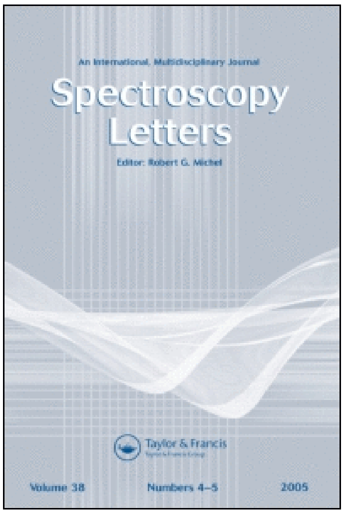

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Felix J. Parodi[a]; Frank R. Fronczek[a]; Nikolaus H. Fischer[a]
[a] Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana

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BIOMIMETIC TRANSFORMATIONS OF A GUAIANOLIDE-1(10)-β-EPOXIDE AND THE MOLECULAR STRUCTURES OF THREE GUAIANOLIDES

FELIX J. PARODI, FRANK R. FRONCZEK AND NIKOLAUS H. FISCHER*

Department of Chemistry, Louisiana State University,

Baton Rouge, Louisiana 70803

ABSTRACT - A reinvestigation of the boron trifluoride-mediated transformations of the guaianolide-1(10)-β-epoxide [1] provided the previously obtained *cis*-eudesmanolide [5] and the fluoroguaianolide [2] as well as two new lactones, the *trans*-guaianolide [4] and the *cis*-guaianolide [3]. The molecular structures of compounds **1**, **3**, and **4** were determined by single crystal X-ray diffraction. The mechanisms of formation of the four lactones from epoxide **1** can be formulated via the carbocationic intermediates **A** and **B**.

INTRODUCTION

The lack of biosynthetic data of sesquiterpene lactones requires that chemical and mechanistic considerations derived from biomimetic transformations be used to provide indirect evidence for their possible biosynthesis. A number of pathways for the biogenesis of pseudoguaianolides via the germacrolide-guaianolide route have been proposed (1-4). It has also been suggested that guaianolide epoxides represent the immediate precursors of this major group of sesquiterpene lactones (4-7). Therefore, a reinvestigation of the BF_3-mediated transformation of a guaianolide-1(10)-β-epoxide [1] was performed to possibly detect pseudoguaianolides such as **6** as minor products . Pseudoguaianolide **6** could be formed from epoxide **1** via intermediate A by BF_3-initiated epoxide opening at C-1 followed by a H-shift from C-5 to C-1 and simultaneous

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*Author to whom correspondence should be addressed.

methyl shift from C-4 to C-5 (4). As in our previous attempt (5), formation of the desired pseudoguaianolide skeleton was not observed. Instead, the previously obtained *cis*-eudesmanolide [5] and fluoro derivative 2 were isolated as major products and the new *trans*-guaianolide [4] and the *cis*-guaianolide [3] were found as minor components. The structure elucidation of compounds **1**, **3**, and **4** and the proposed mechanisms of formation of **2-5** are described in this paper.

RESULTS AND DISCUSSION

The eims spectra of the *cis*-guaianolides **2** and **3** exhibited parent peaks at m/z 286 and 284, respectively. Their ^{1}H- and ^{13}C-nmr data are tabulated in Tables 1 and 2, respectively. The chemical shifts for the deshielded lactonic protons (H-6) in the ^{1}H nmr spectra for 2 (δ 4.52) and 3 ((δ 4.54) must be due to the deshielding effect of the β-oriented hydroxyls at C-10. Compounds **2** and **3** had similar chemical shifts for H-5, the deshielding being due to the proximity of fluorine and hydroxyl substituents in **2** and **3**, respectively. As expected, **2** exhibited a doublet of doublets at δ 2.39 with a 40 Hz coupling constant, which confirmed the presence of a fluorine substituent at C-1 (5). This was further supported by the C-F coupling constant (162 Hz) observed in the ^{13}C-nmr spectrum of **2** (8). The molecular structures of **2** as well as **5** had been previously established by single crystal X-ray analysis (5, 9). Since their high-field ^{1}H- and ^{13}C-nmr data had not been previously reported, they are included in Tables 1 and 2, respectively.

