for 1 h. The solids were removed by filtration and the filtrate was evaporated; the residue was partitioned between benzene and water. Scrubbing of the organic phase with water, drying, and solvent removal left crude product which was triturated with methyl alcohol. This material, 12.4 g (93%), had mp 101 °C. A sample was recrystallized from methyl alcohol: mp 101–102 °C; NMR ($CDCl_3$) δ 2.40 (s, 3, $TosCH_3$), 2.40–3.46 (m, 4, CH_2CH_2), 4.51 (dd, 1, CHTos), 6.75–7.52 (m, 7, Ar H).

Anal. Calcd for $C_{14}H_{15}IO_2S_2$: C, 41.38; H, 3.72. Found: C, 41.60; H, 3.75.

1-(2-Thienyl)-1-(*p*-toluenesulfonyl)prop-3-ylphosphonium Iodide (10d). A solution of 4.06 g (0.01 mol) of **10c**, 2.6 g (0.01 mol) of triphenylphosphine, and 10 mL of toluene was refluxed for 2 h. The mixture was cooled, and the toluene was then decanted from the produced oily layer; this was rubbed with ether to give 4.7 g (70%) of solid product, mp 202–204 °C, which was recrystallized from ethyl alcohol–acetone–ether: mp 204–205 °C; NMR ($CDCl_3$) δ 2.08–3.50 (m, 4, CH_2CH_2), 2.34 (s, 3, $TosCH_3$), 5.78 (dd, 1, CHTos), 6.65–8.02 (m, 22, Ar H).

Anal. Calcd for $C_{32}H_{30}IO_2PS_2$: C, 57.49; H, 4.52. Found: C, 57.38; H, 4.70.

3-Thienyl(*p*-toluenesulfonyl)methane (11a). In analogy to **9a**, **11a** was obtained in 78% yield. Analytical material, obtained from isopropyl alcohol, had mp 102–103 °C: NMR ($CDCl_3$) δ 2.37 (s, 3, $TosCH_3$), 4.30 (s, 2, CH_2Tos), 6.77–7.63 (2 AB, 7, Ar H).

Anal. Calcd for $C_{12}H_{12}O_2S_2$: C, 57.11; H, 4.79. Found: C, 57.26; H, 4.80.

1-(3-Thienyl)-1-(*p*-toluenesulfonyl)-4-methylpent-3-ene (11b). Analogous to **1a**, **11b** was obtained in 77% yield. Analytical material was obtained from diisopropyl ether: mp 99–100 °C; NMR ($CDCl_3$) δ 1.53 (s, 6, $(CH_3)_2$), 2.33 (s, 3, $TosCH_3$), 2.47–3.30 (m, 2, $TosCCH_2$), 4.00–4.20 (m, 1, C=CH), 4.80 (t, 1, TosCH), 6.67–7.53 (2 AB, 7, Ar H).

Anal. Calcd for $C_{17}H_{20}O_2S_2$: C, 63.71; H, 6.29. Found: C, 63.74; H, 6.43.

4,4-Dimethyl-7-(*p*-toluenesulfonyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene (12a). Analogous to **2a**, **12a** was obtained in 92% yield. Analytical material, obtained from diisopropyl ether had mp 107–108 °C: NMR ($CDCl_3$) δ 0.83–1.64 (m, 2, CH_2CCTos), 1.00 and 1.21 (2 s, 6, $(CH_3)_2$), 1.92–2.51 (m, 2, CH_2CTos), 2.38 (s, 3, $TosCH_3$), 4.25 (t, 1, CHTos), 7.02 (s, 2, ThH), 6.96–7.62 (AB, 4, Tos H).

Anal. Calcd for $C_{17}H_{20}O_2S_2$: C, 63.71; H, 6.29. Found: C, 63.55; H, 6.35.

7,7-Dimethyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (12b). Analogous to **3a**, 3 equiv of Dibal-H was used to obtain **12b**. The reaction mixture was stirred for 45 min: yield 72%; NMR ($CDCl_3$) δ 1.30 (s, 6, $(CH_3)_2$), 1.46–2.06 (m, 4, CH_2CH_2), 2.40–2.72 (m, 2, $ThCH_2$), 6.76 (AB, 2, ThH).

Acknowledgment. We thank undergraduate students René A. J. Janssen and Marijn E. J. Dekkers for their enthusiastic collaboration in parts of this project.

Registry No. **1a**, 73838-08-1; **1b**, 73838-09-2; **1c**, 73838-10-5; **1d**, 73838-11-6; **2a**, 73838-12-7; **2b**, 73838-13-8; **2c**, 73838-14-9; **2d**, 73838-15-0; **3a**, 62469-66-3; **3b**, 73838-16-1; **3c**, 73855-13-7; **3d**, 73838-17-2; **7c**, 71370-89-3; **8**, 73838-18-3; **9a**, 20895-79-8; **9c**, 73838-19-4; **9d**, 73838-20-7; **10a**, 73838-21-8; **10b**, 73838-22-9; **10c**, 73838-23-0; **10d**, 73838-24-1; **11a**, 73838-25-2; **11b**, 73838-26-3; **12a**, 73838-27-4; **12b**, 62429-58-7; prenyl bromide, 870-63-3; isopropyltriphenylphosphonium iodide, 1530-33-2; 2-(chloromethyl)thiophene, 765-50-4; ethylene oxide, 75-21-8; triphenylphosphine, 603-35-0.

Supplementary Material Available: NMR data for compounds in Tables I and II and elemental analyses for C and H (2 pages). Ordering information is given on any current masthead page.

Glycosidic Disecoeudesmanolides and Other Secosesquiterpene Lactones from *Picradeniopsis* Species. X-ray Analysis of Bahia I[1]

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Received March 26, 1980

The unusual disecoeudesmanolide glycosides **3a** and **5a** were isolated from an Arizona collection of *Picradeniopsis woodhousei* (Gray) Rydb. in addition to the heliangolide woodhousin (**8a**) and the flavone jaceidin. *P. woodhousei* from New Mexico gave the secoeudesmanolide precursor **7a** of **3a** and **5a**, the woodhousin analogue **8c**, the guaianolide **9**, and the secoheliangolide **11a**. The structures were determined by chemical transformations and spectroscopic means. Eucannabinolide (**13**) and bahia II (**14b**) were isolated from *Picradeniopsis oppositifolia* (Nutt.) Rydb. The stereochemistries of **14b** and its congeners bahia I and bahifolin were settled by X-ray analysis of bahia I (**14a**).

Ivangulin (**1b**),[2,3] eriolangin (**2a**),[4] and eriolanin (**2b**)[4] are the only secoeudesmanolides so far found in nature.[5] We now report isolation and structure determination of the first known disecoeudesmanolides in the form of the glycosides **3a** and **5a** as well as discovery of their putative secoeudesmanolide precursor **7a** and the first secoheliangolide **11a**. The diseco compounds were found on reexamination of *Picradeniopsis woodhousei* (Gray) Rydb. [*Bahia woodhousei* (Gray) Gray] from Arizona[6,8] together with 5,7,4′-trihydroxy-3,6,3′-trimethoxyflavone (jaceidin) and the previously reported heliangolide woodhousin

(1) Supported in part by a grant from the U.S. Public Health Service (CA-13121) through the National Cancer Institute.

(2) Herz, W.; Sumi, Y.; Sudarsanam, V.; Raulais, D. *J. Org. Chem.* **1967**, *32*, 3658.

(3) The stereochemistry of ivangulin at C-4 was settled by total synthesis: Grieco, P. A.; Oguri, T.; Wang, C.-L.; Williams, E. *J. Org. Chem.* **1977**, *42*, 4113.

(4) Kupchan, S. M.; Baxter, R. L.; Chiang, C. K.; Gilmore, C. J.; Bryan, R. F. *J. Chem. Soc., Chem. Commun.* **1973**, 842. Bryan, R. F.; Gilmore, C. J. *Acta Crystallogr., Sect. B* **1975**, *B31*, 2213.

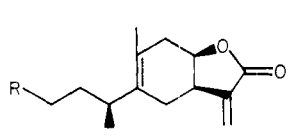
(5) Eriolangin and eriolanin were active against P-388 lymphocytic leukemia in the mouse.[4] Ivangulin exhibited no activity against L-1210 lymphocytic leukemia in the mouse in tests carried out under the auspices of the National Cancer Institute.

(6) Our plant material came from the location of our earlier collection[7] of *P. woodhousei*. It was labeled *Bahia neomexicana* but was identified as *P. woodhousei* by Professor L. C. Anderson.

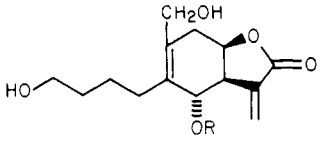
(7) Herz, W.; Bhat, S. V. *J. Org. Chem.* **1972**, *37*, 1906.

