Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally Occurring Substances. 43. Carbon-13 Nuclear Magnetic Resonance Analysis of Bis-Indoline Alkaloids of Two *Voacanga* Species[1-3]

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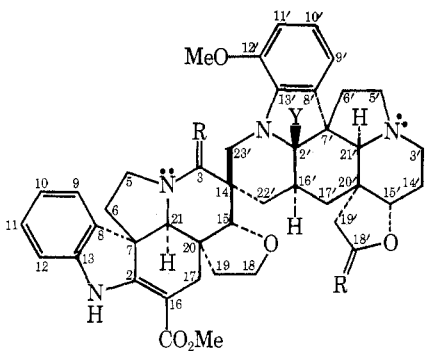
Received March 8, 1976

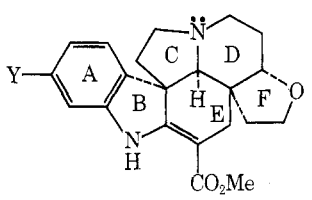
The ^{13}C NMR spectra of the bis-indoline alkaloids vobtusine, vobtusine lactone, and 2′-deoxyvobtusine lactone were recorded and their carbon shifts assigned. With the collected data and those of models the structures of the following natural bases were determined: vobtusine 3-lactam, vobtusine 3-lactam N_b′-oxide, voafolidine, voafoline, isovoafoline, folicangine, subsessiline, and subsessiline lactone.

Several indole alkaloids of high molecular weight were isolated recently from two *Voacanga* species[4,5] one of which proved to be vobtusine, a $C_{43}H_{50}O_6N_4$ alkaloid isolated earlier from *Callichilia subsessilis*[6] and *Hedranthera barteri*[7] and shown by x-ray analysis of its dibromo derivative[8] to possess structure **1a**, a molecular framework composed of a spiro-

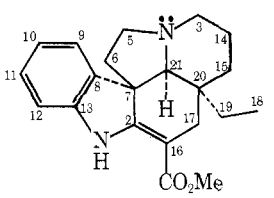


1a, R = R′ = H_2; Y = OH
b, R = H_2; R′ = O; Y = OH
c, R = H_2; R′ = O; Y = H
d, R = R′ = H_2; Y = OH; 2β,16β-dihydro
e, R = H_2; R′ = O; Y = OH; 2β,16β-dihydro
f, R = O; R′ = H_2; Y = OH
g, R = O; R′ = H_2; Y = OH; N_b′-oxide

fused combination of 11-demethoxyvandrikine-like (**2a**) skeleta and a C_1 unit. In order to facilitate the structure analysis of the congeners of vobtusine, all of which were suspected to be based on the same structure pattern, the study was initiated by the ^{13}C NMR analysis of the alkaloids of known constitution vobtusine (**1a**), vobtusine lactone (**1b**),[4] and 2′-deoxyvobtusine lactone (**1c**).[4] In this connection an earlier study of the Aspidosperma bases vandrikine (**2b**), tabersonine (**3a**), and related substances[9] proved very helpful.



2a, Y = H
b, Y = OMe



3a, $\Delta^{14,15}$
b, 14β,15β-oxide

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Since the three indole alkaloid "dimers" are 14,14-disubstituted 11-demethoxyvandrikines (**2a**), comparison of their ^{13}C NMR spectra with those of vandrikine (**2b**)[9] and tabersonine (**3a**)[9] allows direct signal matching for all carbons of ring A, B, C, and E. Whereas C(17) can be confused with C(14′) in vobtusine (**1a**), the ambiguity is relieved on comparison of the shifts of like carbons in the lactones. The identification of vobtusine's C(18) and C(19) shifts and their distinction from the similar C(18′) and C(19′) shifts rest on the δ values of like carbons in the monomer vandrikine (**2b**) and the modification of the latter pair on introduction of the lactone carbonyl group.

With the use of the aromatic carbon shifts of N_a-methyl-2β,16β-dihydrotabersonine[10] and methoxy substitution parameters[11] the methoxylated ring A′ carbon shifts can be assigned. Carbons 2′ and 16′ and the carbons of rings C′ and D′ can be recognized by the field position and multiplicity of their signals and relationship with like carbons of model **2b**. The C(3′) shift of vobtusine (**1a**) differs from that of other aminomethylenes by its perturbation in vobtusine lactone (**1b**) in which, for example, the C(23′) shift, close in magnitude to the δ value of C(3′), is unaffected. The ca. 2 ppm lower field position of C(3′) than that in model **2b** can be ascribed to a diminished γ effect from the ring F′ oxygen of vobtusine (**1a**) in part as a consequence of the conformational transmission induced by the removal of trigonality at the C(2′) and C(16′) sites. As a spectral comparison of vobtusine (**1a**) and its lactone (**1b**) as well as 2β,16β-dihydrovobtusine (**1d**) and its lactone (**1e**) indicates, conversion of ring F′ from a tetrahydrofuran to a γ-lactone unit introduces small, constant shift modifications which with the exception of C(17′) are confined to ring D′ carbons. The shift alteration of C(5) in the dihydro derivatives **1d** and **1e** provides a means of distinguishing this center from C(5′) in the natural product. Carbon 6′ is difficult to differentiate from C(22′). Whereas these two centers and C(17′) and C(23′) have hydrogens 1,3-diaxially disposed toward the 2′-hydroxy group, the expected γ effect is distributed unsymmetrically to the four sites. The shifts of the remaining carbons, those of ring D perturbed by C(14) disubstitution from like centers in vandrikine (**2b**), are constant among the three alkaloid "dimers". All δ values of these compounds are listed in Table I.[12]

