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Ecklonialactone-A and -B, Two Unusual Metabolites from the Brown Alga *Ecklonia stolonifera* Okamura

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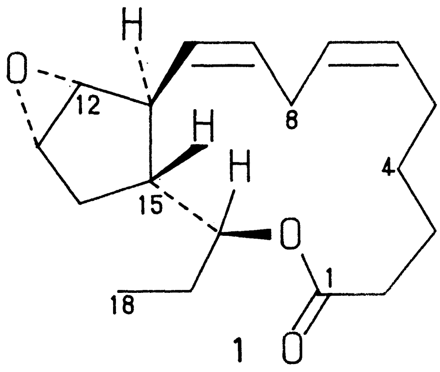
Two new unusual metabolites, ecklonialactone-A and -B have been isolated from the title alga, and their structures were determined by spectral and chemical methods as well as X-ray crystallographic analysis.

Among the brown algae family Laminariaceae, *Ecklonia cava* Kjellman ("Kajime" in Japanese), one of the species of the genus *Ecklonia*, is known to be a suitable food for the abalones *Haliotis* species.[1)] On the other hand,. these abalones feed little on the brown alga *Ecklonia stolonifera* Okamura ("Tsuru-arame"),[2)] thus suggesting that, as have been reported in the case of the brown alga *Dilophus okamurai* Dawson ("Fukurin-amiji"),[3,4)] this alga contains feeding-deterrent substances against the abalones. Although the neutral extract of *E. stolonifera*[5)] did not show distinct feeding-deterrent activity,[6)] an unusual metabolite, named as ecklonialactone-A, isolated from this alga showed a weak activity compared with the control. In this paper we wish to report the structures of two new unique metabolites, ecklonialactone-A (1) and -B (2).

The neutral extract of *E. stolonifera* was subjected to a combination of column chromatography over alumina and silica gel followed by HPLC (Megapak SIL-C_{18}, MeOH/H_2O (85:15)) to give ecklonialactone-A (1) and -B (2) in 0.65 and 0.33% yield, respectively, based on the extract.

Ecklonialactone-A (1), mp 96-98 °C (EtOH), $[\alpha]_D$ -87.7° (c 1.02; $CHCl_3$), had a molecular formula $C_{18}H_{26}O_3$.[7)] Its IR spectrum[8)] showed an intense carbonyl absorption at ν_{max} 1720 cm^{-1} and the ^{13}C NMR spectrum[8)] showed a quaternary carbon at δ 173.6, thus indicating the presence of a lactonic or an esteric group in **1**. Furthermore, ^{13}C and ^{1}H NMR[8)] spectra revealed the presence of two 1,2-disubstituted double bonds and five methine groups, two of which were ascribable to an oxirane grouping [δ 3.23 (1H, br d, J=2.5 Hz) and 3.50 (1H, br d, J=2.5 Hz); δ 61.0 (d) and 57.2 (d)]. Above-mentioned data exhibited that ecklonialactone-A (1), having six degrees of unsaturation, must be composed of a tricyclic skeleton including an



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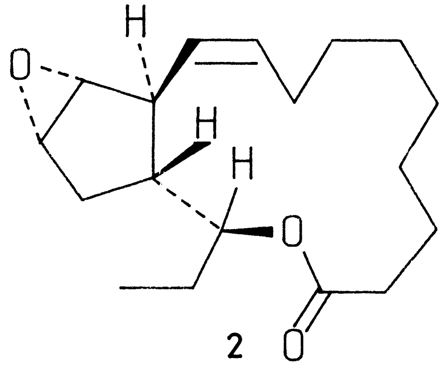

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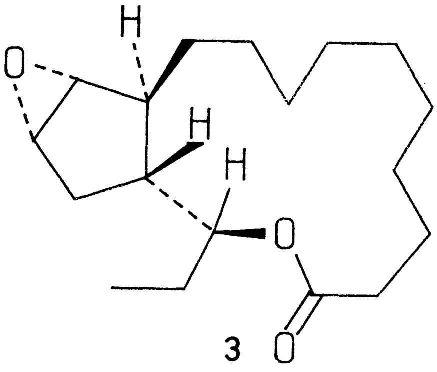

