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Brominated metabolites from an Okinawan *Laurencia intricata*

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Abstract

Two halogenated C_{15} acetogenins, itomanallenes A and B, with a terminal bromoallene moiety along with a halogenated sesquiterpene, itomanol, have been isolated from the red alga *Laurencia intricata* collected in Okinawan waters. Their structures were deduced from 1D and 2D NMR experiments including ^1H–^1H COSY, HSQC, HMBC, and NOESY methods. The alcohol corresponding to itomanallene B seems to be a plausible precursor of itomanallene A, which has an unusual 2,10-dioxabicyclo[7.3.0]dodecene skeleton. Itomanol was found to be a selinane-type bromosesquiterpenoid, and is the first example of a selinane to be isolated from Japanese *Laurencia* species. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Laurencia intricata; Rhodomelaceae; Red alga; C_{15} acetogenin; Sesquiterpene; Halogenated compound; Chemotaxonomy

1. Introduction

Species of the red algal genus *Laurencia* (Rhodomelaceae, Ceramiales) are the most prolific producers of diverse halogenated secondary metabolites (Erickson, 1983; Faulkner, 2001). To date some 25 species of *Laurencia* from Japanese waters, have been studied for their chemical compositions. More than 100 halogenated compounds have been found from *Laurencia* species having an intracellular refractile inclusion known as "*corps en cerise*" which is considered to be the site of synthesis and/or storage of halogenated secondary metabolites (Young et al., 1980). *Laurencia* species without "*corps en cerise*" do not produce any halometabolites (Suzuki and Kurosawa, 1979; Suzuki et al., 1987; Vairappan et al., 2001).

The *Laurencia* species collected from Okinawa, Japan, whose chemical constituents have been investigated, include *L. brongniartii* J. Agardh (Tanaka et al., 1988, 1989), *L. cartilaginea* Yamada (Vairappan et al., 2001), *L. concreta* Cribb (Vairappan et al., 2001), *L. majuscula* (Harvey) Lucas (Masuda et al., 1997; Vairappan et al., 2001), *L. mariannensis* Yamada (Vairappan et al., 2001), *L. nidifica* J. Agardh (Vairappan et al., 2001), *L. snackeyi* (Weber-van Bosse) Masuda as *L. luzonensis* Masuda, *species inedita* (Kuniyoshi et al., 2000, 2001), *L. venusta* Yamada (Sakemi et al., 1986), *L. yonaguniensis* Masuda et Abe, *species inedita* (Takahashi et al., 2002), and two unidentified species (Suzuki et al., 1999, 2002).

As part of a continuing chemical investigation of *Laurencia* species from the Okinawan waters, a sample of *Laurencia intricata* Lamouroux collected at Komesu, Itoman was examined. This sample contained three brominated metabolites, which were named itomanallene A (**1**), itomanallene B (**2**), and itomanol (**3**). The isolation and structures of these brominated compounds is described.

2. Results and discussion

A combination of column and thin-layer chromatography of the MeOH extracts of *L. intricata*, collected at Komesu, Itoman, Okinawa Prefecture, on 29 March 1997, has led to the isolation of itomanallene A (**1**) (0.015% of dry alga), itomanallene B (**2**) (0.004%), and itomanol (**3**) (0.023%).

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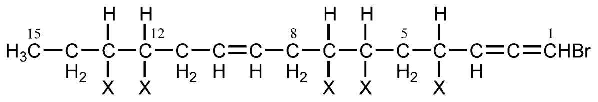
Table 1
^{13}C NMR (100 MHz, DEPT), ^{1}H NMR (400 MHz), and HMBC spectroscopic data[a] for itomanallene A (**1**)

