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PANICUDINE — A NEW ALKALOID FROM *Aconitum paniculatum*

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A structure proposed for panicudine — a C_{20}-diterpene alkaloid of the hetisine type — has been established on the basis of an analysis of IR, UV, mass and ^1H and ^{13}C NMR spectra.

We have continued an investigation of the alkaloids of *Aconitum paniculatum* Lam., cultivated in the Polar-Alpine Botanical Garden [1]. By column chromatography of the total alkaloids obtained from the roots and rhizomes of this plant we have isolated a new base with mp 249-250°C, which has been called panicudine (**1**). High-resolution mass spectrometry showed that the composition of (**1**) corresponded to the formula $C_{20}H_{25}NO_3$ (M^+ 327).

The IR spectrum of panicudine had absorption bands at (cm^{-1}) 3405 (OH), 1718 (C=O), and 1650 (C=C). A study of its PMR spectrum showed the presence in the panicudine molecule of secondary hydroxy (4.02 ppm, m, 1H, $W_{1/2}$ = 10 Hz), exomethylene (4.87 and 4.76 ppm, br.s, 1H each), and tertiary methyl (1.29 ppm, s, 3H) groups and the absence of N-methyl, N-ethyl, and methoxy groups. This indicated that (**1**) belonged to the hetisine type of C_{20}-diterpene alkaloids. The PMR spectrum of (**1**) also contained a singlet at 3.49 ppm (1H, H-20), doublets at 3.12 and 2.95 ppm in the form of an *AB* quartet J = 11.5 Hz, 2H-19), and doublets with triplet components at 2.52 and 2.22 ppm in the form of an *AB* quartet (J = 18 and 1.5 Hz, 2H-15), showing the absence of substituents at C-19 and C-15, respectively. The positions of the substituents in the hetisine skeleton of (**1**) were elucidated by an analysis of the ^{13}C NMR spectrum, in which signals from 20 carbon atoms were

TABLE 1. Chemical Shifts of the Carbon Atoms of Panicudine (**1**) in Py-d_5 and of Spirasine-IV (**3**), Spiradine-A (**4**), and Spirasine-IX (**5**) in $CDCl_3$ [7]

C atom	1	3	4	5
1	34.9 t*	34.9	35.6	35.2
2	66.1 d	19.3	19.2	19.3
3	43.3 t	33.7	33.8	33.9
4	37.7 s	38.0	37.7	38.0
5	62.5 d †	61.2	61.9	61.0
6	99.7 s	65.4	98.7	65.6
7	44.4 t	33.9	45.2	35.2
8	44.2 s	43.0	44.5	44.2
9	49.7 d	48.9	65.2	65.3
10	49.7 s	49.8	51.8	51.0
11	23.4 t	22.7	211.0	211.2
12	54.0 d	53.3	53.3	53.4
13	210.8 s	213.0	27.6	28.3
14	61.9 d †	60.9	43.9	45.0
15	34.0 t*	26.0	29.2	28.4
16	144.9 s	142.7	143.5	144.1
17	110.3 t	110.4	110.9	110.1
18	32.0 q	28.8	30.6	28.8
19	61.9 t	62.7	60.8	63.1
20	70.2 d	70.0	74.6	75.7

*,†The assignments may be interchanged.

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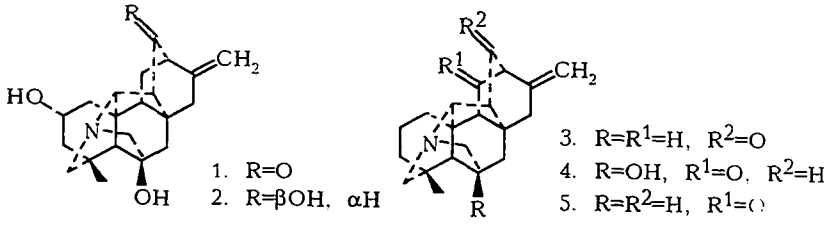
detected. The "off resonance" spectrum showed the presence of 6 quaternary, 6 methine, 7 methylene, and 1 methyl carbon atoms (Table 1). A singlet at 144.9 and a triplet at 110.3 ppm, and also the CS of the singlet signal of C-16 confirmed the presence of an exomethylene group and the absence of a substituent at C-15 [2]. A singlet signal at 99.7 ppm related to a carbinolamine carbon atom [3, 4], and, consequently, there was a tertiary hydroxy group at C-6. The remaining carbonyl and hydroxy groups could be present in the C-1, C-2, C-3, C-7, C-11, and C-13 positions. Singlet signals at 37.7, 44.2, and 49.7 ppm were assigned to the C-4, C-8, and C-10 quaternary carbon atoms, the CSs of which were closest to those of tatsirine (**2**) (δ, ppm: 36.8 (C-4), 44.8 (C-8), and 49.4 (C-10)) [4], which has a hydroxy group at C-2. In fact, the spectrum of (**1**) lacked the triplet signal in the 18.3-19.8 ppm region that is characteristic for the C-2 carbon atom when there is no substituent in ring *A* [5-7]. The presence of a carbonyl group in this position would lead to downfield shifts ($\Delta\delta \sim 5$ ppm) of the signals of the C-4 and C-10 carbon atoms; for example, in geyeridine and delbidine they are observed at 42.8 and 42.3 ppm (C-4) and 55.7 and 55.6 ppm (C-10), respectively [3, 8].

