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STRUCTURE OF VENOXIDINE, AN ALKALOID OF *ALSTONIA VENENATA* R.Br.

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In our earlier publications (1) we have reported the isolation, structure and stereochemistry of alstovenine and venenatine(1,2), the two new epimeric indole alkaloids of *Alstonia venenata* R.Br. We like to report in the present communication the isolation of reserpine (0.03%), kopsinine (0.01%) and of a new indole base which has been named venoxidine (0.01%).

Venoxidine, m.p. 218-19° (dec.), $[\alpha]_D^{25}$ - 58.20° (H_2O), possesses the molecular formula, $C_{22}H_{28}N_2O_5$*. The homogeneity of the base has been established by thin layer as well as by paper chromatography. Venoxidine is soluble in water and alcohols but almost insoluble in all common organic solvents. A solution of the base in chloroform, in which it is only sparingly soluble, sets into a thick gelly on concentration.

Venoxidine is a weak base, pka (H_2O) 4.6, and gives an unstable red picrate, m.p. 222-23° (dec.) and a hydrochloride, $C_{22}H_{28}N_2O_5.HCl$, m.p. 265-66° (dec.) but no methiodide. Two methoxyl groups and two active hydrogen atoms are present in this base which is free from C-methyl and N-methyl groups.

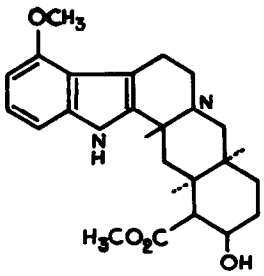
*Satisfactory analyses were obtained for all compounds reported in this communication.

Venoxidine has several absorption maxima in the ultraviolet region: $\lambda_{max.}^{EtOH}$ 224, 268 and 291 m μ (log ϵ , 4.43, 3.77 and 3.60). The infrared spectrum of the base hydrochloride exhibits bands for -OH (2.85 μ), -NH (3.04 μ), for a saturated ester (5.84 μ) and a methoxylated aromatic ring (at 6.16, 6.28 and 6.38 μ). The proton magnetic resonance spectrum of venoxidine in trifluoroacetic acid closely resembles that of venenatine, the two methoxyl singlets (6.05, 6.22 δ) of the latter collapsing to one six-proton signal at 6.0 δ in the spectrum of venoxidine. The mass spectrum of venoxidine recorded a molecular ion peak at 384 and showed a fragmentation pattern identical with that of venenatine. The discrepancy of 16 mass units between the mass spectrometrically derived molecular weight and that for $C_{22}H_{28}N_2O_5$ derived from elemental composition could not be explained until the exact structure of the alkaloid was settled from chemical evidence.

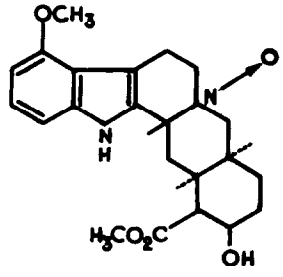
Venoxidine is amenable to catalytic hydrogenation but remains unchanged when treated with $NaBH_4$. On catalytic hydrogenation with PtO_2 in methanol as well as on reduction with zinc and acetic acid, venoxidine furnishes venenatine (I), $C_{22}H_{28}N_2O_4$, m.p. 130° (dec.). The elimination of only one atom of oxygen during this process of reduction indicates the presence of a loosely bound oxygen atom in the molecule probably as an amine oxide (3). This assumption gained credence by the observation that venenatine furnishes venoxidine as the major product on oxidation with hydrogen peroxide in acetic acid as solvent at 25°. No venoxidine could, however, be isolated when the reaction was performed with hydrogen peroxide (30%) alone, presumably because of the hydrolysis (4) of the ester function present

in the base.

The decisive experiment for ascertaining the amine oxide character of the base was its reduction with ferrous sulphate(5), a rather specific reducing agent for the conversion of N-oxides to the corresponding amines. Venoxidine on boiling with this reagent was quantitatively transformed to venenatine, an evidence which conclusively settles the structure of the alkaloid as venenatine N_b-oxide (II).



(I)



(II)

The structure (II) is also consistent with mass spectral observation and the difference of 16 mass units (between the molecular weight of the alkaloid and its molecular ion peak) is evidently due to the loss of oxygen by thermal decomposition(6) as the alkaloid had to be heated to 220° for vaporisation prior to the scanning of the spectrum.

Alkaloid N-oxides are abundant in pyrrolizidine and lupin groups (3) but their occurrence in the indole series is rare (7,8,9,10). So, venoxidine is a new addition to the naturally occurring alkaloid-N-oxide in the indole series.

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