STRUCTURE OF GLAUFIDINE

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From the phenolic ether-soluble material of the epigeal part of Glaucium fimbrilligerum [1] collected in the flowering phase on the slopes of the Baubashata range, Kirgiz SSR (sai Karamazar) we have isolated a new base with $[\alpha]_D$ +182° (c 0.4; CH_3OH), which we have called glaufidine (I).

The UV spectrum of (I) has three maxima, at 223, 269, and 305 nm (log ε 4.51, 4.03, 3.69), which are characteristic for 1,2,10,11-substituted aporphine alkaloids [2, 3].

The IR spectra have absorption bands at 1580, 1610 cm^{-1} (aromatic ring) and 3200-3500 cm^{-1} (OH). The mass spectrum of glaufidine contains the peaks of ions with m/e 357 (M^+), 356, 342, 340, 339, 326, 314, and 178.5 (M^{2+}).

The NMR spectrum (δ scale) has three-proton singlets at 2.48 ppm ($N-CH_3$), 3.66 ppm (OCH_3), 3.85 ppm (OCH_3), and 3.88 ppm (OCH_3). In the aromatic region of the spectrum there are two doublets at 6.79 and 6.99 ppm (J = 8 Hz, ortho aromatic protons) and a one-proton singlet at 6.92 ppm. Methylene and methine protons appear in the form of multiplets in the 2.20-3.50 ppm region. At 4.46 ppm there is a poorly resolved one-proton triplet ($W_{1/2}$ = 5 Hz).

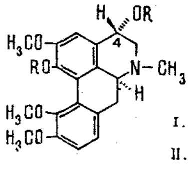
When the base was acetylated with acetic anhydride in pyridine, a diacetyl derivative (II) was obtained with M^+ 441. The NMR spectrum of (II) had signals in the form of three-proton singlets at 2.15 and 2.22 ppm ($2\,OCO-CH_3$), 2.50 ppm ($N-CH_3$), and 3.43, 3.79, and 3.84 ppm ($3\,OCH_3$), a one-proton singlet at 6.91 ppm, one-proton doublets at 6.82 and 6.95 ppm (J = 8 Hz, ortho aromatic protons), and a poorly resolved one-proton triplet ($W_{1/2}$ = 5 Hz) at 5.87 ppm.

The formation of a diacetyl derivative shows that (I) contains two hydroxy groups. The presence in glaufidine of an aporphine nucleus with five oxygen functions and three aromatic protons, and the downfield shift of the weak-field signal in the form of a triplet in the spectrum of (II) shows that one of the oxygen functions is a secondary hydroxy group. The alcoholic hydroxy group may be present at C_4, C_5, or C_7.

The mass spectrum of the base has an ion with m/e 314 (M − 43) which shows the absence of a substituent at C_5 [4, 5]. The appearance in the NMR spectra of (I) and (II) of a geminal proton in the form of a triplet excludes the possibility of the presence of a hydroxy group at C_7. The facts stated above show that the secondary hydroxy group is present at C_4 [3, 6].

When the base was hydrogenated with palladium on carbon, and also when it was treated with PCl_3 followed by reduction with zinc in sulfuric acid, a single product was obtained which was identified as (+)-corydine. The formation of this substance confirms the positions of the substituents in the aromatic part of the molecule and shows the S configuration of the C_{6a} asymmetric center [8]. The CD curve of glaufidine has a positive Cotton effect at 233 nm and a negative effect at 268 nm. The presence of a one-proton triplet at 4.46 ppm in the NMR spectrum of (I) shows that the alcoholic group at C_4 had the α-orientation (pseudoaxial) [9, 10].

Thus, glaufidine is the first aporphine alkaloid of the 1,2,4,10,11-pentasubstituted type, and it has the following structure (I):



I. R=H
II. R=$COCH_3$

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ALKALOIDS OF Veratrum nigrum

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The alkaloids of Veratrum nigrum L. [1] have been studied inadequately. There are reports on the dynamics of the accumulation of the combined alkaloids in various organs according to the vegetation stage of the plant [2], of a preliminary chromatographic separation of the combined alkaloids separated from the epigeal and hypogeal parts [3], and of the isolation of jervine, germerine, and veratroylzygadenine [4]. In view of this, we have undertaken the study of the composition of the alkaloids of this species of Veratrum.

From the combined alkaloids isolated by treating the roots with rhizomes, by the method described for Veratrum lobelianum Bernh. [5], we have isolated by chromatography on a column of cellulose [6] two alkaloids with R_f 0.40 (I), and 0.47 (II) (chloroform, saturated formamide; type "M" ["slow"] paper of the Volodarskii paper mill, impregnated with a 1 : 2 solution of formamide in ethanol).

Alkaloid (I), mp 191-192°C (benzene), $[\alpha]_D^{22}$ −16° (c 0.6 pyridine). IR spectrum (KBr): 1740, 1250 cm^{-1} (ester C=O). The UV spectrum of a sulfuric acid solution of the alkaloid taken 24 h after its dissolution (λ_{max} = 250, 290, 370, 540 nm) had a region at 360 nm of coincidence with the spectrum taken after 1.5 h (the amino alcohol protoverine [7]). In the hydrolysis products of the alkaloid, paper chromatography [8] showed the presence of substances analogous to the hydrolysis products of deacetylprotoveratrine A (III), which we have isolated from Veratrum lobelianum Bernh. [9]: the amino alcohol protoverine (butan-1-ol−CH_3COOH−H_2O (4 : 1 : 5)), acetic acid, (l)-α-methylbutyric acid, and (d)-α-hydroxy-α-methylbutyric acid (butan-1-ol−1.5 N aqueous ammonia (1 : 1)). The methanolysis [10] of (I) converted it into dideacetylprotoveratrine A (IV) [11].

The results of analysis show that the alkaloid (I) is deacetylprotoveratrine A [9]. This is the first time that it has been isolated from Veratrum nigrum L.

Alkaloid (II), mp 202-204°C (benzene), $[\alpha]_D^{20}$ −7° (c 0.88; pyridine). IR spectrum (KBr); 1738, 1250 cm^{-1}. A sulfuric acid solution of the substance had a spectrum in the UV and visible regions taken 24 h after dissolution (λ_{max} 246, 315, 406, 528 nm) that did not coincide with the spectrum taken after 1.5 h (amino alcohol germine) [7]. The products of the alkaline hydrolysis of (II) [8] were shown by paper chromatography with "markers" to contain the amino alcohol germine (butan-1-ol−CH_3COOH−H_2O (4 : 1 : 5)), (l)-α-methylbutyric acid, and (d)-α-hydroxy-α-methylbutyric acid. According to the scheme of determining the positions of acyl groups in Veratrum esters [12], the acids found must occupy position 3 and 15 of the germine, respectively.

The results of analysis permit the conclusion that the alkaloid (II) isolated is germerine. This is the first time that it has been isolated from raw material growing on the territory of the USSR.

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