A vobtusine (**1a**) congener in *Voacanga thouarsii* Roehm and Schult was shown to be a $C_{43}H_{48}O_7N_4$ substance possessing the infrared absorption characteristics of the vinylogous amide function of **1a–c** and a six-membered lactam.[1,5] These facts suggest that the new base could be vobtusine with C(3) or C(3′) in the form of a carbonyl group, a proposal easily tested by the compounds' ^{13}C NMR spectra. Were C(3) in-

Table I. Carbon Shifts of Compounds 1a–e[a]

	3a[b]	1a	1b	1c	1d	1e		2b[b,c]	1a	1b	1c	1d	1e
C(2)	166.7	166.6	166.6	166.7	67.5	67.6	C(2′)		93.7	93.3	75.6	93.7	93.4
C(3)		53.7	53.8	53.8	53.0	53.1	C(3′)	45.7	48.7	48.0	47.8	48.6	48.2
C(5)		50.9	50.9	51.2	55.0	55.1	C(5′)	51.2	51.9	51.8	52.7	51.9	51.8
C(6)		44.9	44.9	45.0	42.1	42.1	C(6′)	45.1	31.1	30.8	37.7	31.2	31.0
C(7)		54.8	54.8	55.0	52.2	52.2	C(7′)	54.2	55.9	55.8	51.0	55.8	55.9
C(8)	137.8	137.6	137.5	137.5	135.4	135.5	C(8′)		134.2	133.0	135.6	134.3	133.1
C(9)	121.4	121.2	121.2	121.4	118.3	118.5	C(9′)		114.5	114.6	114.8	114.5	114.4
C(10)	120.5	120.4	120.4	120.5	122.8	122.9	C(10′)		118.1	118.8	118.3	118.3	119.2
C(11)	127.6	127.4	127.5	127.6	127.7	127.9	C(11′)		110.8	111.1	110.9	110.1	110.7
C(12)	109.2	109.1	109.1	109.2	108.5	108.6	C(12′)		144.9	144.9	145.1	145.2	145.2
C(13)	143.1	142.8	142.8	142.9	150.1	150.2	C(13′)		137.2	136.9	137.9	136.9	136.7
C(14)		39.6	39.5	40.0	39.5	39.6	C(14′)	26.6	25.7	24.7	25.3	25.7	24.8
C(15)		87.4	87.3	87.5	90.0	90.0	C(15′)	79.8	80.3	81.4	82.0	80.3	81.5
C(16)	92.2	94.3	94.2	94.1	38.3	38.4	C(16′)		31.5	31.1	29.4	30.9	30.7
C(17)		27.3	27.3	27.5	26.5	26.6	C(17′)	27.4	32.4	31.7	33.7	32.4	31.8
C(18)		64.2	64.2	64.3	64.6	64.8	C(18′)	64.7	65.1	175.3	175.5	65.1	175.3
C(19)		34.8	34.8	34.8	40.4	40.5	C(19′)	34.6	36.6	41.4	41.5	36.5	41.6
C(20)		47.6	47.6	47.8	40.4	40.5	C(20′)	46.4	44.1	43.4	44.0	44.1	43.4
C(21)		68.9	68.8	68.8	69.8	69.9	C(21′)	68.7	63.6	63.9	65.3	63.5	64.0
C=O	168.8	168.3	168.3	168.4	175.8	175.8	C(22′)		34.1	33.5	39.0	34.1	34.0
OMe	50.8	50.9	50.9	51.0	51.6	51.8	C(23′)		46.1	46.0	52.7	45.4	45.4
							OMe		55.0	55.0	54.9	54.6	54.7

[a] In parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. [b] From ref 9. [c] The previously undifferentiated C(14) and C(17) shifts are resolved by the present study.

