ALKALOIDS OF THREE *ASPIDOSPERMA* SPECIES

RUBEN F. GARCIA M.* and KEITH S. BROWN, JR.†
Centro de Pesquisas de Produtos Naturais, I.C.B., C.C.M., Universidade Federal do Rio de Janeiro, Ilha do Fundão, Rio de Janeiro ZC-32, Brazil

Key Word Index—*Aspidosperma formosanum, A. campus-belus, A. desmanthum*; Apocynaceae; isolation; olivacine; uleine; 3-epiuleine; 1,13-dihydro-13-hydroxyuleine; aspidocarpine; lichexanthone; phthalimide; aspidoalbine.

Plants and sources. Aspidosperma formosanum A. P. Duarte (Formosa, Goiás, Brazil, 1965; APD herbarium register 9387); *A. campus-belus* A. P. Duarte (Campos Belos, Goiás, 1965, APD register 9481); *A. desmanthum* Benth. ex Müll.–Arg. (IPEAN, Belém, Pará, Brazil, 1965, APD register 9798). *Previous work*: None; *A. formosanum* is systematically close to *A. dasycarpon* [1] (Series Tomentosa); *A. campusnbelus* to *A. nigricans* [2] (Series Pyricolla); *A. desmanthum* to *A. exalatum* [3], *A. spruceanum* [2a], and *A. album* [4] (Series Nobile).

Bark. Hot continuous EtOH extraction followed by concn gave in each case about 10% syrupy extract. This was macerated with 2N HOAc, filtered, and divided into standard fractions [5] (letter code; method of obtention; percent of extract in the case of *A. formosanum, A. campus-belus*, and *A. desmanthum*, respectively); A, C_6H_6 extraction of the aq. HOAc solution, 0.87, 2.1, 1.47; B, $CHCl_3$ extraction of the same, 8.7, 1.4, 4.47; C, $CHCl_3$ extraction of the solution after neutralization with HCO_3^-, 2.53, 7.1, 2.2; D, $CHCl_3$ extraction after basification to pH 13 with NaOH, 1.75, 0.8, 0.83.

In the preliminary testing of the various extracts, olivacine (**1**) was noted as the principal base in fraction B of *A. campus-belus*, and a small quantity obtained by direct crystallization from MeOH was compared satisfactorily with material from *A. nigricans* [2].

In large-scale work, the following compounds were isolated (plant; fraction(s), isolation methods, compound name and structure number, yield based on dried bark, mp, other relevant data for characterization, confirmation of identity):

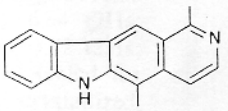
A. desmanthum. C, direct crystallization from MeOH, aspidoalbine (**2**), 0.05%, 174–175° (lit. 174–177° [4], 168° [2a]); MS showing possible impurity of the *N*-acetyl analogue (**3**) at *m/e* 414, but not evident in the NMR; comparison of spectral data [4].

A. formosanum. (1) A,B,C; direct crystallization from MeOH, or basic Al_2O_3 III eluting with hexane–C_6H_6 (1:1) to C_6H_6, or with toluene to toluene–EtOAc (1:1), or with hexane–CH_2Cl_2 (4:1) to CH_2Cl_2, or Si gel eluting with EtOAc–MeOH (9:1); uleine (**4**); 0.64%; 72–78°, but highly variable (known to be poorly crystalline and solvated and show wide melting ranges [2,6]); $[\alpha]_D^{27}$ +20° ($CHCl_3$; *c* 0.94), λ_{max}^{MeOH} nm 213, 307, 315 (log ϵ 4.38, 4.28, 4.24), $\nu_{max}^{CHCl_3}$ cm^{-1} 3534*m*, 2941*s*, 1767*w*, 1637*m*, 1621*m*, 1460*s*, 1445*s*, 1314*s*, 1148*m*, 1125*m*, 1098*m*, 1047*m*, 1007*m*, 977*w*, 935*w*, 911*w*, 873*s*, 839*m*, NMR (100 MHz, $CDCl_3$) δ 8.72 (1Hs, eliminated with D_2O; NH), 7.40–6.80 (4Hm; ArH), 5.18 and 4.84 (2 × 1Hs; $=CH_2$), 3.95 (1Hd, *J* 3 Hz; C-4), 2.16 (3Hs; N-Me), 1.04 (2Hq, *J* 6 Hz; C-14), and 0.76 (3Ht, *J* 6 Hz; C-15), MS M^+ 266 (100%) and fragmentation as published [7], comparison with an authentic sample (B. Gilbert). *Significance*: the large amount of this alkaloid present, its relatively facile isolation, and its unusual and suggestive 1-methylene-4-aminotetrahydrocarbazole structure, have led us to explore chemical transformations into analogues of antischistosomicidal drugs (preazaquinone methides), which will be reported upon in another Journal.

