Scalarane-Based Sesterterpenes from an Indonesian Sponge Strepsichordaia aliena

ARTICLE *in* JOURNAL OF NATURAL PRODUCTS · NOVEMBER 2000

Impact Factor: 3.8 · DOI: 10.1021/np0000771 · Source: PubMed

4 AUTHORS, INCLUDING:

Jorge I Jiménez
American River College
22 PUBLICATIONS **637** CITATIONS

SEE PROFILE

Article

Scalarane-Based Sesterterpenes from an Indonesian Sponge *Strepsichordaia aliena*

Jorge I. Jimnez, Wesley Y. Yoshida, Paul J. Scheuer, and Michelle Kelly

J. Nat. Prod., **2000**, 63 (10), 1388-1392 • DOI: 10.1021/np0000771

Scalarane-Based Sesterterpenes from an Indonesian Sponge *Strepsichordaia aliena*

Jorge I. Jiménez,[†] Wesley Y. Yoshida,[†] Paul J. Scheuer,*[,†] and Michelle Kelly[‡]

Department of Chemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822-2275, and Marine Ecology and Aquaculture Group, National Institute of Water and Atmospheric Research (NIWA), Taihoro Nukurangi, Private Bag 109-695 Newmarket, Auckland, New Zealand

Received February 14, 2000

Investigation of the lipophilic extract of the sponge *Strepsichordaia aliena* revealed six new 20,24-bishomoscalarane sesterterpenes, honu'enone (**1**), phyllofolactones H-K (**3**−**6**), and phyllofenone C (**7**). Structure elucidation of these compounds was secured by spectroscopic methods, 1D and 2D NMR, and accurate mass measurements.

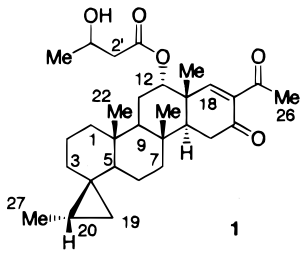
Pentaprenyl terpenoids (sesterterpenes) are widely distributed in fungi, lichens, higher plants, insects, and marine organisms. Their structures are derived from geranyl−farnesyl diphosphate.[1] Scalarane-based sesterterpenes possessing biological activities have been reported from sponges of the order Dictyoceratida.[2]

In a previous paper we reported the structures of 12 new sesterterpenes, honulactones A−L, from an Indonesian sponge *Strepsichordaia aliena* (family Thorectidae).[3] Further investigation of *S. aliena* has led to the isolation and characterization of six new 20,24-bishomoscalarane sestertepenes, honu'enone (**1**), phyllofolactones H−K (**3**−**6**), and phyllofenone C (**7**). Compounds **1** and **7** represent additional examples of 20,24-dimethyl-25-norscalarane sesterterpenes.

Results and Discussion

Honu'enone (**1**) was obtained as a colorless solid exhibiting a molecular ion peak (HRMS) at *m/z* 485.3267 corresponding to $C_{30}H_{44}O_5$. The ^{1}H and ^{13}C NMR spectra of **1** indicated the presence of four singlets and two doublets belonging to methyl groups resonating at δ 0.80, 0.94, 1.08, 1.22, and 2.45; nine methylenes; seven methynes; four quaternary carbons; and a fully substituted quaternary sp^2 carbon (δ 136.7) incorporated into an α,β-unsaturated diketone (two carbonyl carbons at δ 197.6 and 199.3). Initial inspection of the ^{1}H NMR spectrum indicated cyclopropane and hydroxybutanoyl protons similar to those observed for honulactones A and B.[3] However, the ^{1}H and ^{13}C signals associated with the substituted α,β-unsaturated γ-lactone in honulactones A and B were missing in compound **1** (Table 1). Instead, compound **1** showed new signals at δ 7.33 (H-18) corresponding to a trisubstituted sp^2 carbon (δ_C 164.2) and δ 2.45 (H-26) indicative of a methyl ketone (δ 30.7, 199.3). Analysis of the COSY spectrum allowed us to establish the following structural units: C-1 to C-3, C-5 to C-7, C-9 to C-12, C-14 to C-15, C-19 to C-20 to C-27, and C-2′ to C-4′.

