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Alkaloids of *Alstonia boulindaensis* Boiteau*

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From the aerial parts of *Alstonia boulindaensis* Boiteau eleven alkaloids were isolated and identified. Eight of them are new : four possess a vincamajine skeleton, one is a sarpagine derivative, and three other compounds contain the new "indolinolid" chromophore 12.

ALSTONIA boulindaensis Boiteau (Apocynaceae), a new species recently described by Boiteau[1], grows in New Caledonia. This plant was originally designated *Alstonia lanceolifera* S. Moore in our two preliminary papers[2,3], a fact which explains the names given to the compounds isolated from it.

The investigation of the aerial parts led to the isolation of eleven indole alkaloids of which eight are hitherto unknown compounds, belonging to three distinct structural groups :

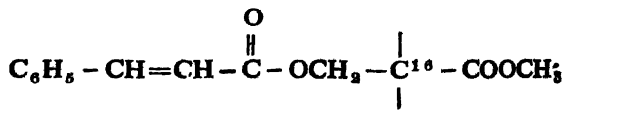
a) seven alkaloids possessing a vincamajine skeleton : 3',4',5'-trimethoxy-17-cinnamoyl-vincamajine **1**, 3', 4', 5'-trimethoxy-17-cinnamoyl–10-methoxy-vincamajine **2**, 3',4',5'-trimethoxy-17-cinnamoyl-10-hydroxy-vincamajine **3**, 3',4',5'-trimethoxy-17-benzoyl-10-hydroxy-vincamajine **4**, 10-methoxy-vincamajine **7**, 3',4',5'-trimethoxy-benzoylvincamajine **5** and 3',4',-5' trimethoxy-benzoyl-methoxy-vincamajine **6**.

While alkaloid **1** has been previously found in *Alstonia constricta*[4], compounds **2**, **3**, **4** and **7** are new and their structure determination was discussed in an earlier paper[2]. The alkaloids **5** and **6** were only isolated in trace amounts, just allowing the determination of their mass spectra.

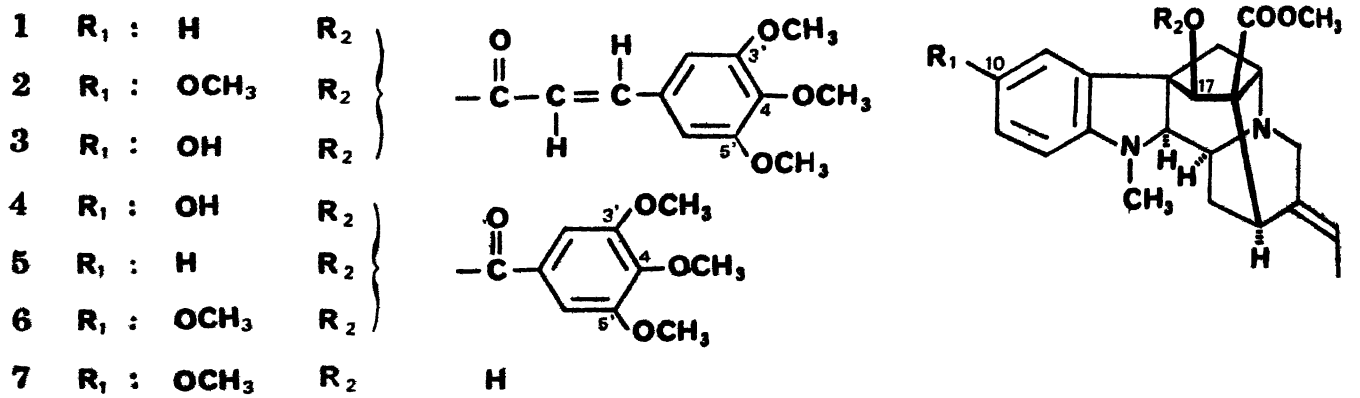
b) one alkaloid with a sarpagine skeleton, Na-methyl-10-methoxy-akuammidine **8**, is also a new compound described in more details in a preliminary communication[2]. Meanwhile it was found to be the major constituent of the root bark of *Alstonia boulindaensis*.

c) three alkaloids possessing a new carbon skeleton[3] : lanciferine **9**, 10-methoxy-lanciferine **10** and 10-hydroxy-lanciferine **11**.

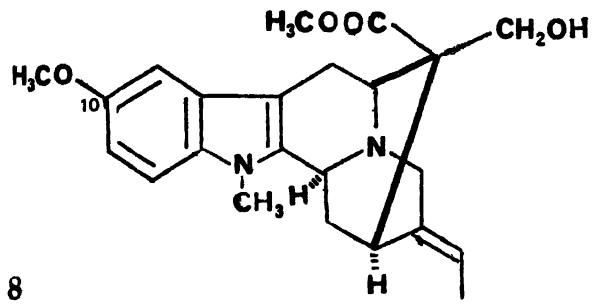
Their structures were determinated by spectral analysis and appropriate chemical reactions. For instance carefully controlled hydrolysis led to the sequence



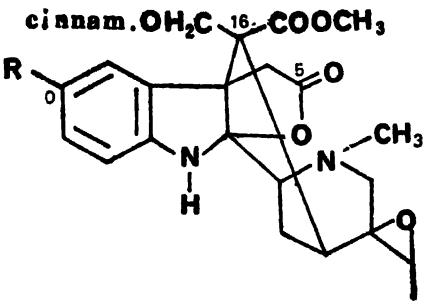
while the "indolinolid" chromophore **12** could be demonstrated by selective ring opening with diazomethane[5]. Finally, their stereochemistry was shown by correlation with picraline and detailed analysis of their CMR spectra[5a].

