STRUCTURE OF VALIVINE

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The total chloroform-extracted material from the epigeal part of *Fritillaria valujevii* Regel has yielded a new base – valivine, with mp 256-258°C, $[\alpha]_D$ –48°, $C_{28}\cdot H_{47}NO_3$ (I). The structure and configuration of valivine have been established on the basis of a study of its IR, NMR, and mass spectra and those of its transformation products.

Having continued the separation of the mother liquor from the combined ether- and chloroform-extracted material from the epigeal part of *Fritillaria valujevii* Regel [1], we have isolated by chromatography on a column of silica gel the new alkaloid valivine with mp 256-258°C, $[\alpha]_D$ –48°, $C_{28}H_{47}NO_3$ (I). The IR spectrum of (I) has absorption bands at (cm^{-1}) 3430, 1055 (hydroxy group), 2975-2835, 1470, 1455 ($-CH_3$; $-CH_2-$), and 2740 ($N-CH_3$). In the mass spectrum of (I) the main ion peaks with m/z 112(100%), 113, 140, 141, 149, 170, 171, 199, 212, 400, 401, 410, 411 $(M-17)^+$, $(M-15)^+$, 445 M^+ are characteristic for typical steroid alkaloids of the edpetilidinine series [2-4]. The acetylation of (I) with acetic anhydride in pyridine gave diacetylvalivine (II). In the IR spectrum of (II) absorption bands appear at (cm^{-1}) 3450, 1048 (hydroxy group), 1740, 1255 (ester group), and 2790 ($N-CH_3$). The spectral characteristics of (I) and (II) are very close to those of rhinolidine (III) and diacetylrhinolidine (IV) [4, 5]. Details of the NMR spectra of compounds (I) and (II) are given in Table 1.

The results of an analysis of the IR, NMR, and mass spectra permit the assumption for (I) of the heterocyclic skeleton of edpetilidinine [2-4], which contains two secondary and one tertiary hydroxy groups.

The formation of a sparingly soluble digitonide of valivine with digitoxin, and also the presence of an absorption band at 1055 cm^{-1} in the IR spectrum of valivine show that it contains a Δ^5-3β-OH group [4, 6-8]. This is also confirmed by the presence of a multiplet at 4.50 ppm from C-3αH in the NMR spectrum of diacetylvalivine [9-11] and the appearance of the signal of the $19-CH_3$ protons at 0.97 ppm in the spectrum of (I), as in that of rhinolidine [4].

In the NMR spectrum of valivine an $18-CH_3$ group gives a signal at 0.92 ppm, as also in the spectrum of rhinolidine, which shows the presence of a secondary OH group at C_{12} or C_{15}. A comparison of the chemical shifts of the protons of the $18-CH_3$ groups of (I) and (II) (with a difference of 0.11 ppm) shows that the hydroxy group is present at C_{15} and has the β-axial orientation [12, 13]. According to the NMR spectra of (I) and (II), the tertiary hydroxy group does not affect the chemical shifts of the $19-CH_3$ protons. Consequently, it cannot be present in the C_8 or C_9 positions.

TABLE 1

Substance	Chemical shift,* δ							
	$19-CH_3$, s	$18-CH_3$, s	$21-CH_3$, d	$OCOCH_3$, s	$N-CH_3$, s	$HC-OH$, m	$HCOCOCH_3$, m	$(C=CH)$, m
I	0,97	0,92	1,08		2,34	3,56; 3,99		5,24
II	0,96	0,81	1,12	1,93; 1,95	2,13		4,50; 5,15	5,21

*s – singlet; d – doublet; m – multiplet.

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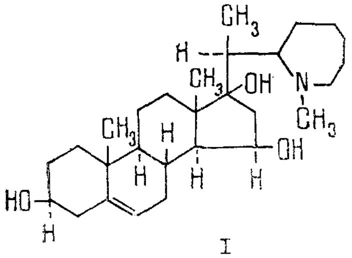
Valivine was not oxidized by periodic acid, which shows the absence of adjacent hydroxyls and excludes the C_{14} position for a hydroxyl [12]. This means that the only possible position for the tertiary hydroxy group remains that at C_{17}. Thus, valivine has the most probable structure and configuration shown by formula (I), below.



I

EXPERIMENTAL

Thin-layer chromatography (TLC) was performed in a fixed layer of KSK silica gel (100 mμm) using the chloroform—methanol (10:1) system. IR spectra were taken on UR-20 spectrometer (in KBr), NMR spectra on a JNM-4H-100 MHz instrument [(I) in $CDCl_3$—CD_3OD (1:1); (II) in $CDCl_3$, with HMDS as internal standard (δ scale)], and mass spectra on an MKh-1310 mass spectrometer.

Isolation of Valivine. Rhinolidine [1] was isolated from the total ether- and chloroform-extracted material. After the removal of the rhinolidine, the mother liquors were combined (160 mg) and rechromatographed on a column of silica gel with elution by chloroform—methanol (10:1.5). This gave valivine with mp 256-258°C (methanol). $[\alpha]_D$ −48° [c. 1.0; chloroform—methanol) (1:1)], R_f 0.46.

Diacetylvalivine. A mixture of 40 mg of valivine, 1 ml of pyridine, and 1 ml of acetic anhydride was kept at room temperature for 3 days. After elimination of the pyridine, the residue was dissolved in 5% sulfuric acid the solution was made alkaline with ammonia and extracted with chloroform, and the solvent was distilled off. When the residue was treated with methanol, crystals were obtained with mp 210-212°C, R_f 0.76.

Mass spectrum: m/z 112 (100%), 113, 125, 138, 144, 150, 167, 168, 169 $(M - 60)^+$, $(M - 59)^+$ $(M - 43)^+$, $(M - 42)^+$, 498, 512, 529 M^+

SUMMARY

The new base valivine has been isolated from the total alkaloids of *Fritillaria valujevii* Regel, and its structure and configuration have been established.

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