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ARTICLE *in* JOURNAL OF NATURAL PRODUCTS · JANUARY 1998

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Unusual Polyoxygenated Monoterpenes from the Antarctic Alga *Pantoneura plocamioides*

Mercedes Cueto,[†] José Darias,*[,†] Juana Rovirosa,[‡] and Aurelio San Martin[‡]

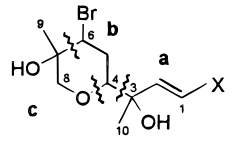
Instituto de Productos Naturales y Agrobiología del CSIC, Avda. Astrofísico F. Sánchez 3, Apdo 195, 38206 La Laguna, Tenerife, Spain, and Dpto. Química, Facultad de Ciencias, Universidad de Chile, Santiago de Chile, Chile

Received December 1, 1995[⊗]

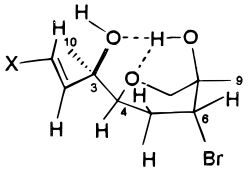
Six new polyoxygenated marine monoterpenes have been isolated from the Antarctic alga *Pantoneura plocamioides*. The structure and relative stereochemistry of these compounds, denominated pantopyranoids A−C (**1**−**3**), and pantoisofuranoids A−C (**4**−**6**) were determined on basis of spectroscopic evidence.

Marine monoterpenes are typical compounds from algae of the Plocamiaceae and Rhizophyllidaceae families (order Gigartinales).[1] Unlike terrestrial monoterpenes that usually include oxygen functionalities, an exceptional aspect of marine monoterpenes is their high degree of halogen substitutions. However, in this first chemical study of *Pantoneura plocamioides* (Delessereaceae, order Ceramiales, a red alga of polar habitat), the alga was found to have an abundance of oxygen-rich monoterpenes from which we have isolated six unusual new monoterpene diols containing an oxane ring.

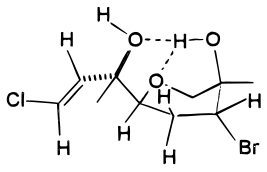
From the chromatographic extract of the algae collected off of King George Island (South Shetland, Antarctic) by scuba, pantopyranoids A−C (**1**−**3**) and pantoisofuranoids A−C (**4**−**6**) were isolated and their structures and relative stereochemistry were determined.



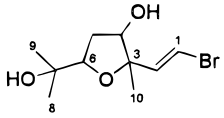
Pantopyranoid A (1) X=Br
Pantopyranoids B-C (2-3) X=Cl



Pantopyranoid A (1) X=Br
Pantopyranoid C (3) X=Cl



Pantopyranoid B (2)



Pantoisofuranoids A-C (4-6)

Results and Discussion

Pantopyranoid A (**1**) was isolated as a colorless oil, $[\alpha]^{25}_D$ −93 (*c* 0.45, $CHCl_3$). The EIMS spectrum showed the molecular ion at *m*/*z* 342/344/346, with relative intensities suggestive of two bromine atoms. The molecular ion (as $[M^+ + 1]$) was confirmed by CIMS and corresponds to the empirical formula $C_{10}H_{16}Br_2O_3$ (HREIMS), implying a monoterpene origin for **1**. The IR spectrum gave absorptions for a hydroxyl group and a double bond (3585 and 1618 cm^{-1}, respectively).

The ^{13}C-NMR spectrum of **1** (Table 1) showed nine signals corresponding to 10 carbons (two carbons have the same chemical shift). Multiplicities of the carbons signals were determined from the DEPT spectrum: two methyls, two methylenes (one bearing oxygen), four methines (two olefinic; one bearing oxygen and the other bromine), and two oxygenated quaternary carbons. The ^{1}H-NMR spectrum (Table 1) showed signals for a trans-disubstituted olefin [δ 6.54 ppm (1H, d, J = 13.4 Hz) and 6.26 (1H, d, J = 13.4 Hz)] and two methines each geminal to a heteroatom [δ 4.69 ppm (1H, dd, J = 1.6, 11.1 Hz) and 4.35 (1H, dd, J = 1.8, 11.2 Hz)]. The protons of one methylene group appeared at δ 2.70 (1H, ddd, J = 1.6, 11.2, 15.7 Hz) and 2.33 ppm (1H, ddd, J = 1.8, 11.1, 15.6 Hz), while two doublets, corresponding to the protons of the methylene geminal to oxygen, appeared at δ 4.02 (1H, d, J = 12.4 Hz) and 3.81 ppm (1H, d, J = 12.4 Hz). The presence of just two methyl groups suggested that the third methyl group, corresponding to a monoterpene skeleton, was oxidized.

