# New Scalarane Class Sesterterpenes from an Indonesian Sponge, Phyllospongia sp.

**ARTICLE** *in* JOURNAL OF NATURAL PRODUCTS · JANUARY 2003

Impact Factor: 3.8 · DOI: 10.1021/np020311i · Source: PubMed

# New Scalarane Class Sesterterpenes from an Indonesian Sponge, *Phyllospongia* sp.

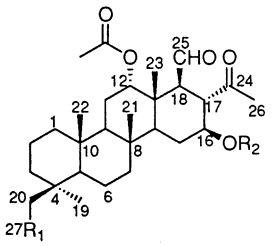
Michael C. Roy,[†] Junichi Tanaka,[†] Nicole de Voogd,[‡] and Tatsuo Higa*,[†]

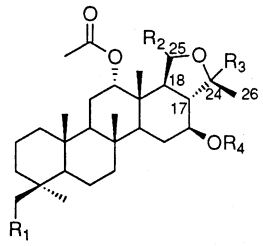
*Department of Chemistry, Biology, and Marine Science, University of the Ryukyus, Nishihara, Okinawa 903-0213, Japan, and Institute of Bio-diversity and Ecosystem Dynamics, University of Amsterdam, P.O. Box 94766, 1090 GT Amsterdam, The Netherlands*

*Received July 11, 2002*

A series of scalarane class sesterterpenes (**1**−**8**) have been isolated from an Indonesian sponge, *Phyllospongia* sp. Their structures were determined by spectroscopic analysis and confirmed by single-crystal X-ray diffraction on compound **1**. The absolute stereochemistry of **1** was established by modified Mosher's method.

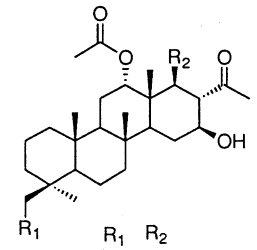
Sesterterpenes are a relatively small group of terpenoids known from terrestrial plants, insects, fungi, lichens, and marine organisms.[1] A number of tetracyclic sesterterpenes of the scalarane class have been reported from marine sponges of the order Dictyoceratida and their predator nudibranchs.[2−4] The scalarane skeletons can vary from $C_{24}$ *nor*-scalarane to $C_{27}$ *dihomo*-scalarane types, the latter having methylation at C19, C20, C23, and/or C24.[5,10] These compounds have been reported to exhibit a wide spectrum of biological activities including cytotoxicity,[2,4,6−13] ichthyotoxicity,[3] antiinflammation,[5] erythroid differentiation,[14] anti-HIV,[15] and antimicrobial properties.[13] When we examined an Indonesian sponge, *Phyllospongia* sp., its crude extract showed cytotoxicity. Separation of the extract gave seven new scalarane derivatives (**1**, **1a**, **3**−**7**) exhibiting weak cytotoxicity. We herein report the isolation and structure determination of these compounds.





| | $R_1$ | $R_2$ |
|---|---|---|
| **1**: | H | H |
| **1a**: | H | Ac |
| **1b**: | H | *R*-MTPA |
| **1c**: | H | *S*-MTPA |
| **2**: | Me | H |

| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| **3**: | H | α-OH | H | H |
| **3a**: | H | α-OAc | H | Ac |
| **3b**: | H | α-OMe | H | H |
| **3c**: | H | β-OMe | H | H |
| **4**: | Me | α-OH | H | H |
| **4b**: | Me | α-OMe | H | H |
| **4c**: | Me | β-OMe | H | H |
| **5**: | H | α-OMe | α-OMe | H |



| | $R_1$ | $R_2$ |
|---|---|---|
| **6**: | H | H |
| **7**: | H | OH |
| **8**: | Me | H |

## Results and Discussion

Upon collection off Makassar, Indonesia, the sample of *Phyllospongia* sp. was frozen, brought to Okinawa, and extracted with MeOH. After concentration, the residue was partitioned between ethyl acetate and water. The organic layer was chromatographed over silica gel followed by ODS HPLC (MeCN/$H_2O$) to give compounds **1**−**8**, which belonged to 24-*homo*- (**1**, **1a**, **3**, **5**), 20,24-*dihomo*- (**2**, **4**), and 25-*nor*-scalaranes (**6**−**8**).

Compound **1** had a molecular formula $C_{28}H_{44}O_5$ as deduced from HREIMS (*m*/*z* 460.3167 $[M]^+$, Δ −1.9 mmu). The IR spectrum of **1** showed absorptions for hydroxyl ($\nu_{max}$ 3453 $cm^{-1}$) and carbonyl ($\nu_{max}$ 1714 $cm^{-1}$) functionalities. Its $^{13}C$ NMR spectrum exhibited a total of 28 signals including resonances for a ketone (δ 213.3 s), an aldehyde (δ 202.6 d), an ester (δ 170.2 s), and two oxymethine carbons (δ 74.8 and 73.8 d). The $^1H$ NMR spectrum also showed signals for an aldehyde (δ 9.48 s), a ketonic methyl (δ 2.41 s), an acetoxy methyl (δ 2.19 s), two oxymethines (δ 5.10, 3.59), and five tertiary methyls (δ 0.80, 0.81, 0.86, 0.87, 0.96). Since the carbonyls account for three out of the seven degrees of unsaturation required by the formula, **1** must be tetracyclic. Analysis of 2D NMR data (COSY, HMQC, HMBC) revealed that **1** is based on a homoscalarane skeleton, having methylation at C24. Complete assignment of the NMR data is given in Tables 1 and 3. The acetoxy group was placed at C12 by an HMBC cross-peak observed between H12 (δ 5.10) and the carbonyl carbon (δ 170.2). Similarly, the positions for the aldehyde, ketone, and hydroxyl were established as shown.

The relative configurations of all asymmetric centers were deduced from coupling constants and NOE data. The chemical shifts of the angular methyl groups (δ 16.0, 16.9, 17.3) suggested that all ring junctions were *trans*.[8] A small coupling constant in the signal at δ 5.10 (brt, $J$ = 2.7 Hz) for H12 indicated it to be equatorial. Large coupling constants ($J$ = 11 Hz) in the signals at δ 3.59, 2.91, and 3.10 suggested the axial disposition of H16, H17, and H18. This observation was further supported by strong NOEs between H16 and H14 and between H16 and H18. Single-crystal X-ray diffraction analysis confirmed the structure of **1**.

To determine the absolute stereochemistry, modified Mosher's method was applied.[17] Treatment of **1** with *R*- and *S*-MTPA in the presence of DCC and DMAP in $CH_2Cl_2$ solution gave the corresponding MTPA esters. Observed chemical shift differences ($\Delta\delta = \delta_S - \delta_R$) were negative for H5, H9, H14, $H_{ax}15$, and H21 and positive for H12, H17, H18, H25, and H26, suggesting the absolute configuration

* To whom correspondence should be addressed. Tel: 81-98-895-8558. Fax: 81-98-895-8538. E-mail: thiga@sci.u-ryukyu.ac.jp.
[†] University of the Ryukyus.
[‡] University of Amsterdam.