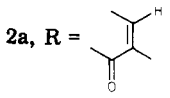
(8) The ditypic genus *Picradeniopsis* was relegated to the allied genus *Bahia* by Ellison[9] but has since been resegregated in work that came to our attention after publication of ref 7.[10]

0022-3263/80/1945-3163$01.00/0



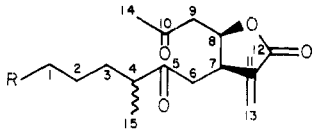
1a, R = CO_2H
b, R = CO_2Me
c, R = CH_2OH

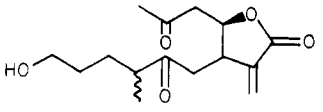




2a, R =

b, R =





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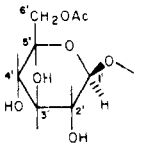
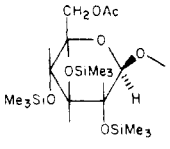


3a, R =



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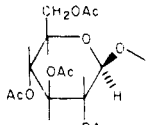
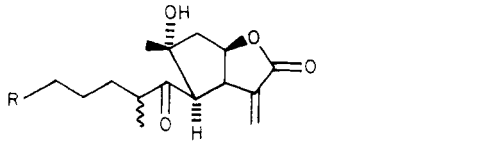
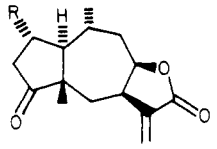


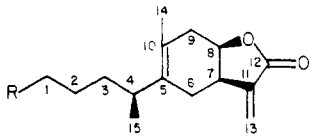
c, R =



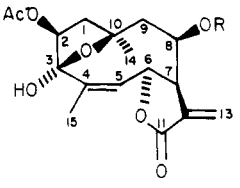
5a, R as in 3a
b, R as in 3c

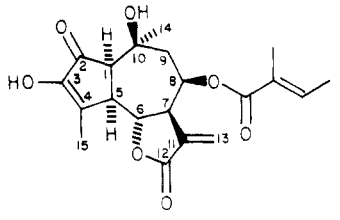


6, R as in 3a



7a, R as in 3a
b, R as in 3c





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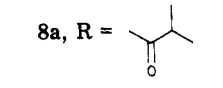
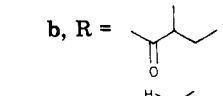
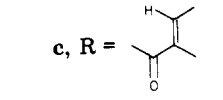


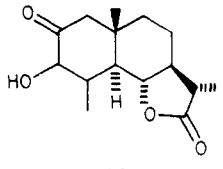
8a, R =



b, R =



c, R =



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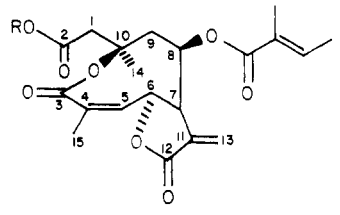


11a, R = H
b, R = Me

(8a),[7,11] while the secolactones **7a** and **11a** were isolated from a Texas collection of *P. woodhousei* together with a woodhousin analogue, **8c**, and a diosphenolic guaianolide, **9**.

We commence with the isomeric noncrystalline lactones **3a** and **5a**, $C_{23}H_{34}O_{11}$ (mass spectra), which were isolated from *P. woodhousei* gathered at the site of our earlier[7] collection in Arizona. Both compounds were α-methylene γ-lactones as evidenced by narrowly split doublets near 6.2 and 5.6 ppm (H-13 of the ^1H NMR spectra in Table I) and an IR band near 1760 cm^{-1}. The ^1H NMR spectrum of **3a** further contained two three-proton singlets at 2.11 and 2.21 ppm, a methyl doublet at 1.11 ppm, and a complex pattern of multiplets in the range 3.2–3.6 ppm whose resolution was not significantly improved by conversion to a trimethylsilyl ether **3b**.

The ^{13}C NMR spectrum of **3a** (Table III) demonstrated the presence of two keto groups (singlets near 212 and 205 ppm), the α-methylene γ-lactone group (singlets at 171.13 and 138.3 ppm, triplet at 122.9 ppm), and another ester group (singlet at 169.8 ppm), presumably an acetate which is also responsible for one of the two methyl singlets in the ^1H NMR spectrum. If this were so, the other methyl had to be that of a methyl ketone. Since the lactone, ketone, and ester groups together accounted for only six of the 11 oxygen atoms of the empirical formula and since the ^{13}C NMR spectrum contained seven signals in the 60–80-ppm region, it was deduced that **3a** was a glycoside, especially since the ^1H NMR spectrum exhibited a sharp doublet at 4.26 ppm (J = 8 Hz) and the ^{13}C NMR spectrum a doublet at 102.6 ppm characteristic of an anomeric proton and carbon, respectively. Formation of a tri- rather than a tetraacetate suggested that the suspected acetate resided on the sugar residue.

Detailed analysis of the ^1H NMR spectrum of the triacetate **3c** with and without $Eu(fod)_3$ where all signals were resolved satisfactorily revealed the nature of both the sugar and the aglycon moieties. Identification of the signal of the anomeric proton as a doublet at 4.48 ppm provided a basis for decoupling experiments which located H-2′, H-3′, H-4′, H-5′ and H-6′. H-5′ was at 3.69 ppm, and the AB pattern of H-6′ was seen at 4.27 and 4.13 ppm. Since on going from **3a** to **3c** H-2′, H-3′, and H-4′ but not H-6′ experienced significant paramagnetic shifts, it was obvious that the lone acetate function of **3a** was located on C-6′. Acid hydrolysis of **3a** gave glucose as in the case of the helenanolide paucin (**6**) which contains the same 6-acetylglucose fragment.[12-14] Enzymatic hydrolysis with β-glucosidase provided experimental proof for the presence of a β-glycosidic linkage already deduced from the large value of $J_{1'2'}$ and resulted in isolation of an aglycon, **4**, albeit in relatively poor yield. The ^{13}C NMR signals of

(9) Ellison, W. L. *Rhodora* **1964**, *67*, 67, 177, 281.
(10) (a) Ellison, W. L. *Southwest. Naturalist* **1966**, *11*, 456. (b) Stuessy, T. F.; Irving, R. S.; Ellison, W. L. *Brittonia* **1973**, *25*, 40.
(11) Herz, W.; Blount, J. F. *J. Org. Chem.* **1978**, *43*, 4887.
(12) Waddell, T. G.; Geissman, T. A. *Phytochemistry* **1969**, *8*, 2371; *Tetrahedron Lett.* **1969**, 515.
(13) Herz, W.; Aota, K.; Holub, M.; Samek, Z. *J. Org. Chem.* **1970**, *35*, 2611. Herz, W.; Aota, K.; Hall, A. L. *Ibid.* **1970**, *35*, 4117.
(14) Cox, P. J.; Sim, G. A. *J. Chem. Soc., Perkin Trans. 2* **1977**, 259.

Table I. ^{1}H NMR Spectra of Glycosides and Derivatives[a]

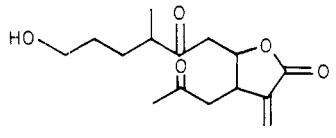
	3a	3c	3c[b]	4	5a	5b	7a	7b	1a	1b	1c
H-1a	3.84 dt (10, 6)	3.85 dt (10, 6)	4.00 m	3.62 br t[c] (6)	3.87 m	3.83 m	3.82 m	3.67 dt (9, 6)			3.42 m
H-1b	3.2-3.7[c]	3.47 dt (10, 6)	3.61 dt (10, 6)	3.62 br td[c] (6)	3.3-3.6[c]	3.47 dt (10, 6)	3.2-3.6[c]	3.44 dt (9, 6)			
H-2[d]	1.56 qu (7)	1.54 m	1.70 qu (7)	1.52[e]	*f*	*f*	1.27	1.30 qu (7)	2.12 m	2.09 br t (7)	
H-3a	1.76 m	1.72 m	1.96 m	1.74	1.88 m	*f*	1.47 m	1.64 m	1.61 m	1.5[c]	1-1.4
H-3b	1.42 m	1.36 m	1.58 m	1.52[e]	1.61 m	*f*	1.02 m	1.08 m	1.47 m	1.5[c]	1-1.4
H-4	2.59 m[c]	2.54 sx (7)	2.79 sx (7)	2.56 sx (7)	2.58 m	2.52 m	2.67 m	2.64 m	2.72 m	2.70 m	2.65 m
H-6	2.94[g]	2.89[g]	3.26[g]	2.89[g]	3.07 d (10)	2.96 d (10)	*f*	*f*	2.20 br dd (15, 6)	2.21 br dd (15, 7)	2.17 br dd (15, 7)
									2.06 dd (15, 4)	2.03 dd (15, 4.5)	2.06 dd (15, 4.5)
H-7	3.20 m	3.21 m	3.77 m	3.21 m	3.87 m	3.83 m	3.2-3.6[c]	3.22 m	3.21 m	3.20 m	3.26
H-8	4.55 dt (4.5, 6)	4.52 dt (5, 6)	5.19 dt (5, 6)	4.52 dt (5, 6)	5.09 dt (7, 5)	5.06 dt (7, 5)	4.94 dt (8.5, 4.5)	4.88 dt (8.5, 4.5)	4.87 dt (8.5, 4.5)	4.84 dt (8.5, 4.5)	4.92 dt (8, 4)
H-9	2.96[h]	2.95	3.38	2.94	2.49 dd (14.5, 7)	2.52 dd (15, 8)	2.46 dd (16, 8.5)	2.38 dd (16, 8.5)	2.37 m[d]	2.36 m[d]	2.42 dd (15, 4)
					1.88 dd (14.5, 5)	*f*	2.27 dd (16, 4.5)	2.30 dd (16, 4.5)			2.28 br dd (15, 4)
H-13a	6.26 d (2.8)	6.28 d (2.8)	6.73 d (2)	6.27 d (2.8)	6.30 d (2)	6.31 d (2)	6.27 d (2.8)	6.24 d (2.8)	6.27 d (3)	6.26 d (3)	6.25 d (2.8)
H-13b	5.64 d (2)	5.64 d (2.5)	5.86 d (1.8)	5.61 d (2.5)	5.58 d (1.8)	5.55 d (1.8)	5.66 d (2)	5.64 d (2)	5.65 d (2.5)	5.64 d (2.5)	5.67 d (2.5)
H-14[c]	2.21	2.19	2.19	2.18	1.37	1.36	1.73 br	1.73 br	1.73 br	1.71 br	1.72 br
H-15[c]	1.11 d (6.5)	1.09 d (7)	1.24 d (7)	1.11 d (7)	1.12 d (7)	1.11 d (7)	0.93 d (7)	0.93 d (7)	0.98 d (7)	0.97 d (7)	0.94 d (7)
H-1′	4.62 d (7.5)	4.48 d (8)	4.71 d (8)		4.26 d (8)	4.47 d (8)	4.26 d (8)	4.50 d (8)			
H-2′	3.2-3.7[c]	4.96 dd (9.5, 8)	5.63[e]		3.3-3.6[c]	4.96 dd (9.5, 8)	3.2-3.6[c]	4.96 dd (9.5, 8)			
H-3′	3.2-3.7[c]	5.20 t (9.5)	5.63[e]		3.3-3.6[c]	5.20 t (9.5)	3.2-3.6[c]	5.22 t (9.5)			
H-4′	3.2-3.7[c]	5.07 t (9.5)	5.41 t (8.5)		3.3-3.5[c]	5.06 t (9.5)	3.2-3.5[c]	5.08 t (9.5)			
H-5′	3.2-3.7[c]	3.69 ddd (9.5, 4.5, 2.5)	4.00 m		3.3-3.6[c]	3.69 ddd (9.5, 4.5, 2.5)	3.2-3.6[c]	3.77 ddd (9.5, 4.5, 2.5)			
H-6′	4.32 m[d]	4.27 dd (12, 4.5)	4.91 dd (12, 4)		4.33 m[d]	4.27 dd (12, 4.5)	4.36 m[d]	4.27 dd (12, 4.5)			
		4.13 dd (12, 2.5)	4.75 dd (12, 2.8)			4.12 dd (12, 2.5)		4.14 dd (12, 2.5)			
misc[i]	2.11 (Ac)	2.22, 2.08, 2.03, 2.00 (Ac)	2.51, 2.48, 2.20, 2.19 (Ac)		2.10 (Ac)	2.11, 2.07, 2.03, 2.01 2.00 (Ac)		2.10, 2.06, 2.04, 2.02 (Ac)		3.64 (OMe)	

