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ALKALOIDS OF *ALSTONIA ANGUSTIFOLIA*

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

Abstract—Thirty-one alkaloids have been isolated from the leaves and from the stem bark of *Alstonia angustifolia* from Malaysia. Twenty of them were known compounds: yohimbine, *O*-acetyl yohimbine, pleiocarpamine, fluorocarpamine, cathafoline, cabucraline, *N*-1 desmethylquaternine, vincamajine, normacusine B, lochnerine, affinisine, akuammicine, 11-methoxyakuammicine, antirhine, alstonisine, alstonerine, alstophylline, macralstonine, villalstonine and tetrahydrocantleyine. Among the 11 novel alkaloids, three were monomers: 19,20-dehydro-10-methoxytalcarpine, 19,20-dehydro-*O*-acetyl yohimbine and hydroxystrictamine, and eight were dimers: villalstonine *N*-4′-oxide, 10-methoxy villalstonine, 10-methoxyvillalstonine *N*-4′-oxide, 10-methoxymacrocarpamine, 10-methoxymacrocarpamine *N*-4′-oxide, angusticraline, alstocraline and foliacraline. Structural elucidation of the new alkaloids was based on spectral data analysis including high field ^{1}H and ^{13}C NMR.

INTRODUCTION

Alstonia angustifolia Wall. (Apocynaceae) is a tree measuring up to 20 m high. As part of a systematic study of the alkaloids of *Alstonia* species [1] and of a chemotaxonomic study of Malaysian plants, we describe herein the alkaloid content of its leaves and stem bark [2, 3]. Plant material was collected and identified by R. Deverre and T. Sevenet and the phytochemical field team of the Department of Chemistry (University of Malaya, Kuala Lumpur, Malaysia) as part of a cooperation research program between C.N.R.S., France and the University of Malaya, Malaysia.

RESULTS AND DISCUSSION

Extractions were conducted in the usual fashion [1] and the yield of alkaloid mixture (AM) was 2.82 g/kg in the leaves and 13.5 g/kg in the stem bark. Alkaloids were separated by means of column chromatography on silica gel or gel filtration using Sephadex LH-20 and by prep. TLC.

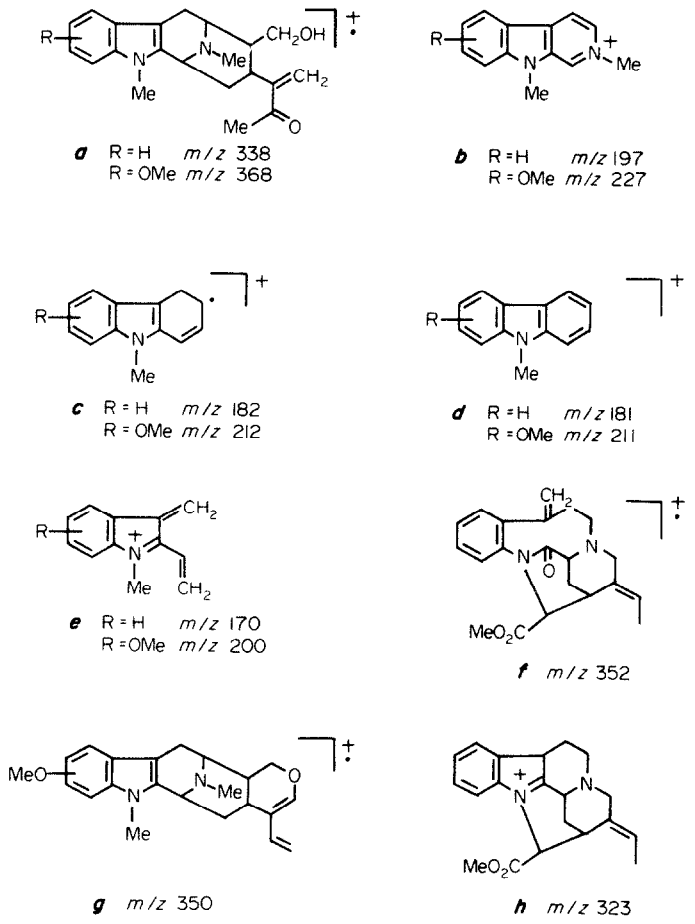
Twenty-seven alkaloids were isolated from the leaves. They were in order of elution from silica gel: alstonisine **1** (0.7% of AM), alstonerine **2** (0.06%), 19,20-dehydro 10-methoxy talcarpine **3** (1%), 19,20-dehydro-*O*-acetyl yohimbine **4** (0.08%), *O*-acetyl yohimbine **5** (1%), vincamajine **6** (0.12%), tetrahydrocantleyine **7** (0.14%), fluorocarpamine **8** (0.14%), pleiocarpamine **9** (0.1%), yohimbine **10** (0.66%), akuammicine **11** (0.1%), affinisine **12** (0.7%), cathafoline **13** (0.04%), cabucraline **14** (0.04%), *N*-1-desmethylquaternine **15** (0.58%), hydroxystrictamine **16** (0.22%), 11-methoxyakuammicine **17** (0.02%), 10-methoxyvillalstonine **18** (0.36%), 10-methoxymacrocarpamine **19** (0.5%), normacusine B **20** (0.2%), lochnerine **21** (0.02%), antirhine **22** (0.22%), 10-methoxy villastonine *N*-4′-oxide **23** (0.13%), foliacraline **24** (0.05%), angusticraline **25** (0.08%), alstocraline **26** (0.13%), and 10-methoxymacrocarpamine *N*-4′-oxide **27** (0.1%).

From the stem bark, nine alkaloids were isolated. They were: macralstonine **28** (0.12%), villastonine **29** (28.2%), villastonine *N*-4′-oxide **30** (0.07%), 11-methoxyakuammicine **17** (0.07%), fluorocarpamine **8** (0.25%), alstophylline **31** (0.07%), alstonisine **1** (0.07%), alstonerine **2** (0.07%) and affinisine **12** (0.05%). Among the 31 alkaloids isolated from the two parts of the plant, compounds **3**, **4**, **16**, **18**, **19**, **23**–**27** and **30** were novel. Known alkaloids **5**–**15**, **17**, **20** and **22** were identified by direct comparison (TLC, UV, IR, mass spectrum, NMR) with authentic samples. Identification of the other known alkaloids was secured by comparison of their spectral properties with literature data: **1** [4, 5], **2** [6], **21** [7], **28** [8], **29** [9, 10], **31** [11].

Fourteen of these bases had, at least in part, the macroline skeleton. They were alkaloids **1**, **2**, **28**, **29** and **31** which had previously been isolated from other *Alstonia* species, the novel monomer **3** and dimers **18**, **19**, **23**–**27** and **30**. Villalstonine **29** was by far the most abundant alkaloid of *A. angustifolia*. Its structure was elucidated *ca* 20 years ago by chemical and spectroscopic means [9, 10, 12]. In order to correctly assign the spectra of the novel compounds, a reinvestigation of the ^{1}H and ^{13}C NMR spectra of **29** was carried out by means of modern 2D NMR techniques. This led to ^{13}C assignments presented in Table 1 which are slightly different from those of ref. [13]. The high field ^{1}H NMR data of all compounds with a macroline unit are given in the Experimental.

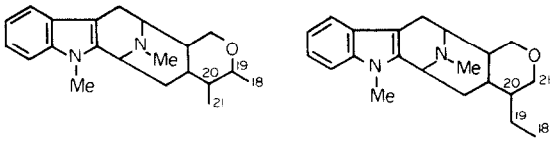
The macroline unit of the novel alkaloids was easily identified from the mass spectra by ions **a**–**e** (Scheme 1) [8, 11]. The ^{1}H NMR spectra also showed several typical signals: three-proton singlets for N-1 and N-4 methyls, a one-proton triplet between 4 and 4.5 ppm (H-17), two doublets of doublets between 3 and 4 ppm (H-17 and H-6) and two doublets between 2 and 3 ppm (H-5 and H-6).

The new dimers belonged to three groups corresponding to the following associations: villalstonine derivatives:



Scheme 1. Diagnostic ions in the mass spectra of the macroline unit.

A macroline type unit + dihydropleiocarpamine unit; macrocarpamine derivatives: B macroline type unit + dihydropleiocarpamine unit and derivatives of a new type: B macroline type unit + cabucraline unit (Scheme 2).

