Phytochemistry, 1974, Vol. 13, pp. 2857 to 2859. Pergamon Press. Printed in England

A NEW ALKALOID FROM *VOACANGA CHALOTIANA*

EZIO BOMBARDELLI, ATTILIO BONATI, BRUNO DANIELI*, BRUNO GABETTA and GIUSEPPE MUSTICH

Laboratorio Ricerche, Inverni della Beffa, 20141 Milano, Italia, and *Istituto di Chimica Organica, Università degli Studi, 20133 Milano, Italia

(*Received* 17 *February* 1974)

Key Word Index—*Voacanga chalotiana*, Apocynaceae, alkaloid, 3-hydroxyvoachalotine

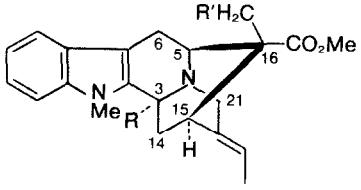
Abstract—The structure of 3-hydroxyvoachalotine, a new indole alkaloid isolated from the root bark of *Voacanga chalotiana*, has been determined by spectroscopic analysis and by chemical correlation with voachalotine

THE ROOT bark of a sample of *Voacanga chalotiana* collected in Angola has been found to contain four new indole alkaloids [1] The present communication is concerned with the structural elucidation of one of the new bases (**1**). The compound, $C_{22}H_{26}N_2O_4$ ($M^+ = 382$), $[\alpha]_D^{22} + 9°$ ($CHCl_3$), showed UV maxima at 229 and 286 nm (1 g ϵ 4·62 and 3·88) characteristic of an indole chromophore. The IR spectrum exhibited carbonyl absorption at 1732 cm^{-1}, as well as an intense OH stretching band at 3450 cm^{-1}. The NMR spectrum (100 MHz, $CDCl_3$) contained signals attributable to four aromatic protons (complex system between δ 7·4 and 6·4), an ethylidene side-chain (methyl group at δ 1·54, *d*, *J* 7 Hz and a vinyl proton at δ 5·24, bq, *J* 7 Hz), a carbomethoxy group and an indolic N–Me resonating at δ 3 61 and 3 32, respectively. The presence of the carbomethoxy and the indolic N–Me functions was corroborated by the occurrence in the MS of the peaks at *m/e* 351 (M^+–OMe), 323 (M^+–CO_2Me), 158 (ion *a*) and 144 (ion *b*). In addition, the NMR spectrum displayed signals for an ABX system (δ_A 1·72, δ_B 1·86, δ_X 3·07, J_{AB} 14 Hz, J_{BX} 4 Hz, J_{AX} 3 Hz), for two protons as a singlet at δ 3·18 and for one proton as a broad doublet (*J* 17 Hz) at δ 4·23. The latter is partially superimposed on the X part of an additional ABX system (δ_A 2·71, δ_B 2 96, δ_X 4·36, J_{AB} 16 Hz, J_{AX} 2 Hz, J_{BX} 5 Hz).

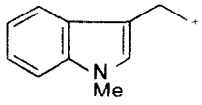
Acetylation of **1** afforded the diacetate (**2**), $C_{26}H_{28}N_2O_6$ ($M^+ = 466$), m.p. 232°, IR bands at 1755 and 1740 cm^{-1}, the nature of the four O atoms of **1** being thus accounted for. The NMR spectrum of **2** (100 MHz, C_6D_6) exhibited four aromatic protons between δ 7·53 and 7·09, the CO_2Me and N–Me functions as singlets at δ 3·36 and 3·24, respectively, and the ethylidene side-chain at δ 5·11 (1H, *bq*, *J* 7 Hz) and δ 1 59 (3H, *d*, *J* 7 Hz); this latter signal partially overlaps an acetyl group signal resonating at unusually high-field (δ 1·55). Furthermore, the NMR spectrum displayed an additional high-field resonating OAc group (δ 1·67), one proton as a double doublet at δ 4·57 (J_1 2·5 Hx, J_2 5 Hz), one proton at δ 3 91 as a broad doublet (*J* 17 Hz), two geminal protons at δ 2·13 and 1·87 as an AB system (*J* 13 Hz) and showing an additional coupling with a proton resonating at about δ 3·10 (*J* 3·5 Hz and 2 Hz, respectively) and, finally, a grouping $-CH_2OAc$ as an AB system (*J* 12 Hz) at δ 4 17 and 3·97 Therefore, the two proton singlet at δ 3·18 in the

[1] GABETTA, B., MARTINELLI, E. and MUSTICH, G. (1974) *Fitoterapia* **45**, 32

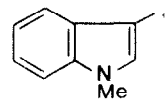
NMR spectrum of **1** must be assigned to a $-CH_2OH$ group which, as indicated by the ion in the MS of **1** at *m/e* 279 (M-103), attributable to the loss of a $CH(CH_2OH)CO_2Me$ fragment, must be located at the same carbon atom bearing the carbomethoxy function The MS fragmentation pattern of alkaloid **1** displayed a striking similarity to that of voachalotine (**3**),[2] the only significant difference being the shift of peaks at *m/e* 183 and 182 at *m/e* 199 (ion *c*) and 198 (ion *d*) in the former, thus indicating for **1** a voachalotine type skeleton bearing one hydroxyl function at the C-ring In particular, the upfield resonances of the two OAc groups are evidence for an interaction between the two ester functions and the aromatic zone, that is the stereochemistry at C-16 in **1** must be the same as that of voachalotine, furthermore, the NMR data are consistent with the location of the additional hydroxyl group at the C-3 position only the ABX system at δ 1·72, 1·86 and 3·07 (δ 1·87, 2·13 and 3·10 in the NMR spectrum of **2**) must be assigned to the protons at C-14 and C-15, while the ABX system at δ 2·71, 2·96 and 4·36 is due to the C-6 and C-5 protons The signals at δ 3·91 (δ 4·23 in the spectrum of **1**) and δ 4·57 in the spectrum of the diacetate **2** must be assigned to one of the C-21 protons and to the C-5 proton, respectively



