ALKALOIDS OF Delphinium dictyocarpum

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UDC 547.944/945

We have investigated Delphinium dictyocarpum collected in the Dzhungarskii Alatau: in the environs of the village of Topolevko (roots, flowering phase) and in the upper reaches of the R. Koktal, Kuyandysai (epigeal part, budding phase). Methyllycaconitine has been isolated previously from this plant collected in the northwestern spurs of the Tarbagatai range (epigeal part, flowering phase) [1].

By chloroform extraction of the epigeal part of D. dictyocarpum we obtained 0.58% of combined alkaloids, from which we isolated methyllycaconitine, eldeline (deltaline), eldelidine, and a new alkaloid which we have called dictyocarpine (I), $C_{26}H_{39}O_8N$, mp 210-212°C, mol. wt. 493 (mass spectrometrically).

The IR spectrum of the base (I) has absorption bands at (cm^{-1}) 3490 (hydroxy groups), 1710 (ester grouping), and 1140 (ether C—O bonds). The NMR spectrum has signals due to a $\diagup\!\!\diagdown$C—CH_3 group (three-proton singlet at 0.91 ppm), to two methoxy groups (three-proton singlets at 3.32 and 3.20 ppm), to a methylenedioxy group (two one-proton singlets at 5.14 and 5.08 ppm), to an >N-ethyl group (three proton triplet at 1.03 ppm), and to an acetoxy group (three-proton singlet at 2.04 ppm). The alkaline hydrolysis of (I) gave an amino alcohol lacking an acetoxy grouping, according to its NMR and IR spectra. Acetylation of the base with acetyl chloride gave a diacetate. Consequently, the developed formula of dictyocarpine is

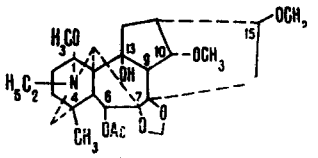
$$C_{19}H_{21}(>N-CH_2-CH_3)(OH)_2(OCH_3)_2(OCOCH_3)(CH_2O_2).$$

When the developed formulas of dictyocarpine and eldeline are compared, it can be seen that they differ by the number of hydroxy and methoxy groups. The similarity of these bases is shown by their mass, NMR, and IR spectra. In the mass spectrum of (I), just as in the mass spectrum of eldeline, the peak of the M−31 ion is the maximum peak, which shows the presence of a methoxy group at C_1 [2]. Second in intensity is the peak of the M−59 ion (20% of the maximum). In the NMR spectrum of (I) there is a signal in the form of a one-proton singlet at 5.42 ppm which shifts upfield by 1.2 ppm when the acetoxy group is saponified. A similar shift is observed in eldeline (5.41 → 4.22 ppm) for the proton at C_6. The presence in dictyocarpine of an acetoxy group at C_6 is confirmed by the peak of the M−59 ion in its mass spectrum, which is also characteristic for eldeline. The dihedral angle made by the β proton at C_5 with an α proton at C_6 is approximately 90-100° and that with a β proton at C_6 is ~30°: in the first case, $J_{calc} \approx 0$ Hz, and in the second $J_{calc} \approx 7$-8 Hz. Thus, as in eldeline [3], the acetoxy group at C_6 has the β configuration. On passing from (I) to its amino alcohol, as on passing from eldeline to eldelidine, an increase in the difference in the chemical shifts (CSs) of the one-proton singlets of the CH_2O_2 group by 4-5 Hz is observed. This permits the methylenedioxy group in dictyocarpine to be placed at C_7 and C_8.