The ir spectrum of the *trans*-fused guaianolide **4** showed absorptions for hydroxyl(s) at 3457 cm^{-1}, a lactone band at 1761 cm^{-1}, and a double bond absorption at 1632 cm^{-1}. The eims gave peaks at m/z 266 [M$^+$], 251 [M$^+$-CH$_3$], 248 [M$^+$-H$_2$O], 233 [M$^+$-H$_2$O-CH$_3$], and 230 [M$^+$-2H$_2$O]. The ^{1}H- nmr COSY spectral data suggested an exocyclic methylene system at C-10 similar to that of compressanolide (10) and a doublet at δ 1.90 was assigned to H-5, which was slightly more deshielded than H-5 of triol **3** (Δδ 0.31). The lactonic proton (H-6) of **4** was also deshielded when compared with the analogous proton of compressanolide (Δδ 0.3). This must be mainly due to the presence of a β-hydroxyl substituent at C-1 in **4**. Furthermore, the C-4-methyl group geminal to the hydroxyl was more strongly deshielded (δ 1.52), when compared with compounds **3** (δ 1.30), due to the deshielding influence of a β-oriented hydroxyl group at C-1.

The molecular structures of compounds **1**, **3**, and **4** were confirmed by single crystal X-ray diffraction. Figure 1 illustrates the molecular structure of epoxide **1**, confirming the β-

Table 1. ^{1}H-nmr Spectral Data of Sesquiterpene Lactones 1-5 [a-c]

Proton	1	2	3	4	5
2α	2.21	1.58	1.65	2.10	3.05 ddd
2β	1.66	1.60	1.03	2.61	2.22 ddd
3α	1.90	2.28	2.10 dddd(2.25)	2.10	1.96 dddd
3β	1.85	1.67	1.03	2.60	2.11 ddd
5	2.24 d	2.52 dd (2.39)	2.04 d (2.21)	1.90 d	2.07 dd
6	4.06 dd	4.28 dd (4.52)	4.29 dd (4.64)	4.28 dd	3.49 dd
7	1.38	1.32 ddd	1.37 dddd	1.72	1.64 dddd
8α	1.68	1.13	1.03	1.70	1.75 dddd
8β	1.35	1.13	1.17	1.92 dd	1.38 dddd
9α	1.92	1.78 dd (br)	1.92 ddd (2.1)	2.36	1.13 ddd
9β	2.16	1.08 d (br)	0.94	2.78	2.34 ddd
11	2.20	1.55	1.58	2.23	2.13 dd
13	1.20 d	0.88 d (1.18)	0.94 d (1.22)	1.21 d	1.21 d
14	1.46 s	0.86 d (1.26)	0.76 s (1.27)	4.90 d 5.08 s	1.55 s
15	1.29 s	1.28 s (1.24)	1.30 s (br)(1.35)	1.52 s	1.52 s

[a] J(Hz): 1: 5,6 = 6,5 = 11.0; 6,7 = 9.8; 13,11 = 7.0. 2: 5,6=6,5=11.2; 5,F=40; 6,F=1.2; 6,7=7,6=9.9; 7,8α=2.5; 7,8β=10.3; 9α,8β=15.0; 9α,9β=9β,9α=15.1; 13,11=6.9; 14,F=0.8. 3: 2α,2β = 15.0; 2α,3β = 6.5; 2β,3α = 6.3; 2α,3α = 3α,2α = 13.6; 3α,3β = 15.0; 5,6 = 6,5 = 11.0; 6,7=7,6 = 9.9; 7,8α = 8α,7 = 3.4; 7,8β = 12.0; 7,11 = 12.1; 8α,8β = 13.8; 8α,9α = 9α,8α = 4; 8α,9β = 5.4; 9α,9β = 13.8; 9α,8β = 13.6; 11,13 = 13,11 = 7.0. 4: 5,6=6,5 = 11.1; 6,7 = 9.4; 13,11=7.0; 9β,8β = 6.6; 9β,9α = 15.0. 5: 2α,3α = 3α,2α = 7.2; 3α,5=5,3α = 2.2;3α,2β = 2β,3α=2.0; 2β,3β = 3β,2β = 5.3; 3α,3β = 3β,3α = 14.2; 2α,2β = 2β,2α=14.8; 3β,2α=2α,3β=13.8; 5,6=6,5=11.2; 6,7 = 7,6= 11.8; 7,8α = 8α,7 = 9β,8α = 8α,9β = 3.5; 9β,8β = 8β,9β = 3.8; 9α,8α = 8α,9α = 4.4; 9α,9β = 9β,9α = 13.9; 8α,8β = 8β,8α = 12.7; 9α,8β = 8β,9α = 12.8; 8β,7=7,8β=12.5; 11,13=13,11=6.8; 11,7=7,11=12.3.

