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PINNATERPENES A, B, AND C, NEW DIBROMODITERPENES FROM THE RED ALGA <u>LAURENCIA</u> <u>PINNATA</u> YAMADA

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The structures of three dibromoditerpenes, isolated from the title alga and designated as pinnaterpenes A, B, and C, were determined on the basis of the X-ray crystallography as well as the chemical and spectral data.

The title alga is a unique <u>Laurencia</u> species characterized by the fact that it contains marine phytosterols[1] with moulting hormone activity related structurally to ecdysones and C_{15} vinyl acetylenic cyclic ethers[2] with (12R,13R)- and (12S,13S)-configurations.[3] Continuous careful examination of components of the alga led to isolation of three dibromoditerpenes instead of bromosesquiterpenes, which have usually been isolated from most of the <u>L</u>. species.[4] We report herein the isolation and structure elucidation of these diterpenes, designated as pinnaterpenes A (**1**), B (**2**), and C (**3**).

Neutral ether-soluble oil (7.5 g) obtained from methanol extracts of the alga (wet, 4 kg), collected at Motsuta point, Hokkaido, in early July,[1,2] was fractionated by repeated chromatography over silica gel to yield **1** (48 mg), **2** (47 mg), and **3** (166 mg).

Pinnaterpene A (**1**), mp 89-93 °C (from hexane-CH_2Cl_2) and $[\alpha]_D$ -23.5° ($CHCl_3$), displayed the following spectra: FD-MS, m/e 432, 430, 428 (1:2:1, base), 450, 448, 446 and EI-MS, m/e 432, 430, 428 (1:2:1), 417, 415, 413 (1:2:1), and 147 (base); IR (KBr), 3580, 1715, 1270, and 1250 cm^{-1}; ^1H NMR, δ 1.03, 1.10, 1.15, and 1.29 (each 3H, s, 4 × ■-$C\underline{H}_3$), 2.03 (3H, s,-$OCOC\underline{H}_3$), 2.56 (1H, d, J = 15 Hz), 2.65 (1H, dd, J = 15 and 3 Hz), 3.93 and 3.95 [each 1H, dd, J = 12, 3 and 12, 4 Hz, 2 × ■-$C\underline{H}(Br)\text{-}CH_2\text{-}$].[5] The highest triplet peaks in the high-resolution EI-MS (HREI-MS)[6] revealed the presence of a fragment cation corresponding to $C_{20}H_{30}Br_2$, which would evidently be formed by elimination of acetic acid [IR, 1715 and 1270 (or 1250) cm^{-1}; ^1H NMR, δ 2.03 (3H, s); ^{13}C NMR[5] (Table 1), δ 171.0 (s) and 21.5 (q)] and water [IR, 3580 cm^{-1}; ^{13}C NMR,[5] δ 71.7 (s)]. These spectral data, coupled with the ^{13}C NMR spectrum indicating the presence of 22 carbon atoms in total, suggested that the molecular formula of **1** would probably be represented by $C_{22}H_{36}O_3Br_2$. The whole structure was elucidated by the X-ray crystallography.[7]

The X-ray measurement was carried out at about -20 °C. The crystal data of **1** were as follows: $C_{22}H_{36}O_3Br_2$, monoclinic, space group $P2_1$, a = 15.404(4), b = 10.329(1), c = 7.410(2) Å, β = 102.13(2)°, Z = 2, D_c = 1.464 g cm^{-3}. 2042 unique intensity data for 2θ < 130° were collected on an automatic, four-circle diffractometer using graphite-monochromated CuKα radiation. The structure was solved by the Monte Carlo direct method,8) and refined by the block-diagonal least-squares method. The absolute configuration was determined by taking account of the anomalous dispersion of bromine atoms for CuKα radiation. The final R value was 0.062. The molecular skeleton of **1** thus obtained is shown in Fig. 1.

The result suggested that pinnaterpene A (**1**) might be an 11-O-acetyl derivative of irieol C, which has recently been isolated from L. irieii by Howard and Fenical.9) In fact, treatment of **1** with hydride reagent ($LiAlH_4$ in ether, 0 °c, 40 min) afforded glycol (**4**), mp 153.5-155.5 °C (from $CHCl_3$) and $[\alpha]_D$ -29.2°, in 63% yield, which was identified as irieol C by direct comparison with an authentic sample, mp 136-137 °C and $[\alpha]_D$ -35.2° (lit.,9,10) amorphous solid and $[\alpha]_D$ 34.2°), isolated from "irieol C fraction" kindly donated by Howard. This transformation establishes the absolute configuration of irieol C.

