acid together with 2.5 g of PtO_2 catalyst were hydrogenated in a Parr shaker for 12 hr to get about 98% of theoretical hydrogen uptake. The acetic acid filtrate was diluted with ether and then with 4 *N* NaOH until the system was alkaline. The ether phase was recovered, dried, and evaporated to 12.0 g of faintly yellow oil. On exposure of this oil for any length of time in the laboratory, fine white crystals began to form on the surface of the container. An oxalate of the material prepared as described by Leithe[23] gave white crystals, mp 136° (lit.[23] 132°). A sample of the oxalate was added to water–ether (50:50) and 4 *N* NaOH was added until the system was strongly basic. The ether layer was processed to give a colorless oil. About 0.5 g of this oil was added to 20 ml of 5% NaOH solution and 2 ml of benzoyl chloride were added wtih stirring. The precipitate was recovered, taken up in ethyl acetate, dried, and worked up to give 500 mg of crystals: mp 158.5° (lit.[23] 162°); $[\alpha]^{25}\mathrm{D}$ $-21.3 \pm 0.06°$ (*c* 3.49, MeOH) (lit.[23] 19.2° for the other isomer).

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.92; H, 9.09; N, 5.92.

(*S*)-α-Cyclohexylethylamine was obtained in the same way. The *N*-benzoyl derivative melted at 159° and had $[\alpha]^{25}\mathrm{D}$ $+20.9 \pm 0.07°$ (*c* 2.57, MeOH).

α-Cyclohexylethylurethans.—These materials were prepared in the same fashion as the α-phenylethylurethans. The following physical data were obtained on the material (*R*)-α-cyclohexylethylurethan: mp 49–50°; $[\alpha]^{25}\mathrm{D}$ $+13.8 \pm 0.2°$ (*c* 1.043, MeOH); nmr (CCl_4) δ 1.09 (3 H, doublet, *J* = 7 Hz, α-CH_3), 1.23 (3 H, triplet, *J* = 7 Hz, --$OCH_2\mathbf{CH_3}$) (the doublet and triplet appear as five lines on a broad base signal which integrates for 12 protons, that is, two CH_3 and six axial protons), 1.75 (5 H, broad signal for equatorial protons), 3.53 (1 H, broad signal for α-H), 4.08 (2 H, quartet, *J* = 7 Hz, –$O\mathbf{CH_2}CH_3$), and 4.53 (1 H, broad exchangeable signal for NH).

Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.29; H, 7.03; N, 10.62. Found: C, 66.47; H, 7.07; N, 10.85.

The (*S*)-α-cyclohexylurethan had mp 51–52° and $[\alpha]^{25}\mathrm{D}$ $-14.32 \pm 0.09°$ (*c* 2.192, MeOH).

Nitroso-α-cyclohexylethylurethans.—The methods described for the syntheses of nitroso-α-phenylurethans were used. The corresponding cyclohexyl compounds could be passed over silica gel to get golden oils which appeared as single spots by tlc using 10% ethyl acetate in hexane developer. At this stage data on (*R*)-nitroso-α-cyclohexylethylurethan were as follows: $[\alpha]^{25}\mathrm{D}$ $+51.0 \pm 0.35°$ (*c* 0.56, MeOH); nmr (CCl_4) δ 1.00 (3 H, doublet, *J* = 7 Hz, α-CH_3), 1.45 (3 H, triplet, *J* = 7 Hz, –$OCH_2\mathbf{CH_3}$) (these five lines appeared on broad base signals integrating for 21 protons which includes the axial and equatorial protons plus impurity), 4.18 (1 H, multiplet, α-H) and 4.47 (2 H, quartet, *J* = 7 Hz, -$O\mathbf{CH_2}CH_3$).

Anal. Calcd for $C_{11}H_{20}N_2O_3$: C, 57.89; H, 8.77; N, 12.28. Found: C, 59.58; H, 9.24; N, 11.40.

These nitroso compounds could not be purified by partition chromatography since, because of their low polarity, they moved at the solvent front. Attempts to purify them by glc resulted in decomposition; consequently no analytically pure samples were obtained.

***ONN*-1-cyclohexylazoxyethanes.**—These materials were prepared as described for the corresponding phenyl compounds. Some purification was effected by silica gel chromatography but the ir spectrum of the material off the silica gel column had a carbonyl peak at 1730 cm^{-1} in addition to a strong azoxy peak at 1495 cm^{-1}. Glc using a 10-in. 10% SF-96 column gave the pure isomers.

For the material (*R*)-*ONN*-1-cyclohexylazoxyethane (III) the following physical data were obtained: mass spectrum *m/e* 184; $[\alpha]^{25}\mathrm{D}$ $-38.24 \pm 0.19°$ (*c* 1.025, MeOH); λ_{max}^{MeOH} 223 nm (ε 8200); nmr (CCl_4) δ 0.97 (3 H, doublet *J* = 7 Hz, α-CH_3) (this doublet appeared as two lines on a broad base signal accounting for the six axial protons), 1.47 (3 H, triplet, *J* = 7 Hz, $-N(\rightarrow O)CH_2\mathbf{CH_3}$) (this triplet appeared as three lines on a broad base signal accounting for five equatorial protons), 3.80 (1 H, broad multiplet, α-H), and 4.08 (2 H, quartet, *J* = 7 Hz, $-N(\rightarrow O)\mathbf{CH_2}CH_3$).

Anal. Calcd for $C_{10}H_{20}N_2O$: C, 65.17; H, 10.94; N, 15.20. Found: C, 64.81; H, 10.94; N, 14.77.

The material (*S*)-*ONN*-1-cyclohexylazoxyethane had *m/e* 184 in the mass spectrum and $[\alpha]^{25}\mathrm{D}$ $+36.00 \pm 0.55°$ (*c* 0.358, MeOH).

Registry No.—I, 24397-77-1; II, 23315-05-1; III, 33290-09-4; V, 33325-77-8; VI, 33290-10-7; urethan of (*R*)-α-phenylethylamine, 14185-43-4; urethan of (*S*)-α-phenylethylamine, 33290-12-9; nitroso-α-phenylurethans, 33290-13-0; (*S*)-α-cyclohexylethylamine *N*-benzoyl derivative, 33325-78-9; (*R*)-α-cyclohexylethylurethan, 33290-14-1; (*S*)-α-cyclohexylethylurethan, 33290-15-2; (*R*)-nitroso-α-cyclohexylethylurethan, 33364-43-1; (*S*)-*ONN*-1-cyclohexylazoxyethane, 33290-16-3.

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Woodhousin, a New Germacranolide from *Bahia woodhousei* (Gray) Gray[1]

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The isolation and structure determination of a new complex germacranolide, woodhousin (1), from *Bahia woodhousei* (Gray) Gray is reported. Jaceidin (4′,5,7-trihydroxy-3,3′,6-trimethoxyflavone) was also found. No homogeneous lactone component could be isolated from *Bahia dissecta* (Gray) Britton.

