SUBHIRSINE - A NEW ALKALOID FROM THE ROOTS OF Convolvulus subhirsutus

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The roots of *Convolvulus subhirsutus* collected on the territory of the Chimkent Province (Kazakh SSR) have yielded a new dimeric alkaloid of the tropane series subhirsine with mp 190-191°C, composition  $C_{3,3}N_{4,0}O_{9}N_{2}$ . Its structure has been established.

Previously, in a study of the alkaloids of the roots of *Convolvulus subhirsutus* Regel et Schmalh. collected in the environs of the village of Dzhilga, Chimkent Province, Kazakh SSR, in the phase of the vigorous growth of the plant, by separating the mixture of bases, into phenolic and nonphenolic fractions, we isolated five alkaloids: convolvine, convolamine [1], phyllalbine [2], convolidine [3], and confoline [4].

From the nonphenolic fraction of the combined material after separation by citratephosphate solution with pH 6.8 and with 10% sulfuric acid (fraction A), we obtained fraction B [4]. The latter was chromatographed on a column of silica gel. From ethereal eluates we isolated a base with mp 190-191°C (acetone),  $R_f$  0.27 (system 1), readily soluble in chloroform and less readily in acetone and ether. We have called it subhirsine (I).

The mass spectrum of (I) shows the peak of the molecular ion  $(M^+ 608)$  and the peak of a doubly charged ion with m/z 304, confirming the molecular weight of the alkaloid can be seen, and also the peaks of ions with m/z 443, 426, 320, 304, 290, 261, 182, and 165, together with those characteristic for tropane nucleus.

The IR spectrum of the alkaloid shows the absorption bands of a conjugated ester carbonyl group (1710 cm<sup>-1</sup>), of an amide carbonyl (1645 cm<sup>-1</sup>), and of a 1,2,4-trisubstituted benzene ring (827, 880, 1600 cm<sup>-1</sup>). The nature of the substitution in the aromatic nucleus was confirmed by the NMR spectrum of (I), which contains the signals from H<sub>a</sub> and H<sub>b</sub> protons in the 7.42-7.62 ppm region (4 H, m) and of H<sub>c</sub> at 6.82 ppm (2 H, d). The signals of methine protons on the  $C_{3\alpha}$  position (5.25 ppm, 2 H, t), from C<sub>1</sub> and C<sub>5</sub> protons (4 H, m), and from the protons of aromatic methoxy groups (3.84 ppm, 12 H, s) were also found.

The results of the mass spectroscopy of (I), its high molecular weight, and its evennumbered mass indicate the dimeric nature of the alkaloid. A comparison of the IR and NMR spectra of (I) and of convolvine shows that they are very similar, on which basis it may be assumed that subhirsine in all probability consist of two convolvine structural units. The absence from the IR spectrum of the absorption band of active hydrogen and the detection of a strong band of an amide carbonyl group indicates the nature of the bond of the two equivalent halves of convolvine through nitrogen atoms by means of a carbonyl group. Such a hypothesis required confirmation by chemical reactions, and for this purpose we performed the alkaline hydrolysis of subhirsine. On hydrolysis, an acid was isolated from the acid fraction and was identified from its  $R_f$  value and by a mixed melting point as veratric acid. From the amino alcohol fraction a substance (II) was obtained with mp 260°C and a molecular weight of 280 (mass-spectrometrically).

The IR spectrum of (II) showed bands of active hydrogen (3390 and 3455 cm<sup>-1</sup>) and the absorption band of an amide carbonyl group (1615 cm<sup>-1</sup>). A diacetyl derivative of the amino alcohol (II) was obtained, with mp 136-137°C (III).

Because of the poor solubility of the amino alcohol (II) in organic solvents, the NMR spectrum of its diacetyl derivative was taken, which clearly showed signals from the protons of a tropane nucleus and of the protons of two acetyl groups (2.01 ppm, 6 H, s). All these

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On the basis of the chemical reactions formed and the spectral characteristics both of the alkaloid itself and of the products of its chemical transformation, and also a comparative study with known alkaloids of this series, structure (I), which agrees well with all its properties, is proposed for subhirsine.

## EXPERIMENTAL

IR spectra were taken on a UR-20 spectrophotometer (molded tablets with KBr), NMR spectra on a JNM-100/100 MHz instrument with hexamethyldisiloxane as internal standard ( $\delta$  scale), and mass spectra on an MKh-1303 mass spectrometer.

For chromatography we used type KSK silica gel, alumina (Brockmann activity grade II), and the following systems of solvents: 1) cyclohexane-chloroform-diethylamine (5:4.5:0.5) and 2) chloroform-methanol-25% ammonia solution (9:1:0.1).

<u>Alkaline Hydrolysis of Subhirsine.</u> A mixture of 50 mg of the alkaloid and 5 ml of 10% methanolic KOH solution was boiled for 5 h. After the end of the reaction, the methanol was driven off in vacuum to dryness. The residue was treated repeatedly with dry ether at the boil on the water bath. The ethereal extracts were combined and concentrated. The residue formed crystals with mp 260°C. After the treatment with ether, the residue was dissolved in 5 ml of 20% sulfuric acid solution and was extracted with ether. The ethereal extract was dried with calcined calcium chloride, filtered, and concentrated, to give crystals with mp 181°C. A mixture with an authentic sample of veratric acid gave no depression of the melting point.

Acetate of the Amino Alcohol (II). A mixture of 5 mg of the amino alcohol (II) and 2 ml of acetic anhydride was left at room temperature. After a day (monitoring by TLC), the excess of acetic anhydride was driven off in vacuum. The residue was dissolved in water and after the solution had been made alkaline with concentrated ammonia it was extracted with ether. The ethereal extract was drived with potassium carbonate and concentrated, giving crystals with mp 137-138°C.

## SUMMARY

On the basis of spectral characteristics and some chemical transformations the structure of subhirsine — a dimeric alkaloid of the tropane series — has been established.

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