Structures of Tabernaelegantines A—D and Tabernaelegantinines A and B, New Indole Alkaloids from *Tabernaemontana elegans*

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The structures of tabernaelegantines A—D [(1)—(4)] and tabernaelegantinines A and B [(5)—(6)], new 'dimeric' indole alkaloids isolated from the root bark of *Tabernaemontana elegans* Stapf. have been determined from their i.r., u.v., mass, and ^1H and ^{13}C n.m.r. spectra. The structural elucidation required the analysis of the carbon-13 spectra of voacangine, dregaminol, and tabernaemontanol. The ^{13}C n.m.r. investigation supports the revision of the reported configurations at C-20 of dregamine and tabernaemontanine.

EXTRACTION of the root bark of *Tabernaemontana elegans* Stapf., an Apocynaceous tree growing in Mozambique, with methanol affords a complex mixture of tertiary bases from which seven new indole alkaloids have been obtained. The isolation procedure has been described already,[1] and the present paper is concerned with the elucidation of structures (1)—(6) for six of the new bases, designated, respectively, tabernaelegantines A (1), B (2), C (3), and D (4) and tabernaelegantinines A (5) and B (6). These alkaloids are new members of the voacamine (7) group; that is, they are ' dimer ' alkaloids composed of coupled vobasine-like and ibogamine-like units. In particular, the structures of the tabernaelegantinines A (5) and B (6) are of considerable biogenetic significance as these two bases contain an extra C_3 unit in the aliphatic portion of the ibogamine unit.

The physical constants and the u.v. absorption maxima of the six alkaloids are reported in Table 1. The four tabernaelegantines have the molecular formula $C_{43}H_{54}N_4O_5$ (high resolution mass spectra) and show very similar spectral properties. Their u.v. spectra (in neutral 95% ethanol) exhibit small differences in intensities only. In particular, tabernaelegantines B (2) and D (4) show at 296 nm a maximum slightly more intense than the absorption at 287 nm, whereas the isomers A (1) and C (3) display an opposite behaviour in this region. However all the spectra are consistent with the presence of indole or alkoxyindole chromophores.

The i.r. spectra also are very similar, the most prominent bands being at 3 450—3 370 (NH) and 1 730 cm^{-1}

[1] B. Gabetta, E. M. Martinelli, and G. Mustich, *Fitoterapia*, 1975, **46**, 195.

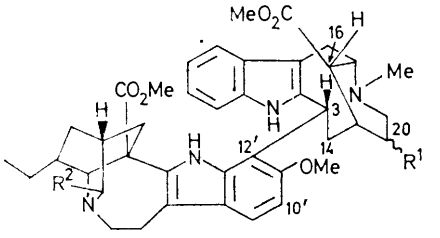
TABLE 1

Physical constants and u.v. spectra

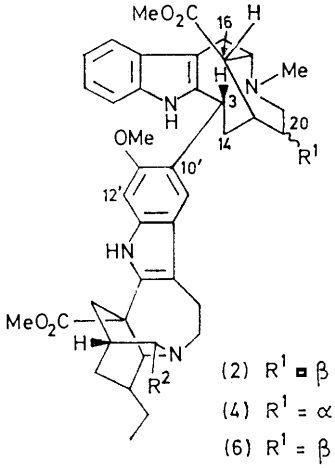
Alkaloid	M.p. (°C) (solvent)	$[\alpha]_D^{20}$ (°) (in $CHCl_3$)	R_F *	$\lambda_{max.}$ (95% EtOH)/nm (log ε)
Tabernaelegantine A (1)	231 (MeOH)	−31.8	0.63	224 (4.70), 285 (4.14), 293 (4.10)
Tabernaelegantine B (2)	199 (Me_2CO)	+14.4	0.48	227 (4.71), 287 (4.09), 296 (4.23)
Tabernaelegantine C (3)	171 (MeOH)	−36.8	0.35	224 (4.76), 285 (4.18), 293 (4.16)
Tabernaelegantine D (4)	206 (MeOH)	+11.3	0.16	226 (4.73), 287 (4.13), 296 (4.16)
Tabernaelegantinine A (5)	160 (n-C_6H_{14})	−53.7	0.60	224 (4.74), 285 (4.18), 293 (4.15)
Tabernaelegantinine B (6)	215 (MeOH)	+39.1	0.11	227 (4.75), 287 (4.14), 295 (4.18)

* On silica gel G (Merck F254); eluant n-hexane–acetone (1 : 1).

