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SOME ALKALOIDS OF *ALSTONIA UNDULATA**

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Abstract—Sixteen indole alkaloids have been identified in the root bark and in the leaves of *Alstonia undulata* from New Caledonia They are vincamedine, tetrahydroalstonine, alstonidine, deplancheine, fluorocarpamine, pleiocarpamine, 11-methoxyakuammicine, cabucraline, desoxycabufiline, cabucraline-*N*(4)-oxide, 11-methoxyakuammicine *N*(4)-oxide, gentiacraline, plumocraline, vincorine, cathafoline and pericyclivine Five *bis* indoles of unknown structure have been isolated The root bark alkaloid mixture contains gentiacraline the first alkaloid made up of an indole and a pyridine alkaloid

INTRODUCTION

Fourteen *Alstonia* species are endemic to New Caledonia [1] In previous work, we have examined the alkaloid content of *A odontophora* [2], *A lanceolata* [3], *A lanceolifera* [4, 5], *A plumosa* [6] and *A sphaerocapitata* [7] Preliminary examination of *A undulata* Guillaum and of *A balansae* Guillaum has shown that these two botanically close species have a similar alkaloid composition *A undulata* has now been investigated in more detail and we herein report on the alkaloid content of its leaves and root bark

RESULTS AND DISCUSSION

The root bark was extracted in the usual fashion [7] to yield 22 8 g/kg of crude alkaloid mixture (AM), which was separated by medium pressure LC Thirteen alkaloids were identified, they are in order of increasing polarity vincamedine **1** (0 5% of AM), tetrahydroalstonine **2** (0 5%), alstonidine **3** (2 5%), deplancheine **4** (1 5%), fluorocarpamine **5** (0 2%), pleiocarpamine **6** (13%), 11-methoxy akuammicine **7** (0 5%), cabucraline **8** (35%), desoxycabufiline **9** (3%), cabucraline-*N*-oxide **10** (2%), 11-methoxy akuammicine-*N*-oxide **11** (2%), gentiacraline **12** (0 5%) and plumocraline **13** (3%)

Among these, only gentiacraline **12** is a novel alkaloid, whose structural determination has been the subject of a preliminary note [8] A complete description of **12** is given in the Experimental

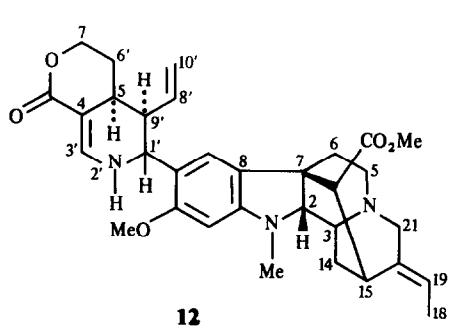
The related tetrahydroalstonine **2** and alstonidine **3** [9] are encountered here for the first time in *Alstonia* species from New Caledonia, their structures have been secured by comparison with authentic samples and by the recording of the 400 MHz ^{1}H NMR spectrum of **2** [10] The isolation of deplancheine **4** is still uncommon but it is the third time that this kind of truncated alkaloid has been found in *Alstonia* species [4, 11] Alkaloids **5**–**11** and **13** are ubiquitous alkaloids of the *Alstonia* from New Caledonia Cabucraline **8**, by far the most abundant alkaloid of the plant, is also part of the dimers **9**, **12** and **13** The presence of pleiocarpamine **6** as the second most abundant base may be responsible for the isolation of plumocraline **13** although no evidence has yet been found of its being an extraction artefact [12]

Besides these alkaloids, a small quantity (< 0 1% of AM) of a low MW compound has been obtained The mass spectrum is similar to that of tetrahydrocantleyine [13] but the two alkaloids have different R_f values on TLC Paucity of material has precluded any further investigation of this alkaloid, which might be related to gentiacraline

Three other dimers, A, B and C, have also been isolated, they will be described with the bisindole alkaloids of the leaves Alkaloid C has also been found in the root bark of *A sphaerocapitata* [7]

Extraction of the leaves gave a 20 g/kg yield of a complicated mixture of alkaloids Purification of these was attempted through a combination of gel permeation chromatography, HPLC and TLC Five monomers were identified, vincorine **14**, cabucraline **8**, cathafoline **15**, tetrahydroalstonine **2** and pericyclivine **16** This latter alkaloid is isolated here for the first time from New Caledonian *Alstonia* species but is related to the well known vincamajine, vincamedine, akuammidine and voachalotine alkaloids

TLC of the alkaloid mixture from the leaves revealed the presence of numerous spots, stained purple with



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*Part 88 in the series "Plants From New Caledonia" For part 87 see ref [7]

