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SPHAEROCOCCENOL A; A NEW REARRANGED BROMO-DITERPENE FROM THE RED ALGA SPHAEROCOCCUS CORONOPIFOLIUS

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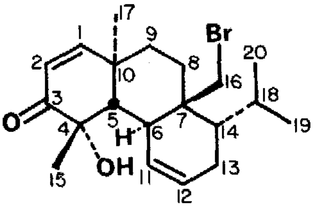
Biosynthesis involving bromination mechanisms is now recognized as a characteristic of at least nine families of the red seaweeds (Rhodophyta)[1]. While bromine-containing diterpenes are not common among these algae, examples of two ring systems, concinndiol[2] and iriediol,[3] are elaborated only by *Laurencia* species.[1] We wish to report herein the structure of a new bromo-diterpene obtained from extracts of the red seaweed *Sphaerococcus coronopifolius* (Good. and Woodw.) Ag. (Sphaerococcaceae). This metabolite appears to result from a methyl migration of a tail to tail diterpene precursor or from more substantial molecular rearrangements.

S. coronopifolius was collected in June, 1975, near La Escala, Spain. The $CHCl_3$-MeOH extract of the partially air-dried alga was chromatographed by conventional methods to yield crystalline sphaerococcenol A (1), mp 184-5° (CCl_4), on ether-benzene (1:9) elution. Sphaerococcenol A, $[\alpha]_D^{25}$ - 93° (c 2.0, $CHCl_3$), the major lipid metabolite, obtained as 15% of the extract, showed infrared and ultraviolet absorptions characteristic of an α,β-unsaturated ketone, $\nu_{c=o}$=1680 cm^{-1}, λ_{max}^{MeOH} = 228nm ε=7,510). High resolution mass spectrometry established the molecular formula as $C_{20}H_{29}O_2Br$ (M^+ measured 380.1353, calculated 380.1351). The second oxygen atom of this molecule belonged to a tertiary alcohol function, since M^+-H_2O fragments were observed in the mass spectrum; an ir band at 3600 cm^{-1} was prominent, and (1) failed to form an