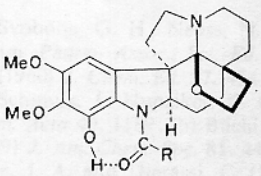
(2) A,B, after preliminary crystallization of uleine; neutral Al_2O_3 I eluting with hexane–C_6H_6 (4:1); 3-epiuleine (**5**); 0.013%; amorphous; UV identical to that of uleine, $\nu_{max}^{CHCl_3}$ cm^{-1} 3521*m*, 2941*s*, 1767*w*, 1637*m*, 1621*m*, 1460*s*, 1445*s*, 1314*s*, 1140*m*, 1125*m*, 1101*m*, 1043*m*, 1010*m*, 978*m*, 952*w*, 910*w*, 870*s*, 823*m*, NMR MHz, $CDCl_3$) δ 7.98

* Present address: Facultad de Ciencias Químicas, Departamento de Química Farmacológica, Universidad de Chile, Santiago. Taken from Master's thesis, C.P.P.N., December 30, 1974.

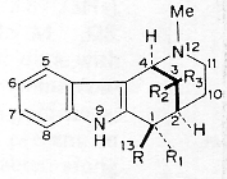
† Present address: Departamento de Zoologia, Instituto de Biologia, Universidade Estadual de Campinas, São Paulo 13.100, Brazil.



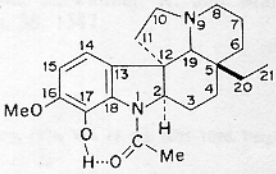
(1)



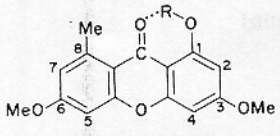
(2) R = Et
(3) R = Me



	R	R_1	R_2	R_3
(4)	$=CH_2$	Et		H
(5)	$=CH_2$	H		Et
(6)	CH_2OH	H		Et



(7)



(8) R = H
(9) R = Ac

(1Hs; NH), 7.40–6.80 (4Hm; ArH), 5.01 and 4.80 (2 × 1Hs; $=CH_2$), 3.86 (1Hd, *J* 2 Hz; C-4), 2.14 (3Hs; N-Me), and 0.96 (3Ht, *J* 6 Hz; C-15); comparison with literature data [8].

(3) C.D. after preliminary crystallization of uleine; EtOAc-soluble fraction over basic Al_2O_3 III eluting with EtOAc–MeOH (19:1), then purification over Florisil, same elution mixture; 1,13-dihydro-13-hydroxyuleine (**6**); 0.0070%; amorphous; $[\alpha]_D^{26}$ −66° (MeOH; *c* 0.25), λ_{max}^{MeOH} nm 219, 283, 290 (log ε 4.56, 3.90, 3.85), $\nu_{max}^{CHCl_3}$ cm^{-1} 3441*m*, 2920*s*, 1460*s*, 1449*sh*, 1380*m*, 1330*m*, 1210*s*, 1150*m*, 1100*m*, 1075*m*, 1040*s*, 1010*s*, 835*s*, NMR (100 MHz, $CDCl_3$) δ 9.18 (1Hs; NH), 7.50–7.06 (4Hm; ArH), 4.06 (2Hs, 1 eliminated with D_2O; C-4 + OH), 3.90 (2Hd, *J* 7 Hz; C-13), 3.10 (1Hm; C-1), 2.24 (3Hs; N-Me), 1.14 (2Hq, *J* 7 Hz; C-14), and 0.82 (3Ht, *J* 7 Hz; C-15), MS M^+ 284 (45%). *m/e* 266 (M^+–H_2O), then fragmentation as in uleine with base peak at *m/e* 168; comparison with an authentic sample (M. Ohashi) and with material prepared by hydroboration of uleine [1d].

