Aristoteline, a Novel Indole Alkaloid: *X*-Ray Structural Determination

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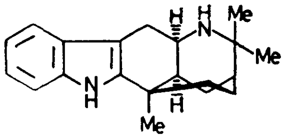
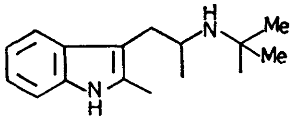
Summary *X*-Ray crystallography shows that aristoteline, the main alkaloid of the New Zealand plant *Aristotelia serrata*, has the novel indole structure (I).

THE New Zealand elaeocarpaceous plant *Aristotelia serrata* ('wineberry') contains at least five alkaloids in the roots and stems, and further bases in the leaves including peduncularine, identical with that isolated from the Tasmanian *A. peduncularis*.[1] The major wineberry alkaloid, aristoteline, was separated by standard methods in *ca.* 0·07% yield from dried plant material, and formed *ca.* 40% of the total alkaloids. After crystallisation from methanol it had m.p. 164° and $[\alpha]_D^{20} + 16°$ (MeOH); the formula $C_{20}H_{26}N_2$ was established by microanalysis and high-resolution m.s. (*cf.* $C_{20}H_{24}N_2$ for peduncularine[1]). Like the latter, aristoteline has a u.v. spectrum closely resembling that of indole, but the Ehrlich test was negative. Both ^1H and ^{13}C n.m.r. spectra were consistent with a 2,3-disubstituted indole, but neither gave evidence of olefinic groups; from its formula aristoteline thus has three rings besides an indole nucleus. Its i.r. spectrum shows an NH stretch, and in fact both nitrogens are secondary, since equilibration of aristoteline with D_2O removes 2 broad 1H resonances at δ 7·59 and 0·96 from the ^1H n.m.r. spectrum, and causes the molecular ion in the m.s. to increase in mass by 2 units; furthermore, under mild conditions aristoteline gives a crystalline *N*-acetyl derivative, m.p. 268—270°, which from its ^1H n.m.r. and u.v. spectra still retains an indolic NH. The ^1H n.m.r. spectrum of aristoteline shows 3 high-field singlets due to C-methyl groups, two of which undergo large and comparable downfield shifts on addition of either europium shift reagent or CF_3CO_2H,[2] while the third is much less affected. This indicates that aristoteline, like peduncularine, may have geminal methyl groups, and that the non-indolic nitrogen is adjacent to them and remote from the remaining methyl group. The m.s. shows intense *M* and $M - CH_3$ ions, and the latter points to a methyl group being attached to a carbon α to a nitrogen atom.[3] Another strong ion arises by loss of C_3H_7N from the molecular ion, as shown by high-resolution m.s. and by the presence of the appropriate metastable ion. In conjunction with the ^1H n.m.r. evidence this suggests that the α carbon atom in fact bears geminal methyl groups. Another α carbon bears a single proton producing a broad absorption around δ 3·6, which shifts downfield on N-acetylation; this proton is coupled to a second resonating around δ 3·05, which in turn is strongly coupled to a third at δ 2·58. The last two are assigned to a methylene group attached to the indole nucleus, and the evidence so far supports the partial structure (II).



(I)



(II)

The complete structure and stereochemistry [(I) and Figure] were finally determined by *X*-ray crystallographic analysis of the hydrobromide, which crystallises from methanol containing a little HBr as large colourless prisms elongated along *b*. *Crystal data:* aristoteline hydrobromide, $C_{20}H_{26}N_2.HBr.CH_4O$, $M = 407$, orthorhombic, $a = 19·462(3)$, $b = 10·443(1)$, $c = 9·889(1)$ Å; $D_m = 1·35$, $D_c = 1·345$ g cm^{-3}, $Z = 4$, space group $P2_12_12_1$, $F(000) = 856$.

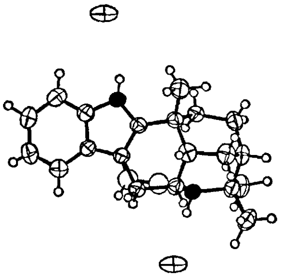


FIGURE. *X*-Ray structure of aristoteline hydrobromide. Nitrogen atoms are shaded, and the methanol of crystallisation can be seen lying below the molecule.

Single-crystal *X*-ray diffraction data between the limits $3° < 2\theta < 126°$ were measured with a Picker FACS-1 *X*-ray diffractometer, using a $\theta,2\theta$ scan technique, with graphite monochromated Cu-K_α radiation. Data were recorded for two complete octants (reflection forms $hk\bar{l}$, $\bar{h}k\bar{l}$) yielding 2859 unique data (about 1430 Bijvoet pairs) having $I > 3\sigma(I)$. Co-ordinates of all non-hydrogen atoms were determined from conventional Patterson and Fourier syntheses. Hydrogen atom co-ordinates were located either by calculation (Ph, CH_2, and N protons) or from difference syntheses (Me hydrogens). All atomic parameters (non-hydrogen with anisotropic, hydrogen with isotropic thermal parameters) were refined by least squares. The absolute configuration of the molecule was determined in the usual way from analysis of the Bijvoet differences due to the anomalous scattering of the bromine atom. At convergence the *R*-factor for the full data set (2859 reflections) was 0·036.

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[1] I. R. C. Bick, J. B. Bremner, and N. W. Preston, *Chem. Comm.*, 1971, 1155.

[2] G. Slomp and J. G. Lindberg, *Analyt. Chem.*, 1967, **39**, 60.

[3] *Cf.* Q. N. Porter and J. Baldas, 'Mass Spectrometry of Heterocyclic Compounds,' Wiley-Interscience, New York, 1971, p. 365, in the case of 2-methylpiperidine.