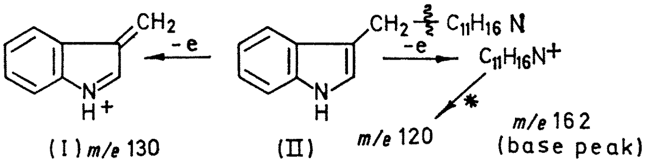
Peduncularine, an Indole–Pyrrolizidine Alkaloid

By I. R. C. BICK,* J. B. BREMNER, and N. W. PRESTON
(*Chemistry Department, University of Tasmania, Hobart,* 7001, *Australia*)
and I. C. CALDER
(*Department of Organic Chemistry, Melbourne University, Melbourne, Victoria, Australia*)

Summary From spectrometric evidence, the alkaloid peduncularine is assigned the novel indole–pyrrolizidine structure (IV) or its mirror image.

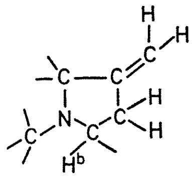
FROM the roots and lower stems of the endemic Tasmanian plant *Aristotelia peduncularis* (Labill.) Hook. f. (Elaeocarpaceae), peduncularine, $[\alpha]_D^{19}$ −24° (c 1·2 in MeOH) has been obtained in 0·003% yield as colourless needles, m.p. 155—157°, together with smaller amounts of at least three other alkaloids. Peduncularine gave a positive Ehrlich test, and its u.v. spectrum closely resembled that of indole. The n.m.r. spectrum showed five aromatic protons, one of which, at τ 2·95 ($CDCl_3$/MeOH), is coupled to the proton on the indole nitrogen (τ −0·1); no aromatic proton absorption occurs above τ 3·0. These data are consistent with an indole nucleus with a free α-position and a β-substituent.[1] The formula $C_{20}H_{24}N_2$ was established by microanalysis and by mass spectrometry, which showed two intense complementary ions at m/e 162 and 130; the latter (I) is given by indole derivatives with a β-carbon chain.[2] The partial structure (II) can thus be written for peduncularine, the presence of the β-methylene group being supported by a 2-proton multiplet around τ 6·8 in the n.m.r. spectrum, in which each proton is coupled to the other (J 13 Hz) and to a third proton at τ 6·47 (designated H^a).



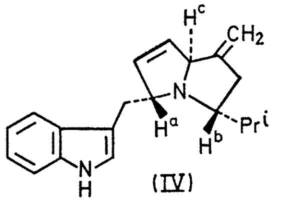
The fragment $C_{11}H_{16}N$ has four centres of unsaturation, including at least two double bonds, since peduncularine has four olefinic protons (n.m.r.) which disappear on hydrogenation over Adam's catalyst to give a tetrahydro-derivative (m.s.): thus the $C_{11}H_{16}N$ fragment has not more than two rings. The nitrogen in this fragment must be tertiary, since the n.m.r. spectrum of peduncularine shows no proton exchangeable with deuterium other than the indolic NH.

The only alkyl group present is isopropyl, which may be inferred from the pair of 3-proton doublets around τ 8·45 in the n.m.r. spectrum and the loss of 42 mass units from the base peak of the m.s. to give the ion m/e 120; however, the isopropyl group cannot be attached to nitrogen since the $M - 15$ peak is only *ca.* 1/10 the intensity of the molecular ion.[3] The nitrogen must thus be in two ring systems, and taking the previous evidence into consideration, the $C_{11}H_{16}N$ fragment has two double bonds only, not conjugated with one another (u.v.).

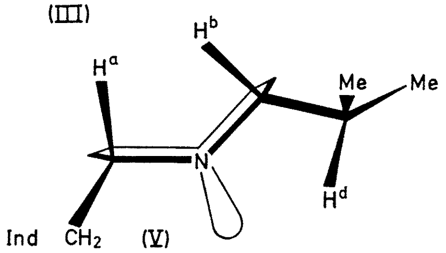
Two of the olefinic protons give singlets in the n.m.r. spectrum (τ 4·66 and 4·78) with no detectable coupling, and are assigned to an exocyclic methylene group, which gives a *C*-methyl on hydrogenation. On the other hand, two protons with a very large coupling resonate around τ 7·69; these must be geminal protons on a ring carbon adjacent to the vinylidene group, and the magnitude of the coupling (J 17 Hz) shows that the dihedral angles made with the π-lobes of the latter group are approximately equal, so that the ring system must be a five-membered one.[4] One of these protons is weakly coupled to a proton (H^b, τ 7·18) which from its chemical shift is on a carbon adjacent to nitrogen (*cf.* III, which summarises the structural evidence so far). The τ 6·47 proton (H^a) and one at τ 5·48 (H^c) are each assigned a similar location, flanked by one and two ethylenic linkages respectively. Apart from the isopropyl and indolylmethyl groups, there remains one such linkage only (C_2H_2) to account for; it can be attached in only one way to form another nitrogen-containing ring in harmony with the chemical shifts of H^a, H^b, and H^c. The structure of peduncularine is thus represented by (IV), in which H^c is coupled to one of the ethylenic protons and H^a to the geminal protons of the indolylmethyl group, while the isopropyl group occupies the remaining position on the carbon bearing H^b.



(III)



(IV)



(V)

The methine proton of the isopropyl group (H^d) resonates at unexpectedly low field (τ 6·48), and has no detectable coupling with H^b. These observations are in accord with the stereochemistry shown in (IV) and (V) (or the mirror image), with the isopropyl group adopting a preferred conformation in which H^d is close to and virtually eclipsed by the lone pair electrons of the nitrogen.[5] At the same time, H^b and H^d form an approximately 90° dihedral angle and the methyl groups are directed away from the bulky indolylmethyl group provided the latter is attached as in (IV) and (V); that it is not freely rotating is shown by the unequal coupling (J 11 and 3Hz) of its methylene protons with H^a.

If a tryptamine residue is subtracted from (IV), a ten-carbon skeleton with an isopropyl group is left, which does not correspond with any so far encountered that are derived from loganin.[6]

We thank Professor W. D. Jackson for assistance in identification of plant material, and the Science Research Council of Great Britain for a 220 MHz n.m.r. spectrum. We are grateful also to Dr. D. H. Williams for helpful discussions, and to the Australian Research Grants Committee for a Post-Doctoral Fellowship to one of us (N.W.P.).

(*Received, July 6th,* 1971; *Com.* 1156.)

---

[1] R. F. M. White, "Physical Methods in Heterocyclic Chemistry", ed. A. R. Katritzky, Academic Press, New York, 1963, vol. 2, p. 133.

[2] J. H. Beynon, "Mass spectrometry and its Applications to Organic Chemistry," Elsevier, Amsterdam, 1960, p. 397.

[3] H. Budziekiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds", Holden-Day, San Francisco, 1964, p. 63.

[4] M. Barfield, and D. M. Grant, *J. Amer. Chem. Soc.*, 1963, **85**, 1899.

[5] S. Yamaguchi, S. Okuda, and N. Nakagawa, *Chem. and Pharm. Bull.* (*Japan*), 1963, **11**, 1465.

[6] A. R. Battersby, R. S. Kapil, J. A. Martin, and L. Mo, *Chem. Comm.*, 1968, 133; A. R. Battersby and B. Gregory, *ibid.*, p. 134; P. Loew and D. Arigoni, *ibid.*, p. 137.