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THE STRUCTURE OF SPIROLAURENONE, A HALOGENATED SESQUITERPENOID FROM THE RED ALGA *LAURENCIA GLANDULIFERA* KÜTZING[1]

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Abstract—The structure of spirolaurenone (1), a halogenated metabolite isolated from the red alga *Laurencia glandulifera* Kützing, was determined on the basis of the chemical and spectroscopic evidence. The absolute configuration of spirolaurenone (1) was established as shown in formula **1** by the chemical correlation with glanduliferol (**18**), a halo-chamigrene derivative isolated from the same alga.

In connection with our continuing studies for constituents of the red algae genus *Laurencia* (Rhodomelaceae), we previously reported the structural elucidation of a sesquiterpene ketone containing bromine, designated as spirolaurenone, which was isolated from the red alga *L. glandulifera* Kützing.[2] Recently we reported the structures of several halochamigrene derivatives isolated from the same alga, some of which are isomeric with spirolaurenone (**1**).[3] The present paper describes the structure of spirolaurenone (**1**), including the absolute configuration, in full details.

Spirolaurenone (**1**), colorless oil, $[\alpha]_D^{17}$ −70.6°, was obtained in 0.014% yield (of dried alga) by column chromatography on alumina and silica gel[4] and analyzed for $C_{15}H_{23}OBr$ by mass spectroscopy *m/e* 300 and 298 (M^+). Spirolaurenone (**1**) was positive to iodoform test and gave a semicarbozone, $C_{16}H_{23}ON_3Br$, m.p. 165–170°.

The PMR spectrum of spirolaurenone (**1**) showed the signals due to two tertiary Me groups at δ 0.95 and 1.11 (each 3H, s) (*gem*-dimethyl group, partial structure A (Fig. 2); further discussed below), an olefinic Me group at 1.70 (3H, br s), an acetyl group at 2.15 (3H, s), a bromomethine proton at 4.25 (1H, t, J = 8.2 Hz) and an olefinic proton at 5.08 (1H, br t, J = 4.0 Hz).

Catalytic hydrogenation of **1** over PtO_2 (or Rh–PtO_2) in EtOH or AcOH produced a saturated alcohol (**2**), $C_{15}H_{28}O$, ν_{max} 3350 cm^{-1}; δ 0.82, 1,12 (each 3H, d, J = 6.0 Hz) and 3.45 (1H, quintet, J = 6.0 Hz), which, on chromium trioxide oxidation, gave the corresponding ketone, dihydrodebromospirolaurenone (**3**), $C_{15}H_{26}O$. The PMR spectrum of **3** showed the signals due to a secondary Me group at δ 0.83 (3H, d, J = 6.0 Hz), two tertiary Me groups at 0.85 and 0.89 (each 3H, s), and an acetyl group at 2.06 (3H, s), disappearing the signals due to the allylic protons (*ca* 2.5), the olefinic proton (5.08) and the bromomethine proton (4.25) in **1**. Furthermore, the ^{13}C NMR spectrum of **1** indicated the presence of one double bond at δ 140.7 (s) and 119.8 (d) ppm, and therefore **1**, having four degrees of unsaturation, must be a bicyclic ketone.

Treatment of **1** with LAH in ether at room temperature afforded an alcohol, spirolaurenol (**4**), with the signals comparable to those of **1** except for the signals at δ 1.18 (3H, d, J = 6.0 Hz) and 3.50 (1H, br quintet, J = 6.0 Hz) due to the Me–CH(OH)–CH< grouping instead of that at 2.15 (3H, s) due to the acetyl group in **1**, which was reconverted into the original ketone (**1**) in good yield by

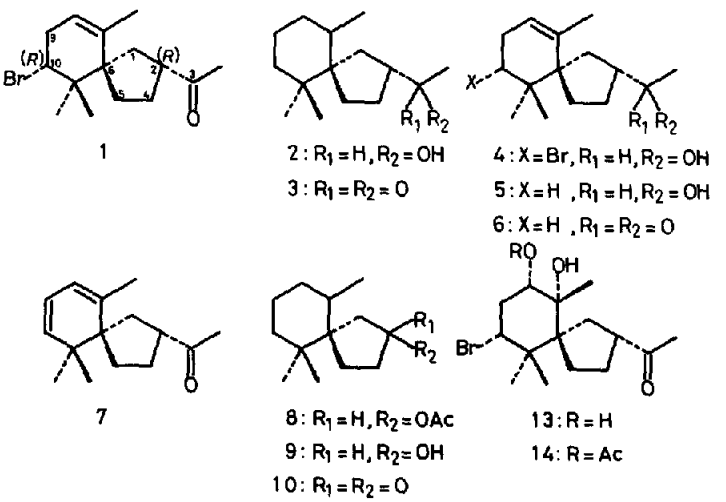


Fig. 1.

treatment with chromium trioxide-pyridine complex. On the other hand, treatment of **1** with LAH in refluxing THF gave a debromo alcohol (**5**), δ 0.87 (6H, br s), 1.14 (3H, d, J = 6.0 Hz), 1.70 (3H, br s), 3.50 (1H, br quintet, J = 6.0 Hz) and 5.10 (1H, m). Oxidation of **5** with chromium trioxide-pyridine complex yielded the corresponding ketone, debromospirolaurenone (**6**), $C_{15}H_{24}O$. The PMR spectrum of **6** was similar to that of **1** except for the signal due to the bromomethine at δ 4.25 in **1**. The splitting patterns (quintet, J = 6.0 Hz) of the signals due to the protons on carbon bearing the OH group in the PMR spectra of **2**, **4** and **5** revealed the presence of a MeCOCH< grouping in **1**.