[b] NOEs: Irradiated (observed): 1: 8β,15(6). 2: 7 (5,9α); 15 (6). 4: 14a (14b); 14b (14a); 15 (6). 5: 6 (3β,8β,11); 14 (5).

[c] 2 and 3 in C_6D_6 ($CDCl_3$), 1, 4 and 5 in $CDCl_3$. All assignments of 1-5 were based on data obtained from COSY experiments at 400 MHz. ^1H ^{13}C correlation spectra were obtained for 1, 2 and 5.

Table 2. ^{13}C-nmr Spectral Data of Sesquiterpene Lactones 1-5 [a-b]

C	1	2	3	4	5
1	69.8 (70.2)[c] s	150.6 d	83.4 s	84.7 s	213.8 s
2	29.4 (29.8) t	30.8 dt	35.9 t[b]	32.1 t	34.4 t
3	37.4 (38.5) t	37.8 t	37.4 t[b]	37.3 t	29.7 t
4	79.6 (79.7) s	80.1 s	80.2 s	80.3 s	72.9 s
5	55.2 (55.4) d	65.6 dd	68.6 d	66.0 d	59.2 d
6	81.6 (81.7) d	81.3 d	82.8 d	84.9 d	82.1 d
7	53.1 (53.4) d	50.1 d	49.9 d	48.6 d	51.7 d
8	23.1 (23.7) t	25.1 t	25.5 t	25.0 t	24.0 t
9	33.4 (33.7) t	35.7 t	35.5 t[b]	38.7 t	35.8 t
10	62.1 (62.4) s	74.3 d	76.3 s	150.8 s	-----
11	40.7 (40.7) d	40.9 d	41.3 d	41.0 d	41.0 d
12	178.0 (178.2) s	177.0 s	178.4 s	178.8.s	158.0 s
13	12.4 (12.4) q	12.7 q	12.9 q	12.5 q	12.3 q
14	23.2 (23.3) q[b]	27.5 q	28.3 q	112.2 t	32.2 q
15	23.2 (23.2) q[b]	22.9 q	22.6 q	28.0 q	30.3 q

[a] Spectra were obtained in $CDCl_3$ at 100 MHz, relative to TMS; multiplicities were based on DEPT spectra for 1-5; ^{1}H ^{13}C correlation spectra were obtained for 1, 2 and 5; compound 2: *J* (Hz): $C_{1,F}$ = 162.0, $C_{5,F}$ = 25.3, $C_{2,F}$ = 25.9, $C_{10,F}$ = 30.4.

[b] Interchangeable assignments.

[c] Data obtained in $(CD_3)_2CO$.

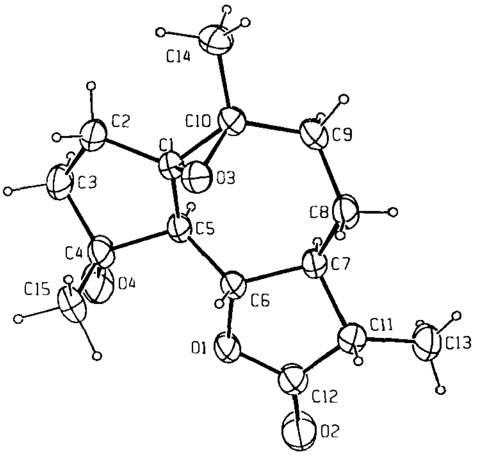


Figure 1. The molecular structure of epoxyguaianolide 1.

