Hz $\geqslant J_{7,13\ cis}$, Table I shows that linearifolin A and fastigilin C must be cis-fused γ-lactones.[20] (2) On the basis of the generalization[21] that cis-fused lactones closed toward C-8 exhibit negative and trans-fused lactones closed toward C-8 exhibit positive lactone Cotton effects, Table II shows that linearifolin A and fastigilin C have the C-8 stereochemistry of helenalin (**4**) and balduilin (**5**). The data of Table II for the trans-fused lactones aromaticin (**6**) and linifolin A (**7**) provide additional evidence for the applicability of the rule to pseudoguaianolides containing a cyclopentenone chromophore.

The β orientation of the C-9 hydroxyl group of **1a** and **1b**, originally deduced on the basis of the values of $J_{8,9}$ and $J_{9,10}$, is supported by the facile isomerization of linearifolin B to linearifolin A which requires that the oxygen substituents at C-8 and C-9 be cis. Since several lines of evidence converge to show that the C-8 oxygen bond is β, the hydroxyl group at C-9 must be β as well. In this orientation, a considerable degree of steric hindrance is suggested by the model, thus accounting for the resistance of **3** to oxidation.

Extraction of *Hymenoxys acaulis* gave, in addition to fastigilin C, 3,3′-dimethoxy-4′,5,7-trihydroxyflavone which has been previously found only in *Nicotiniana tabacum* calyx.[22,23] *Hymenoxys subintegra* Cockll. and *Hymenoxys rusbyi* (Gray) Cockll. also furnished previously known sesquiterpene lactones. The former yielded the modified pseudoguaianolide psilotropin (floribundin, **8**).[24] The latter afforded psilotropin, paucin (**9**)[3,26] and pectolinarigenin (5,7-dihydroxy-4′,6-dimethoxyflavone).

Experimental Section[27]

Isolation of Linearifolin A (1a), Linearifolin B (3) and Hymenoxin from ***Hymenoxys Linearifolia*****.**—Above ground material, wt 3.1 kg, collected by the late Dr. Ralph E. Alston in the vicinity of Austin, Texas, in April 1962 (voucher on deposit in herbarium of the University of Texas, at Austin) was extracted with chloroform and worked up in the usual manner.[28] The crude gum, wt 39.5 g, was taken up in 45 ml of benzene and chromatographed over 500 g of silicic acid, 300-ml fractions being collected. Fractions 1–4 (benzene and chloroform) gave only 0.5 g of gum. Fractions 5–7 (chloroform) contained 3.2 g of gum. Fractions 8–10 (chloroform) gave a gummy solid, 5.7 g, which was recrystallized from acetone to give colorless plates of linearifolin A: mp 187–188°; $[\alpha]^{25}D$ −90.0° (*c* 1.50, $CHCl_3$); uv (EtOH) λ_{max} 218 nm (ϵ 22,500); ir bands ($CHCl_3$) 3665, 3415 (hydroxyl), 1765, 1649 (α,β-unsaturated γ lactone), 1720, 1649, 1270 (ester), 1711, 1580 cm^{-1} (conjugated cyclopentenone).

Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71; O, 26.64. Found: C, 66.40; H, 6.50; O, 27.02.

(17) W. Herz, A. Romo de Vivar, J. Romo, and N. Viswanathan, *Tetrahedron*, **19**, 1359 (1963).
(18) M. T. Emerson, C. N. Caughlan, and W. Herz, *Tetrahedron Lett.*, 621 (1964).
(19) Mazhar-ul-Haque and C. N. Caughlan, *J. Chem. Soc. B*, 956 (1969).

(20) If the rule is generally valid, the $J_{7,13}$ values of **2** (Table I) also suggest that introduction of a carbonyl group at C-9 might have been accompanied by epimerization at C-8. This is certainly compatible with the other coupling constants (model); on the other hand, subtle differences exerted on the conformation of the γ-lactone ring by the new carbonyl group at C-9 might well be responsible for altering $J_{7,13}$'s in cis-fused lactones of this type and require modification of the rule.
(21) T. G. Waddell, W. Stöcklin, and T. A. Geissman, *Tetrahedron Lett.*, 1313 (1969).
(22) C. H. Yang, H. D. Braymer, E. L. Murphy, W. Chorney, N. Scully, and S. H. Wender, *J. Org. Chem.*, **23**, 2063 (1960).
(23) R. Watanabe and S. H. Wender, *Arch. Biochem. Biophys.*, **112**, 111 (1965).
(24) Isolation of this substance was reported almost simultaneously by two laboratories.[3,25] In order to avoid confusion we propose retention of the name suggested by Professor T. A. Geissman.
(25) L. B. de Silva and T. A. Geissman, *Phytochem.*, in press.
(26) T. G. Waddell and T. A. Geissman, *Tetrahedron Lett.*, 515 (1969). These workers propose attachment of the acetate group to C-2′ or C-4′ of the glucose unit.
(27) The experimental conditions specified in ref 3 apply.
(28) W. Herz and G. Högenauer, *J. Org. Chem.*, **27**, 905 (1962).