Although treatment of **1** with 5% KOH in MeOH (reflux 5 min) resulted in only recovery of the starting material, treatment of **1** with 2M KOH in EtOH (reflux 2 hr) afforded a good yield of a conjugated diene, dehydrobromospirolaurenone (**7**), $C_{15}H_{22}O$, ν_{max} 3040, 1710, 1595, 1180 and 725 cm^{-1}; δ 0.97, 1.00 (each 3H, s), 1.79 (3H, br s), 2.07 (3H, s) and 4.8–5.8 (3H, m). The UV spectrum (λ_{max}^{EtOH} 270 nm (ϵ 4700)) of **7** strongly suggested the presence of a dienyl group in a *six*-membered ring.[5]

Moreover, spin decoupling experiments in the PMR spectrum of spirolaurenone (**1**) provided the additional information of the structure. The spin decoupling results were summarized in Table 1, indicating that the allylic protons (H^b) were coupled to both the olefinic proton (H^a), J = 4.0 and 4.0 Hz, and the bromomethine proton (H^c), J = 8.2 and 8.2 Hz, and also to the olefinic Me protons (H^d), long range coupling. These spin decoupling results and dehydrobromination reaction indicated the presence of partial structure B (Fig. 2) in **1**. As mentioned above, spirolaurenone (**1**) involves a *six*-membered ring. It was drawn from the following chemical degradation that the other ring was a *five*-membered.

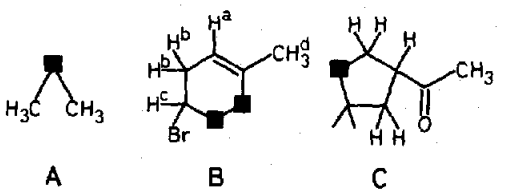


Fig. 2.

Baeyer-Villiger oxidation of **3** with perbenzoic acid in $CHCl_3$ afforded an ester (**8**), ν_{max} 1740 and 1240 cm^{-1}; δ 0.84 (3H, d, J = 6.0 Hz), 0.87 (3H, s), 0.94 (3H, s), 1.93 (3H, s) and 4.90 (1H, m), which was saponified with 5% KOH in MeOH to yield a secondary alcohol (**9**), ν_{max} 3320 and 1070 cm^{-1}; δ 4.15 (1H, m). Oxidation of **9** with chromium trioxide-pyridine complex gave a *five*-membered cyclic ketone (**10**), $C_{13}H_{22}O$ (*m/e* 194; M^+), δ 0.87 (3H, d, J = 6.0 Hz), 0.88 (3H, s), 0.99 (3H, s) and 2.08 (2H, s). The IR spectrum of this ketone (**10**) showed absorption maxima at 1745 and 1410 cm^{-1}, which indicated the presence of one or two methylene group(s) adjacent to the CO group of the 5-membered ring. Two-protons singlet at δ 2.08 in the PMR spectrum of **10** must reveal the presence of a ■–CH_2–CO– (■ denotes quarternary carbon) grouping in **10**.[6] **10** produced the tetradeuterio derivative (*m/e* 198; M^+) on deuteration with NaOD–D_2O, proving spirolaurenone (**1**) to involve partial structure C (Fig. 2).

The ^{13}C NMR spectrum of **1** revealed the signals due to two quarternary carbons at δ 54.6 (s) and 41.8 (s) ppm. Since **1** possesses two tertiary Me groups as above-mentioned, these quarternary carbons can be attributed to two CH_3–■ groups or both one *gem*-dimethyl group and one spiro C atom. Dixon and Naro[7] have studied a number of spiro compounds and indicated that a doublet in the region between 1370 and 1305 cm^{-1} was characteristic of spiro compounds, although the assignment is not always confirmatory owing to their overlapping with absorption due to the *gem*-dimethyl group. The IR spectrum of **1** exhibited absorption maxima at 1392, 1372 and 1352 cm^{-1}, which apparently indicated the presence of the spiro carbon skeleton and/or the *gem*-dimethyl group, and hence **1** must possess both the spiro carbon skeleton and the *gem*-dimethyl group. In view of the aforementioned data, partial structural units A, B and C (Fig. 2) could be combined to formula **11** or **12** (Fig. 3) as the possible planar structures for spirolaurenone (**1**). Formula **11** for spirolaurenone (**1**), however, is preferable to **12** by the following reason.

