Hyrtiosins A – E, Five New Scalarane Sesterterpenes from the South China Sea Sponge *Hyrtios erecta*

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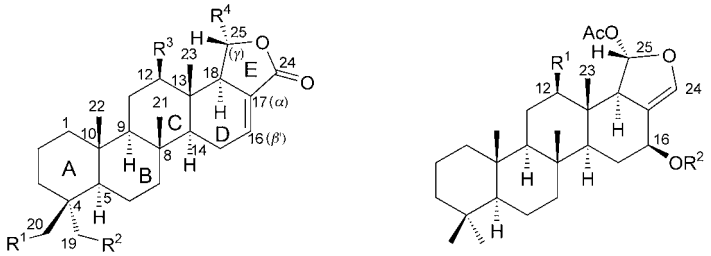
Five new scalarane sesterterpenes, hyrtiosins A – E (**1** – **5**), together with three previously reported sesterterpenes, 25-dehydroxy-12-*epi*-scalarin (**6**), 12-*epi*-scalarin (**7**) and heteronemin (**9**), were isolated from the South China Sea sponge *Hyrtios erecta*. Their structures were determined on the basis of extensive NMR studies and high-resolution MS measurements.

Introduction. – Sponges of the order Dictyoceratida are often prominent members of South Pacific island coral reefs. Their metabolic pattern is highly characterized by sesterterpenes [1], an otherwise rare group of terpenoids. The genus *Hyrtios* of this order has proven to be a rich source of tetra- and pentacyclic sesterterpenes, which exhibit a variety of biological activities, *e.g.*, as antifeedant [2], ichthyotoxic [3], anti-inflammatory [4], cytotoxic [5], and platelet-aggregation inhibitory agents [6]. In the course of our ongoing research program on bioactive metabolites from South China Sea invertebrates [7], we examined the constituents of the sponge *Hyrtios erecta* (family Thorectidae) collected from the Hainan Island, in the South China Sea. In this context, we isolated five new pentacyclic sesterterpenes, named hyrtiosins A – E (**1** – **5**), along with three known related compounds, 25-dehydroxy-12-*epi*-scalarin (**6**) [8], 12-*epi*-scalarin (**7**) [8a], and heteronemin (**9**) [9], all possessing a scalarane skeleton (see *Fig. 1*). Herein, we report their isolation and structural elucidation.

Results and Discussion. – Two separate collections of *H. erecta* were studied; and they were colleted in 2003 from different locations of the Lingshui Bay, Hainan Province, China. Repeated chromatographic separation by silica-gel column chromatography followed by reversed-phase HPLC of the Et_2O-soluble fraction obtained from the Me_2CO extract of the sponge resulted in the isolation of three new sesterterpenes, named hyrtiosins A – C (**1** – **3**), from the collection *03LS-111*, together with previously described 25-dehydroxy-12-*epi*-scalarin (**6**), 12-*epi*-scalarin (**7**), and heteronemin (**9**). Two further new sesterterpenes, named hyrtiosins D and E (**4** and **5**, resp.), were obtained from the second collection *03LS-33*, together with heteronemin (**9**). All new compounds showed considerable structural analogies with the co-occurring known sesterterpenes.

Hyrtiosin A (**1**) was isolated as an amorphous powder and had a molecular formula $C_{29}H_{42}O_6$ as determined by HR-EI-MS and ^{13}C-NMR data. The UV (MeOH) λ_{max} at



1 $R^1 = R^3 = AcO$, $R^2 = R^4 = H$
2 $R^1 = R^4 = H$, $R^2 = R^3 = AcO$
3 $R^1 = R^3 = H$, $R^2 = R^4 = AcO$
6 $R^1 = R^2 = R^4 = H$, $R^3 = AcO$
7 $R^1 = R^2 = H$, $R^3 = AcO$, $R^4 = OH$
8 $R^1 = R^3 = H$, $R^2 = AcO$, $R^4 = OH$

4 $R^1 = OH$, $R^2 = H$
5 $R^1 = H$, $R^2 = Ac$
9 $R^1 = OH$, $R^2 = Ac$

Fig. 1. *Structures of compounds* **1**–**9**

221 nm (ε 4500) and IR bands at 1763, 1736, 1691, and 1242 cm^{-1} indicated the presence of ester-carbonyl and α,β-unsaturated-γ-lactone moieties.