C[b]	^{13}C (δ)	^{1}H (δ)	Multiplicity, J (Hz)	Long-range correlations
1	74.1[c]	6.06	*dd* (5.8, 2.0)	
2	201.2			H-1, H-3, H-4
3	102.5	5.48	*dd* (5.8, 5.8)	H-1, H_2-5
4	74.2[c]	4.86	*dddd* (8.3, 5.8, 5.8, 2.0)	H-1, H-3, H_b-5
5	39.2	2.26	*m* (H_a)	H-3
		1.93	*ddd* (13.2, 8.3, 4.9; H_b)	
6	72.7	3.99	*br s*	H_a-5, H-7, H_2-8, H-13
7	79.8	3.83	*ddd* (10.8, 3.4, 3.4)	H_a-5, H_2-8
8	26.8	2.81	*ddd* (10.8, 10.8, 10.8; H_b)	H-9, H-10
		2.26	*m* (H_b)	
9	127.3	5.55	*ddd* (10.3, 10.3, 7.3)	H_b-8, H-10, H_b-11
10	129.3	5.75	*ddd* (10.3, 10.3, 7.8)	H_b-8, H-9, H_b-11, H-12
11	34.7	3.22	*m* (H_a)	H-9
		2.68	*dd* (14.6, 7.3; H_b)	
12	52.8	3.75	*m*	H_2-11, H-13, H_a-14
13	84.4	3.75	*m*	H_2-11, H-12, H_2-14, H_3-15
14	23.2	2.06	*m* (H_a)	H_3-15
		1.64	*m* (H_b)	
15	11.4	0.96	*t* (7.3)	H-13, H_a-14

[a] Measured in chloroform-d_1.
[b] Assignments were made with the aid of the HSQC spectrum.
[c] Assignments may be interconvertible.



$$H_3C-CH_2-CH(X)-CH(X)-CH_2-CH=CH-CH_2-CH(X)-CH(X)-CH_2-CH(X)-CH=C=CHBr$$

1a: X = O or Br

Fig. 1. Partial structure for itomanallene A (**1**).

Itomanallene A (**1**), a colorless oil, $[\alpha]_D^{22}+99°$ ($CHCl_3$), was found to be $C_{15}H_{20}Br_2O_2$ by interpretation of its ^{13}C NMR spectrum (DEPT) as well as its HR–EIMS. The presence of a terminal bromoallene moiety was readily proved by typical signals in the ^{1}H and ^{13}C NMR spectra (Table 1) [δ_H 6.06 (1H, *dd*, $J=5.8$, 2.0 Hz) and 5.48 (1H, *dd*, $J=5.8$, 5.8 Hz); δ_C 201.2 (C), 102.5 (CH), and 74.1 (CH)], frequently encountered in C_{15} acetogenins found in various *Laurencia* species (Erickson, 1983). Moreover, the ^{1}H NMR spectrum showed the presence of another terminal methyl group [δ_H 0.96 (3H, *t*, $J=7.3$ Hz)], a 1,2-disubstituted double bond [δ_H 5.55 (1H, *ddd*, $J=10.3$, 10.3, 7.3 Hz) and 5.75 (1H, *ddd*, $J=10.3$, 10.3, 7.8 Hz)], and five methine protons adjacent to a bromine or an oxygen atom [δ_H 4.86 (1H, *dddd*, J =8.3, 5.8, 5.8, 2.0 Hz), 3.99 (1H, *br s*), 3.83 (1H, *ddd*, $J=10.8$, 3.4, 3.4 Hz), and 3.75 (2H, *m*)]. The geometry of the double bond was shown to be *Z* from the coupling constant ($J=10.3$ Hz) of the pertinent protons. The ^{1}H–^{1}H COSY spectrum showed the presence of a partial structure **1a** (Fig. 1). Because the IR spectrum of **1** exhibited the absence of hydroxyl and carbonyl functions, the two oxygen atoms were assumed to be involved in ether linkages. In the ^{13}C NMR spectrum, the chemical shift of the methine carbon at C-12 (δ_C 52.8) showed that a bromine atom is attached to this carbon. Furthermore, the remaining substituents of C-4, C-6, C-7, and C-13 were verified to be oxygen atoms based upon the chemical shifts of the pertinent carbons at δ_C 74.2, 72.7, 79.8, and 84.4, respectively. Itomanallene A, which has five degrees of unsaturation, should have two ether rings. In the HMBC spectrum (Table 1), a long-range correlation between C-6 and H-13 established the presence of a nine-membered ether ring with the remaining ether bond between C-4 and C-7 forming a five-membered ether ring. Thus it was unambiguously demonstrated that itomanallene A (**1**) has the same 2,10-dioxabicyclo[7.3.0]dodecene skeleton as neolaurallene (**4**) from *L. intricata* and isolaurallene (**5**) from *L. nipponica* Yamada (Kurata et al., 1982), both of which were collected at Hokkaido, the most northern region of Japan. Neolaurallene (**4**) was first reported from *L. okamurae* Yamada (Suzuki et al., 1984) but *L. intricata* had been incorrectly identified as young *L. okamurae* (Suzuki et al., 1989, 1991).