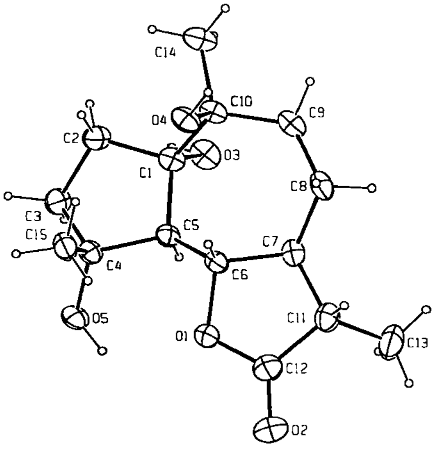


Figure 2. The molecular structure of trihydroxyguaianolide 3.

configuration of the epoxy function. Bond distances are normal, with estimated standard deviations 0.001-0.003 Å. The epoxide is symmetric, with both C-O bonds having length 1.454(2) Å. Its presence forces the seven-membered ring into the chair conformation with a zero torsion angle (-0.6(4)°) about C1-C10, and local mirror plane bisecting the epoxide and passing through C7. Both five-membered rings are in envelope conformations with C4 and C7 at the respective flaps. Since the hydroxyl hydrogen atom is disordered, details of the hydrogen bonding are unclear. It is clear, however, that molecules do not form hydrogen bonded chains. The closest potential hydrogen bond contact is OH oxygen O4 and its symmetry equivalent about the crystallographic twofold axis, O4 ... O4' 2.883(2) Å. There is also a longer, intramolecular contact O4 ... O1, 2.950(2) Å.

Figure 2 illustrates the molecular structure of the triol **3**, confirming that the two OH substituents of the glycol are oriented α at C1 and β at C10. The C10-O4 bond length is 1.442(2) Å, while the other two C-OH bonds have length 1.450(2) Å. The seven-membered ring has a conformation approximating the C_S chair, but the near zero torsion angle (C10-C1-C5-C6, -11.6(3)°) deviates much more from the ideal angle than does that of epoxide **1**, and differences in torsion angle magnitudes across the pseudomirror are larger than in **1**. The five-membered rings both have envelope conformations, but while C7 occupies the flap position of the lactone envelope

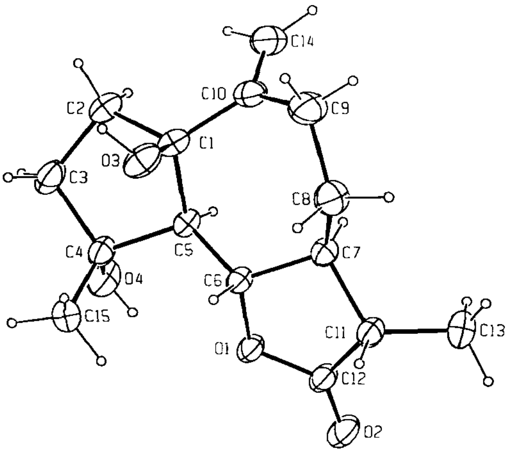
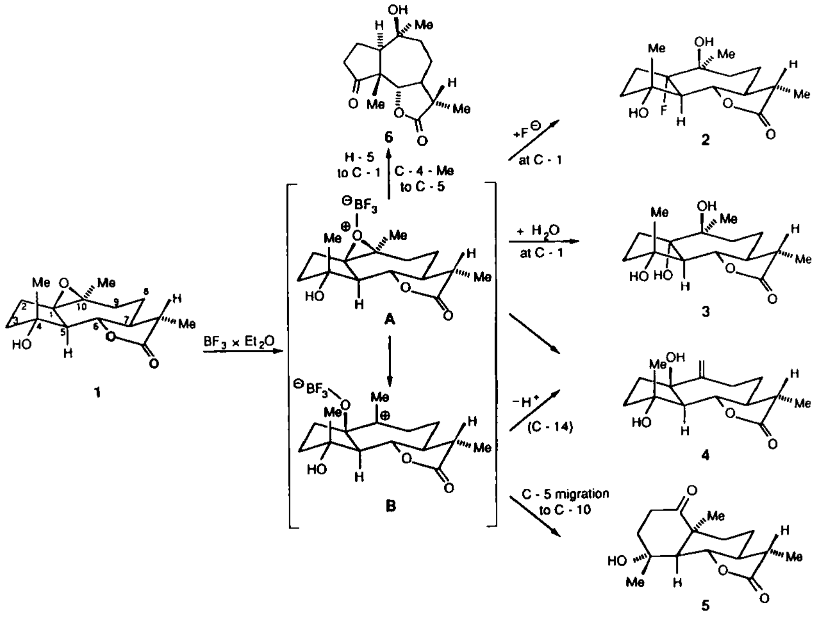


Figure 3. The molecular structure of guaianolide 4.

as in **1**, the other five-membered ring has C3 at the flap. Hydrogen bonding in **3** is extensive but weak. Hydroxyl group 03 forms an intermolecular contact with carbonyl oxygen 02, with 0 ... 0 distance 3.123(2) Å and O-H ... O angle 150 (3)°. Hydroxyl group 04 forms an intermolecular contact with 05, having distance 2.960(2) Å and angle 174(2)°. Hydroxyl group 05 forms a bifurcated contact, intramolecular with 01, 2.953(2) Å, and intermolecular with 03, 3.148(2) Å. The angles at the H atom on 05 are 05-H ... 01 126(2)°, and 05-H ... 03 149(2)°.

