JOC*Note*

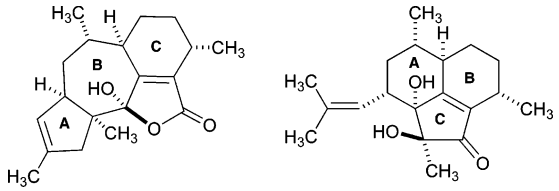
Caribenols A and B, Sea Whip Derived Norditerpenes with Novel Tricarbocyclic Skeletons

Xiaomei Wei,[†] Ileana I. Rodríguez,[†]
Abimael D. Rodríguez,*[,†] and Charles L. Barnes[‡]

Department of Chemistry, University of Puerto Rico, P.O. Box 23346, U.P.R. Station, San Juan, Puerto Rico 00931-3346, and Department of Chemistry, 123 Chemistry Building, University of Missouri—Columbia, Columbia, Missouri 65211

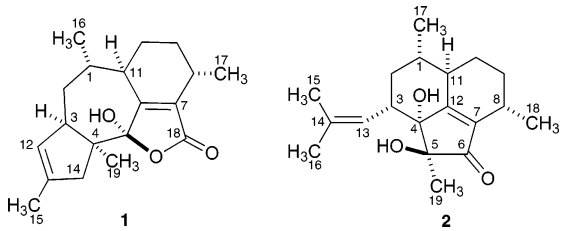
abrodriguez@uprrp.edu

Received April 2, 2007



The extraction of two specimens of *Pseudopterogorgia elisabethae*, each collected from a different location at the San Andrés Archipelago, afforded two new norditerpenes, caribenols A (**1**) and B (**2**). Metabolites **1** and **2** contain unusual carbon skeletons that are previously undescribed and therefore constitute new classes of C_{19} rearranged terpenes. Their molecular structures were established by a combination of single-crystal X-ray analysis and comprehensive 2D NMR measurements.

The West Indian gorgonian octocoral *Pseudopterogorgia elisabethae* (Bayer) has proven to be an extraordinary source of bioactive terpenoids with complex and unique carbon frameworks.[1] In the interest of identifying novel antiinfective and anticancer leads from this chemically prolific animal, we have examined two *P. elisabethae* chemotypes from the San Andrés Archipelago (Colombia). The first chemotype, collected off the shores of Old Providence (Providencia) Island (located at 13°21′N 81°22′W) in March 2002, yielded 11 pseudopterosins, called pseudopterosins P−Z, which were reported in an earlier publication.[2] From the second chemotype, collected near San Andrés Island (located at 12°33′N 81°43′W) in May 1996, were isolated a myriad of structurally diverse terpenoids, many possessing unique structural features (elisabethanes, elisapteranes, cumbianes, and others).[3] In this paper, we report two additional minor norditerpenes, called caribenols A (**1**) and B (**2**),



obtained from each chemotype, respectively, which represent novel diterpene-type skeletons. In each case, the freeze-dried gorgonian was extracted with 1:1 MeOH−$CHCl_3$ (or MeOH−CH_2Cl_2), and the hexane-soluble part of the extract was subjected to size exclusion chromatography followed by column chromatography and normal-phase HPLC to yield compounds **1** and **2**.[4]

Caribenol A (**1**; 9.0 mg) was obtained as a white crystalline material, and the molecular formula $C_{19}H_{26}O_3$ was determined by HRESIMS. The IR spectrum showed absorptions at 3398 (hydroxyl group), 1737 (α,β-unsaturated γ-lactone), and 1648 cm^{-1} (C═C). The UV (MeOH) absorbances at λ_{max} 207 nm (ϵ 9800) and 220 (ϵ 9100) supported the presence of a α,β-unsaturated butyrolactone.

The ^1H NMR spectrum of **1** acquired in C_6D_6 indicated the presence of four methyl groups. Two methyl singlets overlapped at δ 1.56 and two doublets at δ 1.50 (J = 6.9 Hz) and 0.84 (J = 6.7 Hz) accounted for the remaining two methyls. It also exhibited one broad singlet with fine splitting at δ 4.98 (1H), ascribed to a trisubstituted olefin group, and a pair of AB doublets (J = 16.7 Hz) at δ 1.85 and 2.10, due to an isolated methylene unit. Nineteen carbon signals appeared in the ^{13}C NMR spectrum, including a carbonyl carbon signal at δ 169.2 (C18), and olefinic carbon signals at δ 163.1 (C6) and 132.9 (C7) indicated an α,β-unsaturated γ-lactone. The signals at δ 127.1 (CH, C12) and 137.6 (C, C13) suggested a trisubstituted olefin.