10.1021/np020311i CCC: $22.00 
Published on Web 10/25/2002

**Table 1.** $^{13}C$ NMR Data of **1**, **2**, and **6**−**8** in $CDCl_3$ (125 MHz)[a,b]

| no. | 1 | 2 | 6 | 7 | 8 |
|---|---|---|---|---|---|
| 1 | 39.7 t | 40.2 t | 39.7 t | 39.7 t | 40.2 t |
| 2 | 18.4 t | 18.2 t | 18.5 t | 18.5 t | 18.2 t |
| 3 | 41.9 t | 36.6 t | 42.0 t | 41.9 t | 36.9 t |
| 4 | 33.3 s | 36.1 s | 33.3 s | 33.3 s | 36.1 s |
| 5 | 56.5 d | 58.6 d | 56.5 s | 56.5 d | 58.6 d |
| 6 | 18.1 t | 18.1 t | 18.2 t | 18.2 t | 18.1 t |
| 7 | 41.5 t | 41.8 t | 41.2 t | 41.5 t | 41.5 t |
| 8 | 37.9 s | 37.9 s | 37.4 s | 37.4 s | 37.4 s |
| 9 | 52.4 d | 52.8 d | 52.7 d | 52.5 d | 53.1 d |
| 10 | 36.8 s | 36.9 s | 36.9 s | 36.9 s | 36.6 s |
| 11 | 21.7 t | 21.8 t | 22.3 t | 22.6 t | 22.4 t |
| 12 | 74.8 d | 74.9 d | 76.7 d | 74.5 d | 76.7 d |
| 13 | 40.4 s | 40.5 s | 37.7 s | 42.3 s | 37.7 s |
| 14 | 51.1 d | 51.1 d | 49.9 d | 47.1 d | 49.9 d |
| 15 | 30.5 t | 30.4 t | 28.0 t | 29.0 t | 28.1 t |
| 16 | 73.8 d | 73.8 d | 71.2d | 70.6 d | 71.2 d |
| 17 | 52.1 d | 52.1 d | 53.9d | 59.1 d | 53.9 d |
| 18 | 58.3 d | 58.3 d | 38.9 t | 72.9 d | 38.9 t |
| 19 | 33.2 q | 28.5 q | 33.2 q | 33.2 q | 28.5 q |
| 20 | 21.3 q | 24.5 t | 21.3 q | 21.3 q | 24.5 t |
| 21 | 16.9 q | 16.9 q | 16.6 q | 17.2 q | 16.6 q |
| 22 | 16.0 q | 16.8 q | 16.0 q | 16.2 q | 16.8 q |
| 23 | 17.3 q | 17.3 q | 20.7 q | 13.6 q | 20.7 q |
| 24 | 213.3 s | 213.2 s | 212.7 s | 213.2 s | 212.7 s |
| 25 | 202.6 d | 202.6 d | | | |
| 26 | 33.8 q | 33.8 q | 29.1 q | 33.9 q | 29.1 q |
| 27 | | 8.6 q | | | 8.6 q |
| 12-OAc | 170.2 s | 170.2 s | 170.5 s | 172.6 s | 170.5 s |
| | 21.5 q | 21.5 q | 21.4 q | 21.5 q | 21.4 q |

[a] Reference $CDCl_3$ ($\delta_C$ 77.0 ppm). [b] Assignment based on HMQC and HMBC.

**Table 2.** $^{13}C$ NMR Data of **3**−**5** in $CDCl_3$ (125 MHz)[a,b]

| no. | 3 | 3b | 3c | 4 | 4b | 4c | 5 |
|---|---|---|---|---|---|---|---|
| 1 | 39.8 t | 39.8t | 39.8 t | 40.2 t | 40.2 t | 40.2 t | 39.8 t |
| 2 | 18.5 t | 18.5 t | 18.4 t | 18.2 t | 18.2 t | 18.2 t | 18.5 t |
| 3 | 42.0 t | 42.0 t | 41.9 t | 36.6 t | 36.6 t | 36.6 t | 42.0 t |
| 4 | 33.3 s | 33.3 s | 33.2 s[c] | 36.1 s | 36.1 s | 36.1 s | 33.3 s[c] |
| 5 | 56.5 d | 56.4 d | 56.6 d | 58.6 d | 58.6 d | 58.7 d | 56.8 d |
| 6 | 18.2 t | 18.2 t | 18.1 t | 18.1 t | 18.1 t | 18.0 t | 18.2 t |
| 7 | 41.7 t | 41.7 t | 42.0 t | 42.0 t | 42.0 t | 42.0 t | 41.7 t |
| 8 | 37.8 s | 37.7 s | 37.5 s | 37.8 s | 37.7 s | 37.6 s | 37.7 s |
| 9 | 52.9 d | 52.9 d | 52.8 d | 53.3 d | 53.3 d | 53.3 d | 52.9 d |
| 10 | 36.9 s | 36.9 s | 36.8 s | 36.9 s | 36.9 s | 36.9 s | 36.9 s |
| 11 | 22.0 t | 22.1 t | 21.8 t | 22.0 t | 22.1 t | 21.9 t | 22.2 t |
| 12 | 74.6 d | 74.2 d | 75.6 d | 74.6 d | 74.2 d | 75.6 d | 74.2 d |
| 13 | 38.2 s | 38.1 s | 38.9 s | 38.2 s | 38.1 s | 38.9 s | 38.2 s |
| 14 | 52.6 d | 52.8 d | 53.8 d | 52.6 d | 52.8 d | 52.6 d | 52.5 d |
| 15 | 31.3 t | 31.4 t | 31.3 t | 31.3 t | 31.4 t | 31.3 t | 30.5 t |
| 16 | 72.8 d | 72.7 d | 75.3 d | 72.8 d | 72.7 d | 75.3 d | 70.1 d |
| 17 | 52.8 d | 52.4 d | 49.1 d | 52.7 d | 52.4 d | 49.2 d | 54.7 d |
| 18 | 55.9 d | 55.4 d | 52.6 d | 55.9 d | 55.4 d | 53.8 d | 51.7 d |
| 19 | 33.2 q | 33.2 q | 33.2 q[c] | 28.5 q | 28.5 q | 28.5 q | 33.3 q[c] |
| 20 | 21.6 q | 21.3 q | 21.3 q | 24.5 t | 24.5 t | 24.4 t | 21.3 q |
| 21 | 16.9 q | 16.8 q | 17.1 q | 16.8 q | 16.8 q | 16.9 q | 16.8 q |
| 22 | 16.1 q | 16.1 q | 16.0 q | 16.9 q | 16.9 q | 17.0 q | 16.1 q |
| 23 | 16.3 q | 16.5 q | 16.2 q | 16.3 q | 16.5 q | 16.2 q | 16.3 q |
| 24 | 78.2 d | 77.9 d | 80.2 d | 78.1 d | 77.9 d | 80.3 d | 105.5 s |
| 25 | 96.6 d | 104.2 d | 103.7 d | 96.5 d | 104.2d | 103.7 d | 104.8 d |
| 26 | 20.5 q | 20.3 q | 23.4 q | 20.5 q | 20.3 q | 23.4 q | 22.1 q |
| 27 | | | | 8.6 q | 8.6 q | 8.6 q | |
| 12-OAc | 171.1 s | 170.6 s | 170.7 s | 171.1 s | 170.6 s | 170.4 s | 170.8 s |
| | 21.3 q | 21.4 q | 21.5 q | 21.6 q | 21.4 q | 21.5 q | 21.5 q |
| 24-OMe | | | | | | | 48.8 q |
| 25-OMe | | 56.5 q | 54.5 q | | 56.5 q | 54.6 q | 56.4 q |

