TERTIARY ALKALOIDS OF *ALSTONIA SPECTABILIS* AND *ALSTONIA GLABRIFLORA* (APOCYNACEAE)

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Examination of the tertiary base fraction from *Alstonia spectabilis* R.Br. has led to the isolation of villalstonine, macralstonidine, vincamajine, quebrachidine, pleiocarpamine, and $N_{(a)}$-methylsarpagine. Pleiocarpamine, which is a constituent of *Pleiocarpa mutica* Benth. and *Hunteria eburnea* Pichon,[1] and $N_{(a)}$-methylsarpagine have been obtained previously as hydrolysis products respectively of the bis-indoles villalstonine and macralstonidine. Drastic conditions are required for the hydrolysis of these bis-indoles, and it is unlikely that a significant amount of hydrolysis would have occurred during the isolation of the alkaloids. $N_{(a)}$-Methylsarpagine has not previously been isolated directly from natural sources but the quaternary $N_{(b)}$-metho salt has been isolated from *Pleiocarpa mutica*.[2] The occurrence of vincamajine and of esters of both vincamajine and quebrachidine in *Alstonia constricta* were recently reported.[3]

From another New Guinea species, *Alstonia glabriflora* Mgf., the alkaloids villalstonine, macralstonine, pleiocarpamine, and alstophylline have been isolated. Alstophylline, which has been isolated previously as an hydrolysis product of macralstonine and as an alkaloid from *Alstonia macrophylla* Wall.,[4] is one of the major constituents of the tertiary base fraction of *A. glabriflora*.

Experimental

(*a*) *Alkaloids from* Alstonia spectabilis

Bark of *Alstonia spectabilis* R.Br. (Herbarium voucher number, Hoogland 5138) was collected by Dr R. Hoogland in the south-western foothills of the Finisterre Mountains in New Guinea. The milled, dried bark (1090 g) was extracted with methanol, and the acidified concentrate diluted with water and defatted by extraction with light petroleum. The concentrate was basified (NH_3) and extracted repeatedly with diethyl ether to give 4·8 g tertiary bases. Extraction with chloroform then gave a further 7·0 g tertiary bases. The more intractable material extracted by

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[1] Hesse, M., Philipsborn, W. von, Schumann, D., Spiteller, G., Spiteller-Friedmann, M., Taylor, W. I., Schmid, H., and Karrer, P., *Helv. chim. Acta*, 1964, **47**, 878.

[2] Khan, Z. M., Hesse, M., and Schmid, H., *Helv. chim. Acta*, 1965, **48**, 1957.

[3] Crow, W. D., Hancox, N. C., Johns, S. R., and Lamberton, J. A., *Aust. J. Chem.*, 1970, **23**, 2489.

[4] Kishi, T., Hesse, M., Vetter, W., Gemenden, C. W., Taylor, W. I., and Schmid, H., *Helv. chim. Acta*, 1965, **48**, 1349.

chloroform has not been examined in detail. A sample (0·85 g) of the fraction extracted by diethyl ether was heated with benzene and the benzene-soluble portion (0·66 g) added in benzene solution to a column of neutral alumina (Woelm alumina, with 6% water added, activity III).

(i) *Pleiocarpamine.*—Elution with 5% methylene chloride in benzene gave pleiocarpamine (31 mg), colourless crystals from acetone, m.p. 156–158°, $[\alpha]_D$ +123° (*c*, 0·9 in methanol). The i.r., n.m.r., and mass spectra were in agreement with those recorded for pleiocarpamine.[1]

(ii) *Vincamajine.*—Elution with 10% methylene chloride in benzene gave vincamajine (35 mg), colourless crystals from acetone, m.p. 222–223°, $[\alpha]_D$ −53° (*c*, 0·8 in ethanol). The identification was confirmed by a mixed m.p. determination and spectroscopic comparison with authentic vincamajine.

(iii) *Quebrachidine.*—Elution with 20% methylene chloride in benzene gave quebrachidine (26 mg), colourless crystals from acetone, m.p. 275–277°, $[\alpha]_D$ +43° (*c*, 0·6 in $CHCl_3$). The i.r. and mass spectra were in agreement with published spectra.[5]

(iv) *Villalstonine.*—Elution with methylene chloride gave a mixture (310 mg) consisting of villalstonine and macralstonidine. Villalstonine was largely separated from the mixture as the crystalline oxalate[4] (230 mg). Villalstonine oxalate, m.p. 235–240°, $[\alpha]_D$ +15° (*c*, 0·6 in acetone), was purified by crystallization and villalstonine, recovered from the salt as a colourless gum, was shown to have i.r. and n.m.r. spectra identical with those of a reference sample of villalstonine similarly isolated from the tertiary bases of *Alstonia macrophylla*, and in accordance with published spectroscopic data.[6]

