11-HYDROXYPLEIOCARPAMINE – A NEW ALKALOID FROM Vinca erecta

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In an investigation of the epigeal part of Vinca erecta Rgl. et Schmalh., collected on June 1-15, 1965 (in the region of the village of Sagyrdasht, Tajik SSR) in the fruit-bearing period, we established that this plant contained 0.53% of total alkaloids.

The combined alkaloids were separated into a phenolic and a nonphenolic fraction. From the latter we isolated vincamine, vincanine, vinervinine, ervamine, and akuammicine. By separating the phenolic fraction we obtained vincanidine, akuammine, and a base (I) with mp 228-229°C. It is readily soluble in ethanol, chloroform, methanol, acetone, and alkalis, sparingly soluble in ether and benzene, is revealed satisfactorily with Dragendorff's reagent and iodine vapor, and gives no coloration with cerium sulfate.

The IR spectrum of I has absorption bands at 3465 cm^{-1} (hydroxy group), 1742 cm^{-1} (ester carbonyl group), and 860, 840, and 790 cm^{-1} (1,2,4-trisubstituted benzene ring).

The UV spectrum [λ_{max} (in ethanol) 233, 285 nm (log ε 4.25, 3.64)] is characteristic for substituted indole alkaloids [1].

The NMR spectrum of the base taken on a JNM-4H-100/100 MHz spectrophotometer in deuterochloroform exhibits the signals of the protons of an ethylidene group (δ scale, 1.47 ppm, doublet, J = 6 Hz; 5.45 ppm, quartet, J = 7 Hz), of the methoxyl of an ester (3.63 ppm), and of three aromatic protons (6.49-7.15 ppm).

The IR, UV, and NMR spectra showed the absence of NH or $N-CH_3$ groups, and they are similar to the corresponding spectra of pleiocarpamine [2].

The mass spectrum of the base has peaks of ions with m/e 338 (M^+, 100%), 337 $(M-1)^+$ (6%), 323 $(M-15)^+$ (3%), 307 $(M-31)^+$ (9%), 279 $(M-59)^+$ (40%), 196 (12%), differing from the corresponding peaks of pleiocarpamine by 16 mass units. This shows the possible presence of a hydroxy group in the aromatic part of the molecule. The presence of the latter is confirmed by the preparation of an O-methyl ether of the base II. The mass spectrum of II has peaks of ions with m/e 352 (M^+, 100%), 351 $(M-1)^+$ (64%), 337 $(M-15)^+$ (14%), 321 $(M-31)^+$ (12%), 293 $(M-59)^+$ (45%).

The reduction of the alkaloid with zinc in methanolic hydrochloric acid yielded a 2,7-dihydro derivative $C_{20}H_{24}N_2O_3$ (III) with mol. wt. 340 (mass spectrometrically). Qualitative analysis by the color reaction with cerium sulfate and the UV spectrum showed that the base is an indoline derivative.

The results given above on some chemical reactions permit the assumption that the base is a hydroxy derivative of pleiocarpamine, which was first isolated from the plant Pleiocarpa mutica Benth. [3]. Since the IR spectrum of the base has absorption bands characteristic for a 1,2,4-trisubstituted benzene ring, the hydroxy group may be present in position 10 or 11. This is also shown by the chemical shifts and spin-spin coupling constants of the aromatic protons in the NMR spectrum of the base (9-H, δ, 7.15 ppm, 10-H, δ 6.54 ppm, 12-H, δ 7.05 ppm; $J_{9,10} = 7$ Hz, $J_{10,12} = 2$ Hz). By analogy with other alkaloids of similar struc-

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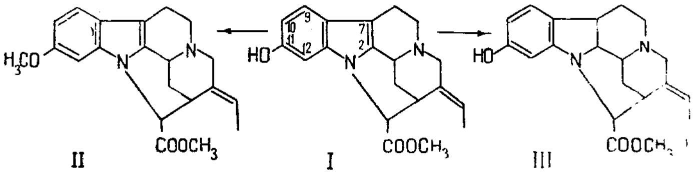
ture, we consider position 11 most probable for the hydroxy group, and for the base we propose the structure of 11-hydroxypleiocarpamine (I).



EXPERIMENTAL

The chloroform extraction of 100 kg of the plant yielded 532 g of total alkaloids, which were treated with benzene. The insoluble part (276 g) was separated off (52% of the total). The benzene-soluble fraction, 255 g (47%), was separated into phenolic (52 g – 20.4%) and nonphenolic (198 g – 77.61%) fractions. The nonphenolic fraction was dissolved in 15 liters of chloroform and separated on an apparatus for polybuffer separation with buffer solutions at various pH values (1-8). The 1st fraction, after working up, yielded 1.68 g of ervamine (0.31%), the 2nd-7th fractions 3.07 g of vincamine (0.58%), and the mother liquor 0.4 g of vincanine (0.07%), 0.3 g of vinervinine (0.05%), and 0.1 g of akuammicine (0.01% of the total weight of the alkaloids). After the extraction of the alkaloids from the chloroform solution with 5% sulfuric acid, the solution was concentrated and treated with 5% acetic acid. The acid solution of the alkaloids was made alkaline with conc.ammonia and extracted with benzene. The resulting combined alkaloids (70 g; 0.07% of the weight of the raw material) were chromatographed on a column of alumina (1 : 15 activity grade II). The 3rd-6th fractions yielded 0.3 g of vinervinine.

Base with mp 228-229°C (I). On standing, a solution of 52 g of the phenolic alkaloids in methanol gave 0.2 g of crystals of vincanidine (0.38%). Then the mother liquor was evaporated and the residue was dried. An acetone solution of the residue deposited 0.75 g of crystals (1.4% of the total phenolic bases) with the composition $C_{20}H_{22}N_2O_3$, mp 228-229°C, M^+ 338 (mass spectrometrically), $[\alpha]_D^{30}$ + 71° (c 0.7; methanol), R_f 0.21 on TLC in silica gel in the ethyl acetate – methanol (9 : 1) system.

O-Methyl Ether of I (II). A solution of 140 mg of the base in 3 ml of a mixture of chloroform and absolute ethanol was treated with 50 ml of an ethereal solution of diazomethane. The mixture was left for 4 days. Then the ethereal solution was washed with 5% KOH solution, dried over sodium sulfate, and concentrated. The oily residue, amounting to 30 mg, had R_f 0.30 on TLC in the system mentioned above and mol. wt. 352 (mass spectrometrically).

The 2,7-Dihydro Derivative of I (III). A solution of 30 mg of the substance in 60 ml of 3 N hydrochloric acid was boiled in the presence of zinc dust under reflux for 1 h. The excess of zinc was filtered off and washed repeatedly with water, and the filtrate was made alkaline with 25% ammonia solution and treated several times with chloroform. The chloroform extract was dried and distilled. TLC of the residue in the same system gave two spots: one with R_f 0.12 giving a red color with cerium sulfate and the other of the base itself with R_f 0.21. Preparative separation yielded the dihydro derivative with R_f 0.12, mol. wt. 340 (mass spectrometrically).

SUMMARY

1. From the epigeal part of Vinca erecta growing in the village of Sagyrdasht, Tajik SSR, we have isolated vincamine, vincanine, vinervinine, ervamine, akuammicine, vincanidine, akuammine, and a new base $C_{20}H_{22}N_2O_3$ with mp 228-229°C, $[\alpha]_D^{30}$ + 71° (c 0.7; methanol).

2. On the basis of IR, UV, NMR, and mass spectra on chemical properties, the structure of 11-hydroxypleiocarpamine has been proposed for the new compound.

LITERATURE CITED

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