Faculty of Pharmaceutical Sciences
University of Tokyo
Hongo, Bunkyo-ku, Tokyo

Received July 13, 1979

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


Keywords—Liliaceae; Veratrum grandiflorum; a new veratrane alkaloid; hosukinidine; a solanidine alkaloid; epirubijervine; illuminated Veratrum

Concerning the biogenesis of C-nor-α-homo steroidal alkaloids, two new cevanine alkaloids, shinonomenine and verafortazine, and a new cevanidine alkaloid, procevine, were isolated from a Veratrum plant cultivated under illumination with a red fluorescent light, after 10 days of etiolation, as described previously. 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-α-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.) Loresen.

Hosukinidine (1a) named after Ainu name "Hosuki" for Veratrum plant: C_{29}H_{43}NO (elementary analysis); mp 176.5–177.5°; [α]_{D}^{25} = 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°; [α]_{D}^{25} = 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 S\(^{2}\)-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-hydroxy 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\(_1\)2\(_1\)2\(_1\), a=33.75±0.07, b=9.43±0.02, c=7.84±0.03 Å, \(α=β=γ\) 90°, \(z=4\). The

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 (20R,22R,25S)-vera-5,12-dien-3β-ol (C-17β side chain, C20α-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 Djerassi2) isolated six methyl-(E)-cholane derivatives with the unexpected 20S stereochemistry (C20α-methyl) from a sea pen, *Pilosarcus 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 C20α-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 veratrobinas,3) the chiral center at C-17 of 1a (17R) retains reverse configuration in contrast to those of jervine and 11-deoxyjervine, and its stereochemistry suggests the formation of 1a via C-nor-D-homo rearrangement from epirubijervine (2a) and successive cleavage of C-16-N bond.

Epirubijervine (2a): C27H14NO4; mp 231–234°; [α]D −32.3° (c 0.22, CHCl3) 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 benzyolation), 5.34 (1H, olefinic proton): afforded on benzyolation 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 androstan derivatives in CMR spectrum. The effect of hydroxyl substituents at C-12 in androstan 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 (δ = −6.44 ppm) because of γ-gauche interaction with β-equatorial hydroxyl group at C-12, and two carbons at C-11 (δ = +10.01 ppm) and C-13 (δ = +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.

---

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, and 2a was identified as 12-epirubijervine ([22R,25S]-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 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.

The authors are indebted to Dr. N. Kamijyo, Government Industrial Research Institute, Osaka, for the use of the diffractometer.

Faculty of Pharmaceutical Sciences, Hokkaido University Kita-ku, Kita-12, Nishi-6 Sapporo, 060 Japan

Faculty of Pharmaceutical Sciences, Kyoto University Sakyo-ku, Yoshida Kyoto, 606 Japan

Kô Kaneko
Noriaki Kawamura
Hiroshi Mitsuhashi
Kenji Ohsaki

Received July 27, 1979


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-acetoxymogomisin 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.