(CO). As the mass spectral fragmentation patterns are, from a qualitative point of view, identical (Table 2), all these data indicate that tabernaelegantines A—D are closely related. The mass spectra of (1)—(4) all contain peaks at *m/e* 675 ($C_{42}H_{49}N_3O_5$), 648 ($C_{41}H_{52}N_4O_3$), 524



(1) R^1 = β-Et, R^2 = H
(3) R^1 = α-Et, R^2 = H
(5) R^1 ▫ β-Et, R^2 = CH_2COMe



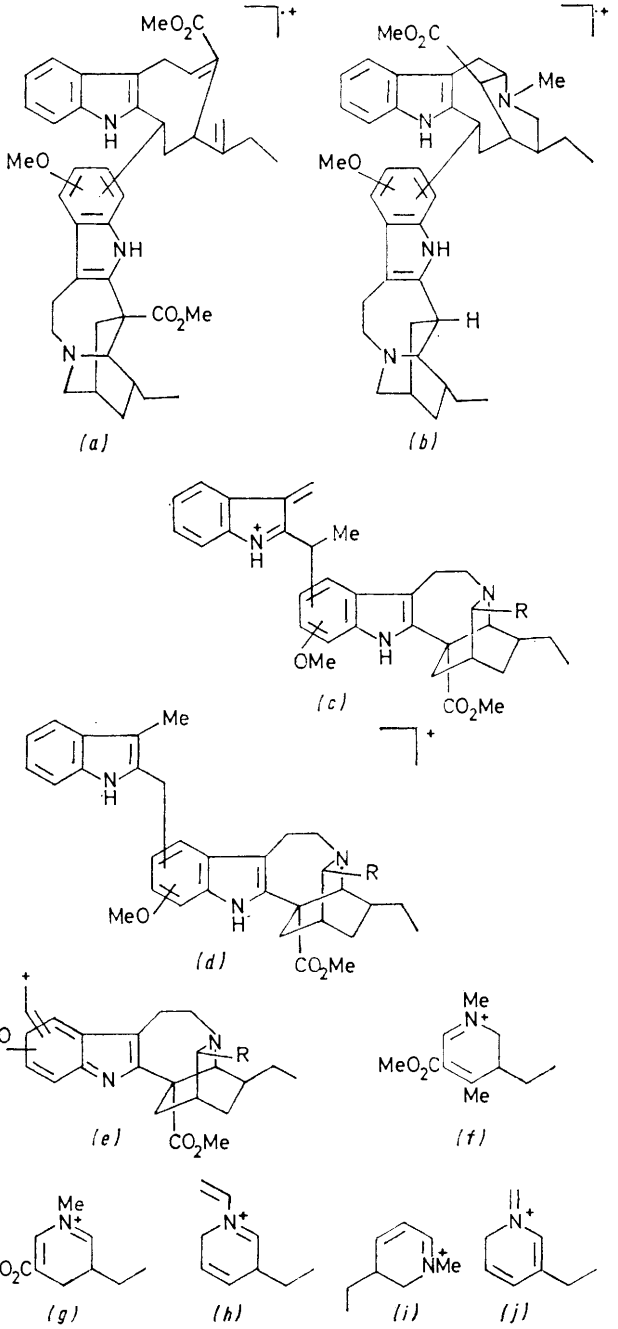
(2) R^1 ▫ β-Et, R^2 = H
(4) R^1 = α-Et, R^2 = H
(6) R^1 = β-Et, R^2 = CH_2COMe

TABLE 2

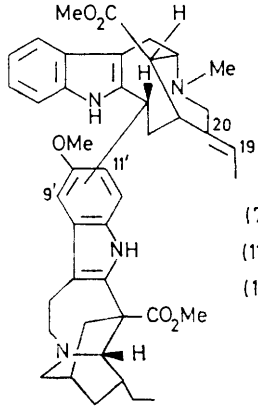
Mass spectral data*

m/e	Relative intensities (%) (1)	(2)	(3)	(4)
720 (M^+ + Me − H)		28		32
706 (M^+)	81	62	36	80
675 [ion (*a*)]	4	4	7	3
648 (*b*)	3	4	3	8
524 (*c*; R = H)	100	100	100	98
511 (*d*; R = H)	14	38	80	100
393 (*e*; R = H)	11	67	13	32
196 (*f*)	20	65	13	18
182 (*g*)	46	96	45	48
136 (*h*)	19	50	26	35
124 (*i*)	14	38	15	21
122 (*j*)	16	41	18	23

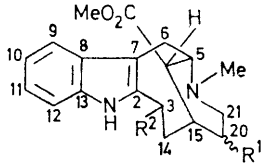
* Obtained at 70 eV; filament current 100 μA; vaporization temperature 130—140 °C.