[a] Reference $CDCl_3$ ($\delta_C$ 77.0 ppm). [b] Assignment based on HMQC and HMBC. [c] Overlaping signals assigned based on HMBC correlation.

at C16 to be *S*. Therefore, the absolute stereochemistry of **1** was determined as shown in the structure.

Compound **1a**, $C_{30}H_{46}O_6$ (*m*/*z* 460.3214 [M − $C_2H_2O$]$^+$, Δ +2.7 mmu), was isolated as a minor component. Similarity of the NMR data with those of **1** suggested that **1a** was an acetyl derivative of **1**. Treatment of **1** with acetic anhydride and pyridine gave a diacetate that showed spectral data identical with those of **1a**.

Compound **2** also showed $^1H$ and $^{13}C$ NMR spectra similar to those of **1**. The only difference was the replacement of a methyl group at C4 in **1** by an ethyl group [$\delta$ 0.75 (3H, t, $J$ = 7.5 Hz), 1.50 (1H, m)/1.16 (1H, dq, $J$ = 14, 7.5 Hz); $\delta_C$ 8.6 q and 24.5 t], as evidenced by HMBC (H27/C4). It was shown to be identical with a dihomoscalarne reported previously from *Carteriospongia foliascenes*.[16]

Compound **3** was isolated as an amorphous solid. The molecular formula $C_{28}H_{46}O_5$ was deduced from HREIMS (*m*/*z* 444.3245 [M − $H_2O$]$^+$, Δ +0.7 mmu). The IR spectrum showed the presence of a hydroxyl ($\nu_{max}$ 3399 cm$^{-1}$) and an ester ($\nu_{max}$ 1714 cm$^{-1}$) group. The $^{13}C$ NMR spectrum exhibited signals for all 28 carbons: seven methyl, seven methylene, nine methine, and five quaternary carbons. The $^1H$ NMR spectrum showed resonances for four oxymethines ($\delta$ 5.26, 4.76, 4.04, and 3.59) and seven methyl groups ($\delta$ 2.07 s, 1.35 d, 0.99 s, 0.86 s, 0.85, 0.80, and 0.80 s). The absence of unsaturations other than an ester carbonyl revealed that **3** must have a pentacyclic structure. This feature suggested that it was also a scalarane-related compound. Acetylation of **3** gave a triacetate (**3a**), demonstrating the presence of two hydroxyl groups. The presence of a 2-hydroxytetrahydrofuran moiety was inferred from signals indicative of a hemiacetal ($\delta$ 5.26; $\delta$ 96.6 d), from COSY and TOCSY (H14/H18, H16/H17, H17/H18, H17/H24, H18/H24, H24/H26), and from HMBC data (H25/C18, H25/C24, H26/C17, H26/C24). These 2D NMR data allowed determination of the gross structure for **3**. The heterocyclic ring was connected to ring D through HMBC cross-peaks (H25/C13, H25/C18, H24/C16). The acetoxy and another hydroxyl were placed at C12 and C16, respectively, by observation of HMBC and shown to have the same configurations as in **1** and **2**.

Irradiation of the signal at $\delta$ 5.26 (H25) produced strong enhancement of the proton signals at H12 and H23, suggesting the $\beta$-orientation of H25. The methyl group at C24 was assigned to have a $\beta$-orientation on the basis of strong NOEs observed among the protons at C24, C16, and C18.

The molecular formula $C_{29}H_{48}O_5$ of **4** was deduced from HREIMS (*m*/*z* 458.3379 [M − $H_2O$]$^+$, Δ −1.4 mmu). It suggested the presence of an additional methyl group relative to **3**. In fact the $^1H$ and $^{13}C$ NMR spectra of **4** were almost identical to those of **3** except for a triplet methyl signal at $\delta$ 0.74 (t, $J$ = 7.5 Hz). The methyl group was shown to be attached at C20 as in **2** by HMBC. The signals for the ring A and B portion were nearly identical with those of **2** (Tables 1 and 2). The relative stereochemistry of **4** was identical with that of **3**, as indicated by comparable chemical shift values of the asymmetric carbons, and confirmed by NOE experiments. The anomeric hydroxyl at C25 in **3** and **4** could be easily methylated with methanol in the presence of a trace amount of an acid to give a pair of diastereomeric products (**3b** and **3c** or **4b** and **4c**). The product ratio ($\alpha$:$\beta$) was approximately 5:1.

Compound **5**, $C_{30}H_{50}O_6$, was obtained as fine needles. The $^1H$ NMR spectrum was similar to that of **3b**. It contained an additional OMe signal ($\delta$ 3.27). A methyl singlet ($\delta$ 1.47) corresponding to H26 was slightly downfield shifted compared to that ($\delta$ 1.36) of **3b**. The presence of two acetal carbons ($\delta$ 105.5 s, 104.8 d) and the absence of an oxymethine proton (H24) signal suggested that the second methoxy group was attached at C24. The $^{13}C$ NMR signals were also comparable to those of **3b** (Table 2). The structure was

