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Epilaurallene, a New Nonterpenoid C_{15}-Bromoallene from the Red Alga *Laurencia nipponica* Yamada[1]

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A new halogenated nonterpenoid C_{15}-compound, epilaurallene, has been isolated as a major constituent from the title alga along with several known compounds, and its structure was determined by the spectral and chemical methods. Epilaurallene is an epimer at C-4 of laurallene and was shown to possess *S*-configuration at C-4.

Within the Japanese species of genus *Laurencia* (Rhodomelaceae), *L. okamurai* Yamada (Mitsude-sozo) collected at various locations have contained laurinterol and debromolaurinterol as the characteristic major metabolites of this species.[2,3] On the other hand, *L. nipponica* Yamada (Ura-sozo) have produced diverse terpenic and nonterpenic C_{15}-metabolites which seem to be mainly dependent upon the growth locality.[4] As part of further studies on the constituents of *L. nipponica*, we examined a specimen collected at Tsukotan, near Oshoro Bay, Hokkaido, and isolated a new nonterpenoid C_{15}-bromoallene, designated as epilaurallene, as a major component. In this paper we describe the isolation and structural elucidation of this compound in full details.

Neutral methanol extracts obtained by the usual methods were submitted to repeated column and thin-layer chromatography to yield epilaurallene (**1**) together with known compounds, 10-bromo-α-chamigrene,[5] laurene,[6] (*E*)-γ-bisabolene 8,9-oxide,[7] cycloeudesmol,[8] (3*E*)-isolaureatin (T-laureatin),[9] isolaureatin,[10] and laureatin.[10]

Epilaurallene (**1**), $C_{15}H_{20}O_2Br_2$ (*m*/*e* 313 and 311; M^+-Br), $[\alpha]_D^{25}$ +175° (*c* 1.00), mp 51—52 °C, showed the very similar IR ($CHCl_3$), ^1H NMR (200 MHz), and mass spectra to those of laurallene (**2**), which has previously been isolated from *L. nipponica* collected at Oshoro Bay and whose structure has been determined as **2** excluding the stereochemistry of C-4 and bromoallene moiety.[11] However, the IR spectra of **1** and **2** in Nujol mulls were clearly distinguishable as shown in Fig. 1. Mixed mp of **1** and **2** revealed no depression, and instead higher mp (56—58 °C) than that of each compound. Furthermore, in the ^{13}C NMR spectra of **1** (Table 1) and **2**,[12] fourteen of the fifteen carbon atoms showed the same chemical shifts while the remaining one carbon, which was assigned to C-4 by proton selective decoupling experiment, revealed the different chemical shift by 0.029 ppm. Above-mentioned data suggest that epilaurallene (**1**) would be an epimer at C-4 of laurallene (**2**). The structure of **1** was established by the following chemical reactions.

Hydrogenation of **1** with PtO_2 in ethanol gave two products, one of which was found to be identical with **3** previously derived from laurallene (**2**).[11] Another hydrogenated product **4**, $C_{15}H_{27}O_2Br$ (*m*/*e* 277 and 275; $M^+-C_3H_7$), showed almost identical spectra (IR and ^1H NMR) with those of **5** also derived from **2**.[11] Treatment of **4** with zinc in acetic acid and methanol