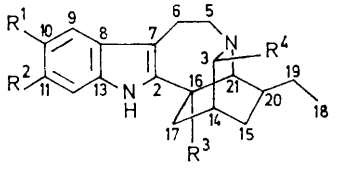
($C_{33}H_{38}N_3O_3$), 511 ($C_{32}H_{37}N_3O_3$), 393 ($C_{24}H_{29}N_2O_3$), 196 ($C_{11}H_{18}NO_2$), 182 ($C_{10}H_{16}NO_2$), 136 ($C_9H_{14}N$), 124 ($C_8H_{14}N$), and 122 ($C_8H_{12}N$). The peaks with lower *m/e* values are of particular diagnostic value, as fragments at *m/e* 196 [ion (*f*)], 182 (*g*), and 124 (*i*) and at *m/e* 136 (*h*) and 122 (*j*) occur [2,3] in the mass spectra of the 19,20-dihydrovobasinols (8) and (9) and voacangine (10), respectively, which suggests that the four tabernaelegantines are built up from 19,20-dihydrovobasine- and voacangine-like units. The most representative ' dimer ' alkaloid of this type is voacamine (7),[4] the mass spectrum of which also shows peaks at *m/e* 524 [ion (*c*)], 511 (*d*), and 122 (*j*), whereas its molecular ion and the ions (*a*), (*b*),



(7) linkage at C-11'
(11) linkage at C-11'; 19,20 dihydro
(12) linkage at C-9'



(8) R^1 = α-Et, R^2 = β-OH
(9) R^1 = β-Et, R^2 = β-OH
(14) R^1 = α-Et, R^2 = O
(15) R^1 = β-Et, R^2 = O
(16) R^1 = EtCH:, R^2 = β-OH



(10) R^1 = OMe, R^2 = H, R^3 = CO_2Me, R^4 = H
(13) R^1 = H, R^2 = OMe, R^3 = CO_2Me, R^4 = H
(17) R^1 = OMe, R^2 = H, R^3 = H, R^4 = H
(18) R^1 = H, R^2 = H, R^3 = CO_2Me, R^4 = H, 15,20-didehydro
(19) R^1 = OMe, R^2 = H, R^3 = CO_2Me, R^4 = H, [3-$^2H_2$]
(20) R^1 = H, R^2 = H, R^3 = CO_2Me, R^4 = CH_2COMe

(*f*), (*g*), and (*i*) contain two less hydrogen atoms than those from the tabernaelegantines, owing to the presence of the 19,20-double bond. Catalytic hydrogenation of voacamine [4] affords a dihydro-derivative (11), which exhibits the same mass spectral fragmentation pattern but differs in physical properties from the tabernaelegantines.

The proton n.m.r. spectra of (1)—(4) also are compatible with 19,20-dihydrovoacamine-like structures. They are characterized (Table 3) by four three-proton singlets near δ 3.9, 3.7, 2.6, and 2.5. These signals fall in the regions where, respectively, the OMe and CO_2Me functions and the NMe and CO_2Me groups of the voacangine and vobasine portions resonate,[4] the high-field shift of the CO_2Me signal of the vobasine unit arising from the diamagnetic anisotropy effect of the indole nucleus. Furthermore, signals for two low-field protons (NH) and six aromatic protons, and a one-proton signal near δ 5 [C(3)H] are present; the most relevant change in comparison with voacamine is the lack of the ethylidene signals and the appearance of an additional ethyl group in the high-field region. The aromatic patterns of (1) and (3) show the presence of two *ortho*-protons, whereas the spectra of (2) and (4) contain, like that of voacamine, a one-proton singlet at 6.78 p.p.m. Alkaloids of the voacamine group are known to isomerize in acidic media.[4] For instance, voacamidine (12) turns into voacamine (7) on refluxing in 2N-hydrochloric acid.[5] The isomerization is partially accompanied by the cleavage of the 3,9'-linkage, so that from this reaction the ibogamine component of the ' dimer ' can also be obtained.[6] After refluxing in methanol and concentrated hydrochloric acid, tabernaelegantines B (2) and D (4) were unchanged, but the same acidic treatment converted tabernaelegantines A (1) and C (3) into (2) and (4), respectively. In both cases minor amounts of isovoacangine (13) were isolated.