Interpretation of the HMBC spectrum revealed correlations between H-3′ (δ 4.15) to C-2′ (δ 43.7)/C-4′ (δ 22.5) and H-2′ (δ 2.45) to C-1′ (δ 171.4)/C-3′ (δ 64.3)/C-4′, confirming the presence of a 3-hydroxybutanoate moiety attached to the oxygenated C-12 carbon [HMBC cross-peak correlation between H-12 (δ 5.09) and C-1′]. Positioning of the methyl ketone at C-17 was based on HMBC correlations observed from H-18 to C-12/C-13/C-14/C-17/C-24 and H-26 to C-17/C-24, thus providing further evidence of the lack of a γ-lactone. HMBC cross-peaks between H-14/H-15 to C-16



1

(δ 197.6) located the second carbonyl carbon at C-16. The cyclopropane signals at C-19 were connected to C-20, and both were connected to C-4: H-19$_{cis}$ and H-19$_{trans}$ showed correlations to C-4/C-20. Finally, the C-27 methyl doublet was placed on the C-20 cyclopropane ring based on HMBC correlation between H-27 and C-4, C-19, and C-20.

The small *J* value observed for H-12 indicated an equatorial hydrogen, which was also corroborated by a strong ROESY cross-peak between H-12 and H-11$_{eq}$/H-11$_{ax}$/H-18/H-23. The C-20 cyclopropane carbon had β-orientation, as a strong ROESY cross-peak was observed between H-20 and H-22. Relative configuration of the CH$_3$-27 group was assigned as *S** supported by ROESY cross-peaks between H-27 and H-3$_{ax}$, C-20, C-22, and H-19$_{trans}$. The all-trans A−B−C−D ring system was also confirmed by cross-peaks observed in the ROESY spectrum: H-11$_{ax}$ to H-21/H-22/H-23, H-15$_{ax}$ to H-21/H-23, and H-9$_{ax}$ to H-5$_{ax}$/H-14$_{ax}$.

The next five compounds were C-12 substituted C$_4$ and C$_5$ hydroxy esters of phyllofolactone A (**2**) previously isolated by Schmitz and co-workers from *Phyllospongia foliascens* collected in the South China Sea.[4,5] The ^{1}H and ^{13}C NMR spectra of compounds **3** and **4** indicated the presence of a 3-hydroxybutanoyl residue at C-12 in ring C, while phyllofolactones J (**5**) and K (**6**) showed a 3-hydroxypentanoyl moiety also attached to ring C at C-12 (Tables 2 and 3). Compounds **3** and **4** are stereoisomers at CH$_3$-26 configuration. 1D NOE experiments indicated that **3** is the β isomer; irradiation of H-24 produced a positive NOE on H-16$_{ax}$ and H-26, while irradiation of H-26 produced a positive NOE on H-16$_{eq}$ and H-24. On the other

* To whom correspondence should be addressed. Tel.: (808) 956-5904. Fax: (808) 956-5908. E-mail: scheuer@gold.chem.hawaii.edu.
[†] Department of Chemistry, University of Hawaii at Manoa.
[‡] Marine Ecology and Aquaculture Group, NIWA.

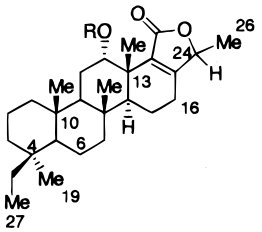
10.1021/np0000771 CCC: $19.00
Published on Web 09/28/2000

Table 1. ^{1}H NMR and ^{13}C NMR Data for Honu'enone (**1**) and Phyllofenone C (**7**)[a,b]

