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TWO NEW SESTERTERPENES FROM A SOUTH CHINA SEA SPONGE

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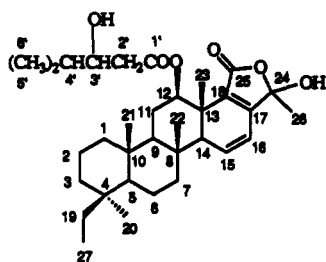
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ABSTRACT.—Two new scalarane derivatives, phyllactones F and G, have been isolated from the sponge *Phyllospongia foliascens*. Compounds **1** and **2** are anomers whose structures were determined on the basis of spectral data. The absolute stereochemistry of phyllactone B [**6**] has been established using Mosher's method, and this permitted verification of the assignments of absolute stereochemistry for all scalarane sesterterpenes isolated from the Chinese sponge *P. foliascens*.

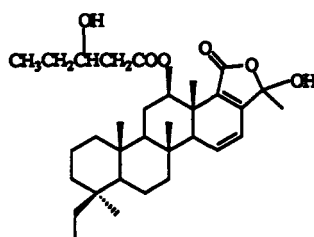
The Chinese sponge *Phyllospongia foliascens* Pallas (Spongiidae) has proved to be a rich source of 20,24-bishomoscalarane sesterterpenes. More than ten sesterterpenes belonging to this group have been reported (1–3) from the sponge *P. foliascens* collected from the Xisha islands and Nansha islands in the South China Sea. Interestingly, the sesterterpene metabolites of *P. foliascens* collected from two localities differ in the

relative stereochemistry at C-12 and C-16. This indicates that the environment has an influence on the metabolic pathway of this sponge. In this paper, we report two new bishomoscalarane sesterterpenes, named phyllactones F and G, isolated from the same sponge and assignment of absolute stereochemistry for the scalarane sesterterpenes.

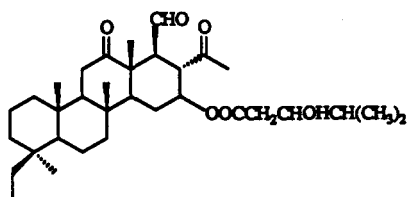
Phyllactones F [**1**] and G [**2**] were obtained together as fine needles by vlc



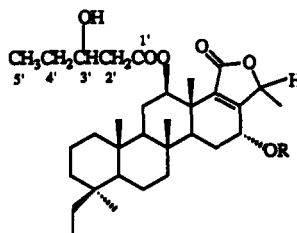
1 Me-26α
2 Me-26β



3 Me-26α
4 Me-26β



5



6 R=H, Me-26β
7 R=(R)-MTPA, Me-26β
8 R=(S)-MTPA, Me-26β

on Si gel followed by flash chromatography and hplc in a silica column. The compound exhibited only one spot on hplc with several solvent systems, but two sets of signals with partial overlapping were revealed clearly in its ^1H - and ^{13}C -nmr spectra (Table 1). This indicated the compound to be a mixture in approximately 1:1 ratio estimated from integration of the ^1H -nmr spectrum. ^1H -nmr and ^{13}C -nmr spectra of phyllactones F and G indicated that they belong to the 20,24-bishomoscalarane sesterterpene group. The ^1H -nmr spectrum showed at least five methyl singlets and one methyl triplet (see Table 1). The ^{13}C resonances,

especially three methine resonances in the region of δ 50–60, are compatible with 20,24-bishomoscalarane sesterterpenes (4). Phyllactones F [1] and G [2] had a cims peak at m/z 543 $[\text{MH}]^+$, 14 mu higher than phyllactones D [3] and E [4] (3). Comparison of the cims data of phyllactones F and G with those of phyllactones D and E indicated that they differ only in the nature of the acyl moiety. In particular, the cims of 1 and 2 showed prominent fragment ion peaks at m/z 525 $[\text{M}-\text{OH}]^+$, 411 $[\text{M}-\text{Me}_2\text{CHCH}(\text{OH})\text{CH}_2\text{COO}]^+$, 393 $[\text{M}-\text{Me}_2\text{CHCH}(\text{OH})\text{CH}_2\text{COO}-\text{H}_2\text{O}]^+$, 367 $[\text{M}-\text{Me}_2\text{CH}(\text{CHOH})\text{CH}_2\text{COO}-\text{H}_2\text{O}-\text{CH}=\text{CH}]^+$,

TABLE 1. Nmr Data for Phyllactones F [1] and G [2] (600 MHz, CDCl_3).

