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TWO *BIS*-INDOLE ALKALOIDS FROM LEAVES OF *ERVATAMIA POLYNEURA*

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Key Word Index—*Ervatamia polyneura*; Apocynaceae; leaves; polyervinine; polyervine; *bis*-indole alkaloids; NMR.

Abstract—Two alkaloids with a *bis*-vincadifformine skeleton, polyervinine and polyervine, have been isolated from the leaves of *Ervatamia polyneura* (Apocynaceae). The structure of polyervinine was determined by spectroscopic methods and confirmed by analysis of several derivatives. The structure of polyervine was educed by spectroscopic comparison with polyervinine.

INTRODUCTION

Trees of the genus *Ervatamia* are widespread in south-eastern Asia and used in traditional medicine for the treatment of ulcerative wounds [1, 2]. In the framework of our chemical studies on *Ervatamia* species [3–8], we have completed a previous investigation of *E. polyneura* (Scortechi ex King and Gamble) King and Gamble which had led to the structural elucidation of several new monomer alkaloids [3, 5]. In this paper, we report on the structural determination of two *bis*-indole alkaloids for which we have proposed the trivial names, polyervinine (**1**) and polyervine (**2**). This work is taken from a thesis [3] and is cited by Teo *et al.* (1990).

RESULTS AND DISCUSSION

Extraction of the crude alkaloid mixture (AM) was as reported previously [5]. Alkaloids were isolated by means of column chromatography and TLC: polyervinine (**1**) (1.2% AM) and polyervine (**2**) (2.0% AM).

Polyervinine (**1**) was obtained as an air-sensitive dark-purple amorphous powder; determination of optical rotation was precluded because of the colour of the solution. The UV–visible absorptions of **1** (203, 316 and 558 nm; neutral pH) were indicative of a highly conjugated system. Upon treatment with base or acid, bathochromic (578 nm) and hypsochromic shifts (363 nm) were observed, respectively. The IR spectrum showed absorptions for conjugated carbonyl groups (1680 and 1600 cm^{-1}) and for OH and/or NH (3360 cm^{-1}).

The *bis*-vincadifformine (vdf) structure of **1** (Scheme 1) and molecular formula $C_{43}H_{46}N_4O_{10}$ were suggested from ^1H and ^{13}C NMR data (Tables 1 and 2). Assignments were ascertained by homo- and heteronuclear 2D experiments. The ^1H NMR spectrum displayed characteristic signals for two ethyl side-chains (*t* at δ0.78 and 0.89) and two deshielded indolic NH (*bs* at δ9.06 and 9.60, exchangeable with D_2O). Three methyl singlets between δ3.8 and 4.0 suggested the presence of methyl ester and/or methoxy groups. The very small number of aromatic protons indicated a high degree of substitution of the aromatic rings.

The ^{13}C NMR spectrum of **1** displayed well-resolved resonances for 43 carbon atoms identified by DEPT sequence as five methyl, nine methylene and 10 methyne groups, in addition to 19 non-protonated carbons. Some signals are characteristic of a *bis*-vdf structure [10]; four quaternary sp^3 carbons at δ47.5, 36.9 (C-20 and 20'), 52.1 and 54.3 (C-7 and 7') and the typical β-anilinoacrylate systems with resonances at δ168.8 and 168.0 (C-22 and C-22'), 51.1 and 51.8 ($2 \times OCH_3$), 98.5 and 92.0 (C-16 and C-16'), 154.2 and 164.6 (C-2 and C-2'). Such a structure implies the presence of 18 sp^2 carbon atoms. As the ^{13}C NMR spectrum of **1** showed only 18 resonances down-field of 90 ppm it was concluded that **1** does not possess any double bonds other than those of the β-anilinoacrylate systems. The reduced number of aromatic protons and the presence of carbon resonances at δ179.5 and 171.8, together with the UV–visible spectroscopic