	honu'enone (**1**)		phyllofenone C (**7**)	
position	^{13}C	^{1}H (mult; J = Hz)	^{13}C	^{1}H (mult; J = Hz)
1	39.6	eq: 1.68, m ax: 0.73, m	40.1	eq: 1.60, m ax: 0.68 (ddd; 4, 13, 13)
2	21.0	1.45, m	17.9	1.40, m
3	33.0	eq: 1.54, m ax: 1.22, m	36.6	eq: 1.67 (ddd; 3, 14, 14) ax: 0.83, m
4	23.1		36.2	
5	50.1	ax: 1.40, m	58.6	ax: 0.94 (dd; 2.2, 13)
6	17.2	1.05, m	18.2	eq: 1.55, m ax: 1.45, m
7	39.0	eq: 1.65, m ax: 1.00, m	41.0	eq: 1.71, m ax: 0.88, m
8	37.8		37.1	
9	50.9	ax: 1.27 (dd; 2.0, 15)	53.6	ax: 1.31 (dd; 3.1, 12.3)
10	36.9		36.8	
11	22.2	eq: 1.97 (dt; 2.6, 15) ax: 1.76 (ddd; 2.4, 15,15)	22.2	1.79, m
12	76.4	eq: 5.09 (t; 2.6)	76.7	eq: 5.11 (t; 2.6)
13	41.3		41.2	
14	48.8	ax: 2.07 (dd; 3.9, 14)	44.1	ax: 1.76, m
15	34.8	eq: 2.52, m ax: 2.41, m	24.0	eq: 1.88 (d; 15) ax: 1.60 (ddd; 4.4, 15, 15)
16	197.6		65.1	5.75 (dd; 1.5, 4.2)
17	136.7		134.9	
18	164.2	7.33, s	153.0	6.70, s
19$_{cis}$	13.6	0.59 (dd; 4.4, 8.9)	28.4	0.82, s
19$_{trans}$		−0.48 (t; 5)		
20	13.3	0.69, m	24.5	a: 1.5, m b: 1.17, m
21	16.2	0.94, s	17.0	0.85, s
22	14.0	0.80, s	16.7	0.84, s
23	18.5	1.17, s	19.8	1.05, s
24	199.3		197.6	
25				
26	30.7	2.45, s	25.8	2.21, s
27	13.1	1.08 (d; 6.3)	8.6	0.74 (t; 7.3)
1′	171.4		171.9	
2′	43.7	2.45, m	43.7	a: 2.53 (dd; 3.3, 16) b: 2.46 (dd; 8.8, 16)
3′	64.3	4.15, m	64.6	4.18, m
3′-OH				2.85, s
4′	22.5	1.23 (d; 6.3)	22.8	1.25 (d; 6.4)
CH_3CO			170.1	
CH_3CO			21.2	2.04, s

[a] Spectra of **1** and **7** were recorded in $CDCl_3$ at 500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR. [b] The numbering system follows that proposed by Kazlauskas et al.[10]

hand, 1D NOE experiments showed that CH_3-26 was α-oriented in phyllofolactone I (**4**): irradiation of H-24 produced a positive NOE on H-16$_{eq}$ and H-26. Similar NOE



R = H	26β-CH_3	**2**
R = $COCH_2CH(OH)CH_3$	26β-CH_3	**3**
R = $COCH_2CH(OH)CH_3$	26α-CH_3	**4**
R = $COCH_2CH(OH)CH_2CH_3$	26β-CH_3	**5**
R = $COCH_2CH(OH)CH_2CH_3$	26α-CH_3	**6**

experiments indicated that CH_3-26 was β-oriented in phyllofolactone J (**5**), although it was α-oriented in compound **6**. In additon, the C-24 chemical shift was diagnostic in confirming the orientation of the CH_3-26: in compounds **4** and **6** (α CH_3-26), C-24 resonates at δ 78.1, as compared to compounds **3** and **5** (β CH_3-26), where it resonates at δ 77.8/77.9 (Table 3). The same carbon chemical shifts correlations were observed for honulactones A−L: C-24 resonates upfield when Me-26 is β-oriented compared to the α-oriented Me-26.[3]

Phyllofenone C (**7**)[6] was obtained as an amorphous solid, $[\alpha]_D$ +16°, with the molecular formula $C_{32}H_{50}O_6$ as established by HRMS. The ^{13}C NMR spectrum of **7** showed 32 signals accounting for three carbonyls (δ 170.1, 171.9, and 197.6), two olefinic carbons (δ 134.9 and 153.0), two methyl ketones (δ 21.2 and 25.8), and three oxymethines (δ 64.6, 65.1, and 76.7).

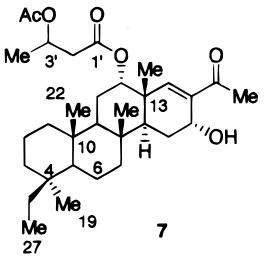
Some features in the ^{1}H NMR observed in phyllofolactones H and I (**3**, **4**) were present in compound **7**: four axial methyl groups (δ 0.82, H-19; 0.84, H-22; 0.85, H-21; and 1.05, H-23), an ethyl side chain; a methyl triplet at δ 0.74 (H-27) coupled to two multiplets at δ 1.17/1.5 (H-20), and a 3-hydroxybutanoyl unit. However, close inspection of the ^{1}H and ^{13}C NMR spectra indicated that the signals associated with the substituted α,β-unsaturated γ-lactone present in phyllofolactones B−D[4,5] and H−K were missing in compound **7** (Tables 2 and 3). Instead, compound **7** showed new signals at δ 6.70 (H-18) corresponding to a trisubstituted sp^2 carbon (δ_C 153), δ 2.04 associated with an acetyl

