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THE ABSOLUTE MOLECULAR STRUCTURE OF PODOPETALINE

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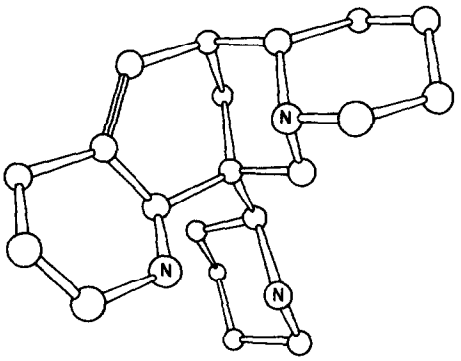
Recent investigations of the alkaloids of the Australian Leguminosae (1) have shown that C_{20}-pentacyclic alkaloids of the ormosanine-piptanthine type are by no means restricted in their occurrence to *Ormosia* and *Piptanthus* species. Structural assignments within this group of alkaloids, some of which occur in optically active form and some as racemates, are particularly difficult because of the large number of possible stereoisomers. For example, there are sixteen possible stereoisomers of the fully-reduced $C_{20}H_{35}N_3$ base ormosanine, without taking account of differences in absolute configuration (2).

An X-ray crystal structure analysis has been carried out on the monohydrobromide of podopetaline, $C_{20}H_{33}N_3$, a new optically-active base which occurs as a major component of the complex mixture of alkaloids from *Podopetalum ormondii* F. Muell. The absolute configuration is not known for any of the *Ormosia* alkaloids (3) and the X-ray analysis of podopetaline monohydrobromide is the first determination of an absolute configuration for any member of this group of alkaloids. Podopetaline therefore provides an absolute chirality reference for this group.

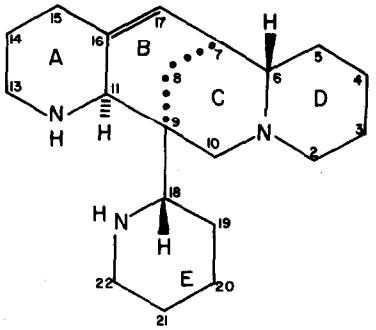
Podopetaline, m.p. 77.5-79°, $[\alpha]_D$ -48° (*c*, 0.95 in methanol), affords a crystalline monohydrobromide, $C_{20}H_{33}N_3$.HBr, m.p. 253-256°, $[\alpha]_D$ - 37° (*c*, 1.3 in methanol). Crystals of podopetaline monohydrobromide are orthorhombic, unit cell dimensions, a = 6.619, b = 10.907, c = 26.806 Å, the space group being $P2_12_12_1$, Z = 4. Intensity data for 1558 independent reflexions of which 849 were significant were measured with CuK_α radiation on a 4-circle diffractometer. The bromine sites, located from a three-dimensional vector map, were used to

derive an approximate electron-density distribution. Subsequent use of least squares refinements and difference synthesis yielded the non-hydrogen atom sites, differentiated the N atoms and defined the location of the double bond in the molecule. Final refinement by least squares has yielded a reliability index R ($\sum\Delta F/\sum F_o$) of 0.075 for the 849 observed reflexions.



I

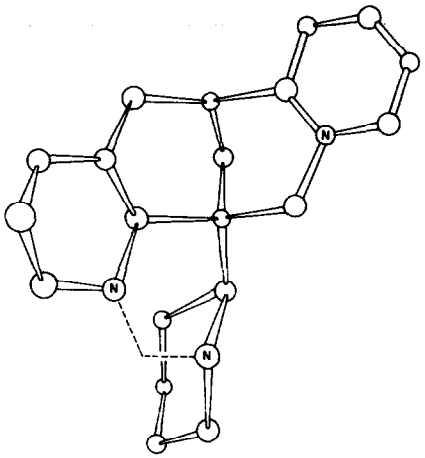
The absolute chirality of the organic cation of podopetaline hydrobromide, determined by reference to selected Bijvoet pairs, is shown in I. On this basis, the absolute structure of podopetaline is represented conventionally in II.



II

Podopetaline has the same relative configuration at C6, C11 and C18 as ormosanine, the structure of which is known from an X-ray structure analysis of jamine (4), an alkaloid identical with the product obtained by reaction of ormosanine with formaldehyde under mild conditions. There is, however, an important difference between the conformation of podopetaline and that of jamine and, presumably, also of ormosanine. Rings A, C, D and E of podopetaline are in the chair form and ring B, which contains the C16-C17 double bond, has five carbon atoms essentially coplanar and C8 out-of-plane (sofa conformation). The chair form for ring C and *cis* C/D ring junction (nitrogen lone pair *cis* to C6-H) contrasts with the conformation of jamine which has a boat form for ring C and the C/D ring junction *trans*. It seems likley that jamine, and presumably ormosanine, have the *trans* C/D conformation because steric interaction between C16-H and the nitrogen lone pair (at N1 in the quinolizidine moiety) makes the *cis* form less stable. In podopetaline, the chair-chair conformations for rings C and D and the *cis* C/D junction can be adopted, and it may be concluded that this represents the more stable conformation in the absence of steric interactions.

To facilitate comparison, the structure of jamine is depicted in III with the same orientation as I, and the absolute configuration opposite to that shown in the original paper (4).



III

The structure reported here for podopetaline has recently been assigned, on the basis of chemical and spectroscopic evidence to ormocastrine, an isomeric alkaloid from *Ormosia semicastrata* (5). However, ormocastrine, m.p. 263° (dec.), $[\alpha]_D$ -29° in methanol, differs markedly in its physical constants from podopetaline.

References

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