New Sesterterpenes from the Sponge *Smenospongia* sp.

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Five new sesterterpenes, three scalarane-type (**1**−**3**) and two linear furanosesterterpenes (**4**, **5**), were isolated from the marine sponge *Smenospongia* sp. collected from Gagu-Do, Korea. The structures of the new compounds, which exhibited moderate cytotoxicity toward the human leukemia cell line K562, were determined from an analysis of spectroscopic data.

Sponges produce a wide variety of structurally unique and biologically active secondary metabolites.[1] Of the diverse carbon skeletons of sponge-derived terpenoids and mixed biogenetic compounds containing polyprenyl moieties, tetracyclic scalarane is recognized as one of the most frequently encountered skeletons of sesterterpenoids.[1,2] Compounds of this structural class are particularly abundant among animals of the order Dictyoceratida and are thus considered to be the important chemotaxonomic markers of these sponges.[3] These compounds also exhibit diverse bioactivities such as antimicrobial,[4] cytotoxic,[2a,c,5,6] anti-inflammatory,[7,8] and platelet-aggregation inhibitory[9] activities as well as important ecological functions including antipredation[10] and ichthyotoxicity.[11]

During the course of our search for bioactive metabolites from marine organisms of Korea, we encountered the brown encrusting sponge *Smenospongia* sp. (order Dictyoceratida, family Thorectidae) from Gagu-do (Island), southwestern Korea. The crude extracts of this specimen exhibited moderate cytotoxicity (LC_{50} 47 μg/mL against the K562 cell line) and brine shrimp lethality (LC_{50} 160 ppm). Bioassay-guided separation of the crude extracts employing solvent-partitioning followed by vacuum flash chromatography, silica, and reversed-phase HPLC yielded several metabolites. Herein we describe the structure determination and bioactivity of five new sesterterpenes of the scalarane (**1**−**3**) and acyclic (**4** and **5**) carbon skeletons.

Compound **1** was isolated as an amorphous solid that analyzed for $C_{29}H_{42}O_6$ by combined HRFABMS and ^{13}C NMR spectrometry. The terpenoidal nature of this compound was apparent from several signals of upfield methyl carbons in the ^{13}C NMR data. Because the presence of two acetoxyl groups, a carbonyl, and a single double bond were revealed from the preliminary analyses of the ^1H and ^{13}C NMR data, the remaining five degrees of unsaturation inherent in the molecule suggested that **1** possessed five rings.

The carbonyl carbon at δ 166.5 (C) in the ^{13}C NMR data, coupled with the absorption band at 1775 cm^{-1} in the IR spectrum, revealed the presence of a γ-lactone in the molecule, while an acetal group was defined on the basis of characteristic chemical shifts of the proton and carbon of a methine (δ_H 6.45, δ_C 93.5). Long-range correlations of the acetal proton with the carbonyls at δ 166.5 and 169.0 in the gHMBC data located the acetal, substituted with an acetoxyl group, at the γ-position of the lactone (Table 1). Similarly, the positioning of a trisubstituted double bond at the α-position of the lactone was determined by the long-range correlations of the olefinic proton at δ 6.92 with the lactone carbonyl and β-methine carbon at δ 56.3.

The remaining part of the molecule was also determined by combined interpretation of ^1H COSY, TOCSY, gHSQC, and gHMBC data. Long-range correlations between the upfield methyl protons and neighboring carbons in the gHMBC data were particularly helpful to construct the six-membered hydrocarbon rings A−D (Table 1). The presence of an oxymethylene, substituted with an acetoxyl group, at the C-23 of the A/B ring juncture was evident from the long-range correlations of the methylene protons at δ 4.59 and 4.15 with C-1, C-9, C-10, and the carbonyl carbon at δ 171.0, which in turn correlated to a methyl proton at δ 2.06.

