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A GERMACRANOLIDE FROM *VICOA INDICA*‡

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Key Word Index—*Vicoa indica*; Compositae, sesquiterpene lactone, germacranolide.

Abstract—The aerial parts of *Vicoa indica* afforded a new sesquiterpene lactone as its acetate (**1**) the structure and relative stereochemistry of which was established by spectral data including X-ray crystallographic analysis.

INTRODUCTION

In previous communications we have reported [1, 2] on the isolation of two germacranolides from *Vicoa indica* D.C. Some more compounds have been isolated by other groups of workers [3–9] from the same plant. Herein, we report on the further chemical investigation of this plant affording a new germacranolide as its acetate (**1**).

RESULTS AND DISCUSSION

The acetone extract of aerial parts of *V. indica* after purification by CC and TLC afforded a new germacranolide as its acetate (**1**). Compound **1** was obtained as a crystalline solid (molecular formula $C_{24}H_{30}O_{10}$, M^+ 478) and showed in its IR spectrum the presence of an α-methylene-γ-lactone and ester carbonyls. Its ^{1}H NMR spectrum (Table 1) revealed the characteristic signals for an α-methylene-γ-lactone, a 2-methylbutyryloxy group, two acetate methyls and a methyl on an epoxide ring. The ^{1}H NMR spectrum along with a ^{1}H-^{1}H 2D COSY experiment showed that H-7 was coupled with H-13a, H-13b and H-8 (δ 4.21, *dd*, J = 8, 10 Hz) confirming the *trans*-lactone junction. H-8 was further *trans* coupled with H-9 (δ 5.04, *d*, J = 10.0 Hz). It also revealed the presence of an epoxide proton H-1, which appeared as a singlet at δ 3.96, indicating the presence of a carbonyl function at C-2. The two doublets at δ 3.07 (J = 12 Hz) and 3.85 (J = 12 Hz) suggested the presence of an exomethylene group at C-4. The two *trans* coupled protons H-5 and H-6 placed the 2-methylbutyryloxy ester group at C-5 and the acetate group at C-6 or vice versa.

The ^{13}C NMR spectrum (Table 1) showed the presence of three ester carbonyls, one lactone carbonyl, and one ring carbonyl at δ 201.87. The spectrum along with an INEPT experiment showed the presence of two exomethylene groups, six oxygenated carbon atoms, one appearing as a singlet and five as doublets.

The above spectral data and ^{13}C-^{1}H decoupling experiment led us to establish the structure of compound **1** as a germacranolide. However, to determine unambiguously the stereochemistry and positions of the functional groups compound **1** was subjected to single crystal X-ray analysis.

The cyclodecane ring adopts a chair-boat-chain conformation while the transfused γ-lactone ring is an envelope and is similar to that reported [1, 10]. The valency angles of the cyclodecane ring vary from 112.3(4)° to 123.5(5)°, the average angle being 115.9(4)°. The large deviation of the valence angle from the tetrahedral value of 109° indicates a considerable amount of angular strain [1, 11]. The largest deviation is found at the fusion of the epoxide ring with the 10-membered ring. In the cyclodecane ring three groups of four atoms each form a good plane viz C(9)—C(10)—C(1)—C(2); C(10)—C(1)—C(5)—C(6) and C(2)—C(4)—C(7)—C(9). The *trans* annular separation C(1)···C(5) = 4.14 Å in the germacranolide is similar to that found in 5β-acetoxy-1α,10α-epoxy-2α,9β-dihydroxy-6α-(2-methylbutyryloxy)germacran-8α,12-olide [12] which showed the absence of *trans* annular interactions as the cyclodecane ring is saturated. The structure is stabilized by intra- and intermolecular hydrogen bonding.

EXPERIMENTAL

MP: Uncorr.; Optical rotation: $CHCl_3$; IR: $CHCl_3$; ^{1}H NMR and ^{13}C NMR: $CDCl_3$ with $SiMe_4$ as int.

