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TWO NEW HALOGENATED SESQUITERPENES FROM THE RED ALGA LAURENCIA MAJUSCULA HARVEY (1)

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In the course of our continuing studies for constituents of the marine red alga genus Laurencia (Rhodomelaceae), we have recently reported (2) the structures of several halogenated and nonhalogenated aromatic sesquiterpenes from L. okamurai Yamada ("mitsudesozo" in Japanese) collected at Nyudogatane, Okino-shima, Tosa Prov., Japan. We collected L. majuscula Harvey ("akasozo") in the same location and investigated its essential oil. There are two new halogenated chamigrene-type sesquiterpenes as the major components in this alga and we report below the structures of these compounds.

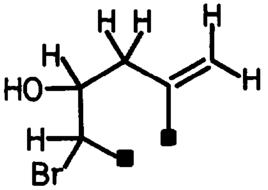
Half-dried algae (ca. 1.8 kg) (3) were extracted with methanol in the usual manner, and the neutral methanol extract (ca. 15 g) was fractionated by column chromatography on neutral alumina. Benzene eluates were rechromatographed over silica gel.

The fraction eluted with benzene gave a halogenated alcohol (1) (10% of neutral oil), $C_{15}H_{20}OBr_2$(m/e 378, 376, 374; M^+), $[\alpha]_D$ -4° (c 1.90; $CHCl_3$); uv, λ_{max}(EtOH) 243 nm (ε 22,000) and λ_{inf} 250 nm (ε 21,000); ir, ν_{max}(film) 3620, 3480, 3080, 1640, 1584, 1393, 1375, 1303, 1079, 1029, 971, 909, 889, 818 and 748 cm^{-1}; mass, m/e (rel. intensity) 378, 376, 374(2), 297, 295(5), 279, 277(16), 241(15), 239(21), 171(6), 131(7), 115(7), 91(30), 85(50), 69(100) and 55(25); cmr ($CDCl_3$), δ 143.2 (s), 137.1 (s), 136.3 (d), 126.9 (d), 117.7 (t), 101.4 (d), 71.9 (d), 70.1 (d), 51.9 (s), 42.8 (s), 37.9 (t), 27.4 (t), 26.6 (q), 26.3 (t) and 21.4 (q).

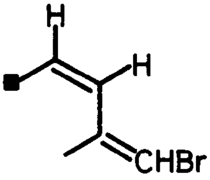
The fraction eluted with ether was further submitted to preparative thin layer chromatography on silica gel to give a halogenated ketone (2a) (20%), $C_{15}H_{19}OBr$ (m/e 296, 294; M^+), $[\alpha]_D$ +91° (c 1.71); uv, λ_{max} 240 nm (ε 30,000); ir, ν_{max}(film) 3070, 3030, 1665, 1615, 1585, 1391, 1381, 1327, 1303, 1270, 901 and 750 cm^{-1}; mass, m/e 296, 294(2), 240, 238(100), 159(70), 144(8), 141(9), 131(36), 115(13), 91(40) and 69(20).

Treatment of 1 with acetic anhydride and pyridine at room temperature yielded an acetate (3), $C_{17}H_{22}O_2Br_2$ (m/e 420, 418, 416; M^+), mp 113-114°, $[\alpha]_D$ -25° (c 1.41); ir, ν_{max}($CHCl_3$) 3085, 1740, 1643, 1587, 1397, 1369, 1305, 1245, 1040, 973, 958, 915, 883 and 820 cm^{-1}.

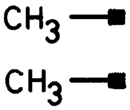
The avove-mentioned spectral data and the double resonance experiments (4) in the pmr spectra (table) of 1 and 3 suggested the presence of the partial structures A, B, C and D in 1.



