

STUDIES ON ACONITUM SPECIES VI.¹ YESOLINE, A NEW C₂₀-DITERPENOID
ALKALOID FROM ACONITUM YESOENSE VAR. MACROYESOENSE (NAKAI) TAMURA.

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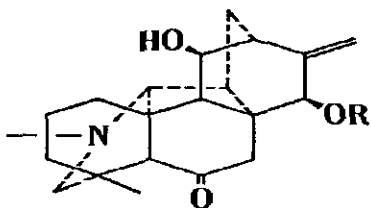
Abstract — A new C₂₀-diterpenoid alkaloid, yesoline, and a known alkaloid, 14-dehydrodelcosine were isolated from *Aconitum yesoense* var. *macroyesoense* (Nakai) Tamura. Structure of the new alkaloid was determined by means of spectral and chemical methods.

The isolation and structure elucidation of fourteen C₂₀-diterpenoid alkaloids and five C₁₉-diterpenoid alkaloids from *Aconitum yesoense* var. *macroyesoense* (Nakai) Tamura were reported in our previous paper.¹ Our continued investigations on the constituents of this plant now resulted in the isolation of a new diterpenoid alkaloid, yesoline (1), and a known alkaloid, 14-dehydrodelcosine (2).²

Alkaloid 2 was identified by comparison of the spectral data with those in literature.²

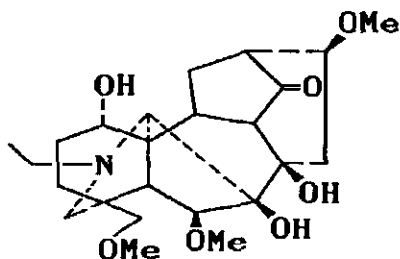
The ¹H-nmr spectrum of yesoline (1), C₃₀H₃₇NO₈, showed signals due to four methyl groups assignable to C-CH₃, N-CH₃, and two OCH₃, signals due to two methines and typical 1,2,4-trisubstituted benzene (See Experimental). The ¹H-nmr, ir, uv, and mass spectral data suggested the presence of veratroyloxy group as an ester. The ¹H-nmr signals at δ 5.23 and 5.41 (each 1H, s, C=CH₂), and ¹³C-nmr signals at 144.5 ppm (s, C-16) and 117.1 ppm (t, C-17) suggested the presence of an exomethylene moiety, and the molecular formula together with the spectral data suggested that the compound was a C₂₀-diterpenoid alkaloid. The ¹³C-nmr spectrum of 1 was similar to that of 15-veratroylpseudokobusine (3),¹ with the exception of presence of a new quartet at 42.8 ppm and a singlet at 203.1 ppm, and the absence of a singlet at ~98 ppm. These data suggested that yesoline was veratroyl ester of *N*-methyl-*N*,6-seco-6-dehydropseudokobusine (6). The structure of yesoline (1) was finally confirmed by the correlation with pseudokobusine (4), already isolated from the same plant,¹ as follows.

Treatment of pseudokobusine (4) with methyl iodide in methanol gave a methiodide

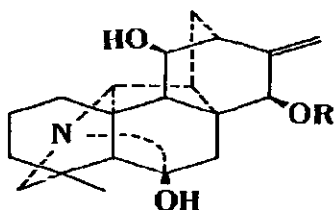


1: R=veratroyl

6: R=H

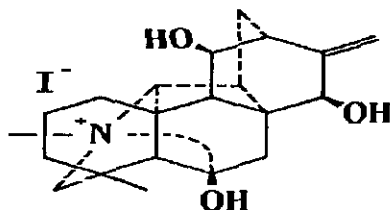


2



3: R=veratroyl

4: R=H



5

5, which was stirred with silver oxide in 50% aqueous methanol³ to give an *N*-methyl ketone 6. On the other hand, alkaline hydrolysis of 1 afforded *N*-methyl-*N*,8-*seco*-6-dehydropseudokobusine (6). The *N*-methyl ketone 6 derived from pseudokobusine and the product derived by the hydrolysis of yesoline showed identical ir and nmr spectra, and the tlc behaviors.

EXPERIMENTAL

All melting points are uncorrected. Ir spectra in KBr disks were taken with a JASCO IRA-2 spectrometer, and uv spectrum was measured in ethanol solution with a Shimadzu D-300 spectrometer. Nmr spectra were measured in CDCl₃ solution with JOEL FX-100 and JOEL GX-270 spectrometers using TMS as an internal standard. Ms spectra were measured with a Shimadzu LKB-9000B spectrometer, and HR-ms spectra were measured with JMS-D300 mass spectrometer. Elemental analyses were performed by the Analytical Center, Hokkaido University.

