

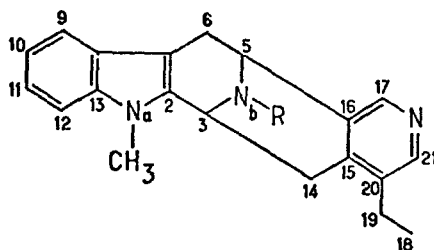
THE STRUCTURE OF SUAVEOLINE, A NEW ALKALOID FROM  
RAUWOLFIA SUAVEOLENS S. MOORE (APOCYNACEAE)

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In the course of our investigations on the alkaloid content of Rauwolfia suaveolens S. Moore, collected from New Caledonia, we were able to isolate from the trunk bark a new alkaloid which we have named suaveoline and for which we propose structure 1. The isolation will be discussed in a full paper (yield : 200mg/10kg of bark). Suaveoline could not be obtained in a crystalline form but the amorphous product appeared to be pure (t.l. c. in various solvent systems),  $[\alpha]_D = 0^\circ \pm 2^\circ$  (CHCl<sub>3</sub>, c = 1). The molecular formula C<sub>20</sub>H<sub>21</sub>N<sub>3</sub> was calculated by high resolution mass spectrometry. Its u. v. spectrum (EtOH) corresponds to that of a modified indole chromophore :  $\lambda_{\max}$ , nm (log.ε) = 227 (4.47), 272 (3.88), 285 (3.82). The nature of this modification becomes obvious after subtraction of the spectrum of voachalotine (1), a Na-methyl indole alkaloid, from that of suaveoline :  $\lambda_{\max}$ , nm : 220 and 265 ;  $\lambda_{\min}$ , 235nm. These last values are comparable with those of a 3,5-disubstituted pyridine (2). The i. r. spectrum showed no band for OH. An attempt to hydrogenate (C Pd/H<sub>2</sub>, ntp) was unsuccessful. The p. m. r. spectrum of suaveoline 1 is represented on fig. 1.



- 1 : R = H  
2 : R = CH<sub>3</sub>  
3 : R = CO CH<sub>3</sub>

Methylation of 1 (C Pd/H<sub>2</sub>) with formaldehyde in methanol, or NaBH<sub>4</sub>, in formaldehyde in the presence of a trace of glacial acetic acid, gave N<sub>b</sub>-methyl derivative 2, crystals from ether, m.p. 194-195°, [ $\alpha$ ]<sub>D</sub> = - 93° (CHCl<sub>3</sub>, c = 0.89). The u.v. spectrum (EtOH) is practically the same as that of 1:  $\lambda_{\max}$ , nm (log  $\epsilon$ ) = 227 (4.57), 272 (4.01), 284 (3.97). The p.m.r. spectrum (CDCl<sub>3</sub>) shows signals at 2.5ppm (S), 3 protons N<sub>b</sub>-CH<sub>3</sub>; 3.6ppm (S), 3 protons N<sub>a</sub>-CH<sub>3</sub>; 4.1-4.3ppm, 2 protons vicinal to N<sub>b</sub>-methyl-group; 7-8.5ppm (M), 6 aromatic protons. Acetylation (acetic anhydride) gave N<sub>b</sub>-acetyl derivative 3, [ $\alpha$ ]<sub>D</sub> = + 7° (CHCl<sub>3</sub>, c = 0.78), crystals from ether, m.p. 207-208°, the i.r. spectrum of which showed band at 1740cm<sup>-1</sup> (tertiary amide) and u.v. spectrum (EtOH) at  $\lambda_{\max}$ , nm (log  $\epsilon$ ): 224 (4.26), 274 (3.6), 286 (3.53). The p.m.r. spectrum (CDCl<sub>3</sub>) exhibits: 2.25ppm (S), 3 protons for N<sub>b</sub>-acetyl group; 3.75ppm (S), 3 protons for N<sub>a</sub>-CH<sub>3</sub>; the signals (S) for two protons are shifted to 5.4ppm and 6.3ppm from their original positions at 4.15ppm and 4.3ppm respectively (H<sub>3</sub> and H<sub>5</sub>).

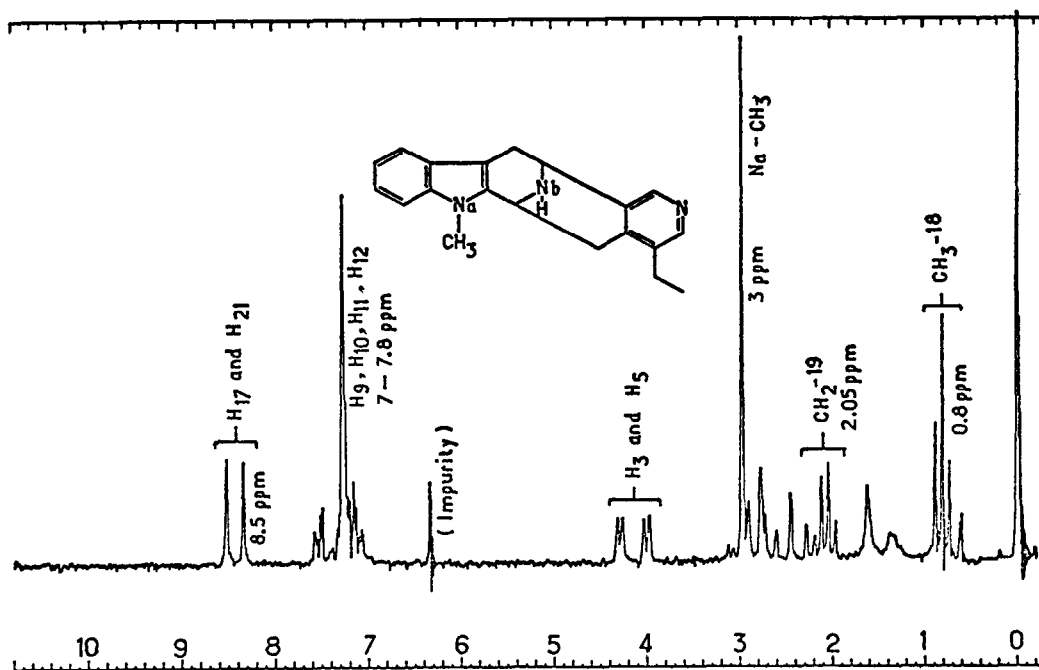


Fig. 1: p.m.r. spectrum of suaveoline, 1, at 100MHz (C<sub>6</sub>D<sub>6</sub>)