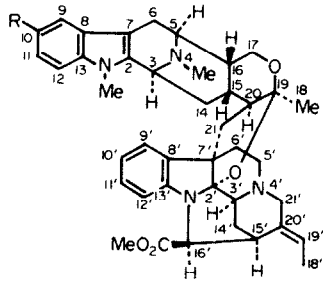


Scheme 2. Types of macroline.

Villastonine derivatives

The mass spectrum of alkaloid **18** gave a $[M]^+$ at *m/z* 690 ($C_{42}H_{50}N_4O_5$ villalstonine + 30 mu) and fragments **a**–**e** corresponding to a methoxylated macroline part. The pleiocarpamine unit was characterized by ions at *m/z* 322, 307, 263, 180, 135, 107 [14] as well as by fragment **f** at *m/z* 352 indicative of a double junction between the two monomers. The ^{1}H NMR spectra of **18** and of **29** were almost superimposable and differed only in the aromatic part (seven aromatic protons) and by the occurrence of a signal for a methoxyl (*s*, δ, 3.90 ppm). ^{13}C NMR data (Table 1) fitted well the proposed structure and the aromatic methoxyl group was located on C-10 according to the typical chemical shifts of C-10 (δ153.8 ppm), C-9 (100.6) and C-11 (110.6) [15].

The mass spectrum of alkaloid **23** displayed the typical fragments of **18** and the peak of highest mass value occurred at *m/z* 690. Comparison of the ^{1}H NMR spectra of **18** and **23** showed, in **23**, a deshielding of the signals of H-3′, of one of the H-5′, and one of H-21′ at δ 4.40, 3.44 and 5.07 ppm, respectively. These features are characteristic of *N*-oxides and this was demonstrated by conversion of **23** into 10-methoxyvillalstonine **18** by sulphurous



29 R = H villastonine
18 R = OMe
23 R = OMe ; N − 4′ → O
30 R = H ; N − 4′ → O

Table 1. ^{13}C NMR 75 MHz; $CDCl_3$ δ values in ppm of alkaloids **29**, **18**, **23**, **32**, **19**, **24**–**26** and **3**

C	**29**	**18**	**23**	**32**[17]	**19**	**24**	**25**	**26**	**3**
2	135.7	135.4	133.4	132.8	133.5	132.4	132.7	132.4	132.6
3	53.3	53.4	53.4	53.8	53.8	52.3	54.3	53.5	53.8
5	54.3	54.4	54.2	54.9	54.8	51.6	53.3	54.4	54.7
6	22.8	22.9	23.0	22.7	22.7	23.3	22.2	23.0	22.9
7	106.6	106.2	106.3	106.6	106.3	106.7	106.0	106.1	105.4
8	126.3	126.6	127.4	126.3	126.6	127	126.6	126.7	126.7
9	118.1	100.6	100.4	117.5	100.3	100.5	101.3	100.6	100.4
10	120.8	153.8	153.8	118.8	153.9	151.9	153.3	152.2	153.7
11	118.8	110.6	110.8	120.8	110.8	109.6	108.7	109.3	110.5
12	108.7	109.4	110.1	108.7	109.5	109.6	108.5	109.3	109.6
13	137.1	132.2	132.1	137.0	132.5	132.4	133.9	133.7	133.8
14	32.4	32.5	32.5	32.3	32.3	29.7	31.3	29.7	32.2
15	32.2*	32.0	31.8	23.8	31.1	32.6	25.3	32.9	31.8
16	37.7*	37.8	37.7	39.0	38.8	38.8	38.2	37.1	38.5
17	65.6	65.6	65.6	66.7	66.8	67.0	59.6	67.4	67.7
18	26.5	26.4	26.3	118.3	118.6	nd	19.6	20.5	22.4
19	98.5	98.6	99.1	126.5	128.9	30.1	34.2	29.7	157.6
20	36.7*	36.7	36.4	115.5	115.3	39.2	47.9	39.4	117.3
21	28.4*	28.3	27.9	144.3	145.5	99.2	93.6	98.8	188.9
N-1 Me	29.0	29.0	29.1	29.1	29.2	29.7	28.8	27.5	29.7
N-4 Me	41.8*	41.8	41.8	41.8	41.8	41.1	41.7	41.7	41.7
OMe	—	56.1	56.0	—	56.0	56.0	56.1	56.1	56.1
2′	91.9	91.8	92.9	66.8	67.0	185	78.7	nd	
3′	51.7	50.8	66.7	54.4	52.0	53.9	47.4	47.6	
5′	47.3	47.2	63.8	49.9	49.2	nd	50.9	49.9	
6′	31.1*	31.1	32.5	21.5	28.0	32	29.7	32.5	
7′	44.0	43.9	42.8	45.7	44.8	nd	42.4	42.1	
8′	132.8	133.6	133.3	133.5	132.5	nd	132.1	132.6	
9′	120.8	120.8	121.4	123.1	123.5	123.9	118.6	118.1	
10′	118.1	118.1	119.0	125.4	119.6	118	124.5	120.3	
11′	126.5	126.6	125.8	127.2	127.1	146.4	156.2	148.8	
12′	109.3	109.3	103.3	107.8	108.4	97.2	92.9	97.5	
13′	146.8	146.7	145.8	147.0	146.3	153.9	151.6	154.1	
14′	27.3	29.1	29.7	29.4	29.6	nd	32.4	33.6	
15′	31.9	31.8	31.2	32.1	31.1	29.3	34.2	34.3	
16′	57.7	57.7	57.5	58.2	57.9	54.7	52.8	52.5	
18′	12.3	12.3	12.7	12.3	12.4	12.9	13.0	13.2	
19′	118.5	118.8	119.8	117.8	118.6	nd	119.1	118.9	
20′	136.8	136.9	nd	135.7	nd	nd	139.1	141.2	
21′	52.8*	52.8	67.4	52.8	52.4	50.3	54.8	54.0	
COOMe	170.8	170.8	170.2	170.3	170.1	171.8	172.9	169.7	
COOMe	51.9	51.7	52.1	51.6	52.0	51.4	51.4	51.5	
ArOMe							55.2	—	
N-1′ Me							33.1	33.6	

* Revised data.
nd: Not detected.

acid [16]. ^{13}C NMR also showed the effects of oxidation in the downfield shifts of C-3′, C-5′ and C-21′ (Table 1).

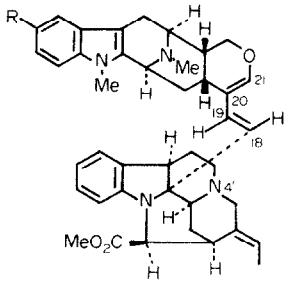
Alkaloid **30** gave UV and mass spectra superimposable with those of villastonine **29**. Examination of its ^1H NMR spectrum suggested an N-4′ oxidation because of the downfield shift of H-21′ (δ 5.16 ppm). This hypothesis was confirmed by the reduction (H_2SO_3) of **30** which yielded a compound identical with **29**.

Macrocarpamine derivatives

Alkaloids **19** and **27** also contained a methoxymacroline unit and a dihydropleiocarpamine unit as shown by mass spectrometry and ^1H NMR. Their two moieties now formed a macrocarpamine skeleton **32** [17] with a **B** macroline type unit. This skeleton was identified by the following spectral features. The IR spectra showed an intense enol-ether band at 1645 cm^{-1}. The mass spectra displayed fragments **g** at *m/z* 350 (= anhydromacrosahline methine + 30 mu) and **h** at *m/z* 323 (Scheme 1) which accounted for a single bond between the two parts. Inspection of ^1H NMR spectra showed signals for *trans* related olefinic protons H-18 and H-19 (AB system with J = 16.5 Hz), while H-21 and H-7′ were observed as a singlet and as a doublet of doublets (J = 10.5 and 7.5 Hz), respectively, at *ca* 6.3 and 2.7 ppm. The structure of **19**

was also deduced from the $[M]^+$ at *m/z* 672, $C_{42}H_{48}N_4O_4$ = macrocarpamine + 30 mu) and from the AMX system (J_{AM} = 8.6 Hz, J_{AX} = 1.1 Hz) formed by three aromatic protons, implying a substitution on C-10 or C-11. ^{13}C assignments (Table 1) were based on literature data related to plumocraline [18] and villalstonine for the dihydropleiocarpamine part and pandicine [19] for the macroline part. These results confirmed structure **19** and allowed location of the methoxyl group on C-10 [15].

