Six New Sesquiterpenoids from the Red Alga *Laurencia nipponica* Yamada[1)]

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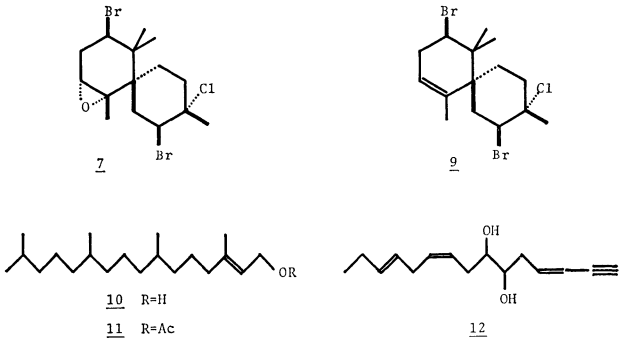
(Received October 1, 1981)

Six new laurane-type sesquiterpenoids were isolated from the red alga *Laurencia nipponica* Yamada and their structures were established on the basis of spectral and chemical evidence.

In the course of our investigation on the constituents from the red alga *L. nipponica* Yamada (Rhodophyta, Rhodomelaceae, Urasozo in Japanese), we have reported[2)] many halogenated or non-halogenated sesquiterpenoids and non-terpenoids consisting of C_{15}-straight carbon skeleton with terminal conjugated enyne or allene moiety. The diversity of terpenoids and non-terpenoids biosynthesis in this alga is found to be greatly dependent upon its growth localities. We wish to report here that this species, collected at Atsuta in the vicinity of Sapporo, Ishikari Bay, Hokkaido, produces six new sesquiterpenoids (**1**, **2**, **3**, **4**, **5**, and **6**) together with already chemically synthesized halochamigrene epoxide (**7**)[3)] as the major component (27% of the neutral essential oil) and the other four known compounds, laurene[4)] (**8**, 1.4%), halochamigrene[3,5)] (**9**, 2.0%), *trans*-phytol (**10**, 2.5%), and *trans*-phytol acetate[6)] (**11**, 0.8%) as the minor components. But surprisingly, this alga does not show the presence of C_{15} non-terpenoids, which are found to be biogenetically derived from laurediol (**12**)[2c)] and have been usually isolated as the major components (20—40%) from this species collected at the several different locations in Japan Sea, including Ishikari Bay.



Half-dried algae[7)] were extracted with methanol and the neutral fraction was obtained from the methanol extract by the usual method. Then the neutral fraction was subjected to separation on a combination of column chromatography over neutral alumina and HPLC to give six new terpenoids (**1**, **2**, **3**, **4**, **5**, and **6**) and five known compounds (**7**, **8**, **9**, **10**, and **11**). Five known compounds were identified by the comparison of IR, ^1H and ^{13}C NMR spectra and the optical rotation with those of the authentic specimens.

The Structure of Isodihydrolaurene (1).[8)] Isodihydrolaurene (**1**); colorless oil, $C_{15}H_{22}$ *m/e* 202 (M^+), $[\alpha]_D$ +33.5° (*c* 1.24, $CHCl_3$), λ_{max}^{EtOH} 205 nm (ε 4,000); had characteristic IR bands at 1655 and 875 cm^{-1} due to an exocyclic methylene group, and it was further supported by ^1H and ^{13}C NMR spectra at δ 4.70 (1H, br.s), 4.77 (1H, br.s), and 105.3 (t). Moreover, the NMR spectra showed signals due to a secondary methyl at δ 0.76 (3H, d, J=7 Hz), a tertiary methyl at 0.98 (3H, s), an olefinic methyl at 1.63 (3H, br.s) and two olefinic protons at 5.34 (2H, m), and 117.8 (d) and 118.8 (d). Treatment of **1** with DDQ in refluxing dioxane resulted in quantitative aromatization to give laurene (**8**), which was identified by the comparison of IR, ^1H and ^{13}C NMR spectra and the optical rotation with those of the authentic specimen. Since the UV spectrum of **1** did not exhibit an absorption due to 1,3-cyclohexadiene moiety,[9)] the

