A New Structural Class of Bisindole Alkaloids from the Seeds of *Catharanthus roseus*: Vingramine and Methylvingramine

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Two new bisindole alkaloids, vingramine (**1**) and methylvingramine (**2**), were isolated from the seeds of *Catharanthus roseus*, Apocynaceae. The structures were determined by HRFABMS as well as one- and two-dimensional NMR experiments. They possess a new bisindole skeleton involving an indole alkaloid part B with loss of 5′,6′-ethylene, a C7′−C16′ linkage, a 14′-O-19′-tetrahydrofuran, and a *N*-4′-isobutyramide group. The 12-methyl vincorine part **A** and part **B** are connected via an 11,10′-biphenyl linkage. The relative configuration was determined by NMR analysis. Biogenetic considerations suggested a rearrangement and a double fragmentation at C6′/C7′ and N4′/C5′ for the formation of **1** from strictamine, further allowing deduction of the absolute configuration of 10 stereocenters: 2*S*, 7*R*, 15*R*, 16*R*, 3′*R*, 14′*S*, 15′*S*, 16′*R*, 19′*S*, and 20′*R*. The alkaloids **1** and **2** display, in vitro, cytotoxic activity against nasopharynx carcinoma KB cells, IC_{50} 5 and 6 μM (4 and 5 μg/mL).

Introduction

Catharanthus roseus (L.) G. Don, a Madagascan periwinkle, produces vinblastine-type bisindole alkaloids,[1] major anticancer agents with a broad spectrum of activity, used clinically in the chemotherapy of numerous haematological and solid tumors.[2] Since the early sixties, intensive efforts have been devoted to design syntheses of these alkaloids (vinblastine, vincristine)[3−5] and derivatives (vindesine, vinorelbine)[2,6] and to search for other sources and other antitumor substances in the Apocynaceae.[7]

Near 30 bisindole alkaloids and over 60 monomers have been isolated from the aerial parts and roots of *C. roseus*[7] (about 260 naturally occurring bisindoles are known). It was generally admitted that seeds of *C. roseus* do not contain alkaloids, Scott's careful sequential studies in 1968, on germinating seedlings,[8,9] detected, only after 24 h, production of alkaloids such as vincoside (revised later to strictosidine),[10] corynantheine, and ajmalicine.[11]

Surprisingly enough, we were able to detect alkaloids in the seeds of a Madagascan *C. roseus* in the dry state, before any germination had occurred. The ethanolic extract showed in vitro cytotoxic activity against P388 murine leukemia cells (80% growth inhibition at 10 μg/mL). Moreover, the bisindole alkaloids found are endowed with an unique, new backbone, very different from those of previously isolated bisindoles from aerial parts and roots of members of the *Catharanthus* genus.[7] We report herein the structure determination of the novel cytotoxic seed alkaloids vingramine (**1**) and methylvingramine (**2**) from spectral data, suggest biogenetic pathways, and subsequently propose absolute configurations of 10 chiral carbon centers.

Results and Discussion

Vingramine (**1**) and methylvingramine (**2**) were isolated as amorphous powders from the CH_2Cl_2 extract of basified seeds of *C. roseus* by repetitive chromatography on Sephadex LH20 and silica gel followed by TLC purification (0.002% and 0.005% yield, respectively).

Pure vingramine (**1**), $[\alpha]_D$ −270.4° ($CHCl_3$, *c* 0.5), analyzed for $C_{46}H_{56}N_4O_8$ deduced from HRFABMS observed $(MH)^+$ at *m*/*z* 793.4193. Of the 21 degrees of unsaturation inherent in this molecular formula, 11 were

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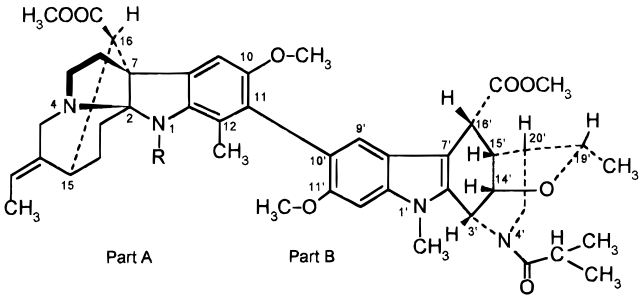
Table 1. ^{1}H NMR Data for Vingramine (1) and Methylvingramine (2)

