ALKALOIDS OF *Delphinium dictyocarpum*

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We have investigated the roots and epigeal part of the plant *Delphinium dictyocarpum* DC. collected in the Dzhungarian Ala-Tau in the upper reaches of the R. Koktal, Kuyandysai (budding stage), and in the region of the village of Topolevka (flowering stage). The isolation from the epigeal part (budding stage, upper reaches of the R. Koktal, Kuyandysai) of eldeline (deltaline) methyllycaconitine, eldelidine, and dictyocarpine and from the roots (flowering stage, environs of the village of Topelevka) of methyllycaconitine, lycoctonine, and of two amorphous bases has been reported previously [1].

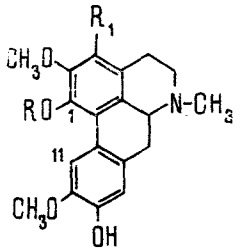
By ordinary chloroform extraction of the epigeal part of the plant collected in the upper reaches of the R. Koktal we obtained 0.52% of combined alkaloids, from which we have isolated eldeline, methyllycaconidine, eldeline, dictyocarpine, and lycoctonine, the aporphine alkaloids isoboldine and N-methyllaurotetanine, and also a new base which we have called dictyzine.

Dictyzine, $C_{21}H_{33}NO_3$ (I), mp 184-186°C (methanol), mol. wt. 347.2404 [high-resolution mass spectrometry (HRMS)], is sparingly soluble in chloroform and more readily in acetone and methanol. The deuteration of (I) showed the presence of three active hydrogen atoms. According to the PMR spectrum, (I) contains a N-methyl and a tertiary C-methyl group. The results of IR, PMR, and mass spectroscopy make it possible to assign (I) to the diterpene alkaloids.

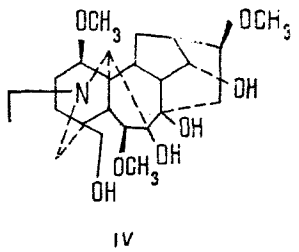
The lack of an authentic sample of N-methyllaurotetanine (II) and the difficulty of its identification on the basis of physicochemical constants [2] induced us to continue work on its identification.

The PMR spectrum (II) has three-proton singlets from an N-methyl group (2.45 ppm) and from three methoxy groups (3.57, 3.77, and 3.79 ppm). Overlapping multiplets from methylene groups are located at 2.1-3.1 ppm. In addition, at 6.50, 6.70, and 7.97 ppm there are one-proton singlets that are characteristic for the aromatic protons at C_3, C_8, and C_{11}, respectively [3]. The position of the hydroxy group (broadened signal at 5.32 ppm) was established on the basis of a consideration of the results of measurements of the intramolecular nuclear Overhauser effect (NOE). When the protons of one of the methoxy groups (3.77 ppm) were irradiated with a strong radiofrequency field, the intensity of the singlet at 7.97 ppm (C_{11}—H) increased by 32%.

The intensity of the signal at 6.50 ppm relating to the C_3—H, also rose, by 30%, but when the protons of the other methoxy group at 3.79 ppm were irradiated there was no NOE between the methoxy groups and the C_8—H. On the other hand, irradiation of the protons of the



II. $R=CH_3$; $R_1=H$
Isoboldine: $R=R_1=H$
V. $R=CH_3$; $R_1=OH$
VI. $R=CH_3$; $R_1=OCH_3$ (C_9-OCH_3)



IV

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methylene groups at C_7 and C_4 led to an increase in the intensity of the signals at 6.50 and 6.70 ppm by 34 and 40%, respectively. These facts permit the unambiguous assignment of the signals at 3.79, 3.77, and 3.57 ppm to the methoxy groups at C_2, C_{10}, and C_1, respectively and the determination of the position of the hydroxy group at C_9.

Chloroform extraction of the roots of the plant collected in the upper reaches of the R. Koktal yielded 1.2% of combined alkaloids, from which we isolated methyllycaconitine, anthranoyllycoctonine, and demethyleneeldelidine [4].

