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NEW MARINE DITERPENOIDS, INCLUDING A UNIQUE HYDROPEROXIDE, FROM A CARIBBEAN GORGONIAN CORAL OF THE GENUS *PSEUDOPTEROGORGIA*

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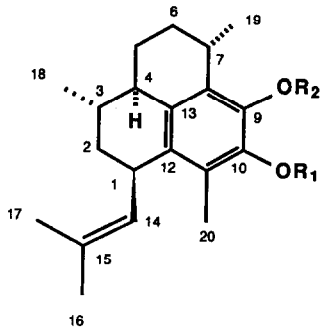
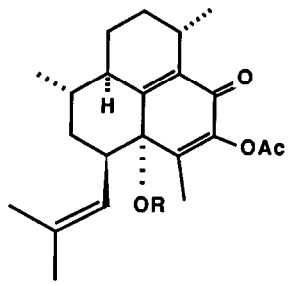
Summary: Three new diterpenoids related to the aglycone components of the recently described pseudopterosins and seco-pseudopterosins have been isolated from an undescribed *Pseudopterogorgia* species from the Caribbean Sea. The new compounds, described on the basis of their NMR properties and chemical interconversions, appear to be related illustrating some interesting rearrangements of a tertiary hydroperoxide in this series.

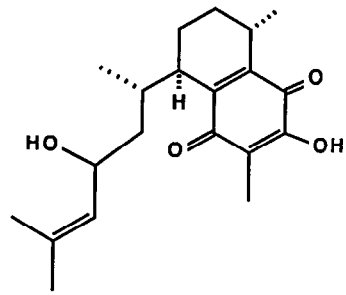
In connection with a comprehensive chemotaxonomic investigation of gorgonian corals of the genus *Pseudopterogorgia*, we encountered several morphologically similar but chemically unique species which appear to be unrecorded. One such species[2], collected near Highborne Cay, Bahamas Islands, in 1982, was found to contain a series of four new diterpenoids, **1a,b, 3,** and **5**. Compounds **1a,b** and **3** possess tricyclic ring skeletons related to the pseudopterosins, a new class of anti-inflammatory glycosides isolated from *P. elisabethae*[3]. Quinone **5** is related to the aglycone portion of the seco-pseudopterosins, another group of glycosides isolated from *Pseudopterogorgia*[4].

Chloroform extraction of the freeze-dried gorgonian yielded a crude extract which was fractionated by silica vacuum flash chromatography with EtOAc/isooctane mixtures. Diterpenoids **1a,b, 3** and **5** were subsequently isolated by silica HPLC from fractions eluted with 25% EtOAc/isooctane. Compounds **1a,b** were obtained as an inseparable equimolar mixture, which appeared to be composed of interconverting monoacetates. Since this mixture could not be investigated with confidence, it was converted to the diacetate **2** with Ac_2O in pyridine. The diacetate **2** showed strong spectral similarities to the aglycone portion of pseudopterosin-C (**6**), a glycoside described by X-ray methods from *P. elisabethae*[3]. The structure of diacetate **2** as proposed, was fully confirmed by synthesis from **6** by hydrolysis followed by reductive acetylation (Zn/HOAc). The synthetic diacetate showed $[\alpha]_D$ -37.4° and was identical to the natural product ($[\alpha]_D$ -41.7°). Since the signs and magnitudes of the optical rotations are nearly identical, diterpenoid **2** possesses the 1**R**, 3**S**, 4**R**, 7**S** absolute configurations.

Diterpenoid **3** (3.5% extract) analyzed for $C_{22}H_{30}O_5$ by HRMS and ^{13}C NMR methods[6]. This compound possessed ^1H and ^{13}C NMR features similar to **2** including one acetate ester, but was recognized as a cross-conjugated cyclohexadienone by its spectral properties [IR: 1645 cm^{-1}; UV: 247 nm (ε = 9300; ^{13}C NMR: 178.0, 156.0, 143.7, 138.0 & 134.0 ppm]. These latter functional groups accounted for only three of the five oxygen atoms in **3**. Since there was only one additional oxygen-bearing carbon in the ^{13}C NMR spectrum of this compound (86.0, s, ppm), compound