Table II. Carbon Shifts of Vobtusine 3-Lactam and Its N_b'-Oxide[a]

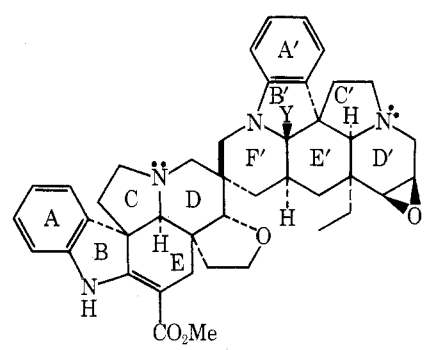
	1f	1g		1f	1g
C(2)	162.6	162.7	C(2′)	93.3	91.3
C(3)	171.2	171.5	C(3′)	48.7	58.9
C(5)	39.1	39.1	C(5′)	51.8	66.9
C(6)	44.9	45.2	C(6′)	31.9	44.9
C(7)	57.4	57.4	C(7′)	55.8	54.9
C(8)	137.5	138.1	C(8′)	133.0	132.3
C(9)	121.2	121.2	C(9′)	113.9	112.7
C(10)	120.8	120.8	C(10′)	118.4	117.9
C(11)	128.4	128.5	C(11′)	112.2	112.7
C(12)	109.5	109.6	C(12′)	146.8	146.8
C(13)	142.8	142.8	C(13′)	135.1	135.2
C(14)	49.0	48.9	C(14′)	25.6	22.6
C(15)	87.2	87.2	C(15′)	80.3	78.5
C(16)	92.4	92.6	C(16′)	31.9	31.0
C(17)	27.1	27.4	C(17′)	32.5	33.4[b]
C(18)	67.6	67.5	C(18′)	65.2	64.8
C(19)	36.2	36.3	C(19′)	36.2	33.9[b]
C(20)	47.8	48.0	C(20′)	43.9	39.2
C(21)	67.1	66.9	C(21′)	63.5	72.2
C=O	167.9	168.0	C(22′)	29.4	29.3
OMe	51.0	51.0	C(23′)	44.1	44.1
			OMe	56.1	56.2

[a] In parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. [b] Signals may be interchanged.

volved in the structural change, an aminomethylene signal can be expected to be replaced by a keto signal and serious shift changes introduced at the spiro carbon and its close neighbors. Inspection of the spectra shows this expectation to be fulfilled and thus the alkaloid to be vobtusine 3-lactam (**1f**). The dramatic shielding of C(5) is in consonance with observations on lactam models.[14] All shifts of **1f** are listed in Table II.

A second vobtusine (**1a**) congener in *V. thouarsii*, a $C_{43}H_{48}O_8N_4$ substance, has been reported to possess closely related infrared absorption bands to those of vobtusine 3-lactam (**1f**).[1,5] The extra oxygen thus most likely is part of an ether linkage or amine oxide moiety. The ^{13}C NMR spectrum of the alkaloid reveals the carbons of the 11-demethoxyvandrikine (**2a**) 3-lactam portion of **1f** and C(22′) and C(23′) to be unchanged and all other nonaromatic carbon shifts to be modified. The 9–15-ppm deshielding of the amino carbons of rings C′ and D′ is in agreement with the shift behavior on conversion of a tertiary amine into an amine oxide.[15,16] Thus the natural base is vobtusine 3-lactam N_b'-oxide (**1g**). Its shifts are cited in Table II. The drastic shift differences between vobtusine 3-lactam (**1f**) and its N_b'-oxide (**1g**) points up the usefulness of monoamine oxide formation as a means of differentiation of individual monomer units of a "dimeric" alkaloid.

Voafolidine (**4a**) and its 2′-deoxy derivative voafoline (**4b**), leaf alkaloids of *Voacanga africana* Stapf., have been shown



4a, Y = OH
b, Y = H

to be related to vobtusine (**1a**), the 15′-oxy substituent being bridged to C(14′) instead of C(18′).[2,4] As a consequence pachysiphine (**3b**)[17] serves as a good ^{13}C NMR spectral model for most of the ring D′ carbons of the alkaloids. The δ values for the monomer base **3b**, shown in Table III, were derived from the aromatic shifts of tabersonine (**3a**)[9] and the nonaromatic shifts of hazuntinine (10,11-dimethoxy-**3b**).[9] The vandrikine-like portion of voafolidine (**4a**) is ^{13}C NMR spectrally identical with the same part of the molecular framework of vobtusine (**1a**). The same relationship exists between voafoline (**4b**) and vobtusine (**1a**). The aromatic carbon shifts of

Table III. Carbon Shifts of Pachysiphine, Voafolidine, and Voafoline[a]