(v) *Macralstonidine.*—Macralstonidine, recovered from the mother liquors from the crystallization of villalstonine oxalate as described,[4] was obtained as colourless crystals, m.p. 295–300°, $[\alpha]_D$ +170° (*c*, 0·9 in $CHCl_3$). The spectroscopic properties were in agreement with those recorded in the literature.[7]

(vi) $N_{(a)}$-*Methylsarpagine.*—A sample (1·08 g) of the tertiary base fraction of *A. spectabilis* extracted into chloroform was heated with a benzene–chloroform mixture (1 : 3) and the solution decanted and added to a column of alumina (Woelm neutral, 1% water added). Examination by t.l.c. of fractions eluted by 20% chloroform in benzene indicated the presence of villalstonine and macralstonidine. Fractions eluted by 5% methanol in chloroform were concentrated and on standing colourless crystals separated from a small volume of solution. Recrystallization from methanol gave $N_{(a)}$-methylsarpagine as colourless prisms, m.p. 300° (dec.), M^+ 324, acetyl derivative, a colourless gum, ν_{max} 1635 cm^{-1} ($CHCl_3$), M^+ 408. A solution of $N_{(a)}$-methylsarpagine (10 mg) was dissolved in methanol (5 ml) and the solution saturated with gaseous methyl chloride. After standing at room temperature for 2 days in a stoppered flask the solution was evaporated by bubbling methyl chloride through it at 40°. Crystallization from a small volume of methanol gave $N_{(a)}$,$N_{(b)}$-dimethylsarpagine chloride, m.p. 275–280° (dec.), $[\alpha]_D$ +38° (*c*, 0·2 in 27·5% methanol in water). The spectroscopic properties were in accordance with those recorded,[2] and the identification was confirmed by a mixed m.p. determination with authentic $N_{(a)}$,$N_{(b)}$-dimethylsarpagine chloride and by comparison of i.r. spectra.

(*b*) *Alkaloids from* Alstonia glabriflora

Bark of *Alstonia glabriflora* Mgf. (Herbarium voucher number TGH 11952) was collected by Dr T. G. Hartley near the village of Omaura in the Eastern Highlands District, Territory of New Guinea. The crude tertiary bases (5·5 g from 477 g dried bark) were isolated in a similar way to the *A. spectabilis* alkaloids, except that they were extracted from the basified solution only into chloroform. Crude alkaloids (1·9 g) were heated with benzene and the benzene-soluble portion (1·3 g) was chromatographed on alumina (Woelm neutral, 6% water added).

[5] "Physical Data of Indole and Dihydroindole Alkaloids." Vol. II. (Eli Lilly: Indiana, U.S.A., 1962); Gorman, M., Burlingame, A. L., and Biemann, K., *Tetrahedron Lett.*, 1963, 39.

[6] Hesse, M., Hürzeler, H., Gemenden, C. W., Joshi, B. S., Taylor, W. I., and Schmid, H., *Helv. chim. Acta*, 1965, **48**, 689.

[7] Waldner, E. E., Hesse, M., Taylor, W. I., and Schmid, H., *Helv. chim. Acta*, 1967, **50**, 1926.

(i) *Alstophylline.*—Fractions eluted by benzene consisted largely of alstophylline (42 mg) which crystallized from methylene chloride–hexane, m.p. 160–162°, $[\alpha]_D$ −122° (*c*, 1·0 in methanol). The identification was confirmed by a mixed m.p. with authentic alstophylline and by comparison of i.r. spectra.

(ii) *Pleiocarpamine.*—The fraction containing pleiocarpamine was eluted by 5% methylene chloride in benzene. By preparative t.l.c. a further quantity of alstophylline (22 mg) was obtained from this fraction as well as purified pleiocarpamine (35 mg), m.p. 156–158°, identical with the compound isolated from *A. spectabilis.*

(iii) *Villalstonine.*—Elution with 20% methylene chloride in benzene gave a fraction from which villalstonine (63 mg) was isolated as the crystalline oxalate, m.p. 235–240°.

(iv) *Macralstonine.*—Several fractions eluted by methylene chloride contained a constituent which crystallized from methanol. Recrystallization from methanol gave macralstonine (54 mg), m.p. 278–280°, $[\alpha]_D$ +22° (*c*, 0·5 in $CHCl_3$). The spectroscopic properties were in accordance with those recorded for macralstonine.[8]

Acknowledgment

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[8] Kishi, T., Hesse, M., Vetter, W., Gemenden, C. W., Taylor, W. I., and Schmid, H., *Helv. chim. Acta*, 1966, **49**, 946.