If now we consider the aromatic patterns of the proton spectra, the evidence so far discussed indicates that the four alkaloids contain an isovoacangine and a 19,20-dihydrovobasine unit, connected through a linkage involving C-3 and C-12' [(1) and (3)] or C-10' [(2) and (4)], respectively. If we assign β-orientations to the C-3 protons of the four isomers on the basis of the arguments advanced by Buchi,[4] there remains the possibility of isomerism only at C-20; that is tabernaelegantines A—D must contain either a dregamine (14) or a tabernaemontanine (15) unit.

The configuration at C-20 for the latter two bases was first investigated by Renner and his co-workers,[2] who suggested the β-axial and α-equatorial orientations for the respective ethyl side chains. A recent *X*-ray crystallographic study has led to the revision of these arguments; [7] thus dregamine and tabernaemontanine must be assigned the absolute configurations shown in formulae (14) and (15).

Dregamine and tabernaemontanine can be spectroscopically differentiated by the high-field regions of their 100 MHz ^1H n.m.r. spectra. The spectrum of dregamine in $CDCl_3$ contains two well separated signals at δ 1.88 and

[2] U. Renner, D. A. Prins, A. I. Burlingame, and K. Biemann, *Helv. Chim. Acta*, 1963, **46**, 2186.
[3] H. Budzikiewicz, C. Djerassi, and D. H. Williams, ' Structure Elucidation of Natural Products by Mass Spectrometry,' Holden-Day, San Francisco, 1964, vol. I, p. 67.
[4] G. Buchi, R. E. Manning, and S. A. Monti, *J. Amer. Chem. Soc.*, 1964, **86**, 4631.
[5] U. Renner and H. Fritz, *Tetrahedron Letters*, 1964, 283.
[6] W. Winkler, *Arch. Pharm.*, 1962, **295**, 895.
[7] A. Husson, Y. Langlois, C. Riche, H. P. Husson, and P. Potier, *Tetrahedron*, 1973, **29**, 3095.

TABLE 3

^{1}H N.m.r. spectra (δ values) *

	(1)	(2)	(3)	(4)	(5)	(6)
NH	7.68	7.68	7.64	7.74	7.63	7.74
	7.62	7.56	7.58	7.59	7.55	7.59
ArH	7.24 [a]	7.14—6.90 [b]	7.26 [a]	7.14—6.84 [b]	7.23 [a]	7.6—6.84 [b]
	7.2—6.9 [c]	6.78 [d]	7.2—6.9 [c]	6.78 [d]	7.15—6.9 [c]	6.79 [d]
	6.83 [a]		6.84 [a]		6.82 [a]	
C(3)H	5.29(m)	5.06(m)	5.27 [e]	5.04(m)	5.27(m)	5.04(m)
ArOMe	3.96	3.91br [f]	3.96	3.92br [g]	3.97	3.93br [h]
CO_2Me	3.70	3.67	3.70	3.67	3.71	3.66
NMe	2.57	2.57	2.64	2.63	2.58	2.63
CO_2Me	2.48	2.43	2.52	2.44	2.52	2.44
CH_2Me	0.94 [i]	0.94 [i]	0.92 [i]	0.92 [i]	0.94 [i]	0.93 [i]
CH_2Me	0.80 [i]	0.86 [i]	0.81 [i]	0.86 [i]	0.80 [i]	0.86 [i]
COMe					2.00	2.09

* 100 MHz; solvent $CDCl_3$; Me_4Si standard.

[a] 1 H, d, J 9 Hz. [b] 5 H, m. [c] 4 H, m. [d] 1 H, s. [e] dd, J 13 and 4 Hz. [f] $W_{\frac{1}{2}}$ 5 Hz. [g] $W_{\frac{1}{2}}$ 9 Hz. [h] $W_{\frac{1}{2}}$ 8 Hz. [i] t, J 7 Hz.

