SHORT REPORT

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Rec. Nat. Prod. 8:4 (2014) 417-421

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Two New Scaralane-type Sesterterpenoids Isolated from the Marine Sponge *Hyrtios erectus*

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(Received September 30, 2013; Revised March 24, 2014; Accepted April 6, 2014)

Abstract: Four sesterterpenoids were isolated from a South China marine sponge of the genus *Hyrtios*, and their chemical structures were elucidated by extensive investigation of HRMS and 2D-NMR spectrum. Two of the compounds were new natural products and characterized to be scalarinether (**1**) and 21-hydroxy-16-deacetyl-12-epi-scalarafuran acetate (**2**). Two known sesterterpenes were identified as scalarin (**3**) and isoscalara furan-A (**4**).

Keywords: Sesterterpenoid; Structure elucidation; *Hyrtios erectus*.

1. Introduction

Compared to diterpenoids and triterpenoids, sesterterpenoids were a small group of natural products, which were widely spread in higher plants, lichens, fungi, insects, and marine organisms [1]. Based on the specifical marine biosynthesis evironment, sponges tended to produce a wide structural range of interesting sesterterpenes which provided a wealth of pharmaceutical lead compounds. Manoalide, a linear natural sesterterpenoid, represented a novel class of anti-inflammation agent by inhibiting phospholipase A_2 [2] and calcium channels [3]. The scientific exploration of the tetracarbocyclic scaralane-type metabolisms has been an attractive field during the last two decades. It's believed that these compounds were useful as chemotaxonomic markers within sponges [4-5]. The biological studies expressed the potential applications of them as therapeutic agents, such as HIF-1 inhibitor [6], HIV-1 integrase inhibitor [7], PTP1B inhibitor [8], antiinflammatory [9] and cytotoxic compounds [10-11]. Structure-activity investigations suggested that the attachment of the hydroxy group instead of acetoxy group at C-12 was considered to be effective in cytotoxicity. The functionalities in the vicinity of C-16, C-19 were proposed as the area that contributed to the bioactivity of the scalaranes. The structural and bioactive diversity have made sesterterpenoids .

In our ongoing studies for searching biologically active natural constituents to relieve the inflammation and pain of lichen planus and oral cavity ulcer, two new scalarane sesterterpenoids scalarinether (**1**) and 21-hydroxy-16-deacetyl-12-epi-scalarafuran acetate (**2**), were isolated from South China Sea marine sponges *Hyrtios erectus*. Their structures were established by MS and 1D-, 2D-NMR techniques. Compounds **3** and **4** were known natural products and identified as scalarin [12]

* Corresponding author: E-mail: yanqiu@xmu.edu.cn; Phone: 086-592-2188681 attractive targets for biomedical purposes.

The article was published by Academy of Chemistry of Globe Publications
www.acgpubs.org/RNP © Published 07/05/2014 EISSN:1307-6167

and isoscalarafuran-A [13] by comparison of their NMR spectroscopic data with those literature reported.

2. Materials and Methods

2.1. Marine Sponge Material

The specimen of *Hyrtios erectus* was collected from Yongxing Island, South China Sea, China, in September 2008. A voucher specimen (MsHE-3) is deposited at the School of Medical, Xiamen University.

2.2 Extration and Isolation

The sponge (1.4 kg, wet wt) which immersed in EtOH was homogenized and then extracted with MeOH. The concentrated dried total extract (18.3 g) was dissolved by dehydrated MeOH to remove the salt. Some water was added to make in a 90% MeOH extraction and then partitioned three times with *n*-hexane to get rid of the lipids. MeOH layer was dried and resuspended in H_2O and then extracted with $CHCl_3$ by three times. The $CHCl_3$-soluble portion (2.3 g) was subjected to flash silica gel column chromatography eluted with an equivalent petroleum ether-ethyl acetate stepwise gradient to obtain 5 fractions. Fraction 3 (1.53 g) was subjected to sephadex LH-20 column (eluted with $CHCl_3$:MeOH = 1:1) and then the ODS column. The fraction eluted by 85% MeOH was concentrated to get crude needles, and which was repurified with silica gel column (petroleum ether-ethyl acetate 3:1) to give compounds **2** (1.4 mg), **3** (821 mg), **4** (158 mg). With the same procedures above, **1** (18 mg) was obtained from Fr. 3.