Earlier investigations of representatives of the genus *Bahia* (tribe Helenieae, Compositae) resulted in the isolation of several closely related guaianolides.[2,3] We now report isolation and structure determination of a new relatively complex germacranolide woodhousin from *Bahia woodhousei* (Gray) Gray,[4] which also contains the flavone jaceidin (4′,5,7-trihydroxy-3,3′,6-trimethoxyflavone).[5–7]

Woodhousin, $C_{21}H_{28}O_8$, mp 183–184.5°, $[\alpha]\mathrm{D}$ $-206.3°$, was a conjugated γ-lactone (ir bands at 1765 and 1662 cm^{-1}; strong uv end absorption). The nmr spectrum (Table I) exhibited the typical two doublets of H_a and H_b in partial structure A. Spin decoupling experiments involving H_a and H_b established the loca-

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[1] Supported in part by grants from the U. S. Public Health Service (GM 05814) and Hoffmann-La Roche, Inc.

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[5] L. Farkas, L. Hörhammer, H. Wagner, H. Rösler, and R. Gurniak, *Chem. Ber.*, **97**, 610 (1964).

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TABLE I

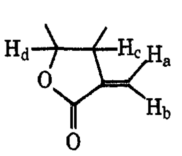
NMR SPECTRA OF WOODHOUSIN AND DERIVATIVES[a]

Compd	H-2	H-5	H-6	H-7	H-8	H-13	H-14[b]	H-15[b]	Ac[b]	H-3′[b]	Misc
1	5.36 d br (5.0)	5.60 c[c]	5.50 c[c]	4.06 m	5.50 c[c]	6.23 d (2.4) 5.60 d (2.0)	1.77 t (1.5)	1.50	2.12	1.07 d (7) 1.05 d (7)	3.23 (OH)[d]
2[d]	5.36 dd $(J_{1a,2} = 2.8)$ $(J_{1b,2}) = 6.5)$	5.76 dq $(J_{5,6} = 5.0)$ $(J_{5,14} = 1.5)$	5.59 qm $(J_{6,7} = 2.0)$ $(J_{6,14} = 1.5)$	3.56 dt $(J_{7,11} = 10.6)$ $(J_{7,8} = 2.4)$	5.22 td $(J_{8,9a} = 6.4)$ $(J_{8,9} = 6.4)$	1.10 d[b] $(J_{11,13} = 7.2)$	1.78 t (1.5)	1.43	2.08	1.12 d (7) 1.12 d (7)	3.07 (OH)[d] 2.80 m (H-11)
3	5.38 d br (5.3)	3.34 $(J_{5,6} = 0)$	5.23 d $(J_{6,7} = 4.5)$	4.30 m	5.50 m[e] $(J_{7,8} = 4.5)$ $(J_{8,9a} = 10.2)$ $(J_{8,9b} = 4.8)$	6.28 d (2.7) 5.63 d (2.3)	1.35	1.46	2.18	1.05 d (7) 1.04 d (7)	3.12 (OH)[d]
4	5.42 dd (3.2, 7.4)	f f	4.80 dd br (12.5, 6)	f f	5.20 dd br (9.5, 4)	1.30 d[b,g] (6.8)	1.10 d[g] (7.0)	1.48	2.15	1.10 d (7) 1.10 d (7)	
5	f	f	4.05[c]	4.15[c]	5.33 ddd (10, 6, 1.8)	1.04 d[b,g] (7.0)	0.86 d[g] (7)	1.25		1.04 d (7) 1.04 d (7)	4.75 dt (11.0, 3.0, H-3)
6	5.47 dd $(J_{1a,2} = 4.8)$ $(J_{1b,2} = 3.2)$	f	4.27 td $(J_{5a,6} = 10.2)$ $(J_{5b,6} = 3.3)$ $(J_{6,7} = 10.2)$	2.7 m	5.90 dd $(J_{7,8} = 6.5)$ $(J_{8,9} = 11.0)$	1.42 d[b,g] (7.0)	1.26 d[g] (6.8)	1.88 d $(J_{9,15} = 1.0)$	2.14	1.15 d (7) 1.15 d (7)	3.52 dd (15.4, 4.8, H-1a) 2.33 dd (15.4, 3.2, H-1b) 5.43 d br (11.0, 1.0, H-9)[h]
7	5.2[c]	f	4.59 dd br (4.5, 12.3)	f	5.2[c]	1.29 d[b,g]	1.08 d[g] (7.0)	5.37 br[i] 5.07 br[i]	2.09	1.08 d 1.08 d	
8a	4.69q[j]	f	3.88 td (10, 3.0)	f	5.96 dd[h] (11.0, 6.0)	1.37 d[b,g] (7.0)	1.17 d[g] (6.8)	1.87 d (1)		1.15 d (7) 1.15 d (7)	5.24 d br (11, 1, H-9)[h] 3.63 d (4.2, OH)
8b	4.73 q[j] (4)	f	4.19 td (10.5, 3.5)	f	5.91 dd[h] (11.5, 6.5)	1.44 d[b,g] (7.0)	1.18 d[g] (6.8)	1.86 d (1)		1.15 d (7) 1.15 d (7)	5.39 d br (11, 1, H-9)[h] 3.59 d (4.2, OH)
9a	4.69 q[j] (3.5)	f	3.67 td (10, 3.0)	f	5.28 dd[c,h] (11.0, 7)	1.38 d[b,g] (6.8)	1.13 d[g] (7)	1.83 d (1)			5.07 d br[c,h] (11.0, 1, H-9)
9b	5.46 dd (5.5, 2.5)	f	4.99 td (10, 3.0)	f	5.30[c]	1.39 d[b,g] (7)	1.32 d[g] (7)	1.89 br	2.13 2.06		3.25 dd (18, 2.5, H-1a) 5.25[c] (H-9)
10		f	3.93[c]	f	5.41 d[h] (11)	1.18 d[b,g] (6.8)	1.40 d[g] (7)	1.98 br		1.15 d (7) 1.15 d (7)	3.17 d (17.8, H-1a) 3.80 d br (17.8, H-1b) 5.50 d br[c] (11, H-9)[h]
11		f	4.54 dd br (12.0, 3.8)	f	5.07 td (7, 2)	1.13 d[b,g] (6.0)	1.07 d[g] (7)	1.90 d (1)	2.22	1.05 d (7) 1.05 d (7)	6.2 br (H-1) 5.10 d (0.8, H-3)
12		f	4.33 dd br (12.0, 3.0)	f	5.07 ddd (11, 7.2)	1.23 d[b,g] (6.0)	1.08 d[g] (7)	1.93 d (1)		1.04 d (7) 1.04 d (7)	6.23 br (H-1) 4.10 br (H-3) 3.66 br (OH) 3.21 dd (11.0, 12.5, H-9a)
13	5.32 dd (9.5, 7.5)	f	4.80[c]	f	4.75 td[c] (12.0, 3.5)	1.06 d[b] (7)	1.34 d[j] (7.0)	1.06 d (7)	2.06	1.06 d (7) 1.06 d (7)	
14	5.30 dd (9.8, 6.5)	f	4.35 ddd (11.5, 4.5, 2.5)	f	f	1.13 d[b] (6.3)	1.30 d[j] (6.8)	1.0 d (6.0)	2.07		
17	k	5.38 dq (11, 1.2)	5.05 dd (11, 1.7)	3.05 quint (1.7)	5.19 m	6.37 d (2.0) 5.83 d (2.0)	1.98 d (1.2)	1.40		1.89 t (1.2) 6.06 br[i] 5.62 br[i]	
18	k		4.48 dd (12.0, 3)	f	5.23 t br (3.5)	1.18[b,l]	1.12 d[l] (7)	1.39		1.14 d (7)[l] 1.13 d (7)[l]	

