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## VENUDELPHINE, A NEW HETISINE-TYPE ALKALOID FROM *DELPHINIUM VENULOSUM*

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**ABSTRACT.**—A new hetisine-type diterpene alkaloid, venudelphine [1], was isolated from the pH 12 fraction of *Delphinium venulosum* (Ranunculaceae) in addition to previously isolated alkaloids. The structure of venudelphine was established by spectral data.

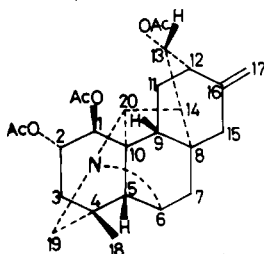
In a previous study (1) with the aerial parts of *Delphinium venulosum* Boiss. (Ranunculaceae), four hetisine-type alkaloids, hetisine, hetisinone, venulol, and venuluson were isolated, the last two compounds being new.

In the present investigation, the pH 12 fraction of the same plant extract yielded another new C<sub>20</sub> alkaloid, venudelphine [1]. The new compound had a molecular formula C<sub>26</sub>H<sub>33</sub>NO<sub>6</sub> (*m/z* 455.2316, calcd 455.2307). The ir spectrum of 1 showed the presence of acetyl signals at 1737, 1730, and 1240 cm<sup>-1</sup>. The uv spectrum had only end absorption at 220 nm. The <sup>1</sup>H-nmr spectrum indicated an exomethylene group at δ 4.99 (1H, br s) and 4.82 (1H, br s) (C-17 protons), three acetyl signals at δ 2.09 (3H, s), 2.01 (3H, s), 1.98 (3H, s), and an Me signal at δ 1.05 (3H, s, Me-18); other signals were at δ 2.82 (1H, br d, *J* = 14 Hz), 2.55 (1H, br d, *J* = 14 Hz) (C-19 protons), 3.86 (1H, s, H-20), and at δ 3.32 (1H, br s, H-6). The signals of hydrogens geminal to acetyl groups were at δ 5.72 (1H, d, *J* = 3.5 Hz, H-1α), 5.31 (1H, dd, *J* = 3.5 and 5 Hz, H-2β), 5.07 (1H, dt,

*J* = 10, 1.5 and 1.5 Hz, H-13β). Spin-decoupling experiments indicated the relationship between H-1 and H-2; when the signals at δ 5.31 (H-2β) and 5.72 (H-1α) were irradiated separately the other signal collapsed to a singlet (H-1) or a doublet (H-2).

The stereochemistries at C-1 and C-2 of 1 were decided by measuring the *J* values and studying Dreiding models. <sup>13</sup>C-nmr and APT spectra of 1 indicated the presence of four Me quartets, six methylene triplets, nine methine doublets, and seven quaternary carbon atoms and thus suggested a hetisine-type compound with three acetyl groups. As the signals at 71.1, 73.1, and 74.9 ppm were doublets in the <sup>13</sup>C-nmr spectrum, the acetyl groups could be situated at C-1, C-2, C-3, C-7, C-11, C-15, and C-19; the signals of two doublets at δ 2.82 and 2.55 in the <sup>1</sup>H-nmr spectrum and the signal of a triplet at 64.10 ppm in the <sup>13</sup>C-nmr spectrum clearly indicated the C-19 protons. When C-15 bears an acetyl group, the signal for C-16 appears at ca. 150–151 ppm (2). Location of the oxygen functions at C-1, C-3, or C-7 adjacent to quaternary carbon atoms (C-10, C-4, and C-8, respectively) will cause them to be further downfield than expected in the <sup>13</sup>C-nmr spectrum (3). Although there were no significant shifts in the signals of C-4 and C-8, the signal for C-10 shifted downfield to 52.8 ppm, indicating an acetyl function at C-1 (4).

Due to the lack of a signal at ca. 18–20 ppm and the spin-decoupling experiments between H-1 and H-2, the second acetyl group was placed at C-2. The



1

third acetyl group could be situated either at C-11 or C-13. The signals at  $\delta$  5.07 (in  $^1\text{H}$  nmr) and at 74.9 ppm (in  $^{13}\text{C}$  nmr) indicated that the acetyl should be at C-13 rather than at C-11. In order to prove this, the related protons beginning from H-20 were irradiated; the signal for H-20 was at  $\delta$  3.86 as a singlet, but because the dihedral angle between H-20 and H-14 ( $\delta$  2.45, 1H, br d,  $J = 10$  Hz) was  $90^\circ$  they did not couple; nevertheless, irradiation of the signal at  $\delta$  3.86 caused a slight sharpening in the signal at  $\delta$  2.45, while irradiation of the latter signal (H-14) collapsed the signal at  $\delta$  5.07 (1H, dt, H-13) into a triplet ( $J = 1.5$  Hz).