Chemical shift arguments and ^{1}H−^{1}H COSY correlations supported by MS data allowed the assignments of fragments **a**−**c** as indicated (**1**). The differentiated chemical shift as well as the values of the respective coupling constants of the methine and methylene protons suggested that the fragments should form part of a ring. This, along with the olefinic unsaturation, is in keeping with the 2 degrees of unsaturation required by the molecular formula. The disubstituted nature of the olefinic carbon atoms as well as the carbinolic moiety of fragment **a** suggested by the ^{1}H- and ^{13}C-NMR data are in agreement with the EIMS spectrum. Both CIMS and EIMS showed an ion at *m*/*z* 149/151 characteristic of fragment **a**. This fragment has been postulated in other acyclic monoterpenes isolated[2] from *Plocamium* species.

* To whom correspondence should be addressed. Phone: 34 22 256847. FAX: 34 22 260135.
[†] Instituto de Productos Naturales y Agrobiología del CSIC.
[‡] Universidad de Chile.
[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1997.

S0163-3864(96)00116-4 CCC: $15.00
Published on Web 01/23/1998

Table 1. ^{1}H- (H^a: $CHCl_3$-*d*, H^b: C_6H_6-d_6) and ^{13}C-NMR (C^a: $CHCl_3$-*d*) Data of Compounds **1**−**6**, and HMBC of Compounds **1** and **4** (400 MHz, δ ppm, (*J*) Hz)

	1			**2**		**3**	
no.	H^a	C^a	HMBC	H^a	C^a	H^a	C^a
1	6.54 d (13.4)	108.75	C2, C3	6.40 d (14.0)	120.78	6.41 d (13.2)	120.87
2	6.26 d (13.4)	139.30	C1, C3	6.12 d (14.0)	136.20	5.98 d (13.2)	134.96
3		76.32			75.88		no obs.
4	4.35 dd (1.8, 11.2)	64.96	C6, C5	4.30 dd (2.0, 11.2)	64.17	4.31 dd (1.4, 11.2)	64.93
5	α: 2.70 ddd (1.6, 11.2, 15.7)	38.37	C4	α: 2.60 ddd (1.7, 11.0, 15.6)	37.38	α: 2.69 ddd (1.6, 11.3, 15.6)	37.98
	β: 2.33 ddd (1.8, 11.1, 15.6)		C6	*β*: 2.38 ddd (2.0, 11.0, 15.6)		*β*: 2.32 ddd (2.0, 11.2, 15.6)	
6	4.69 dd (1.6, 11.1)	57.93	C9, C5, C4, C7	4.66 dd (2.0, 12.0)	57.48	4.65 dd (1.7, 11.3)	57.54
7		76.32			75.88		no obs.
8	α: 4.02 d (12.4)	70.95	C6,C3	α: 4.02 d (12.0)	70.52	α: 4.01 d (12.6)	70.54
	β: 3.81 d (12.4)			*β*: 3.82 d (12.0)		*β*: 3.80 d (12.4)	
9	1.62 (s)	22.13	C6, C8, C7	1.63 (s)	21.80	1.61 s	21.74
10	1.51 (s)	27.88	C4, C1, C3	1.52 (s)	26.00	1.51 s	27.74