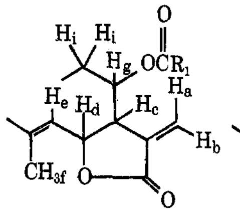
[a] Run at 90 MHz on a Bruker nmr spectrometer in $CDCl_3$ using TMS as internal standard. Chemical shifts are in parts per million. Signals are denoted in the usual way: d, doublet; t, triplet, q, quartet; m, multiplet; c, complex signal whose center is given; br, broadened singlet. Unmarked signals are singlets. Figures in parentheses are line separations or coupling constants in hertz. [b] Three-proton signal. [c] Overlapping signals. [d] Disappeared on addition of D_2O. [e] Outerpart of signal under H-2 and H-13b. [f] Obscured in methylene and methinyl envelope. [g] Tentative assignment on assumption that H-13 is generally at lower field. [h] Part of AB system. [i] One-proton signal. [j] On addition of D_2O H-2 signal collapsed to triplet. [k] Part of ABC multiplet, centered at 3.2. [l] Arbitrary assignment.

tion of the H_c multiplet at the unusually low frequency of 4.06 ppm. H_d was obscured in a multiplet near 5.5 ppm. The presence of partial structure A was further confirmed by formation of a dihydro derivative **2** on sodium borohydride reduction. In the nmr spectrum of **2** the signals of H_a and H_b were replaced by a new methyl doublet and the multiplet of H_c was converted to a doublet of triplets at 3.56 ppm.

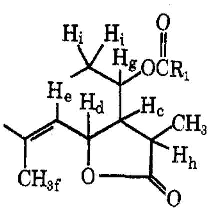
A narrowly split three-proton triplet at 1.77 ppm in the nmr spectrum of woodhousin indicated the presence of a vinyl methyl group which was apparently coupled to a vinyl proton responsible for a multiplet component of a relatively complex signal near 5.6 ppm and to one other proton. The presence of a second, unconjugated double bond indicated by this observation was confirmed by an ir band at 1665 cm^{-1} and by conversion of **1** to an epoxide **3**. In the nmr spectrum of **3**, the signals at 1.77 and 5.6 ppm were replaced by singlets at 1.35 and 3.34 ppm.[8]



A



B



B′

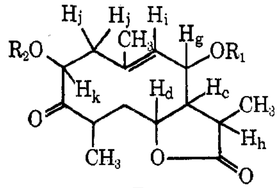
Spin decoupling experiments on **2** allowed expansion of partial structure A for woodhousin to B (modified to B′ in 2).[9] Irradiation at the frequency of the vinyl methyl triplet (H_f) converted a doublet of quartets at 5.76 ppm (H_e) into a doublet and simplified a complex signal at 5.59 ppm (H_d) into a doublet of doublets. Irradiation at the frequency of H_c (4.3 ppm) sharpened a broadened triplet at 5.2 ppm (H_g) and created changes in the signals corresponding to H_d and H_h. The chemical shifts of H_d and H_g were characteristic of protons on carbon carrying ester or lactone functions; the multiplicity of H_g indicated that it was adjacent to a methylene group (H_i). Irradiation at the frequency of H_h collapsed the methyl doublet to a singlet and simplified H_c to a triplet. Conversely, irradiation at the frequencies of H_d or H_g collapsed the H_c signal to a doublet of doublets.

The ir spectrum of woodhousin also indicated the presence of a hydroxyl group and two ester functions (ir bands at 3470, 3440, 1750, and 1730 cm^{-1}).[10] One of the ester functions was an acetate (nmr signal at 2.12 ppm). In view of the molecular formula, the second ester side chain was therefore that of a four-carbon acid. Since **1** was recovered after treatment with acetic anhydride–pyridine, the hydroxyl group was tertiary and not located in the four-carbon side chain because of the presence of two methyl doublets in the nmr spectrum of woodhousin and its derivatives. Hence, the side chain was isobutyric acid. This was corroborated by the mass spectrum which, in addition to the molecular ion (408.1772), exhibited significant peaks at 390.1684 (0.5%, M − H_2O), 384.1603 (4.4%, M − $C_2H_4O_2$), 320.1230 (M − $C_4H_8O_2$), 302.1122 (M − H_2O − $C_4H_8O_2$), 278.1159 (22.5%, M − $C_4H_8O_2$ − C_2H_2O), 277.1048 (M − $C_4H_8O_2$ − C_2H_3O), 261.1104 (7.0%, M − $C_4H_8O_2$ − $C_2H_3O_2$), 260.1043 (38.2%, M − $C_4H_8O_2$ − $C_2H_4O_2$), 242.0918 (10.3%, M − $C_4H_8O_2$ − $C_2H_4O_2$ − H_2O), and 71.0501 (base peak, C_4H_7O).

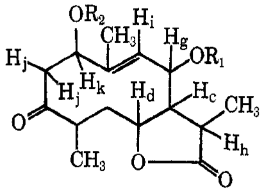
Catalytic hydrogenation of woodhousin (Pd/$BaSO_4$) resulted in the uptake of 2 mol equiv of hydrogen and the formation of a saturated ketol **4** (ir bands at 3432, 1775, 1735, 1728, and 1710 cm^{-1}; CD curve λ_{max} 288 nm, θ +8050). Hydrogenation had obviously resulted not only in reduction of the two double bonds but was accompanied by an isomerization which was responsible for creation of a keto group. It could be rationalized by postulating the presence in woodhousin of a hemiacetal linkage which is cleaved when saturation of the unconjugated double bond forces the ketone and hydroxyl groups out of close proximity. Presence of a hemiacetal grouping would also account for the eighth oxygen atom of the molecular formula.

Occurrence in the nmr spectra of **1**, **2**, **3**, and **4** of a three-proton singlet near 1.45 ppm suggested that the carbon atom carrying the methyl group responsible for this singlet was one terminus of the hemiacetal linkage. This suggestion was confirmed by dehydrating **4** to a mixture of **6** and **7** which were separated by preparative tlc. In the nmr spectrum of **6**, the methyl singlet of **4** at 1.48 ppm had been replaced by a narrowly split vinyl methyl signal at 1.88 ppm; simultaneously, a new vinyl proton resonance at 5.34 ppm (broadened doublet) had made its appearance (Chart I).