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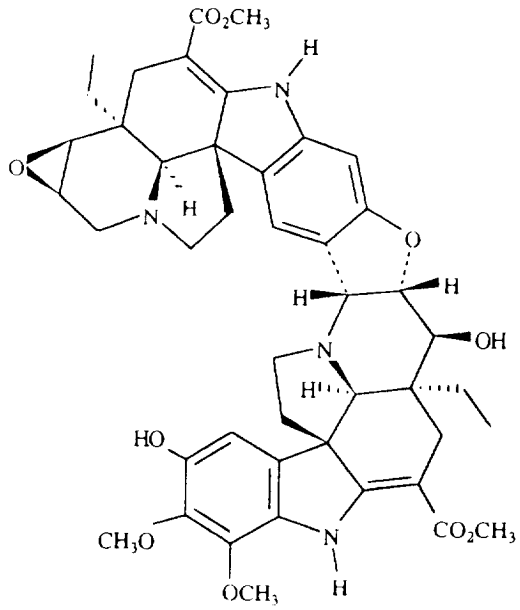
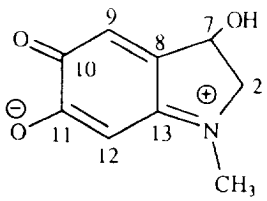
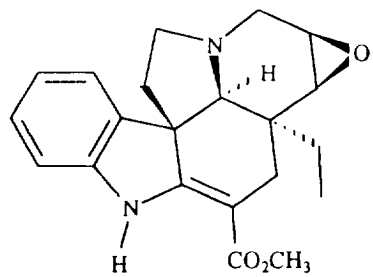


Polyervine (2)



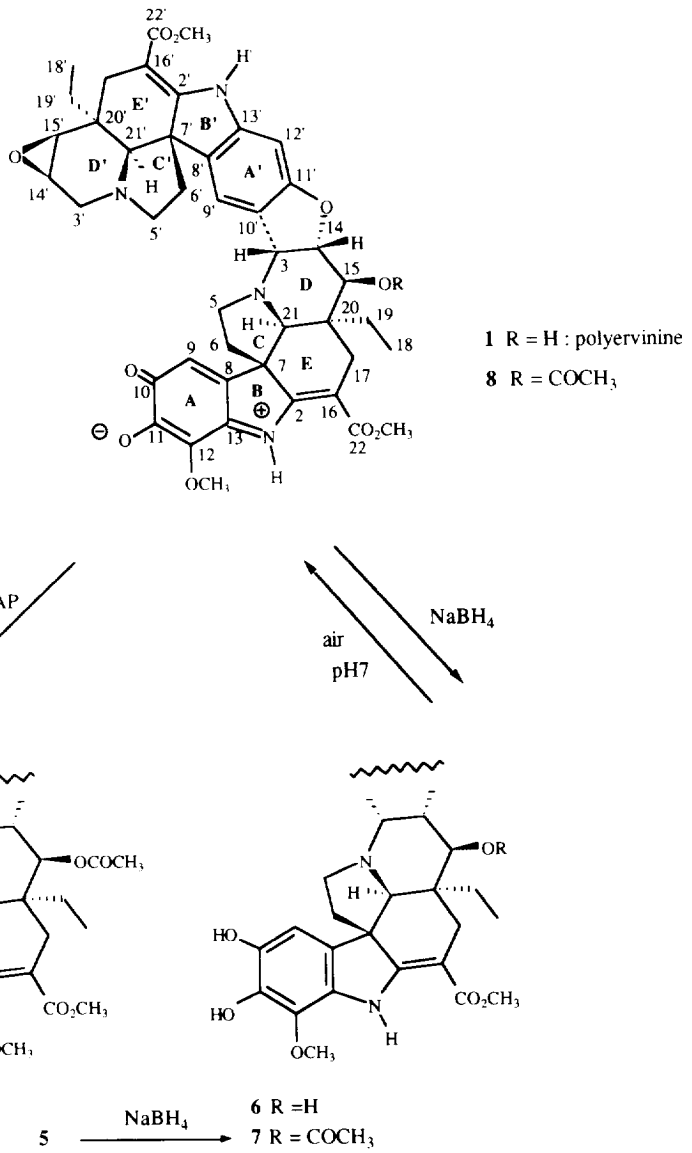
Adrenochrome (3)



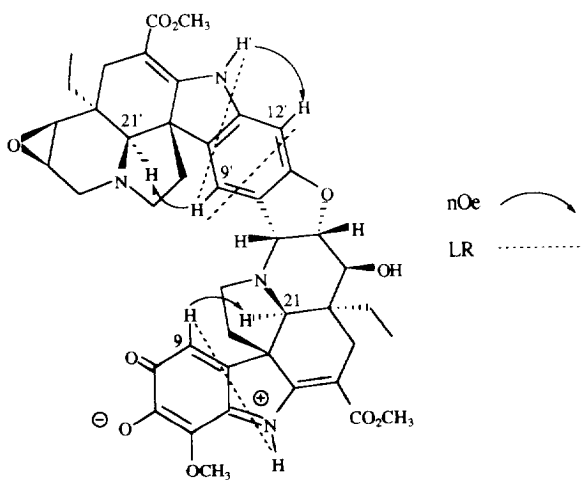
Pachysiphine (4)

