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(*E*,*E*)-8-Acetoxygermacra-1(10),4-dien-6,12-olide, $C_{17}H_{22}O_4$

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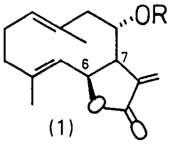
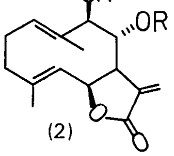
Abstract. $M_r = 290{\cdot}36$, monoclinic, $P2_1$, $a = 7{\cdot}151$ (2), $b = 16{\cdot}421$ (3), $c = 6{\cdot}772$ (1) Å, $\beta = 98{\cdot}18$ (1)°, $V = 787{\cdot}4$ (2) Å^3, $Z = 2$, $D_x = 1{\cdot}225$ g cm^{-3}, Cu $K\alpha$, $\lambda = 1{\cdot}54178$ Å, $\mu = 7{\cdot}11$ cm^{-1}, $F(000) = 312$, $T = 298$ K, $R = 0{\cdot}047$ for 986 independent reflections. The title compound, isolated from *Gochnatia foliolosa* (Compositae), contains a lactone ring with unusual *cis* fusion to the 6,7 positions of the ten-membered germacradiene ring. The *cis* fusion results in the ten-membered ring adopting a chair–boat conformation with the methyl groups *syn* and lying below the plane of the ten-membered ring. Molecular mechanics calculations are reported for the four known *cis*-fused germacranolides.

Introduction. The tribe Mutiseae is one of the least known tribes in the family Compositae, and its small area of distribution implies the tribe is of relatively recent evolutionary origin. The tribe is predominately American with fewer than half of the genera and less than a quarter of the species found elsewhere. Gochnatiinae is the most fragmented and widely distributed subtribe with 21 genera in the Americas and 15 in the Old World. The genus *Gochnatia* is composed of 68 species of which only five (Bohlmann, Zdero, Robinson & King, 1981; Bohlmann, Schmeda-Hirschman, Jakupovic, King & Robinson, 1984; Bohlmann & Zdero, 1979; Dominguez, Franco, Cano & Wolzak, 1978; Bohlmann, Jakupovic, Robinson & King, 1981) have been investigated chemically.

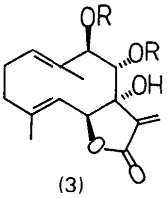
The discovery in *Gochnatia foliolosa* (D. Don) D. Don ex. et A. var. *foliolosa* of the germacranolide (1) (R = acetyl), in which the lactone ring has closed *cis* at the 6 position of the germacradiene ring may be of taxonomic significance. This molecular configuration was reported for compounds (2) and (3) isolated from the genus *Montanoa* (Herz, Govindan & Blount, 1980; Bohlmann & Le Van, 1978) of the tribe Heliantheae and compound (4) isolated from *Ursinia anthemoides* (Samek, Holub, Rychlewska, Grabarczyk & Drozdz, 1979; Rychlewska, 1981). The classification of *Ursinia* has been of some dispute (Heywood & Humphries, 1977). The distribution of the *cis*-fused germacranolides within the genus, the subtribe and the tribe may assist in clarifying taxonomic problems. The germacranolide structures assigned in earlier studies of the *Gochnatia* will be reexamined.



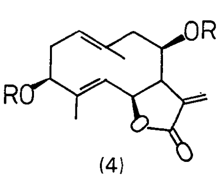
(1)



(2)



(3)



(4)

Experimental. Extracts of *Gochnatia foliolosa* collected in Florida near Concepción, Chile, yielded a crystalline solid, m.p. 388 K, $\lambda(\mathrm{MeOH})_{\max} = 215$ nm (ε 19·72), $\nu(\mathrm{Nujol})_{\max} = 3360$, 2950, 2860, 1760, 1715, 1650,

