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LAUREEPOXIDE, NEW BROMO ETHER FROM THE MARINE RED ALGA *LAURENCIA NIPPONICA* YAMADA[1)]

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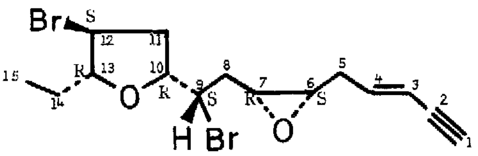
Summary. An interesting bromine containing compound, laureepoxide (1), has been isolated from *L. nipponica* Yamada (Rhodomelaceae, Rhodophyta) and its structure has been determined by the chemical degradations and spectral properties.

Cyclic ethers containing bromine or chlorine, which consist of C_{15} straight carbon skeleton, are common metabolites of several species of the marine red alga *Laurencia*[2)] and usually possess terminal conjugated enyne or allene moieties and seem to be derived from the acyclic precursor, laurediol,[3)] which has been already isolated from this source, *L. nipponica* Yamada. Recently, from our continuing research of *L. nipponica* Yamada, it has been perceived that the constituents of this alga were greatly dependent upon the growth localities. Our investigation of this alga, collected at West Shakotan, Hokkaido, in May and June, led to isolation of new brominated C_{15}-nonterpenoid, laureepoxide (1) and we wish to report herein the structure of this unusual metabolite containing both oxolane and oxirane ring and two bromines. Laureepoxide (1) is a first example containing oxirane ring not yet observed in this group of compounds.

The neutral essential oil from the methanol extract was fractionated on column chromatography over silicic acid and the fractions eluted with benzene gave laureepoxide (1) as a major component (4.9%) together with the known compounds, laurencin, deacetyllaurencin[2a)], laurefucin and acetyllaurefucin[2d)].



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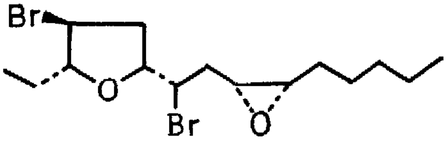

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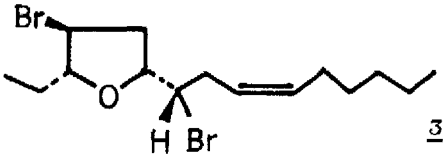
Laureepoxide (1), a colorless oil, $[\alpha]_D$ +25.0° (c; 1.00, $CHCl_3$), $C_{15}H_{20}O_2Br_2$, m/e 390, 392 and 394 (M^+), had the characteristic absorptions due to conjugated enyne group [ν_{max}3300, 2100 cm^{-1}; λ_{max}224(ε 17.000) and $\lambda_{infl.}$230 nm (ε 12.600)] and ether functions (ν_{max}1115, 1065 and 1015 cm^{-1}) but no hydroxyl or carbonyl absorption. The presence of the groups above mentioned has been also confirmed by its ^1H and ^{13}C NMR spectra [^1H; δ 1.00 (3H, t, J=7 Hz), 1.2-2.8 (8H, m), 2.90 (1H, d, J=2, $\underline{H}C{\equiv}C-$), 3.2 (2H, m, $-\underline{H}C\underset{O}{-}C\underline{H}-$), 3.8-4.3 (4H, m), 5.65 (1H, dd, J=16, 2 $-CH{=}C\underline{H}-C{\equiv}CH$) and 6.33 (1H, dt, J=16, 7, $-CH_2-C\underline{H}{=}CH-$), ^{13}C; 140.5, 111.4, 87.3, 81.7, 79.4, 77.0, 55.6, 55.3, 54.7, 46.5, 40.3, 33.1, 31.9, 25.1 and 9.8]. The presence of oxirane and the other ether functions in molecule was strongly suggested by its ^1H NMR [3.2 (2H) and 3.8-4.3 (4H)] and IR absorptions around 1115-928 cm^{-1}.