properties, suggest that **1** belongs to the aminochrome family [11, 12]. These compounds possess an indoline dione chromophore but its zwitterionic quinoniminium form exists predominantly. Confirmation of this hypothesis was obtained by comparing spectroscopic properties (NMR, UV) of **1** with adrenochrome **3**, a dark-red pigment. In the ^{13}C NMR spectrum of **3**, the signals for C-10 and C-11 appear at δ182.8 and 173.3, while **1** and **3** exhibit similar variations in UV absorbance with changes in pH.

Comparison of ^{13}C NMR data of **1** and pachysiphine (**4**) [13] (see Table 2) suggested that one part of the dimer is a substituted pachysiphine linked to the other part through its aromatic ring. The nature of the substituents of the two aromatic rings and the junction-type between the two vdf moieties were determined by a concomitant analysis of long-range (LR), ^{1}H-COSY, NOESY, COLOC, and direct ^{13}C–^{1}H correlation spectra of **1**. In this latter spectrum, three aromatic methines were observed at δ119.1, 93.0 and 118.7. They correlate, respectively, with protons at δ7.07 and 6.35, and with a more shielded one at δ5.02. Because these three proton signals are singlets, one aromatic unit of the dimer is trisubstituted, the other disubstituted at C-10′ and C-11′ (*para* position for the residual aromatic protons). Assignments of these protons and attribution to their respective vdf unit were achieved after observation of NOEs and LR couplings (Scheme 2). The proton at δ6.35 was assigned to H-12′ (pachysiphine half) from NOE with NH′ at δ9.06 and a LR coupling with a second aromatic proton at δ7.07 (H-9′). This latter proton gave a characteristic LR coupling with NH′, as observed in kisantine [14], and also exhibited a NOE with H-21′, which was identified by a ^{1}J correlation with C-21′. The NOE observed for the third proton at δ5.02 with H-21 (aminochrome half), together with the LR coupling to the NH, fixes it on C-9. Quaternary aromatic carbons were attributed from the COLOC spectrum (Scheme 3) which also enabled the identification of a methoxyl group (δ60.2) at C-12. On the pachysiphine moiety, the chemical shift of C-10′ (δ112.6) indicated a C-substitution, while C-11′ (δ 160.8) bears an oxygen atom.



Scheme 1. Polyervinine (**1**) and its derivatives.



Scheme 2. Most significant correlations of compound **1**.

The junction between the two moieties in **1** may involve C-3 and C-14, as well as C-15, which all are methyne groups. From their chemical shifts, two are substituted by oxygen atoms (δC 84.6, δH 5.06; δC 69.1, δH 4.16) and the third δC 59.3, δH 4.81) by a nitrogen atom; this latter is C-3 and is bound to C-10′. Identification of H-14 was made from its multiplicity (*dd*, J = 7.9; 3.7 Hz at δ5.06) and from its correlation with H-3 in the COSY spectrum. To prove the site and nature of the substituents on C-14 and C-15, acetylation of **1** (Ac_2O/DMAP) was carried out to give **5** (Scheme 1). While the chemical shifts of H-14 in **1** and **5** were similar, the resonance at δ4.16 (H-15) was shifted down-field upon acetylation (δ5.57). Therefore, C-14 is a part of an ether group, while the second oxygenated function is a secondary alcohol. Confirmation of the C-10′–C-3 bond and then of substitution of C-15 by an hydroxyl group was accomplished by comparison of the C-3 chem-

Table 1. ^{1}H NMR assignments of polyervinine (**1**), polyervine (**2**) and of the various derivatives of **1** (**5**, **6** and **7**)*

