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THE STRUCTURES OF (3Z)-EPOXYVENUSTIN, (3Z)-VENUSTIN, AND (3Z)-VENUSTINENE, NEW HALOGENATED C_{15}-NONTERPENOIDS FROM THE RED ALGA LAURENCIA VENUSTA YAMADA[1)]

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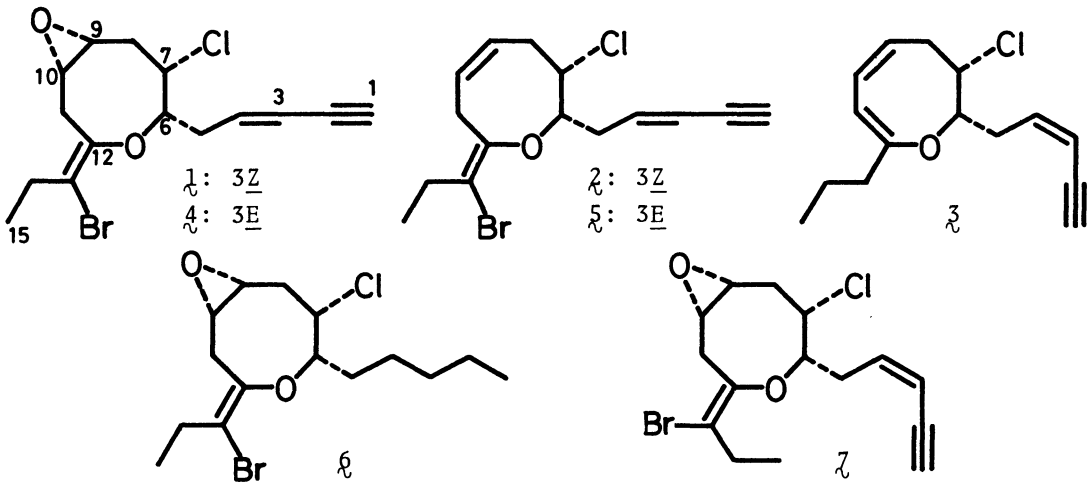
Three new halogenated nonterpenoid C_{15}-compounds have been isolated from the red alga Laurencia venusta Yamada. The structure of (3Z)-epoxyvenustin was confirmed by X-ray diffraction analysis. The structures of (3Z)-venustinene containing a novel propyl side chain and (3Z)-venustin were deduced from their spectral evidence.

In our continuing studies on the secondary metabolites from the Japanese species of genus Laurencia (Rhodomelaceae), we have previously reported the structures of venustin A and B, whose names are now renamed as (3E)-epoxyvenustin and (3E)-venustin respectively, isolated from Laurencia venusta Y. (collected at Moheji, Hokkaido).[2)] In this communication we wish to report the structures of three new acetylenic compounds, which were isolated from L. venusta (collected at Moura, near Asamushi, Aomori Prefecture, in July 23, 1982) and designated as (3Z)-epoxyvenustin, (3Z)-venustin, and (3Z)-venustinene. (3Z)-Venustinene contains a propyl side chain and a conjugated diene moiety not yet encountered in the nonterpenoid C_{15}-metabolites from the genus Laurencia.

Conventional silica gel column chromatography of the neutral methanol extracts gave (3Z)-epoxyvenustin (1), (3Z)-venustin (2), and (3Z)-venustinene (3) in 20%, 3%, and 1.5% yields of the extracts, respectively.