On concentrating fractions 5–10 to small volume, a sparingly soluble yellow crystalline substance separated and was filtered. Recrystallization from dioxane afforded hymenoxin, mp 215–216°, which was identical with authentic hymenoxin from *Hymenoxys scaposa*.[29] Hymenoxin diacetate melted at 167–168° after recrystallization from ethyl acetate.

Continued elution with chloroform and chloroform–methanol 99:1 (fractions 11–18) gave 1.35 g of gum. Fractions 19–24 (chloroform–methanol 99:1) gave 1.4 g of gummy material which on recrystallization from acetone afforded approximately 0.25 g of linearifolin B: mp 214–215°, $[\alpha]D$ −103.8° (*c* 0.80, $CHCl_3$); ir bands at 3580, 3400 (hydroxyl), 1715, 1625, 1229 (unsaturated ester), 1710, 1648 (α,β-unsaturated δ lactone), 1700, and 1580 cm^{-1} (α,β-unsaturated cyclopentenone); mol wt (mass spectrum), 360.1581 (calcd for $C_{20}H_{24}O_6$: 360.1573).

Continued elution with chloroform–methanol 97:3 (fraction 25–30) 19:1 (fractions 31–34) and methanol (fractions 35–40) gave 1.25, 2.5, and 15.6 g of gummy material.

Dehydrolinearifolin A (2).—A solution of 100 mg of linearifolin A in 1 ml of dry pyridine was allowed to stand overnight with 83 mg of CrO_3 in 1 ml of dry pyridine, diluted with water, and extracted with ethyl acetate. The washed and dried organic extract was evaporated at reduced pressure. The residual crystalline mass, wt 96 mg, was recrystallized from ether–ethyl acetate and had mp 245–247° dec: $[\alpha]^{25}D$ +46.7° (*c* 0.75, $CHCl_3$); ir bands at 1787, 1648 (α,β-unsaturated γ lactone), 1720, 1255 (ester), 1720, 1588 (α,β-unsaturated cyclopentenone), and 1710 cm^{-1} (cycloheptanone).

Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19; O, 26.79. Found: C, 67.69; H, 5.81; N, 26.31.

Isolation of Fastigilin C and 3,3′-Dimethoxy-4′,5,7-trihydroxyflavone from *Hymenoxys acaulis*.—Above ground parts of *Hymenoxys acaulis* (Pursh) K. F. Parker, wt 950 g, collected by Mr. R. J. Barr on May 16, 1963, along State Highway 64, 14 miles east of south entrance to Grand Canyon National Park, Coconino County, Ariz. (Barr no. 63-201 on deposit in Florida State University herbarium), was extracted in the usual manner to give 32.9 g of crude gum. This was taken up in 35 ml of benzene and chromatographed over 500 g of silicic acid, 300-ml fractions being eluted. Benzene (fractions 1–4) eluted nothing; fractions 5–15 (benzene–chloroform to chloroform) and fractions 16–19 (chloroform) eluted 10.5 and 4.1 g of gummy mixture. Fractions 20–23 (chloroform to chloroform–methanol 49:1) eluted 1.7 g of gummy solid. Recrystallization from acetone–ether afforded colorless needles, mp 198–200°, which were identified as fastigilin C by comparison with authentic material.

Successive elution with chloroform–methanol 49:1 and 19:1 (fractions 24–31) gave 3.5 g of gum. Fractions 32–34 (chloroform–methanol 19:1) gave 0.6 g of yellow gum. Recrystallization from acetone afforded pale yellow needles of 3,3′-dimethoxy-4′,5,7-trihydroxyflavone: mp 257–260° (lit. mp 254–256°,[30] 258–259°[31]); nmr signals (DMSO-d_6) at 3.83, 3.88 (2 methoxy singlets), 6.20 d (J = 2 Hz, H-8), 6.95 d, br (J = 9 Hz, H-5′), 7.60 (J = 8 Hz, H-6′), and 7.65 br (J = 2 Hz, H-1′); uv λ_{max} 255, 269, and 357.5 nm (ϵ 18,480, 17,380, 17,600); with fused sodium acetate λ_{max} 266, 321, and 375 nm (ϵ 18,040, 10,560, 12,980); with 0.05 M aluminum chloride λ_{max} 267.5, 276, 301, 366, and 408 nm (17,380, 16,500, 7700, 13,640, 15,620); with 0.5 M sodium ethoxide λ_{max} 272.5, 322.5, 414 nm (ϵ 17,600, 9020, 24,860). The triacetate was recrystallized from ethyl acetate and melted at 197–199° (lit.[29] mp 195°): nmr signals at 2.33 (4′- and 7-acetates), 2.47 (5-acetate), 3.81, 3.89 (two methoxyls), 6.86 d (J = 2 Hz, H-6), 7.10 d, br (J = 8 Hz, H-5′), 7.29 d (J = 2 Hz, H-8), 7.70 d, br (J = 8 Hz, H-6′), and 7.71 br (H-2′). Further elution with chloroform–methanol gave 14.3 g of noncrystallizable gum.