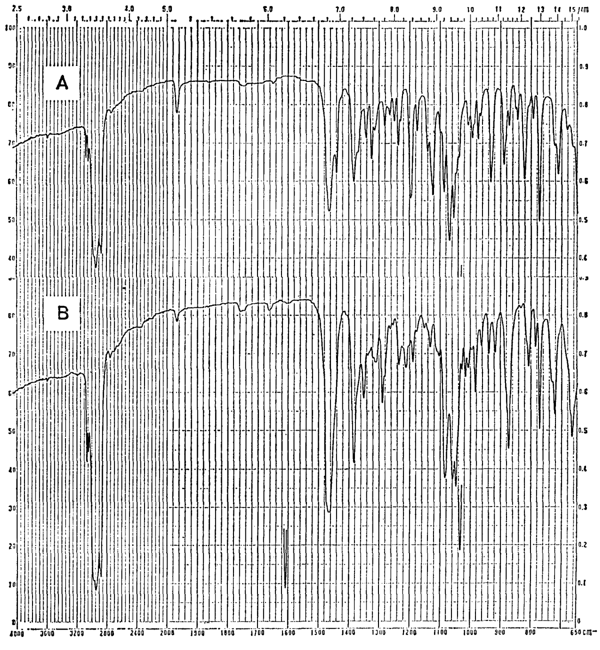


Fig. 1. IR (Nujol) spectra of (A) epilaurallene and (B) laurallene.

TABLE 1. ^{13}C NMR[a] DATA FOR EPILAURALLENE (**1**)

Carbon	δ[b]	Multiplicity
1	74.224	d
2	201.036	s
3	102.693	d
4	73.552	d
5	39.448	t
6	82.925[c]	d
7	79.830[c]	d
8	30.571[d]	t
9	129.469[e]	d
10	127.396[e]	d
11	29.374[d]	t
12	73.406[c]	d
13	57.960	d
14	28.148	t
15	11.241	q

a) Spectrum was recorded at 50.10 MHz. b) The δ values are in ppm downfield from TMS in $CDCl_3$. c) Assignments may be interconvertible. d), e) Assignments may be reversed.

afforded an unsaturated alcohol **6**, $C_{15}H_{28}O_2$ (*m/e* 240; M^+); ν_{max} 3400 and 970 cm^{-1}, δ 3.76 (1H, ddd, J=7, 7, and 3 Hz), 4.1—4.3 (2H, m), and 5.3—5.5 (2H, m), whose spectral data revealed the close resemblance to those of the reduction product **7** of **5**.[11] Compound **6**, when treated with carbon tetrabromide and triphenylphosphine in dry ether, gave a bromide **8**, $C_{15}H_{27}OBr$ (*m/e* 304 and 302; M^+); δ 3.7—4.1 (3H, m) and 5.2—5.5 (2H, m), whose IR spectrum indicated no hydroxyl absorption. Compound **8** was further subjected to Zn–AcOH–MeOH reduction followed by hydrogenation (PtO_2 in ethyl acetate) to yield 4-pentadecanol (**9a**), $C_{15}H_{32}O$ (*m/e* 210; M^+-H_2O), $[\alpha]^{25}_{589}$ +0.87° and $[\alpha]^{25}_{365}$ +3.55°, mp 43 °C; ν_{max} 3350 cm^{-1}, δ *ca.* 3.5 (1H, m). Acetylation of **9a** with acetic anhydride in pyridine gave the corresponding acetate **9b**, $C_{17}H_{34}O_2$ (*m/e* 227; $M^+-C_3H_7$), $[\alpha]^{25}_{589}$ +1.32° and $[\alpha]^{25}_{365}$ +4.25°; ν_{max} 1740 and 1240 cm^{-1}.

On the other hand, compound **3**, on treatment with Raney-Ni in ethanol and successive bromination with carbon tetrabromide and triphenylphosphine in ether, gave a bromide **10**, $C_{15}H_{29}OBr$ (*m/e* 306 and 304; M^+); ν_{max} 1132 and 1080 cm^{-1}, δ 3.3—3.9 (2H, m) and 4.14 (1H, ddd, J=10, 6, and 4 Hz). Moreover, treatment of **10** with zinc in acetic acid and methanol followed by hydrogenation (PtO_2 in ethyl acetate) afforded 4-pentadecanol (**11a**), $C_{15}H_{32}O$, mp 43—44 °C, $[\alpha]^{25}_{589}$ −0.74° and $[\alpha]^{25}_{365}$ −2.17°, which was further converted into the corresponding acetate **11b**, $C_{17}H_{34}O_2$, $[\alpha]^{25}_{589}$ −1.53° and $[\alpha]^{25}_{365}$ −5.60°. The IR, ^1H NMR, and mass spectra of **11a** and **11b** were identical with those of **9a** and **9b**, respectively. Mixed mp of **9a** and **11a** exhibited distinct depression (mp 38 °C).[13]

