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The Structure of Brominated Diterpene from the Marine Red Alga Laurencia obtusa (Hudson) Lamouroux[1)]

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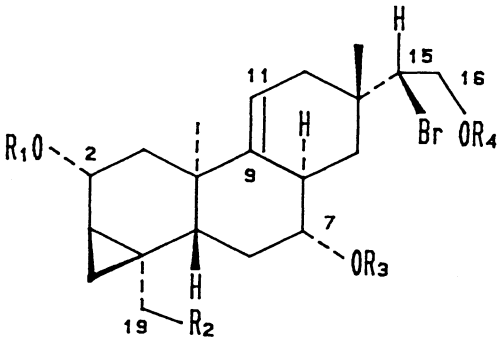
A new brominated diterpene, 15-bromo-2,7,16-trihydroxy-9(11)-parguerene has been isolated from the title alga and its structure including absolute configuration was established by spectral and chemical evidences as well as X-ray crystallographic method.

From the marine red alga Laurencia obtusa (Hudson) Lamouroux collected at Teuri Island, Hokkaido, a cytotoxic diterpene, 15-bromo-2,7,16,19-tetraacetoxy-9(11)-parguerene(1) was isolated as the major metabolite (10% of the neutral oil) together with the inactive one, 15-bromo-2,7,16-trihydroxy-9(11)-parguerene (2) (2%) and the former 1 has already been prepared by acetylation of the natural metabolite 3 obtained from sea hare, Aplysia dactylomela.[2a)]

Although the relative stereostructures of parguerane derivatives except for the configuration at C-15 have been reported,[2)] the absolute stereostructure has not yet been resolved. The establishment of the absolute stereosrtucture of parguerane derivatives will serve to elucidate the problem between the structure and biological activity. We wish to describe here the structure of 2 including the absolute configuration.



1, $R_1 = R_3 = R_4 = Ac$, $R_2 = OAc$
2, $R_1 = R_2 = R_3 = R_4 = H$
3, $R_1 = Ac$, $R_2 = OH$, $R_3 = R_4 = H$
4, $R_1 = Ac$, $R_2 = R_3 = R_4 = H$

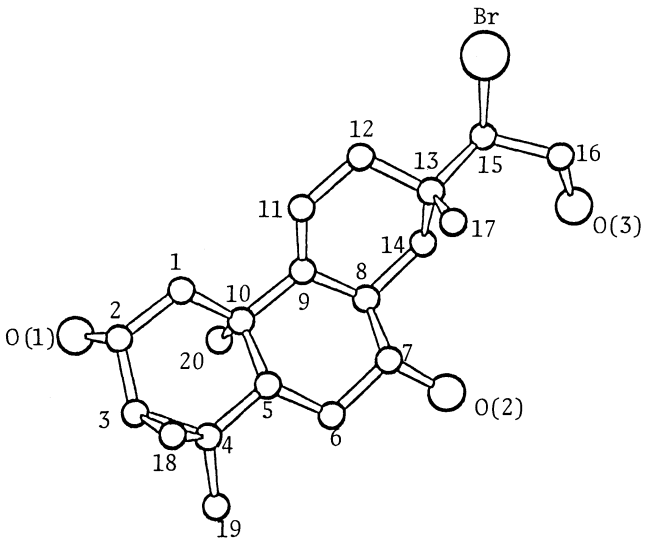


Fig. 1. Perspective view of 2.

Compound 2, mp 173-174 °C, $[\alpha]_D$ -36.4° (c 1.85, $CHCl_3$) was analyzed for $C_{20}H_{31}O_3Br$ [HR-MS: obsd 382.1348, calcd for $C_{20}H_{29}O_2{}^{81}Br$ (M^+-H_2O) 382.1331]. The spectral data[3] of 2 were found to be closely resemble to those of deoxyparguerol(4)[2a] except for the absence of signals due to an acetoxyl group in 4, indicating that the structure of compound 2 would be represented as formula 2. The confirmation of the structure 2 excluding the absolute configuration was performed by the acetylation of 2 with the usual method to afford a triacetate which was identical with the triacetate derived from 4 in all respects. In order to establish the absolute configuration, of 2, a single crystal of 2 (recrystallized from MeOH) was subjected to X-ray crystallographic analysis.

The crystal data of 2 were as follows: $C_{20}H_{31}O_3Br$, tetragonal, space group $P4_1$, a=b=9.796(6), c=38.34(3) Å, Z=8, D_c=1.44 g cm^{-3}. The intensities of 2214 independent reflections with $2\theta<47°$ were measured on a Rigaku four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation. The structure was solved by the direct method and was refined by the block-diagonal least-squares method. The final R value was 0.092. No hydrogen atoms were included for structure factor calculation. The absolute configuration was determined from 10 Friedel pair of reflections, collected on a Mac Science imaging phosphor plate DIP-100 using graphite-monochromated Cu $K\alpha$ radiation. The molecular skeleton with its absolute configuration of 2, is shown in Fig. 1.

It is noteworthy that 15-bromo-2-acetoxy-7,16-dihydroxy-9(11)-parguerene(4) displays cytotoxic properties,[2a] while the trihydroxy compound 2 is inactive, suggesting that the presence of an acetoxyl group at C-2 in the molecule is essential for biological activity.

References

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2) a) F. J. Schmitz, D. P. Michaud, and P. G. Schmidt, J. Am. Chem. Soc., 104, 6415, (1982); b) M. D. Higgs and D. J. Faulkner, Phytochemistry 21, 789, (1982).

3) Mp 173.0-174.0 °C (MeOH); $[\alpha]_D$ -36.4° (c 1.85, MeOH); IR ν_{max} (film), 3394, 1452, 1370, 1248, 1059, and 753 cm^{-1}; ^1H NMR (CD_3OD, 270 MHz), δ 0.02 (1H, dd, J=4.5, 6.0), 0.66 (1H, dd, J=4.5, 10.0), 0.85 (1H, dd, J=6.0, 10.0), 1.07, 1.11, 1.25 (each 3H, s), 3.10 (1H, ddd, J=4.5, 9.5, 10.5), 3.81 (1H, dd, J=9.5, 12.5), 4.05 (1H, dd, J=3.0, 12.5), 4.27 (1H, dd, J=3.0, 9.5), 4.29 (1H, br d, J≃5), and 5.43 (1H, ddd J=1.5, 1.5, 6.0); ^{13}C NMR (CD_3OD, 67.8 MHz), δ CH_3: 20.8, 23.9, and 24.8, CH_2: 22.6, 35.5, 39.3, 40.3, 42.3, and 65.0, CH: 27.5, 39.4, 48.1, 67.2, 67.9, 77.8, and 117.9, C: 18.4, 36.3, 38.5, and 145.6; MS, m/z 382, 380 (0.3:0.3, M^+-H_2O), 364, 362 (3.1:3.2), 349, 347 (2.3:2.6), 346, 344 (0.6:0.6), 331, 329 (1.5:1.5), 283 (10), 238 (19), 183 (18), 169 (18), 157 (24), 145 (20), 143 (23), 131 (26), 119 (27), 105 (44), 91 (41), and 44 (100).

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