Full Papers

New Bromoterpenes from the Red Alga *Laurencia luzonensis*

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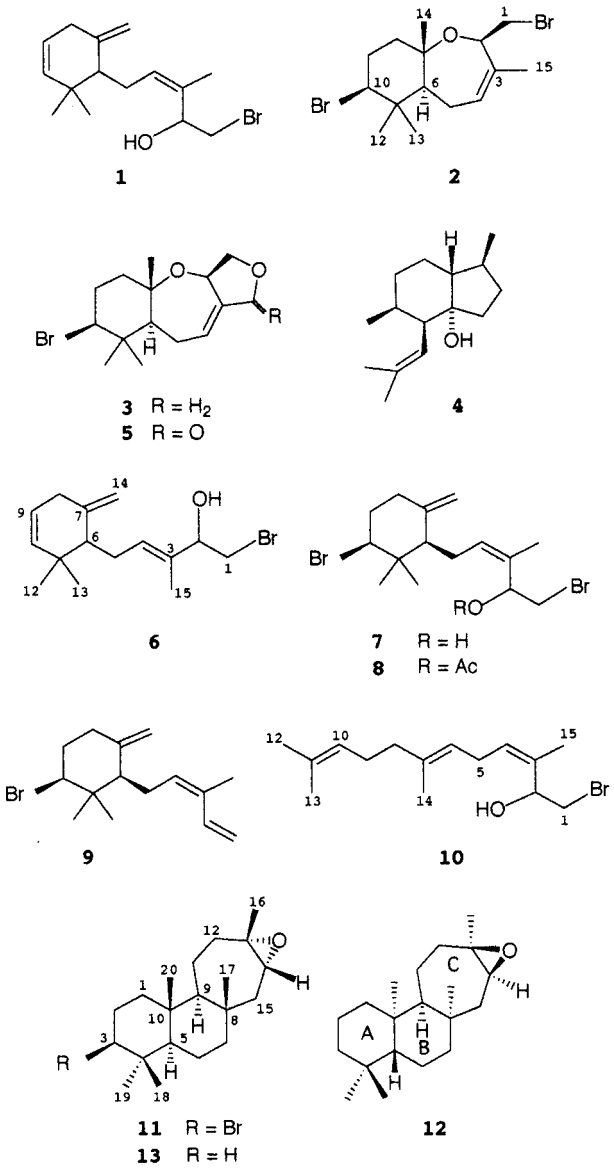
Extraction of a sample of *Laurencia luzonensis* collected off the coast of Kudaka Island, Okinawa, yielded the known sesquiterpenes palisol (**1**), palisadin B (**2**), palisadin A (**3**), pacifigorgiol (**4**), and aplysistatin (**5**), together with five new bromosesquiterpenes, isopalisol (**6**), luzonensol (**7**), luzonensol acetate (**8**), luzonensin (**9**), and (3*Z*,6*E*)-1-bromo-2-hydroxy-3,7,11-trimethyldodeca-3,6,10-triene (**10**). In addition, a new bromoditerpene of unusual structure, 3-bromobarekoxide (**11**), possessing a seven-membered ring fused to *trans*-decalin, was isolated.

Red algae of the genus *Laurencia* have proved to be a rich source of secondary metabolites consisting mainly of sesquiterpenes, C_{15}-acetogenins, and a few di- and triterpenes. More than 300 have been characterized from some 40 species collected in various parts of the world.[1] However, the tropical species *Laurencia luzonensis* has not been examined so far. As it can be collected from Okinawan waters in substantial amounts in season, we decided to investigate its chemical constituents. We now describe the isolation and elucidation of the structure of 11 terpenes, six of which are new, including one with an unusual skeleton.