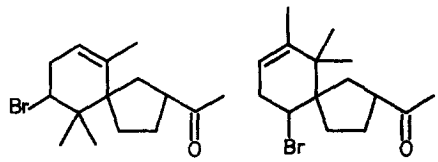
Table 1. Spin decoupling results in the PMR spectrum of **1** in CCl_4 (100 MHz)

Run	Proton (δ) Irradiated		Observed		Multiplicity change	Splitting decoupled (Hz)
1	H^a	5.08	H^b	2.5	m → br d (J=8.2)	4.0
			H^d	1.70	br s* → br s	
2	H^b	2.5	H^a	5.08	br t (J=4.0) → br s	4.0
			H^c	4.25	t (J=8.2) → s	8.2
			H^d	1.70	br s* → br s	
3	H^d	1.70	H^b	2.5	m → dd (J=8.2, 4.0)	
			H^a	5.08	br t (J=4.0) → t (J=4.0)	
4	H^c	4.25	H^b	2.5	m → m**	8.2

Abbreviations; 's' : singlet, 'd' : doublet, 't' : triplet,
'dd' : double doublet, 'm' : multiplet, 'br' : broad

* finely splitted

** narrow multiplet

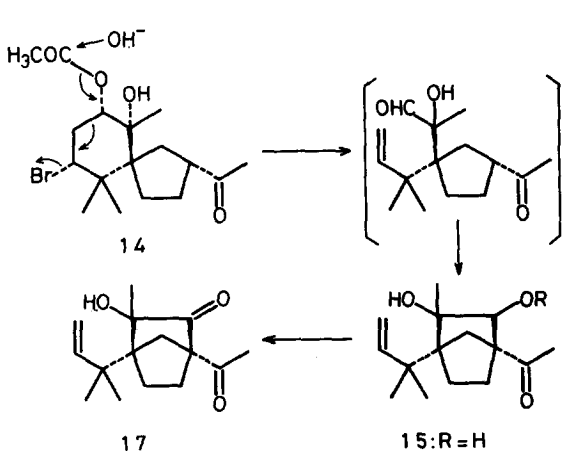


11 12

Fig. 3.

Oxidation of **1** with OsO_4 afforded a glycol (**13**), which, on acetylation with Ac_2O in pyridine, formed the corresponding monoacetate (**14**), $C_{17}H_{27}O_4Br$, m.p. 135–136°, ν_{max} 3640, 1740, 1710, 1030, 1015, 980 and 960 cm^{-1}; δ 1.04, 1.13, 1.22, 2.09, 2.17 (each 3H, s), 4.25 (1H, dd, J = 12.0 and 6.0 Hz) and 4.69 (1H, dd, J = 10.5 and 6.0 Hz). The coupling constant (J = 10.5 and 6.0 Hz) of the signal at δ 4.69 due to the proton on the carbon to which the acetoxyl group is attached revealed that the OAc group was oriented at equatorial configuration and hence the tertiary OH group at axial. Comparison of the chemical shifts of the tertiary Me groups of **1**, **3**, **6** and **7** with those of **13** and **14** suggested that one of the tertiary Me groups and the tertiary OH group would exist at 1,3-diaxial disposition. This implied formula **11** to be preferable to **12**, which would be supported by the following reaction.

Treatment of the monoacetate (**14**) with 5% KOH in MeOH (reflux 5 min) did not give the expected hydrolysis product (**13**) but resulted instead in the formation of a vinyl compound (**15**), $C_{15}H_{24}O_3$, which showed in its IR and PMR spectra the presence of a *gem*-dimethyl group at δ 1.06 and 1.12 (each 3H, s), a –C(CH₃)(OH)– group at ν_{max} 3380 cm^{-1}; δ 1.27 (3H, s), a ■–CH(OH)–■ group at ν_{max} 3380 cm^{-1}; δ 3.42 (1H, s), a CH_2=CH–■ group at ν_{max} 3080, 1630 and 912 cm^{-1}; δ 4.85, 4.89 and 6.03 (each 1H, dd, J = 10.0, 1.7, 18.0, 1.7 and 18.0, 10.0 Hz, respectively) and an acetyl group at ν_{max} 1685 cm^{-1}; δ 2.09 (3H, s). Acetylation of **15** with Ac_2O in pyridine gave a hydroxyacetate (**16**), $C_{17}H_{26}O_4$, indicating the presence of the ■–CH(OAc)–■ group at ν_{max} 1740 and 1240 cm^{-1}; δ 2.04 (3H, s) and 4.60 (1H, s). Oxidation of **15** with chromium trioxide-pyridine complex produced a 5-membered cyclic ketone (**17**), $C_{15}H_{22}O_3$, ν_{max} 3500, 1745, 1699, 1150, 1130, 1010 and 920 cm^{-1}; δ 1.01 (3H, s), 1.05 (6H, br s), 2.11 (3H, s), 4.97, 5.03 and 5.90 (each 1H, dd, J = 18.0, 1.7, 10.0, 1.7 and 18.0, 10.0 Hz). This abnormal reaction could be illustrated as shown in Scheme 1.



