ALKALOIDS OF Delphinium corumbosum

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We have investigated the epigeal part of Delphinium corumbosum Rgr., collected in the budding phase in the upper reaches of the R. Baskan, Dzhungarian Alatau. This plant has not previously been studied chemically.

Chloroform extraction of the epigeal part of D. corumbosum gave 0.51% of total alkaloids, from which we isolated methyllycaconitine, a new alkaloid with the composition $C_{26}H_{41}NO_7$, mp 200-202°C (methanol), $[\alpha]^{24} - 18°$ (c 5; chloroform), which we have called delcorine (I), and a base with mp 93-95°C (hexane). The IR spectrum shows the presence in (I) of hydroxy groups (3520 cm^{-1}) and ether C–O bonds (1100 cm^{-1}). Delcorine contains a N-ethyl group (1.0 ppm; 3H, triplet), a methylenedioxy group (5.01 and 5.07 ppm, 1H, singlets), and four methoxy groups (3.22, 3.28, 3.30, and 3.40 ppm, 3H each, singlets). The acetylation of delcorine with acetyl chloride gave monoacetyldelcorine; NMR spectrum: 2.01 ppm (3H). Consequently, the developed formula of delcorine can be written in the following way: $C_{19}H_{21}(>N-C_2H_5)\ (OH)\ (OCH_3)_4\ (CH_2O_2)$.

The mass spectrum of the alkaloid is characteristic for spectra of diterpene bases with a lycoctonine skeleton and has the maximum peak M−31, which shows the presence of a methoxy group at C_1 [1]. In the NMR spectrum of delcorine there is a signal in the form of a one proton singlet at 4.22 ppm, shifted in delcorine acetate to 5.40 ppm. A similar shift is found on passing from eldeline (II, R_1=OAc; R_2=OCH_3) to eldelidine (II, R_1=OH; R_2=OCH_3) and from dictyocarpine (II, R_1=OAc; R_2=OH) to dictyocarpinine (II, R_1=R_2=OH) [2]. In the IR spectrum of dehydrodelcorine (III), $C_{26}H_{39}NO_7$, obtained by the oxidation of (I) with chromium trioxide, an absorption band appears at 1745 cm^{-1} (cyclopentanone).

As can be seen from Table 1, in the NMR spectrum of dehydrodelcorine there is an increase in the difference of the chemical shifts (CSs) of the protons of the methylenedioxy group in comparison with the CSs of these protons in delcorine by 44 Hz (one-proton doublets at 5.01 and 5.45 ppm, J = 2 Hz). We have observed the same change in the CS on comparing the spectra of eldelidine and dehydroeldelidine (C=O at C_6) and those of dictyocarpinine and didehydrodictyocarpinine (C=O at C_6 and C_{10}). Thus, in delcorine there is an OH group at C_6 and a CH_2O_2 group at C_7 and C_8. Heating with 10% sulfuric acid gave demethylenedelcorine (IV), $C_{25}H_{41}NO_7$, in the NMR spectrum of which the signals of the protons of the methylenedioxy group were absent, while at 3.69 ppm there was a triplet with an intensity of one proton unit with J = 5 Hz, which is characteristic for a proton at C_{10} geminal to a methoxy group [2, 3]. The oxidation of demethylenedelcorine with 1 mole of periodic acid gave demethylenesecodelcorine (V), $C_{25}H_{39}NO_7$; its IR spectrum showed the absorption bands of carbonyl groups in five-membered and six-membered rings (1740 and 1710 cm^{-1}, respectively). The treatment of demethylenesecodelcorine with sulfuric acid gave demethylenesecodemethanoldecorine (VI), $C_{24}H_{35}NO_6$, which is an α,β-unsaturated ketone; λ_{max} 220, 362 mμ (log ε 4.31, 2.62). The NMR spectrum of this substance had signals from three methoxy groups and from two olefinic protons in the form of a one-proton doublet at 5.96 ppm (J = 9 Hz) with additional splitting of ≈ 1.5 Hz and a one-proton multiplet at 6.81 ppm, J_{AX} = 9 Hz, J_{BX} = 7 Hz. The elimination of a molecule of methanol under the conditions given shows the presence of a methoxy group in the seco product in the β position to a carbonyl group [3-6]. According to the IR spectrum of (VI) (1680, 1735 cm^{-1}), this carbonyl group is present in a six-membered ring, and, consequently, one of the methoxy groups in delcorine is located at C_{15}. In the aconite alkaloids, the skeleton of which consists of 19 carbon atoms, the substituent at C_4 is either a methyl, or a hydroxymethyl, or a methoxymethyl group. A hydroxymethyl group is excluded because of the acetylation and the chromium trioxide oxidation reactions, and a methyl group on the basis of the NMR spectrum

