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REACTION OF THE MOLLUSCICIDE GLAUCOLIDE B WITH BENTONITE[1]

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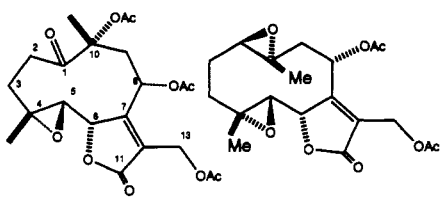
ABSTRACT.—Glaucolide B [**1**] was transformed, under bentonite earth/EtOAc conditions, into compound **3** ([1*R*,4*S*,5*R*,6*S*,8*S*,10*R*]-8,10,13-triacetoxy-1(4)-epoxy-1,5-dihydroxygermacr-7(11)-en-6(12)-olide. The structures of compound **3** and of its derivatives **4** and **5** were established by nmr spectroscopy.

Vernonia species investigated so far contain 13-*O*-acyl sesquiterpene lactones, mainly glaucolides (1), although the structurally related hirsutinolides (2), cadinanolides (3), and vernomargolides (4,5) have also been found in this genus. Some of these compounds have been obtained from glaucolides by acid catalysis (4) or in the presence of Si gel (3,6). These observations have generated doubt about the natural occurrence of some compounds. This paper describes the isolation of glaucolide B [**1**], an antimicrobial and molluscicidal component of many *Vernonia* species (7), from *Vernonia paniculata* (DC.) Gleason (Asteraceae) and its transformation into compound **3**. This transformation was promoted by bentonite earth, which has been used for the opening and rearrangement of natural products containing epoxides (8,9).

The petroleum ether extract of *Vernonia paniculata* contained two main compounds. The major constituent was identified as glaucolide B [**1**] (10) and the minor one as diepoxide **2** (11). Purification of these compounds by cc on bentonite earth using EtOAc as the eluent resulted in the isolation of compound **3**, which was not found in the original extract. Treatment of an EtOAc solution of pure **1** with bentonite also yielded **3**, as the only product.

Elemental analysis and the ms of compound **3** suggested the molecular formula, $C_{21}H_{28}O_{11}$. Its ir spectrum showed absorptions for hydroxyl, α,β-unsaturated-γ-lactone, and ester groups. The ^{1}H- and ^{13}C-nmr spectra revealed that the keto and epoxy functions of the starting material [**1**] were absent in **3**. Instead, **3** possesses an α-hydroxytetrahydrofuran



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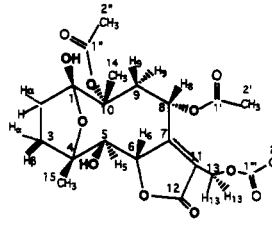

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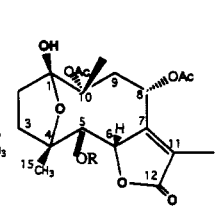

4 R=H
5 R=Ac

[1]Contribution No. 1291 of the Instituto de Química, U.N.A.M.

moiety and a secondary hydroxy group. The former was characterized by the ^{13}C-nmr singlet signals at δ 108.9 and 87.0, attributed to a hemiacetal carbon (C-1) and to a carbon attached to the ethereal oxygen bridge (C-4). The presence of a secondary hydroxyl was inferred from the chemical shift of the doublet at δ 3.52, which is coupled to the signal at δ 5.08 for the proton geminal to the lactone ring (H-6). Therefore, the hydroxy group should be attached to C-5 with a β-orientation in accordance with the observed coupling constant ($J_{5,6}$=9 Hz), indicative of a trans relationship between these protons. This conclusion is supported by the resistance of compound **3** toward dehydration and also by ^{1}H-, ^{13}C-, DEPT, HETCOR, and HMBC (12) nmr experiments, summarized in Tables 1 and 2, which established that the remainder of the molecule stays unchanged. Therefore, structure **3** was proposed.

The relative configuration indicated for **3** was supported by the following nOe enhancements: H-5/H-2, H-3; H-8/H-6, H-14; H-6/H-8, H-15; H-14/H-8, and H-15/H-6.

Hydrogenolysis of compound **3** gave the 13-deacetyloxy derivative **4** as the only product when the reaction was catalyzed by 10% Pd/C. Compound **4** showed a molecular ion by cims at *m/z* 399 in accordance with the proposed structure, which is also supported by the 3H singlet signal at δ 1.91 for the C-13 vinylic methyl. Upon acetylation, compound **4** gave the acetyl derivative **5** whose ^{1}H-nmr spectrum showed signals for three acetate methyl groups, one vinylic methyl group (δ 1.53), and the H-5 signal shifted to lower field.

TABLE 1. ^{13}C- and 2D Nmr Data for **3**.