[a] Run at 270 MHz in $CDCl_3$ with Me_4Si as internal standard. Symbols are as follows: d, doublet; t, triplet; q, quartet; qu, quintet; sx, sextet. Unmarked signals are singlets. Figures in parentheses are coupling constants in hertz. [b] With 0.2 mequiv of $Eu(fod)_3$. [c] Sharpens on adding D_2O. [d] Two protons. [e] Center of AB system. [f] Signal obscured. [g] Center of AB system; $J_{6a,6b} = 18$, $J_{6,7} = 6$ Hz. [h] Center of AB system; $J_{8,9} = 6$ Hz, $J_{9a,9b} = 18$ Hz. [i] Intensity three protons.

C(1′)–C(6′) of **3a** parallel (Table III) those of the sugar part of paucin (**6**) whose structure has been established by X-ray crystallography,[14] and the shift changes accompanying the conversion of **3a** to **3c** are in accordance with expectations.

As for the aglycon part of **3c**, location of H-7 as a multiplet at 3.21 ppm by irradiation at the frequencies of H-13 permitted identification of H-8 by irradiation at the frequency of H-7 and thence recognition of the AB pattern of H-9a,b centered at 2.95 ppm, as well as identification of H-6a,b as an AB system centered at 2.89 ppm. The two AB systems whose chemical shifts and multiplicities indicated that they were α to the two ketone carbonyls were most clearly seen and identified by decoupling in the presence of 0.2 mequiv of $Eu(fod)_3$.

Irradiation at the frequency of the methyl doublet (1.09 ppm) located the H-4 signal at 2.54 ppm and thence, by further decoupling, the multiplets of H-3a,b at 1.72 and 1.36 ppm. These were also coupled to a two-proton quintet at 1.54 (H-2) which in turn was coupled to the two mutually coupled triplets of H-1a,b at 3.85 and 3.47 ppm. Thus the gross structure of the aglycon was either **4** or the biogenetically implausible formula A.



A

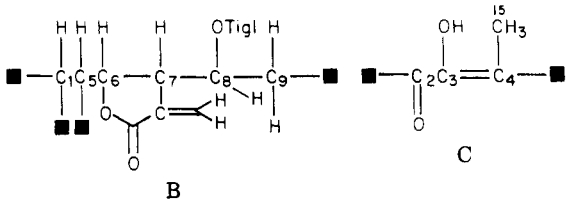
That **4** was correct was shown by our study of the isomeric lactone **5a** which had the same β-D-6′-acetylglucose residue as **3a** (^1H and ^{13}C NMR spectra in Tables I and III, formation of a triacetate, and mass spectral fragmentation). However, in the ^{13}C NMR spectrum of **5a**, the carbonyl singlet of **3a** at 205.63 ppm was replaced by a singlet at 82.20 ppm, whereas in the ^1H NMR spectrum the methyl ketone singlet formerly at 2.21 ppm had moved upfield to 1.37 ppm. The only other change was revealed by decoupling which now showed H-6 as a *one proton doublet*. These features can only be accommodated by formula **5a**, the result of an intramolecular aldol condensation involving C-6 and C-10 of **3a**. Whether **5a** is a true natural product or an artifact formed during the isolation procedure cannot be stated at present.

We defer consideration of the stereochemistries of **3a** and **5a** until we have discussed a third glycosidic lactone, $C_{23}H_{34}O_9$, which was isolated from *P. woodhousei* collected at a site in northwest Texas. The mass spectral fragmentation and detailed analysis of the ^1H and ^{13}C NMR spectra of this substance, **7a**, and its triacetate **7b** (Tables I and III) revealed its general similarity to **3a**, particularly the presence of the β-D-6-acetylglucose moiety, except that the ketone carbonyl singlets in the ^{13}C NMR spectrum were replaced by two singlets in the vinylic carbon region, that the methyl ketone singlet in the ^1H NMR spectrum was replaced by a vinyl methyl singlet at 1.73 ppm, and that the H-6 and H-9 signals had moved upfield. These changes were accommodated most conveniently by the secoeudesmanolide formula **7a** which can be viewed as a biological precursor of **3a** and **5a**.

The proposed structure was established unambiguously by hydrolysis of **7a** to **1c**, oxidation of the latter with pyridinium dichromate[15] to **1a**, and subsequent methylation to **1b** which was identical with ivangulin of established configuration.[2,3,16] This settled the stereochemistry of **7a** at C-4, C-7, and C-8 and, by implication, that of **3a** and **5a** at C-7 and C-8, especially since the coupling constants involving H-7, H-8, and H-8 were quite similar and since a γ-lactone fused trans onto the five-membered ring of **5a** would be impossibly strained. In **5a** the large value of $J_{6,7}$ (10 Hz) indicates that H-6 and H-7 are cis rather than trans; moreover, the paramagnetic shifts of H-7 and H-8 strongly suggest deshielding by, and therefore α orientation of, the hydroxyl group on C-10 (model). However, because C-4 of **3a** and **5a** is an easily epimerizable site, the configuration at **3a** and **5a** at this center is not necessarily that of ivangulin and **7a**. The absolute configurations are as represented in the formulas because the Cotton effects arising from the n,π^* transition of the α,β-unsaturated lactone are all negative as is that of ivangulin;[17] in the CD curves of **3a** and **5a** the minima are displaced to somewhat shorter wavelengths than usual and are weakened as a result of Cotton effects of opposite sign near 290 nm arising from the ketones.

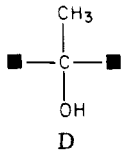
Woodhousin (**8a**) from the Arizona collection of *P. woodhousei* was accompanied by a small amount of the previously unreported **8b** whereas the Texas collection furnished **8c**, whose structure was evident from the ^1H and ^{13}C NMR spectra and the decoupling experiments carried out in $CDCl_3$ and C_6D_6 solution (Tables II and IV). Other lactones from the Texas collection were the diosphenol **9** and the unusual secoheliangolide **11a**, both tiglates like **8c**.

In the case of lactone **9**, after irradiation at the frequencies of H-13 (Table II) had established the location of the H-7 signal at 3.16 ppm, spin decoupling in the usual way permitted deduction of the sequence shown in partial formula B (numbering as in final formula), lactone closure



B

C



D

toward C-6 being assumed because of the relative chemical shifts of H-6 and H-8. Ultraviolet and NMR spectroscopy (Tables II and IV) also indicated the presence of the diosphenolic structural feature C (λ_{max} 265 nm, which shifts to 305 nm on addition of alkali; carbon singlets at 203.48, 169.56, and 164.22 ppm and a vinyl methyl singlet at 2.28 ppm). The remaining two carbon atoms of the molecular formula were represented by D (^1H and ^{13}C NMR spectra).

Combination of B, C, and D was made possible by the paramagnetic shift of H-1 which indicated that it was adjacent to a carbonyl group, i.e., C-2, and by the observation that H-5 was long-range coupled to H-15 (J = 1 Hz), akin to the situation prevailing in the diosphenol **10**.[18]

(15) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

(16) Since ivangulin was no longer available, the comparison was carried out by comparing NMR and IR traces.

(17) Stöcklin, W.; Waddell, T. G.; Geissman, T. A. *Tetrahedron* **1970**, *26*, 2397. The empirical rule formulated by these authors is applicable to eudesmanolides, whose lactone ring is cis fused and closed toward C-8, and hence presumably to ivangulin and its relatives. It is interesting that, as judged by coupling constants, the conformations of **3a** and **5a** do not depart significantly from the conformation of **7a**.

