Glaucine and base (III) were obtained by the preparative separation of fraction AF-1 on a fixed layer of SiO_2/gypsum in the chloroform—benzene (8:2) system.

Thalrugosine and Base (II). Fraction CF-2 was chromatographed on a column of Al_2O_3. The bases were eluted with benzene, ether, chloroform, and methanol, the eluate being collected in 50-ml portions. From the first chloroform fraction, by preparative spearation on plates with SiO_2/gypsum in the cyclohexane—ethyl acetate—DEAE (6:2:2) system we obtained 0.04 g of thalrugosine.

Base (II) was obtained by the comparative separation of the second chloroform fraction on plates with SiO_2/gypsum in the chloroform—methanol—concentrated NH_4OH (12.5:3:0.05) system.

SUMMARY

Glaucine, N-methylnantenine, thalrugosine, magnoflorine, berberine, and the unidentified bases (II) and (III) have been obtained from the roots and rhizomes of *Thalictrum sachalinense*. The main alkaloid in the combined bases of the roots and rhizomes was magnoflorine.

LITERATURE CITED

1. D. Umarova, C. Kh. Maekh, S. Yu. Yunusov, P. G. Gorovoi, and É. V. Boiko, Khim. Prirodn. Soedin., 788 (1976).
2. J. R. C. Bick, J. Harley-Masson, N. Sheppard, and M. J. Vernengo, J. Chem. Soc., 1896 (1961).
3. L. A. Mitscher, Wu-nan Wu, R. W. Doskotch, and I. L. Beal, Chem. Commun., 589 (1971); L. A. Mitscher, Wu-nan Wu, R. W. Doskotch, and J. L. Beal, Lloydia, 35, 167 (1972).
4. M. Shamma and S. Y. Yao, Experientia, 29, 517 (1973).
5. C. Goepel, T. Yupraphat, P. Pachaly, and F. Zymalkowski, Planta Med., 26, 94 (1974).
6. J. S. K. Ayim, D. Dwuma-Badu, N. Y. Fiagbe, A. M. Ateya, D. J. Slatkin, J. E. Knapp, and P. L. Schiff, Lloydia, 40, 561 (1977).
7. Wu-nan Wu, J. L. Beal, L. A. Mitscher, K. N. Salman, and P. Patie, Lloydia, 39, 204 (1976).
8. S. Kh. Maekh, P. G. Gorovoi, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 560 (1976).
9. M. Shamma and J. L. Moniot, Heterocycles, 3, 297 (1975).

STRUCTURE OF A TRANSFORMATION PRODUCT OF PERFORINE AND HAPLOPHYLLIDINE

I. A. Bessonova, M. R. Yagudaev, and S. Yu. Yunusov

UDC 547.944/945

Perforine (I) and haplophyllidine (II) belong to the type of 5,6,7,8-tetrahydrofuranoquinoline derivatives that are found only in the plant *Haplophyllum perforatum* (family Rutaceae) [1]. In their chemical properties, these compounds differ from the furanoquinoline alkaloids. In particular, in contrast to the latter, the methoxy group in position 4 of perforine and haplophyllidine does not undergo saponification when the compounds are heated with strong acids (25% sulfuric or hydrochloric acid), but cyclization followed by elimination of a molecule of methanol, leading to compound (III) is observed.

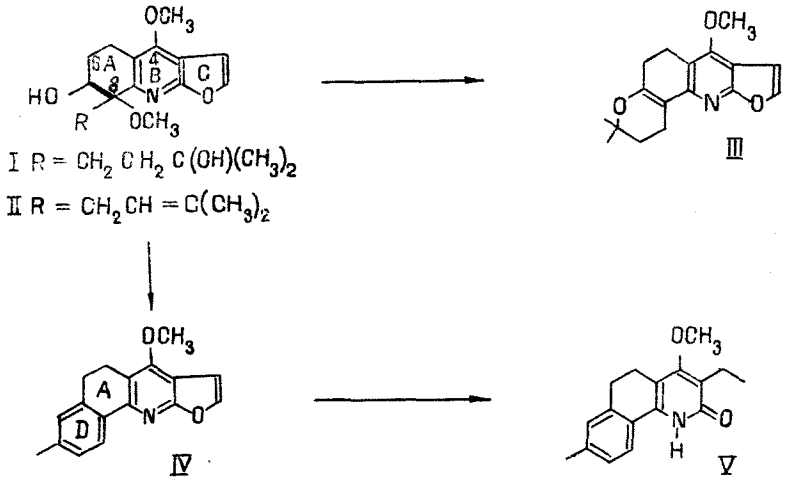
It has been reported previously [2] that the reaction of perforine and haplophyllidine with concentrated sulfuric acid leads to the same product with the composition $C_{17}H_{15}NO_2$ (IV), mol. wt. 265 (mass spectrometry) [2]. In the present paper we consider the structure of (IV). In its composition, (IV) differs from haplophyllidine by CH_3OH, H_2O, and H_2, and from perforine by CH_3OH, $2H_2O$, and H_2. The two oxygen atoms present in (IV) are contained in a methoxy group, which was determined by the method of Vieböch and Brecher, and a furan ring. The presence of the latter was confirmed by the production, when (IV) was subjected to Adams