Irradiation of the signal at  $\delta$  5.07 collapsed the signal at  $\delta$  2.45 to a broad singlet, showing the relation between H-13 and H-14, and indicating that the third acetyl group was at C-13. The stereochemistry at this position was decided by selecting the boat shape ring (C-8, C-9, C-11, C-14) as the reference ring and studying the  $^1\text{H}$ -nmr spectrum using a Dreiding model. When H-13 has an axial ( $\beta$ ) stereochemistry, the dihedral angle between H-13 and H-14 is ca.  $35\text{--}40^\circ$ , which was in agreement with the given coupling constant. The spectral data suggested the given formula for **1**.

## EXPERIMENTAL

**GENERAL EXPERIMENTAL PROCEDURES.**—The ir spectrum was recorded on a Perkin-Elmer 983 instrument in  $\text{CHCl}_3$ ;  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr spectra were determined on a Bruker AC-200 L in  $\text{CDCl}_3$ ; hrms were run on a Kratos MS-30 spectrometer; the optical rotation was determined using an Opt. Act. Ltd. AA-5 polarimeter.

**PLANT MATERIAL.**—*D. venulosum* was collected from Ulukışla-Nigde (Central Turkey) in July 1990 and identified by Dr. R. Ilarslan (Ankara). A voucher specimen is deposited in the Herbarium of the Faculty of Pharmacy, University of Ankara (Ilarslan 1613).

**EXTRACTION AND ISOLATION.**—The plant

material (500 g) was extracted with 70% EtOH by percolation at room temperature. The solvent was evaporated under a vacuum, and the residue was treated with 1.5%  $\text{H}_2\text{SO}_4$  and extracted with  $\text{C}_6\text{H}_6$  before alkaloid extraction. Alkaloids were separated from the remaining aqueous solution as previously described (5). After venulol, hetsisine, and hetsisine were separated from the pH 12 solution (1), the remaining part was fractionated on a Sephadex LH-20 column, eluting with petroleum ether- $\text{CHCl}_3$ -MeOH (7:4:2) and yielding 20 mg of the new compound **1**.

**Venudelpine [1].**— $[\alpha]^{22\text{D}} \pm 0^\circ$  ( $\text{CHCl}_3$ ,  $c = 0.1$ ); ir ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ )  $\nu$  max 3070, 3020, 2970, 2930, 2880, 1737, 1730, 1650, 1450, 1430, 1365, 1240, 1020;  $^1\text{H}$  nmr ( $\text{CDCl}_3$ ) see text;  $^{13}\text{C}$  nmr 73.1 (C-1, d), 71.1 (C-2, d), 36.7 (C-3, t), 37.4 (C-4, s), 54.7 (C-5, d), 67.1 (C-6, d), 35.7 (C-7, t), 43.9 (C-8, s), 63.2 (C-9), 52.8 (C-10, s), 29.2 (C-11, t), 49.4 (C-12, d), 74.9 (C-13, d), 51.6 (C-14, d), 34.1 (C-15, t), 142.1 (C-16, s), 110.6 (C-17, t), 29.2 (C-18, q), 64.1 (C-19, t), 60.3 (C-20, d), 170.8 (COMe, s), 21.0 (COMe, q), 169.9 (COMe, s), 21.2 (COMe, q), 169.7 (COMe, s), 21.5 (COMe, q); hrms  $m/z$  (intensity, %)  $[\text{M}]^+$  455.2316 (10.2) (calcd for  $\text{C}_{26}\text{H}_{33}\text{NO}_6$ , 455.2307),  $[\text{M} - \text{Me}]^+$  440 (8),  $[\text{M} - \text{Ac}]^+$  412 (60),  $[\text{M} - \text{OAc}]^+$  395 (100),  $[\text{M} - \text{OAc} - \text{Ac}]^+$  352 (27),  $[\text{M} - 2 \times \text{OAc} - \text{Ac}]^+$  292 (5), 105 (18), 91 (10).

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