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Table 1. ^1H and ^{13}C NMR (200/50.2 MHz; $CDCl_3$) spectral data of compound **1**

H	δ	J (Hz)	^1H–^1H COSY	C	APT	δ	^{13}C–^1H COSY
1	3.96 *s*			1	CH	65.02	H-1
3a	3.07 *d*	12	H-3b	2	C	201.87	—
3b	3.85 *d*	12	H-3a	3	CH_2	42.00	H-3a, H-3b
5	5.74 *d*	10	H-6	4	C	131.24*	—
6	5.37 *d*	10	H-5	5	CH	76.64	H-5
7	2.79 *ddd*	8, 3.5,	H-8, H-13b,	6	CH	69.00	H-6
		3	H-13a	7	CH	43.04	H-7
8	4.21 *dd*	10, 8	H-9, H-7	8	CH	75.42	H-8
9	5.04 *d*	10	H-8	9	CH	73.55	H-9
13a	6.45 *d*	3.5	H-7	10	C	63.89	—
13b	5.88 *d*	3	H-7	11	C	135.18*	—
14	1.75 *s*			12	C	167.54†	—
15-2H	5.59 *br s*			13	CH_2	125.36	H-13a, H-13b
				14	CH_3	17.81	Me-14
				15	CH_2	126.26	2H-15
				1′	C	175.12†	—
				2′	CH	41.13	H-2′
				3′	CH_2	26.76	H-3′a, H-3′B
				4′	CH_3	11.62	Me-4′
				5′	CH_3	16.61	Me-5′
OMeBu				OAc			
2′	2.4 *m*	7	H-3′, H-5′		C	168.93†	—
3′-2H	1.6 *m*	7	H-2′, H-4′		C	170.66†	—
4′	0.9 *t*	7	H-3′		CH_3	20.79	OAcMe
5′	1.15 *d*	7	H-2′		CH_3	20.79	OAcMe
OAc	2.06 *s*						
	2.17 *s*						

* and † assignments may be interchangeable.

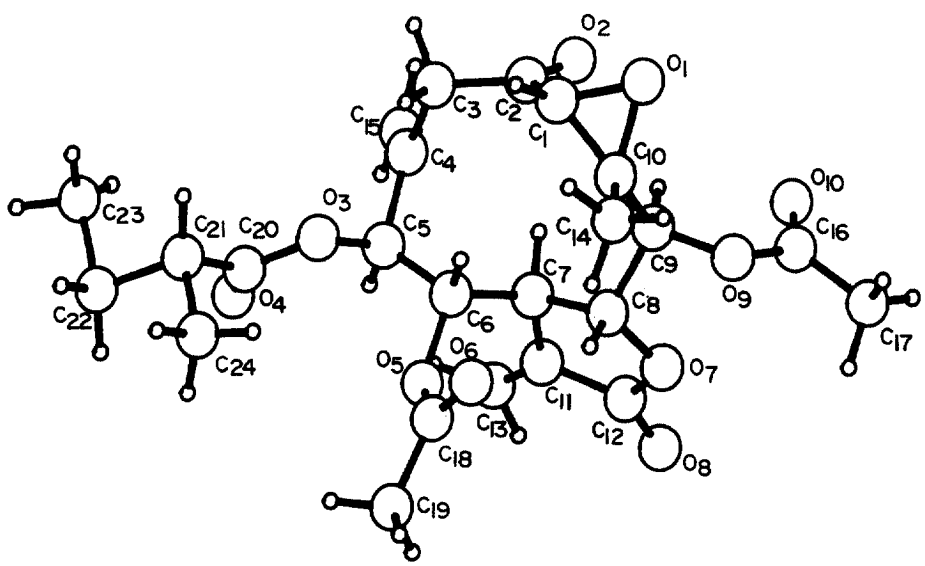

Fig. 1. PLUTO diagram of compound **1** along with crystallographic numbering of atoms.

standard; MS: Finnigan Mat-1020, Automatated GC/MS.