Since the (*R*)-configuration at C-12 in **3** is kept during the transformation procedure from **3** into **11a**, the configuration at C-4 in **11a** is *S*. Furthermore, 4-pentadecanol (**9a**) derived from **4** was apparently indicated to be an enantiomer of (*S*)-4-pentadecanol (**11a**) by comparison of the optical rotations of **9a**, **9b**, **11a**, and **11b** in different wavelength. Consequently, the stereochemistry at C-4 of epilaurallene (**1**) must be *S*-configuration, and hence the configuration at C-4 of laurallene (**2**) must be *R*.

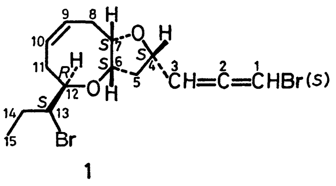
In view of the strong positive rotations of **1** and **2**, which are due to their bromoallene moieties, the absolute configuration of the allene moiety in **1** and **2** would be assigned as *S* by application of Lowe's rule.[14] Thus, the structure of epilaurallene should be represented by formula **1**.

The finding of epilaurallene (**1**) in *L. nipponica* collected at Tsukotan, near Oshoro Bay, prompted us to reinvestigate the metabolites of Oshoro's specimens which have previously contained laurallene (**2**) as the main component. Surprisingly, fresh algae (coll. at several locations in Oshoro Bay, in April and May, 1982) displayed the existence of epilaurallene (**1**) as a major metabolite and absence of laurallene (**2**). These results appear to suggest that the major secondary metabolite(s) of *L. nipponica* sometimes changes or interconverts in a few years (or every year (?)).[15]

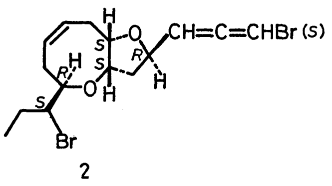
Experimental

All the melting points were uncorrected. The IR spectra were measured on a JASCO A-102 spectrometer. The ^1H NMR spectra were recorded on a JEOL FX-100 spectrophotometer, unless otherwise stated, TMS being used as an internal reference in $CDCl_3$. The ^{13}C NMR spectra were obtained with a JEOL FX-200 spectrophotometer in $CDCl_3$. The optical rotations were measured on a JASCO DIP-181 polarimeter in $CHCl_3$. Aluminium oxide (Merck, activity II-III) and silica gel (Merck, Kieselgel 60, 70—230 mesh) were used for column chromatography. Silica gel (Merck, Kieselgel GF_{254} (Type 60)) was used for preparative thin-layer chromatography. All known compounds were identified by comparison of the spectral data with those of the authentic specimens.

Isolation. *Laurencia nipponica* was collected in April, May, and June 1981, at Tsukotan, near Oshoro Bay,



1



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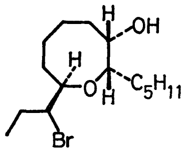

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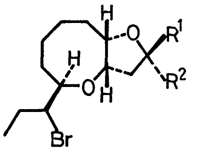
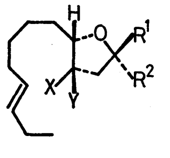


4: R^1=H, R^2=C_3H_7

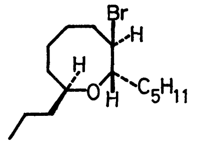
5: R^1=C_3H_7, R^2=H



6: R^1=Y=H, R^2=C_3H_7, X=OH

7: R^1=C_3H_7, R^2=Y=H, X=OH

8: R^1=X=H, R^2=C_3H_7, Y=Br



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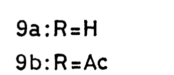
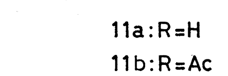