	1	**2**	**5**	**6**	**7**
H-3	4.81 (*bd*, 7.9)	4.81 (*bd*, 7.8)	4.71 (*bd*, 7.9)	4.69 (*bd*, 7.8)	4.59 (*d*, 7.8)
H-5	2.70–2.81 (*m*)	2.84–2.94 (*m*)	2.63–2.79 (*m*)	2.60–2.70 (*m*)	2.68–2.74 (*m*)
H-5	3.04–3.14 (*m*)	2.94–3.03 (*m*)	3.10–3.17 (*m*)	2.74–2.84 (*m*)	2.86–2.91 (*m*)
H-6	1.98 (*dd*, 11.9; 4.5)	1.64–1.73 (*m*)	1.77 (*dd*, 11.8; 4.3)	1.53–1.65 (*m*)	1.52–1.60 (*m*)
H-6	2.02–2.16 (*m*)	1.96–2.17 (*m*)	1.99–2.16 (*m*)	1.82–2.02 (*m*)	1.80–1.95 (*m*)
H-9	5.02 (*s*)	5.57 (*s*)	5.06 (*s*)	5.35 (*s*)	5.29 (*s*)
H-14	5.06 (*dd*, 7.9; 3.7)	5.06 (*dd*, 7.8; 3.7)	4.79 (*dd*, 7.9; 3.1)	4.88 (*dd*, 7.8; 3.8)	4.62 (*dd*, 7.8; 3.1)
H-15	4.16 (*bs*)	4.26 (*bd*, 3.7)	5.57 (*d*, 3.1)	4.04 (*d*, 3.8)	5.42 (*d*, 3.1)
H-17	2.46 (*d*, 15.1)	2.40 (*bd*, 15.4)	2.62 (*dd*, 15.9; 1.8)	2.30 (*d*, 15.5)	2.22 (*bd*, 14.9)
H-17	2.70–2.81 (*m*)	2.70–2.80 (*m*)	2.63–2.79 (*m*)	2.54 (*bd*, 15.5)	2.30 (*d*, 14.9)
CH_3-18	0.78 (*t*, 7.1)	0.71 (*t*, 7.1)	0.86 (*t*, 7.2)	0.60 (*t*, 7.2)	0.57 (*t*, 7.2)
H-19	0.84–0.95 (*m*)	0.84–0.91 (*m*)	0.70–0.80 (*m*)§	0.79–0.88 (*m*)	0.69–0.80 (*m*)
H-19	1.05–1.42 (*m*)	1.11–1.29 (*m*)	1.08–1.29 (*m*)	0.93–1.25 (*m*)	0.88–0.97 (*m*)
H-21	2.46 (*d*, 1.5)†	2.61 (*bs*)	2.30 (*s*)¶	2.59 (*bs*)	2.48 (*bs*)
OCH_3-11	—	3.84 (*s*)	—	—	—
OCH_3-12	3.90 (*s*)	3.88 (*s*)	4.22 (*s*)	3.82 (*s*)	3.78 (*s*)
CO_2CH_3	3.84 (*s*)‡	3.79 (*s*)†	3.88 (*s*)†	3.67 (*s*)‡	3.65 (*bs*)†
N(1)-H	9.60 (*bs*)	8.80 (*bs*)	—	Exchanged	—
H-3′	2.95 (*bd*, 12.9)	2.99 (*bd*, 12.9)	2.92 (*bd*, 12.7)	2.88 (*bd*, 13.0)	2.84 (*bd*, 12.7)
H-3′	3.57 (*bd*, 12.9)	3.59 (*bd*, 12.9)	3.59 (*bd*, 12.7)	3.47 (*bd*, 13.0)	3.44 (*bd*, 12.7)
H-5′	2.70–2.81 (*m*)	2.70–2.80 (*m*)	2.63–2.79 (*m*)	2.60–2.70 (*m*)	2.57–2.64 (*m*)
H-5′	3.04–3.14 (*m*)	3.08 (*bt*, 7.1)	3.06 (*bt*, 7.0)	2.84–2.97 (*m*)§	2.86–2.91 (*m*)
H-6′	1.68 (*dd*, 12.1; 4.5)	1.64–1.73 (*m*)	1.68 (*dd*, 11.6; 4.4)	1.53–1.65 (*m*)	1.52–2.60 (*m*)
H-6′	2.02–2.16 (*m*)	1.96–2.17 (*m*)	1.99–2.16 (*m*)	1.82–2.02 (*m*)	1.80–1.95 (*m*)
H-9′	7.07 (*s*)	7.14 (*s*)	7.02 (*s*)	7.04 (*s*)	6.98 (*s*)
H-12′	6.35 (*s*)	6.34 (*s*)	6.36 (*s*)	6.29 (*s*)	6.28 (*s*)
H-14′	3.24 (*bd*, 3.9)	3.25 (*bd*, 3.8)	3.25 (*bd*, 4.0)	3.18 (*bd*, 3.9)	3.17 (*bd*, 3.9)
H-15′	3.12 (*d*, 3.9)	3.11 (*d*, 3.8)	3.12 (*d*, 4.0)	3.01 (*d*, 3.9)	2.98 (*d*, 3.9)
H-17′	2.52 (*d*, 15.2)	2.54 (*d*, 15.5)	2.53 (*d*, 15.5)	2.43 (*d*, 15.5)	2.39 (*d*, 15.4)
H-17′	2.70–2.81 (*m*)	2.70–2.81 (*m*)	2.63–2.79 (*m*)	2.54 (*bd*, 15.5)	2.57 (*bd*, 15.4)
CH_3-18′	0.89 (*t*, 7.1)	0.80 (*t*, 7.1)	0.86 (*t*, 7.2)	0.75 (*t*, 7.2)	0.72 (*t*, 7.2)
H-19′	1.05–1.42 (*m*)	1.11–1.29 (*m*)	1.08–1.29 (*m*)§	0.93–1.25 (*m*)	1.00–1.18 (*m*)
H-21′	2.48 (*d*, 1.5)†	2.58 (*bs*)	2.44 (*bs*)	2.59 (*bs*)	2.46 (*bs*)
CO_2CH_3	3.80 (*s*)‡	3.80 (*s*)†	3.79 (*s*)†	3.69 (*s*)‡	3.61 (*s*)†
N(1)-H′	9.06 (*bs*)	9.00 (*bs*)	8.97 (*bs*)	Exchanged	Exchanged
N(1)-Ac	—	—	2.30 (*s*)	—	2.07 (*s*)
Ac-15	—	—	2.20 (*s*)	—	1.93 (*s*)

