A New Chamigrane-type Bromo Diether from the Red Alga *Laurencia nipponica* Yamada[1)]

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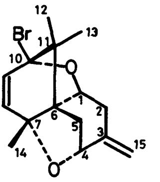
Synopsis. A new halogenated sesquiterpene diether has been isolated from the title alga and its structure was established on the basis of the spectral and chemical evidence.

As part of our studies on the constituents of the red alga *Laurencia nipponica* Yamada ("Ura-sozo") grown in Northern Hokkaido,[2,3)] belonging to the warm current region, we have collected in two locations at Teuri island and Hamamasu. Both specimens displayed the presence of laureatin[4)] (25% and 20% of the extracts) and isolaureatin[4)] (10% and 8%) as the major metabolites. In this paper we report the isolation and the structural determination of a new sesquiterpene bromo diether **1**, which has been obtained as the minor metabolite (0.6%) from the Hamamasu's specimen.

Compound **1**, mp 78—79 °C, $[\alpha]_D^{21}$−54.8 ° ($CHCl_3$), was found to have a molecular formula of $C_{15}H_{19}O_2Br$ by high resolution mass spectrometry. The IR spectrum of **1** showed no hydroxyl and carbonyl absorptions, thus indicating that two oxygen atoms in **1** were involved in ether linkages. The ^{13}C NMR spectrum indicated the presence of an *exo*-methylene group at δ 144.2 and 114.6 and a disubstituted vinyl group at 133.9 and 130.1. Tetracyclic nature, including two ether rings, of **1** was demonstrated from the absence of further unsaturation besides the two double bonds. The ^{1}H NMR spectrum revealed signals at δ 1.02 and 1.14 (each 3H, s) due to two quaternary methyl groups, at 1.24 (3H, s) due to a $CH_3\text{-}\overset{|}{\underset{|}{C}}\text{-O-}$ grouping, at 4.95 and 5.07 (each 1H, br s) due to an *exo*-methylene group, and at 5.82 (2H, br s) due to a disubstituted vinyl group. Furthermore, the spin decoupling studies indicated the presence of $\blacksquare\text{-}\underset{\underset{\text{O-}}{|}}{\text{CH}}\text{-CH}_2\text{-}\blacksquare$ grouping at δ 1.71 (1H, d, J=12 Hz), 2.20 (1H, dd, J=12, 6 Hz), and 4.45 (1H, d, J=6 Hz) and $\blacksquare\text{-}\underset{\underset{\text{O-}}{|}}{\text{CH}}\text{-CH}_2\text{-}\underset{|}{\text{C}}\text{=CH}_2$ grouping at 2.39 (1H, dddd, J=14, 14, 2, 2 Hz), 2.66 (1H, dd, J=14, 5 Hz), and 4.06 (1H, dd, J=14, 5 Hz) (■; quaternary carbon).

In view of the above-mentioned partial structural units coupled with comparisons of the spectral data with those of various chamigrane-type sesquiterpenoids, *e.g.* **2** (pacifenol)[5)] and **3**,[6)] which co-occurred in the same alga, it is suggested that formula **1** would be proposed as possible structure for this bromo diether. The structure **1** was confirmed by the following chemical derivation from the known bromo alcohol **4**,[6)] which has also been isolated from *L. nipponica.*

Treatment of **4** with *N*-bromosuccimide in *t*-BuOH and H_2O at room temperature afforded a dibromo compound **5**, $C_{15}H_{20}O_2Br_2$ (*m/z* 394, 392, and 390; M^+), in 90% yield. The IR and ^{1}H NMR spectra of **5** indicated that the hydroxyl and trisubstituted vinyl groups in **4** disappeared and that an additional ether ring was formed. The formation of the expected diether **5** (not 4-bromo-3,7-epoxy derivative) in the bromonium ion induced cyclization[7)] was supported by the presence of the $CH_3\text{-}\overset{|}{\underset{|}{C}}\text{(Br)-}$ moiety at δ 1.80 (3H, s) in the ^{1}H NMR spectrum of **5**. Treatment of **5** with 1 mol dm^{-3} ethanolic potassium hydroxide gave a dehydrobromination product (20% yield) which was identical with natural bromo diether **1** in all respects (IR, ^{1}H NMR, and MS spectra and undepressed mixed mp). Thus the structure, including the absolute configuration, of the bromo diether is represented by formula **1**.



