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10-EPIDEOXYCUMAMBRIN B AND OTHER CONSTITUENTS OF *STEVIA YACONENSIS* VAR. *SUBEGLANDULOSA*

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Key Word Index—*Stevia yaconensis* var. *subeglandulosa*; Eupatorieae; Compositae; guaianolides; sesquiterpene lactones; X-ray analysis.

Abstract—The aerial parts of *Stevia yaconensis* var. *subeglandulosa* afforded in addition to the known guaianolides ludartin and dehydroleucodin a new guaianolide 10-*epi*-8-deoxycumambrin B whose relative and absolute configurations were established by X-ray crystallography. Chemical transformations of ludartin established its relative and absolute stereochemistry.

INTRODUCTION

Approximately 40 species of the large New World genus *Stevia* (Compositae, tribe Eupatorieae, subtribe Ageratinae [1]) have been studied chemically. Since our most recent summary [2], sesquiterpenes—primarily longipinene derivatives, sesquiterpene lactones of various types and diterpenes of the labdane and kaurane class have been reported from 15 *Stevia* taxa [3–12]. In the present article we describe isolation of the guaianolides ludartin (**1**), 10-epi-8-deoxycumambrin B (**2**) and dehydroleucodin (**4**) from *Stevia yaconensis* Hieron. var. *subeglandulosa*, a taxon limited to northwestern Argentina and possibly parts of Bolivia [13]. Very recently Zdero, Bohlmann and coworkers [12] have obtained two isomers of **1** and **4**, i.e. the guaianolides **10** (estafietin) and **11**, as well as costunolide and several longipinene derivatives from Bolivian *S. yaconensis*.

RESULTS AND DISCUSSION

Ludartin, the major sesquiterpene lactone constituent of our collection of *S. yaconensis* var. *subeglandulosa*, does not seem to have been adequately characterized. It was first isolated in admixture with an 11,13-dihydro derivative from *Artemisia carruthii* by Geissman and Griffin [14] who proposed the stereochemistry shown in formula **1** because of the chemical shift and coupling constants of H-6 and the chemical shift of H-15 in the ^{1}H NMR spectrum of the mixture. We have since pointed out [15] that the chemical shift of H-6 alone is not a good criterion for assigning 3,4-epoxyguaianolide stereochemistry unless both α- and β-epoxides are available for comparison (see also ref. [16]). Subsequent references to ludartin appear to be limited to its detection in minimal amount in *Artemisia sieversiana* [17] with no spectroscopic or other data being provided. Our material had mp 85–86° and was available in an amount sufficient to permit chemical correlation with compounds of known stereochemistry.

^{1}H and ^{13}C NMR data in Tables 1 and 2 provide ample evidence for the gross structure of ludartin and the *trans*-fusion of the lactone ring toward C-6. Deoxygenation (Zn-Cu couple) of ludartin with concomitant hydrogenation of the 11,13-double bond produced a diene **5** apparently identical with 11βH,13-dihydrokauniolide from *Kaunia arbuscularis* [18]. Epoxidation of the diene with *m*-chloroperbenzoic acid afforded all four possible monoepoxides which were separated by column chromatography and HPLC.

Properties of the two monoepoxides which retained the 3,4-double bond corresponded to those of arborescin (**8**) [19–24] and 1,10-epiarborescin (**9**) [23], respectively, the differences in the chemical shifts of H-6 (δ 4.00 for **8**, δ 3.77 for **9**) and H-5 (δ 2.82 for **8**, δ 2.52 for **9**) being particularly significant. The relative and absolute configuration of these substances is secure because of their partial synthesis from (−)-santonin [23].

The two remaining monoepoxides had retained the 1,10-double bond. Their ^{1}H NMR spectra again differed from each other chiefly in the chemical shifts of H-5 and H-6, with the α-orientated epoxide of **6** deshielding H-5 (at δ 2.99) but not H-6 (at δ 3.65), whereas the β-orientated epoxide function of **7** deshielded H-6 (now at δ 3.88) but not H-5 (now at δ 2.77). As **6** was also formed more directly by sodium borohydride reduction of ludartin the epoxide ring of ludartin is α-orientated as postulated originally [14] and the absolute configuration is as depicted in formula **1**. The very small positive Cotton effect of ludartin ($\Delta\varepsilon_{268}^{\mathrm{MeOH}}$ + 0.12) provides another example of the occasional violation of the Stöcklin–Waddell–Geissman rule [25].

