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OKAMURALLENE, A NOVEL HALOGENATED C_{15} METABOLITE FROM THE RED ALGA *LAURENCIA OKAMURAI* YAMADA[1]

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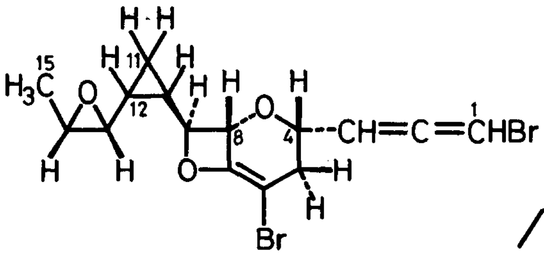
Summary: Okamurallene (1), a novel nonterpenoid C_{15} bromoallene containing cyclopropane ring, has been isolated from the red alga *Laurencia okamurai* Yamada and its structure was determined by the spectral evidence.

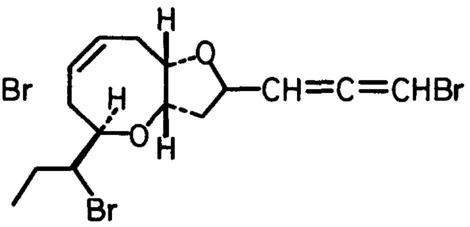
In connection with our interest in the halogenated secondary metabolites of the red algae of the genus *Laurencia* (Rhodomelaceae) and their chemotaxonomic studies, we previously reported that, within the Japanese species of genus *Laurencia*, aromatic sesquiterpenes, laurinterol and debromolaurinterol, were found to be characteristic metabolites of *L. okamurai* Yamada ('Mitsude-sozo' in Japanese).[2] Our further investigations of this species, collected at Bikuni (Hokkaido) and Takahama (Fukui Prefecture),[3] displayed that, as we expected, both specimens have contained laurinterol and debromolaurinterol as the major constituents. In addition, Bikuni's specimen has contained three closely related C_{15}-nonterpenoids as the minor constituents. In this paper we wish to report the structure of one of them, designated as okamurallene, containing bromoallene moiety and cyclopropane ring which is unique feature not yet encountered in the nonterpenoid C_{15} metabolites of *Laurencia*.

The neutral methanol extracts (5.2 g) of Bikuni's alga (300 g) were subjected to combined column and thin-layer chromatography to yield three brominated C_{15}-nonterpenoids along with laurinterol (20% of the extracts), debromolaurinterol (10%) and other aromatic sesquiterpenes.[2]

The more polar compound, okamurallene (1) (2.0%), oil, $[\alpha]_D^{26}$ +160° (c 1.74; $CHCl_3$), was analyzed for $C_{15}H_{16}O_3Br_2$ by mass spectroscopy *m/e* 406, 404



1



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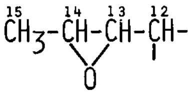
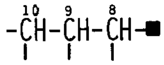
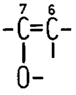


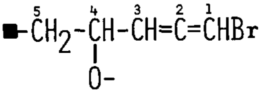
A



B



C



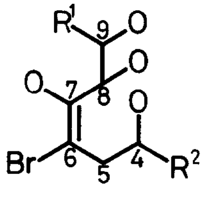
D

and 402 (M^+).[4] Okamurallene (**1**) possesses a bromoallene side chain [IR, ν_{max} (film) 1960 cm^{-1}; ^{1}H NMR (CDCl$_3$), δ 5.44 (1H, dd, *J*=6.0, 6.0 Hz) and 6.10 (1H, dd, *J*=6.0, 1.5 Hz); ^{13}C NMR (CDCl$_3$), δ 202.5 (s), 99.2 (d) and 73.9 (d); mass, *m/e* 287 and 285 (M^+-C_3H_2Br)] as same as laurallene (**2**) isolated from *Laurencia nipponica* Yamada.[5] Furthermore, the ^{1}H and ^{13}C NMR spectra of **1** showed the presence of a $\text{-O-}\underset{|}{\text{C}}\text{HCH}_3$ grouping [δ 1.36 (3H, d, *J*=5.5 Hz); δ 13.7 (q)] and an oxirane ring [δ 2.80 (1H, dd, *J*=4.5, 3.0 Hz) and 3.00 (1H, dq, *J*=4.5, 5.5 Hz); δ 56.1 (d) and 52.7 (d)]. The ^{13}C NMR spectrum revealed the remaining signals at δ 157.6 (s), 91.2 (s), 88.4 (d), 83.6 (d), 72.7 (d), 40.8 (t), 17.0 (d), 12.5 (d) and 10.0 (t). Since the IR spectrum[6] of **1** showed the absence of hydroxyl and carbonyl functionalities, the three oxygen atoms of **1** were assumed to be involved as ether links. In the IR spectrum the intense absorptions at ν_{max} 1660 and 1200 cm^{-1} indicated the presence of a trisubstituted vinyl ether function which was further supported by the observation of two quaternary carbons at δ 157.6 and 91.2 ppm in the ^{13}C NMR spectrum (structural unit **C**).