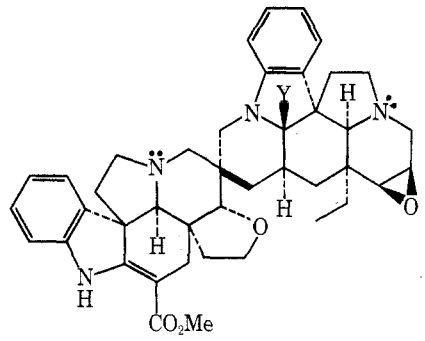
	2b[b]	4a	4b		3b[c]	4a	4b
C(2)	167.4	166.6	166.1	C(2′)	164.9	93.9[d]	76.0
C(3)	45.7	53.7	53.4	C(3′)	49.4	53.4[e]	53.0
C(5)	51.2	50.6	50.3	C(5′)	51.0	52.6[e]	53.0
C(6)	45.1	44.1	44.6	C(6′)	43.9	31.8	39.0
C(7)	54.2	54.6	54.4	C(7′)	54.7	55.4	51.5
C(8)		137.5	137.1	C(8′)	137.5	133.8	135.6
C(9)		121.2	121.5	C(9′)	121.3	121.8	120.8
C(10)		120.5	120.2	C(10′)	120.3	117.4	116.2
C(11)		127.6	127.3	C(11′)	127.6	127.3	127.0
C(12)		109.2	108.9	C(12′)	109.2	107.3	106.3
C(13)		142.9	142.5	C(13′)	142.9	148.8	149.8
C(14)	26.6	40.4	40.3	C(14′)	52.0	53.0	52.5
C(15)	79.8	87.3	87.0	C(15′)	56.2	56.7	56.5
C(16)	93.9	94.1[d]	93.7	C(16′)	90.4	28.5	25.6
C(17)	27.4	27.7	27.4	C(17′)	23.5	28.1	29.9
C(18)	64.7	64.4	64.0	C(18′)	7.1	7.6	7.3
C(19)	34.6	34.9	34.6	C(19′)	26.5	28.1	28.0
C(20)	46.4	47.5	47.3	C(20′)	37.0	36.1	35.9
C(21)	68.7	69.8	69.4	C(21′)	70.9	66.3	67.5
C=O	168.5	168.0	167.8	C(22′)		33.2	38.1
OMe	50.8	51.0	50.6	C(23′)		44.9	48.2

[a] In parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. [b] From ref 9. [c] $\delta(C{=}O) = 168.6$ ppm; $\delta(OMe) = 50.8$ ppm. [d,e] Signals may be reversed.

N_a-methyl-2β,16β-dihydrotabersonine[10] lead to those of ring A′ of **4a** and **4b**, while the shifts of carbons 14′, 15′, 18′, 19′, and 20′ are derived from resonances of like carbons in pachysiphine (**3b**). The aminomethylenes of voafolidine, C(3′) and C(5′), are undifferentiated, the alkaloid's C(6′) and C(22′) shifts are similar to those of vobtusine (**1a**), and of the remaining pairs of methines and nonprotonated carbons one each is deshielded by a directly bound heteroatom. Carbons 17′ and 23′ are shielded in voafolidine (**4a**) vs. vobtusine (**1a**) by the proximate epoxide, as in pachysiphine (**3b**) vs. vandrikine (**2b**), and the removal of a δ effect from the 12′-methoxy group of vobtusine (**1a**), respectively. The fact of the $\Delta\delta$(C-21′) values of voafolidine (**4a**) vs. pachysiphine (**3b**) being nearly identical with those of vobtusine (**1a**) vs. vandrikine (**2b**) shows the stereochemistry of the epoxide unit of **4a** to be the same as that in pachysiphine (**3b**). The strong similarity of the shift differences of all carbons of voafolidine (**4a**) and voafoline (**4b**) vs. those of vobtusine lactone (**1b**) and 2′-deoxyvobtusine lactone (**1c**), except the $\Delta\delta$(C-23′) values, vouch for the identity of the stereoconfigurations of **4a** and **4b**. The conformational environment around C(23′) is different in compounds with the sterically encumbering 12′-methoxy group from those lacking this function, as indicated by a variance of the strength of the γ effect on C(23′) due to the 2′-hydroxy group in the two cases. The carbon shifts of voafolidine (**4a**) and voafoline (**4b**) are listed in Table III.

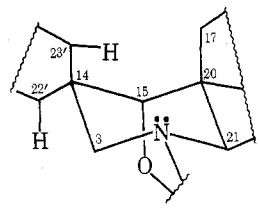
Isovoafoline, a congener of voafolidine (**4a**) and voafoline (**4b**) in *Voacanga africana* Stapf., has been shown to be an isomer of voafoline (**4b**) without the origin of the isomerism having been established.[2,4] A comparison of the ^{13}C NMR spectra of the two isomeric alkaloids establishes the identity of the chiral centers on the periphery of the bases and reveals significant shift differences only of C(18) and ring D and F′ centers, carbons 3, 14, 15, 16′, 22′, and 23′. Among these only C(3) and C(23′) have identical substituents, but can be differentiated by the γ effect of the 2′-hydroxy group on C(23′) in related substances (vide infra). Thus isovoafoline is the C(14) epimer of voafoline (**4b**), as depicted in formula **5b**. Its shifts are listed in Table IV.

