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ALKALOIDS OF *STEMMADENIA GRANDIFLORA**

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Key Word Index—*Stemmadenia grandiflora*; Apocynaceae; indole alkaloids.

Abstract—Extracts from the seeds and leaves of *Stemmadenia grandiflora* yielded 16 alkaloids of the ibogan and plumeran type. 3-Oxovincadifformine, 14β-hydroxyquebrachamine and the *bis*indole alkaloid, 14,15-dehydrotetrastachynine, were hitherto unknown natural products.

INTRODUCTION

Stemmadenia grandiflora (Jacq.) Miers is a Central and South American latex-producing shrub, which grows preferentially along rivers [1, 2]. In Colombia a preparation of the leaves from the plant is used against rheumatic disorders, whereas the latex serves to cure chilblains and skin diseases [2]. Only the bark and the green fruits of *S.grandiflora* have been investigated phytochemically [3, 4] : the occurrence of a proteolytic enzyme (tabernaemontanain) has been described in the green fruits some 40 years ago [3] and a number of indole alkaloids—all of the ibogan-type—were isolated from the bark (and stem) recently [4].

Therefore, we started a chemical investigation of extracts from the seeds and the leaves of *S. grandiflora* with particular emphasis on the alkaloidal constituents. This work has resulted in the isolation of 13 known and three hitherto unknown indole alkaloids of the ibogan and plumeran types, respectively.

RESULTS AND DISCUSSION

Repeated chromatography of extracts from the leaves and seeds yielded the alkaloids **1**–**16** summarized in Table 1. The structure determinations are mainly based on spectroscopic studies.

The spectroscopic data of **10** clearly indicate a 14,15-epoxidized 3-oxovincadifformine (**11**). The relative configuration of the epoxy group can be deduced from ^{1}H NMR arguments: comparison of the ^{1}H NMR of structurally related molecules demonstrate, that the resonance values of the protons at C-19 of the basic vincadifformine (**8**) are particularly sensitive to the introduction of oxygen functions at ring D. Introduction of a 14,15-epoxy-group causes a downfield shift for at least one of these protons, and the induced shift is significantly stronger, if the epoxy group has the α-configuration (Table. 2). An 3-oxo-function also shifts the C(19)H_2 to lower field; this effect ranges from Δδ 0.01 and 0.35 for the conversion vincadifformine (**8**) → 3-oxovincadifformine (**11**) and Δδ 0.08 and 0.18 for tabersonine (**6**) → 3-oxotabersonine (**9**). The values observed for the C(19)H_2 in the ^{1}H NMR spectrum of **10** are therefore indicative for a β-oxirane in a 3-oxovincadifformine (**11**). Consequently, **10** was prepared by oxidation of pachysiphine (**7**) with $KMnO_4$ [6].

The mass spectral fragmentation pattern of **11** closely resembles that of **9** with $[M]^+$ two mass units greater. The coupling system of the four protons at C-14 and C-15 was analysed by decoupling experiments according to Fig. 1.

The deduced structure of 3-oxovincadifformine (**11**) was corroborated by the identity of the isolated compound with the hydrogenation product of **9**.

From its mass spectrum, **13** is recognized as a quebrachamine-type alkaloid with an additional OH-group at ring D. Analysis of the spin systems involved in the splitting of the carbinol hydrogen atom revealed the situation depicted in Fig. 2. The β-configuration of the 14-hydroxy group was established by reductive cleavage of the oxirane ring in conoflorine (**14**) which resulted in an 1:5 mixture of **13** and its 15β-hydroxyisomer. This is a known reaction, which was used during the original structure determination of conoflorine (**14**) [7].

Alkaloid **16** was isolated as a colourless oil; in the presence of air and light it slowly becomes brownish by decomposition. Its chemical stability was enhanced by acetylation, which yielded a di-*O*-acetyl derivative. By EI mass spectrometry (NH_3), the $[M \cdot H]^+$ becomes base (*m/z* 704) which becomes more significant in the spectrum of the diacetyl derivative (*m/z* 788). However, by DCI mass spectrometry (NH_3), the quasi $[M]^+$ becomes base peak (*m/z* 705). High resolution mass spectrometry establishes the elemental composition and thereby the presence of a *bis*indole alkaloid. Key fragments in the mass spectrum of diacetyl-**16** can be assigned to alicyclic systems of a coronaridine and a tabersonine unit; accordingly, on hydrogenation a dihydro compound is produced, which now exhibits a strong key fragment at *m/z* 124 indicative for an aspidospermine-type alkaloid whereas those of the tabersonine-type disappeared. The monomeric structural units deduced from mass spectrometry are corroborated by ^{1}H- and, particularly, ^{13}C NMR. ^{13}C NMR also answers the question about