The structure of hyrtiosin A (**1**) was established as 20-(acetyloxy)-25-dehydroxy-12-*epi*-scalarin, as deduced by detailed analysis of its spectral data and their comparison with those of 25-dehydroxy-12-*epi*-scalarin (**6**).

The ^{1}H-NMR spectrum of **1** (*Table 1*) displayed clearly 4 Me groups at δ 0.86 (*s*), 0.87 (*s*), 0.93 (*s*) and 0.94 (*s*). Further signals at δ 6.87 (*dd*, $J = 6.7$, 3.2 Hz, 1 H) attributable to the β-proton on an α,β-unsaturated carbonyl system, 2 *t* at δ 4.23 ($J = 9.2$ Hz, 1 H) and 4.11 ($J = 9.2$ Hz, 1 H) attributable to a CH_2 group of the γ-lactone, and a *dd* at δ 4.66 ($J = 11.3$, 4.2 Hz, 1 H) for the CH group bearing an AcO group in addition to a *m* at δ 2.86 were observed. These ^{1}H-NMR data are strongly reminiscent of the co-occurring pentacyclic sesterterpene 25-dehydroxy-12-*epi*-scalarin (**6**) [8]. A comparison of all ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*) revealed that **1** differs from **6** only by the presence of an additional AcO group (δ (H) 2.05 (*s*, 3 H); δ (C) 21.5 and 171.3) and by the replacement of one tertiary Me signal by an *AB* system at δ 3.90 and 4.18 (*AB* system, $J = 11.0$ Hz, CH_2(20)). These data can be explained by **1** being an acetyloxy derivative of **6**, in agreement with the molecular-mass difference of 58 observed between **1** and **6**. The location of the AcO group at C(20) (*i.e.*, at the β-positioned Me group attached to C(4) of **6**) was inferred from the replacement of the C(20) Me signal at δ (C) 21.5 with a CH_2O signal at δ (C) 66.8 and by the chemical-shift differences observed in the ^{13}C-NMR spectrum for C(3), C(4), and Me(19) (*Table 2*), which were all consistent with an oxidation of the β-oriented Me group at C(4) of **6** [10]. Finally, the relative configuration of the remaining chiral centers of **1** was shown to be the same as in **6** [8] by the NOESY data, which furnished the correlations displayed in *Fig. 2*.

Hyrtiosin B (**2**) was shown to be a diastereoisomer of **1**, *i.e.*, 19-(acetyloxy)-25-dehydroxy-12-*epi*-scalarin, as follows. Its molecular formula, deduced from HR-EI-MS (*m/z* 486.2999 (M^+)), corresponded to $C_{29}H_{42}O_6$, identical to that of **1**. Comparison of its spectral data (IR: λ_{max} 1765, 1738, 1689, 1240 cm^{-1}; ^{1}H- and ^{13}C-NMR (*Tables 1* and *2*)) with those of **1** clearly indicated that it differs from **1** only within ring A, where the tertiary Me group C(19), instead of C(20), was acetoxylated. Due to the γ-gauche effect, the ^{13}C-NMR signal of C(5) was shifted upfield from δ 57.0 in **1** to 50.3 in **2** supporting the equatorial orientation of the 19-AcO group. The rest of the structure **2** is the same as in hyrtiosin A (**1**).

Table 1. *^{1}H-NMR Data for Compounds* **1**–**5**. δ in ppm, J in Hz.