**Table 3.** $^1$H NMR Data of **1** and **3**−**5** in $CDCl_3$ (500 MHz)[a,b]

| no. | 1 | 3 | 4 | 5 |
|---|---|---|---|---|
| 1 | 1.59 (m)[c] | 1.57 (m) | 1.57 (m) | 1.59 (m) |
| | 0.60 (td, 13, 3.5) | 0.58 (td, 13, 3.5) | 0.60 (td, 13, 3) | 0.59 (td, 13, 3.5) |
| 2 | 1.59 (m) | 1.56 (m) | 1.50 (m) | 1.52 (m) |
| | 1.41 (m) | 1.37 (m) | 1.35 (m) | 1.37 (m) |
| 3 | 1.40 (m) | 1.37 (m) | 1.66 (m) | 1.37 (m) |
| | 1.14 (td, 13.5, 4.5) | 1.12 (td, 14, 4.5) | 0.82 (m) | 1.12 (td, 13, 4.5) |
| 5 | 0.83 (dd, 12, 2) | 0.83 (dd, 12.5, 2) | 0.89 (overlapped) | 0.82 (overlapped) |
| 6 | 1.59 (m) | 1.56 (m) | 1.50 (m) | 1.52 (m) |
| | 1.41 (m) | 1.37 (m) | 1.35 (m) | 1.37 (m) |
| 7 | 1.75 (dt, 12.5, 3.5) | 1.74 (m) | 1.75 (m) | 1.74 (m) |
| | 0.99 (td, 12.5, 3.5) | 1.01 (m) | 0.98 (m) | |
| 9 | 1.29 (dd, 13, 2) | 1.24 (m) | 1.22 (d, 12.5) | 1.21 (m) |
| 11 | 1.82 (m) | 1.75 (m) | 1.74 (m) | 1.68 (m) |
| | 1.68 (td, 13, 2) | 1.70 (m) | 1.65 (m) | |
| 12 | 5.10 (brt, 2.7) | 4.76 (brt, 2.7) | 4.75 (brt, 2) | 4.68 (brt, 2) |
| 14 | 1.51 (dd, 12.5, 2.5) | 1.55 (overlapped) | 1.55 (overlapped) | 1.37 (overlapped) |
| 15 | 1.86 (m) | 1.90 (m) | 1.89 (d, 11) | 1.88 (m) |
| | 1.39 (m) | 1.25 (m) | 1.27 (m) | 1.37 (m) |
| 16 | 3.59 (tdd, 11, 5, 5) | 3.59 (td, 10.5, 5) | 3.58 (td, 10, 4) | 3.81 (td, 10, 4) |
| 17 | 2.91 (t, 11) | 1.40 (overlapped) | 1.39 (overlapped) | 1.77 (dd, 13.5, 10) |
| 18 | 3.10 (d, 11) | 1.97 (dd, 13, 6.5) | 1.96 (dd, 13, 6.5) | 2.28 (dd, 13.5, 6.5) |
| 19 | 0.87 (s) | 0.85 (s) | 0.80 (s) | 0.85 (s) |
| 20 | 0.81 (s) | 0.80 (s) | 1.52 (m) | 0.79 (s) |
| | | | 1.15 (dq, 13.5, 7.5) | |
| 21 | 0.86 (s) | 0.86 (s) | 0.86 (s) | 0.85 (s) |
| 22 | 0.80 (s) | 0.80 (s) | 0.82 (s) | 0.79 (s) |
| 23 | 0.96 (s) | 0.99 (s) | 0.99 (s) | 0.96 (s) |
| 24 | | 4.04 (qd, 6, 12) | 4.03 (qd, 6, 12) | |
| 25 | 9.48 (s) | 5.26 (d, 6.5) | 5.26 (d, 5.5) | 4.72 (d, 6.5) |
| 26 | 2.41 (s) | 1.35 (d, 6) | 1.34 (d, 6) | 1.47 (s) |
| 27 | | | 0.74 (t, 7.5) | |
| 12-OAc | 2.19 (s) | 2.07 (s) | 2.06 (s) | 2.05 (s) |
| 24-OMe | | | | 3.27 (s) |
| 25-OMe | | | | 3.30 (s) |

[a] Internal reference TMS ($\delta_H$ 0.0 ppm). [b] Assignment based on HMQC data. [c] Multiplicity and $J$ = Hz are indicated in parentheses.

elucidated by analysis of 2D NMR and NOE data. Treatment of **1** with methanol in the presence of hydrochloric acid gave a product identical to **5**. Since methanol was used in the extraction and isolation process, **5** must be an artifact.

Compound **6** was isolated as a glassy solid. The molecular formula $C_{27}H_{44}O_4$ was determined by HREIMS (*m*/*z* 414.3104 $[M - H_2O]^+$, $\Delta$ −2.7 mmu). The $^{13}$C NMR spectrum of **6** exhibited signals for all 27 carbons: a ketone ($\delta$ 212.7 s), an ester carbonyl ($\delta$ 170.5 s), two oxymethines ($\delta$ 76.7 and 71.2 d), seven methyls, eight methylenes, four methines, and four quaternary carbons. Both the $^{13}$C and $^1$H NMR data for the ring A and B portion were essentially the same as those of **1**. It also contained an acetoxy ($\delta$ 2.07), an acetyl (methyl ketone, $\delta$ 2.14), and a hydroxyl group ($\delta$ 3.80) as in **1**. However, it lacked an aldehyde group, suggesting that **6** was a 25-norscalarane. Analysis of HMBC data revealed the planar structure. The same stereochemistry as **1** was shown by coupling constant and NOE data.

The molecular formula $C_{27}H_{44}O_5$ of **7**, determined by HREIMS, indicated the presence of an additional oxygen atom compared to **6**. The NMR data ($\delta_H$ 3.27; $\delta_C$ 72.9 d) revealed that it was due to another hydroxyl group which was located at C18 by HMBC correlations (H17/C18; H23/C18; H18/C12, C17, C23). The orientation of the 18-OH was concluded to be $\beta$ from a large coupling constant of H18 ($\delta$ 3.27 dd, $J$ = 11, 3.5 Hz) and a strong NOE between H18 and H16 ($\delta$ 3.73 td, $J$ = 11, 5 Hz). The remaining portion of **7** was shown to be the same as that of **6** by NMR analysis (Tables 1 and 4).

Compound **8** was identified as a known metabolite reported from *Carteriospongia foliascenes*.[16] All isolated compounds (**1**−**8**) exhibited 30−95% inhibition of the growth of KB cells at 10 $\mu$g/mL.

## Experimental Section

**General Experimental Procedures.** Melting points were recorded using an MRK hot plate instrument. Optical rotations were taken on a JASCO DIP-1000 polarimeter, and IR spectra on a JASCO FT/IR-300 spectrophotometer. $^1$H and $^{13}$C NMR spectra were recorded on a JEOL α-500 spectrometer. Mass spectra were measured on a Hitachi M-2500. HPLC was performed on a Hitachi L-6000 pump equipped with an RI monitor (655A-30) and UV detector (L-4000) using an ODS column (COSMOSIL 5C18-AR II, 10 × 250 mm). Kieselgel 60 (70−230 mesh, MERCK) was used for column chromatography. All solvents used were reagent grade.

