ALKALOIDS OF *Stephania hernandifolia*

VII. HERNANDINE

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Continuing a study of the alkaloids of the epigeal part of Stephania hernandifolia, we have obtained from the mother solutions after the separation of hernandifoline [1] a new base with the composition $C_{19}H_{25}O_6N$, which we have callied hernandine (I).

The IR spectrum of (I) (Fig. 1) has a narrow absorption band at 3530 cm^{-1} and a broad one with a maximum at 3260 cm^{-1}. The NMR spectrum of (I) (Fig. 2) exhibits the signals of three hydroxyls (δ 6.53 and 4.01, singlets; 2.68, doublet, J = 11.0 Hz; on the addition of CD_3OD these signals disappear), two methoxyls (δ 3.65 and 3.42 ppm), and a $N-CH_3$ group (δ 2.52 ppm). A two-proton singlet at 6.45 ppm relates to the ortho protons of a benzene nucleus, since on the addition of CD_3OD the singlet is converted into a quadruplet with J = 8 Hz.

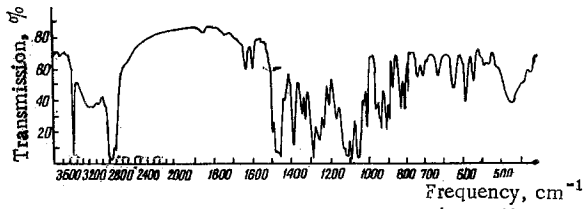


Fig. 1. IR spectrum of hernandine (paraffin oil).

On irradiation of the doublet at 4.82 ppm, J = 6.2 Hz, the quartet at 2.85 ppm, J_1 = 6.2 Hz, J_2 = 10.8 Hz, is converted into a doublet with J = 10.8 Hz, and on irradiation of the quartet at 2.85 ppm the doublets at 4.82 and 1.51 ppm, J = 10.8 Hz, become singlets (see Fig. 2). Consequently, the three protons in (I) form an AMX system (δ_A 1.51 ppm, δ_M 2.85 ppm, δ_X 4.82 ppm, J_{AM} = 10.8 Hz, J_{MX} = 6.2 Hz, J_{AX} = 0). From the value of the coupling constant, the A and M protons are geminal, and the chemical shift of the signal of the X proton (δ 4.82 ppm) is characteristic for the proton of fragment (II) [1-4].

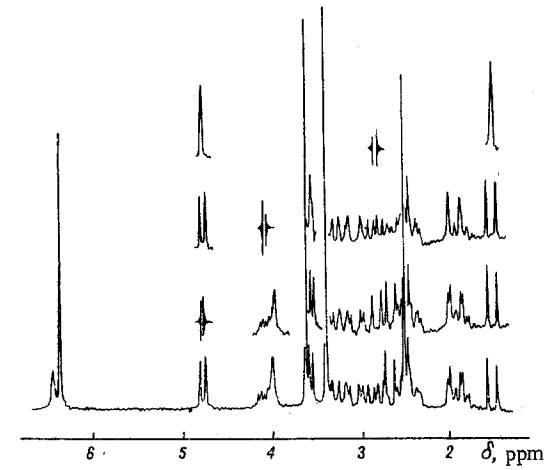
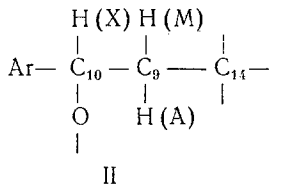


Fig. 2. NMR spectrum of hernandine in $CDCl_3$ (fragments of the double-resonance spectrum are given in the upper position, the position of the beats coincide with the position of the irradiated signals).



