tallized. Recrystallization from acetone afforded 4.60 g (37%) of *trans*-**12b**. The mother liquors were distilled bulb-to-bulb [100–160 °C (0.1 mm)], and the 1.25 g of white solid collected was chromatographed (MPLC, EtOAc) to afford an additional 500 mg (4%) of the *trans*-**12b** followed by 750 mg (6%) of the *cis*-**12b**.

trans-**12b**: mp 117–118 °C; HPLC (EtOAc) t_R 6.2 min; ^{1}H NMR δ 7.1–7.4 (m, 5 H), 3.64 (dd, 1 H, J = 9.5, 12.2 Hz), 3.50 (s, 3 H), 3.45–3.35 (m, 2 H), 3.11–3.00 (m, 1 H), 3.01 (s, 3 H), 2.75 (dd, 1 H, J = 5.7, 17.7 Hz), 2.59 (dd, 1 H, J = 10.3, 17.7 Hz). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.0; H, 6.9; N, 5.7. Found: C, 60.2; H, 7.0; N, 5.6.

cis-**12b**: mp 95–96 °C; HPLC (EtOAc) t_R 7.5 min; ^{1}H NMR δ 7.2–7.4 (m, 3 H), 7.0–7.1 (m, 2 H), 3.74 (dd, 1 H, J = 5.0, 9.2 Hz), 3.65 (s, 3 H), 3.42 (d, 1 H, J = 3.7 Hz), 3.39 (s, 1 H), 3.25–3.15 (m, 1 H), 3.03 (s, 3 H), 2.85 (d, 2 H, J = 5.0 Hz).

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Coronopifoliol, a Diterpene Based on an Unprecedented Tetracyclic Skeleton from the Red Algae *Sphaerococcus coronopifolius*

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The structure of coronopifoliol (1), a novel tetracyclic diterpene isolated from the $CHCl_3$ extracts of *Sphaerococcus coronopifolius*, had been determined on the basis of physicochemical data including 2D NMR spectroscopies, and its biogenetic origin is briefly discussed.

Diterpenes, which are common metabolites of marine brown algae, are much less widespread in Rhodophyta[1], having been found, up to date, only in some algae belonging to the genus *Laurencia*[2] and in the unrelated species *Sphaerococcus coronopifolius*.[3] Particularly, the last organism is yielding an expanding variety of interesting diterpenes based on carbon skeletons that seem to be peculiar to this algae. We wish to describe here the structure of coronopifoliol (1), a novel brominated diterpene possessing an unprecedented tetracyclic ring system.

The dried algae was exhaustively extracted with chloroform, and the residue was subjected to separation on a combination of column chromatography over silica gel and HPLC on RP18 to give 1 (0.001%, based on dry weight). Coronopifoliol had the molecular formula $C_{20}H_{33}BrO_2$, established from HRMS. The mass spectrum showed, in addition to the two very weak molecular ion peaks of equal intensity at m/z 384 and 386, strong peaks at m/z 366, 368 $[(M - H_2O)^+]$, 287 $[(M - H_2O - Br)^+]$, and 269 $[(M - 2H_2O - Br)^+]$, suggesting that the two oxygen atoms are as two hydroxyl groups. This was confirmed by IR absorption at ν_{max} 3450–3300 cm^{-1} and by the ^{13}C NMR spectrum of 1, which also indicated the nature of the two alcoholic functions showing in the lower field region resonances attributable to a $\equiv$C–OH (δ 73.00) and to a =CHOH (δ 75.85) group in addition to that of the bromomethine carbon atom (δ 69.46). The ^{1}H NMR spectrum (C_6D_6, 500 MHz, Table I) of 1 confirmed the last two functionalities [δ 3.41 (1 H, br dd, 14-H) and 3.76 (1 H, dd, 8-H)] and showed the presence of two methyl groups linked to quaternary carbon atoms [3 H singlets at δ 1.13 (16-H_3) and 1.36 (17-H_3)] and of two secondary methyls belonging to an isopropyl function [δ 0.83 and 0.81 (3 H each, d's, 19-H_3 and 20-H_3)].

^{1}H NMR decoupling studies allowed us to formulate the partial structures A, B, and C, showing the interrelation of the pertinent protons as reported in Table II. The values of the coupling constants (see Table I) suggested that the last two structural fragments were most likely parts of six-membered rings.