Isolation procedure -- In the previous paper,¹ we already reported the extraction and isolation of several alkaloids from the rhizoma of the title plant. The column chromatography of remaining crude alkaloid in the previous isolation procedure -1) and -2)¹ gave 33 mg and 15 mg of 1, respectively. They also gave 39 mg and 96 mg of 2, respectively.

Yesoline (1) -- amorphous, (α)_D²³ = -10.6° (c=0.34, ethanol). HR-ms m/z: Calcd for C₃₀H₃₇NO₈ 507.2620, Found 507.2630. Ms: m/z 507 (M⁺), 326 (M⁺-OvR), 165 (veratroyl cation). Ir ν cm⁻¹: 3400, 1700, 1600, 1270. Uv λ max nm (log ϵ): 282 (3.84), 291 (3.61). ¹H-Nmr (δ): 1.45 (3H, s), 2.45 (3H, s), 3.92 (3H, s), 3.93 (3H, s), 4.16 (1H, d, J=5.0 Hz), 5.23 (1H, s), 5.41 (1H, s), 5.66 (1H, s), 6.86 (1H, d, J=8.6 Hz), 7.52 (1H, d, J=2.0 Hz), 7.59 (1H, dd, J=2.0, 8.6 Hz). ¹³C-Nmr (ppm): 203.1 (s, C-6), 165.8 (s, C=O), 153.2 (s, C-4'), 148.7 (s, C-3'), 144.5 (s, C-16), 123.4 (d, C-6'), 122.1 (s, C-1'), 117.1 (t, C-17), 112.1 (d, C-2'), 110.2 (d, C-5'), 78.1 (d), 70.9 (d, C-15), 67.6 (d, C-11), 61.0 (t, C-19), 60.5 (d), 56.7 (d), 55.9 (q, OCH₃x2), 46.1 (t), 45.2 (s), 43.3 (s), 42.8 (q, N-CH₃), 42.7 (d), 41.3 (d), 40.3 (t), 38.1 (s, C-4), 31.8 (t), 31.4 (t), 30.7 (q, C-18), 18.9 (t).

14-Dehydrodelcosine (2) -- Mp 219-221°C (lit.² 212.5-213.5°C). HR-ms m/z: Calcd for C₂₄H₃₇NO₇ 451.2570, Found 451.2562. Ms: m/z 451 (M⁺), 436 (M⁺-15, base peak), 420 (M⁺-OCH₃). Ir ν cm⁻¹: 3450, 1750. ¹H-Nmr (δ): 1.12 (3H, t, J=7.3 Hz), 3.33 (3H, s), 3.34 (6H, s), 4.04 (1H, s).

Pseudokobusine Methiodide (5) -- Pseudokobusine (4, 100 mg) and methyl iodide (1 ml) in methanol (6 ml) were heated under reflux for 3 h. After cooling, the reaction mixture was evaporated and the residue was recrystallized from methanol to afford methiodide (5, 143 mg) in a quantitative yield. Mp 287°C (decomp; lit.⁴ 287°C). Anal: Calcd for C₂₁H₃₀NO₃I: C, 53.51; H, 6.41; N, 2.97; I, 26.92. Found C, 53.67; H, 6.47; N, 2.95; I, 26.81.

N-Methyl-N,6-seco-6-dehydropseudokobusine (6) -- A mixture of methiodide (5, 70 mg), silver oxide (200 mg), and 50% aqueous methanol was stirred for 20 h at room temperature. Filtration of the mixture to remove silver salts and purification of the filtrate by column chromatography on silica gel afforded amorphous N-methyl-N,6-seco-6-dehydropseudokobusine (6, 48 mg) in a quantitative yield. HR-ms m/z: Calcd for C₂₁H₂₉NO₃ 343.2147, Found 343.2152. Ms: m/z 343 (M⁺). Ir ν cm⁻¹: 3400, 1720, 910. ¹H-Nmr (δ): 1.45 (3H, s), 2.29 (3H, s), 3.84 (1H, s), 4.10 (1H, d, J=4.8 Hz, changed into s after addition of D₂O), 5.10 (1H, s), 5.24 (1H, s).

Hydrolysis of yesoline (1) -- Yesoline (1, 7 mg) in a 5% KOH-methanol was stirred for 4 h at room temperature. Usual work-up afforded *N*-methyl-*N*,6-*seco*-6-dehydro-pseudokobusine (6, 3 mg) in 64% yield.

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