The compound (1) consumed 3 moles of hydrogen over PtO_2 in ethanol to give hexahydrolaureepoxide (2), $C_{15}H_{26}O_2Br_2$, m/e 325, 327 and 329 (M^+- C_5H_{11}). Treatment of 2 with potassium selenocyanate$^{4)}$ in methanol-H_2O gave unsaturated dibromo ether (3), $C_{15}H_{26}OBr_2$, m/e 380, 382 and 384 (M^+), $[\alpha]_D$ +43.8° (c; 1.20, $CHCl_3$); δ 0.89 (3H, br. t), 1.01 (3H, t, J=7 Hz), 1.2-1.7 (8H, m), 1.9-2.2 (2H, m), 2.5-2.8 (4H, m), 3.7-4.3 (4H, m) and 5.48 (2H, m); ν_{max}3020, 1400, 1293, 1105, 1074, 1010, 967 and 928 cm^{-1}.

On the other hand, treatment of 2 with zinc powder in acetic acid finally gave diene epoxide (4), $C_{15}H_{26}O$, $[\alpha]_D$ +12.3°, (c; 1.22, $CHCl_3$), ν_{max}3010, 1260, 968, 821 and 720 cm^{-1}, whose ^1H NMR spectrum showed the presence of epoxy protons at δ 2.97 (2H, m), two protons flanked by two double bonds at 2.78 (2H, m) and four olefinic protons at 5.55 (4H, m). The structure of 4 including the absolute configurations at C-6 and 7 was determined to be the antipode of the authentic specimen (5), which was derived from laureatin$^{2b)}$ as described below.

Hexahydrolaureatin (6) was treated with Zn in AcOH to give three products, two of which were unsaturated monobromohydroxy compounds (7), [$C_{15}H_{27}O_2Br$, m/e 318 and 320 (M^+); δ 3.59 (1H, m), 4.05 (1H, m), 4.52 (1H, m), 4.70 (1H, m) and 5.50 (2H, m)] and (8)$^{21)}$. Treatment of 7 with TsCl followed by Zn-AcOH gave unsaturated diol monotosylate (9) in high yield, which was then refluxed in triethyl amine for 2 hr. to yield diene epoxide (5). The comparison of the optical rotation and spectral properties revealed that this epoxide (5) was the antipode of 4 derived from 1.

Furthermore, hydrogenation of 3 gave corresponding dibromoether (10), $C_{15}H_{28}OBr_2$, m/e 353, 355 and 357 (M^+- C_2H_5) and 177 and 179 ($C_6H_{10}OBr$). Debromination of 10 with Ra-Ni afforded tetrahydrofuran derivative (11), $C_{15}H_{30}O$, m/e 226 (M^+), 197 (M^+- C_2H_5) and 99 (M^+- C_9H_{19}). The structure of 10, including the absolute configurations at C-12 and 13, was determined by the chemical correlation to laurencin$^{2a)}$ as follows. Treatment of 10 with Zn-AcOH followed by acetylation and hydrogenation gave two acyclic bromo acetates, $C_{17}H_{33}O_2Br$, (12), $[\alpha]_D$ +3.1°



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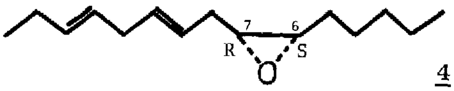

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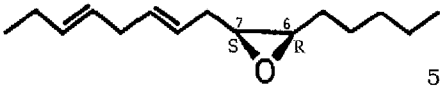

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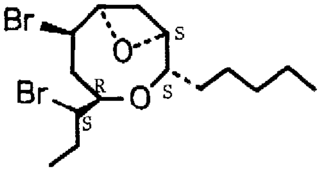

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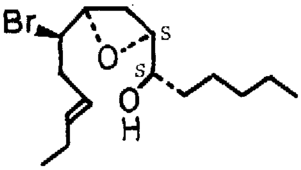

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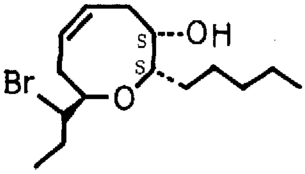