Very useful information was obtained from two-dimensional ^{13}C–^{1}H shift correlated spectroscopy,[4] which led to the assignment of all the protonated carbon resonances in 1, thus confirming the above partial structures. ^{13}C NMR spectrum of 1 also comprised the signals of two quaternary carbon atoms [δ 49.75 (C4) and 41.75 (C7)] which, together with the carbon atom bearing the tertiary OH group (C11), connect the substructures A, B, and C to give structure 1. The positioning of these three fully substituted carbon atoms in structure 1 was accomplished with the aid of long-range 2D ^{13}C–^{1}H shift correlation spectroscopy. By this technique only a limited number of ^2J and ^3J C–H couplings could be evidenced, but these were essential for the confident structural assignment of 1. Thus, the two signals at δ 41.75 (C7) and 73.00 (C11) were observed to correlate with the two Me groups resonating at δ 1.36 (17-H_3) and 1.13 (16-H_3) in the ^{1}H NMR spectrum, respectively. These data in conjunction with the correlations of C12 with 16-H_3 and 17-H_3 and of C10 with 16-H_3 led to the combination of substructures A and C through the carbon atoms C11 and C7.

Ultimately, the correlation of C6 with 17-H_3 clearly indicated that substructure B was linked to C7, thus une-

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(1) Fenical, W. "Marine Natural Products"; Scheuer, P. J., Ed.; Academic Press: New York, 1978; Vol. II, pp 174–245.

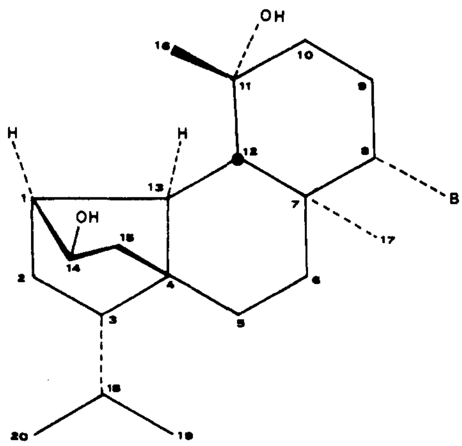
(2) Erickson, K. L. "Marine Natural Products"; Scheuer, P. J., Ed.; Academic Press: New York, 1983; Vol. V, p 132–257.

(3) Cafieri, F.; Fattorusso, E.; Santacroce, C. *Tetrahedron Lett.* **1984**, *25*, 3141 and references cited therein.

(4) Shoolery, J. N. *J. Nat. Prod.* **1984**, *47*, 226.

0022-3263/85/1950-3982$01.50/0

Table I. Nuclear Magnetic Resonance Data for 1 (in C_6D_6)[a]



1

^{13}C, δ	assignment	^1H, δ (multiplicity	^{13}C, δ	assignment	^1H, δ (multiplicity
48.40	1	2.28 (br d)		10α	1.18 (ddd)[d]
	2α	1.18 (m)[d]	44.11		
29.93				10β	1.26 (ddd)
	2β	0.91 (*c*)	73.00	11	
49.94	3	0.91 (c)	48.85	12	1.66 (d)
49.75	4		43.99	13	1.60 (br d)
	5α	1.69 (ddd)	75.85	14	3.41 (br dd)
23.65				15a	1.13 (dd)[d]
	5β	1.20 (ddd)[d]	46.87		
	6α	2.02 (ddd)		15b	1.79 (dd)
38.00			33.86	16	1.13 (s)
	6β	1.33 (ddd)	15.68	17	1.36 (s)
41.75	7		28.63	18	1.61 (m)
69.46	8	3.76 (dd)	23.69	19	0.83 (d)
	9α	2.52 (dddd)	19.09	20	0.81 (d)
31.46					
	9β	1.90 (dddd)			

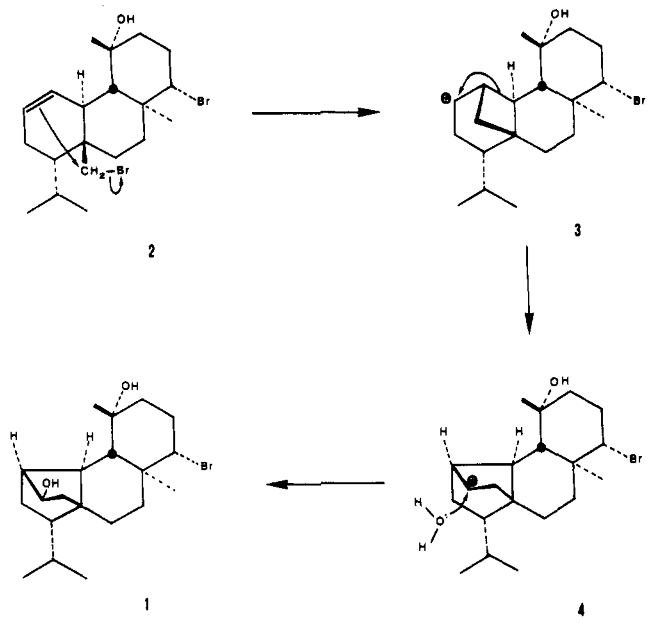
H–H	J, Hz	H–H	J, Hz	H–H	J, Hz
1–2α	3.5	6α–6β	12.5	9β–10α	3.0
1–2β	*b*	5β–6α	3.5	10α–10β	12.0
1–14	*b*	8–9α	12.0	12–13	11.5
1–13	*b*	8–9β	3.0	14–15b	3.0
5α–5β	12.0	9α–9β	12.0	14–15a	8.0
5α–6β	12.0	9α–10β	12.0	15a–15b	12.5
5α–6α	3.5	9α–10α	4.0	18–19	6.5
5β–6β	3.0	9β–10β	3.0	18–20	6.5