The relative stereochemistry of itomanallene A (**1**) was defined by the NOESY spectrum (Fig. 2). The NOE correlations between H-6/H-4 and H-6/H-7 showed that three methine protons, H-4, H-6, and H-7, on the oxolane ring are all *cis*. A NOE between H-6 and H_2-14 confirmed the *trans* relationship between the substituents at C-6 and C-13 on the nine-membered cyclic ethereal ring. Furthermore, the large coupling constant ($J=10.3$ Hz) between H-12 and H-13, which was observed in the ^{1}H NMR spectrum using C_6D_6 as a solvent (Experimental), indicated the *trans* relationship between the substituents at C-12 and C-13 (Fujiwara et al., 1999). Judging from the strong positive rotation of **1**, its bromoallene moiety would be assigned as *S* by application of Lowe's rule (Lowe, 1965). Detailed spectral comparisons of **1** with **4** and **5** indicated that itomanallene A is an epimer at C-4 of neolaurallene (**4**). Consequently, the structure of itomanallene A must be represented by formula **1**, 1*S*, 4*R**, 6*R**, 7*R**, 12*S**, and 13*R**, with the relative configuration between C-3 and C-4 remaining unclear.

Itomanallene B (**2**), a colorless oil, $[\alpha]_D^{22}$ +84° ($CHCl_3$), having a molecular formula of $C_{17}H_{23}BrO_3$, also showed ^{1}H and ^{13}C NMR signals (Table 2) typical of a terminal bromoallene moiety [δ_H 6.07 (1H, *dd*, $J=5.8$, 2.0 Hz) and 5.47 (1H, *dd*, $J=5.8$, 5.8 Hz); δ_C 201.3 (C), 102.0 (CH), and 74.3 (CH)]. The IR spectrum revealed no hydroxyl groups and an acetoxyl group at ν_{max} 1740 cm^{-1}, which was supported by a signal at δ_H 2.08 (3H, *s*) in the ^{1}H NMR spectrum. Detailed analyses of the ^{1}H and ^{13}C NMR, ^{1}H–^{1}H COSY, and HSQC spectra together with the HMBC spectrum (Table 2) indicated that the planar structure of itomanallene B must be as shown by formula **2**. The geometry of double

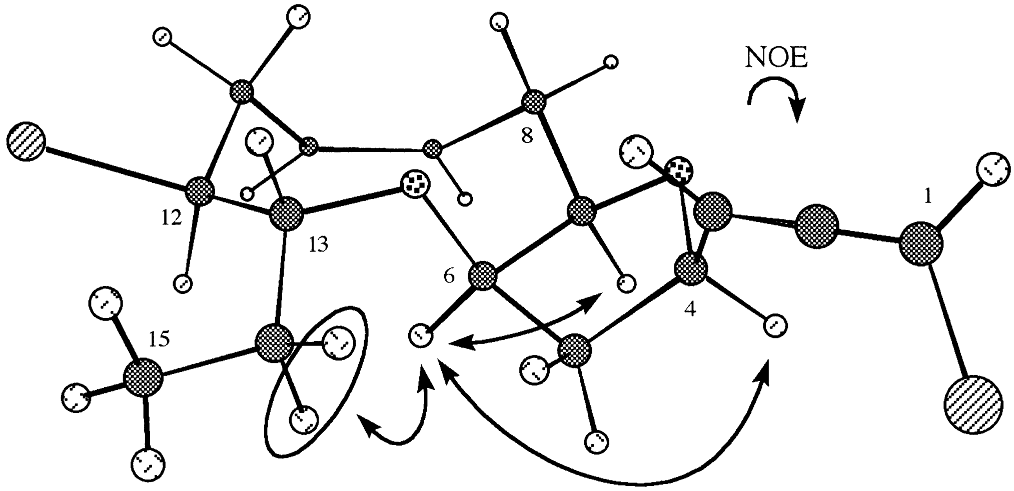


Fig. 2. NOE correlations for itomanallene A (**1**).

bonds was determined by the NOESY spectrum. The NOE correlations between H-9/H-10, H$_2$–8/H$_2$–11, and H-12/H$_2$–14 showed that **2** has *Z*-configuration at C-9 and *E*-configuration at C-12. The chemical shift (δ_H 5.31) of the methine proton of C-6 in the ^{1}H NMR spectrum revealed that the acetoxyl group is attached to this carbon.

