

TWO NEW C₂₀-DITERPENOID ALKALOIDS FROM ACONITUM YESOENSE VAR. MACROYESOENSE (NAKAI) TAMURA[†], STRUCTURES OF DEHYDROLUCIDUSCULINE AND N-DEETHYL-DEHYDROLUCIDUSCULINE

Koji Wada, Hideo Bando, and Takashi Amiya*

Hokkaido Institute of Pharmaceutical Sciences,
7-1, Katsuraoka-cho, Otaru 047-02, Japan

Abstract — Two new C₂₀-diterpenoid alkaloids, dehydrolucidusculine and N-deethyldehydrolucidusculine, and four known alkaloids, kobusine, pseudokobusine, delcosine, and 14-acetyldelcosine, were isolated from roots of Aconitum yesoense var. macroyesoense (Nakai) Tamura. The structures of dehydrolucidusculine and N-deethyldehydrolucidusculine were determined on the basis of their spectral data and the derivation from lucidusculine to dehydrolucidusculine.

The constituents of Aconitum yesoense var. macroyesoense (Nakai) Tamura were investigated many years ago. The isolation of lucidusculine, kobusine, pseudokobusine, delcosine, and 14-acetyldelcosine had been reported by Majima and Morio¹, and Sugimoto *et al.*²⁻⁴ We reinvestigated the constituents of the same plant.

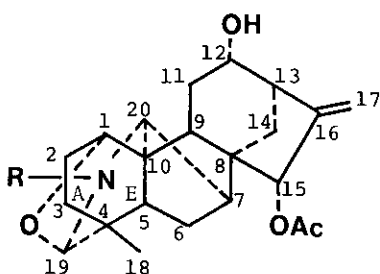
Two new diterpenoid alkaloids, dehydrolucidusculine (1) and N-deethyldehydrolucidusculine (2), were isolated together with four known alkaloids, kobusine (3)^{2,3,5,6}, pseudokobusine (4)^{2,3,6,7}, delcosine (5)^{2,8}, and 14-acetyldelcosine (6)⁴. Identification of 3, 4, 5 and 6 was carried out by comparison of their melting points and spectral data with those of the authentic samples.

Dehydrolucidusculine showed the following properties; mp 186-189°C, $[\alpha]_D^{11} = +2.6^\circ$ (c = 1.0, EtOH), C₂₄H₃₃NO₄. The proton nuclear magnetic resonance (¹H-NMR) spectrum of 1 showed three methyl groups at δ 0.81 (s, C-4CH₃), 1.01 (t, J=7.0 Hz, N-CH₂CH₃) and 2.13 (s, acetyl group), a methine at δ 5.49 (1H, bs, C-15H), and an exomethylene

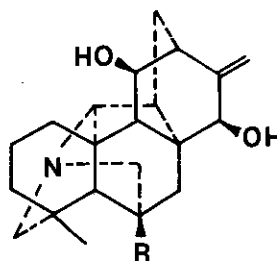
[†] The previous name Aconitum lucidusculum Nakai has been revised as Aconitum yesoense var. macroyesoense (Nakai) Tamura.

at δ 4.92 and 5.12 (each 1H, s, $C=CH_2$). The infrared (IR) spectrum showed absorptions at 3450, 1740, 1635, 1245 and 885 cm^{-1} . These spectra were similar to those of lucidusculine (7).^{2,3,9} The mass spectrum (MS) showed a molecular ion (M^+) peak at m/z 399 as a base peak and m/z 343 ($M^+ - C_3H_4O$). The loss of molecule of acrolein in the MS¹⁰, the IR absorption at 1070 cm^{-1} , and the 1H -NMR signals at δ 3.69 (1H, s, C-19H) and 4.06 (1H, d, $J=4.9\text{ Hz}$, C-18H) suggested the presence of C-1-C-19 inner ether in the new base. On the basis of these spectral data, the compound (1) was assigned to be dehydrolucidusculine.

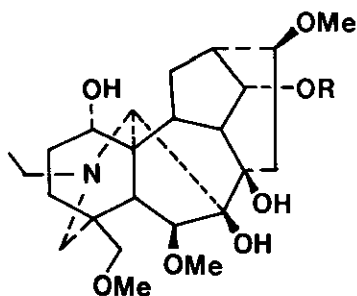
The oxidation of 7 with *N*-bromosuccinimide led to dehydrolucidusculine (1) in 26% yield¹¹, and therefore, its structure was established.