Ce(IV) and tailing into a resinous tar Two alkaloids D and E, were separated from this mixture They were unstable in air and to chlorinated solvents and rapidly decomposed into a host of other purple coloured alkaloids Whereas alkaloids A, B and C of the root bark gave prominent molecular ions at *m/z* 702 (A), *m/z* 730 (B) and *m/z* 732 (C), alkaloids D and E of the leaves yielded ions of low intensity at *m/z* 732 and *m/z* 686, respectively All these compounds are characterized in their ^{1}H NMR spectra by signals corresponding to two ethylidene side chains, four (D and E) or five (A, B, C) methyl singlets, an unsubstituted indole aromatic part (four coupling protons) and a 10,11-disubstituted indole nucleus (two sharp singlets) Their instability has so far precluded any accurate structural determination

As in all other *Alstonia* from New Caledonia, the alkaloid content of *A undulata* consists mainly of indole alkaloids of type I of the Le Men–Taylor classification The high proportion in the root bark of the very nucleophilic cabucraline [7] may be responsible for the formation of gentiacraline, the first isolated alkaloid composed of an indole and a pyridine alkaloid

EXPERIMENTAL

General See ref [7] Plant material was collected near the Nekoro Pass, on the way to Mount Poya (alt 200 m), 18 September 1968, under the reference Sevenet 308 An herbarium specimen is kept at the Laboratoire de Phanérogamie (Museum National d'Histoire Naturelle de Paris)

Extraction and isolation of alkaloids Finely ground root bark (1 kg) was extracted as described in ref [7] From it was obtained 22 8 g of crude AM, which was fractionated on 1 kg Merck silica gel H60 Elution pressure was 7 bar and 30 ml fractions were collected Solvents were $CHCl_3$ (3 1), $CHCl_3$–MeOH (99 1, 4 2 1, 49 1, 9 1, 19 1, 5 1, 9 1, 5 1, 4 1, 3 1, 1 1, 3 1) and MeOH (5 1) Vincamedine **1**, tetrahydroalstonine **2** and alstonidine **3** were eluted in fractions 1–100 (663 mg), deplancheine **4** in fractions 100–200 Fractions 201–276 were almost pure pleiocarpamine **6** (1 7 g) and, although less polar, fluorocarpamine **5** was eluted in fractions 312–336 11-Methoxy akuammicine **7** was in fractions 312–328 along with **5** and **6** Fractions 339–688 contained mixtures of cabucraline **8** (~ 3 g) and of its *N*-oxide **10** Desoxycabufiline **9**, the *N*-oxide of **7**, gentiacraline **12** and plumocraline **13** were recovered in fractions 750–1080

Analogous extraction of the leaves yielded 20 2 g/kg of AM A sample of AM (8 5 g) was separated on 264 g Sephadex LH-20 The elution solvent was MeOH–Me_2CO (7 3), 100 ml fractions were collected Fractions 1–8 contained mixtures of dimers (8 1 g), fractions 9–12 (300 mg) were monomers They were purified by CC (silica gel 9 g) to obtain vincorine **14**, cabucraline **8**, cathafoline **15**, tetrahydroalstonine **2** and pericyclivine **16**