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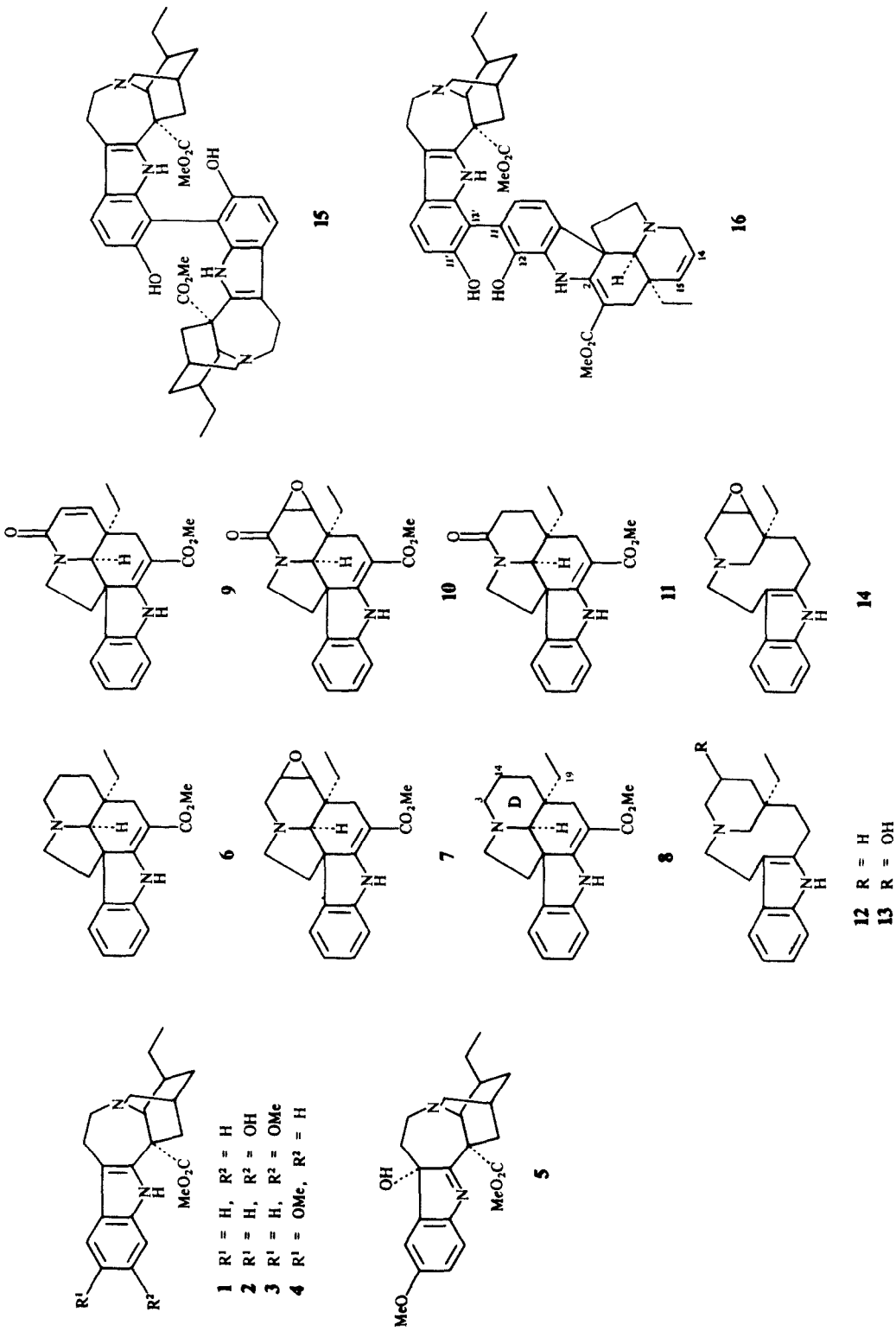
1 R¹ = H, R² = H
2 R¹ = H, R² = OH
3 R¹ = H, R² = OMe
4 R¹ = OMe, R² = H
5
6
7
8
9
10
11
12 R = H
13 R = OH
14
15
16

Table 1. Alkaloids isolated from seeds and leaves of *Stemmadenia grandiflora* (concentrations are given in $\%\cdot10^{-3}$ of dry plant material)

Alkaloid	Concentration in Seeds*†	Leaves*	Leaves†
Coronaridine (**1**)	131.4	5.8	3.6
11-Hydroxycoronaridine (**2**)	traces	1.5	1.3
Isovoacangine (**3**)	—	1.2	0.6
Voacangine (**4**)	1.4	6.5	2.8
Hydroxyindoleninevoacangine (**5**)	0.1	0.4	0.3
Tabersonine (**6**)	331.4	1.2	2.6
Pachysiphine (**7**)	2.0	0.3	—
Vincadifformine (**8**)	2.0	—	—
3-Oxotabersonine (**9**)	1.4	—	—
3-Oxopachysiphine (**10**)	0.9	—	—
3-Oxovincadifformine (**11**)	0.4	—	—
Quebrachamine (**12**)	—	0.7	0.1
14β-Hydroxyquebrachamine (**13**)	—	0.6	—
Conoflorine (**14**)	4.3	5.8	1.4
12,12'-Bis (11-hydroxycoronaridinyl) (**15**)	—	1.5	1.7
14,15-Dehydrotetrastachynine (**16**)	—	0.3	0.6

*Collected July 1983.
†Collected September 1985.

Table 2. Influence of oxygen functions at ring D of vincadifformine (**8**) on the resonances of the protons at C-19.