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1230 cm^{-1}. Prismatic-shaped crystal, 0·35 × 0·34 × 0·20 mm, Syntex $P2_1$ diffractometer, θ:2θ scan, variable scan rate, $2\theta_{\max} = 120°$, graphite-monochromated Cu $K\alpha$ radiation; lattice parameters from least squares of 15 medium-angle reflections ($10·7 \leq 2\theta \leq 31·3°$) with angles measured by centering routine associated with diffractometer system, systematic absences ($k = 2n+1$ for $0k0$) consistent with space group $P2_1$; 1 monitored reflection (121) showed no significant change in intensity; 1089 independent reflections ($0 \leq h \leq 7, 0 \leq k \leq 16, 6 \leq l \leq -6$), 986 had $I > 3\sigma(I)$; Lorentz and polarization, no absorption correction; direct methods (*MULTAN*78; Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) located all heavy atoms; H atoms located in difference Fourier map, fixed at distance of 1·08 Å by scaling but not refined; full-matrix least-squares refinement, $w(|F_o| - |F_c|)^2$ minimized, $w = 1/\sigma^2(F_o)$ (derived from counting statistics); 190 parameters refined, H atoms rescaled, final $R = 0·047$, $R_w = 0·062$ (based on 986 intensities), $S = 3·09$, $(\Delta/\sigma)_{\rm av} = 0·05$, $(\Delta/\sigma)_{\max} = 0·22$, highest peak in difference Fourier map 0·15 e Å^{-3}; locally written programs for data reduction, *MULTAN*78 for direct-methods' calculations and *XRAY*76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) for all others; atomic scattering factors for C and O from Cromer & Mann (1968), H from Stewart, Davidson & Simpson (1965). Table 1 lists atomic positional parameters and $U_{\rm eq}$ values, Table 2 lists observed and calculated bond lengths and Table 3 lists observed and calculated valence and torsion angles.*

Table 1. *Atomic positional parameters* (×10^4) *and equivalent isotropic thermal parameters* (Å^2 × 10^2)

	x	*y*	*z*	$U_{\rm eq}$*
C(1)	2906 (8)	3115 (4)	12247 (9)	60 (3)
C(2)	4447 (8)	3545 (4)	13593 (9)	68 (3)
C(3)	6316 (7)	3049 (4)	13774 (10)	71 (3)
C(4)	5985 (7)	2189 (4)	14467 (8)	61 (3)
C(5)	5406 (7)	1643 (4)	13048 (8)	56 (3)
C(6)	4525 (7)	841 (4)	13366 (8)	56 (3)
O(6)	5538 (5)	208 (3)	12375 (6)	71 (2)
C(7)	2396 (7)	725 (4)	12426 (7)	53 (3)
C(8)	1649 (7)	1307 (3)	10681 (7)	51 (3)
O(8)	278 (5)	879	9283 (5)	60 (2)
C(9)	554 (7)	2048 (4)	11259 (9)	64 (3)
C(10)	1665 (7)	2594 (4)	12806 (8)	56 (3)
C(11)	2381 (9)	−161 (4)	11850 (8)	63 (3)
C(12)	4347 (11)	−395 (4)	11673 (8)	74 (4)
O(12)	4926 (8)	−1027 (3)	11088 (7)	104 (3)
C(13)	939 (11)	−688 (4)	11541 (9)	91 (4)
C(14)	6133 (8)	2053 (4)	16673 (8)	70 (3)
C(15)	1343 (8)	2479 (4)	14944 (9)	72 (3)
C(16)	904 (10)	470 (4)	7814 (8)	62 (3)
O(16)	2541 (6)	469 (3)	7521 (6)	76 (3)
C(17)	−667 (10)	32 (5)	6543 (9)	89 (4)

* $U_{\rm eq} = \frac{1}{3}[U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}aa^*bb^*\cos\gamma + 2U_{13}aa^*cc^*\cos\beta + 2U_{23}bb^*cc^*\cos\alpha]$.

Table 2. *Observed and calculated* (*MM*2) *interatomic distances for* (1) (Å)

