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A C-15 NON-TERPENOID FROM THE RED ALGA *LAURENCIA OKAMURAI**

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Key Word Index—*Laurencia okamurai*; Rhodomelaceae; red alga; C-15 non-terpenoid; aromatic sesquiterpene; halochamigrene derivative.

Abstract—The structure of a new C-15 bromoallene from the red alga *Laurencia okamurai* was deduced by spectral methods.

INTRODUCTION

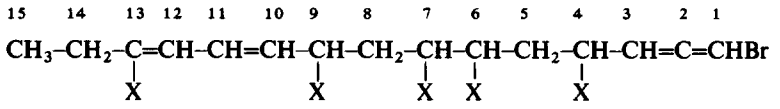
In connection with our continuing studies on the constituents of the red alga *Laurencia okamurai* Yamada [1–4], the Japanese species of the genus *Laurencia* (Rhodophyta), we have examined new samples of this species from six locations. The specimens collected at five of the locations, as anticipated, contained laurinterol [1] and debromolaurinterol [1] as major metabolites. However, the specimen collected at Iwaizaki (Shima pen., Mie prefecture) gave laurinterol in poor yield. Instead it contained halochamigrene derivatives which were very similar to those of the specimen collected at Yasurihama [5, 6], near Iwaizaki, as the major components.

In the course of these studies, neolaurencenyne [6] was found to be a common metabolite of *L. okamurai* and laurequinone [7], which has recently been obtained from *L. nidifica*, was also isolated from the Moura and the Noo specimens. Furthermore, from the Zaga-shima specimen we isolated a new halogenated metabolite (**1**) which is closely related to kumausallene [8] and panacene [9].

RESULTS AND DISCUSSION

The halogenated compound **1**, oil, $[\alpha]_D^{23}$ −215° (*c* 0.985; $CHCl_3$), was analysed for $C_{15}H_{18}O_2Br_2$ by HR-MS. Its IR, UV and ^1H NMR spectra indicated the presence of a terminal bromoallene moiety [ν_{max} 1965 cm^{-1}; δ5.38 (1H, *dd*, *J* = 6 and 6 Hz) and 6.09 (1H, *dd*, *J* = 6 and 1.5 Hz)], an ethyl group [δ1.13 (3H, *t*, *J* = 7 Hz) and 2.57 (2H, *q*, *J* = 7 Hz)] and a conjugated diene moiety [λ_{max} 237 nm (ε27 000) and 243 nm (ε28 000)]. The presence of these moieties was further substantiated by the ^{13}C NMR spectrum (Table 1). Since the IR spectrum showed no hydroxyl and carbonyl absorptions, the two oxygen atoms in **1** were assumed to be involved in ether linkages. Moreover, the ^{13}C NMR spectrum revealed that there were no other double bonds, apart from those of the bromoallene and the conjugated diene moieties, and therefore compound **1**, having six degrees of unsaturation, must be composed of two oxide rings.

Extensive spin decoupling experiments in the ^1H NMR spectrum (Table 1) led to the following partial structure for **1**.



X = Br or O

Placement of the remaining bromine substituent at C-13 was supported by the ^{13}C NMR spectrum which showed no signal due to the vinyl ether moiety at near 150 ppm [10]. Furthermore, the ^1H NMR spectrum contained no signals at about δ3.5–2.9 due to epoxide protons [11] and near δ2.7 due to methylene protons on a 1,3-disubstituted oxetane ring [12, 13]. This meant that the two ether rings must be formed by bonding between C-4 and C-7 and between C-6 and C-9, leading to a planar structure (**1**) which has a 2,6-dioxabicyclo[3.3.0]octane skeleton in the same manner as that of kumausallene (**4**) previously isolated from *L. nipponica* Yamada [8].

Hydrogenation of **1** with platinum oxide in ethyl acetate gave compound **2**, $C_{15}H_{23}O_2Br$, as one of the hydrogenated products. The ^1H NMR spectrum of **2** showed that the terminal bromoallene in **1** was hydrogenated with the release of hydrogen bromide and that the conjugated double bond remained unchanged. Compound **2** was further hydrogenated over platinum oxide in ethanol to give the fully saturated compound **3**, $C_{15}H_{28}O_2$, whose mass spectrum like that of **2** revealed a prominent peak at *m/z* 155, ascribable to a fragment caused by elimination of a C_6 unit. This fragment was comparable to one (base peak) in the spectrum of the hydrogenated product **5** [8] of kumausallene (**4**), and provided good evidence for the presence of the 2,6-

*Part 61 in the series "Constituents of Marine Plants". For Part 60 see Suzuki, M., Segawa, M., Kikuchi, H., Suzuki, T. and Kurosawa, E. (1985) *Phytochemistry* **24**, 2011.