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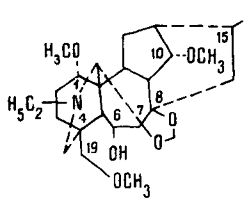
of the base. Thus, the substituent at C_4 in delcorine is a methoxymethyl group. In the mass spectra of delcorine and of demethylenedelcorine the peak of the M − 15 ion amounts to 3% of the maximum (M − 31), which shows the α configuration of the methoxyl at C_1 [7]. The hydroxy group at C_6 in delcorine possesses the β orientation, since in the NMR spectrum the signal of the geminal proton appears in the form of a singlet [2]. The presence in the NMR spectrum of the base of a one-proton triplet at 3.69 ppm with J = 5 Hz indicates that the methoxy group at C_{10} [2, 3] has the α configuration. The ready elimination of a molecule of methanol in demethylenesecodemethanoldelcorine shows that there is a β-methoxy group at C_{15} [3-6].

On the basis of the facts given above, structural formula (I) is proposed for delcorine.



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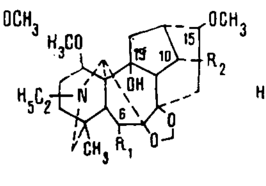

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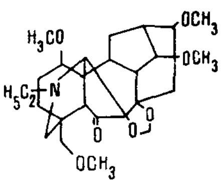

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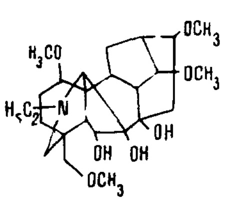

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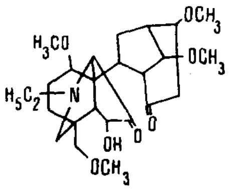
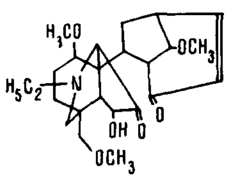


V



VI

The base with mp 93-95°C has mol. wt. 463 (mass spectrometrically). Its IR spectrum has an absorption band at 1100 cm^{-1} (ether C−O bond). The NMR spectrum of the alkaloid exhibits the signals due to a N-ethyl group (three-proton triplet at 1.06 ppm), four methoxy groups (three-proton singlets at 3.22, 3.25, 3.30, and 3.36 ppm), and a methylenedioxy group (two one-proton singlets at 4.86 and 4.96).

EXPERIMENTAL

The homogeneity of the substances was checked by chromatography in a thin layer of type ShSK silica gel in the benzene−methanol (4 : 1) system. The NMR spectra were taken in deuterochloroform on a JNM-4H-100/100 MHz instrument with HMDS as internal standard (the values are given in the δ scale), the mass spectra on an MKh-1303 instrument with a system for direct introduction into the ion source, and the IR spectra on a UR-20 instrument in KBr tablets.

Isolation of the Alkaloids. The comminuted epigeal part of *D. corumbosum* (4.5 kg) was moistened with a 5% solution of sodium carbonate and was exhaustively extracted with chloroform. Five extracts were treated with 5% sulfuric acid. With cooling, the acid solution was made alkaline with sodium carbonate. Extractions with ether gave 20.44 g and extraction with chloroform 2.69 g of mixtures of alkaloids, the total amounting to 0.51% of the weight of the air-dry plant.

When the combined ether-extracted alkaloids were treated with acetone, 5 g of delcorine was obtained with mp 200-202°C (methanol). The material from the mother solution after the separation of the delcorine was dissolved in 2% hydrochloric acid and the solution was washed with water and was then made alkaline with sodium carbonate, with cooling. The alkaline aqueous solution was extracted with ether and with chloroform. This gave a washing chloroform fraction (9.01 g), an alkaline ether-extracted fraction (6 g), and an alkaline chloroform-extracted fraction (0.5 g). The washing chloroform fraction was dissolved in ethanol and the solution was made acidic with 8% perchloric acid. Trituration led to the precipitation of a crystalline mixture (5.68 g) of the perchlorates of methyllycaconitine and of a base with mp 93°C. Fractional recrystallization from ethanol yielded 2 g of methyllycaconitine perchlorate and 0.5 g of the perchlorate of the base with mp 93°C. The methyllycaconitine was shown to be identical with an authentic sample. When the alkaline ether-extracted fraction was concentrated, crystals separated out

TABLE 1

Substance	CH_2O_2, ppm	Δδ, Hz
Eldelidine	4,99 5,06	7
Dehydroeldelidine	5,00 5,44	44
Dictyocarpinine	5,02 5,14	12
Didehydrodictyocarpinine	5,02 5,46	44
Delcorine	5,01 5,07	6
Dehydrodelcorine	5,01 5,45	44

(0.68 g) which were identified as delcorine. The mother solution after the separation of the delcorine was separated according to basicity into 13 fractions. Fractions 5-11 yielded another 1 g of delcorine. The treatment of fraction 12 with an ethanolic solution of perchloric acid gave 0.2 g of methyllycaconitine perchlorate.

