(3*E*)-Laureatin and (3*E*)-Isolaureatin, Halogenated C-15 Non-Terpenoid Compounds from the Red Alga *Laurencia nipponica* Yamada[1)]

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Synopsis. (3*E*)-Laureatin and (3*E*)-isolaureatin have been isolated as major metabolites from the red alga *Laurencia nipponica* Yamada, and their structures were confirmed on the basis of spectral and chemical evidence.

In the course of our continuing studies on the constituents of the red marine algae of the genus *Laurencia* (family Rhodomelaceae), we have reported that *L. nipponica* Yamada ("Ura-sozo"), one of the Japanese species, displayed a marked variation in the major chemical components which seems to be mainly dependent upon the growth locality. The major metabolites from this species collected in the warm current region in Hokkaido are, with some exception,[2,3)] composed of halogenated C-15 non-terpenoids.[4)] As part of our investigations for this species, we have newly collected at several separate locations in Hokkaido and at two locations in Honshū, Oga (Akita Prefecture), and Shichigahama (Miyagi Prefecture). The specimens collected in Hokkaido, as anticipated, contained C-15 non-terpenoids as major metabolites. Laurencin (**1**),[4a)] laureatin (**2**),[4b)] and epilaurallene (**3**)[4c)] were obtained from the specimens of six collecting sites, single site, and two sites, respectively. The major metabolite of Oga's specimen was also C-15 non-terpenoid, laureatin (**2**). On the other hand, the Shichigahama's specimen contained (3*E*)-laureatin (**4**) and (3*E*)-isolaureatin (**5**) as major metabolites, which have previously been obtained as minor components from this species.[5)] We report here the isolation and structural confirmation of these compounds.

(3*E*)-Laureatin (**4**), $C_{15}H_{20}O_2Br_2$, showed the ^1H NMR spectrum very similar to that of laureatin (**2**),[4b)] which has previously been isolated from this species collected at Moheji, except for the signals due to acetylenic and olefinic protons. In the ^1H NMR spectrum of **4**, the signal due to the acetylenic proton was observed in upfield region (δ=2.84) compared with that (δ=3.13) in **2** and the coupling constant between the olefinic protons was 16 Hz. Above-mentioned data coupled with the close resemblance of the ^{13}C NMR spectra (Table 1) of **4** and **2** indicate that **4** is the geometric isomer of the double bond at C-3 of laureatin (**2**). Hydrogenation of **4** over platinum oxide in ethyl acetate gave the hexahydro derivative, $C_{15}H_{26}O_2Br_2$, which was identical with hexahydrolaureatin (**6**)[4b)] in all respects.

The ^1H and ^{13}C NMR (Table 1) spectra of (3*E*)-isolaureatin (**5**), $C_{15}H_{20}O_2Br_2$, again were very similar to those of isolaureatin (**7**),[4b)] an isomer of **2**, except for the signals due to the acetylenic and olefinic protons, thus indicating that **5** is also the geometric isomer of the double bond at C-3 of **7**. Confirmation of the structure of **5** was also obtained by hydrogenation reaction. Hydrogenation of **5** gave the same hexahydro derivative (**8**)[4b)] as that derived from **7**. Accordingly, the structures of (3*E*)-laureatin and (3*E*)-isolaureatin were established as formulae **4** and **5**, respectively.

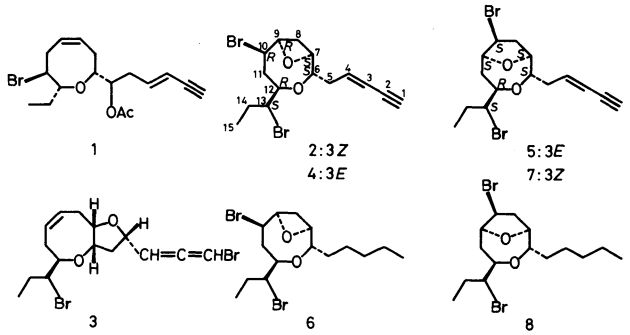

Table 1. ^{13}C NMR Chemical Shifts[a)] for **2**, **4**, **5**, and **7**

Carbon No.	2	4	5	7
1	82.6	77.2	76.6	82.2
2	79.6	81.5	81.6	79.7
3	110.7	111.7	111.5	110.4
4	141.5	141.2	141.6	141.5
5	40.8	41.1	34.4	34.7
6	75.7	76.9	75.2§	75.3‡
7	81.5#	80.7†	80.2	81.2
8	21.8	21.5	33.7	31.1
9	80.8#	80.5†	47.0	47.2
10	51.0	50.7	76.0§	75.7‡
11	29.2	31.8	33.7	33.3
12	73.2	73.4	72.2	71.9
13	65.2	64.5	62.3	63.1
14	28.9	28.3	27.9	28.4
15	12.6	12.7	12.8	12.8

