MAKOMAKINE AND MAKONINE, NEW INDOLE ALKALOIDS FROM ARISTOTELIA SERRATA

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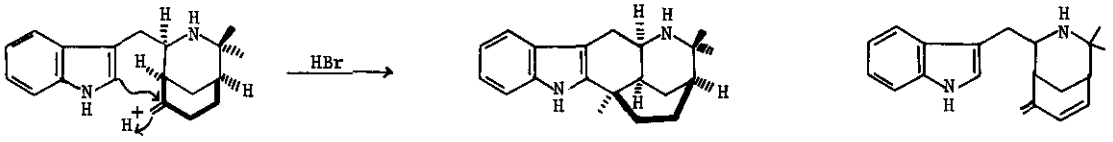
Abstract — A key intermediate, makomakine (I), involved in the proposed scheme of biosynthesis[10] of the Aristotelia alkaloids, has been isolated from an A. serrata extract, together with makonine (II), a dehydro-aristotelinone.

A number of novel indole alkaloids occur in the New Zealand elaeocarpaceous plant Aristotelia serrata W.R.B. Oliver (Maori name: makomako),[1,2,3] and in other Aristotelia spp.[4,5,6,7,8,9] A possible mode of biogenesis of these alkaloids has been put forward[10] involving the hypothetical key intermediate (I). We report the isolation in small amount of a base, m.p. 99-100°, $[\alpha]_D^{19}$ (+) 131.2° (c 0.5, $CHCl_3$), from A. serrata whose structure is shown to correspond with (I). This base, for which the name makomakine is suggested, has an indole nucleus from its U.V. spectrum; its ^1H and ^{13}C n.m.r. spectra show that it has one double bond in a vinylidine group, and from its molecular formula $C_{20}H_{26}N_2$ it must thus have two ring systems in addition to the indole nucleus. Makomakine gives a positive Ehrlich test, and a singlet at δ6.95 in its ^1H n.m.r. spectrum indicates that the 2-position of the indole is unsubstituted. On the other hand, the 3-position evidently bears a methylene group from the strong m/z 130 peak in its m.s.,[11] and from the geminally-coupled pair of protons at δ2.75 and 2.70 in its ^1H n.m.r. spectrum. These are further coupled to a methine proton, which from its chemical shift (δ3.48) is adjacent to N. The non-aromatic nitrogen is secondary: it bears a proton exchangeable with D_2O. Thus far, the structure resembles that of sorelline (III), isolated from A. peduncularis;[6] like the latter base, makomakine has a pair of geminal methyl groups, but it differs from sorelline in having two more hydrogens and one less olefinic group. The tentative structure (I) for makomakine suggested by these data is supported by m.s. and by its ^1H and ^{13}C n.m.r. spectra; the chemical shifts, multiplicities and coupling constants of the aliphatic and olefinic protons are in accord with (I), and the structure was confirmed by a conversion to aristoteline (IV),[1] whose structure and absolute stereochemistry are known from X-ray crystallography. When makomakine (I) was treated at room temperature with 47% hydrobromic acid, it gave crystalline (IV) in 10% yield, identical with the natural alkaloid. This experiment, which fixes at the same time the absolute configuration of

makomakine, supports the suggestion[10] that (I) is a biogenetic precursor of (IV) and of other Aristotelia alkaloids.

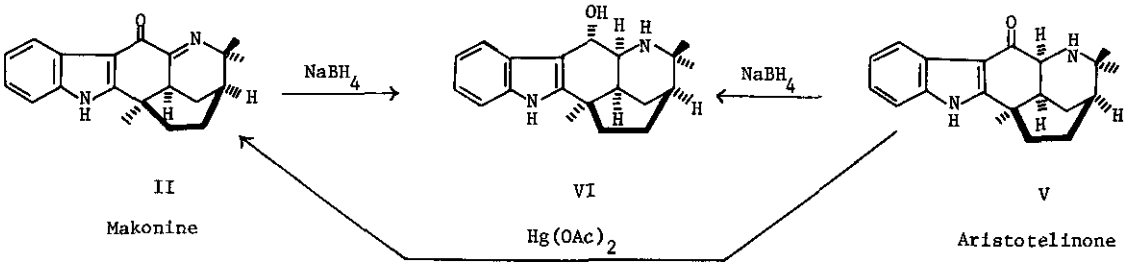


I
Makomakine

IV
Aristoteline

III
Sorelline

Another minor alkaloid, named makonine, was isolated from the same extract as hexagonal crystals, m.p. 310-312° (d), $[\alpha]_D^{19}$ (+) 431.1° (c 0.93, MeOH + $CHCl_3$). Like aristoteline (IV), it gave a negative Ehrlich test, and its n.m.r. spectra showed the presence of a pair of geminal dimethyl groups, plus an extra methyl attached to a quaternary carbon. However, it contained a carbonyl group, and the non-indolic nitrogen appeared to be tertiary. The u.v., i.r. ^1H and ^{13}C n.m.r. spectra were broadly similar to those of aristotelinone[2] (V), which has a carbonyl group conjugated with the indole nucleus, but makonine has two less hydrogens than (V), and an extra olefinic carbon. Structure (II) suggested by these data was confirmed by conversion of aristotelinone into makonine in 25% yield by mercuric acetate oxidation; furthermore, both (II) and (V) on borohydride reduction gave as major product the same secondary alcohol (VI).[2]



II
Makonine

VI

V
Aristotelinone

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