	Obs.	Calc.		Obs.	Calc.
C(1)–C(2)	1·503 (8)	1·504	C(8)–C(9)	1·528 (8)	1·543
C(1)–C(10)	1·326 (9)	1·335	C(8)–O(8)	1·445 (5)	1·467
C(2)–C(3)	1·555 (8)	1·544	C(9)–C(10)	1·515 (8)	1·505
C(3)–C(4)	1·517 (9)	1·507	C(10)–C(15)	1·510 (8)	1·504
C(4)–C(5)	1·336 (8)	1·334	C(11)–C(12)	1·479 (10)	1·479
C(4)–C(14)	1·499 (8)	1·502	C(11)–C(13)	1·340 (10)	1·329
C(5)–C(6)	1·489 (9)	1·489	C(12)–O(6)	1·348 (8)	1·352
C(6)–C(7)	1·576 (7)	1·552*	C(12)–O(12)	1·205 (9)	1·207
C(6)–O(6)	1·481 (8)	1·472	O(8)–C(16)	1·330 (7)	—
C(7)–C(8)	1·554 (7)	1·548	O(16)–C(16)	1·215 (9)	—
C(7) C(11)	1·506 (9)	1·506	C(16)–C(17)	1·498 (9)	—

* Distances differing by more than 3σ.

Discussion. Fig. 1 is an *ORTEP* drawing (Johnson, 1971) of the title compound. The C(6)—C(7) *cis* ring junction of the lactone leads to a chair–boat conformation rather than the chair–chair conformation observed for the *trans*-fused germacranolides. The absolute configuration is assumed to be known from the configuration of C(7) (Herz, Govindan & Blount, 1980). With reference to the lactone ring the two methyl groups lie *syn* and below the plane of the ten-membered ring.

Molecular mechanics calculations (*MM*2; Allinger & Yuh, 1980) have been used to correlate the structures of a series of *trans*-fused germacranolides (Watson, 1984). Preliminary calculations on the ten-membered-ring compounds indicated the observed C=C bond lengths were consistently shorter than calculated, and the observed C—C=C—C torsion angles differed considerably from 0 or 180°. A correlation of the *trans*-fused germacranolides required an increase in the C=C force constant, a reduction of the C—C=C—C torsional barrier and assignment of the lactone ring parameters. All other values assigned by the *MM*2 program were retained, and excellent agreement with all four possible germacradiene structures [(*E,E*), (*E,Z*), (*Z,E*) and (*Z,Z*)] were obtained as well as with epoxide functionalities. The same parameters were used to calculate the minimum-energy conformations for (1), (2), (3) and (4).

The calculated and observed bond lengths in compounds (1), (3) and (4) agree very well with only five distances differing by more than 3σ. The two discrepancies for (1) are associated with the C(6)—C(7) ring fusion and the C—O*R* distance in which the naturally occurring *R* = acetyl has been replaced by *R* = H in the calculations. (2) shows deviations of 5σ and 6σ; however, this probably reflects an optimistic assignment

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* Lists of structure factors, H-atom parameters and thermal parameters for (1), tables of observed and calculated bond lengths, valence angles and torsion angles for (1), (2), (3) and (4) and bar graphs of variances *versus* frequency of occurrence for observed and calculated values have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39841 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

of standard deviations (0·004 Å). The valence-angle deviations $[(|\text{obs.}|-|\text{calc.}|)/\sigma]$ are symmetrically distributed. The six angles in (1) that deviated by more than 3σ are associated with the lactone ring. (2) shows larger deviations ($\pm 8\sigma$) than do the other three compounds; however, the e.s.d.'s of 0·3° are again much smaller. Increasing the e.s.d. to 0·5° leads to a comparable distribution of deviations. Although packing interactions do not appear to affect the equilibrium distances or valence angles, the force-field parameters for the *cis*-fused lactone ring need to be modified.

Table 3. *Observed and calculated* (*MM*2) *valence angles* (°) *and torsion angles* (°) *for* (1)