14

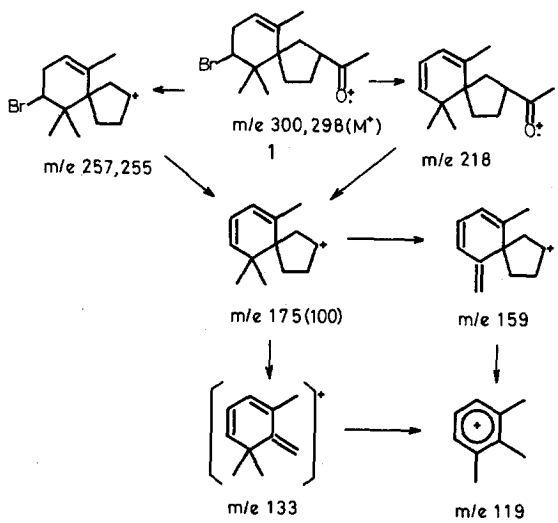
17

15: R = H

16: R = Ac

Scheme 1.

The mass spectra of spirolaurenone (**1**), dihydrodebromospirolaurenone (**3**), debromospirolaurenone (**6**) and dehydrobromospirolaurenone (**7**) supported the proposed structures **1**, **3**, **6** and **7**, respectively. The spectrum of **1** (300 and 298; M^+) showed a base peak at *m/e* 175 (M^+–HBr–$COCH_3$) and significant peaks at *m/e* 257, 255 (M^+–$COCH_3$; 4), 218 (M^+–HBr; 70), 203 (M^+–HBr–CH_3; 24), 159 (60), 133 (73), 119 (69), 105 (57), 91 (60) and 77 (30). The main fragmentations were explicable as shown in Scheme 2. The mass spectrum of **7** (218; M^+) revealed

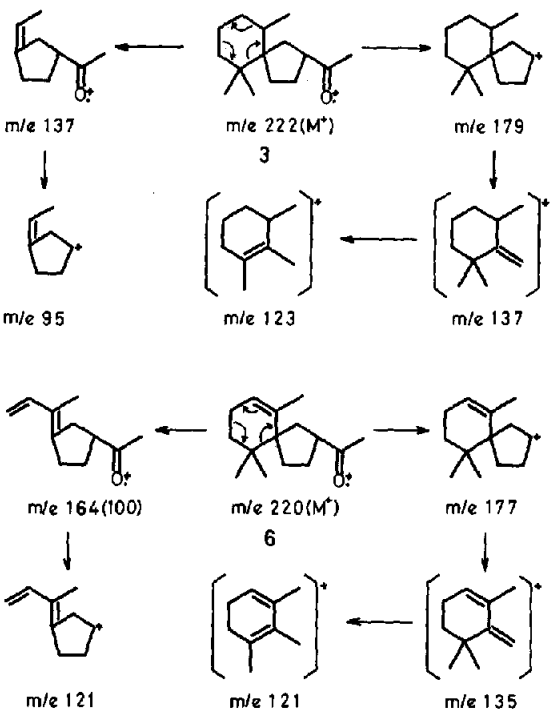


Scheme 2.

a base peak at *m/e* 43 and significant peaks at *m/e* 203 (M^+–CH_3; 8), 175 (M^+–$COCH_3$; 10), 159 (60), 133 (35), 119 (40), 105 (40), 91 (50) and 77 (35). This spectral pattern was similar to that of the lower mass number region of the spectrum of **1** and, therefore, was rationalized reasonably by assuming that degradation of **1** by electron impact, after initial elimination of HBr, proceeded essentially in the same manner as **7**. On the other hand, the main fragmentations of **3** [*m/e* 222 (M^+), 179 (M^+–$COCH_3$; 65), 137 (62), 123 (56), 95 (94) and 43 (100)] and **6** [*m/e* 220 (M^+), 177 (M^+–$COCH_3$; 2), 164 (100), 135 (8), 121 (53) and 93 (17)] would be illustrated as shown in Scheme 3.

The cooccurrence of spirolaurenone (**1**) and several halo-chamigrenes in *L. glandulifera*[3] suggested that the stereochemistry at C-6 and C-10 of **1**[8] might be as same as that of halo-chamigrenes and therefore, in order to confirm the structure and establish the absolute configuration of **1**, we carried out a chemical correlation of **1** with glanduliferol (**18**).

As has previously been described,[3] the B-ring of **18** possesses a twist boat form (formula **18**), which decreases an interaction between the Me group at C-7 and two axial hydrogens at C-2 and C-4 in formula **19**, but, on addition of the shift reagent of $Eu(fod)_3$, changes to a normal chair form from the twist boat form because of a newly generated non-bonded interaction of $Eu(fod)_3$-complex. When **18** is treated with silver oxide, it would be anticipated that the B-ring changes to a normal chair form (formula **20**) from a twist boat form (formula **21**) on account of an interaction between –Cl···Ag and the hydrogens at C-2 and C-4 in the transition state. If the reaction of **18** with silver oxide proceeds with keeping the chair conformation (formula **20**) during the reaction,



Scheme 3.

it seems that **18** yields a ring contracted product.[9] Treatment of **18** with silver oxide in hexane at 50° afforded a high yield (74%) of the expected ring contracted product, which was identical with spirolaurenone (**1**) in all respects.

