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Scalarane Sesterterpenes from the Sponge *Hyatella* sp.

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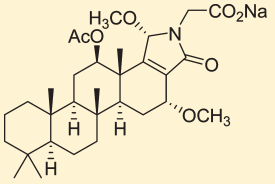
Supporting Information

ABSTRACT: Five new sesterterpenes (**7**−**11**) along with six known compounds (**1**−**6**) were isolated from the sponge *Hyatella* sp., collected off the coast of Soheuksan-do, Korea. Spectroscopic analyses revealed these compounds as scalarane sesterterpenes with oxidized furan moieties (**7**−**10**) and a corresponding lactam (**11**). The compounds exhibited moderate cytotoxicity, antibacterial activity, and weak inhibitory activity against isocitrate lyase.



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Sesterterpenes of the scalarane class are some of the most frequently encountered metabolites in sponges of the order Dictyoceratida.[1−4] During the course of our search for bioactive metabolites from sponges found in Korean waters, several compounds from this structural class have been isolated from the genus *Smenospongia*.[5,6] These compounds exhibited moderate to significant antimicrobial and cytotoxic activities. In our continuing search, we collected the sponge *Hyatella* sp., organic extracts from which have shown moderate brine shrimp lethality (LC_{50} 430 ppm). Guided by bioassay results, several compounds were isolated from an extract of *Hyatella* sp. by combined chromatographic techniques. We report here the structures of five new scalarane sesterterpenes along with six known compounds of the same structural class that is reminiscent of the previous results from the *Hyatella* sponges.[7] Analogous to previous studies, these compounds exhibited moderate antibacterial, cytotoxic, and inhibitory activities against isocitrate lyase (ICL).

Combined spectroscopic analyses identified the structures of compounds **1**−**6** as 12-*epi*-scalarin (**1**),[8] 12-*epi*-19-*O*-methylscalarin (**2**),[9] 12-*O*-deacetyl-12-*epi*-19-deoxy-21-hydroxyscalarin (**3**),[9] 12-*O*-acetyl-16-*O*-methylhyrtiolide (**4**),[10] 12-*O*-deacetyl-19-*O*-methyldeoxoscalarin (**5**),[11] and 12-*epi*-deoxoscalarin (**6**),[8] respectively. The spectroscopic data for these compounds were in good agreement with those reported previously.

The molecular formula of compound **7** was $C_{29}H_{44}O_6$ as determined by combined HRFABMS and ^{13}C NMR analyses. The NMR data of this compound were very similar to those of other sesterterpenes, in particular, the scalarane ethers **5** and **6**. Detailed examination of the ^{13}C NMR data revealed the presence of an additional acetoxy group in this compound that was corroborated by the appearance of an oxymethylene carbon atom at δ 65.4 (Table 1). A corresponding difference was observed in the ^1H NMR spectrum, in which signals attributed to acetoxy and oxymethylene protons appeared at δ 2.07, and 4.34 and 4.60, respectively (Table 2). A combination of ^1H COSY, *g*HSQC, and *g*HMBC analyses supported this interpretation, with an additional acetoxy group at C-23, based on long-range correlations of the oxymethylene protons with those at C-1, C-5, C-9, and C-10 and on the acetoxy carbon atoms. The all-*trans* ring juncture configuration was the same as that observed with other scalaranes, and 5*S**, 8*S**, 9*S**, 10*R**, 12*R**, 13*S**, 14*S**, 18*S**, 19*R** relative configurations were assigned to **7**, based on NOESY cross-peaks at H-5/H-9, H-9/H-12, H-9/H-14, H-11β (δ 1.48)/H-23, H-11β/H-24, H-11β/H-25, H-12/H-18, H-14/H-18, H-15β (δ 2.44)/H-24, H-15β/H-25, H-19/H-25, H-22/H-23, H-23/H-24, and H-24/H-25, respectively. Thus, compound **7** was identified as a 23-acetoxy derivative of **6**.[8]

A closely related metabolite, compound **8** ($C_{27}H_{42}O_5$), was isolated as an amorphous solid. The spectral data of this compound were very similar to those of other scalarane ethers. Comparison of the ^1H and ^{13}C NMR data revealed that one of the acetoxy groups of **7** was replaced with a hydroxy group in **8** at C-12, based on an upfield shift of the H-12 oxymethine proton from δ 4.65 to 3.56 and long-range correlations of this proton with C-9, C-14, and C-25 in the gHMBC data. The NOESY cross-peaks of key protons at the ring junctures indicated the same stereoconfigurations as above and identified **8** as a 12-deacetyl derivative of **7**.

