ALKALOIDS OF *Haplophyllum foliosum*. II.

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In addition to the alkaloids known previously from this plant, haplofoline and folifine, from the epigeal part of *Haplophyllum foliosum* we have isolated norgraveoline with mp 288-289°C (decomp. from acetone), and myrtopsine with mp 201-202°C (from chloroform), $[\alpha]_D - 5°$ (c 0.05; methanol), which were first obtained from *Haplophyllum dubium* and *Myrtopsis sellingii*, respectively. We have confirmed by the PMR-spectroscopic method the positions of the substituents in the dihydrofuran ring of myrtopsine suggested previously on the basis of biogenetic considerations. In addition, it has been established that the substituents are present in the trans form. This is the first time that myrtopsine has been detected in plants of the genus *Haplophyllum*.

Continuing a study of the alkaloid composition of *Haplophyllum foliosum* [1], from the combined ether-extracted nonphenolic alkaloids we have isolated haplofoline and folifine and a base with mp 201-202°C (from chloroform) $[\alpha]_D - 5°$ (c 0.05; methanol) (I) and one with mp 288-289°C (decomp. from acetone). The last-mentioned base was identified as norgraveoline by a direct comparison with a sample obtained from *H. dubium* [2].

The IR spectrum of (I) has the absorption band of active hydrogen at 3260 cm^{-1}, and its UV spectrum [λ_{max} 230, 237 inflection, 265, 272, 283, 313, 326 nm (log ε 4.67, 4.55, 3.83, 3.88, 3.79, 3.62, 3.63)], changing on acidification, is similar to those of the dihydrofuranoquinoline alkaloids of the type of platydesmine (II) [3]. The main peaks in the mass spectrum of (I) are those of ions with m/z (%) 275 (M^+, 100), 200 (100), and 59 (53). The acetylation of (I) gave a monoacetyl derivative (III) with mp 174-175°C (from ether), mol. wt. 317 (mass-spectrometrically), ν 1750 cm^{-1}.

The facts given above and also the PMR spectra of (I) and (III) (Table 1) are similar to the corresponding literature characteristics of myrtopsine, isolated from *Myrtopsis sellingii* [4], with the exception of the following. In the PMR spectra of (I) and (III) the protons of the dihydrofuran ring appear in the form of distinct doublets with the same width, while according to Hifnawy et al. [4] the signals of these protons appear in the form of poorly resolved multiplets of different widths and, in particular, for the multiplets of monoacetylmyrtopsine the values of the intervals of 4.45-4.49 and 6.70-7.10 ppm are given. Furthermore, this paper makes no assignment of these multiplets, because of which two possible structures were proposed for myrtopsine, in one of which the hydroxypropyl group was located in the α position and the hydroxy group in the β position, while the other had the opposite arrangement. The choice between them in favor of (I) was made on the basis of Grundon's biogenetic hypothesis [5].

According to the literature [6], the α protons of a dihydrofuran ring resonate in a weaker field (4.30-5.00 ppm) than the β protons (3.10-4.00 ppm) and a hydroxyisopropyl substituent causes no shift in the signals of these protons. It is generally known that a hydroxy group shifts the signals of the geminal protons downfield by $\approx$2 ppm. A comparison of the PMR spectra of (I) and (II) (Table 1) has shown that they are very close, differing only by the absence from the spectrum of (I) of the two-proton doublet at 3.52 ppm from the β protons of (II) and by the presence in place of this of a one-proton doublet at 5.64 ppm which in the spectrum of (III) undergoes a paramagnetic shift by 1.1 ppm, as is characteristic for protons geminal to a secondary hydroxy group. The signals of the α protons in the spectra of (I-III) appear in one and the same region. Consequently, the hydroxy group in (I) is attached to the β carbon atom, as a result of which the β proton resonates in a weaker field than the α proton.