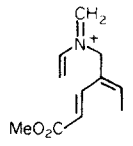
Alkaloid **27** is more polar than **19** and displayed a $[M]^+$ of weak intensity at *m/z* 688, a fragment at *m/z* 672 $[M-16]^+$ and the same ions as found in the mass spectrum of **19**. In the ^1H NMR spectrum of **27**, protons H-3′, H-5′ and H-21′ were deshielded as in *N*-oxides **23** and **30**. As an unambigous proof of structure, **27** was reduced (H_2SO_3) into a compound identical with **19**.



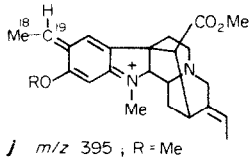
19 R = OMe
27 R = OMe, N − 4′ → O
32 R = H macrocarpamine

New types of derivatives

Alkaloids **25** and **26** presented many spectral analogues. Their UV spectra were the superimposition of substituted indole and indoline chromophores. The IR spectra displayed absorption bands at 1735 (COOMe) and 1620 (>C=C<) cm^{-1}. The prominent ions in the mass spectra featured a methoxymacroline part (ions **a**–**e**) and a cabucraline moiety with ion **i** at *m/z* 194 [20, 21]. This second part was also represented by fragments at *m/z* 395 (**25**) and 384 (**26**) for which structures **j** and **k** were proposed.

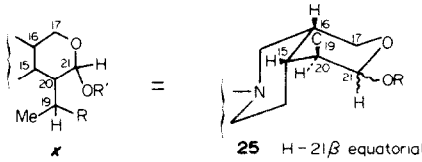


i *m/z* 194



j *m/z* 395, R = Me
k *m/z* 384, R = H

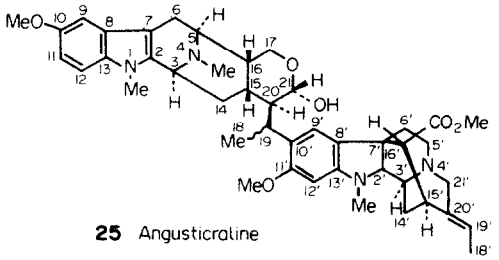
The ^1H NMR spectra of **25** and **26** were analysed with the help of 2D chemical shift correlation (COSY) spectra and comparison with the spectrum of cabucraline **14** [22]. All the signals of cabucraline were present in the spectra of **25** and **26** except for one of the aromatic protons. The five aromatic protons could be separated into two systems: an AMX system assigned to the methoxymacroline part, and two one-proton singlets assigned to H-9′ and H-12′ of the cabucraline part. This allowed location of an additional substitution on C-10′. In the methoxymacroline part most of the protons were easily identified among which Me-18 as a doublet, H-19 and H-20 as multiplets, and a single H-21 located in the olefinic area. The multiplicity and the chemical shift of these protons allowed the deduction of new sort of linkage as shown in partial structure **x**.



x

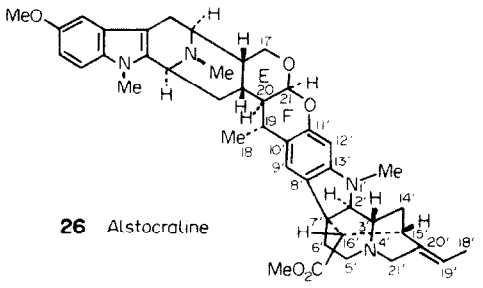
25 H-21β equatorial, R = H
26 H-21α axial, R = C-10′

The mass spectrum of angusticraline **25** showed a $[M]^+$ at *m/z* 736 which indicated a $C_{44}H_{56}N_4O_6$ formula, in agreement with a single link between the two monomers. This bond could be placed between C-19 and C-10′ whose protons are missing. This leaves an hemiketal function which gave an IR absorption at 3340 cm^{-1} (OH) and was responsible for the loss of water in the mass spectrum (ion at *m/z* 718). On the ^1H NMR spectrum, observation of a singlet for H-21 (δ 5.35 ppm) suggested that H-21 and H-20 were equatorial and thus OH-21 α axial. Analysis of the ^{13}C NMR spectrum of **25** fully supported the proposed structure and in particular the presence and position of the two aromatic methoxy groups. The C-18–C-21 appendage was characterized by signals at δ 19.6 ppm (quartet), 34.2, 47.9 and 93.6 ppm (three doublets). Comparison of the spectra of angusticraline **25** and villalstonine **29** showed a 11 ppm deshielding of C-20 in **25**, tentatively explained by loss of a γ-effect [23] due to opening of ring F. The axial orientation of the free hydroxyl induced a 6 ppm shielding of C-17.



25 Angusticraline

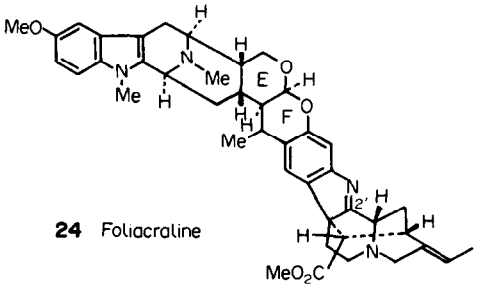
The mass spectrum of alstocraline **26** showed a $[M]^+$ at *m/z* 704, indicative of a $C_{43}H_{52}N_4O_5$ formula; at variance with the mass spectrum of **25**, there was no loss of water in **26** and there was no hydroxyl vibration in the IR spectrum. The elemental composition difference between **25** and **26**, CH_4O, may be explained by demethylation of a methoxy group and loss of water. The presence of ion **k** (*m/z* 384) supported the suggested demethylation hypothesis which was further confirmed by the analysis of



26 Alstocraline

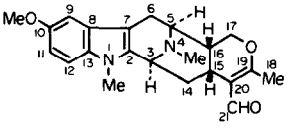
the ^{13}C NMR spectrum (Table 1). Thus, a single aromatic methoxy was detected at δ 56.1 ppm, and signals for a new ring F were observed at δ 29.7 (C-19), 39.4 (C-20), 98.8 (C-21), 120.3 (C-10′) and 148.8 (C-11′). The E–F ring junction was *cis* according to the value of *J* H-21–H-20 (3.1 Hz); protons H-20 and H-21 were α to account for the similar chemical shifts of C-17 in alstocraline **26** and villalstonine **29**. The C-9′ resonances in **26** (118.1 ppm) and **25** (118.6 ppm) were similar, indicating the absence of steric compression with Me-18. It was deduced therefrom that this methyl was axial (α) in accordance with a chemical shift of 20.5 ppm.

The last unknown dimer was foliacraline **24** which was isolated in small amount. Its spectral properties (mass spectrum, ^1H and partial ^{13}C NMR: Table 1) showed the existence of a 10-methoxylated macroline moiety with the same C-18–C-21 appendage as those of angusticraline **25** and alstocraline **26**. The second moiety contained a methyl ester group detected by an IR absorption at 1735 cm^{-1} and by a three-proton singlet at δ 3.58 ppm in the ^1H NMR, and an ethylidene chain (three-proton doublet of doublets at 1.46 and one proton quartet at 5.5 ppm). The $[M]^+$ of **24** occurred at *m/z* 688 ($C_{42}H_{45}N_4O_5$) and corresponded to that of **26** less 16 mu. This difference affected the second moiety and might correspond to a demethylation and an extra unsaturation. Effectively, the signals for the N-1′-Me were missing in the ^1H and ^{13}C NMR spectra and the presence of a N-1′=C-2′ imine bond was suggested by the observation of a quaternary carbon signal (C-2′) at δ 185 ppm. These features brought forward a norcabucraline or strictamine structure for the second part of the molecule. The monomers were linked as in **26** as shown by two one-proton singlets at δ 6.63 and 6.28 ppm (H-9′ and H-12′) and by two quaternary carbons at δ 118 and 146.4 ppm (C-10′ and C-11′). Similarly, the *cis* E–F ring junction was deduced from the H-21 doublet (*J* H-21–H-20 = 3 Hz) and from the chemical shift of C-17 (δ 67 ppm).