	Obs.	Calc.
C(2)C(1)C(10)	126·4 (5)	127·0
C(1)C(2)C(3)	110·5 (5)	109·0
C(2)C(3)C(4)	110·0 (5)	109·1
C(3)C(4)C(5)	116·6 (5)	118·7
C(3)C(4)C(14)	117·1 (5)	115·4
C(5)C(4)C(14)	126·0 (6)	125·6
C(4)C(5)C(6)	·125·7 (5)	128·9*
C(5)C(6)C(7)	116·9 (5)	116·1
C(5)C(6)O(6)	108·1 (4)	109·6
C(7)C(6)O(6)	103·8 (4)	107·2*
C(6)C(7)C(8)	116·1 (5)	116·7
C(6)C(7)C(11)	101·1 (5)	98·0*
C(8)C(7)C(11)	114·1 (4)	111·1*
C(7)C(8)C(9)	115·4 (4)	115·9
C(7)C(8)O(8)	109·1 (4)	108·8
C(9)C(8)O(8)	103·3 (4)	104·9
C(8)C(9)C(10)	114·3 (4)	115·4
C(1)C(10)C(9)	119·4 (4)	120·1
C(1)C(10)C(15)	123·6 (6)	125·0
C(9)C(10)C(15)	116·9 (5)	114·8
C(7)C(11)C(12)	107·5 (5)	110·1*
C(7)C(11)C(13)	129·9 (6)	127·0*
C(12)C(11)C(13)	122·6 (6)	122·9
C(11)C(12)O(6)	109·9 (5)	108·3
C(11)C(12)O(12)	128·7 (7)	128·4
O(6)C(12)O(12)	121·3 (7)	123·1
C(6)O(6)C(12)	110·5 (5)	110·1
C(8)O(8)C(16)	110·5 (4)	
O(8)C(16)O(16)	123·9 (5)	
O(8)C(16)C(17)	111·6 (6)	
O(16)C(16)C(17)	124·5 (6)	
	Obs.†	Calc.
C(1)C(2)C(3)C(4)	−55	−50
C(1)C(10)C(9)C(8)	79	74
C(2)C(3)C(4)C(5)	88	88
C(2)C(1)C(10)C(9)	−164	−167
C(3)C(4)C(5)C(6)	−163	−168
C(3)C(2)C(1)C(10)	93	95
C(4)C(5)C(6)C(7)	114	107
C(5)C(6)C(7)C(8)	21	28
C(6)C(7)C(8)C(9)	−98	−99
C(7)C(8)C(9)C(10)	59	59
C(6)C(7)C(11)C(12)	−22	−22
C(7)C(11)C(12)O(6)	10	12
C(11)C(12)O(6)C(6)	9	5
C(12)O(6)C(6)C(7)	−22	−19
O(6)C(6)C(7)C(11)	26	24
C(6)O(6)C(12)O(12)	−169	−171
C(7)C(11)C(12)O(12)	−173	−172
C(6)C(7)C(11)C(13)	158	159
C(13)C(11)C(12)O(12)	7	7
C(2)C(1)C(10)C(15)	13	11
C(6)C(5)C(4)C(14)	10	7
C(6)C(7)C(8)O(8)	146	143
C(10)C(9)C(8)O(8)	178	178

* Distances differing by more than 3σ.

† E.s.d.'s = 0·8–1·0.

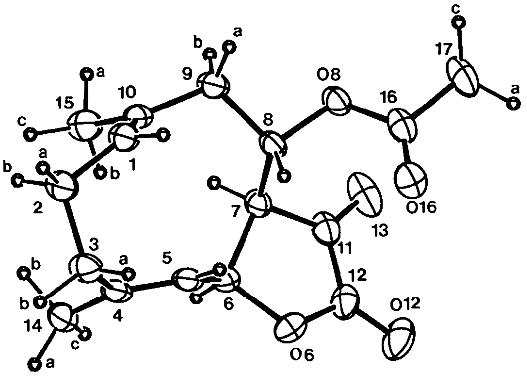

Fig. 1. *ORTEP* drawing of (1). The thermal ellipsoids are drawn at the 50% probability level.

The torsion angles are expected to be more sensitive to packing interactions. There is reasonable agreement between observed and calculated values for (1), (2) and (3); however, (4) shows some deviations as large as ±19°. These torsion angles differ from those observed in the other compounds and from the calculated values. This suggests that packing induces a conformational change. A comparison of the solid-state and solution NMR spectra will be made in order to evaluate these differences. These studies suggest that *MM*2 calculations with properly adjusted force-field parameters provide a good description of the equilibrium structure and can be used to predict solution proton coupling constants.

