Illudalane Sesquiterpenoids of the Alcyopterosin Series from the Antarctic Marine Soft Coral *Alcyonium grandis*

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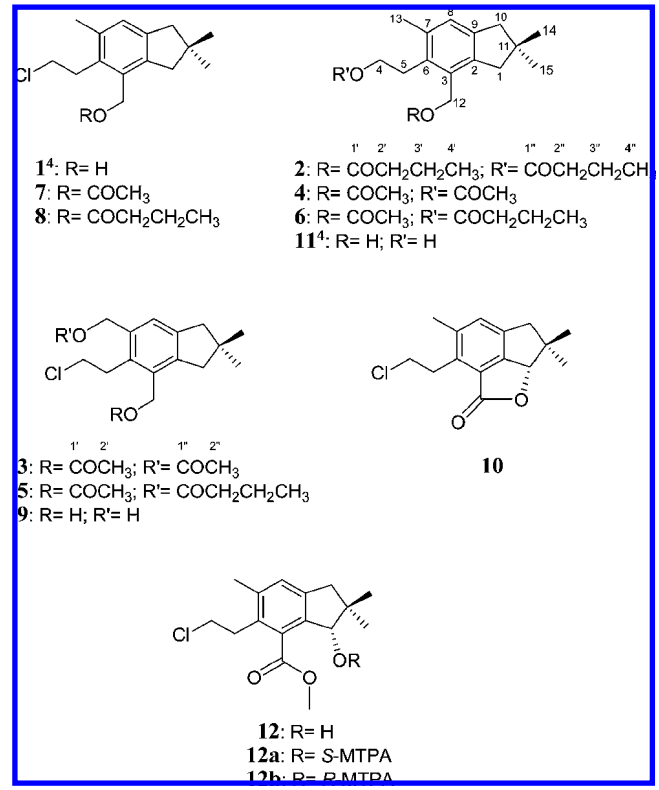
Chemical investigation of the lipophilic extract of the Antarctic soft coral *Alcyonium grandis* led us to the finding of nine unreported sesquiterpenoids, **2**−**10**. These molecules are members of the illudalane class and in particular belong to the group of alcyopterosins, illudalanes isolated from marine organisms. The structures of **2**−**10** were determined by interpretation of spectroscopic data. Repellency experiments conducted using the omnivorous Antarctic sea star *Odontaster validus* revealed a strong activity in the lipophilic extract of *A. grandis* against predation.

Illudalane sesquiterpenes[1] are a group of compounds modestly distributed in nature, being typical metabolites of both fungi of the Basidiomycotina subdivision[2] and ferns of the Pteridaceae family.[3] Among these, alcyopterosins (e.g., alcyopterosin D, **1**) represent a unique set of marine illudalanes isolated from the sub-Antarctic deep sea soft coral *Alcyonium paessleri*.[4] In the alcyopterosins, the six-membered ring of the illudalane skeleton is aromatic and either a chlorine atom or a nitrate ester function is present on the side chain of almost all members of the group.[4] Cytotoxic[4,5] and antispasmodic[6] activities have been reported for illudalane sesquiterpenes. In addition, interesting DNA-binding properties have been described for alcyopterosins and their synthetic analogues.[7,8]

In this paper we report the structure elucidation of nine additional alcyopterosins, compounds **2**−**10**, isolated from an ether extract of the Antarctic soft coral *Alcyonium grandis* Casas, Ramil and Van Ofwegen 1997. Soft corals (order Alcyonacea) are conspicuous members of Antarctic benthic communities and possess a variety of bioactive chemicals.[9] The extract analyzed in this work exhibited feeding-deterrent activity against the generalist Antarctic predator *Odontaster validus.*

