

THE STRUCTURES OF SERRATENONE AND SERRATOLINE, TWO ALKALOIDS FROM
ARISTOTELIA SERRATA

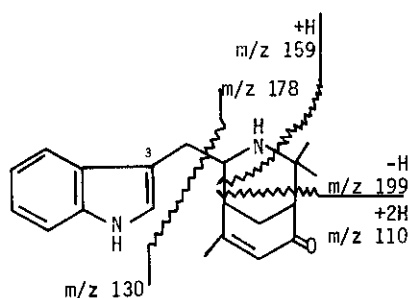
I. Ralph C. Bick*, Mohammad A. Hai, and Nigel W. Preston

Chemistry Department, University of Tasmania, Hobart, Tas., Australia 7001

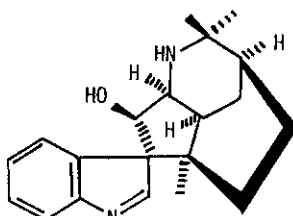
Abstract - Serratenone, a new indole alkaloid from A. serrata, is shown to have structure 1, and the amended structure 3 is established for the indolenine alkaloid serratoline.

The Aristotelia spp. have yielded a range of novel indole alkaloids¹⁻¹³, in particular the New Zealand species A. serrata^{2,9,11,13}. An amorphous base, $[\alpha]_D^{19} -45.3^\circ$ (C 1.0, CHCl₃) has now been isolated from the latter in 0.003% yield, and named serratenone. Its i.r. spectrum suggests that it has an $\alpha\beta$ unsaturated ketone grouping, whose presence is supported by the U.V. spectrum; the latter also indicates the presence of an indole nucleus, and in fact is practically identical with that of an equimolar mixture of tryptamine and mesityl oxide. Both nitrogens in serratenone appear to be secondary, since two broad one-proton peaks in the ¹H n.m.r. spectrum disappear on addition of deuterium oxide. A singlet in the same spectrum at $\delta 7.12$ indicates that a proton is attached to C₂ of the indole ring, and a positive Ehrlich test confirms that this position is unsubstituted; on the other hand C₃ must carry a methylene group from the strong m/z 130 ion in the m.s., and from the pair of geminally coupled protons resonating at $\delta 2.65$ and 2.93. Each of these is further coupled to a methine proton whose chemical shift ($\delta 3.75$) indicates it is attached to a carbon adjacent to nitrogen. From the strong M-15 ion in the m.s., the aliphatic nitrogen is also attached to a carbon bearing a methyl group, and since the ¹H n.m.r. spectrum shows a 6-proton singlet corresponding to a gem dimethyl group, the part structure Ar-CH₂-CH-NH-CMe₂ can be deduced. The methine proton in this sequence is further coupled to another methine proton, which in turn is coupled allylically to the only olefinic proton in the spectrum, and also to a pair of geminal protons. The latter are further coupled to another methine proton, which from its chemical shift ($\delta 2.00$) and lack of further coupling is assigned a location adjacent to the carbonyl group. The olefinic proton is also coupled allylically to a methyl group attached to an olefinic carbon. These data point to structure 1, which is in full accord with the mass spectrum of serratenone.

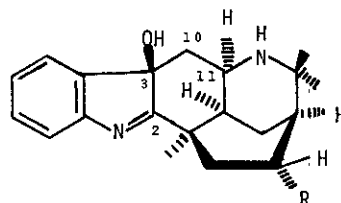
The alkaloid serratoline, isolated previously from A. serrata, proved to be a hydroxyindolenine for which structure 2 was deduced⁹. A reexamination of the previous data, together with further