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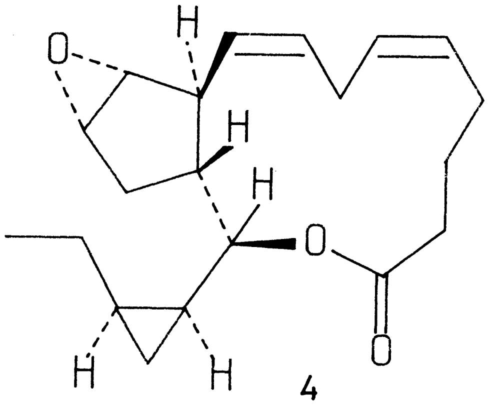

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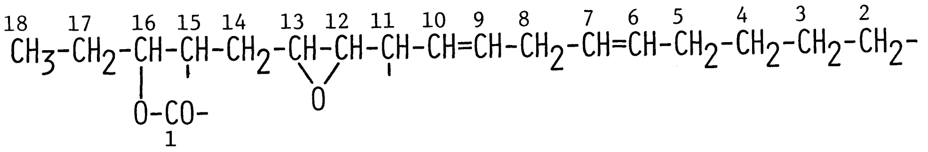
oxirane ring and probably a lactone ring. The ^1H-^1H 2D COSY spectra (in $CDCl_3$ and in C_6D_6) coupled with ^1H-^{13}C COSY spectrum provided the following partial structure (Fig. 1) for **1**. Judging from the chemical shifts [δ 2.40 (2H, m) and δ 33.6 (t)] for the protons and the carbon at C-2, this carbon (C-2) must be connected to the carbonyl group, leading to a planar formula **1** for ecklonialactone-A. Thus in order to establish the structure, we have carried out an X-ray crystallographic study of **1**.



$$\overset{18}{CH_3}-\overset{17}{CH_2}-\underset{\underset{1}{O-CO-}}{\overset{16}{CH}}-\overset{15}{CH}-\overset{14}{CH_2}-\overset{13}{CH}\underset{O}{\diagdown\diagup}\overset{12}{CH}-\overset{11}{CH}-\overset{10}{CH}=\overset{9}{CH}-\overset{8}{CH_2}-\overset{7}{CH}=\overset{6}{CH}-\overset{5}{CH_2}-\overset{4}{CH_2}-\overset{3}{CH_2}-\overset{2}{CH_2}-$$

Fig. 1. Partial structure for **1**.

The crystal data of **1** were as follows: $C_{18}H_{26}O_3$, monoclinic, space group $P2_1$, a=10.636(6), b=10.076(3), c=8.418(5) Å, β=111.80(5)°, Z=2, D_c=1.152 g cm^{-3}. The intensities of 1166 independent reflections with $2\theta<45°$ were measured on a Rigaku four-circle diffractometer with graphite-monochromated Mo Kα radiation. The structure was solved by the direct method, and was refined by the block-diagonal least-squares method. Hydrogen atoms were located in a difference Fourier map, and were included in the refinement. The final R value was 0.108. The molecular skeleton of **1**, including the relative configuration, is illustrated in Fig. 2.

Ecklonialactone-B (**2**), $C_{18}H_{28}O_3$,[7] mp 64-66 °C (EtOH), $[\alpha]_D$ -49.3° (c 1.08: $CHCl_3$), showed spectral data[9] very similar to those of **1**. The ^1H and ^{13}C NMR spectra revealed the presence of one 1,2-disubstituted double bond and five methine groups which are also present in **1**, thus suggesting that ecklonialactone-B is the dihydro derivative of **1**.

