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BROMOCORODIENOL, A DITERPENOID BASED ON A NOVEL BICYCLIC SKELETON FROM THE RED ALGA *SPHAEROCOCCUS CORONOPIFOLIUS*

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Summary: The structure of bromocorodienol (3) has been determined on the basis of physical and chemical evidence and its role in the metabolic pathway of geranylgeraniol in *Sphaerococcus coronopifolius* is briefly discussed.

The red alga *Sphaerococcus coronopifolius* is an unusually prolific source of diterpenoids[1-7] based on two tricyclic skeletons which appear substantially rearranged. Bromosphaerol (1) and presphaerol (2)[8] are representative of these two classes of compounds which until now have been isolated only from this organism. We wish to describe here the isolation from this alga of a new bromoditerpene alcohol, bromocorodienol (3), based on a further unprecedent skeleton.

Fresh material, found near Salerno Bay (Summer 1983), was homogenized and extracted with methanol; the chloroform-soluble material from the decanted methanol was repeatedly chromatographed on SiO_2 gel (230-400 mesh, Merck) columns using benzene as eluent. The appropriate fractions were purified by HPLC using a RP 8 column (Varian) eluted with CH_3CN to give 3 (0.004% based on fresh material), mp 89-91° (from CH_3CN), $[\alpha]_D = +34.3°$ (c 1.5, $CHCl_3$). 3 had molecular formula $C_{20}H_{33}BrO$ established by HRMS (m/z 368.1723, $C_{20}H_{33}{}^{79}BrO$ requires 368.1715). Infrared analysis revealed strong OH absorption at $\nu_{max}^{CHCl_3}$ 3600-3400 cm^{-1}.

Analysis of the ^{1}H-NMR spectrum (500 MHz, $CDCl_3$,Table), which was particularly detailed, and extensive double resonance experiments allowed assignment of the structure 3. The doublets at δ 0.76 and 0.83 are due to the methyls of an isopropyl group since they collapsed to two singlets by irradiation at the frequency (δ 1.41) of an 1-H multiplet, and the singlets at δ 1.00 and 1.22 are due to two t-Me's, one of which linked to an oxygen-bearing carbon atom. This spectrum also comprises a bromomethine signal at δ 3.94 (dd) which is coupled to the signals at δ 2.48 (H-12ax) and 2.08 (H-12eq); the 13ax and 13eq proton signals are clearly visible as multiplets at δ 1.44 and 1.66 respectively.

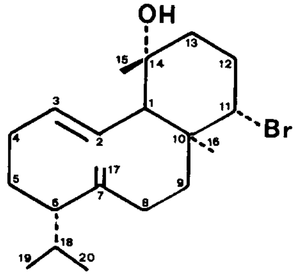
In the olefinic region the narrow multiplets at δ 4.75 and 4.81 are attributable to the protons of the exocyclic methylene group while the 1-H double doublet at δ 5.51 coupled to the signal at δ 1.53 (1H, d) can be assigned to H-2 and the 1-H multiplet at δ 5.59 is due to H-3. The latter signal was proved to be coupled with the protons attached to C-4 which resonate at δ 2.21 and 1.77. The multiplet at δ 1.72 broadened by long-range coupling with the vinyl proton at δ 4.75 was assigned to H-6. The protons linked to C-8 resonate at δ 1.93 (ddd broadened by long-range coupling) and in the region at δ 1.82-1.75; finally the protons linked to C-9 appear as multiplets at δ 1.26 and 2.27.

Additional evidence to confirm structure **3** was obtained by mass spectrum in which intense fragmentation peaks at m/z (%) 353, 355 $(M-CH_3)^+$ (4.92); 350, 352 $(M-H_2O)^+$ (13.53); 335, 337 $(M-H_2O-CH_3)^+$ (3.69); 325, 327 $(M-C_3H_7)^+$ (17.83); 314, 316 $(M-C_4H_6)^+$ (35.67); 307, 309 $(M-C_3H_7-H_2O)^+$ (17.22); 296, 298 $(M-C_4H_6-H_2O)^+$ (100); 289 $(M-Br)^+$ (88.56); 288 $(M-HBr)^+$ (14.76); 281, 283 $(M-C_4H_6-H_2O-CH_3)^+$ (7.38); 271 $(M-H_2O-Br)^+$ (84.87); 245 $(M-C_3H_7-HBr)^+$ (51.66); 227

Table – Nuclear Magnetic Resonance Data for Bromocorodienol-

^{13}C chemical shift	assignment	^{1}H chemical shift
61.7	1	1.53 (d)
134.4	2	5.51 (dd)
126.3	3	5.59 (ddd)
	4a	2.21 (m)
	4b	1.77 (m°)
	5a	°° (m)
	5b	°° (m)
55.2	6	1.72 (ddd°°°)
153.8	7	
	8a	1.93 (ddd°°°)
	8b	°°
	9a	2.27 (ddd)
	9b	1.26 (ddd)
44.9	10	
68.9	11	3.94 (dd)
	12ax	2.48 (dddd)
	12eq	2.08 (dddd)
	13ax	1.44 (ddd)
	13eq	1.66 (ddd)
71.6	14	
30.7	15	1.22 (s)
14.4	16	1.00 (s)
112.2	17a	4.75 (bs)
	17b	4.81 (bs)
29.8	18	1.40 (o)
20.5 and 21.5	19 and 20	0.76 and 0.83 (d)