Compound **9** ($C_{28}H_{44}O_4$) was isolated as an amorphous solid. The NMR data of this compound were similar to those of the other scalaranes and compound **5** in particular. A combination of 2D NMR experiments readily identified this compound as a 12-acetyl derivative of **5**, with the same relative configurations

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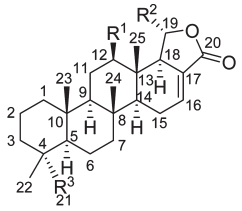
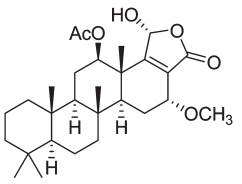


1 : R^1 = OAc, R^2 = OH, R^3 = CH_3
2 : R^1 = OAc, R^2 = OCH_3, R^3 = CH_3
3 : R^1 = OH, R^2 = H, R^3 = CH_2OH



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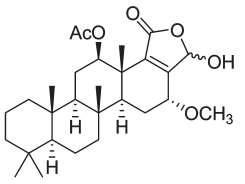

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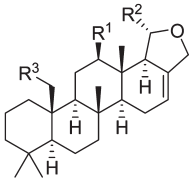
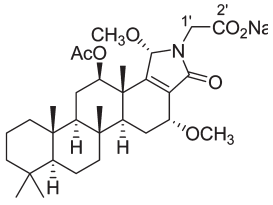


5 : R^1 = OH, R^2 = OCH_3, R^3 = H
6 : R^1 = OAc, R^2 = OH, R^3 = H
7 : R^1 = OAc, R^2 = OH, R^3 = OAc
8 : R^1 = OH, R^2 = OH, R^3 = OAc
9 : R^1 = OAc, R^2 = OCH_3, R^3 = H



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(Tables 1 and 2). The structural similarity of **9** with the hemiacetal **6** suggests that this compound is an isolation artifact, despite its stability in prolonged exposure to MeOH at room temperature.

The molecular formula of compound **10** was $C_{28}H_{42}O_6$, as determined by HRFABMS. Despite the general similarity with other scalaranes, the ^{13}C NMR data of this compound showed many more signals than anticipated from the mass data. Several key signals were present as pairs with a 2.5:1 intensity ratio; the same phenomenon was observed in the ^1H NMR data (Tables 1 and 2). Furthermore, many signals in both the ^1H and ^{13}C NMR spectra were very broad and severely hindered NMR-based structure determination. This problem was mitigated by changing the NMR solvent from chloroform-*d* to pyridine-d_5. The change in solvent significantly enhanced the signals and shifted the intensity ratio to 10.1:1, thereby enabling a structural determination of the major component in **10**.

The 2D NMR data in pyridine-d_5 indicate the presence of acetoxy and methoxy groups at C-12 and C-16, respectively, based on the correlations of H-12 and H-16 with neighboring protons and carbons in the COSY and HMBC data. Additionally, the ^{13}C NMR spectrum of **10** showed characteristic signals of a furan-derived, α,β-unsaturated-γ-hydroxybutyrolactone that is frequently found at the terminus of scalarane sesterterpenes; δ_C 169.7 (C), 159.7 (C), 140.3 (C), and 96.7 (CH). However, significant differences in chemical shifts from those of **1**−**4** suggested a different mode of oxidation for **10**. In this portion of the molecule, long-range correlations in the gHMBC data between the H-16 proton at δ 4.40 and the lactone carbon atoms at δ 159.7, 140.3, and 96.7 determined the position of the γ-lactone at C-17 to C-20 with the carbonyl and hydroxy groups at C-19 and C-20, respectively. Thus, the planar structure of compound **10** was identified as a scalarane lactone bearing diverse oxygenated substituents.

The configurations at the asymmetric carbon centers were assigned based on NOESY experiments. As in compounds **7**−**9**, sequential 1,3-diaxial cross-peaks between the bridge-head methyl and methine protons and axial protons confirmed all-*trans* orientations for the ring junctures. On the basis of the coupling constants (11.4 and 4.5 Hz) and cross-peaks with H-7α and H-14, H-12 was assigned an α-orientation. Similarly, cross-peaks at H-15α/H-16, H-15β/H-16, and H-15α/OMe indicated a β-orientation for H-16. An additional cross-peak at H-20/OMe indicated an α-orientation for H-20. Thus, the overall relative configurations for **10** were 5*S**, 8*R**, 9*R**, 10*S**, 12*R**, 13*S**, 14*S**, 16*R**, 20*R**.

