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ALKALOIDS OF *Delphinium retropilosum*

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Elasine, methyllycaconitine, lycoctonine, and the new alkaloid delretine have been isolated from the plant Delphinium retropilosum, *and the structure of delretine has been determined.*

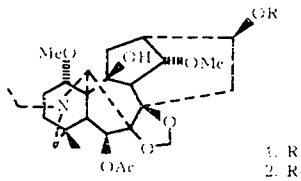
Representatives of the genus *Delphinium* L., which produce diterpene alkaloids, belong to some of the most valuable alkaloid-bearing plants of the Ranunculaceae family [1]. Alkaloids isolated from these plants have been described in a large number of publications [2], but many species of this genus have not hitherto been investigated. Such plants include *Delphinium retropilosum* L. In the literature available to us there is no information on the chemical composition of this plant and its use in folk medicine [3].

Delphinium retropilosum, a plant 65-85 cm tall, is found in Western and Eastern Siberia [4]. We have investigated the alkaloids of the hypogeal and epigeal parts of the plant gathered in the Kemerovo oblast (Kemerovo region, valley of the R. Tom'). We obtained the total alkaloids from the roots and epigeal part in the usual way; they amounted to 0.65 and 0.8%, respectively, on the weights of the air-dry raw materials. By column chromatography and by forming salts from the mixtures of bases of the roots and epigeal parts we isolated four (**1-4**) and two (**1**, **2**) alkaloids, respectively.

Base (**1**), with the composition $C_{28}H_{41}NO_9$, mp 218-219°C, dissolves in chloroform, acetone, and methanol, is sparingly soluble in alcohol and ether, and crystallizes from hexane. This base is new, and we have called it delretine (**1**). In the IR spectrum of (**1**) there was a narrow absorption band of a hydroxy group at 3545 cm^{-1}, high-intensity bands at 1737 cm^{-1} (ester carbonyl group) and 1244 cm^{-1} ("ester band"). Analysis of the PMR spectrum ($CDCl_3$, δ, ppm) showed the presence of the following functional groups in (**1**): methylenedioxy (4.88 and 4.80; s, 1 H each), two methoxyls (3.40 and 3.18; s, 3H each), two acetoxy groups (2.00 and 1.96; s, 3H each), an N-ethyl group (0.99, t, 3H, J = 7.5 Hz) and an 18-methyl group (0.80, s, 3H). These facts showed that delretine belongs to the norditerpenoid alkaloids with a lycoctonine skeleton.

The mass spectrum of (**1**) contained the peaks of ions with *m/z* 535 (M^+), 520, and 504 (100), which are typical for lycoctonine alkaloids. The fact that the (M-31) ion had the maximum intensity showed the presence of a methoxy group at C-1 [5]. The chemical shifts and multiplicities of the one-proton signals at 5.40 ppm (br.s) and 4.66 ppm (dd, J = 7 and 10 Hz) showed that they belonged to the H-6α and H-16α gem-acetoxy protons, respectively

An analogous pattern is observed in the spectra of eldeline, dictyocarpine, etc., for H-6α (5.42-5.34 ppm) [6, 7], and corumdephine, delbiterine for H-16α (dd, J = 7 and 10 Hz, 4.66 and 4.73 ppm) [8, 9]. Consequently, the acetoxy groups of (**1**) were present in positions 6 and 16 and had the β-orientation. In the spectrum of (**1**) the proton at C-14 resonated in the form of a triplet signal at 4.09 ppm (J = 5 Hz). Its chemical shift was typical for alkaloids containing a methoxy group at C-14 and a hydroxy group at C-10 [6, 10, 11]. The facts given above permit us to propose for delretine the structure (**1**).



1. R = Ac
2. R = H

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The crystalline base (**2**) has the composition $C_{26}H_{39}NO_8$, mp 116-118°C. It formed a perchlorate with mp 213-215°C. Its spectral characteristics (IR, mass and PMR spectra) coincided with those of elasine, which has been isolated in the form of an amorphous substance from *D. elatum* [12]. The structure of elasine differs from that of delretine by the absence of the acetyl group at C-16. We acetylated elasine and obtained its monoacetyl derivative, which, according to a mixed melting point, TLC, and IR, PMR and mass spectra, was identical with delretine. 16-Acetylelasine has been described in the literature [12], but this is the first time that it has been isolated from a plant.

Base (**3**) had the composition $C_{37}H_{50}N_2O_{10}$, amorphous, giving a crystalline perchlorate with mp 190-192°C. The PMR and IR spectra of (**3**) were identical with those of methyllycaconitine [8, 13].