The epigeal part of the plant collected in the environs of the village of Topilevka contained 0.34%, and the roots 0.98% of combined alkaloids. From the combined alkaloids of the epigeal part we isolated methyllycaconitine, lycoctonine, delectine [5], N-acetyldelectine [4], O-acetyldelectine [6], and a new base which we have called dictyonine.

Dictyonine, $C_{33}H_{37}NO_{10}$ (III), mp 246-248°C (acetone), mol. wt. 607.2417 (HRMS) readily dissolved in chloroform and methanol, and less readily in ether. According to the PMR spectrum, (III) contains a N-methyl group, a tertiary C-methyl group, three acetoxy groups, and one benzoyl group. Its IR, PMR, and mass spectra permit (III) to be assigned to the diterpene alkaloids and its formula to be developed as

$$C_{19}H_{18}(>N—CH_3)\ (CH_3COO)_3\ (C_6H_5COO)\ (OH)_2.$$

From the combined alkaloids of the roots of the plant, in addition to the methyllycaconitine and lycoctonine found previously, we have isolated delectine, N-methyllaurotetanine, and the new bases delectinine and delporphine.

Delectinine, $C_{24}H_{39}NO_7$ (IV), mp 167-169°C (hexane—acetone), mol. wt. 453.2753 (HRMS) dissolves readily in chloroform, methanol, and acetone. Its IR spectrum shows absorption bands at 3445 cm^{-1} (hydroxy groups) and 1100 cm^{-1} (ether C—O bonds). The PMR spectrum of (IV) contains signals due to a N-ethyl group (0.99 ppm, triplet, 3 H), and three methoxy groups (3.20, 3.29, and 3.37 ppm; singlets each with an intensity of 3H). The mass spectrum shows the peaks of the ions M^+ 453, M − 15, M − 31 (100%), and M − 33.

The features of the IR, PMR, and mass spectra that have been given are identical with those of the amino alcohol from delectine [5]. A direct comparison of the two compounds showed their identity. Consequently, delectinine has the structure (IV), and this is the first time that it has been found in plants.

Delporphine $C_{20}H_{23}NO_5$ (V) is a phenolic base with mp 116-117°C (ethanol), $[\alpha]_D$ +68° (c 0.25; ethanol). The IR spectrum of (V) has absorption bands at 3420 cm^{-1} (hydroxy groups), 1520, and 1595 cm^{-1} (aromatic ring). The mass spectrum of delporphine has the peaks of the ions M^+ 357 (100%), M^{++} 178.5, 356, 342, 340, 326, 314, and 283. The PMR spectrum of (V) shows the signals of a N-methyl group (2.43 ppm; singlet, 3H), of three methoxy groups (3.62, 3.79, and 3.86 ppm; singlets, each 3H), and of two aromatic protons (6.66 and 7.79 ppm; singlets, 1H each). The results of mass and PMR spectroscopy, the magnitude of the specific rotation [7] and also the UV spectrum [λ_{max} 217, 283, 304, 315 nm (log ε 4.54, 4.13, 4.08, 4.01)] [8] permit delporphine to be assigned to the 1,2,3,9,10-pentasubstituted aporphine alkaloids.

The three-proton singlet in the PMR spectrum of (V) at 3.62 ppm relates to the methoxyl at C_1 [3], and the one-proton singlets at 6.66 and 7.79 ppm to the aromatic protons at C_8 and C_{11}, respectively. When a strong radiofrequency field was imposed on the protons of the methoxy group at 3.79 ppm, the intensity of the singlet at 7.79 ppm (C_{11}—H) increased by 30%. Irradiation of any of the three methoxy groups did not lead to a change in the intensity of the second singlet at 6.66 ppm (C_8—H). On the other hand, the value of the NOE observed between C_8—H and the methylene protons at C_7 was 38%. Consequently, one of the hydroxy groups in the molecule of (V) is located at C_9. In the PMR spectrum of the diacetyl derivative of (V) the greatest change relative to the spectrum of the base itself is observed in the methylene region (downfield displacement). A similar change in the same region of the spectrum is observed on comparing the spectra of the bases (V) and (II) in solution in $CDCl_3$ and deuteropyridine. In the first case, these changes can be explained by the closeness of the acetyl residue to the methylene protons at C_4, and in the second case by the closeness to them of pyridine molecules associated with the hydroxy groups. This can be the case if the second hydroxy group in the molecule of (V) is present at C_3. Judging from the facts given, delporphine corresponds to structure (V). To confirm the proposed structure, delporphine was methylated with diazomethane in ether. The reaction products identical with

an authentic sample of thalicsimidine (VI) according to thin-layer chromatography and the specific yellow-brown color, changing to orange [9].