Consequently, the structure of **1**, including the absolute configuration, is represented by formula **1**, in which the absolute stereochemistry of the acetyl group at C-2 has been assigned as *R*-configuration on the basis of the reaction mechanism as shown in Scheme 4.

Two possible biogenetic pathways, "bisabolene" route and "monocyclofarnesol" route, from farnesol to halogenated chamigrenes have been proposed.[10] As have been described by Gonzalez *et al.* in *Laurencia obtusa*,[11] the "bisabolene" route seems to be preferable to the "monocyclofarnesol" route in the biogenesis in *L. glandulifera* (Scheme 5). Cyclization of farnesyl pyrophosphate with subsequent loss of proton can generate γ-bisabolene. Two carbonium ions, **22** and **23**, are given by a brominium ion induced ring closure of γ-bisabolene or a ring closure of a bromohydrin, which is derived from γ-bisabolene epoxide by attack of bromide ion. Deprotonation of the carbonium ion (**22**) gives (−)-(19*R*)-10-bromo-α-chamigrene (**24**),[3] from which can be derived other halogenated chamigrenes (**25**, **26**, **27** and **18**),[3] and spirolaurenone (**1**). Alternative deprotonation of the carbonium ion (**22**) gives also (−)-(10*R*)-10-bromo-β-chamigrene derivatives.[11] Aromatization of another carbonium ion (**23**) gives bromocuparene (**28**),[12] which further yields laurene (**29**).[13] Furthermore, several halogenated sesquiterpene phenols and the related ethers from *L. glandulifera*,[14,15] e.g. laurenisol (**30**), are also derived from the carbonium ion (**23**).

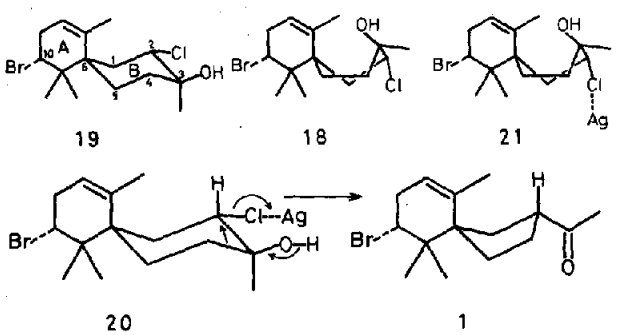
EXPERIMENTAL

All the m.ps are uncorrected. The UV and IR spectra were measured on a Nihon-Bunko ORD/UV-5 spectrometer and a IR-S spectrometer, respectively. The PMR spectra were recorded on a JEOL 3H-60 spectrometer or a Hitachi H-60 spectrometer, TMS being used as an internal reference in a CCl_4 soln, unless otherwise stated. The ^{13}C NMR spectrum was recorded on a JEOL JNM-FX100 spectrometer in a $CDCl_3$ soln. The optical rotations were measured in a $CHCl_3$ soln. Silica gel (Mallinckrodt, 100 mesh) was used for column chromatorgaphy.

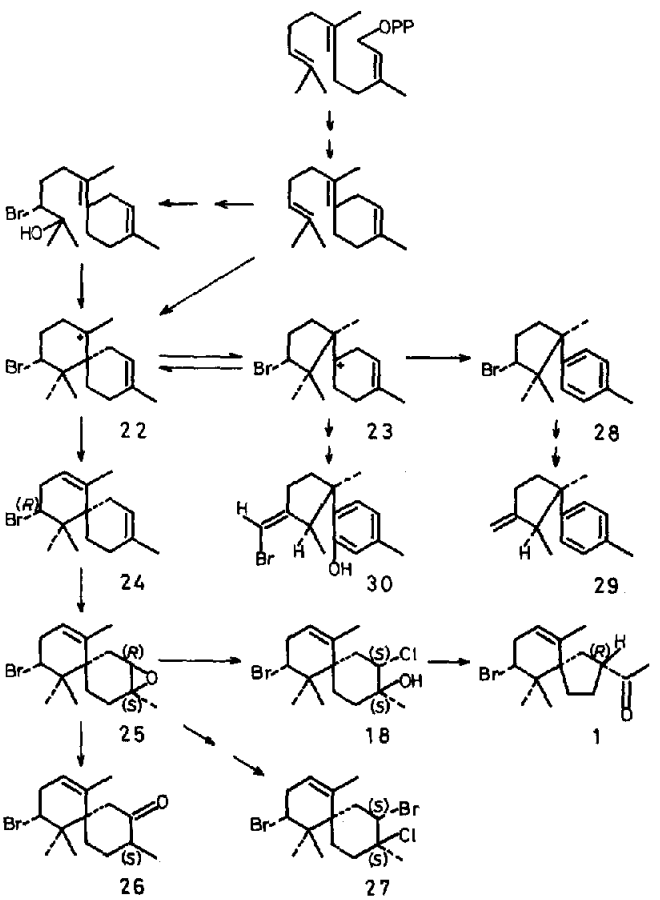
Spirolaurenone (**1**); colorless oil; $[\alpha]_D^{17}$ −70.6° (*c*, 1.26); UV, λ_{max}^{EtOH} 288 nm (ε 110); IR; ν_{max}^{film} 3025, 1715, 1665, 1392, 1372, 1352, 1180, 1160, 837, 790, 760 and 739 cm^{-1}; PMR (100 MHz), δ 0.95 (3H, s), 1.11 (3H, s), 1.70 (3H, br s), 2.15 (3H, s), *ca* 2.5 (2H, m), 2.85 (1H, m, W_H = 27 Hz), 4.25 (1H, t, J = 8.2 Hz) and 5.08 (1H, br t, J = 4.0 Hz); ^{13}C NMR, δ 211.1 (s), 140.7 (s), 119.8 (d), 63.0 (d), 54.6 (s), 54.4 (d), 41.8 (s), 35.8 (t), 35.6 (t), 35.1 (t), 31.3 (t), 29.3 (q), 24.0 (q), 20.0 (q) and 17.1 (q); mass, *m/e* (relative intensity) 300, 298 (M^+, 15), 257, 255 (4), 218 (70), 203 (24), 175 (100), 159 (60), 133 (73), 119 (69), 105 (57), 91 (60) and 77 (30). **1** gave positive iodoform test and a semicarbazone; m.p. 165–170° (from EtOH). (Found: C, 53.96; H, 7.31: N, 11.44. $C_{16}H_{26}ON_3Br$ requires: C, 53.90; H, 7.53; N, 11.79%).