Compound **10** was isolated as an inseparable 2.5:1 mixture. Previous studies have shown that scalarane lactones occasionally exist as inseparable diastereomers at the hydroxy-bearing center (C-20 for **10**).[7b] Under acidic conditions, these diastereomers slowly interconvert.[12] As a consequence, in prior work, the configuration could be determined only after separating **10** as the corresponding acetyl derivatives of the diastereomers.[8] In the present study, interestingly, changing the solvent from chloroform to pyridine resulted in a rapid shift in the isomeric ratio of

Table 1. ^{13}C NMR Assignments for Compounds 7−11[a]

position	7	8	9	10	11
1	37.7	38.0	39.7	40.0	41.0
2	19.8	19.8	18.4	19.2	19.7
3	43.3	43.3	42.0	42.6	43.3
4	34.4	34.4	33.3	33.76	34.4
5	57.9	58.0	56.4	56.6	58.0
6	20.0	20.1	18.1	18.9	19.4
7	41.3	41.4	41.3	41.9	42.6
8	38.6	38.5	37.5	37.5	38.4
9	59.4	60.0	58.1	58.1	59.5
10	41.9	41.9	37.4	37.9	38.8
11	24.4	27.0	23.5	25.6	24.4
12	84.2	82.3	83.0	76.6	78.6
13	39.3	41.1	37.5	42.5	43.7
14	56.2	55.8	53.7	50.9	50.8
15	24.6	24.8	22.1	22.4	23.4
16	117.8	118.3	116.4	70.8	70.5
17	137.6	136.8	136.2	159.7	134.8
18	62.5	62.5	60.0	140.3	160.6
19	100.9	100.7	106.2	169.7	86.6
20	69.1	69.1	68.3	96.7	171.0
21	33.8	33.8	33.3	33.78	33.9
22	21.9	21.9	21.3	21.9	21.9
23	65.4	65.8	16.6	16.5	16.9
24	17.0	17.0	16.5	17.8	18.1
25	10.5	9.6	10.0	15.7	17.6
1′					43.4
2′					176.2
12-OAc	172.84		170.0	171.6	173.1
	21.6		21.5	22.5	21.8
16-OMe				57.7	57.5
19-OMe			55.2		50.0
23-OAc	172.82	172.8			
	21.2	21.2			

[a] Data were obtained in MeOH-d_4 for **7**, **8**, and **11**, $CDCl_3$ for **9**, and pyridine-d_5 solutions for **10**, respectively. Data were measured at 150 MHz (**7**, **9**) and 125 MHz (**8**, **10**, and **11**), respectively.

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Table 2. ^{1}H NMR Assignments for Compounds 7−11[a]