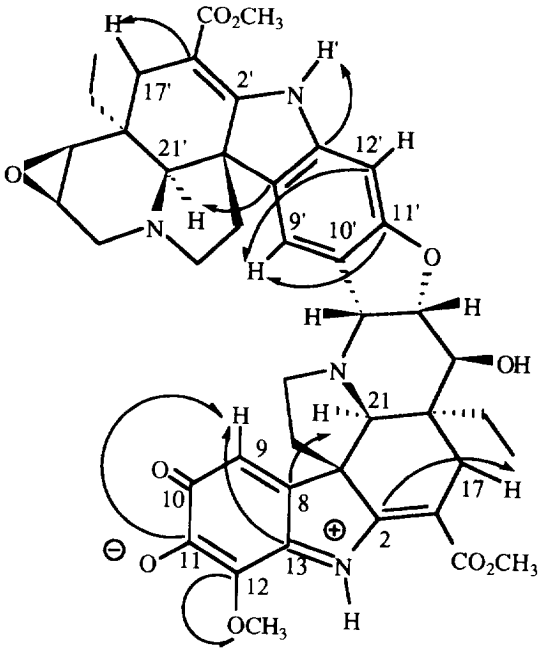
*Chemical shift values (δ) are reported in ppm from TMS at 300 MHz except for **7** (500 MHz); signal multiplicity and coupling constants (Hz) are shown in parentheses. Spectra of compounds **1**, **2** and **5** were recorded in $CDCl_3$; three drops of CD_3OD were added for compounds **6** and **7**.

†‡§Values with the same index and within the same column are interchangeable.

¶Partially masked signal.

ical shift in **1** with that of criophylline [15]. Final spectroscopic evidence of the zwitterionic iminoquinone form was obtained from the mass spectrum of **1**. Although EI does not give rise to any significant peak, the FAB spectrum exhibited an ion at *m/z* 781. Iminoquinone alkaloids are well-known to be easily disproportionated under FAB conditions and to display a $[MH + 2]^+$ peak [16, 17]. It is a rare case but typical for quinone-like compounds. The base peak observed at *m/z* 781 $[M + 3]^+$ matches the formula $C_{43}H_{46}N_4O_{10}$ and is consistent with the proposed structure **1**.

The stereochemistry of the different asymmetric centres in **1** was deduced from the NOE experiment and by chemical shift analogy; stereochemistry at C-7′, C-14′, C-15′, C-20′ and C-21′ has been established by comparison with pachysiphine [13] and the C/D ring junction is proposed to be *trans* according to Daudon *et al.* [18]. The relative configuration of C-3 was deduced from the shielding of C-5 and C-21 relative to the monomeric alkaloid, pachysiphine (**4**). This shielding results from a 1,3-diaxial interaction, as reported for criophylline [15] or pandicine [19], and is also a proof of a *trans*-C/D ring junction. Therefore, the doublet of N-(4) is β, H-21 α and, for biogenetic reasons, the C-6/C-7 bond is β, while the ethyl side-chain is α. A β configuration for H-14 is imposed by the dihydrofuran ring and, finally, the α-orientation of H-15 is deduced from its NOE with CH_3-18 in **5**. Dreiding models show that H-9 faces the shielding



Scheme 3. Most significant correlations in COLOC spectrum of compound **1**.

zone of the aromatic ring of the pachysiphine unit. This is consistent with the strong shielding of this proton compared to H-9 of iminoquinone alkaloids, such as vincarubine [10] or flexicorine [20], and has already been reported in a related substituted dimer [14].

