Chemistry of Natural Compounds, Vol. 32, No. 4, 1996

STRUCTURE OF PANICULADINE

I. A. Bessonova and Sh. A. Saidkhodzhaeva

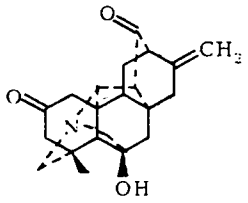
UDC 547.944/945

The new alkaloid paniculadine has been isolated from the epigeal parts of the cultivated plant Aconitum paniculatum *Lam., and its structure has been established by spectral and chemical methods.*

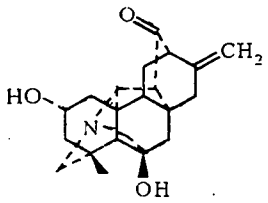
Continuing a study of the alkaloid composition of *Aconitum paniculatum* Lam. (panicled monkshood) [1], we have investigated the roots and rhizomes of this plant cultivated in the Polar-Alpine Botanical Garden [2]. The raw material, gathered in the stage of the withering of the epigeal part, was sent to us by A. P. Gorelova. The alkaloid content was 0.56% on the weight of the air-dry raw material. From the total alkaloids we isolated panicudine [3], paniculamine [4], and a new base with mp 276-278°C, which we have called paniculadine (**1**).

Paniculadine is insoluble in water and ether, sparingly soluble in ethanol and methanol, and less soluble in acetone and chloroform, and it crystallizes from acetone. It has the composition $C_{20}H_{23}NO_3$ (M^+ 325). Its IR spectrum showed absorption bands of hydroxy (3194 cm^{-1}), carbonyl (1717 and 1708 cm^{-1}) and exomethylene (1651 cm^{-1}) groups. Its composition differs from that of panicudine (**2**) by two hydrogen atoms.

Analysis of the PMR spectra of (**1**) and (**2**) taken in deuteropyridine showed the presence in the spectrum of each alkaloid of the signal of an 18-methyl group in the weak field (at 1.50 and 1.49, ppm, respectively), which is characteristic of hetisine alkaloids with a hydroxy group at C-6 [5]. The signals of exomethylene groups were observed in the form of broadened singlets, at 4.62 and 4.79 ppm. Consequently, paniculadine is an alkaloid of the hetisine type containing a tertiary hydroxyl in position 6. The two remaining oxygen atoms are present in the form of carbonyl groups. Three singlet signals at 210.1, 210.9, and 99.0 ppm in the ^{13}C NMR spectrum of paniculadine (**1**) confirmed the presence in it of a tertiary hydroxy group at C-6 and two carbonyl groups.



1



2

The UV spectrum of (**1**) showed a maximum in the 301 nm region, which is characteristic for β,γ-unsaturated ketones. Consequently, one carbonyl group could be located in position 11 or 13. In the ^{13}C NMR spectra of known hetisine alkaloids with a carbonyl group at C-13, the signal of the C-11 carbon atom is observed in the 22.7-23.4 ppm region (spirazine IV [6], panicudine [3]), while for those with a carbonyl at C-11 the C-13 signal appears at 27.6–28.3 ppm (spirazine A [6], spirazine IX [6]).

A triplet signal in the 3.2 region of the spectrum of (**1**) showed that its β,γ-unsaturated carbonyl group is in position 13. The location of the second carbonyl group was established by a comparison of the ^{13}C NMR spectra of paniculadine and panicudine (Table 1).

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (3712) 89 14 75. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 576-579, July-August, 1996. Original article submitted February 5, 1996.