Table 1. ^{13}C and ^{1}H NMR data for **1** ($CDCl_3$, TMS as int. standard)

Carbon	^{13}C*	^{1}H† J (Hz)
1	73.9	6.09 *dd* 6, 1.5
2	201.9	
3	101.1	5.38 *dd* 6, 6
4	76.7	4.70 *dddd* 8, 6, 6, 1.5
5	41.4‡	1.96 *ddd* 13.5, 8, 5.5
		2.30 *ddd* 13.5, 6, ~0
6	84.1§	4.81 *ddd* 5.5, 4.5, ~0
7	83.8§	4.74 *dd* 4.5, 4.5
8	40.7‡	1.73 *ddd* 13.5, 10, 4.5
		2.26 *dd* 13.5, 6
9	79.7	4.52 *ddd* 10, 6, 6
10	130.0‖	5.61 *dd* 13.5, 6
11	130.5‖	6.32 *dd* 13.5, 10
12	133.3‖	6.42 *d* 10
13	132.2	
14	29.8	2.57 *q* 7
15	13.4	1.13 *t* 7

*50.10 MHz with the aid of INEPT method.
†200 MHz.
‡,§Assignments may be reversed.
‖Assignments may be interconvertible.

dioxabicyclo[3.3.0]octane skeleton with propyl and C_6 side chains in **2** and **3**.

On detailed analysis of the coupling constants (Fig. 1) in the ^{1}H NMR spectra of compound **1** and kumausallene (**4**), the stereochemistries at C-4, C-6, C-7 and C-9 were determined. The bromoallenic side chain in kumausallene (**4**) is in the *exo*-configuration in which a pseudo-equatorial conformation can be assumed. As a result the dihedral angle between H_β-5 and H-6 is approximately 90°, corresponding to the observed J-value of 0 Hz. However, since the 1-bromo-3-hexenyl side chain in **4** is in the *endo*-configuration, the coupling constant between H-7 and H_β-8 is observed as 3.5 Hz. On the other hand, the coupling constants between H_β-5 and H-6 and between H-7 and H_β-8 in **1** were observed as ~0 Hz and 0 Hz, respectively, and therefore the two side chains at C-4 and C-9 in **1** both had the *exo*-configuration. The *cis* relationship between H-6 and H-7 was also indicated by them having a coupling constant (4.5 Hz) comparable with that of **4**.

Consequently, the relative configurations of the four chiral centres at C-4, C-6, C-7 and C-9 were assigned as in formula **1**. Furthermore, the *E*-configuration of the double bond at C-10 was indicated by the values (J = 13.5 Hz in $CDCl_3$ and J = 15 Hz in C_6D_6) of the coupling constants between the pertinent olefinic protons. The double bond at C-12 in **1** was assigned *E*-configuration by the observation of a nuclear Overhauser enhancement (about 10%) between H-11 and H_2-14.

