Alstonerine, a New Indole Alkaloid from *Alstonia muelleriana*

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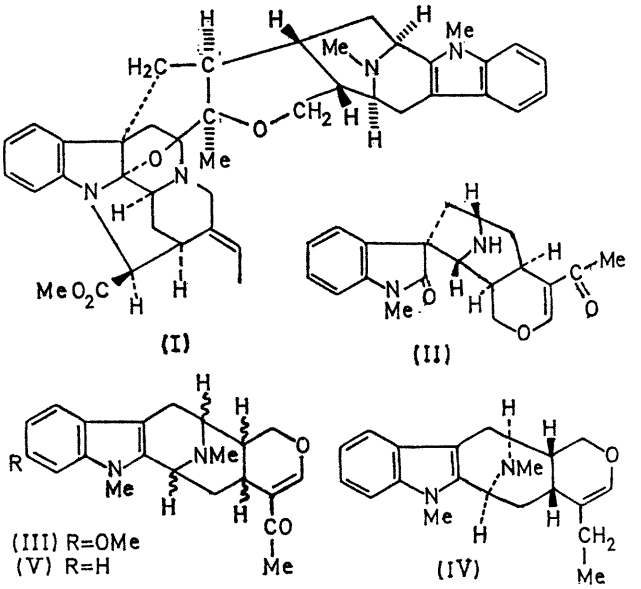
Summary Alstonerine, an alkaloid from *Alstonia muelleriana*, is a new member of the small group of indolohomotropane alkaloids consisting of alstophylline and the non-pleiocarpamine portion of villalstonine.

THE alkaloids of *Alstonia muelleriana* Domin.[1,2] are thought to be closely related to those of the *A. macrophylla* group[3] of *Alstonia* alkaloids, because of the presence in *A. muelleriana* of villalstonine (I)[4,5] and "Alkaloid C" (II).[6] We now report the structure of a new alkaloid, alstonerine (previously called Alkaloid D[1,2]), which bears an important relationship to these two compounds.

Alstonerine, m.p. 172—173°, $[\alpha]_D^{25}$ −195° (EtOH), λ_{max} (EtOH) 231, 261, 284, 293 nm (ϵ 38,000, 10,300, 8300, 7100), ν_{max} ($CHCl_3$) 1660 and 1621 cm.$^{-1}$, has the molecular formula $C_{21}H_{24}N_2O_2$ (microanalysis and mass spectrum; M^+ at *m/e* 336). The i.r. peaks at 1660 and 1621 cm.$^{-1}$ suggest the presence of an oxo-enol ether function, O C ‖ | –C–C=CH–O–C–, and the u.v. spectrum is a summation of those of this chromophore[7] and an indole nucleus. In the n.m.r. spectrum of alstonerine picrate a 1-H singlet at δ 7·55 arises from the enol ether vinyl proton. The aromatic region contains four protons from the indole nucleus, resonating at *ca.* δ 7·35, with no pyrrole N–H or indole α-H signals. A 3-H singlet at δ 2·08 is consonant



with a CH_3CO- group, permitting the expansion of the oxo-enol ether structural element to $CH_3CO-C(C)=CH-O-C-$. Two further methyl group signals, at δ 2·84 and δ 3·77, are assigned to aliphatic and indolic $N-CH_3$ groups respectively. This evidence, taken together with the absence from the n.m.r. spectrum of any signals at higher field than δ 2·0, suggests a polycyclic structure resembling that of the unusual indolohomotropane alkaloid alstophylline (III).[8] Indeed, the mass spectral fragmentation pattern was virtually identical with that of the ajmaline derivative (IV), prepared by Schmid and co-workers,[8] except for the displacement of the molecular ion (*m/e* 322) and a small peak at *m/e* 253 in compound (IV) to *m/e* 336 and 267 respectively in alstonerine. We therefore suggest the structure (V) for alstonerine, without implying at this time that alstonerine has the same stereochemistry as alstophylline, although similarities in the optical rotations and the mass spectra of the two alkaloids would support this.

Alstonerine is closely related to "Alkaloid C" (II) and to the non-pleiocarpamine portion of villalstonine (I). The possibility of its being a biogenetic precursor of "Alkaloid C" has *in vitro* analogy.[9] Work in progress in our laboratory indicates that the alstonerine skeleton is incorporated into further dimeric alkaloids of *A. muelleriana*.

We thank the Office of Research Administration of The University of Michigan for support of this work, and Mrs. Gloria Cook for valuable assistance.

(*Received, September 8th*, 1969; *Com.* 1362.)

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