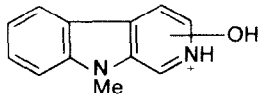
(1) R = R' = OH
(2) R = R' = OAc
(3) R = H, R' = OH



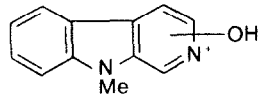
(a)



(b)



(c)



(d)

$NaBH_4$ reduction of the carbinol-amine linkage and transannular cyclization transformed alkaloid **1** into voachalotine, thus supporting for the new base the absolute stereochemistry depicted in structure **1**

EXPERIMENTAL

M ps were corrected NMR were recorded using a 100 MHz instrument

3-Hydroxyvoachalotine (**1**) The alkaloid, isolated from the root bark of *Voacanga chalotiana* Pierre ex Stapf as previously described,[1] exhibited the following properties m p 247 (from EtOAc) $[\alpha]_D^{22}$ + 9 (*c* 1 CHCl$_3$) UV (MeOH) λ_{max} 229 and 286 nm (log ϵ 4·62 and 3·88) ν_{max} 249 nm (log ϵ 3·34), infl at 278 and 289 nm (log ϵ 3·85 and 3·87), IR (KBr) 3450 and 1740 cm^{-1} NMR (CDCl$_3$) 7·4–6·4 (4H, *m*), 5·24 (1H, *bq J* 7 Hz) 4·36 (1H, *dd*, J_1 2 Hz, J_2 5 Hz), 4·23 (1H, *bd J* 17 Hz) 3·61 (3H s) 3·32 (3H s) 3·18 (2H s), 3·07 (1H, *dd*, J_1 4 Hz, J_2 3 Hz) 2·96 (1H, *dd*, J_1 16 Hz, J_2 5 Hz), 2·71 (1H *dd* J_1 16 Hz J_2 2 Hz), 1·86 (1H *dd* J_1 14 Hz, J_2 4 Hz) 1·72 (1H *dd* J_1 14 Hz, J_2 3 Hz), 1·54 (3H *d*, *J* 7 Hz), MS *m/e* 382 (M$^+$ 85%), 365(20) 351(27), 323(17) 279(59), 251(19), 199(66), 198(100) 158(16) 144(30), 143(33) (Calc for $C_{22}H_{26}N_2O_4$ C 69·09 H 6·85 N 7·32 Found C 69·01 H, 6·91, N, 7·34)

3-Hydroxyvoachalotine diacetate (**2**) **1** (30 mg) was treated for 16 hr with Ac_2O (2 ml) in C_5H_5N soln Usual working up gave **2** m p 232 (from EtOAc) UV (MeOH) λ_{max} 228 and 285 nm (log ϵ 4·55 and 3·86) ν_{max} 249

[2] ACHENBACH, H (1966) *Tetrahedron Letters* 4405

nm (log ε 3 35), infl at 278 and 293 nm (log ε 3 84 and 3 79), IR (KBr) 1755, 1740, 1625 cm^{-1}, NMR (C_6D_6) 7 53–7 09 (4H, *m*) 5 11 (1H, *bq*, *J* 7 Hz), 4 57 (1H, *dd*, J_1 2 5 Hz, J_2 5 Hz), 4 17 (1H, *d*, *J* 12 Hz), 3 97 (1H, *d*, *J* 12 Hz), 3 91 (1H, *bd*, *J* 17 Hz), 3 36 (3H, *s*), 3 24 (3H, *s*), 2 13 (1H, *dd*, J_1 13 Hz, J_2 3 5 Hz), 1 87 (1H, *dd*, J_1 13 Hz, J_2 2 Hz), 1 67 (3H, *s*), 1 59 (3H, *d*, *J* 7 Hz), 1 55 (3H, *s*), MS *m/e* 466 (M^+, 73%), 424(25), 423(23), 408(89), 366(14), 365(50), 364(15), 363(25), 351(12), 349(14), 348(29), 347(100), 333(14), 331(12), 322(13), 321(46), 279(20), 261(42), 221(23), 199(38), 198(51), 195(30), 182(20), 181(19), 169(12), 168(20), 167(17), 158(13), 144(30), 143(35)

Transformation of **1** *into voachalotine* **1** (20 mg) was treated in MeOH soln for 3 days with $NaBH_4$ (35 mg). Dilution with H_2O, extraction with $CHCl_3$ and evaporation gave a residue which was refluxed (90 min) in AcOH and then evaporated under red pres. The resulting residue was diluted with H_2O, neutralized with Na_2CO_3 and extracted with CH_2Cl_2. Preparative TLC (eluant hexane–EtOAc–MeOH 5 4 1) yielded voachalotine (8 mg), identified by comparison with authentic material.