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Note

Voatriafricanines A and B, Trimeric Vobasine-Aspidosperma-Aspidosperma Alkaloids from *Voacanga africana*

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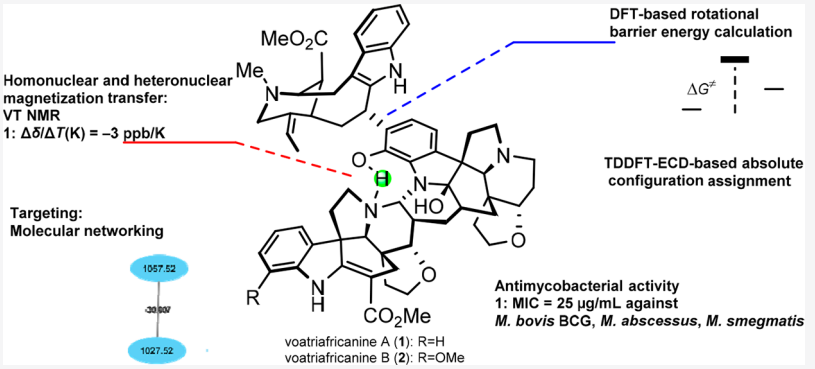

ABSTRACT: Voatriafricanines A and B (**1** and **2**), the first examples of vobasine-aspidosperma-aspidosperma monoterpene trisindole alkaloids, were isolated from the stem barks of *Voacanga africana*, guided by a molecular networking strategy. Their structures, including absolute configurations, were elucidated by spectroscopic methods and ECD calculations. Compounds **1** and **2** possess intramolecular hydrogen bonding, sufficiently robust to transfer homonuclear and heteronuclear magnetizations. Compound **1** exhibited potent antimycobacterial activity with no discernible cytotoxic activity.

After a century of intensive efforts, the discovery of monoterpene indole alkaloids (MIAs) still remains among the most exciting and dynamic areas of plant natural product (NP) research.[1−3] Although a growing number of unexpected structural motifs have been described in this group of NPs, the continual discovery of intricate MIAs may, undoubtedly, offer unprecedented molecular architectures with fundamental downstream lessons. As part of our research program directed toward the streamlined hypothesis-driven reinvestigation of previously investigated plants,[4−9] we endeavored toward the phytochemical study of *Voacanga africana* Stapf (Apocynaceae). This plant has been the subject of extensive phytochemical isolation efforts since 1959, resulting in the description of a wealth of monomers and dimers belonging to the aspidosperma- and iboga-type alkaloids.[10] Economically, with over 1600 tons of seeds exported annually from Ghana and Ivory Coast, *V. africana* is an important source of additional income for harvesters and exporters in West Africa.[11] Here we describe the use of a molecular networking-targeted strategy to identify the naturally occurring voatriafricanines A and B (**1** and **2**), representing the first examples of vobasine-aspidosperma-aspidosperma monoterpene trisindole alkaloids.

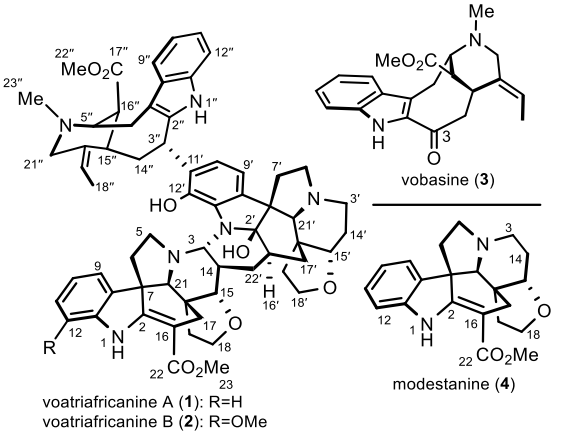

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Table 1. ^{1}H and ^{13}C (600 and 150 MHz) NMR Spectroscopic Data for 1 in $CDCl_3$

