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Two New *Veratrum* Alkaloids, Hosukinidine and Epirubijervine from Illuminated *Veratrum* Plant

Hosukinidine, (20*R*,22*R*,25*S*)-veratra-5,12-dien-3β-ol, and epirubijervine, (22*R*,25*S*)-solanid-5-ene-3β,12β-diol, were isolated from illuminated *Veratrum* plant.

Keywords——Liliaceae; *Veratrum grandiflorum*; a new veratranine alkaloid; hosukinidine; a solanidanine alkaloid; epirubijervine; illuminated *Veratrum*

Concerning the biogenesis of C-nor-D-homo steroidal alkaloids, two new cevanine alkaloids, shinonomenine and veraflorizine, and a new cevanidane alkaloid, procevine, were isolated from a *Veratrum* plant cultivated under illumination with a red fluorescent light, after 10 days of etiolation, as described previously.[1] The isolation of these three alkaloids, in addition to isorubijervine, from illuminated *Veratrum* plant suggests the biogenesis of cevanine alkaloid via the formation of C-18-N bond from isorubijervine, before C-nor-D-homo rearrangement.

In continuation of our work on the separation of alkaloids which accumulate particularly in illuminated plants but not found in etiolated plants, two new alkaloids, hosukinidine (**1a**) from the rhizomes and epirubijervine (**2a**) from the aerial part, were isolated from hydrolytic fraction of the illuminated *Veratrum grandiflorum* (Max.) Loesen.

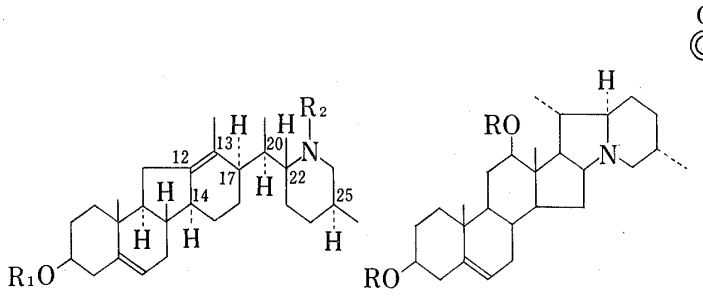
Hosukinidine (**1a**) named after Ainu name "Hosuki" for *Veratrum* plant: $C_{27}H_{43}NO$ (elementary analysis); mp 176.5—177.5°; $[\alpha]_D$ −56.5° (*c* 0.27, MeOH); IR: 3600, 1045 cm^{-1}; MS *m/e*: 397 (M^+), 125, 98 (base peak), afforded on acetylation in pyridine N,O-diacetate (**1b**): mp 195—197°; $[\alpha]_D$ −55.6° (*c* 0.23, $CHCl_3$); IR: 1715, 1615, 1235, 1030 cm^{-1}; PMR: δ 2.03 (3H, s, –OAc) 2.07 (3H, s, –NAc).

The PMR spectrum of **1a** exhibited a singlet at δ 0.98, indicative of C-19 methyl group of a steroidal ring system with Δ^5-double bond, two doublets at δ 0.80 and 0.84 (3H each, J=7 Hz), corresponding to two secondary methyl groups at C-21 and C-27, a singlet at δ 1.56 (3H) for a vinyl methyl, and a signal at δ 5.38 (1H) for an olefinic proton. Multiplet centered at δ 3.48 is associated with α-hydrogen at C-3 (bearing β-hydroxyl group) and this signal shifted downfield to δ 4.64 on acetylation.

In the mass spectrum of **1a**, the base peak at *m/e* 98 is assigned to the methyl piperidyl side chain moiety as a result of a bond fission between C-20 and C-22 of **1a**. In the light of these spectral data, **1a** was considered to be a C-nor-D-homo steroidal alkaloid having veratranine skeleton, and hosukinidine is represented by formula **1a**, except for the configurations at C-17, -20, -22, and -25.