	1[a])	**2**[a])	**3**[b,c])	**4**[a])	**5**[b])
H_α–C(1)	0.95 (*m*)	0.93 (*m*)	0.78 (*m*)	0.76 (*m*)	0.75 (*m*)
H_β–C(1)	1.69 (*m*)	1.64 (*m*)	1.69 (*m*)	1.66 (*m*)	1.66 (*m*)
H_α–C(2)	1.45 (*m*)	1.44 (*m*)	1.46 (*m*)	1.46 (*m*)	1.57 (*m*)
H_β–C(2)	1.45 (*m*)	1.44 (*m*)	1.60 (*m*)	1.46 (*m*)	1.57 (*m*)
H_α–C(3)	1.00 (*m*)	1.36 (*m*)	1.32 (*m*)	1.05 (*m*)	0.95 (*m*)
H_β–C(3)	1.69 (*m*)	1.36 (*m*)	1.32 (*m*)	1.34 (*m*)	1.12 (*m*)
H–C(5)	1.00 (*m*)	1.13 (*m*)	1.07 (*m*)	0.79 (*m*)	0.79 (*m*)
CH_2(6)	1.45 (*m*)	1.55 (*m*)	1.38 (*m*)	1.39 (*m*)	1.38 (*m*)
H_α–C(7)	0.95 (*m*)	0.93 (*m*)	0.92 (*m*)	0.87 (*m*)	1.35 (*m*)
H_β–C(7)	1.77 (*m*)	1.73 (*m*)	1.67 (*m*)	1.77 (*m*)	1.78 (*m*)
H–C(9)	1.03 (*m*)	1.05 (*m*)	0.87 (*m*)	0.85 (*m*)	0.78 (*m*)
H_α–C(11)	2.20 (*m*)	2.02 (*m*)	1.35 (*m*)	1.29 (*m*)	1.39 (*m*)
H_β–C(11)	2.37 (*m*)	2.37 (*m*)	1.56 (*m*)	1.68 (*m*)	1.57 (*m*)
H_α–C(12)	4.66 (*dd*, *J* = 11.3, 4.2)	4.68 (*dd*, *J* = 11.3, 3.9)	1.38 (*m*)	3.42 (*dd*, *J* = 11.3, 3.9)	1.16 (*m*)
H_β–C(12)	–	–	1.88 (*m*)	–	1.81 (*m*)
H–C(14)	1.34 (*m*)	1.36 (*m*)	1.28 (*m*)	0.86 (*m*)	1.03 (*m*)
H_α–C(15)	1.84 (*m*)	1.85 (*m*)	2.29 (*m*)	1.97 (*m*)	2.03 (*m*)
H_β–C(15)	1.45 (*m*)	1.44 (*m*)	2.05 (*m*)	1.28 (*m*)	1.38 (*m*)
H–C(16)	6.87 (*dd*, *J* = 6.7, 3.2)	6.87 (*dd*, *J* = 7.1, 2.9)	6.87 (*dd*, *J* = 7.0, 3.1)	4.26 (*m*)	5.40 (*m*)
H–C(18)	2.86 (*m*)	2.88 (*m*)	2.50 (*m*)	2.37 (*m*)	2.34 (*m*)
Me(19)	0.93 (*s*)	–	–	0.80 (*s*)	0.85 (*s*)
H_a–C(19)	–	3.87 (*d*, *J* = 11.0)	3.87 (*d*, *J* = 11.0)	–	–
H_b–C(19)	–	3.63 (*d*, *J* = 11.0)	3.61 (*d*, *J* = 11.0)	–	–
Me(20)	–	0.83 (*s*)	0.88 (*s*)	0.77 (*s*)	0.80 (*s*)
H_a–C(20)	4.18 (*d*, *J* = 11.0)	–	–	–	–
H_b–C(20)	3.90 (*d*, *J* = 11.0)	–	–	–	–
Me(21)	0.94 (*s*)	0.97 (*s*)	0.83 (*s*)	0.82 (*s*)	0.85 (*s*)
Me(22)	0.87 (*s*)	0.89 (*s*)	0.92 (*s*)	0.80 (*s*)	0.84 (*s*)
Me(23)	0.86 (*s*)	0.87 (*s*)	0.82 (*s*)	0.71 (*s*)	0.85 (*s*)
H–C(24)	–	–	–	6.27 (*t*, *J* = 1.9)	6.09 (*s*)
H_a–C(25)	4.23 (*t*, *J* = 9.2)	4.24 (*t*, *J* = 9.2)	6.45 (*d*, *J* = 1.3)	6.76 (*d*, *J* = 1.4)	6.34 (*d*, *J* = 1.4)
H_b–C(25)	4.11 (*t*, *J* = 9.2)	4.11 (*t*, *J* = 9.2)	–	–	–
AcO–C(12)	2.05 (*s*)	2.05 (*s*)	–	–	–
AcO–C(16)	–	–	–	–	2.07 (*s*)
AcO–C(19)	–	2.05 (*s*)	2.07 (*s*)	–	–
AcO–C(20)	2.05 (*s*)	–	–	–	–
AcO–C(25)	–	–	2.14 (*s*)	2.10 (*s*)	2.10 (*s*)

[a]) *Bruker AV-500-MHz* spectrometer, δ referenced to $CDCl_3$ (δ(H) 7.26). [b]) *Varian Mercury-400-MHz* spectrometers, δ referenced to $CDCl_3$ (δ(H) 7.26). [c]) Assignments were tentatively made by the comparison with those of model compound **8**.