	4				**5**			**6**		
no.	H^a	H^b	C^a	HMBC	H^a	H^b	C^a	H^b	H^b	C^a
1	6.31 d (13.6)	6.22 d (13.4)	105.85	C2, C3	6.47 d (13.6)	6.39 d (13.5)	107.56	6.41 d (13.6)	6.40 s	106.83
2	6.17 d (13.6)	5.98 d (13.4)	141.33	C1	6.32 d (13.6)	6.22 d (13.5)	137.86	6.37 d (13.6)	6.40 s	138.90
3			88.33				86.76			87.90
4	3.84 m	3.57 d (5.2)	75.41	C3, C6	4.05 m	3.75 dd (6.7, 8.4)	78.18	3.93−3.89 m	3.54 dd (2.0, 5.0)	76.64
5	α: 2.30 m	α: 1.69 dd (3.2, 13.8)	34.73		α: 2.15 m	α: 1.47 ddd (3.9, 6.7, 12.8)	34.43	α: 2.41 ddd (5.5, 9.2, 14.2)	1.75 m	34.95
	β: 1.94 dd (3.1, 14.0)	*β*: 1.77 ddd (5.2, 9.3, 13.8)			*β*: 1.85 m	*β*: 1.88 ddd (6.0, 8.4, 12.8)		*β*: 2.00 ddd (1.0, 3.7, 14.3)	1.75 m	
6	3.84 m	3.32 dd (3.3, 9.4)	83.66		4.05 m	3.47 m	84.30	3.93−3.89 m	3.37 dd (4.8, 8.5)	83.20
7			71.66				70.51			71.92
8	1.17 s	1.09 s	26.40	C6, C7, C9	1.12 s	0.91 s	26.01	1.16 s	0.78 s	26.31
9	1.34 s	0.78 s	27.63	C6, C7, C8	1.26 s	0.96 s	27.41	1.22 s	0.78 s	27.62
10	1.37 s	1.32 s	20.99	C2, C3, C4	1.30 s	1.15 s	24.25	1.35 s	1.05 s	23.95

HMQC and HMBC data were used to confirm the fragments **a**−**c** and establish the connectivity between them. The linkage C-3/C-4 was established by the correlation between C-4 and Me-10, C-6/C-7 was established by the correlation C-6 and Me-9 and also C-6 and H-8. The correlation of the quaternary carbon atoms (δ 76.32 ppm) with the olefinic protons (δ 6.26 and δ 6.54 ppm) and with the methyl groups (δ 1.62 and δ 1.51 ppm) delineated the two quaternary carbon atoms C-3 and C-7, while fragment **c** was internally confirmed by the correlation of C-8 with Me-9. The correlation H-8 and C-6 confirms the linkage of the fragments **c/a**.

Pantopyranoids B (**2**) and C (**3**) have a retention times (HPLC) very close to that of pantopyranoid A (**1**). In the CIMS spectra of (**2**) and (**3**) molecular ions [M^+ + 1] were observed at *m*/*z* 299/301/303 with relative intensities suggestive for chlorine and a bromine. EIMS gave the empirical formula $C_{10}H_{16}BrClO_3$ for each and showed a base peak at *m*/*z* 105/107. This suggested that in pantopyranoids B (**2**) and C (**3**) the vinyl halogen substituent is chlorine (fragment **a** in **2** and **3**).

The NMR data for pantopyranoids B (**2**) and C (**3**) are practically superimposable on that for pantopyranoid A (**1**) (Table 1). The most significant difference was the carbon chemical shift of an olefinic resonance. This was observed at δ 108.75 ppm in pantopyranoid A (**1**) but appeared at δ 120.78 and 120.87 ppm in pantopyranoids B (**2**) and C (**3**). This variation in the chemical shift can be rationalized[3] by the substitution of the bromine by a chlorine atom in pantopyranoids B (**2**) and C (**3**). The spectroscopic similarity between pantopyranoids A (**1**), B (**2**), and C (**3**) suggests that the three compounds are isomeric, chlorine being the vinyl substituent in **2** and **3** and bromine in **1**.

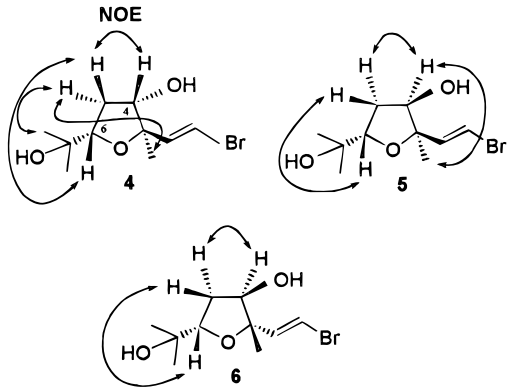
The relative stereochemistry of the chiral centers of the ring was determined by a study of the coupling constants and 2D ROESY experiments. In 2D ROESY ($CDCl_3$) experiments the H-4 and H-6 protons gave a NOE with different protons of the C-5 methylene, indicating that H-4 and H-6 are trans, establishing a relative trans stereochemistry for the lateral side chain and the bromine atom. On the other hand, the C-9 methyl group and H-4 showed a NOE with the same proton of the C-5 methylene, suggesting that H-4 and C-9 methyl have the same stereochemistry.