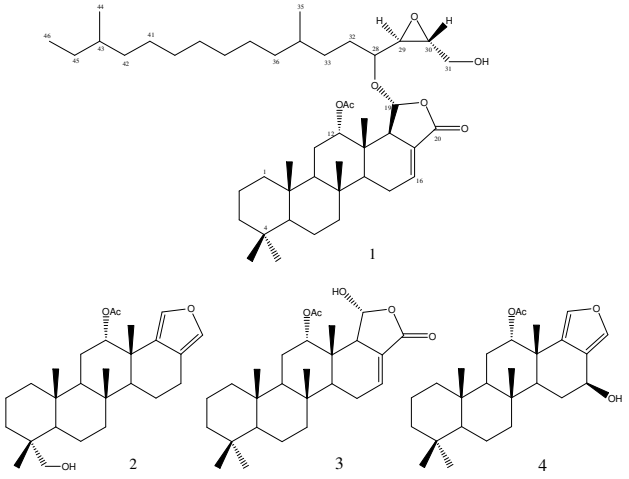

Figure 1. Structures of compounds **1**-4.

Compound **1**, white amorphous, $[\alpha]_D^{25}$ = +25.3 (*c* 0.11, $CHCl_3$); ESI-TOF-MS: *m/z*: 741.6 $[M+H]^+$; HRFAB-MS: *m/z*: 741.5814, (calcd. for $C_{46}H_{77}O_7$, 741.5664); for ^{1}H-NMR and ^{13}C-NMR see Table **1**.

Compound **2**, white amorphous, $[\alpha]_D^{25}$ = +61.3 (*c* 0.004, $CHCl_3$); ESI-TOF-MS: *m/z*: 429.3 $[M+H]^+$; HR-ESI-MS: *m/z*: 429.2698, (calculated for $C_{27}H_{41}O_4$, 429.2999); for ^{1}H-NMR and ^{13}C-NMR see Table **1**.

3. Results and Discussion

3.1. Structure elucidation

Compound **1** was obtained as a white amorphous powder, which molecular formula was established as $C_{46}H_{76}O_7$ on the basis of a molecular ion peak at *m/z* 741.5814 $[M+H]^+$ in the HR-FAB-MS (calculated value, 741.5664). Five angular methyls at δ 0.80 (*s*, 3H), 0.81 (*s*, 3H), 0.82 (*s*, 3H), 0.86 (*s*, 3H), and 0.93 (*s*, 3H) in DEPT spectrum suggested a normal scaralane-type frame structure,

Table 1. ^{1}H NMR data for compounds **1** and **2** (at 500 MHz in $CDCl_3$, δ in ppm, *J* in Hz).