The final structural proof of **1a** was elucidated by the X-ray crystal structure analysis of its hydrochloride (**1c**), colorless needles, mp 285° (dec.). Crystals of **1c** are orthorhombic, space group $P2_12_12_1$, a=33.75±0.07, b=9.43±0.02, c=7.84±0.03 Å, $\alpha=\beta=\gamma$ 90°, z=4. The

1) K. Kaneko, N. Kawamura, T. Kuribayashi, M. Tanaka, H. Mitsuhashi, and H. Koyama, *Tetrahedron Lett.*, **1978**, 4801.



1a: $R_1=R_2=H$ hosukinidine
1b: $R_1=R_2=Ac$
1c: $R_1=H$, $R_2=HCl$ salt

2a: R=H epiribijervine
2b: R=benzoyl

Fig. 1

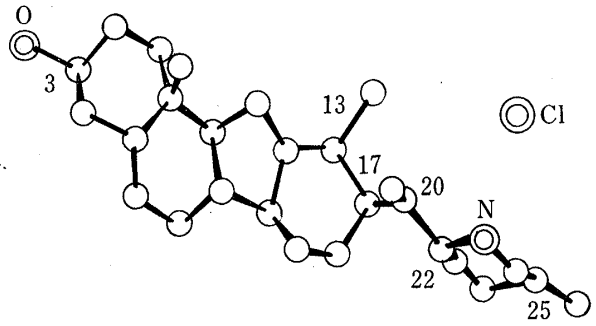


Fig. 2. Perspective Drawing of the Molecule showing Absolute Configuration of Hosukinidine (**1a**)

three-dimensional diffraction data were collected with a Rigaku four-circle diffractometer, using θ–2θ scan technique and graphite monochromated Cu–Kα radiation. The structure was refined by full-matrix anisotropic least-squares calculations to R 0.061.

From these evidences, **1a** was identified as (20*R*,22*R*,25*S*)-veratra-5,12-dien-3β-ol (C-17β side chain, $C_{20}\alpha$-methyl). It is generally known that the stereochemistry at C-20 in naturally occurring steroids has been settled as R-configuration, but recently, Vanderah and Djerassi[2] isolated six methyl-(E)-cholanate derivatives with the unexpected 20*S* stereochemistry ($C_{20}\alpha$-methyl) from a sea pen, *Ptilosarcus gurneyi* Gray. **1a** has no functional group in the neighborhood of C-20, and **1a** is found in the nonsaponifiable alkaloids and microbial hydrolytic alkaloids prepared from illuminated *Veratrum* plants, so that it seems most reasonable to conclude that **1a** is not an artifact through hydrolysis with hydrochloric acid. Therefore, **1a** is the first compound which possesses $C_{20}\alpha$-methyl group to be isolated from the plant kingdom.

From the fact that chiral center at C-17 in jervanine alkaloid has been settled as S-configuration from X-ray crystal structure analysis of veratrobasine,[3] the chiral center at C-17 of **1a** (17*R*) retains reverse configuration in contrast to those of jervine and 11-deoxojervine, and its stereochemistry suggests the formation of **1a** *via* C-nor-D-homo rearrangement from epirubijervine (**2a**) and sucessive cleavage of C-16-N bond.

Epirubijervine (**2a**): $C_{27}H_{43}NO_2$; mp 231—234°; $[\alpha]_D$ −32.3° (*c* 0.22, $CHCl_3$) MS *m/e*: 413 (M^+), 220, 150 (base peak); PMR: δ 0.85 and 1.03 (3H each, s, 18- and 19-Me), 0.84 and 0.99 (3H each, d, J=6 Hz, 21- and 27-Me), 3.42 (2H, m, 3α-, and 12α-H, these signals shifted downfield to δ 4.86 on benzoylation), 5.34 (1H, olefinic proton): afforded on benzoylation in pyridine O,O-dibenzoate (**2b**): mp 264—267°; IR: 1710, 1280, 1120 cm^{-1}; PMR: δ 7.34—8.14 (10H, m, aromatic protons).