Connectivities from C1 to C3 and from C8 to C11 were inferred from the COSY cross-peaks, including correlations from H-1 to H-11 and H_3-16, H-3 to H-12, and H-8 to H_3-17. Long-range couplings of H-12 with H-14β and H_3-15 and of H_3-19 with both H_2-14, indicated connectivity from C12 to C15 and C19. Further connectivities among the isolated spin systems in **1** were determined by the correlations in the HMBC spectra: C3 [H_3-19], C4 [H-14α, H_3-19], C5 [H_3-19], C7 [H_3-17], C13 [H-12, H-14α, H_3-15], C14 [H-12, H_3-15, H_3-19], and C18 [H-8]. Confirmation of the substitution pattern as well as the connectivities of all the ring systems found in **1** came from

* To whom correspondence should be addressed. Tel: (787) 764-0000. Ext. 4799. Fax: (787) 756-8242.
[†] University of Puerto Rico.
[‡] University of Missouri—Columbia.

(1) Heckrodt, T. J.; Mulzer, J. *Top. Curr. Chem.* **2005**, *244*, 1−41.
(2) Rodríguez, I. I.; Shi, Y.-P.; García, O. J.; Rodríguez, A. D.; Mayer, A. M. S.; Sánchez, J. A.; Ortega-Barria, E.; González, J. *J. Nat. Prod.* **2004**, *67*, 1672−1680.
(3) (a) Rodríguez, A. D.; González, E.; Huang, S. D. *J. Org. Chem.* **1998**, *63*, 7083−7091. (b) Rodríguez, A. D.; Ramírez, C.; Rodríguez, I. I.; Barnes, C. L. *J. Org. Chem.* **2000**, *65*, 1390−1398. (c) Rodríguez, A. D.; Ramírez, C.; Rodríguez, I. I. *Tetrahedron Lett.* **1999**, *40*, 7627−7631. (d) Rodríguez, A. D.; Shi, Y.-P. *Tetrahedron* **2000**, *56*, 9015−9023. (e) Rodríguez, A. D.; Ramírez, C.; Shi, Y.-P. *J. Org. Chem.* **2000**, *65*, 6682−6687. (f) Rodríguez, A. D.; Ramírez, C. *Org. Lett.* **2000**, *2*, 507−510. (g) Rodríguez, A. D.; Ramírez, C.; Rodríguez, I. I. *J. Nat. Prod.* **1999**, *62*, 997−999.
(4) For a complete list of crossover products, see the Supporting Information.

10.1021/jo070649n CCC: $37.00
Published on Web 08/23/2007

TABLE 1. ^{1}H NMR (300 MHz), ^{13}C NMR (75 MHz), ^{1}H−^{1}H COSY, NOESY, and HMBC Spectral Data of Caribenol A (1)[a]