The soft coral *A. grandis* was collected in the Weddell Sea (Antarctica), during the Austral Summer of 2003−2004. The biological material was frozen at −20 °C and transferred to the laboratory in Spain, where it was later extracted with acetone. In a further Antarctic campaign in January 2006, the Et_2O-soluble portion of the acetone extract was tested in a repellency assay against *O. validus*, and it displayed significant activity. Subsequently, a portion of the extract (365 mg) was transferred to our laboratory in Italy and submitted to chemical investigation. TLC analysis of the extract showed the presence of a series of spots at R_f 0.35−0.75 (light petroleum ether/Et_2O, 8:2). The extract was then submitted to purification steps including molecular exclusion, silica gel, and reversed-phase chromatography (see Experimental Section) to give pure compounds **2** (1.3 mg), **3** (0.5 mg), **4** (0.6 mg), **5** (1.2 mg), **6** (1.3 mg), **7** (2.8 mg), **8** (0.7 mg), **9** (0.5 mg), and **10** (1.0 mg).

Preliminary ^{1}H NMR analysis of the new compounds showed their close structural relationship, in particular indicating that they exhibited the same illudalane aromatic carbon skeleton as that reported for the alcyopterosins (i.e., alcyopterosin D,[4] **1**). Four groups of molecules could be recognized: compounds **2**, **4**, and **6**, exhibiting oxygen functional groups at both C-4 and C-12; compounds **3**, **5**, and **9**, bearing chlorine at C-4 and oxygen functions at both C-13 and C-12; compounds **7** and **8**, with a chlorine at C-4 and an oxygenated group at C-12; and compound **10**, displaying an unusual tricyclic arrangement. The structure elucidations are reported starting from the main metabolite **7**. Other alcyopterosins are described subsequently according to the above functionalization groupings.



Compound **7** exhibited the molecular formula $C_{17}H_{23}O_2Cl$ as deduced by HRESIMS on the sodiated molecular peak at 317.1286 (M + Na). The ^{1}H NMR spectrum appeared to be very simple and displayed three singlet signals at δ_H 1.14 (6H), 2.08 (3H), and 2.33 (3H), which were attributed to two tertiary methyls (H_3-14 and H_3-15), an acetyl group, and an aromatic methyl (H_3-13), respectively. Five methylene signals at δ_H 2.69 (2H, s, H_2-10), 2.74 (2H, s, H_2-1), 3.15 (2H, t, J = 9 Hz, H_2-5), 3.57 (2H, t, J = 9 Hz, H_2-4), and 5.12 (2H, s, H_2-12) and a single aromatic methine at δ_H 7.01 (1H, s, H-8) completed the spectrum. These data were consistent with the alcyopterosin carbon skeleton containing chlorine and acetyl functional groups. The ^{13}C NMR spectrum displayed signals attributable to six sp^2 aromatic carbons (one CH and five quaternary

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Table 1. ^{1}H NMR Data[a] (400 and 600 MHz, $CDCl_3$) of Compounds **7**, **8**, and **10**

	7	**8**	**10**
position	δ_H (J in Hz)	δ_H (J in Hz)	δ_H (J in Hz)
1	2.74, s	2.74, s	5.28, s
4	3.57, t (9)	3.57, t (9)	3.80, m
5	3.15, t (9)	3.15, t (9)	3.54, m
			3.28, m
8	7.01, s	7.26, s	7.15, s
10	2.69, s	2.69, s	2.48, d (15)
			3.30, m
12	5.12, s	5.13, s	
13	2.33, s	2.42, s	2.42, s
14	1.14, s	1.14, s	1.45, s
15	1.14, s	1.14, s	0.44, s
2′	2.08, s	2.30, m	
3′		1.62, m	
4′		0.94, t (7)	

[a] Assignments made by ^{1}H−^{1}H COSY, HSQC, and HMBC (J = 10 Hz) experiments.