position	7	8	9	10	11
1α	0.96, m	0.93, m	0.88, m	0.66, m	0.89, m
1β	2.17, ddd (13.3, 3.0, 3.0)	2.16, ddd (13.3, 3.0, 3.0)	1.64, br d (12.7)	1.48, m	1.64, m
2α	1.46, m	1.47, m	1.42, m	1.32, m	1.41, m
2β	1.68, m	1.68, m	1.58, m	1.52, m	1.58, m
3α	1.21, ddd (13.2, 12.3, 3.5)	1.19 ddd (13.7, 13.7, 4.1)	1.13, ddd (13.2, 13.2, 4.1)	1.12, ddd (13.3, 13.3, 3.3)	1.19, m
3β	1.39, br d (13.2)	1.40, br dd (13.7, 2.7)	1.35, br dd (13.2, 1.6)	1.33, m	1.37, br d (13.2)
5	0.95, m	0.92, m	0.81, m	0.65, dd (12.4, 1.5)	0.89, m
6α	1.59, br dd (14.0, 2.2)	1.72, m	1.32, m	1.37, m	1.65, m
6β	1.42, m	1.40, m	1.52, m	1.58, m	1.48, m
7α	0.91, m	0.89, m	0.90, m	0.91, ddd (12.4, 12.4, 2.7)	0.96, m
7β	1.68, br d (11.6)	1.57, br dd (13.8, 2.3)	1.68, ddd (12.7, 3.2, 3.2)	1.75, br d (12.4)	1.88, br d (12.9)
9	1.17, br d (12.8)	1.12, br d (12.3)	0.98, br d (12.2)	0.82, m	0.99, m
11α	1.88, br dd (12.7, 3.9)	1.74, m	1.84, ddd (11.1, 4.1, 1.3)	1.83, br dd (12.8, 2.4)	1.93, dd (12.6, 3.2)
11β	1.48, m	1.47, m	1.40, m	1.60, ddd (12.8, 12.2, 11.4)	1.50, m
12	4.65, dd (11.4, 3.9)	3.56, dd (11.4, 4.5)	4.65, dd (11.4, 4.4)	5.26, dd (11.4, 4.5)	4.62, dd (11.4, 4.4)
14	1.47, br d (11.7)	1.34, dd (12.0, 5.2)	1.27, dd (11.0, 5.7)	1.56, m	1.58, m
15α	2.24, br d (17.9)	2.21, m	2.07, br d (18.3)	2.11, br d (13.9)	2.13, m
15β	2.44, br dd (17.9, 11.7)	2.41, ddd (12.0, 12.0, 2.6)	2.02, m	1.54, m	1.71,ddd(14.5,12.6,3.8)
16	5.51, br s	5.50, br s	5.51, br s	4.40, br d (3.5)	3.99, d (3.8)
18	2.28, br s	2.24, br s	2.32, br s		
19	5.39, d (4.3)	5.30, d (5.9)	5.02, d (3.4)		5.67, s
20	4.35, d (11.5)	4.42, br d (11.8)	4.25, br d (10.9)	6.57, s	
	4.09, d (11.5)	4.14, br d (11.8)	4.10, d (10.9)		
21	0.87, s	0.86, s	0.83, s	0.864, s	0.86, s
22	0.83, s	0.84, s	0.79, s	0.79, s	0.84, s
23	4.60, d (12.5)	4.57, d (12.5)	0.81, s	0.77, s	0.88, s
	4.34, d (12.5)	4.32, d (12.5)			
24	0.93, s	0.94, s	0.92, s	0.858, s	0.97, s
25	0.97, s	0.86, s	0.86, s	1.21, s	1.23, s
1′					4.26, d (17.1)
2′					3.35, d (17.1)
12-OAc	2.04, s		2.05, s	2.37, s	2.00, s
16-OMe				3.51, s	3.43, s
19-OMe			3.32, s		2.84, s
20-OH				10.20, br s	
23-OAc	2.07, s	2.06, s			

[a] Data were obtained in MeOH-d_4 for **7**, **8**, and **11**, $CDCl_3$ for **9**, and pyridine-d_5 solutions for **10**, respectively. Data were measured at 600 MHz (**7**, **9**) and 500 MHz (**8**, **10**, and **11**), respectively.

10 to 10.1:1. Furthermore, redissolution of **10** in chloroform instantly recreated a 2.8:1 mixture, which was nearly identical to the original ratio.

The molecular formula of compound **11** was $C_{31}H_{46}NO_7Na$ as determined by combined HRFABMS and ^{13}C NMR analyses. The spectroscopic data of this compound were similar to those obtained from other scalaranes. NMR data aided by 2D analyses identified a 12-acetoxy-16-methoxyscalarane framework, as for **4** and **10**, for this compound. The remaining structural features of **11** were determined by combined NMR techniques. Long-range coupling of H-16 at δ 3.99 with quaternary carbon atoms at δ 171.0, 160.6, and 134.8 in the gHMBC data identified these shifts as due to C-20, C-18, and C-17, respectively. These carbon atoms represented an α,β-unsaturated carbonyl system supported by long-range correlations between H-14 and H-25 and C-18. Additional correlations of unsaturated carbonyl carbon atoms at C-17, C-18, and C-20 with a methine proton at δ 5.67 revealed a methine carbon atom at C-19, indicative of a γ-lactam moiety. This moiety was further attached to a methoxy group, based on mutual proton−carbon correlations between the methine and the methoxy group (Tables 1 and 2). Finally, long-range coupling of isolated methylene protons at δ 4.26 and 3.35 with C-19, C-20, and the remaining carbonyl carbon atom at δ 176.2 indicated a carboxymethylene group attached to the nitrogen atom. This interpretation was further supported by the chemical shifts of C-19 (δ 86.6) and C-1′ (δ 43.4) as well as the significant upfield shift of the former from the corresponding carbons of the analogous compounds (δ 99−105 for **1**, **2**, and **4**). Thus, the structure of **11** was that of a scalarane metabolite bearing a glycine-derived lactam moiety. Previous studies have revealed that sponge-derived sesterterpenes occasionally exist as mixed biogenetic products due to condensation with amino acids.[4,13,14] In addition to the same relative configurations of the A−D rings as those given above, a 19*S** configuration was assig-