**Animal Material.** The sponge (600 g, wet weight) was collected at a depth of 10−15 m by hand using scuba in Makassar, Indonesia, in August 2001. The specimen was frozen after collection. The sample was identified as *Phyllospongia* sp. (order Dictyoceratida, family Spongiidae) by one (N.V.) of us. A voucher specimen (9710A08) is deposited in our laboratory in Okinawa.

**Extraction and Isolation.** The frozen sample was brought to Okinawa and extracted with MeOH (1.2 L × 3). After concentration, the residue of the extract was partitioned between EtOAc and water to give a solid mixture (15 g). Half of the mixture (7.8 g) was separated on silica gel using $CH_2Cl_2$ with increasing amounts of MeOH to give 10 fractions. Fractions 6−8 were subjected to further purification by ODS HPLC using MeCN/$H_2O$ (90:10 and 65:35) to afford compounds **1**−**8**.

**Compound 1:** colorless crystals (MeOH/$H_2O$, 95:5, 163 mg); mp 185−187 °C; $[\alpha]_D^{23}$ +138° (*c* 0.83, $CHCl_3$); IR (film) $\nu_{max}$ 3453, 2935, 1714, 1238, 736 cm$^{-1}$; $^1$H and $^{13}$C NMR ($CDCl_3$), see Tables 1 and 3; EIMS *m*/*z* 460 $[M]^+$ (5), 424 (75), 354 (100),

**Table 4.** $^1$H NMR Data of **6**−**8** in $CDCl_3$ (500 MHz)[a,b]

| no. | 6 | 7 | 8 |
|---|---|---|---|
| 1 | 1.58 (m)[c] | 1.57 (m) | 1.55 (m) |
| | 0.61 (td, 13, 3.5) | 0.63 (td, 12.5, 3.5) | 0.68 (td, 12.5, 3.5) |
| 2 | 1.58 (m) | 1.58 (m) | 1.48 (m) |
| | 1.37 (m) | 1.38 (m) | 1.39 (m) |
| 3 | 1.38 (m) | 1.35 (m) | 1.65 (m) |
| | 1.12 (td, 14, 4.5) | 1.14 (td, 13.5, 4) | 0.86 (m) |
| 5 | 0.83 (dd, 12.5, 2.5) | 0.84 (overlapped) | 0.87 (dd, 9, 5) |
| 6 | 1.57 (m) | 1.58 (m) | 1.52 (m) |
| | 1.37 (m) | 1.39 (m) | 1.41 (m) |
| 7 | 1.75 (dt, 12.5, 3) | 1.75 (dt, 12, 3) | 1.76 (dt, 12.5, 3) |
| | 0.96 (td, 12.5, 3) | 0.96 (td, 12, 3) | 0.95 (td, 12.5, 3) |
| 9 | 1.21 (t, 7.5) | 1.33 (brt, 12.5) | 1.21 (t, 7.5) |
| 11 | 1.70 (dd, 8, 3) | 1.66 (m) | 1.69 (dd, 9, 3) |
| 12 | 4.76 (t, 2.5) | 4.90 (t, 2.5) | 4.76 (brt, 3) |
| 14 | 1.30 (m) | 1.11 (dt, 12.5, 2.5) | 1.30 (m) |
| 15 | 1.88 (dd, 10.5, 5) | 1.81 (m) | 1.88 (m) |
| | 1.35 (m) | 1.36 (m) | 1.32 (m) |
| 16 | 3.80 (brt, 9.5) | 3.73 (td, 11, 5) | 3.80 (brt, 11) |
| 16-OH | 2.68 (brd, 3) | | 2.65 (brs) |
| 17 | 2.57 (ddd, 13.5, 10, 4) | 2.71 (t, 11) | 2.57 (ddd, 13.5, 9.5, 3.5) |
| 18 | 1.30 (m) | 3.27 (dd, 11, 3.5) | 1.35 (m) |
| 18-OH | | 2.90 (d, 3.5) | |
| 19 | 0.85 (s) | 0.86 (s) | 0.80 (s) |
| 20 | 0.80 (s) | 0.81 (s) | 1.49 (m) |
| | | | 1.16 (dq, 14, 7.5) |
| 21 | 0.83 (s) | 0.88 (s) | 0.82 (s) |
| 22 | 0.79 (s) | 0.82 (s) | 0.81 (s) |
| 23 | 1.09 (s) | 1.02 (s) | 1.08 (s) |
| 26 | 2.14 (s) | 2.25 (s) | 2.14 (s) |
| 27 | | | 0.74 (t, 7.5) |
| 12-OAc | 2.07 (s) | 2.12 (s) | 2.07 (s) |

[a] Internal reference TMS ($\delta_H$ 0.0 ppm). [b] Assignment based on HMQC data. [c] Multiplicity and $J$ = Hz are indicated in parentheses.

311 (50), 205 (80), 191 (80); HREIMS *m/z* 460.3167 (calcd for $C_{28}H_{44}O_5$, 460.3186).

**Compound 1a:** glass (9 mg); $[\alpha]_D^{23}$ +108° (*c* 0.64, $CHCl_3$); IR (film) $\nu_{max}$ 2933, 1737, 1716, 1371, 1234, 1025, 755 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 9.48 (1H, s), 5.11 (1H, brt, $J$ = 2.7 Hz), 4.67 (1H, td, $J$ = 10, 5 Hz), 3.19 (1H, d, $J$ = 11.5 Hz), 3.09 (1H, dd, $J$ = 11.5, 11 Hz), 2.34 (3H, s), 2.20 (3H, s), 2.03 (3H, s), 0.97 (3H, s), 0.86 (3H, s), 0.84 (3H, s), 0.80 (3H, s), 0.79 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 211.0 (s, C24), 202.2 (d, C25), 170.2 (s, C12−OAc), 169.6 (s, C16−OAc), 75.8 (d, C12), 74.7 (d, C16), 58.4 (d, C18), 56.4 (d, C5), 52.3 (d, C9), 50.7 (d, C17), 49.1 (d, C14), 41.9 (t, C3), 41.3 (t, C7), 40.4 (s, C13), 39.7 (t, C1), 38.0 (s, C8), 36.8 (s, C10), 33.2 (s, C4), 33.1 (q, C19), 33.0 (q, C26), 25.9 (t, C15), 21.7 (t, C11), 21.5 (q, C12−OAc), 21.3 (q, C20), 21.0 (q, C16−OAc), 18.4 (t, C2), 18.0 (t, C6), 17.2 (q, C23), 16.9 (q, C21), 16.0 (q, C22); EIMS *m/z* 502 $[M]^+$ (2), 460 (5), 430 (60), 354 (100), 311 (40), 205 (50), 191 (70); HREIMS *m/z*. 460.3214 (calcd for $C_{28}H_{44}O_5$, 460.3187).