no.	δ_H, mult (*J*, Hz)	δ_C	no.	δ_H, mult (*J*, Hz)	δ_C	no.	δ_H, mult (*J*, Hz)	δ_C
1 (NH)	9.07, s					1″(NH)	8.28, s	
2		166.3	2′		95.8	2″		138.6
3	4.35, d (12.0)	71.0	3′	3.44, ov.	49.2	3″	5.31, dd (13.0, 2.4)	37.6
				2.46, ov.				
5	3.76, ov.	53.2	5′	3.75, m	51.8	5″	4.45, m	60.3
	3.03, td (10.9, 5.7)			1.54, m				
6	2.46, ov.	44.8	6′	2.95, m	29.8	6″	3.59, m	21.1
	2.29, ov.			1.34, ov.			3.82, ov.	
7		56.8	7′		55.5	7″		129.4
8		135.3	8′		134.5	8″		107.1
9	8.08, d (7.3)	122.5	9′	6.42, d (7.3)	112.2	9″	7.54, m	117.5
10	7.14, brt (7.3)	122.6	10′	6.29, d (7.3)	119.6	10″	7.10, ov.	119.6
11	7.18, brt (7.3)	128.7	11′		132.4	11″	7.12, ov.	122.2
12	6.85, d (7.3)	109.7	12′		141.3	12″	7.13, ov.	110.0
13		143.0	13′		134.2	13″		135.8
14	1.94, ov.	40.0	14′	2.00, ov.	25.1	14″	2.51, ov.	34.6
				2.28, ov.			2.25, ov.	
15	3.62, d (9.1)	87.6	15′	3.47, brs	79.6	15″	3.95, ov.	33.1
16		94.1	16′	2.09, ov.	34.8	16″	3.19, ov.	44.8
17	2.74, d (15.7)	34.4	17′	1.93, ov.	31.8	17″		169.0
	2.32, d (15.7)			0.98, brd (13.0)				
18	3.75, ov.	66.0	18′	3.94, ov.	65.3	18″	1.48, brd (7.0)	12.7
				3.84, ov.				
19	1.55, ov.	39.8	19′	2.26, ov.	37.1	19″	5.52, brq (7.0)	124.9
	1.35, ov.			1.51, ov.				
20		48.8	20′		44.8	20″		132.8
21	4.16, s	67.2	21′	2.74, s	64.7	21″	4.03, m	51.5
							3.47, ov.	
22		168.6	22′	1.97, ov.	33.1	22″	2.54, s	50.7
				1.68, ov.				
23	3.82, s	51.5				23″	2.89, s	40.5
			12′-OH	14.39, s				

As a way to explore the chemical diversity of the alkaloid extract of the stem barks of *V. africana*, its LC-MS/MS data were acquired and organized following the classical molecular networking workflow.[12] At this stage, the MIADB[13] spectral library (hosted by GNPS[12]) annotation yielded 18 hits (Table S3, Supporting Information), with five of them being previously described in the plant (ibogaine, tabersonine, vobtusine, voacamine, vobasine). On examination of the global molecular network (Figure S2, Supporting Information), a small unannotated molecular family (A) (Figure S4, Supporting Information) constituted of two nodes at *m/z* 1027.52 and 1057.52 attracted our attention. These unusual, elevated masses were reminiscent of oligomers, and their generated molecular formulas did not match any natural product databases (*Dictionary of Natural Products*[14] and *Reaxys*[15]). Ultimately, these observations fueled our isolation efforts toward the above-mentioned masses of molecular family A for rigorous structural elucidation.