The ^{1}H and ^{13}C NMR spectra of a second lactone, mp 123–124°, and extensive decoupling which will not be detailed here showed that it was either **2** or **3a**. A lactone of mp 117–119° to which formula **3a** was tentatively assigned by analogy with cumambrin B (**3b**) was first isolated from *Artemisia nova* [26] and subsequently found in *A. frigida* [17], *Pyrethrum pyrethroides* [27] and

Table 1. ^{1}H NMR spectra of compounds **1**, **2**, **3a**, **6** and **7** ($CDCl_3$, 270 MHz)

H	**1**	**1** (C_6D_6)	**2**	**2** ($CDCl_3$-C_6D_6 1:1)	**3a***	**6**	**7**
1	—	—	2.55 *m*	2.25 *m*	2.55 *d*	—	—
2a	2.71 *br d*	2.40 *br d*	2.55 *m*	2.39 *ddd*	2.35 *br d*	2.72 *br d*	2.67 *br d*
2b	2.44 *dquint*	1.90 *br d*	2.48 *m*	2.22 *m*	2.28 *m*	2.45 *dquint*	2.48 *dquint*
3	3.38 *br*	2.96 *br*	5.48 *br s*	5.37 *br s*	5.47 *br s*	3.39 *br s*	3.31 *d*
5	3.09 *br d*	2.75 *br*	2.85 *br t*	2.59 *br t*	2.78 *br t*	2.99 *br d*	2.77 *br d*
6	3.64 *dd*	2.88 *dd*	4.50 *t*	4.33 *t*	4.23 *dd*	3.65 *dd*	3.89 *t*
7	2.77 *m*	1.90 *ddddd*	2.60 *m*	2.25 *m*	3.17 *ddddd*	1.84 *dddd*	1.81 *dddd*
8a	2.12 *m*	1.24 *ddd*	1.95 *m*	1.6 *m*	2.25 *dddd*	1.84 *m*	1.91 *m*
8b	1.30 *ddd*	0.59 *dddd*	1.78 *tt*	1.3 *m*	1.46 *dddd*	1.25 *m*	1.28 *m*
9a	2.25 *br dd*	1.61 *br dd*	~2.1	1.35 *m*	1.96 *dddd*	2.18 *m*	2.12 *m*
9b	2.06 *m*	1.50 *ddd*	~1.7	1.7 *m*	1.70 *m*	2.04 *ddd*	2.13 *m*
11	—	—	—	—		2.22 *dq*	2.25 *dq*
13	6.12 *d*	5.98 *d*	6.16 *d*	6.07 *d*	6.17 *d*	1.23 *d*†	1.23 *d*†
	5.38 *d*	4.15 *d*	5.45 *d*	5.19 *d*	5.44 *d*		
14†	1.66 *br s*	1.34 *br s*	1.30	1.04 *s*	1.19 *s*	1.69 *dd*	1.68 *br s*
15†	1.69 *br s*	1.70 *br s*	1.88 *br s*	1.88 *br s*	1.87 *br s*	1.63 *s*	1.63 *s*

*400 Mz, from [17].

†Intensity 3 protons.

‡Shifted to 1.61 on addition of TAI.

J (Hz): Compound **1**: 2a, 2b = 18; 2a, 3 = 2b, 3 = 2b, 14 = 3, 5 = 3, 15 = 1 − 1.5; 5, 6 = 7, 8b = 11; 6, 7 = 10; 7, 8a < 1; 8a, 8b = 8a, 9a = 8b, 9a = 12; 7, 13a = 3.5; 7, 13b = 3; 8a, 9b = 1.5; compound **2**: 1, 5 = 5, 6 = 6, 7 = 10; 2a, 2b = 17; 2a, 3 = 2b, 3 = 8b, 9 = 2; 3, 5 = 1; 3, 15 = 1.5; 7, 13a = 3.3; 7, 13b = 3; compound **6**: 2a, 2b = 18; 2a, 14 = 1; 2b, 3 = 2b, 14 = 5, 14 = 1.5; 5, 6 = 10; 6, 7 = 9; 7, 11 = 12; 7, 8a or 7, 8b = 3; 8a, 9b = 6; 8b, 9b = 2; 9a, 9b = 14; 11, 13 = 7; compound **7**: same as compound **6** except 5,6 = 6,7 = 10; 2b, 3 = 2; 7, 8a or 7, 8b = 3.