In addition to these spectral data, the CMR spectrum of **2a** is explained well as the structure of epiruvijervine. Djerassi *et al.*[4] reported the effect of hydroxyl substituents of androstane derivatives in CMR spectrum. The effect of hydroxyl substituents at C-12 in androstane and solanidanine showed a similar tendency for chemical shifts with regard to β-carbons (C-11 and C-13) and γ-carbons (C-9, -14, -17, and -18). The resonance of C-18 shifted upfield ($\Delta\delta$=−6.44 ppm) because of γ-gauche interaction with β-equatorial hydroxyl group at C-12, and two carbons at C-11 ($\Delta\delta$=+10.01 ppm) and C-13 ($\Delta\delta$=+5.74 ppm) shifted downfield because of β-effect with equatorial hydroxyl group at C-12, so that it seems most reasonable to conclude that **2a** is identical with 12-epirubijervine.

2) D.J. Vanderah and C. Djerassi, *Tetrahedron Lett.*, **1977**, 683; D.J. Vanderah and C. Djerassi, *J. Org. Chem.*, **43**, 1442 (1978).
3) G.N. Reeke, Jr., R.L. Vincent, and W.N. Lipscomb, *J. Am. Chem. Soc.*, **90**, 1663 (1968).
4) H. Eggert, C.L. VanAntwerp, N.S. Bhacca, and C. Djerassi, *J. Org. Chem.*, **41**, 71 (1976).

The melting point of **2a** was not depressed by admixture with authentic specimen of 12-epirubijervine which was synthesized according to the method of Pelletier,[5] and **2a** was identified as 12-epirubijervine [(22*R*,25*S*)-solanid-5-ene-3β,12β-diol].

No pertinent biogenetic researches for jervanine and veratranine alkaloids on plants have been reported. **2a** corresponds to the starting material of Narayanan's hypothesis of C-nor-D-homo rearrangement[6] and **1a** coincides with the compound cleaved at C-16-N bond, after C-nor-D-homo rearrangement from **2a**, except the orientation at C-21 methyl group. However, the reversion of C-21 methyl group from **2a** to **1a** still remains uncertain.

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5) S.W. Pelletier and D.M. Locke, *J. Am. Chem. Soc.*, **79**, 4531 (1957).
6) C.R. Narayanan, *Fortschr. Chem. Org. Naturstoffe*, **20**, 298 (1962).

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The Constituents of *Schizandra chinensis* Baill.[1] The Cleavage of the Methylenedioxy Moiety with Lead Tetraacetate in Benzene, and the Structure of Angeloylgomisin Q

Cleavage of the methylenedioxy moiety with lead tetraacetate in benzene to diphenol was described. Piperonylic acid methyl ester (**5**), 3,4-methylenedioxytoluene (**6**), 2,3-methylenedioxyanisole (**7**) and gomisin A (**8**) afforded protocatechuic acid (**10**), 3,4-dihydroxytoluene (**11**), 2,3-dihydroxyanisole (**12**) and compound **13**, respectively, by the reaction. The structure of angeloylgomisin Q, isolated from the fruits of *Schizandra chinensis* Baill. (Schizandraceae), was elucidated as **4** with the aid of the above reaction.

Keywords——cleavage of methylenedioxy moiety; lead tetraacetate; *Schizandra chinensis* Baill.; Schizandraceae; dibenzocyclooctadiene lignan; angeloylgomisin Q

In the course of the studies on the constituents of *Schizandra chinensis* Baill. (Schizandraceae), we have found that treatment of gomisin N(**1**) with lead tetraacetate [$Pb(OAc)_4$] in AcOH gave 6β-acetoxygomisin N(acetylgomisin O, **2**), but treatment of **1** with the reagent in dry benzene gave an unexpected diphenol (**3**).[1] This communication deals with the further cleavage reactions of the methylenedioxy moiety with $Pb(OAc)_4$ in dry benzene, and also describes the structure elucidation of a new lignan, angeloylgomisin Q, isolated from the fruits of the same plant.

1) Y. Ikeya, H. Taguchi, I. Yosioka, and H. Kobayashi, *Chem. Pharm. Bull.* (Tokyo), in press.