It must be mentioned that (V) has been obtained previously as an intermediate in the synthesis of (±)-thalicsimidine [10]. Magnoflorine [11] and higenamine (dl-demethylcoclaurine) [12] have been obtained from plants of the genus Aconitum.

EXPERIMENTAL

The homogeneity of the substances was checked by chromatography in a thin layer of type KSK silica gel in the benzene–methanol (4:1) and chloroform–methanol (20:1) systems and in alumina of "for chromatography" grade in the chloroform–methanol (50:1) system. The UV spectra were taken on a Hitachi spectrophotometer (in ethanol), the PMR spectra in $CDCl_3$ on a JNM-4H-100/100 MHz instrument with HMDS as internal standard (the values are given in the δ scale), and the mass spectra on a MKh-1303 instrument fitted with a system for the direct introduction of the sample into the ion source (the high-resolution mass spectra were recorded on a MS-902 mass spectrometer with a DS-30 data-processing system (UK)).

Isolation of the Alkaloids from the Epigeal Part of the Plant (upper reaches of the R. Koktal). The chloroform extraction of 51 kg of air-dry plant yielded 244.8 g of ether-soluble and 18.4 g of chloroform-soluble alkaloids. The combined ether-soluble alkaloids, by treatment with acetone, gave 76.9 g of eldeline. The material from the mother liquor was dissolved in ethanol, and the solution was acidified with 10% ethanolic perchloric acid. On trituration, methyllycaconitine perchlorate deposited (63.2 g). The mother liquor was evaporated, the residue was dissolved in water, the solution was made alkaline with sodium carbonate, with cooling, and was extracted with ether. The ethereal extract was treated with 4% caustic potash solution, after which it was washed with water and dried over sodium sulfate. This gave 106.7 g of nonphenolic fraction of the combined ether-soluble bases. The alkaline solution was saturated with ammonium chloride and extracted with ether and then with chloroform (to exhaustion). This gave 4.8 g of ether-soluble and 2.6 g of chloroform-soluble fractions of the phenolic part.

The phenolic fraction was chromatographed on a column of silica gel (1:20). The alkaloids were eluted with chloroform–methanol (200:1) (12 fractions); (100:1) (fractions 13-21); (50:1) (fractions 22-29), and (20:1) (fractions 30-35), the fraction volume being 50 ml. On treatment with acetone, fraction 14 deposited 0.18 g of eldelidine: fractions 16-17, on acidification with 10% ethanolic hydrobromic acid, gave 0.12 g of N-methyllaurotetanine hydrobromide; fractions 19-20, on treatment with methanol, gave 0.06 g of isoboldine; and the acetone treatment of fractions 30-35 yielded 0.11 g of lycoctonine.

Treatment of the nonphenolic part of the combined ether-soluble alkaloids with acetone gave 16.9 g of eldeline. The material from the mother liquor was dissolved in 10% hydrochloric acid, and, with cooling, the solution was acidified with sodium bicarbonate and was extracted with ether, after which the aqueous alkaline solution was made strongly alkaline with sodium carbonate and was extracted with chloroform. This gave 79.4 g of ether-soluble and 11.2 g of chloroform-soluble fractions. The treatment of the ether-soluble fraction with acetone led to the separation of 28.7 g of eldeline. The mother liquor after the removal of eldeline was separated into 9 fractions of differing basicity. The treatment of fractions 7-9 with acetone yielded 1.2 g of dictyzine.