The structure of compound **4** is illustrated in Figure 3, which shows the β configuration of the OH group of C1. The seven-membered ring has a twisted conformation somewhat resembling the C_2 half-chair, with C9 on the local diad axis, but deviations from ideal torsion angles are large. As in **1** and **3**, the lactone ring has the envelope conformation with C7 at the flap. The five-membered ring of the guaianolide skeleton has the envelope conformation also, but in this case C1 is in the flap position. Molecules are linked in chains along the c axis direction by intermolecular hydrogen bonds involving OH group 03 and carbonyl oxygen atom 02, with 0 ... 0 distance 2.853(1) Å and angle at H 172(2)°.

Scheme 1 outlines the transformations of guaianolide-1(10)-β-epoxide **1**, which was the major reaction product of the peracid oxidation of dehydromichelliolide [guaian-1(10)-en-6,12-olide]. BF_3-Complexation would lead to cation A which could be attacked at C-1 by either F^- or



Scheme 1. BF_3-Initiated transformations of guaianolide-1(10)-β-epoxide [1].

H_2O to form *cis*-guaianolides **2** (5) or **3**, respectively. Alternatively, opening of the epoxide at C-10 and loss of a proton from the C-10 methyl would provide the 1β-hydroxy-*trans*-guaianolide **4**. As previously discussed (5), the formation of the *cis*-eudesmanolide **5** could involve cleavage of the C-10-oxygen bond to form carbocation **B** followed by bond migration of C-5 to C-10 with formation of a ketone moiety at C-1.

EXPERIMENTAL

BF_3-CATALYSED REACTION OF GUAIANOLIDE 1(10)-β-EPOXIDE [**1**].---A solution of the epoxide **1** (180 mg) in 18 ml of dry ether was treated with 1.8 ml of BF_3-etherate (11, 12) and left at room temperature for 1 h. After quenching with 40 ml of water, the organic layer was washed with 5% aq. $NaHCO_3$ and H_2O until neutral, dried over Na_2SO_4, filtered and evaporated *in vacuo* to give 130 mg of a dark brown gum. Preparative tlc over silica gel using Et_2O afforded seven fractions. Rechromatography of fractions 4, 5, and 6 (C_6H_6/EtOAc, 3:1; 3x)

Table 3. Crystal Data and X-ray Data Collection Parameters of Guaianolides **1**, **3**, and **4**

Compound	**1**	**3**	**4**
Formula	$C_{15}H_{22}O_4$	$C_{15}H_{24}O_5$	$C_{15}H_{22}O_4$
FW	266.3	284.4	266.3
Crystal System	Monoclinic	Orthorhombic	Monoclinic
Space group	C2	$P2_12_12_1$	$P2_1$
Cell constants			
a, Å	15.853(7)	10.285(2)	8.571(2)
b, Å	8.681(2)	18.391(3)	9.693(3)
c, Å	10.757(2)	7.834(2)	8.989(2)
β, °	107.55(3)	-	110.60(2)
V, $Å^3$	1411.4(13)	1481.7(9)	699.1(6)
Z	4	4	2
D_c, g cm^{-3}	1.253	1.275	1.265
μ(CuKα), cm^{-1}	6.9	7.4	7.0
Temp., °C	25	25	26
Crystal size, mm	0.28 x 0.44 x 0.44	0.12 x 0.18 x 0.36	0.15 x 0.40 x 0.40
θ limits, deg	2-75	2-75	2-75
Scan speeds, deg. min^{-1}	0.72 - 3.30	0.63 - 3.30	0.43 - 3.30
Min. transmission, %	83.6	80.8	90.3
Unique data	1558	1765	1534
Observed data	1529	1459	1484
Criterion	$I>0$	$I>3\sigma(I)$	$I>3\sigma(I)$
Variables	256	242	260
R	0.041	0.040	0.028
R_w	0.053	0.044	0.040
Resid. density, e^- $Å^{-3}$	0.22	0.20	0.14
Extinction	$4.0(7) \times 10^{-6}$	$1.7(2) \times 10^{-6}$	$9.6(9) \times 10^{-6}$
Hydrogen Atoms	OH not found; others refined iso	Me H fixed; others refined iso	Refined iso

and 8 (cyclohexane/EtOAc, 1:4) provided pure **5** (26 mg) **4** (13 mg), **1** (27 mg), **2** (18 mg), and **3** (7 mg).