Table 2. ^{13}C NMR spectra of compounds **1**, **2**, **6** and **7** (67.89 MHz, $CDCl_3$)*

C	**1**	**2**	**6**	**7**
1	133.85 *s*‡	48.86 *d*	133.40 *s*‡	133.67 *s*‡
2	33.62 *t*†	33.64 *t*†	33.43 *t*†	34.70 *t*†
3	63.78 *d*	126.06 *d*	63.60 *d*†	64.12 *d*†
4	67.09 *s*	141.70 *s*‡	66.95 *s*	67.40 *s*
5	52.46 *d*†	56.16 *d*†	51.80 *d*†	51.80 *d*†
6	80.72 *d*	84.13 *d*†	80.29 *d*†	82.10 *d*†
7	54.51 *d*	50.52 *d*†	57.61 *d*†	55.23 *d*†
8	25.81 *t*	23.24 *t*	27.37 *t*†	27.01 *t*†
9	33.95 *t*	40.32 *t*	34.21 *t*†	34.70 *t*†
10	134.92 *s*‡	73.61 *s*	134.90 *s*‡	133.89 *s*‡
11	139.44 *s*	140.28 *s*‡	41.16 *d*†	41.50 *d*‡
12	169.5 *s*	170.40 *s*	177.70 *s*	178.03 *s*
13	117.76 *t*	118.68 *t*	12.09 *q*†	12.06 *q*†
14	22.65 *q*†	33.02 *q*†	22.32 *q*†	23.60 *q*
15	19.00 *q*	17.70 *q*†	18.87 *q*†	18.90 *q*†

*Multiplicities established by DEPT pulse sequence.

†Assignment by single frequency heteronuclear decoupling.

‡Assignments may be interchanged.

an *Eriocephalus* species [28] although no further evidence for the originally proposed C-10 configuration was adduced. However, a comparison (see Table 1) of the 400 MHz ^{1}H NMR spectrum of the presumed **3a** from *Artemisia frigida* [17]§ with that of our substance from *S. yaconensis* revealed obvious differences in the chemical shifts of the easily identifiable H-6, H-7 and H-14 signals as well as those of others which are partially obscured such H-2a,b and H-8a,b. In particular the paramagnetic shift of H-6 and the diamagnetic shift of H-7 in the ^{1}H NMR spectrum of our substance could be associated with a change of C-10 stereochemistry from **3a** to **2**.

To verify this conclusion an X-ray analysis of our substance was undertaken. Crystal data are given in the Experimental section. Fig. 1 is a stereoscopic view of the molecule which shows that the hydroxylactone from *S. yaconensis* indeed possesses formula **2** and that the provisional assignment **3a** by Irwin and Geissman [26] for 8-deoxocumambrin B from *A. nova* was correct. A partial listing of torsion angles is given in Table 3; lists of bond lengths, bond angles, all torsion angles, final atomic and final anisotropic thermal parameters are deposited at the Cambridge Crystallographic Data Center. The torsion angles in Table 3 show that the 7-membered ring is a slightly distorted C_s chair with the plane of symmetry passing through C-8 and midway through the C-1, C-5 bond whereas in the somewhat similar bahia 1 (**12**) the seven-membered ring is a twist chair with an axis of symmetry passing through C-8 [29]. The cyclopentene ring is a somewhat distorted flattened envelope ($\Sigma|\omega| = 35°$), flatter than that of **12**, with H-1 as the flap, whereas the α-methylene-γ-lactone ring is significantly puckered ($\Sigma|\omega| = 107°$) and approximates a half chair