Hydrogenation of **2** with Pt-catalyst in ethyl acetate gave the hydrogenated product whose IR and ^1H NMR spectra were identical with those of compound **3**[10] derived from **1** by hydrogenation. Comparison of the chemical shifts of the proton and the carbon at C-11 in **1** and **2** [δ 3.09 (br d, J=9.5 Hz) in **1** and δ 3.03 (br d, J=9.9 Hz) in **2**; δ 40.1 in **1** and δ 40.0 in **2**] indicated that ecklonialactone-B (**2**) is the 6,7-dihydro derivative of ecklonialactone-A (**1**).

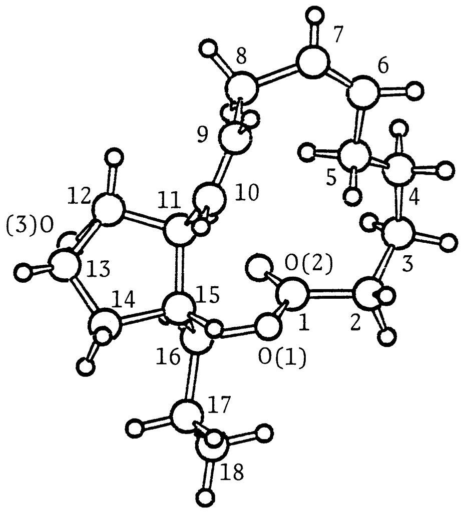


Fig. 2. A perspective view of ecklonialactone-A (**1**).

The structure of ecklonialactone-A (**1**) is very similar to that of hybridalactone (**4**)[11,12] which has previously been isolated from the red alga Laurencia hybrida.

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5) Alga was collected in May 1987 at near Tsuruoka, Yamagata prefecture.

6) Feeding-deterrent activity was evaluated by comparing the number of biting traces left on the cellulose plates with that of the phosphatidylcholine.[4] The water-soluble fraction showed a considerably strong activity.

7) HR-MS; **1**: m/z 290.1864 (calcd for $C_{18}H_{26}O_3$, 290.1881), **2**: m/z 292.2045 (calcd for $C_{18}H_{28}O_3$, 292.2038).

8) Spectral data for **1**; IR ($CHCl_3$), ν_{max} 1720, 1398, 1380, 1362, 1342, 1263, 1107,

1089, 1019, 975, 950, 930, 913, and 840 $\mathrm{cm^{-1}}$; ^{1}H NMR (270 MHz, $\mathrm{CDCl_3}$), δ 0.81 (3H, t, J=7.3 Hz, H_3-18), 1.3-1.5 (3H, m, H_2-4 and H-17), 1.6-1.8 (3H, m, H_2-3 and H-17), 1.8-2.1 (5H, m, H_2-5, H_2-14, and H-15), 2.40 (2H, m, H_2-2), 2.65 (1H, m, H-8), 3.09 (1H, br d, J=9.5 Hz, H-11), 3.1 (1H, m, H-8), 3.23 (1H, br d, J=2.5 Hz, H-12), 3.50 (1H, br d, J=2.5 Hz, H-13), 4.91 (1H, m, H-16), 5.09 (1H, ddd, J=10, 9.5, 1.5 Hz, H-10), and 5.3-5.5 (3H, m, H-6, H-7, and H-9); ^{13}C NMR (67.9 MHz, $\mathrm{CDCl_3}$), $\mathrm{CH_3}$: δ 8.7 (C-18), $\mathrm{CH_2}$: δ 24.3 (C-3), 25.3 (C-17), 26.0 (C-5), 26.3 (C-8), 28.1 (C-4), 28.8 (C-14), and 33.6 (C-2), CH: δ 40.1 (C-11), 46.0 (C-15), 57.2 (C-13), 61.0 (C-12), 78.6 (C-16), 127.5 (C-10), 128.0 (C-7), 129.5 (C-6 or C-9), and 129.8 (C-9 or C-6), C: δ 173.6 (C-1); MS (70 eV), m/z (rel. intensity) 290 (1.3; M^+), 273 (1.4), 272 (6), 261 (3.3), 243 (4.7), 232 (9.2), 159 (21), 145 (28), 131 (61), 117 (100), 105 (67), 97 (73), 93 (41), 91 (86), 81 (40), 79 (75), 77 (43), 67 (63), 57 (36), 55 (53), 53 (28), 43 (22), 41 (96), and 39 (34).

