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ARISTOSERRATENINE AND TASMANINE: STRUCTURES AND ABSOLUTE CONFIGURATIONS

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Abstract - The structure of the *Aristotelia* alkaloid aristoserratenine (1) has been determined by spectroscopic means, and confirmed by rearrangement to aristoteline (2). The structure of tasmanine (3) has been confirmed similarly, and the configuration at the spiro carbon of each base has been determined by nOe experiments.

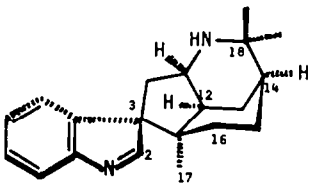
RESULTS AND DISCUSSION

The alkaloid aristoserratenine (1) was isolated amongst the minor bases of the New Zealand plant *Aristotelia serrata* (J.B. et G. Forst) W.R.B. Oliver, in which it occurs to the extent of about 0.0009%. It proved to be isomeric with aristoteline[1,2,4] (2), the major alkaloid of the plant, but its uv spectrum showed it to be an indolenine, the C-2 position of which must be unsubstituted from the appearance of a sharp singlet at δ8.00, and a doublet at δ178.7 in the ^{1}H and ^{13}C nmr spectra respectively. The remainder of the ^{13}C spectrum of aristoserratenine (1) closely corresponds with that of aristoteline (2) except for the singlet attributed to C-3 that appears at δ104 in the latter spectrum; this singlet is shifted to δ70.8 in the spectrum of 1, consistent with the signal from the spiro carbon of an indolenine nucleus. The rest of the ^{1}H nmr spectrum of aristoserratenine (1) likewise corresponds in general terms with that for aristoteline (2), and decoupling experiments permitted a sequence of protons to be traced in the spectrum of 1 which parallels that for 2; the mass spectra of the two alkaloids are also very similar, and the evidence thus points to an indolenine structure of type 1 for aristoserratenine.

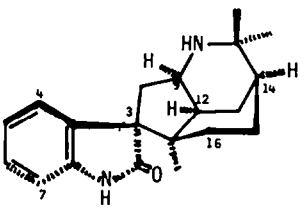
This conclusion has been confirmed by an acid-catalysed rearrangement of aristoserratenine into (+)-aristoteline (2) in 47% yield; since the absolute stereochemistry of 2 is known, this experiment at the same time fixes that of 1 except for the configuration at the spiro carbon C-3. In order to clarify the stereochemistry at this point, a series of nOe experiments was undertaken on aristoserratenine, in the course of which a 27% decrease in signal intensity of the *endo* proton attached to C-16 was observed on irradiation of H-2[3]: these two protons must thus be located relatively close to one another in space, and no comparable effect was observed on protons in other positions. Conversely, irradiation of the C-16 *endo* proton produced a similar, though predictably smaller, negative enhancement of the H-2 signal. These data support the configuration at C-3 shown in structure 1, which thus represents the absolute stereochemistry of aristoserratenine.

The alkaloid tasmanine (3) was first isolated from the Tasmanian species *A. peduncularis*[4], but it has subsequently been found to occur in *A. serrata* to the extent of about 0.0015%. Its structure and relative stereochemistry were deduced[4] from spectroscopic evidence.

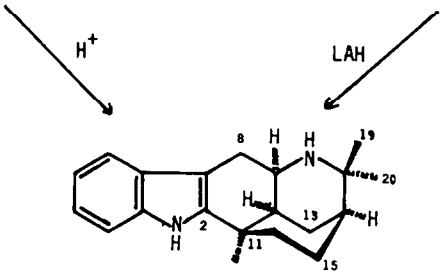
This structure has now been confirmed by LAH reduction of tasmanine (3), which gave (+)-aristoteline (2) in 30% yield. This experiment also fixed the absolute stereochemistry of 3 except for



1 Aristoserratenine



3 Tasmanine



2 (+)-Aristoteline

the spiro centre (C-3). In a previous study of tasmanine[4], some evidence for the configuration at this centre relative to the rest of the molecule was adduced from the anisotropic effects of the carbonyl group, and of the aromatic ring, on H-12 and on the protons attached to C-16 respectively. As formulated in 3, H-12 lies in the deshielding zone of the carbonyl group, and resonates at distinctly lower field (δ2.55) than H-14 (δ1.31), which is remote from the carbonyl. Similarly, H_{endo}-16 as formulated in 3 lies close to the plane of the aromatic ring, and is distinctly deshielded (δ3.00) as compared to H_{exo}-16 (δ0.75). However, further consideration shows that comparable chemical shifts would be expected for these protons if the configuration at the spiro carbon C-3 were reversed: the H-12 proton would then be deshielded by the aromatic ring, and H_{endo}-16 by the carbonyl group. The values for the corresponding protons H-12, H-14, H_{endo}-16 and H_{exo}-16 in aristoserratenine (1) for which the reverse stereochemistry at C-3 has been deduced as compared to that for tasmanine (3), are in fact δ2.02, 1.39, 3.16 and 1.00 respectively.

More reliable evidence concerning the configuration at C-3 was sought from nOe experiments on tasmanine, and it was found that irradiation of the aromatic proton H-4 produced a distinct enhancement in the signal due to H_{endo}-16 and vice versa. In a molecular model corresponding to 3, the two protons in question are close to one another in space, but with the epimeric configuration at the spiro atom, they would be too remote for a nuclear Overhauser effect to take place: structure 3 thus represents the absolute configuration for all chiral centres in tasmanine.