**Compound 2:** glass (60 mg); $[\alpha]_D^{23}$ +128° (*c* 1.07, $CHCl_3$), lit.[13] $[\alpha]_D^{23}$ +95° (*c* 0.27); IR (film) $\nu_{max}$ 3448, 2933, 1714, 1238, 736 cm$^{-1}$; $^1$H NMR ($CDCl_3$) data identical with those reported;[13] $^{13}$C NMR ($CDCl_3$), see Table 1; EIMS *m/z* 474 $[M]^+$ (20), 368 (100), 325 (75), 219 (90), 205 (90); HREIMS *m/z* 474.3331 (calcd for $C_{29}H_{46}O_5$, 474.3342).

**Compound 3:** solid (70 mg); mp 128−130 °C; $[\alpha]_D^{23}$ +42° (*c* 1.80, $CHCl_3$); IR (film) $\nu_{max}$ 3399, 2931, 1714, 1265, 736 cm$^{-1}$; $^1$H and $^{13}$C NMR ($CDCl_3$), see Tables 2 and 3; EIMS *m/z* 462 $[M]^+$ (5), 356 (80), 205 (100), 191 (90); HREIMS *m/z* 444.3245 (calcd for $C_{28}H_{44}O_4$, 444.3238).

**Compound 4:** solid (37 mg); $[\alpha]_D^{23}$ +38° (*c* 0.99, $CHCl_3$); IR (film) $\nu_{max}$ 3399, 2931, 1714, 1265, 736 cm$^{-1}$; $^1$H and $^{13}$C NMR ($CDCl_3$), see Tables 2 and 3; EIMS *m/z* 458 $[M - H_2O]^+$ (80), 370 (75), 219 (98), 205 (100); HREIMS *m/z* 458.3379 (calcd for $C_{29}H_{46}O_4$, 458.3393).

**Compound 5:** fine needles (MeOH−$H_2O$, 95:5) (7.5 mg); mp 170−171 °C; $[\alpha]_D^{23}$ +58° (*c* 0.50, $CHCl_3$); IR (film) $\nu_{max}$ 3448, 2942, 1716, 1249, 736 cm$^{-1}$; $^1$H and $^{13}$C NMR ($CDCl_3$), see Tables 2 and 3; EIMS *m/z* 505 $[M - H]^+$ (10), 446 (45), 428 (50), 386 (100); HREIMS *m/z* 505.3481 (calcd for $C_{30}H_{49}O_6$, 505.3525).

**Compound 6:** glass (18 mg); $[\alpha]_D^{23}$ +41° (*c* 1.24, $CHCl_3$); IR (film) $\nu_{max}$ 3444, 2933, 1714, 1247, 736 cm$^{-1}$; $^1$H and $^{13}$C NMR ($CDCl_3$), see Tables 1 and 4; EIMS *m/z* 432 $[M]^+$ (5), 414 (15), 372 (90), 354 (100), 205 (50), 191 (50); HREIMS *m/z* 414.3104 (calcd for $C_{27}H_{42}O_3$, 414.3131).

**Compound 7:** glass (7 mg); $[\alpha]_D^{23}$ +27° (*c* 0.48, $CHCl_3$); IR (film) $\nu_{max}$ 3440, 2933, 1712, 1263, 736 cm$^{-1}$; $^1$H and $^{13}$C NMR ($CDCl_3$), see Tables 1 and 4; EIMS *m/z* 448 $[M]^+$ (10), 388 (20), 302 (90), 258 (35), 192 (100); HREIMS *m/z* 430.3096 (calcd for $C_{27}H_{42}O_4$, 430.3081).

**Compound 8:** glass (14 mg); $[\alpha]_D^{23}$ +34° (*c* 0.95, $CHCl_3$), lit.[16] $[\alpha]_D$ +36° (*c* 0.78, $CH_2Cl_2$); IR (film) $\nu_{max}$ 3446, 2933, 1714, 1245, 736 cm$^{-1}$; $^1$H and $^{13}$C NMR ($CDCl_3$), see Tables 1 and 4; EIMS *m/z* 446 $[M]^+$ (5), 428 (20), 386 (90), 368 (100), 357 (95), 219 (60), 205 (60); HREIMS *m/z* 428.3287 (calcd for $C_{28}H_{44}O_3$, 428.3287).

**Acetylation of 1 and 3.** A sample of **1** (9.4 mg) was treated with acetic anhydride (0.25 mL) and pyridine (0.25 mL) in the usual manner to give 10.0 mg of **1a**. Similar treatment of **3** (4.1 mg) gave **3a** (4.5 mg). Product **1a** showed IR and $^1$H and $^{13}$C NMR spectra identical with those of **1a** isolated from the sponge.

**Compound 3a:** glass; IR (film) $\nu_{max}$ 2933, 1733, 1371, 1245, 1034, 755 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 6.04 (1H, d, $J$ = 6.5 Hz), 4.79 (1H, td, $J$ = 10.5, 5 Hz), 4.62 (1H, brs), 3.96 (1H, qd, $J$ = 10, 6 Hz), 2.29 (1H, dd, $J$ = 13, 7 Hz), 2.12 (3H, s), 2.05 (3H, s), 2.01 (3H, s), 1.22 (3H, d, $J$ = 6 Hz), 1.04 (3H, s), 0.86 (3H, s), 0.85 (3H, s), 0.79 (6H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 170.7 (s, OAc), 170.4 (s, OAc), 169.9 (s, OAc), 95.5 (d, C25), 78.6 (d, C24), 74.5 (d, C12), 73.8 (d, C16), 56.6 (d, C5), 53.3 (d, C18), 52.8 (d, C9), 51.9 (d, C17), 49.5 (d, C14), 41.9 (t, C3), 41.6 (t, C7), 39.8 (t, C1), 38.1 (s, C13), 37.9 (s, C8), 36.9 (s, C10), 33.3 (s, C4), 33.2 (q, C19), 26.9 (t, C15), 21.7 (q, C26), 21.6 (q, C20), 21.3 (q, OAc), 21.2 (q, OAc), 19.6 (q, OAc), 18.4 (t, C2), 18.1 (t, C6), 17.0 (q, C21), 16.1 (q, C23), 15.7 (q, C22); EIMS *m/z* 503 $[M - H]^+$ (40), 487 (30), 443 (80), 426 (100), 205 (10), 191 (15).

**Preparation of MTPA Esters of 1.** A solution of **1** (2.0 mg) in $CH_2Cl_2$ (0.3 mL) was treated with DMAP (0.5 mg), DCC (2.0 mg), and *R*-MTPA (5.0 mg) at room temperature for 6 h. The reaction mixture was filtered off and purified by HPLC

(Si) using $CH_2Cl_2$/EtOAc to furnish *R*-MTPA ester (**1b**, 0.6 mg). *S*-MTPA ester (**1c**, 1.2 mg) was similarly prepared using *S*-MTPA.