(18) Bhedi, D. N.; Shaligram, A. M.; Rao, A. S. *Indian J. Chem., Sect. B* **1976**, *14B*, 658.

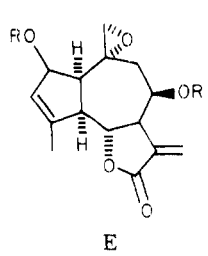
Table II. ^{1}H NMR Spectra of Other Lactones[a]

	8c	8c[b]	9	11a	11a[b]	11b
H-1	2.45 dd (14, 5.5), 2.13 br d (14)	2.16 dd (14, 5.5), *d*	2.93 d (7)	2.96[c]	2.66[c]	2.91[c]
H-2	5.39 br d (5.5)	5.44 br d (5.5)				
H-5	5.75 dq (3.5, 1.5)	5.68 dq (3.5, 1.5)	3.22 br dd (11, 7)	6.38 dq (3, 1.5)	5.92 dq (3, 1.5)	6.37 dq (3, 1.5)
H-6	5.64 ddq (3.5, 3, 1)	5.80 tq (3, 1)	4.71 dd (11, 10)	5.72 tq (3, 1)	5.58 m	5.71 m
H-7	4.06 br ddd (3, 2.5, 2.2, 2)	4.08 m	3.15 dddd (10, 3.5, 3, 2)	3.18 dddd (3, 3, 2.5, 2)	2.79 m	3.16 m
H-8	5.57 br dd (10, 5)	5.68 br dd (10, 5)	5.78 ddd (4, 3, 2)	5.42 ddd (8, 6, 3)	5.32 ddd (8, 6, 3)	5.41 ddd (8, 6, 3)
H-9	2.44 dd (15, 10), 2.04 dd (15, 5)	2.40 dd (15, 10), 1.91 dd (15.5)	2.33 dd (15, 4), 2.09 dd (15.3)	2.50 dd (15, 6), 2.38 dd (15, 8)	2.27[c]	2.41[c]
H-13	6.25 d (2.5), 5.61 d (2.2)	6.27 d (2.5), 5.31 d (2.2)	6.33 d (3.5), 5.64 d (3)	6.32 d (2.5), 5.68 d (2)	6.20 d (2.5), 5.06 d (2)	6.32 d (2.5), 5.67 d (2)
H-14[e]	1.53	1.73	1.22	1.83	1.74	1.80
H-15[e]	1.81 t (1.5)	1.82 t (1.5)	2.28 br (1)	1.90 t (1.5)	1.61 t (1.5)	1.89 t (1.5)
H-3'	6.71 dq (7, 1.5)	6.89 dq	6.74 dq (7, 1.5)	6.76 dq (7, 1.5)	6.89 dq	6.77 dq (7, 1.5)
H-4'[e]	1.79 br d (7)	1.35 br d	1.80 br d (7)	1.76 br d (7)	1.36 br d	1.76 br d (7)
H-5'[e]	1.76 br	1.28 br	1.79 br	1.74 br	1.37 br	1.79 br[f]

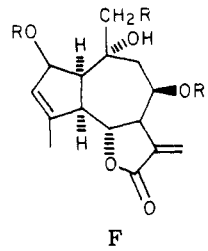
[a] Run at 270 MHz in $CDCl_3$ unless specified otherwise. Unmarked signals are singlets. [b] Run in C_6D_6. [c] Center of AB system, J_{AB} = 15 Hz. [d] Obscured signal. [e] Three proton intensity. [f] Also contains OMe signal.

Consequently, partial structure D had to be inserted between C-1 and C-9, thus giving rise to the guaianolide skeleton of **9**.

The coupling constants involving H-1, H-5, H-6, H-7, and H-8 require the relative stereochemistry depicted in the formula which at H-1 and H-5 is that demanded by the usual anti-Markovnikov-orientated cyclization of a chair-folded germacradiene precursor.[19] However, the values of $J_{8,9a,b}$ (4 and 3 Hz) differ considerably from the values of $J_{8,9a,b}$ ($J_{8,9a,b}$ = 9 Hz) in those lactones of types E and F or their epoxides for which data are available,[20-22]



E



F

indicating that the conformation is different. Moreover, the H-7 signal of **9** exhibits a normal chemical shift whereas the near-twist chair conformation adopted by the cycloheptane rings of E and F, with the C_α axis passing through C-8,[20b,23] results in a deshielding of H-7 by the α-oriented hydroxyl group of F to ~4 ppm.[20]

A conformation of **9** in which the dihedral angles involving H-8 and H-9 satisfy the observed coupling constants is a somewhat deformed chair with the C_s plane passing through C-8. In this conformation, depending on the configuration at C-10, either the methyl or the hydroxyl is close to H-6, but the absence of an NOE involving H-6 and H-14 suggests a β orientation of the C-10 hydroxyl. This places the C-10 methyl group near the shielding zone of the carbonyl at C-2, which may account for its diamagnetic displacement to 1.22 ppm. The absolute configuration is assumed to be that of other lactones from *Picradeniopsis* and Compositae in general.[24]

The infrared spectrum of the remaining lactone (**11a**, $C_{20}H_{24}O_8$) suggested that it was a carboxylic acid. This was confirmed by preparation of a methyl ester, **11b**. The sequence H-5 through H-9 was deduced by spin decoupling in the usual way, with H-13a and H-13b as points of departure. $J_{7,13}$ was less than 3 Hz, and H-5 and H-6 were coupled to H-15 at 1.90 ppm, the former allylically and the latter homoallylically, all features characteristic of heliangolides with a trans-fused lactone ring closed to C-6. However, the chemical shifts of H-5, 0.6 ppm downfield from H-5 of an ordinary heliangolide (cf. **8c** of Table III), and of the corresponding carbon doublet, 14 ppm downfield from C-5 of **8c** (Table IV), were such that the 4,5 double bond had to be conjugated.

Since keto groups were absent (^{13}C NMR, UV, and CD), the appearance in the ^{13}C NMR spectrum of a fourth carbonyl singlet at 164.22 ppm in addition to the three required by the tigloyl ester, the γ-lactone, and the carboxyl groups indicated that the conjugation was due to a second lactone function linking C-3 to the quaternary center next to C-9, i.e., C-10 (carbonyl singlet at 82.02 ppm). To accommodate the spectroscopic evidence, C-10 also had to carry a second methyl group (three-proton singlet at 1.83 ppm) as well as the remaining two carbon atoms of the molecular formula in the form of a CH_2CO_2 residue (carbon triplet at 26.93 ppm, AB quartet at 2.96 ppm). This completed formulation of the acid as the 2,3-secoheliangolide **11a**, the first representative of this type. Pycnolide (**12**), the first 2,3-seco-*trans,trans*-ger-

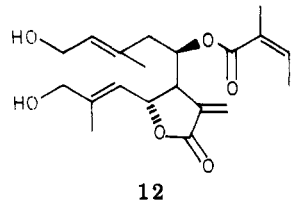
(19) Herz, W. *Isr. J. Chem.* **1977**, *16*, 32.
(20) (a) Herz, W.; Poplawski, J.; Sharma, R. P. *J. Org. Chem.* **1975**, *40*, 199. (b) Karlsson, B.; Pilotti, A.-M.; Wiehager, A.-C.; Wahlberg, I.; Herz, W.; *Tetrahedron Lett.* **1975**, 2245. (c) Herz, W.; Murari, R.; Govindan, S. *Phytochemistry* **1979**, *18*, 1337. (d) Herz, W.; Kumar, N. *Ibid.*, in press.
(21) (a) Bohlmann, F.; Mahanta, P. K.; Suwita, A.; Suwita, A.; Natu, A. A.; Zdero, C.; Dorner, W.; Ehlers, D.; Grenz, M. *Phytochemistry* **1977**, *16*, 1973. (b) Bohlmann, F.; Zitzkowski, P.; Suwita, A.; Fiedler, L. *Ibid.* **1978**, *17*, 2101.
(22) Ito, K.; Sakakibara, Y.; Haruna, M. *Chem. Lett.* **1979**, 1473.
(23) McPhail, A. T.; Sim, G. A. *Tetrahedron* **1973**, *29*, 1751.
(24) The lactone Cotton effect of **9** which should be negative[17] is swamped by the cyclopentenone chromophore which gives rise to a minimum near 300 nm and a maximum near 256 nm.