0009-3130/96/3204-0561$15.00

TABLE 1. Chemical Shifts of the Carbon Atoms of Paniculadine (1) and of Panicudine (2) in Deuteropyridine

C atom	1	2	C atom	1	2
1	43.7 t	34.9	11	23.2 t	23.4
2	210.1 s*	66.1	12	53.2 d	54.8
3	52.4 t	43.3	13	210.0 s*	210.8
4	43.9 s	37.7	14	61.1 d**	61.9
5	61.0 d**	62.5	15	33.2 t	34.0
6	99.0 s	99.7	16	143.7 s	144.9
7	44.1 t	44.4	17	110.6 t	110.3
8	44.7 s	44.2	18	30.4 q	32.0
9	48.6 d	49.7	19	63.2 t	61.9
10	54.8 s	49.7	20	71.8 d	70.2

*, **The assignments may be interchanged.

The main difference between the spectra consists in the fact that in the spectrum of (1) the signal of C-2 is observed in the form of a singlet at 210.1 ppm, while in the spectrum of (2) it is in the form of a doublet at 66.1 ppm. The presence of the carbonyl group at C-2 causes considerable downfield shifts of the triplet signals of the carbon atoms C-1 and C-3 ($\Delta\delta$ 12.8 and 9.1 ppm) and of the singlet signals from the quaternary carbon atoms C-4 and C-10 ($\Delta\delta$ 6.2 and 5.1 ppm) relative to their positions in the spectrum of (2), which is due to the β- and γ-effects of the carbonyl group, respectively.

In the spectra of alkaloids containing a carbonyl group at C-2 (geyerine, geyeridine, delbidine, hetisine) the chemical shifts of the carbon atoms C-1, C-3, C-4, and C-10 appear in the 43.2-45.2, 49.9-51.6, 42.3-45.9, and 55.7-56.6 ppm regions, respectively [7-9], i.e., close to those observed in the spectrum of paniculadine (see Table 1). Consequently, paniculadine has the structure (1). Structure (1) has been confirmed chemically: the oxidation of panicudine with the Jones reagent [10] gave dehydropanicudin, which was identical with paniculadine according to a mixed melting point, TLC, and mass and PMR spectra.

EXPERIMENTAL

For general observations, see [3].

^1H and ^{13}C NMR spectra were taken on a Tesla BS 567A instrument at frequencies of 100 MHz (0 — HMDS) and 25.142 MHz (0 — TMS), respectively. The ^{13}C NMR spectra were obtained under conditions of complete and incomplete decoupling from protons. Mass spectra were taken on a MKh-1310 instrument (EI, 70 eV).

Isolation of the Alkaloids. The air-dry comminuted roots and rhizomes of panicled monkshood (44 g) were covered with 80% alcohol (5 × 2.5 liters). The alcoholic solution was evaporated in vacuum, and the residue was partitioned between water (A) and chloroform (B). The aqueous solution (A) was made alkaline with sodium carbonate, and the alkaloids were extracted with chloroform, the distillation of this extract then giving 4.1 g of alkaloids. The chloroform solution (B) was extracted with 5% sulfuric acid. The acid extract was washed with chloroform, made alkaline with sodium carbonate, and shaken with chloroform (C). The concentrated chloroform solution (C) deposited 0.2 g of crystals, which were separated into fractions soluble (0.08 g) and insoluble (0.12 g) in methanol. The methanol-soluble fraction, after crystallization from a mixture of ethanol, chloroform, and hexane, gave panicudine (2), mp 247-248°C (40 mg) [3]. The methanol-insoluble fraction was chromatographed on alumina, and the alkaloids were eluted with chloroform. The first chloroform eluates yielded paniculadine (1), mp 276-278°C (from acetone) (60 mg), while the subsequent ones gave panicudine (2) (20 mg) and paniculamine (10 mg), mp 213-214°C [4].

After the separation of the crystals, the chloroform solution (C) was evaporated, to give a mixture of alkaloids (1.17 g). The total amount of bases obtained was 5.47 g, or 0.56% on the weight of the dry raw material.

Paniculadine (1), mp 276-278°C (acetone).

UV spectrum (EtOH, λ_{max}, nm): 301 (lg ε 5.11).