As the conformational representations of rings D and F′ of

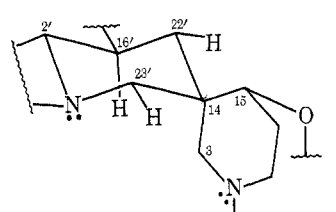


5a, Y = OH
b, Y = H

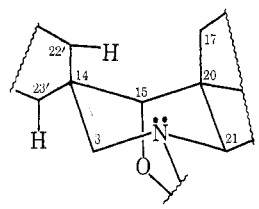
voafoline (**4b**), i.e., **6a** and **6b**, respectively, and isovoafoline (**5b**), i.e., **7a** and **7b**, respectively, illustrate, N_a′ and C(16′) of



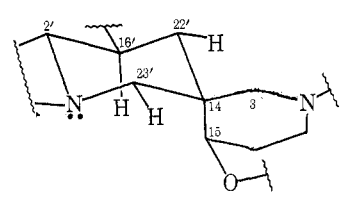
6a



6b



7a



7b

voafoline (**4b**) are involved in 1,3-diaxial interactions with C(3), while C(15), equatorially oriented toward ring F′, feels no such effects. Contrastingly, N_a′ and C(16′) of isovoafoline (**5b**) perturb C(15), while leaving C(3) unaffected. Owing to these specific γ effects C(3) is upfield and C(15) downfield in voafoline (**4b**) with respect to isovoafoline (**5b**). The 1,3-diaxial interactions of the N_b electron pair and C(17) with C(23′) in voafoline (**4b**), i.e., a strongly shielding γ effect and a mild deshielding δ effect, appears to be nearly balanced by the 1,3-diaxial involvement of the C(15) ether oxygen with C(22′), i.e., a strong γ effect. In view of this balance the inverted interactions of isovoafoline (**5b**) lead to only minimal shift differences at C(22′) and C(23′). Thus the C(3) and C(15) shifts establish the C(14) stereochemistry (see Table V). Had these alkaloids been 15-deoxy compounds, the C(22′) and C(23′) shifts would have been equally diagnostic.

Folicangine, another *V. africana* alkaloid, has been shown to be converted into isovoafolidine, an isomer of voafolidine (**4a**), on reduction with sodium borohydride.[2,4] Inspection of the ^{13}C NMR spectra of the reduction product showed it to be 14-isovoafolidine (**5a**). As in the case of voafoline (**4b**) and isovoafoline (**5b**) only the carbons sensitive to a configurational change at C(14) exhibit shift differences (cf. Table V). A similar study of the borohydride reduction products of subsessiline[1,2,4] and subsessiline lactone,[1,2] alkaloids of *Callichilia subsessilis*, proved them to be 14-isovobtusine (**8a**) and 14-isovobtusine lactone (**8b**), respectively (cf. Table V). Thus the alkaloids isovoafoline (**5b**), folicangine, subsessiline, and subsessiline lactone, whose detailed structures were unknown, possess a common C(14) configuration opposite to that of vobtusine (**1a**). All carbon shifts of the 14-iso compounds **5a**, **5b**, **8a**, and **8b** are listed in Table IV.

The following general comments can be made on the basis of the shift difference data. In agreement with observations

Table IV. Carbon Shifts of Isovoafolidine, Isovoafoline, Isovobtusine, and Isovobtusine Lactone[a]

	5a	5b	8a[b]	8b[b]		5a	5b	8a[b]	8b[b]
C(2)	166.6	166.1	166.7	166.7	C(2′)	94.1	76.9	94.4[c]	94.3[d]
C(3)	58.0	57.7	58.0	58.3	C(3′)	53.5[e]	53.1[e]	48.8	48.2
C(5)	51.4	51.0	51.4	50.9	C(5′)	52.8[e]	52.7[e]	52.0	51.9
C(6)	44.4	44.1	44.4	44.4	C(6′)	31.7	39.1	31.3	31.3
C(7)	55.0	54.5	54.8	54.8	C(7′)	55.5	51.6	56.4	56.4
C(8)	137.8	137.4	137.9	137.8	C(8′)	133.5	135.9	134.2	133.1
C(9)	121.4	121.0	121.5	121.4	C(9′)	121.2	121.0	113.5	113.6
C(10)	120.5	120.2	120.5	120.5	C(10′)	117.4	116.3	118.5	119.4
C(11)	127.5	127.4	127.5	127.6	C(11′)	127.1	126.8	110.3	110.6
C(12)	109.1	108.8	109.1	109.2	C(12′)	109.0	108.1	146.0	146.1
C(13)	142.9	142.6	142.8	142.9	C(13′)	148.3	149.4	136.8	136.4
C(14)	39.0	38.8	38.9	38.9	C(14′)	53.0	52.5	25.5	25.0
C(15)	80.2	80.6	81.5	81.5	C(15′)	56.6	56.4	80.4	81.4
C(16)	94.3	93.9	94.3[c]	93.9[d]	C(16′)	28.8	26.1	32.4[e]	32.0
C(17)	27.9	27.9	28.1	28.4	C(17′)	29.6	29.6	32.6[e]	32.0
C(18)	62.7	62.5	63.7	64.0	C(18′)	7.6	7.3	65.3	175.4
C(19)	34.8	34.6	35.1	34.9	C(19′)	28.1	27.9	36.8	41.7
C(20)	47.1	46.8	47.9	47.9	C(20′)	36.3	36.0	44.4	43.5
C(21)	70.0	69.6	69.9	69.9	C(21′)	66.5	67.9	63.7	63.6
C=O	168.1	167.6	168.1	168.2	C(22′)	34.8	39.9	35.1	34.9
OMe	50.9	50.5	50.9	50.9	C(23′)	44.2	49.1	46.5	46.3
					OMe			55.0	55.0