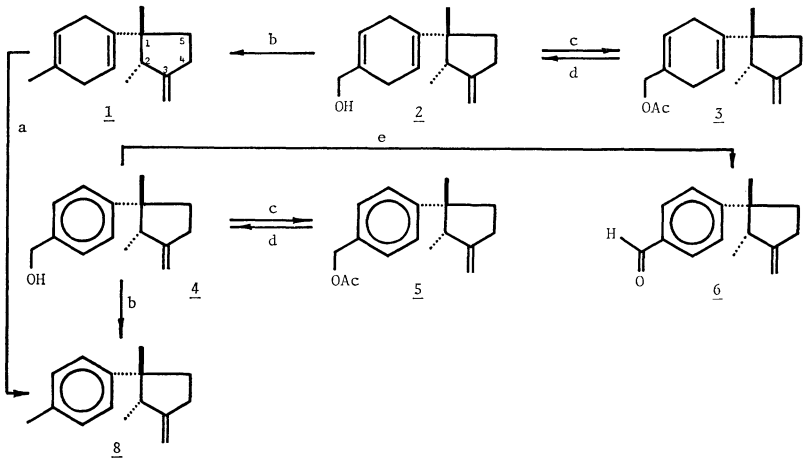


Fig. 1. a) DDQ-dioxane, reflux 80 min; b) 1) MsCl-Et_3N, 0 °C, 1 h; 2) $LiAlH_4$-THF, reflux 0.5 h; c) Ac_2O-Py, room temp, 18 h; d) K_2CO_3-MeOH, room temp, 1.5 h; e) CrO_3-2Py, CH_2Cl_2, room temp, 5 min.

structure of isodihydrolaurene, including the absolute configuration, should be represented by the formula **1**.

The Structures of Isodihydrolaurenol (2) and Isodihydrolaurenol Acetate (3). The ^{1}H NMR spectrum of **2** was almost identical with that of **1** except for an olefinic methyl at δ 1.63 in **1** and, instead of it, showed signals due to a hydroxymethyl group at 2.26 (1H, br.s, -OH) and 3.85 (2H, br.s, $-CH_2OH$). The structure of **2** was confirmed by the chemical correlation with **1**. When alcohol (**2**) was treated with MsCl and Et_3N in CH_2Cl_2 followed by reduction with LAH, **2** was converted to **1**. The spectral evidence and chemical correlation reaction defined the structure of isodihydrolaurenol as shown in the formula **2**. Moreover acetylation of **2** with acetic anhydride and pyridine generated the natural product (**3**) in quantitative yield.

The Structures of Laurenol (4) and Laurenol Acetate (5). Laurenol (**4**); colorless oil, $[\alpha]_D$ +34.7° (*c* 0.26, $CHCl_3$), $C_{15}H_{20}O$ *m/e* 216 (M^+), λ_{max}^{EtOH} 257 nm (ε 290), ν_{max}^{film} 3340 cm^{-1}; showed in ^{1}H NMR spectrum signals due to a secondary methyl at δ 0.67 (3H, d, J=7 Hz), a tertiary methyl at 1.23 (3H, s), a hydroxymethyl at 4.44 (2H, s), an exocyclic methylene at 4.77 (2H, br.s) and four aromatic protons at 7.05 (4H, br.s), and the signals were found to be well corresponding with the structure **4**. The structure of **4** was further confirmed by chemical correlation with **8** as shown in Fig. 1. The structure of **5** was established by acetylation of **4** with acetic anhydride in pyridine.

The Structure of Laurenal (6). Laurenal; colorless oil, $[\alpha]_D$ +33.2° (*c* 0.23, $CHCl_3$), $C_{15}H_{18}O$ *m/e* 214 (M^+), λ_{max}^{EtOH} 258 (ε 12700) and 205 nm (17500), ν_{max}^{film} 2820, 2730, and 1700 cm^{-1}; exhibited the presence of an aromatic aldehyde group in ^{1}H NMR at δ 9.88 (1H, s), IR and UV spectra. Collins oxidation[10] of **4** gave an aldehyde in 85% yield, whose spectral data and the optical rotation were identical with those of natural aldehyde (**6**).

Experimental

The IR and UV spectra were recorded on a JASCO model A-102 and Hitachi model 134 spectrophotometers, respectively. The ^{1}H NMR spectra were determined using a JEOL JNM-PS-100 spectrometer in CCl_4 solution with TMS as an internal standard and the ^{13}C NMR spectra were obtained with a Bruker SXP4-100 spectrometer in $CDCl_3$. A JASCO model DIP-SL was used for the measurement of the optical rotation in $CHCl_3$. Alumina (Merck, activity II—III) and silica gel (Merck, Kieselgel 60) were used for the column chromatography and HPLC was performed on a JASCO Finpac SIL-C_{18}.