Voatriafricanine A (**1**) was obtained as a brown amorphous solid. Its UV spectrum showed characteristic absorption maxima at 233, 254, 296, and 330 nm, corresponding to indole,[16] indoline, and *β*-anilinoacrylate chromophores.[17] The molecular formula of **1** was established to be $C_{62}H_{70}N_6O_8$ using the HRESIMS data at *m/z* 1027.5324 $[M + H]^+$ (calcd 1027.5328) requiring 31 sites of unsaturation. Analysis of the ^{1}H NMR spectrum (Table 1) in conjunction with the aid of HSQC, HMBC, and COSY spectra (Figures S13−S15, Supporting Information) provided evidence for the presence of a hydrogen-bonded phenol group proton [δ_H 14.39 (1H, s)], two NH protons [δ_H 8.28 (1H, s), 9.07 (1H, s)], an *ortho*-disubstituted benzene ring [δ_H 8.08 (1H, d, *J* = 7.3 Hz), 7.14 (1H, brt, *J* = 7.3 Hz), 7.18 (1H, brt, *J* = 7.3 Hz), 6.85 (1H, d, *J* = 7.3 Hz)], an *ortho*-tetrasubstituted benzene ring [δ_H 6.42 (1H, d, *J* = 7.3 Hz), 6.29 (1H, d, *J* = 7.3 Hz)], four aromatic protons [δ_H 7.54 (1H, m), 7.10−7.13 (3H, overlapped)], one nitrogen methyl [δ_H 2.89 (3H, s)], two methyl ester groups [δ_H 3.82 (3H, s), 2.54 (3H, s)], and an ethylidene group [δ_H 5.52 (1H, brq, *J* = 7.0 Hz), 1.48 (3H, brd, *J* = 7.0 Hz)]. Moreover, two bridgehead nitrogen methines [δ_H 4.16 (1H, s), 2.74 (1H, s)] were typical of two aspidosperma-type scaffolds,[18] and one methine signal [δ_H 5.31 (1H, dd, *J* = 13.0, 2.4 Hz)] was typical of an H-3 proton in the C-3-tethered vobasine unit.[16] In line with its elemental composition, these observations strongly supported that **1** was a trimeric MIA constituted by two aspidosperma units and one vobasine unit. Further analysis of the NMR data revealed that much of the signals had a close resemblance to those previously reported for the bisindole voacandimine A[17] [a modestanine (**4**)[19] dimer linked by a piperidine linkage]. The noticeable difference between **1** and voacandimine A resulted from the hydration of the double bond C-2′−C-16′ and its replacement by a hemiaminal carbon [δ_C 95.8 (C-2′)] and an sp^3 methine [δ_C 34.8 (C-16′)] in **1**. The cursory comparison of the spectral data of **1** to those of voacandimine A led to pinpoint some

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significant differences in the signal patterns related to H-15 (δ_H 3.62 (1H, d, J = 9.1 Hz), indicating its *trans* diaxial disposition to H-14 in **1** (H-14 appeared as a broad singlet in voacandimine A), whereas the unaltered magnitude of the $^3J_{H,H}$ coupling constant between H-3 and H-14 (J = 9.1 Hz) determined an identical *trans*-fused piperidine connection.

These spectroscopic data hinted that **1** could correspond to a diastereoisomer of voacandimine A with opposed configurations of both C-3 and C-14. The remaining NMR signals were ascribed to a vobasine (**3**)[20] in which the keto group C-3 (δ_C 189.9) was replaced by a methine [δ_H 5.31 (1H, dd, J = 13, 2.4 Hz), δ_C 37.6] in **1**.

The connection of the hydrovoacandimine A unit to the vobasine unit via a C-3″−C-11′ bond was established from HMBC correlations of H-3′′ to C-10′, C-11′, and C-12′ (Figure 1). Analysis of the 1D and 2D NMR spectra (Figure 1)

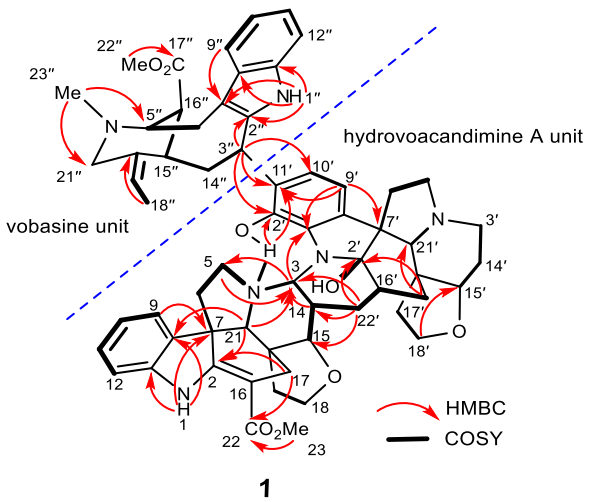

Figure 1. Selected 2D NMR correlations for **1**.

allowed the assignment of the gross structure of **1** to be the first example of a monoterpene trisindole alkaloid constituted by a vobasine-aspidosperma-aspidosperma skeleton.