Table 2. ^{1}H NMR Data for Phyllofolactones H−K (**3**−**6**)[a,b]

	^{1}H (mult; J = Hz)			
position	phyllofolactone H (**3**)	phyllofolactone I (**4**)	phyllofolactone J (**5**)	phyllofolactone K (**6**)
1	eq: 1.68, m	eq: 1.66, m	eq: 1.65, m	eq: 1.66, m
	ax: 0.58 (ddd; 4, 13, 13)	ax: 0.58 (ddd; 4, 13, 13)	ax: 0.59 (ddd; 4, 13, 13)	ax: 0.59 (ddd; 4, 13, 13)
2	*c*	*c*	*c*	*c*
3	*c*	*c*	*c*	*c*
4				
5	ax: 0.86 (dd; 2, 13)	ax: 0.86 (dd; 2, 13)	ax: 0.86, m	ax: 0.87, m
6	*c*	*c*	*c*	*c*
7	eq: 1.83 (dt; 3, 13)	eq: 1.83 (dt; 3, 13)	eq: 1.83 (dt; 3, 13)	eq: 1.83 (dt; 3, 13)
	ax: 0.99 (ddd; 4, 13, 13)	ax: 1.01 (ddd; 4, 13, 13)	ax: 0.99 (ddd; 4, 13, 13)	ax: 1.01 (ddd; 4, 13, 13)
8				
9	ax: 1.16, m	ax: 1.17, m	ax: 1.17, m	ax: 1.18, m
10				
11	eq: 2.01 (dt; 3, 15)	eq: 2.02 (dt; 3, 15)	eq: 2.02 (dt; 3, 15)	eq: 2.03 (dt; 3, 15)
	ax: 1.69, m	ax: 1.69, m	ax: 1.71, m	ax: 1.69, m
12	eq: 5.60 (t; 2.7)	eq: 5.58 (t; 3)	eq: 5.60 (t; 2.7)	eq: 5.58 (t; 2.7)
13				
14	ax: 1.49, m	ax: 1.50, m	ax: 1.50, m	ax: 1.50, m
15	eq: 1.91 (dd; 6.5, 12)	eq: 1.91 (dd; 7, 13)	eq: 1.91 (dd; 7, 12)	eq: 1.91 (dd; 7, 12)
	ax: 1.55, m	ax: 1.56, m	ax: 1.54, m	ax: 1.53, m
16	eq: 2.35, m	eq: 2.31, m	eq: 2.36, m	eq: 2.32, m
	ax: 2.19 (ddd; 7, 12, 15)	ax: 2.24, m	ax: 2.20 (ddd; 7, 12, 15)	ax: 2.24 (ddd; 7, 11, 15)
17				
18				
19	0.79, s	0.79, s	0.79, s	0.79, s
20	a: 1.51, m	a: 1.52, m	a: 1.50, m	a: 1.49, m
	b: 1.17, m	b: 1.14, m	b: 1.15, m	b: 1.15, m
21	0.82, s	0.83, s	0.83, s	0.83, s
22	0.88, s	0.89, s	0.89, s	0.89, s
23	1.17, s	1.18, s	1.17, s	1.18, s
24	4.77 (q; 6.7)	4.75 (q; 6.5)	4.77 (q; 7)	4.76 (q; 6.6)
25				
26	1.35 (d; 7)	1.34 (d; 6.8)	1.36 (d; 6.8)	1.35 (d; 6.9)
27	0.73 (t; 7.4)	0.73 (t; 7.4)	0.73 (t; 7.4)	0.73 (t; 7.4)
1′				
2′	a: 2.36 (dd; 4, 16)	2.33 (d; 6)	a: 2.38 (dd; 3, 16)	a: 2.36 (dd; 3, 15.5)
	b: 2.31 (dd; 8.5, 16)		b: 2.30 (dd; 9, 16)	b: 2.30 (dd; 9, 15.5)
3′	4.09, m	4.11 (q; 6.3)	3.82, m	3.83, m
3′-OH	3.08, s	3.04, s	3.00, s	2.99, s
4′	1.18 (d; 6.3)	1.18 (d; 6.3)	1.45, m	1.45, m
5′			0.94 (t; 7.5)	0.94 (t; 7.4)

[a] Spectra of **3**−**6** were recorded in $CDCl_3$ at 500 MHz. [b] The numbering system follows that proposed by Kazlauskas et al.[10]. [c] Superimposing signals.

unit, δ 2.45 (H-26) indicative of a methyl ketone (δ_C 30.7, 199.3), and δ 5.75 (H-16) for an oxymethine proton.