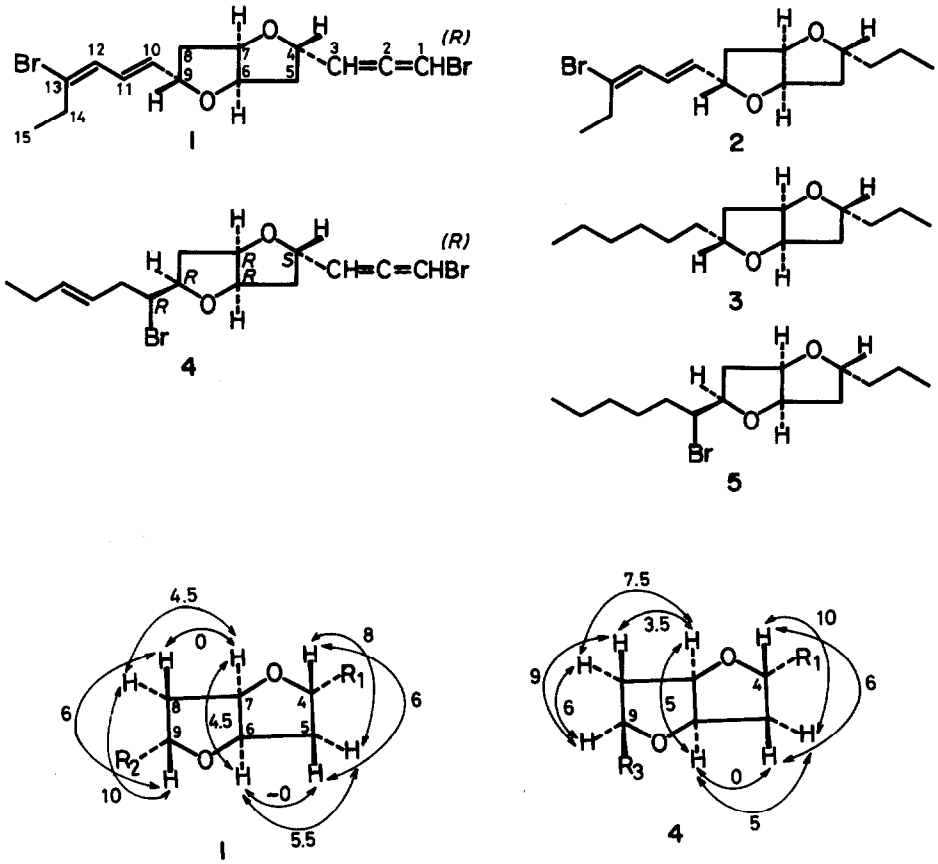


Fig. 1. The coupling constants (Hz) for the new bromoallene (**1**) and kumausallene (**4**).

In view of the strong negative rotation of **1**, the absolute configuration of the bromoallene moiety in **1** was assigned *R*-configuration by application of Lowe's rule [14].

Thus, the structure of the new C-15 bromoallene is represented by formula **1**. This is the second example of a C_{15} non-terpenoid compound from the genus *Laurencia* with a 2,6-dioxabicyclo[3.3.0]octane skeleton.

EXPERIMENTAL

^1H and ^{13}C NMR: 100 MHz and 200 MHz, $CDCl_3$ unless otherwise stated, TMS as int. standard (coupling constant, *J* in Hz); Low and high resolution MS: 70 eV; Optical rotations: $CHCl_3$; CC: silica gel (Merck, Kieselgel 60, 70–230 mesh); prep. TLC: silica gel 60 F_{254} (Merck). All known metabolites were identified by comparison of the spectral data with those of the authentic specimens. Yields are based on the weights of the extracts.

Collection, extraction and isolation. Samples were collected from six different sites: Kamuimisaki (Shakotan pen., Hokkaido; August 17, 1982), Esashi (Hokkaido; July 24, 1982), Moura (Aomori prefecture; July 23, 1982), Noo (Niigata prefecture; July 6, 1983), Iwaizaki (Shima pen., Mie prefecture; June 30, 1983) and Zaga-shima (Ago Bay, Mie prefecture; June 30, 1983). Extraction and isolation were carried out by conventional methods as described in the case of Zaga-shima's specimen.

Zaga-shima specimen. Half-dried alga (40 g) was extracted with MeOH, and the resulting MeOH soln was treated in the usual manner [1] to give a neutral oil (0.9 g) which was successively fractionated by CC over silica gel. The fraction eluted with hexane was rechromatographed on a silica gel column to yield isolaurene (0.3%) [15], neolaurencenyne (0.5%) [6] and (−)-α-bromocuparene (0.6%)* [16].

The first C_6H_6 fraction was further subjected to prep. TLC to give isolaurinterol (2%) [1] and debromoisolaurinterol (1%) [1, 3]. The next C_6H_6 fraction gave a mixture of laurinterol (17%) [1] and debromolaurinterol (4%) [1], which was separated via their acetates. The last C_6H_6 fraction was repeatedly subjected to a combination of silica gel CC and TLC to yield the new bromoallene **1** (4%) along with prepacifenol (3%) [17], prepacifenol epoxide (1%) [18], pacifenol (9%) [19] and johnstonol (1%) [20]. *Iwaizaki's specimen* contained neolaurencenyne (1.5%) [6], laurencenyne (0.5%) [6], laurinterol (1%) [1], deoxyprepacifenol (0.3%) [21], prepacifenol epoxide (13%) [18], pacifenol (20%) [19] and johnstonol (5%) [20]. *Kamuimisaki, Esashi, Moura and Noo specimens.* These contained laurinterol [1] and debromolaurinterol [1] in 30–40% yields together with neolaurencenyne (*ca* 1%) [6] and previously reported minor metabolites [3], e.g. isolaurene (*ca* 1%), (−)-α-bromocuparene (2–3%) and isolaurinterol (3–5%). Laurequinone [7] was also obtained from Moura's and Noo's specimens in 0.3% and 1% yields, respectively.

