Pergamon 0031-9422(95)00232-4 Phytochemistry, Vol. 40, No. 1, pp. 335 336, 1995

0031-9422/95 $9.50 + 0.00

VICOGENIN, A 28-NOR-12-OLEANENEPENTOL FROM *VICOA INDICA*

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(*Received* 21 *November* 1994)

Key Word Index—*Vicoa indica*; Compositae; vicogenin; triterpenoid; 28-nor-12-oleanenepentol.

Abstract—Vicogenin, a new triterpenoid, has been isolated from the chloroform extract of *Vicoa indica* and its structure assigned as 28-nor-12-oleanene-2β,3β,16β,17β,23-pentol on the basis of its spectroscopic properties.

INTRODUCTION

Vicoa indica DC known as 'Banjouri' in Hindi, is used as a tribal antifertility drug in Bihar State, India. Previous work resulted, *inter alia*, in the isolation of a monoterpenoid diol vicodiol [1], the sesquiterpenoid lactones vicolides A–D [2], and, more recently, a 28-nor-12-oleanene triterpenoid glycoside vicoside A **1** [3]. We now report on the isolation and structural elucidation of vicogenin (**2**), the desformyl aglucone of vicoside A, whose structure has been independently confirmed by X-ray analysis [4].

RESULTS AND DISCUSSION

The chloroform extract of the aerial part of the plant was chromatographed over silica gel. Elution with $CHCl_3$–MeOH (9:1) afforded vicogenin (**2**), $C_{29}H_{48}O_5$ ([M–H_2O]$^+$458), ν_{max} 3400, 1620, 830 cm^{-1}. Its ^1H and ^{13}C NMR spectra revealed the presence of six tertiary methyl groups (see Experimental), one primary, one tertiary and four secondary oxygenated carbons and a trisubstituted double bond, whose carbon chemcial shifts [δ_c 124.0(*d*) and 144.6(*s*)] were suggestive of a 12-oleanene skeleton [5]. It was apparent that a methyl group had been lost. Acetylation afforded a tetra-acetate, **3**, which still retained hydroxyl absorption in its IR spectrum. The mass spectrum of **2** did not show a parent ion, the highest peak being at *m/z* 458 [M–H_2O]$^+$. The mass spectrum of **3** also showed a ready loss of water (*m/z* 626 [M–H_2O]$^+$). The retro-Diels Alder fragments at *m/z* 239 and 236 in the mass spectrum of vicogenin indicated that three hydroxyls were situated in rings A/B and two in rings D/E. Ready loss of water from the ring D/E fragment gave rise to the base peak at *m/z* 218.

The hydroxylation pattern of ring A was readily revealed as 2β,3β,23 by inspection of the ^1H NMR chemical shifts and coupling constants of vicogenin and its acetate and comparison with literature values [6]. In **2**, H-3α appears at δ_H 3.62 (*d*, *J* = 5.0Hz) while the multiplicity of H-2α is obscured because of overlap with the third secondary hydroxyl proton (H-16α) at δ_H 4.16. However, the ^1H NMR spectrum of **3** in C_6D_6 clearly shows H-2α as a doublet of triplets (*J* = 3.7, 3.0Hz) at δ_H5.63 and simultaneously reveals the other proton (H-16α) as a doublet of doublets (*J* = 11.2, 6.2Hz) at δ_H 5.73. The high-field nature of the primary alcohol protons [δ_H 3.28 and 3.52 (AB*q*, *J* = 11.8 Hz)] indicates their attachment to C-23 [5]. Comparison of the ^{13}C NMR data of **3** and methyl 2β,3β,16α,23-tetracetoxy-12-oleanen-28-oate [6] confirmed these assigments. The shifts are identical, except for those associated with C-15 to C-18. The coupling constants of the remaining secondary hydroxyl proton (see above) of **2** are consistent with the presence of a 16β hydroxyl group [7]. The tertiary hydroxyl group must be sited at C-17 because H-18 [δ_H 2.45 (*dd*, *J* = 13.8, 3.9 Hz)] is clearly visible. Thus, vicogenin is a 17-hydroxy-28-nor-12-oleanene derivative.