EXPERIMENTAL

Aristoserratenine - This alkaloid was obtained by ptlc separation from the minor alkaloids of *A. serrata* as an amorphous solid, $[\alpha]_D^{19}$+58° (C=0.9, $CHCl_3$); λ_{max} (MeOH): 259, 226nm (log ε_{max} 3.57, 4.38); ν_{max} ($CHCl_3$): 3230, 2950, 2910, 1700, 1610, 1580, 1550, 1450, 1375, 1210, 1165, 1100, 1020, 660, 750, 650 cm^{-1}. ^1H Nmr: 8.0 (1H, s, H-2); 7.15-7.6 (4H, m, H-4 - H-7); 3.83 (1H, ddd, $J_{9/8exo}$=6.6 Hz, $J_{9/12}$=5.0 Hz, $J_{9/8endo}$=0.9 Hz, H-9), 3.16 (1H, td, J_{gem}=14Hz, $J_{16endo/15exo}$=14Hz, $J_{16endo/15exo}$=14 Hz, $J_{16endo/15endo}$=5.5 Hz, H-16_{endo}); 2.37 (1H, dd, J_{gem}=14.7 Hz, $J_{8exo/11}$=6.6 Hz, H-8_{exo}); 2.17 (1H, d9a, J_{gem}=13.3 Hz, $J_{13a/14}$=$J_{13a/12}$=$J_{13a/15endo}$=2.5 Hz, H-13a); 2.02 (1H, dt, $J_{12/9}$=5.0 Hz, $J_{12/13a}$=$J_{12/13b}$=2.5 Hz, H-12); 1.99 (1H, ddqa, J_{gem}=14 Hz, $J_{15endo/16endo}$=5.5 Hz, $J_{15endo/16exo}$=$J_{15endo/14}$=$J_{15endo/13a}$=2.5 Hz, H-15_{endo}); 1.87 (1H, dd, J_{gem}=14.7 Hz, $J_{8endo/9}$=0.9 Hz, H-8_{endo}); 1.66 (1H, dt, J_{gem}=13.3 Hz, $J_{13b/12}$=2.5 Hz, H-13b); 1.61 (1H, ttd, J_{gem}=$J_{15exo/16endo}$=1.5 Hz, H-15_{exo}); 1.39 (1H, q1, $J_{14/13a}$=$J_{14/13b}$=$J_{14/15exo}$=$J_{14/15endo}$=2.5 Hz, H-14); 1.0-1.6 (1H, br, H-10); 1.22 and 1.17 (6H, 2s, H-19 and H-20); 1.00 (1H, ddd, J_{gem}=14 Hz, $J_{16exo/15exo}$= 5.0 Hz, $J_{16exo/15endo}$=2.5 Hz, H-16_{exo}); 0.66δ (3H, s, H-17). ^{13}C Nmr: 178.7 (d, C-2); 155.7 (s, C-7a); 139.3 (s, C-3a);127.6 (d, C-5); 125.5 (d, C-6); 124.8 (d, C-4); 120.6 (d, C-7); 70.8 (s,

C-3); 54.0 (s, C-18); 53.4 (d, C-9); 46.8 (s, C-11); 46.2 (d, C-12); 39.5 (t, C-8); 36.0 and 27.4 (2 qa, C-19 and C-20); 32.2 (t, C-16); 30.2 (d, C-14); 25.2 and 23.7 (2t, C-13 and C-15); 19.7δ (qa, C-17).

Acid-Catalysed Rearrangement of Aristoserratenine (1) to Aristoteline (2) - Aristoserratenine (15 mg) was dissolved in 2 ml of 5% (w/v) sulphuric acid, and the resulting solution was refluxed for 8 hr, then cooled to room temperature, basified with ammonia (d 0.88) and extracted with chloroform (3 x 15 ml). The combined chloroform extracts were dried (Na_2SO_4) and evaporated to dryness *in vacuo*. The residue (13 mg), when purified by ptlc (silica gel impregnated with 0.5 M KOH, 2.5% MeOH/$CHCl_3$), afforded 7 mg of a base (47% yield) as the major component, which crystallised from methanol as colourless crystals, mp 82-85° (solute), 162-163.5° (after drying; lit.[1] 163-164°) and proved identical ([α], Rfs, uv, ir, ms, mp and mmp) with (+)-aristoteline (1).

LAH Reduction of Tasmanine (3) - To a solution of tasmanine (20 mg, 0.06 mmole) in 10 ml of dry THF was added 15 mg of LAH in 5 ml of THF, and the mixture was refluxed for 5 hr. The excess of LAH was destroyed with water, the solvents were removed *in vacuo*, and the residue was treated with water (20 ml) containing a few drops of 5% aqueous sodium hydroxide solution. The mixture was extracted with chloroform (20 ml x 4), and the combined extracts were washed with water, dried (Na_2SO_4) and evaporated to dryness. Analysis of the residue (14 mg) by tlc (10% MeOH/$CHCl_3$) showed the presence of two components, which were separated by ptlc with the same solvent system. The major (more polar) component (6 mg) crystallised from methanol and proved identical (Rf, [α], ir, uv, ms, mp and mmp) with (+)-aristoteline.

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