The stereochemistry on the oxolane ring was partly determined. A *cis* relationship between the substituents at C-6 and C-7 was shown by a NOE correlation between H-6 and H-7. The bromoallene moiety of **2** was also assigned as *S* from the strong positive optical rotation. Thus the structure of itomanallene B would be represented by formula **2**, including the relative configuration of 6*R** and 7*R**. The closely related oxolane bromoether, graciosallene has been isolated from *Laurencia obtusa* collected at Graciosa (Canary Islands) (Norte et al., 1988).

The third brominated metabolite, itomanol (**3**), a colorless oil, $[\alpha]_D^{23}$ −50° ($CHCl_3$), was found to be $C_{15}H_{25}BrO$ by HR–EIMS. Its IR spectrum exhibited an absorption at ν_{max} 3550 cm^{-1} due to a hydroxyl group. The ^{1}H NMR spectrum (Table 3) indicated the presence of a tertiary methyl group at δ_H 1.03 (3H, *s*), a vinyl methyl group at δ_H 1.85 (3H, *br s*), two secondary methyl groups at δ_H 0.96 (3H, *d*, J=6.4 Hz) and 1.03

Table 2
^{13}C NMR (100 MHz, DEPT), ^{1}H NMR (400 MHz), and HMBC spectral data[a] for itomanallene B (**2**)

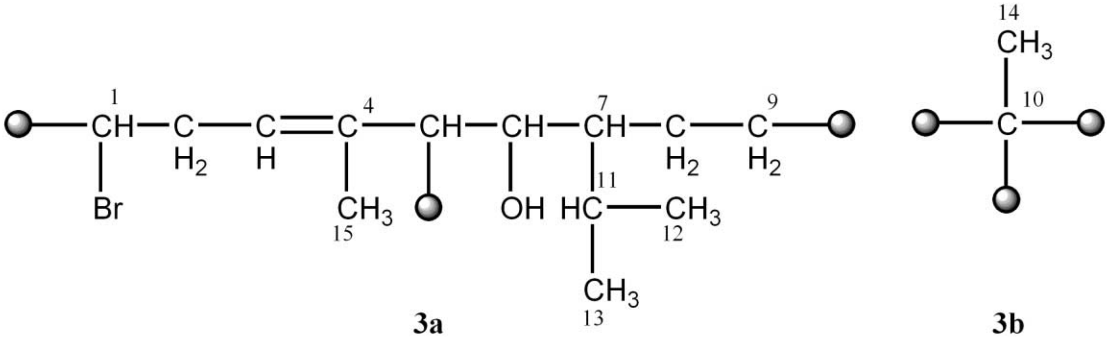
C[b]	^{13}C (δ)	^{1}H (δ)	Multiplicity, *J* (Hz)	Long-range correlations
1	74.3	6.07	*dd* (5.8, 2.0)	H-3
2	201.3			H-1, H-3, H-4
3	102.0	5.47	*dd* (5.8, 5.8)	H-1, H$_2$-5
4	73.5	4.81	*dddd* (7.3, 5.8, 5.4, 2.0)	
5	39.0	2.24	*ddd* (13.7, 5.4, 1.5; H$_b$)	H-3
		2.18	*ddd* (13.7, 7.3, 4.9; H$_a$)	
6	74.6	5.31	*m*	H$_2$-5, H$_2$-8
7	80.6	3.97	*ddd* (7.3, 7.3, 3.4)	H$_2$-5, H$_2$-8
8	27.1	2.39	*m*	
9	124.7	5.38	*m*	H$_2$-8, H$_2$-11
10	130.6	5.49	*m*	H$_2$-8, H$_2$-11
11	30.5	2.74	*br t* (6.8)	
12	126.8	5.33	*m*	H$_2$-11, H$_b$-14
13	132.8	5.47	*m*	H$_2$-11, H$_2$-14, H$_3$-15
14	25.6	2.00	*m* (H$_a$)	H$_3$-15
		1.30	*m* (H$_b$)	
15	13.8	0.96	*t* (7.3)	H$_2$-14
	21.1	2.08	*s* (Ac)	
	170.4		(Ac)	H$_3$-Ac

[a] Measured in chloroform-*d*$_1$.
[b] Assignments were made with the aid of the HSQC spectrum.