NOE difference experiments provided an easy solution to the uncertainty concerning the configuration of the D/E ring fusion and also enabled unambiguous assignment of the ^1H methyl resonances. A large NOE (~ 12%) between H-12 and H-18 supports the normal *cis* D/E ring junction (17β-OH, 18β-H). Inspection of models reveals that such a large effect is only possible for the *cis* (β) stereochemistry. Thus vicogenin is 28-nor-12-oleanene-2β,3β,16β,17β,23-pentol (**2**) and represents a further addition to the small group of 17-hydroxy-28-nor-12-oleanenes [8, 9].

The NOE experiments were run in a mixture of CD_3OD and $CDCl_3$, which resulted in better resolution of the methyl resonances [δ 0.90, 0.92, 1.00 (6H), 1.25 and 1.30; cf. 0.91 (6H), 1.00 (6H), 1.20 and 1.26 in CD_3OD]. Irradiation of the lower field H-23 gave a NOE at the

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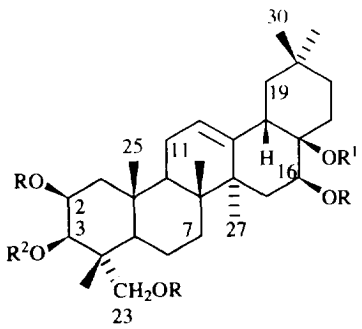

1 R = H; R¹ = CHO; R² = β-D-glu
2 R = R¹ = R² = H
3 R = R² = Ac; R¹ = H

methyl at δ_H 0.92, which is therefore Me-24. Irradiation of Me-24 readily identified Me-25 at δ_H 1.30. In view of the large NOEs induced at Me-25 and H-18 by irradiation of the six-proton signal at δ_H 1.00, this must contain Me-26 and Me-30. The Me-27 at δ_H 1.25 was identified by irradiation of H-16 (the simultaneous irradiation of H-2 gave a NOE at H-3). The highest field methyl at δ_H 0.90 is, by exclusion, Me-29.

EXPERIMENTAL

All mps uncorr. IR: KBr discs or in CCl_4 solution; ^1H (200 MHz) and ^{13}C (50 MHz) NMR: $CDCl_3$ or CD_3OD. Shifts are relative to $CHCl_3$ at 7.25 ppm or CD_2HOD at 3.30ppm for protons and $CDCl_3$ at 77.0 ppm or CD_3OD at 49.0 ppm for ^{13}C. EIMS: 70 eV, direct inlet.