	1 in Py-d_5, δ, J (Hz); HMBC: C connections		**1** in $CDCl_3$, δ		**2** in $CDCl_3$, δ	
C no.	**A**	**B**	**A**	**B**	**A**	**B**
N-CH_3	–	3.86, s; 2′,13′	–	3.74	2.98	3.78
3	1.65, m	6.21, d, J = 4.6; 2′,1″,7′,15′,14′,21′	2.07	5.90	1.90	5.95
	2.65, m	–	2.50	–	2.42	–
5	2.80, m	–	2.80	–	2.78	–
	3.70, m	–	3.65	–	3.50	–
6	2.10, m	–	2.20	–	2.10	–
	2.70, m	–	2.50	–	2.60	–
9	7.38, s; 7,8,10,11,13	7.50, s; 7′,10′,11,11′,13′	6.90	7.05	6.85	7.02
10-OCH_3	3.68, s; 10	–	3.55	–	3.54	–
11-OCH_3	–	3.65, s; 11′	–	3.78	–	3.80
12	–	7.08, s; 8′,10′,11′,13′	–	6.80	–	6.80
12-CH_3	2.02, s; 11,12,13	–	1.83	–	2.12	–
14	1.80, m	4.48, t, J = 4.8; 3′,19′,20′	1.78	4.30	1.75	4.35
	2.00, m	–	1.88	–	1.85	–
15	3.75, m	3.05, m	3.68	3.05	3.68	3.10
16	3.15, d, J = 4.5; 2,6,7,8,14,15,17,20	4.39, d, J = 7.9; 2′,7′,15′,17′,20′	2.90	4.35	2.89	4.38
17-OCH_3	3.77, s; 17	3.65, s; 17′	3.79	3.71	3.75	3.80
18-CH_3	1.60, d, J = 6.6; 19,20	1.31, d, J = 6.3; 19′,20′	1.62	1.34	1.68	1.35
19	5.38, q, J = 6.8; 15,18,21	4.25, m	5.45	4.25	5.48	4.28
20	–	2.05, m	–	2.02	–	2.05
21	3.13, d, J = 14.6; 2,15	3.60, m; 1″	3.05	3.48	3.08	3.50
	4.05, d, J = 14.6	3.60, m	3.95	3.64	3.98	3.67
2″	–	2.75, s; 1″,3″	–	2.80	–	2.80
3″	–	1.18, d, J = 6.3; 1″,2″,4″	–	1.19	–	1.20
4″	–	0.72, d, J = 6.3; 1″,2″,3″	–	0.96	–	1.00



Vingramine **1** : R=H

Methylvingramine **2** : R=CH_3

defined from ^{13}C NMR ($CDCl_3$) data as 3 ester/amide carbonyls and 16 sp^2 carbon atoms. Hence, vingramine (**1**) must possess 10 rings. However, in this solvent three proton signals near δ 4.3 were entangled and prevented an unambiguous assignment of resonances. This problem was overcome by performing NMR experiments in pyridine-d_5.

Analysis of vingramine (**1**) by 1D and 2D ^{1}H and ^{13}C NMR (Tables 1 and 2) established three spin systems: aminoethyl (**i**), 4-(methoxycarbonyl)butyl (**ii**), and 2-butenylamino (**iii**), in which two methylenes at δ_C 54.8 and 58.1 may be vicinal to a nitrogen atom (Figure 1). Four other fragments were defined, by ^2J and ^3J, ^{1}H−^{13}C long-range correlations (HMBC),[12] as isobutanoyl (**iv**), tetrahydrofuranyl (**v**), 10-methoxy-12-methyldihydroindolyl (**vi**), and *N*-methyl-11′-methoxyindolyl (**vii**) groups,[13a] respectively. Concerning fragment **v**, the ^{1}H−^{1}H COSY spectrum revealed one hexyl spin system (C3′−C14′−C15′−C20′−C19′−C18′) bearing two side chains: 15′-methine and 20′-methylene. ^{13}C shifts of C14′ and C19′