Analysis of the 2D NMR spectra revealed that the chelated phenol signal at OH-12′ [δ_H 14.39 (1H, s)] displayed subtle, but unexpected ^{1}H−^{1}H COSY (Figure S13, Supporting Information) correlations with H-21 [δ_H 4.16 (1H, s)], H-3 [δ_H 4.35 (1H, d, J = 12.0 Hz)], and H-5 [δ_H 3.03 (1H, td, J = 10.9, 5.7 Hz)], in addition to its HMBC correlations with C-12′ and C-11′ (Figure S15, Supporting Information). Interestingly, the chemical shift of OH-12′ was remarkably deshielded in **1** compared to voacandimine A (δ_H 12.76) and other dimeric alkaloids that possess this functional group at this position. Moreover, Takayama et al. did not report on those puzzling 2D NMR correlations in the course of their elucidation of voacandimine A.[17] The presence of the additional monomer in **1** may increase the spatial proximity between OH-12′ and N-4 to enable this through-space scalar coupling. These so-called "through-bond" and "through-space" NMR spectroscopic J coupling effects are a well-described phenomenon.[21] Although most NMR textbooks describe the indirect spin−spin (scalar) J-coupling of nuclear magnetic momenta as a purely through-bond interaction mediated by the covalent link of two atoms, it has recently been demonstrated that through-space scalar couplings can be observed between two hydrogen nuclei.[22] Although less common, a case of through-hydrogen bond $^3J_{H,H}$ coupling has been described across adenine−uracil base pairs in RNA.[23] Hydrogen bonds generally weaken as a consequence of a temperature increase due to larger thermal motion, and H-bond weakening leads to an upfield shift of the proton resonance to a greater extent in the case of intermolecular interactions. Thus, to characterize the hydrogen-bonding strength of the hydroxy proton (OH-12′), its dependency on the temperature has been investigated through a variable-temperature ^{1}H NMR experiment (243 to 303 K, $CDCl_3$, 10 mM, Figure S5-A, Supporting Information) and a temperature coefficient determination [$\Delta\delta/\Delta T$(K)]. The temperature coefficient of OH-12′ was −3 ppb/K (Figure S5-B, Supporting Information), confirming its robustness and intramolecular nature.[24]

The absolute configuration of **1** was determined by a combination of ROESY studies, ^{1}H−^{1}H J-coupling constant magnitude analysis, extensive molecular modeling, and DFT calculations. In the vobasine unit, the ROESY correlations observed between H-15″ (δ_H 3.95) and H_3-18″ (δ_H 1.48) established the *E*-configuration of the ethylidene side chain. The configuration of C-16″ was assigned as *S* by the characteristic highly shielded chemical shifts of the methoxy group at C-16″ (δ_H 2.54), due to the anisotropic effect of the indole ring.[16] H-3″ was assigned a β-orientation by comparing its coupling constant values (dd, J = 13, 2.4 Hz) with the literature.[16] Collectively, ROESY correlations observed between (i) H-3″ and H-15′′, (ii) H-15′′ and H-16′′, and (iii) H-16′′ and H-5′′ further confirmed the relative configuration of this unit. Regarding the hydrovoacandimine A unit, ROESY correlations observed between H-9, H-21, H-14, H-19, H-16′, H-19′, and H-21′ suggested that they were cofacial and randomly assigned as α-oriented (red arrows, Figure 2). On