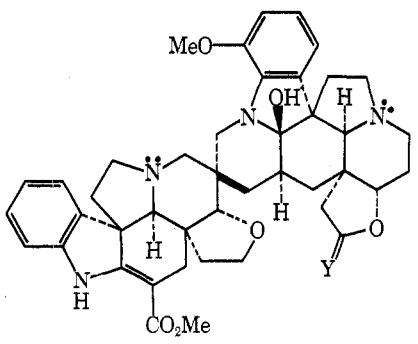
[a] In parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. [b] Based on only a proton-decoupled spectrum because of low sample size. [c,d] Signals may be reversed. [e] Signals in any vertical column may be reversed.

Table V. Carbon Shift Differences Indicative of C(14) Configuration[a]

	4a	5a	4b	5b	1a	8a	1b	8b
δ(C-3)	53.7	58.0	53.4	57.7	53.7	58.0	53.8	58.3
δ(C-14)	40.4	39.0	40.3	38.8	39.6	38.9	39.5	38.9
δ(C-15)	87.3	80.2	87.0	80.6	87.4	81.5	87.3	81.5
δ(C-18)	64.4	62.7	64.0	62.5	64.2	63.7	64.2	64.0
δ(C-16′)	28.5	28.8	25.6	26.1	31.5	32.4	31.1	32.0
δ(C-22′)	33.2	34.8	38.1	39.9	34.1	35.1	33.5	34.9
δ(C-23′)	44.9	44.2	48.2	49.1	46.1	46.5	46.0	46.3
Δδ(C-3)	4.3		4.3		4.3		4.5	
Δδ(C-14)	−1.4		−1.5		−0.7		−0.6	
Δδ(C-15)	−7.1		−6.4		−5.9		−5.8	
Δδ(C-18)	−1.7		−1.5		−0.5		−0.2	
Δδ(C-16′)	0.3		0.5		0.9		0.9	
Δδ(C-22′)	1.6		1.8		1.0		1.4	
Δδ(C-23′)	−0.7		0.9		0.4		0.3	

[a] $\Delta\delta = \delta(\text{iso}) - \delta(\text{normal})$, in parts per million.

on quaternary carbon shifts[11] the δ values of the spiro carbon common to the two monomer units of the bis-indoline alkaloids suffers only minor perturbation from the normal to the 14-iso series, being slightly shielded in the latter. The aforementioned difference of ring F′ conformation depending on C(12′) substitution, as indicated by the magnitude of the γ effect of the 2′-hydroxy group on C(23′), is reflected also by the shift differences of C(15), C(18), and C(16′). The presence of a 12′-methoxy group reduces the magnitude of the reciprocal γ effects at C(15) and C(16′). The subtle conformational distortion of ring F′ is even observable through the shift of the distant C(18), presumably by conformational transmission via C(15)-H. In contrast to the sensitivity of all ring F′-related centers involved in strong steric interactions the sterically unencumbered C(3) is insensitive to ring F′ conformation.



8a, Y = H_2
b, Y = O

As the shift analysis of anhydrovobtusine[18,19] (cf. numbers on formula **9**) indicates, dramatic substitution changes of ring F′ and consequent alteration of the interaction of ring F′ centers with ring D sites lead to shift modification of the carbons shown above to be diagnostic of the C(14) stereochemistry. Whereas the absence of models precludes complete shift assignment of the carbons, the C(15) shift can be recognized and is found to be anomalous for the normal vobtusine series.

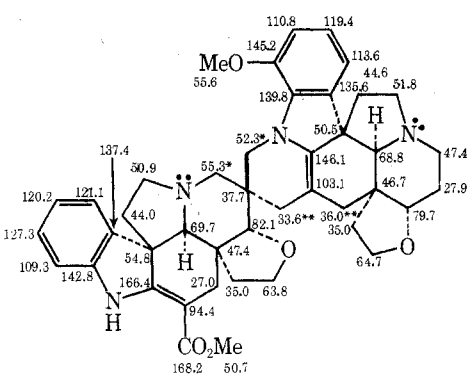
The chemical tie-up of folicangine with isovoafolidine (**5a**) by borohydride reduction[4] and the liberation of a 2′-hydroxy

Table VI. Carbon Shifts of Folicangine, Subsessiline, and Subsessiline Lactone[a]