Compound	δ [ppm]		Δδ [ppm]	
Vincadifformine (**8**)	0.98	0.64	—	—
Pachysiphine (**7**) (=14β,15β-epoxyvincadifformine)	0.98	0.92	±0	+0.28
Lochnericine (=14α,15α-epoxyvincadifformine)	1.42	1.15 [5]	+0.44	+0.51
3-Oxovincadifformine (**11**)	0.99	0.99	+0.01	+0.35
Tabersonine (**6**) (=14,15-dehydrovincadifformine)	1.00	0.86	—	—
3-Oxotabersonine (**9**)	1.08	1.04	+0.08	+0.18
10	1.26	1.08		

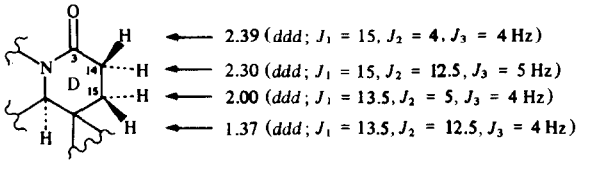

Fig. 1. Shifts and coupling constants of the protons at C-14 and C-15 in **11**.

the substitutions of the benzene rings and the positions of the linkage between hydroxycoronaridine and hydroxytabersonine. The highly, non-symmetrically substituted biphenyl unit in **16** causes atropisomerism of the molecule and thereby doubling of all ^{1}H NMR signals. The largest difference in chemical shift is observed for the signals from NH of the 11-hydroxycoronaridine part ($\Delta\delta\sim0.2$ ppm at room temperature in $CDCl_3$); coalescence occurs around 60° (in CD_3OD). In the noise-decoupled ^{13}C NMR, only the resonances of carbons near to the centre of steric hindrance appear significantly doubled with a maximum effect for C-2 of the tabersonine part ($\Delta\delta\sim0.8$ ppm), whereas the carbon atoms of the alicyclic ring systems remain as (broadened) singlets. The spectroscopic data of **16** (UV, ^{1}H-, and ^{13}C NMR) are in good agreement with those published for tetrastachynine (14,15-dihydro-**16**) [8]; major alterations are observed only for the NMR resonances of atoms located in ring D of the tabersonine part of the molecule.

From a chemotaxonomic point of view the occurrence of ibogan and plumeran type alkaloids is a characteristic of *Stemmadenia* species. As far as seeds of *Stemmadenia* species are concerned, coronaridine (**1**) and tabersonine (**6**) are two of the major alkaloids [9]. Quebrachamine (**12**) was isolated from a *Stemmadenia* species only once [10], but **12** has never been found in a *Tabernaemontana* species. This fact corroborates the botanical classification of *S. grandiflora*. *Bis*indole alkaloids are rare constituents in *Stemmadenia* species, the only report describes the presence of voacamine [11] in *S. donnell-smithii* [10]. The

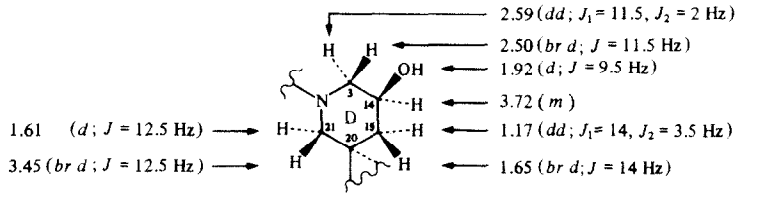

Fig. 2. Shifts and coupling constants of the protons at ring D of **13**. (Broadening of protons at C-3, C-15 and C-21 is caused by long-range coupling (~1Hz) between these protons).

isolation of the 3-oxo-alkaloids **9**–**11** raises the question whether these compounds are genuine natural products. Therefore, we exposed solutions of **6** (in petrol) to daylight. After two days **9** was detected among the decomposition products. On the other hand, a solution of **8** treated in the same way, was unchanged after several weeks. Therefore, we believe **10** and **11** to be genuine natural products, whereas the already known **9** [6, 12] could be an artefact.

The comparison of spectroscopic data enables us to determine the unknown configuration of the epoxidized 3-oxovincadifformine isolated by Aimi *et al.* from *Amsonia elliptica* [6]; the reported ^{1}H resonances for H-(14), H-(15) and H-(21) are indicative for the β-structure of the 14,15-epoxy group.

EXPERIMENTAL

Plant material. Seeds and leaves were collected in July 1983 and in September 1985 in the Tayrona Parque Nacional (Provincia Magdalena, Colombia). Botanical identification was performed by Mr Roberto Jaramillo (Herbario Nacional de Colombia, Bogotá, Colombia); herbarium specimen are kept under no. 272/77 at the Herbario Nacional de Colombia.

General. Mps: uncorr. IR spectra were recorded in $CHCl_3$. Unless otherwise stated UV and CD-measurements were taken in MeOH, ^{1}H NMR spectra at 400 MHz and ^{13}C NMR at 100 MHz in $CDCl_3$; int. ref. TMS. MS were obtained by EI at 70 eV, unless otherwise stated. TLC was performed on precoated plates (Nano plates Sil-20 UV, Macherey–Nagel) using S-1 = petrol–EtOAc (4:1); S-2 = petrol–Me_2CO (1:1); S-3 = cyclohexane–EtOAc (7:3); S-4 = Me_2CO; S-5 = $CHCl_3$–MeOH (99:1). Detection: UV and ceric ammonium sulphate reagent [13].