Isolation. Half-dried algae (4.6 kg), collected at Atsuta in Ishikari Bay, Hokkaido, in July 1980, were extracted with 10 L of methanol for two weeks and the methanol solution was concentrated to about 1.5 L under reduced pressure and the residue was percolated with ether. The ether solution was shaken with 5% NaOH for removing acidic part and then dried over anhydrous Na_2SO_4. After evaporation of solvent, the dark greenish neutral oil (52 g) was obtained and then subjected to column chromatography over neutral alumina. The fraction eluted with hexane gave pure laurene (**8**, 1.4% of the neutral fraction) and halochamigrene (**9**, 2.0%), and crude isodihydrolaurene (**1**), and the last was further purified on HPLC with CH_3CN–H_2O (95:5) to give the pure material of **1** (2.5%). The fraction eluted with hexane–benzene (1:1) yielded halochamigrene epoxide (**7**, 27%). The fraction eluted with benzene–ethyl acetate (10:1) was further subjected to HPLC with MeOH–H_2O (80:20) to give isodihydrolaurenol (**2**, 0.51%), isodihydrolaurenol acetate (**3**, 0.2%), laurenol (**4**, 0.51%), laurenol acetate (**5**, 0.2%), laurenal (**6**, 0.03%), *trans*-phytol (**10**, 2.5%), and *trans*-phytol acetate (**11**, 0.8%).

Isodihydrolaurene (1). Colorless oil; $[\alpha]_D$ +33.5° (*c* 1.24, $CHCl_3$); λ_{max}^{EtOH} 205 nm (ε 4000); ν_{max}^{film} 3070, 3020, 1655, 1370, 1165, 1090, 1020, 950, 875, and 775 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.76 (3H, d, J=7 Hz), 0.98 (3H, s), 1.39 (1H, ddd, J=11, 6, 6, α-H on C-5), 1.63 (3H, br.s), 1.8—2.5 (3H), 2.19 (1H, br.q, J=7), *ca.* 2.5 (4H, m), 4.70 (1H, br.s), 4.77 (1H, br.s), and 5.34 (2H, m, W_H=9); ^{13}C NMR ($CDCl_3$) δ 17.5 (q), 22.8 (q), 25.8 (q), 27.4 (t), 28.6 (t), 31.8 (t), 32.8 (t), 48.8 (d), 49.5 (s), 105.3 (t), 117.8 (d), 118.8 (d), 130.9 (s), 139.2 (s), and 157.9 (s). Found: *m/e* 202.1714. Calcd for $C_{15}H_{22}$: M, 202.1719.

Isodihydrolaurenol (2). Colorless oil; $[\alpha]_D$ +40.0° (*c* 1.52, $CHCl_3$); λ_{max}^{EtOH} 205 nm (ε 6000); ν_{max}^{film} 3300, 3070, 3020, 1690, 1655, 1425, 1370, 1095, 1055, 1030, 1005, 960, 880, 810, 785, and 755 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.77 (3H, d, J=7 Hz), 0.99 (3H, s), 1.42 (1H, ddd, J=12.5, 5.5, 5.5), 1.8—2.6 (4H), 2.26 (1H, br.s, -OH), 2.62 (4H, m), 3.85 (2H, br.s, $-CH_2OH$), 4.73, 4.78, 5.42, and 5.59 (1H each, br.s). Found: *m/e* 218.1643. Calcd for $C_{15}H_{22}O$: M, 218.1668.

Isodihydrolaurenol Acetate (3). Colorless oil; $[\alpha]_D$ +40.0° (*c* 0.21, $CHCl_3$); λ_{max}^{EtOH} 206 nm (ε 9700); ν_{max}^{film} 3080, 3030, 1740, 1655, 1370, 1245, 1230, 1025, 960, 887, and 802 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.77 (3H, d, J=7 Hz), 0.99 (3H, s), 1.43 (1H, ddd, J=12, 5, 5), 1.9—2.6 (3H), 1.97 (3H, s), 2.13 (1H, br.q, J=7), 2.65 (4H, m), 4.37 (2H, br.s), 4.71, 4.78, 5.39 and 5.66 (1H each, br.s). Found: *m/e* 260.1782. Calcd for $C_{17}H_{24}O_2$: M, 260.1776.

Laurenol (4). Colorless oil; $[\alpha]_D$ +34.7° (*c* 0.26, $CHCl_3$); λ_{max}^{EtOH} 257 (ε 290), 263 (ε 330) and 272 nm (ε 230); ν_{max}^{film} 3340, 3060, 3020, 1655, 1615, 1515, 1415, 1370, 1030, 1020, 880, 840, 815 and 805 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.67 (3H, d, J=7 Hz), 1.23 (3H, s), 1.6—2.6 (5H), 2.06 (1H, br.s, -OH), 4.44 (2H, s, $-CH_2OH$), 4.77 (2H, br.s), and 7.05 (4H, br.s). Found: *m/e* 216.1496. Calcd for $C_{15}H_{20}O$: M, 216.1511.