To provide an interpretation of the observed high *J* value (over 11 Hz) for the coupling of the respective H-4 with H-5α and H-6 with H-5*β* in all three compounds, the geometry of compounds **1**−**3** was investigated by performing molecular mechanics calculations using PCMODEL.[4] The forcefield MMX was employed, and the molecules were optimized within the unrestricted Hartree−Fock (UHF) formalism performing a full self-consistent-field (SCF) process. In each of the boat conformations drawn for pantopyranoids A−C, the dihedral angle H-4−C-4−C-5−H-5α was fixed at 0 degrees, and then the structures were minimized. After minimization the resulting conformations 1−3 showed H-bond interactions of the C-7−OH proton with both the C-3 and ring oxygens. The coupling constants for H-4 and H-6 measured by the program (for example, *J* = 9.56, 2.85 and *J* = 9.89, 2.20, respectively, for pantopyranoid A) are in good agreement with the observed *J* values for these compounds.

Compounds **1** and **3** are assigned the same relative stereochemistry at C-4, C-6, and C-7 on the basis of the almost identical nature of the ^{1}H-NMR and ^{13}C-NMR values of the significant protons and carbons of the ring. From the ^{13}C-NMR data (Table 1) it can be seen that

the chemical shift of Me-10 in compounds **1** and **3** is similar (δ 27.88 and δ 27.74, respectively), suggesting analogous relative space environments. A variation in the chemical shift on the order of $\Delta\delta = 1.80$ ppm is observed for C-10 of compound **2**, however, suggesting an opposite stereochemistry at C-3. Because the nature of the halogen substituents at C-1 does not influence the chemical shift of the Me-10 of compounds **1** and **3**, the variation observed in the chemical shift of the Me-10 in compound **2** can be attributable to steric factors. This observation, in addition to the fact that the chlorinated compound **2** is 0.25 kcal/mol less stable than the corresponding epimer **3**, allows us to propose the relative stereochemistry represented in 2 for C-3 of pantopyranoid B, which gave the most hindered Me-10.

Pantoisofuranoids A−C (**4**−**6**) were obtained from the (1:1) hexanes−EtOAc fraction of the crude extract by successive chromatography on Si gel followed by recycling-HPLC (RHPLC). Pantoisofuranoid A (**4**) (10 mg) is a colorless oil, $[\alpha]^{25}_D$ −72° (*c* 0.4, $CHCl_3$). The CIMS gave the molecular ion at *m/z* 265/267 [$M^+ + 1$] corresponding to $C_{10}H_{17}BrO_3$ and indicating two degrees of unsaturation. The EIMS spectrum showed a fragment ion at *m/z* 247/249 [$M^+ - OH$]. Bands at 3582 (OH) and 1623 (C=C) cm^{-1} were detected in the IR spectrum.



The ^{1}H-NMR (Table 1) showed two trans-disubstituted olefinic protons at δ 6.31 (1H, d, $J = 13.6$ Hz) and δ 6.17 (1H, d, $J = 13.6$ Hz). The multiplet at δ 3.84 (2H, m) was assigned to protons geminal to alcoholic and ring oxygens, and the protons at δ 2.30 (2H) were exchangeable with D_2O, indicating two hydroxyl groups. A methylene multiplet appeared at δ 1.94 (1H, dd, $J =$ 3.1, 14.1 Hz) and 2.30 (1H, m) and three methyl groups, geminal to oxygen, were located at δ 1.17, 1.34, and 1.37 (3H, s, each). A ^{1}H−^{1}H COSY NMR spectrum showed coupling between the protons at δ 3.84 and the methylene protons at δ 2.30 and 1.94.