(3Z)-Epoxyvenustin (1), $C_{15}H_{18}O_2BrCl$ (m/z 348, 346, and 344; M^+), mp 72-73 °C (from hexane), $[\alpha]_D^{20}$ -44.1° (c 1.00; $CHCl_3$), showed the presence of a conjugated cis-pentenyne side chain in its UV [λ_{max}^{EtOH} 212 nm (ε 18,000), λ_{inf} 220 (ε 17,000) and 231 nm (ε 10,500)], ^{1}H NMR [δ 3.17 (1H, d, J=2 Hz), 5.60 (1H, br d, J=11 Hz), and 6.10 (1H, ddd, J=11, 7, 7 Hz)], and mass [m/z 65] spectra. Furthermore, comparison of the spectral data[3] of 1 with those of (3E)-epoxyvenustin (4)[2] exhibited the presence of the same oxocane ring bearing a pentenyne side chain, an oxirane ring, a bromopropylidene moiety, and a chlorine atom as in 4, thus indicating that the structure of (3Z)-epoxyvenustin must be represented by formula 1. This was confirmed by the following chemical correlation. Hydrogenation of 1 over PtO_2 in ethyl acetate gave the hexahydro compound, $C_{15}H_{24}O_2BrCl$ (m/z 354, 352, and 350; M^+), $[\alpha]_D^{21}$ +7.02° (c 0.78), which was identical with the hydrogenation product (6)[2] of (3E)-epoxyvenustin (4) in all respects. However, the stereochemistry of the oxirane ring had not been confirmatively settled.[2] Therefore, in order to establish the structure including the absolute configuration, a single crystal of 1 was submitted to X-ray crystallographic analysis.

The crystal data for 1 were as follows: $C_{15}H_{18}O_2BrCl$, orthorhombic, space group $P2_12_12_1$, a=9.527(4), b=21.621(7), c=7.423(5) Å, Z=4, D_c=1.501 g cm^{-3}. 1037 unique intensity data for 2θ<50° were collected on an automated four-circle diffractometer with graphite-monochromated Mo Kα radiation, using the θ-2θ scanning technique.[4] The structure was solved by the Monte Carlo direct method, using the 20 strongest reflections as the starting set.[5] The 2nd random phase set led to the correct solution; an E-map based on 447 phases revealed the locations of all the non-hydrogen atoms. After the structure had been well refined by the block-diagonal least-squares method with anisotropic temperature factors, the absolute configuration was determined by taking account of the anomalous dispersion of halogen atoms for Mo Kα radiation. The R ratio for the two enantiomeric structures, 1.16, rejected one of them at the 99.5% confidence level.[6] A difference Fourier map afforded all the hydrogen atoms except that of the ethynyl group. Further least-squares refinements were performed including the hydrogen atoms and the anomalous-dispersion effects. The final R value was 0.052. The molecular structure of 1 thus obtained is shown in Fig. 1. Consequently, the absolute structure of (3E)-epoxyvenustin is represented by formula 4. (3Z)-Epoxyvenustin (1) is the geometrical isomer of the double bond at C-12 of epoxyrhodophytin (7) also isolated from an undescribed Laurencia species.[7]

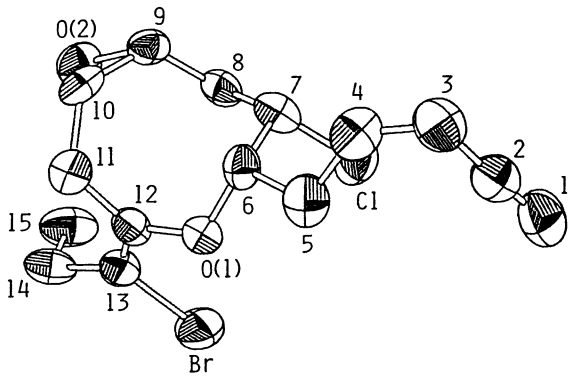


Fig. 1. A perspective view of the 1 molecule.

(3Z)-Venustin (2), $C_{15}H_{18}OBrCl$ (m/z 332, 330, and 328; M^+), $[\alpha]_D^{20}$ -103° (c 1.14), is an isomer of (3E)-venustin (5)[2] and could readily be assigned formula 2 by detailed comparison of the spectral properties[3] of 2 with those of 5.

The third metabolite, (3Z)-venustinene (3), mp 38-39 °C (from MeOH-H_2O), $[\alpha]_D^{23}$ -184° (c 1.00), was analyzed for $C_{15}H_{19}OCl$ by high resolution mass spectroscopy m/z 250.1128 (calcd for $C_{15}H_{19}OCl$; 250.1125). The UV spectrum of 3 showed absorption maxima at λ_{max}^{EtOH} 267 nm (ε 4,900) due to a conjugated diene moiety and at λ_{inf} 231 nm (ε 8,000), λ_{max} 221 nm (ε 10,600), and λ_{inf} 214 nm (ε 9,800) due to a conjugated terminal enyne group. The mass spectrum[3] indicated the presence of propyl (m/z 209 and 207; $M^+-C_3H_7$) and pentenyne (m/z 187 and 185; $M^+-C_5H_5$) side chains, which was also supported by the ^1H NMR spectrum. Since the IR spectrum[3] revealed no hydroxyl and carbonyl functions, the sole oxygen atom in 3, having six degrees of unsaturation, was assumed to be involved as an ether link. From above-mentioned data coupled with the spin decoupling experiments in the ^1H NMR spectrum (Table 1), the following partial structure could be deduced.