Spin decoupling experiments on **6** permitted expansion of B′ to D or E. Irradiation at the frequency of the vinyl methyl doublet sharpened the broad vinyl doublet of H_i. Conversely, irradiation of H_i collapsed the methyl doublet to a singlet and converted a doublet of doublets of 5.90 (H_g, now allylic and hence shifted to lower field) to a doublet. Irradiation at the frequency of H_g collapsed the H_i doublet and caused some changes at 2.70 ppm (H_c). Irradiation of H_c collapsed H_g to a doublet and converted a triplet of doublets at 4.27 ppm (H_d, no longer allylic, hence displaced toward higher field in comparison with **1** and probably also shielded by the new double bond) to a doublet of doublets. The remaining low-field signal at 5.47 ppm could be assigned to a proton (H_k) under carbon carrying the second ester function. H_k was clearly identifiable by double irradiation as the X part of an ABX system whose A and B components (H_{j_1} and H_{j_2} at 3.52 and 2.33 ppm) were gemately coupled to each other ($|J_{j_1,j_2}|$ = 15.4 Hz).



D



E

Controlled hydrolysis of **6** yielded two isomeric monohydroxy ester lactones $C_{19}H_{26}O_6$ (**8a** and **8b**) and a small amount of a diol $C_{15}H_{22}O_5$ (**9a**). The nmr spectrum of **8b** indicated disappearance of the acetyl function; simultaneously the signal corresponding to H_k had moved upfield. On the other hand, the two superimposed methyl doublets of the isobutyryl group were still in evidence and the chemical shifts of H_d and H_g had remained unaltered. Acetyla-

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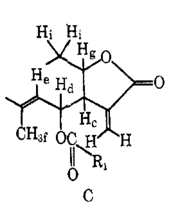
[8] In **3**, $J_{5,6}$ = 0, thus giving rise to a singlet for H-5.

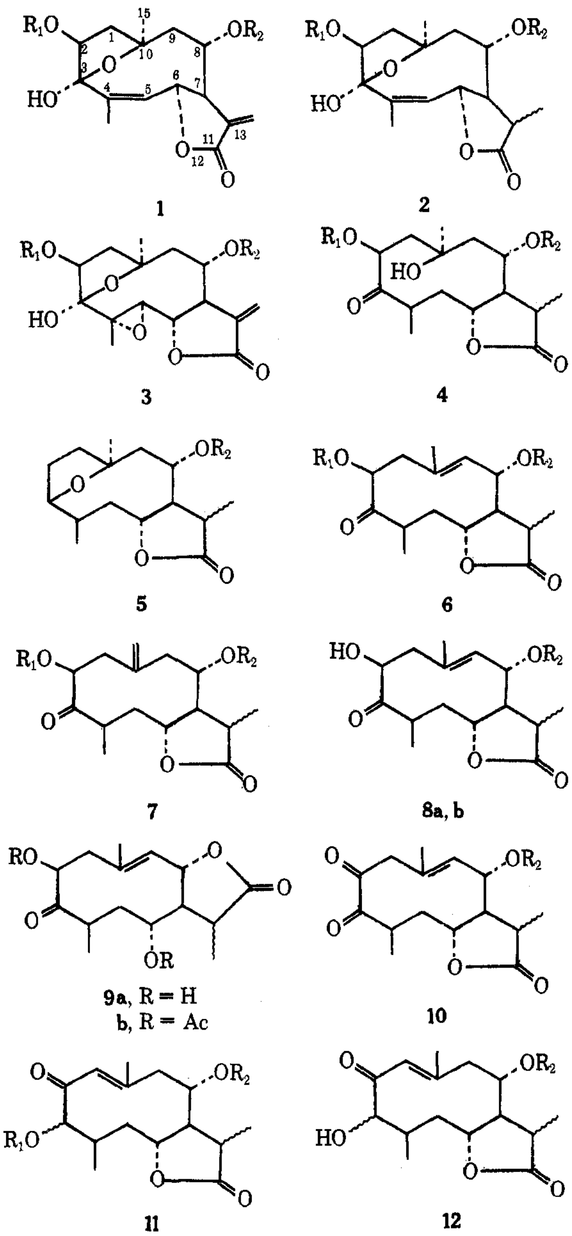
[9] In the interest of clarity, the results are discussed in terms of structure B, although at this point the alternative partial structure C could not yet be excluded.



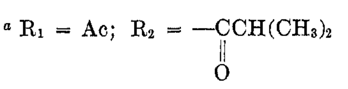
C

[10] The possibility that ketone functions were responsible for the two carbonyl bands was excluded by the lack of appropriate n,π* transitions in the uv and CD curves.

CHART I[a]



[a] R_1 = Ac; R_2 =


$R_2 = -\overset{\displaystyle O}{\underset{}{}}\!\!\!\!\!\! \; \mathrm{C}(=\mathrm{O})\mathrm{CH}(\mathrm{CH_3})_2$

tion of **8b** regenerated **6**[11a] thus ruling out the absence of a rearrangement during the partial hydrolysis of **6** to **8b**. Hence R_1 is isobutyryl and R_2 is acetyl.

Compound **8b** gave a positive α-ketol test with Benedict's reagent and could be oxidized to an unconjugated α diketone **10**. Since **6** was recovered unchanged or prolonged treatment with basic alumina,[11b] formula E for **6** was ruled out and formula D for **6** (R_1 = isobutyryl; R_2 = acetyl) and hence **1** for woodhousin was established, pending definition of the lactone ring orientation[9] (*vide infra*). This formula also explains the observation that catalytic hydrogenation of **1** with platinum oxide–acetic acid–perchloric acid is accompanied by hydrogenolysis of the acetate function to **5**.

The nmr spectrum of the isomeric anhydro derivative **7** contained no vinyl methyl resonance but had two additional signals in the low-field region characteristic of an exocyclic methylene group (see Table I). Treatment of **7** with basic alumina gave an α,β-unsaturated ketone **11** [$\lambda_{\max}$ 235 nm (ϵ 9850)] whose nmr spectrum (Table I) had signals consonant with the proposed formula. The formation of this compound requires migration of the acetate function from C-2 to C-3 under basic conditions.[12] Controlled hydrolysis of **7** afforded, again with rearrangement, an α,β-unsaturated ketol **12** [$\lambda_{\max}$ 243 nm (ϵ 6300)] which gave a positive Benedict's test and retained the isobutyryl function at C-8 (nmr spectrum).

We now turn to the question of lactone ring orientation.[13] This was settled by studying the catalytic hydrogenation of **6**. Use of platinum oxide in acetic acid–perchloric acid resulted not only in the production of **13** by saturation of the double bond but was also accompanied by hydrogenolysis and formation of **14**. Disappearance of the isobutyrate function under these conditions showed that it was attached to C-8 and that the lactone ring of woodhousin had to be closed to C-6. Hence woodhousin is correctly represented as **1** (exclusive of stereochemistry).