The mass spectrum of suaveoline, 1 (fig. 2) can be correlated with that of ajmaline 4 (3), except the peak at m/e 286 (M<sup>+</sup> - 17) probably due to the elimination of NH<sub>3</sub> from the molecular ion. Likewise, the major peak at m/e 183 is characteristic of a N(a)-methyltetrahydrocarboline as voachalotine (1).

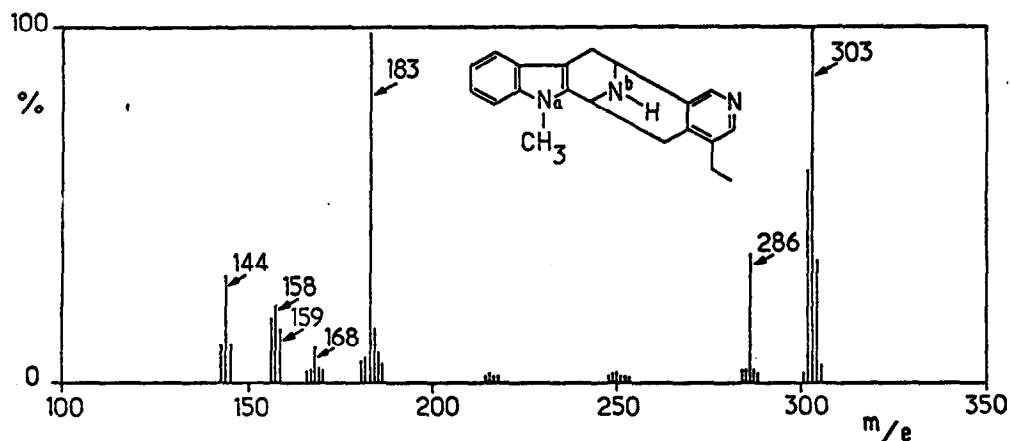
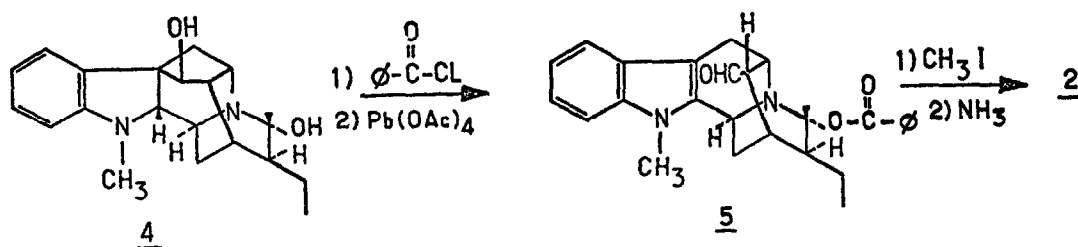


Fig. 2 : Mass spectrum of suaveoline, 1.

Confirmation of the structure of suaveoline by partial synthesis

Compound 2 was prepared from ajmaline 4 in four steps (4). 21-O-benzoyl-ajmaline (5), prepared by refluxing ajmaline 4 in benzene solution with benzoyl chloride, was treated with  $Pb(AcO)_4$  giving 5. This aldehyde 5 was refluxed with  $CH_3I$  to give a quaternary ammonium salt which was dissolved in ammonia solution and warmed to obtain a product whose i. r., u. v., mass spectrum and mixed m. p. were identical with those of  $N_b$ -methyl suaveoline 2. The principal steps are shown below :



The isolation of suaveoline raises the question of whether it is an artefact or not ; suaveoline is indeed present among the alkaloids obtained using ammonia for alka-  
lisation of the plant material ; however, it can also be isolated, although in lesser

amount, from the total alkaloids obtained using sodium carbonate in place of ammonia for alkanisation.

The isolation of suaveoline from a Rauwolfia species is also noteworthy and reminiscent not only of that of N<sub>b</sub>-C<sub>21</sub> seco-sarpagine compounds in the same botanical genus, but also of that of the biogenetically related compounds (i. e. Alstophylline (4) ) from the botanically related genus Alstonia.

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#### References

- (1) J. Pecher, N. Defay, M. Gautier, J. Peeters, R.H. Martin and A. Vandermeers, Chem. and Ind., 1960, p. 1481.
- (2) R. A. Friedel, M. Orchin, U. V. Spectra of Organic Compounds, Wiley & Sons, 1951.
- (3) K. Biemann, P. Bommer, A.L. Burlingame and W.J. McMurry, J. amer. chem. Soc., 1964, 86, 4624.
- (4) T. Kishi, M. Hesse, C.W. Gemenden, W.I. Taylor and H. Schmid, Helv. chim. Acta, 1965, 48, 1349.
- (5) F. A. L. Anet (Mrs), D. Chakravarty (née Mukharjee) and Sir Robert Robinson, J. chem. Soc., 1954, p. 1249.