7

Long-range heteronuclear correlations revealed the following connections: (a) attachment of the 3-hydroxybutanoate unit to ring C through C-12; (b) the singlet methyl (δ_H 2.45) is attached to C-24 (δ_C 197.6), and the latter is connected to ring D through C-17: HMBC correlation between H-26 to C-17; (c) the ethyl side chain and one angular methyl group were found to be attached to C-4 in ring A: HMBC cross-peaks between H-19/H-20/H-27 and C-4; (d) HMBC correlations placed the last oxymethine proton on C-16: cross-peaks between H-14/H-15/H-18 and C-16.

The small coupling constants for H-12 and H-16 revealed α-orientation for both oxymethine protons. The ethyl side chain was assigned β-orientation because a strong ROESY cross-peak was observed between H-20 and H-22. Finally, the acetyl unit was connected to the butanoyl unit through the oxygen at C-3′.

Uncommon, but not unique, the lack of C-25 in phyllofenone C (**7**) is also found in phyllofenone A and other 25-norscalaranes isolated from sponges of the genus *Phyllospongia* (syn. *Carteriospongia*),[7] *Strepsichordaia lendenfeldi*,[2a] *Dictyoceratida* spp.,[8] *Halichondria* spp.,[8] and *Hyrtios erecta*.[9] Further biological evaluation of compounds **1** and **3**−**7** is under way.

Experimental Section

Spectral Analysis. NMR spectra were determined on a General Electric GN Omega 500 spectrometer operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C. ^{1}H chemical shifts are referred to $CDCl_3$; ^{13}C chemical shifts are referred to $CDCl_3$ (77.0 ppm). Homonuclear ^{1}H connectivities were determined by using the 2D double-quantum filtered COSY and 1D decoupling experiments. Homonuclear ^{1}H NOEs were obtained by difference NOE experiments using a 2-s irradiation period. One-bond heteronuclear ^{1}H−^{13}C connectivities were determined by 2D proton-detected HMQC experiments; two- and three-bond ^{1}H−^{13}C connectivities were determined by 2D proton-detected HMBC experiments. HRMS were determined in the DCI and FAB modes. Optical rotations were measured on a JASCO-DIP-700 instrument using CH_2Cl_2 at 20 °C at the sodium D line (589 nm).

Table 3. ^{13}C NMR Data for Phyllofolactones H−K (**3**−**6**)[a,b]

position	phyllofolactone H (**3**)	phyllofolactone I (**4**)	phyllofolactone J (**5**)	phyllofolactone K (**6**)
1	40.0	40.0	40.0	40.0
2	18.0	18.0	18.0	18.0
3	36.5	36.5	36.5	36.6
4	36.1	36.1	36.1	36.1
5	58.7	58.7	58.7	58.7
6	18.1	18.1	18.1	18.1
7	41.7	41.7	41.5	41.6
8	37.5	37.5	37.5	37.5
9	53.4	53.5	53.4	53.5
10	37.0	37.0	37.0	37.0
11	21.0	20.9	20.9	21.0
12	74.5	74.6	74.5	74.6
13	38.4	38.4	38.4	38.4
14	51.1	51.4	51.1	51.4
15	16.9	17.0	16.9	17.0
16	24.0	24.4	24.0	24.4
17	164.2	164.3	164.1	164.3
18	132.7	132.6	132.7	132.6
19	28.4	28.5	28.5	28.5
20	24.4	24.5	24.5	24.5
21	16.7	16.6	16.7	16.6
22	16.8	16.7	16.8	16.7
23	21.4	21.2	21.4	21.2
24	77.9	78.1	77.8	78.1
25	171.3	171.3	171.3	171.3
26	18.6	18.6	18.6	18.6
27	8.6	8.6	8.6	8.6
1′	171.5	171.4	171.7	171.5
2′	43.4	43.4	41.8	41.7
3′	64.2	64.3	69.4	69.4
3′-OH				
4′	22.2	22.3	29.2	29.3
5′			10.0	10.0