The ^{13}C-NMR spectrum together with the information from a DEPT spectrum showed the presence of 10 carbon atom signals, which can be assigned to three CH_3, one CH_2, four CH (two olefinic and two bearing oxygen) and two nonprotonated carbons atoms bearing oxygens. The disubstituted nature of the olefinic carbons and their chemical shifts are in accordance with a bromovinylic bond. Because pantoisofuranoid A (**4**) has only two quaternary carbon atoms, one of them must be substituted by a gem-dimethyl and by oxygen. A further oxygen must be geminal to a methyl group.

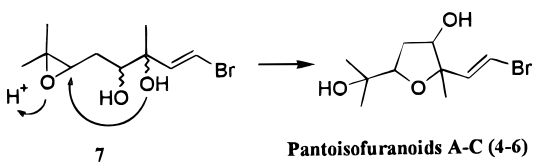
The ^{1}H−^{1}H COSY experiment established the connectivity of the H-4−H-6 fragment. The coupling constants for these protons (ABX_2) suggested that they formed part of a ring. The AB protons of the system appeared as an isolated multiplet at δ 3.84 (2H) in $CDCl_3$ but were resolved in C_6H_6-d_6 as two doublets of doublets at δ 3.57 and 3.32 (C_6D_6) (Table 1).

Proton−carbon chemical shift correlations for all the carbons directly bonded to protons were established by a HMQC (C_6D_6) experiment, and a correlation of C-6 with H-4 in a HMBC (C_6D_6) experiment confirmed the assignment of these signals. The gem-dimethyl group at C-7 was indicated by correlations of C-8 with Me-9 and of C-9 with Me-8, and also by correlations of C-7 with Me-8 and Me-9. The third methyl group was linked to the quaternary C-3 by correlations of C-3 with Me-10. Furthermore, the C-2 and C-3 carbons must be linked due to the correlations between C-2 and Me-10. The C-3/C-4 linkage was established by correlations of C-4 and Me-10, and the correlation of C-6 with Me-8 and Me-9 established the overall structure **4**, with the requisite two degrees of unsaturation.

Of the two hydroxy groups of the molecule only one gave an acetyl derivative on treatment of **4** with Ac_2O and pyridine at room temperature, suggesting that the other was a tertiary hydroxyl group. The presence of a hydroxylated isopropyl group was supported by the mass spectrum of **4**, which gave a base peak at *m/z* 59 consistent with a fragment C_3H_7O.

Pantoisofuranoids B and C (**5** and **6**) gave ^{1}H- and ^{13}C-NMR spectra that were very similar to those of pantoisofuranoid A (**4**) (Table 1), suggesting that the differences were in the stereochemistry at the C-3, C-4, and C-6 chiral centers. The stereochemistry of each compound was determined by 2D ROESY experiments. In the 2D ROESY (C_6D_6) of compound **4**, NOEs were observed between H-4 and H-6 to the H-5β methylene proton and from the C-9 and C-10 methyl groups to the H-5α proton (δ 2.30) of the methylene, thus establishing the relative stereochemistry of the three chiral centers.

In compound **5** (C_6D_6) a NOE effect was observed between H-6 and H-5β, H-4 and H-5α, and H-4 and Me-10. These data showed that compound **5** is epimeric of **4** at the C-4 hydroxyl group. The ROESY ($CDCl_3$) experiment on compound **6** showed a strong interaction of the overlapping H-4 and H-6 protons with H-5α and also with H-5β, indicating that H-4 and H-6 are necessarily on opposite sides of the plane, as is the case with compound **5**. The compound, therefore, must be the C-3 epimer **6** of compound **5**. The possibility that the naturally occurring compounds **4**−**6** were formed from a 6,7-epoxide such as **7** by intramolecular attack by the tertiary alcohol when exposed to Si gel during the purification process may be discarded, inasmuch as a prior purification of the crude extract with Sephadex LH-20 afforded a residue that could be identified from its ^{1}H-NMR spectrum as containing compounds **4**−**6**.