Table 2. ^{13}C NMR Data[a] (300 MHz, $CDCl_3$) of Compounds **2**−**10**

	2	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
position	δ_C	δ_C	δ_C	δ_C	δ_C	δ_C	δ_C	δ_C	δ_C
1	46.5	46.6	46.4	47.1	46.5	46.4	46.4	47.7	87.9
2	142.3	142.4	142.4	143.4	142.4	141.9	142.5	143.4	139.9
3	135.5	133.5	135.5	134.6	135.6	134.3	134.6	137.1	n.d.
4	63.7	44.0	63.9	44.0	63.7	43.2	44.5	44.8	44.7
5	28.6	32.6	29.7	32.6	28.6	33.2	31.6	32.1	30.4
6	132.8	134.3	132.8	135.2	132.9	133.1	133.3	n.d.	133.7
7	130.4	130.9	130.3	131.1	130.3	130.3	130.5	134.2	n.d.
8	127.9	127.9	127.7	127.8	127.7	127.7	127.7	125.9	132.0
9	142.3	145.6	142.4	145.6	142.4	142.5	142.5	142.9	139.4
10	47.7	47.6	47.6	46.7	47.7	47.6	47.7	46.5	49.1
11	39.7	39.8	39.7	40.4	39.7	40.3	39.7	39.6	54.9
12	61.9	65.1	62.1	65.1	62.1	62.1	61.9	64.0	161.7
13	20.0	61.7	20.0	61.5	21.0	20.9	21.4	60.2	19.3
14	28.9	28.9	29.0	28.9	29.0	28.9	28.9	29.0	26.4
15	28.9	28.9	29.0	28.9	29.0	28.9	28.9	29.0	18.7
1′	173.3	170.6	170.6	171.1	170.2	170.8	173.6		
2′	36.2	21.0	21.0	21.1	22.3	19.8	36.2		
3′	18.4						18.1		
4′	13.6						13.4		
1″	173.1	171.1	170.9	173.5	172.7				
2″	36.2	21.0	21.0	36.1	36.2				
3″	18.4			18.4	18.4				
4″	13.6			13.7	13.7				

[a] Assignments made by HSQC and HMBC (J = 10 Hz) experiments.

C) and nine sp^3 carbons (three CH_3, two of which resonated at the same value, five CH_2, one CH, and one quaternary C) along with the signals at δ_C 170.8 (CO) and 19.8 (CH_3) due to the carbons of the acetyl function. Comparison of ^{1}H and ^{13}C NMR spectra of compound **7** with literature data[4] clearly indicated that **7** was the acetyl derivative of alcyopterosin D (**1**). Analysis of 2D-NMR experiments (^{1}H−^{1}H COSY, HSQC, and HMBC) of 12-acetylalcyopterosin D (**7**) allowed complete proton and carbon assignments as reported in Tables 1 and 2.

The molecular formula of compound **8** ($C_{19}H_{27}O_2Cl$) exhibited 28 additional mass units (C_2H_4) with respect to compound **7**. NMR data of **8** were substantially similar to those of **7** (Tables 1 and 2) and suggested that the unique difference between the two metabolites was in the nature of the acyl residue at C-12. Analysis of the ^{1}H−^{1}H COSY spectrum of compound **8** indicated that an *n*-butanoyl group was present rather than the acetyl group present in **7**. NMR analysis of 12-*n*-butanoylalcyopterosin D (**8**) led to the proton and carbon assignments listed in Tables 1 and 2.

Analysis of the ^{1}H and ^{13}C NMR spectra of **2**, molecular formula $C_{23}H_{34}O_4$, revealed the absence of chlorine and the presence of four additional carbon and two oxygen atoms with respect to compound **8**. Compound **2** contained an acyloxy group linked to C-4 [δ_H 4.15 (t, J = 8 Hz); δ_C 63.7] in the place of the chlorine substituent. The ^{1}H−^{1}H COSY spectrum of **2** clearly indicated the presence of two equivalent spin systems consistent with two *n*-butanoyl moieties esterified to 4-OH and 12-OH. This structural hypothesis was confirmed by analysis of HSQC and HMBC experiments, which also led us to assign all carbon and proton resonances (Tables 2 and 3). Compound **2** was the 4,12-bis-*n*-butanoyl derivative of the previously reported alcyopterosin O (**11**).[4]

Table 3. ^{1}H NMR Data[a] (400 and 600 MHz, $CDCl_3$) of Compounds **2**, **4**, and **6**