The ir spectrum of diol **9a** displayed only two carbonyl bands at 1764 and 1708 cm^{-1}, indicating loss of both side chains. This was confirmed by the nmr spectrum. Acetylation of **9a** gave a diacetate **9b**; comparison of the nmr spectra of **9a** and **9b** (Table I) indicated that a doublet of doublets at 5.28 ppm had to be associated with the proton under the lactone ether oxygen. Multiplicity and chemical shift required that this be assigned to H-8, *i.e.*, that complete hydrolysis of **6** to **9a** was accompanied by lactone ring reorientation from C-6 to C-8. The implications of this finding will be considered subsequently.

Lastly we consider the stereochemistry of woodhousin. In the nmr spectra of **1**, **2**, and **3**, the signal corresponding to H-7 has an abnormally low chemical shift (4.06 ppm) which indicated that H-7 is close to the oxygen of the tetrahydrofuran ring. If the usual assumption is made that the C-7 side chain is β and equatorial as in all sesquiterpene lactones of authenticated stereochemistry, this proximity requires, as is seen by construction of Dreiding models, α-oriented

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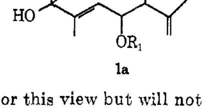
[11] (a) Because of the similarity of the nmr spectra, we assume that **8a** and **8b** are C-11 epimers. The only significant difference in the nmr spectra is the chemical shift of H-9 (see Table I). (b) Under these conditions a β-acyloxy ketone is generally transformed to an α,β-unsaturated ketone.

[12] For analogous isomerizations of steroidal and triterpenoid α-acetoxy ketones, see L. F. Fieser and R. Stevenson, *J. Amer. Chem. Soc.*, **76**, 1728 (1954); N. S. Leeds, D. K. Fukushima, and T. F. Gallagher, *ibid.*, **76**, 2943 (1954); H. Henbest, D. N. Jones, and G. P. Slater, *J. Chem. Soc.*, 4442 (1961); D. Lavie, E. Glotter, and Y. Shvo, *Tetrahedron*, **19**, 1377 (1963); A. Lablache-Combier, B. Lacoume, and J. Levisalles, *Bull. Soc. Chim. Fr.*, 897 (1966); A. D. Boul, P. M. Fairweather, J. M. Hall, and G. D. Meakins, *J. Chem. Soc. C*, 1199 (1971).

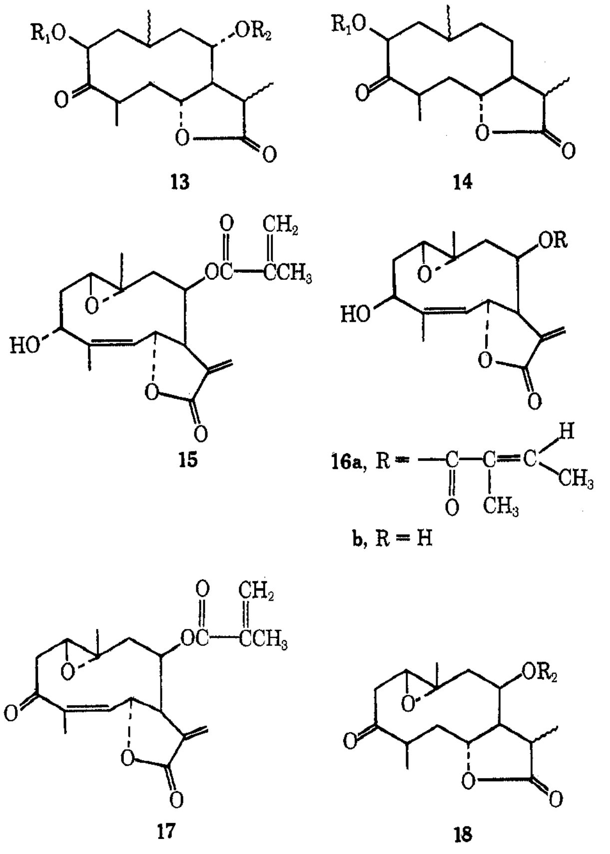
[13] On the basis of our experience with germacranolides, it seemed logical to associate the signal near 4–4.5 ppm in the nmr spectra of **6**, **7**, **8b**, **10**, **11**, and **12** with the proton under the lactone function (H$_d$) rather than with H$_g$, the latter being associated with the doublet of doublets or broad triplet at lower field. This would lead to formula **1** for woodhousin in preference to **1a**. Extensive decoupling experiments on **12** and related compounds provided confirmation for this view but will not be detailed here because the formation of **14** from **6** furnished decisive chemical evidence in favor of **1**.


1a

3-hydroxyl and C-10 methyl groups and incorporation of a cisoid C-4–C-5 double bond.[14] An attempt to provide more positive evidence for the latter point by means of showing the existence of a nuclear Overhauser effect in **1** or **2** failed because H-5 was not sufficiently differentiated from the other low-field protons.[15]

Values of $J_{4,5}$, $J_{5,6}$, $J_{6,7}$, and $J_{8,9}$ given in Table I did not permit a unique assignment of stereochemistry to the centers at C-6 and C-8. However, a comparison of **12** with a substance **18** prepared from erioflorin (**15**)[17] *via* **17** (Chart II) proved instructive.

CHART II[a]

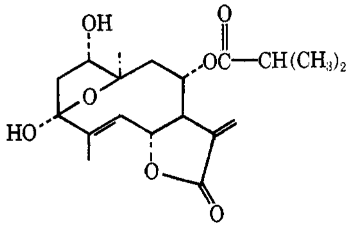


$^{a}R_1 = \mathrm{Ac};\ R_2 = -\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH(CH_3)_2}$

Inspection of models indicated that, if the configurations of **12** and **18** at C-6 were identical, the conformations of **12** and **18** should be almost the same. In fact, coupling constants and chemical shifts of H-6 in **12** and **18** were very similar, thus leading to the conclusion that H-6 in **12** and in woodhousin is also β. On the other hand, $J_{7,8}$ and $J_{8,9}$ in **12** and **18** differed considerably, an observation which suggested that H-8 of woodhousin was β instead of α as in erioflorin. This deduction is substantiated by the formation of **9a** during the hydrolysis of **6** since it has been shown[18] that germacranolides containing α-oriented lactonizable groups at C-6 and C-8 preferentially lactonize toward C-8.[19]

A clue to the stereochemistry at C-2 is furnished by the nmr spectrum of **3** which exhibits the H-2 resonance as a slightly broadened doublet ($J_{1a,2} = 5.3$ Hz, $J_{1b,2} < 1$ Hz). This is only possible if H-2 is α or pseudoaxial (model). Our failure to effect facile elimination of the β-oriented oxygen function at C-2 is in accord with this inference.