Extraction and chromatography. Seeds: dried and ground seeds (350 g) were extracted with petrol at room temp, yielding 70 g of crude extract. The extract was redissolved in petrol and treated with 2% HCl. The acidic aq layer was adjusted to pH 9 with NH_3 and the crude alkaloids extracted with $CHCl_3$ (yield: 2 g extract A). Leaves: Dried and ground leaves (500 g) were extracted successively with petrol and MeOH at room temp, yielding 6 g and 28 g of crude extracts, respectively. The crude MeOH extract was redissolved in MeOH–H_2O (1:1) and extracted with $CHCl_3$ (yield: 3.5 g extract B).

Extract A was repeatedly chromatographed over silica gel (Macherey–Nagel no. 81538) using petrol–Me_2CO, petrol–EtOAc and cyclohexane–EtOAc as eluents and compounds **1**, **2**, **4** to **11** and **14** were isolated. Purification of these alkaloids was performed by chromatography over Fractogel PVA 500 (Merck) with MeOH.

Extract B was sepd over Al_2O_3 (basic, act. II-III, Woelm) into four fractions (B1–B4) using $CHCl_3$–MeOH with increasing concns of MeOH. Chromatography of the alkaloid containing fraction B2 over Sephadex LH 20 using MeOH–$CHCl_3$ (7:3) sepd the dimeric from the monomeric compounds. Further chromatography over silica gel, Fractogel and Al_2O_3 (neutral, act. II-III) with the eluents described under extract A afforded compounds **1**–**7** and **12**–**16**.

Coronaridine (**1**). Amorphous (450 mg); TLC (S-1): R_f 0.32, blue; $[\alpha]_D^{21}$ −40° ($CHCl_3$; *c* 1.05); spectral properties identical with published data [14, 15].

11-*Hydroxycoronaridine* (**2**). Colourless oil (10 mg); TLC (S-3): R_f 0.21, grey-green; $[\alpha]_D^{21}$ −32° ($CHCl_3$; *c* 0.45); spectral properties identical with published data [16].

Isovoacangine (**3**). Colourless crystals (8 mg), mp 154–156°; TLC (S-1): R_f 0.21, brown; $[\alpha]_D^{21}$ −43° ($CHCl_3$; *c* 0.34); spectral properties identical with published data [10, 16, 17].

Voacangine (**4**). Colourless crystals (40 mg), mp 135–137°; TLC (S-1): R_f 0.22, brown; $[\alpha]_D^{21}$ −41° ($CHCl_3$; *c* 1.02); spectral properties identical with published data [15,18].

Hydroxyindoleninevoacangine (**5**). Colourless oil (2 mg); TLC (S-3): R_f 0.25, yellow; $[\alpha]_D^{21}$ −61° ($CHCl_3$; *c* 0.11); spectral properties identical with published data [19].

Tabersonine (**6**). Amorphous (800 mg); TLC (S-1): R_f 0.30, yellow with blue edge; $[\alpha]_D^{21}$ −243° ($CHCl_3$; *c* 1.24); spectral properties identical with published data [20, 21].

Pachysiphine (**7**). Colourless oil (8 mg); TLC (S-1): R_f 0.11, yellow with blue edge; $[\alpha]_D^{21}$ −354° ($CHCl_3$; *c* 0.38); IR ν_{max} cm^{-1}: 3380, 1670, 1605; UV λ_{max} (log ε): 228 (3.84), 299 (3.88), 328 (3.99); ^{1}H NMR: δ 0.72 [3H, *dd*, $J_1 = J_2 = 7.5$ Hz, Me(18)], 0.92 (1H, *dq*, $J_1 = 15$, $J_2 = 7.5$ Hz, H-19a), 0.98 (1H, *dq*, $J_1 = 15$, $J_2 = 7.5$ Hz, H-19b), 1.70 (1H, *dd*, $J_1 = 11.5$, $J_2 = 4.5$ Hz, H-6α), 2.07 (1H, *ddd*, $J_1 = J_2 = 11.5$, $J_3 = 6.5$ Hz, H-6β), 2.46 (1H, *d*, $J = 2$ Hz, H-21), 2.54 (1H, *d*, $J = 15$ Hz, H-17β), 2.70 (1H (*dd*, $J_1 = 15$, $J_2 = 2$ Hz; H-17α), 2.71 (1H, *ddd*, $J_1 = 11.5$, $J_2 = 8$, $J_3 = 4.5$ Hz, H-5α), 2.89 (1H, *d*, $J = 13$Hz, H-3α), 3.02 (1H, *br dd*, $J_1 = 8$, $J_2 = 6.5$ Hz, H-5β), 3.06 (1H, *d*, $J = 4$ Hz, H-15), 3.26 (1H, *br d*, $J = 4$ Hz, H-14), 3.59 (1H, *dd*, $J_1 = 13$, $J_2 = 1$ Hz, H-3β), 3.78 (3H, *s*,CO_2Me), 6.81 (1H, *br d*, $J = 7.5$ Hz, H-12), 6.87 (1H, *ddd*, $J_1 = J_2 = 7.5$, $J_3 = 1$ Hz, H-10), 7.14 (1H, *ddd*, $J_1 = J_2 = 7.5$, $J_3 = 1$ Hz, H-11), 7.17 (1H, *br d*, $J = 7.5$ Hz, H-9), 8.98 (1H, *br s*, NH); MS *m/z* (rel. int.): 352 (39 [M]$^+$), 221 (8), 215 (9), 214 (34), 195 (7), 194 (7), 180 (11), 168 (20), 167 (21), 154 (20), 151 (13), 139 (17), 138 (100), 123 (8), 109 (10), 108 (60); other data see ref. [22].