In order to confirm the aminochrome structure of **1**, we have prepared some derivatives (Scheme 1) and studied their spectral data (Tables 1 and 2). Borohydride reduction of **1** led to the slightly yellow coloured compound **6**. Spontaneous oxidation of **6** upon exposure to air gave back **1** and prohibited isolation except in an inert atmosphere. The acetylated derivative **5** gave a ^{1}H NMR spectrum which displayed two acetyl groups (δ2.20 and 2.30) and only one NH indole resonance (δ8.97) attributed to NH′ from its NOE with H-12′. While one acetate of **5** was easily located on C-15, location of the second acetyl group was not so straightforward. It could be either on NH or on the oxygen atom borne by C-11. Because **5** was yellow, we assumed that the zwitterionic iminoquinone form was no longer present and that acetylation had occurred at position 1. This was confirmed by the *ca* 10 ppm shielding of C-11. Reduction of **5** ($NaBH_4$) led to **7** which also spontaneously reoxidized to compound **8** in the presence of air. Like **1**, compound **8** displayed a dark-blue colour at alkaline pH

Table 2. ^{13}C NMR assignments of polyervinine (**1**), polyervine (**2**), pachysiphine (**4**) [13] and derivatives of **1***

	1	2	4	5	6	7		1	2	4	5	6	7
C2	154.2	164.3†		165.5†	166.8	168.8†	C2′	164.6	165.0†	164.9	164.9†	165.6	165.5
C3	59.3	59.5		59.1	59.2	59.0	C3′	49.2	49.2	49.4	49.7	49.2	49.5
C5	45.6	45.9		46.1	46.2	46.5	C5′	51.2	51.1	51.0	51.2	50.9	50.9
C6	41.2	41.8		40.3	42.1	42.5	C6′	44.2	44.3	43.9	44.3	44.3¶	44.4
C7	52.1	54.8‡		53.2‡	55.6	53.8‡	C7′	54.3	54.4‡	54.7	54.0‡	54.0	55.9‡
C8	157.4	133.5		154.7	125.5†	125.4§	C8′	131.4	130.9	137.5	131.0	130.4	130.3
C9	118.7	103.9		117.7	98.3	98.0	C9′	119.1	119.3	121.3	118.9	119.1	118.9
C10	179.5††	143.5		179.5	148.6	148.6	C10′	112.6	113.8	120.3	113.3	114.9	115.0
C11	171.8††	138.7		162.7	141.8	141.8	C11′	160.8	161.0	127.6	159.9	160.6	159.7
C12	131.2	136.7		148.4	128.7	128.7	C12′	93.0	93.0	109.2	93.0	92.9	93.0
C13	140.9	128.7		134.8	125.4†	125.1§	C13′	145.4	145.0	142.9	145.2	144.6	144.4
C14	84.6	85.0		82.5	85.3	82.7	C14′	52.1	52.1	52.0	52.2	52.3	52.3
C15	69.1	69.5		69.4	69.7	70.9	C15′	56.3	56.3	56.2	56.4	56.6	56.6
C16	98.5	90.7§		122.6	88.3	87.6	C16′	92.0	91.3§	90.4	92.1	91.0	91.1
C17	22.6	22.2		27.8	22.1	21.8	C17′	23.5	23.5	23.5	23.5	23.3	23.3
C18	7.6†	7.4		7.2§	6.6‡	6.6¶	C18′	7.4†	7.4	7.1	7.4§	7.1‡	6.9¶
C19	26.8‡	26.4¶		26.7	26.2§	27.2¶	C19′	26.9‡	26.7¶	26.5	26.7	26.5§	26.1¶
C20	47.5	44.8		47.9	44.4¶	44.0	C20′	36.9	37.0	37.0	37.2	37.1	37.1
C21	65.2	65.3		64.8	65.0	64.1	C21′	71.9	71.7	70.9	72.0	71.4	71.3
C22	168.8§	168.7‖		168.7¶	168.9‖	167.4	C22′	168.0§	168.8‖	168.6	166.3¶	169.0‖	167.4
$CO_2\underline{C}H_3$	51.1§	50.9**		51.1¶	50.7**	50.7‖	$CO_2\underline{C}H_3$	51.8§	51.0**	50.8	52.4¶	50.5**	50.5‖
OCH_3-11	—	60.9		—	—	—	$O\underline{C}OCH_3$-15′	—	—	—	—	170.1	170.8
OCH_3-12	60.2	60.4		60.7	59.8	59.7	$OCO\underline{C}H_3$-15′	—	—	—	21.1	—	20.8
N(1)-$\underline{C}OCH_3$		—		168.2	—	168.9†		—	—	—		—	
N(1)-$CO\underline{C}H_3$		—		20.4	—	20.3		—	—	—		—	