The complete structure and stereochemistry deduced for woodhousin (Figure 1) is identical at the relevant centers C-1, C-4, C-6, C-7, C-8, and C-10, with that recently proposed for orizabin (**19**)[20] by correlation through ciliarin (**20**)[21] with zexbrevin (most probable structure[22] **21**). The correspondence in all significant detail between the nmr spectra of woodhousin and orizabin[20] provides additional support for the proposed identical stereochemistry as do the CD curves (Figure 2) which are very similar.[23,25] The correspondence of physical properties also requires that orizabin and ciliarin be reformulated as Δ^4-*cis*-germacranolides if our



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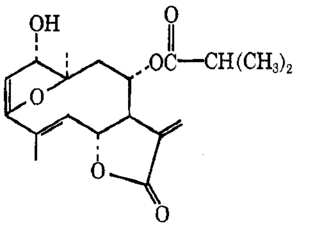

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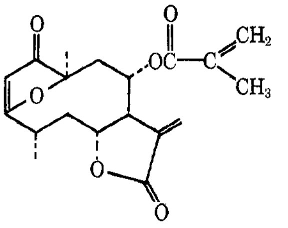

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(14) Construction of a Dreiding model containing a trans C-4–C-5 double bond proved impossible.

(15) Woodhousin would not be the first germacranolide with a cis C-4–C-5 double bond. Professor D. Rogers of Imperial College, London, has drawn our attention to the fact that the constitutional formula (C-4–C-5 bond trans) given for heliangine by N. Nishikawa, K. Kamiya, A. Takabatake, H. Oshio, Y. Tomiie, and I. Nitta, *Tetrahedron*, **22**, 3601 (1966), is in error since the pictorial representation and the coordinate list in the paper by the Japanese authors indicate the presence of a cis C-4–C-5 bond. Hence, erioflorin[16] (**15**), which has been correlated with heliangin (now written as **16a**) without saturating the double bonds also possesses a cis C-4–C-5 double bond.

(16) S. J. Torrance, T. A. Geissman, and M. R. Chedekel, *Phytochemistry*, **8**, 2381 (1969).

(17) We wish to thank Professor T. A. Geissman for a generous sample of erioflorin.

(18) H. Yoshioka, W. Renold, and T. J. Mabry, *Chem. Commun.*, 148 (1970).

(19) The nmr spectrum of **17** also provides convincing evidence for the cis arrangement of the C-4–C-5 double bond in erioflorin. In the Dreiding model of **17** with a trans Δ^4 bond, the H-6–H-7 dihedral angle is approximately 160°, which is much too large for the observed value (1.7 Hz) of $J_{6,7}$. By contrast, the H-6–H-7 dihedral angle in the model with a cis Δ^4 bond is ~100°, which is in excellent agreement with the observed coupling constant.

(20) A. Ortega, C. Guerrero, A. R. de Vivar, J. Romo, and A. Palafox, *Rev. Latinoamer. Quim.*, **2**, 38 (1971).

(21) A. Ortega, A. Romo de Vivar, E. Diaz, and J. Romo, *ibid.*, **1**, 81 (1970).

(22) A. Romo de Vivar, C. Guerrero, E. Diaz, and A. Ortega, *Tetrahedron*, **26**, 1657 (1970).

(23) The observed positive Cotton effect due to the lactone n,π* transition is at variance with the negative Cotton effect predicted on the basis of a recently formulated rule[24] for germacranolides whose lactone ring is transfused and closed toward C-6. However, it should be noted that heliangenol (**16b**, stereochemistry authenticated by X-ray analysis) also exhibits[24] a positive Cotton effect. Obviously, dissymmetry effects are altered by introduction of a cis C-4–C-5 double bond.

(24) W. Stöcklin, T. G. Waddell, and T. A. Geissman, *Tetrahedron*, **26**, 2397 (1970).

(25) We are grateful to Dr. A. Romo de Vivar for a sample of orizabin.

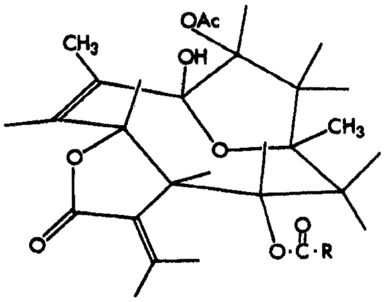

Figure 1.—Model of woodhousin.

conclusions concerning the Δ^4 double bond of woodhousin are correct.

Extraction of *Bahia dissecta* (Gray) Britton followed by extensive chromatography did not result in isolation of homogeneous sesquiterpene lactone fractions.

Experimental Section[26]

Isolation of Woodhousin and Jaceidin.—Finely ground *Bahia woodhousei* (Gray) Gray, wt 1.2 kg, collected by Mr. R. Barr on Sept 16, 1963, along U. S. 60 near Vernon, Apache Co., Arizona (Barr No. 63-467, on deposit in herbarium of Florida State University), was extracted with chloroform and worked up in the usual manner.[27] The crude gum, wt 14 g, was chromatographed over 200 g of silicic acid (Mallinckrodt, 100 mesh), 300-ml fractions being collected in the following order: 1–10 (benzene), 11–20 (benzene–$CHCl_3$, 3:1), 21–30 (benzene–$CHCl_3$, 1:1), 31–40 (benzene–$CHCl_3$, 1:3), 41–50 ($CHCl_3$), 51–59 ($CHCl_3$–CH_3OH, 97:3), 60–69 ($CHCl_3$–CH_3OH, 19:1), 70–75 ($CHCl_3$–CH_3OH, 9:1). All fractions were monitored by tlc. Fractions 21–26 which showed a major spot on tlc were combined and recrystallized from ethyl acetate–hexane to give pure woodhousin, wt 1.98 g, which melted at 183–184.5°: $[\alpha]_D$ −206.3° (*c* 4.26); uv end absorption 207 nm (ϵ 19,000); ir bands at 3570, 3440, 1765, 1750, 1730, 1662, and 1665 cm^{-1}.

Anal. Calcd for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91; O, 31.34; mol wt, 408.1784. Found: C, 62.18; H, 6.91; O, 31.29; mol wt (mass spectrum), 408.1772.

Fractions 28–29 gave jaceidin which was recrystallized from methanol and then melted at 127–135° (lit.[5] 127–133°): wt 0.26 g; nmr spectrum identical with reported[7] spectrum; ir and uv (ethanol, ethanol–sodium acetate, aluminum chloride, sodium methoxide) superimposable on spectra of an authentic specimen;[28] mixture melting point undepressed.

Anal. Calcd for $C_{18}H_{16}O_8 \cdot H_2O$: C, 57.14; H, 4.80; O, 38.06. Found: C, 57.23; H, 4.71; O, 38.07.

Dihydrowoodhousin (2).—To a solution of 0.115 g of **1** in 8 ml of methanol was added with stirring 0.080 g of $NaBH_4$ in 2 ml of methanol at 0°. Stirring was continued for 1 hr at 0°. The solution was acidified, evaporated at reduced pressure, diluted with 10 ml of water, and extracted with chloroform. The washed and dried extract was evaporated and the residue (**2**) was recrystallized from ethyl acetate–hexane: yield 75 mg; mp 156–159°; ir bands at 3578, 3450, 1765, 1750, and 1728 cm^{-1}.

Anal. Calcd for $C_{21}H_{30}O_8$: C, 61.45; H, 7.37; O, 31.18. Found: C, 61.21; H, 7.43; O, 30.57.

