AN INVESTIGATION OF THE ALKALOIDS OF Physochlaina dubia

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UDC 547.944

The chloroform extraction of the roots of Physochlaina dubia Pasch. (Ph. alaica E. Korot.), collected on May 16, 1971 in the flowering phase in the Rishtan region of the Fergana oblast, yielded 1.25% of total alkaloids. Separation of the mixture of bases according to their solubilities in various organic solvents gave hyoscyamine [1] and base (I) with mp 61-62°C. The IR spectrum of (I) showed absorption bands at (cm^{-1}) 710 and 760 (monosubstituted) and 1722 (ester carbonyl group) and a broad band at 3380-3420 cm^{-1} (active hydrogen). Its UV spectrum, like the spectrum of hyoscyamine [2], has a broad band at 243-262 nm.

The NMR spectrum of (I) is close to that of hyoscyamine, showing signals of the protons of a $N-CH_3$ group (δ 2.32 ppm, 3H, singlet), a three-proton multiplet (δ 2.88 ppm, protons at C_1, C_5, and in a hydroxy group), a two-proton doublet of a hydroxymethylene group (δ 3.78 ppm), and the signals of the protons of a monosubstituted benzene ring (δ 7.25 ppm, 5H).

The molecular weight of (I) found by mass spectrometry (M^+ 305) differed from that of hyoscyamine by 16 m/e. This shows that the alkaloid (I) is apparently a hydroxy derivative of hyoscyamine. This was confirmed by the formation of a diacetyl derivative of (I) with mp 74.5-75.5°C (M^+ 389). Since compound (I) is a monosubstituted nonphenolic derivative, the second hydroxy group is probably located in the tropane moiety of the molecule.

In the mass spectra of the tropane and some pyrrolidine alkaloids, the main direction of fragmentation is the α-cleavage of the ring with the subsequent elimination of a molecule of ethylene [3]. The mass spectrum of (I) shows a similar pattern: the peak of an ion with m/e 261, the appearance of which is explained by a metastable peak with m/e 224 was recorded. Furthermore, the mass spectrum showed peaks of ions with m/e 140, 96, 95, and 94, which are characteristic for alkaloids of the tropane series [3]. The formation of the peak of an ion with m/e 261 with the elimination of hydroxyethylene shows that in (I) the second hydroxy group is located at C_6.

Consequently, the base (I) that we have isolated from the plant for the first time has the structure of 6-hydroxyhyoscyamine.

In its melting point and some other properties, 6-hydroxyhyoscyamine hydrobromide in similar to the hydrobromide of the substance with structure (I) synthesized by G. Fodor et al. [4].

EXPERIMENTAL

By the usual chloroform extraction (8 extractions), 14 kg of the roots yielded 175 g of total alkaloids, TLC of which on silica gel in the methanol–benzene (9 : 1) system showed three spots with R_f 0.18, 0.35, 0.70.

Isolation of Hyoscyamine. A solution of 25 g of the combined alkaloids in 200 ml of 10% H_2SO_4 was brought to pH 8 with conc. ammonia solution, and the resins that precipitated were separated off. Then

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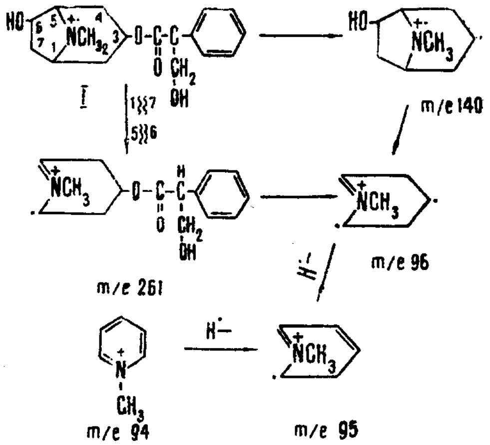
Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. M. I. Kalinin Andizhan State Medical Institute. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 493-495, July-August, 1972. Original article submitted January 25, 1972.



an excess of ammonia was added, and the precipitate that deposited was separated off, washed with water, and dried. This gave 18 g of hyoscyamine with mp 109-110°C benzene), R_f 0.18.

6-Hydroxyhyoscyamine (I). After the separation of hyoscyamine, the alkaloids in the mother liquor were extracted with chloroform. The residue after the volatilization of the chloroform (3 g) was treated with benzene. This gave (I) with mp 61-62°C (benzene), $[\alpha]_D^{20} - 13.5°$ (c 1.9; methanol), R_f 0.35, hydrobromide with mp 156-157°C (acetone).

Diacetyl-(I) (II). A solution of 0.15 g of the base in 5 ml of acetic anhydride was left for 24 h. This gave 0.18 g of compound (II) with mp 74.5-75.5°C (ether). NMR spectrum, δ, ppm: 1.97 (singlet, 6H), 2.32 (singlet, 3H). The NMR spectra were recorded in $CDCl_3$ on a JNM-4-H 100/100 MHz instrument with HMDS as internal standard.

Mass spectrum: M^+ 389 (10%); m/e: 329 (14%); 182 (100%); 122 (30%); 96 (11%); 95 (76%); 94 (55%).

SUMMARY

The roots of Physochlaina dubia collected in the flowering phase have yielded hyoscyamine (72% of the total alkaloids) and base (I). By a study of its IR, UV, NMR, and mass spectra and its chemical properties, the structure of 6-hydroxyhyosciamine has been established for (I).

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