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THREE NOVEL ALKALOIDS FROM ERVATAMIA ORIENTALIS

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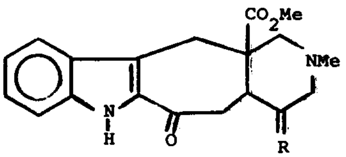
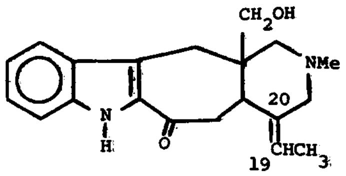
Ervatamine, 20-epiervatamine and 19,20-dehydroervatamine are related indole alkaloids of a novel type obtained from extracts of Ervatamia orientalis (Apocynaceae). In this communication we report evidence for their structures which are unusual in that they lack indolylethylamine moieties.

The spectral characteristics of 19,20-dehydroervatamine (1), $C_{21}H_{24}N_2O_3$, m.p. 198-200° (dec.), $[\alpha]_D$ + 53° indicate the following groupings: a 2-acylindole grouping (ν_{max} 1650cm^{-1}; λ_{max} 242, 315 mμ, log ϵ 4.11, 4.28), a methyl ester (ν_{max} 1740cm^{-1}, three proton n.m.r. singlet at 6.44τ), an N-methyl (three proton n.m.r. singlet at 7.73τ) and a $>C=CHCH_3$ grouping (three proton doublet at 8.42τ, J = 6.5Hz). $LiAlH_4$ reduction of 1 formed a mixture of epimeric diols which was converted to a single crystalline ketol (2), $C_{20}H_{24}N_2O_2$ (M^+, 324.1840), m.p. 120-140° $[\alpha]_D$ + 67° by careful oxidation with CrO_3/pyridine[1]. The n.m.r. spectrum of the derived O-acetate showed the signals for the protons geminal to the acetoxyl group as a clean AB quartet (τ_A5.87, τ_B6.22, J_{AB} = 11 Hz) demonstrating that the methoxycarbonyl group of 1 is located on a fully substituted carbon.



1 R = $CHCH_3$

7, 8 R = $<^{H}_{CH_2CH_3}$



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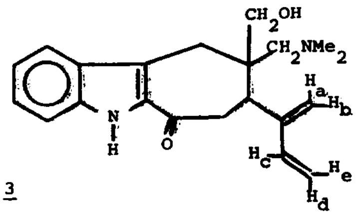

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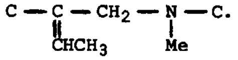
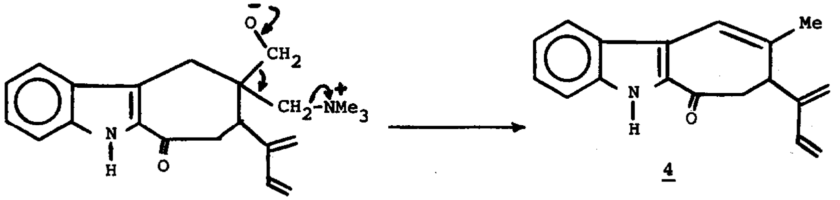
The methiodide of the ketol (2) underwent a vinylogous 1,4-Hofmann elimination under mild conditions to form the conjugated diene (3), $C_{21}H_{26}N_2O_2$, m.p. 138-138.5°, $[\alpha]_D$ + 4° which has a broadened short wavelength u.v. absorption (230-240mμ) due to the diene chromophore. In addition the 2-substituted butadiene grouping was revealed by inspection of the n.m.r. spectrum: the five vinylic protons gave rise to a doublet of doublets (3.70τ, J = 17.5, 10 Hz; H_c), two broadened singlets (4.85, 5.05τ; H_a, H_b) and obscured signals from two other protons (H_d, H_e, signals partly underneath those of H_a, H_b). The presence of such a grouping in 3 shows that 1 has the partial structure



$C-\underset{\underset{CHCH_3}{\|}}{C}-CH_2-\underset{\underset{Me}{|}}{N}-C.$

A neutral product $C_{18}H_{17}NO$, (M^+, 263.1303) m.p. 141-4° $[\alpha]_D$ + 255° was obtained from brief treatment of the methiodide of 3 with KOtBu in *t*-butanol. The n.m.r. spectrum of the product showed that the 2-substituted butadiene grouping was retained but additional signals were observed due to a new vinylic proton (br.s, 3.11τ) and a deshielded vinylic methyl (d, 7.93τ, J∿1Hz). In addition the u.v. spectrum (λ_{max} 233, 252, 333, 390(sh)mμ; log ε 4.51, 4.52, 4.11 and 3.83) revealed an extended chromophore. These observations are consistent with structure 4 which is considered to arise from the methiodide by loss of formaldehyde and trimethylamine[2] followed by isomerization of the double bond thus formed into conjugation with the indole moiety.



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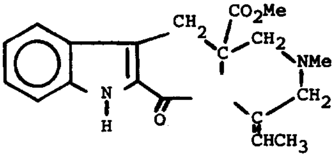
Partial structure 5 is indicated for 19,20-dehydroervatamine by the above evidence and though there are several possible structures combining 5 with the C_2H_3 residue only one has a methylene group adjacent to the ketone functionality. That this is the case for 19,20-dehydroervatamine was shown NaBH$_4$ reduction of 1 to give a mixture of epimeric alcohols which underwent smooth dehydration with glacial acetic acid.[3] The product was the α-vinyl indole (6) and n.m.r. signals for two additional vinyl protons at 3.56τ (d of d, J = 11, 3Hz) and 4.48τ (partially obscured) showed it to be a disubstituted alkene. Thus 19,20-dehydroervatamine has a methylene grouping adjacent to the ketone and is represented by structure 1.



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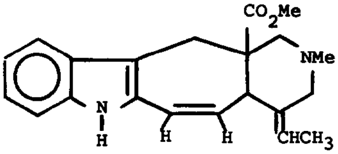

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Ervatamine (7), $C_{21}H_{26}N_2O_3$ (M^+, 354.1949) m.p. 92-8° (solvated by MeOH), $[\alpha]_D$ -3.7° and 20-epiervatamine (8) $C_{21}H_{26}N_2O_3$ (M^+, 354.1950) m.p. 185-7° (dec.), $[\alpha]_D$ -22° were seen to lack an ethylidene functionality (n.m.r.) but in other respects they showed properties very similar to those of 1. Prolonged catalytic hydrogenation of 1 followed by reoxidation of the reduced carbonyl functionality gave ervatamine together with a small amount of 20-epiervatamine thus demonstrating that they are the epimeric dihydro derivatives 7 and 8 as was suspected from the spectral and analytical observations.

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