Table 2. ^{13}C NMR Data for Compounds 1 and 2

	1 in Py-d_5		**1** in $CDCl_3$		**2** in $CDCl_3$	
C no.	**A**	**B**	**A**	**B**	**A**	**B**
2	95.0	132.3	94.1	131.8	97.7	131.3
3	26.8	46.0	26.7	45.7	20.8	45.6
5	54.8	–	54.3	–	54.3	–
6	41.4	–	40.5	–	40.2	–
7	58.7	108.1	58.1	107.6	56.7	107.5
8	135.0	121.1	137.7	120.0	136.3	120.7
9	107.8	122.5	106.9	121.8	106.7	121.8
10	152.0	120.2	151.6	119.5	150.3	119.2
11	129.3	155.5	128.2	154.9	129.3	154.9
12	119.8	92.7	119.3	92.2	118.0	92.0
13	142.0	139.2	140.6	138.7	141.2	138.4
14	26.8	75.4	26.5	75.2	26.2	75.2
15	35.6	40.3	35.2	39.8	34.8	39.6
16	51.1	39.4	50.6	39.1	50.7	39.0
17	174.0	173.3	173.6	173.1	173.0	173.8
18	13.8	16.7	13.6	16.4	13.5	16.4
19	122.8	77.1	123.6	76.9	123.2	76.8
20	139.0	40.0	137.9	39.7	137.9	39.7
21	58.1	39.1	57.6	39.0	58.0	38.9
N-CH_3	–	30.3	–	30.3	32.0	29.7
17-OCH_3	51.6	51.9	51.7	52.1	52.0	51.6
10-CH_3	57.1	–	57.1	–	57.0	–
11-OCH_3	–	55.7	–	56.1	–	56.0
12-CH_3	15.3	–	14.9	–	16.7	–
1″	–	175.9	–	176.1	–	176.1
2″	–	30.8	–	30.7	–	30.2
3″	–	19.1	–	18.8	–	18.8
4″	–	19.8	–	20.0	–	19.9

at δ 75.4 and 77.1 indicated their oxymethine nature. HMBC correlation between C19′ and H14′ revealed that C14′ was close to C19′. Hence, a tetrahydrofuran ring was established. The carbonyl resonance at δ 173.3 was correlated to H16′ at δ 4.39 and methoxyl at δ 3.65. Thus, the methoxycarbonyl group was attached to methine C16′.

The partial structures **i**−**vii** were connected through HMBC spectra rich in correlations. The first moiety **A** (Figure 2) was consistent with the fragments **i**, **ii**, **iii**, and **vi**. The strongly deshielded sp^3 quaternary C-2 carbon at δ 95.0 of the dihydroindole group **vi** was a diagnostic signal indicating that C-2 was linked to

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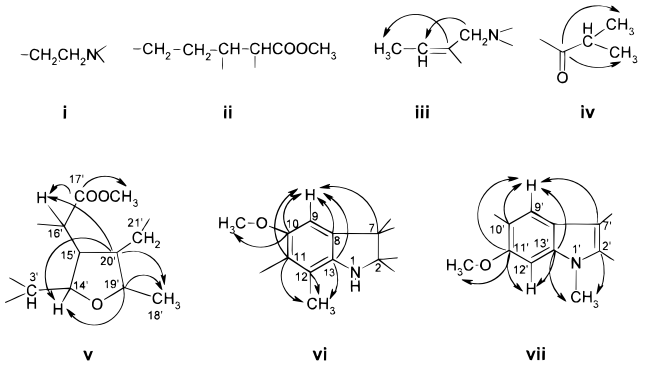

Figure 1. Structural fragments **i**−**vii** of vingramine (**1**) with some HMBC correlations.