position	δ_H, mult, intrgt (*J*, Hz)	δ_C (mult)[b]	^{1}H−^{1}H COSY	NOESY	HMBC[c]
1	1.13, m, 1H	30.9 (CH)	H2α*β*, H11, H_3-16	H10*β*, H14*β*, H_3-16	H_3-16
2α	1.35, dd, 1H (2.8, 14.5)	39.3 (CH_2)	H1, H2*β*, H3	H2*β*, H3, H11, H_3-16	H_3-16
2*β*	2.19, m, 1H		H1, H2α, H3	H2α, H3, H12, H_3-16	
3	2.51, br m, 1H	53.7 (CH)	H2α*β*, H12	H2α*β*, H12, H_3-19	H2α, H12, H14α, H_3-19
4		49.3 (C)			H2α, H12, H14α, H_3-19
5		109.3 (C)			H_3-19
6		163.1 (C)			
7		132.9 (C)			H_3-17
8	2.32, m, 1H	27.9 (CH)	H9α*β*, H_3-17	H9*β*, H10*β*, H_3-17	H_3-17
9α	0.96, m, 1H	31.9 (CH_2)	H8, H9*β*, H10α*β*	H9*β*, H11, H_3-17	H_3-17
9*β*	1.62, m, 1H		H8, H9α, H10α*β*	H8, H9α, H_3-17	
10α	0.85, m, 1H	28.5 (CH_2)	H9α*β*, H10*β*, H11	H10*β*, H_3-16	
10*β*	1.75, m, 1H		H9α*β*, H10α, H11	H1, H8, H10α	
11	1.76, m, 1H	43.1 (CH)	H1, H10α*β*	H2α, H9α, H_3-16	H2α, H_3-16
12	4.98, br s, 1H	127.1 (CH)	H3, H14*β*, H_3-15	H2*β*, H3, H_3-15	H2*β*, H14α, H_3-15
13		137.6 (C)			H12, H14α, H_3-15
14α	1.85. br d, 1H (16.7)	47.0 (CH_2)	H14*β*, H_3-19	H14*β*, H_3-15, H_3-19	H12, H_3-15, H_3-19
14*β*	2.10, br d, 1H (16.7)		H14α, H_3-19	H1, H14α	
15	1.56, s, 3H	16.3 (CH_3)	H12	H12, H14α	
16	0.84, d, 3H (6.7)	22.1 (CH_3)	H1	H1, H2α*β*, H10α, H11	H2α
17	1.50, d, 3H (6.9)	18.5 (CH_3)	H8	H8, H9α*β*	
18		169.2 (C)			H8
19	1.56, s, 3H	25.4 (CH_3)	H14α*β*	H3, H14α	H14α

[a] Spectra were recorded in C_6D_6 at 25 °C. Chemical shift values are in parts per million relative to TMS. Assignments were aided by HMQC experiments. [b] ^{13}C NMR multiplicities were obtained from a DEPT-135 experiment. [c] Protons correlated to carbon resonances in the ^{13}C column.

additional HMBC correlations found in Table 1 and the NOESY spectra, establishing the gross structure of caribenol A. A search of the literature did not reveal any known compounds of this skeletal type. While the spectral data of compound **1** were in full accord with the proposed structure for the molecule, an unambiguous proof of the structure was highly desirable. The structure of caribenol A (**1**) was, therefore, confirmed by a single-crystal X-ray diffraction experiment, which also yielded its relative stereochemistry (ORTEP drawing in the Supporting Information).[5] Hence, the 5,7,6-tricarbocyclic norditerpene caribenol A (**1**) presents a novel carbon skeleton.

Caribenol B (**2**; 3.1 mg) was obtained as a transparent oil, and its molecular formula $C_{19}H_{28}O_3$ was determined by HRES-IMS. IR bands at 3412 (s, br), 1704 (s), and 1632 cm^{-1} (m-s) pointed to hydroxyl, conjugated ketone carbonyl, and C=C functions. The UV (MeOH) spectrum, with maxima at λ_{max} 202 (ϵ 13 000) and 227 nm (ϵ 7000), was reminiscent of a five-membered α,*β*-unsaturated ketone functionality.[6] The ^{1}H and ^{13}C NMR data (Table 2) of **2** showed signals for an isobutenyl (C13−C16) group, a fully substituted α,*β*-unsaturated cyclopentenone ring (C4−C7, C12), and a *vic*-glycol moiety (C4−C5), a pattern with no similarity to that of any previously known metabolite.[7] The observed correlations in the COSY spectra indicated an uninterrupted $CH_3CHCH_2CH_2CHCH(CH_3)CH_2$-$CHCH{=}C(CH_3)_2$ (C18−C8−C9−C10−C11−C1(C17)−C2−C3−C13−C14(C15,C16)) spin system (Figure 1). The long-range heteronuclear correlations (Figure 1) of H-11 (δ 2.17) to C7 (δ 136.7) and C12 (δ 175.3), H_3-18 (δ 1.25) to C7, H-2*β* (δ 1.40) to C4 (δ 76.2), and H_3-19 (δ 1.23) to C4, C5 (δ 77.6), and C6 (δ 207.9), connected C4, C5, C6, C7, and C12 with the substructure to form the perhydroacenaphthene-type ring array depicted in structure **2**.[8] Thus, the planar structure of caribenol B was elucidated and represents a novel norditerpene ring system.

