Phytochemistry, Vol. 21, No. 8, pp. 2160–2161, 1982.
Printed in Great Britain.

0031-9422/82/082160-02$03.00/0

ALKALOIDS OF THE STEM BARK OF *ALSTONIA LANCEOLIFERA**

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(*Received* 13 *October* 1981)

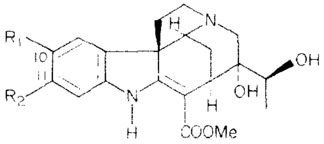
Key Word Index—*Alstonia lanceolifera*; Apocynaceae; stem bark; indole alkaloids.

Abstract—Nine indole alkaloids were identified from the stem bark of *Alstonia lanceolifera*: (−)-lochnericine, 10,11-dimethoxy 1-methyldeacetylpicraline 3′,4′,5′-trimethoxybenzoate, 10,11-dimethoxy-1-methylpicraline, akuammiline, picraline, 10-methoxy-nor-*C*-fluorocurarine, 11-methoxyakuammicine, 10-methoxycompactinervine and 11-methoxycompactinervine.

In a previous paper in this series [1], we reported on the alkaloid content of the leaves of the neocaledonian *Alstonia lanceolifera* S. Moore [2]. Here we describe the alkaloid content of the aerial bark, collected by one of us (T.S., voucher no. Sevenet 795). A previous report on the alkaloids of *A. lanceolifera* [3, 4] incorrectly identified the plant species and it has now been corrected to *A. boulindaensis* Boiteau [2, 5].

Following the usual technique of extraction [6], the ground stem bark yielded 7.85 g crude alkaloid mixture (AM) per kg. Ten alkaloids amongst which two had not previously been described were separated by medium pressure liquid chromatography and prep. TLC. They are, in order of increasing polarity: **1**, (−)-lochnericine (0.05% AM); **2**, 10,11-dimethoxy-1-methyldeacetylpicraline 3′,4′,5′-trimethoxybenzoate (8% AM); **3**, 10,11-dimethoxy 1-methylpicraline (6% AM); **4**, akuammiline (18.4% AM); **5**, picraline (6.4% AM); **6**, 10-methoxy-nor-*C*-fluorocurarine (0.05% AM); **7**, 11-methoxyakuammicine (0.6% AM); **8**, 10-methoxycompactinervine (0.1% AM); and **9**, 11-methoxycompactinervine (0.2% AM) also known as alstovine. The tenth alkaloid, **10**, has a polarity intermediate between those of **1** and **2**; its structure has not been firmly established.

Alkaloids **1**, **4** and **5** are classical among the Apocynaceae and were identified by TLC (direct comparison), MS, IR, UV, NMR and $[\alpha]_D$. The 10,11-dimethoxy-1-methylpicralines **2** and **3** are typical *Alstonia* alkaloids and have been recently described in *A. lanceolata* and in the leaves of *A. lanceolifera* [1, 6]. Alkaloid **7**, first determined by Le Quesne [7, 8] in *A. muelleriana*, was also found by us in *A. odontophora* [9]. The 10-methoxycompactinervine (**8**) proved to be identical with the original sample from *A. lanceolata*; 11-methoxycompactinervine (**9**) presented very similar physical data and its structure was ascertained by direct comparison with a sample of alstovine from *A. vitiensis* provided by Dr. Thal [10].