	2	**4**	**6**
position	δ_H (J in Hz)	δ_H (J in Hz)	δ_H (J in Hz)
1	2.73, s	2.74, s	2.74, s
4	4.15, t (8)	4.15, t (8)	4.15, m
5	3.03, t (8)	3.03, t (8)	3.02, m
8	7.01, s	7.01, s	7.01, s
10	2.69, s	2.69, s	2.69, s
12	5.15, s	5.15, s	5.15, s
13	2.35, s	2.35, s	2.36, s
14	1.13, s	1.14, s	1.14, s
15	1.13, s	1.14, s	1.14, s
2′	2.29, m	2.06,[c] s	2.06, s
3′	1.64, m	2.07,[c] s	
4′	0.93,[b] t (7)		
2″	2.29, m		2.35, m
3″	1.64, m		1.67, m
4″	0.94,[b] t (7)		0.94, t (7)

[a] Assignments made by ^{1}H−^{1}H COSY, HSQC, and HMBC (J = 10 Hz) experiments. [b,c] Values with the same superscript may be interchanged.

Compound **4** had the molecular formula $C_{19}H_{26}O_4$, and spectroscopic data were similar to those of compound **2**. Two acetyl signals (δ_H 2.06 and 2.07) in the proton spectrum of **4** replaced signals due to the *n*-butanoyl moieties in the ^{1}H NMR spectrum of **2**, clearly indicating that the difference between **4** and **2** was in the nature of the acids esterified to the hydroxy groups at C-4 and C-12. In particular, compound **4** was the 4,12-bis-acetyl derivative of alcyopterosin O.[4] The ^{1}H and ^{13}C NMR data of **4** were in agreement with the proposed structure. All resonances were assigned as reported in Tables 2 and 3 by 2D NMR experiments.

Analysis of the spectroscopic data of compound **6**, $C_{21}H_{30}O_4$ by the HRESIMS, revealed structural features similar to those of compounds **2** and **4**. But, in this case, both an acetyl group and an *n*-butanoyl group were present in the molecule, as indicated by a singlet at δ_H 5.15 and a multiplet at δ_H 4.15 in the ^{1}H NMR spectrum. Thus the hydroxy groups at C-4 and C-12 were esterified by these acids. The positions of the acid residues were evident from analysis of the HMBC spectrum of **6**. Diagnostic long-range correlations were observed between C-1′ (δ_C 170.2) and both H_3-2′ (δ_H 2.06) and H_2-12 (δ_H 5.15) as well as between C-1″ (δ_C 172.7) and both H_2-3″ (δ_H 1.67) and H_2-4 (δ_H 4.15), inferring the indicated substitution pattern. Thus, compound **6** was 12-acetyl-4-*n*-butanoylalcyopterosin O. NMR assignments are reported in Tables 2 and 3.

The ^{1}H NMR spectrum of **3**, which had the molecular formula $C_{19}H_{25}O_4Cl$, showed some similarities to that of acetylalcyopterosin D (**7**), only differing in the presence of two signals at δ_H 5.14 (2H, s, H_2-13) and δ_H 2.10 (3H, s, −OAc) rather than the aromatic methyl singlet at δ_H 2.33 of compound **7**. Analysis of the HMBC spectrum confirmed this suggestion, as significant long-range correlations were observed between the two oxymethylenes at δ_H 5.13 and 5.14 and carbonyl carbons at δ_C 170.6 and 171.1, respectively. All proton and carbon assignments of 13-acetoxy-12-acetylalcyopterosin D (**3**) were made by 2D NMR experiments (Tables 2 and 4).