II

The observed nuclear Overhauser effect (NOE) [5] between the X proton and the aromatic proton confirms the presence of fragment (II) in the molecule of (I) (on irradiation of the aromatic singlet, the integral intensity of the doublet at 4.82 ppm rises by 14%). The

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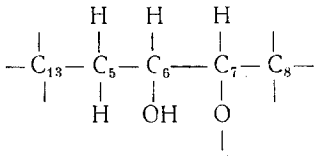
absence of spin-spin coupling between the A and X protons is characteristic of the analogous fragment in the hasubanan alkaloids with a hemiketal bridge in the $C_{10} - C_8$ position [4].

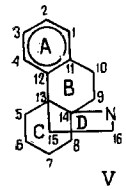
The irradiation of the multiplet at 4.15 ppm converts the doublet at 3.58 ppm, J = 3.8 Hz, into a singlet and the quartets at 3.09 ppm, J_1 = 3.5 Hz, J_2 = 14.6 Hz and at 1.95 ppm, J_1 = 2.4 Hz, J_2 = 14.6 Hz, into doublets with J = 14.6 Hz (see Fig. 2). Consequently, the 3.09 and 1.95 ppm signals can be ascribed to the protons of a methylene group, and the multiplet at 4.15 ppm and the doublet at 3.58 ppm to the methine protons of the fragment (III).



III

At C_6 there is an OH group, as is shown by the contraction of the multiplet at 4.15 ppm after the addition of CD_3OD and on the irradiation of the 2.68 ppm doublet. Addition to the C_6 and C_7 oxygen atoms is shown by the values of the chemical shifts of the C_6 – H and C_7 – H protons.

The methoxyl at 3.65 ppm is aromatic, since a NOE is observed between the aromatic proton and the protons of the methoxy group (the integral intensity of the singlet at 6.45 ppm rises by ~15% on irradiation of the signal of the methoxyl). The signals forming a complex pattern in the 1.5-3.5 ppm region belong to the other four protons of (I). Thus, the functions of all 25 protons in the molecule of (I) have been determined.



V

Information on the carbon skeleton of (I) is given by its mass spectrum (Fig. 3). A metastable peak with m/e 147.5 shows that the ion corresponding to the maximum peak of the spectrum with m/e 231 arise from the molecular ion. A comparison of the mass spectra of (I) and of metaphanine (IV) [6] (see Fig. 3) permits the conclusion that (I) has the hasubanan skeleton (V). Such a skeleton is in harmony with the IR

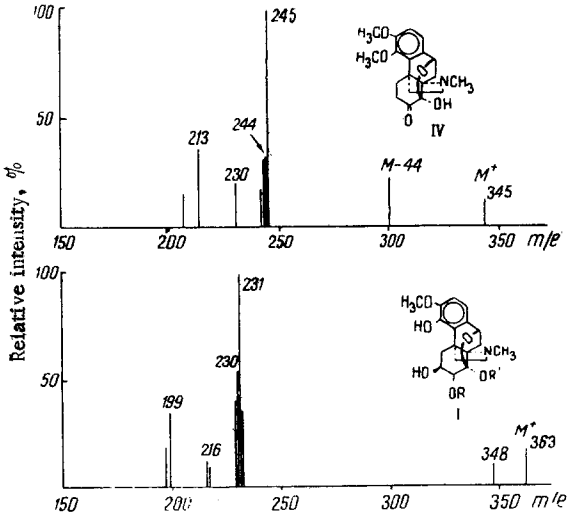
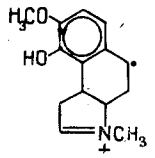


Fig. 3. Mass spectrum of hernandine (I) and of metaphanine (IV).

and NMR spectra: fragments (II) and (III) are included in the hasubanan skeleton, and the protons of the ethanamine bridge form a complex pattern in the region above 4 ppm. The shift of the peaks of moderate mass numbers in the mass spectrum of (I) by 14 units as compared with the spectrum of metaphanine is due to the fact that there is a hydroxyl in position 4 of (I). An analogous shift has been found in the spectrum of the hasubanan alkaloid aknadinine with a hydroxyl at C_4 and a methoxyl at C_3 [7]. Consequently, the ion with m/e 231 in the spectrum of (I) has structure (VI) [6].