The IR and mass spectra of base (**4**), with the composition $C_{25}H_{41}NO_7$, mp 115-120°C, coincided with those of lycoctonine [14].

EXPERIMENTAL

PMR spectra were taken on a Tesla BS 567 A instrument, frequency 100 MHz ($CDCl_3$, 0—HMDS), and IR spectra on a Fourier IR spectrometer, model 2000 (Perkin-Elmer). Mass spectra were obtained on MKh-1310 and MS-3301 instruments.

For TLC we used Silufol in ethyl acetate—methanol—ammonia (10:5:3 drops) and alumina (LSL 254 5/40) in the chloroform—methanol (100:1) system.

Isolation of the Alkaloids. The air-dry comminuted roots (123 g) and epigeal part (170 g) of *Delphinium retropilosum* were treated with a solution of sodium carbonate, and the alkaloids were extracted with chloroform. The bases were extracted from the concentrated chloroform solution with 5% sulfuric acid. From the acid solutions, in the usual way, we obtained 0.81 g of a mixture of bases from the roots, and 1.39 g from the epigeal part.

The mixture of alkaloids (0.81 g) was chromatographed on alumina. Elution was performed with ether, ether—chloroform (1:2), chloroform, chloroform—methanol (50:1), and methanol, 100-ml fractions being collected. The first fractions (1-4) of the ethereal eluates yielded delretine (13 mg), the following ones (5-10) elasine (30 mg) and (13-24) methyllycaconitine, the latter giving a perchlorate (0.124 g) with mp 190-192°C. Lycoctonine, with mp 115-120°C (15 mg), was obtained from the methanolic eluates.

An alcoholic solution of the alkaloids obtained from the epigeal part was acidified with perchloric acid. The crystals of elasine perchlorate that deposited were recrystallized from alcohol, mp 213-215°C. The elasine perchlorate was converted into the free base. After treatment with a solution of sodium carbonate, the residual mother liquor was shaken with chloroform, and distillation of the resulting extract yielded 0.65 g of a mixture of alkaloids. This mixture (0.65 g) was chromatographed on alumina. Elution was performed with chloroform, chloroform—methanol (50:1), and methanol, 100-ml fractions being collected. The first chloroform fractions yielded delretine (5 mg), and the subsequent ones elasine (80 mg).

Delretine (1), mp 218-219°C (from hexane).

IR spectrum (ν, cm^{-1}): 3545, 2952, 2931, 2873, 2834, 1736, 1447, 1380, 1367, 1302, 1244, 1161, 1134, 1105, 1086, 1044, 1014, 983, 972.

Mass spectrum, *m/z* (I_{rel}, %): 535 (M^+, 4), 520 ($M-15^+$, 3), 504 ($M-31^+$, 100), 476 ($M-59^+$, 12).

Elasine (2). White crystalline substance with mp 116-118°C (from petroleum ether—ether; hexane).

IR spectrum (ν, cm^{-1}); 3448, 2962, 2938, 2872, 1745, 1458, 1368, 1295, 1246, 1217, 1197, 1160, 1129, 1100, 1084, 1049, 985, 964.

Mass spectrum, *m/z* (I_{rel}, %): 493 (M^+, 4), 478 ($M-15^+$, 3), 462 ($M-31^+$, 100), 434 ($M-59^+$, 20).

PMR spectrum ($CDCl^3$, δ, ppm): 5.42 (1H, br.s, H-6α), 4.92 and 4.87 (1H each, s, O-CH_2-O), 4.22 (1H, t, J = 5 Hz, H-14β), 3.43 and 3.19 (3H each, s, OCH_3), 2.00 (3H, s, $OCOCH_3$), 1.00 (3h, t, J = 7 Hz, N-CH_2-$\underline{CH_3}$), 0.82 (3H, s, 18-CH_3).

Preparation of 16-Acetylelasine. Elasine was acetylated as described in [12]. 16-Acetylelasine, mp 216-218°C (from hexane), M^+ 535, identified by direct comparison with delretine (mixed melting point, TLC, mass, IR, and PMR spectra).

Methyllycaconitine (3). Light yellow amorphous compound giving a perchlorate with mp 190-192°C (from alcohol). Identified by direct comparison (mixed melting point of the perchlorates and by TLC and PMR spectra) with an authentic specimen obtained from *D. corumbosum* [8].

Lycoctonine (4), mp 115-120°C. Identified by direct comparison with a specimen isolated from *A. septentrionale* (TLC, IR and mass spectra) [14].

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