The chloroform fraction was chromatographed on a column of alumina (1:20). The alkaloids were eluted with chloroform (19 fractions) and with chloroform–methanol (5:1) (fractions 20-24), the fraction volume being 150 ml. On treatment with acetone, fractions 7-20 gave 0.88 g of dictyocarpine and the same treatment of fractions 21-23 yielded 0.37 g of dictyzine.

Isoboldine, mp 123-125°C (methanol). A mixture with an authentic sample gave no depressions of the melting point.

N-Methyllaurotetanine, $[\alpha]_D$ +80° (c 0.2; chloroform); hydrobromide mp 210-211°C (decomp., absolute ethanol).

Isolation of Alkaloids from the Roots of the Plant (upper reaches of R. Koktal). The chloroform extraction of 8 kg of the air-dry roots gave 113 g of combined alkaloids, which were dissolved in ethanol, and the solution was acidified with 10% ethanolic perchloric acid. On trituration, methyllycaconitine perchlorate (53 g) was deposited. The mother solu-

tion was evaporated, the residue was dissolved in water, the solution was made alkaline with sodium carbonate, with cooling, and the alkaloids were extracted with ether (part A) and then with chloroform (part B).

Part A was divided into eleven fractions of different basicities. Fractions 8-11 were combined and treated with acetone, to give 3.34 g of demethyleneeldelidine.

Part B was separated into nine fractions of different basicities. Fractions 7-9, on treatment with acetone, yielded 2.26 g of demethyleneeldelidine.

Fractions 1-7 of part A and fractions 1-6 of part B were combined, dissolved in benzene, and separated according to basic strength by means of citrate-phosphate buffers. This gave 15 fractions at pH 7.2 and three fractions each at pH 6.8, 6.4, 6, and 5.6.

Fractions 1-5 at pH 7.2 (3.4 g) were chromatographed on a column of silica gel (1:70). Substances were eluted with ether, 20 fractions of 200 ml being collected. The treatment of fractions 9-18 with acetone led to the separation of 0.62 g of demethyleneeldelidine.

Fractions 1-3 at pH 6.4 (8 g) were chromatographed on a column of silica gel (1:70), the alkaloids being eluted with ether–methanol (100:1) (19 fractions), (50:1) (fractions 29-45), and (25:1) (fractions 46-59). The acetone treatment of fractions 20-31 yielded 0.07 g of anthranoyllycoctonine, and fractions 50-59, on acidification with 10% ethanolic perchloric acid, yielded 0.52 g of methyllycaconitine perchlorate.

Demethyleneeldelidine, mp 98-100°C (hexane–acetone), $[\alpha]_D$ +30° (c 1.2; chloroform). A mixture with an authentic sample of demethyleneeldelidine gave no depression of the melting point.

Isolation of Alkaloids from the Epigeal Part of *D. dictyocarpum* (village of Topolevka). Chloroform extraction of 48 kg of air-dry epigeal part of the plant yielded 170.7 g of combined alkaloids. These were dissolved in ethanol and the solution was acidified with 10% ethanolic perchloric acid. After 24 h, 134.1 g of methyllycaconitine perchlorate had deposited. The mother liquor was evaporated, the residue was dissolved in water and, with cooling, the solution was made alkaline with sodium carbonate and was extracted with ether (part A) and with chloroform (part B).

Part A was separated into 13 fractions of different basicities. Fractions 3-4 (part C) were chromatographed on a column of alumina (1:70). The alkaloids were eluted with ether, 300-ml fractions being collected. The treatment of fraction 11 with ether gave 0.08 g of dictyonine, and the treatment of fractions 17-22 with acetone gave 0.109 g of N-acetyldelectine.

Fractions 5-9 (part D) from the separation of part A according to basicity were reseparated according to basicity into 22 fractions. Fractions 4-8 (2.2 g) were chromatographed on a column of alumina (1:70), the substances being eluted with ether, and fractions with a volume of 250 ml being collected. Fractions 6-7, on treatment with methanol, deposited 1.11 g of O-acetyldelectine.

Fractions 12-13 (4.1 g) from the separation according to basic strength of part D were chromatographed on a column of silica gel (1:100). The alkaloids were eluted with ether (36 fractions), ether–methanol (100:1) (fractions 37-47), and ether–methanol (50:1) (fractions 48-58), 350-ml fractions being collected. From fractions 24-36 by treatment with a mixture of hexane and acetone 0.17 g of delectine was isolated.