The stereochemistry at the asymmetric carbon centers were assigned on the basis of ROESY and 1-D NOESY experiments. The ROESY cross-peaks H-22/H-23 and H-23/H-24 assigned axial orientations for C-22, C-23, and C-24 on the molecular plane. This spatial proximity was extended to the lactone ring by the cross-peaks H-24/H-25 and H-19/H-25. Conversely, a series of NOE correlations H-1α/H-3α, H-1/H-9, H-3α/H-5, H-5/H-6α, H-6α/H-7α, H-7α/H-14, and H-9/H-14, coupled with the characteristic splitting pattern of the ring juncture protons H-5, H-9, and H-14 in the ^1H NMR spectra (Table 1), assigned axial orientations for all of these protons at the opposite side of the molecular plane, thereby *trans* orientations for all of the ring junctures in the molecule. The orientation of H-18 was assigned to be α on the basis of the ROESY cross-peak H-14/H-18. Hence, the structure of compound **1** was determined to be 12-deacetoxy-23-acetoxy-19-*O*-acetylscalarin, a sesterterpene lactone of the scalarane class.[12]

The molecular formula of compound **2** was deduced as $C_{27}H_{40}O_5$ by combined HRFABMS and ^{13}C NMR analyses. The spectral data for this compound were very similar to those of **1**, with the loss of signals for an acetoxyl group in the ^1H and ^{13}C NMR data as the most noticeable change. A combination of 2-D NMR experiments showed that **2** possessed a ring structure identical to that of **1**. The structural difference was traced to the replacement of the acetoxyl group with a hydroxyl group at C-19, as evidenced by the significant upfield shift of the H-19 protons at δ 5.64

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Table 1. ^{1}H and ^{13}C NMR Assignments for Compounds **1** and **3**[a]

	1				3		
no.	δ_H	δ_C		HMBC	δ_H	δ_C	
1α	0.74, ddd (13.7, 13.7, 2.0)	34.9	CH_2	C-2, C-3, C-5, C-10	0.70, ddd (13.2, 13.2, 3.4)	34.4	CH_2
β	2.08, br d (13.7)				2.21, br d (13.2)		
2α	1.45, m	18.4	CH_2	C-3	1.48, m	18.5	CH_2
β	1.59, m				1.59, br ddd (14.2, 13.2, 13.2)		
3α	1.16, m	41.6	CH_2	C-4, C-5	1.17, ddd (13.2, 13.2, 3.9)	41.8	CH_2
β	1.45, br d (12.2)				1.43, br d (13.2)		
4		33.0	C			33.0	C
5	0.98, br d (12.7)	56.9	CH	C-4, C-6, C-23	0.94, br d (12.2)	56.9	CH
6α	1.56, br d (13.7)	17.9	CH_2	C-4, C-5, C-7	1.52, m	17.9	CH_2
β	1.39, dddd (13.7, 13.2, 12.7, 2.9)				1.36, m		
7α	1.05, ddd (13.2, 12.7, 3.9)	42.0	CH_2	C-6, C-8, C-9, C-14, C-24	1.01, m	42.52	CH_2
β	1.80, br d (12.7)				1.84, br d (12.7)		
8		37.7	C			38.1	C
9	1.00, br d (13.2)	61.7	CH	C-5, C-23	0.88, br d (13.2)	61.9	CH
10		40.7	C			42.46	C
11α	1.76, br d (13.2)	19.7	CH_2		1.77, m	20.4	CH_2
β	1.65, ddd (13.2, 13.2, 12.2)				1.71, dddd (13.2, 12.7, 12.7, 3.4)		
12α	1.16, m	41.1	CH_2	C-9, C-11, C-25	1.01, m[b]	41.9	CH_2
β	1.73, br d (13.2)				1.79, m		
13		34.0	C			36.9	C
14	1.34, dd (11.2, 5.4)	54.8	CH	C-8, C-9, C-13, C-15, C-16, C-18, C-24, C-25	1.03, br d (11.7)	56.5	CH
15	2.39, ddd (20.5, 5.4, 3.4)	24.2	CH_2	C-8, C-13, C-14, C-16, C-17	2.08, m;[b] 1.36, m[b]	28.4	CH_2
	2.14, br dd (20.5, 11.2)						
16	6.92, br dd (3.4, 3.4)	137.4	CH	C-14, C-18, C-20	5.41, dd (9.8, 6.8)	69.5	CH
17		126.0	C			114.2	C
18	2.65, m	56.3	CH	C-12, C-13, C-14, C-16, C-17, C-19, C-25	2.33, br s	63.4	CH
19	6.45, d (5.9)	93.5	CH	C-13, C-18, C-20, carbonyl(19)	6.33, d (1.5)	98.3	CH
20		166.5	C		6.10, d (1.5)	134.7	CH
21	0.88, s	33.8	CH_3	C-3, C-4, C-5, C-22	0.87, s	33.9	CH_3
22	0.84, s	21.9	CH_3	C-3, C-4, C-5, C-21	0.77, s	21.8	CH_3
23	4.59, d (12.2); 4.15, d (12.2)	64.7	CH_2	C-1, C-9, C-10, carbonyl(23)	4.02, d (11.7); 3.88, d (11.7)	62.8	CH_2
24	0.98, s	15.8	CH_3	C-7, C-8, C-9, C-14	1.03, s	16.7	CH_3
25	0.83, s	14.7	CH_3	C-12, C-13, C-14, C-18	0.87, s	14.4	CH_3
16-OAc						170.1	C
					2.11, s	21.1	CH_3
19-OAc		169.0	C			170.0	C
	2.14, s	20.9	CH_3	carbonyl(19)	2.07, s	21.2	CH_3
23-OAc		171.0	C				
	2.06, s	21.2	CH_3	carbonyl(23)			