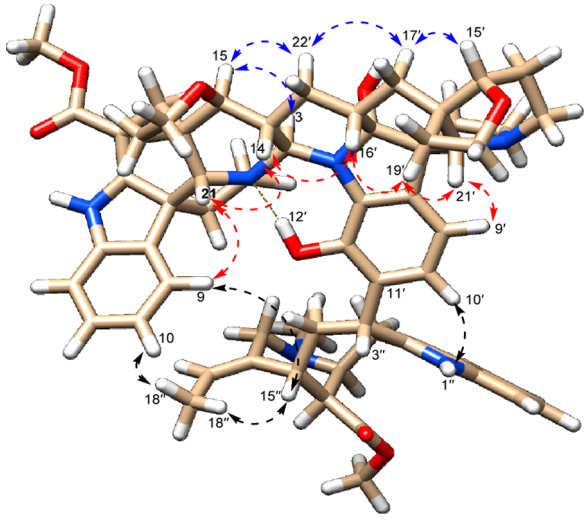

Figure 2. Selected 2D ROESY correlations for **1** (calculated at the B3LYP/6-31G* level).

the other hand, the ROESY cross-peaks observed between H-3, H-15, H-22′a, H-17′a, and H-15′ indicated that these protons were β-oriented (blue arrows, Figure 2). Furthermore, the β-configuration of the OH group at C-2′ was deduced from the upfield chemical shift of C-6′ (δ_C 29.8) owing to a γ-gauche effect.[17,18,25] At last, the conformation of **1** through the C-3″−C-11′ bond was assigned by the interunit ROESY correlations of H-9/H-15′′, H-10/H_3-18″, and NH-1′′/H-10′, as shown in

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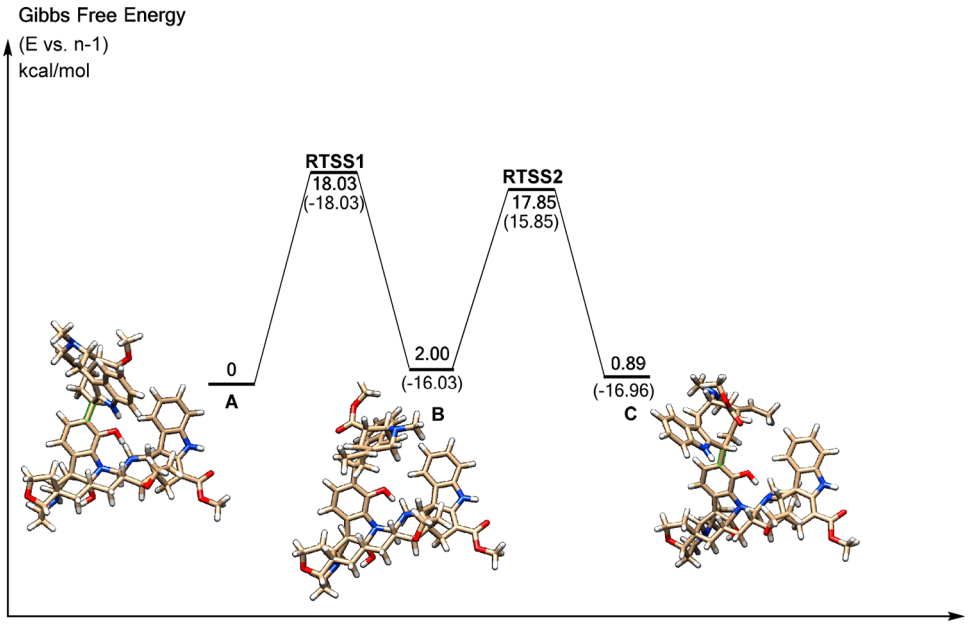

Figure 3. Free energy profile connecting minima A, B, and C to rotational transition state structures (RTSS1 and RTSS2) involved in the rotation of **1** through C-3″−C-11′ (calculated at the B3LYP/6-31G* level of theory).

the lowest-energy conformer 3D model of **1** (black arrows, Figure 2).

The energy barriers to rotation of **1** across this bond were calculated in the framework of DFT. Two rotational transition state structures (RTSSs) **1** and **2** were calculated at the B3LYP/6-31G* level (Figure 3). Free energy barriers $\Delta G^{\ddagger}_{298.15\ K}$ of 18.0 and 17.9 kcal/mol, equal to the 18 kcal/mol value considered surmountable by thermal activation at room temperature,[26] confirmed the free rotation through the C-3″−C-11′ bond. Thus, the relative configuration of **1** was established as shown.