Results and Discussion

A freshly collected sample of *L. luzonensis* Masuda (Rhodomelaceae) was allowed to partially dry out for 2 days and then extracted by steeping in 95% ethanol for several more days. The concentrated extract was initially separated by chromatography over silica gel and then purified by HPLC to afford the terpenes **1**−**11**. The known bromosesquiterpenes were readily identified as palisol (**1**), palisadin B (**2**), palisadin A (**3**), aplysistatin (**5**), and the hydroxysesquiterpene pacifigorgiol (**4**), by comparing their spectral data with those reported.[2−4]

The new sesquiterpenes **6**−**10** were all isolated as colorless oils. Isopalisol (**6**), molecular formula $C_{15}H_{23}BrO$ as deduced from its LR EIMS and ^{13}C NMR data (Table 1), required four sites of unsaturation. Three were due to the presence of three double bonds [δ 145.00 (s), 136.86 (d), 133.38 (s), 128.43 (d), 123.10 (d), and 109.67 (t)]. Thus, **6** must be monocyclic. Comparison of its NMR data (Tables 1 and 2) with those of palisol (**1**) revealed that they are closely related. The 2D NMR data confirmed that they share the same gross structure. The only difference between **1** and **6** is the geometry of the C-3 double bonds. The ^{13}C resonances for C-2 and C-15 in **1**, which has the *Z* geometry, are observed at δ 70.27 and 17.46, respectively. As the corresponding resonances for **6** are δ 76.51 and 12.16, it must therefore be the *E*-isomer.



A major constituent, named luzonensol (**7**), was given the molecular formula $C_{15}H_{24}Br_2O$ on the basis of the LR

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Table 1. ^{13}C NMR Chemical Shifts (δ) for **6**−**10** in CDCl

carbon no.	6	7	8	9	10
1	38.50 (t)	36.92 (t)	31.19 (t)	113.73 (t)	37.56 (t)
2	76.51 (d)	70.13 (d)	71.86 (d)	133.60 (d)	70.13 (d)
3	133.38 (s)	133.11 (s)	132.00 (s)	132.36 (s)	133.23 (s)
4	128.43 (d)	129.89 (d)	129.79 (d)	130.59 (d)	128.98 (d)
5	25.22 (t)	24.65 (t)	24.79 (t)	24.77 (t)	26.56 (t)
6	52.36 (d)	53.17 (d)	52.86 (d)	52.20 (d)	121.88 (d)
7	145.50 (s)	145.31 (s)	145.61 (s)	145.59 (s)	135.99 (s)
8	32.44 (t)	37.15 (t)	37.37 (t)	37.44 (t)	36.61 (t)
9	123.10 (d)	35.57 (t)	35.77 (t)	35.77 (t)	26.61 (t)
10	136.86 (q)	66.70 (d)	67.00 (d)	67.23 (d)	124.14 (d)
11	37.14 (s)	41.61 (s)	42.00 (s)	42.12 (s)	131.52 (s)
12	25.10 (q)	16.60 (q)	16.50 (q)	28.42 (q)	25.67 (q)
13	30.25 (q)	28.41 (q)	28.32 (q)	16.22 (q)	16.13 (q)
14	109.67 (t)	110.00 (t)	109.94 (t)	110.10 (t)	17.67 (q)
15	12.16 (q)	17.37 (q)	17.50 (q)	19.70 (q)	17.50 (q)
OAc			20.10 (q)		
OAc			170.00 (s)		

EIMS and ^{13}C NMR data (Table 1). The latter disclosed the presence of two double bonds and thus the monocyclic nature of the compound. Studies of the 1D and 2D NMR spectra (COSY, HMQC, HMBC) indicated a monocyclofarnesane skeleton bearing a side-chain similar to that of palisol (**1**). The second bromine atom was located in the ring at the C-10 position, as attested by the relevant chemical shifts (δ (C), 66.70, δ (H) 4.15 (dd, J = 11.5, 4.5 Hz)). The relative configuration of the ring portion, namely the diequatorial disposition of the C-6 and C-10 substituents, was determined by the observed NOESY correlation between the protons at the C-10 and C-6 positions (δ 1.83 (br d, J = 10 Hz)). The C-3 double bond was assigned the *Z* configuration on the basis of the ^{13}C signals of the C-2 and C-15 atoms (δ 70.13 and 17.37, respectively), which closely parallel those of palisol (**1**).

A small amount of the acetyl derivative of **7**, luzonensol acetate (**8**) of molecular formula $C_{17}H_{26}Br_2O_2$, was also obtained. The presence of an acetoxy group was shown by the NMR data (δ (H) 2.09 (3H, s); δ (C) 170.0 (s), 20.10 (q)). Acetylation of **7** gave an acetate that was identical with **8** as confirmed by the IR (1730 cm^{-1}) and NMR spectra (Tables 1 and 2).

