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THE STEREOCHEMISTRY OF VINCAMINE

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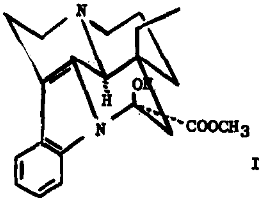
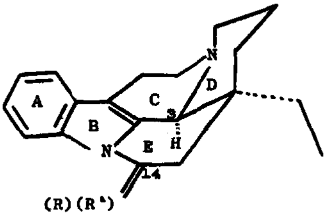
The recent communication by Clauder and co-workers[1] claiming that vincamine is I prompts us to publish data which indicate that vincamine (R = OH, R' = $COOCH_3$) must be represented by the alternate expression II with the conformation shown being the favored one.



I



II

(a) Wenkert[2] has shown that in eburnamonine the C-3 hydrogen and the C-16 ethyl side chain are cis to one another. Since vincamine has been chemically related to eburnamonine[3], the same stereochemistry must prevail in vincamine.

(b) The infrared spectrum of vincamine in chloroform solution shows a relatively simple absorption pattern near 3.4μ characteristic

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[1] O. Clauder, K. Gesztes and K. Szasz, Tetrahedron Letters 1147 (1962).

[2] E. Wenkert, J. Am. Chem. Soc. 84, 98 (1962).

[3] J. Mokrý, I. Kompiš and P. Šefčovič, Tetrahedron Letters 433 (1962).

of a cis fused C/D quinolizidine system as in II.[4]

(c) The nmr spectrum of vincamine in $CDCl_3$ solution shows a peak at 3.92 ppm for the C-3 proton. Such an absorption is also exhibited by the yohimbine-reserpine-heteroyohimbine alkaloids possessing a cis fused C/D quinolizidine system.[5]

(d) The pseudo first-order rates of methiodide formation[6] of the alkaloids or their derivatives determined on 3 mg. of each compound were:

Vincamine (R = OH, R' = $COOCH_3$) 6.0×10^{-4} $sec.^{-1}$
Vincaminol (R = OH, R' = CH_2-OH) 9.3×10^{-4} $sec.^{-1}$
Vincanorine (rac.-eburnamonine) (R,R' = =O) 2.5×10^{-4} $sec.^{-1}$
Apovincamine 8.8×10^{-4} $sec.^{-1}$

These relatively slow rates of salt formation are characteristic of a rather hindered N_b as in II above, where approach of the methyl iodide molecule is hindered by the ethyl side chain.

The stereochemistry at C-14 cannot be determined with complete certainty at present, in spite of the easy elimination of water from vincamine to give apovincamine.[7] The two substituents at this carbon atom in vincamine are respectively quasi-axial and quasi-equatorial, and the molecule is flexible enough in ring E to allow a quasiequatorial substituent in one conformation to become quasiaxial in another.

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[4] M. Shamma and J. B. Moss, J. Am. Chem. Soc. 84, 1739 (1962).

[5] E. Wenkert, B. Wickberg and C. Leicht, Tetrahedron Letters 822 (1961).

[6] M. Shamma and J. B. Moss, J. Am. Chem. Soc. 83, 5038 (1961).

[7] J. Trojánek, O. Štrouf, J. Holubek and Z. Čekan, Tetrahedron Letters 702 (1961).