$$\overset{15}{CH_3}\text{-}\overset{14}{CH_2}\text{-}\overset{13}{CH_2}\text{-}\overset{12}{C}(\overset{C1}{})(\overset{O}{})\overset{11}{\text{-}CH}\text{=}\overset{10}{CH}\text{-}\overset{9}{CH}\text{=}\overset{8}{CH}\text{-}\overset{7}{CH_2}\text{-}\overset{6}{CH}\text{-}\overset{5}{CH_2}\text{-}\overset{4}{CH}\text{=}\overset{3}{CH}\text{-}\overset{2}{C}\equiv\overset{1}{C}\text{-}H$$

Since the ^1H and ^{13}C NMR spectra (Table 1) of 3 indicated the absence of an oxirane ring, the oxygen atom in 3 could be attached to C-12. Furthermore, the mass spectrum showed no fragment ion due to a hexenyne side chain containing a chlorine atom, indicating that the remaining substituent at C-6 is not chlorine atom but oxygen atom, and hence the chlorine atom must be attached to C-7. The chemical shift (δ 3.13) of the acetylenic proton and the coupling constant (J=11 Hz) between the olefinic protons at C-3 and C-4 revealed the double bond at C-3

Table 1. ^1H and ^{13}C NMR data for (3Z)-venustinene (3)

Carbon	^{13}C δ[a]	^1H δ[b]	Multiplicity, J (Hz)
1	80.0	3.13	d, $J_{1,3}$ = 2
2	82.5		
3	130.5	5.55	br d, $J_{3,4}$ = 11
4	140.8	6.00	ddd, $J_{4,3}$ = 11, $J_{4,5}$ = 7, 7
5	39.2[c]	2.5∿3.0	m
6	76.0	4.97	ddd, $J_{6,7}$ = 2, $J_{6,5}$ = 9, 5
7	59.1	3.86	ddd, $J_{7,6}$ = 2, $J_{7,8}$ = 12, 5
8	35.6[c]	2.5∿3.0	m
9	110.9	5.30	ddd, $J_{9,10}$ = 10, $J_{9,8}$ = 8, 8
10	122.4	5.86	dd, $J_{10,9}$ = 10, $J_{10,11}$ = 6
11	97.1	4.58	d, $J_{11,10}$ = 6
12	160.2		
13	34.6	2.04 2.17	ddd, $J_{13,13}$ = 14, $J_{13,14}$ = 7, 7
14	21.1	1.55	tq, $J_{14,13}$ = 7, 7, $J_{14,15}$ = 7, 7, 7
15	13.6	0.92	t, $J_{15,14}$ = 7, 7

a) Spectrum was measured at 50.10 MHz in $CDCl_3$ (TMS=0). b) Spectrum was recorded at 200 MHz in $CDCl_3$ (TMS=0). c) Assignments may be interconvertible.

to be Z. The cis-relationship between the chlorine atom at C-7 and the pentenyne side chain at C-6 was suggested by the coupling constant (J=2 Hz) between the protons at C-7 and C-6, whose J-value was consistent with that of (3Z)-epoxy-venustin (1).

Thus the structure of (3Z)-venustinene would be represented by formula 3, which is the first example of halogenated C_{15}-nonterpenoid with a propyl side chain at C-12, whereas the C_{15}-nonterpenoids from the genus Laurencia generally contain bromopropyl or ethyl side chain at C-12 or C-13, respectively. It is biologically interesting that Moura's L. venusta has exclusively synthesized (3Z)-metabolites while Moheji's specimen has synthesized only (3E)-metabolites.[8]

References

1) Part 55 of "Constituents of Marine Plants". Part 54, K. Kurata, T. Suzuki, M. Suzuki, E. Kurosawa, A. Furusaki, K. Suehiro, T. Matsumoto, and C. Katayama, Chem. Lett., 1983, 561.