TABLE 4

^{13}C N.m.r. data (δ values) *

Carbon	(8)	(9)	(10)	(1)	(2)	(3)	(4)	(5)	(6)
2	137.1	137.1		136.3	135.6	136.2	135.9	136.0	135.2
3	66.9	67.1		34.7	35.1	34.7	36.6	34.9	37.0
5	59.0	59.2		59.4	59.7	59.2	59.5	59.2	59.3
6	19.3	17.7		17.9	17.6	19.5	19.9	17.8	19.3
7	107.8	107.9		109.1	110.3	109.0	110.0	108.7	110.6
8	129.4	129.4		129.7	130.4	129.6	129.5	129.4	129.9
9	118.0	118.0		118.2	118.3	118.1	117.9	117.8	117.2
10	119.1	119.1		119.4	118.6	119.4	119.5	119.1	118.5
11	121.9	121.9		122.1	121.5	122.1	122.1	121.9	121.1
12	110.6	110.6		110.0	110.0	110.0	110.4	109.9	109.7
13	135.8	135.8		137.0	136.2	136.9	136.2	136.6	135.9
14	30.6	38.2		36.9	37.1	29.2	31.5	36.8	30.9
15	28.9	30.3		35.2	35.1	33.1	31.9	35.2	31.8
16	50.3	44.2		44.0	44.1	49.9	49.8	43.8	49.7
18	11.6	12.8		12.9	13.0	11.4	10.7	12.8	11.4
19	23.6	25.6		25.7	25.8	23.5	22.9	25.6	23.5
20	43.8	42.9		43.1	43.2	43.9	41.6	43.0	43.8
21	49.3	47.13		47.0	47.2	49.5	48.4	46.7	49.7
CO_2Me	175.4	176.0		172.6	172.7	172.0	169.5	172.2	171.5
CO_2Me	50.3	50.4		50.0	50.0	49.9	50.3	49.8	49.7
NMe	42.4	42.9		43.1	43.2	42.5	41.0	43.0	42.3
2′			137.8	136.3	135.1	136.2	135.5	136.0	134.8
3′			51.7	51.3	51.6	51.3	51.5	54.6	55.1
5′			53.3	53.0	53.2	53.0	53.4	51.3	51.4
6′			22.2	22.1	22.2	22.1	22.0	22.0	22.0
7′			110.2	110.5	111.1	110.3	110.1	110.1	109.7
8′			129.3	124.6	122.9	124.5	122.7	124.4	122.4
9′			100.9	117.1	117.6	117.1	117.3	116.9	118.0
10′			154.1	105.1	127.9	105.1	126.9	104.9	127.6
11′			111.3	152.1	153.8	152.1	153.4	151.8	153.3
12′			111.9	114.9	93.0	115.1	93.2	114.7	92.7
13′			130.9	135.4	138.2	135.3	139.0	135.2	137.9
14′			27.4	27.2	27.5	27.1	27.3	30.6	32.9
15′			32.1	32.0	32.2	31.9	31.8	26.6	27.0
16′			55.2	54.7	55.2	54.6	54.9	54.2	54.7
17′			36.5	35.0	36.5	35.1	36.1	35.8	37.5
18′			11.7	11.6	11.7	11.6	11.7	11.6	11.7
19′			26.8	26.6	26.8	26.6	26.8	26.6	26.7
20′			39.1	38.9	39.3	38.9	39.1	38.2	38.4
21′			57.5	57.6	57.7	57.6	57.6	58.6	58.3
CO_2Me'			52.6	52.3	52.5	52.3	52.7	52.2	52.4
CO_2Me'			175.9	174.9	176.2	175.0	175.8	174.4	175.5
ArO*Me*			56.0	57.0	56.0	56.8	56.1	56.7	55.8
CH_2·COMe								46.7	46.7
CH_2·COMe								208.2	208.3
CH_2·CO*Me*								30.6	30.9

* Solvent $CDCl_3$; Fourier transform instrument operating at 25.2 MHz; standard internal Me_4Si.

1.32 for the C-19 and C-20 protons, which, in the spectrum of tabernaemontanine, form into a complex multiplet centred at δ 1.50. However, these data cannot be used for determining the configurations at C-20 of compounds (1)—(4) owing to the complexity of these regions in the spectra of the ' dimers '. Hence, as carbon-13 spectroscopy is much more sensitive to changes in steric relationship between groups, an examination of the carbon spectra of dregaminol (8) and tabernaemontanol (9) was undertaken. The results of this investigation are summarized in Table 4.