Carbon	δ (mult.)[a]	^{13}C-^{1}H direct coupling ^{1}J[b]	^{13}C-^{1}H long-range coupling	
			^{2}J	^{3}J
1	108.7 s			3β, 9β, 14
2	34.6 t	[c]		
3	33.9 t	3β[d]		5, 15
4	86.6 s		3β, 5, 15[d]	6[c]
5	76.1 d	5	6	15[c]
6	81.7 d	6		8
7	168.4 s		6, 8	5, 9β, 13, 13′
8	68.4 d	8	9β	
9	42.1 t	9β	8	15
10	87.0 s		9β, 14	8
11	123.2 s		13, 13′	6, 8
12	170.7 s			6, 13, 13′
13	55.8 t	13, 13′		
14	17.4 q	14		9[b]
15	22.0 q	15		5
OAc-8				
1′	169.7 s			
2′	20.6 q	2′	2′	8
OAc-10				
1″	171.4 s			
2″	22.2 q	2″	2″	
OAc-13				
1‴	170.3 s			
2‴	21.0 q	2‴	2‴	13, 13′

[a]δ in ppm; (mult.)=DEPT multiplicity.
[b]XHCORR, HMQC, CHORTLE (PROTON) (12).
[c]Two couplings observed, but proton signal could not be assigned.
[d]Additional coupling observed, but proton signal could not be assigned.

TABLE 2. ^{1}H-Nmr Spectral Data for Compounds **3–5**.

Proton	Compounds		
	3[a]	**4**[b]	**5**[b]
2	2.11 m	2.2 m	2.2 m
2β	2.15 m	2.2 m	2.2 m
3	2.11 m	2.2 m	2.2 m
3β	1.81 m	1.8 m	1.8 m
5	3.52 d (9)	3.49 d (9)	4.85 d (9)
6	5.08 d (9)	4.96 d (9)	5.05 d (9)
8	5.87 t (3)	5.81 dd (8,4)	5.86 d, d (8,4)
9β	2.57 dd (12,3)		2.53 d (4)
9α			
13	4.89 d (16)	1.91 br	1.90 s
13′	4.72 d (16)		
14	1.60 s	1.61 s	1.61 s
15	1.48 s	1.48 s	
OAc	2.02, 2.05, 2.08	2.00, 2.06	2.11, 2.05, 2.01

[a]300 MHz, $CDCl_3$, TMS as internal standard, δ values, *J* values in parentheses.
[b]80 MHz, $CDCl_3$, TMS as internal standard, δ values, *J* values in parentheses.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mps are uncorrected. Ir spectra were recorded in $CHCl_3$ solutions using a Nicolet FT-5X spectrometer. Eims were taken on a Hewlett-Packard 5985-B mass spectrometer at 70 eV. Nmr measurements were performed on either a Varian FT80-A or a Bruker AM-300 spectrometer (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C). The ^{13}C-nmr measurements were acquired with composite-pulse decoupling, namely, the wide-band alternating phase low-power technique for zero-residue splitting (WATZ-16).

PLANT MATERIAL.—Aerial parts of *Vernonia paniculata* (DC.) Gleason were collected near Matatlán, Oaxaca, México, during August 1991. Herbarium specimens (MEXU-262818) were deposited at the Herbarium of the Instituto de Biología, UNAM.

EXTRACTION AND ISOLATION.—Aerial parts of the plant (500 g) were extracted with petroleum ether at room temperature. After solvent evaporation, 40 g of extract were obtained. Tlc of this extract revealed the presence of two main components. After prep. tlc of 80 mg of the extract (Si gel, petroleum ether-EtOAc, 9:1) glaucolide B [**1**] (R_f 0.4; 40 mg) and compound **2** (R_f 0.3; 12 mg) were isolated. Both compounds displayed spectroscopic data in accordance with those previously reported (10,11).

Compound **3**.—(a) A $CHCl_3$ solution of the original extract (10 g) was percolated through a column of bentonite earth ("Tonsil") (200 g) (8) first with $CHCl_3$ and then with EtOAc. Fractions eluted with EtOAc contained compound **3** (5.9 g), which was purified by crystallization from Me_2CO/petroleum ether. (b) An EtOAc solution of glaucolide B [**1**] (98 mg) was quantitatively transformed into **3** when it was percolated through a column of bentonite. Compound **3**: mp 140–142°; ir ($CHCl_3$) ν max 3600, 3450, 1770, 1230 cm^{-1}; cims *m/z* 457 $[M+1]^+$; *anal.*, calcd for $C_{21}H_{28}O_{11}$, C 55.26, H 6.18, found C 55.59, H 6.03; ^{13}C-nmr data, see Table 1; ^{1}H-nmr data, see Table 2.

Compound **4**.—An EtOH solution of compound **3** (200 mg) was hydrogenated with 10% Pd/C (22 mg). The suspension was stirred for 2 h, filtered, and solvent removed *in vacuo*. The resulting residue was purified by successive crystallizations from Me_2CO/petroleum ether to yield 189 mg of compound **4**: mp 95–97°; ir ($CHCl_3$) ν max 3600, 3400, 1750 cm^{-1}; cims *m/z* 399 $[M+1]^+$ (100), 381 (42), 339 (80), 321 (85); ^{1}H-nmr data, see Table 2.

Compound **5**.—A solution of compound **4** (97.3 mg) in pyridine (1 ml) and Ac_2O (1 ml) was

left to stand until completion and worked up as usual to obtain, after crystallization from Me_2CO/petroleum ether, 87.8 mg of compound **5**: mp 65–67°; ir ($CHCl_3$) ν max 3400, 1760, 1740 cm^{-1}; cims *m/z* 441 $[M+1]^+$ (13), 423 (44), 381 (100), 363 (24), 321 (85); ^{1}H-nmr data, see Table 2.

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