To determine the relative stereochemistry of caribenol B (**2**), a combination of NOESY experiments and molecular modeling analysis was employed. The overall conformations of the six-membered rings can be described as a chair (ring A) and half-chair (ring B), respectively. In the NOESY spectrum, the strong correlations of H-1 (δ 1.32) to H-3 (δ 2.36) and of H-11 (δ 2.17) to H_3-17 (δ 1.04) indicated that H-11, H_3-17, and the isobutenyl group at C-3 were α in orientation and H-1 and H-3 were *β* in configuration (arbitrary relative assignments). The observed strong NOESY correlations of H-8 (δ 2.39) and H-10*β* (δ 1.19) implied that H_3-18 was α in orientation.[9] Because the five-membered *vic*-glycol moiety could exist in several different conformations, a conformational analysis was essential for the determination of the configurations of both the 4- and 5-hydroxyl groups. The conformation with minimized energy by molecular modeling is shown in Figure 2. A relatively large coupling constant (9.0 Hz) between the protons at C3 and C13 indicated

(5) Crystal data for caribenol A (**1**) at 173(2) K: $C_{19}H_{26}O_3$, M_r = 302.40, orthorhombic, space group $P2_12_12_1$, a = 8.5337(8) Å, b = 12.4631(11) Å, c = 15.9278(14) Å, V = 1694.0(3) Å^3, Z = 4, ρ_{calcd} = 1.186 Mg m^{-3}, F_{000} = 656, λ(Mo Kα) = 0.710 73 Å, μ = 0.078 mm^{-1}. Data collection and reduction: crystal size 0.50 × 0.10 × 0.10 mm^3, θ range 2.07−24.72°, 6047 reflections collected, 1622 independent reflections (R_{int} = 0.0292), final R indices ($I > 2\sigma(I)$) R1 = 0.0337, wR2 = 0.0747 for 207 variable parameters, GOF = 1.059. CCDC 618665 (**1**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax (+44)1223-336-033; deposit@ccdc.cam.ac.uk).

(6) Lambert, J. B.; Shurvell, H. F.; Lightner, D. A.; Cooks, R. G. *Organic Structural Spectroscopy*; Prentice Hall: Upper Saddle River, NJ, 1998; pp 304−344.

(7) Blunt, J. W.; Copp, B. R.; Hu, W.-P.; Munro, M. H. G.; Northcote, P. T.; Prinsep, M. R. *Nat. Prod. Rep.* **2007**, *24*, 31−86, and previous articles in this series.

(8) For three structurally related diterpenoids based on a similar ring array, although with distinct alkylation/substitution patterns, see: (a) Rodríguez, A. D.; Rodríguez, I. I. *Tetrahedron Lett.* **2002**, *43*, 5601−5604. (b) Rodríguez, I. I.; Rodríguez, A. D.; Wang, Y.; Franzblau, S. G. *Tetrahedron Lett.* **2006**, *47*, 3229−3232. (c) König, G. M.; Wright, A. D.; Angerhofer, C. K. *J. Org. Chem.* **1996**, *61*, 3259−3267.

(9) The ^{13}C NMR resonances of **2** ascribable to C-8 (δ_C 28.0) and C-18 (δ_C 18.2) are highly comparable with those of **1** (27.9 and 18.5 ppm) and amphilectolide (27.3 and 17.8 ppm), suggesting that these compounds must possess the same relative stereochemistry at C-8; see the Supporting Information and: Rodríguez, A. D.; Ramírez, C.; Medina, V.; Shi, Y.-P. *Tetrahedron Lett.* **2000**, *41*, 5177−5180.