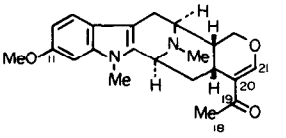


24 Foliacraline

Alkaloid **3** gave the typical signals (mass spectrum, ^1H NMR) for a 10- or 11-methoxylated macroline and its spectral properties were reminiscent of those of alstophylline **31**. Both compounds had the same composition ($[M]^+$ *m/z* 366, $C_{22}H_{26}N_2O_3$) and their mass spectra displayed similar fragments. Two intense IR absorptions at 1615 and 1635 cm^{-1} corresponded to an α, β unsaturated carbonyl. The slight differences observed in the UV spectra of **3** and **31** suggested a different position for the methoxy group. In **3**, its location on C-10 was deduced from ^{13}C NMR (Table 1). ^1H NMR spectra of **3** and **31** recorded at 20° were similar and presented broad signals. At 45°, the resolution of the spectrum of **31** was better and in particular for the N-4 methyl which could not be observed at 20°. This phenomenon might be explained by the presence of rotamers around the C-19–C-20 bond. The assignment of the protons of **3** was supported by a COSY spectrum and fitted well the proposed structure. The vinylogous ester group was characterized by a singlet for H-21 at δ 9.65 ppm and by a singlet for Me-18 at δ 2.18 ppm. The structure **3**: 19,20-dehydro 10-methoxytalcarpine was also supported by the ^{13}C NMR spectrum (Table 1) which was assigned by comparison with that of villalstonine. Carbons C-19, C-20 and C-21 appeared at low field besides the eight carbons of the indole nucleus. The most deshielded CH (δ 188.9 ppm) was assigned to C-21 and the signals at δ 157.6 and 115.9 ppm to C-19 and C-20, respectively.

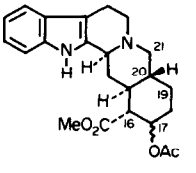


3



31 Alstophylline

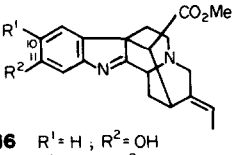
Alkaloid **4** was an indole derivative (UV spectrum) whose spectral properties (mass spectrum, IR, ^1H NMR) were similar to those of *O*-acetylyohimbine **5** [24]. Its $[M]^+$ at *m/z* 394 ($C_{23}H_{26}O_4N_2$) was accompanied by a strong $[M-1]^+$ reminiscent of the indoloquinolizidines; it corresponded to the $[M]^+$ of **5**, less 2 mass units, suggesting the presence of an extra unsaturation. The ^1H NMR spectrum showed a single olefinic proton (H-19) which was superimposed on the H-17 signal at δ 5.53 ppm. These data allowed consideration of two structures: 19,20-dehydro or 20,21-dehydro-*O*-acetylyohimbine. The latter was excluded because of the absence of an enamine band in the IR spectrum. Paucity of alkaloid **4** did not allow for determination of the configurations of C-16 and C-17. Compound **4** might be identical to one of the two derivatives **4a, b** prepared by Brown and Pratt [25].



5 17βH
4a Δ-19,20 ; 17αH
4b Δ-19,20 ; 17βH

The structure of alkaloid **16** (= 11-hydroxystrictamine) was established by comparison of its spectral properties with those of the novel 10-hydroxystrictamine **33** whose structure was determined in our laboratory (J. Vercauteren, personal communication). Alkaloid **33** was also isolated from *Vinca minor* (Vercauteren, personal communication) and *A. deplanchei*, var. *ndokoaensis* [22].

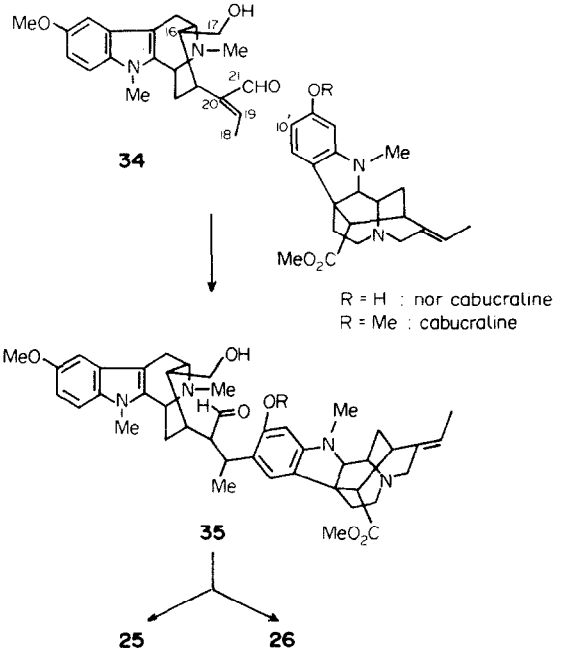
The structural elucidation of **16** and **33** will be the subject of a forthcoming publication.



16 R^1 = H ; R^2 = OH
33 R^1 = OH ; R^2 = H

CONCLUSIONS

The alkaloids of *A. angustifolia* belong to type I of the Le Men and Taylor classification [26]. The macroline skeleton is preponderant and its high reactivity is shown by frequent dimerizations. Angusticraline **25** and alstocraline **26** associate for the first time macroline and cabucraline and their biogenesis may be explained in the following manner (Scheme 3): the nucleophilic C-10′ of cabucraline gives a Michael reaction with unsaturated aldehyde **34** (=opened form of a talcarpine). An analogous mechanism may explain the formation of foliacraline **24**. The generated aldehyde **35** affords a propitious geometry to form hemiketal **25** (R=Me) or ketal **26** (R=H).



Scheme 3. Proposed biogenesis of angusticraline **25** and alstocraline **26**.

A. angustifolia is a new example of a plant with macroline alkaloids belonging to the Monuraspermum section of the genus *Alstonia*, as *A. spectabilis*, *A. muelleriana*, *A. macrophylla* and *A. glabriflora*. Macroline alkaloids constitute a real marker of this section.

EXPERIMENTAL

General. Plant material was collected in the State of Yohore (Malaysia) and identified by R. Deverre and one of us (T. S.). Voucher specimens are kept in the herbarium of the Department of Chemistry of the University of Malaya.

Mps: uncorr. ^{1}H NMR were measured in $CDCl_3$ at 300, 400 and 500 MHz. Chemical shifts are given in ppm and coupling constants in Hz. Colour reactions (CR) were obtained by spraying TLC plates with a solution of Ce-IV $(NH_4)_2SO_4$.

Extraction and isolation of alkaloids. Dried ground leaves (2.75 kg) were wetted with 50% NH_4OH and lixiviated by means of 45 l of EtOAc. The lixiviate was extracted with 2% H_2SO_4 until Mayer's test was negative, the acid layer sepd, made alkaline with NH_4OH and extracted with $CHCl_3$. The $CHCl_3$ soln was washed with H_2O, dried (Na_2SO_4) and evapd *in vacuo* to give 13.12 g of crude alkaloid mixture (AM) (4.77 g/kg). Purified AM were obtained by performing a lixiviation of dried ground leaves (200 g) with CH_2Cl_2 prior to the extn of alkaloids. The yield of purified AM was 2.82 g/kg. Crude AM (6.8 g) was chromatographed on a silica gel column (210 g) which was packed in $CHCl_3$ and eluted in 160 ml fractions with $CHCl_3$ (fractions 1–40), $CHCl_3$–MeOH (99:1) (50–76), $CHCl_3$–MeOH (19:1) (77–93), $CHCl_3$–MeOH (9:1) (94–104) and MeOH (105–110). The fractions were analysed by TLC and pooled according to their composition. Alkaloids **1** and **2** were in fr. 15–20, **3** in fr. 15–35, **4–6** in fr. 20–55, **7** in frs 45–60, **8** and **9** in fr. 59–67, **10** in fr. 65–83, **11** in fr. 70–80, **12–15** in fr. 70–93, **16** and **17** in fr. 81–83, **18** and **19** in fr. 81–104, **20–25** in fr. 94–104, **25** in fr. 94–110, alkaloid **27** in fr. 105–110.

In the same manner, 3.5 kg of dried ground stem bark gave 72 g of crude AM (20.57 g/kg). Yield of purified AM was 13.5 g/kg. Crude AM (8 g) was fractionated by filtration on a column of Sephadex LH 20 gel (80 g) packed in $CHCl_3$–MeOH (22:3). Elution solvents were $CHCl_3$–MeOH (22:3) (1–10), (91:9) (11–19), and (19:1) (20–27); fractions (10 ml) were analysed by TLC. Alkaloids **28** and **29** were in fractions 9–19, alkaloids **1**, **17**, **30** and **31** in fr. 16–19, alkaloids **2** and **8** in fr. 16–23 and alkaloid **12** in fr. 20–23.