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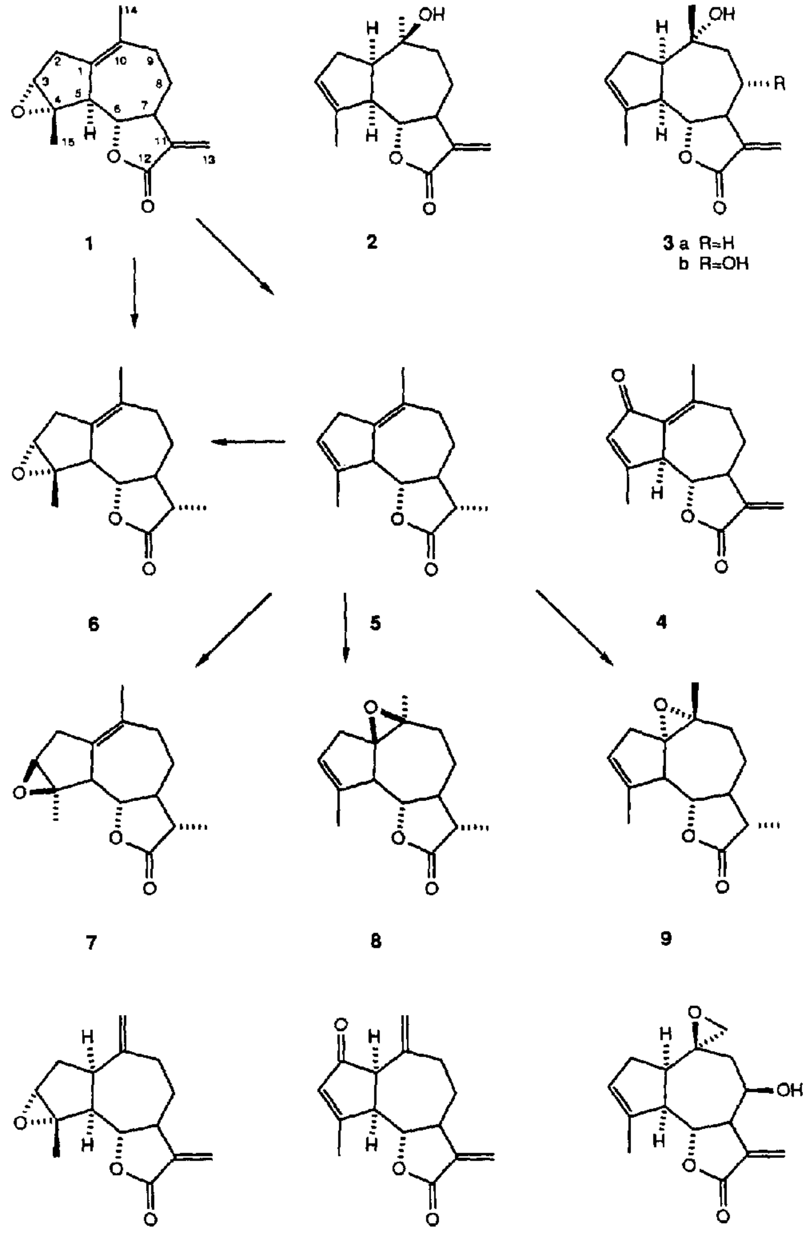
§The material obtained by the German workers [17] from *A. frigida* was noncrystalline, but apparently identical with the solid originally isolated by Irwin and Geissman [26] as indicated by the chemical shifts of H-6 and H-14.



1 2 3 a R=H b R=OH

6 5 4

7 8 9

10 11 12

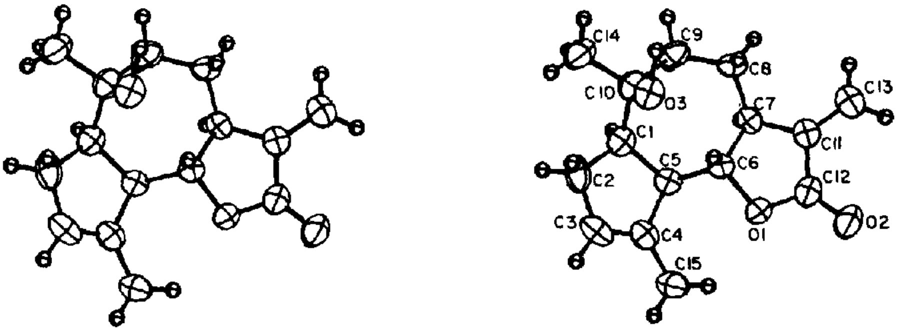


Fig. 1. Stereoscopic view of compound 2.