Compound **1**. Oil; $[\alpha]_D^{23}$ −215° (*c* 0.985); UV λ_{max}^{EtOH} nm (ε): 237 (27 000) and 243 (28 000), and λ_{inf} 254 (19 000); IR ν_{max}^{film} cm^{-1}: 3060, 1965, 1650, 1610, 1320, 1200, 1190, 1150, 1075, 1030, 990, 965, 915, 885 and 845; ^1H NMR (200 MHz, C_6D_6): δ0.96 (3H, *t*, *J* = 7 Hz), 1.24 (1H, *ddd*, *J* = 13.5, 10, 4.5 Hz), 1.50 (1H, *ddd*, *J* = 13.5, 8, 5.5 Hz), 1.95 (1H, *dd*, *J* = 13.5, 6 Hz), 1.99 (1H, *ddd*, *J* = 13.5, 6, ~ 0 Hz), 2.31 (1H, *q*, *J* = 7 Hz), 4.27 (1H, *ddd*, *J* = 10, 6, 6 Hz), 4.31 (1H, *dd*, *J* = 4.5, 4.5 Hz), 4.41 (1H, *ddd*, *J* = 5.5, 4.5, ~ 0 Hz), 5.49 (1H, *dddd*, *J* = 8, 6, 6, 2 Hz), 5.05 (1H, *dd*, *J* = 6, 6 Hz), 5.33 (1H, *dd*, *J* = 15, 6 Hz), 5.69 (1H, *dd*, *J* = 6, 2 Hz), 6.19 (1H, *dd*, *J* = 15, 11 Hz) and 6.42 (1H, *d*, *J* = 11 Hz); MS *m/z* (rel. int.): 392, 390 and 388 $[M]^+$ (8:16:8), 311 and 309 $[M-Br]^+$ (57:57), 273 and 271 $[M-C_3H_2Br]^+$ (19:18), 244 and 242 $[M-C_3H_2Br-C_2H_5]^+$ (20:20), 231 and 229 $[M-C_6H_8Br]^+$ (9:10), 149 (53), 125 (72), 109 (99), 107 (66), 81 (81), 79 (100), 77 (65) and 65 (51); HR-MS *m/z*: 389.9643. Calc. for $C_{15}H_{18}O_2$ $^{79}Br^{81}Br$: 389.9654.

Hydrogenation of **1**. Compound **1** (12 mg) was hydrogenated in EtOAc over PtO_2-catalyst. After removal of the catalyst and the solvent, the residual oil was chromatographed on TLC to give **2** (4 mg); oil; $[\alpha]_D^{21}$ +9.02° (*c* 0.35); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1650, 1610, 1320, 1150, 1125, 1097, 1065, 1035, 963 and 918; ^1H NMR: δ1.12 (3H, *t*, *J* = 7 Hz), 2.57 (2H, *q*, *J* = 7 Hz), 4.03 (1H, *m*), 4.52 (1H, *ddd*, *J* = 10, 6, 6 Hz), 4.6–4.8 (2H, *m*), 5.61 (1H, *dd*, *J* = 13.5, 6 Hz), 6.29 (1H, *dd*, *J* = 13.5, 10 Hz) and 6.43 (1H, *d*, *J* = 10 Hz); MS *m/z* (rel. int.): 316 and 314 $[M]^+$ (0.4:0.4), 273 and 271 $[M-C_3H_7]^+$ (0.2:0.2), 235 $[M-Br]^+$ (1.5), 155 $[M-C_6H_8Br]^+$ (92) and 71 (100).

Hydrogenation of **2**. Compound **2** (4 mg) was hydrogenated in EtOH over PtO_2. After the usual work-up, the resulting oily substance was purified by TLC to give **3** (2 mg); oil; $[\alpha]_D^{20}$ +5.13° (*c* 0.20); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1130, 1077, 1038 and 910; ^1H NMR: δ4.0–4.4 (2H, *m*) and 4.6–4.7 (2H, *m*); MS *m/z* (rel. int.): 240 $[M]^+$ (3), 197 $[M-C_3H_7]^+$ (35), 155 $[M-C_6H_{13}]^+$ (78) and 71 (100).

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*Previously we reported that the sign of the specific rotation of α-bromocuparene was positive. However, further examination showed that the sign is negative.

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