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NATURAL PRODUCTS OF DEGRADATION OF THE ASPIDOSPERMA ALKALOID SKELETON[1]

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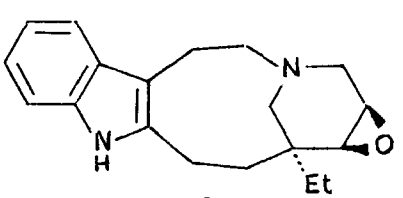
Abstract: The structure analysis of two minor alkaloids of Voacanga africana Stapf. is presented.

The extraction of the leaves of the plant Voacanga africana Stapf. has led to the isolation of the known alkaloids vobtusine and voacamine, of three indole alkaloid monomers: voaphylline (1) and its derivatives[2,3] and of eight bis-indolinic bases such as voafoline (2a), isovoafoline (2a) and voafolidine (2b).[2,4,5] By the utilization of a sensitive separation technique (partitioning of indole alkaloid monomers from dimers by the passage of their solutions through Sephadex LH 20 columns) it now has been possible to isolate two more minor bases of the following novel constitution.



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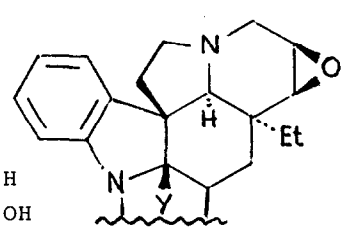
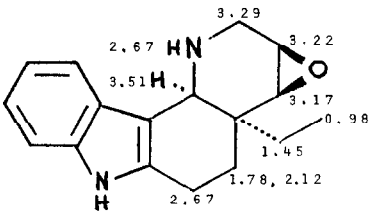
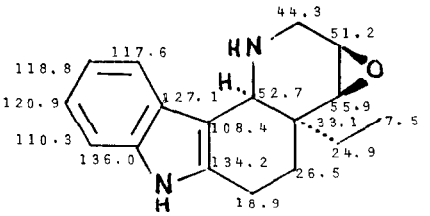


2a, Y = H
b, Y = OH

One base, mp 233-235° C (crystallized from benzene), $[\alpha]_{578}$ +109° (c = 0.1, $CHCl_3$), is a pentacyclic $C_{17}H_{20}N_2O$ substance whose UV spectrum [λ_{max}^{EtOH} 227 nm (log ε 4.29), 277 (3.83), 293 (3.74)] shows the presence of an indole chromophore. Its mass spectrum [m/e 268 (M^+, 100%), 267 (34), 251 (12), 239 (28), 225 (36), 210 (36), 208 (37), 197 (37), 182 (24), 180 (33), 171 (63), 170 (42), 169 (39), 168 (51), 167 (34), 166 (31), 158 (43), 157 (45), 144 (21), 143 (27), 130 (30)] confirms the indole unit by the 130, 143 and 144 fragments and reveals the presence of an ethyl group (M-29 fragment) and an aminomethine moiety (M-1 fragment). The infrared spectrum ($CHCl_3$) confirms the indole moiety (weak 1600 and 1625 cm^{-1} absorption bands) and exhibits a non-indolic NH band (3480 cm^{-1}), which is replaced in the acetylation product (m/e 310 = M + 42) by an intense amide carbonyl band (1610 cm^{-1}). The 400 MHz ^1H NMR spectrum [δ($CDCl_3$) 0.98 (t, 3, J = 7 Hz), 1.45 (q, 2, J = 7 Hz), 1.78 (dd, 1, J = 14, 5 Hz), 2.12 (m, 1), 2.67 (m, 3), 3.17 (d, 1, J = 4 Hz), 3.22 (d, 1, J = 4 Hz), 3.29 (AB, 2), 3.51 (s, 1), 7.05, 7.56 (d, 1 each, J = 7 Hz), 7.10, 7.22 (t, 1 each, J = 7 Hz), 8.00 (s, 1, indole NH)] confirms the ethyl group (0.98 and 1.45 ppm signals) and the benz-unsubstituted indole system (7.1-7.6 and 8.00 ppm signals). The 25.2 MHz ^{13}C NMR spectrum ($CDCl_3$) reveals the alkaloid to possess a 2,3-disubstituted indole unit, an ethyl group attached to a quaternary carbon center, three methylenes of which one is bonded to the secondary amino group and another to the indole moiety and three methines of which one must be an aminomethine and the remaining ones oxirane methines in view of the upfield position of their signals.