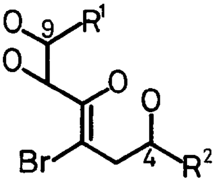
Moreover, the detailed spin decoupling studies in the ^{1}H NMR (100 MHz and 200 MHz) spectra of **1** provided additional information of the structure. Irradiation of the one-proton multiplet centered at δ 4.28 caused the double doublet at δ 6.10 and the double doublet at δ 5.44 to collapse each to doublets (*J*=6.0 Hz). In the same double resonance experiment, the signals of methylene protons observed as an ABX pattern at δ 2.44 (dd, *J*=13.5, 5.0 Hz) and 1.90 (dd, *J*=13.5, 10.0 Hz), the latter of which overlapped with the signal of another methine proton, was simplified each to doublets (*J*=13.5 Hz), proving that the methylene group must be flanked on one side by a fully substituted center. These results showed the presence of structural unit **D** (■; quaternary carbon) in the molecule. Irradiation of the doublet methyl signal at δ 1.36 collapsed the double quartet at δ 3.00 to a doublet (*J*=4.5 Hz), while irradiation at δ 3.00 simplified the doublet at δ 1.36 to a sharp singlet and converted the double doublet at δ 2.80 into a doublet (*J*=3.0 Hz), indicating that the methyl group must be attached to the oxirane ring. Furthermore, irradiation at δ 2.80 collapsed the signal at δ 3.00 to a quartet (*J*=5.5 Hz) and effected a change in the shape of the three-protons multiplets at δ ca. 1.1∿1.3. Irradiation at δ ca. 1.2 affected not only the one-proton multiplet at δ ca. 1.9 but also caused the signal at δ 2.80 to collapse to a doublet (*J*=4.5 Hz). Above results indicated the presence of structural unit **A** in the molecule.

Structural unit **B** was also derived from the spin decoupling experiments as follows. Irradiation of the one-proton double doublet (*J*=6.5, 6.5 Hz) at δ 5.06 collapsed the one-proton doublet (*J*=6.5 Hz) at δ 5.31 to a singlet and also changed the appearance of the multiplet at δ ca. 1.9. Conversely, by irradiation at δ ca. 1.9, the double doublet at δ 5.06 was simplified to a doublet (J=6.5 Hz) and the appearance of the multiplets at δ ca. 1.1∿1.3 was also changed. Since the ^{13}C NMR spectrum revealed that any double bond except for the bromoallene and the trisubstituted vinyl ether moieties is not present, two protons at C-8 (δ 5.31) and C-9 (δ 5.06) were ascribed to the protons on carbons bearing oxygen atom or bromine atom. Above results permitted the deduction of unit **B** in the molecule.

All elements except for a methylene group and one bromine atom implied by the molecular formula of okamurallene (**1**) have now been defined and are comprised in the structural units **A**, **B**, **C** and **D**. The ^{1}H NMR chemical shifts of the C$_{10}$-H and the C$_{12}$-H reveal that no bromine atom or oxygen atom must be attached to these carbons. Therefore, the remaining methylene group (δ 1.1∿1.3) can be inserted between C-10 and C-12 accompanied by linking C-10 and C-12 to form a cyclopropane ring[7] which is suggested by the decoupling data and by the typical three signals due to a 1,2-disubstituted cyclopropane at δ 17.0 (d), 12.5 (d) and 10.0 (t) in the ^{13}C NMR spectrum.[8] Thus **1**, having seven degrees of unsaturation, must contain other two oxide rings. Since the C$_{15}$-nonterpenoid cyclic ethers of *Laurencia* seem to be derived from a straight-chain C$_{15}$-precursor, e.g. laurediol from *L. nipponica*,[9] the double bond (unit **C**) necessitates being linked to C-8 at one end and to C-5 at the other end. The ^{13}C NMR chemical shifts (δ 157.6 and 91.2) of the trisubstituted vinyl ether function indicate that the fourth substituent of **C** must be not oxygen atom but bromine atom, leading to structures, **E**, **F**, **G** and **H**.