Epoxywoodhousin (3).—A solution of 88 mg of **1** in 4 ml of dry chloroform was allowed to stand with 44 mg of *m*-chloroperbenzoic acid overnight at 0°. The reaction mixture was diluted with chloroform, washed, dried, and evaporated. The residue was recrystallized from ethyl acetate–hexane: yield 58 mg; mp 198–201°; ir bands at 3560, 3440, 1775, 1755, 1730, and 1660 cm^{-1}.

Anal. Calcd for $C_{21}H_{28}O_9$: C, 59.43; H, 6.65; O, 33.92. Found: C, 59.31; H, 6.68; O, 34.38.

Tetrahydrowoodhousin (4).—A solution of 0.586 g of **1** in 40 ml of ethyl acetate was reduced at atmospheric pressure with 0.76 g of prereduced 5% $Pd/BaSO_4$ for 5 hr. The filtered solution was evaporated and the residue purified by preparative tlc. The product was recrystallized from ethyl acetate: yield 0.430 g; mp 181–183°; $[\alpha]^{27}_D$ −35.5° (*c* 1.417); CD curve λ_{max} 288 nm (θ +8051); ir bands (KBr) at 3432, 1775, 1735, 1728, and 1710 cm^{-1}.

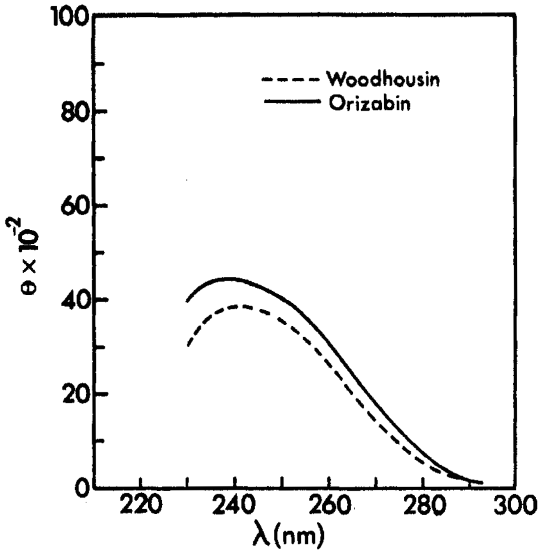

Figure 2.—CD curves.

Anal. Calcd for $C_{21}H_{32}O_8$: C, 61.15; H, 7.82; O, 31.03. Found: C, 61.53; H, 7.86; O, 30.81.

2-Deacetoxy-3-dehydroxytetrahydrowoodhousin (5).—A solution of 0.13 g of **1** in 5 ml of acetic acid containing 2 drops of perchloric acid was stirred with 40 mg of platinum oxide in a hydrogen atmosphere for 4 hr, filtered, and evaporated. The residue was subjected to preparative tlc. The major fraction was recrystallized from ethyl acetate–hexane: yield 80 mg; mp 99–101°; ir bands at 1770 and 1725 cm^{-1}; no CD absorption.

Anal. Calcd for $C_{19}H_{30}O_5$: C, 67.43; H, 8.93; O, 23.64. Found: C, 67.18; H, 8.92; O, 23.69.

Anhydrotetrahydrowoodhousin (6 and 7).—To a solution of 0.374 g of **4** in 5 ml of pyridine was added with stirring 0.8 ml of thionyl chloride at 0°. Stirring was continued at this temperature for 15 min. Excess thionyl chloride was decomposed with ice water and the mixture was extracted with chloroform. The washed and dried extract was evaporated and the residue was purified by preparative tlc. Fraction 1 gave 0.126 g of **6** and fraction 2 gave 0.120 g of **7**; 0.096 g of starting material was recovered. Recrystallization of **6** from ethyl acetate–hexane afforded material which melted at 164–166°: $[\alpha]^{24}_D$ +206.8 (*c* 2.05); CD curve λ_{max} 284 nm (θ +11660); ir bands at 1770, 1750, 1728 (double intensity), and 1656 cm^{-1}.

Anal. Calcd for $C_{21}H_{30}O_7$: C, 63.94; H, 7.69; O, 28.39. Found: C, 64.26; H, 7.58; O, 28.31.

7 was a gum and had ir bands at 1770, 1763, 1740, 1722, and 1639 cm^{-1}; CD curve λ_{max} 290 nm (θ +11030).

Anal. Calcd for $C_{21}H_{30}O_7$: C, 63.94; H, 7.69; O, 28.30. Found: C, 64.04; H, 7.85; O, 28.43.

Hydrolysis of 6. A.—A solution of 100 mg of **6** in 4 ml of 80% aqueous methanol containing 40 mg of potassium carbonate was stirred at room temperature for 40 min (nitrogen atmosphere). The solvents were removed, water was added, and the mixture was thoroughly extracted with chloroform. The washed and dried extract was evaporated and the residue was subjected to preparative tlc. The least polar fraction (**8a**) was recrystallized from ethyl acetate–hexane and melted at 165–169°: yield 8 mg; ir bands at 3470, 1770, 1723, 1709, and 1653 cm^{-1}; positive Benedict's test.

Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01; O, 27.24. Found: C, 64.91; H, 8.21; O, 27.09.

A second fraction (**8b**) was recrystallized from ethyl acetate–hexane and melted at 124–126°: yield 8 mg; ir bands at 3470, 1770, 1723, 1710, and 1656 cm^{-1}; positive Benedict's test.

Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01; O, 27.24. Found: C, 64.97; H, 7.88; O, 26.89.

The most polar fraction **9a** was recrystallized from ethyl acetate–hexane and melted at 201–204°: yield 5 mg; ir bands at 3470, 1764, 1708, and 1660 cm^{-1}; positive Benedict's test; mol

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[26] Experimental conditions specified by W. Herz, S. V. Bhat, and A. L. Hall, *J. Org. Chem.*, **35**, 1110 (1970), apply. High-resolution mass spectra were run at 70 MeV on a MS-9 high-resolution mass spectrometer.

[27] W. Herz and G. Högenauer, *ibid.*, **27**, 905 (1962).

[28] We wish to thank Professor H. Wagner for a sample of jaceidin.

wt (mass spectrometry), 282.1462 (calcd for $C_{15}H_{22}O_5$, 282.1466). There was insufficient material for an elementary analysis. Acidification of the aqueous layer, from the original extraction, followed by extraction with chloroform and the usual work-up gave an additional 20 mg of **8b**, mp 118–120°.

B.—A solution of 50 mg of **6**, 30 mg of sodium bicarbonate, and 10 ml of 80% aqueous methanol was stirred at room temperature for 8 hr. The solvent was removed at reduced pressure and the residue was subjected to preparative tlc after the usual work-up. The major fraction was recrystallized from ethyl acetate–hexane, melted at 124–126°, yield 15 mg, and was identified as **8b**.

Acetylation of 8b.—A solution of 15 mg of **8b** in 1 ml of pyridine and 0.5 ml of acetic anhydride was left overnight at room temperature and then worked up in the usual way. Recrystallization from ethyl acetate–hexane gave 10 mg of **6**: mp 164–166°; mixture melting point undepressed; nmr and ir spectra superimposable on that of an authentic sample.

