

M. Alimova, I. A. Israilov,  
M. S. Yunusov, N. D. Abdullaev, and S. Yu. Yunosov

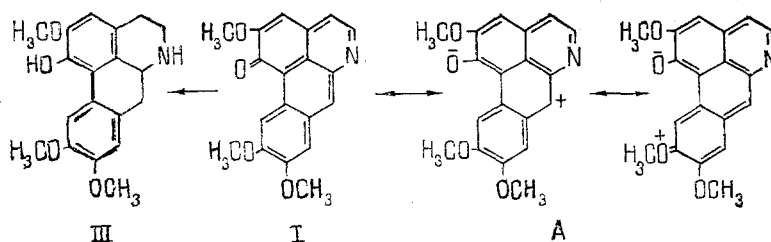
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The alkaloid composition of the roots of *Corydalis paniculigera* Rgl., collected in the flowering phase in the Alai range, has been studied. Chloroform extraction yielded 0.39% of total alkaloids, from which were isolated wilsonirine, thalicmidine, coclaurine, stylophine, dihydrosanguinarine, sanguinarine, oxosanguinarine, adlumine, adlumidine, bicucculine, sibiricine, protopine, pancorine, and corunnine, and new alkaloids which have been called pancoridine (I) and pancorinine (II). The structures of (I) and (II) have been established on the basis of spectral characteristics and also the production of wilsonirine on their reduction in sulfuric acid.

We have investigated the roots of *Corydalis paniculigera* Rgl. [1] collected in the flowering phase in the Alai range (Alauddinsai). Chloroform extraction yield 0.39% of total alkaloids (0.21% in the ethereal and 0.18% in the chloroform fraction). From the ethereal fraction we isolated wilsonirine, thalicmidine, coclaurine, stylophine, dihydrosanguinarine, sanguinarine, oxosanguinarine, adlumine, adlumidine, bicucculine, sibiricine, protopine, pancorine [2], and the new alkaloid, pancoridine. From the chloroform fraction we obtained corunnine [3] and new alkaloids which have been called pancoridine (I) and pancorinine (II). All the known alkaloids that were isolated were identified on the basis of spectral characteristics and direct comparison with authentic samples, and corunnine on the basis of spectral characteristics and the production of thalicmidine on its reduction with zinc in sulfuric acid.

Pancoridine is an optically inactive base with a bright orange color. According to high-resolution mass spectrometry (mol. wt. 321.0987) and elementary analysis, the alkaloid has the composition  $C_{19}H_{15}O_4$ .

The UV spectrum of the base has absorption maxima at 218, 236, 259, 277, 298, 312, 340, 402, and 466 nm, and the IR spectra has absorption bands at 1505, 1580, and 1635  $cm^{-1}$ . The mass spectrum of (I) shows the peak of the molecular ion with  $m/z$  321, and also the peaks of ions with  $m/z$  306, 290, and 160.5 ( $M^{++}$ ). The PMR spectrum of the base taken in trifluoroacetic acid has the signals from three methoxy groups at 3.75 ppm (6 H) and 3.82 ppm (3 H). In the aromatic region of the spectrum there are signals in the form of one-proton singlets at 6.77, 7.08, 8.51, and 9.07 ppm and one-proton doublets at 7.68 and 8.53 ppm ( $J = 5.5$  Hz). When the base was reduced with zinc in sulfuric acid, a product was obtained which was identified as wilsonirine (III) [4, 5] (melting point, TLC, IR spectrum). The facts given above permit structure (I) to be proposed for pancoridine. A compound with such a structure has been synthesized previously [6]



Scheme 1

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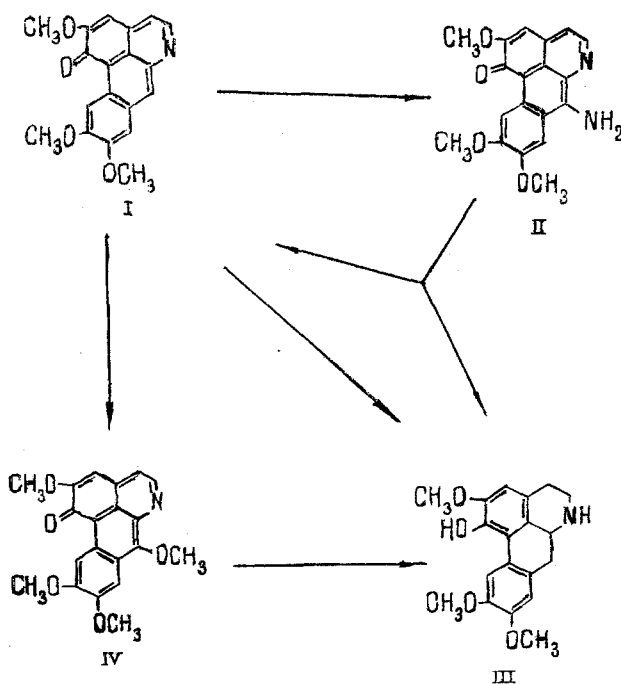
The properties and spectral characteristics of (I) agree with those of the synthetic substance.