[a] NMR data were obtained in $CDCl_3$ solutions. Assignments were aided by a combination of ^{1}H COSY, TOCSY, gHSQC, and gHMBC experiments. [b] Due to the overlapping with other signals, splitting patterns were not accurately measured.

in the ^{1}H NMR spectra of **2** as well as the loss of long-range coupling between this proton and the acetoxyl group in the gHMBC data. Thus, the structure of compound **2** was established as 12-deacetoxy-23-acetoxyscalarin.

The molecular formula of compound **3** was assigned as $C_{29}H_{44}O_6$ by HRFABMS and ^{13}C NMR analyses. The spectral data for this compound were highly compatible with those of other scalaranes. However, detailed examination of the ^{1}H and ^{13}C NMR data revealed that signals of protons and carbons of ring D and the lactone moiety of **1** were shifted significantly. First, the replacement of the γ-lactone with another structural moiety was strongly suggested from the loss of both the signal of the carbonyl carbon in the ^{13}C NMR data and a characteristic absorption band in the IR data. The newly appearing moiety was defined to be a dihydrofuran on the basis of the long-range correlations of the acetal proton at δ 6.33 with the olefinic carbons at δ 134.7 and 114.2 and the methine carbon at δ 63.4 in the gHMBC data (Table 1). Similarly, an acetoxyl group was placed at C-16 by the long-range correlations of an oxymethine proton at δ 5.41 with the olefinic carbons, C-15 at δ 28.4, and a carbonyl carbon at δ 170.1. The removal of an acetyl group from C-23 was apparent from the significant upfield shifts of the H-23 oxymethylene protons as well as the loss of long-range correlations between these and a carbonyl carbon in the gHMBC data. The structure of the remaining portion of the molecule was defined to be identical to **1** by combined 2-D NMR analyses. The β-orientation of the newly appearing C-16 acetoxyl group was secured by the ROESY cross-peaks H-14/H-16, H-14/H-18, and H-16/H-18. Thus, the structure of compound **3** was determined to be 12-dehydroxy-23-hydroxyheteronemin.[13]