Alstonisine **1**. ^{1}H NMR (400 MHz, $CDCl_3$): 8.26 (*dd*, $J=7$, 1.5 Hz, H-12), 7.63 (*s*, H-21), 7.35 (*br dd*, $J=7$, 1.5 Hz, H-11), 7.32 (*br dd*, $J=7$, 1.5 Hz, H-10), 6.88 (*dd*, $J=7$, 1.5 Hz, H-9), 4.45 (*t*, $J=11$ Hz, H-17), 4.42 (*ddd*, $J=11$, 4, 1.5 Hz, H-17), 3.68 (*br d*, $J=7$ Hz, H-5), 3.40 (*m*, H-14), 3.20 (*s*, N-1 Me), 3.18 (*br s*, H-3), 2.52 (*dd*, $J=13$, 7 Hz, H-6), 2.26 (*m*, H-15), 2.23 (*s*, Me-18), 2.19 (*d*, $J=13$ Hz, H-6), 1.96 (*m*, H-16), 1.55 (*ddd*, $J=15$, 11, 3 Hz, H-14).

Alstonerine **2**. ^{1}H NMR (400 MHz, $CDCl_3$): 7.54 (*s*, H-21), 7.48 (*d*, $J=7$ Hz, H-9), 7.34 (*d*, $J=7$ Hz, H-12), 7.21 (*t*, $J=7$ Hz, H-11), 7.10 (*t*, $J=7$ Hz, H-10), 4.42 (*t*, $J=11$ Hz, H-17), 4.19 (*dd*, $J=11$, 4 Hz, H-17), 3.9 (*br s*, H-3), 3.66 (*s*, N-1 Me), 3.33 (*dd*, $J=16$, 7 Hz, H-6), 3.11 (*br d*, $J=7$ Hz, H-5), 2.61 (*m*, H-15), 2.42 (*d*, $J=16$ Hz, H-6), 2.31 (*s*, N-4 Me), 2.09 (*s*, Me-18), 1.9 (*m*, H-16), 1.8 (*m*, H-14), 1.45 (*m*, H-14).

19,20-*Dehydro*-10-*methoxytalcarpine* **3**. CR (grey); $[\alpha]_D = -140°$ (EtOH; *c* 0.5); mp 300°, Me_2CO; UV λ_{max}^{MeOH} nm: 230, 270, 315 (sh); IR ν_{max}^{KBr} cm^{-1}: 1635, 1615; MS *m/z* (rel. int.): 366 $[M]^+$ (69), 351, 297, 254, 242 (11), 227 (67), 212 (14), 211 (32), 200 (100); ^{1}H NMR (400 MHz, $CDCl_3$): 9.65 (*s*, H-21), 7.21 (*d*, $J=8.8$ Hz, H-12), 6.93 (*d*, $J=2.4$ Hz, H-9), 6.85 (*dd*, $J=8.8$, 2.4 Hz, H-11), 4.48 (*t*, $J=11$ Hz, H-17), 4.22 (*dd*, $J=11$, 4 Hz, H-17), 3.9 (*s*, OMe), 3.86 (*br s*, H-3), 3.63 (*s*, N-1, Me), 3.31 (*dd*, $J=16.5$, 6.8 Hz, H-6), 3.10 (*br d*, $J=6.8$ Hz; H-5), 2.63 (*m*, H-15), 2.48 (*d*, $J=16.5$ Hz, H-6), 2.35 (*s*, N-4 Me), 2.18 (*s*, Me-18), 2.12 (*m*,H-14), 1.80 (*m*, H-14); ^{13}C NMR see above.

19,20-*Dehydro*-O-*acetylyohimbine* **4**. CR (brown); $[\alpha]_D = +75°$ (MeOH; *c* 0.1); UV λ_{max}^{MeOH} nm: 227, 283, 290; IR $\nu_{max}^{CHCl_3}$: 3380, 2860, 2800, 2740, 1730, 1250; MS *m/z* (rel. int.): 394 $[M]^+$ (100), 393 (84), 351, 335, 170 (26), 169 (32), 156 (35); ^{1}H NMR (400 MHz, $CDCl_3$): 7.8 (*br s*, N-1-H), 7.43 (*d*, $J=8$ Hz, H-12), 7.30 (*d*, $J=8$ Hz, H-9), 7.15 (*t*, $J=8$ Hz, H-11), 7.09 (*t*, $J=8$ Hz, H-10), 5.53 (*br s*, H-17 and H-19), 3.75 (*s*, COOMe), 2.05 (*s*, OCOMe).

10-*Methoxy villalstonine* **18**. CR (purple); $[\alpha]_D = +39°$ ($CHCl_3$; *c* 0.66); UV λ_{max}^{MeOH} nm: 233, 250 (sh), 289, 315 (sh); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1735, 1610; MS *m/z* (rel. int.): 690 $[M]^+$ (17), 675, 660, 631, 368 (35), 352, 338 (42), 322 (80), 307, 263 (96), 227 (75), 212, 211, 200 (29), 180 (100), 135, 121 (60), 107 (25); ^{1}H NMR (500 MHz, $CDCl_3$): 7.21 (*d*, $J=8$ Hz, H-12), 6.99 (*d*, $J=2$ Hz, H-9), 6.98 (*dd*, $J=8$, 7.6 Hz, H-10′), 6.88 (*d*, $J=7.6$ Hz, H-9′), 6.81 (*dd*, $J=8$, 2 Hz, H-11), 6.69 (*t*, $J=8$ Hz, H-11′), 6.15 (*d*, $J=7.8$ Hz, H-12′), 5.36 (*q*, $J=6.7$ Hz, H-19′), 4.44 (*d*, $J=3.6$ Hz, H-16′), 4.19 (*br d*, $J=11.8$ Hz, H-21′), 3.93 (*t*, $J=11.8$ Hz, H-17), 3.9

(*s*, OMe), 3.85 (*br s*, H-3), 3.72 (*m*, H-3′ and H-17′), 3.71 (*s*, COOMe), 3.58 (*s*, N-1 Me), 3.25 (*dd*, $J = 16.5$, 6.5 Hz, H-6), 3.21 (*br d*, $J = 3.5$ Hz, H-15′), 3.12 (*ddd*, $J = 14$, 13, 2.5 Hz, H-5′), 2.92 (*d*, $J = 11.8$ Hz, H-21′), 2.91 (*d*, $J = 6.5$ Hz, H-5), 2.68 (*m*, H-5′ and H-14′), 2.42 (*d*, $J = 16.5$ Hz, H-6), 2.41 (*m*, H-14), 2.39 (*m*, H-21), 2.30 (*s*, N-4 Me), 2.08 (*m*, H-16), 2.03 (*ddd*, $J = 13.2$, 12, 4.2 Hz, H-6′), 1.68 (*dd*, $J = 12.5$, 3.5 Hz, H-14′), 1.61 (*m*, H-15), 1.59 (*m*, H-21), 1.55 (*dd*, $J = 6.5$, 2 Hz, Me-18′), 1.43 (*br d*, $J = 12.5$ Hz, H-14), 1.24 (*s*, Me-18), 1.16 (*m*, H-20), 1.11 (*br d*, $J = 13.2$ Hz, H-6′); ^{13}C NMR see above.