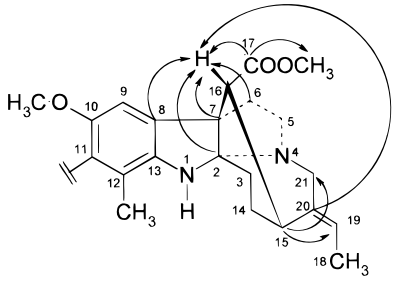

Figure 2. Structure part **A** with selected HMBC correlations.

another nitrogen[14] or oxygen atom. The indole fragment **vi** was connected to the methyl pentanoate group **ii** by cross-peaks between H16 and C8, C7, and C2. The aminoethyl group **i** was attached to C7 due to correlation between C6 and H16. The butenylamino group **iii** was connected to C15 that showed HMBC correlations with H21 and H19 as well as between H16 and C20. The final connection between C2 and H3 or H14 was lacking. However, C2−C3 ring-closure was necessary for satisfying the five ring requirement for part **A**, since part **B** was composed of five rings (vide infra). These data allowed identification of an *N*-demethylvincorine[13b] skeleton with an exceptional C12-methyl substituent for the vingramine **A** moiety.

Another quite intriguing moiety **B** was constructed by connecting the isobutanoyl **iv**, the tetrahydrofuranyl **v**, and the *N*-methylindolyl **vii** fragments. The cross-peak between the H3′ at δ 6.21 in fragment **v** and the isobutanoyl carbonyl-1″ at δ 175.9 indicated the amide nature of this carbonyl group. The strongly deshielded methine H3′ at δ 6.21 (δ_C 46.0), in the tetrahydrofuran fragment **v**, suggested vicinal linkages with both the amide nitrogen atom and the indole double bond. Unfortunately, each of two protons, H3′ at δ 6.21 as well as H16′ at δ 4.39, were correlated with both C-2′ (δ 132.3) and C-7′ (δ 108.1) of indole **vii** and lacked the critical cross-peak with the indole C8′ at δ 121.1 in the HMBC spectrum.

Finally, ROESY experiments (Figure 4) displayed two pairs of interactions between δ_H 6.21 and $\delta_{N'\text{-}CH3}$ 3.86 on one hand, and between δ_H 4.39 and $\delta_{H9'}$ 7.50 on the other. Hence, the methine CH-3′ (δ 6.21) could be linked to C2′; this assignment was further corroborated by HMBC correlations of H3′ with C2′, C7′, C14′, C15′, and C1″.

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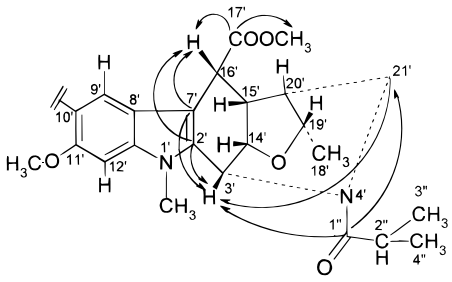


Figure 3. Structure part **B** with selected HMBC correlations.

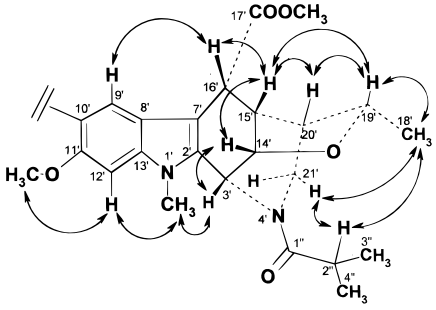


Figure 4. Selected NOEs of part **B** of vingramine (**1**).

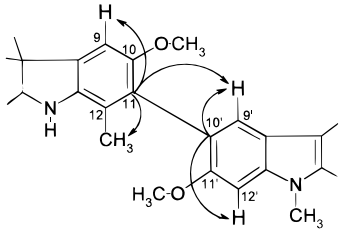


Figure 5. Selected HMBC correlations of the C11−C10′ biphenyl linkage of vingramine (**1**).

