*Chemistry of Natural Compounds, Vol. 31, No. 4, 1995*

# ALKALOIDS OF *Haplophyllum perforatum*

**Kh. A. Rasulova and I. A. Bessonova**

UDC 547.944/945

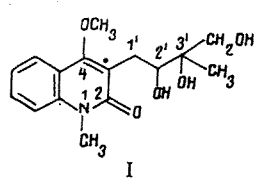
*The alkaloids of the epigeal parts of* Haplophyllum perforatum *plants gathered from three growth sites have been studied. In addition to known compounds, the new alkaloid haplosamine has been isolated. Its structure has been established on the basis of spectral results and has been confirmed by direct comparison with the product of the hydrolysis of dubinidine methiodide.*

The plant *Haplophyllum perforatum* Kar. et Kir. (fam. Rutaceae) is one of the clear examples of a marked change in alkaloid composition as a function of the vegetation period [1, 2], the organ [3], and, in particular, the growth site of the plant [4, 5]. Many new alkaloids characteristic only of this plant (modified furanoquinolines [6, 7], glycoalkaloids [8]) are produced in it only from definite growth sites. *H. perforatum* from new collection sites is therefore an independent object of chemical study.

We have studied the alkaloids of the epigeal parts of plants gathered from new growth sites (Republic of Kazakhstan); I) environs of Kuyuk Pass, Dzhambuskaya oblast, beginning of vegetation; II) Zhylga village, Chimkent oblast, flowering; and III) along the Chulan-Kurga-Suzak road, Suzak region, Chimkent oblast, end of flowering. The raw material was extracted with methanol. Mixtures of alkaloids were obtained from the concentrated methanolic extract by the usual method, and the following were isolated from these by column chromatography: from (I) – evoxine and haplopine; from (II) – evoxine and haplamine; and from (III) skimmianine and a new base with mp 132-133°C, which we have called haplosamine. The known alkaloids were identified by direct comparison with authentic samples.

Haplosamine dissolves in chloroform, and, more sparingly, in water and methanol. It crystallizes from alcohol, acetone and ethyl acetate in the form of colorless prisms.

Its UV spectrum contained maxima at 3552, 3430, and 3225 $cm^{-1}$ (OH groups) and intense absorption at 1630 $cm^{-1}$ (amide carbonyl). In the PMR spectrum there were the signals of four adjacent aromatic protons at (ppm) 7.82 (doublet of doublets, 1H, J = 8 and 2.5 Hz, H-5) and 7.37 (multiplet, 3H, H-6, 7, 8), of the protons of C-methyl, methylimide, and methoxy groups at 1.15, 3.68, and 3.92 (singlets, 3H each), and of the nonequivalent benzyl protons of the side chain at 3.00 (dd, J = 2.5 and 13.5 Hz) and 2.77 (dd, J = 8.5 and 13.5 Hz). In the 4.10-3.90 ppm region a three-proton multiplet of the protons of hydroxymethyl and hydroxymethylene groups were observed. There were also broadened singlets at 5.07, 3.55, and 3.12 ppm (3 OH) which disappeared on the addition of trifluoroacetic acid. These facts, and also the spectrum of the base, were identical with published characteristics for 3-(2′,3′-dihydroxy-3′-hydroxymethylbutyl)-4-methoxy-N-methylquinolin-2-one, obtained in the hydrolysis of dubinidine methiodide in an aqueous solution of ammonia [9]. A direct comparison of the base isolated with an authentic sample showed their identity. Consequently, haplosamine has the structure (**1**).




I

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (3712) 89 14 75. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 586-587, July-August, 1995. Original article submitted October 17, 1994.

0009-3130/95/3104-0487$12.50 ©1996 Plenum Publishing Corporation

## EXPERIMENTAL

**General Observations**. The spectra of the substances were obtained on the following instruments: Hitachi EPS-3T (alcohol); UR-20, tablets with KBr; and Tesla BS-567 A 100 MHz ($\delta$-scale, 0 – TMS, in deuterochloroform).

Chromatographic monitoring was performed by TLC (LSL 5/40 alumina, neutral; Silufol) in the solvent systems: toluene–ethyl acetate–acetic acid (5:4:1); ethyl acetate–methanol (2:1); and benzene–methanol (4:1).

**Isolation of the Alkaloids.** The dried comminuted epigeal parts of (I) (420 g), (II) (460 g), and (III) (960 g) were extracted with methanol. The evaporated methanolic extracts were dissolved in chloroform and the solutions were shaken with 10% sulfuric acid. The acid solutions were made alkaline with ammonia, and the alkaloids were extracted with chloroform. Samples (I), (II), and (III) yielded 0.94, 2.06, and 3.3 g of mixtures of bases (0.22, 0.45, and 0.35% of the weight of the dry epigeal parts), respectively.

By chromatography on alumina, the 0.94 g of alkaloids from (I) yielded 30 mg of evoxine and 20 mg of haplopine. Similarly, the separation of the 2.06 and 3.3 g of alkaloids isolated from (II) and (III) gave 0.91 g of evoxine, 0.2 g of skimmianine, and 26 mg of haplosamine. The neutral fraction obtained from (II) yielded 0.42 g of haplamine.

**Haplosamine**, mp 132-133°C, (from acetone, alcohol, and ethyl acetate). UV spectrum ($C_2H_5OH$, $\lambda_{max}$, nm); 229, 244 infl., 265, 274, 284, 312, 326, 340 (log $\varepsilon$ 5.18, 4.72, 4.39, 4.49, 4.40, 4.32, 4.42, 4.29).

The spectrum did not change on acidification.

IR spectrum (KBr, $\nu_{max}$, $cm^{-1}$): 3552, 3430, 3225, 1633, 1595, 1510, 1470, 1420, 1370, 1340, 1230, 1110.

Mass spectrum, *m/z*(%): 289 ($M-H_2O^+$, 1.5), 276(4), 271(5), 268(12), 258(10), 240(3), 232(100), 216(15), 203(43), 202(38), 188(53), 172(20), 160(8), 144(18), 134(13), 122(13), 115(10), 105(10), 91(14), 77(18).

## REFERENCES


1. S. Yu. Yunusov and G. P. Sidyakin, Zh. Obshch. Khim., **22**, 1055 (1952).
2. Kh. A. Abdullaeva, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prir. Soedin, 219 (1978).
3. D. M. Razakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prir. Soedin., 682 (1976).
4. D. M. Razakova, I. A. Bessonova, Kh. A. Abdullaeva, and S. Yu. Yunusov, Khim. Prir. Soedin., 395 (1983).
5. Kh. A. Rasulova and I. A. Bessonova, Khim. Prir. Soedin., 249 (1992).
6. Z. Sh. Faizutdinova, I. A. Bessonova, and S. D. Yunusov, Khim. Prir. Soedin., 360 (1968).
7. D. M. Razakova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prir. Soedin., 246 (1983).
8. Kh. A. Rasulova, I. A. Bessonova, M. R. Yagudaev, and S. Yu. Yunusov, Khim. Prir. Soedin., 876 (1987); 94 (1988).
9. I. A. Bessonova, E. G. Mil'grom, Ya. V. Rashkes, A. D. Vdovin, D. M. Razakova, Khim. Prir. Soedin., 418 (1993).