Fractions 18-20 (1.6 g) from the separation of part D according to basicity were dissolved in ethanol, the solution was acidified with 10% perchloric acid, and 0.53 g of methyllycaconitine perchlorate separated out.

Fractions 10-13 (2.3 g) from the separation of part A according to basicity was chromatographed on a column of alumina (1:100). The alkaloids were eluted with chloroform (17 fractions), chloroform–methanol (100:1) (fractions 18-26) and (10:1) (fractions 27-38), the volume of the fractions being 70 ml. From fractions 33-38 by treatment with acetone, 0.33 g of lycoctonine was obtained.

Delectine, mp 107-109°C (hexane–acetone), $[\alpha]_D$ +49° (c 0.67; chloroform).

N-Acetyldelectine, mp 116-118°C (acetone), $[\alpha]_D$ +30° (c 0.33; chloroform).

O-Acetyldelectine, mp 118-120°C (methanol, $[\alpha]_D$ +42° (c 0.83; chloroform).

Dictyocarpine, mp 200-202°C (hexane—acetone), $[\alpha]_D$ −14° (c 0.76; chloroform).

Isolation of Alkaloids from the Roots of *D. dictyocarpum* (village of Topolovka). The chloroform extraction of 11 kg of air-dry roots yielded 108 g of combined alkaloids; these were dissolved in ethanol and the solution was acidified with 10% ethanolic perchloric acid, which gave 80.1 g of methyllycaconitine perchlorate. The mother solution was evaporated the residue was dissolved in water, and, with cooling, the solution was made alkaline with sodium carbonate and was extracted with ether (part A) and then with chloroform (part B).

Part A was chromatographed on a column of alumina (1:20). The alkaloids were eluted with ether (32 fractions) and with ether—chloroform (10:1) (fractions 33-43) and (1:1) (fractions 44-50) and then with chloroform (fractions 51-60) and with chloroform—methanol (50:1) (fractions 63-67). From fractions 20-49 by acidification with 10% ethanolic hydrobromic acid was obtained 0.115 g of N-methyllaurotetanine hydrobromide, from fractions 54-59 by treatment with ether 0.2 g of delectine, and from fractions 63-64 by treatment with acetone 0.24 g of lycoctonine. Fraction 66, on treatment with acetone, gave 0.17 g of delectinine.

The chloroform extract (part B) was treated with a 4% solution of caustic potash and washed with water. This gave 12 g of nonphenolic fraction of part B.

The alkaline solution was saturated with ammonium chloride and extracted with ether and then with chloroform. This gave 0.6 g of ether-soluble and 0.48 g of chloroform-soluble fractions of phenolic bases.

The ether-soluble fraction of phenolic bases was chromatographed on a column of silica gel (1:70). The alkaloids were eluted with chloroform—methanol (20:1), 5-ml fractions being collected. The treatment of fractions 15-20 with ethanol led to the separation of 0.17 g of delporphine.

Delectinine, mp 167-169°C (hexane—acetone), $[\alpha]_D$ +42° (c 0.67; chloroform). A mixture with a sample of the amino alcohol from delectine gave no depression of the melting point.

Delporphine, mp 116-117°C (ethanol), $[\alpha]_D$ +68° (c 0.25; ethanol).

Acetylation of Delporphine. A mixture of 0.05 g of the base, 2 ml of acetic anhydride, and 0.5 ml of pyridine was left at room temperature for 2 days. After the usual working up, 0.057 g of a chromatographically homogeneous substance was obtained. PMR spectrum: 2.26 and 2.29 ppm (2 $OCOCH_3$).

SUMMARY

From the plant *Delphinium dictyocarpum* DC, in addition to alkaloids described previously, we have isolated N-methyllaurotetanine, isoboldine, and the new bases dictyzine, dictyonine, delectinine and delporphine. The structure of 1,2,10-trimethoxy-3,9-dihydroxyaporphine has been established for delporphine.

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