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ARISTOMAKINE, A NOVEL INDOLE ALKALOID FROM ARISTOTELIA SERRATA

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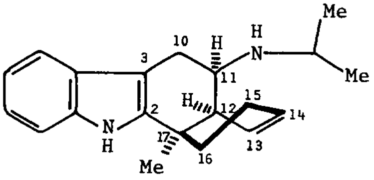
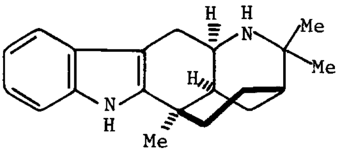
Abstract: The isolation and structural determination of aristomakine (I), an unusual indole alkaloid with an N-isopropyl group, is reported.

Indole alkaloids from Aristotelia spp.[1-10] are distinguished by the incorporation into their structures of a monoterpene unit which has not undergone previous rearrangement to loganin, although considerable subsequent rearrangement may take place. Aristomakine, $[\alpha]_D^{22}$ -79.1° (c 1.5 in $CHCl_3$), was isolated in 0.0008% yield from dried whole plant material of the New Zealand species A. serrata W.R.B. Oliver (Maori name: makomako). It is isomeric with aristoteline (II),[2,3] the major alkaloid of the plant, but n.m.r. spectroscopy showed it had one double bond, and hence one less ring than (II). From its u.v. spectrum, aristomakine has an indole nucleus, which as for (II) is substituted at C-2 and C-3 from the -ve Ehrlich test. This substitution is confirmed by the n.m.r. spectra; furthermore, the ^{13}C spectra of aristomakine and (II) show a close correspondence in resonance of their C-2 carbons (δ 136.3 and 135.9), suggesting that these carbons carry similar substituents: thus the only quaternary aliphatic carbon in aristomakine, which must bear the methyl group producing a 3-proton singlet at δ 1.36 in its ^1H n.m.r. spectrum, is presumably attached at C-2. This inference is supported by a series of strong ions between m/z 180 and 183 in the m.s. of both aristomakine and (II). The m/z 181 fragment from (II) has been formulated as (III)[3] and is considered to arise from the ion radical (IV).[3] The non-indolic nitrogen of aristomakine is secondary: it bears one proton exchangeable with D_2O, and the ^{13}C n.m.r. spectrum shows signals at δ 51.5 and 46.6 corresponding to two α methine carbons. Of the two protons which can be assigned to these methine groups, one produces a septet at δ 3.10 in the ^1H n.m.r. spectrum, and is coupled to two sets of geminal methyl protons; thus aristomakine has an N-isopropyl group. The other proton, resonating at δ 3.44, is coupled to two geminal protons which from their chemical shifts (δ 2.90 and 2.30) can be attributed to a methylene group attached to C-3 of the indole nucleus. These observations suggest a structure such as (I) with a skeleton of type (IV) for aristomakine. Structure (I) is supported by the m.s., in which the base peak appears at m/z 124 and is accompanied by a strong complementary ion at m/z 170. These ions may be formulated as (V) and (VI) and could arise by α-cleavage and retro-Diels-Alder fission of (I). Structure (I) has been confirmed by a series of decoupling experiments, which have established a sequence of protons attached to a chain of carbon atoms extending from C-10 to C-16. The protons in this sequence all show the expected chemical shifts, multiplicities, and coupling constants corresponding in structure and relative stereochemistry to (I).

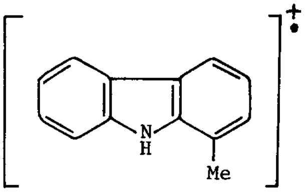
It seems likely that aristomakine, with its unusual N-isopropyl group, is formed biosynthetically by cleavage of the piperidine ring of (II), with retention of configuration at the chiral centres 11, 12 and 17.



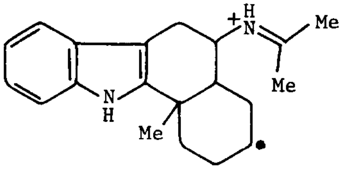
(I), Aristomakine



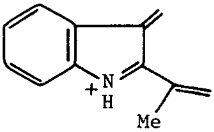
(II), Aristoteline



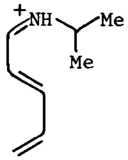
(III), $^{m}/z$ 181



(IV), $^{m}/z$ 294



(VI), $^{m}/z$ 170



(V), $^{m}/z$ 124

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