FOLIOSIDINE ACETONIDE

V. A. Tel'nov, I. A. Bessonova, and S. Yu. Yunusov

UDC 547.944/945

Continuing the separation of the chloroformic fraction of the combined alkaloids of Haplophyllum foliosum Vved., we have obtained a base in the form of its hydrochloride with the composition $C_{19}H_{25}O_5N$, mp 119-120°C (I). The same base was isolated by chromatography on alumina of the combined alkaloids obtained after the isolation of dubinidine.

The base is nonphenolic, optically active, and readily soluble in organic solvents, crystallizing from petroleum ether. The UV spectrum has the maxima characteristic for 4-alkoxyquinolin-2-ones (λ_{max} 215, 233, 250, 275 inflection, 284, 315 inflection, 323 nm; log ε 4.63, 4.50, 4.43, 3.84, 3.80, 3.44, 3.50, respectively) and almost coincides with the UV spectra of 4-methoxy-1-methylquinolin-2-one derivatives substituted in position 8 [1].

The IR spectrum of I has the absorption band of an amide carbonyl group with a high integral intensity at 1650 cm^{-1} and lacks the absorption bands of hydroxy groups. A functional analysis showed the presence of a methoxy and a N-methyl group. The base contains a gem-dimethyl group, since oxidation by the Kuhn–Roth method yielded acetone.

The NMR spectrum of the base (Fig. 1) shows six groups of signals with a ratio of their intensities of 1 : 2 : 1 : 3 : 6 : 12, corresponding to the 25 hydrogen atoms of the base.

In the strong-field region there are three singlets at τ 8.60 (3H), 8.68(6H), and 8.87 (3H) and a poorly resolved singlet at τ 6.15 (6H) showing the presence in the base of four C-methyl, one N-methyl, and one methoxy groups. The three-proton signal at τ 5.94 corresponds to the $-O-CH_2-CH-O-$ grouping. In the weak field region of the spectrum there is a one-proton singlet at τ 4.07 showing the absence of substitution at C_3 of the quinoline nucleus, a two-proton doublet at τ 2.94, and a one-proton triplet at τ 2.47 with approximately the same distances between the components (J = 5 Hz), representing an ABX system, the chemical shifts of the A and B protons coinciding and the constants J_{AX} and J_{BX} differing [2]. In this case, the triplet corresponds to a proton at C_5, since in the 4-methoxyquinoline nucleus this proton appears in a weaker field [3]. A direct comparison of the NMR spectra of I and of foliosidine (II) showed that they are very similar and differ only by the absence of signals from protons of hydroxy groups and by the presence of signals from the protons of four $C-CH_3$ groups in the spectrum of I instead of two $C-CH_3$ groups in the spectrum of II. The nature of the splitting of the signals from the aromatic protons in the spectra of I and II is the same. All these facts enable us to assume that in I a gem-dimethyl group is attached to two adjacent oxygen atoms of the side chain of foliosidine. In actual fact, when I was heated in ethanolic solution with hydrochloric acid a phenolic base with mp 232°C, identical with the norfoliosidine obtained from foliosidine under similar conditions [1] and a nonphenolic base with mp 140°C which proved to be foliosidine were obtained. The latter was also formed by heating I with dilute sulfuric acid. On the other hand, the condensation of foliosidine with acetone in the presence of acid led to the formation of a substance with mp 119°C which gave no depression of the melting point with our base. Their IR spectra were also identical. Thus, base I is foliosidine acetonide. Since on treating the combined alkaloids we used acetone and acid, the base I is probably formed from foliosidine and is not a natural alkaloid; this will be checked subsequently.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 724-727, November-December, 1970. Original article submitted October 20, 1970.

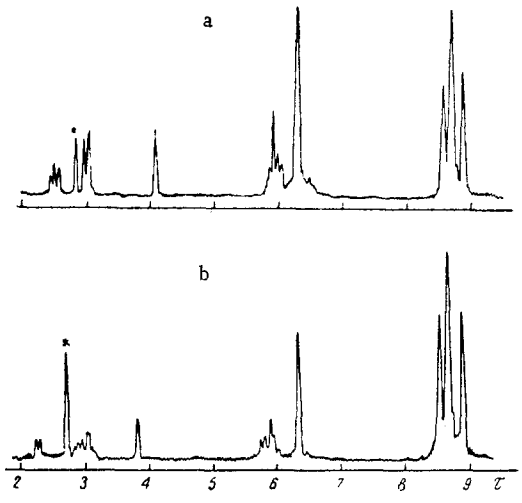
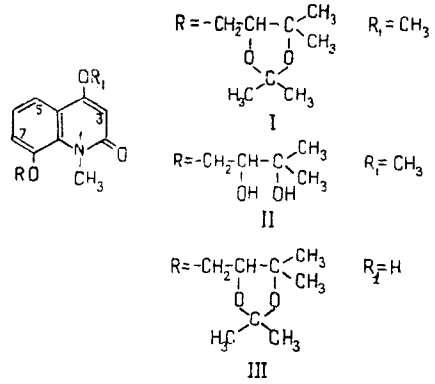


Fig. 1. NMR spectra of foliosidine acetonide (a) and norfoliosidine (b).