Table 3. Selected torsion angles (deg) in compound **2** with standard deviation in parentheses

C(1)–C(2)–C(3)–C(4)	7.8 (0.6)
C(2)–C(3)–C(4)–C(5)	−1.1 (0.6)
C(3)–C(4)–C(5)–C(1)	−6.0 (0.5)
C(4)–C(5)–C(1)–C(2)	10.2 (0.5)
C(5)–C(1)–C(2)–C(3)	−10.7 (0.5)
C(5)–C(6)–C(7)–C(8)	83.6 (0.5)
C(6)–C(7)–C(8)–C(9)	−61.2 (0.5)
C(7)–C(8)–C(9)–C(10)	68.4 (0.6)
C(8)–C(9)–C(10)–C(1)	−83.8 (0.5)
C(9)–C(10)–C(1)–C(5)	55.5 (0.6)
C(10)–C(1)–C(5)–C(6)	11.2 (0.6)
C(1)–C(5)–C(6)–C(7)	−73.9 (0.5)
C(6)–C(7)–C(11)–C(12)	25.0 (0.4)
C(7)–C(11)–C(12)–O(1)	−9.0 (0.5)
C(11)–C(12)–O(1)–C(6)	−12.6 (0.5)
C(12)–O(1)–C(6)–C(7)	28.5 (0.4)
O(1)–C(6)–C(7)–C(11)	−31.7 (0.4)
C(13)–C(11)–C(12)–O(2)	−14.2 (0.8)

whose axis passes through C-12 and bisects the C-6, C-7 bond rather than an envelope. The C=C–C=O and the O(1)–C(6)–C(7)–C(11) torsion angles (ω_2 and ω_3 of [30]) are both negative and thus of like sign. Hence, either by Beecham's rule [31] which relates the chirality of the lactone chromophore (the sign of ω_2) in *trans*-fused lactones to the sign of the lactone Cotton effect or a later suggestion [32] that the sign of ω_3 and the magnitude of the C(5)–C(6)–C(7)–C(8) torsion angle (ω_4 of [30]) provide a better correlation with the sign of the Cotton effect, 10-*epi*-8-deoxycumambrin B, if represented by absolute configuration **2** should exhibit a negative Cotton effect in the 250 nm region. This is indeed the case with $\Delta\varepsilon_{256}^{\mathrm{MeOH}}$ −0.83. Hence the absolute configuration of **2** is as depicted in the formula.

Dehydroleucodin (**4**), the third sesquiterpene lactone found in our collection of *S. yaconensis* has been isolated repeatedly from Anthemideae [33–37]. Its appearance in a *Stevia* species has no precedent although it has been reported in two *Kaunia* species (Eupatorieae, subtribe Oxylobinae) [18], and *Austrobrickellia patens* (Eupatorieae, subtribe Alomiinae) [38] and 11βH, 13-dihydroleucodin has been found in *Stevia pilosa* [10].

EXPERIMENTAL

Extraction of S. yaconensis. Aerial parts (1.6 kg) of *S. yaconensis* Hieron. var. *subeglandulosa*, collected by R. R. G. in Cuestecilla del Rodeo, Departamento Ambato, Catamarca Province, Argentina, in March 1987 and identified by Dr Luis Ariza Espinar (voucher on deposit in Museo Botanico de Cordoba [CORD]), were exhaustively extracted with $CHCl_3$ at room temp. Removal of solvent afforded 99.8 g of residue which was partitioned between MeOH (750 ml), hexane (3 l) and H_2O (250 ml). The MeOH–H_2O layer was concd at red. pres. and the remaining aq. layer extracted with $CHCl_3$. Evaporation of the $CHCl_3$ extract furnished 32.8 g of a residue which was adsorbed on 60 g of silica gel and chromatographed over 1 kg of the same adsorbent packed in C_6H_6, 250 ml fractions being collected in the order Me_2CO–Me_2CO (1:49), Me_2CO–C_6H_6 (1:9) and EtOAc.

Fractions 15–18 were combined and recrystallized from C_6H_6–petrol to give 5.2 g of ludartin (**1**). Fractions 21–23 (1.1 g) were rechromatographed over 40 g of silica gel packed in C_6H_6, the polarity being increased with Me_2CO. This yielded 194 mg of dehydroleucodin (**4**) IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1776, 1690, 1640, 1620; EIMS *m/z* (rel. int.): 244 $[M]^+$ (100), 229 $[M-15]^+$ (16), 216 $[M-CO]^+$ (9), ^{1}H NMR spectrum coincident with literature data [32]. Fractions 24–28 after recrystallization from Et_2O gave 780 mg of 10-*epi*-8-deoxocumambrin B (**2**).