Isolation of Psilotropin (8) from *Hymenoxys subintegar*.—Above ground parts of *Hymenoxys subintegra* Cockll., wt 1.8 kg, collected by Mr. R. J. Barr on July 31, 1968, 1 mile west of Deer Lake, Kaibab Plateau near North Rim of Grand Canyon, Coconino County, Ariz. (Barr no. 68-419 on deposit in herbarium of Florida State University), was extracted with chloroform and worked up in the usual fashion. The crude gum, wt 31 g, was taken up in 30 ml of chloroform and chromatographed over 220 g of silicic acid, 300-ml fractions being collected. Fractions 1–5 (benzene–chloroform 1:1 and 1:3) gave 5.6 g of crude psilotropin. Recrystallization from acetone afforded crystals melting at 143–144°. Further elution with benzene–chloroform 1:3 (fractions 12–20) gave 10.6 g of gum; chloroform (fractions 25–29), 19:1 (fractions 30–32), and 93:7 (fractions 33–41) eluted 1.5, 3.8, 3.9, and 5.1 g of gum, respectively.

Isolation of Psilotropin (8), Paucin (9) and Pectolinarigenin from *Hymenoxys rusbyi*.—Above ground parts of *Hymenoxys rusbyi* (Gray) Cockll., wt 22.5 kg, collected by Mr. R. J. Barr on July 5, 1968, 26 miles north of Globe, Gila County, Ariz., at 6100 ft (Barr no. 68-597 on deposit in herbarium of Florida State University), was extracted with chloroform and worked up in the usual fashion. A 150 g portion of the crude gummy lactone fraction (total wt 350 g) was taken up in 150 ml of benzene and chromatographed over 1 kg of silicic acid, 800-ml fractions being collected. Fractions 1–8 (benzene and benzene–chloroform 1:1) gave only oily material (4.2 g). Fractions 9–34 (benzene–chloroform 1:1 to chloroform–methanol 19:1) gave 32 g of gummy semisolid. Recrystallization from acetone afforded colorless needles, mp 143°, which were identified as psilotropin by direct comparison with material isolated previously.

Fractions 40–43 also contained a crystalline yellow compound sparingly soluble in $CHCl_3$ which crystallized on concentrating the fractions. It was filtered and recrystallized from dioxane. The material melted at 217–219° and was identified as pectolinarigenin by direct comparison with a sample of pectolinarigenin isolated previously[32] from *Iva nevadensis* M. E. Jones. The acetate was identical with diacetylpectolinarigenin.

Continued elution with chloroform–methanol 19:1 gave, in fractions 44–45, 64 g of gummy material and, in fractions 46–49, 2.5 g of crystalline solid. After recrystallization from acetone the colorless needles melted at 177–179° and were identified as paucin by comparison with authentic material isolated previously. Continued elution with chloroform–methanol gave 39 g of gum.

Isomerization of Linearifolin B.—An nmr tube containing a $CDCl_3$ (0.5 ml) solution of linearifolin B (30 mg) was allowed to stand at room temperature for 5 weeks. After the solvent had evaporated, the recovered crystals were diluted with pyridine-d_5 (0.5 ml) and the nmr spectrum was run. The spectrum indicated the material to be a mixture of two compounds; this conclusion was further confirmed by a tlc experiment (*ca.* linearifolin A:B, 3:1). The pyridine-d_5 solution was diluted with water and extracted with ethyl acetate. After washing and drying, the organic layer was evaporated at reduced pressure to give a crystalline mixture which was recrystallized from acetone to give linearifolin A (15 mg) as a colorless needles, mp 187–188°, which was identical in all respects with linearifolin A.

Acetylation of Linearifolin B.—Linearifolin B (15 mg) in pyridine (0.4 ml) was treated with acetic anhydride at room temperature overnight. The reaction mixture was diluted with water and extracted with ethyl acetate. After washing and drying, the ethyl acetate layer was evaporated at reduced pressure to give a gum (16 mg), which was a mixture of linearifolin A and B acetates (*ca.* 1:1) by tlc.

Registry No.—**1a**, 26305-86-2; **1b**, 6995-12-6; **2**, 26358-39-4; **3**, 26358-40-7; **4**, 6754-13-8; **5**, 6895-47-2; **6**, 5945-42-6; **7**, 5988-99-8; **8**, 26305-91-9; 3,3′-dimethoxy-4′,5,7-trihydroxyflavone, 4382-17-6; 3,3′-dimethoxy-4′,5,7-trihydroxyflavone triacetate, 26305-93-1.

(29) We wish to thank Professor T. J. Mabry for an authentic sample.

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