The absolute configuration of **1** was elucidated by comparing its experimental ECD curve with a computationally derived theoretical spectrum (Figure 4). The consensus of both spectra allowed the absolute configuration of voatriafricanine A (**1**) to be assigned as shown.

Voatriafricanine B (**2**) was isolated as a yellow amorphous solid. Its molecular formula was determined to be $C_{63}H_{72}N_6O_9$ from its monocharged molecular ion at m/z 1057.5421 [M + H]$^+$ in the HRESIMS, indicating a molecular weight of 30 mass units higher than **1**. The ^{1}H and ^{13}C NMR data of **2** (Table S6, Supporting Information) are strikingly similar to those of voatriafricanine A (**1**), exhibiting the same deshielded hydrogen-bonded phenol OH-12′ resonating at δ_H 14.94. The main differences between ^{1}H NMR spectra of **2** and **1** were the presence of an additional signal for a methoxy group at δ_H 3.88 in **2** in conjunction with a pronounced upfield shift of the indole aromatic signals. This observation was further confirmed by the location of the additional methoxy group at C-12 from the HMBC cross-peak between δ_H 3.88 and δ_C 144.4, typical of the C-12 position.[27] These observations, in combination with an analysis of COSY, HSQC, and HMBC spectra, strongly suggested that **2** corresponds to 12-methoxy-voatriafricanine A. The relative configuration of **2** was determined to be identical with that of **1** based on the similarity of the ROESY correlations. The absolute configuration of compound **2** was determined by comparing its experimental ECD spectrum with the spectrum of **1** (Figure S9, Supporting Information).

Inspired by previous studies,[28] the *in vitro* antibacterial activities of compounds **1** and **2** were evaluated against *Mycobacterium smegmatis*, *M. abscessus*, *M. bovis* BCG, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* (Table 2). While voatriafricanine B (**2**) was inactive against all tested bacteria, voatriafricanine A (**1**) showed good antimycobacterial activity on the three mycobacterial species. This activity was

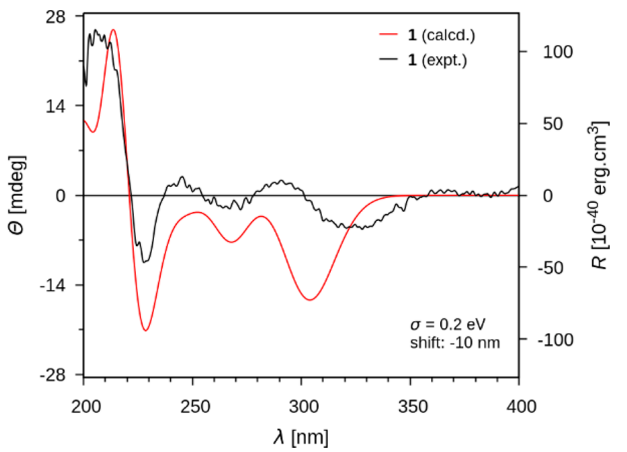

Figure 4. ECD spectra of **1** (experimental and calculated at the B3LYP/6-31G* level).

Table 2. Minimum Inhibitory Concentration (MIC, μg/mL) of 1 and 2[a]

sample	*M. smegmatis*	*M. abscessus*	*M. bovis*	*S. aureus*	*P. aeruginosa*
1	25	25	25	>100	>50
2	>100	>100	>100	>100	>100
standards[b]	0.1	0.1	0.1	1	0.1

[a]Values are mean of three independent experiments. [b]Vancomycin (*S. aureus*), cetrimide (*P. aeruginosa*), rifampicin (*M.* spp).