Compound **5** had the molecular formula $C_{21}H_{29}O_4Cl$ and was structurally related to compound **3**. Analysis of the NMR spectra (Tables 2 and 4) revealed that **5** differed from **3** only in the nature of the ester attached to C-13. An *n*-butanoyl moiety was present in

Table 4. ^{1}H NMR Data[a] (400 and 600 MHz, $CDCl_3$) of Compounds **3**, **5**, and **9**

	3	**5**	**9**
position	δ_H (J in Hz)	δ_H (J in Hz)	δ_H (J in Hz)
1	2.73, s	2.73, s	2.73, s
4	3.63, t (9)	3.62, t (8)	3.76, t (8)
5	3.20, t (9)	3.20, t (8)	3.30, t (8)
8	7.20, s	7.19, s	7.19, s
10	2.77, s	2.77, s	2.82, s
12	5.13, s	5.13, s	4.69,[c] s
13	5.14, s	5.14, s	4.71,[c] s
14	1.15, s	1.14, s	1.16, s
15	1.15, s	1.14, s	1.16, s
2′	2.08,[b] s	2.10, s	
2″	2.10,[b] s	2.31, t (7)	
3″		1.66, app. sext (7)	
4″		0.94, t (7)	

[a] Assignments made by ^{1}H−^{1}H COSY, HSQC, and HMBC (J = 10 Hz) experiments. [b,c] Values with the same superscript may be interchanged.

the molecule, as indicated by the typical multiplets at δ_H 2.31 (2H, t, J = 7 Hz, H_2-2″), 1.66 (2H, app. sext, J = 7 Hz, H_2-3″), and 0.94 (3H, t, J = 7 Hz, H_3-4″) in the ^{1}H NMR spectrum. Compound **5** was thus 12-acetyl-13-*n*-butanoxyalcyopterosin D.

The spectroscopic data of compound **9** ($C_{15}H_{21}O_2Cl$) indicated that it was a diol related to both **3** and **6**. The ^{1}H NMR spectrum of **9** lacked the two acetyl signals present in the spectrum of **3** and displayed two singlets due to the isolated methylenes H_2-12 and H_2-13 at high field shifted values (δ_H 4.69 and 4.71) with respect to the corresponding signals in **3** (δ_H 5.13 and 5.14). The proposed structure was confirmed by comparing a synthetic sample obtained by acetylation of **9** with compound **3**. The proton and carbon assignments of 13-hydroxyalcyopterosin D (**9**) are reported in Tables 2 and 4.

Compound **10** had the molecular formula $C_{15}H_{17}O_2Cl$, implying seven unsaturation degrees. The ^{1}H and ^{13}C NMR spectra of **10**, named alcyopterosin P, revealed a structural arrangement different from those of the other co-occurring alcyopterosins. According to the molecular formula, the presence of a lactone moiety fused to the bicyclic alcyopterosin framework was strongly suggested by both a carboxyl signal at δ_C 161.7 in the ^{13}C NMR spectrum and the strong IR band at 1765 cm^{-1}. The ^{1}H NMR spectrum lacked two methylene signals attributed to H_2-1 and H_2-12 of the alcyopterosin skeleton, displaying in their place a methine singlet at δ_H 5.28 (s, H-1), which was correlated in the HMBC spectrum to the carboxyl carbon at δ_C 161.7. These data suggested the location of the carboxyl at C-12, and subsequently the lactone moiety had to involve C-1, C-2, and C-3. The remaining part of the molecule was the same as alcyopterosins **7** and **8** (see Tables 1 and 2 for NMR assignments).

The absolute configuration at C-1 was determined by applying the modified Mosher method[10,11] on the methyl ester derivative **12**, obtained from **10** by methanolysis and subsequent opening of the lactone ring. Treatment of compound **12** with (*R*)- and (*S*)-MTPA chlorides in dry CH_2Cl_2 and DMAP afforded the corresponding (*S*)-MTPA (**12a**) and (*R*)-MTPA (**12b**) esters, respectively. The two Mosher derivatives were characterized by 2D-NMR experiments (^{1}H−^{1}H COSY, HSQC, HMBC), and some selected ^{1}H NMR data and $\Delta\delta$ ($\delta_S - \delta_R$) are reported in the Experimental Section. The $\Delta\delta$ values observed for the signals of protons close to the hydroxyl group at C-1 indicated the *S* configuration as depicted in formula **12**, and the same configuration was assigned to C-1 of the corresponding lactone, alcyopterosin P (**10**).