9a: R=H

9b: R=Ac



11a: R=H

11b: R=Ac

Hokkaido. The neutral methanol extracts (*ca.* 1% of the half-dried alga) obtained by the conventional methods were fractionated by column chromatography over alumina. The fraction eluted with hexane was chromatographed on silica-gel column to yield 10-bromo-α-chamigrene[5] (1% of the extracts) and laurene[6] (0.5%). The fraction eluted with benzene was repeatedly subjected to a combination of silica gel column and thin-layer chromatography to give a mixture of fatty acid esters (10%; main component, methyl palmitate), (3*E*)-isolaureatin[9] (1%), isolaureatin[10] (1%), laureatin[10] (3%), and (*E*)-γ-bisabolene 8,9-oxide[7] (2%). The fraction eluted with ether was further chromatographed on silica-gel column to yield epilaurallene (**1**) (25%), cycloeudesmol[8] (1%), and an unidentified alcohol (0.5%).

*Epilaurallene (**1**)*: Mp 51—52 °C (from hexane or MeOH); $[\alpha]^{25}_{D}$ +175° (*c* 1.00); IR (Nujol), ν_{max} 3060, 3025, 1959, 1190, 1120, 1085, 1065, 1053, 928, 818, 765, and 706 cm^{-1}; ^{1}H NMR (200 MHz), δ 1.09 (3H, t, *J*=7 Hz), 1.7—2.8 (8H, m), 4.0—4.2 (3H, m), 4.24 (1H, m), 4.85 (1H, m), 5.46 (1H, dd, *J*=5 and 5 Hz), 5.7—6.0 (2H, m), and 6.07 (1H, dd, *J*=5 and 2 Hz); MS, *m/e* (rel intensity) 313, 311 (2; M^+-Br), 275, 273 (58; $M^+-C_3H_2Br$), 193 (14; $M^+-C_3H_2Br-HBr$), 149 (9), 123 (15), 121 (15), 109 (31), 107 (75), 81 (30), 79 (100), 77 (38), 67 (69), 65 (29), 55 (56), and 41 (62).

Found: C, 45.94; H, 5.14; Br, 40.75%. Calcd for $C_{15}H_{20}O_2Br_2$: C, 45.88; H, 5.06; Br, 40.55%.

*Hydrogenation of **1**.* The hydrogenation of **1** (40 mg) was performed in EtOH over PtO_2-catalyst. After removal of the catalyst and the solvent, the residual oil was chromatographed on silica-gel column to give **3** (10 mg) and **4** (15 mg). The polar product **3**; colorless oil; $[\alpha]^{27}_{D}$ +11.1° (*c* 0.718); IR (film), ν_{max} 3450, 1285, 1213, 1128, 1107, 1090, 1053, 958, and 797 cm^{-1}; ^{1}H NMR, δ 0.89 (3H, br t, *J*=6 Hz), 1.06 (3H, t, *J*=7 Hz), and 3.5—4.1 (4H, m); MS, *m/e* 240 (1; M^+-HBr), 223, 221 (1), 199 (2), 141 (12), 123 (95), 83 (35), 81 (100), 67 (53), 55 (91), 44 (30), and 42 (50): These spectral data were consistent with those of one of the hydrogenation product **3** of laurallene (**2**).[11] The less polar product **4**; colorless oil; $[\alpha]^{27}_{D}$ +17.0° (*c* 1.17); IR (film), ν_{max} 1277, 1088, 1066, 920, and 795 cm^{-1}; ^{1}H NMR, δ 0.92 (3H, br t, *J*=6 Hz), 1.08 (3H, t, *J*=7 Hz), 3.6—4.2 (4H, m), and 4.35 (1H, m); MS, *m/e* 277, 275 (10; $M^+-C_3H_7$), 197 (68), 95 (35), 81 (53), 69 (43), 67 (21), 55 (92), 44 (31), and 42 (100).