Table 3
^{13}C NMR (100 MHz, DEPT), ^{1}H NMR (400 MHz), and HMBC spectral data[a] for itomanol (**3**)

C[b]	^{13}C (δ)	^{1}H (δ)	Multiplicity, *J* (Hz)	Long-range correlations
1	67.1	4.18	*dd* (8.8, 8.8)	H$_2$-9, H$_3$-14
2	36.0	2.56	*m*	H-1
3	121.9	5.24	*br s*	H$_3$-15
4	135.5			H$_3$-15
5	51.5	2.19	*br d* (8.3)	H-1, H$_3$-14, H$_3$-15
6	70.0	3.99	*ddd* (8.3, 4.9, 3.9)	H-11
7	45.2	1.53	*m*	H$_2$-9, H$_3$-12, H$_3$-13
8	20.1	1.63	*m*	H$_2$-9
		1.42	*dddd* (14.7, 7.3, 6.8, 2.4)	
9	37.4	1.62	*m*	H-1, H$_2$-8, H$_3$-14
		1.54	*m*	
10	36.8			H-1, H$_2$-9, H$_3$-14
11	27.4	1.72	*ddd* (6.4, 6.4, 2.0)	H$_3$-12, H$_3$-13
12	22.1	1.03	*d* (6.4)	H-11, H$_3$-13
13	21.5	0.96	*d* (6.4)	H3–12
14	17.1	1.03	*s*	H-1, H$_2$-9
15	22.0	1.85	*s*	
		1.33	*br d* (3.9; OH)	

[a] Measured in chloroform-*d*$_1$.
[b] Assignments were made with the aid of the HSQC spectrum.



3a **3b**

Fig. 3. Partial structures for itomanol (**3**).

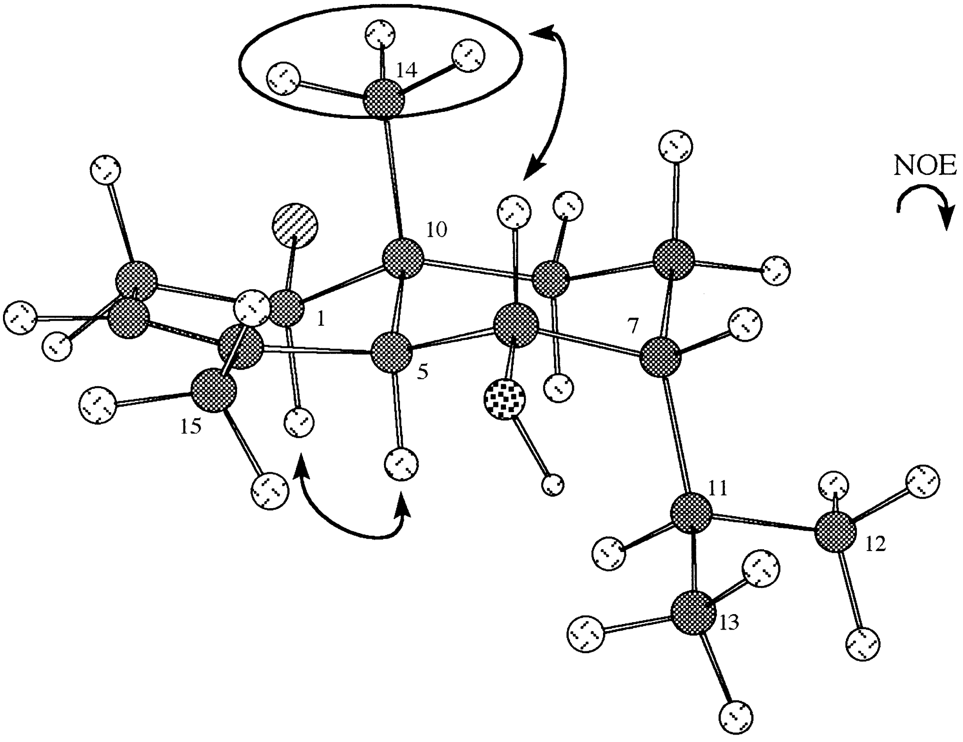
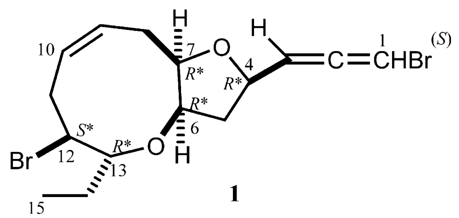