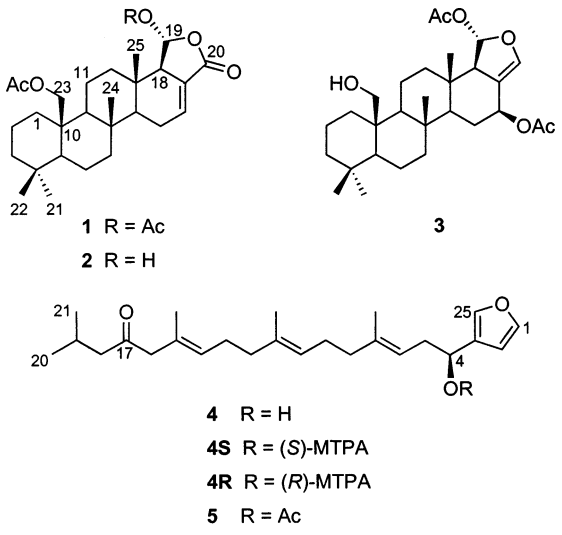
Compound **4** was isolated as an amorphous solid that analyzed for $C_{25}H_{38}O_3$ by HRFABMS and ^{13}C NMR spectrometry. The presence of the signals of a carbonyl carbon at δ 209.6 and 10 olefinic carbons in the region δ 145−105 in the ^{13}C NMR data suggested that **4** possessed only one ring. Three downfield protons at δ 7.38 (2H) and 6.41 (1H) in the ^{1}H NMR data and small coupling constants (1 Hz) among these protons were indicative of a 3-substituted furan moiety, which was confirmed by long-range correlations between these protons and neighboring carbons in the gHMBC data. Accordingly, the remaining part of **4** had an acyclic structure that was determined to be a linear array of tetraisoprene on the basis of combined ^{1}H COSY and gHMBC experiments. A hydroxyl group was placed at C-4 by the long-range correlations of the oxymethine proton

at δ 4.66 with C-2, C-3, and C-5. The carbonyl group was similarly assigned at C-17 by its long-range correlations with H-16 and H-18.

The absolute stereochemistry of the asymmetric carbon center at C-4 was determined by Mosher's method. Measurement of the difference of chemical shifts between the corresponding protons in the ^{1}H NMR data of **4S** and **4R**, prepared following the standard method, showed that $\Delta\delta$-(**4S**−**4R**) for H-2 was +68.9 Hz, while those for H-5, H-6, and H-24 were −25.4, −16.4 (two protons of H-5), −57.6, and −17.6 Hz, respectively. Thus, the configuration at C-4 was assigned to be *S* for compound **4**, which was designated as 4-hydroxy-9-deoxoidiadione.[10]

The molecular formula of compound **5** was deduced as $C_{27}H_{40}O_4$ by HRFABMS and ^{13}C NMR analyses. The ^{1}H and ^{13}C NMR data of this compound were very similar to those of **4**, with the appearance of signals for an acetyl group {δ_H 2.04 (3H, s), δ_C 170.4 (C), 21.2 (CH_3)} as the most noticeable difference. Upon the downfield shift of H-4 from δ 4.66 in **4** to 5.75 in **5**, the newly appeared substituent was positioned at C-4, which was confirmed by combined 2-D NMR experiments. Hence, the structure of **5** was defined to be the 4-*O*-acetyl derivative of **4** and designated as 4-acetoxy-9-deoxoidiadione.[10]

Sponge-derived sesterterpenoids exhibit diverse and potent bioactivities.[1] In our measurement, these compounds displayed moderate cytotoxicity toward the human leukemia cell-line K562 with LC_{50} 4.9, 11.2, 0.02, 3.0, and 31.6 μg/mL for **1**−**5**, respectively. It is noteworthy that changes of functional groups in the scalarane sesterterpenoids, as noticed between **2** and **3**, resulted in the significant difference of bioactivity as much as 3 orders of magnitude.



Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO digital polarimeter using a 5 cm cell. UV spectra were obtained in methanol using a Milton-Roy spectrophotometer. IR spectra were recorded on a Mattson GALAXY spectrophotometer. NMR spectra were recorded in $CDCl_3$ solutions containing Me_4Si as internal standard, on a Varian Unity 500 spectrometer. Proton and carbon NMR spectra were measured at 500 and 125 MHz, respectively. Mass spectra were obtained by using a JEOL JMS-HX 110 high-resolution mass spectrometer and provided by the Korea Basic Science Institute, Taejeon, Korea. All solvents used were spectral grade or were distilled from glass prior to use.

Animal Material. Specimens of the horny sponge *Smenospongia* sp. (sample number 00SH-19) was collected by scuba at 15−20 m depth off the shore of Gagu-Do (Island), southwestern Korea in July 2000. The specimens were massive (80 mm × 95 mm × 70 mm) and had several locally opened oscules (1−5 mm in diameter). The color was dark reddish brown in life and turned to dark brown in alcohol. Texture was firm and compressible but readily cut and torn off. The surface was covered with sharply pointed low conules (<1 mm in height, 1−3 mm apart). All fibers were dark brown in color and were concentrically laminated. The primary fibers (100−225 μm in diameter) were cored with small amounts of sand and spicules, while the secondary fibers (50−150 μm in diameter) were devoid of detritus. A voucher specimen (registry No. Spo. 43) is currently on deposit at the Natural History Museum, Hannam University, Korea, under the curatorship of C.J.S.

Extraction and Isolation. The fresh collection was immediately frozen using dry ice and kept at −25 °C until investigated chemically. The specimens were defrosted (wet wt 0.85 kg), macerated, and repeatedly extracted with MeOH (2 L × 2) and CH_2Cl_2 (2 L × 2). The combined crude extract (ca. 49 g) was partitioned between CH_2Cl_2 and H_2O. The former layer (13.1 g) was subjected to reversed-phase vacuum flash chromatography using gradient mixtures of MeOH and H_2O as eluents (elution order: 50%, 40%, 30%, 20%, 10% aqueous MeOH, 100% MeOH) and finally acetone. The fraction (1.2 g) eluted with 100% MeOH was separated by semi-preparative reversed-phase HPLC (YMC ODS-A column, 1 cm × 25 cm, 15% aqueous MeOH) to yield, in order of elution, **2**, **3**, **4**, **1**, and **5**. Final purification was accomplished by reversed-phase HPLC (10% aqueous MeOH) to afford 10.3, 29.3, 21.7, 18.1, and 16.9 mg of **1**−**5**, respectively.

12-Deacetoxy-23-acetoxy-19-*O*-acetylscalarin (1): amorphous solid; $[\alpha]^{25}_D$ −22.9° (*c* 0.11, MeOH); UV (MeOH) λ_{max} (log ϵ) 221 (3.79) nm; IR (KBr) ν_{max} 2930, 2850, 1775, 1740, 1375, 1235, 1200 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; HRFABMS *m*/*z* 509.2879 [M + Na]$^+$ (calcd for $C_{29}H_{42}O_6Na$, 509.2883).