Position	δ_c^a		δ_H^a	
	1 or 2	1 or 2	1 or 2	1 or 2
1	40.0	39.9		
2	17.9	17.9		
3	36.6	36.6		
4	36.1	36.1		
5	58.6	58.6		
6	18.1	18.1		
7	40.9	40.8		
8	37.4	37.4		
9	58.5	58.4		
10	37.4	37.4		
11	24.5	24.3		
12	75.5	75.3	5.19 dd, 11, 4	5.22 dd, 11, 4
13	40.1	40.1		
14	57.1	56.8		
15	139.5	139.3	6.34 dd, 10, 3, 5	6.39 dd, 10, 3, 5
16	119.4	119.1	6.42 dd, 10, 2	6.43 dd, 10, 2
17	158.2	158.0		
18	132.1	132.0		
19	28.7	28.5	0.80 s	0.82 s
20	24.5	24.5		
21	16.6	16.6	0.85 s	0.85 s
22	18.9	18.8	1.04 s	1.04 s
23	12.6	12.6	1.09 s	1.09 s
24	102.8	102.8		
25	168.4	168.4		
26	24.1	24.0	1.56 s	1.66 s
27	8.6	8.6	0.75 t, 7	0.75 t, 7
1'	173.7	173.3		
2'	39.9	39.8	2.49 m	2.49 m
3'	73.0	72.8	3.90 m	3.90 m
4'	33.2	33.1	1.76 m	1.76 m
5'	18.4	18.2	0.94 d, 6, 8	0.96 d, 6, 8
6'	17.7	17.7	0.94 d, 6, 8	0.96 d, 6, 8

^aEach value may be interchanged.

133 [Me₂CHCHOHCH₂COOH₂]⁺, 115 [Me₂CHCHOHCH₂CO]⁺. Ir bands at 3400 and 1750 cm⁻¹, along with ¹H and ¹³C-nmr data of the 3-hydroxy-4-methylpentanoyl moiety (see Table 1) were consistent with those of compound **5** (5). The location of the 3-hydroxy-4-methylpentanoyl group at C-12 was determined by comparison of the nmr data of **1** and **2** with those of phyllactones A–E (3) and by consideration of the origin of these compounds. This position of oxygenation agrees with that of all previously reported scalarane derivatives (6,7). The observed coupling constants for H-12 ($J_{11ax,12ax} = 11$ Hz; $J_{11eq,12ax} = 4$ Hz) indicated an H-12 α stereochemistry.

In arguments similar to the one applied in the structural elucidation of **3** and **4**, the structure of rings D and E was proposed for phyllactones F [**1**] and G [**2**]. The nmr data (see Table 1) of this moiety are in good agreement with those of phyllactones D and E (3). From the above evidence, phyllactones F and G are C-24 anomers like phyllactones D and E (3) and can be assigned the structures **1** and **2**.

This work also gave us the opportunity to assign absolute stereochemistry to the scalarane sesterterpenes. To our knowledge the absolute stereochemistry of any scalarane sesterterpene has never been unambiguously assigned. The secondary alcohol functionality at C-16 enabled an investigation of the absolute stereochemistry of phyllactone B [**6**] (3) using a modified Mosher's method (8,9). Thus, alcohol **6** was converted to (*R*)- and (*S*)-MTPA esters (**7** and **8**, respectively). The $\Delta\delta$ ($\delta_S - \delta_R$) observed for H-24, H-26 were -58.55, -25.46 Hz respectively, while those observed for H-12, H-23, H-22, H-21, H-19, H-27 were +4.85, +2.94, +19.47, +12.61, +2.02, +2.51 Hz, respectively [for convenience, δ values were given in Hz (400 MHz)]. From the MTPA determination rule (8,9), the positive and negative $\Delta\delta$ value observed for the signals of protons in the left and the