10-*Methoxymacrocarpamine* **19**. CR (greenish turns purple on standing); UV λ_{max}^{MeOH} nm: 217 (sh), 232, 252, 284; IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1750, 1730, 1635, 1615; MS *m/z* (rel. int.): 672 [M]$^+$ (32), 613, 599, 350, 323, 322, 307, 263, 227 (56), 212, 211, 200 (46), 180, 135 (100), 121, 107 (35); ^{1}H NMR (500 MHz, $CDCl_3$): 7.27 (*d*, $J = 8.6$ Hz, H-12), 6.92 (*d*, $J = 7.9$ Hz, H-9′), 6.90 (*d*, $J = 1.1$ Hz, H-9), 6.88 (*dd*, $J = 8.6$, 1.1 Hz, H-11), 6.83 (*t*, $J = 7.9$ Hz, H-11′), 6.56 (*t*, $J = 7.9$ Hz, H-10′), 6.29 (*s*, H-21), 5.85 (*d*, $J = 7.9$ Hz, H-12′), 5.52 (*d*, $J = 16.5$ Hz, H-19), 5.46 (*q*, $J = 6.7$ Hz, H-19′), 4.56 (*d*, $J = 16.5$ Hz, H-18), 4.43 (*br d*, $J = 12.3$ Hz, H-21′), 4.25 (*t*, $J = 11.4$ Hz, H-17), 4.13 (*d*, $J = 3.7$ Hz, H-16′), 3.96 (*dd*, $J = 11.4$, 4.1 Hz, H-17), 3.90 (*s*, OMe), 3.85 (*m*, H-3), 3.83 (*m*, H-3′), 3.72 (*s*, COOMe), 3.64 (*s*, N-1 Me), 3.24 (*dd*, $J = 16.6$, 7.1 Hz, H-6), 3.17 (*br d*, $J = 3.7$ Hz, H-15′), 3.10 (*m*, H-21′), 3.05 (*d*, $J = 7.1$ Hz, H-5), 3.03 (*m*, H-5′), 2.67 (*dd*, $J = 10.5$, 7.6 Hz, H-7′), 2.42 (*d*, $J = 16.6$ Hz, H-6), 2.35 (*s*, N-4 Me), 2.14 (*br d*, $J = 13.2$ Hz, H-14′), 2.03 (*m*, H-14 and H-14′), 1.91 (*m*, H-15 and H-16), 1.84 (*m*, H-14 and H-5′), 1.82 (*m*, H-6′), 1.62 (*m*, H-6′), 1.58 (*dd*, $J = 6.7$, 1.7 Hz, Me-18′); ^{13}C NMR: see above.

10-*Methoxy villalstonine* N-4′ *oxide* **23**. CR (purple) $[\alpha]_D = +27°$ ($CHCl_3$; $c = 0.7$); UV λ_{max}^{MeOH} nm: 233, 288, 316 (sh); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1735, 1610; MS *m/z* (rel. int.): 690 (32), 647, 617, 368, 352 (26), 338 (74), 322 (37), 263, 227 (67), 212, 211, 200 (39), 180, 135 (68), 121 (100), 107 (30); ^{1}H NMR (500 MHz, $CDCl_3$): 7.21 (*d*, $J = 8.8$ Hz, H-12), 7.05 (*t*, $J = 7.7$ Hz, H-10′), 7.01 (*d*, $J = 2.5$ Hz, H-9), 6.94 (*d*, $J = 7.7$ Hz, H-9′), 6.88 (*dd*, $J = 8.8$, 2.5 Hz, H-11), 6.78 (*t*, $J = 7.7$ Hz, H-11′), 6.19 (*d*, $J = 7.7$ Hz, H-12′), 5.57 (*q*, $J = 6.8$ Hz, H-19′), 5.07 (*br d*, $J = 12.5$ Hz, H-21′), 4.46 (*d*, $J = 3.6$ Hz, H-16′), 4.40 (*br s*, H-3′), 3.96 (*t*, $J = 12.1$ Hz, H-17), 3.90 (*s*, OMe), 3.83 (*br s*, H-3), 3.77 (*dd*, $J = 12.1$, 4.8 Hz, H-17), 3.72 (*s*, COOMe), 3.58 (*s*, N-1 Me), 3.44 (*m*, H-5′ and H-21′), 3.30 (*m*, H-15′), 3.26 (*dd*, $J = 16$, 6.6 Hz, H-6), 2.83 (*br d*, $J = 12.5$ Hz, H-14′), 2.61 (*br d*, $J = 12.5$ Hz, H-14′), 2.40 (*m*, H-6, H-14 and H-21), 2.31 (*s*, N-4 Me), 2.11 (*m*, H-16), 1.92 (*ddd*, $J = 13.2$, 12, 4.2 Hz, H-6′), 1.66 (*m*, H-15), 1.64 (*d*, $J = 6.5$ Hz, Me-18′), 1.64 (*m*, H-21), 1.27 (*s*, Me-18), 1.25 (*m*, H-6′), 1.23 (*m*, H-20); ^{13}C NMR see above.

Foliacraline **24**. CR (green), $[\alpha]_D = +55°$ ($CHCl_3$; *c* 0.3); UV λ_{max}^{MeOH} nm: 220, 228, 289, 302 (sh); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1630; MS *m/z* (rel. int.): 688 [M]$^+$ (13), 628 (8), 368 (10), 350 (10), 324 (30), 322 (28), 281 (15), 255 (20), 227 (100), 213 (30), 212 (33), 211 (30), 200 (85), 107 (100); ^{1}H NMR (300 MHz, $CDCl_3$): 7.18 (*d*, $J = 8.7$ Hz, H-12), 6.94 (*d*, $J = 2.3$ Hz, H-9), 6.86 (*dd*, $J = 8.7$, 2.3 Hz, H-11), 6.63 (*s*, H-9′), 6.28 (*s*, H-12′), 5.5 (*q*, $J = 6$ Hz, H-19′), 5.44 (*d*, $J = 3$ Hz, H-21), 5.01 (*d*, $J = 2$ Hz, H-3′), 4.2 (*t*, $J = 11$ Hz, H-17), 3.9 (*m*, H-17 and H-21′), 3.88 (*s*, OMe), 3.58 (*s*, COOMe and N-1 Me), 3.3 (*m*, H-21′ and H-14′), 3.2 (*dd*, $J = 16.2$, 5.8 Hz, H-6), 3.0 (*d*, $J = 5.8$ Hz, H-5), 2.68 (*q*, $J = 6.8$ Hz, H-19), 2.4 (*d*, $J = 16.2$ Hz, H-6), 2.36 (*s*, N-4 Me), 2.15 (*m*, H-14′), 1.67 (*br s*, H-20), 1.46 (*dd*, $J = 6$ Hz, Me-18′), 1.18 (*d*, $J = 6.8$ Hz, Me-18).

Angusticraline **25**. CR (orange turns pink and purple on standing); $[\alpha]_D = +6°$ (MeOH, *c* 1.1); UV λ_{max}^{MeOH} nm (log ε): 215 (3.57), 230 (3.53), 280 (sh) (3.0), 303 (sh) (3.05), 317 (sh) (2.63); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3340, 1740, 1615; HRMS *m/z* (rel. int.): 736.4228 (calcd for $C_{44}H_{56}N_4O_6$ 736.4256) [M]$^+$ (25), 718.4006 (calcd for $C_{44}H_{54}N_4O_5$ 718.3996) (9), 395.2321 (calcd for $C_{24}H_{31}N_2O_3$ 395.2309) (100), 381, 368, 227 (42), 212, 211, 200 (26), 194 (13), 188, 174, 157; ^{1}H NMR (500 MHz, $CDCl_3$): 6.96 (*d*, $J = 8.7$ Hz, H-12), 6.85 (*d*, $J = 2.5$ Hz, H-9), 6.76 (*dd*, $J = 8.7$, 2.5 Hz, H-11), 6.39 (*s*, H-12′), 5.39 (*q*, $J = 7.2$ Hz, H-19′), 5.38 (*s*, H-9′), 5.35 (*s*, $W_{1/2} = 2$ Hz, H-21), 4.44 (*t*, $J = 11.7$ Hz, H-17), 4.0 (*m*, H-3′), 3.91 (*br d*, $J = 15.7$ Hz, H-21′), 3.88 (*s*, COOMe and OMe), 3.73 (*s*, OMe), 3.72 (*br s*, H-3), 3.64 (*m*, H-5′), 3.51 (*br s*, H-15′), 3.44 (*dd*, $J = 11.7$, 4.8 Hz, H-17), 3.34 (*s*, N-1 CH_3), 3.09 (*dd*, $J = 16.1$, 6.9 Hz, H-6), 2.92 (*m*, H-6′), 2.89 (*d*, $J = 15.7$ Hz, H-21′), 2,83 (*d*, $J = 6.9$ Hz, H-5), 2.81 (*m*, H-14), 2.77 (*d*, $J = 3.9$ Hz, H-16′), 2.59 (*m*, H-5′), 2.33 (*s*, N-1′ Me), 2.28 (*m*, H-14′), 2.27 (*s*, N-4 Me), 2.22 (*s*, H-2′), 2.16 (*m*, H-19), 2.13 (*d*, $J = 16.1$ Hz, H-6), 2.04 (*m*, H-16), 1.59 (*br d*, $J = 13$ Hz, H-14′), 1.47 (*dd*, $J = 7.2$, 2.2 Hz, Me-18′), 1.31 (*m*, H-20), 1.11 (*m*, H-14), 1.08 (*d*, $J = 6.8$ Hz, Me-18), 0.87 (*m*, H-6′); ^{13}C NMR see above.