Dihydrodebromospirolaurenone (**3**). The hydrogenation of **1** (150 mg) was performed in EtOH (or AcOH) over PtO_2. After removal of the catalyst and the solvent, the residual oil was chromatographed to give **2** (125 mg); IR, ν_{max}^{film} 3350, 1140 and 895 cm^{-1}; PMR, δ 0.82 (3H, d, J = 6.0 Hz), 0.83 (3H, s), 0.95 (3H, s), 1.12 (3H, d, J = 6.0 Hz) and 3.45 (1H, quintet, J = 6.0 Hz). To a soln of chromium trioxide (100 mg) and pyridine (3 ml) complex was added a soln of **2** (69 mg) in pyridine (0.5 ml), and the mixture was allowed to stand at room temp. overnight. After being worked up in the usual manner, the product was purified by chromatography to yield **3** (56 mg); $[\alpha]_D^{18}$ 0° (*c*, 1.00); IR, ν_{max}^{film} 1710, 1375, 1360, 1170 and 950 cm^{-1}; PMR, δ 0.83 (3H, d, J = 6.0 Hz), 0.85 (3H, s), 0.89 (3H, s) and 2.06 (3H, s); mass, *m/e* 222 (M^+, 40), 179 (65), 137 (62), 123 (56), 109 (92), 95 (94) and 43 (100).

Spirolaurenol (**4**). To a soln of **1** (47 mg) in dry ether (10 ml) was added LAH (5 mg), and the mixture was stirred for 24 hr at room temp. Water was cautiously added to the mixture cooled in an ice bath, and then the salts were filtered off. The ethereal soln was washed with water, dried over Na_2SO_4 and evaporated. The



Scheme 4.



Scheme 5. Possible biogenetic pathways of halogenated metabolites from *Laurencia glandulifera*.

residual substance was chromatographed to afford **4** (25 mg); $[\alpha]_D^{20}$ −50° (*c*, 2.30); IR, ν_{max}^{film} 3400, 3020, 1660, 1393, 1384, 1373, 1115, 1063, 1045, 952, 893, 835, 790, 760 and 739 cm^{-1}; PMR, δ 0.95 (3H, s), 1.10 (3H, s), 1.18 (3H, d, J = 6.0 Hz), 1.70 (3H, br s), *ca* 2.5 (2H, m), 3.50 (1H, br quintet, J = 6.0 Hz), 4.36 (1H, t, J = 8.2 Hz) and 5.00 (1H, m); mass, *m/e* 221 (M^+-Br) and 220 (M^+-HBr). Acetate of **4**; $[\alpha]_D^{22}$ −69° (*c*, 1.10); IR, ν_{max}^{film} 3020, 1740, 1660, 1393, 1382, 1373, 1230, 1055, 1044, 1020, 955, 936, 835, 790, 760 and 740 cm^{-1}; PMR, δ 0.92 (3H, s), 1.08 (3H, s), 1.20 (3H, d, J = 6.0 Hz), 1.70 (3H, br s), 1.96 (3H, s), *ca* 2.5 (2H, m), 4.31 (1H, t, J = 8.2 Hz), 4.75 (1H, quintet, J = 6.0 Hz) and 5.00 (1H, m); mass, *m/e* 344 and 342 (M^+). Oxidation of **4** (54 mg) with CrO_3–Py was carried out in the usual manner. The product (45 mg) was identified as **1** by comparisons of the spectral data.