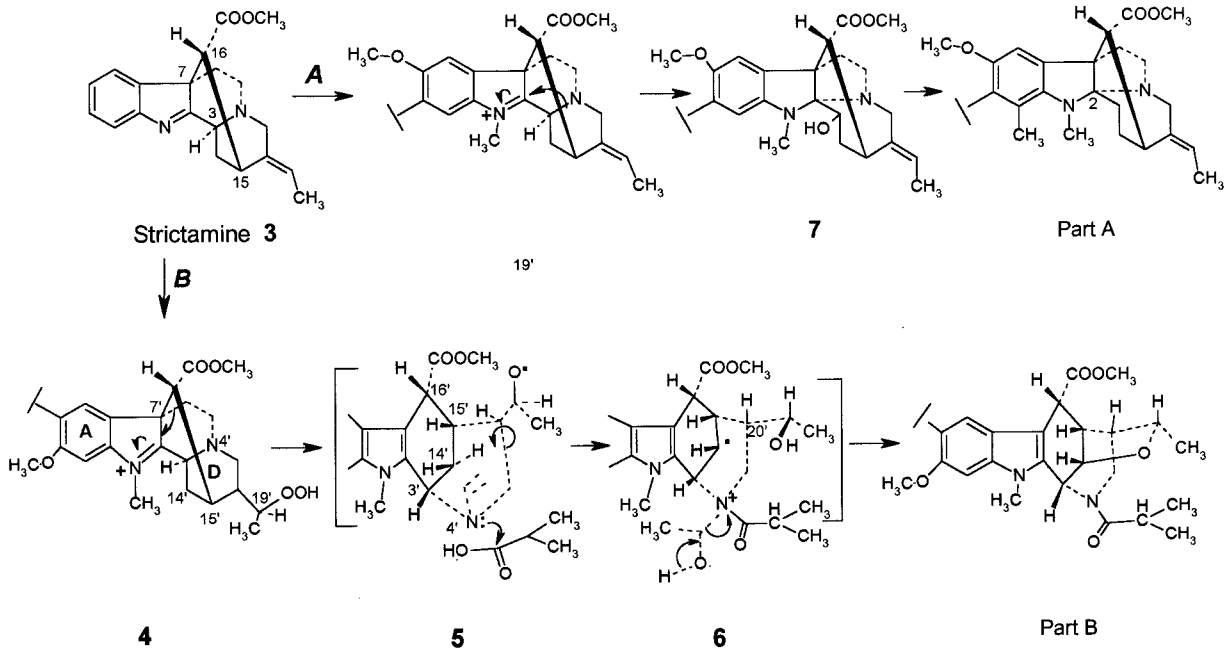
The carbon at δ 39.4, bearing the H16′ at δ 4.39 and the ester group, was thus linked to C7′ and assigned the C-16′ position. H16′ also showed HMBC connections with C20′, C17′, as well as C2′ and C7′. The tenth and last ring required cyclization of the amide nitrogen with methylene-21′ (δ_C 39.1 and δ_H 3.60) of the tetrahydrofuran spin system **v**. This piperidine ring was ascertained by deshielding of the CH_2-21′ shift and HMBC cross-peaks between carbonyl-1″ and H21′ as well as between H3′ and C21′ (Figure 3). Hence, vingramine (**1**) possessed the alkaloid substructure moiety **B**. These results revealed an unusual lack of a C5′, C6′-ethylene group, a C7′−C16′ bond preserved, a condensed pentacyclic skeleton and a *N*-4′-amide, for the indole alkaloid moiety **B**.

The biphenyl linkage of C11 of part **A** with C10′ of part **B** was established by HMBC connections between C11 and H9′ as well as C11/H9, C11/$CH_3$12, C10′/H9′, and C10′/H12′ (Figure 5).

The additional NOE interactions (Figure 4) defined the relative spatial arrangement of the six methine protons on the tricyclic cage structure for part **B**. The H-3′, H-14′, H-15′, and H-16′ were found on the same side, H-19′ and H-20′ were parallel to the indole plane, and methyl-18′ was close to H-21′ and H-2″ on the other side. Hence, the relative configurations were determined as 3′*R**, 14′*S**, 15′*S**, 16′*R**, 19′*S**, and 20′*R**.