12-Deacetoxy-23-acetoxyscalarin (2): amorphous solid; $[\alpha]^{25}_D$ −33.1° (*c* 0.23, MeOH); UV (MeOH) λ_{max} (log ϵ) 220 (3.80) nm; IR (KBr) ν_{max} 3400 (br), 2935, 2855, 1740, 1455, 1390, 1240, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.86 (1H, br s, H-16), 5.64 (1H, br s, H-19), 4.58 (1H, d, *J* = 12.2 Hz, H-23), 4.17 (1H, d, *J* = 12.2 Hz, H-23), 2.45 (1H, br s, H-18), 2.35 (1H, dd, *J* = 20.5, 4.9 Hz, H-15), 2.12 (1H, dd, *J* = 20.5, 11.2 Hz, H-15), 2.08 (1H, br d, *J* = 13.2 Hz, H-1), 2.07 (3H, s, OAc), 1.89 (1H, br d, *J* = 13.7 Hz, H-12), 1.79 (1H, br d, *J* = 12.7 Hz, H-7), 1.77 (1H, br d, *J* = 12.7 Hz, H-11), 1.63 (1H, br ddd, *J* = 13.2, 12.7, 12.2 Hz, H-11), 1.58 (1H, m, H-2), 1.56 (1H, br d, *J* = 13.7 Hz, H-6), 1.44 (2H, br dd, *J* = 12.7, 2.9 Hz, H-2, H-3), 1.39 (1H, dddd, *J* = 13.7, 13.2, 13.2, 3.4 Hz, H-6), 1.31 (1H, dd, *J* = 11.2, 4.9 Hz, H-14), 1.28 (1H, br dd, *J* = 13.7, 12.2 Hz, H-12), 1.17 (1H, ddd, *J* = 13.7, 12.7, 3.9 Hz, H-3), 1.05 (1H, ddd, *J* = 13.2, 12.7, 3.4 Hz, H-7), 1.00 (1H, dd, *J* = 13.2, 3.9 Hz, H-9), 0.98 (1H, dd, *J* = 13.2, 3.9 Hz, H-5), 0.98 (3H, s, H-24), 0.88 (3H, s, H-21), 0.83 (3H, s, H-22), 0.82 (3H, s, H-25), 0.75 (1H, ddd, *J* = 13.2, 13.2, 3.9 Hz, H-1); ^{13}C NMR ($CDCl_3$) δ 171.1 (C, OAc), 167.6 (C, C-20), 136.4 (CH, C-16), 127.7 (C, C-17), 98.6 (CH, C-19), 64.8 (CH_2, C-23), 61.7 (CH, C-9), 59.1 (CH, C-18), 56.8 (CH, C-5), 54.8 (CH, C-14), 42.0 (CH_2, C-7), 41.6 (CH_2 × 2, C-3, C-12), 40.7 (C, C-10), 37.7 (C, C-8), 34.9 (CH_2, C-1), 33.9 (C, C-13), 33.7 (CH_3, C-21), 33.0 (C, C-4), 24.1 (CH_2, C-15), 21.8 (CH_3, C-22), 21.2 (CH_3, OAc), 19.7 (CH_2, C-11), 18.4 (CH_2, C-2), 17.9 (CH_2, C-6), 15.9 (CH_3, C-24), 15.0 (CH_3, C-25); HRFABMS *m*/*z* 467.2773 [M + Na]$^+$ (calcd for $C_{27}H_{40}O_5Na$, 467.2770).

12-Deacetoxy-23-hydroxyheteronemin (3): amorphous solid; $[\alpha]^{25}_D$ −38.1° (*c* 0.25, MeOH); IR (KBr) ν_{max} 3450 (br), 2945, 2850, 1745, 1455, 1365, 1235, 1030 cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; HRFABMS *m*/*z* 511.3036 [M + Na]$^+$ (calcd for $C_{29}H_{44}O_6Na$, 511.3034).

4-Hydroxy-9-deoxoidiadione (4): amorphous solid; $[\alpha]^{25}_D$ −5.5° (*c* 0.29, MeOH); IR (KBr) ν_{max} 3435 (br), 2925, 2870, 1710, 1445, 1365, 1230, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.38 (2H, br d, *J* = 1.0 Hz, H-1, H-25), 6.41 (1H, br s, H-2), 5.23 (1H, t, *J* = 6.8 Hz, H-14), 5.17 (1H, t, *J* = 6.8 Hz, H-6), 5.09 (1H, t, *J* = 6.8 Hz, H-10), 4.66 (1H, t, *J* = 7.8 Hz, H-4), 3.01