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9α-Bromo-16α-methylprednisolone* (I), $C_{22}H_{29}BrO_5$, and 9α-Bromoprednisolone (II), $C_{21}H_{27}BrO_5$

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Abstract. (I): $M_r = 453{\cdot}4$, monoclinic, $P2_1$, $a = 6{\cdot}550\,(6)$, $b = 14{\cdot}46\,(1)$, $c = 10{\cdot}75\,(1)$ Å, $\beta = 100{\cdot}9\,(5)°$, $V = 999{\cdot}8$ Å^3, $Z = 2$, $D_m = 1{\cdot}505\,(3)$, $D_x = 1{\cdot}506$ g cm^{-3}, $\lambda(\mathrm{Cu}\,K\alpha) = 1{\cdot}5418$ Å, $\mu = 28{\cdot}51$ cm^{-1}, $F(000) = 472{\cdot}0$, $T = 293$ K, $R = 0{\cdot}072$ for 1749 unique reflections. (II): $M_r = 439{\cdot}3$, monoclinic, $P2_1$, $a = 7{\cdot}737\,(6)$, $b = 14{\cdot}92\,(1)$, $c = 8{\cdot}94\,(1)$ Å, $\beta = 103{\cdot}6\,(5)°$, $V = 1003{\cdot}1$ Å^3, $Z = 2$, $D_m = 1{\cdot}452\,(3)$, $D_x = 1{\cdot}455$ g cm^{-3}, $\lambda(\mathrm{Cu}\,K\alpha) = 1{\cdot}5418$ Å, $\mu = 28{\cdot}27$ cm^{-1}, $F(000) = 456{\cdot}0$, $T = 293$ K, $R = 0{\cdot}075$ for 1650 unique reflections. The molecules of both compounds have very similar stereochemistry with minor differences in some torsion angles. Ring *A* is almost planar, rings *B* and *C* have chair conformations while ring *D* is a C(13) envelope. The molecules are packed by O(3)···O(17) (compound I) and O(3)···O(17) and O(3)···O(11) (compound II) intermolecular hydrogen bonds.

Introduction. Samples of the compounds were kindly supplied by the late Dr C. L. Hewett of Organon Laboratories Limited. The study was intended to give information on the stereochemistry of these two closely related compounds which might throw light on their physiological activity.

Experimental. D_m measured by flotation ($KI/Na_2S_2O_3$ in H_2O). Prismatic crystals grown from ethanol. Equi-dimensional crystals approximately 0·3 × 0·3 × 0·3 mm selected for X-ray diffraction measurements. Cell dimensions obtained initially from rotation photographs and more accurately from high-angle reflections on Weissenberg photographs using a local least-squares program. Intensity data: Leeds–Cox integrating Weissenberg camera; multiple-film photographs taken about: (I): *a*(layers 0–4), *b*(layers 0–2), *c*(layers 0–4); (II): *a*(layers 0–5), *b*(layers 0–12). Intensities derived using a Joyce–Loebl microdensitometer, Lorentz and polarization but no absorption corrections applied. (I): 1749, (II): 1650 measured reflections (2290 and 2300 in Cu sphere respectively), Friedel pairs merged; index range (I): $h \pm 8$, $k\,0/18$, $l\,0/13$; (II): $h\,-8/9$, $k\,0/19$, $l\,0/11$. Heavy-atom methods used to solve structures employing a locally written Fourier synthesis program. Program packages *SHELX76* (Sheldrick, 1976), *XANADU* (Roberts & Sheldrick, 1975) and *PLUTO* (Motherwell & Clegg, 1978) also used, with all calculations performed on the Dundee University DEC-10 computer. Refinement on *F* magnitudes, using blocked full-matrix least squares, with *SHELX76*. All atoms except H refined using anisotropic temperature factors. H atoms included as fixed atoms at calculated positions, with isotropic temperature factors fixed at 1·5 times that of the parent atom. Final refinements involved: (I): 252 refined parameters, $R = 0{\cdot}072$, unit weights, max. shift/e.s.d. = 0·058, av. shift/e.s.d. = 0·005, max. diff. peak = 1·00 e Å^{-3}, min. diff. peak = −0·95 e Å^{-3}. (II): 243 refined parameters, $R = 0{\cdot}075$, unit weights, max. shift/e.s.d. = 0·055, av. shift/e.s.d. = 0·004, max. diff. peak = 0·73 e Å^{-3}, min. diff. peak = −0·76 e Å^{-3}. Scattering factors from *International Tables for X-ray Crystallography* (1974).

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* Prednisolone is 11β,17α,21-trihydroxypregna-1,4-diene-3,20-dione.

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