Communications to the Editor

[Chem. Pharm. Bull.
31(1) 360—361 (1983)]

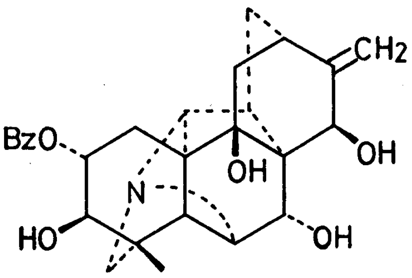
THE STRUCTURE AND ABSOLUTE CONFIGURATION OF SADOSINE

Toshihiko Okamoto,*,[a] Hidenao Sanjoh,[a] Kentaro Yamaguchi,[a]
Yoichi Iitaka,[a] and Shin-ichiro Sakai[b]
Faculty of Pharmaceutical Sciences, Tokyo University,[a] Hongo, Bunkyo-ku,
Tokyo, Japan and Faculty of Pharmaceutical Sciences, Chiba University,[b]
1-33 Yayoi-cho, Chiba 260, Japan

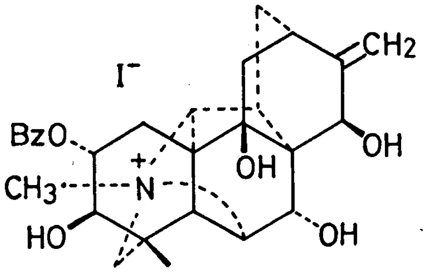
The structure and absolute configuration of sadosine, a new C_{20}-diterpene alkaloid isolated from *Aconitum japonicum* Thunb., have been determined by X-ray crystallography of sadosine and its methiodide.

KEYWORDS——diterpene alkaloid; *Aconitum japonicum* Thunb., *Ranunculaceae*; sadosine; X-ray analysis; absolute configuration

Sadosine, $C_{27}H_{31}NO_6$,[1)] is a new diterpene alkaloid isolated from *Aconitum japonicum* Thunb.,[2)] a plant native to Sado Island, Niigata Prefecture, Japan. This alkaloid was isolated from the base fraction, extracted from methanol extract of the dry roots, as the minor component. We report here the structural determination of sadosine by the single crystal X-ray analysis of sadosine and its methiodide.



(I)



(II)

Recrystallization of sadosine from acetone gave colorless needle crystals, mp 222 - 224°C: $[\alpha]_D^{25}$ + 53.1° (c 0.96, CH_3OH). MS: *m/z* 465 (M^+). The 100 MHz ^1H-NMR spectrum in CD_3OD showed signals due to C(4) methyl (3H,s) at δ 1.19, C(3) proton (1H, d,J=3.0 Hz) at δ 3.67, C(7) proton (1H,d,J=4.0 Hz) at δ 4.44, C(15) proton (1H,br s) at δ 4.52, exocyclic methylene (2H,br s) at δ 5.00, C(2) proton (1H,m) at δ 5.40 ppm. The ^{13}C-NMR spectrum of (I) in CD_3OD exhibited the following signals: δ 25.6, 25.7, 34.0, 36.1, 37.6, 39.9, 41.7, 48.3, 50.0, 51.4, 62.3, 65.0, 67.7, 71.1, 71.3, 74.6, 75.6, 80.6, 110.1, 129.5, 130.1, 131.0, 134.2, 155.4, and 166.5 ppm which revealed the presence of a C(4) methyl group, a ketone group, an exocyclic methylene, eight carbons of C-N and C-O bond, and other characteristic features for the atisine-type skeleton.

The crystal, tetragonal I4 with a=23.267(11), b=23.369(11), c=8.955(4)Å, Dc=1.51

g/cm^3 for Z=4. One octant of the data on a crystal of dimensions ca. 0.16 X 0.23 X 0.53 mm was collected to the maximum 2θ of 130° using the θ-2θ scan technique with CuKα radiation (λ=1.5418Å), and, after Lorentz and polarization corrections were applied, they were used for structure determination. The structure was solved by the direct method with the weighted multisolution tangent refinement program MULTAN[3] and refined by the block-diagonal least-squares method using HBLS IV. The final R value was 0.072 including hydrogen atoms.

Bond length between oxygen, nitrogen and carbon atoms have standard deviations of approximately 0.01Å and bond angles have standard deviations of approximately 0.5°. All bond distances and angles have typical values. The X-ray analysis showed that (I) is the correct stereochemical structure of sadosine with the hydroxy group having the α-configuration at the C(7) and the benzoate group having the α-configuration at the C(2).

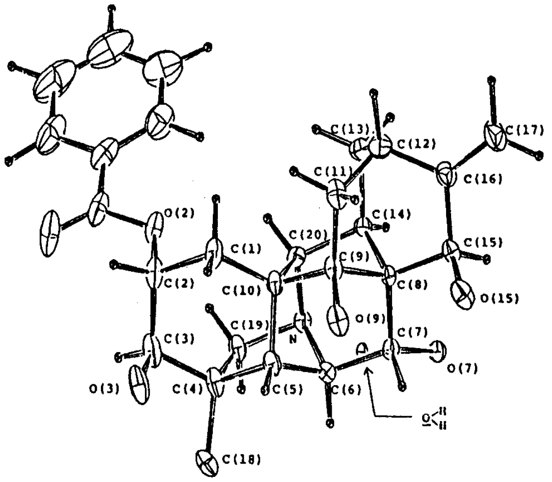


Figure. ORTEP Drawing of Sadosine Hydrate

We prepared sadosine methiodide (II) in order to determine the absolute configuration. This methiodide was prepared by treating sadosine with methyl iodide in methanol solution. Recrystallization of the methiodide from acetone gave colorless platy crystals, mp 279 - 281°C (dec.).

crystal data: Monoclinic $P2_1$, a=11.656(5), b=11.725(5), c=9.567(4)Å, β=93.61(5)°, Dc=1.50 g/cm^3, Z=2. A θ-2θ scan method with graphite monochromated CuKα radiation was used to measure 1844 independent reflexions with 2θ values below 120°. The structure was solved by the heavy atom method and refined by the block-diagonal least-squares method. The absolute configuration of methiodide (II) was determined on the basis of the anisotropic refinement of the non-hydrogen atoms with anomalous dispersion corrections for iodine which gave the R factor 0.051. The structure and absolute configuration of sadosine was then assigned (I) shown as sadosine hydrate in the Figure.

REFERENCES AND NOTES

1) Sadosine was crystallized as mono-hydrate from acetone. *Anal.* Calcd for $C_{27}H_{31}NO_6\cdot H_2O$: C, 67.06, H, 6.88, N, 2.90. Found: C, 66.75, H, 6.88, N, 2.99.
2) E. Ochiai, T. Okamoto, S. Sakai, M. Kaneko, K. Fujisawa, U. Nagai, and H. Tani, *Yakugaku Zasshi*, 76, 550 (1956).
3) P. Main, M. M. Woolfson, and G. Germain (1971). MULTAN. A system of computer programs for the automatic solution of crystal structures from X-ray diffraction data. Univs. of York, England, and Louvain, Belgium.

(Received December 10, 1982)