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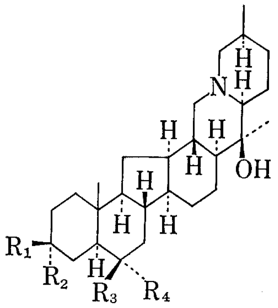
Isobaimonidine, a New *Fritillaria* Alkaloid from the Aerial Part of *Fritillaria verticillata*

The third epimer of verticine, isobaimonidine, was isolated from the aerial part of *Fritillaria verticillata*, and its absolute configuration was chemically determined as (22*S*, 25*S*)-5α-cevanine-3α,6α,20β-triol.

Keywords——Liliaceae; *Fritillaria verticillata*; a new *Fritillaria* alkaloid; a epimer of verticine; 5α-cevanine-3α-ol series; alkaloid from aerial part

In the course of our biogenetic studies on *Fritillaria* alkaloids, we have already reported two new cevanine alkaloids, baimonidine (2) from the aerial part, and isoverticine (3) from the bulb of the mature *Fritillaria verticillata* WILD. var. *Thunbergii* BAKER, Liliaceae.[1] In continuation of our work on the separation of alkaloids in the same mature plant, a new minor alkaloid, isobaimonidine (1) was isolated from the aerial part.



Compound	R1	R2	R3	R4
Isobaimonidine (**1**)	H	OH	H	OH
Baimonidine (**2**)	H	OH	OH	H
Isoverticine (**3**)	OH	H	OH	H
Verticine (**4**)	OH	H	H	OH
6α-Ol-3-one deriv. (**5a**)	=O		H	OH
Verticinone (**6**)	OH	H	=O	

Fig. 1

Isobaimonidine (**1**), [mp 238—241°; $[\alpha]_D$ −59.2° (*c* 0.25, $CHCl_3$); IR $\nu_{\max}^{CHCl_3}$: 3600, 3550—3100, 2780 and 1020 cm^{-1}], revealed a parent molecular peak at *m/e* 431 and a base peak at *m/e* 112[2] in mass spectrum. The IR spectrum of **1** showed diagnostic absorption bands contributed to *trans*-quinolizidine moiety at 2780 cm^{-1},[3] and hydroxyl group at 3600, and 3550—3100 cm^{-1}. The ^{1}H-NMR spectrum (100 MHz) of **1** exhibited three methyl signals, two singlets at δ 0.80 and 1.02, a doublet at δ 1.07, and two multiplets centered at δ 3.33 ($W_{1/2}$=24 Hz) and 4.16 ($W_{1/2}$=8 Hz), which associated with hydrogens bearing hydroxyl group. Thus it can be concluded that **1** is a cevanine alkaloid having a tertiary and two secondary hydroxyl groups. The chemical shifts of the methyl protons and the half height width of protons bearing hydroxyl group in **1** have analogies with those of verticine (**4**)[4] and those of its epimers,[1] as shown in Table I, and suspect the structure of **1** as 5α-cevanine-3α,6α,20β-triol.

In order to establish the absolute configuration of **1**, we conducted the conversion of **4** to **1**. **4** was oxidized with Fetizon's reagent (Ag_2CO_3 on Celite)[5] to 6α-ol-3-one deriv. (**5a**), [MS *m/e*: 429 (M^+), 414, 411, and 112 (base peak); IR $\nu_{\max}^{CHCl_3}$ cm^{-1}: 3600, 3570—3150, 2800, 1700, 1130, and 1030; ^{1}H-NMR: in Table I; CD (*c* 3.58×10^{-1}, methanol) $[\theta]_{288}$ (nm):

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Table I. ^1H Chemical Shifts in ppm Relative to TMS in $CDCl_3$

Compound	C-3	C-6	C-19[a]	C-21[a]	C-27[b]
1	4.16[c]	3.33[d]	0.80	1.02	1.07
2	4.24[c]	3.84[c]	1.02	1.05	1.11
3	3.63[d]	3.85[c]	1.03	1.03	1·09
4	3.50[d]	3.44[d]	0.81	1.02	1.11
5a	—	3.45[d]	1.06	1.02	1.12
6	3.56[d]	—	0.76	1.02	1.10

Multiplicity: *a*) s, *b*) d, $J=7$ Hz, *c*) m, $W_{1/2}=8$ Hz, *d*) m, $W_{1/2}=24$ Hz.

+3000 (positive maximum); ref. verticinone (**6**),[4] CD (c 4.78×10^{-1}, methanol) $[\theta]_{295}$ (nm): −2800 (negative maximum)[6]].

5a was acetylated by usual manner, resulting 6α-acetate (**5b**) was reduced with isobornyloxyaluminum dichloride.[7] The product, after being saponified, was purified by column chromatography on silica gel and afforded **1** and **4**, 38% and 15% yield, respectively. The physical constants of **1** agreed completely with those of natural product and melting point of **1** was not depressed by admixture with the natural product.

1 corresponds 3rd epimer of **4**, concerning configurations of hydroxyl groups at C-3 and C-6 in 5α-cevanine skeleton, then it seems most reasonable to suspect that **4** and its three epimers, **1**, **2**, and **3** are derived from common precursor which is transformed from solanidine.[8] It is interesting to note that regarding configuration of hydroxyl group at C-3 in 5α-cevanine alkaloid, α-hydroxyl epimers, **1** and **2**, were only isolated from the aerial part, but not found from the bulb, on the contrary, β-hydroxyl epimers, **3** and **4**, were mainly isolated from the bulb. On the basis of these consideration, the biogenesis of *Fritillaria* alkaloid are subject under active investigations.

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