Pinnaterpene B (**2**), mp 152-154 °C (from hexane-benzene) and $[\alpha]_D$ -20.6° ($CHCl_3$), was assigned molecular formula $C_{22}H_{36}O_4Br_2$ on the basis of the HRFD-MS,6) and formed its monoacetate (**2a**), oil and $[\alpha]_D$ -17.9° ($CHCl_3$). The spectra of **2** and **2a** suggested that **2** would differ from **1** only in monohydroxylation at C-18 of **1**: **2**, FD-MS, m/e 527, 525, 523 (1:2:1), 508, 506, 504 (1:2:1), and 448, 446, 444 (1:2, base); IR (KBr), 3280, 1740, and 1250 cm^{-1}; ^1H NMR, δ 1.04, 1.11, and 1.35 (each 3H, s, 3 × ■-CH_3), 2.03 (3H, s,-$OCOCH_3$), 2.49 (1H, d, J = 14 Hz), 2.62 (1H, dd, J = 15 and 4 Hz), 2.71 (1H, dq, J = 5 and 13 Hz, 2-axial-H), 3.2 (2H, br s, 2 OH), and 3.9 (4H, m): **2a**, EI-MS, m/e 508, 506, 504 (1:2:1), 448, 446, 444 (1:2:1), and 145 (base); IR ($CHCl_3$), 3550, 1735, and 1260 cm^{-1}; ^1H NMR, δ 1.04, 1.10, and 1.29 (each 3H, s), 2.03 and 2.06 (each 3H, s), 3.86 and 3.94 [each 1H, dd, J = 12 and 4 Hz, 2 × ■-CH(Br)-CH_2-], 4.22 and 4.65 (each 1H, ABq, J = 13 Hz, ■-CH_2OAc). This presumption was supported by the appearance of a new triplet peak at δ 64.0 in the ^{13}C NMR spectrum (Table 1) instead of the methyl signal at δ 16.1 in that of **1**.

Compound **2**, when treated with tosyl chloride in pyridine (20 °C for 2 d, 40 °C for 1 d, 60 °C for 1 d, and reflux for 1 d), was converted into cyclic ether (**5**), $C_{22}H_{34}O_3Br_2$, oil and $[\alpha]_D$ +7.1°, in 26% yield: **5**, EI-MS, m/e 508, 506, 504 (1:2:1, M^+), 448, 446, 444 (1:2:1), and 121 (base); IR ($CHCl_3$), 1731, 1263, and 1018 cm^{-1}; ^1H NMR, δ 1.04, 1.12, and 1.22 (each 3H, s), 2.02 (3H, s), 3.52 and 4.11 (each 1H, ABq, J = 9 Hz, ■-CH_2O-), 3.94 [1H, dd, J = 12 and 5 Hz, ■-CH(Br)-CH_2-], and 4.16 [1H, dd, J = 9, 8 Hz, ■-CH(Br)-CH_2-]. The same compound (**5**) was also obtained by oxidation of **1** with lead(IV) acetate and iodine in benzene (reflux, 2 d)11) in 67% yield, establishing that **2** is 18-hydroxypinnaterpene A.

Pinnaterpene C (**3**), amorphous solid and $[\alpha]_D$ +29.2° ($CHCl_3$), was analyzed for $C_{22}H_{34}O_4Br_2$ by the HRFD-MS.6) The spectra suggested that **3** would be an 18-hydroxy derivative of the cyclic ether (**5**) and hence possess a hemi-acetal structure: FD-MS, m/e 524, 522, 520 (1:2:1), 507, 505, 503 (1:2:1, base), and 464, 462, 460

Table 1. ^{13}C NMR spectra of pinnaterpenes

Carbon number	Compound A (1)	 B (2)	 C (3)
1	65.0 (d)	64.8 (d)	65.0 (d)
2	30.4 (t)	30.4 (t)	32.4 (t)
3	40.4 (t)	37.5 (t)	32.5 (t)
4	71.7 (s)	71.2 (s)	83.1 (s)
5	60.0 (d)	61.1 (d)	58.8 (d)
6	32.9 (d)	32.8 (d)	36.0 (d)
7	31.9 (t)	31.8 (t)	31.9 (t)
8	43.6 (t)	43.6 (t)	40.7 (t)
9	47.1 (s)	50.8 (s)	62.3 (s)
10	46.3 (t)	46.2 (t)	46.7 (t)
11	83.8 (s)	83.9 (s)	83.5 (s)
12	37.9 (t)	37.0 (t)	37.1 (t)
13	30.1 (t)	30.4 (t)	30.4 (t)
14	64.8 (d)	63.3 (d)	63.6 (d)
15	36.6 (s)	36.5 (s)	36.6 (s)
16	45.3 (t)	45.3 (t)	45.2 (t)
17	32.3 (q)	32.3 (q)	22.0 (q)
18	16.1 (q)	64.0 (t)	99.0 (d)
19	22.8 (q)	22.8 (q)	22.9 (q)
20	31.1 (q)	30.7 (q)	32.4 (q)
CH_3CO	171.0 (s)	171.0 (s)	170.8 (s)
	21.5 (q)	21.6 (q)	21.7 (q)