TABLE 2. ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), ^{1}H−^{1}H COSY, NOESY, and HMBC Spectral Data of Caribenol B (2)[a]

position	δ_H, mult, intrgt (J, Hz)	δ_C (mult)[b]	^{1}H−^{1}H COSY	NOESY	HMBC[c]
1	1.32, m, 1H	37.7 (CH)	H2αβ, H11, H$_3$-17	H3, H10β	H2α, H$_3$-17
2α	1.63, m, 1H	37.0 (CH$_2$)	H1, H2β, H3	H2β, H13, H$_3$-17	H$_3$-17
2β	1.40, dt, 1H (3.5, 13.5)		H1, H2α, H3	H2α, H3, H$_3$-17	
3	2.36, m, 1H	41.5 (CH)	H2αβ, H13	H1, H2β, H$_3$-15	H2α
4		76.2 (C)			H2β, H$_3$-19
5		77.6 (C)			H$_3$-19
6		207.9 (C)			H$_3$-19
7		136.7 (C)			H9β, H11, H$_3$-18
8	2.39, m, 1H	28.0 (CH)	H9αβ, H$_3$-18	H9α, H10β, H$_3$-18	H$_3$-18
9α	1.23, m, 1H	31.4 (CH$_2$)	H8, H9β, H10αβ	H9β, H10α, H11	H$_3$-18
9β	1.88, m, 1H		H8, H9α, H10αβ	H8, H9α, H10β, H$_3$-18	
10α	2.13, m, 1H	26.4 (CH$_2$)	H9αβ, H10β, H11	H9α, H10β, H$_3$-17	
10β	1.19, m, 1H		H9αβ, H10α, H11	H1, H8, H9β, H10α	
11	2.17, m, 1H	41.0 (CH)	H1, H10αβ	H9α, H$_3$-17	H2αβ, H$_3$-17
12		175.3 (C)			H11
13	5.44, br d, 1H (9.0)	123.5 (CH)	H3, H$_3$-15, H$_3$-16	H2α, H$_3$-16, H$_3$-19	H3, H$_3$-15, H$_3$-16
14		132.2 (C)			H$_3$-15, H$_3$-16
15	1.62, br s, 3H	18.4 (CH$_3$)	H13	H3	H13, H$_3$-16
16	1.74, br s, 3H	26.0 (CH$_3$)	H13	H13	H$_3$-15
17	1.04, d, 3H (6.5)	19.6 (CH$_3$)	H1	H2αβ, H10α, H11	
18	1.25, d, 3H (6.5)	18.2 (CH$_3$)	H8	H8, H9β	
19	1.23, s, 3H	21.5 (CH$_3$)		H13	
4-OH	3.43, br s, 1H (exchangeable)[d]				
5-OH	2.81, br s, 1H (exchangeable)[d]				

[a] Spectra were recorded in $CDCl_3$ at 25 °C. Chemical shift values are in parts per million relative to TMS. Assignments were aided by HSQC experiments. [b] ^{13}C NMR multiplicities were obtained from a DEPT-135 experiment. [c] Protons correlated to carbon resonances in the ^{13}C column. [d] Values with identical superscripts within the same column may be interchanged.

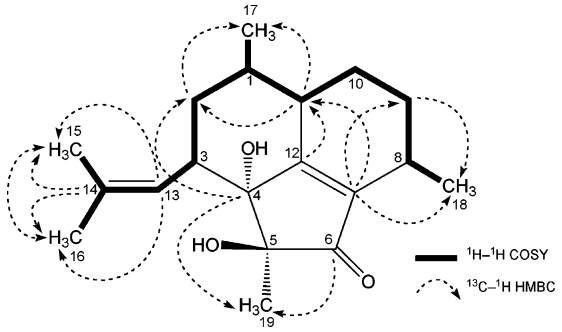


FIGURE 1. Partial structures for caribenol B (**2**) generated from ^{1}H−^{1}H COSY and HMBC spectral data.

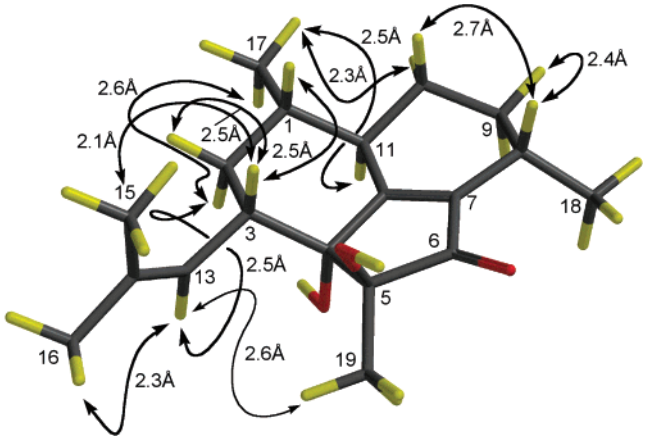


FIGURE 2. Conformation of **2** with minimized energy. The arrows show the NOE correlations, and the data are the distances in Å between correlated protons.