Another new monocyclofarnesane was named luzonensin (**9**). The LR EIMS and ^{13}C NMR data (Table 1) gave a molecular formula of $C_{15}H_{23}Br$, indicating four degrees of unsaturation. The presence of three double bonds as evidenced by the ^{13}C resonances requires that **9** be monocyclic. Comparison of its NMR data with those of **7** and **8** suggests that all three have the same ring structure, namely, an equatorial bromine substituent at C-10 and an exocyclic methylene group at the C-7 position (δ 145.59 (s), 110.10 (t)). Accordingly, the two other double bonds must be in the side-chain. The ^1H and ^{13}C signals (Tables 1 and 2), as assigned by the 2D correlation, show that they are conjugated and originate at the C-1 terminus.

The geometry of the C-3 double bond was shown to be *Z* by the NOE observed between the contiguous protons attached at the C-4 and C-15 positions. Similarly, the NOE seen between the protons at C-6 and C-10 confirmed that the configuration of the ring substituents in **9** is the same as that in **7** and **8**.

The remaining sesquiterpene turned out to be the acyclic bromhydrin **10**. The molecular formula $C_{15}H_{25}BrO$ was deduced from the LR EIMS and ^{13}C NMR data (Table 1). Six olefinic carbon signals (δ 135.99, 133.23, 131.52, 128.98, 124.14, and 121.88) accounted for the three sites of unsaturation required by the formula, thereby establishing the acyclic structure. A hydroxy group was indicated by the IR absorption band at 3417 cm^{-1}. The ^1H NMR spectrum displayed four signals, each characterizing a vinyl-substituted methyl group (δ 1.72, 1.68, 1.63, and 1.61) suggestive of the sesquiterpenic nature of **10**. The overall structure of **10** was corroborated by 2D NMR analysis (Table 1). The C-3 double bond clearly has the Z configuration in view of the tell-tale ^{13}C resonances exhibited by the C-2 and C-15 carbon atoms (δ 70.13 and 17.50), which are essentially identical to those of **1** and **7**. The *E* geometry of the C-6 double bond was inferred from the relatively high field signal observed for the C-14 atom (δ 17.67). It can therefore be concluded that **10** is (3*Z*,6*E*)-1-bromo-2-hydroxy-3,7,11-trimethyldodeca-3,6,10-triene.

Evidently, **10** is the biogenetic precursor to the cyclized entities **1**−**3** and **5**−**9**, all of which have the snyderane[1] skeleton. For example, addition of brominium ion to the isopropenyl entity in **10** would bring about cyclization to **7** and **8**. Thereafter, protonation of the exocyclic double bond in **7** followed by nucleophilic attack of the neighboring hydroxy group affords the seven-membered cyclic ether **2**. It is worth noting that, since the absolute structures of palisadin B (**2**) and its 12-hydroxy derivative are known,[2] the configuration of the hydroxy substituent in **10** can be designated as *R*. Palisadin A (**3**) and aplysistatin (**5**) are derived from **2** by hydroxylation of the 15-methyl substituent followed by cyclization.

Dehydrobromination of **7** accounts for the formation of palisol (**1**). However, it is difficult to say at what stage the side-chain isomerizes to give isopalisol (**6**). The formation of luzonensin (**9**) undoubtedly arises by brominium-initiated cyclization of (3*Z*,6*E*)-3,7,11-trimethyldodeca-1,3,6,-10-tetraene. Most probably, the latter process constitutes an alternative biogenetic path, but for the other bromosesquiterpenes it does raise the question of the timing of

Table 2. ^1H NMR Chemical Shifts (δ) and Coupling Constants (J in Hz) for **6**−**10** in $CDCl_3$