The occurrence of sesquiterpenes of the alcyopterosin series in the Antarctic soft coral *A. grandis* is in agreement with the chemical data reported for the sub-Antarctic species *A. paessleri*.[4] This secondary metabolite pattern seems to be a distinctive character for both species, suggesting a close taxonomic relationship. Alcyopterosins have not been reported so far from other soft corals or from any other marine organisms. The extract containing alcyopterosins was active in a repellency assay on *O. validus*.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO DIP 370 digital polarimeter. The UV spectra and CD curves were recorded on a Agilent 8453 spectrophotometer and a JASCO 710 spectropolarimeter, respectively. The IR spectra were taken on a Bio-Rad FTS 155 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on DRX 600, Avance 400, and DPX 300 MHz Bruker spectrometers in $CDCl_3$, with chemical shifts reported in ppm referred to $CHCl_3$ as internal standard (δ 7.26 for proton and δ 77.0 for carbon). ESIMS and HRESIMS were measured on a Micromass Q-TOF Micro spectrometer coupled with a HPLC Waters Alliance 2695. The instrument was calibrated by using a PEG mixture from 200 to 1000 MW. Silica gel chromatography was performed using precoated Merck F_{254} plates and Merck Kieselgel 60 powder. HPLC purification was carried out on a Shimadzu LC-10AD liquid chromatograph equipped with a UV SPD-10A wavelength detector.

Collection and Extraction of the Animal Material. Specimens of *A. grandis* were collected in the Western Weddell Sea (Antarctica) at 597.6 m depth during the ANT XXI/2 cruise of *R/V Polarstern* (AWI; Bremerhaven, Germany), from November 2003 to January 2004, using a bottom trawl. The biological material was immediately frozen at −20 °C and then transferred to the laboratory in Spain. Subsequently the sample was extracted with acetone (25 mL × 3). The organic solvent was removed under reduced pressure, and the residual water was partitioned with Et_2O and subsequently with *n*-butanol. An aliquot of the Et_2O extract (16.7 mg) was used for the ecological tests. The remaining part (365 mg) was transferred to ICB in Naples (Italy) and chemically analyzed. A voucher specimen was fixed in 10% formalin for taxonomical determination, and it is stored at Dept. of Animal Biology (Invertebrates), University of Barcelona (sample code #1152).

Purification of Compounds 2−10. An aliquot (183 mg) of the Et_2O extract of *A. grandis* was fractionated on Sephadex LH-20 chromatography using a mixture of $CHCl_3$/MeOH (1:1) as eluent to yield three fractions: A (18.7 mg), B (5.3 mg), and C (17.4 mg). Fraction A was chromatographed on a silica gel column (light petroleum ether/Et_2O gradient), affording pure compounds **2** (1.3 mg), **3** (0.5 mg), and **4** (0.6 mg) and a mixture, which was separated on preparative TLC (SiO_2, C_6H_6/light petroleum ether, 8:2) to give compounds **5** (1.2 mg) and **6** (1.3 mg). Fraction B was submitted to preparative TLC (SiO_2, light petroleum ether/Et_2O, 9:1) to give pure **7** (2.8 mg) and a mixture (3.0 mg), which was further purified by preparative TLC (SiO_2, C_6H_6/light petroleum ether, 8:2) to yield compound **8** (0.7 mg). Fraction C was subjected to reversed-phase HPLC using a Supelco Discovery C18 column (25 cm × 10 mm, particle size = 5 μm) eluted with a 20 min gradient from 80 to 100% CH_3OH in H_2O (flow rate 2 mL/min) to give pure compounds **9** (0.5 mg) and **10** (1.0 mg).