No.	Compound **1**		No.	Compound **2**	
	δC	δH (*J* Hz)		δC	δH (*J* Hz)
1	39.90 (t)	1.60, 0.60 (2H, m)	1	39.1 (t)	
2	18.11 (t)	1.53, 1.36 (2H, m)	2	18.2 (t)	
3	42.14 (t)	1.35, 1.12 (2H, m)	3	37.6 (t)	
4	33.43 (s)		4	35.0 (s)	
5	56.62 (d)	0.84 (1H, m)	5	49.3 (d)	
6	18.58 (t)	1.36, 1.14 (2H, m)	6	18.5 (t)	
7	41.49 (t)	1.71, 1.04 (2H, m)	7	41.2 (t)	
8	38.08 (s)		8	38.1 (s)	
9	52.66 (d)	1.29 (1H, m)	9	52.6 (d)	
10	36.96 (s)		10	37.0 (s)	
11	22.16 (t)	1.86, 1.67 (2H, m)	11	29.7 (t)	
12	74.55 (d)	4.82 (1H, br)	12	75.3 (d)	5.37 (1H, d, 2.8)
13	37.33 (s)		13	38.9 (s)	
14	49.85 (d)	1.70 (1H, m)	14	51.2 (d)	
15	23.86 (t)	2.34, 2.08 (2H, m)	15	22.3 (t)	
16	129.62 (d)	6.55 (1H, d, 3.0)	16	18.0 (t)	
17	131.42 (s)		17	120.4 (s)	
18	47.33 (d)	3.01 (1H, m)	18	132.3 (s)	
19	87.35 (d)	4.67 (1H, d, 4.5)	19	135.1 (d)	6.98 (1H, br s)
20	166.59 (s)		20	136.6 (d)	7.06 (1H, br s)
21	33.43 (q)	0.86 (3H, s)	21	71.8 (t)	3.49, 3.13 (1H, each, d, 10.5)
22	21.50 (q)	0.81 (3H, s)	22	17.2 (q)	0.79 (3H, s)
23	16.45 (q)	0.82 (3H, s)	23	16.3 (q)	0.90 (3H, s)
24	16.10 (q)	0.93 (3H, s)	24	17.5 (q)	0.95 (3H, s)
25	15.28 (q)	0.80 (3H, s)	25	26.7 (q)	1.29 (3H, s)
26	170.03 (s)		26	170.8 (s)	
27	21.66 (q)	2.04 (3H, s)	27	21.5 (q)	1.93 (3H, s)
28	81.40 (d)	3.34 (1H, ddd, 2.5, 6.5, 9.0)			
29	65.26 (d)	3.41 (1H, br d, 9.0)			
30	64.25 (d)	3.09 (1H, br d, 9.0)			
31	58.01 (t)	4.28 (1H, dd, 11.0, 6.0); 4.07 (1H, dd, 9.0, 6.0)			
32	24.66 (t)	1.42, 1.29 (2H, m)			
33	31.88 (t)	1.75, 1.52 (2H, m)			
34	28.12 (d)	1.27 (1H, m)			
35	22.84 (q)	0.87 (3H, d, 6.0)			
36	39.22 (t)	1.15 (2H, m)			
37-42	27-31 (t)	1.2-1.4 (12H, m)			
43	34.55 (d)	1.29 (1H, m)			
44	19.40 (q)	0.84 (3H, d, 3.7)			
45	36.81 (t)	1.28 (2H, m)			
46	11.60 (q)	0.85 (3H, t, 2.0)			

as confirmed by the HMBC correlations. ^{1}H, ^{13}C-NMR and the HMBC correlations [δ 6.55 (*s*, br, 1H, H-16) and δ 23.86 (C-15), 47.33 (C-18), 49.85 (C-14), 166.59 (C-20)] indicated one α,β-unsaturated-γ-lactone. An acetal group was located at C-19, which was validated by the HMBC cross-peaks between the acetal proton at δ 4.67 (*d*, J = 4.5 Hz) and two carbons at δ 37.33 (C-13), 166.59 (C-20). Additional acetyl substituent was assigned to C-12 on the basis of the correlations of δ 4.82 (*br*, 1H), 2.04 (*s*, 3H) with the acetyl carbon at δ 170.03 (C-28) at the HMBC spectrum. Of the oxygenated carbons for compound **1**, two high-field methine carbons at δ 65.26 (C-29), 64.25 (C-30) were attributed to one epoxide ring. Interpretation of ^{1}H-^{1}H COSY and HSQC spectra led to the following partial scaralane ring, which were further confirmed by the HMBC correlations for δ 3.09 (m, 1H, H-30)/ δ 81.40 (C-28), 65.26 (C-29), 58.01 (C-31) and the COSY cross peaks between δ 4.28, 4.07 and an exchangeable proton at δ 4.96. The HMBC cross peak between δ 4.67 (d, J = 4.5 Hz, 1H, H-19) and δ 81.40 (C-28) indicated that fraction A was adjacent to the scaralane ring through the moiety C_{19}-O-C_{28}, while the two downshift carbon signals at δ 81.40 (C-28) and 87.35 (C-19) could also confirm the existence of the ether. The long fatty chain was established as partial structure B by the detailed interpretation of HMBC and ^{1}H-^{1}H COSY spectrum of the methyls (*Figure 2*).