°overlapped with other signals
°°overlapped with other signals in the region 1.82-1.75
°°°broadened by long-range coupling



3

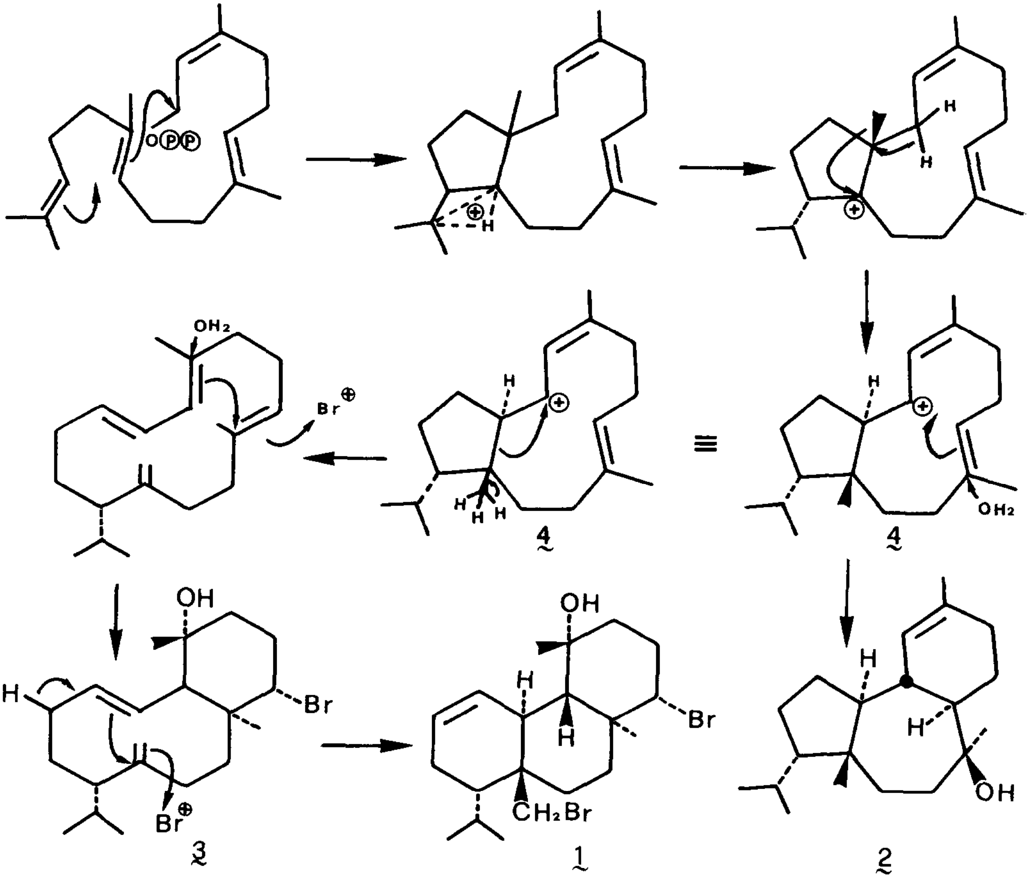
J (Hz) 1-2=10; 2-3=15; 3-4a=7; 3-4b=7; 5a-6=3; 5b-6=3; 6-18=6.8; 8a-8b=16; 8a-9a=4.5; 8a-9b=4.5; 8b-9a=14; 9a-9b=14; 11-12ax=13; 11-12eq=4; 12ax-12eq=13; 12ax-13eq=4; 12ax-13ax=13; 12eq-13eq=4; 12eq-13ax=4; 13ax-13eq=13; 18-19=6.8; 18-20=6.8

$(M-C_3H_7-H_2O-HBr)^+$ (46.74) are present and by ^{13}C-NMR spectrum ($CDCl_3$, 62.90 MHz) which showed, in addition to the signals reported in Table and assigned on the basis of selective decoupling experiments, six methylene signals at δ 41.10, 39.51, 31.63, 30.85, 27.80, 25.58.

Final proof of the correctness of the formula 3 and the definition of the absolute stereochemistry at C-1, C-6, C-10, C-11 and C-14 was provided by treatment of 3 with NBS in anhydrous acetone at room temp. for 0.5 h which afforded bromosphaerol (1) (15% yield). The E configuration of the C-2 double bond is clearly indicated by the large coupling constant (J 15 Hz) between H-2 and H-3.

Bromocorodienol is composed of an irregular diterpenoid skeleton of an unprecedent nature from which bromosphaerol (1) could be biosynthesized by a bromonium-ion induced carbocyclization, which we reproduced under laboratory conditions as described above. Its biosynthesis starting from geranylgeranylpyrophosphate could be formulated by the biogenetic scheme depicted in figure which involves C-1 C-11 and C-10 C-14 cyclizations; the resulting carbonium-ion, after a rearrangement, by methyl and hydrogen shifts could generate the ion 4 from which bromocorodienol (3) could be originated by proton elimination and opening of the pentatomic ring and

Scheme



by subsequent cyclization of the resulting diene, induced by a bromonium-ion. This biogenetic pathway also accounts for the co-occurrence of presphaerol- and bromosphaerol-type diterpenoids in the S. coronopifolius. In fact the intermediate **4** could evolve to **2** as reported in the scheme

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8. For **1** the absolute configuration has been determined[3] while only the relative stereochemistry of **2** has been established[4].

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