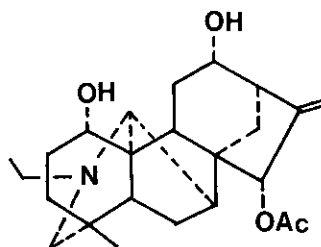
1: R = Et
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 2: R = H
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3: R = H
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 4: R = OH
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5: R = H
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 6: R = Ac
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7
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N-Deethyldehydrolucidusculine (2) showed the following properties; amorphous powder, $[\alpha]_D^{17} = -9.6^\circ$ ($c=0.27$, EtOH), $C_{22}H_{29}NO_4$, the IR absorptions at 3400, 1730, 1650, 1240, 1070 and 885 cm^{-1} , and the 1H -NMR signals at δ 0.86 (3H, s, C-4CH₃), 2.14 (3H, s, acetyl group), 3.87 (1H, s, C-19H), 4.15 (1H, d, $J=4.8\text{ Hz}$, C-18H), 4.93 and 5.16 (each 1H, s, $C=CH_2$), and 5.50 (1H, s, C-15H). The MS showed a molecular ion peak at m/z 371 and the 1H -NMR spectrum was very similar to that of 1, but did not show

a methyl group of an N-ethyl moiety which was revealed nearly at δ 1.01 in the case of 1. The spectrum of 2 suggested that its structure was assigned to be N-deethyldehydrolucidusculine. Compound 2 is the third with respect to the reported C_{20} -diterpenoid alkaloids having a secondary amino group ($>N-H$).¹²

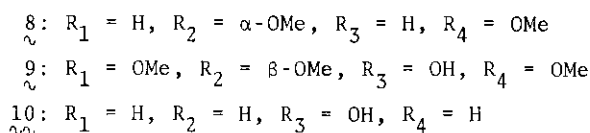
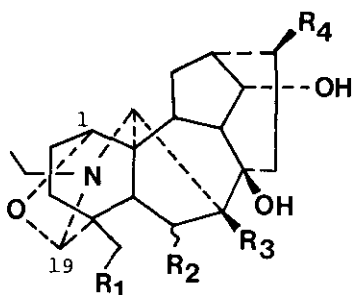
The structures of dehydrolucidusculine (1) and N-deethyldehydrolucidusculine (2) were confirmed by carbon-13 (^{13}C -) NMR spectrum, and the assignments were made by comparison with the spectra of lucidusculine (7) and other published ^{13}C -NMR data for related diterpenoid alkaloids.¹³ The chemical shift patterns in 1 and 2, were very similar to that of 7. In the ^{13}C -NMR spectrum of 1, the appearance of a new doublet at 92.8 ppm, the disappearance of a triplet at $\sim$ 58 ppm, the upfield shift of C-1, the C-4 resonance downfield as the result of β effect, and the C-3, C-5 and C-18 resonances upfield as the result of γ effect, afforded evidence for the presence of C-1-C-19 inner ether in 1. The assignments of C-1 (67.6 ppm) and C-19 (92.8 ppm) were determined by selective decoupling method at C-1H and C-19H, respectively. The ^{13}C -NMR data of pentagynine (8), 18-methoxygadesine (9) and graciline (10) have been reported.¹³ Compounds 8, 9 and 10 are C_{19} -diterpenoid

Table 1. ^{13}C -Chemical Shifts and Assignments for Dehydrolucidusculine (1), N-Deethyldehydrolucidusculine (2), and Lucidusculine (7).⁹

Carbon	<u>1</u>	<u>2</u>	<u>7</u>	Carbon	<u>1</u>	<u>2</u>	<u>7</u>
1	67.6	67.8	69.9	13	48.3	48.1	48.8
2	29.7	29.6	31.6	14	30.2	30.2	36.5
3	24.5	23.7	30.5	15	77.7	77.7	77.5
4	37.7	37.8	34.0	16	151.7	151.6	153.1
5	33.7	34.0	47.7	17	110.4	110.5	109.5
6	23.8	23.5	23.7	18	18.9	19.0	26.4
7	46.8	46.8	43.7	19	92.8	87.8	57.9
8	49.4	49.4	49.6	20	65.6	57.5	65.7
9	45.8	45.6	37.7	N-CH ₂	48.3	----	50.8
10	51.7	50.6	52.5	CH ₃	14.1	----	13.4
11	28.1	28.1	29.1	O=C	170.7	170.6	170.6
12	76.1	76.1	75.5	CH ₃	21.5	21.5	21.6

a) δ (ppm) downfield from TMS in $CDCl_3$.

alkaloids, and compounds 1 and 2 are C₂₀-diterpenoid bases. Nevertheless, the A and E rings in each of 8, 9 and 10 are the same as those of 1. Compound 2 has the secondary amino group in stead of the N-ethyl group. By comparison with the spectra of 8, 9 and 10 with those of 1 and 2 it could be presumed that the assignments of the resonances of C-1 and C-19 in each of 8, 9 and 10 must be reversed. The ¹³C-NMR spectrum of 2 was similar to that of 1, but did not show the N-ethyl group which was revealed nearly at 48.3 and 14.1 ppm in the case of 1. The C-19 and C-20 resonances upfield as the result of disappearance of the N-ethyl group were observed.¹⁴



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