Vincadifformine (**8**). Colourless oil (7 mg); TLC (S-1): R_f 0.28, yellow with blue edge; $[\alpha]_D^{21}$ −542° ($CHCl_3$; *c* 0.30); spectral properties identical with published data [20, 23].

3-*Oxotabersonine* (**9**). Colourless oil (4.5 mg); TLC (S-2): R_f 0.27, yellow with blue edge; $[\alpha]_D^{21}$ −82° ($CHCl_3$; *c* 0.23); IR ν_{max} cm^{-1}: 3385, 1660, 1605; UV λ_{max} (log ε): 296 (4.14), 329 (4.19); ^{1}H NMR: δ 0.87 (3H, *dd*, $J_1 = J_2 = 7.5$ Hz, Me (18)), 1.04 (1H, *dq*, $J_1 = 15$, $J_2 = 7.5$ Hz, H-19a), 1.08 (1H, *dq*, $J_1 = 15$, $J_2 = 7.5$ Hz, H-19b), 1.89 (1H, *dd*, $J_1 = 12$, $J_2 = 5.5$ Hz, H-6α), 1.96 (1H, *ddd*, $J_1 = J_2 = 12$, $J_3 = 7$ Hz, H-6β), 2.07 (1H, *d*, $J = 15.5$ Hz, H-17β), 2.62 (1H, *dd*, $J_1 = 15.5$, $J_2 = 2$ Hz, H-17α), 3.39 (1H, *ddd*, $J_1 = J_2 = 12$, $J_3 = 5.5$ Hz, H-5α), 3.79 (3H, *s*,CO_2Me), 3.98 (1H, *br s*, H-21), 4.32 (1H, *dd*, $J_1 = 12$, $J_2 = 7$ Hz, H-5β), 5.96 (1H, *d*, *J*

= 10 Hz, H-14), 6.45 (1H, *d*, *J* = 10 Hz, H-15), 6.89 (1H, *br d*, *J* = 7.5 Hz, H-12), 6.94 (1H, *br dd*, $J_1 = J_2 = 7.5$ Hz, H-10), 7.22 (1H, *br dd*, $J_1 = J_2 = 7.5$ Hz, H-11), 7.23 (1H, *br d*, *J* = 7.5 Hz, H-9), 9.04 (1H, *br s*, NH); MS *m/z* (rel. int.): 350 (9 $[M]^+$), 228 (16), 227 (100), 214 (3), 196 (13), 195 (88), 168 (20), 167 (29), 154 (13); other data see ref. [6].

3-*Oxopachysiphine* (**10**). Colourless oil (3 mg); TLC (S-2): R_f 0.32, yellow with blue edge; $[\alpha]_D^{21} - 205°$ ($CHCl_3$; *c* 0.14); IR ν_{max} cm^{-1}: 3390, 1670 (sh), 1660, 1615; UV λ_{max} (log ε): 296 (4.02), 328 (4.13); ^1H NMR: δ 0.80 (3H, *dd*, $J_1 = J_2 = 7.5$ Hz, Me (18)), 1.08 (1H, *dq*, $J_1 = 15$, $J_2 = 7.5$ Hz, H-19a), 1.26 (1H, *dq*, $J_1 = 15$, $J_2 = 7.5$ Hz, H-19b), 1.74 (1H, *ddd*, $J_1 = J_2 = 12$, $J_3 = 7$ Hz, H-6β), 1.80 (1H, *br dd*, $J_1 = 12$, $J_2 = 5.5$ Hz, H-6α), 1.88 (1H, *d*, *J* = 15.5 Hz, H-17β), 2.69 (1H, *dd*, $J_1 = 15.5$, $J_2 = 2$ Hz, H-17α), 3.25 (1H, *ddd*, $J_1 = J_2 = 12$, $J_3 = 5.5$ Hz, H-5α), 3.47 [1H, *d*, *J* = 4 Hz, H-15 (or 14)], 3.61 [1H, *d*, *J* = 4 Hz, H-14 (or 15)], 3.67 (1H, *d*, *J* = 2 Hz, H-21), 3.80 (3H, *s*, CO_2Me), 4.46 (1H, *dd*, $J_1 = 12$, $J_2 = 7$ Hz, H-5β), 6.88 (1H, *br d*, *J* = 7.5 Hz, H-12), 6.93 (1H, *br dd*, $J_1 = J_2 = 7.5$ Hz, H-10), 7.21 (1H, *br d*, *J* = 7.5 Hz, H-9), 7.22 (1H, *br, dd*, $J_1 = J_2 = 7.5$ Hz, H-11), 8.98 (1H, *br s*, NH); MS *m/z* (rel. int.): 366 (53 $[M]^+$), 228 (18), 227 (100), 215 (12), 214 (72), 196 (11), 195 (65), 182 (9), 180 (10), 168 (25), 167 (27), 155 (11), 154 (40), 127 (10).

