9,9-Dibromotrimethylenequinazolone (XXIV). Compound (XXII) (3 g) was brominated under the conditions described above. After the appropriate working up, the residue was recrystallized from ethanol–acetone, to give 3.08 g of a product with mp 175°C (decomp.) (lit.: 189-191°C [5]). Mass spectrum: 346/344/342, 265/263, 185, 184. PMR spectrum: 3.30 (2H, m, H-10, H-10'); 4.15 (2H, m, H-11, H-11'); 7.67 (3H, m, H-6, H-7, H-8); 8.35 (1H, dd, J_o = 7.5 Hz, J_m = 1.5 Hz, H-5). By recrystallization after separation on a column of Al_2O_3 the mother liquors yielded very small amounts of the initial (XXII) and of 9-bromo-DOV (XXVIII).

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ALKALOIDS OF THE EPIGEAL PART OF Aconitum orientale

STRUCTURE OF ORGETINE

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UDC 547.944/945

From the total alkaloids of the epigeal part of the plant Aconitum orientale have been isolated the known alkaloid kobusine and a new alkaloid, which has been called orgetine. A structure has been put forward for orgetine on the basis of spectral characteristics (IR, PMR, ^{13}C NMR, and mass spectra) and the production of a triacetate.

Continuing the separation of the total alkaloids of the epigeal part of Aconitum orientale [1], we have isolated kobusine and a new base, which has been called orgetine (I).

Orgetine has the composition $C_{20}H_{27}NO_3$. The IR spectrum of the base contained absorption bands of hydroxy groups at 3300-3500 cm^{-1}. The PMR spectrum revealed the signals of a tertiary C-methyl group and a terminal methylene group, and also one-proton signals at (ppm) 3.00 (doublet, J = 12 Hz), 3.82 (broadened singlet), and 3.97 (doublet, J = 5 Hz).

The acetylation of a mixture of orgetine and kobusine with acetic anhydride in the presence of pyridine led to a triacetyl derivative of orgetine (II) in the IR spectrum of which the absorption bands of hydroxy groups had disappeared, which showed the completeness of acetylation. The absence of the signals of an N-alkyl substituent from the PMR spectra of compounds (I) and (II) and the heterocyclic skeleton of the molecule obtained on replacing the hydroxyls by hydrogen permitted orgetine to be assigned to the alkaloids of the hetisine type and to be considered as an isomer with respect to the positions of the hydroxy groups.

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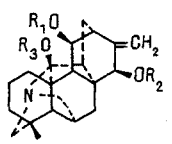
TABLE 1. Chemical Shifts of the Carbon Nuclei of Orgetine (I), Nominine (III), and 9-Hydroxynominine (IV)

Carbon	I	III	IV	Carbon	I	III	IV
1	30,6	33,3	28,9	11	70,6	27,1	38,5
2	19,6	19,8	19,6	12	41,2	34,0	35,1
3	35,9	34,2	33,4	13	41,4	32,9	33,4
4	37,9	37,3	38,0	14	40,7	44,0	41,5
5	61,9	61,2	54,6	15	73,2	74,9	73,2
6	67,8	65,4	64,8	16	149,8	156,8	154,6
7	29,5	27,0	24,5	17	114,8	108,3	109,9
8	47,2	45,7	35,1	18	27,7	28,9	29,0
9	54,5	43,8	79,2	19	60,5	62,8	62,4
10	50,2	49,7	52,8	20	97,4	71,8	72,3

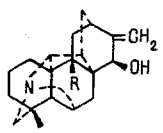
A comparison of the PMR spectra of orgetine and its triacetate showed that in the alkaloid two of the hydroxy groups are secondary and one tertiary, since on acetylation shifts were observed of the signals of only two protons geminal to hydroxy groups. A signal at 3.82 ppm had shifted to 4.97 ppm, and one at 3.97 ppm to 5.00 ppm. A one-proton broadened singlet at 3.82 ppm was assigned to C-15–H on the basis of the following facts. In the PMR spectrum of orgetine triacetate, in addition to the shift of the C-15–H signal, an increase in the difference between the chemical shifts of the α- and β-protons of the terminal methylene group was observed (for orgetine the difference was 0.10 ppm, and for its triacetate 0.25 ppm). The same shift takes place on passing from pseudokobusine to 15-benzoylpseudokobusine [2], and is obviously due to the influence of the anisotropic field of the carbonyl group at C-15 on the protons of the terminal methylene group.