Laurenol Acetate (5). Colorless oil; $[\alpha]_D$ +23.6° (*c* 0.42, $CHCl_3$); λ_{max}^{EtOH} 255 (ε 300), 261 (ε 330), 267 (ε 270), and 271 nm (ε 200); ν_{max}^{film} 3070, 3020, 1740, 1655, 1615, 1515, 1430, 1375, 1360, 1225, 1075, 1030, 1020, 965, 880, 825, and 815 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.69 (3H, d, J=7 Hz), 1.26 (3H, s), 1.6—2.6 (5H), 2.00 (3H, s), 4.81 (2H, br.s), 4.94 (2H, s), and 7.12 (4H, br.s). Found: *m/e* 258.1626. Calcd for $C_{17}H_{22}O_2$: M, 258.1620.

Laurenal (6). Colorless oil; $[\alpha]_D$ +33.2° (*c* 0.23, $CHCl_3$); λ_{max}^{EtOH} 258 (ε 12700) and 205 nm (ε 17500); ν_{max}^{film} 3070, 3030, 2820, 2730, 1700, 1655, 1605, 1570, 1415, 1385, 1370, 1310, 1215, 1175, 1075, 1015, 880, and 825 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.69 (3H, d, J=7 Hz), 1.28 (3H, s), 1.8—2.8 (5H), 4.85 (2H, m), 7.29 (2H, br.d, J=8), 7.71 (2H, br.d, J=8) and 9.88 (1H, s). Found: *m/e* 214.1371. Calcd for $C_{15}H_{18}O$: M, 214.1358.

Aromatization of 1. A mixture of **1** (16 mg) and DDQ (24 mg) in freshly distilled dioxane (2 ml) was refluxed under nitrogen atmosphere. After cooling, the resulting

suspension was filtered through a column of neutral alumina (2 g) and eluted with hexane to give colorless oil (15 mg), whose spectral data and optical rotation were identical with those of the authentic specimen of laurene (**8**).[4]

*Conversion of Isodihydrolaurenol (**2**) into **1**.* To a cooling solution of **2** (10 mg) in dry CH_2Cl_2 containing dry Et_3N (10 μl) was gradually added distilled MsCl (5 μl). The mixture was stirred for 1 h at 0 °C, and then poured into ice water. Ether-extract was successively washed with 1 M HCl, 5% $NaHCO_3$, and brine, and then dried over anhydrous Na_2SO_4. After evaporation of the solvent, the resulting crude mesylate (12 mg), colorless oil, was reduced with LAH (20 mg) in refluxing THF (1 ml) for 0.5 h under nitrogen atmosphere. Ice was added to the cooled solution at 0 °C to decompose the excess of LAH. After the usual work-up, the resulting oily material was purified by column chromatography over silicic acid to give pure **1** (9 mg).

*Acetylation of **2**.* A solution of **2** (20 mg) in acetic anhydride (0.2 ml) and pyridine (0.2 ml) was allowed to stand overnight at room temperature and then worked up in the usual way to give monoacetate (**3**) (22 mg).

*Transformation of **4** into **8**.* To a cooling solution of **4** (12 mg) in dry CH_2Cl_2 (0.3 ml) containing dry Et_3N (10 μl) at 0 °C was gradually added distilled MsCl (6 μl) and stirred for 1 h at 0 °C. The reaction mixture was poured into ice–water and extracted with ether. After the usual work-up, the resulting crude mesylate (17 mg) was treated with LAH (20 mg) in refluxing THF (1 ml) for 0.5 h under nitrogen atmosphere. After usual manner for separation, the resulting oily material was chromatographed over silicic acid to give hydrocarbon (**8**) (11 mg).

*Acetylation of **4**.* Acetylation of **4** (20 mg) was carried out in the same manner as that of **2** to give **5** (22 mg).

*Collins Oxidation of **4** into **6**.* Dry CrO_3 (15 mg) was added to the solution of dry CH_2Cl_2 (0.5 ml) and dry pyridine (23 μl) in a dried two necked flask and the mixture was stirred at room temperature under nitrogen atmosphere for 5 min. Then a solution of **4** (6 mg) in dry CH_2Cl_2 (0.25 ml) was added to the resulting burgundy colored solution and it was stirred for an additional 5 min. After addition of ether, filtration and washing with ether, the ethereal solution was shaken with 5% $NaHCO_3$ and dried over anhydrous Na_2SO_4. After removal of the solvent, the oily substance (5 mg) was obtained, whose spectral data and the optical rotation were identical with those of natural aldehyde (**6**).

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