Hyrtiosin C (**3**) showed the molecular formula $C_{29}H_{42}O_6$, the same as compound **1** and **2**, as indicated by its HR-EI-MS. But their ^{1}H-NMR spectra (*Table 1*) were significantly different. Careful comparison of ^{1}H-NMR data of **2** and **3** revealed that the main differences are located in the rings C and E. Hyrtiosin C (**3**) was tentatively determined as 19-(acetyloxy)-12-de(acetyloxy)-25-*O*-acetylscalarin.

Table 2. *^{13}C-NMR Data of Compounds* **1**, **2**, *and* **4**–**6**. δ in ppm.

	1[a])	**2**[a])	**4**[a])	**5**[b])	**6**[a])
C(1)	39.7 (*t*)	39.2 (*t*)	40.0 (*t*)	39.9 (*t*)	39.8 (*t*)
C(2)	18.0 (*t*)	17.9 (*t*)	18.3 (*t*)	18.2 (*t*)	18.0 (*t*)
C(3)	36.3 (*t*)	35.7 (*t*)	41.9 (*t*)	42.0 (*t*)	41.5 (*t*)
C(4)	37.0 (*s*)	36.5 (*s*)	33.5 (*s*)	33.3 (*s*)	33.3 (*s*)
C(5)	57.0 (*d*)	50.3 (*d*)	56.6 (*d*)	56.5 (*d*)	56.5 (*d*)
C(6)	18.2 (*t*)	17.6 (*t*)	18.6 (*t*)	18.6 (*t*)	18.5 (*t*)
C(7)	41.7 (*t*)	41.1 (*t*)	42.1 (*t*)	42.1 (*t*)	42.0 (*t*)
C(8)	37.4 (*s*)	37.4 (*s*)	37.5 (*s*)	37.6 (*s*)	37.4 (*s*)
C(9)	58.5 (*d*)	58.4 (*d*)	58.9 (*d*)	61.3 (*d*)	58.4 (*d*)
C(10)	37.3 (*s*)	37.4 (*s*)	38.0 (*s*)	38.0 (*s*)	37.4 (*s*)
C(11)	23.6 (*t*)	23.7 (*t*)	27.3 (*t*)	17.1 (*t*)	23.4 (*t*)
C(12)	82.6 (*d*)	82.6 (*d*)	80.7 (*d*)	40.6 (*t*)	82.7 (*d*)
C(13)	38.8 (*s*)	38.9 (*s*)	42.6 (*s*)	36.7 (*s*)	38.8 (*s*)
C(14)	53.5 (*d*)	53.5 (*d*)	54.9 (*d*)	56.1 (*d*)	53.6 (*d*)
C(15)	23.5 (*t*)	23.4 (*t*)	26.4 (*t*)	28.2 (*t*)	23.7 (*t*)
C(16)	135.7 (*d*)	135.7 (d)	68.0 (d)	69.5 (d)	135.6 (*d*)
C(17)	126.6 (*s*)	126.5 (*s*)	125.1 (*s*)	114.3 (*s*)	126.5 (*s*)
C(18)	49.7 (*d*)	49.7 (*d*)	64.2 (*d*)	63.7 (*d*)	49.7 (*d*)
C(19)	27.3 (*q*)	72.6 (*t*)	33.3 (*q*)	33.3 (*q*)	33.3 (*q*)
C(20)	66.8 (*t*)	17.2 (*q*)	21.3 (*q*)	21.3 (*q*)	21.4 (*q*)
C(21)	16.5 (*q*)	16.6 (*q*)	17.4 (*q*)	17.3 (*q*)	16.6 (*q*)
C(22)	17.0 (*q*)	17.0 (*q*)	16.4 (*q*)	16.3 (*q*)	16.6 (*q*)
C(23)	9.0 (*q*)	9.0 (q)	8.9 (*q*)	14.7 (*q*)	9.0 (*q*)
C(24)	169.5 (*s*)	169.5 (*s*)	135.2 (*d*)	134.8 (*d*)	169.4 (*s*)
C(25)	67.7 (*t*)	67.7 (*t*)	102.0 (*d*)	98.4 (*d*)	67.7 (*t*)
*Ac*O–C(12)	170.2 (*s*), 21.0 (*q*)	170.3 (*s*), 21.0 (*q*)	–	–	170.1 (*s*), 21.3 (*q*)
*Ac*O–C(16)	–	–	–	169.9 (*s*), 21.1 (*q*)	–
*Ac*O–C(19)	–	171.2 (*s*), 21.5 (*q*)	–	–	–
*Ac*O–C(20)	171.3 (*s*), 21.5 (*q*)	–	–	–	–
*Ac*O–C(25)	–	–	171.4 (*s*), 21.4 (*q*)	170.1 (*s*), 21.2 (*q*)	–