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Table 3. Results of Bioactivity Tests[a]

	MIC (μg/mL)							
	Gram(+) bacteria			Gram(−) bacteria			K562	ICL
compound	A	B	C	D	E	F	LC_{50} (μM)	IC_{50} (μM)
1	>100	6.25	>100	>100	6.25	>100	28.3	111.9
2	>100	>100	>100	>100	>100	>100	38.4	40.8
3	>100	>100	>100	>100	>100	>100	31.1	133.2
4	25	0.78	25	12.5	3.125	50	36.7	ND[c]
5	>100	>100	>100	>100	>100	>100	24.6	ND
6	>100	>100	>100	>100	>100	>100	31.3	55.3
7	>100	0.78	>100	>100	3.125	>100	39.5	ND
8	25	6.25	12.5	12.5	12.6	>100	19.5	107.4
9	>100	>100	>100	>100	>100	>100	>100	ND
10	25	<0.39	25	12.5	1.56	50	14.8	ND
11	50	6.25	25	50	25	100	27.0	176.4
ampicillin	1.56	0.78	0.39	1.56	1.56	6.25		
doxorubicin							9.7	
3NP[b]								27.9

[a] A: *Staphylococcus aureus* (ATCC 6538p), B: *Bacillus subtilis* (ATCC 6633), C: *Micrococcus* sp. (IFO 12708), D: *Salmonella typhimurium* (ATCC 14028), E: *Proteus vulgaris* (ATCC 3851), F: *Escherichia coli* (ATCC 25922). [b] 3-Nitropropionic acid. [c] ND, due to the strong initial absorption, inhibitory activity was not adequately measured.

ned on the basis of a NOESY analysis. The presence of methoxy groups at C-16 and C-19 raises the possibility of this compound as an isolation artifact, despite the lack of plausible precursor in the extract.

Sponge-derived scalarane sesterterpenes typically exhibit diverse bioactivities.[2−4] The compounds described here exhibited moderate to weak cytotoxicity against a K562 cell line, and some were comparable to doxorubicin. Several compounds also exhibited antibacterial activity against both Gram-positive and Gram-negative bacteria, with the exception of *E. Coli*. Although none of these compounds were active against pathogenic fungi, some moderately inhibited isocitrate lyase, a key enzyme in fungal metabolism.

EXPERIMENTAL SECTION

General Experimental Procedures. Optical rotations were measured on a JASCO P-1020 polarimeter using a 1 cm cell. UV spectra were recorded on a Hitachi U-3010 spectrophotometer, and IR spectra were recorded on a JASCO 300E FT-IR spectrometer. NMR spectra were recorded in $CDCl_3$, MeOH-d_4, and pyridine-d_5 solutions containing Me_4Si as an internal standard on Bruker Avance 500, 600, and Avance II 900 spectrometers. Proton and carbon NMR were measured at 900 and 225 MHz (Supporting Information for **10**), 600 and 150 MHz (**7** and **9**), and 500 and 125 MHz (**8**, **10**, and **11**), respectively. Mass spectrometric data were obtained from the Korea Basic Science Institute (Daegu) and acquired on a Jeol JMS 700 mass spectrometer, Korea. All solvents were spectroscopic grade or distilled from glass prior to use.

Animal Material. Specimens of *Hyatella* sp. (voucher number 07SH-2) were collected by hand from a depth of 20 m using scuba equipment off the shore of Soheuksan-do, West Sea, Korea, on June 18, 2007. According to K.J.L., the sponge was massive, measuring 160 × 120 mm with a thickness of 65 mm. The whole sponge was lacunose. The surface is unarmored and finely conulose, with tuberculate oscules 40−80 mm in diameter. The texture was compressible and the color was purple and beige. The fiber skeleton was comprised of simple cored primary fibers and uncored secondary fibers. The primary fibers at the surface were 40−50 μm in diameter and partially inside 50−80 μm in diameter. The secondary fibers were 20−55 μm in diameter, producing polygonal meshes. A voucher specimen (registry no. SPO. 57) is on deposit at the Natural History Museum at Hannam University, Daejeon, Korea, under the curatorship of Chung J. Sim.