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clearly bactericidal, as *M. bovis* BCG proliferation could not be recovered after transfer on medium without voatriafricanine A (**1**) but did not involve loss of outer membrane cell wall integrity, as vancomycin was unable to synergize with **1**.[29] Notably, compounds **1** and **2** showed no cytotoxicity (IC_{50} > 25 μg/mL) on the human SiHa cell line. The specific and toxic activity of **1** toward pathogenic *Mycobacterium* spp. (*M. bovis* BCG and *M. abscessus*) should be further investigated.

EXPERIMENTAL SECTION

General Experimental Procedures. The optical rotations were measured in MeOH at 25 °C on a Polaar 32 polarimeter. Ultraviolet (UV) spectra were measured on a Lightwave II+ WPA 7126 V. 1.6.1 spectrophotometer. ECD spectra were measured at 25 °C on a JASCO J-810 spectropolarimeter. Infrared (IR) spectra were recorded with a PerkinElmer type 257 spectrometer. Exact mass HRESIMS data were recorded using an Agilent 6530 Accurate-Mass QTOF mass spectrometer (Agilent Technologies, Santa Clara, CA, USA) in positive ion mode. ^1H, ^{13}C, and 2D NMR spectra were recorded on a Bruker AM-600 (600 MHz) apparatus equipped with a microprobe TXI 1.7 mm, and a Bruker AM-600 (600 MHz) equipped with a cryoprobe TCI 5 mm using $CDCl_3$ as solvent. The solvent signals were used as references. Multiplicities are described by the following abbreviations: s = singlet, d = doublet, t = triplet, q = quadruplet, brs = broad singlet, brd = broad doublet, ddd = doublet of doublet of doublets, dq = doublet of quadruplets, dt = doublet of triplets. Sunfire preparative C18 columns (150 × 19 mm, i.d. 5 μm, Waters) were used for preparative HPLC separations with a Waters Delta Prep equipped with a binary pump (Waters 2525) and a UV−visible diode array detector (190−600 nm, Waters 2996). Silica 330, 80, and 120 g Grace cartridges were used for flash chromatography with an Armen Instrument−spot liquid chromatography flash apparatus. Chemicals and solvents were purchased from Sigma-Aldrich.

Plant Material. The fresh bark of *V. africana* [Yaounde National Herbarium voucher specimen No. HNY/1949; Victor Nana (collector)] was collected from the campus of the University of Yaoundé I, Cameroon, in December 2019 and oven-dried at 30 °C.

Extraction and Isolation. The air-dried and powdered bark of *V. africana* (2.3 kg) was extracted three times with MeOH at room temperature. The resulting extract was concentrated under reduced pressure to obtain a crude extract (231 g). The obtained extract was dissolved in a MeOH−H_2O 10% mixture and alkalinized with NH_3 (pH = 12), then extracted with CH_2Cl_2 (3 × 1.5 L, 1 h each, 20 °C, atmospheric pressure). The mixture was concentrated under vacuum at 38 °C to yield 50.5 g of an alkaloid extract. A part of this residue (VADCM, 25 g) was subjected to flash chromatography using a silica 330 g Grace cartridge with a gradient of CH_2Cl_2−MeOH (100:0 to 0:100) at 80 mL/min to afford 15 fractions, VA1−VA15, according to their TLC profiles. Fraction VA4−VA6 (14.7 g) was subjected to a second flash chromatography using a silica 120 g Grace cartridge with a gradient of CH_2Cl_2−MeOH (100:0 to 0:100) at 80 mL/min to afford 13 fractions, VA.B1−VA.B13, according to their TLC profiles. VA.B6 (1.72 g) was then submitted to Sephadex LH20 (4 cm × 90 cm) and eluted with a mixture of MeOH−CH_2Cl_2 (8:2) to afford 15 fractions, VA.B6.1−VA.B6.15, according to their TLC profiles. VA.B6.7 (761 mg), named KQ, was subjected again to Sephadex LH20 (4 cm × 90 cm) and eluted with a mixture of MeOH−CH_2Cl_2 (8:2) to afford 13 fractions, KQ1−KQ13, according to their TLC profiles. KQ4 underwent a preparative HPLC separation using a gradient of MeOH−H_2O with 0.1% formic acid (gradient 10−80% in 25 min) to give compound **1** (10.1 mg, yield = 0.000 44%) and compound **2** (4.1 mg, yield = 0.000 178%).