Fig. 4. NOE correlations for itomanol (**3**).

(3H, *d*, $J=6.4$ Hz) (probably isopropyl), two methine groups at δ_H 3.99 (1H, *ddd*, $J=8.3$, 4.9, 3.9 Hz) and 4.18 (1H, *dd*, $J=8.8$, 8.8 Hz), an olefinic proton at δ_H 5.24 (1H, *br s*), and a hydroxyl proton at δ_H 1.33 (1H, *br d*, $J=3.9$ Hz; D_2O exchangeable). The ^1H–^1H COSY spectrum as well as the ^{13}C NMR and HSQC spectra showed the presence of partial structural units **3a** and **3b** in the molecule (Fig. 3). In the ^1H NMR spectrum, the signal of *ddd* of the methine proton at C-6 was changed into *dd* by the addition of D_2O, indicating that a hydroxyl group is attached to C-6. In the ^{13}C NMR spectrum, the chemical shift (δ_C 67.1) of the methine carbon at C-1 in **3a** indicated that a bromine atom is attached to this carbon. Itomanol (**3**), which has three degrees of unsaturation, must contain two carbocyclic rings. Confirmation of the partial structural units and determination of their connectivities were made with the aid of the HMBC spectrum. Long-range correlations between C-10/H-1, C-14/H-1, C-1/H_3–14, C-5/H-1, and C-5/H_3–14 confirmed the connection of C-10 with C-1 and C-5 to form a six-membered ring system. Furthermore, long-range correlations between C-14/H_2-9, C-10/H_2-9, C-9/H-1, C-9/H_3-14, and C-1/H_2-9 confirmed the connection of C-10 with C-9. Thus the planar structure **3** was unambiguously assigned for itomanol.

The relative stereochemistry of itomanol (**3**) was determined by the NOESY spectrum (Fig. 4). The NOE correlations between H-1/H-5 and H-6/H_3-14 established that H-5 was *cis* to the axial proton at C-1 and *trans* to the angular methyl group at C-14, while methyl group at C-14 was shown to be *cis* to the axial proton at C-6. Furthermore, a NOE between H-5/H-11 showed that the configuration between H-5 and the isopropyl group is *cis*. Thus the structure of itomanol,



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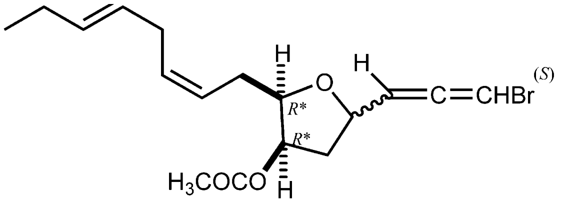

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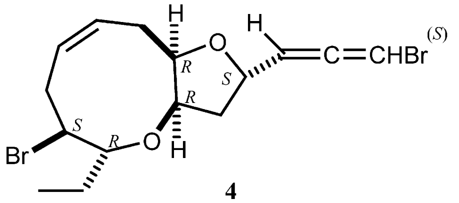

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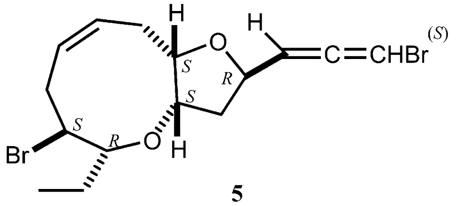

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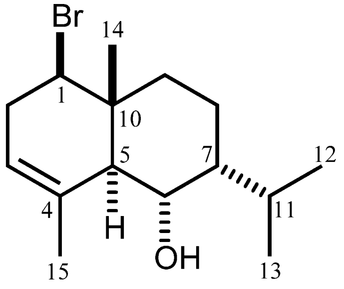

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including the relative configuration, was assigned as (1*R**,5*S**,6*S**,7*R**,10*R**)-1-bromo-6-hydroxyselin-3-ene. The determination of absolute configuration of the secondary hydroxyl group at C-6 in itomanol (**3**) by application of the modified Mosher's method failed because no MTPA esters could be formed, presumably due to steric hindrance.

