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THE STRUCTURE AND ABSOLUTE CONFIGURATION OF HANAMISINE

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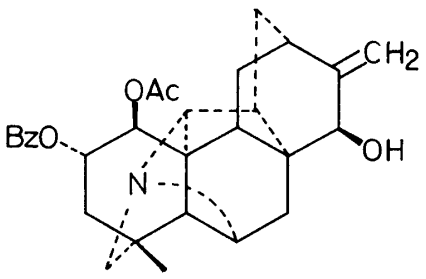
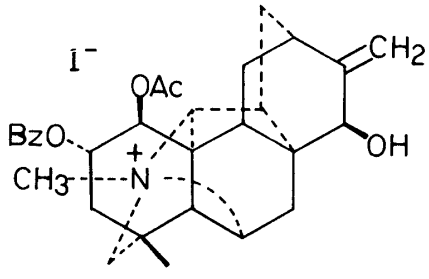
The structure and absolute configuration of hanamisine (I), a new C_{20}-diterpene alkaloid isolated from *Aconitum sanyoense* Nakai and *A. s. var. tonense* Nakai, have been determined by X-ray crystallography of hanamisine methiodide.

KEYWORDS——diterpene alkaloid; *Aconitum sanyoense* Nakai; *Aconitum sanyoense var. tonense* Nakai; *Ranunculaceae*; hanamisine; X-ray analysis; absolute configuration

We investigated previously the components of *Aconitum sanyoense* Nakai, a plant native to Mt. Hanamiyama, Okayama Prefecture, Japan.[1] A few alkaloids: hypognavine,[2] isotalatizidine (Kajigamori base) and hanamiyama base, were isolated from this plant, but the structure of hanamiyama base has remained to be determined. Recently, we reinvestigated the components of the same plant collected at the same place, and isolated a new diterpene alkaloid, named hanamisine (344 mg), from the base fraction (3.93 g) obtained from methanol extract of the dry roots (859 g). Hanamisine was also found as a minor base of *Aconitum sanyoense var. tonense* Nakai collected at Kuzure, Matsumoto, Nagano Prefecture, Japan.[3] Hanamiyama base was identified as deacetylhanamisine, prepared by treating hanamisine with 1% aq. K_2CO_3 in methanol solution. We report here the results of the structural determination of hanamisine by the single crystal X-ray analysis of its methiodide.



(I)



(II)

Recrystallization of hanamisine from acetone gave prisms, mp 124 - 127°C; $[\alpha]_D^{25}$ + 122.6° (c 1.06, MeOH); MS *m/z* 475 (M^+). The 100 MHz ^{1}H-NMR spectrum in CD_3OD

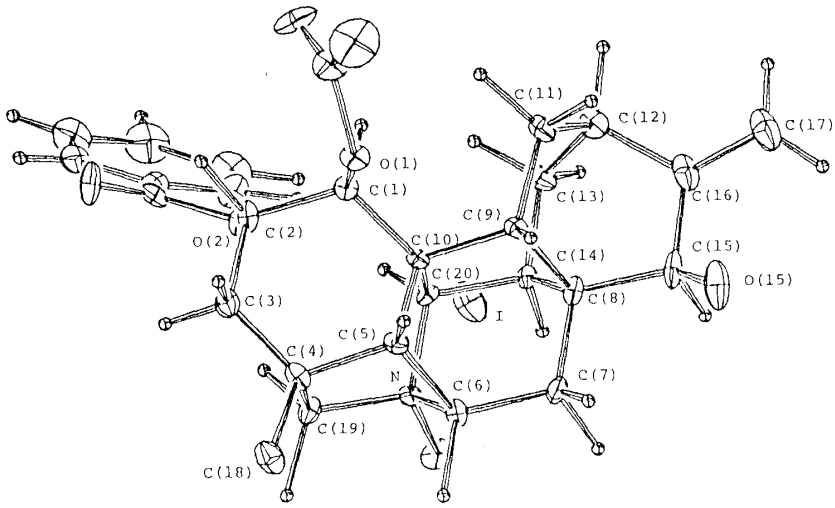


Fig. 1. ORTEP Drawing of the Compound (II)

showed signals due to C(4) methyl (3H,s) at δ 1.08, acetyl group (3H,s) at δ 2.10, exocyclic methylene (2H,m) at δ 4.96, C(15) proton (1H,br s) at δ 3.98, C(1) and C(2) proton (2H,m) at δ 5.30 ppm. The ^{13}C-NMR spectrum in CD_3OD exhibited the following signals: δ 20.8, 27.6, 29.1, 33.3, 34.2(X2), 34.7, 37.1, 43.6, 44.8, 45.8, 53.4, 57.6, 63.5, 66.3, 70.4, 70.9, 71.5, 74.2, 109.5, 129.6, 130.1, 130.7, 134.3, 155.7, 165.9 and 171.0 ppm, which revealed the presence of an acetyl group, a benzoyl group, a hydroxy group, an exocyclic methylene and other signals attributable to the atisine type skeleton.

Hanamisine methiodide (II) was prepared by treating hanamisine with methyl iodide in methanol solution. Recrystallization of the methiodide from ethyl acetate - acetone (1:1) gave prismatic crystals, mp 253 - 256°C.

Crystal data: Orthorhombic $P2_12_12_1$, a=14.207(6), b=15.273(6), c=12.941(6)Å, Dc= 1.46 g/cm^3, Z=4. A θ-2θ scan method with graphite monochromated CuKα radiation was used to measure 2884 independent reflections with 2θ values below 160°. The structure was solved by the heavy atom method and refined by the block diagonal least-squares method. The final R value was 0.067. The absolute configuration obtained by using anomalous dispersion effects of iodine atoms shown in Fig. 1. The structure and absolute configuration of hanamisine have been determined to be (I) from the X-ray diffraction analysis.[4)]

REFERENCES AND NOTES

1) E. Ochiai, T. Okamoto, S. Sakai, and A. Saito, *Yakugaku Zasshi*, 76, 1414 (1956).
2) S. Sakai, K. Yamaguchi, I. Yamamoto, and T. Okamoto, *Chem. Pharm. Bull*, 30, 4573 (1982).
3) Abstracts of Papers, 26th Meeting of Kanto Branch, Pharmaceutical Society of Japan, Chiba, November, 1982, p. 95.
4) The final atomic coordinates have been deposited with the Cambridge Crystallographic Data Center, Cambridge, England. The list of Fo and Fc values may be obtained from one of the author (K. Y.) upon request.

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