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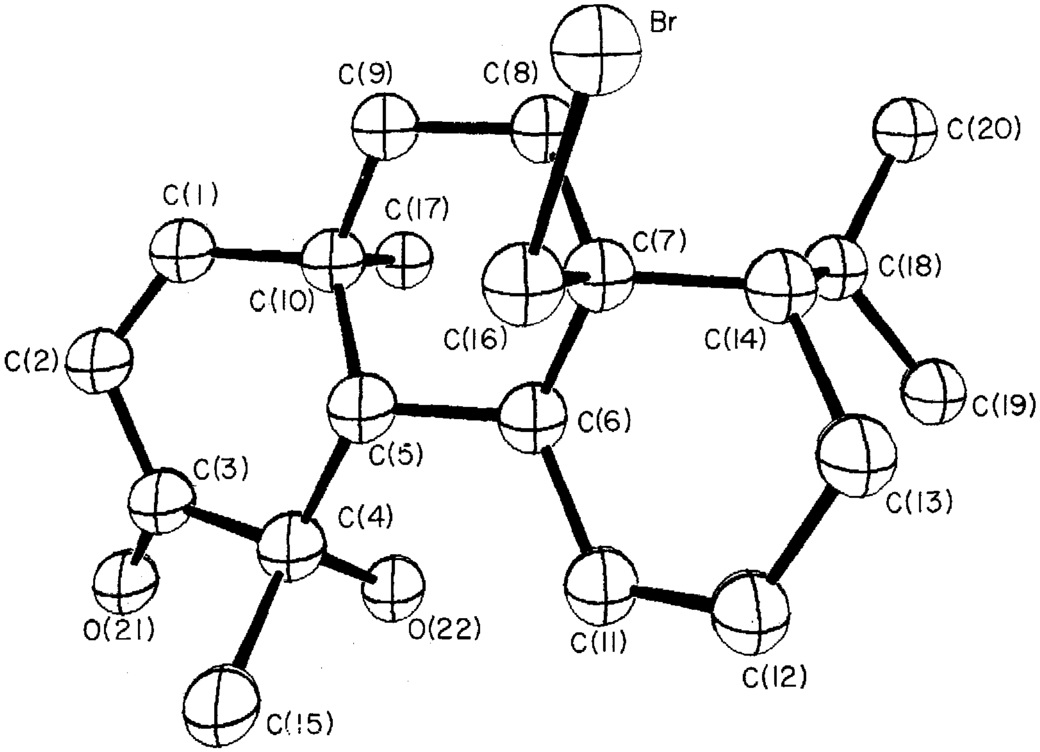
acetate under mild conditions (Ac_2O/py 25°). Other structural features were extractable from both the ^1H and ^{13}C nmr spectra. At 220 MHz ($CDCl_3$), proton bands at δ6.80 d (1H), J = 10 Hz and δ6.06 d (1H), J = 10 Hz, defined the isolated AB system of the α,β-unsaturated ketone. Two additional olefin protons appeared at δ6.03 d (1H), J = 10 Hz and δ5.73 m (1H). An interesting AB quartet, with doublet components at δ3.98 and δ3.70 (J = 11 Hz), was suggestive that the remaining bromine atom formed a bromomethyl group, rather than the more typical secondary bromine substituent. The remaining bands were centered at δ3.13 s (1H), δ2.96 m (1H), δ1.3-2.3 multiple bands (9H), with four methyl bands at δ1.34 s (3H), δ1.09 s (3H), δ0.98 d (3H), J = 7 Hz, δ0.94 d (3H), J = 7 Hz. The ^{13}C spectrum (20 MHz, $CDCl_3$ ppm rel. to tms) was composed of the following bands: a singlet carbonyl carbon at 200.7 ppm, four olefin carbons at 159.7, 126.2, 125.3, and 122.3 ppm (all doublets by double resonance decoupling), a quaternary hydroxyl-containing carbon at 73.1, various bands for allylic, methine and methylene carbons at 39.9 (d), 38.0 (t), 37.6 (s), 34.6 (d), 33.4 (t), 30.9, 29.1, 23.7, 23.6, and four methyl quartets at 22.4, 20.2, 19.2 and 17.3 ppm. Careful consideration of these combined data gave no correlation with known diterpene systems. Hence, the structure of this new diterpene was determined unequivocally by X-ray diffraction methods

Clear crystals of sphaerococcenol A belong to the orthorhombic space group $P2_12_12_1$ with unit cell axes a = 8.168(4), b = 14.386(5), c = 15.810(6)Å. The calculated density was 1.36 g/cc for four molecules of $C_{20}H_{29}O_2Br$ per unit cell. Reflections with $\theta \leq 57°$ were measured using an ω scan technique on a four-circle diffractometer, using monochromated CuK_α radiation (1.54178 Å). Of the 1473 reflections measured, 1382 with $F_o \geq 3\sigma(F_o)$ were considered observed (94%). The structure was solved routinely with a multiple solution weighted tangent formula approach.[4] Phase refinements and electron density synthesis revealed all 23 non-hydrogen atoms.[5] The hydrogen positions were calculated and included in the model. Anisotropic refinements of the heavy atoms and isotropic refinement of the hydrogens brought the conventional R-factor to 0.062. Anomalous scattering correction for the bromine gave, after several cycles of refinement, final R-factors of 0.059 and 0.067 for the molecule and its mirror image, respectively.[6] See reference 7 for additional crystallographic details

The configruations of the substituents are: 4-OH α, 4-CH_3 β, 5-H β, 6-H α, 7-CH_2Br β, and 10-CH_3 α. The isopropyl group at C-14 is α and, in the solid state, held in an eclipsed conformation. This may also be true in solution, since each methyl component of the isopropyl appears as a separate doublet in the nmr spectrum. All bond distances and angles agree well with generally accepted values, and there are no abnormally short intermolecular contacts.[8]



A computer generated drawing of the final X-ray model of sphaerococcenol A.

Sphaerococcenol A cannot be disected into isoprene subunits. However, if the bromomethyl carbon (C-16) bonded to C-7 has its terpenoid origin at C-6, biosynthetic mechanisms can be drawn from a tail to tail farnesyl-isoprene precursor. This migration could conceivably occur from a C-6, C-7 cyclopropane intermediate which could react with Br^+ to yield the exhibited bromomethyl group.

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