4,12-Bis-*n*-butanoylalcyopterosin O (2): colorless oil; UV (CH_2Cl_2) λ_{max} (log ϵ) 226 (3.57) nm; IR (liquid film) ν_{max} 2929, 1745, 1173 cm^{-1}; ^{1}H and ^{13}C NMR in Tables 3 and 2; HRESIMS *m/z* 397.2298 (calcd for $C_{23}H_{34}O_4Na$, 397.2355).

13-Acetoxy-12-acetylalcyopterosin D (3): colorless oil; UV (CH_2Cl_2) λ_{max} (log ϵ) 228 (4.07), 233 (3.56) nm; IR (liquid film) ν_{max} 1752, 1246, 1019 cm^{-1}; ^{1}H and ^{13}C NMR in Tables 4 and 2; HRESIMS *m/z* 375.1338 (calcd for $C_{19}H_{25}O_4ClNa$, 375.1339).

4,12-Bis(acetyl)alcyopterosin O (4): colorless oil; UV (CH_2Cl_2) λ_{max} (log ϵ) 227 (3.64) nm; IR (liquid film) ν_{max} 2935, 1768 cm^{-1}; ^{1}H and ^{13}C NMR in Tables 3 and 2; HRESIMS *m/z* 341.1718 (calcd for $C_{19}H_{26}O_4Na$, 341.1729).

12-Acetyl-13-*n*-butanoxyalcyopterosin D (5): colorless oil; UV (CH_2Cl_2) λ_{max} (log ϵ) 227 (4.12) nm; IR (liquid film) ν_{max} 2956, 1738, 1227 cm^{-1}; ^{1}H and ^{13}C NMR in Tables 4 and 2; HRESIMS *m/z* 403.1645 (calcd for $C_{21}H_{29}O_4ClNa$, 403.1652).

12-Acetyl-4-*n*-butanoylalcyopterosin O (6): colorless oil; UV (CH_2Cl_2) λ_{max} (log ϵ) 227 (4.34) nm; IR (liquid film) ν_{max} 2923, 1739, 1237 cm^{-1}; ^{1}H and ^{13}C NMR in Tables 3 and 2; HRESIMS *m/z* 369.2038 (calcd for $C_{21}H_{30}O_4Na$, 369.2042).

12-Acetylalcyopterosin D (7): colorless oil; UV (CH_2Cl_2) λ_{max} (log ϵ) 226 (3.57) nm; IR (liquid film) ν_{max} 1739, 1224, 1024 cm^{-1}; ^{1}H and ^{13}C NMR in Tables 1 and 2; HRESIMS *m/z* 317.1286 (calcd for $C_{17}H_{23}O_2ClNa$, 317.1284).

12-*n*-Butanoylalcyopterosin D (8): colorless oil; UV CH_2Cl_2) λ_{max} (log ϵ) 226 (3.36) nm; IR (liquid film) ν_{max} 2969, 1738, 1227 cm^{-1}; ^1H and ^{13}C NMR in Tables 1 and 2; HRESIMS *m*/*z* 345.1581 (calcd for $C_{19}H_{27}O_2ClNa$, 345.1567).

13-Hydroxyalcyopterosin D (9): colorless oil; UV (CH_2Cl_2) λ_{max} (log ϵ) 227 (3.69) nm; IR (liquid film) ν_{max} 2935, 1229 cm^{-1}; ^1H and ^{13}C NMR in Tables 4 and 2; HRESIMS *m*/*z* 291.1128 (calcd for $C_{15}H_{21}O_2ClNa$, 291.1128).

Alcyopterosin P (10): colorless oil; $[\alpha]_D$ −822.9 (*c* 0.07, $CHCl_3$); UV (CH_2Cl_2) λ_{max} (log ϵ) 227 (3.72) nm; IR (liquid film) ν_{max} 2929, 1765, 1073 cm^{-1}; ^1H and ^{13}C NMR in Tables 1 and 2; HRESIMS *m*/*z* 287.0790 (calcd for $C_{15}H_{17}O_2ClNa$, 287.0815).