[a] ^{13}C–^1H shift correlated 2D NMR spectrum via ^1J showed the interrelation of all the protonated carbons with the pertinent proton(s). The correlations via ^2J and ^3J are described in the text. [b] Very small. [c] Part of a further coupled AB system. [d] Visualized by difference decoupling experiments.

quivocally establishing the position of the last quaternary carbon (C4). In fact, the only way to accomodate this carbon atom was its incorporation in the structure 1 through linkages with C8, C15, C13, and C5.

The overall relative stereochemistry of coronopifoliol was finally assigned on the basis of J values in the ^1H NMR spectrum and of NOE measurements (see Figure 1). The axial nature of 8-H was evidenced by its large coupling constant with 9-H_{ax}. Analogously the trans diaxial relationship between 12-H and 13-H was concluded from the pertinent J value (11.0 Hz). Enhancements of 9-H_{ax} and 13-H signals on irradiation at 7-Me showed their cis relationship thus establishing that the ring junction at C7 and C12 is trans diequatorial. Irradiation at 11-Me produced a relevant enhancement of 1-H while 9-H_{ax} was completely unaffected; this could be explained only assuming an equatorial nature of 11-Me. The stereochemistry of C1 and C4 was established from the NOE found between 6-H_{ax} and 15-H^b, whereas a positive enhancement of 2-H_β and 3-H produced by irradiation at 14-H enabled us to assign the relative stereochemistry of C13 and C3.

Scheme I



The determination of the absolute configuration of the C14 center was carried out by Horeau's method,[5] which gave a preponderance of (+)-α-phenylbutyric acid. Thus the absolute stereochemistry of coronopifoliol was assumed to be as shown.

Compound 1 contains a unique carbocyclic ring system which further increases the number of irregular diterpenoid carbon skeletons synthetized by *S. coronopifolius*. A biogenetic relationship between coronopifoliol and bromosphaerol (2), which is one of the most abundant diterpenes of this algae, may be hypothesized. In fact the novel ring system in 1 could be generated by a nucleophilic attack on the bromomethylene carbon of bromosphaerol (2) followed by a rearrangement of the resulting carbonium ion 3, thus giving 4, the immediate precursor of coronopifoliol (see Scheme I). The above pathway represents a further step of the general biogenetic scheme of diterpenes in *S. coronopifolius* recently proposed starting from geranylgeraniol.[3]

Experimental Section

IR spectra were recorded on a Perkin-Elmer 157 spectrometer in $CHCl_3$ solution.

^1H NMR spectra, spin-decoupling experiments, and NOE measurements were performed on a Bruker WM 500 spectrometer in C_6D_6 solution with Me_4Si as internal reference, with δ 0. ^{13}C NMR spectra and 2D experiments were determined on a Bruker WM 250 instrument in C_6D_6 solution.

Determination of nuclear Overhauser effects and decoupling difference experiments were performed with the aid of Aspect 2000 microprograms which allowed direct accumulation of FID's. The sample used for NOE measurements was previously degassed by bubbling argon through the solution for 40 min.

^{13}C–^1H shift correlated 2D NMR spectra were carried out with a Bruker microprogram. The shift correlation with polarization transfer via J coupling experiments were performed by adjusting the fixed delays D_3 and D_4 to give maximum polarization for J_{C-H} = 135 Hz when ^1J couplings were used; for detecting ^{13}C–^1H long range correlation D_3 and D_4 were adjusted to give maximum polarization for J_{C-H} = 5.0 and 6.5 Hz in two different experiments.

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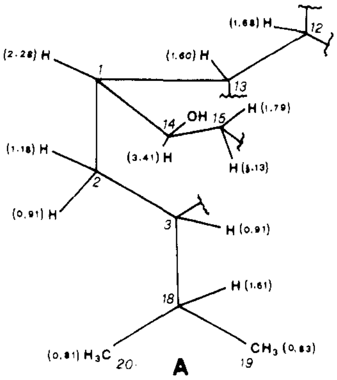
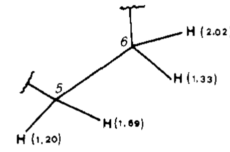
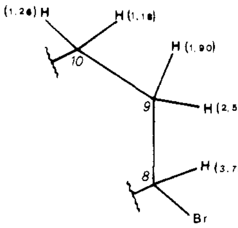
(5) Horeau, A. *Tetrahedron Lett.* **1962**, 965.