a) Measured at 25.0 MHz in $CDCl_3$ (TMS=0).
#, †, §, ‡; Assignments may be reversed.

Experimental

The melting point was uncorrected. The IR spectra were recorded on a JASCO A-102 spectrophotometer and the UV spectra on a Shimadzu UV-240 spectrophotometer. The ^1H and ^{13}C NMR spectra were measured on a JEOL JNM-FX 100 spectrometer, using $CDCl_3$ as the solvent and tetramethylsilane as the internal standard. The low and high resolution mass spectra were obtained by a JEOL JMS-D300 spectrometer. Specific rotations were measured on a JASCO DIP-140 polarimeter in $CHCl_3$ unless otherwise stated. Aluminium oxide (Merck, activity II—III) and silica gel (Merck, Kieselgel 60, 70—230 mesh) were used for column chromatography. Silica gel 60 F_{254} (Merck) was used for preparative thin-layer chromatography. All known com-

pounds were identified by comparison of the spectral data with those of the authentic specimens.

Collection. Algae were collected in Hokkaido at Kabutosaki ('Kabutoiwa')[4a,6] (Oshoro Bay, near Otaru, May 7, 1982), Ebisuiwa (Oshoro Bay, May 7, 1982), Poromaisaki (Oshoro Bay, May 7, 1982), Bikuni (East Shakotan, June 30, 1982), Moiwa (Tomari, West Shakotan, June 30, 1982), Terugishi (West Shakotan, June 30, 1982), Raiden (near Iwanai, June 24, 1982), Sametorima (near Raiden, June 24, 1982), and Benkei Point (Suttsu, June 24, 1982). Furthermore, algae were collected in Honshū at Oga (Akita Prefecture, July 20, 1981) and Shichigahama (near Shiogama, Miyagi Prefecture, April 26, 1982).

Extraction and Isolation. Extraction and isolation were carried out by conventional methods as described in the case of Shichigahama's specimen. Major metabolites; laurencin (**1**): Kabutosaki (10% of the extract), Bikuni (13%), Terugishi (15%), Raiden (15%), Sametorima (10%), and Benkei Point (15%); laureatin (**2**): Moiwa (15%, isolaureatin 5%) and Oga (17%, isolaureatin 5%); epilaurallene (**3**): Ebisuiwa (20%) and Poromaisaki (13%, laurencin 5%).

Isolation of (3*E*)-Laureatin (4) and (3*E*)-Isolaureatin (5). Dried alga (150 g) collected at Shichigahama was extracted with methanol, and the methanol extract was treated with 10% aqueous Na_2CO_3 in the usual manner to give a neutral brown oil (3 g). The neutral oil (1.2 g) was chromatographed over alumina column. The earlier benzene fraction was further chromatographed over silica-gel column to yield crude (3*E*)-isolaureatin (**5**) (60 mg as a pale yellow oil) and (3*E*)-laureatin (**4**) (130 mg as crystals). The successive benzene fraction was subjected to repeated preparative TLC to afford prepacifenol (20 mg),[7] pacifenol (70 mg),[8] and diacetate of laurediol (20 mg).[5] Purification of **4** and **5** was performed by recrystallization and preparative TLC, respectively.