This is the first time that pancoridine has been isolated from a plant.

Pancorinine is an optically inactive base having, according to high-resolution mass spectrometry (molecular weight, 336.1108) and elementary analysis, the composition  $C_{19}H_{16}N_2O_4$ . The base has characteristic colorations — in alkaline and neutral solutions claret-colored and in acid solutions red. In its UV spectrum there are absorption maxima at 232, 247, 265, 276, 287, 296, 376, 412, 440, 526, and 566 nm and in the IR spectrum absorption bands at 1250, 1510, 1545, and 1650  $cm^{-1}$ . The mass spectrum shows the peak of the molecular ion with  $m/z$  336, and also the peaks of ions with  $m/z$  305 and 292.

The PMR spectrum of pancorinine is characterized by 3 H singlet signals at 3.74, 3.83, and 3.95 ppm from three methoxy groups, 1 H singlets at 7.24, 7.45, and 8.63 ppm, and mutually coupled doublets with  $J = 5.5$  Hz at 8.20 and 8.54 ppm. The facts given above permit the base to be assigned to the oxoaporphine alkaloids.

When pancorinine was reduced with zinc in sulfuric acid, first pancoridine (I) was formed (melting point, TLC, PMR and mass spectra) and further reduction led to wilsonirine (III). The empirical formula of pancorinine (II) differs from that of pancoridine (I) by NH, and compound (II) contains one aromatic proton less than (I).



Scheme 2

The results obtained permitted the assumption that (II), unlike pancoridine, contains a primary amino group, and the characteristics of the PMR spectrum and the ease of hydrolysis permitted its position to be determined as at C<sub>7</sub>. This assumption was confirmed by the fact that when pancoridine was treated with ammonia at room temperature for 20 hours it was converted completely into pancorinine. Under similar conditions, sodium methanolate and pancoridine in methanol gave 7-methoxypancoridine (IV). When (IV) was reduced with zinc in sulfuric acid, a product identical with wilsonirine (III) (TLC) was obtained. The ease with which pancoridine enters into these reactions, due, in all probability, to the existence of the mesomeric structure A, has thrown doubt on the existence of pancorinine in the plant, since ammonia was used in the process of isolating the alkaloids. When the alkaloids were isolated without ammonia, pancorinine was still detected but in considerably smaller amounts, while at the same time the amount of pancoridine rose sharply.

The assignment of the signals of the methoxy groups and aromatic protons in the PMR spectrum of pancorinine was performed on the basis of the following facts. When it was irradiated with an additional radiofrequency field having  $\nu = 820$  Hz (C<sub>4</sub>-H), the intensity

of the signal at 7.24 ppm increased by 9% (through the suppression of long-range spin-spin coupling) while the other two singlets at 7.45 and 8.63 ppm remained unchanged. Consequently, the singlet at 7.24 ppm belongs to the C<sub>3</sub>-H atom. Furthermore a NOE was detected between the protons of the methoxy groups and the corresponding aromatic protons in the ortho positions with respect to them, which resonated at 3.95 ppm (C<sub>2</sub>-OCH<sub>3</sub>) and 7.24 ppm (C<sub>3</sub>-H) (12%); 3.74 ppm (C<sub>9</sub>-OCH<sub>3</sub>), and 7.45 (C<sub>8</sub>-H) (13%); and 3.83 (C<sub>10</sub>-OCH<sub>3</sub>) and 8.63 ppm (C<sub>11</sub>-H) (16%).

#### EXPERIMENTAL

For chromatography we used type KSK silica gel, and for TLC the following solvent systems: chloroform-ethanol (9:1) and (4:1); and benzene-ethanol (9:1) and (4:1). UV spectra were taken on a Hitachi spectrometer in ethanol, IR spectra on a UR-20 instrument (tablets with KBr), PMR spectra on a JNM-4H-100/100 MHz instrument with HMDS as standard ( $\delta$  scale) in CF<sub>3</sub>COOH, and mass spectra on MKh-1303 and MKh-1310 spectrometers.

Isolation and Separation of the Total Alkaloids. By the usual chloroform extraction [7], 7.5 kg of roots of *C. paniculigera* yielded 16.9 g of ethereal fraction and 12.5 g of chloroform fraction of combined alkaloids. The ethereal fraction was separated into phenolic (1.7 g) and nonphenolic (15.2 g) parts. Treatment of the nonphenolic material with methanol yielded a mixture of crystals (6.2 g) from which, by fractional crystallization from methanol-chloroform 1.9 g of sanguinarine and 4.1 g of protopine were isolated. The residual mother liquor was chromatographed on a column of silica gel. The alkaloids were eluted with benzene and with benzene-ethanol. The benzene fractions yielded 0.07 g of dihydrosanguinarine, 0.5 g of sanguinarine, and 0.03 g of stylophine, and the benzene-ethanol (99:1) and (98:2) fractions yielded 0.2 g of adlumidine, 0.04 g of adlumine, and 0.3 g of bicucculine. The (96:4) and (9:1) fractions gave 0.3 g of oxosanguinarine, 0.25 g of sibiricine, and 1 g of protopine, and the (4:1) fractions gave 0.21 g of pancorine.