The plant material was collected by Dr P. Brindha, Department of Botany, Captain Srinivasa Murti Research Institute for Ayuveda, Madras. A voucher specimen is deposited in the herbarium of the Institute. The shade-dried and coarsely ground plant material (6 kg) was extracted with $CHCl_3$ by cold percolation for 48hr. The extract was chromatographed over silica gel. Elution with $CHCl_3$–MeOH (9:1) afforded a crude fraction, which was purified by repeated CC over silica gel and crystallization to give 28-nor-12-oleanene-2β,3β,16β, 17β,23-pentol (**2**) (vicogenin) (65 mg), mp 245° (ex $CHCl_3$), $C_{29}H_{48}O_5$, ([M–H_2O]$^+$ 458) IR ν_{max}^{KBr} cm^{-1}: 3400, 2920, 1635, 1450, 1380, 1360, 1050,1040, 995, 960, 820, 760; ^1H NMR (CD_3OD):δ_H 0.91 (6H, Me-24 and Me-29), 1.00 (6H, Me-26 and Me-30), 1.20 (Me-27), 1.26 (Me-25), 2.45 (*dd*, J = 13.6, 3.9 Hz, H-18), 3.28 and 3.52 (AB*q*, J = 11.8Hz,2H-23), 3.62 (*d*, J = 5.0Hz, H-3), 4.10 (m, H-2 and H-16), 5.25 (*t* J = 3.5Hz, H-12); ^{13}C NMR (CD_3OD): δ_C45.2 (C-1), 66.3 (C-2), 73.4 (C-3), 42.7 (C-4), 50.2 (C-5), 18.8 (C-6), 31.6 (C-7), 40.9 (C-8), 48.4 (C-9), 37.8 (C-10), 24.7 (C-11), 124.0 (C-12), 144.6 (C-13), 44.8 (C-14), 37.1 (C-15), 72.2 (C-16), 74.9 (C-17), 48.7 (C-18), 49.5 (C-19), 31.6 (C-20), 35.7 (C-21), 33.7 (C-22), 67.4 (C-23), 14.1 (C-24), 18.0 (C-25), 17.5 (C-26), 27.1 (C-27), 33.2 (C-29), 24.6 (C-30); EIMS (rel.int.) *m/z* (%): 458 [M$^+$–18]$^+$ (1.9), 440 (1.6), 409 (1.0), 239 (6.6), 236 (1.3), 221 (3.8), 218 (100), 205 (6.6), 204 (6.1), 203 (18.5), 200 (5.9), 189 (36.5), 133 (10.2), 121 (13.9), 118 (13.8), 109 (11.3), 107 (16.2), 105 (14.3), 95 (16.2), 93 (13.7), 91 (12.0), 84 (17.0), 79 (10.0), 69 (19.1).

Acetate **3**. Vicogenin (30 mg) in dry pyridine (5 ml) was treated with Ac_2O (1 ml) at temp. for 12hr. the usual work-up afforded **3** (20 mg), mp 91°, $C_{37}H_{56}O_9$, ([M–18]$^+$ 626) IR $\nu_{max}^{CCl_4}$ cm^{-1} 3400, 1735, 1650; ^1H NMR ($CDCl_3$): δ_H 0.70, 0.95, 0.98, 1.02, 1.21 and 1.22 (*t*-Me), 1.98, 2.03, 2.05 and 2.06 (Ac), 2.45 (*dd*, J = 12.0, 5.0 Hz, H-18), 3.67 and 3.84 (AB*q*, J = 11.8 Hz, 2H-23), 4.90 (*d*, J = 4.0 Hz, H-3), 5.32 (*t*, J = 3.5 Hz, H-12), 5.40 (*m*, H-2 and H-16); ^{13}C NMR ($CDCl_3$): δ_C 41.5 (C-1), 69.5 (C-2), 71.9 (C-3), 40.0 (C-4), 47.5 (C-5), 17.5 (C-6), 32.4 (C-7), 39.7 (C-8), 47.4 (C-9), 36.5 (C-10), 23.5 (C-11), 123.7 (C-12), 142.0 (C-13), 43.4 (C-14), 30.9 (C-15), 69.5 (C-16), 73.2 (C-17), 49.0 (C-18), 47.7 (C-19), 30.7 (C-20), 35.7 (C-21), 31.3 (C-22), 65.4 (C-23), 13.8 (C-24), 16.4 (C-25), 17.2 (C-26), 26.3 (C-27), 32.4 (C-29), 24.0 (C-30), 170.8, 170.4, 170.3, 170.1, 21.2, 21.15, 20.8 and 20.7 (acetates); E/MS *m/z* (rel.int.): 626 [M–18]$^+$ (0.2), 566 (2.1), 218 (42.0), 203 (7.6), 201 (5.0), 189 (15.7), 173 (49.0), 95 (5.9), 81 (7.2), 69 (7.4), 55 (7.9), 43 (100).

Acknowledgements—The authors thank Dr P. Brindha, Department of Botany, Captain Srinivasa Murti Drug Research Insitute, for collection and identification of plant material, the Director, Central Council for Research in Ayurveda and Siddha, New Delhi, for financial support, and Mr B.Jayakumar for secretarial assistance.

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