**Compound 1b:** glass (0.6 mg); $[\alpha]_D^{23}$ +188° (*c* 0.04, $CHCl_3$); IR (film) $\nu_{max}$ 2931, 1747, 1716, 1236, 1170, 1020, 757 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 9.43 (1H, s, H25), 7.26−7.45 (5H, mult., Ph), 5.10 (1H, brt, $J$ = 2.5 Hz, H12), 4.86 (1H, td, $J$ = 11, 5 Hz, H16), 3.59 (3H, brd, $J$ = 1 Hz, OMe), 3.14 (1H, d, $J$ = 11.5 Hz, H18), 3.07 (1H, dd, $J$ = 11.5, 11 Hz, H17), 2.20 (3H, s, OAc), 2.20/1.36 (2H, m, H15), 1.76 (3H, s, H26), 1.62 (1H, m, H14), 1.41 (1H, m, H9), 0.97 (3H, s, H23), 0.87 (3H, s, H19), 0.87 (1H, overlapped, H5), 0.85 (3H, s, H21), 0.81 (3H, s, H20), 0.80 (3H, s, H22).

**Compound 1c:** glass (1.2 mg); $[\alpha]_D^{23}$ +106° (*c* 0.08, $CHCl_3$); IR (film) $\nu_{max}$ 2931, 1743, 1716, 1234, 1184, 1016, 757 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 9.45 (1H, s, H25), 7.26−7.45 (5H, mult., Ph), 5.11 (1H, brt, $J$ = 2.5 Hz, H12), 4.84 (1H, td, $J$ = 11, 5 Hz, H16), 3.42 (3H, brd, $J$ = 1 Hz, OMe), 3.16 (1H, d, $J$ = 11.5 Hz, H18), 3.09 (1H, dd, $J$ = 11.5, 11 Hz, H17), 2.25/1.25 (2H, m, H15), 2.21 (3H, s, H26), 2.11 (3H, s, OAc), 1.62 (1H, m, H14), 1.33 (1H, m, H9), 0.96 (3H, s, H23), 0.87 (3H, s, H19), 0.85 (1H, overlapped, H5), 0.83 (3H, s, H21), 0.81 (3H, s, H20), 0.80 (3H, s, H22).

**Methylation of 3 and 4.** A few drops of HCl (0.1 N) were added to a methanolic solution of **3** (16.0 mg), and the solution was allowed to stand at room temperature for 10 min. The solvent was evaporated under a stream of nitrogen, and the product mixture was purified by ODS HPLC ($MeOH/H_2O$) to give compounds **3b** and **3c**. Similar treatment of **4** (12.0 mg) gave **4b** and **4c**.

**Compound 3b:** glass (11.0 mg); $[\alpha]_D^{23}$ +32° (*c* 0.7, $CHCl_3$); IR (film) $\nu_{max}$ 3442, 2931, 1716, 1251 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.72 (1H, d, $J$ = 6.5 Hz, H25), 4.70 (1H, brt, $J$ = 2.7 Hz, H12), 3.92 (1H, qd, $J$ = 5.5, 9.5 Hz, H24), 3.57 (1H, td, $J$ = 10, 4.5 Hz, H16), 3.30 (3H, s, C25−OMe), 2.04 (3H, s, C12−OAc), 1.95 (1H, dd, $J$ = 12.5, 6.5 Hz, H18), 1.89 (1H, ddd, $J$ = 12, 5, 5 Hz)/1.25 (1H, m, H15), 1.70/1.00 (2H, m, H7), 1.58/1.38 (4H, m, H2, H6), 1.56 (1H, m)/0.60 (1H, td, $J$ = 12, 6.5 Hz, H1), 1.50 (1H, m, H17), 1.40 (1H, m, H14), 1.36 (3H, d, $J$ = 5.5 Hz, H26), 1.23 (1H, m, H9), 0.98 (3H, s, H23), 0.86 (3H, s, H21), 0.85 (3H, s, H19), 0.82 (1H, overlapped, H5), 0.80 (6H, s, H20, H22); $^{13}C$ NMR ($CDCl_3$), see Table 2; EIMS *m*/*z* 476 $[M]^+$ (30), 445 (30), 416 (65), 356 (100), 338 (30), 191 (50).

**Compound 3c:** glass (2.0 mg); IR (film) $\nu_{max}$ 3399, 2931, 1714, 1265 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.95 (1H, brt, $J$ = 2 Hz, H12), 4.54 (1H, d, $J$ = 4 Hz, H25), 3.88 (1H, qd, $J$ = 5, 9.5 Hz, H24), 3.46 (1H, tdd, $J$ = 10, 5, 5 Hz, H16), 3.27 (3H, s, C25−OMe), 2.09 (3H, s, C12−OAc), 1.90 (1H, m, H17), 1.87/1.38 (2H, m, H15), 1.70 (1H, m, H18), 1.57/1.36 (4H, m, H2, H6), 1.56 (1H, m)/0.57 (1H, td, $J$ = 13, 6.5 Hz, H1), 1.39 (3H, d, $J$ = 6 Hz, H26), 1.36/1.11 (2H, m, H7), 1.27 (1H, brd, $J$ = 13 Hz, H14), 1.20 (1H, brd, $J$ = 13 Hz, H9), 1.17 (3H, s, H23), 0.87 (3H, s, H21), 0.85 (3H, s, H19), 0.83 (1H, overlapped, H5), 0.80 (6H, s, H20, H22); $^{13}C$ NMR ($CDCl_3$), see Table 2; EIMS *m*/*z* 476 $[M]^+$ (60), 416 (75), 356 (100), 191 (40).

**Compound 4b:** solid (7.5 mg); $[\alpha]_D^{23}$ +27° (*c* 0.51, $CHCl_3$); IR (film) $\nu_{max}$ 3444, 2931, 1716, 1249 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.72 (1H, d, $J$ = 6.5 Hz, H25), 4.69 (1H, brt, $J$ = 2.7 Hz, H12), 3.91 (1H, qd, $J$ = 5.5, 9.5 Hz, H24), 3.56 (1H, td, $J$ = 10, 4.5 Hz, H16), 3.30 (3H, s, C25−OMe), 2.04 (3H, s, C12−OAc), 1.95 (1H, dd, $J$ = 13, 6 Hz, H18), 1.88 (1H, d, $J$ = 11. 5 Hz)/1.24 (1H, m, H15), 1.70/0.98 (2H, m, H7), 1.57 (1H, m)/0.60 (1H, td, $J$ = 12, 6.5 Hz, H1), 1.50 (1H, m, H14), 1.50/1.15 (2H, m H20), 1.46/1.35 (4H, m, H2, H6), 1.36 (3H, d, $J$ = 5.5 Hz, H26), 1.35 (1H, m, H17), 1.16 (1H, m, H9), 0.98 (3H, s, H23), 0.85 (3H, s, H21), 0.82 (1H, overlapped, H5), 0.82 (3H, s, H22), 0.80 (3H, s, H19), 0.74 (3H, t, $J$ = 7.5 Hz, H27); $^{13}C$ NMR ($CDCl_3$), see Table 2; EIMS *m*/*z* 490 $[M]^+$ (45), 459 (35), 430 (55), 370 (100), 219 (10), 205 (35).