The absolute configuration of vingramine (**1**, $[\alpha]_D$ −270.4°) may be deduced from inspection of the bio-

Scheme 1. Suggested Biogenetic Pathways for Structural Parts A and B of Vingramine (1) and Methylvingramine (2)



genetic formation of part **A** and part **B** (Scheme 1) derived from a key intermediate, strictamine **3**, well defined by X-ray analysis,[15] bearing an 1,2-imine bond. In this pathway, the configurations of C-16 and C-16′ were not modified and should be *R* as observed for vincorine ($[\alpha]_D$ −142°).[13b] The indole alkaloid part **B** should be generated via path B by double fragmentation and rearrangement. The first C6′−C7′ cleavage would be induced by methylation at *N*-1 of imine **4**. The more probable second C4′−C5′ scission may occur by formation of isobutyramide **5**, hydration of the enamine **6**, followed by breakdown of the derived carbinol promoted by quaternary N-4′, as acetaldehyde. Such amide-producing N4−C5 cleavage has been reported.[6a] Another biogenetic hypothesis is that oxidation of C-5′ and methylation of C-6′ take place without elimination of C5′−C6′ to form the isobutanoyl group. Subsequently, conversion of C-20′ would invert the piperidine D ring from boat **5** to the less hindered twist conformation **6**. Then, the 19′-hydroperoxyl group would get close enough to the C-14′ area to experience enzymatic rearrangement. The mechanism is likely of the free-radical type, the initiating step involving 1,5-internal hydrogen abstraction by C19-oxy radical formed by homolytic cleavage, thus activating the δ-carbon radical.[16] Then, ring closure takes place between 19′-hydroxyl and the C-14′ carbocation in position δ from the α side, to form a tetrahydrofuran cycle. A recent synthetic sequence of a quite analogous, albeit tetracyclic, structure instead of the pentacyclic part **B** of vingramine (**1**), was described in order to build simultaneously the C7−C6 and C7−C16 bonds of akuammiline type alkaloids.[17]

The absolute configuration of each chiral center is preserved as are those of C3, C7, C15, and C16 of strictamine **3**[15] in this rearrangement, and the NOE interactions of alkaloid **1** are in good agreement with spatial proton arrangements. Hence, the absolute configurations 3′*R*, 14′*S*, 15′*S*, 16′*R*, 19′*S*, and 20′*R* are proposed for part **B** of vingramine (**1**). There is no inversion of stereochemistry at either C-3′ or C-15′; however, introduction of an ether oxygen at C-14′ led to a change in the nomenclature for C-3′ (*S* → *R*) and C-15′ (*R* → *S*).

Moreover, strictamine **3** may also be a precursor of vincorine, part **A** of vingramine (**1**) produced by loss of *N*-methyl-1 from alkaloid (**2**), provided by path A via deformocorymine (**7**).[18] Thus, part **A** should possess the known absolute configurations 2*S*, 7*R*, 15*R*, and 16*R*.

It would appear that in the seeds of *C. roseus*, in contrast to other parts of the plant, monomer alkaloids undergo oxidative coupling into 11,10′-bisindole at an early step of biogenesis before more complex rearrangements take place.[9,19] The biphenyl bisindoles of the other Apocynaceae, unknown in the *Catharanthus* species, were found in various biogenetic states, such as 10,11′-dimethoxyvincamajinyl-cathafolines before skeleton rearrangement;[20] pelankine,[21] cabufiline,[22] desoxycabufiline,[22] and (11-methoxyvancamajinyl)-vincorines[23a] after half-rearrangement to vincorine; peceyline and peceylanine[21] after two-portion skeleton rearrangements into the vincorine−vincovine[23b] type of alkaloids.