Debromospirolaurenone (**6**). To a soln of **1** (145 mg) in THF (20 ml) was added LAH (100 mg), and the mixture was refluxed for 3 hr with continuous stirring, cooled and mixed with water. After filtration of the salts and evaporation of the filtrate under reduced pressure, the residue was repeatedly extracted with ether, and the combined ethereal soln was dried over Na_2SO_4 and evaporated. The residual oil was purified by chromatography to give **5** (30 mg); IR, ν_{max}^{film} 3350, 3020, 1660, 960 and 895 cm^{-1}; PMR, δ 0.87 (6H, br s), 1.14 (3H, d, J = 6.0 Hz), 1.70 (3H, br s), 3.50 (1H, br quintet, J = 6.0 Hz) and 5.10 (1H, m). Oxidation of **5** (23 mg) with CrO_3-Py was carried out in the usual manner. The product was purified by chromatography to yield **6** (15 mg); $[\alpha]_D^{23}$ −80° (c, 0.75); IR, ν_{max}^{film} 3020, 1710, 1390, 1370, 1355, 1165, 950 and 823 cm^{-1}; PMR, δ 0.85 (3H, s), 0.90 (3H, s), 1.69 (3H, br s), 2.09 (3H, s) and 5.15 (1H, m); mass, *m/e* 220 (M^+, 2), 205 (2), 177 (2), 164 (100), 135 (8), 121 (53), 105 (15), 93 (17), 91 (17), 77 (11), 55 (12) and 43 (19).

Dehydrobromospirolaurenone (**7**). A soln of **1** (101 mg) in 2M KOH–EtOH (13 ml) was refluxed for 2 hr under N_2. After being cooled, the mixture was poured into water and most of the EtOH was removed under reduced pressure. The residue was extracted with ether. The ethereal soln was washed with saturated brine and dried over Na_2SO_4. After evaporation of the solvent, the residual oily material was chromatographed to give **7** (50 mg); $[\alpha]_D^{23}$ +23° (*c*, 1.37); UV, λ_{max}^{EtOH} 270 nm (ϵ 4700); IR, ν_{max}^{film} 3040, 1710, 1595, 1180 and 725 cm^{-1}; PMR, δ 0.97 (3H, s), 1.00 (3H, s), 1.79 (3H, br s), 2.07 (3H, s) and 4.8–5.8 (3H, m); mass, *m/e* 218 (M^+, 13), 203 (8), 175 (10), 159 (60), 133 (35), 119 (40), 105 (40), 91 (50), 77 (35), 55 (30) and 43 (100).

Baeyer–Villiger oxidation of **3**. To a soln of **3** (55 mg) in $CHCl_3$ (0.5 ml) was added a soln of perbenzoic acid (50 mg) in $CHCl_3$ (2.5 ml). The mixture was allowed to stand at room temp in the dark for 140 hr. The $CHCl_3$ soln was then shaken with 5% $NaHCO_3$aq and water, and dried over Na_2SO_4. After evaporation of the solvent, the residual oil was purified by chromatorgaphy to afford an oily ester (**8**; 50 mg); IR, ν_{max}^{film} 1740, 1382, 1365, 1240, 1190, 1040 and 1020 cm^{-1}; PMR, δ 0.84 (3H, d, J = 6.0 Hz), 0.87 (3H, s), 0.94 (3H, s), 1.93 (3H, s) and 4.90 (1H, m). Saponification of **8** (50 mg) was carried out with 5% KOH–MeOH (5 ml) (reflux for 10 min) by the usual method. The product was purified by chromatography to give **9** (45 mg); IR, ν_{max}^{film} 3320 and 1070 cm^{-1}; PMR, δ 0.86 (3H, d, J = 6.0 Hz), 0.90 (3H, s), 0.95 (3H, s), 3.03 (1H, s: OH) and 4.15 (1H, m).

C_{13}-*Ketone* (**10**). Oxidation of **9** (41 mg) with CrO_3-Py was carried out in the usual manner. The product was chromatographed to yield **10** (32 mg); IR, ν_{max}^{film} 1745, 1410, 1393, 1385 and 1165 cm^{-1}; PMR, δ 0.87 (3H, d, J = 6.0 Hz), 0.88 (3H, s), 0.99 (3H, s) and 2.08 (2H, s); mass, *m/e* 194 (M^+, 48), 137 (20), 123 (100), 110 (50), 83 (75) and 55 (70).

Deuterium exchange of **10** was effected by treating **10** (30 mg) in NaOD (0.5 ml), prepared by adding Na (13 mg) to D_2O (0.5 ml) in N_2 atmosphere, and dioxane (1 ml) at 100° for 10 min. After being cooled, the solvent was distilled off under reduced pressure. To the product was added a mixture of D_2O (0.5 ml) and

dioxane (1 ml), and the mixture was heated and most of the solvent was then evaporated under reduced pressure. The same procedure was further repeated three times, and finally the residue was extracted with dry ether. Removal of the ether yielded C_{13}-ketone-d_4 (18 mg); mass, *m/e* 198 (M^+).