4: Mp 77—78 °C (methanol); $[\alpha]_D^{18}$ +36.6° (*c* 0.95); UV (ethanol), λ_{max} 224 nm (ε 16000) and λ_{inf} 215 (ε 13000) and 231 nm (ε 13000); IR ($CHCl_3$), ν_{max} 3310, 1285, 1140, 1085, 1045, 967, 947, 905, and 803 cm^{-1}: ^1H NMR (100 MHz), δ=1.08 (3H, t, *J*=7 Hz, H-15), 1.7—2.0 (2H, m, H-14), 2.4—3.1 (6H, m, H-5, H-8, and H-11), 2.84 (1H, d, *J*=2 Hz, H-1), 3.7—4.0 (2H, m, H-6 and H-13), 4.21 (1H, ddd, *J*=10, 7, 3 Hz, H-10), 4.45 (1H, ddd, *J*=5, 5, 4 Hz, H-12), 4.65 (1H, ddd, *J*=8, 5.5, 1.5 Hz, H-7), 4.97 (1H, ddd, *J*=8, 5.5, 3 Hz, H-9), 5.47 (1H, br dd, *J*=16, 2 Hz, H-3), and 6.18 (1H, ddd, *J*=16, 7, 7 Hz, H-4); ^{13}C NMR, in the Table 1; EI-MS (70 eV), *m/z* (rel intensity) 394, 392, 390 (0.2:0.4:0.2; M^+), 329, 327, 325 (0.6:1.3:0.7; $M^+-C_5H_5$), 313, 311 (0.9:0.8; M^+—Br), 247, 245 (21:22), 179, 177 (25:27), 165 (66), 149 (19), 147 (44), 119 (37), 107 (35), 105 (27), 93 (47), 91 (33), 81 (24), 79 (43), 77 (38), 71 (20), 69 (30), 67 (59), 65 (44), 57 (22), 55 (54), 53 (28), 44 (37), 43 (27), and 41 (100). Found: *m/z* 391.9815. Calcd for $C_{15}H_{20}O_2{}^{79}Br^{81}Br$: M, 391.9809.

5: Colorless oil; $[\alpha]_D^{15}$ −8.73° (*c* 1.11); UV (ethanol), λ_{max} 224 nm (ε 14000) and λ_{inf} 214 (ε 11000) and 232 nm (ε 11700); IR ($CHCl_3$), ν_{max} 3310, 2150, 1287, 1135, 1110, 963, 945, and 842 cm^{-1}; ^1H NMR (100 MHz), δ=1.07 (3H, t, *J*=7 Hz, H-15), 1.6—2.7 (8H, m, H-5, H-8, H-11, and H-14), 2.83 (1H, d, *J*=2 Hz, H-1), 3.56 (1H, dd, *J*=7, 7 Hz, H-6), 3.8—4.5 (5H, m, H-7, H-9, H-10, H-12, and H-13), 5.55 (1H, br dd, *J*=16, 2 Hz, H-3), and 6.23 (1H, ddd, *J*=16, 7, 7 Hz, H-4); ^{13}C NMR, in the Table 1; EI-MS, *m/z* 394, 392, 390 (0.5:0.9:0.4; M^+), 329, 327, 325 (0.4:0.9:0.5; $M^+-C_5H_5$), 313, 311 (1.6:1.6; M^+—Br), 247, 245 (45:47), 179, 177 (32:33), 165 (80), 149 (20), 147 (46), 119 (33), 109 (18), 107 (29), 105 (21), 95 (25), 93 (44), 91 (22), 81 (27), 79 (31), 77 (21), 69 (38), 68 (22), 67 (53), 65 (30), 55 (60), 53 (21), 43 (31), and 41 (100). Found: *m/z* 389.9847. Calcd for $C_{15}H_{20}O_2{}^{79}Br^{79}Br$: M, 389.9830.

Hydrogenation of (3*E*)-Laureatin (4). **4** (12 mg) was hydrogenated in ethyl acetate over PtO_2-catalyst to give **6** (10 mg); oil; $[\alpha]_D^{20}$ +26.5° (*c* 1.00) and $[\alpha]_D^{18}$ +28.3° (*c* 0.78, CCl_4); whose spectral data were consistent with those of hexahydrolaureatin (**6**)[4b] derived from laureatin (**2**).

Hydrogenation of (3*E*)-Isolaureatin (5). **5** (9 mg) was hydrogenated in ethyl acetate over PtO_2-catalyst to yield **8** (9 mg); oil; $[\alpha]_D^{18}$ +5.79° (*c* 0.97) and $[\alpha]_D^{19}$ −0.62° (*c* 0.69, CCl_4); whose spectral data were identical with those of hexahydroisolaureatin (**8**)[4b] derived from isolaureatin (**7**).

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