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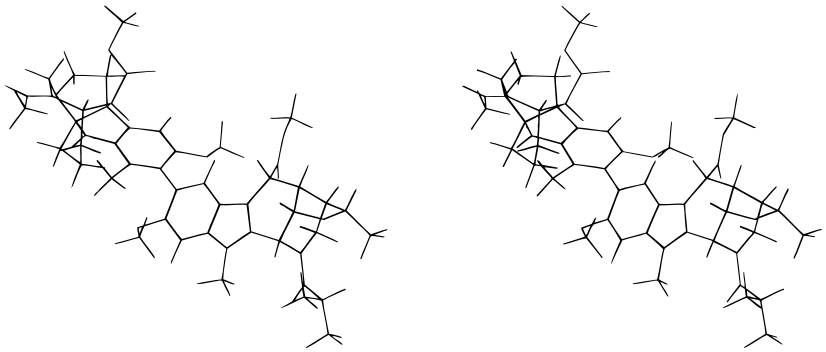

Figure 6. Stereoview of energy-minimized structure of vingramine (**1**).

The energy-minimized structure of vingramine (**1**, Figure 6) was obtained by molecular mechanics/molecular dynamics simulation calculations in vacuo.[24] The starting structure was built up with experimental distance restraints based on NOE (2−4 Å). The configuration of C15*R*, C7*R*, C3′*R*, and C15′*S* dictated automatically remaining configurations of bisindole **1** as obtained above by biogenetic considerations. The lowest energy structure of **1** possesses a dihedral angle C10−C11−C10′−C11′ of 132°. However, the stereochemistry of C11/C10′ atropisomerism remains unknown and calls for further study.

The second new alkaloid, named methylvingramine (**2**), $[\alpha]_D$ −278.0° ($CHCl_3$), analyzed for $C_{47}H_{58}N_4O_8$ deduced from HRFABMS: $(MH)^+$ at *m*/*z* 807.4403. Alkaloid **2** possesses 14 Da more than compound **1**. The NMR analysis ($CDCl_3$) presented great structural similarity with vingramine (**1**) and revealed additional resonances at δ_H 2.98 (3H) and δ_C 32.0. This methyl was assigned to the *N*-methyl-1 group on part **A** of vingramine (**1**) by HMBC connections with C-2 at δ 97.7 and C-13 at δ 141.2.

The structures of the bisindole alkaloids **1** and **2** are exceptional due to the particular rearrangement of part B, the presence of an isobutyramide group and a C14′-O-C19′ tetrahydrofuran ring, a 12-methyl on the vincorine part **A**, and a biphenyl linkage rather unusual in *Catharanthus* alkaloids.

Vingramine (**1**) and methylvingramine (**2**) displayed moderate cytotoxicity against human nasopharynx carcinoma cells (KB cells) with IC_{50} values of 5 and 6 μM (4 and 5 μg/mL), respectively, in comparaison with vinblastine: IC_{50} 8 nM. The antiproliferative activity of alkaloids **1** and **2** is due to inhibition of tubulin assembly in mitosis, as for vinblastine.[2a]

Conclusion

Most of the *Catharanthus* bisindole alkaloids are composed of a dihydroindole moiety, typically vindoline, and another indole alkaloid moiety connected via an aromatic C-10 and aliphatic C-16′ bond. Some examples of C6−C7 bond scission of indole alkaloids are reported in the Apocynaceae: vinoxine[25] (*Vinca minor*), fluorocarpamine[26] (*Alstonia pulmosa*), pseudoindoxyl ajmalicine[27] (*C. roseus*), melonine and celastromeine[28] (*Melodinus celastroides*), and 6,7-secoangustilobine A[29] (*Alstonia congensis*).

Vingramine (**1**) and methylvingramine (**2**) are the first examples of alkaloids found in *Catharanthus roseus* seeds; moreover, they belong to a new structural class involving an uncommon indole alkaloid skeleton with loss of 5′,6′-ethylene, *N*-4′-amide features, and a tetrahydrofuran ring formed by cyclization between the C14′ and C19′-oxygen. The absolute configuration of vingramine (**1**) and methyl vingramine (**2**) was proposed for 10 chiral centers 2*S*, 7*R*, 15*R*, 16*R*, 3′*R*, 14′*S*, 15′*S*, 16′*R*, 19′*S*, and 20′*R*. This new structural class may offer the opportunity of synthesizing new and possibly less neurotoxic anticancer drugs.