The aromatic carbon shifts of (8) and (9) are consistent with the presence of indole units and can be assigned on the basis of chemical shift theory.[8] The non-aromatic regions are characterized by the presence of five doublets, four triplets, three quartets, and one singlet. The shifts of the *O*- and *C*-methyl groups and the carbonyl function are derived from chemical shift theory. As regards the methyne resonances, the assignments of C-3, -5, -15, and -20 [the last occurs in the aromatic region in the spectrum of vobasinol (16)] are based on simple electronegativity considerations. The remaining methyne carbon, C-16, resonates at δ 44.2 in (9) and at 50.3 in (8). Molecular models of both (8) and (9) show that, if the ethyl group at C-20 has a β-axial orientation, C-16 experiences a strong steric interaction with C-19. Therefore, the high-field resonance of C-16 in (9) indicates that the ethyl side chain is β-oriented.

The triplet resonances are due to C-21, -14, -19, and -6. The two spectra show signals in the regions δ 48 (C-21), 24 [C-19, shifted downfield in the spectrum of (16)], and 18 (C-6), whereas the C-14 signal falls at δ 30.6 and 38.2 in (8) and (9), respectively. The resonances associated with C-14 are correctly assigned, as they are the sole signals which show significant shifts in the spectra of the parent compounds, dregamine (14) and tabernaemontanine (15) (39.4 and 45.8, respectively). The marked difference in C-14 chemical shifts also arises from the stereochemistry at C-20: if the ethyl side chain is α-equatorially oriented, C-19 interacts sterically with the C(14)–α-H linkage and, as a consequence, the C-14 signal moves to higher field. Hence, carbon-13 spectroscopy also points to the revision of the original stereochemical assignments and, on the basis of the observed differences in chemical shift of C-14 and -16, this technique should provide valuable information about the stereochemistry at C-20 of the tabernaelegantines. However, unambiguous carbon signal assignment of the spectra of these bases required examination of the spectrum of isovoacangine (13) as well. Owing to the extremely small amount of (13) at our disposal, the investigation was carried out on its isomer, voacangine (10), which possesses the same aliphatic skeleton. Inspection of the carbon spectrum of ibogaine (17) also appeared useful, as the removal of the methoxycarbonyl function from the voacangine skeleton predictably affects only the C-20 and -17 signals, which are expected [9] to move to lower and higher field, respectively. Additional evidence for the correctness of the carbon shift assignments of the quinuclidine system was also provided by inspection of the spectrum of catharanthine (18).

The aromatic carbon shifts of voacangine are consistent with the presence of a 10-methoxyindole unit (Table 4). The non-aromatic region contains signals for thirteen carbon atoms (three quarters, six triplets, three doublets, and one singlet). Apart from the C-16 and methyl signals, which are easily attributable on the basis of their multiplicity and of chemical shift theory, the doublet resonances are for C-21, -20, and -14 and are readily assigned since they have markedly different chemical shifts: C-21 (δ 57.5) is linked to N_b whereas the C-20 signal (39.1) is shifted downfield relative to C-14 (27.4) owing to the β-effect of C-21. In the spectrum of ibogaine (17), C-14 (δ 26.6) and C-21 (57.6) show no significant change, whereas C-20 suffers the expected downfield shift (2 p.p.m.). Furthermore, the high-field region of the catharantine (18) spectrum contains doublets for only two carbon atoms, C-21 (δ 61.9) and C-14 (30.9).

The six triplet resonances of the voacangine spectrum are for C-3, -5, -6, -15, -17, and -19. C-3 and -5 are linked to the N_b and their signals are shifted downfield (δ 53.3 and 51.7) relative to those of the other methylene carbon atoms. In the ibogaine (17) spectrum, these two signals fall at 54.3 and 50.1, but it is possible to allocate these resonances by an investigation of the spectrum of [3-$^2H_2$]ibogaine (19),[10] which indicates that the low-field signal must be attributed to C-5.

The C-17 resonance at δ 36.5 in the spectrum of voacangine is distinguished from the other methylene signals by its high-field shift (34.1) in the spectrum of ibogaine, whereas, of C-15 and -19, the signal of the former is expected to be the farthest downfield as it is subject to many β-effects. Furthermore, in the catharanthine spectrum the C-15 signal moves to δ 123.5, whereas C-19 still resonates in the δ 26 region.