right segments, respectively, showed clearly that the absolute configuration of **6** at C-16 is *R*. According to the relative configuration determined by nmr data and nOe's (3), the absolute configurations of asymmetric centers C-4, C-12, C-24 in **6** were assigned as *S*, *R*, and *S*. The absolute stereochemistry of C-5, C-8, C-9, C-10, C-13, and C-14 as shown is compatible with the known absolute stereochemistry of common steroids and triterpenes. This result, together with biogenetic relationships, implies that phyllactones F [**1**] and G [**2**] and the reported scalarane sesterterpenes (1–3) have the absolute stereochemistry as shown. It seems likely that this conclusion extends to all reported scalarane sesterterpenes, since the "traditional" absolute stereochemistry drawn for the scalarane sesterterpenes is presumably in accord with the known absolute stereochemistry of common steroids and triterpenes.

Unfortunately, we could not define the relative configuration of C-3' on the 3-hydroxypentanoyl residue of phyllactone B [**6**] by nOe. Furthermore, it is surprising that the 3'-OH of the 3-hydroxypentanoyl moiety was not transformed to the corresponding MTPA ester. Therefore, the absolute stereochemistry of C-3' remains unknown.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—General procedures are as described previously (3), except that nmr spectra were recorded on a Bruker AMX-600 and the MTPA work was done on a 400 MHz instrument. Biological material was described previously (3).

ISOLATION OF PHYLLACTONES F AND G.—The sun-dried specimens (dry wt ca. 800 g) were repeatedly extracted with MeOH at room temperature. The MeOH extract was concentrated under reduced pressure and partitioned between EtOAc-petroleum ether (1:4) and H₂O. The organic fraction was separated and dried over anhydrous Na₂SO₄. Evaporation of the solvent yielded a viscous oil (54 g) that was subjected to vlc on Si gel. Elution with varying proportions of petroleum ether/EtOAc (0–100% EtOAc) yielded nine

fractions. Flash chromatography of the fifth and sixth fractions (20–30% EtOAc in petroleum ether) followed by normal phase hplc with 20% EtOAc in hexane as eluent yielded a mixture (5 mg) of phyllactones F [1] and G [2] in a 1:1 ratio. We could not separate this mixture by chromatography on Si gel even by hplc.

Phyllactones F and G.—Needles from MeOH: uv λ max (MeOH), 290 nm ($\epsilon=5998$), 204 nm ($\epsilon=5823$); ir (CHCl₃) γ max cm⁻¹, 3400 (br, OH), 1750 (ester), 1710 (α,β -unsaturated- γ -lactone); cims m/z (% rel. int.) [MH]⁺ 543 (100), [M-OH]⁺ 525 (40), 411 (52), 393 (53), 367 (24), 133 (55), 115 (87); eims m/z (% rel. int.) 410 (64), 395 (96), 393 (66), 381 (32), 366 (63), 351 (32), 270 (68), 255 (100), 205 (64); ¹H and ¹³C nmr see Table 1.

SYNTHESIS OF R- AND S-MTPA ESTERS OF PHYLLACTONE B.—A solution of **6** (2.4 mg, 4.5 μ mol), dimethylaminopyridine (3 mg, 24.5 μ mol), and triethylamine (1.5 μ l) in 0.25 ml of CH₂Cl₂ (distilled from P₂O₅) was treated with S-(+)-MTPA chloride (3.6 μ l, 19.3 μ mol), and the mixture stood at room temperature for 18 h. A quench of 3-[(dimethylamino)propyl]amine (2.4 μ l, 19.1 μ mol) was added, and after 15 min the solvent was evaporated and the residue was subjected to preparative tlc on Si gel plate (5% MeOH in CH₂Cl₂) to give the R-MTPA ester **7** of phyllactone B as an oil (1.3 mg). The S-MTPA ester **8** was obtained in the same manner.

R-MTPA ester 7.—[α]_D +53° ($c=0.10$, CHCl₃); cims m/z (% rel. int.) 747 (68), 647 (6), 629 (26), 529 (8), 515 (82), 429 (24), 415 (100), 397 (98), 395 (62), 235 (27), 227 (79), 119 (54), 101 (29).

S-MTPA ester 8.—[α]_D +31° ($c=0.10$, CHCl₃); cims m/z (% rel. int.) 747 (100), 647 (9),

629 (31), 529 (16), 515 (54), 395 (80), 235 (64), 227 (88), 119 (52), 101 (24).

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