that the two protons have a nearly 180° dihedral angle in the preferred conformation. In addition, H-13 showed NOE correlations with both H$_3$-19 (δ 1.23) and H-2α (δ 1.63), and H$_3$-15 (δ 1.62) correlated with H-3 (δ 2.36), requiring an α,β (diaxial) 4,5-glycol functionality. The calculated distances between the NOE correlated protons are shown in Figure 2 and are highly consistent with the experimentally determined NOESY data.

Including **1** and **2**, a total of eight norditerpenes have been isolated thus far from this gorgonian species.[3a−d] While the biosynthetic origin of these intriguing C$_{19}$ terpenes remains uncertain, a biogenetic pathway involving the posterior rearrangement of either an amphilectane or a serrulatane-based precursor should not be ruled out.[10] Putative biogenetic pathways for some of these metabolites, including **1** and **2**, are given as Supporting Information.

Compounds **1** and **2** were found to have strong inhibitory activity (61% and 94%, respectively) against *Mycobacterium tuberculosis* (H$_{37}$Rv) (ATCC 27294) at a concentration range of 128−64 μg/mL.[11] At lower concentrations, however, their inhibitory activities were significantly diminished. From these results it was determined that caribenol A (**1**) and caribenol B (**2**) have MIC (μg/mL) values of >128 and 63, respectively. Furthermore, caribenol A (**1**) demonstrated weak in vitro antiplasmodial activity against chloroquine-resistant *Plasmodium falciparum* W2 (IC$_{50}$ 20 μg/mL).[12]

Experimental Section

Molecular Modeling. A system composed of rings A−C was constructed and submitted to conformational analysis. Each of the obtained conformations for caribenol B (**2**) was further submitted to full geometry optimization using AM1 semiempirical methods.

(10) (a) Coleman, A. C.; Kerr, R. G. *Tetrahedron* **2000**, *56*, 9569−9574. (b) Ferns, T. A.; Kerr, R. G. *J. Org. Chem.* **2005**, *70*, 6152−6157.
(11) Collins, L. A.; Franzblau, S. G. *Antimicrob. Agents Chemother.* **1997**, *41*, 1004−1009.
(12) Corbett, Y.; Herrera, L.; González, J.; Cubilla, L.; Capson, T.; Colley, P. D.; Kursar, T. A.; Romero, L. I.; Ortega-Barria, E. *J. Trop. Med. Hyg.* **2004**, *70*, 119−124.

The McSpartan '04 molecular modeling program was used to calculate the conformer distribution of each possible structure; key inter-proton distances were then measured on the lowest energy conformer. These distances are given in Figure 2 together with selected observed NOESY correlations. In order to obtain theoretical $^3J_{H,H}$ coupling constants for the minimum energy conformations produced in conformational analysis, we applied the Haasnot−Altona parametrization of the Karplus equation to the endocyclic angle geometries.[13]

Extraction and Isolation Procedures for *P. elisabethae* Collected at Old Providence Island To Obtain Caribenol A (1). Healthy specimens of *P. elisabethae* were collected by scuba at depths of 80−100 ft from the coral reefs off Old Providence Island, Colombia. The collection was partially air-dried (1.8 kg), freeze-dried, and kept frozen prior to homogenization in a mixture of 1:1 CH_2Cl_2−MeOH (5 × 4 L). After filtration and concentration the crude gummy extract (400 g) was suspended in water (1 L) and extracted successively with hexane (4 × 2 L), CH_2Cl_2 (4 × 2 L), and EtOAc (3 × 2 L). The hexane extract (323 g) was chromatographed on a large silica gel column by stepwise elution with 9:1 hexane−CH_2Cl_2, CH_2Cl_2, and MeOH. A total of 26 fractions, designated I−XXVI, were obtained. Fraction XIX (7.1 g) was dissolved in toluene, filtered over sand and Celite, and chromatographed on a Bio-Beads SX-3 column eluted with toluene. After size-exclusion chromatography, a terpene-rich portion (fraction D, 500 mg) stemming from fraction XIX was purified by HPLC (semipreparative, Cyano column using 98.5:1.5 hexane−2-propanol; all separations were monitored simultaneously by refractive index and UV absorption). The third fraction (15 mg) obtained from the latter separation was further purified by analytical HPLC (Cyano column in 99.5:0.5 hexane−2-propanol) to afford caribenol A (**1**; 9.0 mg).