**Compound 4c:** glass (1.5 mg); $[\alpha]_D^{23}$ +52° (*c* 0.14, $CHCl_3$); IR (film) $\nu_{max}$ 3444, 2931, 1716, 1249 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.95 (1H, t, $J$ = 2.7 Hz, H12), 4.54 (1H, d, $J$ = 3.5 Hz, H25), 3.87 (1H, qd, $J$ = 6, 8.5 Hz, H24), 3.46 (1H, tdd, $J$ = 10, 5, 5 Hz, H16), 3.27 (3H, s, C25−OMe), 2.10 (3H, s, C12−OAc), 1.91 (m, H17), 1.86/1.37 (2H, m, H15), 1.70 (1H, m, H18), 1.59 (1H, m)/0.58 (1H, td, $J$ = 12.5, 3.5 Hz, H1), 1.55/1.37 (4H, m, H2, H6), 1.50/1.15 (2H, m, H20), 1.39 (3H, d, $J$ = 6 Hz, H26), 1.36/1.15 (2H, m, H7), 1.26 (1H, dd, $J$ = 12.5, 2.5 Hz, H14), 1.20 (1H, dd, $J$ = 12.5, 2.5 Hz, H9), 1.16 (3H, s, H23), 0.86 (3H, s, H21), 0.83 (1H, overlapped, H5), 0.81 (3H, s, H22), 0.80 (3H, s, H19), 0.74 (3H, t, $J$ = 7.5 Hz, H27); $^{13}C$ NMR ($CDCl_3$), see Table 2; EIMS *m*/*z* 490 $[M]^+$ (12), 459 (20), 430 (40), 370 (100), 219 (10), 205 (55).

**X-ray Diffraction of 1.**[18] Suitable colorless crystals of **1** were obtained by recrystallization ($MeOH/H_2O$, 95:5). The crystal (0.40 × 0.25 × 0.40 mm) belonged to the orthorhombic system, space group $P2_12_12_1$, with $a$ = 7.9045(3) Å, $b$ = 10.6863(7) Å, $c$ = 30.072(1) Å, $V$ = 2540.1(2) $Å^3$, $Z$ = 4, $D_{calcd}$ = 1.204 $g/cm^3$, $\lambda$(Mo K$\alpha$) = 0.71069 Å. Intensity data were measured on a Rigaku RAXIS-RAPID diffractometer up to 2$\theta$ of 55°. A total of 3309 reflections were collected. The structure was solved by direct methods (SIR 92) and refined by full-matrix least-squares procedure. The non-hydrogen atoms were given anisotropic thermal parameters. The refinement converged to a final $R$ = 0.068, $R_w$ = 0.055 for 2535 observed reflections [$I > 3.00\sigma(I)$] and 298 variable parameters.

**Acknowledgment.** We thank A. Trianto, Diponegoro University, for his help with the collection of the sponge. We also thank S. Aoki and M. Kobayashi, Osaka University, for the cytotoxicity assay. Financial support from the Ministry of Education, Culture, Sports, Science, and Technology of Japan is gratefully acknowledged.

**Supporting Information Available:** ORTEP drawing of the X-ray structure of **1** and $^1H$ and $^{13}C$ NMR spectra of compounds **1**−**7**. This material is available free of charge via the Internet at http://pubs.acs.org.

## References and Notes

(1) Jiménez, J. I.; Yoshida, W. Y.; Scheuer, P. J.; Kelly, M. *J. Nat. Prod.* **2000**, *63*, 1388−1392.
(2) Miyamoto, T.; Sakamoto, K.; Amano, H.; Arakawa, Y.; Nagarekawa, Y.; Komori, T.; Higuchi, R.; Sasaki, T. *Tetrahedron* **1999**, *55*, 9133−9142.
(3) Fontana, A.; Mollo E.; Ortea, J.; Gavagnin, M.; Cimino, G. *J. Nat. Prod.* **2000**, *63*, 527−530.
(4) Fontana, A.; Cavaliere, P.; Ungur, N.; D′Souza, L.; Parameswaram, P. S.; Cimino, G. *J. Nat. Prod.* **1999**, *62*, 1367−1370.
(5) Alvi, K. A.; Crews, P. *J. Nat. Prod.* **1992**, *55*, 859−865.
(6) De Rosa, S.; Puliti, R.; Crispino, A.; De Giulio, A.; Mattia, C. A.; Mazzarella, L. *J. Nat. Prod.* **1994**, *57*, 256−262.
(7) Youssef, D. T. A.; Yamaki, R. K.; Kelly, M.; Scheuer, P. J. *J. Nat. Prod.* **2002**, *65*, 2−6.
(8) Crews, P.; Bescansa, P. *J. Nat. Prod.* **1986**, *49*, 1041−1052.
(9) Jiménez, J. I.; Yoshida, W. Y.; Scheuer, P. J.; Lobkovsky, E.; Clardy, J.; Kelly, M. *J. Org. Chem.* **2000**, *65*, 6837−6840.
(10) De Rosa, S.; Crispino, A.; De Giulio, A.; Iodice, C.; Tommonaro, G.; Zavodnik, N. *Tetrahedron* **1998**, *54*, 6185−6190.
(11) Tsuchiya, N.; Sato. A.; Hata, T.; Sato, N.; Sasagawa, K.; Kobayashi, T. *J. Nat. Prod.* **1998**, *61*, 468−473.
(12) Miyaoka, H.; Nishijima, S.; Mitome, H.; Yamada, Y. *J. Nat. Prod.* **2000**, *63*, 1369−1372.
(13) Bowden, B. F.; Coll, J. C.; Li, H.; Cambie, R. C.; Kernan, M. R.; Bergquist, P. R. *J. Nat. Prod.* **1992**, *55*, 1234−1240.
(14) Aoki, S.; Higuchi, K.; Isozumi, N.; Matsui, K.; Miyamoto, Y.; Itoh, N.; Tanaka, K.; Kobayashi, M. *Biochem. Biophys. Res. Commun.* **2001**, *282*, 426−431.
(15) Chang, L. C.; Otero-Quintero, S.; Nicholas, G. M.; Bewley, C. A. *Tetrahedron* **2001**, *57*, 5731−5738.
(16) Braekman, J. C.; Daloze, D.; Kaisin, M.; Moussiaux, B. *Tetrahedron* **1985**, *41*, 6403−6414, and references therein.
(17) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092−4096.
(18) Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre (deposition number CCDC184433). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

NP020311I