	10	11a	11b		10	11a	11b
C(2)	165.8	165.9	165.7	C(2′)	93.9[b]	94.6[c]	93.9[d]
C(3)	91.8	91.9	91.9	C(3′)	53.7[e]	49.0	48.4
C(7)	59.1	59.1	*h*	C(5′)	53.3[e]	53.2	52.9
C(8)	136.1	137.1	*h*	C(6′)	30.5	31.1	31.5
C(9)	121.4	122.4	122.3	C(7′)	53.7	54.4	54.4
C(10)	121.0	120.9	120.9	C(8′)	135.9	136.0	135.8
C(11)	127.8	127.7	127.8	C(9′)	122.2	114.6	114.6
C(12)	109.1	109.0	109.1	C(10′)	118.1	118.8	119.1
C(13)	142.9	142.9	142.8	C(11′)	127.8	111.1	111.6
C(14)	38.1	38.1	38.2	C(12′)	106.9	145.8	145.9
C(15)	87.5	87.6	87.5	C(13′)	147.8	136.2	136.0
C(16)	93.0[b]	92.8[c]	92.7[d]	C(14′)	52.9	26.1	25.2
C(18)	67.3	67.2	67.3	C(15′)	56.5	80.9	81.9
C(20)	49.9	49.9	50.0	C(16′)	32.2	32.8	32.2
C(21)	70.6	70.6	70.7	C(17′)	29.6	34.4[f]	33.7[g]
C=O	168.1	168.1	168.0	C(18′)	7.6	65.0	175.2
OMe	51.0	50.9	51.0	C(19′)	28.0	35.8	40.6
				C(20′)	35.5	44.1	43.4
				C(21′)	67.7	65.8	65.9
				OMe		55.6	55.6

	10	11a	11b
NCH_2	47.5, 51.2	49.0, 50.9	48.9, 50.8
CH_2	33.9, 38.0, 38.6, 41.6	34.0,[f] 38.1, 38.6, 41.5	34.0,[g] 37.7, 38.6, 41.4

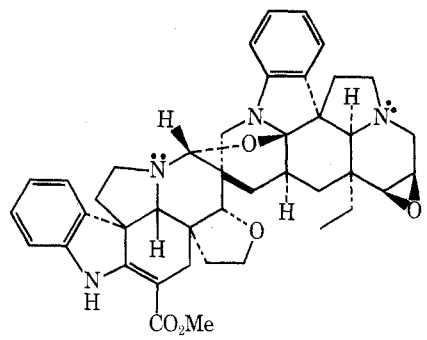
[a] In parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm. [b-g] Signals may be reversed. [h] Signal missing because of low sample size.



9

group in this reaction indicates the tetradecacyclic, $C_{42}H_{46}O_5N_4$ alkaloid to be a didehydroisovoafolidine whose C(2′) oxygen is bridged to an amino carbon. In accord with this view the ^{13}C NMR spectra of folicangine differ from those of isovoafolidine (**5a**) primarily by the absence of one aminomethylene and the presence of a methine substituted by two heteroatoms. The spectra of monodeuterated isovoafolidine, prepared by the reduction of folicangine by sodium borodeuteride,[4] reveal the disappearance of the C(3) signal. Thus the structure of folicangine is **10**.[20] The relationship of folicangine to isovoafolidine (**5a**) is mimicked by that of subsessiline (amataine[19]) to isovobtusine (**8a**), even to the extent of sodium borodeuteride reduction of subsessiline placing a deuterium at C(3) of isovobtusine (**8a**).[1] Therefore the structure of subsessiline is **11a**.[20] Since the difference of the shifts of subsessiline and subsessiline lactone are like those of vobtusine (**1a**) and vobtusine lactone (**1b**), the structure of subsessiline lactone is **11b**.[20]

The chemical shifts of rings A′, B′, C′, D′, and E′ of the three 3,2′ ethers, **10**, **11a**, and **11b**, are altered only minimally from the values of their 2′-hydroxy alkaloid counterparts of either normal or 14-iso configuration. However, the introduction of the 3,2′-ether bridge causes dramatic shift changes at many of the carbons of the remaining rings, precluding rigorous shift assignment of the leftover methylenes (see Table VI). The drastic shift perturbations of the carbons of rings C, D, E, and the D-attached tetrahydrofuran cannot be accommodated by a H(3α) configuration, since this stereochemistry, depicted in conformation **12**, introduces merely a ring F′ boat form into the skeleta of the 2′-hydroxy-14-iso compounds, thus affecting, at worst, only the C(3), C(5), C(14), C(15), and C(21) shifts. More deep-seated conformational changes must be involved in shift alteration of centers far removed from the ether-bridging site, such as the lower limit $\Delta\delta$ values of 3, 4, 6, and 4 ppm for C(6), C(7), C(17), and C(19), respectively. Thus it appears that folicangine, subsessiline, and subsessiline lactone possess a H(3β) configuration, as illustrated in formulas **10**, **11a**, and **11b**. This stereochemistry demands that



