Communications to the Editor

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THE STRUCTURE OF IGNAVINE

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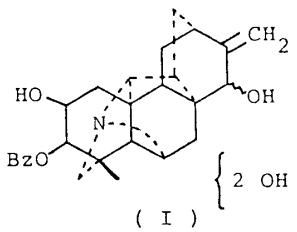
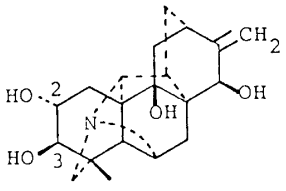
The structure and absolute configuration of ignavine (III), a diterpene alkaloid isolated from certain plants of the Aconitum species, have been determined by X-ray crystallography of ignavine methiodide.

KEYWORDS——diterpene alkaloid; Aconitum; *Ranunculaceae*; ignavine; X-ray analysis; absolute configuration

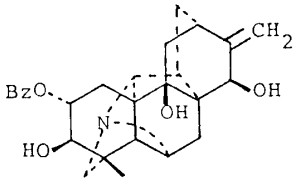
Ignavine, $C_{27}H_{31}NO_5 \cdot H_2O$,[1] a diterpene alkaloid isolated from the roots of Aconitum species, assumed to be *Aconitum Japonicum* Thunb., collected at Katsuyama Fukui Prefecture, Mt. Nasu Tochigi Pref., Nobeyama Nagano Pref., and also at Sado-island Niigata Pref., was initially assigned structure (I) on the basis of chemical studies.[2] In 1970, Pelletier reported the structure (II) for anhydroignavinol,[3] the alkaline hydrolysis product of ignavine, from a single-crystal X-ray analysis of its methiodide. The absolute configuration indicated for (II) was based only on analogy with the other diterpene alkaloid. Further, it was not decided whether the position of a benzoate group in ignavine was C(2) or C(3). Now we report the results of structural determination of ignavine methiodide by a single-crystal X-ray analysis, and the structure of ignavine is represented by formula (III) including the absolute configuration.



(I)



(II)



(III)

Ignavine methiodide was recrystallized from acetone, mp 300 - 304°C (dec.). The crystal was monoclinic $P2_1$ with the unit cell dimensions of a = 11.563(6), b = 11.898(6), c = 9.582(5)Å, β = 97.96(5)°; Z = 2, Dc = 1.58 g/cm^3. In all, 2539 unique non-zero reflections were recorded. The structure was solved by the heavy atom method. The iodine ion was treated as anisotropic; all other atoms were assumed to have isotropic thermal factors. After refinement, the average estimated standard deviation of

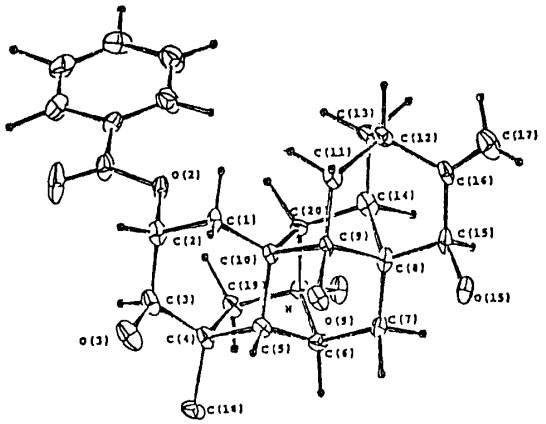


Figure 1. ORTEP Drawing of Compound (III)

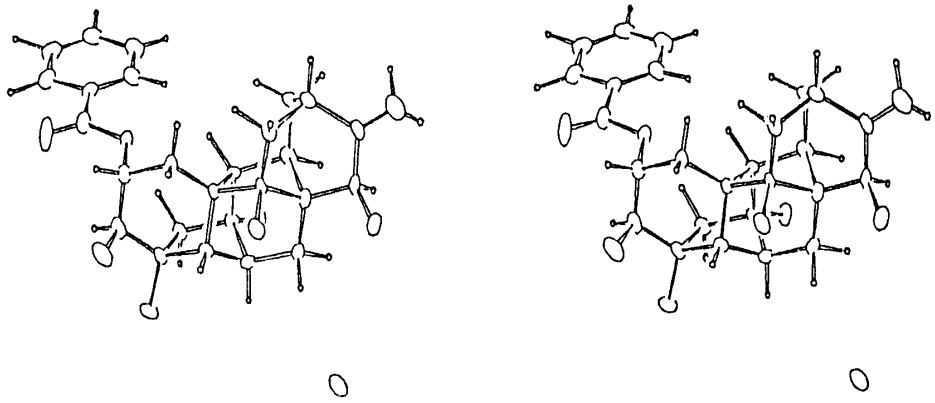


Figure 2. Stereoscopic View of Compound (III)

bond length was 0.01 Å and the average standard deviation of bond angles was 0.6°. Anisotropic refinement of the atomic parameters for nonhydrogen atoms, with anomalous dispersion corrections for iodine atoms converged the R factor 0.097 and 0.087 respectively for the two enantiomers. On the basis of Hamilton's test, the absolute configuration of the structure was assigned as shown in Figure 1.[4] From the X-ray diffraction analysis, the structure of ignavine has been determined to be (III) with an benzoate group having the α - configuration at the C(2) position.

REFERENCES AND NOTES

1) Initially, the molecular formula of ignavine was assigned to $C_{27}H_{31}NO_6$, but should be corrected to $C_{27}H_{31}NO_5 \cdot H_2O$ by the following data; *Anal.* Calcd for $C_{27}H_{31}NO_5 \cdot H_2O$: C, 69.36, H, 7.11, N, 3.00. Found: C, 69.17, H, 7.31, N, 3.02. MS: $C_{27}H_{31}NO_5$ *m/z* 449 (M^+).

2) E. Ochiai, and T. Okamoto, *Chem. Pharm. Bull.* 7, 556 (1959).

3) S. W. Pelletier, S. W. Page, and M. Gary Newton, *Tetrahedron Lett.*, 4825 (1970).

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 authors (K. Y.) upon request.

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