carbon no.	6	7	8	9	10
1	3.45 (m)	3.49 (dd, 10.0, 9.0) 3.40 (dd, 10.0, 4.5)	3.54 (dd, 10.5, 8.5) 3.38 (dd, 10.5, 6.0)	5.20 (br d, 17.5) 5.11 (br d, 11.0)	3.40 (dd, 10.0, 3.5) 3.45 (dd, 10.0, 10.0)
2	4.22 (t, 5.0)	4.74 (dd, 9.0, 4.5)	5.80 (dd, 8.0, 6.0)	6.78 (dd, 17.5, 11.0)	4.80 (m)
4	5.48 (m)	5.29 (6, 5.5)	5.35 (br t, 6.0)	5.28 (br t, 8.0)	5.35 (m)
5	2.25 (m), 2.90 (m)	2.45 (m), 2.25 (m)	2.58 (m), 2.20 (m)	2.55 (m), 2.37 (m)	2.75 (m)
6	2.00 (m)	1.83 (br d, 10.0)	1.92 (br d, 10.0)	1.90 (br d, 11.0)	5.05 (m)
8	2.64 (br s)	2.35 (m), 2.04 (m)	2.35 (m), 2.10 (m)	2.33 (m), 2.02 (m)	2.00 (m)
9	5.52 (m)	2.30 (m), 2.08 (m)	2.25 (m), 2.15 (m)	2.25 (m), 2.08 (m)	2.05 (m)
10	5.37 (s, 10.0)	4.15 (dd, 11.5, 4.5)	4.15 (dd, 11.5, 4.0)	4.16 (dd, 11.5, 5.0)	5.05 (m)
12	0.95 9s)	0.87 (s)	0.88 (s)	0.87 (s)	1.68 (s)
13	1.02 (s)	1.20 (s)	1.25 (s)	1.22 (s)	1.72 (s)
14	4.86 (s), 4.60 (s)	4.91 (br s), 4.56 (br s)	4.94 (s), 4.61 (s)	4.91 (br s), 4.50 (br s)	1.63 (s)
15	1.65 (br s)	1.69 (br s)	1.64 (br s)	1.78 (br s)	1.61 (br s)
OAc			2.09 (s)		

bromhydrin formation, namely, whether it occurs before or after cyclization.

The isolation of pacifigorgiol (**4**) from *Laurencia* was surprising. It has only been previously isolated from a gorgonian coral and has never been found in algae or any other marine organisms. Furthermore, the highly rearranged carbon skeleton of **4** is completely different from those of the other sesquiterpenes isolated from *L. luzonensis*.

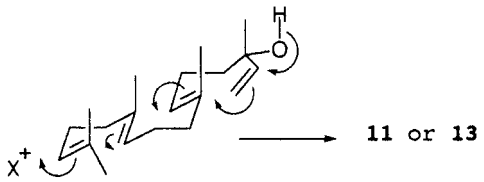
The final bromoterpene (**11**) isolated from the extract was also a surprise. It was obtained as colorless crystals, mp 165 °C. The molecular formula $C_{20}H_{33}BrO$ was deduced from the LR EIMS and ^{13}C NMR data. The monobrominated nature of **11** was revealed by the molecular ion peak which appeared as a doublet (*m/z* 368, 370) of equal intensity. The presence of an epoxide ring was evident from the carbon signals (δ 60.52 (s), 60,45 (d)) in conjunction with the characteristic proton resonance at δ 2.70 (dd, J = 7.5, 7.5 Hz). The absence of olefinic signals in the ^1H and ^{13}C NMR spectra means that **11** is tetracyclic and comprises three carbocyclic rings. The five singlet methyl resonances (δ 0.87, 0.93, 1.02, 1.05, and 1.32) in the ^1H NMR spectrum strongly suggest that **11** is a diterpene. More conclusively, analysis of the 1D and 2D NMR spectra (COSY, HMQC, HMBC, NOESY) enabled the structure to be established as a central seven-membered ring to which are fused *trans*-decalin and an epoxide.

From the preceding evidence, **11** appeared to be the 3β-bromo derivative of the known diterpene barekoxide (**12**), which had been isolated from the sponge *Chelonaplysilla erecta*.[5] In fact, comparison of the NMR data of **11** and **12** showed that they were very much the same except for the signals of the A ring portion. We therefore assumed that **11** would have the same relative stereochemistry as **12**, in which the A/B and B/C junctions were purported to be trans- and cis-fused, respectively. However, since the absolute configuration of **12** was unknown, the bromo derivative **11**, by virtue of its heavy atom, provides a convenient means for determining the absolute structure of **11** and by extension that of **12** as well.

