

THE RELATIVE CONFIGURATION AT C<sub>(22)</sub> AND C<sub>(23)</sub> IN VERATRAMINE  
AND JERVINE

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CONSIDERATION of the stereochemistry of the piperidine moiety of veratramine (I)<sup>1</sup> shows that the side chain on C<sub>(22)</sub> must be the conformation determining substituent and hence equatorial. Therefore, if the hydroxyl group on C<sub>(23)</sub> is configurationally cis to this substituent, the hydroxyl will be largely in the axial conformation; on the other hand, if these two groups are trans, the hydroxyl will be equatorial. If, therefore, the axial or equatorial nature of the hydroxyl group were known, the relative configuration at the centres C<sub>(22)</sub> and C<sub>(23)</sub> in veratramine could be established.

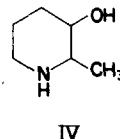
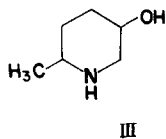
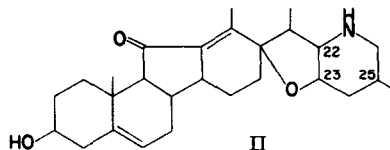
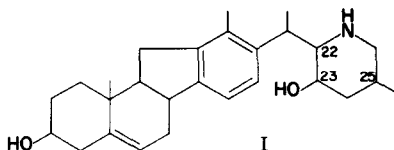
We have recently suggested that the axial or equatorial nature of the hydroxyl group in 3-hydroxypiperidine derivatives may readily be deduced from the hydroxyl stretching frequencies in the 3 $\mu$  region:<sup>2</sup> only the axial

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<sup>1</sup> Ch. Tamm and O. Wintersteiner, J. Amer. Chem. Soc. 74, 3842 (1952).

<sup>2</sup> J. Sicher and M. Tichý, Coll. Czech. Chem. Comm. 22, 2081 (1958).

hydroxyl can engage in hydrogen bonding with the ring nitrogen atom. The spectrum of a 3-hydroxypiperidine derivative containing a hydroxyl group in the axial conformation will therefore exhibit two concentration independent hydroxyl bands (free and associated) in the 3 $\mu$  region, while that of a derivative with an equatorial hydroxyl group will show only a single hydroxyl band (free).



cis, m.p. 48.5 - 49.5°  
 $\nu(\text{OH})_{\text{free}}$  3625  $\text{cm}^{-1}$   
 $\nu(\text{OH})_{\text{assoc}}$  3532  $\text{cm}^{-1}$   
trans, m.p. 97 - 97.5°  
 $\nu(\text{OH})_{\text{free}}$  3624  $\text{cm}^{-1}$

cis, m.p. 94.5 - 95.5°  
 $\nu(\text{OH})_{\text{free}}$  3632  $\text{cm}^{-1}$   
 $\nu(\text{OH})_{\text{assoc}}$  3526  $\text{cm}^{-1}$   
trans, m.p. 138.5 - 139.5°  
 $\nu(\text{OH})_{\text{free}}$  3632  $\text{cm}^{-1}$

In accordance with this rule we have found that of the two pairs of pipercolinol derivatives, III and IV, prepared as models for a semi-quantitative study to be reported on a subsequent occasion, the cis-isomers exhibit two hydroxyl bands in the 3 $\mu$  region, the trans-isomers only a single

hydroxyl band.<sup>3</sup> On the basis of these considerations we have already been able to determine the relative configuration of the propyl and hydroxyl group in the alkaloid  $\phi$ -conhydrine (trans-2-propyl-5-hydroxypiperidine).

We have now found that the spectrum of veratramine contains a single OH band (3619 cm<sup>-1</sup>). This proves that the hydroxyl group on C<sub>(22)</sub> is equatorial and therefore that the substituents on C<sub>(22)</sub> and C<sub>(23)</sub> in veratramine (I) are trans to each other. It has been shown by Wintersteiner and Moore<sup>4</sup> that the configurations at C<sub>(22)</sub> and C<sub>(23)</sub> in jervine (II) are the same as those in veratramine. Our results therefore also establish the relative configurations at C<sub>(22)</sub> and C<sub>(23)</sub> in jervine and hence show that the tetrahydrofuran ring in jervine is annelated to the piperidine ring in a trans fashion. The position of the methyl group on C<sub>(25)</sub> in both alkaloids relative to the hydroxyl group remains undecided.

We are greatly indebted to Dr. O. Wintersteiner (Squibb Institute for Medical Research, New Brunswick, N.J.) for a sample of veratramine and for very valuable comment on the relation between veratramine and jervine.

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<sup>3</sup> The spectra were measured by Dr. M. Horák of this Institute. For the technique used see J. Sicher, M. Horák and M. Tichý, Coll. Czech. Chem. Comm. 24, 950 (1959).

<sup>4</sup> O. Wintersteiner and M. Moore, J. Amer. Chem. Soc. 78, 6193 (1956).