Ludartin ([3R, 4S, 5S, 6S, 7S]-3,4-*epoxyguaia*-1(10),. 11(13)-*dien*-6, 12-*olide*) (**1**). Mp 85–86° from C_6H_6-petrol; CD curve (MeOH; *c* 0.86 × 10^{-3} M) $[\theta]_{298}$ O, $[\theta]_{268}$ +400, $[\theta]_{257}$O, $[\theta]_{236}$ −5350, $[\theta]_{223}$ −4000 (last reading); IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1764, 1668, 1255, 825; EIMS *m/z* (rel. int.): 246 $[M]^+$ (2), 231 $[M-15]^+$ (30), 43 (76); ^{1}H and ^{13}C NMR spectra in Tables 1 and 2.

10-epi-8-*Deoxycumambrin* B ([1R, 5R, 6S, 7S, 10S]-10-*hydroxyguaia*-3,11 (13)-dien-6,12-olide) (**2**). Mp 123–124° from Et_2O; CD curve (MeOH, 1.068 × 10^{-3} M) $[\theta]_{256}$ −2735, $[\theta]_{229}$ −695 (last reading); IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3487, 3023, 1741, 1660, 1154; EIMS *m/z* (rel. int.): 248 $[M]^+$ (2), 230 $[M-H_2O]^+$ (30), 215 (11), 121 (15), 107 (100); ^{1}H and ^{13}C NMR spectra in Tables 1 and 2.

Reduction of ludartin. To a soln of 65 mg of ludartin in 15 ml of dry MeOH was added 35 mg of $NaBH_4$ in portions with stirring at room temp. After 60 min the mixture was acidified with dil. HCl, diluted with H_2O and extracted with $CHCl_3$. The washed and dried extract was evapd at red. pres. Flash chromatography of the residue (60 mg) gave 43 mg of **6** (see below) as a gum.

A mixture of 100 mg of **1** and 2.5 g of Zn-Cu couple in 40 ml of EtOH was refluxed for 3 days, filtered through silica gel H and concd at red. pres. The oily residue (97 mg) was purified by flash chromatography over silica gel H with Me_2CO–hexane as eluent, yielding 54 mg of 11βH, 13-dihydrokauniolide [5*S*, 6*S*, 7*S*, 11*S*]-guaia-1 (10), 4-dien-6,12-olide (**5**) [18] as a gum; IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1773, 967; EIMS *m/z* (rel. int.): 232 $[M]^+$ (60.2), 217 $[M-15]^+$ (18.8), 204 $[M-CO]^+$ (2.7), 203 (3.4), 189 (12.3), 175 (22.8); 105 (100); ^{1}H NMR (80.13 MHz, $CDCl_3$): δ 5.50 (*ddq*, *J* = 3, 3, 1.5 Hz, H-3), 3.65 (*dd*, *J* = 10.4, 8.8 Hz, H-6), 3.28 (*br d*, *J* = 10.4 Hz, H-5), 2.96 (H-2a, b, centre of AB system), 2.15 (*m*, obscured, H-11), 1.90 (*tdd*, *J* = 2.5, 1.5, 1 Hz. H-15), 1.71 (*q*, *J* = 1.6 Hz, H-14), 1.23 (*d*, *J* = 6.4 Hz, H-13).