Experimental Section

General Information. 1D and 2D ^1H and ^{13}C NMR were performed in either $CDCl_3$ or pyridine-d_5 on a Bruker AC-300 spectrometer (^1H: 300.13 and ^{13}C: 75.45 MHz) referenced to TMS (δ = 0). ROESY spectra were recorded with 1.5 s relaxation delay, 300 ms mixing time, and apodization with a shifted sine bell and baseline corrections. HRFABMS were measured on a ZAB2-SEQ (VG analytical).

Isolation of Vingramine (1) and Methylvingramine (2). Seeds of *C. roseus* (500 g) were harvested in Madagascar and the plants cultured from the seeds identified by Dr. Lucile Allorge, Muséum National d'Histoire Naturelle, Paris, France. Powdered seeds were defatted with cyclohexane, basified with ammonia, and extracted by CH_2Cl_2. The concentrated extract was extracted by 5% HCl, and the aqueous layer made alkaline with ammonia was extracted with CH_2Cl_2. The organic layer was washed with water, concentrated to dryness, and yielded 1.2 g of residue. The alkaloidal residue was separated into four fractions on a Sephadex LH20 column eluted with MeOH. The chromatography of fraction 2 on silica gel, eluted by CH_2Cl_2/MeOH (95:5), furnished crude **2** (25 mg) and **1** (10 mg) and was further purified by preparative TLC (CH_2Cl_2/MeOH = 95:5).

Vingramine (1). $C_{46}H_{56}N_4O_8$. Amorphous. $[\alpha]_D$ −270.4° ($CHCl_3$, *c* 0.5). HRFABMS: *m*/*z* 793.4193 $(MH)^+$ (calcd 793.4176 for $C_{46}H_{57}N_4O_8$). IR (KBr) ν cm^{-1}: 1738, 1637, 1250, 1213, 1170. UV (MeOH), λ_{max}, nm (log ϵ): 217 sh (4.69), 231 (4.80), 280 (4.33), 303 sh (4.30).

Methylvingramine (2). $C_{47}H_{58}N_4O_8$. Amorphous. $[\alpha]_D$ −278.0° ($CHCl_3$, *c* 0.5). HRFABMS: *m*/*z* 807.4403 $(MH)^+$ (calcd 807.4332 for $C_{47}H_{59}N_4O_8$). IR (KBr) ν cm^{-1}: 1738, 1634,

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1250, 1213, 1169. UV (MeOH), λ_{max}, nm (log ϵ): 216 (4.89), 234 sh (4.57), 280 (4.12), 297 (4.12), 310 sh (4.11).

MM/MD Simulation Calculation. The energy-minimized structure was obtained by molecular mechanics force field using HyperChem software packages (Hypercube, INC. 419 Phillip Street Waterloo, Ontario N2L 3X2, Canada). The structure was first built with steric constraints: 7*R*, 15*R*, 16*R*, 3′*R*, 15′*S*, and 16′*R*, and distance restraints based on the NOE (2−4 Å). The energy minimization was carried out using a geometry optimization algorithm with conjugate gradient iterations to reach the root-mean-square of the gradients 0.001 kcal (Å·mol)$^{-1}$. Then, the structure was submitted to molecular dynamics using a simulated annealing procedure. The temperature was raised to 1000 K by steps of 100 K, and the dynamics were run for 200 ps, in vacuo. The lower energy minimum structure was again calculated by geometry optimization to obtain the energy-minimized structure.

Determination of Biological Activity. The cytotoxicity assays were carried out in 96-well microtiter plates in triplicate against P388 murine leukemia or human nasopharynx carcinoma KB cell lines (3×10^3 cells/mL). Cell growth was estimated by colorimetric measurement of stained Golgi apparatus in living cells by neutral red. Optical density was determined at 540 nm on a Titertek Multiskan photometer after 48 h for P388 cells and 72 h incubation for KB cells.

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Supporting Information Available: ^{1}H and ^{13}C NMR, HMBC (Py-d_5) spectra of vingramine (**1**), and ^{1}H and ^{13}C NMR ($CDCl_3$) spectra of methylvingramine (**2**) (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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