Alstocraline **26**. CR (orange turns yellow on standing); $[\alpha]_D = +3°$ (MeOH, *c* 0.7); UV λ_{max}^{MeOH} nm (log ε): 227 (4.02), 282 (4.45), 295 (sh) (4.44); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1620; HRMS *m/z* (rel. int.): 704.3807 (calcd. for $C_{43}H_{52}N_4O_5$ 704.3937) [M]$^+$ (67), 689, 674.3737 (calcd for $C_{42}H_{50}N_4O_4$ 674.3644) (14), 381 (30), 368 (19), 338, 227 (86), 212, 211, 200 (78), 197, 194 (100), 188 (30), 174 (33), 170, 158, 139 (42); ^{1}H NMR (500 MHz, $CDCl_3$): 7.18 (*d*, $J = 8.7$ Hz, H-12), 6.94 (*d*, $J = 2.5$ Hz, H-9), 6.85 (*dd*, $J = 8.7$, 2.5 Hz, H-11), 6.45 (*s*, H-12′), 6.14 (*s*, H-9′), 5.50 (*q*, $J = 7$ Hz, H-19′), 5.43 (*d*, $J = 3.1$ Hz, H-21), 4.37 (*m*, H-3′), 4.18 (*t*, $J = 11.7$ Hz, H-17), 4.03 (*br d*, $J = 15.5$ Hz, H-21), 3.97 (*dd*, $J = 11.7$, 5.2 Hz, H-17), 3.95 (*m*, H-5′), 3.87 (*s*, COOMe), 3.86 (*m*, H-3), 3.68 (*s*, OMe), 3.60 (*m*, H-15′), 3.58 (*s*, N-1 Me), 3.24 (*dd*, $J = 16$, 4, 6.6 Hz, H-6), 3.08 (*d*, $J = 15.5$ Hz, H-21′), 3.04 (*m*, H-6′), 2.91 (*d*, $J = 6.6$ Hz, H-5), 2.86 (*d*, $J = 3.6$ Hz, H-16′), 2.76 (*m*, H-5′), 2.64 (*s*, N-1′ Me), 2.60 (*m*, H-19), 2.52 (*s*, H-2′), 2.35 (*m*, H-14 and H-16), 2.35 (*d*, $J = 16.4$ Hz, H-6), 2.34 (*m*, H-14′), 2.32 (*s*, N-4 Me), 1.87 (*m*, H-15), 1.68 (*br d*, $J = 14.6$ Hz, H-14′), 1.62 (*m*, H-20), 1.53 (*m*, H-6′), 1.52 (*m*, H-14), 1.51 (*dd*, $J = 7$, 2.6 Hz, CH_3-18′), 1.24 (*d*, $J = 7.1$ Hz, CH_3-18); ^{13}C NMR see above.

10-*Methoxymacrocarpamine* N-4′ *oxide* **27**. CR (pale purple turns green on standing); $[\alpha]_D = -9°$ (MeOH, *c* 0.1); UV λ_{max}^{MeOH} nm: 220 (sh), 230, 254, 290; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1735, 1635, 1610; MS *m/z* (rel. int.): 688 (1), 672 (25), 613, 350, 323, 322, 263, 227 (36), 212, 211, 200 (35) 180, 135 (100), 107 (37); ^{1}H NMR (300 MHz, $CDCl_3$): 7.24 (*d*, $J = 8.5$ Hz, H-12), 6.94 (*d*, $J = 7.7$ Hz, H-9′), 6.89 (*d*, $J = 8.5$ Hz, H-11), 6.87 (*s*, H-9), 6.83 (*t*, $J = 7.7$ Hz, H-11′), 6.61 (*t*, $J = 7.7$ Hz, H-10′), 6.34 (*s*, H-21), 5.85 (*d*, $J = 7.7$ Hz, H-12′), 5.68 (*d*, $J = 16.4$ Hz, H-19), 5.58 (*q*, $J = 6.7$ Hz, H-19′), 5.17 (*br d*, $J = 12.9$ Hz, H-21′), 4.49 (*d*, $J = 16.4$ Hz, H-18)) 4.29 (*t*, $J = 11.5$ Hz, H-17), 4.12 (*d*, $J = 3.7$ Hz, H-18), 4.29 (*t*, $J = 11.5$ Hz, H-17), 4.12 (*d*, $J = 3.7$ Hz, H-16′), 4.0 (*m*, H-3′), 3.98 (*dd*, $J = 11.4$, 4.6 Hz, H-17), 3.87 (*s*, OMe), 3.86 (*br s*, H-3), 3.8 (*m*, H-21′), 3.75 (*s*, N-1 Me), 3.65 (*s*, COOMe), 3.46 (*m*, H-5′), 3.23 (*dd*, $J = 16.4$, 6.6 Hz, H-6), 3.21 (*br d*, $J = 3.7$ Hz, H-15′), 3.05 (*d*, $J = 6.6$ Hz, H-5), 2.86 (*m*, H-7′), 2.72 (*m*, H-14′), 2.41 (*d*, $J = 16.4$ Hz, H-6), 2.34 (*s*, N-4 Me), 2.21 (*m*, H-6′), 2.10 (*m*, H-14′), 1.91 (*m*, H-16 and H-14), 1.87 (*m*, H-6′), 1.77 (*m*, H-14), 1.63 (*dd*, $J = 6.7$, 1.7 Hz, Me-18′).

Macralstonine **28**. ^{1}H NMR (300 MHz, $CDCl_3$; mixt of isomers and of rotamers; signals of the major component only are given): 7.58 (*s*, H-21′), 7.40–7.10 (*m*, H-9, H-10, H-11, H-12), 6.9 (*s*, H-12′), 6.75 (*s*, H-9′), 4.45 (*m*, H-17, H-17′), 4.20 (*m*, H-17, H-17′), 4.05 (*br s*, H-3), 3.98 (*s*, OMe), 3.8 (*br s*, H-3′), 3.65 (*s*, N-1 Me), 3.60 (*s*, N-1′ Me), 3.40 (*dd*, $J = 16$, 7 Hz, H-6), 3.20 (*dd*, $J = 15$, 6 Hz, H-6′), 3.05 (*d*, $J = 7$ Hz, H-5), 2.40 (*s*, N-4 Me), 2.28 (*s*, N-4′ Me), 2.15 (*s*, Me-18′), 1.70 (*s*, Me-18).

Villalstonine **29**. ^{1}H NMR (500 MHz, $CDCl_3$): 7.55 (*d*, $J = 8$ Hz, H-9), 7.32 (*d*, $J = 8$ Hz, H-12), 7.22 (*td*, $J = 8$, 1 Hz, H-11), 7.15 (*td*, $J = 8$, 1 Hz, H-10), 6.97 (*td*, $J = 8$, 1 Hz, H-10′), 6.87 (*dd*, $J = 8$, 0.5 Hz, H-9′), 6.68 (*td*, $J = 8$, 0.5 Hz, H-11′), 6.14 (*d*, $J = 8$ Hz, H-12′), 5.36 (*qd*, $J = 6.5$, 1 Hz, H-19′), 4.42 (*d*, $J = 3.5$ Hz, H-16′), 4.19 (*br d*, $J = 12.5$ Hz, H-21′), 3.97 (*t*,

$J = 11.8$ Hz, H-17), 3.84 (*br s*, H-3), 3.74 (*br s*, H-3'), 3.71 (*dd*, $J = 11.8$, 4.5 Hz, H-17), 3.66 (*s*, COOMe), 3.6 (*s*, N-1 Me), 3.27 (*dd*, $J = 16.5$, 6.5 Hz, H-6), 3.20 (*br d*, $J = 3.5$ Hz, H-15'), 3.12 (*br dd*, $J = 14$, 2.5 Hz, H-5), 2.95 (*d*, $J = 12.5$ Hz, H-21'), 2.91 (*d*, $J = 6.5$ Hz, H-5), 2.71 (*m*, H-5'), 2.68 (*m*, H-14'), 2..45 (*d*, $J = 16.5$ Hz, H-6), 2.43 (*m*, H-14), 2.37 (*m*, H-21), 2.29 (*s*, N-4 Me), 2.10 (*m*, H-16), 2.01 (*ddd*, $J = 13.2$, 12, 4.2 Hz, H-6), 1.69 (*br dd*, $J = 12.5$, 2.9 Hz, H-14'), 1.62 (*m*, H-15), 1.57 (*dd*, $J = 12$, 4.2 Hz, H-21), 1.54 (*dd*, $J = 6.5$, 2 Hz, Me-18'), 1.42 (*br d*, $J = 12.5$ Hz, H-14), 1.24 (*s*, Me-18), 1.15 (*m*, H-20), 1.12 (*br d*, $J = 13.2$ Hz, H-6'); ^{13}C NMR see above.