10 *by Oxidation of* **7**. **7** (6 mg) was oxidized with $KMnO_4$ (4 mg) in Me_2CO (2 ml) according to the procedure described for the oxidation of **6** [6]; purification was by TLC (silica gel, S-2).

3-*Oxovincadifformine* (**11**). Colourless oil (1.5 mg); TLC (S-2): R_f 0.39, yellow with blue edge; $[\alpha]_D^{21} - 315°$ ($CHCl_3$; *c* 0.12); IR ν_{max} cm^{-1}: 3395, 1675, 1650, 1615; UV λ_{max} (log ε): 226 (4.01,sh), 297 (4.02), 328 (4.14); ^1H NMR: δ 0.70 (1H, *t*, *J* = 7.5 Hz, Me (18)), 0.99 (2H, *q*, *J* = 7.5 Hz, H-19), 1.37 (1H, *ddd*, $J_1 = 13.5$, $J_2 = 12.5$, $J_3 = 4$ Hz, H-15β), 1.84 (1H, *dd*, $J_1 = 12$, $J_2 = 5.5$ Hz, H-6α), 1.93 (1H, *d*, *J* = 15.5 Hz, H-17β), 2.0 (1H, *ddd*, $J_1 = 13.5$, $J_2 = 5$, $J_3 = 4$ Hz, H-15α), 2.0 (1H, *ddd*, $J_1 = J_2 = 12$, $J_3 = 7.5$ Hz H-6β), 2.30 (1H, *ddd*, $J_1 = 15$, $J_2 = 12.5$, $J_3 = 5$ Hz, H-14α), 2.39 (1H, *ddd*, $J_1 = 15$, $J_2 = J_3 = 4$ Hz, H-14β), 2.65 (1H, *dd*, $J_1 = 15.5$, $J_2 = 2$ Hz, H-17α), 3.42 (1H, *ddd*, $J_1 = J_2 = 12$, $J_3 = 5.5$ Hz, H-5α), 3.47 (1H, *d*, *J* = 2 Hz, H-21), 3.79 (3H, *s*, CO_2Me), 4.16 (1H, *dd*, $J_1 = 12$, $J_2 = 7.5$ Hz, H-5β), 6.87 (1H, *br d*, *J* = 7.5 Hz, H-12), 6.92 (1H, *ddd*, $J_1 = J_2 = 7.5$, $J_3 = 1$ Hz, H-10), 7.18 (1H, *br d*, *J* = 7.5 Hz, H-9), 7.21 (1H, *ddd*, $J_1 = J_2 = 7.5$, $J_3 = 1$ Hz, H-11), 9.0 (1H, *br s*, NH); MS *m/z* (rel. int.): 352 (38 $[M]^+$), 228 (16), 227 (100), 214 (34), 196 (8), 195 (50), 182 (4), 180 (5), 168 (12), 167 (13), 154 (18), 138 (5); other data see ref. [6].

11 *by Hydrogenation of* **9**. **9** (1 mg) was hydrogenated at room temp in MeOH using PtO_2 as catalyst. After 10 min the mixt was filtered and the solvent evapd to obtain 1 mg oily product identical with **11**.

Quebrachamine **12**. Colourless crystals (4 mg), mp 145–147°; TLC (S-3): R_f 0.38, pink; $[\alpha]_D^{21} + 114°$ ($CHCl_3$; *c* 0.21); IR ν_{max} cm^{-1}: 3470; UV λ_{max} (log ε): 227 (4.41), 284 (3.89), 291 (3.86); ^1H NMR: δ 0.84 [3H, *dd*, $J_1 = J_2 = 7.5$ Hz, Me (18)], 1.07–1.34 (5H, *m*), 1.49 (1H, *d*, *J* = 12 Hz, H-21a), 1.53-1.64 (2H, *m*), 1.92 (1H, *ddd*, $J_1 = 14$, $J_2 = 7$, $J_3 = 2$ Hz), 2.24 (1H, *ddd*, $J_1 = 12$, $J_2 = 11$, $J_3 = 3$ Hz), 2.33 (1H, *ddd*, $J_1 = J_2 = 11.5$, $J_3 = 4.5$ Hz), 2.42 (1H, *ddd*, $J_1 = 11.5$, $J_2 = 4.5$, $J_3 = 3$ Hz), 2.46 (1H, *m*), 2.67 (1H, *ddd*, $J_1 = 15$, $J_2 = 7$, $J_3 = 2$ Hz), 2.74 (1H, *ddd*, $J_1 = 15$, $J_2 = 10$, $J_3 = 2$ Hz), 2.83 (1H, *ddd*, $J_1 = 15$, $J_2 = 4.5$, $J_3 = 3$ Hz), 2.93 (1H, *ddd*, $J_1 = 15$, $J_2 = 11.5$, $J_3 = 4.5$ Hz), 3.24 (1H, *br d*, *J* = 12 Hz, H-21b), 7.03–7.11 (2H, *m*), 7.27 (1H, *m*), 7.47 (1H, *m*), 7.69 (1H, *br s*, NH); MS *m/z* (rel. int.): 282 (100 $[M]^+$), 253 (16), 210 (6), 196 (6), 168 (9), 167 (8), 158 (10), 157 (43), 156 (23), 154 (10), 152 (9), 144 (23), 143 (31), 141 (11), 138 (30), 130 (12), 128 (11), 126 (21), 125 (51), 124 (48), 122 (11), 115 (8), 110 (52), 108 (9), 96 (20); for other data see refs. [10, 24].