2) M. Suzuki and E. Kurosawa, Chem. Lett., 1980, 1177.

3) 1: IR, ν_{max} (Nujol) 3300, 2100, 1660, 1200, 1140, 1072, 990, 831, 755, and 730 cm^{-1}; ^1H NMR (100 MHz; $CDCl_3$), δ 1.12 (3H, t, J=7 Hz; C_{15}-CH_3), 2.46 (2H, q, J=7 Hz; C_{14}-CH_2), 3.17 (1H, d, J=2 Hz; C_1-H), 4.13 (1H, ddd, J=11, 5, 2 Hz; C_7-H), 4.35 (1H, ddd, J=7, 7, 2 Hz; C_6-H), 5.60 (1H, br d, J=11 Hz; C_3-H), and 6.10 (1H, ddd, J=11, 7, 7 Hz; C_4-H); ^{13}C NMR (25.1 MHz; $CDCl_3$), δ 144.5 (s), 139.9 (d), 111.7 (s), 111.2 (d), 82.8 (d), 79.7 (s), 76.9 (d), 59.9 (d), 53.3 (d), 52.0 (d), 34.3 (t), 34.1 (t), 29.7 (t), 28.7 (t), and 13.5 (q); MS (rel. intensity), m/z 348, 346, 344 (1:6:5, M^+), 311, 309 (1:1, M^+-Cl), 267, 265 (12:36, M^+-Br), 150, 148 (50:50), 117 (53), 115 (44), 91 (57), 65 (92), 57 (58), and 41 (100); HR-MS, m/z 344.0155 (Calcd for $C_{15}H_{18}O_2{}^{79}Br^{35}Cl$, 344.0178).
2: UV, λ_{max} (EtOH) 222 nm (ε 17,000), λ_{inf} 214 nm (ε 16,000) and 231 nm (ε 12,000); ν_{max} ($CHCl_3$) 3300, 2100, 1655, 1260, 1135, and 980 cm^{-1}; δ 1.09 (3H, d, J=7 Hz; C_{15}-CH_3), 2.44 (2H, q, J=7 Hz; C_{14}-CH_2), 3.14 (1H, d, J=2 Hz; C_1-H), 3.98 (1H, ddd, J=11, 5, 2 Hz; C_7-H), 4.43 (1H, ddd, J=7, 7, 2 Hz; C_6-H), 5.56 (1H, br d, J=11 Hz; C_3-H), ca. 5.2 (2H, m, C_9-H and C_{10}-H), and 6.12 (1H, ddd, J=11, 7, 7 Hz; C_4-H); δ 147.4 (s), 140.8 (d), 130.4 (d), 125.4 (d), 110.7 (d), 107.0 (s), 82.5 (d), 79.8 (s), 76.3 (d), 63.4 (d), 33.9 (t), 32.5 (t), 29.8 (t), 29.6 (t), and 13.4 (q); m/z 332, 330, 328 (M^+); HR-MS, m/z 328.0213 (Calcd for $C_{15}H_{18}O^{79}Br^{35}Cl$, 328.0228).
3: ν_{max} ($CHCl_3$) 3300, 2100, 1633, 1620, 1185, 1165, 1103, and 1092 cm^{-1}; m/z 252, 250 (1:3, M^+), 215 (4, M^+-Cl), 209, 207 (0.3:1, M^+-C_3H_7), 187, 185 (2:5, M^+-C_5H_5), 123 (43), 110 (81), 91 (60), 81 (100), 77 (33), 71 (94), 65 (36), and 43 (89).

4) The intensity measurement was made at the High Energy X-Ray Diffraction Laboratory of Hokkaido University.

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6) W. C. Hamilton, Acta Crystallogr., 18, 502 (1965).

7) B. M. Howard, W. Fenical, K. Hirotsu, B. Solheim, and J. Clardy, Tetrahedron, 36, 171 (1980).

8) (3E)-Venustinene could not be detected in the previous Moheji's extracts.

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