Table III. ^{13}C NMR Spectra of Glycosidic Lactones and Derivatives[a]

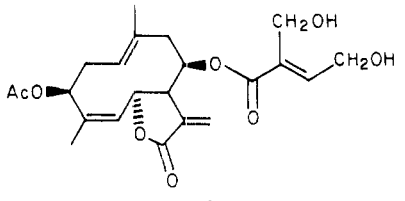
carbon	3a	3a[b]	3c	5a	6[b]	7a	7b
1	69.56 t	68.43 t	69.56 t	69.33 t	51.84 d	69.88 t	69.41 t
2	29.05 t[d]	28.64 t[d]	29.66 t[d]	27.90 t[d]	76.64 d[d,e]	30.64 t[d]	30.68 t[d]
3	27.08 t[d]	26.68 t[d]	26.99 t[d]	27.08 t[d]	44.77 t	28.38 t[d]	28.33 t[d]
4	45.64 d[c]	44.71 d	45.61 d	47.43 d[c]	215.31	33.75 d[c]	33.75 d
5	212.35	212.21	211.72	215.51	50.88	140.51	140.41
6	48.57 t[c]	47.78 t	48.68 t	63.22 d[c]	35.26 t[f]	27.67 t[d]	27.41 t[d]
7	39.26 d[c]	38.50 d	39.29 d	46.54 d[c]	38.18 d	37.31 d	37.32 d
8	78.92 d[c]	78.14 d	78.78 d	81.62 d[c]	79.15 d[d]	77.79 d[c]	77.19 d
9	45.41 t	44.10 t	45.61 t	47.73 t[c]	36.04 t[f]	35.46 t[c]	35.60 t
10	205.63	205.36	204.88	82.20	28.62 d	125.05	125.05
11	138.30	139.00	138.22	137.98	140.04	134.39	134.42
12	171.30	170.10	170.49	171.42	170.02	171.18	170.46
13	122.94 t	121.09 t	122.79 t	123.95 t	122.16 t	122.70 t	122.28 t
14	30.54 q	30.12 q	30.55 q	26.47 q[c]	19.37 q	19.40 q[c]	19.34 q
15	16.09 q	15.71 q	16.21 q	14.84 q	20.59 q	19.02 q[c]	19.15 q
1′	102.61 d	102.73 d	100.70 d	102.64 d	103.57 d	102.47 d	100.05 d
2′	73.73 d[e]	73.47 d[e]	71.79 d[e]	73.75 d[e]	73.33 d	73.53 d[e]	71.53 d[e]
3′	76.37 d	76.40 d	72.75 d	76.47 d	76.72 d[e]	76.23 d	72.92 d
4′	70.26 d	69.96 d	68.46 d	70.25	70.14 d	70.08 d	68.56 d
5′	73.47 d[e]	73.22 d[e]	71.30 d[e]	73.52 d[e]	73.33 d	73.48 d[e]	71.39 d[e]
6′	63.73 t	63.62 t	61.30 t	63.78 t	63.44 t	63.79 t	63.05 t
1″	169.76	169.10	170.11, 169.8, 169.32 (2)	170.45	168.89	171.13	170.46, 169.99, 169.33, 169.10
2″	20.91 q	20.59 q	21.21 q, 20.70 q, 20.93 q, 20.66 q, 20.56 q		20.59 q	20.88 q	20.64 q, 20.60 q, 20.56 q (2)

[a] Run at 67.9 MHz in $CDCl_3$ unless specified otherwise with Me_4Si as internal standard. Unmarked signals are singlets. Numbers in parentheses are coupling constants in hertz. [b] Run in Me_2SO-d_6. [c] Assignment by single-frequency off-resonance decoupling. [d-f] Assignments may be interchangeable.

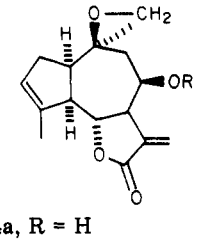
macradienolide, was isolated earlier[25] from a *Liatris* species.



12

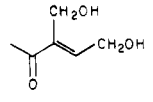


13

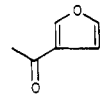


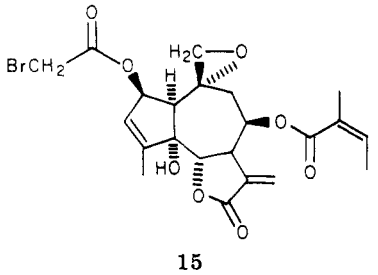
14a, R = H

b, R =



c, R =





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The C-5, C-6, C-7 stereochemistry of **11a** is dictated by the observed coupling constants which are not significantly different from those of a furanoid heliangolide of type **8**. However, the coupling constants involving H-8 and H-9 are somewhat different due to cleavage of the 2,3-bond which allows C-7 to rotate outward and thus alters the dihedral angles involving these protons (model). This is also indicated by the diamagnetic shift of the H-7 signal which is almost at the normal frequency (2.9–3.0 ppm) for heliangolides lacking the 3,10 ether linkage. The stereochemistry at C-10 which participates in the second curious feature of **11a**, the medium-sized lactone ring, is assumed to be unaltered from that of other C-10-oxygenated heliangolides; the absolute stereochemistry cannot be deduced from the CD curve due to the superposition of two lactone Cotton effects but H-7 is presumed to be α as usual.

The discovery of the unusual secolactones **3a**, **5a**, **7a**, and **11a** in *Picradeniopsis woodhousei* made it of interest to determine whether such compounds were characteristic constituents of the genus, the only other representative of which is *P. oppositifolia* (Nutt.) Rydb. [*Bahia oppositifola* (Nutt.) DC.].[10] In an earlier study of a Colorado collection of this species,[26] at that time subsumed in *Bahia*, we had isolated only the guaianolide bahifolin (**14c**) and 5,7-dihydroxy-3,6,3′,4′-tetramethoxyflavone. Examination of a collection from New Mexico has now yielded the antileukemic heliangolide eucannabinolide (**13**)[27,28] and the guaianolide bahia II (**14b**),[29] but again no seco- or diseco-lactones were found.

(25) Herz, W.; Sharma, R. P. *J. Org. Chem.* **1975**, *40*, 392; **1976**, *41*, 1248.

(26) Herz, W.; Bhat, S. V.; Crawford, H.; Wagner, H.; Maurer, G.; Farkas, L. *Phytochemistry* **1972**, *11*, 371.

(27) (a) Drozdz, B.; Grabarczyk, H.; Samek, Z.; Holub, M.; Herout, V.; Sorm, F. *Collect. Czech. Chem. Commun.* **1972**, *37*, 1546. (b) Herz, W.; Wahlberg, I. *J. Org. Chem.* **1973**, *38*, 2485. (c) Holub, M.; Samek, Z. *Collect. Czech. Chem. Commun.* **1977**, *42*, 1053. (d) Herz, W.; Govindan, S. V. *Phytochemistry*, in press.

(28) Eucannabinolide exhibited significant activity against P-388 lymphocytic leukemia in the mouse in tests carried out under the auspices of the National Cancer Institute.

Table IV. ^{13}C NMR Spectra of Other Lactones[a]

carbon	8c	9	11a	14a	14b	14c
1	42.55 t[c]	53.90 d[g]	29.63 t	46.80 d	47.83 d	48.83 d
2	80.43 d[d]	203.48	169.56[f]	31.84 t	32.61 t	32.93 t
3	108.50	150.65[c]	164.22	125.92 d	126.19 d	126.02 d
4	138.01	148.31[c]	131.52	140.83	141.17	141.95
5	131.94 d	49.73 d[d]	145.52 d[b]	56.06 d	56.11 d	56.11 d
6	76.87 d[d]	77.53 d[g]	77.20 d[c]	78.64 d	79.83 d	80.01 d
7	50.17 d	47.55 d[d]	51.63 d[b]	53.52 d	49.82 d	49.26 d
8	72.59 d	65.12 d	74.29 d[c]	66.56 d	66.87 d	66.45 d
9	41.85 t[c]	45.73 t[g]	41.08 t[b]	38.03 t	36.29 t	35.65 t
10	83.27	74.60	82.02	57.71	56.22	55.67
11	136.46	133.90	136.03	135.51	134.20	134.11
12	170.26	168.86	169.56[f]	e	169.15	169.01
13	122.95 t	122.36 t	124.20 t	121.40 t	122.44 t	122.48 t
14	28.93 q	27.19 q	22.46 q	52.20 t	52.16 t	52.07 t
15	21.79 q	14.42 q	17.85 q	17.62 q	17.29 q	17.20 q
1′	166.91	166.54	166.78		166.06	162.11
2′	127.85	127.72	127.60		131.59	118.40
3′	138.30 d	138.73 d	139.11 d		144.60 d	109.73 d
4′	14.43 q	14.42 q	14.52 q		58.92 d	143.97 d
5′	11.90 q	12.12 q	11.86 q	11.86 q	56.76	148.12 d
misc	169.09					
	21.24 q					

[a] Same as in Table III. [b-d] Assignments may be interchangeable. [e] Solubility in $CDCl_3$ too small to permit observation of weak signal. [f] Double intensity, separately visible in Me_2SO-d_6 solution. [g] Assignment by simple frequency off-resonance decoupling.

Table IX. Torsion Angles (degrees) in 14a with Standard Deviations in Parentheses

C(5)-C(1)-C(2)-C(3)	−26.3 (3)
C(1)-C(2)-C(3)-C(4)	15.8 (4)
C(2)-C(3)-C(4)-C(5)	2.0 (4)
C(3)-C(4)-C(5)-C(1)	−18.8 (4)
C(4)-C(5)-C(1)-C(2)	27.3 (3)
C(10)-C(1)-C(5)-C(6)	37.2 (4)
C(1)-C(5)-C(6)-C(7)	−62.9 (3)
C(5)-C(6)-C(7)-C(8)	96.4 (3)
C(6)-C(7)-C(8)-C(9)	−48.1 (3)
C(7)-C(8)-C(9)-C(10)	−32.0 (4)
C(8)-C(9)-C(10)-C(1)	84.4 (4)
C(9)-C(10)-C(1)-C(5)	−62.4 (4)
O(1)-C(6)-C(7)-C(11)	−18.5 (3)
C(6)-C(7)-C(11)-C(12)	17.1 (3)
C(7)-C(11)-C(12)-O(1)	−9.6 (3)
C(11)-C(12)-O(1)-C(6)	−2.9 (3)
C(12)-O(1)-C(6)-C(7)	13.8 (3)
O(2)-C(12)-C(11)-C(13)	−11.5 (6)

Table X. Coupling Constants for 14a-c[a]

	14a	14b	14c
$J_{1,5}$	10	9.5	10
$J_{5,6}$	10	9.5	10
$J_{6,7}$	10	9.5	8.5
$J_{7,8}$	3	3.5	4
$J_{8,9}$	5, 5	6, 6	8, 8

[a] Run in $CDCl_3$ at 270 MHz. Coupling constants expressed in hertz.