In the proof of the structure of some aconitine alkaloids, it was shown that when there is an α-hydroxy group at C_{10} and no substitutents at C_9 and C_{11}, the signal of the geminal proton is always present at about 4.1 ppm in the form of a poorly resolved triplet with $J \approx 5$ Hz [4, 5]. The replacement of the hydroxy group by a methoxy group shifts the signal of the C_{10} proton in delphatine to 3.52 ppm [6] and in 10-methyltalatisamine to 3.6 ppm. In the NMR spectrum of eldeline (OCH_3 at C_{10}) there is a signal in the form of a one-proton triplet at 4.09 ppm ($J \approx 5$ Hz). Taking the given information into account, it may be concluded

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 498-502, July-August, 1972. Original article submitted January 26, 1972.

that this downfield shift of the signal is caused by the descreening influence of an OH group at C_{13}. The latter has the β configuration [3, 4]. The corresponding signal in the NMR spectrum of dictyocarpine and its amino alcohol is located at 4.55 ppm ($J \approx 5$ Hz). It follows from what has been said above that in compound (I) there is an α-OH group at C_{10} the geminal proton of which is descreened by a hydroxy group at C_{13}.



Eldeline (Deltaline)

The chloroform extraction of the roots of D. dictyocarpum gave 1.83% of combined alkaloids; from them we obtained methyllycaconitine, lycoctonine, and the new bases (II) and (III). Base (II) is amorphous with mol. wt. 453 (mass spectrometrically). Its IR spectrum has absorption bands at 3440 cm^{-1} (hydroxy group) and 1100 cm^{-1} (ether C–O bonds). The NMR spectrum shows a three-proton triplet at 1.01 ppm ($>N-CH_2-CH_3$) and three-proton singlets at 3.28, 3.40, and 3.47 ppm (3 OCH_3). The mass spectrum of (II) is characteristic for the mass spectra of the diterpene alkaloids with a lycoctonine skeleton and its maximum peak is M–31, which shows the presence of a methoxy group at C_1 [2]. The acetylation of (II) with acetic anhydride in pyridine gave a diacetate. This shows that the two hydroxy groups are apparently secondary. The presence in its NMR spectrum of a one-proton triplet at 4.1 ppm ($J \approx 5$ Hz) shows that one of them is located at C_{10}. On the basis of the similarity of the mass, NMR, and IR spectra of substance (II) and of lycoctonine, the following developed formula may be written for the former:

$$C_{19}H_{21}(>N-CH_2-CH_3)(OH)_4(OCH_3)_3.$$

Base (III) is amorphous with mol. wt. 541 (mass spectrometrically). IR spectrum (cm^{-1}): 3400 (OH), 1720 (ester carbonyl), 1593 (aromatic ring). NMR spectrum: three-proton triplet at 1.01 ppm ($>N-CH_2-CH_3$), three-proton singlets at 3.20, 3.31, and 3.36 ppm (3 OCH_3), and signals at 7.45-8.05 ppm (five aromatic protons of a benzoyloxy group).

EXPERIMENTAL

The homogeneity of the substances was checked by chromatography in a thin layer of ShSK silica gel in the benzene–methanol (4:1) system. The NMR spectra (deuterochloroform) were taken 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 an MKh-1303 instrument fitted with an all-glass system for the direct introduction of the sample into the ion source.

Isolation of the Alkaloids. 1. The chloroform extraction of 18 kg of the epigeal part of D. dictyocarpum gave 105.9 g (0.58%) of total alkaloids. These were dissolved in ethanol, and the solution was acidified with 10% perchloric acid. On trituration, microcrystalline methyllycaconitine perchlorate deposited (27.9 g). After the separation of this precipitate the mother liquor was evaporated, the residue was dissolved in water, and the solution was washed with chloroform, made alkaline with sodium carbonate with cooling, and exhaustively extracted with chloroform. This gave a washing chloroform fraction A (62.5 g) and an alkaline chloroform fraction B (15.5 g). The treatment of fraction A with acetone gave 35.5 g of eldeline. After this had been separated off, the mother liquor of fraction A was evaporated, and the residue was dissolved in 5% sulfuric acid. The acid solution was washed with chloroform, made alkaline with sodium carbonate with cooling, and extracted with ether and chloroform. The ethereal fraction deposited crystals (7 g) identified as eldeline.

