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THE STRUCTURE OF HEYNEANINE (20-HYDROXYCORONARIDINE) AND ITS INTERRELATION WITH CORONARIDINE

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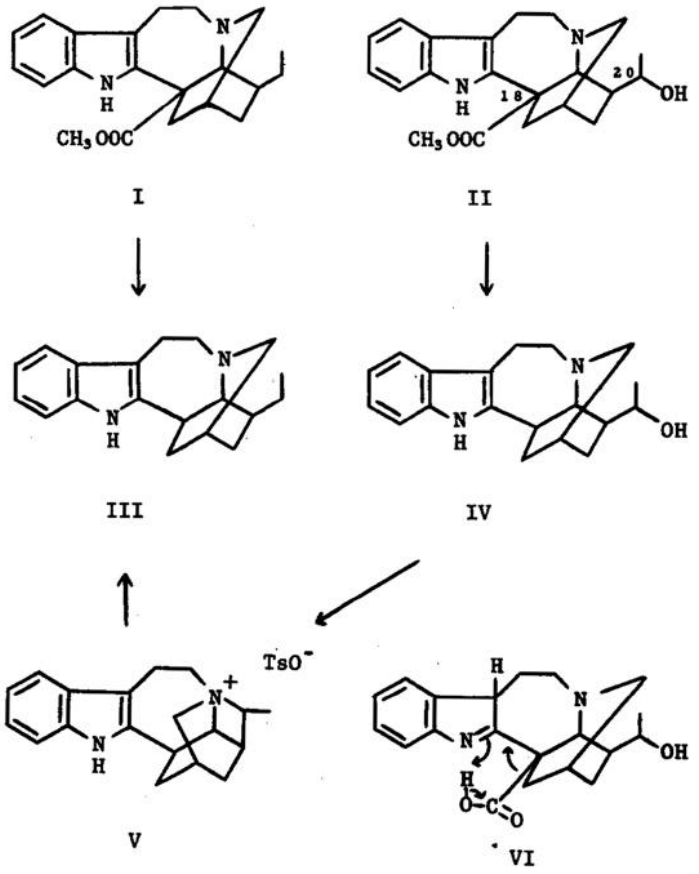
Two recent reports have described the isolation of a new alkaloid from Tabernaemontana heyneana Wall. (1) and Conopharyngia jollyana (2). The new alkaloid was characterized as 20-hydroxycoronaridine on the basis of physical evidence, and Govindachari et al. have indicated that an approach to confirm the structure chemically had been undertaken (1). The appearance of the latter reports prompts us to record our isolation of heyneanine (20-hydroxycoronaridine (II)) from Ervatamia dichotoma (Roxb.) Blatter and proof of structure of heyneanine by interrelation with coronaridine (I) by conversion to ibogamine (III).

In an earlier report, we described the isolation of coronaridine (I) from the petroleum ether-extractable alkaloids of the fruits of E. dichotoma (3). In the present study, partition of the ethanol extract of the root bark between ether and 4% hydrochloric acid gave a crude alkaloid fraction upon neutralization of the acid and extraction with ether. The ether layer was extracted with 1% sodium hydroxide to remove the phenolic bases. The non-phenolic alkaloids were chromatographed on neutral alumina, and coronaridine was eluted with benzene. Elution with benzene-chloroform (1:1) gave a fraction which was further fractionated by partition chromatography. The material was dissolved in the upper phase of the system ethylene chloride-Skellysolve B-methanol-water (2.5:15:20:0.3) and chromatographed on a column of Celite 545 impregnated with Bromcresol Purple and lower phase of the solvent system (4). Six purple bands were visible on the column. After elution, the third band yielded solid

which was crystallized from Skellysolve B to yield heyneanine, m.p. 160-161°, $[\alpha]_D^{30}$ -19° (c 0.80, chf.). The molecular formula, $C_{21}H_{26}N_2O_3$, was assigned on the basis of elemental analysis and osmometric molecular weight determination (360).

The ultraviolet spectrum (λ_{max}^{EtOH} 225, 284, 292 mμ; ϵ_{max} 32,500, 7,400, 6,500) and infrared spectrum ($\lambda_{max}^{chf.}$ 2.91 μ (indole NH), 5.80 and 8.03 μ ($COOCH_3$)) resembled those of coronaridine (I). In addition, the infrared spectrum of heyneanine showed a band at 3.15 μ which indicated the presence of a hydroxyl group. The n.m.r. spectrum showed an indole NH signal at 1.90 τ, a 4-proton multiplet in the aromatic region between 2.4 τ and 3.0 τ, indicating that the indole ring was unsubstituted, a sharp singlet at 6.26 τ, confirming the presence of the carbomethoxy group, and a doublet (3H) centered at 8.90 τ (J=6.5 cps) and a diffuse (1H) quartet centered at 5.82 τ (J=6.5 cps), indicating the presence of the $-CHOHCH_3$ group. Structure II was first considered for heyneanine on the basis of the physical data outlined above. This structure has been confirmed by an efficient degradation to ibogamine (III).

Saponification of heyneanine with alcoholic potassium hydroxide followed by decarboxylation in hydrochloric acid solution (5, 6) gave the expected de-carbomethoxy derivative IV, $C_{19}H_{24}N_2O \cdot 1/2\ CH_3OH$, m.p. 158-159° and 223-224°. The loss of the carbomethoxy group was confirmed by absence of absorption at 5.80 and 8.03 μ from the infrared spectrum of IV. Treatment of IV with p-toluenesulfonyl chloride and pyridine gave the quaternary p-toluenesulfonate salt (V), $C_{26}H_{30}N_2O_3S$, m.p. 270-271°. The presence of the p-toluenesulfonate anion was indicated by the absorption at 8.48, 8.96, 9.68 and 9.89 μ in the infrared spectrum of V (cf. 7-9). Treatment of the tosylate salt (V) with lithium aluminum hydride in benzene-ether under reflux (cf. 10) gave ibogamine (III), m.p. 161-163°, $[\alpha]_D^{27}$ -53° (c 0.40, EtOH), in 75% yield. The product was characterized by direct comparison (IR, mixed m.p., mixed t.l.c. in three solvent systems) with a sample prepared by a hydrolysis and decarboxylation sequence from coronaridine. Assignment of the carbomethoxy group of heyneanine to C-18 is indicated by the close spectroscopic and biogenetic analogy to the companion alkaloid coronaridine. This location is strongly


N
N
H
CH3OOC
I
N
N
H
CH3OOC
18
20
OH
II
N
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N
N
H
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IV
TsO⁻
N+
N
H
V
H
N
N
H
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C
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OH
VI

supported by the facile decarboxylation of the corresponding acid in dilute hydrochloric acid. The latter reaction, believed to proceed by the illustrated mechanism (VI), is probably facilitated by the almost planar geometry of the aromatic rings, C-18, and the carboxyl group (11).

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