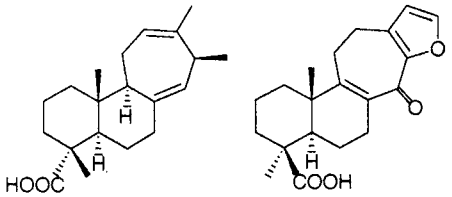
Accordingly, a single crystal of **11** was prepared and submitted to X-ray analysis. Its absolute structure, described in a preliminary publication,[6] reveals that the A/B ring fusion is certainly trans, but that the B/C ring junction is trans as well. Despite the syn-diaxial array and attendant mutual interactions of the C-18, C-20, and C-17 methyl groups, the cyclohexane and cycloheptane rings adopt regular chair conformations. Obviously, the relative configuration previously assigned to **12** was not correct and requires amendment. Final proof was secured by the reductive debromination of **11**. Treatment with tributyltin hydride and AIBN in DMSO afforded a product (**13**) that exhibited virtually the same ^1H and ^{13}C NMR data as those reported for barekoxide. In other words, the absolute structure of barekoxide could be that of **13** or its enantiomer. However, the fact that natural and semisynthetic barekoxide (**13**) have optical rotations of the same sign confirms that the absolute configuration of sponge-derived barekoxide is correctly represented by **13**.

The foregoing findings not only establish the absolute structures of the barekoxides but also record the occurrence of an unusual type of diterpene in *Laurencia*. Natural products composed of a *trans*-decalin fused to a seven-membered ring are quite uncommon. The few examples known are of terrestrial origin. Strobal and strobic acid (**14**) were isolated from *Pinus strobus* L and their absolute configurations determined by degradation and CD.[7,8] Significantly, the configurations of the C-5, C-9, and C-10 atoms in **11** and **13** are the same as those in **14**. Similarly, extracts of the plant *Ballota hispanica* have yielded hispanonic (**15**) and hispaninic acids (**16**),[9] the absolute configurations of which were elucidated by X-ray diffraction.[10] A 2D NMR study further showed that the chair and half-chair conformations of the A and B rings observed in the crystal were also adopted in solution.[11] The A/B ring fusions in **15** and **16** are trans, and the configurations of the C-5 and C-10 atoms are the same as those in 3-bromobarekoxide (**11**).

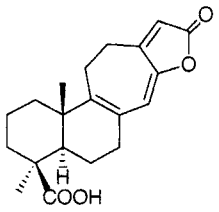
Scheme 1



17 X = Br or H



14 **15**



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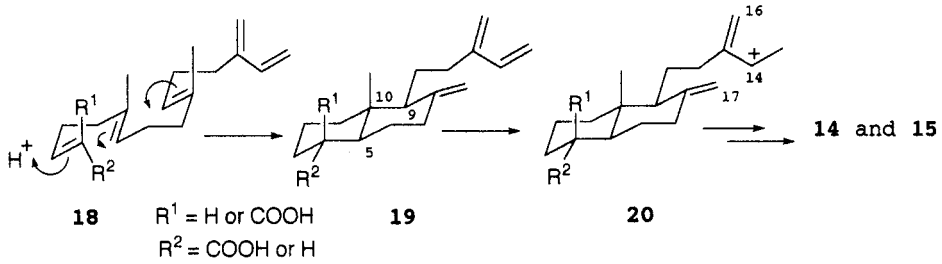
Clearly, all three metabolites (e.g., **11**, **14**, and **15**) arise initially by similar stereoselective biogenetic pathways. Bromination or protonation of geranyllinalool (**17**) creates a steroid-like tetracyclic array affording **11** or **13** directly in a concerted manner (Scheme 1). However, formation of **14** and **15** requires an interrupted proton-triggered cyclization of a hypothetical precursor such as **18** which stops at the labdane stage (Scheme 2). The formation of **19** implants the C-5, C-9, and C-10 stereocenters, which are the same as those in **11**. Thereafter, the stereochemically less critical construction of the seven-membered rings in **14** and **15** could proceed stepwise from **19** by ring enlargement of intermediate cyclohexenylmethyl cations.[12] Another possibility is direct formation of the fused cycloheptane ring. Intramolecular electrophilic addition of either the C-14 or C-16 terminus of the allylic cation **20** onto the C-17 methylene group would give the strobane or hispanane carbon skeletons and eventually **14** or **15**.

In summary, the red alga genus *L. luzonensis* has provided a rich harvest of bromosesquiterpenes and 3-bromobarekoxide (**11**), an unusual diterpene containing a seven-membered ring hitherto only observed in natural products of terrestrial origin. Moreover, the carbon frameworks of **11** and barekoxide (**13**) of sponge origin were shown to have the same absolute configurations. Furthermore, the barekoxides, together with strobic, hispanonic,

Scheme 2



and hispaninic acids possess the same configurations at the C-5 and C-10 stereocenters, thereby indicating that their biogeneses share similar stereochemical features.