The relative stereochemistry of C-12 and C-19 were determined by comparing coupling constants with values reported for similar compounds. A trans relationship for H-29 and H-30 was confirmed by 1D-GOESY spetrum. When H-19 was irradiated, two 1D-GOESY singals to H-28 and H-30 and no signal to H-29 were observed, which revealed that C-29 and C-30 were a part of a trans-epoxide. Thus, the structure of compound **1** was elucidated to be scalarinether.

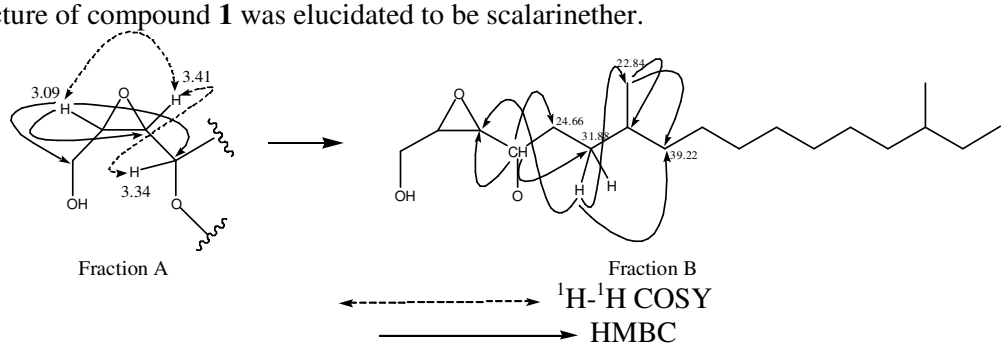

Figure 2. The key ^{1}H-^{1}H COSY and HMBC correlations of the long fatty chain of compound 1

Compound **2** was obtained as a minor component. The molecular formula was established as $C_{27}H_{40}O_4$ by high resolution mass measurement. The ^{1}H-NMR spectrum of 2 displayed the presence of four singlets in higher fields belonging to angular methyl groups resonating at δ 0.79, 0.90, 0.95, and 1.29, which was different from the characteristic scalarane skeleton. The HMQC correlations between δ 3.13 (*d*, J = 10.5 Hz, 1H), 3.49 (*d*, J = 10.5 Hz, 1H) and δ 71.8 (C-21) suggested the presence of a hydroxylated methylene group. The connection of this group to C-4 was confirmed by the HMBC cross-peaks between the angular methyl protons at δ 0.79 and δ 71.8 (C-21), 49.3 (C-5), 37.8 (C-3), 35.0 (C-4). The correspondence of hydroxylated methylene protons were not observed maybe because of the few quality of this compound. HMBC cross-peak between δ 1.93 (3H, s) and δ 170.8 (C-27) indicated the presence of an acetoxyl group, which was suggested to be located at C-12 through the correlation between the angular methyl protons at δ 1.29 (3H, s, Me-25) and δ 38.9 (C-13), 51.2 (C-14), 75.3 (C-12), 132.3 (C-18) in HMBC spectrum similar with most of the scalaranes. The magnitude of the J-coupling for H-12 (1H, δ 5.37, br d, J = 2.8 Hz) to H-11 indicated that H-12 was equatorial and the axial C-12 acetyl group occupied the α-face. The proton signals at δ 6.98 (1H, br s, H-19) and 7.06 (1H, br s, H-20) are representative of a disubstituted furan moiety. Fusion of the furan moiety to the six-membered ring through C-17 and C-18 was secured by detailed HMBC correlations. Thus, compound 2 was estimated as 21-hydroxy-16-deacetyl-12-epi-scalarafuran acetate.

Acknowledgments

This paper was supported by the National Natural Sciences Foundation of China (No. 81373273), the Youth Scientific Research of Fujian Health Department (2013-2-105), and Xiamen Science & Technology Bureau Project (No. 3502Z20113010, 3502Z20134046).

Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/RNP

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