1a R_1=H, R_2=Ac
1b R_1=Ac, R_2=H
2 R_1=R_2=Ac
6 R_1=H, R_2= 3'OAc-ß-D-xylose

3 R = OH
4 R = H

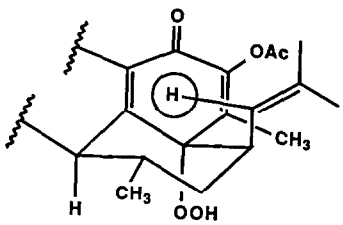
5

NMR Data for Diterpenoids **2**, **3** and **5**[a]

C#	2		3		5	
	^{1}H (CCl_4)	^{13}C ($CDCl_3$)	^{1}H ($CDCl_3$)	^{13}C ($CDCl_3$)	^{1}H ($CDCl_3$)	^{13}C (Bz-d_6)
1	3.60, m	35.7	2.95, m	26.9	4.59, ddd (6,8,8)	66.6
2	nr	39.0	1.42, ddd (5,13,13)	37.2	1.50, m	43.8
3	nr	30.0	nr	33.8	1.96, m	33.7
4	2.38, bd (5.5)	42.3	2.38, m	40.6	2.99, m	33.7
5	nr	27.2	nr	25.2	nr	26.3
6	nr	29.6	nr	19.0	nr	25.8
7	3.01, m	27.7	2.95, m	42.8	2.99, m	26.2
8	-	136.5	-	134.0	-	144.0
9	-	138.9	-	178.0	-	188.0
10	-	138.2	-	156.0	-	151.0
11	-	130.4	-	139.0	-	127.0
12	-	136.1	-	86.0	-	183.0
13	-	133.1	-	144.2	-	133.0
14	5.18, d (9)	129.1	4.69, d (10)	122.0	5.21, d (8)	129.0
15	-	127.3	-	144.0	-	147.0
16	1.75, bs	17.7	1.60, bs	20.3	1.74, bs	20.8
17	1.70, bs	25.6	1.57, bs	25.9	1.70, bs	17.3
18	1.05, d (6.1)	20.9	0.98, d (6.3)	20.1	0.83, d (7)	18.3
19	1.14, d (7.2)	22.4	1.11, d (6.9)	18.0	1.10, d (7)	18.1
20	1.87, s	11.7	1.78, s	10.7	1.92, s	8.3
Ac	2.21, s	20.5	2.27, s	19.9		
	2.19, s	20.4				
Ac		168.7		168.0		
		168.4				
OOH			8.21, bs (D_2O ex.)			

a ^{1}H spectra were recorded at 360 MHz and ^{13}C spectra were recorded at 50 MHz in the solvents indicated. Proton assignments were made on the basis of comparisons with similar compounds and by coupling analyses determined by single frequency decoupling and COSY experiments. ^{13}C assignments were made by comparison with similar compounds. These assignments are insecure and may be interchanged. nr = not resolved.

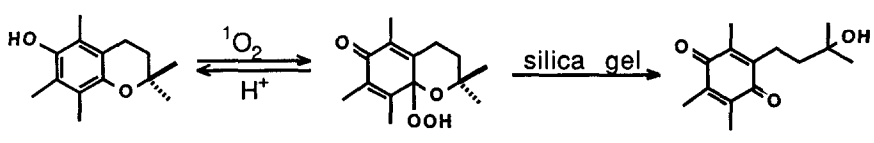
3 was concluded to be a tertiary hydroperoxide. This conclusion was supported by a proton NMR broad singlet resonance at δ 8.21 (D_2O-exc.) assigned to the hydroperoxy proton. Sodium borohydride reduction 1.3H⁻ eq/0°/1 hr.) yielded the alcohol **4**. Alcohol **4** was almost indistinguishable from **3** by ^1H NMR, with the exception of a significant downfield shift of the C-2 axial proton from δ 1.42 in **3** to δ 1.98 in **4**. This result suggested that the hydroperoxide functionality bore a 1,3-diaxial relationship with the newly formed hydroxyl. Consideration of two conceivable structures for **3** resulted in the assignment as shown. An alternative to **3** was carefully considered in which the -OOH is placed at C-13, the acetoxyl is placed at C-9, and the cyclohexadienone is placed at C-8 to C-12 (CO at C-10). Structure **3** was strongly favored since the olefinic proton at C-14 is forced into the π -cloud of the cyclohexadienone system only in this isomer. The C-14 proton in **3** is unusually shielded to δ 4.69.