[a]) ^{13}C-NMR Spectra were recorded at 125 MHz; δ referenced to $CDCl_3$ (δ(C) 77.0). [b]) ^{13}C-NMR Spectra were recorded at 100 MHz; δ referenced to $CDCl_3$ (δ(C) 77.0).

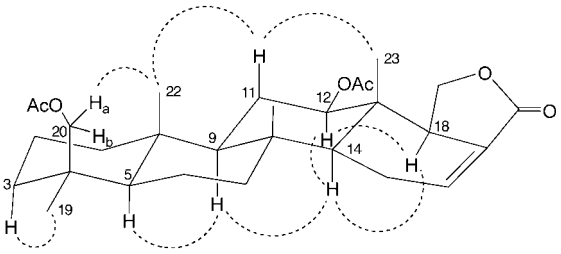


Fig. 2. *Selected key NOSEY correlations of hyrtiosin A* (**1**)

In the ^{1}H-NMR of **3**, the absence of the typical H–C(12) signal at δ 4.68 from ring C and the appearance of a new signal at δ 6.45 from ring E, together with the disappearance of *AB*-type signals attributable to CH_2(25), indicated that the second AcO group, at C(12) in **2**, was at C(25) in **3**. The splitting pattern of H–C(25) (*d*, J = 1.3 Hz) matches that of the co-occurring compound **7** [8a] and of model compound **8** [11], and indicated that the AcO group at C(25) was also α-oriented. Unfortunately, the scarcity of the material did not allow us to confidently record its ^{13}C-NMR spectrum as well as to measure its optical rotation.

Hyrtiosin D (**4**) had the molecular formula $C_{27}H_{42}O_5$ as established by HR-ESI-MS and ^{13}C-NMR data. Its ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*) were very similar to those of co-occurring heteronemin (**9**) [9], except for the absence of an acetyl group in **4**, thus indicating that **4** was an *O*-deacetyl derivative of **9**. Analysis of 2D-NMR spectra (^{1}H,^{1}H COSY, HMQC, HMBC) of **4** readily allowed to place two OH groups at C(12) and C(16), and an AcO group at C(25). Furthermore, the splitting patterns and the coupling constants of H–C(12), H–C(16), and H–C(25) (see *Table 1*) closely resemble those of **9** [9], indicating that their relative configuration is the same. The missing acetyl group at O–C(16) caused the expected upfield-shift of H–C(16) (from δ 5.33 in **9** to 4.26 in **4**), in accord with the proposed structure **4** as a 16-*O*-deacetylheteronemin.

Hyrtiosin E (**5**), 12-dehydroxy-heteronemin, yielded an EI-MS molecular-ion peak at *m/z* 472, *i.e.,* 16 mass units less than that of **9**. The ^{1}H- and ^{13}C-NMR spectra of **5** (*Tables 1* and *2*) revealed a close relationship with **9**. The presence of two AcO groups at C(16) and C(25) of the molecule was evident. Comparison of NMR data of **5** with those of **9** disclosed that the only difference between them resided in ring C. A significant upfield shift of C(12) (from δ 80.4 in **9** to 40.6 in **5**) implied that the OH group at C(12) was absent. Moreover, the observation that Me(23) is deshielded by 6 ppm compared to **9** further supports the postulated structure **5** for this isolate [9b].

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Experimental Part

General. Reversed-phase HPLC: *Agilent 1100* liquid chromatograph, with a *VWD G1314A* detector at 210 nm; purification with one semi-prep. *ODS-HG-5* (column 5 μm, 10 mm (i.d.) × 25 cm). Optical rotations: *Perkin-Elmer 341-MC* polarimeter; in $CHCl_3$. UV Spectra: *Varian Cary-300-BIO* spectrophotometer; λ_{max} (ε) in nm. IR Spectra: *Nicolet Magna-FT-IR-750* spectrometer: $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Varian Mercury-400* and *Bruker AV-500* spectrometer; with residual $CHCl_3$ (δ (H) 7.26, δ (C) 77.0) as internal standard; chemical shifts δ in ppm, coupling constants *J* in Hz. MS: *Finnigan MAT-95* instrument for EI and *Q-Tof-Micro-YA019* instrument; for ESI; in *m/z*.