9) Spectral data for 2; IR ($\mathrm{CHCl_3}$), ν_{max} 1720, 1403, 1373, 1345, 1180, 1149, 1092, 1002, 985, 970, 955, 930, and 845 $\mathrm{cm^{-1}}$; ^{1}H NMR (270 MHz, $\mathrm{CDCl_3}$), δ 0.81 (3H, t, J=7.3 Hz, H-18), 1.2-1.5 (9H, m, H_2-4, H_2-5, H_2-6, H_2-7, and H-17), 1.6 (1H, m, H-3), 1.71 (1H, m, H-17), 1.8-2.0 (4H, m, H-3, H_2-14, and H-15), 2.08 (2H, m, H_2-8), 2.38 (2H, m, H_2-2), 3.03 (1H, br d, J=9.9 Hz, H-11), 3.25 (1H, br d, J=2.6 Hz, H-12), 3.50 (1H, br d, J=2.6 Hz, H-13), 4.96 (1H, m, H-16), 5.12 (1H, br dd, J=10, 9.9 Hz, H-10), and 5.47 (1H, m, H-9); ^{13}C NMR (67.9 MHz, $\mathrm{CDCl_3}$), $\mathrm{CH_3}$: δ 8.7 (C-18), $\mathrm{CH_2}$: δ 24.1 (C-3), 25.3 (C-17), 25.3 x 2, 26.2, 26.8 x 2(C-4, C-5, C-6, C-7, and C-8), 28.8 (C-14), and 33.5 (C-2), CH: δ 40.0 (C-11), 46.3 (C-15), 57.0 (C-13), 61.0 (C-12), 78.6 (C-16), 128.2 (C-10), and 131.8 (C-9), C: δ 173.8 (C-1); MS (70 eV), m/z 292 (6; M^+), 275 (4), 274 (13), 263 (7), 245 (12), 244 (16), 234 (10), 177 (20), 163 (24), 149 (54), 147 (20), 145 (21), 135 (21), 133 (35), 131 (21), 121 (34), 120 (22), 119(77), 109 (18), 108 (19), 107 (46), 106 (44), 105 (100), 97 (18), 96 (24), 95 (30), 94 (21), 93 (71), 92 (79), 91 (65), 81 (62), 80 (79), 79 (72), 77 (33), 69 (28), 67 (67), 57 (48), 55 (76), 53 (23), 43 (28), 41 (99), and 39 (25).

10) Spectral data for 3; $[\alpha]_D$ +14.5° (c 0.550; $\mathrm{CHCl_3}$); IR ($\mathrm{CHCl_3}$), ν_{max} 1720, 1405, 1385, 1375, 1360, 1347, 1255, 1175, 1147, 1085, 970, 955, 942, 916, and 841 $\mathrm{cm^{-1}}$; ^{1}H NMR (270 MHz, $\mathrm{CDCl_3}$), δ 0.81 (3H, t, J=7.3 Hz), 2.13 (1H, br d, J=7.0 Hz), 2.36 (1H, d, J=7.0 Hz), 2.38 (1H, d, J=8.0 Hz), 3.31 (1H, br d, J=2.5 Hz), 3.44 (1H, br d, J=2.5 Hz), and 4.88 (1H, m); MS (70 eV), m/z 294 (5; M^+), 277 (2), 266 (6), 251 (13), 247 (7), 237 (4), 236 (3), 219 (3), 191 (4), 137 (12), 123 (19), 121 (15), 109 (13), 97 (13), 95 (23), 94 (10), 93 (31), 81 (40), 80 (100), 79 (23), 69 (18), 67 (43), 66 (11), 57 (37), 55 (38), 43 (15), 41 (48), and 39 (9); HR-MS: m/z 294.2176 (calcd for $C_{18}H_{30}O_3$, 294.2195).

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