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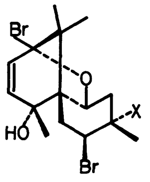
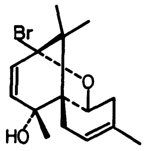


2: X=Cl
3: X=OH



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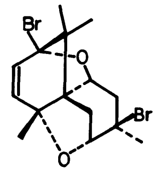

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Experimental

All the mps were uncorrected. The IR spectra were measured on a JASCO A-102 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-PS-100 and JEOL JNM-FX200 spectrometer, respectively, using tetramethylsilane as an internal reference in $CDCl_3$. The low and high resolution mass spectra were taken at 70 eV with a JEOL JMS-D300 spectrometer. Optical rotations were determined on a JASCO DIP-140 polarimeter in $CHCl_3$. Aluminium oxide (Merck, activity II-III) and silica gel (Merck, Kieselgel 60, 70—230 mesh) were used for column chromatography.

Collection. Algae were collected at Teuri island (Haboro) and Hamamasu (*ca.* 40 km southwest of Rumoi[3)]) early in August 1980.

Isolation. The neutral MeOH extracts (5 g; *ca.* 2% of the half-dried alga), obtained from the Hamamasu's specimen in the usual manner, was fractionated by column chromatography on alumina. The fraction eluted with hexane-benzene (1:1) was rechromatographed on silica-gel column to yield laureatin[4)] (1 g) and isolaureatin[4)] (400 mg) together with deoxyprepacifenol[8)] (25 mg), (3*Z*)-isoprelaurefucin[9)] (170 mg), and spirolaurenone[10)] (40 mg). The fraction eluted with benzene was further submitted to column chromatography on silica gel to give **1** (30 mg) as a crystalline material along with cycloeudesmol[11)] (65 mg). The fraction eluted with benzene-ethyl acetate (10:1) was repeatedly chromato-

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graphed over silica gel to yield pacifenol[5] (100 mg), 2,10-dibromo-3-chloro-α-chamigren-9-ol[12] (10 mg), and laureacetal-A[13] (10 mg). The following fraction eluted with ethyl acetate was submitted to repeated silica-gel column chromatography to afford laureacetal-B[14] (60 mg), 4,10-dibromo-1,10-epoxychamigra-8-ene-3,7-diol[6] (10 mg), and 10-bromo-1,10-epoxychamigra-2,8-diene-4,7-diol[15] (65 mg).

1: Mp 78—79 °C (hexane–diisopropyl ether); $[\alpha]_{\mathrm{D}}^{21}$ −54.8° (c 1.43); IR, $\nu_{\max}$ (Nujol) 1160, 1090, 1050, 1030, 1020, 985, 935, 915, and 865 cm^{-1}; ^{1}H NMR (100 MHz), in the text; ^{13}C NMR (50.1 MHz), δ=144.2 (s, C3), 133.9 (d, C8 or C9), 130.1 (d, C9 or C8), 114.6 (t, C15), 98.8 (s, C10), 84.7 (s, C7), 81.2 (d, C4), 78.0 (d, C1), 55.5 (s, C6), 47.7 (s, C11), 31.1 (t, C2), 26.9 (t, C5), 23.9 (q, C14 or C13), 23.3 (q, C13 or C14), and 20.1 (q, C12); MS, m/z (rel intensity) 312, 310 (0.2; M$^+$), 297, 295 (1; M$^+$−CH$_3$), 231 (9; M$^+$−Br), 200, 198 (32), 171 (40), 133 (88), 121 (100), 119 (37), 91 (36), 57 (42), 43 (77), and 41 (71). Found: m/z 295.0333. Calcd for $C_{14}H_{16}O_2{}^{79}Br$: M−CH$_3$, 295.0333.