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 597-601, September-October, 1978. Original article submitted May 18, 1978.

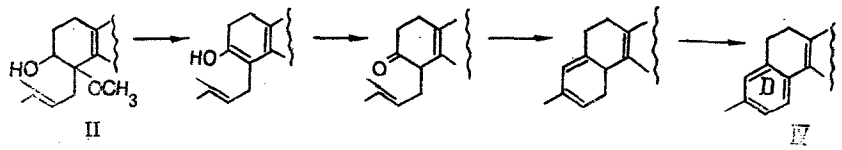
0009-3130/78/1405-0513$07.50

hydrogenation, of a tetrahydro derivative (V), mol. wt. 269 (mass spectrometry) the IR spectrum of which contained a strong absorption band (1647 cm^{-1}) characteristic of 2-quinolones [3].

The UV spectrum of (IV) differs from those of (I-III) and of the alkaloids of the furanoquinoline type [2]. Its IR spectrum contains absorption bands at (cm^{-1}) 3158, 3130 (furan ring), 1605, 1590, 1570, 1539 (aromatic system), and 875, 830 (1,2,4-substituted benzene ring). This information, and also the total number of rings and unsaturated bonds (R) calculated from the molecular formula of (IV), which is 11 [in the 5,6,7,8-tetrahydrofuranoquinoline system R = 7, and the benzene ring introduced into the (IV) molecule increases this



number by 4] [4], permits the assumption that in the reactions of (I) and (II) with concentrated sulfuric acid the elimination of a molecule of methanol and intramolecular condensation with the splitting out of a molecule of water accompanied by the aromatization of the resulting ring D take place:



The characteristics of its PMR spectrum (in CCl_4) confirm the structure (IV). In the spectrum of (IV) (Fig.1) there are signals the chemical shifts of which are typical for the protons of a methyl group bound to a benzene ring (2.28 ppm, 3H, broadened singlet), of two benzyl methylene groups (2.77 ppm, 4H, broadened singlet), a methoxy group at C_4 (4.08, 3H, singlet), a furan ring (7.38 and 6.70 ppm, doublets, 1H each, J = 2.5 Hz), and a 1,2,4-substituted benzene ring. In the spectrum, the three protons of the benzene ring give a pattern corresponding to an ABX three-spin system. The chemical shifts of the protons of this system have the values δ_A 6.83, δ_B 6.98, and δ_X 8.10 ppm. The ortho-coupling constant of the B and X protons is 8.5 Hz. It is difficult to determine the meta-coupling constant of the A and B protons from the spectrum because of their long-range allyl spin–spin coupling with the protons at C_6 ($ArCH_2$) and the $ArCH_3$ protons; the para-coupling constant $J_{AX} \approx 0$. Consequently, we made use of the method of double and triple resonance.

On irradiation with an additional frequency corresponding to the resonance transitions of the $ArCH_2$ protons (ν_2 277 Hz), the intensity of the signal of the A proton rises, and a meta constant with a B proton of approximately 2 Hz appears, and with the simultaneous superimposition of frequencies of 277 and 228 Hz; i.e., under triple resonance conditions, the meta-coupling constant appears clearly in the signals of the A and B protons, their intensities rising considerably, obviously because of an intramolecular nuclear Overhauser effect (NOE) between the irradiated $ArCH_2$ and $ArCH_3$ protons and the observed A and B protons.