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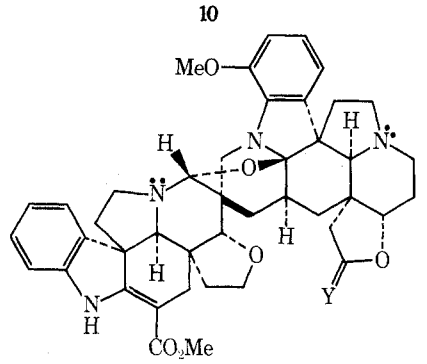
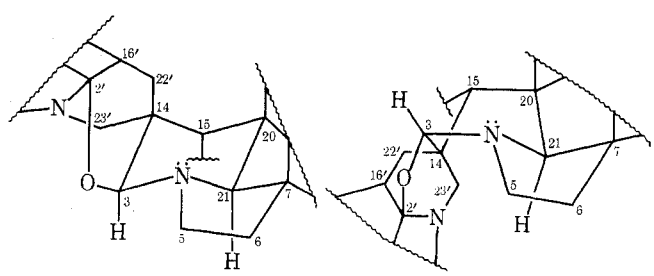
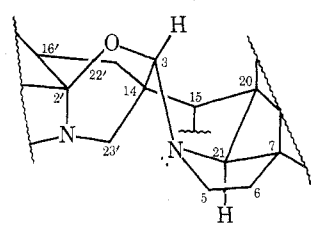


11a, Y = H_2
b, Y = O

ring D be constrained into a boat form. However, the resultant, strong, nonbonded interactions of H(21) and H(23′β) (cf.



12 **13**



14

conformation **13**) can be expected to convert the usual C/D trans configuration of the *Aspidosperma* bases[21] to a *cis*-indolizidine system. The consequently new nonbonded interactions in conformation **14** of the alkaloids **10**, **11a**, and **11b** are sufficiently complex and all-pervasive to lead to the observed general shift changes.

Experimental Section

The ^{13}C NMR spectra were recorded on a Varian XL-100-15 spectrometer operating at 25.2 MHz in the Fourier transform mode. All samples were run in 0.05–0.5 M deuteriochloroform solutions. Except for substances **8a**, **8b**, and **11b**, all compounds were submitted to proton-noise decoupling, single-frequency off-resonance decoupling, and low-power, noise-modulated decoupling,[22] to establish carbon shifts and degrees of protonation. In select instances partially relaxed Fourier transform spectra, obtained by the 180°–τ–90° inversion recovery method, were recorded for verification of the latter. For the alkaloids examined by this technique τ intervals in the range of 0.070–0.080 s were found to distinguish qualitatively methine from methylene carbons by making the latter null. The shifts enumerated on formula **9** are in parts per million downfield from Me_4Si [$\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm]. The starred numbers indicate possible signal reversal.

Anhydrovobtusine (9). The following represents an improved method of preparation of **9**.[18,19] A solution of 1.0 g of vobtusine (**1a**) in a minimum of methylene chloride was added to a solution of 2 g of *p*-toluenesulfonic acid in 200 ml of anhydrous benzene in the presence of a Dean-Stark water separator and the mixture refluxed for 4 h. It then was poured into 200 ml of water, made basic to pH 10, and extracted with chloroform. The extract was washed with water, dried over sodium carbonate, and evaporated. Chromatography of the resin, 1 g, on Baker silica gel (activity I) and elution with methylene chloride–methanol yielded 700 mg of **9** and 100 mg of apovobtusine, identical in all respects with the reported compounds.[18]

Registry No.—**1a**, 19772-79-3; **1b**, 19772-81-7; **1c**, 19772-80-6; **1d**, 59803-47-3; **1e**, 59796-71-3; **1f**, 50924-04-4; **1g**, 50924-05-5; **3b**, 2447-58-7; **4a**, 32063-91-5; **4b**, 31947-67-8; **5a**, 33055-38-8; **5b**, 31947-66-7; **8a**, 59829-32-2; **8b**, 59829-33-3; **10**, 32340-00-4; **11a**, 31148-60-4; **11b**, 59796-72-4.

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Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally Occurring Substances. 48. Dimeric Quinolinic *Melodinus* Alkaloids[1]

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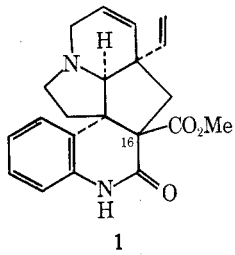
Received March 22, 1976

The *Melodinus* C_{41} alkaloids scandomelonine and episcandomelonine are shown by ^{13}C NMR spectroscopy to be 19 epimers of 10-(3′α-pachysiphinyl)meloscandonine. A similar study of the C_{42} *Melodinus* bases scandomeline and episcandomeline reveals them to be structurally related, 19-epimeric carbinolamines.

The New Caledonian plant *Melodinus scandens* Forst. has been shown to produce a large array of alkaloids containing inter alia the two unusual quinolones scandine (**1**) and meloscandonine (**2**).[2-7] Further fractionation of the plant extract now has yielded four "dimeric" alkaloids, scandomelonine,[6] episcandomelonine, scandomeline,[6] and episcandomeline. The present communication presents their structure analysis mostly by the use of ^{13}C NMR spectroscopy.

Scandomelonine and episcandomelonine are $C_{41}H_{42}O_5N_4$



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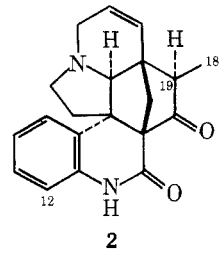

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