Table II. ^{1}H NMR Decoupling Experiment Data for 1 (in C_6D_6)

irradiated signal (multiplicity)	modified signal[a]	assignments
1.61 (m)	0.83 (d → s), 0.81 (d → s), 0.91 (m → *b*)	 **A**
0.91 (*d*)	1.61 (m → heptet), 1.18 (m → d), 2.28 (br d → *c*)	
1.18 (m)	0.91 (m → *b*) 2.28 (br d → br s)	
2.28 (br d)	1.60 (br d → d), 3.41 (br dd → dd), 1.18 (m → *b*)	
1.60 (br d)	1.66 (d → s), 2.28 (br d → *c*)	
1.66 (d)	1.60 (br d → br s)	
3.41 (br dd)	2.28 (br d → *c*), 1.79 (dd → d), 1.13 (dd → d)	
1.79 (dd)	1.13 (dd → d), 3.41 (br dd → br d)	
1.13 (dd)	1.79 (dd → d), 3.41 (br dd → br d)	
2.02 (ddd)	1.33 (ddd → dd), 1.69 (ddd → dd), 1.20 (ddd → dd)	 **B**
1.33 (ddd)	2.02 (ddd → dd), 1.69 (ddd → dd), 1.20 (dd → d)	
1.69 (ddd)	1.20 (ddd → dd), 1.33 (ddd → dd), 2.02 (ddd → dd)	
1.20 (ddd)	1.33 (ddd → dd), 2.02 (ddd → dd), 1.69 (ddd → dd)	
3.76 (dd)	2.52 (dddd → ddd), 1.90 (dddd → ddd)	 **C**
2.52 (dddd)	3.76 (dd → d), 1.90 (dddd → ddd) 1.18 (ddd → dd), 1.26 (ddd → dd)	
1.90 (dddd)	3.76 (dd → d), 2.52 (dddd → ddd) 1.18 (ddd → dd), 1.26 (ddd → dd)	
1.26 (ddd)	1.18 (ddd → dd), 2.52 (dddd → ddd) 1.90 (dddd → ddd)	
1.18 (ddd)	1.26 (ddd → dd), 1.90 (dddd → ddd) 2.52 (dddd → ddd)	

[a] Multiplicity before irradiation → multiplicity after irradiation. [b] The initial multiplet was simplified. [c] The initial signal was sharpened. [d] Part of a further coupled AB system.

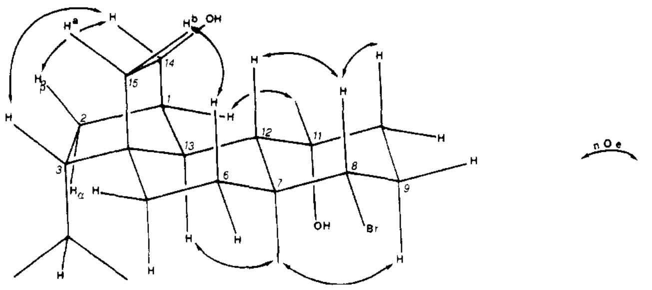


Figure 1.

Low-resolution mass spectra were recorded at 70 eV on an AEI MS 30 instrument. High-resolution mass spectra were obtained on an AEI MS 902 spectrometer.

Optical rotation was measured with a Perkin-Elmer 141 polarimeter with a 10-cm microcell.

Isolation of 1. Freeze-dried and ground *S. coronopifolius* (3 kg), collected in the Bay of Naples near Massalubrense (spring, 1984), was exhaustively extracted with $CHCl_3$; and the extract was taken to dryness; the residue (11 g) was chromatographed on a SiO_2 (100 g) column and eluted with $CHCl_3$ containing increasing amounts of Et_2O. The fractions eluted with $CHCl_3$–Et_2O (7:3) yielded 100 mg of crude 1. Final purification was achieved by HPLC (Varian 5000 instrument) on a RP18 (1 × 25 cm, Merck) column using CH_3CN as eluent to give 30 mg of 1: $[\alpha]_D$ −28.6° (*c* 0.7 in $CHCl_3$); high-resolution mass measurement calcd for $C_{20}H_{33}{}^{79}BrO_2$ 384.1664, found 384.1658.

Determination of the Absolute Configuration of C14 in 1 by Horeau's Method. 1 (7.7 mg, 0.2 mmol) and 60 mg of racemic α-phenylbutyric acid anhydride were dissolved in 5 mL of dry pyridine. Conventional workup[5] led to the isolation of a preponderance of (+)-α-phenylbutyric acid (optical yield 11%).

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