Continuing the separation of the nonphenolic fraction of the combined alkaloids of *Haplophyllum foliosum* Vved. [1], we have obtained a new optically active base — folisine, C₁₅H₁₇O₄N, mol. wt. 275 (mass spectrometry). The substance has no methoxy group but has a N-methyl group. The base dissolves readily in acids and sparingly in acetone and ether, is insoluble in alkalis, and crystallizes from methanol.

The IR spectrum of folisine shows strong absorption bands at 3200, 3415, and 3510 cm⁻¹ for a hydroxy group and at 1520, 1540, 1555, 1590, and 1628 cm⁻¹, which are typical for 2-alkoxy-4-quinolones [2]. The fact that folisine is an alkaloid of the 4-quinolone series is shown by its UV spectrum, which is similar to that of ifflaiamine [3].

In the NMR spectrum of the base in the weak-field region there are two signals from four adjacent aromatic protons: a three-proton multiplet at 2.15-2.65 ppm from H₆, H₇, and H₈, and a one-proton doublet at 1.8 ppm from H₅. The downfield shift of the H₅ signal by 60 Hz relative to the center of the multiplet of the other aromatic protons shows the 2-alkoxy-4-quinolone structure of this alkaloid. A one-proton triplet at 4.75 ppm, a two-proton doublet at 6.60 ppm (J=8 Hz), and a three-proton singlet at 6.22 ppm (N—CH₃) show that folisine is a N-methyl-dihydrofurano-4-quinoline alkaloid with a substituting group in the α position of the dihydrofuran ring. The NMR spectrum has two singlets at 6.17 ppm (2H) and 8.87 ppm (3H) from

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\text{CH}_3
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the lateral substituent \( \text{CH}_2\text{OH} \). These results permit the conclusion that folisine differs from dubinidine [4] only by the presence of a methylimide group in place of a methoxy group.

The mass spectrum of folisine - m/e 275 (M) (100%), 244 (29), 226 (15), 215 (14), 214 (38), 202 (53), 201 (15), 200 (69), 189 (59), 188 (70), 176 (38), 175 (22), 134 (20) - confirms the proposed structure (I) for this base. The main peaks are due to the splitting off of the side chain attached to the dihydrofuran ring with the formation of an oxonium ion having m/e 200 and by the cleavage of the Cα—Cβ and O—Cα bonds with the migration of hydrogen from the tertiary hydroxy group (an ammonium ion with m/e 188 is formed) [5-7]. On oxidation with periodic acid, folisine gave a ketone (II) the IR spectrum of which lacks the absorption bands of hydroxy groups and has a band at 1730 cm⁻¹ (carbonyl group). The NMR spectrum of (II) lacks the two-proton singlet of a hydroxymethyl group, and the signal of the C-methyl group appears at τ 7.81 ppm (Δτ=1.06), which is characteristic for a methyl group attached to a carbonyl group. The struc-
ture of the alkaloid was shown definitively by the passage from dubinidine (III) to (I) by the reaction of dubinidine methiodide (IV) with anhydrous pyridine. (See scheme on following page.)

Substances (I) and (III) have not been obtained previously, and isodubinidine, isolated from the products of the saponification of (IV) by ethanolic alkali [8] is \( \beta \)-hydroxy-\( \alpha \)-hydroxymethyl-\( \alpha \)-dimethyl-\( \alpha \),\( \beta \)-dihydrofuran-4-quinolone [7].

We have performed the usual isomerization of dubinidine [9] and have isolated substances (I) and (IV) from the reaction products. In determining the melting point of dubinidine methiodide, it was observed that at 160°C the substance melted with effervescence, and then it solidified and remelted at 226°C, i.e. it behaved similarly to platydesmine methiodide [6, 10]. Substance (IV) was heated to the melting point and, after cooling, it was recrystallized from methanol. The resulting substance was identical in melting point, IR spectrum, and TLC behavior with folisine.

**EXPERIMENTAL**

The combined nonphenolic alkaloids (40 g) were chromatographed on alumina (900 g). Folisine was isolated from the chloroform-methanol eluates.

Folisine (I). The substance had mp 236-237°C (from methanol), \([\alpha]_{D}^{23} = 123^\circ \) (c 1.22; methanol); UV spectrum, \( \lambda_{max} \) nm: 215, 237, 251 (inflection), 299 (inflection), 310, 321 (log e 4.50; 4.43; 4.24; 4.01; 4.12; 4.07); Rf 0.38. Folisine hydrochloride with mp 230°C precipitated on the addition of ether to a solution of the base in ethanolic hydrogen chloride. It gave a depression of the melting point in admixture with folisine.

**Oxidation of Folisine with Periodic Acid.** To a solution of 0.2 g of periodic acid in 2 ml of water was added 0.1 g of folisine. It immediately deposited white crystals of the ketone (II), which were filtered off with suction, and washed with water, mp 144°C (from ethanol).

**Conversion of Dubinidine into Folisine (I).** A. A mixture of 0.3 g of dubinidine methiodide and 10 ml of anhydrous freshly distilled pyridine was heated in the water bath for 7 h. On the following day, the solution yielded crystals with mp 235°C showing no depression of the melting point with folisine; their IR spectra and thin-layer chromatograms were identical.

B. A mixture of 0.3 g of dubinidine and 1 ml of methyl iodide was heated in a sealed tube at 100°C for 3 h. The tube was opened and the excess of methyl iodide was evaporated off. The substance obtained, with mp 235°C (from methanol), was identical with folisine. Yield 0.25 g. The methanolic mother solution deposited crystals of dubinidine methiodide.

C. Dubinidine methiodide (0.1 g) was heated until it melted. After melting with effervescence, it immediately crystallized. After cooling and recrystallization from methanol, folisine was obtained with mp 235°C. Yield 0.6 g.

**SUMMARY**

1. From the mixture of alkaloids of *H. foliosum* has been isolated a new base — folisine — which is 1-methyl-\( \alpha \),\( \beta \)-dihydrofuran-4-quinolone with a substituting group on the \( \alpha \)-carbon atom.

2. The transition from dubinidine to folisine has been effected by the reaction of dubinidine methiodide with anhydrous pyridine.

3. When dubinidine is heated with methyl iodide in a sealed tube, the usual isomerization takes place and folisine is formed.

**LITERATURE CITED**