Biomimetic Synthesis and Structure of the Bisindole Alkaloid Alstonisidine

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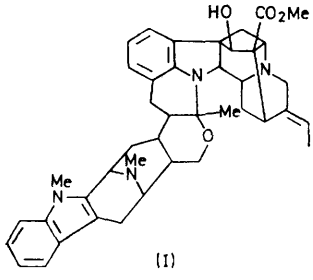
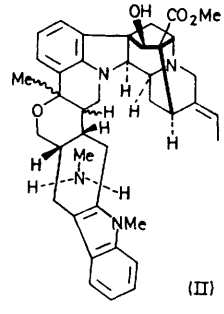
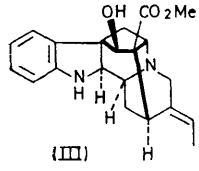
Summary Alstonisidine, a bisindole alkaloid from *Alstonia muelleriana*, is assigned the revised structure (II) on the basis of its biomimetic synthesis from quebrachidine (III) and macroline (IV).



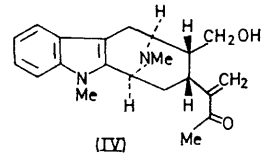
(I)



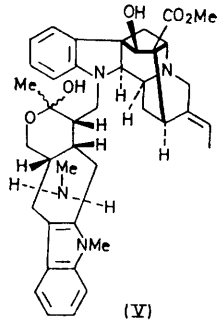
(II)



(III)



(IV)



(V)

THE bisindole structure (I) was suggested[1] for alstonisidine,[2] in preference, from data then available, to the isomeric (II; no stereochemistry).[3] Both structures can be conceived as arising from reaction of quebrachidine (III)[4] with macroline (IV).[5] More recent isolation[3] of quebrachidine from *A. muelleriana* supports this concept.

We now report that, in accord with model reactions,[3] quebrachidine (III) and macroline (IV) react in 0·2 N-aqueous hydrochloric acid at 20° for 72 h giving the labile amino-hemiacetal (V). This compound reverts to (III) and (IV) on warming or treatment with more concentrated acids, and slowly during chromatography. Structure (V) follows from these properties and from spectral data [ν_{KBr} 3570, 3430 (O–H), 1735 cm^{-1} (ester C=O); M^+ at *m/e* 690; other major peaks at *m/e* 672, 659, 481, 365, 321, and lower values characteristic of each parent alkaloid]. The stereochemistry tentatively assigned at the new asymmetric centre is based on equatorial orientation of the quebrachidine-bearing $-CH_2-$ group. Treatment of (V) with BF_3 etherate at 0° for 6h gave only alstonisidine, which must therefore be (II). This structure is also compatible with the data previously adduced.[1] The stereochemistry at the new ring junction is uncertain, but a *trans*-fusion, with α-Me and β-H, is likely. Crystallographic work is in progress. This synthesis parallels the biomimetic synthesis of villalstonine,[6] and may similarly reflect the biogenetic pathway.

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