8 R_1 = OMe, R_2 = H
9 R = H, R_2 = OMe

10-methoxy-nor-*C*-fluorocurarine (**6**) is a new alkaloid with properties similar to those given by Rakimov *et al.* for vincanicine (**11**) [11]. The mass spectrum of **6** showed a M^+ at *m/z* 322 ($C_{20}H_{22}O_2N_2$) and fragments at *m/z* 293, 279 and 121 (base peak). The IR spectrum showed absorptions for N–H (3360 cm^{-1}) and a conjugated aldehyde (2750, 1650 cm^{-1}); the UV had maxima at 245, 290 and 375 nm, a sign of an extended chromophore as in nor-*C*-fluorocurarine [12]. The ^{1}H NMR spectrum ($CDCl_3$) showed a one-proton singlet at δ 9.45, a three-proton multiplet centered at δ 7.0, signals for an ethylidene side chain at δ 5.5 and 1.75 and a three-proton singlet at δ 3.85 (OMe). All these data lead us to propose a methoxy-nor-*C*-fluorocurarine structure for **6**. Location of the aromatic methoxyl group was not an easy task owing to the complexity of the NMR spectrum in deuterochloroform. It was rewarding to record it in deuterobenzene where an ABX system was analysed, yielding the following coupling constants: $J_{AB} = 7$ Hz, $J_{AX} = 1.7$ Hz, $J_{BX} = 0$. This pattern fitted substitution on C-10 or C-11; substitution on C-9 and C-12 should have shown two large *ortho* coupling constants. To ascertain the locus of the substitution, a straightforward chemical correlation between **6** and 11-methoxyakuammicine **7** was attempted according to Scheme 1.

The final compounds **11** and **12**, presented almost identical physical constants but were definitively different on TLC (color with ceric sulphate spray and mobility). Given the stereospecificity of the sodium

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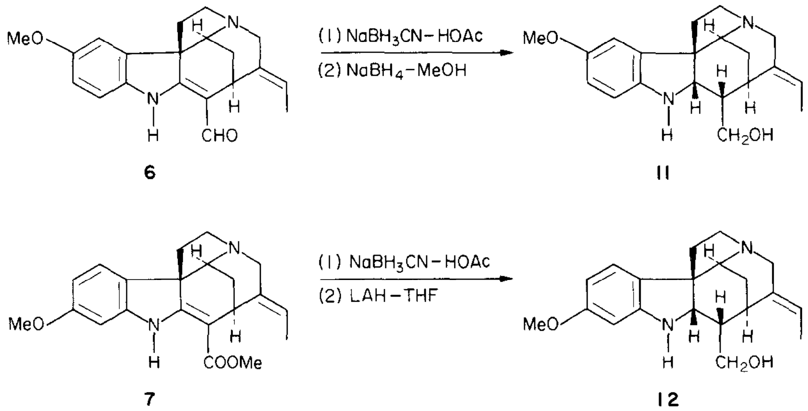
*Part LXXVI in the series "Plants from New Caledonia." For Part LXXV see S. Bassou, H. Mehri and M. Plat (1981) *Planta Med.* (submitted).



Scheme 1.

cyanoborohydride reduction of 2, 16 double bonds, in the α-methylene indoline system [13], compound **6** is the 10-methoxy-nor-*C*-fluorocurarine.

As previously noted during our *Alstonia* studies, the alkaloids of *A. lanceolifera* (stem bark) belong to the type I of the Le Men–Taylor classification with the predominance of the picraline type. An exception is lochnericine (**1**), type II aspidospermane also found in trace quantities in *A. lanceolata.*

EXPERIMENTAL

General. Mps are uncorr. Rotations were determined in $CHCl_3$ and unless otherwise stated NMR were measured in $CDCl_3$ solns; chemical shifts are given in δ values with TMS as int. standard. Chromatography was performed on a medium pressure LC packed with Merck H-60 Si gel. Prep. TLC plates were Whatman K-6F. Colour reactions (CR) were obtained by spraying plates with a soln of cerium (IV) ammonium sulfate.