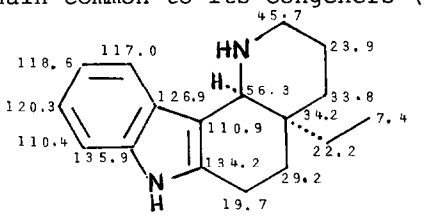
3a



3b

The above data and ^{13}C NMR spectral comparison with synthetic models 4 and 5[6] indicate structure 3 as the relative configuration of the new alkaloid. The natural base thus represents a new indole alkaloid structure type, having lost

oxidatively the two carbons of the usual ethanamino bridge of the Aspidosperma alkaloid skeleton. It retains the trans relationship of the epoxide and ethyl sidechain common to its congeners (1 and 2).



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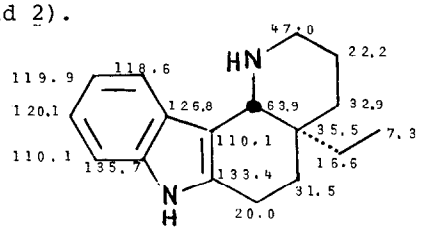

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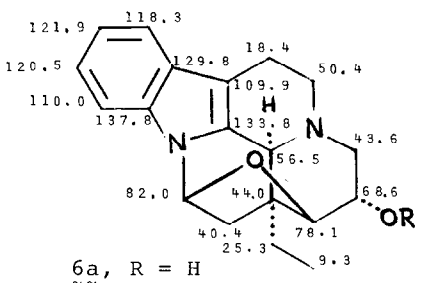
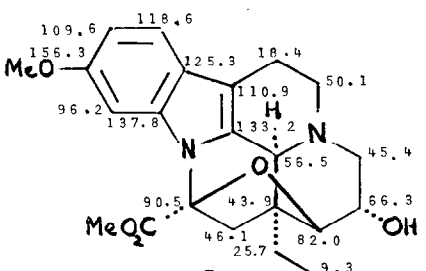
The second minor Voacanga africana base, mp 241-243° C, $[\alpha]_{578}$ -250° (c = 0.1, $CHCl_3$), m/e 310 (M^+, 40%), 251 (10), 209 (50), 208 (base), 180 (10), is a hexacyclic $C_{19}H_{22}N_2O_2$ compound with an indole chromophore [UV: λ_{max}^{EtOH} 232 nm (log ε 4.37), 274 (3.87), 283 (3.83), 292 (3.63)] and a hydroxy group [IR: OH 3200 (m) cm^{-1}; no C=O; on acetylation — no OH, C=O 1735 (s) cm^{-1}]. Its 60 MHz ^1H NMR spectrum [δ($CDCl_3$) 1.10 (t, 3, J = 7 Hz, Me), 2.15 (s, 1, OH, exchangeable in D_2O), 3.70 (m, 2, CHOH, CHOR), 4.15 (s, 1, NCH), 6.00 (dd, 1, J = 4, 2 Hz, NCHO), 7.0-7.6 (m, 4, aromatic Hs), no ca. 7.5 ppm NH signal] and the 90 MHz ^1H NMR spectrum of its acetate [δ($CDCl_3$) 0.97 (t, 3, J = 7 Hz, Me), 1.97 (s, 3, COMe), 3.50 (d, 1, J = 3 Hz, CHOR), 4.12 (s, 1, NCH), 4.68 (dd, 1, J = 5, 3 Hz, CHOAc), 5.85 (dd, 1, J = 4, 2 Hz, NCHO), 6.8-7.4 (m, 4, aromatic Hs)] reveals the presence of an ethyl group attached to a non-protonated carbon, an aminomethine, a hydroxy group and ether bridge bonded only to secondary carbon sites and an N-substituted indole moiety. These data and, finally, the close resemblance of the carbon shifts of the acetate (6b)[7,8] with those recorded for vincarodine (7)[9] indicate structure 6a to be the relative configuration of the new alkaloid.[10]



6a, R = H
6b, R = Ac



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7. The numbers on formula 3a represent hydrogen shifts and those on formulas 3b, 4, 5, 6b and 7 carbon shifts [δ(TMS) = $\delta(CDCl_3)$ + 76.9 ppm].
8. The acetyl δ(CO) and δ(Me) values are 169.6 and 21.2 ppm, respectively.
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10. T. D. J. H. and E. W. acknowledge with gratitude the support of the work at Rice University by the U. S. Public Health Service.

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