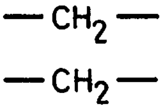
A



B



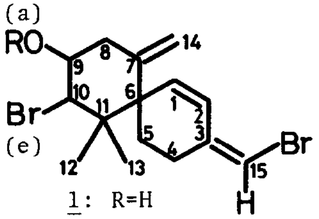
C



D

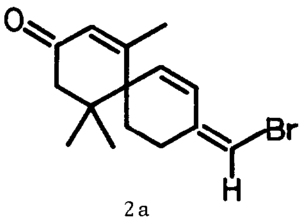
The cmr spectrum of 1 indicates the presence of the three double bonds and, hence, 1, having five degrees of unsaturation, must be a bicyclic alcohol. As is usually observed in the pmr spectra of 10-bromochamigrene derivatives from genus *Laurencia*, the bromine at C-10 in proximity to the *gem*-dimethyl group at C-11 results in a ca. 0.20 ppm shift to lower magnetic field of the more eclipsed methyl. Furthermore, in the cmr spectrum of 1, the peaks at 51.9 (s) and 42.8 (s), which are characteristic of halogenated chamigrene derivatives and assignable to C-6 and C-11, respectively, indicate the presence of a chamigrene-skeleton in 1. The coupling constants for the proton α to the bromine (C_{10}-H) (J=3 Hz in 1 and J=4 Hz in 3) indicate that the vicinal bromine and hydroxyl groups in 1 are *cis* configuration. The closely spaced multiplet ($W_{1/2}$=ca. 10 Hz) for the proton α to the hydroxyl (C_9-H) is consistent with axial OH at C-9 and therefore equatorial Br at C-10.

Jones oxidation of 1 gave a ketone (4), $C_{15}H_{18}OBr_2$ (m/e 376, 374, 372; M^+), mp 87-88°, $[\alpha]_D$ +39° (c 0.89); uv, λ_{max} 243 nm (ε 21,000); ir, $\nu_{max}(CHCl_3)$ 1740, 1630, 1585, 1395, 1380, 1305, 923, 911 and 861 cm^{-1}. The ir spectrum of 4 indicates the presence of equatorially α-brominated six-membered ring ketone (5).

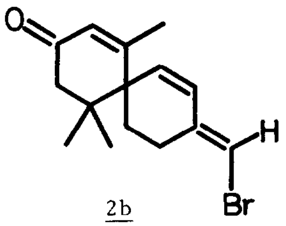


1: R=H

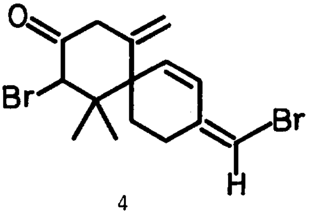
3: R=Ac



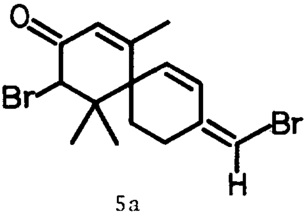
2a



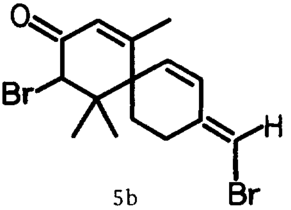
2b



4



5a



5b

TABLE

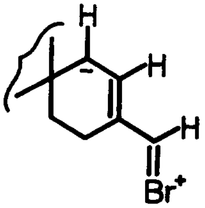
Nuclear Magnetic Resonance Data (100 MHz, δ-value; CCl_4)

Compound Carbon	1	3	4	5a	5b	2a	2b
1	6.61 d (J=10)	6.63 d (J=10)	6.71 d (J=10)	6.80 d (J=10)	6.39 d (J=10)	6.79 d (J=10)	6.38 d (J=10)
2	6.06 br d (J=10)	6.06 br d (J=10)	5.95 br d (J=10)	5.95 br d (J=10)	5.75 br d (J=10)	5.89 br d (J=10)	5.69 br d (J=10)
4	1.7- m	1.8- m	2.0- m	1.7- m	1.7- m	1.7- m	1.7- m
5	2.3	2.3	2.5	2.7	2.7	2.6	2.6
8	2.59 d (J=2)	2.45 m 2.72 m	3.31 s	5.90 br s	5.90 br s	5.77 br s	5.77 br s
9	4.09 m	5.18 m					
10	4.54 d (J=3)	4.45 d (J=4)	4.92 s	4.96 s	4.96 s	1.7- m 2.6	1.7- m 2.6
12	0.99 s	1.03 s	0.97 s	1.08 s	1.08 s	1.03 s	1.03 s
13	1.22 s	1.22 s	1.18 s	1.17 s	1.17 s	1.06 s	1.03 s
14	4.83 br s 5.11 br s	4.83 br s 5.03 br s	4.85 br s 5.08 br s	1.88 br s	1.88 br s	1.88 br s	1.88 br s
15	5.87 br s	5.88 br s	5.96 br s	6.00 br s	6.26 br s	5.97 br s	6.23 br s