(4) A,B. after preliminary crystallization of uleine; basic Al_2O_3 III eluting with toluene to toluene–EtOAc (9:1), then purification over Si gel eluting with EtOAc–MeOH (19:1); (+)-aspidocarpine (**7**); 0.013%, 169–170° (lit. [9] 168.5–169.5°); $[\alpha]_D^{25}$ +174° ($CHCl_3$; *c* 2.2), λ_{max}^{MeOH} nm 228.3, 262.5 (log ε 4.38, 3.72), ν_{max}^{KBr} cm^{-1} 2834*s*, 1629*s*, 1580*s*, 1439*s*, 1245*s*, 1080*s*, 801*s*, NMR (60 MHz, $CDCl_3$) δ 10.94 (1Hs, eliminated with D_2O; OH.....O=C), 6.63 (2 × 1Hd, nearly superimposed; ArH), 4.10 (1Hm; C-2), 3.86 (3Hs; OMe), 3.15 (2Hm; C-10?), 2.30 (3Hs; COMe), and 0.65 (3Ht, *J* 8 Hz; C-21), MS M^+ 370 (25%), base peak at *m/e* 124; comparison with an authentic sample (B. Gilbert) [2].

(5) A; direct crystallization (MeOH) or Florisil eluting with $CHCl_3$; lichexanthone (**8**); 0.0038%; 185–191° (lit. [10] 186–187°); λ_{max}^{MeOH} nm 242, 306 (log ε 4.37, 4.09), λ_{infl} 252, 269, 340 (log ε 4.18, 3.88, 3.63), $\lambda_{max}^{MeOH-NaOH}$ nm 239, 270, 308, 347, (log ε 4.54, 4.22, 4.12, 3.73), ν_{max}^{KBr} cm^{-1} 2941*w*, 1642*s*, 1613*s*, 1570*m*, 1307*m*, 1274*s*, 1205*s*, 1159*s*, 1028*m*, 840*s*, 820*s*, NMR (100 MHz, $CDCl_3$) δ 13.30 (1Hs, eliminated with D_2O; OH.....O=C), 6.64 (2Hs; C-5,7), 6.29 (2Hs; C-2,4), 3.85 (3Hs; OMe), 3.82 (3Hs; OMe), 2.85 (3Hs; ArMe), MS M^+ 286.074 (calcd for $C_{16}H_{14}O_5$, 286.084); O-acetate (**9**), not crystallized, ν_{max}^{KBr} cm^{-1} 2909*m*, 1754*m*, 1610*s*, 1570*m*, 1439*m*, 1262*m*, 1208*s*, 1159*m*, 1140*s*, 1063*m*, 898*m*, 830*m*, NMR (100 MHz; $CDCl_3$) δ 6.70 (1Hd, *J* 3 Hz; C-2), 6.61 (2Hs; C-5,7), 6.51 (1Hd, *J* 3 Hz; C-4), 3.89 (3Hs), 3.87 (3Hs). 2.53 (3Hs, ArMe), 2.40 (3Hs, ArOCOMe), MS M^+ 328, base peak at *m/e* 286; comparison of spectral data with those of a sample isolated from the lichen *Graphina confluens* Fée (D. O. Laux [11], O. R. Gottlieb). *Significance*: this compound probably came from a lichen present on the bark of *A. formosanum* and originally extracted along with it, though the quantity isolated is quite large, corresponding to at least 400 mg of lichen per kg of bark; this amount would have been noticed by the collector or in the laboratory, but no lichen was obviously present or reported. Perhaps some lichens can excrete metabolites into the bark itself.

(6) A; Florisil, eluting with $CHCl_3$–EtOAc (9:1); phthalimide; 0.0036%; 199–200° (MeOH); λ_{max}^{MeOH} nm 223.5, 292.5, NMR (60 MHz, acetone-d_6) δ 7.88 (4Hs; ArH), 2.87 (1Hs, eliminated with D_2O; CONHCO); comparison with a commercial sample. *Significance*: the source of this compound is problematical; chromatographic solvents were redistilled, and the large amount isolated (154 mg) makes it unlikely that it was due to contamination. While this cannot be rigorously eliminated, confirmation is desirable through recollection.

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