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# NEW AROMATIC SESQUITERPENOIDS FROM THE RED ALGA LAURENCIA OKAMURAI YAMADA (1)

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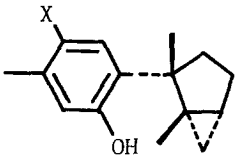
Many halogenated metabolites have been isolated from the marine red algae genus Laurencia (Rhodomelaceae), and various species of Laurencia are known to contain, although some overlap is noted, unique halogenated compounds (species-specific ?)(2).

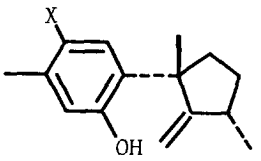
In connection with our interest in algal natural products we have examined the essential oils of the red algae L. okamurai Yamada collected from two different locations. Previously, we reported (3) the isolation of laurinterol (1a), debromolaurinterol (1b), aplysin (5a) and debromoaplysin (5b) as the major components and aplysinol (6) as the minor one, from L. okamurai collected in August at Hakata-shima, the Inland Sea of Japan. We collected L. okamurai early in June, 1977, at Nyudogatane, Okino-shima, Tosa Province, Japan, and examined. This alga displayed no aplysin, debromoaplysin and aplysinol, but instead yielded three new sesquiterpenes and several known sesquiterpenes, which have previously been described from other Laurencia species, together with laurinterol and debromolaurinterol. Reported below are the structures of these interesting new compounds.

Half-dried algae (ca. 700g) were extracted with methanol, and the methanol extract (ca. 10g), after separation of the acidic and basic components, was fractionated by column chromatography on neutral alumina; (i) hexane fraction, (ii) hexane-benzene fraction and (iii) benzene fraction.

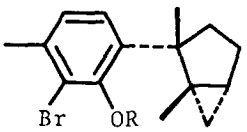
Sesquiterpene phenols. Benzene fraction (iii) gave laurinterol (1a) (30% of neutral oil) and debromolaurinterol (1b)(20%) along with isolaurinterol (2a)(0.5%) and debromoisolaurinterol (2b)(0.5%) (4). Hexane-benzene fraction (ii) was rechromatographed on silica gel. Benzene eluate consisted of a complex mixture of fatty acid methyl ester. Hexane eluate gave new halogenated phenol (3)(0.1%), designated as neolaurinterol, $C_{15}H_{19}OBr$ (m/e 296 and 294, $M^+$); m.p. 62-63°; $[\alpha]_D$ -14° (c 0.57; $CHCl_3$); $\nu_{max}(CHCl_3)$ 3580, 1607, 1190 and 1135 $cm^{-1}$; δ (100 MHz, $CCl_4$) ca. 0.5 (2H, m), ca. 1.1 (1H, m), 1.27, 1.37, 2.33 (each 3H, s), 5.64 (1H, s; $D_2O$ exchangeable), 6.61 (1H, d, J=8 Hz) and 7.28 (1H, d, J=8 Hz). The pmr spectrum of neolaurinterol (3) displayed the signals comparable to those of laurinterol (1a) except for in the lower magnetic field region (aromatic protons of 1a; each singlet at δ 6.42 and 7.47).



1a: X=Br
1b: X=H



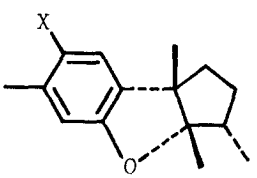
2a: X=Br
2b: X=H



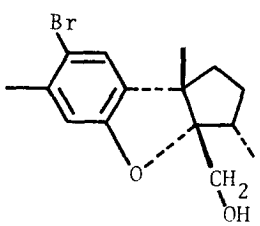
3: R=H
4: R=Ac

Treatment of 3 with acetic anhydride and pyridine at room temperature (overnight) afforded an acetate (4) in low yield (40%), whereas 1a was acetylated quantitatively under the same condition. The above-mentioned data indicates that the ortho-position of the hydroxyl group of 3 might be substituted by the bromine atom. Confirmation of the structure of 3 was obtained by the following reaction. Debromolaurinterol (1b) was treated with NBS in $CCl_4$ (5) at room temperature (1 hr) to yield a brominated product, $[\alpha]_D$ -17° (c 1.19), (70% yield), which was identical with natural 3 by the comparison of spectral data. Thus, neolaurinterol is represented by formula 3, including absolute stereochemistry.