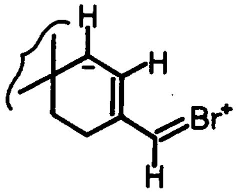
4 was unstable for light and spontaneously isomerized to a mixture of α,β-unsaturated ketones (5a) and (5b), and the latter isomer (5b) gradually increased with time. The more stable isomer (5b) showed the ir spectrum (ν_{max}(film) 3065, 3030, 1676, 1620, 1585, 1390, 1375, 1303, 1169, 885, 859 and 800 cm^{-1}) very similar to that of 5a except the signals due to a double bond group (ν_{max} 800 cm^{-1} in 5b and 760 cm^{-1} in 5a). In addition, in the pmr spectra (table) of 5a and 5b, the distinct difference was observed; e.g., in the spectrum of 5b, absorptions due to three olefinic protons appeared at δ 6.39 (d, J=10 Hz), 5.75 (br d, J=10 Hz) and 6.26 (br s) instead of absorptions at δ 6.80 (d, J=10 Hz), 5.95 (br d, J=10 Hz) and 6.00 (br s) in 5a.

Treatment of 3 with 5% methanolic KOH (5 min reflux) gave a ketonic mixture (2a) and (2b), one of which was identical with natural ketone (2a). Natural ketone (2a) was also isomerized to the more stable isomer (2b). In the ir and pmr spectra (table) of 2a and 2b, the distinct difference similar to that of 5a and 5b was observed.

The assignments of Z-configuration at C-3 and C-15 for 5a and 2a and E-configuration for 5b and 2b could be made as follows. In the pmr spectra of 5a, 5b, 2a and 2b, the signals of C_{15}-H in 5b and 2b appeared in 0.26 ppm lower field region than those in 5a and 2a. The substituent effects on the chemical shifts of ethylenic protons reveal that the ethylenic proton having a β-substituted cis-oriented double bond resonates in the lower magnetic field region than the one having a β-substituted trans-oriented double bond (6). Furthermore, the signals of C_2-H in 5a and 2a appeared in 0.20 ppm lower field region than those in 5b and 2b. These chemical shifts are due to the deshielding being caused by C_{15}-Br, which is situated close to C_2-H in 5a and 2a. The large upfield shifts were also observed for the signals of C_1-H, 0.41 ppm in 5b and 2b. Since it would be anticipated that the resonance structure (E) contributes more largely to the hybrid than the structure (F) because of a non-bonded interaction between the hydrogen at C-2 and the bromine at C-15 (7), the bromine at C-15 in E-form of 5b and 2b causes an addition in the electron density at δ-carbon atom (C-1) more than the bromine at C-15 in Z-form of 5a and 2a, and hence decreases the deshielding of the δ-proton (C_1-H) in 5b and 2b.



E



F

Consequently, 1, 3 and 4 possess Z-configuration at C-3 and C-15 as well as 5a and 2a.

As described above, the structures of new halogenated sesquiterpenes (1) and (2a) from L. majuscula would be represented most favorably by formulae 1 and 2a, which are the second examples of halogenated chamigrene from the genus Laurencia with a halogen atom on a methyl group at C-15 (8).

References

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(2) M. Suzuki and E. Kurosawa, Tetrahedron Letters, 2503 (1978).
(3) Algae were collected at Nyudogatane, Okino-shima, Tosa Prov., Japan, early in June, 1977.
(4) Full details of NMDR experiments will be discussed in a full paper.
(5) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules", Methuen & Co. Ltd., London and John Wiley & Sons, Inc., New York, 1958, pg. 139.
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