Extraction and Isolation. Freshly collected specimens were immediately frozen and stored at −25 °C until use. The combined specimens (4.6 kg, wet wt) were lyophilized, macerated, and repeatedly extracted with CH_2Cl_2 (3 L × 3) and MeOH (3 L × 3). The combined extracts (151.71 g) were successively partitioned between H_2O and *n*-BuOH; the latter fraction was repartitioned between 15% aqueous MeOH (9.55 g) and *n*-hexane (22.32 g). The MeOH layer was separated by C_{18} reversed-phase vacuum flash chromatography using a sequential mixture of MeOH and H_2O as eluents (elution order: 50%, 40%, 30%, 20%, 10% MeOH(aq) and 100% MeOH), acetone, and finally EtOAc.

On the basis of the results of ^{1}H NMR and cytotoxicity analyses, the fractions eluted with 20% MeOH(aq) (0.3 g), 10% MeOH(aq) (0.89 g), and 100% MeOH (1.79 g) were chosen for separation. The fraction eluted with 20% MeOH(aq) was separated by semipreparative reversed-phase HPLC (YMC-ODS column, 10 mm × 250 mm, 35% MeOH-(aq)) to yield two peaks rich with secondary metabolites. Further purification of the first and second peaks by reversed-phase HPLC (60% MeCN(aq)) afforded compounds **11** and **3**, respectively, as amorphous solids.

An aliquot (0.65 g) of the 10% MeOH(aq) fraction was separated by normal-phase HPLC (YMC-Pack silica column, 10 mm × 250 mm, 40% EtOAc in *n*-hexane) to yield, in order of elution, compounds **1**, **4**, **7**, and **8**. These metabolites were then purified by analytical HPLC (YMC-ODS-A column, 4.6 mm × 250 mm, 60% MeCN(aq)).

The 100% MeOH fraction was separated and purified by reversed-phase HPLC (5% MeOH(aq)) to yield compounds **9**, **5**, **2**, **10**, and **6**, in order of elution, as pure compounds. The purified metabolites were isolated in the following amounts: 5.0, 10.1, 4.6, 12.0, 3.7, 6.3, 15.0, 9.8, 8.6, 9.0, and 6.4 mg of **1**−**11**, respectively.

Compound 7:. white, amorphous solid; $[\alpha]_D^{25}$ −33.8 (*c* 0.51, MeOH); IR (ZnSe) ν_{max} 3435 (br), 2924, 1738, 1615, 1371 cm^{-1};

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^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; HRFABMS m/z 511.3038 $[M + Na]^+$ (calcd for $C_{29}H_{44}O_6Na$, 511.3036).

Compound 8:. white, amorphous solid; $[\alpha]_D^{25}$ −3.6 (c 0.80, MeOH); IR (ZnSe) ν_{max} 3430 (br), 2924, 1738, 1604, 1464, 1370 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; HRFABMS m/z 469.2932 $[M + Na]^+$ (calcd for $C_{27}H_{42}O_5Na$, 469.2930).

Compound 9:. white, amorphous solid; $[\alpha]_D^{25}$ −24.0 (c 0.83, MeOH); IR (ZnSe) ν_{max} 2927, 1739, 1611, 1465, 1389 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; HRFABMS m/z 467.3141 $[M + Na]^+$ (calcd for $C_{28}H_{44}O_4Na$, 467.3137).

Compound 10:. white, amorphous solid; $[\alpha]_D^{25}$ −9.4 (c 0.35, MeOH); UV (MeOH) λ_{max} (log ε) 205 (3.74), 252 (3.23) nm; IR (ZnSe) ν_{max} 3430 (br), 2930, 1738, 1586, 1462, 1387 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; HRFABMS m/z 497.2875 $[M + Na]^+$ (calcd for $C_{28}H_{42}O_6Na$, 497.2879).

Compound 11:. white, amorphous solid; $[\alpha]_D^{25}$ −3.0 (c 0.60, MeOH); UV (MeOH) λ_{max} (log ε) 207 (3.88), 250 (3.05) nm; IR (ZnSe) ν_{max} 3430 (br), 2926, 1735, 1693, 1608, 1387 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; HRFABMS m/z 590.3075 $[M + Na]^+$ (calcd for $C_{31}H_{46}NO_7Na_2$, 590.3070).

Biological Assays. Cytotoxicity assays were performed in accordance with the protocols in refs 15 and 16. Antimicrobial and isocitrate lyase inhibition assays were performed according to the methods given in refs 17 and 18, respectively.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra of compounds **7**−**11** and pictures of the sponge specimen are available free of charge via the Internet at http://pubs.acs.org.

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