Five halogenated selinane derivatives have previously been obtained from *Laurencia* species; (+)-(1*S*,4*R*,5*S*,10*S*)-1-bromo-4-hydroxyselin-7-ene from a Mexican *Laurencia* sp. (the Gulf of California) (Howard and Fenical, 1977) and an Australian *Laurencia* sp. (New South Wales) (Rose and Sims, 1977), (+)-(1*S*,4*R*,5*S*,6*R*,7*R*,10*S*)-1-bromo-6-chloro-4-hydroxyselinane (heterocladol), from the South Australian *L. filiformis* (C. Agardh) Montagne f. *heteroclada* (Harvey) Saito et Womersley (near Port MacDonnell) (Kazlauskas et al., 1977), (+)-(1*S*,4*R*,5*S*,7*R*,10*S*)-1-bromo-4-hydroxy-7-chloroselinane from a South Australian *Laurencia* sp. (New South Wales) (Rose et al., 1978), (+)-(1*R*,4*R*,5*S*,6*S*,7*R*,10*R*)-1-bromo-6-acetoxy-4-hydroxyselinane (austradiol acetate), and (+)-(1*R*,4*R*, 5*S*, 6*S*,7*R*,10*R*)-1-bromo-4,6-diacetoxyselinane (austradiol diacetate) from a Western Australian *Laurencia filiformis* (Yanchep) (Brennan and Erickson, 1982).

Itomanol (**3**) is a new congener of halogenated selinane-type sesquiterpenoids and a stereoisomer of lankalapuol A, (1*R*,5*R*,6*R*,7*R*,10*R*)-1-bromo-6-hydroxyselin-3-ene, which has previously been isolated from the sea hare *Aplysia dactylomela* (Baker et al., 1988).

3. Experimental

3.1. General

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz), TMS as int. standard; Low and high resolution MS: 70 eV; CC: silica gel (Merck, Kieselgel 60, 70–230 mesh); Prep. TLC: silica gel plate (Merck, Kieselgel 60 F_{254S})

3.2. Collection

A sample of *Laurencia intricata* was collected at Komesu, Itoman, Okinawa Prefecture, on 29 March, 1997. The voucher specimens are deposited in the Herbarium of the Graduate School of Science, Hokkaido University (SAP 071779-071781).

3.3. Extraction and isolation

The partially dried alga (133 g) was extracted with MeOH. The MeOH solution was concentrated in vacuo and partitioned between Et_2O and H_2O. The Et_2O solution was washed with water, dried over anhydrous Na_2SO_4, and evaporated to obtain a dark green oil (1.01 g). The extracts were then fractionated by Si gel CC with a step gradient (hexane and EtOAc). The fraction eluted with hexane/EtOAc (9:1) was further submitted to repeated prep. TLC with toluene or toluene/EtOAc (4:1) to give itomanallene A (**1**) (20.2 mg; 0.015% based on dry alga), itomanallene B (**2**) (5.2 mg; 0.004%), and itomanol (**3**) (30.5 mg; 0.023%).