Delcorine (I). After three recrystallizations from methanol and drying in vacuum, it melted at 200-202°, $[\alpha]_D^{24} -18°$ (c 5); chloroform). Delcorine hydrochloride, mp 117-118°C (acetone).

Found %: C 65.3; 65.0; H 9.58, 9.23; N 2.88; 2.78. $C_{26}H_{41}NO_7$. Calculated, %: C 65.1; H 8.56; N 2.92. mol. wt. 479.

Delcorine Acetate (VII). A mixture of 0.1 g of delcorine and 7 ml of acetyl chloride was kept in a sealed tube at 40-50°C for 50 h. The excess of acetyl chloride was evaporated off, 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–methanol system (4 : 1), amorphous delcorine acetate was isolated with mol. wt. 521. NMR spectrum: 2.01 ppm (3H, singlet).

Dehydrodelcorine (III). A mixture of 0.15 g of delcorine in 23 ml of acetone and 0.25 g of chromium trioxide in 9 ml of acetone was left at room temperature for three days. The acetone was distilled off, the residue was dissolved in 10% sulfuric acid, and the excess of chromium trioxide was decomposed with sodium sulfite. The solution was made alkaline and was extracted with ether. The residue after the evaporation of the solvent was chromatographed on a column of alumina (1 : 30), the reaction products being eluted with ether. This gave dehydrodelcorine, mp 135-136°C (ether). Mol. wt. 477. IR spectrum: 1747 cm^{-1}.

Demethylenedelcorine (IV). A mixture of 1 g of delcorine and 25 ml of 10% sulfuric acid was heated in the steam bath for 10 h. With cooling, the reaction mixture was made alkaline with sodium carbonate and was extracted with chloroform. The solvent was distilled off and the residue was treated with petroleum ether, giving 0.7 g of a product with mp 80-83°C (petroleum ether); mol. wt. 467.

Demethylenesecodelcorine (V). A solution of 0.5 g of demethylenedelcorine and 0.28 g of periodic acid in 50 ml of distilled water was left at room temperature for 3 h. The reaction mixture was made alkaline, and the product was extracted with chloroform. The residue from the distillation of the solvent was dried and was treated with acetone, giving 0.2 g of a crystalline product with mp 170-171°C, mol. wt. 465. IR spectrum: 1710, 1740 cm^{-1}. UV spectrum: λ_{max} 217, 360 mμ (log ε 4.62, 2.62).

Demethylenesecodemethanoldelcorine (VI). A solution of 0.1 g of demethylenesecodelcorine in 1.5 ml of ethanol and 7 ml of 30% sulfuric acid was heated in the steam bath for 2 h. The cooled reaction mixture was made alkaline with sodium carbonate and was extracted with chloroform. The solvent was distilled off and the residue was treated with acetone, whereupon 0.07 g of a crystalline substance with mp 103-105°C precipitated; mol. wt. 433.

Dehydroeldelidine. A mixture of 0.6 g of eldelidine in 90 ml of acetone and 0.9 g of chromium trioxide in 30 ml of acetone was left at room temperature for five days. The reaction product was treated as described above in the preparation of dehydrodelcorine. mp of dehydroeldelidine 120-122°C (from hexane). Mol. wt. 463. IR spectrum: 1740 cm^{-1}. NMR spectrum: 1.01 ppm (3 H, triplet, $>N{-}C_2H_5$), 0.87 ppm (3H, singlet, $\geqslant C{-}CH_3$), 3.30, 3.32, 3.37 ppm (3H, singlets, 3 OCH_3), 5.00 and 5.44 ppm (1H, singlets, CH_2O_2).

Didehydrodictyocarpinine. Dictyocarpinine (0.05 g) was oxidized with chromium trioxide as described above. This gave 0.03 g of amorphous didehydrodictyocarpinine. NMR spectrum: 5.02 and 5.46 ppm (1H, singlets, CH_2O_2); mol. wt. 447.

SUMMARY

From Delphinium corumbosum Rgl. have been isolated methyllycaconitine, a new base which has been called delcorine, and a base with mp 93-95°C. On the basis of its chemical and spectral characteristics, a lycoctonine skeleton has been established for delcorine with α-methoxy groups at C_1 and C_{10}, a β-hydroxy group at C_6, a methylenedioxy group at C_7 and C_8, a β-methoxy group at C_{15}, and a methoxy group at C_{19}.

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