STRUCTURE OF VINCANIDINE, AN ALKALOID FROM THE ROOTS OF Vinca erecta

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We isolated vincanidine in 1952 from the phenolic part of the total alkaloids of the roots of V. erecta [1]. By repeating the elemental analysis and determining the molecular weight we corrected the formula of vincanidine (I), which is C_{19}H_{20}O_{2}N_{2}. In the infrared spectrum of vincanidine the absorption region of the OH group and the secondary nitrogen atom is not characteristic, as a result of the formation of an intramolecular hydrogen bond. Vincanidine methiodide shows the presence of an OH group at 3380 cm\(^{-1}\) and a secondary nitrogen atom at 3160 cm\(^{-1}\). The compound showed the presence of two active hydrogen atoms by the Tserevitinov method. Vincanidine has an intense absorption band at 1660 cm\(^{-1}\), characteristic for a free carbonyl group conjugated with a double bond. This frequency is associated with the presence of a complex 2-methyleneindoline chromophore conjugated with an aldehyde group [2-6]. On ozonolysis vincanidine forms acetaldehyde, which points to the presence of an ethylidene side group. According to this vincanidine has the following developed formula:

\[
\text{C}_{19}\text{H}_{17}(=\text{N}−\text{H})(=\text{N}−)(\text{OH})−\text{C}(=\text{O})_2\text{H}
\]

The ultraviolet spectrum of vincanidine is close to that of vincanine and has three maxima, \(\lambda_{\text{max}} = 242, 291,\) and 375 m\(\mu\) [7].

The character of the ultraviolet and infrared absorption curves and the high rotatory power give grounds for the view that vincanidine contains the chromophoric system of 2-methyleneindoline conjugated with an aldehyde group and also a phenolic hydroxyl in a benzene ring. Also, the phenolic hydroxyl of vincanidine is not methylated with diazomethane and dimethyl sulfate.

\[
\text{HO}\quad \text{N}\quad \text{OCH}_3
\]

Vincanidine differs from vincanine by the presence of a phenolic hydroxyl, and it is therefore possible that the same heterocyclic system lies at the basis of both of them. To establish the basic skeleton of vincanidine it is desirable to eliminate the aldehyde and hydroxy groups. By heating vincanidine with 20% hydrochloric acid we obtained a base of composition C_{18}H_{20}ON_2 (II), m.p. 185-188° (decomp.) and \([\alpha]_D -176.1°\) (alcohol, in the infrared spectrum of which the carbonyl group is absent. The ultraviolet spectrum of this base has two maxima, \(\lambda_{\text{max}} 222\) and 262 m\(\mu\), which are characteristic of bases of 3H-indole derivatives [8]. In the reduction of the 3H-indole base (II) with zinc and sulfuric acid in absolute methanol and with sodium borohydride in an acid medium we obtained a crystalline base, m.p. 240-242° (decomp.), of composition C_{18}H_{22}ON_2 (III); \([\alpha]_D -106.6°\) (alcohol). The infrared spectrum of (III) showed the presence of an OH group at 3570 cm\(^{-1}\) and a secondary nitrogen atom at 3390 cm\(^{-1}\). The base (III) contains two active hydrogen atoms, which indicates the presence of a hydroxy group.
and a secondary nitrogen atom. The ultraviolet spectrum of the base contains two maxima, \( \lambda_{\text{max}} \) 245 and 292 \( \mu \), which is characteristic for indole bases. When reduced with sodium borohydride in an alkaline medium and with an Adams platinum catalyst in alcohol, the 3H-indole base (II) forms a base of m.p. 160-161° (IV), composition C\(_{18}\)H\(_{20}\)ON\(_2\). Its ultraviolet spectrum contains three maxima, \( \lambda_{\text{max}} \) 222, 276, and 294 \( \mu \), characteristic for indole derivatives. On the basis of the formation of 3H-indole (II), indoline (III), and indole (IV) bases, the following structures may be assigned to vincanidine and its breakdown products:

\[ \text{HO} \]
\[ \text{H} \]
\[ \text{CH}_{3} \]
\[ \text{N} \]
\[ \text{HO} \]
\[ \text{H} \]
\[ \text{CH}_{3} \]
\[ \text{N} \]
\[ \text{HO} \]
\[ \text{H} \]
\[ \text{CH}_{3} \]
\[ \text{N} \]

Vincanidine is not methylated with diazomethane, but its breakdown products are readily methylated with formation of crystalline O-methyl ethers. To eliminate the hydroxy group from the indoline base (III) the amorphous tosyl ester was prepared, and by the reduction of this with Raney nickel we isolated a crystalline dihydro tosyl ester of m. p. 153° (VI), \([\alpha]_{D}^{20} -123.3°\) (chloroform), composition C\(_{15}\)H\(_{16}\)N\(_2\)OSO\(_2\)C\(_6\)H\(_4\)CH\(_3\). The ultraviolet spectrum of this ester has the maxima: \( \lambda_{\text{max}} \) 246, 276, 303 \( \mu \). Work on the establishment of the position of the phenolic hydroxyl continues.

**EXPERIMENTAL**

Vincanidine (I) was isolated from the phenolic part of the total alkaloids of *Vinca erecta*. After purification with methanol it charred without melting at 250-280°; \([\alpha]_{D}^{20} = 548.6°\) (c 0.853, methanol). Found: C 73.5; 73.7; H 6.58; 6.53; N 9.1; 8.9; H\(_{\text{act}}\) 0.58%. C\(_{18}\)H\(_{20}\)O\(_2\)N\(_2\). Calculated: C 73.99; H 6.54; N 9.09; H\(_{\text{act}}\) 0.33%. Ultraviolet spectrum (\( \lambda_{\text{max}} \)) 242 (log \( \epsilon \) 3.95); 291 (log \( \epsilon \) 3.26), 375 (log \( \epsilon \) 4.14).

Ozonolysis of (I). 0.045 mg of (I) was dissolved in 5 ml of dry chloroform, and ozone was passed into the solution for two hours at 0°. Chloroform was then vacuum-distilled off at room temperature, 10 ml of ice water was added to the residue, and the mixture was steam-distilled. The distillate passed into a cooled saturated solution of 2,4-dinitrophenylhydrazine in 2% HCl. The precipitated crystals had m. p. 136-139°, undepressed by admixture of acetone 2,4-dinitrophenylhydrazone.

Decarbonylation of (I). 3 g of (I) was dissolved in 70 ml of 20% HCl, and an evacuated tube containing the substance was heated for three hours at 115-120°. Solvent was driven off, and we obtained 1.81 g of the 3H-indole base (II), m. p. 185-188° (decomp.) (from acetone), \([\alpha]_{D}^{14} = -176.1°\) (c 1.328 ethanol). Found: C 76.9; 76.7; H 7.37; 7.61; N 10.07% C\(_{18}\)H\(_{20}\)ON\(_2\). Calculated: C 77.1; H 7.71; N 9.99%. Ultraviolet spectrum (\( \lambda, \mu \)) 222 (log \( \epsilon \) 4.3); 262 (log \( \epsilon \) 3.66).