14β-*Hydroxyquebrachamine* (**13**). Colourless crystals (3 mg), mp 123–126°; TLC (S-4): R_f 0.37, pink; $[\alpha]_D^1 + 86°$ ($CHCl_3$; *c* 0.14); IR ν_{max} cm^{-1}: 3630, 3470; UV λ_{max} (log ε): 225 (4.42), 283 (3.79), 290 (3.75); ^1H NMR: δ 0.85 [3H, *dd*, $J_1 = J_2 = 7.5$ Hz, Me (18)], 1.13 (1H, *dq*, $J_1 = 15$, $J_2 = 7.5$ Hz, H-19a), 1.17 (1H, *dd*, $J_1 = 14$, $J_2 = 3.5$ Hz, H-15α), 1.18 (1H, *dq*, $J_1 = 15$, $J_2 = 7.5$ Hz, H-19b), 1.61 (1H, *d*, *J* = 12.5 Hz, H-21α), 1.65 (1H, *br d*, *J* = 14 Hz, H-15β), 1.84 (1H, *ddd*, $J_1 = 15$, $J_2 = 9.5$, $J_3 = 1.5$ Hz), 1.92 (1H exch,*d*,*J* = 9.5 Hz, OH), 2.34 (1H, *ddd*, $J_1 = 15$, $J_2 = 9$, $J_3 = 1.5$ Hz), 2.36 (1H, *ddd*, $J_1 = J_2 = 11$, $J_3 = 5$ Hz), 2.50 (1H, *br d*, *J* = 11.5 Hz, H-3β), 2.59 (1H, *dd*, $J_1 = 11.5$, $J_2 = 2$ Hz, H-3α), 2.59 (1H, *ddd*, $J_1 = 11$, $J_2 = 4.5$, $J_3 = 3$ Hz), 2.75 (1H, *ddd*, $J_1 = 15$, $J_2 = 9$, $J_3 = 1.5$ Hz), 2.83 (1H, *ddd*, $J_1 = 15$, $J_2 = 9.5$, $J_3 = 1.5$ Hz), 2.95 (1H, *ddd*, $J_1 = 15$, $J_2 = 5$, $J_3 = 3$ Hz), 3.01 (1H, *ddd*, $J_1 = 15$, $J_2 = 11$, $J_3 = 4.5$ Hz), 3.45 (1H, *br d*, *J* = 12.5 Hz, H-21β), 3.72 (1H, *m*, H-14), 7.03–7.11 (2H, *m*), 7.26 (1H, *m*), 7.45 (1H, *m*), 7.72 (1H exchangeable, *br s*, NH); MS *m/z* (rel. int.): 298 (100 $[M]^+$), 280 (5), 269 (4), 251 (10), 211 (22), 210 (14), 199 (10), 182 (6), 180 (5), 168 (11), 167 (7), 158 (13), 157 (61), 156 (35), 154 (33), 149? (9), 144 (25), 143 (37), 142 (22), 141 (23), 140 (24), 130 (13), 128 (11), 126 (33), 124 (18), 122 (8), 115 (8), 110 (8); for other data see refs [7, 25].

Conoflorine (**14**). Colourless crystals (40 mg), mp 166–167°; TLC (S-1): R_f 0.15, pink; $[\alpha]_D^1 + 26°$ ($CHCl_3$; *c* 0.64); spectral properties identical with published data [7, 21, 26].

13 by *reduction of* **14**. **14** (8 mg) in dry THF (2 ml) was added to a suspension of $LiAlH_4$ (15 mg) in 4 ml THF and refluxed for 2 hr. Excess $LiAlH_4$ was destroyed by addn of EtOAc and then H_2O. Extraction with $CHCl_3$ followed by CC (Al_2O_3, neutral, S-5) yielded **13** (0.8 mg) and its isomer (4 mg), whose spectral properties were identical with published data for 15β-hydroxyquebrachamine (conoflorinol A [7] or voaphyllinol A [25]).

12,12′-Bis(11-*hydroxycoronaridinyl*) (**15**). Colourless oil (14 mg); TLC (S-3): R_f 0.20, green; $[\alpha]_D^{21} - 41°$ ($CHCl_3$; *c* 0.75); spectral properties identical with published data [27].

