

# STRUCTURE OF FOLIMININE

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From the combined chloroform-soluble nonphenolic alkaloids obtained from the epigeal part of *Haplophyllum foliosum* [1] by chromatography on a column of alumina we have isolated a new alkaloid which has been called foliminine.

Foliminine has the composition  $C_{17}H_{17}O_3N$ , mp 107–108°C, mol. wt. 283 (mass spectrometry); it is optically inactive and forms a hydrochloride. The IR spectrum of the base [ $\lambda_{\max}$  252, 314, 328, 340 nm ( $\log \epsilon$  4.55; 3.80; 3.79; 3.73)] is characteristic for the furanoquinoline alkaloids [2]. The IR spectrum has no absorption band of a hydroxy group and shows absorption maxima at 3140 and 3170  $\text{cm}^{-1}$  (furan ring). The absorption bands of the CH vibrations of the furan ring are located at shorter wavelengths than is the case with other representatives of this group of alkaloids [3]. However, the fact that foliminine belongs to the furanoquinoline group of alkaloids is shown by its NMR spectrum (Fig. 1), in which there are eight signals with an intensity ratio of 1:1:1:1:3:2:2:6 corresponding to the 17 hydrogen atoms of the base. Doublets at 2.15 and 3.10 ppm ( $J = 9$  Hz) correspond to the ortho protons of an aromatic ring. Consequently, the benzene ring of foliminine is substituted in the 5,6 or 7,8 positions. Two other doublets at 2.64 and 3.28 ppm ( $J = 3$  Hz) are due to the protons of the furan ring, since in the product of the hydrogenolysis of the base –

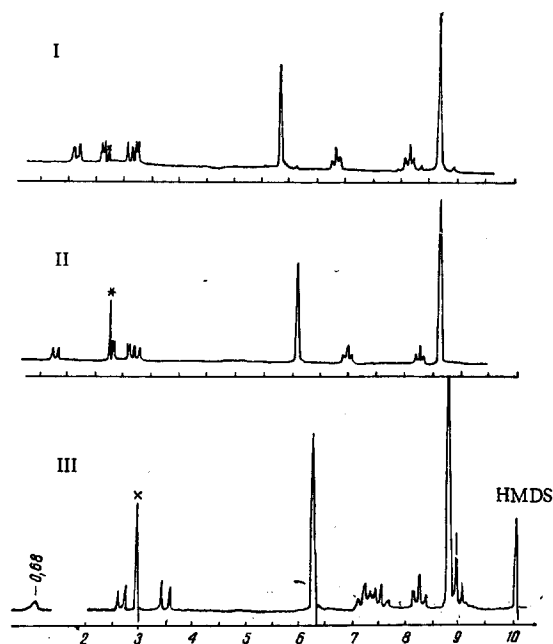


Fig. 1. NMR spectra of foliminine (I), isofoliminine (II) (on a JNM-4H100/100 MHz instrument), and tetrahydrofoliminine (III) (on a JNM-C-60 HL instrument) in  $\text{CDCl}_3$ ,  $\tau$  scale.

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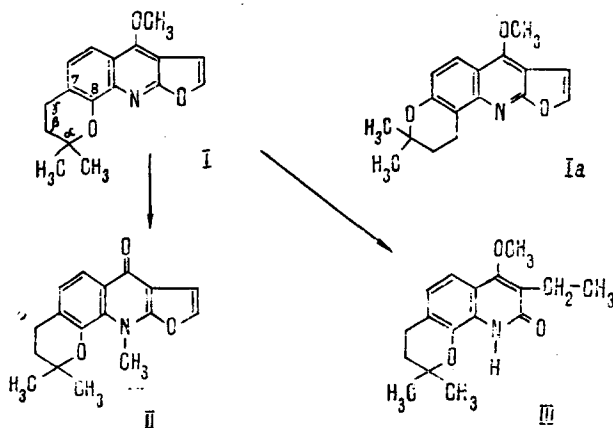
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tetrahydrofoliminine— these signals have disappeared. The presence in the NMR spectrum of foliminine of a three-proton singlet at 5.88 ppm, two triplets at 6.88 and 8.17 ppm of two proton units each ( $J = 7$  Hz); and a six-proton singlet at 8.70 ppm permits the assumption that the base has a methoxy group in position 4 and a dimethyl-dihydropyran ring condensed with the benzene ring in the 5,6 or 7,8 position. In order to investigate this, we performed an isomerization reaction with methyl iodide, obtaining isofoliminine (II), the IR and UV spectra of which are typical for N-methylfuranodihydroquinolin-4-one derivatives. In the NMR spectrum of (II) (see Fig. 1) the signals of the aromatic protons appear at 1.82 and 3.26 ppm ( $J = 9$  Hz). The considerable downfield shift of the signal in comparison with the initial base as the result of the influence of a carbonyl group in position 4 [14] shows that it is due to a proton at  $C_5$ , and therefore the benzene ring of the quinoline nucleus is substituted in the 7,8 positions. If it were substituted in the 5,6 positions, this signal would have undergone a strong diamagnetic shift [5].