7 **Pantoisofuranoids A-C (4-6)**

The compounds **1**−**6** are distinguished by the number of oxygen substituents they contain that exceeds that of halogen substituents, supporting our hypothesis that a direct relationship exists between oxygen-containing marine monoterpenes and latitude. Only a very few of the more than 150 marine polyhalogenated monoterpenes found in the literature incorporate oxygen. With the exception of cartilagineal,[5] isolated from *Plocamium cartilagineum* from the Californian coast, the small number of the described[6−12] acyclic oxygenated monoterpenes come from marine species located in austral latitudes.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer model 241 polarimeter using a Na lamp at 25 °C. IR spectra were obtained with a Perkin-Elmer 1650/FTIR spectrometer in $CHCl_3$ solutions. EIMS spectra were taken on a Hewlett-Packard 5995 spectrometer; CIMS spectra were determined with a Hewlett-Packard 5998 spectrometer using methane as the reactive gas and HRMS spectra on a VG Micromass ZAB-2F spectrometer. ^{1}H-NMR and ^{13}C-NMR, HMQC, HMBC, ROESY, and COSY spectra were measured employing a Bruker AMX 400 instrument operating at 400 MHz for ^{1}H NMR and at 100 MHz for ^{13}C NMR, using TMS as internal standard. Two-dimensional spectra were obtained with the standard Bruker software. RHPLC separations were performed with a Japan Analytical LC-908. The gel filtration column (Sephadex LH-20) used hexane−MeOH−$CHCl_3$ (2:1:1) as solvent. Merck Si gel 7734 and 7729 were used for column chromatography. The spray reagent for TLC was H_2SO_4−H_2O−AcOH (1:4:20).

Plant Material. *Pantoneura plocamioides* was collected by a scuba off King George Island (South Shetland, Antarctic) at −18 m. A voucher specimen has been deposited at the Museo de Historia Natural, Santiago de Chile.

Extraction and Isolation of Monoterpenoids. The dried alga (1.4 kg) was extracted with Me_2CO at room temperature, and the Me_2CO extract was concentrated to give a dark green residue (39 g). This extract was chromatographed by flash chromatography on Si gel. The fraction eluted with hexanes−EtOAc (7:3) (4.78 g) was chromatographed on a Sephadex LH-20 column with hexane−MeOH−$CHCl_3$ (2:1:1) as eluent, affording a fraction (1.026 g) that was further separated by Si gel chromatography to give a fraction (53 mg) that contained a complex mixture that was separated by RHPLC, using a Jaigel-sil column (20 × 250 mm), to give pantopyranoid A (**1**) (4.3 mg), pantopyranoid B (**2**) (10 mg), and pantopyranoid C (**3**) (6 mg). The fraction eluted with hexanes−EtOAc (1:1) (4.58 g) was chromatographed on a Sephadex LH-20 column with hexane−MeOH−$CHCl_3$ (2:1:1) as eluent, affording a fraction (2.513 g) that was further separated by Si gel chromatography to give a fraction (60 mg) that contained a complex mixture that was separated with recycling HPLC to give pantoisofuranoid A (**4**) (10 mg), pantoisofuranoid B (**5**) (6.2 mg) and pantoisofuranoid C (**6**) (2 mg).

Pantopyranoid A (1): colorless oil; $[\alpha]_D$ −93° (*c* 0.45, $CHCl_3$,); IR ν_{max} 3582; 1618 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m/z* 343/345/347 [$M^+ + 1$; 9, 21, 14], 247/249 (5, 3), 207 (14), 149/151 [C_4H_6OBr; 100, 100], 133/135 [C_4H_6Br; 27, 22], 89 (16); CIMS 341/343/345 [$M^+ - 1$], 343/345/347 [$M^+ + 1$], 371/373/375 [$M^+ + 29$], 383/385/387 [$M^+ + 41$]; HRMS *m/z* [$M^+ + 2$] 347.956 (calcd for $C_{10}H_{16}O_3{}^{81}Br_2$ 347.958).

Pantopyranoid B (2): colorless oil; $[\alpha]_D$ −83° (*c* 5.00, $CHCl_3$); IR ν_{max} 3582; 1621 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m/z* 299/301/303 [$M^+ + 1$; 7, 10, 5], 105/107 [C_4H_6OCl 100, 91], 89 (22); CIMS 297/299/301 [$M^+ - 1$], 299/301/303 [$M^+ + 1$], 327/329/331 [$M^+ + 29$], 339/341/343 [$M^+ + 41$]; HRMS *m/z* [$M^+ - 1$], 298.987 (calcd for $C_{10}H_{15}O_3{}^{35}Cl^{81}Br$ 298.987).