14,15-*Dehydrotetrastachynine* (**16**). Colourless oil (6 mg); TLC (S-3): R_f 0.18, grey-green; $[\alpha]_D^{21} - 31°$ ($CHCl_3$; *c* 0.26); CD nm (Δε): 335 (−12.51), 291 (+6.04), 243 (+10.45); IR ν_{max} cm^{-1}: 3540, 3440, 3390, 1720, 1675, 1615; UV λ_{max}^{EtOH} (log ε): 230 (4.42), 294 (4.24), 338 (4.16); +NaOH: 244 (4.40, sh), 294 (4.22), 360 (4.18); ^1H NMR: δ0.67 and 0.75 (3H, 2 × *dd*, $J_1 = J_2 = 7.5$ Hz, Me (18)), 0.85–0.95 (4H, *m*), 1.00–1.23 (2H, *m*), 1.25–1.37 (1H, *m*), 1.40–1.50 (1H, *m*), 1.51–1.65 (1H, *m*), 1.67–1.80 (2H, *m*), 1.82–1.92 (2H, *m*), 2.04–2.20 (1H, *m*, H-6α), 2.42–2.54 (2H, *m* H-17β, H-17′α), 2.58–2.65 (1H, *m*, H-17α), 2.72–2.86 (3H, *m*), 2.90–2.97 (1H, *m*), 2.98–3.08 (1H, *m*), 3.09–3.28 (4H, *m*), 3.36–3.43 (1H, *m*), 3.44–3.52 (1H, *m*, H-3β), 3.50 and 3.56 (1H, 2 × *br s*, H-21′), 3.65 and 3.71 (3H, 2 × *s*, CO_2Me'), 3.78 and 3.79 (3H, 2 × *s*, CO_2Me), 5.72–5.86 (2H, *m*, H-14,H-15), 6.82–6.95 (2H, *m*), 7.0 and 7.05 (1H, 2 × *d*, *J* = 7.5 Hz), 7.38 and 7.40 (1H, 2 × *d*, *J* = 7.5 Hz), 7.46 and 7.64 (1H, 2 × *br s*, NH), 9.01 and 9.04 (1H, 2 × *br s*, NH); (CD_3OD, 60°), e.g. δ 5.72 (1H, *br d*, *J* = 10 Hz, H-15), 5.83 (1H, *ddd*, $J_1 = 10$, $J_2 = 4.5$, $J_3 = 1.5$ Hz, H-14), 6.76 (1H, *d*, *J* = 8 Hz), 6.93 (1H, *d*, *J* = 7.5 Hz), 7.0 (1H, *d*, *J* = 7.5 Hz), 7.30 (1H, *d*,*J* = 8 Hz); ^{13}C NMR: δ 7.6 (C-18), 11.6 (C-18′), 22.1 (C-6′), 26.8 (C-19′), 27.2 (C-17 or C-14′), 27.3 (C-14′ or C-17), 28.8 (C-19), 32.0 (C-15′), 36.2 (C-17′), 38.9 (C-20′), 41.1 (C-20), 44.2 and 44.6 (C-6), 50.3 and 50.4 (C-5), 51.1 ($CO_2\underline{Me}$ or C-3), 51.2 (C-3 or $CO_2\underline{Me}$), 51.8 and 51.9 (C-3′), 52.6 and 52.7 ($CO_2\underline{Me}'$), 53.1 (C-5′), 55.0 (C-16′), 56.2 (C-7), 57.4 and 57.6 (C-21′), 70.1 (C-21), 92.6 and 92.8 (C-16), 99.5 and 99.6 (C-12′), 109.5 and 109.6 (C-10′), 110.9 and 111.1 (C-7′), 114.9 and 115.1 (C-9), 119.4 and 119.6 (C-9′), 120.2 and 120.5 (C-11 or C-10), 121.8 and 122.1 (C-10 or C-11), 123.5 and 123.7 (C-8′), 124.8 (C-14), 132.7 and 133.2 (C-13 or C-13′), 133.1 (C-15), 134.4 and 134.9 (C-13′ or C-13), 135.9 and 136.1 (C-2′), 138.2 and 138.3 (C-8), 139.8 and 140.3 (C-12), 148.3 and 149.0 (C-11′), 165.9 and 166.7 (C-2), 168.8 and 169.0 ($\underline{C}O_2Me$), 175.4 ($\underline{C}O_2Me'$); MS *m/z* (rel. int.): 704 (~0.08 $[M]^+$), 136 (2), 135 (9),

108 (5), 107 (100), 106 (50), 93 (4), 92 (88); DCIMS (NH_3) *m/z*: 705 $[M+1]^+$.

Acetylation of **16**. **16** (1 mg) was acetylated (room temp, 24 hr) in 2 ml Ac_2O–pyridine (1:1). Purification by TLC (silica gel, S-3): 0.8 mg colourless oil; TLC (S-3): R_f 0.27, pale grey-brown; MS *m/z* (rel. int.): 788.3781 ($C_{46}H_{52}N_4O_8$; 5 $[M]^+$), 394.5 (~1), 394 (~1.5 $[M]^{2+}$), 136.1126 ($C_9H_{14}N$; 33), 135.1048 ($C_9H_{13}N$; 100), 124 (7), 122.0970 ($C_8H_{12}N$; 22), 121 (9), 107.0735 (C_7H_9N; 16).

*Hydrogenation of diacetyl-***16**. Diacetyl-**16** (0.5 mg) was hydrogenated in MeOH using PtO_2: 0.5 mg colourless oil; TLC (S-3): R_f 0.31, pale grey-brown; MS *m/z* (rel.int.): 790 (6 $[M]^+$), 338 (1), 136 (12), 125 (9), 124 (100).

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Addition on proof: very recently Prof. P. Potier informed us that he also had isolated compound **16** from the Caribbean *Tabernaemontana citrifolia*.

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