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12-epi-Heteronemin : New Sesterterpene From The Marine Sponge *Hyrtios erecta*

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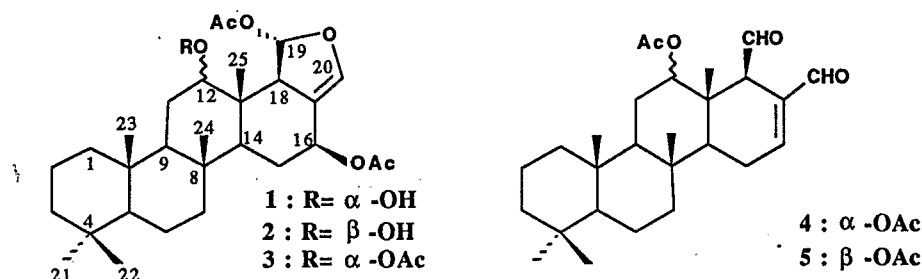
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Abstract: 12-epi-heteronemin, a novel tetracycyclic sesterterpene was isolated from the marine sponge *Hyrtios erecta* and its structure has been established through spectral studies.

Sponges of the order of Dictyoceratida are known as a source of sesterterpenes, an otherwise rare group of terpenoids. Tetracyclic sesterterpenes of the scalarane type have been frequently reported from sponges of the genus *Hyrtios*. A study on the methanolic extract of the sponge *Hyrtios erecta*, collected in New Caledonia in 1988, has now led to the isolation of a new member of this class of sesterterpenes: 12-epi-heteronemin **1** and to the previously described heteronemin **2**¹ and 12-epi-heteronemin acetate **3**².

The methanol extract (4.7 g) of lyophilized *Hyrtios erecta* (500 g), was fractionated by silicagel chromatography using a gradient of MeOH in CH₂Cl₂. The fraction eluted with 5% MeOH/CH₂Cl₂ (1.3 g) was a crystallized mixture of two major compounds, further separated on silica gel (hex/AE 8:2), Sephadex LH-20 (CHCl₃/MeOH 4:6) column chromatography and preparative tlc (CH₂Cl₂/Acetone 95:5), thus affording two crystallized pure compounds. The minor one (0.1% animal dry weight), heteronemin **2**, was easily identified by its accordance with the spectral data given in the literature³, m.p: 182°C, [α]_D = -37 (c 0.009, Chf).

We shall here discuss the structure elucidation of the major (0.5% animal dry weight) and less polar compound **1**, m.p: 175°C, [α]_D = -35 (c 0.01, Chf).



The spectral data in the ¹H NMR spectrum of **1** were almost identical with those of heteronemin **2**, with the exception of the proton H-12, which appeared at δ 3.84 ppm as a typical broad triplet (*J* = 2.7 Hz) for an equatorial proton, whereas the ¹H NMR of heteronemin **2** indicated the presence of an axial proton at δ 3.44 ppm (*J* = 3.9, 11.3 Hz). This was confirmed by comparison of the ¹³C NMR data, by the shielded signal at δ 71.52 ppm (δ 80.51 ppm for **2**) and the deshielded signal at δ 56.86 ppm (δ 64.18 ppm for **2**), respectively



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attributed to the C-12 and C-18 carbons (Table 1). Thus, compound **1** was identified as 12-epi-heteronemin. U.V., I.R. and MS data, supported this structural assignment⁴.

n°	heteronemin 2		12-epi-heteronemin 1	
	¹³ C	¹ H	¹³ C	¹ H
1	39.91		39.61	1.61 m
2	18.17 ^a		18.14 ^a	1.58 m
3	42.03		41.96	1.04 ax and 1.34 eq
4	33.21 ^b		33.24 ^b	
5	56.51		56.30	
6	18.56 ^a		18.52 ^a	1.36 m
7	41.82		41.76	0.98 ax and 1.72 eq
8	37.41		38.05	
9	58.75		50.92	1.38 ax
10	38.06		36.85	
11	27.20		24.75	1.64 m
12	80.51	3.44 J=3.8, 11.3	71.52	3.84 brt J=2.7, 2.7
13	42.70		41.60	
14	54.67		49.90	1.37 ax
15	27.99		28.29	1.34 ax and 2.04 eq
16	69.33	5.34	69.15	5.34 dddd J=10.1, 6.2, 2.1, 1.2
17	114.41		115.38	
18	64.17	2.40	56.86	3.02 d J= 1.3
19	101.63	6.74 d J=1.3	100.35	6.27 d J= 1.3
20	135.34	6.14 t J=2	134.48	6.11 t J= 2
21	33.23 ^b	0.87	33.19 ^b	0.80 eq
22	21.34	0.77	21.26	0.76 ax
23	16.31	0.79	16.24	0.78 ax
24	17.31	0.81	16.81	0.81 ax
25	8.75	0.81	14.61	0.81 ax
OAc	21.24	2.07	21.36	2.05
OAc	21.03	2.07	20.99	2.06
CO	171.30		171.81	
CO	170.06		169.96	

Assignments were determined by ¹H-¹H COSY, ¹H-¹³C correlations via HMQC and HMBC NMR experiments, *J* values are expressed in Hz, ^{a-b}: Assignments may be reversed.

Hyrtilos erecta from Australian Barrier Reef and Red Sea localities have already yielded a variety of sesterterpenes of which heteronemin is the dominant metabolite. Thus, it is surprising that in the New Caledonia sample, 12-epi-heteronemin **1** is the major compound (0.5%) and has not been isolated to-date. Marine sponges can biosynthesize several isomers of tetracarbocyclic sesterterpenes such as scalaradial **4**, 12-epi-scalaradial **5** and 12-18-diepi-scalaradial, which were isolated from *Spongia nitens*⁵ and *Cacospongia mollior*⁶, all of which are PLA₂ inhibitors⁷. Similarly, 12-epi-heteronemin acetate and 12-epi-scalaradial **5** have been reported from *Hyrtilos erecta*². Hence, 12-epi-heteronemin can be considered as the missing piece of this series. Further studies on the chemical behaviour and on the biological activities of **1** and derivatives are in progress.

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4. UV (MeOH) 210 (ε, 13859), IR (film) 3545 (alcohol), 1732, 1748 and 1237 (acetate) cm⁻¹; MS: m/e 470 (17%), 428 (30%), 386 (17%), 368 (100%), 350 (30%), 191 (47%).
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