*Voatriafricanine A (**1**):* yellow amorphous powder; $[\alpha]^{25.0}_D$ +360 (*c* 0.05, MeOH); IR ν_{max} 3400, 1720 cm^{-1}; UV (MeOH) λ_{max} (log ε) 254.7 (2.42), 296.1 (3.3), 330 (3.0) nm; ^1H and ^{13}C NMR data, see Table 1; HRESIMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{62}H_{70}N_6O_8$, 1027.5328; found 1027.5324; MS/MS spectrum was deposited in the GNPS spectral library under the identifier CCMSLIB00006675746

*Voatriafricanine B (**2**):* yellow amorphous powder; $[\alpha]^{25.0}_D$ +320 (*c* 0.06, MeOH); IR ν_{max} 3400, 1720 cm^{-1}; UV (MeOH) λ_{max} (log ε) 288.8 (2.42), 293.6 (3.25), 330 (3.0) nm; ^1H and ^{13}C NMR data, see Table S5; HRESIMS (ESI) *m/z* $[M + H]^+$ calcd for $C_{63}H_{72}N_6O_9$, 1057.5434; found 1057.5421; MS/MS spectrum was deposited in the GNPS spectral library under the identifier CCMSLIB00006675747

Data-Dependent LC-HRMS² Analyses. LC-ESI-HRMS² analyses were achieved by coupling the LC system to a hybrid quadrupole time-of-flight mass spectrometer, Agilent 6530 (Agilent Technologies, Massy, France), equipped with an ESI source, operating in positive ion mode. Source parameters were set as follows: capillary temperature at 320 °C, source voltage at 3500 V, sheath gas flow rate at 10 L min^{-1}. The divert valve was set to waste for the first 3 min. MS scans were operated in full-scan mode from *m/z* 100 to 1700 (0.1 s scan time) with a mass resolution of 11 000 at *m/z* 922. MS1 scan was followed by MS^2 scans of the three most intense ions above an absolute threshold of 5000 counts. Selected parent ions were fragmented with three collision energies fixed at 30, 50, and 70 eV and an isolation window of 1.3 amu. A calibration solution was used, containing two internal reference masses (purine, $C_5H_4N_4$, *m/z* 121.050873, and HP-921 [hexakis(1*H*,1*H*,3*H*-tetrafluoropentoxy)-phosphazene], $C_{18}H_{18}O_6N_3P_3F_{24}$, *m/z* 922.0098). A permanent MS/MS exclusion list criterion was set to prevent oversampling of the internal calibrant. LC-UV and MS data acquisition and processing were performed using MassHunter Workstation software (Agilent Technologies, Massy, France).

LC-MS/MS Processing and Molecular Networking Parameters. The MS^2 data files related to the alkaloid extract of the barks of *V. africana* were converted from the .d (Agilent) standard data-format to .mzXML format using the MSConvert software, part of the ProteoWizard package.[30] A molecular network was created using the online Molecular Networking workflow (version release_8) at GNPS[12] (http://gnps.ucsd.edu) with a parent mass tolerance of 0.02 Da and an MS/MS fragment ion tolerance of 0.02 Da. A network was then created where edges were filtered to have a cosine score above 0.65 and more than six matched peaks. Further edges between two nodes were kept in the network if, and only if, each of the nodes appeared in each other's respective top 10 most similar nodes. The spectra in the network were then searched against GNPS spectral libraries. All matches kept between network spectra and library spectra were required to have a score above 0.6 and at least six matched peaks. The molecular networking data were analyzed and visualized using Cytoscape (ver. 3.6.0).[31]

Biological Evaluation. See S1, Supporting Information.

Computational Details. See S7 and S8, Supporting Information.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.jnatprod.1c00812.

UHPLC-DAD-MS2 analysis, 1D and 2D NMR spectra for **1** and **2**; Cartesian coordinates of the conformers of **1** (PDF)

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Notes

The authors declare no competing financial interest.

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