Bahifolin (**14c**) was correlated[26] with bahia I (**14a**) and bahia II (**14b**) from *Bahia pringlei*[29] and *B. absinthifolia* var. *dealbata*.[26] The relative and absolute stereochemistries of these compounds at C-1, C-4, C-5, C-6, and C-7 were derived from coupling constants and from a circuitous correlation with isophotosantonic acid lactone.[30] The stereochemistry assigned to C-8, originally[29] based on application of Horeau's method which has occasionally proved unreliable, is consonant with the observed coupling constants ($J_{7,8} \approx 4$ Hz, $J_{8,9a} = J_{8,9b} \approx 8$ Hz);[26] however, the stereochemistry at C-10 remained uncertain.

To settle the stereochemistry of **14a–c** in all detail, we undertook an X-ray analysis of **14a**. Crystal data are listed in the Experimental Section. Figure 1a is a stereoscopic drawing of the molecule which confirms the earlier deductions and shows that the C-10 oxygen atom is β; the figure also represents the absolute configuration because of the correlation with isophotosantonic acid lactone.[30] Tables V–VIII, listing final atomic and final anisotropic thermal parameters, bond lengths and bond angles, are available as supplementary material. Table IX lists selected torsion angles.

The cycloheptane ring of **14a**, like that of euparotin bromoacetate (**15**) with an α-oriented oxygen on C-14,[23] is a twist chair with an approximate axis of symmetry through C-8 [$\Sigma_2 = 28°$, $\Sigma_s = 160°$, $\Sigma_2/(\Sigma_2 + \Sigma_s) = 0.15$]. This is shown more clearly in Figure 1b which presents a side view of the molecule. The cyclopentene and the α,β-unsaturated γ-lactone ring are both somewhat distorted envelopes but are less flat than those of **15**, with $\Sigma|\omega_1|$ values of 88 and 61°, respectively. The C(13)–C(11)–C(12)–O(2) angle is −11.5°; the chirality of the C=C—C=O chromophore thus corresponds with the observed negative Cotton effect (see Experimental Section) in accordance with Beecham's rule[31] as appears to be generally true for trans-fused lactones on six- and seven-membered rings.

In Table X, coupling constants for protons in the cycloheptane rings of **14a–c**, determined at 270 MHz under identical conditions, are tabulated. Small but seemingly significant differences exist for $J_{7,8}$ and $J_{8,9}$ which suggest that in solution the cycloheptane ring of **14a**, and to a lesser extent that of **14b**, may approximate the C_s conformation earlier postulated for **9** rather than the C_2 conformation as in the solid state which requires relatively large values for $J_{8,9a}$ and $J_{8,9b}$ (see Figure 1b).

Experimental Section

Extraction of *Picradeniopsis woodhousei* (Gray) Rybd. (A). Above-ground parts of *P. woodhousei* (3.5 kg) collected by

(29) Romo de Vivar, A.; Ortega, A. *Can. J. Chem.* **1969**, *47*, 2849.
(30) Romo, J.; Lopez, V. *Bol. Inst. Quim. Univ. Nacl. Auton. Mex.* **1969**, *21*, 82.
(31) Beecham, A. F. *Tetrahedron* **1972**, *28*, 5543.

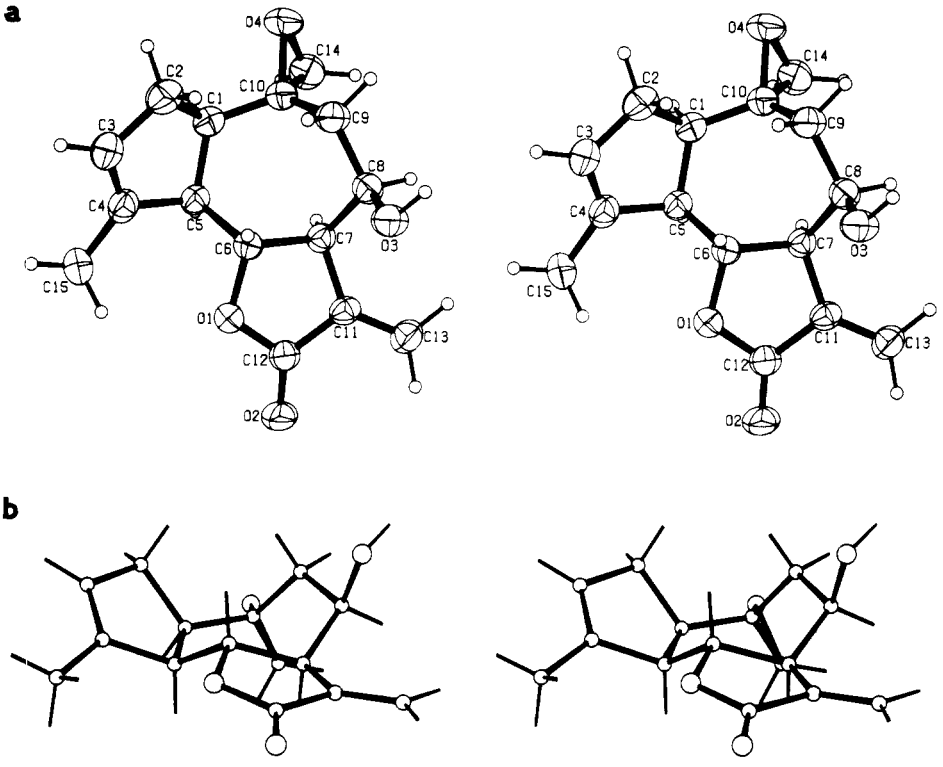

Figure 1. (a) Stereoscopic view of bahia I (**14a**) with ellipsoids of thermal motion. (b) Side view of framework.

Mr. R. J. Barr on Sept. 5, 1970, along U.S. 60 near Vernon, Apache Co., Arizona (Barr No. 70-101 on deposit in the herbarium of Florida State University),[6] was extracted with $CHCl_3$ and worked up in the usual way.[32] The crude gum (53 g) was chromatographed over 1.75 kg of silicic acid (Mallinckrodt, 100 mesh), the following fractions being obtained: 1 (benzene, 5 L), 2 ($CHCl_3$–benzene, 1:9, 2 L), 3 ($CHCl_3$–benzene, 1:4, 2 L), 4 ($CHCl_3$–benzene, 1:1, 6 L), 5 ($CHCl_3$–benzene, 3:1, 4 L), 6–8 ($CHCl_3$, 4, 4, and 6 L), 9–13 (MeOH–$CHCl_3$, 1:19, 2, 1, 0.75, 0.5, and 0.5 L), 14–15 (MeOH–$CHCl_3$, 1:9, 4 and 8 L), 16 (MeOH–$CHCl_3$, 1:4, 4 L).

Fraction 10 (0.95 g) was further purified by TLC (MeOH–$CHCl_3$, 1:49) and gave a mixture of woodhousin (**8a**) and **8b** (0.62 g, mp 174–179 °C) as indicated by the ^1H and ^{13}C NMR spectra and by comparison with authentic woodhousin. Fractions 11–16 (25 g), which represented complex mixtures (TLC), were combined, preadsorbed on 50 g of silicic acid, and rechromatographed over 500 g of the same adsorbent, 400-mL fractions being collected as follows: 1A–9A ($CHCl_3$), 10A–13A (MeOH–$CHCl_3$, 1:99), 14A–27A (MeOH–$CHCl_3$, 3:97), 28A–30A (MeOH–$CHCl_3$, 3:47). Fractions 1A–3A which were homogeneous (2.5 g) were combined, further purified by TLC (MeOH–$CHCl_3$, 1:19), and identified as woodhousin. Fraction 5A (60 mg) was recrystallized from methanol and identified as jaceidin by direct comparison with an authentic sample. Fraction 24A (0.8 g) was homogeneous by TLC; further purification by TLC (MeOH–$CHCl_3$, 3:17) led to isolation of pure **3a** which could not be induced to crystallize and polymerized gradually: IR (film) 3370 (vbr), 1755, 1735, 1710 cm^{-1}; UV λ_{max} 210 nm (ϵ 7950); CD $[\theta]_{274}$ +1600, $[\theta]_{238}$ -320, $[\theta]_{232}$ -172 (last reading); ^1H NMR and ^{13}C NMR spectra are given in Tables I and III.

Anal. Calcd for $C_{23}H_{34}O_{11}$: mol wt 486.2101. Found: mol wt (mass spectrum) 486.2094.

Other significant peaks in the high-resolution mass spectrum were at m/e (composition, relative intensity) 282 ($C_{15}H_{22}O_5$, 1.9), 265 ($C_{15}H_{21}O_4$, 46.9), 247 ($C_{15}H_{19}O_3$, 13.2), 205 ($C_8H_{13}O_6$, 23.2), 187 ($C_8H_{11}O_{51}$, 50.2), 127 ($C_6H_7O_3$, 78.9), and 115 ($C_6H_{11}O_2$, 100).

Fractions 28–30 (0.9 g) were combined and repurified by TLC (MeOH–$CHCl_3$, 3:17) to give **5a** which could not be induced to crystallize: IR ($CHCl_3$) 3400 (br), 1755, 1740, 1700 cm^{-1}; UV λ_{max} 210 nm (ϵ 7600); $[\alpha]_D$ +13.9° (*c* 0.0187, $CHCl_3$); CD (MeOH) $[\theta]_{286}$ +9000, $[\theta]_{246}$ -1350, $[\theta]_{232}$ +4000 (last reading); ^1H and ^{13}C NMR spectra are given in Tables I and III.

Anal. Calcd for $C_{23}H_{34}O_{11}$: mol wt 486.2101. Found: mol wt (mass spectrum) 486.2101.