(2H, s, H-16), 2.49 (1H, ddd, J = 14.2, 7.8, 6.8 Hz, H-5), 2.44 (1H, ddd, J = 14.2, 7.8, 6.8 Hz, H-5), 2.28 (2H, d, J = 6.8 Hz, H-18), 2.12 (3H, m, H-13, H-19), 2.05 (2H, m, H-9), 2.03 (2H, m, H-8), 2.01 (2H, m, H-12), 1.64 (3H, s, H-24), 1.61 (3H, s, H-22), 1.60 (3H, s, H-23), 0.89 (6H, d, J = 6.8 Hz, H-20, H-21); ^{13}C NMR ($CDCl_3$) δ 209.6 (C, C-17), 143.2 (CH, C-1), 139.4 (C, C-7), 139.0 (CH, C-25), 135.0 (C, C-11), 129.5 (CH, C-14), 128.9 (C, C-15), 128.7 (C, C-3), 124.2 (CH, C-10), 119.3 (CH, C-6), 108.6 (CH, C-2), 66.7 (CH, C-4), 54.5 (CH_2, C-16), 50.5 (CH_2, C-18), 39.8 (CH_2, C-8), 39.3 (CH_2, C-12), 36.7 (CH_2, C-5), 26.7 (CH_2, C-13), 26.4 (CH_2, C-9), 24.4 (CH, C-19), 22.6 (CH_3 x 2, C-20, C-21), 16.40 (CH_3, C-22), 16.36 (CH_3, C-24), 16.0 (CH_3, C-23); HRFABMS m/z 409.2719 $[M + Na]^+$ (calcd for $C_{25}H_{38}O_3$Na, 409.2719).

(*S*)-MTPA Esterification of 4. To a stirred solution of 2.7 mg of **4** in 0.5 mL of dry pyridine was added 20 μL of (−)-MTPA chloride. The mixture was allowed to stand under N_2 at room temperature for 3 h. After confirming the consumption of starting material by TLC, 0.5 mL of H_2O, 0.3 mL of CH_2Cl_2, and 1 mL of MeOH were added sequentially. After removing the solvents under vacuum, the residue was redissolved in 2 mL of 20% EtOAc/hexane, filtered through a silica Sep-Pak column, and then separated by silica HPLC (20% EtOAc/hexane) to afford 1.3 mg of **4S**: ^{1}H NMR ($CDCl_3$) δ 7.46−7.34 (7H, m, H-1, H-25, Ph), 6.430 (1H, t, J = 1.0, 1.0 Hz, H-2), 5.984 (1H, dd, J = 7.3, 6.8 Hz, H-4), 5.249 (1H, dd, J = 7.3, 6.8 Hz, H-14), 5.079 (1H, t, J = 7.3 Hz, H-10), 5.012 (1H, dd, J = 7.3, 6.8 Hz, H-6), 3.462 (3H, s, OMe), 3.018 (2H, s, H-16), 2.643 (1H, dt, J = 14.7, 7.3 Hz, H-5), 2.522 (1H, dt, J = 14.7, 6.8 Hz, H-5), 2.295 (2H, d, J = 6.8 Hz, H-18), 2.14−2.09 (3H, m, H-13, H-19), 2.05 (2H, m, H-9), 2.03−2.00 (4H, m, H-8, H-12), 1.618 (3H, br s, H-22), 1.590 (3H, br s, H-23), 1.548 (3H, br s, H-24), 0.901 (6H, d, J = 7.3 Hz, H-20, H-21).