A one-proton doublet at 3.97 ppm (J = 5 Hz) was assigned to C-11–α-H on the basis of a study of a model and a comparison with the spectra of kobusine and its diacetate.

The third hydroxy group in orgetine is tertiary but was nevertheless acetylated by acetic anhydride at room temperature. Such behavior is observed for tertiary α-carbinolamines, which limited the location of this hydroxy group to position 20 or 6. It is known that the acetylation of a hydroxy group at C-6 is not infrequently accompanied by cleavage of the C-6–N bond [3], which was not observed on the acetylation of orgetine. Consequently, the tertiary hydroxy group may be located at C-20, and the structure of orgetine be represented by formula (I).



I. $R_1=R_2=R_3=H$
II. $R_1=R_2=R_3=Ac$



III. R=H
IV. R=OH

A further confirmation of the suggested structure was obtained in a study of the ^{13}C NMR spectrum of orgetine. In the ^{13}C NMR spectrum of orgetine (under conditions of complete suppression of carbon-proton interactions) 20 signals, corresponding to the 20 carbon atoms of orgetine, were observed. The multiplicities of these signals were determined on the basis of the off-resonance spectrum. The assignments of the signals were made by a comparison with the spectra of nominine (III) and 9-hydroxynominine [4] and are given in Table 1.

A weak-field singlet at 97.4 ppm was assigned to C-20, just as for other alkaloids containing α-carbinolamine carbon [5]. The close values of the chemical shifts of C-15 in orgetine (I), nominine (III), and 9-hydroxynominine (IV) permitted the assumption that the hydroxy groups at C-15 in these alkaloids have the same configuration.

EXPERIMENTAL

For chromatography we used brand LS 5/40 silica gel (Czechoslovakia) and alumina (Brockman activity grade II).

IR spectra were taken on a UR-20 spectrometer, mass spectra on an MKh-1310 spectrometer fitted with a system for the direct introduction of the sample into the ion source, and PMR (100 MHz) and ^{13}C NMR (25.4 MHz) spectra on a BS-567A spectrometer in deuterochloroform with the addition of deuteromethanol. Chemical shifts are given relative to the internal standard TMS on the δ scale.

Separation of the Chloroform Fraction [1]. The chloroform fraction of the total alkaloids from the epigeal part of Aconitum orientale was treated with acetone, and 1.05 g of a crystalline mixture consisting of two alkaloids was isolated. The crystalline fraction was separated by the formation of acetates.

Acetylation of the Crystalline Mixture. A solution of 0.5 g of the crystalline mixture, 5 ml of acetic anhydride, and 0.2 ml of pyridine was kept at room temperature for 60 h. The excess of acetic anhydride was evaporated off, the residue was dissolved in water, the solution was made alkaline, and the reaction products were extracted with ether. After the solvent had been distilled off, the products were separated on a column of alumina. Elution with ether–methanol (50:1) yielded 0.31 g of orgetine triacetate. Ether–methanol (10:1) eluates gave 0.09 g of a product that was identified as kobusine diacetate.

Alkaline Hydrolysis of Orgetine Triacetate (II). A solution of 0.22 g of orgetine triacetate in 10 ml of 5% methanolic KOH was boiled for 1 h. The solvent was evaporated off, and the residue was dissolved in water and extracted with chloroform. After evaporation and the elimination of the solvent with the aid of acetone, 0.12 g of orgetine was isolated.

Orgetine (I), mp 280-282°C (acetone), $C_{20}H_{27}NO_3$ (M^+ 329.19895, HRMS), $[\alpha]_D^{22}$ +40° (c 0.36; C_2H_5OH). IR spectrum: 3300-3500 cm^{-1} (OH groups).

PMR spectrum, ppm: 1.28 (3H, s, 18-CH_3), 3.00 (1H, d, J = 12 Hz), 3.82 (1H, s, H-15), 3.97 (1H, d, J = 5 Hz, α-H-11), 5.05 and 5.15 (each 1H, br. s, H-17β and H-17α).

Mass spectrum: M^+ 329 (100%).

Orgetine triacetate (II), mp 128-130°C. IR spectrum: 1740 cm^{-1} (ester carbonyl).

PMR spectrum, ppm: 1.00 (3H, s, 18-CH_3); 1.93; 1.97; 2.03 (each 3H, $COCH_3$ × 3); 2.85 (1H, d, J = 12 Hz, H-19β); 2.93 (1H, d, J = 12 Hz, H-19α; 5.12 and 5.37 (each 1H, br. s, H-17β and H-17α).

Mass spectrum: M^+ 455.

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