Villalstonine N-4'-*oxide* **30**. CR (pale green); UV λ_{max}^{MeOH} nm: 230, 250 (sh), 286, 293 (sh); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1730, 1610; MS *m/z* (rel. int.): 660 (46), 617, 601, 352 (30), 338 (64), 322 (36), 308, 307, 263, 251, 197 (100), 182, 181, 180, 170 (42), 135 (48), 121 (59), 107 (20); ^{1}H NMR (300 MHz, $CDCl_3$, 45°C): 7.55 (*d*, $J = 7.8$ Hz, H-9), 7.31 (*d*, $J = 7.8$ Hz, H-12), 7.25 (*t*, $J = 7.8$ Hz, H-11), 7.16 (*t*, $J = 7.8$ Hz, H-10), 7.06 (*td*, $J = 7.8$, 1.2 Hz, H-10'), 6.94 (*dd*, $J = 7.3$, 1.2 Hz, H-9'), 6.80 (*td*, $J = 7.3$, 1.2 Hz, H-11'), 6.19 (*d*, $J = 7.8$ Hz, H-12'), 5.61 (*q*, $J = 6.5$ Hz, H-19'), 5.16 (*br d*, $J = 13.2$ Hz, H-21'), 4.46 (*d*, $J = 3.5$ Hz, H-16'), 4.09 (*m*, H-17), 3.89 (*dd*, $J = 11.4$, 4.8 Hz, H-17), 3.82 (*m*, H-21'), 3.72 (*s*, COOMe), 3.61 (*s*, N-1 CH_3), 3.32 (*br d*, $J = 3.2$ Hz, H-15'), 2.74 (*br d*, $J = 14.6$ Hz, H-14'), 2.70 (*m*, H-14), 2.66 (*m*, H-21), 2.59 (*br dd*, $J = 14.6$, 3.2 Hz, H-14'), 1.76 (*br d*, $J = 15.2$ Hz, H-6'), 1.65 (*m*, H-21), 1.64 (*dd*, $J = 6.8$, 2 Hz, Me-18'), 1.52 (*m*, H-15), 1.26 (*s*, Me-18), 1.23 (*m*, H-20).

Alstophylline **31**. ^{1}H NMR (300 MHz, $CDCl_3$, 45°): 7.56 (*s*, H-21), 7.34 (*d*, $J = 8.4$ Hz, H-9), 6.82 (*dd*, $J = 8.4$, 2 Hz, H-10), 6.77 (*d*, $J = 2$ Hz, H-12), 5.03 (*t*, $J = 10.8$ Hz, H-17), 4.65 (*br s*, H-3), 4.25 (*br d*, $J = 10.8$ Hz, H-17), 3.90 (*s*, OMe), 3.72 (*d*, $J = 6.6$ Hz, H-5), 3.65 (*s*, N-1 Me), 3.48 (*dd*, $J = 16.2$, 6.6 Hz, H-6), 3.05 (*d*, $J = 16.2$ Hz, H-6), 2.88 (*s*, N-4 Me), 2.70 (*m*, H-15), 2.54 (*m*, H-14), 2.40 (*m*, H-14), 2.25 (*m*, H-16), 2.10 (*s*, Me-18).

Chemical correlations (*reduction of* **23**, **27** and **30**). To 5 mg of each alkaloid dissolved in CH_2Cl_2 was added 1 ml of H_2SO_3. The soln was stirred at room temp. for 10 min. The reaction mixt was then poured into H_2O, made alkaline with NH_4OH and extracted with $CHCl_3$. After drying (Na_2SO_4) and evapn, 4 mg of reduced alkaloid (identical to **18**, **19**, **29**, respectively) was obtained.

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REFERENCES

1. Legseir, B., Cherif, A., Richard, B., Pusset, J., Labarre, S., Massiot, G. and Le Men-Olivier, L. (1986) *Phytochemistry* **25**, 1735.
2. Ghedira, K. (1986) Ph.D. thesis Reims.
3. Zeches-Hanrot, M., Ghedira, K., Le Men-Olivier, L. and Massiot, G. (1986) 7–9 May. Communication Poster, first International Congress 'Plantes et substances naturelles d'intérêt thérapeutique', Monastir, Tunisia.
4. Elderfield R. C. and Gilman, R. E. (1972) *Phytochemistry* **11**, 339.
5. Nordman, C. E. and Nakatsu, K. (1963) *J. Am. Chem. Soc.* **85**, 353.
6. Cook. J. M., Le Quesne, P. W. and Elderfield, R. C. (1969) *J. Chem. Soc., Chem. Comm.* 1306.
7. Poisson, J., Le Men, J. and Janot, M.-M., (1957) *Bull. Soc. Chim. Fr.* 610.
8. Kishi, T., Hesse, M., Vetter, W., Gemenden, C. W., Taylor, W. I. and Schmid, H. (1966) *Helv. Chim. Acta* **49**, 946.
9. Hesse, M., Hurzeler, H., Gemenden, C. W., Joshi, B. S., Taylor, W. I. and Schmid, H. (1965) *Helv. Chim. Acta* **48**, 689.
10. Hesse, M., Bodmer, F., Gemenden, C. W., Joshi, B. S., Taylor, W. I. and Schmid, H. (1966) *Helv. Chim. Acta* **49**, 1173.
11. Kishi, T., Hesse, M., Gemenden, C. W., Taylor, W. I. and Schmid, H. (1965) *Helv. Chim. Acta* **48**, 1349.
12. Nordman, C. E. and Kumra, S. K. (1965) *J. Am. Chem. Soc.* **87**, 2059.
13. Das, B. C., Cosson, J. P., Lukacs, G. and Potier, P. (1974) *Tetrahedron Letters* 4299.
14. Hesse, M., Philipsborn, W., Schumann, D., Spiteller, G., Spiteller-Friedmann, M., Taylor, W. I., Schmid, H. and Karrer, P. (1964) *Helv. Chim. Acta* **47**, 878.
15. Verpoorte, R., Van Beek, T. A., Riegman, R. L. M., Hylands, P. J. and Bisset, N. G. (1984) *Org. Magn. Res.* **22**, 328.
16. Verpoorte, R. (1976) Thesis Doct. Sc. Phys. Leiden, Holland.
17. Mayerl, F. and Hesse, M. (1978) *Helv. Chim. Acta* **61**, 337.
18. Massiot, G., Vercauteren, J., Jacquier, M. J., Levy, J. and Le Men-Olivier, L. (1981) *C. R. Acad. Sci. Paris* Ser. II, 191.
19. Kan-Fan, C., Massiot, G., Das, B. C. and Potier, P. (1981) *J. Org. Chem.* **46**, 1481.
20. Mamatas-Kalamaras, S., Sevenet, T., Thal, C. and Potier, P. (1975) *Phytochemistry* **14**, 1637.
21. Mansour, M. A. H., Le Men-Olivier, L., Lévy, J. and Le Men, J. (1974) *Phytochemistry* **13**, 2861.
22. Cherif, A. (1988), Ph.D. thesis, Reims.
23. Breitmaier, E. and Voelter, W. (1974) *^{13}C NMR spectroscopy*. Verlag Chemie, Weinheim.
24. Robert, G. M. T. (1982) Thesis Doct. Sc. Phys. Paris Sud.
25. Brown, R. T. and Pratt, S. B. (1980) *J. Chem. Soc., Chem. Commun.* 165.
26. Le Men, J. and Taylor, W. (1965) *Experientia* **21**, 508.