STRUCTURE OF VINCARIDINE AND VINCARICINE

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Vincaridine [1, 2] and vincaricine [3] have been isolated from the epigeal part of Vinca erecta Rgl. et Schmalh.

Vincaridine (I) contains one methoxyl group. The IR spectrum of vincaridine has absorption bands of a O-substituted benzene ring and ester and NH groups; the UV spectrum of the base (Table 1) is characteristic for indoline alkaloids. The NMR spectrum of vincaridine (Table 2) has the signals of four aromatic protons, three protons of the methoxyl of an ester, and four protons of an ethylidene group.

Table 1

Chromophore	C_2H_5OH λ mμ (log ε)	70% $HClO_4$ γmμ (log ε)
Picrinine [5]	237, 287 (3.90, 3.51)	239, 244, 305 (3.65, 3.64, 3.67)
Vincaridine	238, 289 (3.87, 3.52)	240, 244, 300 (3.77, 3.75, 3.79)
Indole product from vincaridine	227, 283, 291 (4.13, 3.58, 3.57)	—
Vincaricine	236, 308 (3.85, 3.48)	255, 343 (3.97, 4.02)
Indole product from vincaricine	220, 282 (4.82, 4.53)	—

The action of zinc in hydrochloric acid on vincaridine gave an indole product [4]. A comparison of the UV, IR, mass, and NMR spectra, and also some chemical properties, of vincaridine and picrinine (I) showed that they were identical.

Table 2

Group	Number of protons	Picrinine [5]	Vincaridine	Vincaricine
$CH_3CH{=}C$	4	1.58—5.44	1.46 d, 5.40 q	1.45 d, 5.36 q
CH_3COO	3	3.74	3.62 s	3.67 s
$CH_3O{-}Ar$	3	—	—	3.62 s
H—C—O	1	4.92	4.79 s	4.73 s
H—Ar	4	—	6.60—6.8	—
H—Ar	3	—	—	6.53—6.69

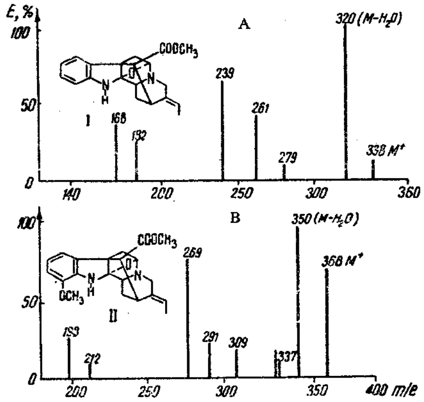
Note: The NMR spectra were taken in a JNM 4H-100 instrument; d) doublet; q) quartet; s) singlet.

Vincaricine (II), $C_{21}H_{24}N_2O_4$, has two methoxyl groups. In its IR spectrum the absorption bands appear of a NH group, an ester carbonyl group, and a 1, 2, 3-trisubstituted benzene ring; the UV spectrum of the base is characteristic of the indoline alkaloids containing a methoxyl group in the benzene ring (see Table 1). When the UV spectrum of the base was recorded in concentrated perchloric acid solutions, a bathochromic shift was observed (Table 1)

The action of zinc in hydrochloric acid on vincaricine yielded an oily product the UV spectrum of which was characteristic of the indole bases [4]. Consequently, the chromophoric group of the molecule of vincaricine is analogous to that of the molecules of the alkaloids picroline and picrinine [5, 6]. On the basis of the spectral features and elementary analysis, the formula of the alkaloid can be developed in the following way:

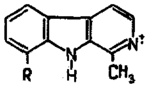
$$C_{18}H_{17}\ (NH)\ ({=}N{-})\ ({-}COOCH_3)\ (OCH_3)\ ({-}O{-}).$$

When vincaricine was oxidized by a modified Kuhn-Roth method, we detected acetic acid, which indicates the pressure of an ethylidene group, as is confirmed by the presence in the NMR spectrum of the base of signals at $\delta = 1.45$ and $\delta = 5.36$ ppm. Furthermore, the NMR spectrum of vincaricine has a three-proton singlet of the methoxyl



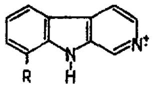
Mass spectra of picrinine (vincaridine) (A) and vincaricine (B).

of an ester (see Table 2).