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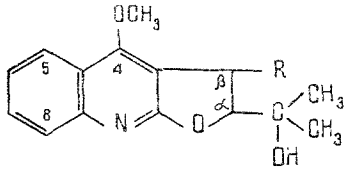
TABLE 1. Chemical Shifts of the Protons of Compounds (I), (II), and (III) (ppm)



I. R = OH
II. R = H
III. R = OAc

Compound	H_5	$H_{6,7,8}$	βCH–OH βCH–OAc	OCH_3	α CH	βCH₂	$C(CH_3)_2$	OAc
I	8,02 d J=8,5 Hz	7,78–7,05m	5,64d J=3 Hz	4,42 s	4,31d J=3 Hz		1,30 s 1,22s	
II	7,88 d J=8,5 Hz	7,60–7,00m		4,12 s	4,50d J_1=7Hz J_2=9 Hz	3,52d J=8Hz	1,25 s 1,20 s	
III	7,98 d J=8 Hz	7,60–7,00m	6,74 d J=1,5 Hz	4,16 s	4,39d J=1,5Hz		1,33 s 1,27 s	2,04 s

Note. s – singlet; d – doublet; q – quartet; m – multiplet.

Thus, an analysis of the PMR spectra of (I-III) unambiguously shows that the alkaloid isolated has the structure (I) and is identical with myrtopsine.

With the cis arrangement of the α and β protons in (I), the dihedral angle between them found from Dreiding models is small (≈0°) while when they have the trans arrangement Φ ≈ 120°, The theoretical values of the vicinal coupling constants of these protons obtained by the use of these angles are approximately 10 and 3.8 Hz, respectively [7]. A comparison of these with the experimentally observed spin–spin coupling constant of the α and β protons in (I) (Table 1) shows the trans orientation of the protons of the dihydrofuran ring of myrtopsine. The somewhat lowered value of the experimental constant is obviously due to the presence of an electronegative substituent on the β carbon atom [7]. Thus, it has been established that the substituents in the dihydrofuran ring of myrtopsine are present in the trans form.

It must be mentioned that in deuterochloroform [8], the α proton and the two β protons of (II) give, in the PMR spectrum, three one-proton quartets which are characteristic for an ABX system, while in methanol (Table 1) a degeneration of the spectrum takes place and the observed pattern in the form of a weakly resolved one-proton quartet and an unsymmetrical two-proton doublet approximates to a spectrum of the AA'X type.

EXPERIMENTAL

UV spectra were recorded on a Hitachi EPS-3T spectrophotometer (in ethanol), IR spectra on a UR-20 instrument (KBr), PMR spectra on a JNM-C-60/60 MHz spectrometer (δ scale, CD_3OD), and mass spectra on a MKh-1303 spectrometer. For TLC (silica gel L 5/40 μ) the toluene–ethyl acetate–methanol–formic acid (5 : 4 : 2 : 1) solvent system was used.

Separation of the Alaloids. For the isolation of the mixture of alkaloids from the raw material and the principle of its separation, see [1]. When the chromatography of the total ether-extracted nonphenolic bases on a column of alumina was continued, treatment with chloroform, of the ethereal eluates following edulinine gave myrtopsine (I) (0.1 g), which was crystallized from methanol and then from chloroform. The chloroform eluates yielded, successively, haplofoline (0.05 g), mp 272-273°C (from methanol), folifine (0.5 g), mp 224-225°C (from methanol), and norgraveoline (0.05 g). Haplofine and folifine were identified by direct comparison with authentic samples obtained previously from this plant [9].

Platydesmine (II), mp 138-139°C (from ether–acetone) [10].

Monoacetylmyrtopsine (III) (20 mg) was obtained from myrtopsine (23 mg) by a method described in the literature [4].

SUMMARY

1. In addition to haplofoline and folifine, obtained previously, the epigeal part of the plant *Haplophyllum foliosum* has yielded myrtopsine and norgraveoline. This is the first time that myrtopsine has been detected in plants of the genus *Haplophyllum*.

2. The positions of the substituents in the dihydrofuran ring of myrtopsine suggested previously on the basis of biogenetic considerations has been confirmed by NMR spectroscopy.

It has been established that the substituents in the dihydrofuran ring of myrtopsine are present in the trans form.

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