LEUCOSTININE A FROM *Aconitum barbatum*

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UDC 547.944/945

In the search for sources of songorine, we studied *Aconitum barbatum* Pers. The known alkaloids delcosine, lycoctonine, songorine, and the new base bataconine were isolated earlier from the aerial part of this plant collected near Ulan-Bator during vegetation [1]. Roots of *A. barbatum* from Altai collected in July contained songorine [2]. According to the literature, the Mongol and Siberian populations of *A. barbatum* can be used as sources of the biologically valuable alkaloid songorine. Thus, the aerial part of the plant contained 1.5% total alkaloids, of which the songorine fraction was 14%. The alkaloid content of *A. barbatum* roots is 1.7%. The songorine concentration is 36% of the total bases [3].

We did not find songorine in flowerheads and leaves of *A. barbatum* collected in Irkutsk Oblast′ during flowering but did isolate leucostinine A. Leucostinine A was first observed in 1996 by Chinese researchers in roots of *A. leucostomum* [4]. In 1999, Swiss scientists isolated this same alkaloid from flowers of *A. lycoctonum* but reported it as a new base, 6-*O*-acetyldemethylenedelcorine [5]. Thus, different names have been given to a single compound [4, 5]. Both groups of researchers established the structure using mass, PMR, and ^{13}C NMR spectra (DEPT, COSY). Chemical shifts in ^{13}C NMR spectra of both alkaloids are practically identical. However, assignments for C-5, C-9 and C-10, and C-13 were interchanged among themselves [4, 5] (Table 1).

We used a heteronuclear method (^{1}H—^{13}C HMBC) to assign signals in the PMR and ^{13}C NMR spectra of leucostinine A and to confirm that the Swiss researchers had interpreted correctly the NMR spectra. Figure 1 shows the principal correlations in the 2D HMBC spectrum. The chemical shift of the N atom was obtained from the ^{15}N—^{1}H HMBC spectrum, in which there are correlations with H-17 (3.01), H-19 (2.69), and the ethyl CH_3 (1.04).

Leucostinine A: $C_{27}H_{43}NO_8$. Mass spectrum (EI, 70 eV, *m/z*, I_{rel}, %): 509 (4) $[M]^+$, 494 (3) $[M - 15]^+$, 478 (100) $[M - 31]^+$, 450 (21) $[M - 60]^+$, 434 (10) $[M - 15 - 60]^+$. ^{15}N NMR spectrum (40.5 MHz, $CDCl_3$, δ, ppm, CH_3NO_2 internal standard): 344.0. Table 1 gives the PMR and ^{13}C NMR spectra.

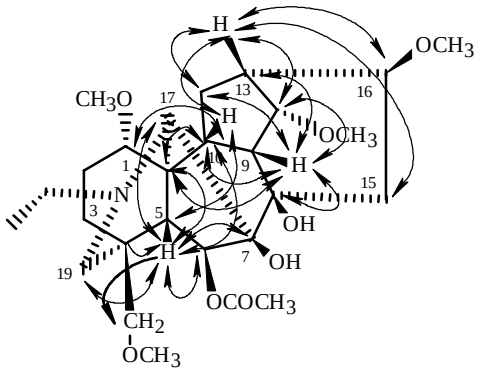

Fig. 1. Principal correlations in the 2D HMBC spectrum of **1**.

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0009-3130/07/4301-0119

TABLE 1. PMR and ^{13}C NMR Spectra of Leucostinine A (400 and 101.6 MHz, $CDCl_3$, δ, ppm, J/Hz)