*^{13}C spectra were recorded under the same conditions as for ^{1}H spectra (see Table 1). Carbon chemical shift values (δ) are given in ppm from TMS at 75 MHz, except for **7** (125 MHz).

†,‡,§,¶,‖,**,††Interchangeable values within the same column.

and a dark-purple colour at neutral pH. The ^{1}H NMR spectrum of **8** contained signals for only one acetyl group (δ2.20) and two NH signals (δ NH 9.57) and NH' 9.05, see Experimental). In the reduced derivatives, **6** and **7**, chemical shifts of aromatic carbons are consistent with an *o*-diphenol pattern.

The structure of polyervine (**2**) was deduced from spectroscopic comparison with **1** and its reduced derivatives. The $[MH]^+$ of **2** appeared at *m/z* 795 (in a FAB experiment), corresponding to the formula $C_{44}H_{50}O_{10}N_4$. Alkaloid **2** gave a yellow coloured solution and UV spectrum consistent with a reduced chromophore, as in derivative **6**. The ^{1}H NMR spectrum of **2** was similar to that of **1**, with the exception of an extra OCH_3 resonance (δ3.84) located at C-11 from a COLOC experiment and by the deshielding of H-9 compared to **1** (see Table 1) confirming the reduced form of **2**. Because of the very close similarity of chemical shifts and couplings of **1** and **2**, all asymmetric centres of **2** must have the same stereochemistry as those of **1**. Polyervine (**2**) is probably identical to a compound, named conophylline, recently isolated from *Tabernaemontana divaricata* [21, 22]; it also occurs in *T. glandulosa* [23].

The proposed configurations for **1** and **2** are those of conophylline determined by an X-ray study [22]. Our analysis of NMR spectra leads to consistent relative configurations within monomeric units of dimers **1** and **2**. To the best of our knowledge, polyervinine (**1**) is the first aminochrome *bis*-indole alkaloid to be isolated. Its quinonimine form exhibits a structural relationship with the cytotoxic alkaloid, vincarubine [10], and the active form of 10-hydroxyellipticine, a potent anti-tumoral agent [24].

EXPERIMENTAL

General. ^{1}H NMR were recorded either at (300 MHz) or 500 MHz. Merck silica gel, 230–400 mesh, was used for flash CC and Whatman kieselgel K6F was used for prep. TLC.

Plant material. Ervatamia polyneura (Scortechi ex King and Gamble) King and Gamble was collected in April 1984 at Selangor Genting Simpha (Malaysia) in the framework of a collaborative research program between the CNRS and the University of Malaya. A voucher sample has been deposited at the Herbarium of the Department of Phytochemistry (University of Malaya).

Extraction. See Ref. [5].

Isolation. The crude alkaloid mixt. (5.5 g) was fractionated by silica gel CC (step gradient: CH_2Cl_2 to MeOH). Frs 14–17 (CH_2Cl_2–MeOH, 99:1) containing crude polyervinine were combined (500 mg) and further purified by silica gel prep. TLC to give polyervinine (**1**) (70 mg; yield 1.2%). Polyervine (**2**) was in frs 11–13 (790 mg; CH_2Cl_2–MeOH, 99:1) and was purified using the same method as described for (**1**) (115 mg; yield 2%).

Polyervinine (**1**). Amorphous purple powder. Ceric sulphate TLC (CR) pale yellow; R_f 0.56 ($CHCl_3$–MeOH, 24:1). UV λ_{max}^{MeOH} nm (log ε): 203 (4.49), 244 (*sh*, 4.11) 316 (4.18), 393 (*sh*, 3.35), 538 (3.33); + HCl: 203, 240, 314, 363; + NaOH: 210, 250 (*sh*), 316, 400 (*sh*), 578. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3360, 1680, 1600. FAB$^+$ HR *m/z* $[MH + 2]^+$ 781.3495 (calcd for $C_{43}H_{49}N_4O_{10}$, 781.3449). ^{1}H and ^{13}C NMR: see Tables 1 and 2.