Treatment of 4 with NBS in t*-BuOH–H$_2$O.* To a soln of **4**[6] (30 mg) in t-BuOH (1 ml) and H_2O (1 ml) was gradually added recrystallized NBS (19 mg) at 0 °C. After the mixture had been stirred for 1 h at room temperature, water was added, and the mixture was extracted with ether. The ethereal soln was washed with saturated brine, dried over anhydrous Na_2SO_4, and evaporated to leave an oily substance, which was purified by column chromatography over silica gel to give **5** (34 mg); mp. 97—98 °C (hexane–diisopropyl ether); $[\alpha]_{\mathrm{D}}^{23}$ −29.4° (c 1.49); IR, $\nu_{\max}$ (Nujol) 1265, 1160, 1105, 1050, 1040, 1030, 1015, 1005, 982, 958, 950, 935, 925, 910, 880, 865, 815, 765, and 743 cm^{-1}; ^{1}H NMR (100 MHz), δ=1.03, 1.14, 1.25, 1.80 (each 3H, s), 2.13 (2H, m), 2.33 (1H, br s), 2.43 (1H, s), 3.74 (1H, dd, J=10, 9 Hz), 4.26 (1H, dd, J=4, 2 Hz), and 5.84 (2H, br s); MS, m/z 394, 392, 390 (0.3:0.5:0.3; M$^+$), 379, 377, 375 (0.3:0.5:0.3; M$^+$−CH$_3$), 313, 311 (40; M$^+$−Br), 231 (5; M$^+$−Br−HBr), 199 (20), 162 (20), 133 (85), 121 (100), 113 (34), 71 (37), 43 (69), and 41 (48).

Conversion of 5 into 1. A soln of **5** (30 mg) in 1 mol dm^{-3} ethanolic KOH (1.5 ml) was refluxed for 2 h and then worked up in the usual way to give an oily product which was further purified by silica-gel column chromatography to yield a crystalline substance (5 mg) (20 mg of **5** was recovered), mp 77—78 °C, $[\alpha]_{\mathrm{D}}^{22}$ −51.0° (c 1.21), whose spectral data were consistent with those of natural **1**.

References

1) Part 64 of "Constituents of Marine Plants." Part 63; M. Suzuki, M. Segawa, T. Suzuki, and E. Kurosawa, *Bull. Chem. Soc. Jpn.*, **58**, 2435 (1985).

2) M. Suzuki, M. Segawa, T. Suzuki, and E. Kurosawa, *Bull. Chem. Soc. Jpn.*, **56**, 3824 (1983).

3) M. Suzuki, M. Segawa, H. Kikuchi, T. Suzuki, and E. Kurosawa, *Phytochemistry*, in press.

4) T. Irie, M. Izawa, and E. Kurosawa, *Tetrahedron*, **26**, 851 (1970).

5) J. J. Sims, W. Fenical, R. M. Wing, and P. Radlick, *J. Am. Chem. Soc.*, **93**, 3774 (1971).

6) T. Suzuki, *Chem. Lett.*, **1980**, 541.

7) E. Demole and P. Enggist, *Helv. Chim. Acta*, **54**, 456 (1971).

8) C. Ireland, M. O. Stallard, D. J. Faulkner, J. Finer, and J. Clardy. *J. Org. Chem.*, **41**, 2461 (1976).

9) E. Kurosawa, A. Fukuzawa, and T. Irie, *Tetrahedron Lett.*, **1973**, 4135.

10) M. Suzuki, N. Kowata, and E. Kurosawa, *Tetrahedron*, **36**, 1551 (1980).

11) T. Suzuki, A. Furusaki, H. Kikuchi, and E. Kurosawa, *Tetrahedron Lett.*, **22**, 3423 (1981).

12) W. Fenical, *Phytochemistry*, **15**, 511 (1976).

13) T. Suzuki, A. Furusaki, N. Hashiba, and H. Kurosawa, *Tetrahedron Lett.*, **1977**, 3731.

14) T. Suzuki and E. Kurosawa, *Chem. Lett.*, **1979**, 301.

15) K. Kurata, A. Furusaki, C. Katayama, H. Kikuchi, and T. Suzuki, *Chem. Lett.*, **1981**, 773.