The furanoquinoline structure of this alkaloid is also confirmed by the hydrogenolysis reaction. On hydrogenation over a platinum catalyst, foliminine absorbs four atoms of hydrogen, forming tetrahydrofoliminine (III). The IR and UV spectra of (III) agree with 4-alkoxydihydroquinolin-2-one structure.

The NMR spectrum of (III) lacks the signals of the protons of the furan ring, and instead of these there are signals at 8.89 and 7.42 ppm in the form of a three-proton triplet and a two-proton quartet from a  $-CH_2-CH_3$  group and a broadened signal at  $-0.68$  ppm from an NH group.

The facts presented above give grounds for considering that foliminine must correspond to one of the possible structures (I) and (Ia).



The fact that all the alkaloids isolated from *H. foliosum* with the exception of skimmianine and haplopine either contain no substituents in the benzene ring (graveoline, folimidine, 1-methyl-2-phenyldihydroquinoline-4-one, dubinidine, folifine, haplofoline, folisine) or have an alkoxy or hydroxy substituent in position 8 (robustinine, folimine, folifidine, folifinine, foliosidine) permits the assumption that structure (I) is more likely for foliminine.

## EXPERIMENTAL

The conditions for isolating the alkaloids and for taking the spectra have been given previously [6, 7].

The combined nonphenolic chloroform-soluble alkaloids (60 g) were chromatographed on alumina (1100 g). The ether-chloroform eluates yielded 0.6 g of a noncrystallizing oil, which was rechromatographed on alumina. Treatment of the ethereal eluates with ethanolic hydrochloric acid yielded a hydrochloride with mp  $188^{\circ}\text{C}$  (from ethanol), which was suspended in aqueous ammonia solution. The base was extracted with ether. The yield of (I) was 400 mg, mp  $107-108^{\circ}\text{C}$  (from acetone-water),  $R_f$  0.81 [TLC; silica gel-gypsum (20:1); ethyl acetate]. The substance dissolves readily in acetone and chloroform.

Main peaks in the mass spectrum of (I):  $283 M^+$  (97%), 268 ( $M-15$ ) (21%), 240 ( $M-43$ ) (100%), 228 ( $M-55$ ) (56%).

**Isofoliminine.** A mixture of 100 mg of the base and 2 ml of freshly distilled methyl iodide was heated in a sealed tube in the boiling water bath for 10 h. Isofoliminine was obtained with mp  $203^{\circ}\text{C}$  (from ethanol),  $R_f$  0.39 (ethyl acetate). Isofoliminine is readily soluble in chloroform and acetone and in the light acquires a pink color.

UV spectrum:  $\lambda_{\max}$  238 inflection, 266, 323 nm ( $\log \epsilon$  4.03, 4.60, 3.77); in an acid medium  $\lambda_{\max}$  261, 326, 335 nm ( $\log \epsilon$  4.51, 3.81, 3.79). IR spectrum,  $\text{cm}^{-1}$ : 3150, 3120, 1630, 1600, 1540, 1517.

Mass spectrum: 283  $\text{M}^+$  (100%), 268 (M-15) (9%), 240 (M-43) (6%), 228 (M-55) (50%).

Tetrahydrofoliminine. The hydrogenation of 40 mg of the base in 15 ml of ethanol was performed over a platinum catalyst for 1 h. The catalyst was removed and the solution was concentrated, and on standing it deposited crystals of (III) with mp 224-225°C (from ethanol), Rf 0.64 (ethyl acetate). The substance is readily soluble in chloroform.

UV spectrum:  $\lambda_{\max}$  221, 231 inflection, 250, 259, 287, 313 inflection, 325, 339 nm ( $\log \epsilon$  4.67, 4.45, 3.99, 4.03, 3.79, 3.99, 4.23, 4.20). The spectrum undergoes no change in an acid medium.

IR spectrum,  $\text{cm}^{-1}$ : 1650, 1580, 1500. Mass spectrum: 287  $\text{M}^+$  (100%), 272 (M-15) 41%, 258 (M-29) 16%, 244 (M-43) 10%, 232 (M-55) 40%, 216 (M-71) 37%, 202 (M-85) 12%.

#### CONCLUSIONS

From the combined alkaloids of the epigeal part of Haplophyllum foliosum (family Rutaceae) the new alkaloid foliminine, with the composition  $\text{C}_{17}\text{H}_{17}\text{O}_3\text{N}$  has been isolated, and for it the most probable structure of 7, 8-( $\alpha,\alpha$ -dimethyl- $\beta,\gamma$ -dihydropyrano)-4-methoxyfuranoquinoline has been proposed.

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