Guaianolide [**3**].---$C_{15}H_{24}O_5$; colorless crystals; mp 205-206°; eims <u>m/z</u> (% rel. int.)284 $[M]^+$ (0.1), 266 $[M\text{-}H_2O]^+$ (0.6), 248 $[M\text{-}2H_2O]^+$ (6.8), 230 $[M\text{-}3H_2O]^+$ (1.7), 205 (4.3), 190 (13.8), 99 (13.3), 97 (37.8), 95 (11.2), 71 (15.4), 55 (21.6), 43 $[MeCO]^+$ (100.0), ir ν_{max} (neat) 3434 (OH), 1755 (γ-lactone).

Table 4. Coordinates for epoxyguaianolide 1

Atom	x	y	z	B_{eq}(Å^2)
O1	0.66433(8)	0	0.0506(1)	5.55(4)
O2	0.6966(1)	0.0088(5)	-0.1360(1)	9.89(8)
O3	0.74486(8)	-0.1507(2)	0.4430(1)	4.32(3)
O4	0.5272(1)	0.1534(3)	0.1405(2)	7.14(5)
C1	0.7025(1)	-0.0006(3)	0.4176(2)	3.74(3)
C2	0.6284(1)	0.0288(3)	0.4781(2)	4.67(4)
C3	0.5532(1)	0.1005(4)	0.3691(2)	5.33(5)
C4	0.5678(1)	0.0457(4)	0.2425(2)	4.92(5)
C5	0.6700(1)	0.0546(3)	0.2756(2)	3.95(3)
C6	0.7116(1)	-0.0335(3)	0.1877(2)	4.08(4)
C7	0.8067(1)	0.0113(3)	0.1996(2)	4.07(4)
C8	0.8751(1)	-0.0511(3)	0.3191(2)	4.87(5)
C9	0.8725(1)	0.0247(4)	0.4455(2)	5.14(5)
C10	0.7960(1)	-0.0143(3)	0.4974(2)	3.96(4)
C11	0.8139(1)	-0.0452(4)	0.0686(2)	5.06(5)
C12	0.7219(1)	-0.0112(5)	-0.0202(2)	6.21(6)
C13	0.8858(1)	0.0251(6)	0.0206(2)	7.35(8)
C14	0.8186(1)	-0.0001(3)	0.6439(2)	4.84(4)
C15	0.5316(1)	-0.1145(4)	0.2057(3)	6.36(6)

$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$

Table 5. Coordinates for trihydroxyguaianolide 3

Atom	x	y	z	B_{eq}(Å^2)
O1	0.5214(2)	0.67543(9)	0.0810(3)	4.02(4)
O2	0.4964(2)	0.5592(1)	0.0172(3)	6.59(6)
O3	0.8485(2)	0.8322(1)	0.2199(3)	4.17(4)
O4	0.5605(2)	0.8320(1)	0.4860(2)	3.28(3)
O5	0.5250(2)	0.8039(1)	-0.1449(2)	3.81(4)
C1	0.7107(2)	0.8412(1)	0.2528(3)	2.89(5)
C2	0.6623(3)	0.9164(1)	0.1947(4)	3.59(6)
C3	0.6092(3)	0.9052(1)	0.0149(4)	3.92(6)
C4	0.5399(3)	0.8328(1)	0.0262(3)	3.06(5)
C5	0.6361(2)	0.7866(1)	0.1336(3)	2.71(5)
C6	0.5794(2)	0.7200(1)	0.2175(3)	2.82(5)
C7	0.6760(2)	0.6697(1)	0.3048(3)	3.03(5)
C8	0.6937(3)	0.6896(1)	0.4916(3)	3.68(6)
C9	0.7610(3)	0.7621(2)	0.5206(4)	3.69(6)
C10	0.6980(2)	0.8312(1)	0.4497(3)	3.02(5)
C11	0.6192(3)	0.5943(1)	0.2720(4)	3.77(6)
C12	0.5398(3)	0.6046(2)	0.1113(4)	4.26(7)
C13	0.7169(4)	0.5320(2)	0.2590(5)	5.42(8)
C14	0.7607(3)	0.8975(2)	0.5368(4)	4.59(7)
C15	0.4063(3)	0.8398(2)	0.1078(3)	3.57(5)