3.4. Itomanallene A (**1**)

Oil; $[\alpha]_D^{23}$ +99° ($CHCl_3$; *c* 0.44); IR ν_{max} ($CHCl_3$) cm^{-1}: 3010, 2920, 1515, 1450, 1240, 1200, 1120, 1050, 990, 905; ^1H and ^{13}C NMR ($CDCl_3$), see Table 1; ^1H NMR (C_6D_6); δ 0.85 (3H, *t*, J=7.3 Hz, H_3-15), 1.28 (1H, *ddq*, J=14.6, 10.3, 7.3 Hz, H_b-14), 1.42 (1H, *ddd*, J=13.2, 7.8, 4.9 Hz, H_b-5), 1.83 (1H, *ddd*, J=13.2, 6.8, 2.0 Hz, H_a-5), 1.88 (1H, *ddq*, J=14.6, 1.5, 7.3 Hz, H_a-14), 2.16 (1H, *ddd*, J=11.7, 7.3, 3.4 Hz, H_b-8), 2.55 (1H, *dd*, J=14.2, 7.8 Hz, H_b-11), 2.77 (1H, *ddd*, J=11.7, 10.7, 10.3 Hz, H_a-8), 3.02 (1H, *ddd*, J=14.2, 10.3, 6.8 Hz, H_a -11), 3.39 (1H, *br s*, H-6), 3.43 (1H, *ddd*, J=10.3, 6.8, 1.5 Hz, H-12), 3.54 (1H, *ddd*, J=10.7, 3.4, 3.4 Hz, H-7), 3.60 (1H, *ddd*, J=10.3, 10.3, 1.5 Hz, H-13), 4.64 (1H, *dddd*, J=7.8, 6.8, 5.9, 2.0 Hz, H-4), 5.12 (1H, *dd*, J=5.9, 5.9 Hz, H-3), 5.26 (1H, *ddd*, J=10.3, 10.3, 7.3 Hz, H-9), 5.45 (1H, *ddd*, J=10.3, 10.3, 7.8 Hz, H-10), 5.73 (1H, *dd*, J=5.9, 2.0 Hz, H-1); LR-FDMS *m*/*z* (rel. int.): 394, 392, 390 (48:100:50) $[M]^+$, 313, 311 (15:14) $[M–Br]^+$, 275, 273 (26:27) $[M–C_3H_2Br]+$; LR–EIMS *m*/*z* (rel. int.): 365, 363, 361 (0.6:1.2:0.7) [M–C2H5]+, 313, 311 (41:42) $[M–Br]^+$, 275, 273 (86:87) $[M–C_3H_2Br]^+$, 255, 253 (11:10) $[M–C_3H_6BrO]^+$, 231, 229 (12:12) $[M–C_6H_{10}Br]+$, 219, 217 (8:9) $[M–C_6H_6BrO]+$, 193 (22), 67 (100); HR–EIMS *m*/*z*: 362.9395. Calc for $C_{13}H_{15}{}^{79}Br^{81}BrO_2$, 362.9418 $[M–C_2H_5]$.

3.5. Itomanallene B (**2**)

Oil: $[\alpha]_D^{23}$ +84° ($CHCl_3$; *c* 0.18); IR ν_{max} ($CHCl_3$) cm^{-1}: 2920, 1740, 1370, 1260, 1030, 800; ^1H and ^{13}C NMR, see Table 2; LR–EIMS *m*/*z* (rel. int.): 313, 311 (3:3) $[M–CH_3CO]^+$, 275 (23), 273 (23), 247, 245 (18:18) $[M–C_8H_{13}]^+$, 217 (20), 187 (38), 185 (38), 111 (37), 43 (100); HR–EIMS *m*/*z*: 311.0636. Calc. for $C_{15}H_{20}{}^{79}BrO_2$, 311.0647 $[M–CH_3CO]$.

3.6. Itomanol (**3**)

Oil; $[\alpha]_D^{23}$ –50° ($CHCl_3$; *c* 0.31); IR ν_{max} ($CHCl_3$) cm^{-1}: 3550, 2910, 1720, 1460, 1380, 1260, 1190, 1130, 1020, 975, 960, 800; ^1H and ^{13}C NMR, see Table 3; LR–EIMS *m*/*z* (rel. int.): 302, 300 (4:4) $[M]^+$, 284, 282 (12:12) $[M–H_2O]+$, 269, 267 (5:5) $[M–H_2O–CH_3]+$, 241, 239 (13:12) $[M–H_2O–C_3H_7]+$, 221 (15) $[M–Br]+$, 203 (88) $[M–H_2O–Br]+$, 189 (17), 187 (18), 159 (23), 119 (96), 107 (100); HR–EIMS *m*/*z*: 300.1060. Calc. for $C_{15}H_{25}{}^{79}BrO$, 300.1089 [M].

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