The crude product (205 mg) from Zn-Cu reduction of 230 mg of ludartin was dissolved in 10 ml of dry CH_2Cl_2 with stirring, cooled to 0° and mixed with 179 mg of *m*-chloroperbenzoic acid. After 12 hr at room temp, the reaction mixture was worked-up in the usual way to yield 196 mg of a crude product. Purification by flash chromatography afforded 20 mg of **5**, 8 mg of arborescin (**8**) and 116 mg of a mixture of at least 3 epoxides. Separation by HPLC (RSilC-18, 10 μm column, MeOH–H_2O 2:1; 3 ml/min) yielded 31 mg of **9** (R_t 30.5 min), 5 mg of **6** (R_t 33 min) and 16 mg of **7** (R_t 41 min). Arborescin ([1*R*, 5*R*, 6*R*, 7*S*, 10*S*, 11*S*] − 1(10)-epoxyguai-3-en-6,12-olide) (**8**) [19–23] had IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1170, 1637, 1230; EIMS *m/z* (rel. int.): 248 $[M]^+$ (6), 233 $[M-15]^+$ (5), 215 (32), 205 (4), 91 (100); ^{1}H NMR (80.13 MHz, $CDCl_3$): δ 5.55 (*m*, $W_{1/2}$ = 4.7 Hz, H-3), 4.00 (*dd*, *J* = 10.4, 8.8 Hz, H-6), 2.82 (*m*, H-5), 1.94 (*br d*, *J* = 0.83 Hz, H-15), 1.33 (*s*, H-14), 1.19 (*d*, *J* = 7.2 Hz, H-13); 10-epiarborescin ([1*S*, 5*R*, 6*R*, 7*S*, 10*R*, 11*S*]-1 (10)-epoxyguai-3-en-6,12-olide) (**9**) [23] had mp 90–92°; EIMS *m/z* (rel. int.): 248 $[M]^+$ (7.4), 233 $[M-15]^+$ (1.2), 215 (2.1), 215 (2.1), 205 (3.7), 96 (100); ^{1}H NMR (80.13 MHz, $CDCl_3$): δ 5.56 (*m*, $W_{1/2}$ = 4.2 Hz, H-3), 3.77 (*dd*, *J* = 11.2, 9.6 Hz, H-6, 2.86 (*br d*, *J* = 12.6 Hz, H-2a), 2.52 (*br d*, *J* = 11.2 Hz, H-5), 1.94 (*m*, H-15), 1.33 (*s*, H-14), (*d*, *J* = 6.4 Hz, H-13).

11βH, 13-*Dihydroludartin* ([3*R*, 4*S*, 5*S*, 6*S*, 7*S*, 11*S*]-3,4-*epoxyguai*-1(10)-en-6,12-*olide* (**6**). Almost crystalline gum, IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1777, 1638, 1233; EIMS *m/z* (rel. int.) 248 $[M]^+$ (6.8), 233 $[M-15]^+$ (6.8), 215, 205 (6.5), 91 (100); ^{1}H and

^{13}C NMR spectra in Tables 1 and 2.

(3S, 4R, 5S, 6S, 7S, 11S)-3,4-*Epoxyguai*-1(10)-*en*-6, 12-*olide* (7). Mp 106–108°; IR ν_{max}^{KBr} cm^{-1}: 1770, 1628, 1230; EIMS *m/z* (rel. int.): 248 $[M]^+$ (92.5), 233 (21.4), 220 (5.2), 206 (20.4), 205 (27.2), 191 (14.7), 190 (29.2), 178 (11.5), 177 (20.0), 175 (47.6), 163 (17.9), 161 (28.3), 160 (41.7), 159 (39.2), 149 (37.5), 135 (74.3), 133 (100); ^{1}H and ^{13}C NMR spectra in Tables 1 and 2.

X-Ray analysis of **2**. Single crystals of **2** prepared by slow evaporation of an Et_2O soln were orthorhombic, space group $P2_12_12_1$ with $a = 9.130$ (9), $b = 10.497$(11), $c = 13.688$(9) Å, $d_{calcd} = 1.26$ g/cm^3 for $Z = 4$ ($M_r = 248.32$). The intensity data were measured on a CAD 4 Enraf Nonius diffractometer (Mo radiation, monochromated, θ–2θ scans). The size of the crystal used for data collection was *ca* 0.20 × 0.30 × 0.30 mm^3. No absorption correction was necessary ($\mu = 0.805$). A total of 1262 reflections were measured for $\theta \leq 50°$ of which 992 were considered to be observed $[I \geq 2\sigma(I)]$. The structure was solved by direct methods using MULTAN 78 [39] and refined by full-matrix least squares methods. In the final refinement anisotropic thermal parameters were used for non-hydrogen atoms. Methyl and hydroxyl hydrogen atoms were located from a difference Fourier map; the remaining hydrogen atom parameters were calculated assuming idealized geometry. Hydrogen atom contributions were included in the structure factor calculations but their parameters were not refined. The final discrepancy indices were $R = 4.9$ and $R_w = 6.5$ for the 992 observed reflections. The final difference Fourier map was essentially featureless with no peaks greater than 0.16 e Å^{-3}.

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