Fortuitously, hydroperoxide **3** was found to spontaneously decompose ($T^{1/2}$ = 3 weeks at RT) to the monoacetate mixture **1a,b**. Acetylation of the mixture yielded diacetate **2**, which showed $[\alpha]_D$ -41.9°. Thus, hydroperoxide **3** is fully defined as the C-12 hydroperoxide with the absolute stereochemistry as shown including C-12 = **R**.

Diterpenoid **5**, isolated as an orange oil (0.5% of the extract), analyzed for $C_{20}H_{28}O_4$ by HRMS and ^{13}C NMR methods. Analysis of mass spectral and ^{13}C NMR data indicated that **5** was a bicyclic *p*-benzoquinone. The UV spectrum of **5**, which showed a large base-induced shift from 279 to 326 nm, indicated the presence of an *ortho* hydroxyl functionality on the benzoquinone ring (a diosphenol). Further, spin-decoupling ^1H NMR experiments positioned an allylic alcohol at C-1 and defined protons along the 8-carbon side chain between C-4 and C-15. Comparison of these data with several derivatives of the seco-pseudopterosins showed that **5** possessed the same aglycone skeleton[4]. NMR analysis of coupling constants for **5** showed that the protons at C-3, C-4 and C-7 had identical relative stereochemistries as in the seco-pseudopterosins, and as in pseudopterosin-C, **6**. No information could be interpreted, however, to assign the absolute configurations at these centers.[7].

Over the past decade careful isolation procedures have resulted in the isolation of numerous hydroperoxides from marine sources[8]. Although not immediately obvious, compounds **1,b, 3**, and **5** appear to be related through oxidation and acid catalyzed rearrangement. Matsumoto *et al.* have recently shown that chromanol **7** is converted to the hydroperoxide **8** with singlet oxygen. They further showed that acid catalyzed decomposition of **8** yielded starting material, and that silica gel transformed the hydroperoxide to the *p*-benzoquinone **9**[9]. These observations are highly analogous to the reactivities and to the structural relationships between diterpenoids **1a,b, 3** and **5**, suggesting that similar chemistry is involved in their formation and interconversions.



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References

1. This paper is dedicated to the memory of Carl A. Harvis, a bright scholar and unique individual, who lost his life in an unfortunate diving accident on 7 July, 1985.

2. We thank Dr. Frederick M. Bayer, Smithsonian Institution, Washington, D.C. for providing taxonomic support for these studies.

3. Look, S.A., Fenical, W., Matsumoto, G., and Clardy, J., *J. Org. Chem.* **51**, 5140 (1986).

4. Look, S.A., and Fenical, W., *Tetrahedron* **43**, 3363 (1987).

5. For **2**, a yellow oil; $[\alpha]_D$ -41.7° (c 0.02, MeOH); UV (EtOH) 282, 220 nm; IR ($CHCl_3$) 3500, 2960, 2390, 1790 cm^{-1}.

6. For **3**, a yellow oil; $[\alpha]_D$ -11.3° (c 0.006, MeOH); UV (EtOH) 247 nm (ε = 9300); IR ($CHCl_3$) 3020, 2400, 1760, 1645 cm^{-1}; HRMS M^+ *m/z* = 374.2096, M^+-O *m/z* = 358.2172, *m/z* = 342.2201, 282.1953.

7. For **5**, an orange oil, UV (MeOH) 321 nm (ε = 3100), 279 nm (ε = 8900), 220 nm (ε = 13,200), KOH 326 nm (ε = 4600), 281 nm (ε = 7500), 223 nm (ε = 15,700); IR ($CHCl_3$) 3000, 1640-1650 cm^{-1}; HRMS 332 (weak, no HR) M^+-H_2O *m/z* = 314.1868, *m/z* = 248.1434, 205.9996.

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