E



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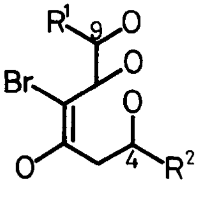
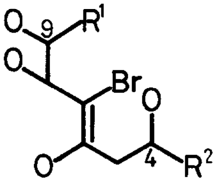


G



H

A study of Dreiding models indicated that only four possible structures are given by the following ether closures; (i) bonding between C-4 and C-8 and between C-7 and C-9 by oxygen atoms in **E**, (ii) bonding between C-4 and C-7 and between C-8 and C-9 by oxygen atoms in **F** and (iii) bonding between C-4 and C-6 and between C-8 and C-9 by oxygen atoms in **G** and **H**, the latter three structures of which, however, can be ruled out because of the presence of an additional oxirane ring for which there is no evidence. Hence okamurallene would be represented by formula **1** as a planar structure.

The stereochemistries at C-4, C-8, C-9, C-13 and C-14 were deduced with the aid of the coupling constants in the ^{1}H NMR spectrum. The configuration of the proton at C-4 was found to be axial since the methylene protons at C-5 were observed as the AB parts of the ABX system at δ 2.44 and 1.90, with a geminal coupling constant of 13.5 Hz and additional couplings of 5.0 Hz ($J_{eq,ax}$) and 10.0 Hz ($J_{ax,ax}$). Furthermore, the coupling constant, J=6.5 Hz, between the protons at C-8 and C-9 on oxetane ring seemed to show that the stereochemistry of the protons at C-8 and C-9 is *trans* to each other.[10] The *cis* stereochemistry of the oxirane ring between C-13 and C-14 was indicated by the value (4.5 Hz) of the coupling constant between the pertinent epoxide methines.[11] The *cis* relationship between the C_4-H and the C_8-H was confirmed by the observation of a nuclear Overhauser enhancement (ca. 15%) between these two protons. But the stereochemistry of the cyclopropane ring remains unsettled.

Thus the structure of okamurallene would be represented by formula **1**, which is the first example of the nonterpenoid C_{15}-compounds from the genus *Laurencia* with a cyclopropane ring, a bromine atom at C-6 and a substituent at C-8.

References and Notes

1. Part 46 of "Constituents of Marine Plants". Part 45, T. Suzuki, A. Furusaki, H. Kikuchi, E. Kurosawa and C. Katayama, *Tetrahedron Letters*, in press.
2. M. Suzuki and E. Kurosawa, *Bull. Chem. Soc. Jpn.*, 52, 3352 (1979) and references cited therein.
3. Algae were collected at Bikuni, Shakotan peninsula, Hokkaido, in August, 1979, and Takahama, Fukui Prefecture, in May, 1979.
4. Molecular formula was confirmed by the high resolution mass spectral analysis; obsd m/e 401.9499, $C_{15}H_{16}O_3{}^{79}Br_2$ requires: 401.9467.
5. A. Fukuzawa and E. Kurosawa, *Tetrahedron Letters*, 1979, 2797.
6. IR data of **1**: ν_{max}(film) 3040, 1960, 1660, 1200, 1119, 1035, 995, 945, 922, 865 and 840 cm^{-1}.
7. Although the reason why the C_{10}-H (δ ca. 1.9) resonates at considerably lower field region as a cyclopropane methine proton is not clear, this down field shift appears to be explicable by the deshielding effect of the β-substituents,[12] probably the oxetane oxygen atom and/or the oxirane ring.
8. J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, 1972, pg. 161.
9. E. Kurosawa, A. Fukuzawa and T. Irie, *Tetrahedron Letters*, 1972, 2121.
10. F. Piozzi, A. Quilico, T. Ajello, V. Sprio and A. Melera, *Tetrahedron Letters*, 1965, 1829.
11. K. Tori, T. Komeno and T. Nakagawa, *J. Org. Chem.*, 29, 1136 (1964).
12. (a) J. D. Graham and M. T. Rogers, *J. Am. Chem. Soc.*, 84, 2249 (1962); (b) D. J. Patel, M. E. H. Howden and J. D. Roberts, *ibid.*, 85, 3218 (1963).

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