With the chemical shifts of the models (8), (9), and (10) established, the ^{13}C n.m.r. analysis of the ' dimers ' is simple. The aromatic signals corresponding to the dregamine or tabernaemontanine units remain almost unaffected, and the substitution at C-10′ or -12′ can be easily deduced. In fact, in the case of a C-10′ linkage a high-field doublet is present at δ *ca.* 93, characteristic [11] of C-12′ of an 11′-methoxy-substituted unit, whereas C-10′ resonates as a singlet at δ *ca.* 127. If the substitution is at C-12′, C-10′ and -12′ resonate at *ca.* 105 and 115, respectively.

Of the saturated carbon signals, only the resonances of C-3, -14, and -15 are perturbed by the replacement of the C-3 hydroxy-group of (8) and (9) (upfield shifts for C-3

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and -14, downfield shift for C-15).[12] The remaining signals can be easily assigned by a simple subtractive process.

The stereochemistry at C-20 of (1)—(4) can be deduced, from the above considerations. Tabernaelegantines A (1) and B (2) show C-16 resonances at δ 44.0 and 44.1, and those of C-14 at 36.8 and 37.1, whereas in tabernaelegantines C (3) and D (4) these carbons resonate at 49.9 and 49.8, and at 29.2 and 31.5, respectively. These shifts support β- and α-orientations for the ethyl side chains, respectively, as shown in structures (1)—(4).

In addition to the aromatic patterns of the proton and carbon spectra, the differences in substitution at C-10′ or -12′ are reflected in (i) the C-3 proton resonance (*ca.* 0.23 p.p.m. upfield shift if the substitution is at C-10′); (ii) the shape of the 290 nm region of the u.v. spectra (Table 1); (iii) the shape of the 11′-methoxy-signal in the proton spectra [dramatic broadening (Table 3) if the substitution is at C-10′]; (iv) the possibility of interconversion between the two pairs (1) and (2), and (3) and (4), as only a 3,12′-bond can be converted into a 3,10′-bond; (v) a mass spectral peak 14 mass units greater than the molecular weight if the substitution is at C-10′ (Table 2).

The mass spectrum of voacamine also shows an $M + 14$ peak arising from intermolecular methyl transfer involving the voacangine methoxycarbonyl group as methyl donor and N_b of the vobasinol component as acceptor.[13] The quaternary ammonium salt thus formed can undergo Hofmann degradation, the proton abstractor being the carboxylate anion.

Molecular models of the tabernaelegantines indicate that rotation about the 3,12′-bond of (1) and (3) is sterically more inhibited than that around the 3,10′-bond of (2) and (4); this accounts for the possibility of conversion in acidic media of the former alkaloids into the more stable ones [(2) and (4)]. Furthermore, the isovoacangine methoxycarbonyl groups of (1) and (3) appear to be crowded by the dihydrovobasinol units, and consequently unavailable for ion–molecule collisions in the mass spectrometer. No transmethylation processes are in fact observed in the case of (1) and (3), even at higher vaporization temperatures, whereas the intensities of the $M + 14$ peaks exhibited by (2) and (4) appear to be dependent on vaporization temperature (the spectra reported in Table 2 were recorded at 130—140 °C).

In addition, the molecular models show that in the most stable conformations of (2) and (4) the aromatic methoxy-groups of the isovoacangine units are linked to the indole NH group of the dihydrovobasine component by strong hydrogen bonding, which causes broadening of the OMe signals in the proton spectra. On the other hand, the restricted rotation about the 3,12′-bonds of (1) and (3) inhibits the formation of such intramolecular hydrogen bonds, so that the shapes of the methoxy-signals are in this case unaffected.

Tabernaelegantinines A (5) and B (6) have the molecular formula $C_{46}H_{58}N_4O_6$. They are two further members of the voacamine family, as suggested by their proton and carbon n.m.r. spectral properties (Tables 3 and 4). In particular the aromatic regions of the carbon spectra are almost identical with those of (1) and (2), respectively. In addition, the mass spectrum of tabernaegantinine B (6) contains, like (2) and (4), the ion at *m/e* 776 ($M + 14$, 23%) indicating the presence of a 3,12′-bond.