Atom	Leucostinine A [3] (DEPT)	6-*O*-Acetyldemethylenedelcorine [4] (DEPT)	Leucostinine A* (HSQC, COSY, HMBC)	
	^{13}C	^{13}C	^{13}C	^{1}H
1	83.95	84.0	84.08	2.95 (1H, t, 8.1)
2	25.96	26.0	26.08	2.04 (2H, m)
3	31.79	31.9	31.9	1.33 (1H, m); 1.75 (1H, m)
4	38.56	38.6	38.66	-
5	43.24	51.7	51.63	1.65 (1H, $W_{1/2}$ = 5.2)
6	81.06	81.1	81.18	5.30 (1H, $W_{1/2}$ = 3.2)
7	88.87	88.9	89.00	-
8	76.33	77.1	76.47	-
9	51.53	43.3	43.33	2.97 (1H, t, 4.8)
10	37.27	45.8	45.79	1.88 (1H, m)
11	48.39	48.5	48.49	-
12	28.73	28.8	28.84	1.81 (1H, m); 2.42 (1H, dd, 14.5, 4.9)
13	45.60	37.5	37.44	2.35 (1H, m)
14	84.31	84.4	84.42	3.68 (1H, t, 4.8)
15	37.93	38.0	38.05	1.52 (1H, dd, 16.3, 5.8), 2.87 (1H, dd, 16.3, 6.9)
16	82.12	82.2	82.21	3.18 (1H, dd, 5.8, 6.9)
17	66.08	66.0	66.25	3.01 (1H, s)
18	78.57	78.6	78.66	3.04 (1H, d, 9.3); 3.14 (1H, d, 9.3)
19	52.67	52.8	52.73	2.49 (1H, dd, 11.8, 2.0), 2.69 (1H, d, 11.8)
$N\underline{CH_2}CH_3$	51.17	51.1	51.30	2.87 (2H, dd, 7.1, 3.6)
$NCH_2\underline{CH_3}$	14.18	14.1	14.30	1.04 (3H, t, 7.1)
$-OCOCH_3$	172.47	172.4	172.59	-
$-OCO\underline{CH_3}$	21.54	21.5	21.68	2.04 (3H, s)
OCH_3-1	55.64	55.6	55.79	3.24 (3H, s)
OCH_3-14	57.67	57.7	57.81	3.40 (3H, s)
OCH_3-16	56.25	56.3	56.39	3.31 (3H, s)
OCH_3-18	59.41	59.4	59.54	3.27 (3H, s)

*Chemical shift for the compound isolated in this work.

Flowerheads and leaves (with the former dominating) of *A. barbatum* (90 g) were wetted with saturated Na_2CO_3 solution and extracted exhaustively with $CHCl_3$. The concentrated $CHCl_3$ extract was treated repeatedly with H_2SO_4 (5%). The H_2SO_4 extract was neutralized with Na_2CO_3 solution until the pH was 9-10 and extracted with $CHCl_3$. The solvent was evaporated to afford a fraction of bases (2.7 g, 3% of the air-dried weight of raw material). This fraction was repeatedly separated by column and flash chromatography over Al_2O_3 and silica gel (impregnated with Na_2CO_3, 3%) with gradient elution by hexane:acetone, hexane:chloroform, and chloroform:methanol to afford leucostinine A (9 mg) as an amorphous colorless substance.

Isolation of leucostinine A from *A. barbatum* is the third instance of occurrence of this compound in the plant world.

REFERENCES

1. N. Batbayar, D. Batsuren, M. N. Sultankhodzhaev, and M. S. Yunusov, *Khim. Prir. Soedin.*, 237 (1988).
2. I. Yu. Bagryanskaya, Yu. V. Gatilov, Zh. Ganbaatar, S. A. Osadchii, M. M. Shakirov, E. E. Shul′ts, and G. A. Tolstikov, *Izv. Akad. Nauk, Ser. Khim.*, 2000 (2001).
3. Zh. Ganbaatar, Author's Abstract of a Candidate Dissertation in Chemical Sciences, N. N. Vorozhtsov Novosibirsk Inst. Org. Chem., Sib. Div., Russ. Acad. Sci., (2003).
4. J. Yue, J. Xu, Q. Zhao, H. Sun, and Y. Chen, *J. Nat. Prod.*, **59**, 277 (1996).
5. Y. Chen and A. Katz, *J. Nat. Prod.*, **62**, 798 (1999).