## Communications to the Editor

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# THE STRUCTURE OF HYPOGNAVINE

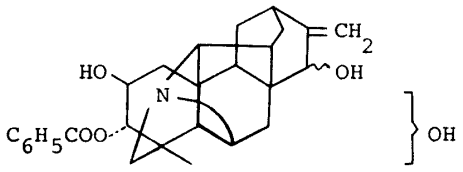
Shin-ichiro Sakai,*[,a] Keiichi Yamaguchi,[a] Ichiro Yamamoto,[a] and Toshihiko Okamoto[b]

Faculty of Pharmaceutical Sciences, Chiba University,[a] 1-33 Yayoi-cho, Chiba 260 Japan and Faculty of Pharmaceutical Sciences, Tokyo University,[b] Hongo, Bunkyo-ku, Tokyo 113, Japan

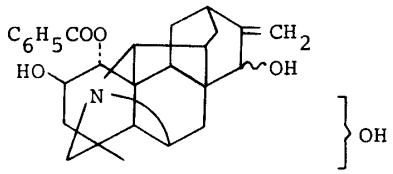
The structure and absolute configuration of hypognavine (IIIb), a major diterpene alkaloid from *Aconitum sanyoense* Nakai (Sanyo bushi), were established on the basis of X-ray analysis and the CD spectrum of a hypognavine derivative, acetylhypognavinone (IV).

KEYWORDS —— diterpene alkaloid; *Aconitum sanyoense* Nakai; *Ranunculaceae*; hypognavine; acetylhypognavinone; X-ray analysis; CD spectrum; absolute configuration

Hypognavine, $C_{27}H_{31}NO_5$, a diterpene ester alkaloid native to *Aconitum sanyoense* Nakai, was initially assigned structure (I) or (II), the structural skeleton being first proposed as a heptacyclic ring diterpene alkaloid on the basis of chemical studies[1] by one (S. S.) of us in 1958.




(I)

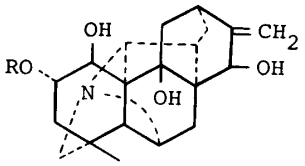



(II)

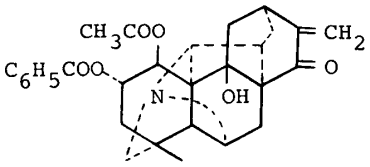
In 1971, Pelletier presented the structure of hypognavinol (IIIa), an alkaline hydrolysis product of hypognavine, based on a single crystal X-ray analysis of hypognavinol methiodide.[2] However, the absolute configuration indicated for (IIIa) was based only on analogy with the other atisine type diterpene alkaloids.

We now report the results of a structural determination of acetylhypognavinone (IV) by single crystal X-ray analysis. The absolute configuration indicated for (IV) was proved to be correct on the basis of CD spectral comparison with the other diterpene alkaloid having a known absolute configuration. Therefore, the structure of hypognavine is represented by formula (IIIb).

Acetylhypognavinone, $C_{29}H_{31}NO_6$, was recrystallized from EtOH to prisms, mp 265°C.[3] The mass spectrum revealed a base peak at m/z 430.2000 corresponding to




(IIIa) R = H
(IIIb) R = $C_6H_5CO$-




(IV)

$C_{27}H_{28}NO_4$ ion ( calcd. 430.1985 $M^+ - CH_3CO_2$ ). The crystals were orthorhombic, space group $P2_12_12_1$, Z= 4; a= 10.254(4), b= 24.121(10), c= 9.615(7) Å, and Dx=1.37 g/cm$^3$. Intensity data of 2716 unique reflections with Fo > 2σ(Fo) were measured on a Rigaku diffractometer, AFC-5, by using monochromated Cu Kα radiation. Scanning was made by ω - 2θ scanning technique within the range $3° \leq 2\theta \leq 150°$. The direct method MULTAN[4] was used to solve the structure. The atomic positional and thermal parameters were refined by a block diagonal least squares procedure. The final R value was 0.069. The elucidated structure of acetylhypognavinone is shown in Fig. 1 and 2, and therefore, the absolute configuration of acetylhypognavinone is represented as (IV) or its mirror image.

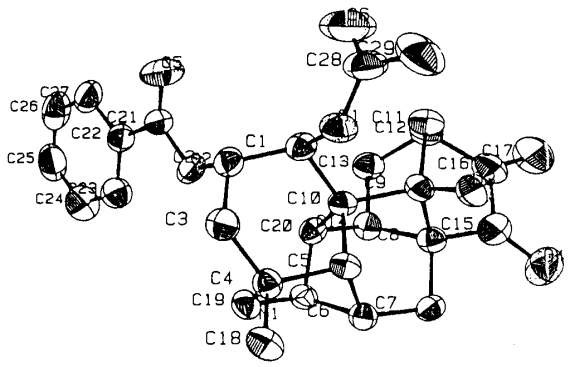



Fig. 1. An ORTEP Drawing of the Structure of (IV)

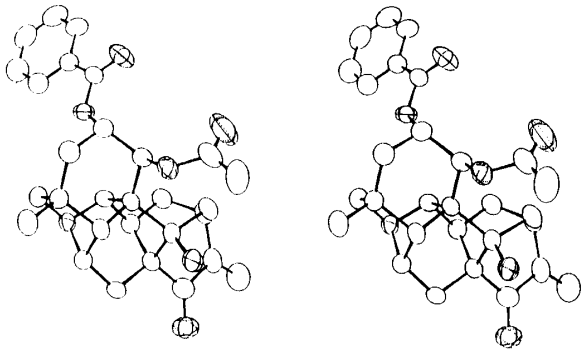
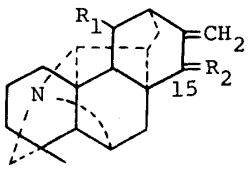
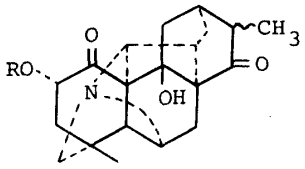


Fig. 2. Stereoscopic View of the Structure of (IV)

The CD spectrum of (IV) exhibited CD maxima at $\lambda_{ext}^{dioxane}$ nm(Δε): 340(0.32), 353(0.43), 368(0.42), 388(0.16 sh.), and the curve between 300 - 400 nm is almost superimposable on that of 15-dehydronominine (Va),[5] mp 136-138°C, which was derived from a known base kobusine (Vb). The absolute configuration of (Vb) is also indicated on the basis of CD spectrum correlation[5] with a diterpene alkaloid spiradine A methiodide whose absolute configuration was determined by X-ray analysis




(Va) $R_1$ = H
$R_2$ = O
(Vb) $R_1$ = OH
$R_2$ = 




(VIa) R = $C_6H_5CO$-, (VIb) R = H

using the anomalous dispersion of the iodide ion.[6]

A benzoyloxy group on carbon 1 indicated in the alternative structure (II) of hypognavine was erroneously assumed from the positive Zimmerman's color test (active methylene group) of ketodihydrohypognavinone (VIa).[3] However, compound (VIa) has no methylene group neighboring to C-1 ketone. Therefore, an α-ketol (1-keto) derivative (VIb) which was obtained by alkaline hydrolysis of the benzoyl group, was probably in an equilibrium with another α-ketol (2-keto) isomer with an active methylene group at C-3.

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REFERENCES AND NOTES

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5) See the following communications. "submitted"
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