Analysis of mass-spectrometric results also confirms the structure (IV). The strongest peaks of ions in the spectrum of (IV) are those of the molecular ion, which has the maximum intensity, and of the $(M-1)^+$ ion arising through the detachment of hydrogen from the methyl group attached to the benzene ring. The peaks of the other ions, with the exception of an ion with m/e 250, which is formed by the splitting off of a methyl radical from the methoxy group,

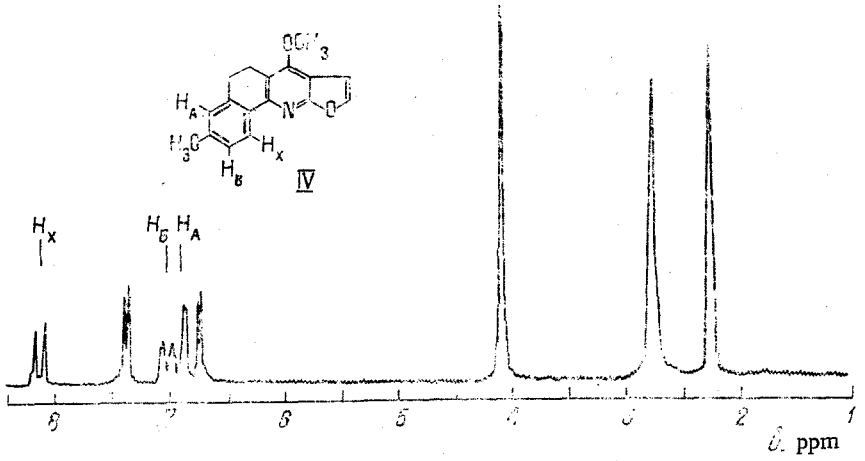
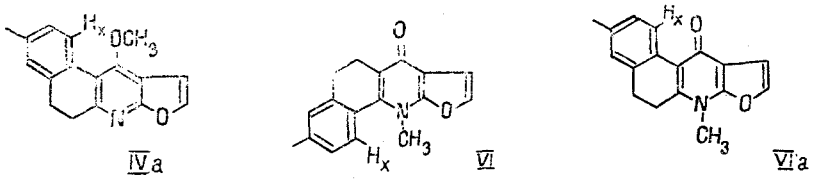


Fig. 1. NMR spectrum of compound (IV).

are of very low intensity. The spectrum of (IV) includes the peak of the doubly charged ion M^{++}. Such behavior under mass-spectrometric conditions is characteristic for aromatic compounds [5].

Structures (I) and (II) have been established as the most probable for perforine and haplophyllidine, respectively (for these alkaloids, structures with the OH substituent at C_6 and the OCH_3 and R substituents at C_5 are equiprobable). A consideration of the NMR spectra of (IV) (equivalence of the protons of the methylene groups of ring A, appearing in the form of a broadened singlet the chemical shift of which is typical for $ArCH_2$ [6a]; the absence of a NOE between the protons of the OCH_3 group and H_X on irradiation with the additional frequency ν_2 408 Hz corresponding to the resonance of the methoxy group) permits formula (IV) to be regarded as correct. If the cyclization product had the structure (IVa), the methylene protons of ring A could not be equivalent (the protons of a methylene group attached in the α position of a pyridine ring resonate in the weaker field at 3.00-3.15 ppm [6b]) and an NOE should be expected between the adjacent protons of the methoxy group and H_X [see formula (IVa)]:



For a definitive proof of the structure (IV) [and, correspondingly, of (I) and (II)] we isomerized (IV) with methyl iodide [7], since the conversion of compound (IV) into an iso compound would permit an unambiguous answer to the question of the position of linkage of rings A/D. If the iso compound had the structure (VIa), its PMR spectrum would show a paramagnetic shift of the H_X signal relative to its position in the spectrum of the initial compound by approximately 0.9 ppm [8] as a consequence of the anisotropic influence of the carbonyl group. We obtained an iso compound (VI) in the PMR spectrum of which (in $CDCl_3$) the signals of the aromatic protons of ring D appeared in the form of a multiplet in the 7.42-7.06-ppm region. Consequently, in the spectrum of (VI) there is a diamagnetic shift of the H_X signal ($\Delta\delta$ = 0.7 ppm) which is obviously due to the weakening of the aromaticity of ring B and to the screening of the N-methyl group in comparison with the initial compound [in the PMR spectrum of (IV) taken in $CDCl_3$, δH_X = 8.18 ppm]. This fact unambiguously indicates that the cyclization product has the structure (IV).

The determination of the structure of products (IV) confirms the structures (I) and (II) previously put forward for perforine and haplophyllidine [2].

EXPERIMENTAL

The UV spectra were taken on a Hitachi EPS-3T spectrophotometer (in C_2H_5OH), the IR spectra on a UR-20 instrument (in KBr), the mass spectra on an MKh-1303 instrument, and the PMR spectra on a JNM-4H 100/100 MHz spectrometer (0 — HMDS, δ scale). For TLC we used KSK silica gel with 5% gypsum in the toluene—ethyl acetate—formic acid (5:3:1) solvent system, with Dragendorff's reagent to reveal the substances on the chromatogram.