Acetylation of 9a.—**9a** (4 mg), 0.1 ml of acetic anhydride, and 0.15 ml of pyridine was allowed to stand overnight and worked up in the usual manner. The residue was a gum (**9b**): wt 4 mg; nmr spectrum (see Table I); mol wt (mass spectrum), 366.1668 (calcd for $C_{19}H_{26}O_7$, 366.1677).

Oxidation of 8b.—A solution of 20 mg of **8b** in acetone containing a few drops of Jones reagent was stirred at 0° for 0.5 hr. Excess reagent was destroyed by addition of methanol and solvents were removed at reduced pressure. The residue **10** was purified by preparative tlc but remained a gum and had ir bands at 1775, 1724, 1708, and 1658 cm^{-1}.

Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48; O, 27.40. Found: C, 64.48; H, 7.46; O, 27.61.

Isomerization of 7.—A solution of 0.5 g of **7** in benzene was placed on a column of 5 g of basic alumina and left overnight. Elution with chloroform gave 0.35 g of gum (**11**) which had ir bands at 1770, 1735, 1728, 1700, and 1633 cm^{-1}; λ_{max} 235 nm (ϵ 9850); mol wt (mass spectrum), 394.2006 (calcd for $C_{21}H_{30}O_7$, 394.1990).

Hydrolysis of 7.—A solution of 99 mg of **7** in 4 ml of 80% aqueous methanol was hydrolyzed in the same manner as **6**. The crude product was purified by preparative tlc. Fraction 1, 20 mg, was a gum which had ir bands at 1775, 1725, 1638, and 1629 cm^{-1}; λ_{max} 237 nm (ϵ 7700). Fraction 2 was a solid (**12**) and was recrystallized from ethyl acetate–hexane: mp 169–172°; yield 35 mg; ir bands at 3480, 1768, 1728, 1680, and 1637 cm^{-1}; λ_{max} 243 nm (ϵ 6300).

Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01; O, 27.24; mol wt, 352.1884. Found: C, 64.42; H, 7.98; O, 27.31; mol wt, 352.1896.

Preparation of 13 and 14.—A solution of 80 mg of **6** in 7 ml of acetic acid containing 2 drops of perchloric acid was stirred with 40 mg of platinum oxide for 5 hr. Work-up as described for **5** and preparative tlc gave two fractions. Fraction 1 (**14**) was recrystallized from ethyl acetate–hexane: yield 8 mg; mp 172–175°; ir bands at 1762 and 1723 cm^{-1}.

Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44; O, 25.77; mol wt, 310.1779. Found: C, 64.96; H, 8.12; O, 26.20; mol wt (mass spectrum), 310.1824.

Fraction 2 (**13**) was recrystallized from ethyl acetate–hexane: yield 41 mg; mp 196–198°; ir bands at 1765 and 1723 cm^{-1} (double intensity).

Anal. Calcd for $C_{21}H_{32}O_7$: C, 63.62; H, 8.14; O, 28.25. Found: C, 63.78; H, 8.52; O, 28.02.

Oxidation of Erioflorin.—A solution of 0.190 g of erioflorin (**15**) in 10 ml of acetone was mixed with 0.2 ml of Jones reagent and stirred at room temperature for 10 min. Excess reagent was destroyed by addition of methanol, the solvent removed *in vacuo*, the residue diluted with water and extracted with chloroform. The washed and dried chloroform extract was evaporated and the residue was recrystallized from ethyl acetate–hexane. The yield of **17** was 0.165 g: mp 169–172°; ir bands at 1763, 1718, 1705, 1662, and 1630 cm^{-1}. The analysis was not satisfactory, mol wt (mass spectrum), 346.1548 (calcd for $C_{19}H_{22}O_6$, 346.1530).

Hydrogenation of 17.—A solution of 0.052 g of **17** in 25 ml of ethyl acetate was hydrogenated with 0.54 g of 5% $Pd/BaSO_4$ for 4 hr at atmospheric pressure. Filtration and evaporation gave a solid (**18**) which was recrystallized from ethyl acetate–hexane: yield 0.039 g; mp 183–186°; ir bands at 1770, 1775, and 1720 cm^{-1}; CD curve λ_{max} 285 nm (θ +6390) (c 0.29 mg/ml).

Anal. Calcd for $C_{19}H_{28}O_6$: C, 64.75; H, 8.01; O, 27.24. Found: C, 64.88; H, 7.87; O, 27.48.

Extraction of *Bahia dissecta*.—Finely ground *Bahia dissecta* (Gray) Britton, wt 0.75 kg, collected by Mr. R. Barr on Sept 17, 1963, at Big Lake 10 miles south of Eager, Apache Co., Arizona (Barr No. 63-477, on deposit in herbarium of Florida State University), was extracted with chloroform and worked up in the usual way. The crude gum, wt 12 g, was chromatographed over 200 g of silicic acid as described for the extract of *B. woodhousei*, the eluate being monitored by tlc. All fractions showed several spots on tlc.

Registry No.—**1**, 33143-54-3; **2**, 33143-55-4; **3**, 33143-56-5; **4**, 33143-57-6; **5**, 33143-58-7; **6**, 33143-59-8; **7**, 33143-60-1; **8a**, 33143-61-2; **8b**, 33143-62-3; **9a**, 33143-63-4; **9b**, 33143-64-5; **10**, 33143-65-6; **11**, 33143-66-7; **12**, 33143-67-8; **13**, 33143-68-9; **14**, 33143-69-0; **17**, 33143-70-3; **18**, 33143-71-4.

Notes

A New Etherification Method

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While carrying out research on phosphorus-bearing steroids,[1] we found that the presence of catalytic amounts of acid, in a solution of a steroidal alcohol in dialkyl phosphite, caused the unexpected formation of the corresponding ether. In the absence of acid, the mixed steroidal alkyl phosphite, whose formation can be easily explained, is the main product. Thus, if cholesterol (**1**) is heated for several hours in $HOP(OCH_3)_2$, cholesteryl methyl phosphite (**2**) is the main product. The structure of compound **2** is unequivocally deduced from its nmr spectrum [δ 3.74 d, J = 12 Hz, $P(O)(OCH_3)$; 6.81 d, J = 696 Hz, P(O)H; and 4.24 m, C-3α H], mass spectrum [m/e 386 (100%), $M\cdot^+ - P(O)(OCH_3)$; 368 (57%), $M\cdot^+ - HOP(O)(OCH_3)H$ ("McLafferty" rearrangement); and 353 (29%), $M\cdot^+ - 96 - CH_3\cdot$], ir, and elemental analysis (see Experimental Section). If, on the other hand, p-TsOH (or some other acid) is present in the dimethyl phosphite solution, 3β-methoxycholest-5-ene (**3**)[2] is the

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[1] Y. Kashman and M. Sprecher, *Tetrahedron*, **27**, 1331 (1971).

[2] E. Müller and I. Page, *J. Biol. Chem.*, **101**, 127 (1933).