(*R*)-MTPA Esterification of 4. 4R was prepared using (+)-MTPA chloride following the same procedure for **4S**. From 2.7 mg of **4** was obtained 1.6 mg of **4R**: ^{1}H NMR ($CDCl_3$) δ 7.45−7.33 (7H, m, H-1, H-25, Ph), 6.292 (1H, br d, J = 1.0 Hz, H-2), 5.966 (1H, dd, J = 7.8, 6.8 Hz, H-4), 5.242 (1H, t, J = 6.8 Hz, H-14), 5.128 (1H, dd, J = 7.8, 6.8 Hz, H-6), 5.082 (1H, t, J = 7.3 Hz, H-10), 3.525 (3H, s, OMe), 3.023 (2H, s, H-16), 2.694 (1H, dt, J = 14.7, 7.8 Hz, H-5), 2.554 (1H, dt, J = 14.7, 6.8 Hz, H-5), 2.301 (2H, d, J = 6.8 Hz, H-18), 2.14−2.09 (3H, m, H-13, H-19), 2.05 (2H, m, H-9), 2.03−1.99 (4H, m, H-8, H-12), 1.606 (3H, br s, H-22), 1.600 (3H, br s, H-23), 1.583 (3H, br s, H-24), 0.894 (6H, d, J = 7.3 Hz, H-20, H-21); $\Delta\delta$(**4S**−**4R**) H-2, +68.9 Hz; H-4, −8.8 Hz; H-5, −25.4 Hz, −16.4 Hz; H-6, −57.6 Hz; H-10, −1.5 Hz; H-14, +2.7 Hz; H-16, −2.2 Hz; H-18, −2.3 Hz; H-20/H-21, + 3.2 Hz; H-22, +6.4 Hz; H-23, −4.9 Hz; H-24, −17.6 Hz.

4-Acetoxy-9-deoxoidiadione (5): amorphous solid; $[\alpha]^{25}_D$ −19.2° (c 0.34, MeOH); IR (KBr) ν_{max} 2930, 2850, 1735, 1710, 1445, 1370, 1235, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.40 (1H, br s, H-25), 7.37 (1H, dd, J = 2.0, 1.5 Hz, H-1), 6.39 (1H, br d, J = 2.0 Hz, H-2), 5.75 (1H, t, J = 7.8 Hz, H-4), 5.24 (1H, t, J = 6.8 Hz, H-14), 5.07 (2H, br t, J = 6.8 Hz, H-6, H-10), 3.01 (2H, s, H-16), 2.59 (1H, ddd, J = 14.7, 7.8, 6.8 Hz, H-5), 2.48 (1H, ddd, J = 14.7, 7.8, 6.8 Hz, H-5), 2.28 (2H, d, J = 6.8 Hz, H-18), 2.11 (3H, m, H-13, H-19), 2.05 (2H, m, H-9), 2.04 (3H, s, Ac), 2.01 (4H, m, H-8, H-12), 1.61 (6H, br s, H-22, H-24), 1.59 (3H, br s, H-23), 0.89 (6H, d, J = 6.8 Hz, H-20, H-21); ^{13}C NMR ($CDCl_3$) δ 209.6 (C, C-17), 170.4 (C, Ac), 143.0 (CH, C-1), 140.3 (CH, C-25), 138.5 (C, C-7), 134.8 (C, C-11), 129.5 (CH, C-14), 128.9 (C, C-15), 124.8 (C, C-3), 124.2 (CH, C-10), 118.6 (CH, C-6), 109.0 (CH, C-2), 68.4 (CH, C-4), 54.5 (CH_2, C-16), 50.5 (CH_2, C-18), 39.7 (CH_2, C-8), 39.3 (CH_2, C-12), 33.4 (CH_2, C-5), 26.7 (CH_2, C-13), 26.5 (CH_2, C-9), 24.4 (CH, C-19), 22.6 (CH_3 × 2, C-20, C-21), 21.2 (CH_3, Ac), 16.4 (CH_3, C-22), 16.3 (CH_3, C-24), 15.9 (CH_3, C-23); HRFABMS m/z 451.2824 $[M + Na]^+$ (calcd for $C_{27}H_{40}O_4$Na, 451.2820).

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