Sesquiterpene ethers. Hexane fraction (i) was rechromatographed on silica gel. Earlier hexane eluates consisted of a mixture of hydrocarbons (vide infra) and successive eluates were further submitted to thin layer chromatography over silica gel to yield two new ether compounds. The less polar halogenated compound (7) (0.2%), designated as isoaplysin, $C_{15}H_{19}OBr$ (m/e 296 and 294, $M^+$), $[\alpha]_D$ -33° (c 0.69), had the following spectral characteristics; $\nu_{max}$(film) 1620, 1597, 1501, 1275, 1265, 950 and 802 $cm^{-1}$; δ 1.09 (3H, d, J=6 Hz), 1.50 (3H, s), 2.26 (3H, s), 3.55 (2H, s), 6.50 (1H, br. s), 6.58 (1H, br. d, J=8 Hz) and 6.82 (1H, d, J=8 Hz); m/e (relative intensity) 296, 294 (47), 281, 279 (7), 239, 237 (7), 215 (35), 201 (20), 199 (12), 173 (16), 159 (100), 145 (15), 135 (75), 121 (31), 115 (11), 107 (11) and 91 (12).



5a: X=Br
5b: X=H



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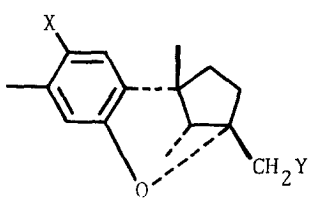
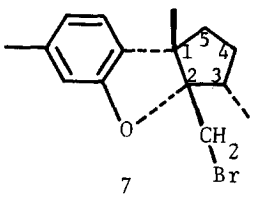


9a: X=Br, Y=H
9b: X=Br, Y=OH
9c: X=H , Y=Br



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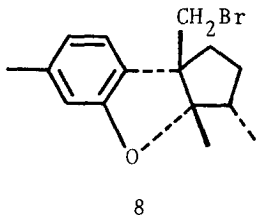

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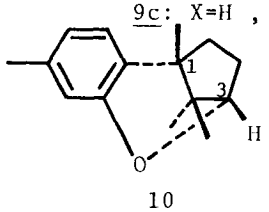

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TABLE

$^{13}C$ nmr shifts (δ, ppm downfield from $(CH_3)_4Si$, $CDCl_3$)

| Compound Carbon | 5b | 7 | 9a | 9b | 9c | 10 |
|---|---|---|---|---|---|---|
| | 158.8(s) | 158.7(s) | 152.3(s) | 151.6(s) | 152.3(s) | 152.4(s) |
| | 137.7(s) | 138.2(s) | 136.4(s) | 136.5(s) | 137.4(s) | 137.0(s) |
| | 133.3(s) | 132.9(s) | 130.1(s) | 130.3(s) | 127.7(s) | 130.5(s) |
| | 122.5(d) | 122.1(d) | 128.4(d) | 128.6(d) | 124.7(d) | 124.0(d) |
| | 120.6(d) | 121.4(d) | 117.4(d) | 117.5(d) | 121.2(d) | 120.6(d) |
| | 109.3(d) | 109.3(d) | 114.4(s) | 114.9(s) | 115.8(d) | 115.8(d) |
| C-2 | 98.8(s) | 97.1(s) | 46.4(d) | 43.1(d) | 44.3(d) | 41.0(s) |
| C-1 | 54.0(s) | 55.5(s) | 44.9(s) | 44.9(s) | 45.1(s) | 45.7(s) |
| C-3 | 46.1(d) | 43.7(d) | 85.3(s) | 87.4(s) | 85.7(s) | 86.2(d) |
| C-5 | 42.6(t) | 42.6(t) | 42.2(t) | 41.8(t) | 41.8(t) | 41.4(t) |
| C-4 | 31.2(t) | 31.5(t) | 37.3(t) | 33.0(t) | 34.5(t) | 30.1(t) |
| | 23.5(q) | 34.5(t) | 23.0(q) | 66.0(t) | 36.4(t) | 21.0(q) |
| | 21.4(q) | 22.9(q) | 22.5(q) | 22.5(q) | 21.0(q) | 20.5(q) |
| | 20.0(q) | 21.5(q) | 20.4(q) | 20.0(q) | 20.5(q) | 18.2(q) |
| | 13.1(q) | 13.8(q) | 7.4(q) | 7.9(q) | 7.2(q) | 15.0(q) |