In view of the fact that the assignment of the signals from the aromatic protons for foliosidine [4] differs from that for foliosidine acetonide, we have studied the NMR spectrum of norfoliosidine acetonide (III).

As was to be expected, in the spectrum of III the signal from the proton at C_5 is displaced downfield by 8 Hz as compared with the signal from the same proton in the spectrum of I, and this shows that the signal in the weaker field is due to the proton at C_5 and not that at C_7. In the spectrum of III, the aromatic protons appear in the form of a one-proton quartet at τ 2.39 and a two-proton multiplet with a center at 3.00. There is no signal from the protons of a methoxy group. The other protons are found at τ 4.03 (H_3), 5.80-6.10 (−O−CH−CH_2−O−), 6.31 (N−CH_3), 8.56, 8.65, and 8.83 (4C−CH_3 groups).

EXPERIMENTAL

Isolation of Foliosidine Acetonide. A solution of 313 g of the combined chloroformic alkaloids in 600 ml of acetone was acidified with 10% HCl. On cooling, dubinidine hydrochloride (48.5 g) deposited. On the following day folifine (14.1 g) [6] crystallized from the mother solution. The acid acetonic mother solution was made alkaline with sodium carbonate, distilled to small volume, and again acidified with 10% HCl. On cooling, 18 g of the hydrochloride of I with mp 156.5-157.5°C (ethanol−ether) deposited. When ammonia was added to an aqueous solution of the hydrochloride of I, the colorless base deposited with mp 119-120°C (petroleum ether), $[\alpha]_D^{20}$ + 51° (c 2.5; methanol); picrate of I mp 182-183°C (ethanol).

The combined nonphenolic alkaloids (18.3 g) after the separation of the dubinidine were chromatographed on alumina (550 g). The ethereal eluates yielded foliosidine acetonide.

Oxidation of Foliosidine Acetonide. 0.1 g of the base was treated with 0.8 g of chromic anhydride, 1 ml of conc. sulfuric acid, and 3 ml of water, and the mixture was heated. The volatile products were trapped in a 0.1% solution of 2,4-dinitrophenylhydrazine hydrochloride. A precipitate of acetone 2,4-dinitrophenylhydrazone with mp 123-124°C (ethanol) was formed.

Action of Hydrochloric Acid on Foliosidine Acetonide. A solution of 0.35 g of the base in 5.5 ml of ethanol and 1.5 ml of conc. HCl was heated in the water bath for 6 h. Then the ethanol was driven off and the residue was dissolved in 4% caustic soda solution. The alkaline solution was washed with chloroform and acidified with acetic acid. The resulting precipitate of norfoliosidine (0.14 g) was separated off, mp 231-235°C (ethanol).

The chloroformic extract was dried over sodium sulfate and was then distilled. On treatment with acetone the residue crystallized. The yield of foliosidine was 0.13 g, mp 139°C.

Hydrolysis of Foliosidine Acetonide. A mixture of 0.2 g of the base and 10 ml of 5% sulfuric acid was heated on the sand bath for 1 h. The acid solution was cooled and made alkaline with ammonia. This gave foliosidine (0.18 g) with mp 140-141°C (acetone).

Preparation of Foliosidine Acetonide. A solution of 0.6 g of foliosidine in 30 ml of acetone was treated with 1 ml of conc. sulfuric acid. After 12 h, the acid solution was brought to slight alkalinity with anhydrous sodium carbonate. The acetone solution was separated from the precipitate and evaporated.

The residue was treated with ether. The ethereal solution was evaporated to small volume and petroleum ether was added. On cooling, foliosidine acetonide (0.31 g) precipitated with mp 119-120°C (petroleum ether).

Norfoliosidine acetonide (0.13 g) was obtained from norfoliosidine (0.2 g) by the method described above, mp 246-247°C (ether).

SUMMARY

Foliosidine acetonide has been isolated from the mixture of alkaloids from H. foliosum.

LITERATURE CITED

1. V. I. Pastukhova, G. P. Sidyakin, and S. Yu. Yunusov, KhPS [Chemistry of Natural Compounds], 1, 27, 1965.
2. V. I. Ionin and B. A. Ershov, NMR Spectroscopy in Organic Chemistry [in Russian], 1967, pp. 33, 161.
3. A. V. Robertson, Austral. J. Chem., 16, 451, 1963.
4. M. R. Yagudaev and S. Yu. Yunusov, KhPS [Chemistry of Natural Compounds], 4, 201, 1968.
5. G. P. Sidyakin, M. Eskairov, and S. Yu. Yunusov, ZhOKh, 30, 338, 1960.
6. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, KhPS [Chemistry of Natural Compounds], 3, 257, 1967.