Other significant peaks in the high-resolution mass spectrum were at m/e (composition, relative intensity) 282 ($C_{15}H_{22}O_5$, 2.0), 265 ($C_{15}H_{21}O_4$, 63.8), 247 ($C_{15}H_{19}O_3$, 5.2), 205 ($C_8H_{13}O_6$, 16.0), 187 ($C_8H_{11}O_5$, 19.8), 127 ($C_6H_7O_3$, 54.9), and 115 ($C_6H_{11}O_2$, 100).

The triacetate **5b** was prepared by dissolving 0.1 g of **5a** in 1 mL of dry pyridine and 0.5 mL of acetic anhydride. After 12 h at room temperature, the usual workup followed by TLC (MeOH–$CHCl_3$, 1:9) gave the triacetate which could not be induced to crystallize. The ^1H NMR spectrum is given in Table I.

Anal. Calcd for $C_{29}H_{40}O_{14}$: mol wt 612.24178. Found: mol wt (mass spectrum) 612.24178.

Other significant peaks in the high-resolution mass spectrum were at m/e (composition, relative intensity) 331 ($C_{14}H_{19}O_9$, 35.8), 271 ($C_{12}H_{15}O_7$, 12.0), 265 ($C_{15}H_{21}O_4$, 35.5), 247 ($C_{15}H_{19}O_3$, 6.3), and 169 ($C_8H_9O_4$, 100).

(B). *P. woodhousei* (0.55 kg) collected by Dr. T. F. Stuessy on Aug. 1, 1969, 2 miles southeast of Lariat, Bailey Co., Texas, on route 84 (1503 Stuessy on deposit in the herbarium of The Ohio State University) was extracted as usual. The crude gum (20 g) was preadsorbed on 40 g of silicic acid and chromatographed over 530 g of the same adsorbent packed in $CHCl_3$, 300-mL fractions being collected as follows: 1–11 ($CHCl_3$), 12–14 (MeOH–$CHCl_3$, 1:49), 15–24 (MeOH–$CHCl_3$, 1:24), 25–27 (MeOH–$CHCl_3$, 1:9). Fractions 8–9, which showed one major spot on TLC, were combined (2.7 g) and triturated with EtOAc–benzene to give solid **8c** (1.8 g) which was recrystallized from EtOAc–hexane: mp 176–178 °C; $[\alpha]_D$ -167.5° (*c* 0.835, $CHCl_3$); IR ($CHCl_3$) 3560, 3440, 1775, 1740, 1700 cm^{-1}; UV (MeOH) λ_{max} 214 nm (ϵ 19 100); CD (MeOH) $[\theta]_{232}$ +6700, $[\theta]_{222}$ +1580 (last reading). The ^1H and ^{13}C NMR spectra are given in Tables II and IV.

Anal. Calcd for $C_{22}H_{28}O_8$: mol wt 420.1784. Found: mol wt (mass spectrum) 470.1772.

Other significant peaks in the high-resolution mass spectrum were at m/e (composition, relative intensity) 378 ($C_{20}H_{26}O_7$, 0.4), 320 ($C_{17}H_{20}O_6$, 6.5), 278 ($C_{15}H_{18}O_5$, 36.9), 260 ($C_{15}H_{16}O_4$, 100), 242 ($C_{15}H_{14}O_3$, 19.0), 232 ($C_{14}H_{16}O_3$, 55.2), and 98 ($C_5H_6O_2$, 54.5).

(32) Herz, W.; Högenauer, G. *J. Org. Chem.* **1962**, *27*, 905.

Fractions 12–15 (0.42 g) were combined and purified by TLC (MeOH–$CHCl_3$, 9:91) to yield 0.13 g of **11a** which could not be induced to crystallize: $[\alpha]_D$ −132.0° (*c* 0.258, $CHCl_3$); IR ($CHCl_3$) 3480, 3200 (centers of broad bands), 1760 and 1760 (double intensity) cm^{-1}; UV (MeOH) λ_{max} 215 nm (ϵ 17 600); CD (MeOH) $[\theta]_{230}$ +3900, $[\theta]_{224}$ −3500 (last reading). ^1H and ^{13}C NMR spectra are given in Tables II and IV.

Anal. Calcd for $C_{20}H_{24}O_8$: mol wt 392.1471. Found: mol wt (mass spectrum) 392.1475.

Other significant peaks in the high-resolution mass spectrum were at *m/e* (composition, relative intensity) 293 ($C_{15}H_{17}O_6$, 1.5), 275 ($C_{15}H_{15}O_5$, 7.9), 231 ($C_{14}H_{15}O_3$, 2.1), 105 (C_8H_9, 10.2), 97 ($C_5H_5O_2$, 27.1), and 83 (C_5H_7O, 100).

The methyl ester **11b** was prepared by allowing 10 mg of **11a** to stand with 1 mL of MeOH and 1 drop of concentrated H_2SO_4 at room temperature for 10 h. Workup in the usual way gave a 4:1 mixture of **11b** and **11a** which was separated by TLC (MeOH–$CHCl_3$, 3:47). The ^1H NMR spectrum of **11b** is reported in Table II. The mass spectrum showed M^+ as a very weak peak at *m/e* 406; other significant peaks were at *m/e* 307, 275, 257, and 83 (base peak).

Fraction 15, which exhibited one spot on TLC, was purified by TLC (MeOH–$CHCl_3$, 9:91) and gave 0.5 g of **9** which could not be induced to crystallize: it gave a positive $FeCl_3$ test; $[\alpha]_D$ +48.0° (*c* 0.107, $CHCl_3$); UV (MeOH) λ_{max} 215 nm (ϵ 17 200), 265 (8130), the second band moving to 305 nm on addition of 2 drops of 1 N NaOH; IR ($CHCl_3$) 3480, 1760, 1700, 1650 cm^{-1}; CD (MeOH) $[\theta]_{300}$ −2650, $[\theta]_{256}$ +6580, $[\theta]_{236}$ +4800, $[\theta]_{228}$ +5800 (last reading). ^1H and ^{13}C NMR spectra are given in Tables II and IV.

Anal. Calcd for $C_{20}H_{24}O_7$: mol wt 376.1521. Found: mol wt (mass spectrum) 376.1466.

Other significant peaks in the high-resolution mass spectrum were at *m/e* (composition, relative intensity) 358 ($C_{20}H_{22}O_6$, 3.4), 276 ($C_{15}H_{16}O_5$, 13.8), 258 ($C_{15}H_{14}O_4$, 31.8), 165 ($C_9H_9O_3$, 100), and 12 ($C_7H_7O_2$, 51.6).

Fraction 20 (1.58 g) exhibited one major spot on TLC; purification by preparative TLC (MeOH–$CHCl_3$, 3:22) yielded 0.9 g of **7a** which could not be induced to crystallize: $[\alpha]_D$ −26.5° (*c* 0.900, $CHCl_3$); IR ($CHCl_3$) 3400 (vbr), 1760, 1750 cm^{-1}; UV (MeOH) λ_{max} 211 (ϵ 9000); CD (MeOH) $[\theta]_{242}$ −615, $[\theta]_{230}$ +585 (last reading); ^1H and ^{13}C NMR spectra are given in Tables I and III.

Anal. Calcd for $C_{23}H_{34}O_9$: mol wt 454.2201. Found: mol wt (mass spectrum) 454.2195.

Other significant peaks in the high-resolution mass spectrum were at *m/e* (composition, relative intensity) 279 ($C_{16}H_{23}O_4$, 100), 261 ($C_{16}H_{21}O_3$, 23.3), 250 ($C_{15}H_{22}O_3$, 75.6), 233 ($C_{15}H_{21}O_4$, 73.0), 232 ($C_{15}H_{20}O_2$, 50.1), 205 ($C_8H_{13}O_6$, 17.9), 191 ($C_{12}H_{15}O_2$, 65.3), 187 ($C_8H_{11}O_5$, 24.1), and 127 ($C_6H_7O_3$, 30.9).

Reactions of 3a. (a). Preparation of the triacetate **3c** was carried out as described above for **5b** with 0.1 g of **3a**. The product was purified by TLC (MeOH–$CHCl_3$, 1:9) but could not be induced to crystallize: IR (film) 1750 (vs), 1710, 1230 cm^{-1}. ^1H and ^{13}C NMR spectra are given in Tables I and III.

Anal. Calcd for $C_{29}H_{40}O_{14}$: mol wt 612.2418. Found: mol wt (mass spectrum) 612.2355.

(b). A mixture of 26 mg of **3a** and 1 mL of 6% aqueous H_2SO_4 was warmed on a steam bath for 75 min, cooled, and thoroughly extracted with $CHCl_3$. TLC of the $CHCl_3$ extract showed a complex pattern. The aqueous extract was neutralized with 20% aqueous K_2CO_3, the mixture was evaporated at room temperature, and the residue was extracted with MeOH. The extract was spotted on Whatman paper No. 1 along with the sugar obtained by hydrolysis of paucin carried out under identical conditions as well as with a number of other representative hexoses, and this was developed with *n*-BuOH–Py–H_2O (6:4:3, first set) and with *n*-BuOH–acetic acid–H_2O (4:1:5, upper layer; second set). After the paper was dried, sprayed with aniline phthalate, and heated for 5 min at 110 °C, the spots due to the sugar from **3a** and paucin correspond to those of D-(+)-glucose in each set; the R_f's of the osazones corresponded also.