Extractions. Conducted as described previously [1]. 4.39 g of crude alkaloid mixture was obtained from 560 g ground stem bark. Five such extractions were performed and the resulting 7.39 g AM were chromatographed on 1 kg Si gel under a pressure of 10 bar. $CHCl_3$ was the solvent (1.5 l.), then $CHCl_3$–MeOH (49:1; 10 l.), (19:1; 1.5 l.), 9:1; 1.5 l.), (17:13; 3 l.), (17:3; 3 l.). **1** (5 mg) was in fractions 148–161, **2** (678 mg) in fractions 257–261; **3** (507 mg) in fractions 272–300; fractions 318–322 contained pure **4** (1.54 g); fractions 326–329 contained **5** (544 mg). **6** was isolated from fractions 333–339 by prep. TLC (3 mg); **7** in fractions 350–430 (50 mg); **8** in fractions 431–549 (10 mg) and **9** in fractions 565–570 (13 mg).

*Spectral properties of new alkaloids. 10-Methoxy-nor-*C*-fluorocurarine* (**6**). CR: yellow; $[\alpha]_D -405°$ (c 0.25); UV λ_{max}^{MeOH} nm: 215, 245, 290, 375; IR ν^{CHCl_3} cm^{-1}: 3360, 2750, 1650, 1590, 1560; MS m/z (rel. int.): 322 $[M]^{+\cdot}$, 293, 279, 252, 202, 121 (100); ^1H NMR ($CDCl_3$) δ 9.35 (1H, *s*), 6.90 (3H, *m*), 5.5 (1H, *m*), 1.20 (1H, *brs*), 3.85 (3H, *s*), 1.75 (3H, *d*, $J = 7$ Hz); ^1H NMR (C_6D_6) δ 9.55 (1H, *s*), 7.10 (1H, *d*, $J = 1.7$ Hz), 6.90 (1H, *d*, $J = 7$ Hz), 6.50 (1H, *dd*, $J = 7$, 1.7 Hz), 5.15 (1H, *m*), 3.30 (3H, *s*), 1.50 (3H, *d*, $J = 7$ Hz). *11-Methoxy compactinervine* (**9**). CR blue; mp 239° (EtOH); $[\alpha]_D -486°$ (c 1.1); UV λ_{max}^{MeOH} nm: 260, 305, 337; IR ν^{CHCl_3} cm^{-1}: 3760, 3440, 3380, 1670, 1630, 1600, 1200, 1130, 1110; MS m/z (rel. int.): 386 $[M]^{+\cdot}$, 369, 355, 313, 298, 256(100), 255, 239, 224; ^1H NMR ($CDCl_3$) δ 8.60 (1H, *s*), 7.10 (1H, *m*), 6.50 (2H, *m*), 3.85 (3H, *s*), 3.75 (3H, *s*), 1.10 (3H, *d*, $J = 7$ Hz). *Unknown alkaloid* (**10**). CR pink–orange; UV λ_{max}^{MeOH} nm: 220, 295; IR ν^{CHCl_3} cm^{-1}: 3500, 1740, 1665, 1620, 1450, 1250; MS m/z (rel. int.): 408 $[M]^{+\cdot}$, 349, 335, 263, 168, 135 (100); ^1H NMR($CDCl_3$) δ 7.80–7.00 (4H, *m*), 4.60 (1H, *t*, $J = 4$ Hz), 3.60 (3H, *s*), 2.30 (3H, *s*), 1.80 (3H, *s*). *Reduction product of 11-methoxy akuammicine* (**7**→**12**). CR pink–orange; UV λ_{max}^{MeOH} nm: 212, 247(sh), 302; IR ν^{CHCl_3} cm^{-1}: 3380, 1620, 1500, 1460, 1160; MS m/z (rel. int.): 326, 309, 295, 180, 174, 173, 166(100). *Reduction product of 10-methoxy-nor-*C*-fluorocurarine* (**6**→**11**). CR purple; UV λ_{max}^{MeOH} nm: 220, 245, 300; IR ν^{CHCl_3} cm^{-1}: 3400, 1610, 1500, 1450, 1150; MS m/z (rel. int.): 326, 309, 295, 174, 173, 166(100).

Acknowledgements—Thanks are due to Dr. Thal for kindly providing a sample of alstovine and to Professor J. Lévy for interest in this work.

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