Extraction and Isolation Procedures for *P. elisabethae* Collected at San Andrés Island To Obtain Caribenol B (2). *P. elisabethae* colonies were collected by hand using scuba at depths of 80−100 ft off San Andrés Island, Colombia. The gorgonian was sun-dried and kept frozen prior to its extraction. The dry animal (1.0 kg) was blended with MeOH−$CHCl_3$ (1:1) (11 × 1 L), and after filtration, the crude extract was evaporated under vacuum to yield a green residue (284 g). After the crude extract was partitioned between hexane and H_2O, the resulting hexane extract was concentrated in vacuo to yield 178 g of an oil, a portion of which (128 g) was separated by flash chromatography (silica gel (780 g) with stepwise elution of acetone in hexane (0−100%) and then 100% MeOH). Fractions were pooled on the basis of their TLC and NMR profiles to yield seven primary fractions, I−VII. The fraction obtained from 60% acetone in hexane (fraction IV (83.3 g)) was separated into 16 subfractions (a−p) by silica gel (600 g) column chromatography using a step gradient of EtOAc−hexane mixtures. Fraction f (15.5 g) was dissolved in a small volume of toluene, filtered, and loaded onto a Bio-Beads SX-3 column with toluene as eluent. Four fractions were obtained: fraction f1 (1.5 g), fraction f2 (2.4 g), fraction f3 (7.2 g), and fraction f4 (4.0 g). The penultimate terpenoid-rich fraction (f3) was further purified by column chromatography over silica gel (200 g) using 50% $CHCl_3$ in hexane. The most polar fraction (f3-H, 113 mg) stemming from the latter chromatographic separation was further purified by HPLC (Partisil-10 column in 97.5:2.5 hexane−2-propanol; all separations were monitored simultaneously by refractive index and UV absorption) to afford pure caribenol B (**2**; 3.1 mg).

Caribenol A (1): crystalline solid; $[\alpha]^{20}_D = +40.0°$ (*c* 1.0, $CHCl_3$); IR (film) 3398, 3087, 2929, 1737, 1648, 1376, 1245 cm^{-1}; UV (MeOH) λ_{max} 207 (ϵ 9800), 220 nm (ϵ 9100); ^1H NMR (C_6D_6, 300 MHz) and ^{13}C NMR (C_6D_6, 75 MHz) (see Table 1); HRESIMS *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{26}O_3$ 303.1960, found 303.1958.

Caribenol B (2): colorless oil; $[\alpha]^{20}_D = +26.8°$ (*c* 0.7, $CHCl_3$); IR (film) 3412, 2929, 1704, 1632, 1454, 1376 cm^{-1}; UV (MeOH) λ_{max} 202 (ϵ 13 000), 227 nm (ϵ 7000); ^1H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) (see Table 2); HRESIMS *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{28}O_3Na$ 327.1936, found 327.1931.

Acknowledgment. We thank Dr. Juan A. Sánchez (Universidad de Los Andes, Bogotá) for providing logistic support during the specimen collections. The Institute for Tuberculosis Research of the University of Illinois at Chicago and the Institute for Tropical Medicine and Health Sciences (Panama) provided in vitro antituberculosis and antimalarial activity data, respectively. I.I.R. thanks the US Department of Education GAANN Fellowship Program (Grant No. P200A030197-05) for financial support. This work was partially supported by the NIH-SCORE Program (Grant No. S06GM08102) of the University of Puerto Rico.

Supporting Information Available: X-ray crystallographic data (in CIF format) and an ORTEP drawing for **1**, description of crossover products isolated, known norditerpenes from *P. elisabethae*, key ^1H and ^{13}C NMR chemical shift comparison of caribenol B (**2**) and amphilectolide, plausible biosynthetic pathways, and 1D and 2D NMR spectra for **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO070649N

(13) Haasnot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783−2792.