OsO_4 *Oxidation of* **1**. To a soln of **1** (210 mg) in benzene (6.5 ml, S-free) containing dry pyridine (1 ml) was added OsO_4 (250 mg). The mixture was allowed to stand at room temp. for 170 hr, then the solvent was removed. To the residue was added CH_2Cl_2 (7 ml) and a soln of KOH (300 mg) and mannitol (2 g) in water (20 ml). The mixture was stirred at room temp. for 5 hr and then an additional volume of CH_2Cl_2 was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 soln was concentrated, and the residue was extracted with ether. The ethereal soln was washed successively with water, 1M HClaq and saturated brine, dried over Na_2SO_4 and evaporated. The oily product was purified by chromatography to give **13** (220 mg); IR, $\nu_{max}^{CHCl_3}$ 3450, 1700, 1395, 1372, 1353, 1170, 1160, 1080, 1055, 1030, 1010, 920 and 860 cm^{-1}; PMR ($CDCl_3$), δ 1.02 (3H, s), 1.21 (3H, s), 1.25 (3H, s), 2.18 (3H, s), 3.46 (1H, br t) and 4.26 (1H, br t).

Acetate **14** of **13**; m.p. 135–136° (from diethyl ether); $[\alpha]_D^{22}$ +54° (*c*, 1.47); IR, $\nu_{max}^{CHCl_3}$ 3640, 1740, 1710, 1398, 1378, 1030, 1015, 980, 960, 910 and 865 cm^{-1}; PMR δ 1.04 (3H, s), 1.13 (3H, s), 1.22 (3H, s), 2.09 (3H, s), 2.17 (3H, s), 4.25 (1H, dd, J = 12.0 and 6.0 Hz) and 4.69 (1H, dd, J = 10.5 and 6.0 Hz); mass, *m/e* 333, 331 (M^+-$COCH_3$). (Found: C, 54.63; H, 7.49. $C_{17}H_{27}O_4Br$ requires: C, 54.40; H, 7.25).

Vinyl compound (**15**). A soln of **14** (150 mg) in 5% KOH–MeOH (15 ml) was refluxed for 5 min under N_2. After being cooled, the mixture was poured into water and extracted with ether. The ethereal soln was washed with saturated brine, dried over Na_2SO_4 and evaporated. The residual oil was chromatographed to yield **15** (70 mg); $[\alpha]_D^{23}$ −17° (*c*, 1.16); IR, ν_{max}^{film} 3380, 3080, 1685, 1630, 1380, 1363, 1090, 1008 and 912 cm^{-1}; PMR, δ 1.06 (3H, s), 1.12 (3H, s), 1.27 (3H, s), 2.09 (3H, s), 3.42 (1H, s), 4.85 (1H, dd, J = 10.0 and 1.7 Hz), 4.89 (1H, dd, J = 18.0 and 1.7 Hz) and 6.03 (1H, dd, J = 18.0 and 10.0 Hz); mass, *m/e* 252 (M^+).

Hydroxyacetate (**16**). Acetylation of **15** (33 mg) was carried out with Ac_2O–Py in the usual manner. The acetylated product was purified by chromatography to give **16** (35 mg); $[\alpha]_D^{23}$ −28° (*c*, 1.76); IR, ν_{max}^{film} 3500, 3080, 1740, 1698, 1630, 1380, 1367, 1240, 1045, 1010 and 910 cm^{-1}; PMR, δ 1.08 (3H, s), 1.12 (3H, s), 1.42 (3H, s), 2.04 (3H, s), 2.07 (3H, s), 4.60 (1H, s), 4.83 (1H, dd, J = 10.0 and 1.7 Hz), 4.88 (1H, dd, J = 18.0 and 1.7 Hz) and 6.03 (1H, dd, J = 18.0 and 10.0 Hz).

Saponification of **16** (33 mg) was carried out with 5% KOH–MeOH (reflux for 5 min) in the usual manner. The original vinyl compound (**15**) (27 mg) was obtained and identified by comparisons of the spectral data.

Hydroxyketone (**17**). To a soln of CrO_3–Py complex was added a soln of **16** (32 mg) in pyridine, and the mixture was set aside at room temp. overnight. After being worked up in the usual manner, the oily product was chromatographed to give **17** (16 mg); $[\alpha]_D^{23}$ −42° (*c*, 0.52); IR, ν_{max}^{film} 3500, 1745, 1699, 1390, 1372, 1360, 1150, 1130, 1100 and 920 cm^{-1}; PMR, δ 1.01 (3H, s), 1.05 (6H, s), 2.11 (3H, s), 4.97 (1H, dd, J = 18.0 and 1.7 Hz), 5.03 (1H, dd, J = 10.0 and 1.7 Hz) and 5.90 (1H, dd, J = 18.0 and 10.0 Hz); mass, *m/e* 250 (M^+).

Conversion of glanduliferol (**18**) *to spirolaurenone* (**1**). To a soln of **18** (29 mg) in hexane (3 ml) was added silver oxide (*ca* 50 mg), and the mixture was stirred for 15 min at 50° under N_2. After the silver salts were filtered off and washed with hexane, the combined hexane soln was then shaken with Na_2SO_4. After filtering Na_2SO_4, the solvent was evaporated under reduced pressure. The residual oily substance was purified by chromatography to give **1** (19 mg), $[\alpha]_D^{22}$ −77° (*c*, 0.89), which was identified by comparisons of the IR, PMR and mass spectra.

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