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MINOR ALKALOIDS OF *ALSTONIA SCHOLARIS* ROOT

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Key Word Index—*Alstonia scholaris*; Apocynaceae; root bark; indole alkaloids; akuammicine; akuammicine-N_b-methiodide; akuammicine-N_b-oxide; ψ-akuammigine; N_b-demethylechitamine; tubotaiwine.

Plant. Alstonia scholaris R.Br. *Plant part.* Root bark. *Source.* Botanical Garden, Department of Medical Sciences, Thailand. Voucher sample No. ALST 101-731 deposited with the Collection of Materia Medica and Herbaria, University of Bradford.

Previous work. Isolation of echitamine [1] and echitamidine [2]. *Present work.* Six previously unreported alkaloids were detected; five were isolated and identified and one was identified by co-TLC.

EXPERIMENTAL

Alkaloids were extracted in 2% ammoniated MeOH and fractionated by extraction into $CHCl_3$ at pH 1, pH 8 and pH 11 (weak, intermediate and strong base fractions).

Weak base fraction. After separation and purification by PLC, 6 alkaloids were detected. ψ-Akuammigine (chromogenic tests, UV, IR, MS, co-TLC with authentic alkaloid). *Tubotaiwine*, amorphous pale yellow powder; UV: λ_{max} 230, 295, 327, λ_{min} 263, 306 nm; IR$_\gamma$KBr 3400 *m*, 2950 *m*, 1670 *s*, 1603 *s*, 1465 *m*, 1440 *m*, 1275 *m*, 1230 *s*, 1145 *s*, 740 *s* cm^{-1}; MS *m/e* 324, 307, 293, 267, 229, 182, 181, 180, 167, 95, 71; TLC data agrees with tubotaiwine [3]. *Akuammicine*, co-TLC (8 systems) with authentic alkaloid. *Akuammicine-N_b-oxide*, off-white amorphous powder; UV: λ_{max} 228, 294, 327, λ_{min} 260, 307 nm; IR$_\gamma$KBr 3400 *m*, 2930 *m*, 1655 *s*, 1600 *s*, 1464 *s*, 1430 *m*, 1225 *s*, 1100 *m*, 755 *m* cm^{-1}; MS *m/e* 338, 336, 322, 320, 307, 280, 263, 252, 234, 226, 220, 156, 144, 130, 121, 115, 92; reduction product identical with authentic akuammicine (co-TLC, 8 systems). *Akuammicine-N_b-methiodide*, off-white amorphous powder; UV: λ_{max} 228, 294, 328, λ_{min} 260, 307 nm; IR$_\gamma$KBr 3400 *m*, 2950 *m*, 1660 *s*, 1605 *s*, 1470 *m*, 1435 *m*, 1230 *s*, 1100 *s*, 750 *s* cm^{-1}; MS *m/e* 336, 322, 307, 291, 277, 264, 234, 220, 206, 195, 180, 167, 158, 142, 127, 121, 115, 106, 93; identical with synthetic akuammicine-N_b-methiodide (UV, IR, MS, co-TLC). *Hydroxy-19,20-dihydroakuammicine*, white amorphous powder; UV: λ_{max} 225, 297, 328, λ_{min} 265, 305 nm; IR$_\gamma$KBr 3400 *s*, 2910 *s*, 1665 *s*, 1460 *s*, 1435 *m*, 1230 *m*, 1190 *m*, 1090 *m*, 740 *s* cm^{-1}; MS *m/e* 340, 322, 309, 295, 281, 241, 225, 214, 209, 194, 180, 167, 156, 154, 139, 115, 109, 94; acetyl deriv. MS *m/e* 382, 323, 295, 283, 268, 225, 214, 194, 180, 167, 156, 154, 149, 121, 98, 94.

Intermediate base fraction. Separation and purification by PLC yielded 2 alkaloids. *18- or 19-Hydroxy-19,20-dihydroakuammicine*, off-white amorphous powder; UV: λ_{max} 225, 291, 325, λ_{min} 260, 307 nm; IR$_\gamma$KBr 3400 *m*, 2950 *s*, 1670 *m*, 1605 *s*, 1460 *m*, 1430 *m*, 1250 *s*, 1080 *s*, 1020 *s*, 800 *s* cm^{-1}; MS *m/e* 340, 338, 322, 295, 281, 241, 225, 215, 214, 208, 194, 180, 167, 156, 154, 139, 115, 107, 94; acetyl deriv. MS *m/e* 382, 323, 295, 283, 268, 225, 214, 194, 180, 167, 154, 145, 130, 121, 98, 94; reduction product of O-acetyl deriv. UV: λ_{max} 217, 247, 297, λ_{min} 232, 270 nm; MS *m/e* 342, 311, 297, 225, 212, 199, 144, 130, 123, 115, 111, 109, 97, 95. *N_b-Demethylechitamine*, off-white crystals; mp 238–240°; UV: λ_{max} 215, 243, 302, λ_{min} 227, 268 nm; IR$_\gamma$KBr 3450 *s*, 3350 *s*, 2975 *s*, 1735 *s*, 1605 *m*, 1485 *m*, 1470 *s*, 1450 *m*, 1210 *m*, 1110 *s*, 1070 *m*, 805 *m*, 750 *s* cm^{-1}; MS *m/e* 370, 353, 326, 171, 157, 154, 144, 143, 130; NMR (60 MHz, $CDCl_3$) δ 6.4–7.5 (5H, *m*, aromatic ring + NH), 5.5 (1H, *q*, *J* 6.5 Hz, olefinic proton), 3.85 (3H, *s*, COOMe), 3.2 (1–2H, broad signal), 1.5 (3H, *dd*, *J* 6.5 Hz, allylic C-Me); methylation yielded a compound identical with echitamine iodide prepared from isolated echitamine.

Strong base fraction. PLC separation and purification yielded the main alkaloid. *Echitamine* (as chloride), white short needle crystals; mp 274° (dec.); elemental analysis C 62.90%, H 6.93%, N 6.57%, O 15.26%, Cl 8.34% (agrees with $C_{22}H_{29}N_2O_4^+Cl^-$); UV: λ_{max} 214, 237, 294, λ_{min} 224, 258 nm; IR$_\gamma$KBr 3500 *m*, 3280 *s*, 3000 *m*, 2930 *m*, 1735 *s*, 1608 *m*, 1595 *m*, 1485 *s*, 1445 *m*, 1305 *m*, 1270 *m*, 1210 *s*, 1085 *s*, 1055 *s*, 1040 *s*, 755 *s* cm^{-1}; MS *m/e* 384, 383, 369, 353, 194, 152, 144, 130, 124; NMR (60 MHz, $CDCl_3$) free base: δ 6.55–7.65 (5H, *m*, aromatic ring + NH), 5.5 (1H, *q*, olefinic proton), 4.62 (1H, *s*, OH), 3.75 (3H, *s*, COOMe), 2.3 (3H, *s*, N-Me), 1.55–1.75 (3H, *dd*, allylic C-Me). The principal alkaloid found was echitamine (0.21% as chloride) accompanied by 0.002% N_b-demethylechitamine. ψ-Akuammigine comprised 0.0004% and the akuammicine group alkaloids isolated were <0.0001% akuammicine, 0.0004% akuammicine-N_b-oxide, 0.00035% akuammicine-N_b-methiodide, 0.00045% tubotaiwine and 0.001% echitamidine isomers which could not be adequately differentiated from one another.

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