Plants collected during October 1991 near the National Chemical Laboratory Campus were shade dried and powdered. The powder (4 kg) was extracted with Me_2CO to give an extract (190 g), a portion (100 g) of which was fractionated over silica gel (60–120 mesh) using Me_2CO–petrol as eluent in increasing proportions of Me_2CO. Eight broad fractions were collected: A (23 g), B (12 g), C (8 g), D (4 g), E (4.5 g), F

(5 g), G (7 g) and H (29 g). 500 mg of fraction (G) on acetylation at room temp. and repeated CC and prep. TLC yielded compound **1** (85 mg), 6β,9β-diacetoxy-4(15)-en-1α,10α-epoxy-5α-(2-methylbutyryloxy)-2-oxo-7,8α-germacranolide (**1**), mp 200–2°; $[\alpha]_D^{25}$ +12.25°; (*c*, 0.32, $CHCl_3$). IR ν_{max} cm^{-1}: 1780 (C=O), 1760 (γ-lactone), 1745–1730 (CO_2R), 1650 (unsaturation): ^1H and ^{13}C NMR Table 1; MS *m/z*. (rel. int.): 478 $[M]^+$ (0.5), 418 (2), 394 (2), 394 (0.8), 376 (2), 334 (2.2), 318 (2.2), 274 (4), 258 (3.5), 85 (17) and 57 (100).

X-ray analysis of compound **1**

Single crystals of the compound were grown from Me_2CO–petrol (2:1).

Crystal data

$C_{24}H_{30}O_{10}$, $M = 478.48$ orthorhombic $a = 9.759(2)$, $b = 14.595(2)$, $c = 17.351(3)$ Å, $V = 2471.3(7)$ Å^3, space group $P2_12_12_1$ (D_2^4 No. 19). $D_c = 1.286$ g cm^{-3}, $Z = 4$ $F(000) = 1016$ (25 machine centred reflection $12 \leqslant \theta \leqslant 18°$). A colourless crystal of size $0.06 \times 0.12 \times 0.6$ mm was chosen for data collection. $\mu(Mo\text{–}K_\alpha) = 0.1$ mm^{-1}.

Data collection and processing

Enraf-Nonius CAD4 diffractometer, graphite monochromated Mo-K_α radiation ($\lambda = 0.7107$ Å), ω-2θ scan mode, ($1.87 \leqslant \theta \leqslant 23.37°$), 2074 unique reflections 1636 with ($I \geqslant 2\sigma I$).

Structure solution and refinement

The structure was solved by direct methods (MULTAN-80) using NRCVAX programs [12]. Atomic co-ordinates are depicted in Table 2. Full matrix, least-squares refinement [13] on F^2 with all non-hydrogen atoms anisotropic, H-atoms geometrically determined and confirmed by a difference Fourier were held fixed during the refinement, converged to final $R_1[F^2 \geqslant 2\sigma(F)^2] = 0.0561$, wR_2 [all data] = 0.1703, $S(F^2) = 1.043$ for 2074 reflections and 308 refined parameters. The weighting scheme $w^{-1} = [\sigma^2 (F_o^2) + 0.1204\ p^2 + 0.6810\ p]$. $P = 1/3$ [max $(F_o^2, O) + 2F_c^2$] gave satisfactory agreement analysis. An extinction correction [13] refined to 0.008(3) and the final ΔF synthesis showed no peaks outside the range $-0.262 \rightarrow +0.302$ eÅ^{-3}. The PLUTO diagram of the molecule is depicted in Fig. 1.

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Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters (Å$^2 \times 10$) for $C_{24}H_{30}O_{10}U$(eq) is defined as one third of the trace of the orthogonalized Uij tensor