Animal Material. Sponge samples 03LS-33 and 03LS-111 were collected in January, 2003, by scuba techniques at a depth of − 10 m from the different locations of the Lingshui Bay, Hainan Province, China. Both of the sponge samples were frozen immediately and transferred to the Shanghi Institutes for Biological Sciences (SIBS), where it was kept at − 20° until extraction. The voucher specimens are stored for inspection at the SIBS, under registration No. 03LS-33 and No. 03LS-111, resp.

Extraction and Isolation. The frozen sponges 03LS-111 (138 g dry weight) were cut into small pieces and exhaustively extracted with Me_2CO at r.t. The extract was concentrated, and the resulting residue was extracted with Et_2O and BuOH. The Et_2O-soluble portion was repeatedly chromatographed (silica gel, increasing amounts of AcOEt in light petroleum ether): mixture of sesterterpenoids **1**–**3**, **6**, **7**, and **9**. This mixture was further purified by reversed-phase HPLC (*ODS-18* column (10 mm (i.d.) × 25 cm), MeCN/H_2O 88 : 12): pure **1** (3.1 mg), **2** (2.3 mg), **3** (0.6 mg), **6** (3.3 mg), **7** (6.9 mg), and **9** (4.3 mg), all as amorphous white powder.

Analogously to the procedure applied to the collection 03LS-111, a mixture of sesterterpenoids **4**, **5**, and **9** was isolated from sponge 03LS-33 (86 g dry weight). This mixture was further purified by reversed-phase HPLC (*ODS-18* column (10 mm (i.d.) × 25 cm), MeOH/H_2O 85 : 15): pure **4** (3.1 mg), **5** (5.4 mg), and **9** (6.4 mg), all as amorphous white powder.

Hyrtiosin A (=(*5a*S,*5b*R,*7a*R,*8*S,*11a*R,*11b*R,*13*R*13a*S,*13b*R)*-13-(Acetyloxy)-8-[(acetyloxy)methyl]-5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a,13b-hexadecahydro-5b,8,11a,13a-tetramethylchryseno[1,2-c]furan-

*3(1*H*)-one*; **1**): Amorphous white powder. $[\alpha]_D^{20} = +5$ ($c = 0.17$, $CHCl_3$). IR (KBr): 3435, 2926, 1763, 1736, 1691, 1242. UV (MeOH): 221 (4500). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. EI-MS: 486 (M^+), 444, 426, 366, 353, 257, 249, 189. HR-EI-MS: 486.2992 ($C_{29}H_{42}O_6^+$; calc. 486.2981).

*Hyrtiosin B (=(5a*S*,5b*R*,7a*R*,8R,11a*R*,11b*R*,13*R*,13a*S*,13b*R*)-13-(Acetyloxy)-8-[(acetyloxy)methyl]-5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a,13b-hexadecahydro-5b,8,11a,13a-tetramethylchryseno[1,2-*c*]furan-3(1*H*)-one;* **2**): Amorphous white powder. $[\alpha]_D^{20} = +7$ ($c = 0.16$, $CHCl_3$). IR (KBr): 3458, 2926, 1765, 1738, 1689, 1240. UV (MeOH): 221 (5500). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. EI-MS: 486 (M^+), 426, 366, 353, 271, 257, 229, 189. HR-EI-MS: 486.2999 ($C_{29}H_{42}O_6^+$; calc. 486.2981).

*Hyrtiosin C (=(1*R*,5a*S*,5b*R*,7a*R*,8*R*,11a*R*,11b*S*,13*S*,13a*S*,13b*R*)-1-(Acetyloxy)-8-[(acetyloxy)methyl]-5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a,13b-hexadecahydro-5b,8,11a,13a-tetramethylchryseno[1,2-*c*]furan-3(1*H*)-one;* **3**): Amorphous white powder. ^{1}H-NMR ($CDCl_3$, 400 MHz). *Table 1*. EI-MS: 486 (M^+), 444, 426, 366, 353, 316, 249, 230, 189. HR-EI-MS: 486.2980 (M)$^+$ $C_{29}H_{42}O_6^+$; calc. 486.2981).

