# ALKALOIDS OF *Corydalis*

I. A. Israilov, M. U. Ibragimova,
M. S. Yunusov, and S. Yu. Yunusov

UDC 547.943

Eight alkaloids have previously been isolated from *Corydalis gortschakovii* collected in the western Tien-Shan in the flowering stage [1-3]. Continuing a study of this plant collected in the Pamir-Alai in the budding and incipient flowering period, in addition to the alkaloids mentioned we isolated d-corydine and isoboldine, identified by a direct comparison with authentic samples [4-6], and also bracteoline and domesticine, which were identified spectrally and by the preparation of their methyl ethers [7-9], and also a base with mp 225-226°C.

From the tubers of *Corydalis sewertzovii*, collected in the flowering period in the Chimkent oblast of the Kazakh SSR, in addition to sanguinarine, protopine, and allocryptopine, which have been isolated previously [10, 11], we obtained heleritrine, corlumine, and dihydrosanguinarine, which were identified by direct comparison with authentic samples [12], and bases with mp 188-189°C and 195-196°C.

The alkaloids of *Corydalis intermedia* (L) Merat Nouv. have not previously been studied. This plant grows widely in the European part of the Soviet Union [13]. The plant was collected in the flowering period in the Kostroma oblast. From the epigeal part by chloroform extraction we isolated 0.4% of combined alkaloids, from which we isolated protopine, α-allocryptopine, isoboldine, a base with mp 168-170°C, and an amorphous base.

## EXPERIMENTAL

The NMR spectra were taken on a JNM-4H-100/100 MHz instrument in deuterochloroform with HMDS as internal standard (δ scale), and the mass spectra on an MKh-1303 instrument fitted with a system for direct introduction into the ion source. The purity of all the alkaloids was checked by chromatography in a thin layer of ShSK silica gel in the benzene–chloroform–methanol (5:1:1) system.

The air-dry plant *C. gortschakovii* (35.5 kg) was extracted with chloroform by the usual method. This gave 267.8 g of ether-soluble and 86.2 g of chloroform-soluble combined alkaloids (CA). The ether-soluble CA were treated with 1 N KOH, washed with water, and evaporated. The yield of nonphenolic CA was 199.7 g. Ammonium chloride was added to the alkaline solution, and the alkaloids were extracted with ether (49.17 g of CA) and then with chloroform (15.77 g of CA). The nonphenolic CA were treated with methanol. This yielded 28.41 g of a crystalline mixture of bases which was converted into the hydrobromides.

Fractional crystallization from ethanol gave 10 g of isocorydine hydrobromide. The sparingly soluble fraction of the hydrobromides was converted into the free bases and these were chromatographed on a column of alumina. The benzene eluate was treated with acetone. This precipitated 3.7 g of corydine. The mother solution of the nonphenolic Ca (166.5 g) was separated according to basicities into seven fractions. The washing chloroform solution was treated with methanol, leading to the separation of 0.97 g of l-adlumine. Methanol was added to fractions 6-7. The crystals of protopine that deposited were separated off (1.75 g).

The mother solutions of fractions 6-7 were combined and separated according to basicities into five fractions. The last two fractions were treated repeatedly with a 4% solution

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Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 612-615, September-October, 1975. Original article submitted July 6, 1974.

of KOH. Ammonium chloride was added to the alkaline solution and the alkaloids were extracted with ether. The residue from the ether extract was treated with acetone, and 0.28 g of sendaverine was obtained. From the nonphenolic fraction, l-domesticine tartrate was isolated. The free base was obtained in the usual way and was recrystallized from ether, mp 154-155°C, $[\alpha]_D^{18}$ −56° (c 0.5; chloroform). UV spectrum: $\lambda_{\max}^{\text{ethanol}}$ 219, 283, 313 nm (log ε 4.15, 3.99, 4.13); mass spectrum: m/e 325 ($M^+$), 324, 310, 282. NMR spectrum (ppm): 2.43 ($N{-}CH_3$), 3.80 ($OCH_3$), 5.86 ($CH_2O_2$), 6.45, 6.68, 7.86 (3H, Ar protons).

The O-methyl ether of domesticine was obtained by methylating the alkaloid with diazomethane, and after recrystallization from a mixture of acetone and water it had mp 137-138°C.

The combined nonphenolic alkaloids after the preparation of the domesticine tartrate were dissolved in water, the solution was made alkaline, and the alkaloids were extracted with ether. The residue from the ethereal extract was treated with acetone, giving 0.65 g of cryptopine.