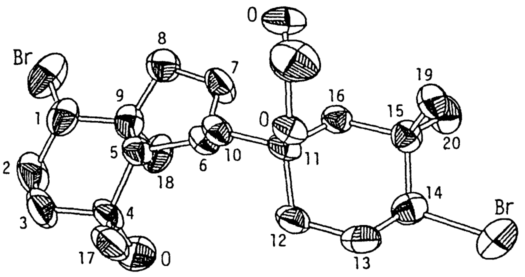
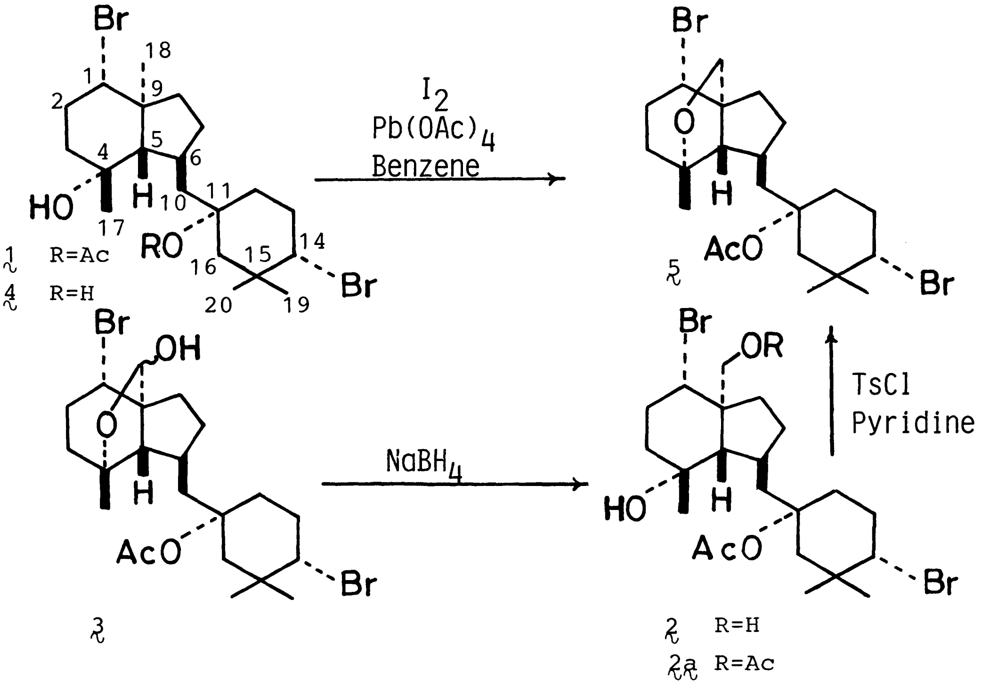


Fig. 1 The structure of 1 determined by the X-ray crystallographic method



(1:2:1); IR (neat), 3420, 1730, and 1245 cm^{-1}; ^{1}H NMR, δ 1.03, 1.11, and 1.30 (each 3H, s), 2.01 (3H, s), 2.58 (1H, dd, J = 15 and 3 Hz), 3.16 [1H, d, J = 4 Hz, ■-CH(O$\underline{\mathrm{H}}$)-O-, disappeared on addition of D_2O], 3.94 and 4.10 (each 1H, dd, J = 12, 4 and 12, 6 Hz), and 5.33 [1H, d, J = 4 Hz, ■-C$\underline{\mathrm{H}}$(OH)-O-, s on addition of D_2O]; ^{13}C NMR (Table 1), δ 99.0 (d, 18-C) and 83.1 (s, 4-C). As expected, the compound (**3**) with the hemi-acetal moiety was reduced smoothly with sodium borohydride in ethanol (room temp, 2 d) to give pinnaterpene B (**2**) in 65% yield. Pinnaterpene C is therefore represented by formula **3**.

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3) These cyclic ethers are considered to be formed *in vivo* from a new precursor, (3E,6Z,9Z,12Z)-pentadeca-3,6,9,12-tetraen-1-yne, rather than laurediol; *cf*., H. Kigoshi, Y. Shizuri, H. Niwa, and K. Yamada, Tetrahedron Lett., **22**, 4729 (1981); E. Kurosawa, A. Fukuzawa, and T. Irie, ibid., 2121 (1972).

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5) The NMR spectra were measured in chloroform-*d* at 200 and/or 400 MHz for ^{1}H and at 25.2 MHz for ^{13}C, respectively. The abbreviation ■ denotes a quaternary carbon atom.

6) HR-MS: **1**, m/e 428.0727 (calcd for $C_{20}H_{30}Br_2$, 428.0715): **2**, m/e 523.1008 (calcd for $C_{22}H_{37}O_4Br_2$, 523.1059): **3**, m/e 520.0870 (calcd for $C_{22}H_{34}O_4Br_2$, 520.0824).

7) The details will be described in a full paper.

8) A. Furusaki, Acta Crystallogr., Sect. A, **35**, 220 (1979).

9) B. M. Howard and W. Fenical, J. Org. Chem., **43**, 4401 (1978).

10) Howard and Fenical[9] reported that irieol C, amorphous solid (not crystalline), had $[\alpha]_D$ 34.2° (no sign). However, a sample, isolated in our laboratory from "irieol C fraction" donated by Howard and identified as irieol C (IR and ^{1}H NMR), had mp 136-137 °C and $[\alpha]_D$ -35.2°.

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