[a] Spectra of **3**−**6** were recorded in $CDCl_3$ at 125 MHz. [b] The numbering system follows that proposed by Kazlauskas et al.[10]

Animal Material. The sponge was collected at Turtle Bay, Sangakali, eastern Indonesia, at a depth of 23 m, in March 1996 (2° 04′ 59″ N, 118° 23′ 41″ E). In life, the sponge is fan-shaped to palmitate−digitate, with 2-mm diameter oscules on one surface; the opposite surface has radiating channels, both surfaces are covered with small conules. The texture is quite tough, but very flexible; the external color in life is maroon−purple; interior, cream. The skeleton consists of simple radiating cored primary fibers and golden vermiform tertiary fibers that are linked by short junctions. The surface has a layer of sand grains on it. The sponge is closely comparable to *S. aliena* (order Dictyoceratida, family Thorectidae, subfamily Phyllosponginae). A voucher specimen has been deposited in the Natural History Museum, London (BMNH 1999.7.12.1).

Extraction and Isolation. The freeze-dried sponge (81.0 g) was extracted in dichloromethane−isopropyl alcohol (DCM−IPA) (1:1; 1.0 L) overnight, filtered, and concentrated under reduced pressure to dryness yielding 3.03 g of crude extract. The crude extract was loaded on a Sephadex LH-20 column (30 × 2.5 cm) equilibrated in DCM. The column was eluted using a gradient profile as follows: (1) DCM, DCM/acetone (1:1), and methanol. Eight major fractions (A−H) were collected and concentrated to dryness. Reversed-phase HPLC (Phenomenex Ultracarb 10 ODS 30; 250 × 22 mm; 80% aqueous MeCN to 100% MeCN in 40 min at 6.0 mL/min and monitoring at 220 nm) of fraction B afforded six fractions [fraction 1 (35.2 mg), fraction 2 (77.2 mg), fraction 3 (32.4 mg), fraction 4 (118.1 mg), fraction 5 (44.7 mg), and fraction 6 (90.3 mg)]. Fractions 4 and 6 were further separated by normal-phase HPLC (Microsorb Si; 300 × 7.0 mm; solvent A = hexanes, solvent B = 1:1 hexanes/isopropyl alcohol, starting with solvent A at 0 min to 100% solvent B in 35 min at 2.0 mL/min and monitoring at 220 nm) to yield honu'enone (1.3 mg), phyllofolactone H (3.8 mg), phyllofolactone I (2.8 mg), phyllofolactone J (2.0 mg), phyllofolactone K (1.2 mg), and phyllofenone C (1.3 mg).

Honu'enone (**1**): colorless solid, 1.3 mg (0.0016% based on dry wt); $[\alpha]_D$ +16.0° (*c* 0.4, CH_2Cl_2); ^1H and ^{13}C NMR data, see Table 1; assignments made by interpretation of COSY, HMQC, and HMBC data; HRFABMS *m/z* obsd 485.3267 $[M + H]^+$ ($C_{30}H_{45}O_5$, Δ 2.7 ppm).

Phyllofolactone H (**3**): amorphous solid, 3.8 mg (0.0047% based on dry wt); $[\alpha]_D$ +78.5° (*c* 1.3, CH_2Cl_2); ^1H and ^{13}C NMR data, see Tables 2 and 3; assignments made by interpretation of COSY, HMQC, and HMBC data; HRDCIMS *m/z* obsd 518.38674 $[M + NH_4]^+$ ($C_{31}H_{52}NO_5$, Δ −4.2 ppm).

Phyllofolactone I (**4**): amorphous solid, 2.8 mg (0.0035% based on dry wt); $[\alpha]_D$ +61.9° (*c* 0.93, CH_2Cl_2); ^1H and ^{13}C NMR data, see Tables 2 and 3; assignments made by interpretation of COSY, HMQC, and HMBC data; HRDCIMS *m/z* obsd 518.383471 $[M + NH_4]^+$ ($C_{31}H_{52}NO_5$, Δ 2.1 ppm).