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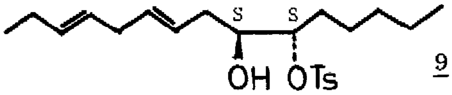

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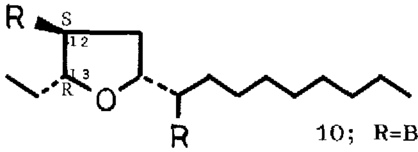
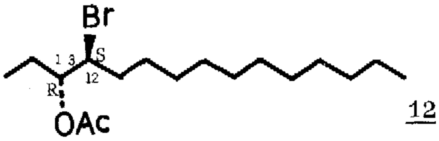


10; R=Br

11; R=H



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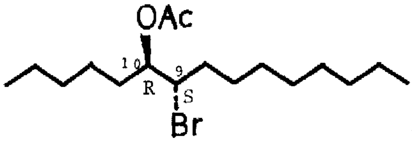

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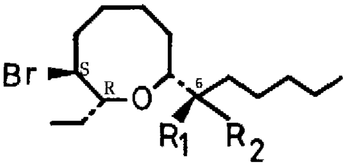
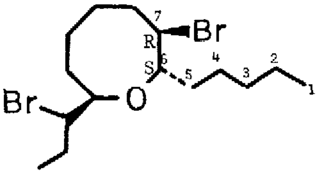


14; R_1=OH, R_2=H: C-6, R

15; R_1=H, R_2=Br: C-6, S



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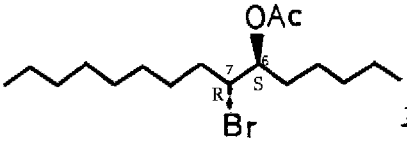

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(c; 0.65, $CHCl_3$), ν_{max}1740, 1301, 1235, 1124, 1089, 1020 and 965 cm^{-1}; δ 0.88 (3H, br.t) 0.91 (3H, t, J=7 Hz), 2.08 (3H, s), 4.08 (1H, dt, J=7, 7) and 4.87 (1H, dt, J=7, 7)] and (13) [$[\alpha]_D$ -31.1° (c; 0.51, $CHCl_3$), ν_{max}1740, 1230, 1128 and 1022 cm^{-1}; δ 0.89 (6H, br.t), 2.09 (3H, s), 4.03 (1H, td, J=6, 3), 4.99 (1H, td, J=6, 3). The reaction product (12) was related to the authentic specimen derived from octahydrodeacetyllaurencin (14)[2a]. Treatment of 14 with carbon tetrabromide and triphenyl phosphine[5] in dry methylene chloride gave dibromide (15), [$C_{15}H_{28}$

OBr_2, m/e 382, 384 and 386 (M^+); δ 3.62 (2H, m) and 4.02 (2H, m)]. Dibromide (15) was then treated with Zn-AcOH followed by acetylation and hydrogenation to give three compounds, one of which was identical with 12 by comparison of optical rotation and spectral properties. These results indicated that the configurations at C-12 and 13 in 12 should be represented by S and R, respectively, and therefore C-12 and 13 in 1 by S and R.

Confirmation of the remaining stereochemistry at C-9 and 10 in 1 came from the following chemical degradation of 8 derived from laureatin. Hydrogenation of 8 followed by bromination with carbon tetrabromide and triphenyl phosphine in $CH_2Cl_2$⁵⁾ gave saturated dibromide (16), $C_{15}H_{28}OBr_2$, δ 0.90 (3H, br.t), 1.06 (3H, t, J=7) and 3.6-4.2 (4H, m). The dibromide (16) was then treated with Zn-AcOH followed by acetylation and hydrogenation to give two compounds, one of which (17) was found to be the antipode of 13 by comparison of the optical rotation and spectral properties. These results came to the conclusion that the configurations at C-9 and C-10 in 13 are S and R, respectively, and consequently laureepoxide should be represented by formula 1.

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