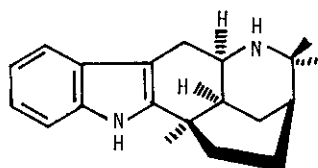
1 Serratene



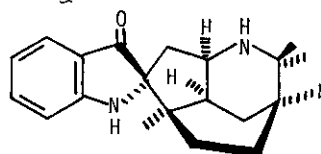
2



3 Serratoline, R = H
Aristotelinine, R = OH



4 Aristoteline



5 Aristotelone

evidence from ^1H and ^{13}C n.m.r. spectroscopy, has led to this structure being revised to **3**. In particular, the ^{13}C n.m.r. spectrum showed the presence of a quaternary carbon resonating at $\delta 189.0$, which corresponds to C_2 of an indolenine. Another signal at $\delta 83.9$ from a quaternary carbon suggested that the hydroxyl group is attached to C_3 ; on the other hand, a singlet previously reported⁹ at $\delta 7.30$ in the ^1H n.m.r. spectrum, which was attributed to a proton attached to C_2 , must have been due to impurity since this signal could not be observed with a purified and recrystallised sample of serratoline. Structure **3** is consistent with the previous evidence⁹ that serratoline could be reduced with borohydride to an indoline, which could then be dehydrated to aristoteline (**4**)², and the reverse transformation has now been effected by oxidation of **4** with benzoyl hydroperoxide, followed by reduction with sodium dithionate: the product proved identical with naturally occurring serratoline. Since the absolute stereochemistry of aristoteline is known from X-ray crystallography², its correlation with serratoline enables not only the structure but also the absolute stereochemistry of the latter to be deduced for all chiral centres except that bearing the hydroxyl group (C_3). A molecular model shows that with the hydroxyl attached as in **3**, $\text{H}-\text{C}_{11}$ makes equal dihedral angles with the geminal protons on C_{10} , whereas with the reverse configuration at C_3 , the angles are very different. The absolute configuration as in **3** is established from the fact that the coupling constants of the C_{10} geminal protons with $\text{H}-\text{C}_{11}$ are each 2.9 Hz; the structure and stereochemistry for the rest of the molecule has been confirmed by an extended series of proton decoupling experiments. The alkaloid aristotelinine from *A. chilensis*, whose structure **5** was established by X-ray crystallography⁴, is thus 19-hydroxy-serratoline.

Although serratoline is resistant to rearrangement with base⁹, it is readily transformed in fair yield on boiling with dilute sulphuric acid into a crystalline ψ -indoxyl (6), m.p. 217-218°C, $[\alpha]_D +41^\circ$ (CHCl₃), whose m.p., i.r. and mass spectra are in agreement with those reported for aristotelone³, another naturally occurring base from *A. chilensis*. A direct comparison has not been possible for lack of an authentic sample, but we believe the two to be identical.

We thank the Australian Research Grants Committee for financial support, the National NMR Centre, Canberra, for spectra, the Australian Development Assistance Bureau for an Australian Commonwealth Scholarship (to M.A.H.), and the New Zealand Forestry Service for supply of plant material.

REFERENCES

1. I.R.C. Bick, J.B. Bremner, N.W. Preston, and I.C. Calder, J. Chem. Soc., Chem. Commun., 1971, 1155.
2. B.F. Anderson, G.B. Robertson, H.P. Avey, W.F. Donovan, I.R.C. Bick, J.B. Bremner, A.J.T. Finney, N.W. Preston, R.T. Gallagher, and G.B. Russell, J. Chem. Soc., Chem. Commun., 1975, 511.
3. D.S. Bhakuni, M. Silva, S.A. Matlin, and P.G. Sammes, Phytochemistry, 1976, 15, 574.
4. M. Bittner, M. Silva, E.M. Gopalakrishna, W.H. Watson, V. Zabel, S.A. Matlin, and P.G. Sammes, J. Chem. Soc., Chem. Commun., 1978, 79.
5. N. Chaichit, B.M. Gatehouse, I.R.C. Bick, M.A. Hai and N.W. Preston, J. Chem. Soc., Chem. Commun., 1979, 874.
6. I.R.C. Bick, M.A. Hai, and N.W. Preston, Heterocycles, 1979, 12, 1563.
7. H.P. Ros, R. Kyburz, N.W. Preston, R.T. Gallagher, I.R.C. Bick, and M. Hesse, Helv. Chim. Acta, 1979, 62, 481.
8. R. Kyburz, E. Schöpp, I.R.C. Bick, and M. Hesse, Helv. Chim. Acta, 1979, 62, 2539.
9. I.R.C. Bick, M.A. Hai, N.W. Preston, and R.T. Gallagher, Tetrahedron Lett., 1980, 21, 545.
10. V. Zabel, W.H. Watson, M. Bittner, and M. Silva, J. Chem. Soc., Perkin Trans. I, 1980, 2842.
11. M.A. Hai, N.W. Preston, R. Kyburz, E. Schöpp, I.R.C. Bick, and M. Hesse, Helv. Chim. Acta, 1980, 63, 2130.
12. R. Kyburz, E. Schöpp, I.R.C. Bick, and M. Hesse, Helv. Chim. Acta, 1981, 64, 2555.
13. I.R.C. Bick and M.A. Hai, Heterocycles, 1981, 16, 1301.

Received, 4th January, 1983