Description of new alkaloids Gentiacraline (**12**) $C_{32}H_{39}N_3O_5$ (colour reaction (CR) yellow–orange), $[\alpha]_D = -332°$ (*c* 0 27), UV λ_{max}^{MeOH} nm (log ε) 222 (4 37), 255 (3 85) and 295 (4 3), IR ν_{max} cm^{-1} 3400, 3260, 1740, 1680, 1620, 1580, 1250, 1230, MS *m/z* (rel int) 546 (35), 545 (100), 473 (30), 420, 395, 369, 336, 259, 202, 194 (98), 177, 167, HRMS *m/z* 545 2984 (calc 545 3001), 194 1168 (calc for $C_{11}H_{16}NO_2$ 194 1179), ^{1}H NMR (400 MHz) 7 95 (*dd*, *J* = 6, 1 Hz, H-3′), 6 7 (*s*, H-9), 6 25 (*s*, H-12), 5 7 (*dt*, 17, 10, H-8′), 5 58 (*q*, 7, H-19), 5 45 (*t*, *J* = 6 Hz, N-2′H), 5 25 (*dd*, 17, 2, H-10′), 5 2 (*dd*, 10, 2, H-10′), 4 65 (*dd*, 6, 1, H-3′), 4 48 (*br d*, 5, H-3), 4 4 (*ddd*, 11, 4, 3, H-7′) 4 15 (*t*, 11, H-7′), 4 09 (*d*, 16, H-21), 4 (*dt*, 6, 14, H-5), 3 95 (*s*, CO_2Me), 3 85 (*s*, OMe), 3 65 (*br s*, H-15), 3 25 (*dt*, H-6), 3 15 (*d*, 16, H-21), 2 92 (*d*, 4, H-16), 2 85 (*dd*, 14, 7, H-5), 2 75 (*s*, NMe), 2 65 (*br s*, H-2), 2 42 (*m*, H-14), 2 4 (*m*, H-9′), 2 35 (*m*, H-5′), 1 8 (*dd*, 15, 3, H-6′), 1 7 (*dd*, 14, 3, H-14), 1 55 (*dd*, 7, 2 5, Me-18), 1 5 (*m*, H-6), 1 45 (*m*, H-6′) *Alkaloid A* (CR purple), UV λ_{max}^{MeOH} nm 220, 255 (sh), 290, IR ν_{max} cm^{-1} 3420, 1735, 1620, MS *m/z* (rel int) 702 (100), 687 (20), 643 (10), 566, 549, 368 (5), 336 (25), 335 (100), 321 (5), 194 (15), 183 (10), 136 (20), ^{1}H NMR (400 MHz) δ6 45 (*s*, 1H), 6 2 (*s*, 1H), 5 35 (*q*, *J* = 7 Hz, 1H), 5 2 (*q*, *J* = 7 Hz, 1H), 4 8 (*s*, H), 4 2 (*m*, 2H), 3 9 (*s*, 3H), 3 15 (*s*, 3H), 2 9 (*s*, 3H), 2 7 (*s*, 3H), 1 6 (*d*, *J* = 7 Hz, 3H), 1 35 (*d*, *J* = 7 Hz, 3H) *Alkaloid B* (CR green), UV λ_{max}^{MeOH} nm 220, 267, 285 (sh), IR ν_{max} cm^{-1} 3380, 1740, 1715, 1470, 1210; MS *m/z* (rel int) 730 (3), 702 (0 5), 671, 654, 627 (1), 366 (15), 365 (12), 335 (10), 289 (15), 196 (30), 194 (25), 167 (100), ^{1}H NMR (400 MHz) 6 15 (*s*, 2H), 5 3 (*m*, 2H), 3 95 (*s*, 3H), 3 7 (*s*, 3H), 3 05 (*s*, 3H), 2 8 (*s*, 3H), 2 45 (*s*, 3H), 1 66 (*d*, *J* = 7 Hz, 3H), 1 45 (*d*, *J* = 7 Hz, 3H) *Alkaloid C* (CR purple), $[\alpha]_D = -22°$ (*c* 1), UV λ_{max}^{MeOH} nm 220, 250 (sh), 285, 295, IR ν_{max} cm^{-1} 3350, 1730, 1610, 1210, 1200, MS *m/z* (rel int) 732 (20), 702 (5), 629 (10), 368 (8), 365 (10), 194 (10), 140 (45), 123 (70), 83 (100), ^{1}H NMR (400 MHz) δ6 18 (*s*, 1H), 6 16 (*s*, 1H), 5 28 (2*q*, 2H), 4 85 (*s*, 1H), 4 2 (*d*, *J* = 8 Hz, 1H), 3 9 (*s*, 3H), 3 6 (*s*, 3H), 3 0 (*s*, 3H), 2 8 (*s*, 3H), 2 63 (*s*, 3H), 1 6 (*d*, *J* = 7 Hz, 3H), 1 25 (*d*, *J* = 7 Hz, 3H) *Alkaloid D* (CR purple), UV λ_{max}^{MeOH} nm 225, 285, 295, IR ν_{max} cm^{-1} 3400, 1735, 1615, 1490, 1470, 1450, 1430, MS *m/z* (rel int) 734, 733, 732 (1), 416 (20), 368 (10), 335 (40), 321 (100), 169 (50), 168 (45), ^{1}H NMR (400 MHz) δ6 3 (*s*, 1H), 6 25 (*s*, 1H), 3 85 (*s*, 3H), 3 65 (*s*, 3H), 3 1 (*s*, 3H), 2 5 (*s*, 3H), 1 6 (*d*, *J* = 7 Hz, 3H), 1 3 (*d*, *J* = 7 Hz, 3H) *Alkaloid E* (CR purple), UV λ_{max}^{MeOH} nm 225, 290, IR ν_{max} cm^{-1} 3360, 1730, 1610, 1190, 1160, MS *m/z* (rel int) 686 (1), 685 (2), 626, 533, 473, 335 (15), 279 (2), 223, 182 (20), 107 (100), 106 (60), 105 (55), 92 (95), ^{1}H NMR (400 MHz) δ6 4 (*s*, 1H), 6 25 (*s*, 1H), 3 75 (*s*, 3H), 3 55 (*s*, 3H), 3 0 (*s*, 3H), 2 25 (*s*, 3H), 1 5 (*d*, *J* = 7 Hz, 3H), 1 15 (*d*, *J* = 7 Hz, 3H)

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