$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$

Table 6. Coordinates for guaianolide 4

Atom	x	y	z	B_{eq}(Å^2)
O1	0.6905(1)	0	0.4648(1)	3.38(2)
O2	0.7514(2)	0.0018(2)	0.2455(1)	4.81(3)
O3	0.8002(1)	0.0631(2)	0.9545(1)	4.04(2)
O4	0.3543(1)	-0.0178(2)	0.5474(2)	4.98(3)
C1	0.6852(2)	0.1589(2)	0.8516(2)	3.11(3)
C2	0.5218(2)	0.1601(2)	0.8863(2)	3.90(3)
C3	0.4451(2)	0.0193(3)	0.8295(2)	4.61(4)
C4	0.5003(2)	-0.0225(2)	0.6899(2)	3.46(3)
C5	0.6243(2)	0.0931(2)	0.6845(1)	2.74(2)
C6	0.7643(2)	0.0519(2)	0.6290(1)	2.76(2)
C7	0.8810(2)	0.1668(2)	0.6183(2)	3.11(3)
C8	1.0148(2)	0.1985(2)	0.7788(2)	4.27(4)
C9	0.9557(2)	0.2942(3)	0.8845(2)	5.36(4)
C10	0.7715(2)	0.2969(2)	0.8576(2)	3.90(3)
C11	0.9422(2)	0.1091(2)	0.4888(2)	3.49(3)
C12	0.7898(2)	0.0329(2)	0.3831(2)	3.40(3)
C13	1.0064(2)	0.2139(3)	0.3974(2)	5.48(4)
C14	0.6921(3)	0.4167(3)	0.8423(2)	5.15(4)
C15	0.5717(2)	-0.1679(2)	0.7114(2)	4.47(4)

$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* a_i \cdot a_j$

1β-*Hydroxycompressanolide* [4].---$C_{15}H_{22}O_4$; colorless crystals; mp 166-170°; eims m/z (% rel. int.): 266 $[M]^+$ (8.9), 251 $[M\text{-}Me]^+$ (1.0), 248 $[M^+\text{-}H_2O]$ (6.5), 233 $[M\text{-}H_2O\text{-}Me]^+$, (2.1), 230 $[M\text{-}2H_2O]^+$ (2.6), 220 $[M\text{-}H_2O\text{-}CO]^+$ (11.4), 205 $[M\text{-}H_2O\text{-}CO\text{-}Me]^+$ (4.1), 190 (63.5), 99 (43.4), 71 (32.1), 55 (85.5), 43 $[MeCO]^+$ (100.0); ir ν_{max} (neat) 3457 (OH), 1761 (γ-lactone), 1632 (C=C).

X-RAY DATA FOR LACTONES **1**, **3**, and **4**. Data were collected on an Enraf-Nonius CAD4 diffractometer with CuKα radiation (λ = 1.54184 Å) and a graphite monochromator. Crystal data and data collection parameters are given in Table 3. Data were collected by ω-2θ scans of variable speed, designed to yield approximately equal relative precision for all significant reflections. One octant of data was measured for the orthorhombic crystal, one quadrant for the monoclinic crystals. Data reduction included corrections for backround, Lorentz-polarization, and absorption effects. Absorption corrections were based on ψ scans. Structures were solved by direct methods and refined by full-matrix least squares on F with weights $w = \sigma^{-2}(Fo)$, using the Enraf-Nonius SDP (13). Nonhydrogen atoms were treated anisotropically. Hydrogen atoms were located by difference maps, and their handling is detailed in Table 3. The OH hydrogen atom of compound **1** is disordered about a two-fold axis, and was not located. Secondary extinction coefficients were refined for all structures. Final R factors and residual electron densities are given in Table 3. Coordinates for guaianolides **1**, **3**, and **4** are given in Tables 4 through 6, respectively.

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