The phenolic CA (49.17 g) were separated according to their basicities into eight fractions. Fractions 1-6 yielded a crystalline mixture of corydine and isocorydine hydrobromides. The action of methanol on fraction 8 yielded 0.59 g of isoboldine. The mother liquors of fraction 8 were treated with an ethanolic solution of hydrochloric acid. This gave 1.81 g of a crystalline mixture of hydrochlorides. This mixture was recrystallized from ethanol. The hydrochloride, readily soluble in ethanol, was dissolved in water, and the solution was made alkaline and was extracted with ether. The residue from the evaporation of ether was treated with methanol, giving 0.17 g of isoboldine. By the same method, 0.38 g of corgoine was isolated from the hydrochloride sparingly soluble in ethanol.

Fraction 7 was again separated according to basicities into seven fractions. The last fraction yielded 0.11 g of isoboldine, and the methanolic mother liquor yielded 0.05 g of bracteoline with mp 218-221°C, $[\alpha]_D$ + 35.8° (c, 0.16; chloroform).

UV spectrum: $\lambda_{\max}^{\text{ethanol}}$ 223, 282, 310 nm (log ε 4.45, 4.04, 4.08); mass spectrum: m/e 327 ($M^+$), 326, 312, 284. NMR spectrum (ppm): 2.50 ($N{-}CH_3$), 3.70 [6H $(OCH_3)_2$], 7.90, 6.40, 6.65 (3H; Ar protons).

The O,O-dimethyl ether of bracteoline was obtained by methylating the alkaloid with diazomethane, mp 97-98°C (hexane); $[\alpha]_D^{18}$ + 111° (c 0.4; chloroform).

The mother liquors from the phenolic CA after the isolation of the isoboldine, corgoine, and bracteoline were combined (4.17 g) and chromatographed on a column of alumina (1:30). The alkaloids were eluted with petroleum ether, benzene–diethyl ether (1:100, 1:10, and 1:1), ether–chloroform (1:100, 1:10, 1:1), chloroform, and chloroform–methanol (1:10, 1:1). The chloroform fractions 10-15 on treatment with methanol yielded 0.14 g of sendaverine, and the chloroform–methanol fractions 1-6 yielded a base with mp 225-226°C. The remaining chloroform and chloroform–methanol (1:1) fractions were combined and passed through a column of silica gel. Elution was performed with benzene–methanol–chloroform (5:1:1). Fractions 5-10 yielded 0.05 g of bracteoline.

The alkaloids were extracted from 810 g of the dry tubers of *C. sewertzovii* with chloroform by the usual method. In the extraction of the alkaloids from the chloroform solution with 10% sulfuric acid, a sulfate precipitates. It was separated off and dissolved in water, and the solution was made alkaline with concentrated ammonia and was extracted with ether (2.76 g) and then with chloroform (0.46 g).

The separation [4] of the ether-soluble fraction yielded 0.84 g of sanguinarine and 0.27 g of heleritrine. The acid solution after the separation of the insoluble sulfate was made alkaline, and the alkaloids were extracted with ether and then with chloroform. The ethereal CA was separated into phenolic (0.87 g) and nonphenolic (4.23 g) fractions. On the addition of methanol, the nonphenolic part crystallized; the crystals were separated and by fractional crystallization from a mixture of chloroform and methanol protopine (0.21 g), allocryptopine (0.3 g), and corlumine (0.79 g) were obtained. The methanolic mother solution deposited crystals, and these were chromatographed on a column of silica gel with elution of the alkaloids by benzene–methanol–chloroform (5:1:1). Fractions 1-4 yielded 0.02 g of a base with mp 195-196°C, and the subsequent fractions yielded protopine (0.13 g). The mother solution of the nonphenolic Ca (2.93 g) was chromatographed on a column of alumina (1:60), the alkaloids being eluted with benzene, benzene–methanol (99:1; 98:2; 95:5; 9:1; and 1:1) and methanol. The benzene–methanol (99:1) fractions yielded 85 mg of dihydrosanguinarine.

The phenolic CA (0.87 g) were chromatographed on a column of silica gel. The benzene–methanol (98:2) fraction deposited 0.18 g of a base with mp 188-189°C.

By the usual chloroform extraction, 100 g of the air-dry epigeal part of *C. intermedia* yielded 0.4 g of CA, which was chromatographed on a column of silica gel. The alkaloids were eluted with benzene, benzene–methanol (99:1; 98:2; 95:5; 1:1) and with methanol. The benzene–methanol (99;1) fractions yielded a base with mp 168-170°C (15 mg); the benzene–methanol (98:2) fractions gave isoboldine (30 mg); the (95:5) eluent gave 82 mg of protopine and 65 mg of allocryptopine; and the (1:1) mixture gave 10 mg of an amorphous base.

## SUMMARY

Fifteen bases have been isolated from three species of *Corydalis*. Dihydrosanguinarine has been isolated from a plant of the genus *Corydalis* for the first time.

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