*Conversion of **4** into **6**.* To a soln of **4** (96 mg) in MeOH (6 ml) containing 350 μl of acetic acid was added activated Zn-dust (350 mg), and the mixture was refluxed for 4 h. After cooling and filtering off Zn-dust, the mixture was extracted with ether. The ether soln was washed successively with water, 5% aqueous $NaHCO_3$, and water. After drying over Na_2SO_4, the solvent was removed to leave residual oil, which was purified by column chromatography on silica gel to afford **6** (72 mg); colorless oil; $[\alpha]^{25}_{D}$ +4.5° (*c* 1.57); IR, ν_{max} 3400, 1070, 1020, and 970 cm^{-1}; ^{1}H NMR, δ 0.93 (3H, br t, *J*=6 Hz), 0.96 (3H, t, *J*=7 Hz), 1.8—2.3 (4H, m), 3.76 (1H, ddd, *J*=7, 7, and 3 Hz), 4.1—4.3 (2H, m), and 5.3—5.5 (2H, m); MS, *m/e* 240 (3; M^+), 197 (4), 141 (4), 123 (13), 100 (12), 95 (14), 82 (86), 81 (39), 57 (100), 55 (53), and 42 (22).

*Conversion of **6** into **8**.* A soln of **6** (72 mg) in dry ether (8 ml) was refluxed with triphenylphosphine (160 mg) and carbon tetrabromide (200 mg) for 4 h in N_2 atmosphere and then cooled. The subsequent removal of the solvent gave a residual substance, which was purified by repeated column chromatography on alumina or silica gel to yield **8** (45 mg); colorless oil; $[\alpha]^{25}_{D}$ −8.6° (*c* 1.09); IR (film), ν_{max} 1091, 1028, and 977 cm^{-1}; ^{1}H NMR, δ 0.93 (3H, br t, *J*=6 Hz), 0.96 (3H, t, *J*=7 Hz), 1.8—2.2 (4H, m), 3.7—4.1 (3H, m), and 5.2—5.5 (2H, m); MS, *m/e* 304, 302 (1; M^+), 261, 259 (1), 223 (17), 135 (18), 95 (56), 81 (53), 69 (71), 67 (56), 55 (95), and 42 (100).

*4-Pentadecanol (**9a**) from **8**.* To a soln of **8** (45 mg) in MeOH (4 ml) containing 250 μl of acetic acid was added activated Zn-dust (300 mg), and the mixture was refluxed for 3 h. After being cooled and then filtered off, the mixture was extracted with ether. The ether soln was worked up as usual to give an oily residue, which was chromatographed on silica-gel column to yield an unsaturated alcohol (23 mg); colorless oil, IR (film), ν_{max} 3350, 1260, 1020, and 967 cm^{-1}; ^{1}H NMR, δ 0.93 (3H, br t, *J*=6 Hz), 0.96 (3H, t, *J*=7 Hz), *ca.* 3.5 (1H, m), and 5.2—5.6 (4H, m); MS, *m/e* 224 (0.2; M^+), 206 (1), 110 (33), 96 (26), 82 (34), 81 (34), 68 (48), 67 (50), and 55 (100). The hydrogenation of the unsaturated alcohol was carried out in ethyl acetate over PtO_2-catalyst. After removal of the catalyst and the solvent, the product was purified by column chromatography on silica gel to give **9a** (18 mg); colorless crystals; mp 43 °C; $[\alpha]^{25}_{D}$ +0.87° (*c* 1.87), $[\alpha]^{25}_{577}$ +1.04°, $[\alpha]^{25}_{546}$ +1.25°, $[\alpha]^{25}_{435}$ +2.30°, and $[\alpha]^{25}_{365}$ +3.55°; IR (Nujol), ν_{max} 3350 cm^{-1}; ^{1}H NMR, δ 0.8—1.0 (6H) and *ca.* 3.5 (1H, m); MS, *m/e* 210 (2; M^+-H_2O), 185 (19; $M^+-C_3H_7$), 97 (34), 73 (100; $M^+-C_{11}H_{23}$), and 55 (91).