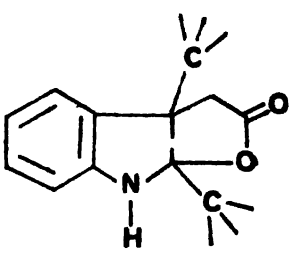


*Plantes de Nouvelle Cale'donie. Partie n° 52 (Laboratoire des plantes me'dicinales du C.N.R.S, Noume'a, Nouvelle-Cale'donie)



8





12

9 R : H

10 R : OCH_3

11 R : OH

The position of the aromatic methoxy group of **10** on C-10 was shown using CMR techniques.

A new alkaloid, nareline, was recently isolated from *Alstonia scholaris*[6]. It derives from picraline skeleton also, but does not possess the characteristic Nb-C_6 bond, as alkaloids **9**, **10** and **11**.

The above results combined with those obtained by Cosson and Mamatas-Kalamaras[7,8] demonstrate that the alkaloids of *Alstonia* species from New-Caledonia are restricted to the biogenetic type I *Corynanthe*, indicating some kind of biochemical and toxonomical archaism.

Experimental

Extraction : Powdered twigs and leaves of *Alstonia boulindaensis* (18 kg) were percolated by ethanol until negative Mayer test and the extract was concentrated under reduced pressure. After treatment with 20% acetic acid (20 l) the precipitated pigments were filtered over kielselgur.

Extraction of the aqueous phase at *p*H 3 with ether furnished 10 g of weak bases A from which alkaloids **1**, **2**, **6** and **7** could be isolated.

The remaining aqueous phase is adjusted to *p*H 8 with sodium hydroxide and extracted with methylene chloride yielding 374 g of bases B.

Isolation of alkaloids **9**, **10** and **11** : 374 g of bases B filtered over a tenfold excess of silicagel (activity I) with ether as solvent. The residue obtained in this manner (90 g) was rechromatographed over 30 times its weight of silicagel (activity I).

Benzene : ether 1/1 eluted 4 g of a mixture of alkaloids **9** and **10** while pure ether eluted 4 g of a fraction containing essentially alkaloid **11**.

Compounds **9** and **10** are separated by preparative tlc using methylene chloride with 0.25% MeOH. Compound **11** was purified by repeated crystallization from ether-methanol.

Lanciferine **9** $C_{31}H_{32}N_2O_7$ (M = 544)

m.p. 259-262° (from ethanol). $[\alpha]_{578}^{20} = -60°$ (chloroform, c = 1). Formula $C_{31}H_{32}N_2O_7$ (High resolution mass spectrometry) : (Found : 544.2209 ; Calc : 544.2209). UV spectrum (EtOH) : 236 (3.87), 280 (4.20). IR spectrum (KBr) : 3400 (NH), 1765 (lactone), 1740 (ester), 1715 (conjugated ester), 1640 (conjugated olefin), 1610 (dihydroindole). PMR spectrum ($CDCl_3$) : 1.20 (d, 3H, J_{HH} = 6 Hz, (-18 H_3) ; 2.40 (s, 3H, NCH_3) ; 3.60 (s, 3H, $COOCH_3$) ; 4.60 (s., 1H, N*H*, disappears on addition of D_2O) ; 5.90 (d, J_{HH} = 16 Hz, olefinic proton from cinnamic part); 6.4-7.5 (m, 10H, 9 aromatic protons + olefinic proton from cinnamic part). Mass spectrometry : m/e(abondance%) 544 (M^+) (9), 224 (23), 180(10), 138 (100), 131 (28), 122 (10), 110 (45), 103 (16), 94 (45), 77 (10), 70 (17).

10-Methoxy lanciferine **10** $C_{32}H_{34}N_2O_8$ (M = 574)

m. p. = 251-254° (from methanol) ; $[\alpha]_{578}^{20} = -64°$ (chloroforom, c = 1). Formula $C_{32}H_{34}N_2O_8$ (High resolution mass spectrometry) (Found : 574.2308 , Calc : 574.2315). UV spectrum : 238 (3.92), 281 (4.18). IR spectrum : same characteristic frequencies as **9** PMR spectrum : very similar to **9** with additional signal to 3.50 ppm (s, 3H, Ar-CH_3). Mass spectrometry : 574 (M^+) (17), 224 (7), 138 (100), 131 (10), 122 (5), 120 (5), 110 (11), 103 (8), 94 (10), 77 (4), 70 (5).

10-Hydroxy lanciferine **11** $C_{31}H_{32}N_2O_8$ (M = 560)

m.p. = 228-231° (from ether methanol) ; $[\alpha]_{578}^{20} = -48°$ (chloroform, c = 1). Formula $C_{31}H_{32}N_2O_8$ (High resolution mass spectrometry) : (Found : 560.2160 ; Calc : 560.2158). UV spectrum : 240 (3.89), 280 (4.19). IR sepctrum : very similar to **9** with additional hydroxyband (3500-3200 cm^{-1}). PMR spectrum : same typical frequencies as **9**, with additional signal to 5.80 ppm (1H disappears on addition of D_2O). Mass spectrometry : 560 (M^+) (20), 224 (8), 138 (100), 131 (18), 122 (5), 120 (7), 110 (10), 103 (10), 94 (20), 77 (7), 70 (7).

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