IR spectrum (KBr, ν, cm^{-1}): 3194, 2952, 2941, 2923, 2907, 2877, 1717, 1708, 1651, 1458, 1421, 1352, 1339, 1293, 1268, 1218, 1164, 1032, 1010, 915, 862.

PMR spectrum (100 MHz, Py-d_5, ppm, J, Hz): 1.50 (3H, s, 18-Me), 1.59 (2H, m), 1.88 (2H, s), 1.97 (1H, s), 2.00 (2H, s), 2.05 (1H, s), 2.17 (2H, s), 2.20 (3H, s), 2.25-2.45 (3H, m), 2.63 (1H, s), 2.85 (1H, t, 7 Hz, H-12), 3.32 (1H, d, 12 Hz, H-19α), 4.62 and 4.79 (s, 1H each, 2H-17).

Mass spectrum, *m/z* (I_{rel}, %): 325 (M^+, 100), 310 (5), 308 (4), 297 (26), 282 (5), 270 (13), 269 (28), 254 (10), 242 (14), 240 (11), 224 (25), 192 (10), 191 (17), 190 (10), 176 (25), 175 (10).

Panicudine (2), mp 247-248°C.

PMR spectrum (100 MHz, Py-d_5): 1.49 (3H, s, 18-Me), 1.10-2.40 (13H, m), 2.07 (2H, s), 2.55 (1H, s), 2.82 (1H, d, 7 Hz, H-12), 3.32 and 3.63 (d, 1H each, 12 Hz, 2H-19), 4.16 (1H, s, H-20), 4.22 (1H, br.s, H-2β), 4.62 and 4.79 (s, 1H each, 2H-17).

Formation of Dehydropanicudine. A solution of 60 mg of panicudine in 20 ml of acetone was treated with 0.2 ml of the Jones reagent at −15°C [10], and the mixture was stirred for 30 min. To destroy the excess of oxidant, 1 ml of methanol was added to the reaction mixture, and it was evaporated to a volume of 10 ml. It was then poured into 30 ml of water, made alkaline with sodium carbonate, and extracted with chloroform. The chloroform extract was washed with water and evaporated. The concentrated chloroform solution deposited crystals with mp 262-265°C (37 mg). The dehydropanicudine gave no depression of the melting point with paniculadine (**1**). Their TLC characteristics and mass and NMR spectra coincided completely.

REFERENCES

1. I. A. Bessonova, Sh. A. Saidkhodzhaeva, and S. K. Usmanov, Khim. Prir. Soedin., 914 (1995).
2. A. P. Gorelova, Introduction of Monkshoods into the Subarctic [in Russian], Apatity (1986).
3. I. A. Bessonova, Sh. A. Saidkhodzhaeva, and M. S. Faskhutdinov, Khim. Prir. Soedin., 838 (1995).
4. I. M. Yusupova, I. A. Bessonova, and B. Tashkhodzhaev, Khim. Prir. Soedin., 277 (1995).
5. G. de la Fuente, J. A. Gavin, M. Reina, and R. D. Acosta, J. Org. Chem., **55**, 342 (1990).
6. Atta-ur Rahman, Handbook of Natural Products Data, Vol. 1, Diterpenoid and Steroidal Alkaloids, Elsevier, Amsterdam (1990), pp. 241, 247, 281.
7. B. S. Joshi, H. K. Desai, E. A. El-Kashoury, S. W. Pelletier, and J. D. Olsen, Phytochemistry, **28**, 1561 (1986).
8. J. A. Grina, D. R. Schroeder, E. T. Wydallis, F. R. Stermitz, J. Melman, and J. L. Capinera, J. Org. Chem., **51**, 390 (1986).
9. J. A. Glinski, B. S. Joshi, Q. P. Jiang, and S. W. Pelletier, Heterocycles, **27**, 185 (1988).
10. C. Djerassi, R. R. Engle, and A. Bowers, J. Org. Chem., **21**, 1547 (1956).