(c). A mixture of 0.1 g of **3a**, 9 mL of acetate buffer (prepared by mixing 2 mL of 0.2 M aqueous acetic acid and 8 mL of 0.2 aqueous NaOAc to give a pH of ~5.2), and 35 mg of β-glucosidase was kept in an incubator at 37 °C for 70 h and then thoroughly extracted with $CHCl_3$. The washed and dried extract was purified by TLC (MeOH–$CHCl_3$, 1:9) to give 40 mg of starting material and 15 mg of **4**, whose ^1H NMR spectrum is given in Table I. The low-resolution mass spectrum exhibited a very weak molecular ion at *m/e* 282; other significant peaks were at *m/e* 264, 224, 206, 153, and 115.

Anal. Calcd for $C_{15}H_{22}O_5$: mol wt 282.1467. Found: mol wt (mass spectrum, peak matching) 282.1460.

Reactions of 7a. (a). Acetylation of 0.2 g of **7a** with 2 mL of Ac_2O and 5 mL of anhydrous pyridine at room temperature overnight followed by the usual workup and TLC (MeOH–$CHCl_3$, 1:9) gave 0.18 g of triacetate **7b** as a gum whose ^1H and ^{13}C NMR spectra are given in Tables I and III.

Anal. Calcd for $C_{29}H_{40}O_{12}$: mol wt 580.2519. Found: mol wt (mass spectrum) 580.2500.

Other significant peaks in the high-resolution mass spectrum appeared at *m/e* (composition, relative intensity) 331 ($C_{14}H_{19}O_9$, 35.7), 271 ($C_{12}H_{15}O_7$, 10.6), 250 ($C_{15}H_{22}O_3$, 0.4), 233 ($C_{15}H_{21}O_2$, 6.3), 191 ($C_{12}H_{15}O_2$, 4.7), 169 ($C_8H_9O_4$, 100), and 109 ($C_6H_5O_2$, 40.8).

(b). Acid hydrolysis of 55 mg of **7a** was carried out as previously described for **3a**. The sugar in the aqueous portion of the hydrolysate was identified as D-(+)-glucose as described for **3a**. The $CHCl_3$ extract of the hydrolysate was homogeneous by TLC; evaporation gave the gummy aglycon **1c** (25 mg) which exhibited the ^1H NMR signals listed in Table I. It was dissolved without further purification in 0.5 mL of DMF, treated with 210 mg of pyridinium dichromate, stirred at room temperature for 10 h, diluted with 5 mL of H_2O, and extracted with $CHCl_3$. The washed and dried extract was evaporated; the residual syrup (20 mg) after purification by TLC (MeOH–$CHCl_3$, 1:9) yielded 8 mg of **1a** which was pure by TLC and NMR criteria (Table I): mass spectrum, *m/e* 264 (M^+), 246, 228, 218, 200, 191, 145, 107, 71, 57 (base peak). Esterification of 20 mg of **1a** (0.5 mL of MeOH, 1 drop of concentrated H_2SO_4) at room temperature overnight followed by the usual workup and TLC (MeOH–$CHCl_3$, 1:9) gave unreacted acid and 12 mg of **1b** whose IR and 270 MHz ^1H NMR spectra (Table I) were identical with those of ivangulin.

Extraction of *Picradeniopsis oppositifolia* (Nutt.) Rydb. Extraction of 0.8 kg of *P. oppositifolia* collected by Dr. T. F. Stuessy on Aug. 3, 1969, on a dirt ranch road 1 mile north of the junction of routes 39 and 56, Abbott, Colfax Co., New Mexico (Stuessy 1515 on deposit in the herbarium of The Ohio State University), with $CHCl_3$ in the usual way gave 7.5 g of crude gum which was purified by preparative TLC plates coated with silica gel (60 $PF_{254+366}$, EM reagent, 2 mm thick) with the solvent mixture MeOH–$CHCl_3$, 1:24. This led to isolation of 1.4 g of a seemingly homogeneous fraction (TLC) which was eventually deduced to be a 3:2 mixture of bahia II (**14b**) and eucannabinolide (**13**) on the basis of a detailed analysis of the ^1H and ^{13}C NMR spectra and comparison with the spectra of pure **13** and **14b**. The previously unreported CD curves of bahia I (**14a**) and bahia II in MeOH are as follows: **14a**, $[\theta]_{248}$ −1415, $[\theta]_{238}$ −1170, $[\theta]_{218}$ −6015 (last reading); **14b**, $[\theta]_{248}$ −2030, $[\theta]_{222}$ 0 (last reading).

X-ray Analysis of Bahia I. Single crystals of bahia I[22] were prepared by slow crystallization from MeOH. They were orthorhombic, space group $P2_12_12_1$, with a = 7.617 (2) Å, b = 12.213 (3) Å, c = 13.8765 (4) Å, and d_{calcd} = 1.349 g cm^{-3} for Z = 4 ($C_{15}H_{18}O_4$, mol wt 262.31). 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 × 0.40 mm was used for data collection. A total of 1030 reflections were measured for $\theta < 57°$ of which 977 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple-solution procedure[33] 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 final discrepancy indices are R = 0.034 and R_w = 0.041 for the 977 observed reflections. The final difference map has no peaks greater than ±0.2 eA^{-3}.

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

Acknowledgment. We wish to thank Dr. Tod F. Stuessy, The Ohio State University, for collections and valuable correspondence.

Registry No. **1a**, 73971-64-9; **1b**, 14271-37-5; **1c**, 73971-65-0; **3a**, 73971-66-1; **3c**, 73971-67-2; **4**, 73971-68-3; **5a**, 73985-91-8; **5b**, 73985-92-9; **6**, 26836-43-1; **7a**, 73971-69-4; **7b**, 73971-70-7; **8a**, 33143-54-3; **8b**, 73971-71-8; **8c**, 73971-72-9; **9**, 73971-73-0; **11a**, 73971-74-1; **11b**, 73971-75-2; **13**, 38458-58-1; **14a**, 24268-44-8; **14b**, 24268-45-9; **14c**, 35682-60-1.

Supplementary Material Available: Final atomic parameters (Table V), final anisotropic thermal parameters (Table VI), bond lengths (Table VII), and bond angles (Table VIII), for **14a** (4 pages). Ordering information is given on any current masthead page.

Phase-Transfer Alkylation of Heterocycles in the Presence of 18-Crown-6 and Potassium *tert*-Butoxide

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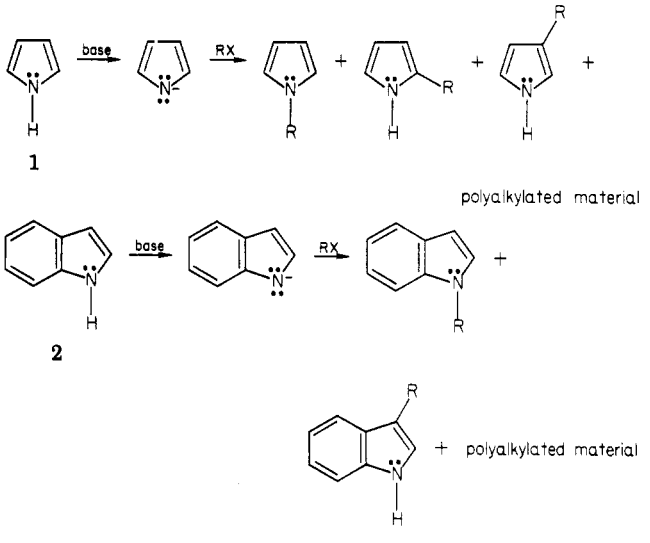
Received January 4, 1980

It has been found that the N-alkylation of heterocyclic compounds bearing an acidic hydrogen atom attached to nitrogen can be accomplished in diethyl ether via a phase-transfer process in which 18-crown-6 is employed as the catalyst and potassium *tert*-butoxide is employed as the base. In this manner, pyrrole (**1**), indole (**2**), pyrazole (**3**), imidazole (**4**), benzimidazole (**5**), benzotriazole (**6**), carbazole (**7**), and methyl indole-3-acetate (**8**) can be successfully alkylated. The procedure is convenient and mild and generally gives rise to exclusive N-alkylation.

The N-alkylation of heterocyclic compounds bearing an acidic hydrogen atom attached to nitrogen, like pyrrole (**1**) or indole (**2**), is generally accomplished by the treatment of these compounds with an appropriate base followed by the treatment of the resulting salt with an alkylating agent (Scheme I).[1] However, since the pyrrolyl and indolyl anions exhibit ambident behavior as nucleophiles, alkylation can occur at carbon as well as at nitrogen.[1,2] Thus, when these species are alkylated, substantial quantities of 2- and 3-alkylpyrrole or 3-alkylindole may contaminate the N-alkylated product along with some polyalkylated material. In many instances, the major products are those derived from C-alkylation.

The amount of N-alkylation relative to C-alkylation depends upon a number of factors, including the base employed for the deprotonation of the heterocycle, the solvent, and the alkylating agent. Thus, for salts derived from pyrrole or indole, the base (and hence, the cation associated with the pyrrolyl or indolyl anion) can influence the ratio of N to C alkylation.[2e-h] Although nitrogen alkylation generally predominates when the cation is a sodium or potassium ion, carbon alkylation usually predominates with harder[3] cations like lithium or magnesium

Scheme I



which are tightly bound to nitrogen.[4] The solvent can dramatically influence the ratio of N to C alkylation,[2e-h,5] and dipolar aprotic solvents can give rise to predominant N-alkylation of salts derived from pyrrole or indole even when magnesium is the counterion.[2e,f,5c] Finally, the alkylating agent can influence the ratio of N to C alkylation. For example, when compared to other alkylating agents, allylic or benzylic halides generally afford a greater proportion of C-alkylated material.[2e,5a,c,6]

During the past decade, several new procedures have been developed in which the N-alkylation of pyrrole or

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