*Acetylation of **9a**.* Acetylation of **9a** (15 mg) was carried out with acetic anhydride in pyridine in the usual manner. The acetylated product was purified by column chromatography on silica gel to give **9b** (13 mg); colorless oil; $[\alpha]^{25}_{D}$ +1.32° (*c* 1.06) and $[\alpha]^{25}_{365}$ +4.25°; IR (film), ν_{max} 1740, 1240, and 1020 cm^{-1}; ^{1}H NMR, δ 0.8—1.0 (6H), 2.04 (3H, s), and 4.88 (1H, dddd, *J*=6, 6, 6, and 6 Hz); MS, *m/e* 227 (1; $M^+-C_3H_7$), 210 (2; M^+-CH_3COOH), 115 (7; $M^+-C_{11}H_{23}$), 97 (5), 83 (4), 69 (4), 55 (6), and 43 (100).

*Conversion of **3** into **10**.* To a soln of **3** (110 mg) in EtOH (15 ml) was added freshly prepared W-7 Raney nickel (from 1.5 g of Al–Ni alloy) and then 2 M KOH (1 ml), and the mixture was refluxed for 2 h. After removal of the catalyst, water was added and the most of the solvent was evaporated under reduced pressure. The residue was extracted with ether, and the ether soln was washed with water, dried over Na_2SO_4, and evaporated to leave the debromo alcohol (78 mg); IR (film), ν_{max} 3420, 1125, 1075, 1046, 1012, and 948 cm^{-1}; ^{1}H NMR, δ 0.8—1.0 (6H) and 3.4—3.8 (3H, m); MS, *m/e* 242 (3; M^+), 82 (100), 57 (59), and 55 (56). Bromination of the above debromo alcohol (150 mg) was performed with triphenylphosphine (300 mg) and carbon tetrabromide (400 mg) in dry ether (10 ml) under the similar reaction conditions in the case of **6** to give **10** (105 mg); colorless oil; $[\alpha]^{27}_{D}$ −5.8° (*c* 0.24); IR (film), ν_{max} 1180, 1132, and 1080 cm^{-1}; ^{1}H NMR, δ 0.9—1.0 (6H), 3.3—3.9 (2H, m), and 4.14 (1H, ddd, *J*=10, 6, and 4 Hz); MS, *m/e* 306, 304 (1; M^+), 263, 261 (1), 125 (27), 82 (80), 69 (94), 55 (100), and 42 (8).

*(S)-4-Pentadecanol (**11a**) from **10**.* To a soln of **10** (105 mg) in MeOH (6 ml) containing 350 μl of acetic acid was added activated Zn-dust (200 mg), and the mixture was refluxed for 2 h. After the usual work-up, the resulting unsaturated alcohol was hydrogenated, without further purification, with PtO_2 in ethyl acetate and then purified by column chromatography on silica gel to give **11a** (48 mg); colorless crystals; mp 43—44 °C; $[\alpha]^{25}_{D}$ −0.74° (*c* 3.33), $[\alpha]^{25}_{577}$ −0.78°, $[\alpha]^{25}_{546}$ −0.92°, $[\alpha]^{25}_{435}$ −1.75°, and $[\alpha]^{25}_{365}$ −2.17°; The spectral properties were identical with those of **9a**.

*Acetylation of **11a**.* Acetylation of **11a** (18 mg) was carried out with acetic anhydride in pyridine by the usual method to give **11b** (15 mg); colorless oil; $[\alpha]^{25}_{D}$ −1.53° (c 1.57) and $[\alpha]^{25}_{365}$ −5.60°; The spectral properties were identical with those of **9b**.

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14) G. Lowe, *Chem. Commun.*, **1965**, 411; In the case of isolaurallene[16)] and obtusallene-I,[17)] which reveal the strong negative rotations and were shown to possess *R*-configuration at the bromoallene moiety by X-ray diffraction analysis, Lowe's rule can well be applied in order to determine the absolute stereochemistry of the bromoallene.

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