The phenolic part of the ether fractions of the total alkaloids was chromatographed on a column of silica gel. The alkaloids were eluted with benzene and with benzene-ethanol mixtures in various ratios. The fractions eluted by benzene gave 0.3 g of pancoridine, those eluted by the (9:1) mixture 0.15 of wilsonirine and 0.008 g of thalicmidine, and the (4:1) mixture yielded 0.05 g of coclaurine. The chloroform fraction of combined alkaloids (12.5 g) was chromatographed on a column of silica gel. The alkaloids were eluted with chloroform and with chloroform-ethanol. The chloroform fractions yielded 3.5 g of pancoridine and 3 g of pancorinine, and from the fractions eluted by chloroform-ethanol (99:1) and (98:2) 1.1 g of corunnine was obtained.

Protopine, mp 205–206°C (chloroform-ethanol). Adlumine, mp 179–180°C (chloroform-methanol). Adlumidine, mp 220–221°C (chloroform-methanol). Bicucculine, mp 194–195°C (chloroform-methanol). Oxosanguinarine, mp 365–366°C (ethanol). Dihydrosanguinarine, mp 187–188°C (ethanol). Sanguinarine, mp 242–243°C (ethanol). Sibiricine, mp 204–205°C (ethanol). Wilsonirine, mp 211–212°C (ethanol). Thalicmidine, mp 192–193°C (methanol), coclaurine, mp 208–209°C (ethanol). Stylophine, mp 203°C (ethanol). Corunnine, mp 255–257°C (chloroform). Pancorine, mp 254–256°C (ethanol). Pancoridine, mp 218–219°C (chloroform-methanol). Pancorinine, mp 289–290°C (chloroform-methanol).

Amination of (I). A solution of 0.1 g of pancoridine in 10 ml of chloroform was treated with 2 ml of ammonia, and the reaction mixture was left at room temperature for 20 h. After the usual working up and crystallization from chloroform-methanol, 0.098 g of a product identical with pancorine was obtained.

Methoxylation of (I). To a solution of 0.05 g of metallic sodium in 20 ml of dry CH<sub>3</sub>OH was added 0.1 g of pancoridine. The mixture was left at room temperature for 20 h, after which the solvent was distilled off, the residue was dissolved in water, and the reaction product was extracted with chloroform. The chloroform solution was evaporated and the residue was crystallized from ether. This gave 0.08 g of (IV) with mp 204–205°C. UV spectrum:  $\lambda_{\max}$  224, 234, 249, 278, 290, 302, 398, 482, 515 nm. IR spectrum: 1240, 1510, 1540, 1630 cm<sup>-1</sup>. Mass spectrum: m/z 350 (M<sup>+</sup>), 336, 322, 292.

PMR, ppm: 3.75 (s, 6 H); 3.81 (s, 3 H); 4.04 (s, 3H); 6.81, 7.27, 9.16 (s, 1 H each); and 7.73 and 8.52 (d, J = 5.5 Hz, 1 H each).

Reduction of (I). A solution of 0.2 g of pancoridine in 20 ml of 10% H<sub>2</sub>SO<sub>4</sub> was treated with 30 g of zinc dust, and the mixture was heated at 100°C for 18 h. After the end of the reaction, the zinc dust was separated off, the acid solution was made alkaline with ammonia, and the reaction product was extracted with chloroform. The solvent was distilled off and the residue was crystallized from ethanol to give 0.16 g of a product with mp 210–211°C, identical with an authentic sample of wilsonirine (melting point, TLC, IR spectrum).

Reduction of (II) [production of (I)]. A solution of 0.1 g of pancorinine in 10 ml of 10% H<sub>2</sub>SO<sub>4</sub> was treated with 20 g of zinc dust and left at room temperature for 12 h. Then the zinc dust was separated off, the acid solution was made alkaline with sodium carbonate, and the reaction product was extracted with chloroform. After the solvent had been distilled off, the residue was crystallized from chloroform-methanol, giving 0.08 g of a product identical with pancoridine.

Reduction of (II) (production of (III)). A solution of 0.1 g of pancorinine in 10 ml of 10% H<sub>2</sub>SO<sub>4</sub> was treated with 20 g of zinc dust, and the mixture was heated at 100°C for 20 h. Then the zinc dust was separated off, the acid solution was made alkaline with sodium carbonate, and the reaction product was extracted with chloroform. After the solvent had been distilled off, the residue was crystallized from ethanol, giving 0.075 g of a reaction product identical with wilsonirine.

Reduction of (IV). The method described above for pancoridine was used for the reduction of 0.1 g of (IV). The reduction product obtained (0.06 g) proved to be identical with wilsonirine (III).

#### SUMMARY

The alkaloid composition of the roots of *Corydalis paniculigera* has been studied for the first time, and 16 alkaloids have been isolated among which pancoridine and pancorinine proved to be new. The structures of these alkaloids have been established.

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