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NEW ALKALOIDS FROM *Haplophyllum*

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The new alkaloid foliphorin is isolated from Haplophyllum foliosum *(Rutaceae). Spectral data establish the structure as 1-methyl-4-methoxy-8(2′-O-acetyl-3′-hydroxy-3′-methylbutyloxy)-2-quinolone. Dihydro-haplamine, which is observed for the first time in nature, is obtained from* Haplophyllum perforatum.

In continuation of the study of alkaloids from plants of the *Haplophyllum* genus (Rutaceae) [1], new alkaloids with mp 83-84°C (**1**) and 231-232°C (**2**), respectively, were isolated from the above-ground parts of *H. foliosum* Vved. and *H. perforatum* Kar. et Kir.

Compound **1**, called foliphorin, has the formula $C_{18}H_{23}NO_6$, M^+ 349 (mass spectrometry).

The UV spectrum of foliphorin exhibits maxima at 214, 233, 251, 285, and 326 nm, characteristic of 2-quinolone alkaloids [2] and similar to the spectrum of foliosidin (**3**) [3, 4]. The IR spectrum contains absorption bands for active H (3300 cm^{-1}), ester (1741 cm^{-1}), and amide carbonyl (1638 cm^{-1}).

The mass spectrum of foliphorin has the same set of peaks (*m/z* 307, 292, 248, 205, 174, 162, 59) as foliosidin [4], with the exception of the molecular ion, which is located at higher mass (M^+ 349) and differs from the corresponding peak of **3** (M^+ 307) by 42 amu.

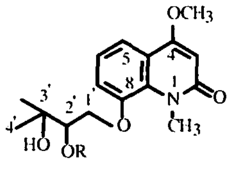
This fact and the presence in the IR spectrum of **1** of an absorption band for an ester suggests that the isolated alkaloid is an acetyl derivative of foliosidin. The ^1H NMR spectra of foliphorin confirm this.

Signals in the spectrum of **1** and **3** [4, 5] appear for the four aromatic protons at δ 7.63 (1H, m, H-5), 7.12 (2H, m, H-6, H-7), and 6.00 ppm (1H, s, H-3), for the O-methylene protons (4.35 ppm, 1H, dd, J_1 = 10 Hz, J_2 = 3 Hz, and 4.17 ppm, 1H, dd, J_1 = 10 Hz, J_2 = 7 Hz), methoxyl (3.90 ppm, 3H, s), N-methyl (3.82 ppm, 3H, s), and gem-dimethyl (1.31 and 1.27 ppm, 3H each, s) groups.

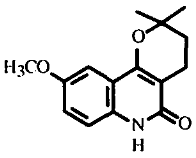
However, in contrast with foliosidin, the spectrum of foliphorin contains a signal for only one hydroxyl group at 5.15 ppm (1H, s). A 3-proton singlet at 2.11 ppm belonging to the protons of the acetyl group is seen instead of the signal of the second hydroxyl. Furthermore, the signal for H-2′ in the spectrum of foliphorin shifts to weak field by more than 1 ppm compared with the same signal in the spectrum of foliosidin. It occurs at 5.34 ppm (1H, dd, J_1 = 7 Hz, J_2 = 3 Hz). Hence, this proton is geminal to the acetoxy group that according to this should be located on C-2′.

Thus, foliphorin (**1**) differs from foliosidin in that the secondary hydroxyl group of the latter is acetylated in **1**. Foliphorin has the structure 1-methyl-4-methoxy-8(2′-O-acetyl-3′-hydroxy-3′-methylbutyloxy)-2-quinolone (**1**).

The UV spectrum of **2** exhibits absorption bands at 216, 232, 278, 287, and 334 nm. This is characteristic of 2-quinolone derivatives [2]. Its IR spectrum contains absorption bands for active H at 3150 cm^{-1} and an amide carbonyl at 1650 cm^{-1}.



1: R=$COCH_3$; **3**: R=H



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The mass spectrum of the alkaloid has a peak for the molecular ion with *m/z* 259 (M^+, ·100%), which differs from the corresponding peak of haplamine [6] by 2 amu. This suggests that the isolated compound is a dihydro derivative of haplamine that was prepared previously from it [7]. Direct comparison of the samples demonstrated that they are identical.

Thus, the isolated alkaloid is dihydrohaplamine and has the structure **2**. Dihydrohaplamine is observed for the first time in nature.

EXPERIMENTAL

General comments. Silica gel KSK was used for column chromatography. Thin-layer chromatography used the same grade of silica gel with 5% gypsum and toluene-ethylacetate-acetic acid (5:4:1) eluent. The chromatograms were visualized with Dragendorf reagent.

UV, IR, PMR, and mass spectra were recorded on a Lambda 16 UV/VIS spectrometer, Perkin—Elmer System 2000 FT-IR, Tesla BS-567 A (100 MHz, $CDCl_3$, δ-scale, 0 = HMDS), and MX 1310 with a direct probe into the ion source, respectively.

Isolation of Foliphorin from *H. foliosum*. Mother liquor (1 g) after purification of techical foliosidin (3.5 g) that was isolated from 50 kg of the above-ground part of the plant (Takzhikistan, flowering phase) was treated with ether (100 ml). The solid after evaporation of solvent (0.45 g) was crystallized twice from a hexane-ether (7:3) mixture to give foliphorin (70 mg). The method for isolating foliosidin has been published [8].

Foliphorin (1), mp 83-84°C (from hexane-ether).

UV spectrum (ethanol, cm^{-1}): λ_{max} 214, 233, 251, 274 (sh), 285, 326; λ_{max} 219, 241, 281, 298.

IR spectrum (ν_{max}, cm^{-1}): 3300 (OH), 1741 (O–CO), 1638 (N–CO), 1576, 1490, 1397, 1241, 1073, 1061, 825, 794, 735.

Mass spectrum, *m/z* (%): 349 (M^+, 43), 334 (M - 15, 31), 307 (9).

Isolation of Dihydrohaplamine from *H. perforatum*. Mother liquor (5 g) after purification of technical haplamine (20 g) that was isolated from 20 kg of the above-ground part of the plant (Dzhungarskii Alatau, flowering phase) was treated twice with a warm mixture of hexane-ether (7:3) (100 ml each). The solutions were combined. The solid (1.5 g) after distillation of the solvent were chromatographed on a silica-gel column (1:100) using ether. The solid from the first eluates was separated and crystallized from acetone to give dihydrohaplamine (50 mg).

The method for isolating haplamine has been published [7].

Dihydrohaplamine (2), mp 231-232°C (acetone).

IR spectrum (ν_{max}, cm^{-1}): 3150 (NH), 1650 (N–CO), 1604, 1503, 1480, 1460, 1420, 1370, 1315, 1220, 1170, 1120, 1040, 860, 820, 770, 715.

Mass spectrum, *m/z* (%): 259 (M^+, 100), 216 (45), 204 (65), 203 (71), 188 (28), 168 (25).

^1H NMR and UV spectral data of **2** have been published [7].

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