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

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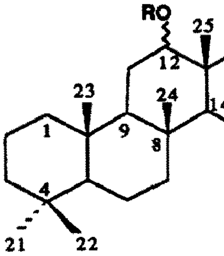
Abstract: 12-epi-heteronemin, a novel tetracarbocyclic sesterterpene was isolated from the marine sponge *Hyrtios erecta* and its structure has been established through spectral studies.

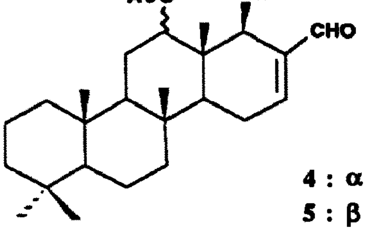
Sponges of the order of Dictyoceratida are known as a source of sesterterpenes, an otherwise rare group of terpenoids. Tetracyclic sesterterpenes of the scalarane type have been frequently reported from sponges of the genus *Hyrtios*. A study on the methanolic extract of the sponge *Hyrtios erecta*, 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 CH_2Cl_2. The fraction eluted with 5% MeOH/CH_2Cl_2 (1.3 g) was a crystallized mixture of two major compounds, further separated on silica gel (hex/AE 8:2), Sephadex LH-20 ($CHCl_3$/MeOH 4:6) column chromatography and preparative tlc (CH_2Cl_2/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 literature[3], m.p: 182°C, $[\alpha]_D = -37$ (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, $[\alpha]_D = -35$ (c 0.01, Chf).



1 : R= α -OH
2 : R= β -OH
3 : R= α -OAc



4 : α -OAc
5 : β -OAc

The spectral data in the ^{1}H 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 ^{1}H 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 ^{13}C 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 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 assignment[4].

Table 1: ^{1}H-(300 MHz) and ^{13}C-(75 MHz) NMR data of heteronemin **2** and 12-epi-heteronemin **1** ($CDCl_3$)

	heteronemin 2		12-epi-heteronemin 1	
n°	^{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 ^{1}H-^{1}H COSY, ^{1}H-^{13}C correlations via HMQC and HMBC NMR experiments, *J* values are expressed in Hz, [a-b]: Assignments may be reversed.

Hyrtios 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 PLA_2 inhibitors[7]. Similarly, 12-epi-heteronemin acetate and 12-epi-scalaradial **5** have been reported from *Hyrtios 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.

References

1. Kazlauskas, R.; Murphy, P.T.; Quinn, R.J.; Wells, R.J. *Tetrahedron Lett.*, **1976**, *30*, 2631-2634.
2. Crews, P.; Besansca, P. *J. Nat. Prod.*, **1986**, 49, 1041-1052.
3. Kashman, Y.; and Rudi, A. *Tetrahedron*, **1977**, *33*, 2997-2998.
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%).
5. Cimino, G.; De Stefano, S.; Di Luccia, A. *Experientia*, **1979**, *35*, 1277-1278.
6. Cimino, G.; De Stefano, S.; Minale, L. *Experientia*, **1973**, *29*, 934-935.
7. Potts, B.C.M.; Faulkner, D.J. *J. Nat. Prod.*, **1992**, 55, 1701-1717.

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