The C-11 and C-13 positions remained possible for the carbonyl group, since the UV spectrum of panicudine had a maximum in the 300 nm region that is characteristic for a β,γ-unsaturated ketone. Moreover, the location of a carbonyl group at C-1, C-3, or C-7 would cause a considerable downfield shift of the singlet signals as a result of the β-effect, which was not observed. The choice between the C-11 and C-13 positions for the keto group was made by comparing the ^{13}C NMR spectra of (**1**) with those of spirasine-IV (**3**), spiradine-A (**4**), and spirasine-IX (**5**) (Table 1) [7], having a carbonyl group in position 13 (spirasine-IV) or 11 (spiradine-A, spirasine-IX). The results of the analysis showed that, regardless of the position of the carbonyl group — at C-11 or C-13 — the CSs of the signals of the C-12 carbon atom were almost identical. The CSs 23.4 (t), 49.7 (d), 49.7 (s), and 61.9 (d) in the spectrum of panicudine were closer to those of the signals of C-11, C-10, C-9, and C-14 of spirasine-IV than to those of the C-13, C-10, C-14, and C-9 signals of spiradine-A and spirasine-IX, which have a carbonyl group at C-11. Consequently, the carbonyl group is present in the C-13 position, and panicudine has the structure of 6-hydroxy-11-deoxy-13-dehydrohetisine (**1**).



EXPERIMENTAL

The IR spectrum was obtained on a Perkin-Elmer model 2000 Fourier IR spectrometer; the UV spectrum on a Perkin-Elmer UV-VIS Lambda-16 spectrophotometer; and the ^1H and ^{13}C NMR spectra on a Tesla BS 567 A instrument at frequencies of 100 and 25 MHz, respectively (for ^1H in CD_3OD and for ^{13}C in deuteropyridine). The ^{13}C NMR spectra were obtained under conditions of complete and partial decoupling of C–H interactions. The mass spectrum was taken on a Kratos MS 25 RF chromato-mass spectrometer (ionizing energy 70 eV, source temperature 200°C, temperature of direct injection 120-150°C, collector current 100 μA).

Chromatographic monitoring was affected by TLC (Al_2O_3, KSK and Silufol) in the solvent systems chloroform–methanol (4:1) and ethyl acetate–methanol–ammonia (10:5:3 drops).

For the isolation of the alkaloids, see [1]. On treatment with acetone, fractions 19-21 deposited crystals of technical panicudine with mp 215-217°C.

Panicudine — mp 249-250°C (from EtOH–$CDCl_3$–C_6H_{14}).

UV spectrum (EtOH, λ_{max}, nm): 205, 300.

IR spectrum (KBr, ν, cm^{-1}) 3405, 2931, 1718, 1650, 1423, 1342, 1278, 1219, 1171, 1143, 1066, 1037, 1015, 965, 947, 902, 867, 822.

PMR spectrum (ppm, J; Hz): 1.29 (3 H, s, 18-Me), 2.20 (1 H, s, $W_{1/2}$ = 5, H-14), 2.22 and 2.52 (dt, each 1 H, J = 18 and 1.5, 2 H-15), 2.74 (1 H, br.d, J = 4, H-12), 2.95 and 3.12 (d, each 1 H, J = 11.5, 2 H-19), 3.49 (1 H, s, H-20), 4.02 (1H, m, $W_{1/2}$ = 10, Hβ-2), 4.76 and 4.87 (s, each 1 H, $W_{1/2}$ = 4, 2 H-17).

Mass spectrum, *m/z* (I_{rel} %): 327 (M, 100), 310 (32), 299 (14), 282 (6), 254 (12), 240 (7), 224 (7), 191 (15), 190 (13), 178 (15), 176 (16), 160 (60), 148 (10), 128 (12), 118 (32), 105 (18), 91 (30), 84 (11), 77 (18), 55 (18). HRMS: Found 327.18133 $C_{20}H_{25}NO_3$; Calculation 327.18345.

REFERENCES

1. I. M. Yusupova, I. A. Bessonova, and B. Tashkhodzhaev, Khim. Prir. Soedin., 277 (1995).
2. A. G. Gonzalez, G. de la Fuente, M. Reina, R. Diaz, and I. Timon, Phytochemistry, **25**, 1971 (1986).
3. J. A. Grina, D. R. Schroeder, E. T. Wydallis, F. R. Stermitz, J. Melman, and J. L. Capinera, J. Org. Chem., **51**, 390 (1986).
4. X. Zhang, J. K. Snyder, B. S. Joshi, J. A. Glinski, and S. W. Pelletier, Heterocycles, **31**, 1879 (1990).
5. S. I. Sakai, I. Yamamoto, K. Hotoda, K. Yamaguchi, N. Aimi, E. Yamanaka, J. Haginiwa, and T. Okamoto, J. Pharm. Soc. Jpn., **104**, 222 (1984).
6. F. Sun, X. T. Liang, and D. Q. Yu, J. Nat. Prod., **51**, No. 1, 50; No. 5, 923 (1988).
7. Atta-ur-Rahman, Handbook of Natural Products Data, Vol. 1, Diterpenoid and Steroidal Alkaloids, Elsevier, Amsterdam (1990), p. 241.
8. B. S. Joshi, H. K. Desai, E. A. El Kashoury, S. W. Pelletier, and J. D. Olsen, Phytochemistry, **26**, 1561 (1986).