A

R = H;
R = OCH$_3$



b

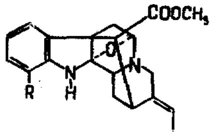
R = H;
R = OCH$_3$

The fragmentation of vincaricine under the action of electron impact takes place similarly to the fragmentation of picrinine. As can be seen from Table 3, the fragments of vincaricine differ from the corresponding ions of picrinine by 30 m/e. This shows the presence in vincaricine of a methoxyl group, which may be present in the benzene ring at $C_{(9)}$ or $C_{(12)}$ (IR spectrum). Vincaricine is a trisubstituted benzene derivative, which is shown by the presence in the NMR spectrum of the signals of three aromatic protons. In the NMR spectrum of vincaricine, the singlet at δ 3.62 ppm apparently relates to a methoxyl group at $C_{(12)}$ [7].

Table 3

Base	M^+	a	b	$(M-H_2O)$	$(M-CH_3O)$	$(M-COOCH_3)$	$(M-CO_2CH_3+$ $+H_2O)$	$M-CO+$ $+C-COOCH_3$
Picrinine [5]	338	—	—	320	307	279	—	239
Vincaridine	338	182	168	320	307	279	261	239
Vincaricine	368	212	198	350	337	309	291	269

On the basis of the results given, structure II may be proposed for vincaricine.



R = H
R = OCH$_3$

EXPERIMENTAL

Isolation of vincaridine (I). The nonphenolic ethereal fraction of the total alkaloids of **Vinca erecta** (40 g) was dissolved in 100 ml of benzene and the solution was passed through a column of alumina (1 : 30, activity grade II). On elution with benzene–ether (1 : 9), fractions XV–XX yielded a base with mp 217–218° C (from methanol), $[\alpha]_D^{22}$ − 58° (c 0.73; chloroform), mol. wt. 338 (mass spectrometry R_f 0.72 [butan-1-ol–CH_3COOH–water (5 : 1 : 5)] and R_f 0.22 in a thin layer of silica gel in the benzene–methanol (9 : 1) system; IR spectrum, cm^{-1}: 3390, 1730, 760.

Vincaridine hydrochloride has mp 186–187° C (methanol).

N-Acetylvincaridine. A mixture of 0.07 g of vincaridine and 2 ml of acetic anhydride was heated at 90° C for 2 hr. This gave N-acetylvincaridine with mp 208–209° C (ether–acetone), R_f 0.43 [ethyl acetate–methanol (9 : 1)], IR spectrum: 1630 cm^{-1}.

Indole product from vincaridine. In a similar manner to vincaricine, under the action of zinc in hydrochloric acid 0.1 g of vincaridine yielded 0.08 g of an indole base with R_f 0.85.

Vincaricine (II). After the extraction of 300 kg of epigeal part of **Vinca erecta** growing in the Fergana region, the mother liquor was treated with 5% acetic acid. This gave 350 g of combined benzene alkaloids (0.116% of the weight of the dry plant), which were dissolved in 250 ml of benzene and chromatographed through a column of alumina (1 : 10), activity grade II. On elution with benzene–ether (8 : 2), the fourth to ninth fractions yielded 20 g of a mixture of two alkaloids: vincaricine and a base with mp 177–179° C. After four recrystallizations from benzene, 1.52 g of vincaricine was obtained with mp 187–189° C (0.005% of the weight of the dry plant). Vincaricine has R_f 0.19 in TLC on silica gel [ethyl acetate–methanol (9 : 1)], R_f 0.89 [butanol–acetic acid–water (20 : 1 : 20)], $[\alpha]_D^{22}$ ± 5° (c 0.6;

chloroform); IR spectrum, cm^{-1}: 3180, 1750, 770.

Indole product from vincaricine. Over 20 min, 1.5 g of zinc dust was added in portions to a solution of 100 mg of the base in 15 ml of concentrated hydrochloric acid at −20 to −30° C. The reaction mixture was poured into ice water (150 ml) and the excess of zinc dust was filtered off. With cooling, the filtrate was made alkaline with concentrated ammonia and was extracted with ether. The ethereal solution was dried and evaporated.

This gave a pale yellow oily product with R_f 0.81 [ethyl acetate–methanol (9 : 1) system]. Yield 70 mg. When 10 mg of the base was oxidized by the Kuhn–Roth method, acetic acid was detected.

CONCLUSIONS

1. Picrinine and a new base, vincaricine, have been isolated from the epigeal part of Vinca erecta Rgl. et Schmalh.
2. The structure of vincaricine has been established by a study of its IR, UV, NMR, and mass spectra and its chemical properties.

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