Acetylation of 9. 13-Hydroxyalcyopterosin D (**9**, 0.5 mg) was dissolved in dry C_5H_5N (0.5 mL) and treated with Ac_2O (two drops) at room temperature for 8 h. After evaporation, the residue was filtered on a Pasteur pipet-SiO_2 column (light petroleum ether/Et_2O) to give the diacetyl derivative **3** (0.5 mg).

Methanolysis of 10. Alcyopterosin P (**10**, 1.0 mg) was dissolved in anhydrous MeOH (1 mL), and an excess of Na_2CO_3 was added. The solution was stirred at room temperature for 4 h and filtered, and the solvent evaporated. The crude product was purified on a Pasteur column (light petroleum ether/Et_2O), affording 0.8 mg of pure **12**: $[\alpha]_D$ −18.9 (*c* 0.08, $CHCl_3$); ^1H NMR ($CDCl_3$) δ_H 7.14 (1H, s, H-8), 4.57 (1H, s, H-1), 3.97 (3H, s, −OMe), 3.52 (2H, m, H_2-4), 3.18 (2H, m, H_2-5), 2.90 (1H, d, J = 16 Hz, H-10a), 2.54 (1H, d, J = 16 Hz, H-10b), 2.37 (3H, s, H_3-13), 1.18 (3H, s, H_3-15), 1.02 (3H, s, H_3-14); ESIMS $(M + Na)^+$ *m*/*z* 319.

Preparation of MTPA Esters. (*R*)- and (*S*)-MTPA-Cl (10 μL) and a catalytic amount of DMAP were separately added to two different aliquots of the alcohol **12** (1.0 mg each) in dry CH_2Cl_2 (0.5 mL), and the resulting mixtures were allowed to stand at room temperature for 12 h. After the usual workup the reaction mixtures were purified on preparative TLC (SiO_2, light petroleum ether/Et_2O, 7:3), affording pure (*S*)- and (*R*)-MTPA esters of **12**, respectively.

(*S*)-MTPA ester (12a): selected ^1H NMR values ($CDCl_3$) δ_H 7.17 (1H, s, H-8), 6.22 (1H, s, H-1), 3.80 (3H, s, −OMe), 3.65 (2H, m, H_2-4), 3.56 [(3H, s, −OMe (MTPA)], 3.22 (2H, m, H_2-5), 2.90 (1H, d, J = 16 Hz, H-10a), 2.48 (1H, d, J = 16 Hz, H-10b), 2.40 (3H, s, H_3-13), 1.02 (3H, s, H_3-15), 0.95 (3H, s, H_3-14).

(*R*)-MTPA ester (12b): selected ^1H NMR values ($CDCl_3$) δ_H 7.14 (1H, s, H-8), 6.19 (1H, s, H-1), 3.84 (3H, s, -OMe), 3.58 (2H, m, H_2-4), 3.36 [3H, s, -OMe (MTPA)], 3.14 (m, 2H, H_2-5), 2.92 (1H, d, J = 16 Hz, 1H, H-10a), 2.53 (1H, d, J = 16 Hz, 1H, H-10b), 2.38 (3H, s, H_3-13), 1.15 (3H, s, H_3-15), 1.07 (3H, s, H_3-14).

Biological Assays. Individuals of the Antarctic omnivorous predator the sea star *Odontaster validus* were collected in the South Shetland Islands (Livingston and Deception Is.) on board the *B/O Hespérides* during January 2006 for feeding−repellence assays. Experiments took place at the Spanish Base "Gabriel de Castilla" in Deception Island, Antarctica, during the same period. Dry Et_2O extracts from specimens of *A. grandis* were diluted in solvent (Et_2O) and coated into shrimp pieces. These shrimp pieces were then presented to the sea stars. Natural concentration (as that obtained from the soft coral) was used for the tests. After 24 h the number of shrimp pieces eaten out of a total of 10 pieces was compared in treatment versus control experiments. The tests were carried out following the detailed methodology reported in previous works.[12,13]

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Supporting Information Available: ^1H, ^{13}C NMR and HMBC spectra of compounds **2**−**10** are available free of charge via the Internet at http://pubs.acs.org.

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