	x	*y*	*z*	U(eq)
O(1)	6735(4)	8019(3)	435(3)	83(1)
O(2)	7335(4)	6343(3)	−319(2)	77(1)
O(3)	2701(3)	4935(3)	222(2)	58(1)
O(4)	2197(6)	3488(4)	157(8)	226(6)
O(5)	3596(3)	4942(2)	1735(2)	58(1)
O(6)	3091(5)	6333(3)	2173(3)	91(1)
O(7)	7437(4)	5684(3)	2378(2)	66(1)
O(8)	8203(5)	4320(3)	2742(3)	95(2)
O(9)	7801(4)	7407(3)	2017(3)	74(1)
O(10)	9803(5)	6920(6)	1577(4)	139(3)
C(1)	5719(6)	7362(4)	212(4)	68(2)
C(2)	6146(5)	6543(4)	−231(3)	60(1)
C(3)	4992(5)	5957(4)	−560(3)	60(1)
C(4)	4992(5)	4973(4)	−285(3)	55(1)
C(5)	4114(4)	4741(3)	400(3)	50(1)
C(6)	4434(5)	5306(3)	1120(3)	48(1)
C(7)	5960(4)	5276(3)	1334(3)	47(1)
C(8)	6415(5)	6070(3)	1861(3)	53(1)
C(9)	7089(5)	6867(4)	1431(3)	58(1)
C(10)	6091(6)	7517(4)	1045(3)	64(1)
C(11)	6497(5)	4447(3)	1739(3)	53(1)
C(12)	7450(6)	4770(4)	2337(3)	64(1)
C(13)	6322(7)	3579(5)	1612(4)	87(2)
C(14)	5155(6)	8059(4)	1540(4)	80(2)
C(15)	5716(6)	4321(5)	−637(3)	74(2)
C(16)	9160(8)	7277(5)	2072(5)	89(2)
C(17)	9726(9)	7649(6)	2812(5)	119(3)
C(18)	2927(5)	5531(5)	2195(3)	65(1)
C(19)	1999(7)	5051(5)	2745(4)	89(2)
C(20)	1841(6)	4263(5)	136(5)	95(2)
C(21)	396(6)	4622(5)	−42(5)	104(3)
C(22)	−604(13)	3806(10)	−171(12)	319(17)
C(23)	−208(18)	3753(19)	−1009(10)	245(10)
C(24)	−194(13)	4900(12)	731(7)	194(7)

REFERENCES

1. Dhaneshwar, N. N., Bhat, U. G., Nagasampagi, B. A. and Tavale, S. S., *Acta Crystallographica*, 1983, **C39**, 362.
2. Sawaikar, D. D., Rojatkar, S. R. and Nagasampagi, B. A., *Phytochemistry*, 1994, **37**, 585.
3. Purushothaman, K. K., Vasanth Sardha, Cox, P. J., Akinniyi, J. A., Connoly, J. D., Raycraft, D. S. and Sim, A. S., *Journal of Chemical Research* (*S*), 1981, 374, *Journal of Chemical Research* (*M*), 437.
4. Purushothaman, K. K. and Vasanth Saradha, *Indian Journal of Chemistry*, 1986, **25B**, 417.
5. Balakrishna, K., Vasanth Saradha, Bima Rao, R. and Purushothaman, K. K., *Indian Drugs*, 1989, **26**, 708.
6. Vasanth Saradha, Kundu, A. B., Purushothaman, K. K., Patra, A., Vasantha Pattabhi and

Connolly, J. D., *Journal of Natural Products*, 1990, **52**, 354.
7. Vasanth Saradha, Kundu, A. B., Panda, S. K. and Patra, A., *Phytochemistry*, 1991, **30**, 3053.
8. Vasanth Saradha, Kundu, A. B. and Patra, A., *Journal of Natural Products*, 1992, **55**, 1149.
9. Chowdhary, B. L., Hussaini, F. A. and Shoeb, A., *Journal of Crude Drug Research*, 1990, **28**, 121.
10. Hilderbrandt, R. L., Wieser, J. D. and Montgomery, L. K., *Journal of the American Chemical Society*, 1973, **95**, 8598.
11. Cox, P. J. and Sim, G. A., *Journal of the Chemical Society, Perkin Transaction*, 2, 1974, 1355.
12. Gabe, E. J., Page, Y.-Le., Charland, J. P., Lee, F. L. and White, P. S., *Journal of Applied Crystallography*, 1989, **22**, 384.
13. Sheldrik, G. M., SHELXL-93, Program for the refinement of crystal structures. University of Gottingen, Germany, 1993.