In comparison to the tabernaelegantines, the tabernaelegantinines (5) and (6) contain three additional carbon atoms, involved in a $CH_2{\cdot}CO{\cdot}CH_3$ grouping (3H as a singlet in the δ 2 region of the proton spectra; CO at 208, CH_2 at 46, and CH_3 at δ 30 in the carbon spectra). This grouping must be placed in the isovoacangine unit as, in addition to the peaks at *m/e* 762 (M^+, 87 and 48%, respectively), 731 (M — Me, 6 and 5%), 719 (M — COMe, 3 and 12%), 705 (M — $CH_2{\cdot}$COMe, 26 and 15%), 673 (M — CH_2COMe — OMe — H, 12 and 3%), 196 [ion (*f*), 26 and 39%], 182 [ion (*g*), 89 and 95%], 136 [ion (*h*), 9 and 21%], 124 [ion (*i*), 9 and 19%], and 122 [ion (*j*), 14 and 25%], the mass spectra of (5) and (6) contain the ions (*c*) (R = CH_2COMe, *m/e* 580, 100, and 86%), (*d*) (R = $CH_2{\cdot}$COMe, *m/e* 567, 13, and 100%), and (*e*) (R = $CH_2{\cdot}$COMe, *m/e* 449, 7 and 20%) shifted by +56 m.u. in comparison with the corresponding ions of the tabernaelegantines. Ions at *m/e* 522 [(*c*) — Me_2CO, 56 and 70%] and 509 [(*d*) — Me_2CO, 6 and 29%)] are also present.

The aliphatic regions of the carbon spectra show that (5) and (6) possess opposite configurations at C-20. In fact, C-16 and -14 resonate at δ 43.0 and 36.8 in (5), and at 49.7 and 30.9 in (6), in agreement with an axial and an equatorial orientation, respectively, of the C-20 ethyl side chains. In addition, a comparison of the carbon shifts of the isovoacangine units of (1)—(4) and (5) and (6) shows that in the tabernaelegantinines one of the aminomethylene carbon signals is a doublet thus indicating that the $CH_2{\cdot}CO{\cdot}CH_3$ grouping is at either C-3′ or -5′. The substitution does not notably affect the resonances of C-6′, -17′, and -20′, whereas those of C-14′ and -15′ suffer, respectively, downfield and upfield shifts. These chemical shift changes can be explained if the $CH_2{\cdot}CO{\cdot}CH_3$ grouping is at position 3′, as in this case C-14′ experiences a β-effect and C-15′ interacts sterically with the substituent and consequently resonates at higher field. The configurations at C-3′ of these alkaloids are therefore those represented in the stereostructures (5) and (6).

A compound having an ibogamine-like skeleton carrying an extra C_3 unit has been recently isolated,[14] and the location of this unit at position 3 has been proposed on the basis of the chemical reactivity of this centre. The nature of the tabernaelegantinines suggests that the assignment of structure (20) to this alkaloid is probably correct. As acetone has been used for their separation,

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the possibility that these alkaloids are artefacts cannot be excluded.[15] However, if they are genuine products, we consider that nucleophilic attack of an acetoacetyl-CoA unit at C-3 of a 3,4-dehydroibogamine component, followed by decarboxylation, is the most probable mechanism of formation of this kind of compound.

EXPERIMENTAL

^{1}H N.m.r. spectra were determined with a Varian XL-100 spectrometer. High resolution mass measurements were obtained with a Varian MAT 311 instrument. ^{13}C N.m.r. spectra were recorded at 25.2 MHz with a Varian XL-100 instrument equipped with Fourier transform facility.

Conversion of Tabernaelegantine A (1) *into Tabernaelegantine B* (2).—Tabernaelegantine A (200 mg) dissolved in methanol (10 ml) and concentrated hydrochloric acid (1 ml) was heated under reflux for 24 h. Sodium carbonate solution and methylene chloride were added and the organic phase was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel to afford pure isovoacangine (13) (15 mg), starting material (75 mg), and (2) (90 mg).

Conversion of Tabernaelegantine C (3) *into Tabernaelegantine D* (4).—A solution of tabernaelegantine C (50 mg) in methanol (8 ml) and concentrated hydrochloric acid (1 ml) was heated under reflux for 16 h. The mixture was diluted with sodium carbonate solution and extracted with methylene chloride, and the extract was evaporated. Preparative t.l.c. [silica gel; EtOAc–MeOH–H_2O (100 : 5 : 2)] yielded compounds (3) (13 mg), (13) (8 mg), and (4) (26 mg).

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