Fraction B was dissolved in 5% sulfuric acid, and the solution was made alkaline with sodium carbonate with cooling and was extracted with ether and chloroform. The ethereal fraction (9.07 g) was divided according to basic strengths into eleven fractions. Fractions 6-8 crystallized. The crystals from fraction 6 consisted of a mixture of eldeline and dictyocarpine. Fractions 7 and 8 gave 0.3 g of dictyocarpine with mp 210-212°C (hexane–acetone). Fractions 9 and 10 were combined and chromatographed on a column of alumina (1:100). Elution with a mixture of chloroform and methanol (50:1) yielded eldelidine with mp 227-230°C.

2. The chloroform extraction of 3 kg of the roots of D. dictyocarpum gave 55 g (1.83%) of total alkaloids; these were dissolved in ethanol, and the solution was acidified with 8% perchloric acid solution. On trituration, methyllycaconitine perchlorate deposited (37.3 g). The mother solution, after the separation of this precipitate, was evaporated; the residue was dissolved in water, the solution was washed with chloroform (fraction A) and was then made alkaline with sodium carbonate, with cooling, and was extracted with benzene (fraction B) and with chloroform (fraction C). The solvents were distilled off. Fraction A was dissolved in 5% sulfuric acid, the solution was washed with chloroform, made alkaline with sodium carbonate, with cooling, and extracted with chloroform. The alkaline chloroform fraction was separated according to basicity into eleven fractions. Fractions 6-8 were combined and chromatographed on a column of alumina (1:70). Elution with a mixture of benzene and methanol (50:1) gave base (III) (0.4 g). Fractions 10 and 11 were combined and treated with methanol. This gave 0.2 g of lycoctonine.

Fraction B was separated according to basicities into eight fractions. Fractions 5-8 were combined and chromatographed on a column of alumina (1:50). Elution with a mixture of benzene and methanol (1:1) gave 0.3 g of the base (II).

Fraction C was separated according to basicities into seven fractions. Fractions 6 and 7 were combined and chromatographed on a column of alumina (1:70). Elution with a mixture of chloroform and methanol (25:1) gave 0.05 g of base (II) and 0.1 g of lycoctonine.

Saponification of Dictyocarpine. A mixture of 0.07 g of the base and 10 ml of 5% methanolic alkali was heated in the water bath for 30 min. The solvent was evaporated off, and the residue was diluted with water, with cooling, and was extracted with ether. A crystalline substance deposited with mp 204-205°C (ether), M^+ 451.

Dictyocarpine Diacetate. A mixture of 0.07 g of the base and 7 ml of acetyl chloride was kept in a sealed tube at 40-50°C for 30 h. The excess of acetyl chloride was evaporated off, and the residue was dissolved in water with cooling, and the solution was made alkaline and was extracted with ether. After preparative separation in a thin layer of silica gel in the benzene–acetone (1:1) system, an amorphous diacetate was isolated with M^+ 577. NMR spectrum: 2.02 ppm (3 $OCOCH_3$).

Diacetate of the Base (II). A mixture of 0.2 g of the base (II), 4 ml of acetic anhydride, and a few drops of pyridine was left at room temperature for three days. The residue after the elimination of the solvent was treated with ice water, made alkaline with sodium carbonate, and extracted with ether. The reaction product was purified on a column of alumina (1:100). Elution with a mixture of benzene and methanol (100:1.5) gave an amorphous chromatographically homogeneous substance with M^+ 537. NMR spectrum: 2.0 ppm (2 $OCOCH_3$).

10-Methyltalatisamine. A mixture of 0.5 g of talatisamine, 1 ml of methyl iodide, and 0.15 g of sodium hydride in 30 ml of dioxane was boiled for 2 h. It was then filtered, and the filtrate was evaporated. On treatment with benzene the reaction product crystallized, mp 107-110°C (from hexane), M^+ 435; NMR spectrum: 3.20 (3H); 3.22 (3H); 3.25 (3H); 3.33 (3H).

SUMMARY

From the roots and epigeal part of Delphinium dictyocarpum from two growth sites have been isolated methyllycaconitine, eldeline, eldelidine, lycoctonine, the new base dictyocarpine, and bases (II) and (III). The lycoctonine skeleton has been proposed for dictyocarpine and the positions of the substituting groups have been suggested.

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