The pmr and cmr (table) spectra of 7 are very similar to those of debromoaplysin (5b). In the pmr spectra of 7 and 5b, however, the distinct difference was observed; e.g., in the spectrum of 5b, absorptions due to two tertiary methyls appeared at δ 1.21 and 1.27, instead of one tertiary methyl at δ 1.50 and two-proton singlet at δ 3.55 attributed to $BrCH_2$- group in the spectrum of 7, suggesting that the tertiary methyl group and the $BrCH_2$- group are in cis configuration to each other. Debromination of 7 with LAH in refluxing THF yielded a debromo ether, $[\alpha]_D$ -53° (c 0.15), which was identified as debromoaplysin (5b) by the comparison of spectral data. On the basis of the above data, two possible structures, 7 and 8, can be written for isoaplysin.

The choice in favour of structure 7 for isoaplysin was made with the aid of $^{13}C$ chemical shift. In the cmr spectra of 7 and 5b, the distinct difference, 2.4 ppm, was observed for the signals of C-3 appeared at 43.7 in 7 and 46.1 in 5b. The comparative upfield shifts were also observed for the signals of C-2 and C-4 in the cmr spectra of filiformin (9a) (6), filiforminol (9b) (6) and 9c (7). These upfield shifts were explained by the effects due to additional γ-substituents, and, consequently, the $BrCH_2$- group in 7 must be attached to C-2. The structure 7 for isoaplysin will also be explicable well from the biogenetic consideration, demonstrating that the presence of substituents has not been recognized on the benzylic methyl group at C-1 of this type of sesquiterpenes.

The polar nonhalogenated compound (10)(0.4%), $C_{15}H_{20}O$ (m/e 216, $M^+$), $[\alpha]_D$ -25° (c 0.68), exhibited in its spectra [$\nu_{max}$(film) 1620, 1578, 1505, 1397, 1379, 1247, 1160, 1039 and 808 $cm^{-1}$; δ 0.87, 0.96, 1.22, 2.20 (each 3H, s), 4.02 (1H, br. d), 6.40 (1H, br. s), 6.48 (1H, br. d, J=8 Hz) and 6.85 (1H, d, J=8 Hz); m/e 216 (100), 201 (75), 173 (71), 159 (40), 148 (80), 147 (30), 145 (20), 135 (22), 133 (18), 121 (17), 115 (11), 105 (10) and 91 (15)] the presence of three tertiary methyls, including gem-dimethyl group (cmr (table) 41.0 (s)), one of which was shifted to higher magnetic field by an anisotropic effect of the aromatic nucleus, and aromatic methyl and 2,5-disubstituted phenol ether group. In addition, the cmr spectrum of 10 indicates the presence of the aromatic ring and further no double bond, and, hence, the compound (10), having six degrees of unsaturation, must contain other two rings, one of which is the ether ring and the other may be a five-membered carbocyclic ring. Furthermore, in the cmr spectrum of 10, the peaks at 86.2 (d) and 45.7 (s), which are assignable to C-3 and C-1, respectively, are similar to those of (9a) (6) and (9b) (6) and 9c (7). This indicates that the ether oxygen is combined with C-3, having one proton. In view of the above-mentioned data and the standpoint of biogenesis, the structure of this ether compound would be represented as 10.

Sesquiterpene hydrocarbons. Repeated silica gel column and thin layer chromatography of the mixture of hydrocarbons yielded isolaurene (0.7%), α-bromocuparene (1%) and α-bromoisocuparene (0.3%), previously isolated from L. glandulifera Kützing and L. nipponica Yamada (8)(9).

## References

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