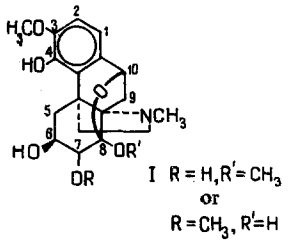


VI

On the basis of the structure of the ion with m/e 231 and the chemical shifts of the protons of the methylene group at C_5 [8], fragment (III) must be ascribed to ring C.

Summarizing what has been said, two variants of structure I may be arrived at.

The configuration of the substituent at C_6 was determined from the value of the spin-spin coupling between the protons of the CH_2 group and C_6–H. The absence of the large constant characteristic for diaxial protons enables the OH group at C_6 to be regarded as axial.



I R = H, R′ = CH_3
or
R = CH_3, R′ = H

The similarity of the spectral characteristics of hernandine and hernandifoline [1] confirms the conclusions arrived at concerning the structure of the new alkaloid.

EXPERIMENTAL

The IR spectrum of (I) was taken on a UR-10 instrument (paraffin oil), and the NMR spectrum on a HA-100D spectrometer ($CDCl_3$; internal standard HMDS, samples degassed); the mass spectrum was obtained on a MKh-1303 instrument (U_{ion} 30V, t_{ev} 150°C) by Yu. S. Nekrasov.

Hernandine (I). The chloroformic mother solution after the separation of the adduct of hernandifoline [1] was evaporated in vacuum. The resinous residue was treated several times with 10% hydrochloric acid. The combined acid solutions were exhaustively extracted with ether and the extract was washed with 10% ammonia solution and then with water. After drying over sodium sulfate, the chloroform was evaporated off and the residue was crystallized from ethanol. This gave 0.2 g of hernandine with mp 197-199° C $[\alpha]_D^{20}$ – 33° (c 1.8; ethanol).

Found %: C 62,24; H 6,95; N 3,95. *M* 363 (mass spectrometric). $C_{19}H_{25}O_6N$.
Calculated %: C 62,80; H 6,88; N 3,85. *M* 363.

SUMMARY

The epigeal part of Stephania hernandifolia has given a new hasubanan alkaloid with the composition $C_{19}H_{25}O_6N$, mp 197-199° C (ethanol), $[\alpha]_D^{20}$ – 33° (c 1.8; ethanol), which has been called hernandine, and for which a partial structure has been proposed.

LITERATURE CITED

1. D. A. Fesenko, I. I. Fadeeva, T. N. Il'inskaya, M. E. Perel'son, and O. N. Tolkachev, Khim. Prirodn.

Soedin., 7, 157 (1971) [in this issue].
2. D. B. MacLean, R. A. Bell, J. K. Saunders, C. Y. Chen, and R. H. F. Manske, Can. J. Chem., 47, No. 19, 3593 (1969).
3. R. H. F. Manske, R. G. A. Rodrigo, D. B. MacLean, D. E. F. Gracey, and J. K. Saunders, Can. J. Chem., 47, No. 19,3589 (1969).
4. M. Tomita, T. Ibuka, Y. Inubushi, and K. Takeda, Tetrahedron Lett., No. 48, 3605 (1964).
5. R. A. Bell and J. K. Saunders, Can. J. Chem., 48, No. 7,1114 (1970).
6. M. Tomita, A. Kato, and T. Ibuka, Tetrahedron Lett., No. 15, 1019 (1965).
7. B. K. Moza, B. Bhaduri, D. K. Basu, J. Kunitomo, Y. Okamoto, E. Yuge, Y. Nagai, and T. Ibuka, Tetrahedron, 26, No. 2, 427 (1970).
8. I. I. Fadeeva, M. E. Perel'son, T. No. Il'inskaya,and A. D. Kuzovkov, Farmatsiya, 2, 28 (1970).