The preparation of (IV) from (I) and (II) has been described previously [2].

Substance (IV), mp 125-126°C, $[\alpha]_D^{24}$ ±0 (c 2.17; chloroform); UV spectrum, λ_{max}: 219, 232 (inflection), 250 (inflection), 281 (inflection), 295, 315 (log ε 4.40, 4.32, 4.00, 4.24, 4.32, 4.36). Mass spectrum, m/e (%): 265 (100, M^+), 264 (33), 250 (15), 234 (6), 222 (6), 192 (8), 132.5 (4).

Hydrogenation of (IV). Substance (IV) (0.5 g in 15 ml of ethanol) was hydrogenated with hydrogen over a platinum catalyst for 2 h. The catalyst was filtered off with suction and the filtrate was evaporated to give compound (V) with mp 232-233°C (from ethanol). UV spectrum, λ_{max}, nm: 240 (inflection), 260, 270, 282, 302, 338 (inflection), 352 (log ε 3.97, 3.78, 3.63, 3.50, 3.46, 4.09, 4.13); the spectrum did not change on acidification. IR spectrum, cm^{-1}: 3138, 1647 (NH—CO). Mass spectrum, m/e (%): 269 (100, M^+), 268 (75), 254 (90). PMR spectrum (in $CDCl_3$): 7.95 (1H, doublet, J_{ortho} = 8 Hz, H_X); 7.06 (1H, quartet, J_{ortho} = 8 Hz, $J_{meta} \approx 2$ Hz, H_B); 6.97 (1H, doublet, $J_{meta} \approx 2$ Hz, H_A); 3.70 (3H, singlet, OCH_3); 2.90-2.45 (6H,, multiplet, 3 CH_2—Ar); 2.30 (3H, broadened singlet, Ar—CH_3); 1.19 (3H, triplet, J = 7.5 Hz, CH_2—CH_3).

Isomerization of (IV) to (VI). In a sealed tube, 0.15 g of substance (IV) was heated on a boiling-water bath for 10 h with a mixture of 2 ml of methanol and 3 ml of methyl iodide. The residue after the evaporation of the solvents was chromatographed on a column of alumina. The residue obtained by the evaporation of chloroform eluates was dissolved in 10% sulfuric acid. The acid solution was washed with ether, made alkaline, and extracted with ether, and the distillation of the ether then yielded the iso compound (VI) with mp 198-200°C. It dissolved readily in chloroform, acetone, and methanol. In the light, the solutions turned pink. UV spectrum, λ_{max}, nm: 227 (inflection), 254, 291 (inflection), 309, 324 (inflection), 332 (inflection) (log ε 4.11, 4.23, 4.08, 4.18, 4.03, 3.72); in an acid medium, λ_{max}, nm: 214 (inflection), 227 (inflection), 248 (inflection), 256 (inflection), 298 (inflection), 330 (log ε 4.31, 4.15, 3.93, 3.90, 4.00, 4.20). IR spectrum: 1630 cm^{-1}. Mass spectrum, m/e (%): 265 (65, M^+), 264 (100), 250 (15). The PMR spectrum of a sample dried at 100°C (in $CDCl_3$, ppm): 7.42-7.06 (3H, multiplet, aromatic protons); 7.27 and 6.98 (doublets, 1 H each, J = 2.3 Hz, protons of a furan ring); 3.90 (3H, singlet, OCH_3), 2.90-2.50 (4H, multiplet, 2 CH_2—Ar); 2.35 (3H, broadened singlet, Ar—CH_3).

SUMMARY

The structure of compound (IV) formed by the action of concentrated sulfuric acid on perforine and haplophyllidine has been established, and thus unambiguously confirms the structures proposed previously for these alkaloids.

LITERATURE CITED

1. I. A. Bessonova and S. Yu. Yunusov, Khim. Prirodn. Soedin., 303 (1977).
2. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 360 (1968).
3. N. J. McCorkindale, Tetrahedron, 14, 223 (1961).
4. J. Beynon, Mass Spectrometry and Its Applications to Organic Chemistry, Elsevier, Amsterdam (1960).
5. H. Budzikiewicz, C. Djerassi, and D. Williams, Interpretation of Mass Spectra of Organic Compounds, Holden-Day, San Francisco (1964).
6. Varian NMR Spectra Catalogs, Varian Associates, Palo Alto, California, 2 (1963).
7. Y. Asahina, T. Ohta, and M. Inubuse, Ber., 63, 2045 (1930).
8. S. R. Johns, I. A. Lamberton, and A. A. Sioumis, Aust. J. Chem., 20, 1975 (1967).