Phyllofolactone J (**5**): amorphous solid, 2.0 mg (0.0025% based on dry wt); $[\alpha]_D$ +55.3° (*c* 0.8, CH_2Cl_2); ^1H and ^{13}C NMR data, see Tables 2 and 3; assignments made by interpretation of COSY, HMQC, and HMBC data; HRDCIMS *m/z* obsd 532.398571 $[M + NH_4]^+$ ($C_{32}H_{54}NO_5$, Δ 3.1 ppm).

Phyllofolactone K (**6**): amorphous solid, 1.2 mg (0.0015% based on dry wt); $[\alpha]_D$ +53.8° (*c* 0.8, CH_2Cl_2); ^1H and ^{13}C NMR data, see Tables 2 and 3; assignments made by interpretation of COSY, HMQC, and HMBC data; HRDCIMS *m/z* obsd 532.399877 $[M + NH_4]^+$ ($C_{32}H_{54}NO_5$, Δ 0.6 ppm).

Phyllofenone C (**7**): amorphous solid, 1.3 mg (0.0016% based on dry wt); $[\alpha]_D$ +16.0° (*c* 0.4, CH_2Cl_2); ^1H and ^{13}C NMR data, see Table 1; assignments made by interpretation of COSY, HMQC, and HMBC data; HRFABMS *m/z* obsd 553.35051 $[M + Na]^+$ ($C_{32}H_{50}O_6Na$, Δ 1.5 ppm).

Cytotoxicity Testing. Cytotoxicity assays were carried out by Instituto Biomar, S. A., Madrid, Spain.

Acknowledgment. We thank, NSF, the Sea Grant College Program, Instituto Biomar, S. A., and PharmaMar, S. A. for financial support.

Supporting Information Available: ^1H and ^{13}C NMR spectra for all compounds are available. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Crews, P.; Naylor, S. In *Fortschr. Chem. Org. Naturst.*; Herz, W., Grisebach, H., Kirby, G. W., Tamm, Ch., Eds.; Springer: New York, 1985; Vol. 48, pp 203−269. (b) Hanson, J. R. *Nat. Prod. Rep.* **1996**, *13*, 529−535, and earlier reports.
(2) (a) Jahn, T.; König, G. M.; Wright, A. D. *J. Nat. Prod.* **1999**, *62*, 375−377. (b) Sera, Y.; Adachi, K.; Shizuri, Y. *J. Nat. Prod.* **1999**, *62*, 152−154. (c) Rueda, A.; Zubía, E.; Ortega, M. J.; Carballo, J. L.; Salvá, J. *J. Org. Chem.* **1997**, *62*, 1481−1485. (d) De Rosa, S.; Crispino, A.; De Giulio, A.; Iodice, C.; Tommonaro, G. *Tetrahedron* **1998**, *54*, 6185−6190. (e) Jaspars, M.; Jackson, E.; Lobkovsky, E.; Clardy, J.; Diaz, M. C.; Crews, P. *J. Nat. Prod.* **1997**, *60*, 556−561.
(3) Jiménez, J. I.; Yoshida, W. Y.; Scheuer, P. J.; Lobkovsky, E.; Clardy, J.; Kelly, M. *J. Org. Chem.* **1999**, submitted.
(4) Zeng, L.; Fu, X.; Su, J.; Pordesimo, E. O.; Traeger, S. C.; Schmitz, F. J. *J. Nat. Prod.* **1991**, *54*, 421−427.
(5) Fu, X.; Zeng, L.; Su, J.; Schmitz, F. J. *J. Nat. Prod.* **1999**, *62*, 644−646.
(6) Phyllofenone A and B[5] were isolated from *P. foliascens* [Zeng, L.; Fu, X.; Su, J.; Chen, S.; Snyder, J. K. *Chem. Res. Chin. University* **1991**, *7*, 100−106].
(7) Braekman, J. C.; Daloze, D.; Kaisin, M.; Moussiaux, B. *Tetrahedron* **1985**, *41*, 4603−4614.
(8) Nakagawa, M.; Hamamoto, Y.; Ishibana, M. *Tetrahedron Lett.* **1987**, *28*, 431−434.
(9) (a) Crews, P.; Bescansa, P.; Bakus, G. J. *Experientia* **1985**, *41*, 690−691. (b) Crews, P.; Bescansa, P. *J. Nat. Prod.* **1986**, *49*, 1041−1052.
(10) Kazlauskas, E.; Murphy, P. T.; Wells, R. J.; Daly, J. J. *Aust. J. Chem.* **1980**, *33*, 1783−1797.

NP0000771