Pantopyranoid C (3): colorless oil; $[\alpha]_D$ −205° (*c* 0.2, $CHCl_3$); IR 3582; 1618 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m/z* 105/107 [C_4H_6OCl; 100, 91], 89 (22), 77-(22); CIMS 297/299/301 [$M^+ - 1$], 299/301/303 [$M^+ + 1$], 327/329/331 [$M^+ + 29$], 339/341/343 [$M^+ + 41$].

Pantoisofuranoid A (4): colorless oil; $[\alpha]^{25}_D$ −72° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3582; 1619 cm^{-1}; ^{1}H NMR ($CDCl_3$); ^{1}H NMR (C_6D_6); ^{13}C NMR, see Table 1; EIMS *m/z* 247/249 [$M^+ - OH$, 3, 2]; 149/151(14, 11), 133/135 (31/26), 109 (62), 105/107 [C_2H_2Br; 8, 7], 59 [C_3H_7O, 100]; CIMS 263/265 [$M^+ - 1$], 265/267 [$M^+ + 1$], 293/295 [$M^+ + 29$], 305/307 [$M^+ + 41$].

Pantoisofuranoid B (5): colorless oil; $[\alpha]^{25}_D$ −147° (*c* 0.20, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3583; 1602 cm^{-1}; ^{1}H NMR ($CDCl_3$); ^{1}H NMR (C_6D_6); ^{13}C NMR, see Table 1; EIMS *m/z* 247/249 [$M^+ - OH$, 8, 9], 149/151(59, 32), 133/135 (28/27), 109(48), 105/107 [C_2H_2Br; 12, 9], 59 [C_3H_7O, 100]; CIMS 263/265 [$M^+ - 1$], 265/267 [$M^+ + 1$], 293/295 [$M^+ + 29$], 305/307 [$M^+ + 41$].

Pantoisofuranoid C (6): colorless oil; $[\alpha]^{25}_D$ −45° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3582; 1623 cm^{-1}; ^{1}H NMR ($CDCl_3$); ^{1}H NMR (C_6D_6); ^{13}C NMR, see Table 1; EIMS *m/z* 247/249 [$M^+ - OH$, 4, 4], 149/151(38, 32), 133/135 (31/26), 109(69), 105/107 [C_2H_2Br, 16, 15], 59 [C_3H_7O, 100]; CIMS 263/265 [$M^+ - 1$], 265/267 [$M^+ + 1$], 293/295 [$M^+ + 29$], 305/307 [$M^+ + 41$].

Acetylation of Pantoisofuranoid A (4). A solution of **4** (5 mg) in dry C_5H_5N (1.5 mL) was treated with Ac_2O (1 mL) and stirred at room temperature for 2 h and then was poured into 10% aqueous HCl and extracted with $CHCl_3$. The organic layer was washed with H_2O and brine, dried (Na_2SO_4), and concentrated. The residue was purified by RHPLC to give 4 mg of the acetate derivative, which was identified by ^{1}H NMR: colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.13 (9H, s), 1.93−2.0 (1H, m), 2.08 (3H, s), 2.34−2.20 (1H, m), 3.81 (1H, t, J = 7.7 Hz), 5.12 (1H, dd, J = 4.2, 6.9 Hz), 6.24 (1H, d, J = 13.6 Hz), 6.38 (1H, d, J = 13.6 Hz); EIMS *m/z* 168 [$M^+ - OAc-Br$, 22] 105/107 (35,14), 59 (35), 54 (100); CIMS 305/307 [$M^+ - 1$], 307/309 [$M^+ + 1$].

Acknowledgment. This work was supported by the Comisión Interministerial de Ciencia y Tecnología (CICYT) (ANT94-0047) and Instituto Antártico Chileno (INACH). M. Cueto acknowledges a fellowship from the Programa Nacional de la Antártida. We are grateful to Dr. Eliana Ramírez (Museo de Historia Natural de Chile) for the taxonomic classification of the alga.

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NP9601162