Adrenochrome (**3**). Commercial sample. UV λ_{max}^{MeOH} nm: 231, 301, 480. ^{1}H NMR ($CDCl_3$ + CD_3OD, 500 MHz, 15°): δ6.47 (*d*, *J* = 2 Hz, H-9), 5.28 (*s*, H-12), 4.88 (*ddd*, *J* = 6.8, 3.0, 2.0 Hz, H-7), 3.91 (*dd*, *J* = 12.2, 3.0 Hz, H-2), 3.50 (*dd*, *J* = 12.2, 6.8 Hz, H-2'), 2.98 (*s*, NCH_3). ^{13}C NMR ($CDCl_3$ + CH_3OD, 75 MHz, 15°): δ182.8 (C-10), 173.3 (C-11), 159.1 (C-13), 155.0 (C-8), 125.9 (C-9), 91.3 (C-12), 65.4 (C-7), 62.8 (C-2), 33.6 (N-CH_3).

Reduction of **1**–**6**. Because of the instability of **6**, the reaction was carried in an NMR tube. To a soln of **1** (10 mg) in $CDCl_3$ (2 ml) was added 2 drops of CD_3OD and 2 mg of $NaBH_4$. After gas release, the tube was closed for the recording of NMR. UV $\lambda_{max}^{MeOH + NaBH_4}$ nm: 203, 247, 332. ^{1}H and ^{13}C NMR: see Tables 1 and 2.

Acetylation of **1**–**5**. To a soln of **1** (25 mg, 0.03 mmol) in CH_2Cl_2 (8 ml) was added 4 mg of DMAP and 3 ml of Ac_2O. The reaction mixt. was stirred at room temp. for 20 hr and then washed with an aq. soln of 10% $CuSO_4$ (2 × 10 ml) and with H_2O (3 × 10 ml). The organic layer was dried and evapd *in vacuo*. The residue was purified by TLC to give **5** (10 mg, 39%). CR TLC purple R_f 0.69 ($CHCl_3$–MeOH, 99:4). UV λ_{max}^{MeOH} nm: 204, 246 (*sh*), 320, 402; + HCl 203, 241, 316, 362; + NaOH 211, 250 (sh), 324, 442. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3360, 2940, 2800, 2720, 1770, 1730, 1690, 1670, 1630, 1605, 1470, 1430, 1370, 1260. ^{1}H and ^{13}C NMR see Tables 1 and 2.

Reduction of **5**–**7**. The reaction was performed as described as for the reduction of **1**. ^{1}H and ^{13}C NMR: see Tables 1 and 2.

Oxidation of **7**–**8**. Upon exposure to air, **7** was spontaneously oxidized to give **8**. ^{1}H NMR ($CDCl_3$): δ9.57 (*bs*, NH), 9.05 (*bs*, NH'), 7.04 (*s*, H-9'), 6.38 (*s*, H-12'), 5.58 (*d*, *J* = 3.1 Hz, H-15), 5.05 (*s*, H-9), 4.78 (*dd*, *J* = 7.9, 3.1, H-14), 4.71 (*d*, *J* = 7.9 Hz, H-3), 3.91 (*s*, OCH_3-12), 3.84 (*s*, CO_2CH_3), 3.80 (*s*, CO_2CH_3), 3.6 (*d*, *J* = 12.7 Hz, H-3'), 2.20 (*s*, $COCH_3$), 0.92 (*t*, *J* = 7 Hz, $CH_3$18), 0.86 (*t*, *J* = 7 Hz, CH_3-18').

Polyervine (**2**). Brown amorphous powder. CR TLC purple, R_f 0.62 ($CHCl_3$–MeOH, 14:1). UV λ_{max}^{MeOH} nm (log ε): 203 (4.61), 231 (*sh*, 4.30), 253 (*sh*, 4.12), 313 (4.16), 331 (4.20). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3360, 1670, 1605; FAB$^+$ HR *m/z* $[M]^+$ 795.3614 (calcd for $C_{44}H_{51}N_4O_{10}$, 795.3605). ^{1}H and ^{13}C NMR: see Tables 1 and 2.

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