*Hyrtiosin D (=(1*S*,4*S*,5a*S*,5b*R*,7a*S*,11a*S*,11b*R*,13*R*,13a*S*,13b*R*)-1,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a,13b-Octadecahydro-5b,8,8,11a,13a-pentamethylchryseno[1,2-*c*]furan-1,4,13-triol 1-Acetate;* **4**): Amorphous white powder. $[\alpha]_D^{20} = -16$ ($c = 0.16$, $CHCl_3$). IR (KBr): 3458, 2926, 1738, 1689, 1240. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 469.2940 ($[M + Na]^+$, $C_{27}H_{42}NaO_5^+$; calc. 469.2930).

*Hyrtiosin E (=(1*S*,4*S*,5a*S*,5b*R*,7a*S*,11a*S*,11b*R*;13a*S*,13b*R*)-1,4,5,5a,5b,6,7,7a,8,9,10,11,11a,11b,12,13,13a,13b-Octadecahydro-5b,8,8,11a,13a-pentamethylchryseno[1,2-*c*]furan-1,4-diol Diacetate*; **5**): Amorphous white powder: $[\alpha]_D^{20} = -67.9$ ($c = 0.52$, $CHCl_3$). IR (KBr): 3109, 2922, 1732, 1684, 1223. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. EI-MS: 472 (M^+), 412, 376, 370, 152. HR-EI-MS: 472.3221 ($C_{29}H_{42}O_6^+$; calc. 472.3253).

REFERENCES

[1] P. Crews, S. Naylor, *Prog. Chem. Org. Nat. Prod*. **1985**, *48*, 203.
[2] R. P. Walker, J. E. Thompson, D. J. Faulkner, *J. Org. Chem*. **1980**, *45*, 4976.
[3] J. C. Braekman, D. Daloze, M. Kaisin, B. Moussiaux, *Tetrahedron* **1985**, *41*, 4063.
[4] H. Kikuchi, Y. Tsukitani, I. Shimizu, M. Kobayashi, I. Kitagawa, *Chem. Pharm. Bull*. **1983**, 31, 552.
[5] B. F. Bowden, J. C. Coll, H. Li, R. C. Cambie, M. R. Kernan, P. R. Bergquist, *J. Nat. Prod.* **1992**, *55*, 1234; X. Fu, L. Zeng, J. Su, M. Paris, P. Potier, *J. Nat. Prod*. **1992**, *55*, 1607.
[6] R. Kazlauskas, P. T. Murphy, R. J. Wells, *Aust. J. Chem.* **1982**, *35*, 51.
[7] W. Zhang, Y.-W. Guo, E. Mollo, G. Cimino, *Helv. Chim. Acta* **2004**, *87*, 2341; W. Zhang, Y.-W. Guo, E. Mollo, G. Cimino, *Helv. Chim. Acta* **2004**, *87*, 2919; X.-C. Huang, D. Zhao, Y.-W. Guo, H.-M. Wu, Z.-H. Wang, Y.-S. Lin, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3117.
[8] a) G. Cimino, S. D. Stefano, L. Minale, E. Trivellone, *J. Chem. Soc., Perkin Trans. 1* **1977**, 1587; b) A. Fontana, E. Mollo, J. Ortea, M. Gavagnin, G. Cimino, *J. Nat. Prod.* **2000**, *63*, 527.
[9] a) M. L. Bourguet-Kondracki, M. T. Martin, C. Debitus, M. Guyot, *Tetrahedron Lett*. **1994**, *35*, 109; b) P. Crews, P. Bescansa, *J. Nat. Prod.* **1986**, *49*, 1041.
[10] A. R. Lal, R. C. Cambie, C. E. F. Rickard, P. R. Bergquist, *Tetrahedron Lett.* **1994**, *35*, 2603; L. Gomez-Paloma, A. Randazzo, L. Minale, C. Debitus, C. Roussakis, *Tetrahedron* **1997**, *53*, 10451; J.-M. Fang, C.-I. Lang, W.-L. Chen, Y.-S. Cheng, *Phytochemistry* **1991**, *30*, 2793.
[11] G. Ryu, S. Matsunaga, N. Fusetani, *J. Nat. Prod.* **1996**, *59*, 515.

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