Experimental Section

General Experimental Procedures. IR spectra were recorded on a Jasco FT IR-300 spectrometer and optical rotation on a Jasco DIP-1000 digital polarimeter. NMR spectra were recorded on a JEOL 500 MHz FT NMR spectrometer with TMS as internal standard. LR EIMS were measured on a Hitachi M-2500 instrument. The columns used for HPLC were normal-phase LiChrosorb Si60 (7 μm) and reversed phase μ-Bondapak C18 (Waters).

Plant Material. The alga (5.2 kg) of *L. luzonensis* Masuda (Rhodomelaceae) was collected off the coast of Kudaka Island, Okinawa, in May 1998. After washing with freshwater it was allowed to dry in the air at room temperature for 2 days to give semidried material (3.5 kg). A dried voucher specimen (MK 9805-1) is kept in our laboratory of the Department of Chemistry, Biology, and Marine Science, University of the Ryukyus in Okinawa.

Extraction and Isolation. After extraction with 95% EtOH, the extract was concentrated and the resulting residue was partitioned between AcOEt and H_2O to give an oil (12.5 g). Separation of the oil on silica gel by using a step gradient consisting of hexane, CH_2Cl_2, and AcOEt gave 13 fractions. The first fraction was eluted with hexane and further separated on a small column (SiO_2, hexane) followed by HPLC purification (Si60, hexane) to furnish luzonensin (**9**) as an oil (3.4 mg). Fraction 5 was eluted (hexane−CH_2Cl_2, 2:1) and further separated into four subfractions (SiO_2, hexane−CH_2Cl_2). Separation of subfraction 5 on PTLC (RP-18, MeOH−MeCN−$CHCl_3$, 4:4:1) gave palisadin B (**2**) as a colorless solid (10.6 mg), which displayed NMR data identical with those reported.[2] Repeated separation of subfraction 3 by HPLC (Si60, hexane, AcOEt) gave, in order of elution, pacifigorgiol (**4**), 3-bromobarekoxide (**11**), (3*Z*,6*E*)-1-bromo-2-hydroxy-3,7,11-trimethyldodeca-3,6,10-triene (**10**), palisol (**1**), isopalisol (**6**), and luzonensol (**7**) in quantities of 16.1, 58.5, 3.4, 21.3, 5.1, and 290.0 mg, respectively. Separation of subfraction 4 on PTLC (Si60, hexane−CH_2Cl_2, 1:1) followed by HPLC (Si60, hexane−$CHCl_3$, 5:2) furnished luzonensol acetate (**8**) and **2** in amounts of 0.4 and 8.1 mg, respectively. Further separation of subfraction 5 on a column (Si60, hexane−AcOEt, 20:3) followed by HPLC (Si60, hexane−AcOEt, 20:3 → 20:4) yielded palisadin A (**3**) as an oil (129 mg) and aplysistatin (**5**) as colorless crystals (119 mg). Bromosesquiterpenes **1**−**3**, **5**, and hydroxysesquiterpene **4** were identified by comparing their NMR spectra with those reported.[2−4]

Isopalisol (6): colorless oil, $[\alpha]^{27}_D$ −31.88° (*c* 0.59, $CHCl_3$); IR (film) ν_{max} 3417, 3014, 2923, 1650, 1444, 1068, 993 cm^{-1}; ^{1}H and ^{13}C NMR data (see Tables 1 and 2); LR EIMS (70 eV) *m*/*z* 282 (3), 280 (3, $M^+ - H_2O$), 265, (8), 201 (15), 121 (100), 105 (48), 93 (55).

Luzonensol (7): colorless oil, $[\alpha]^{27}_D$ −39.58° (*c* 2.26, $CHCl_3$); IR (film) ν_{max} 3411, 3081, 2971, 1646, 1440, 1068, 993 cm^{-1}; ^{1}H and ^{13}C NMR data (see Tables 1 and 2); LR EIMS (70 eV) *m*/*z* 364 (3), 362 (6), 360 (3, $M^+ - H_2O$), 281 (100), 201 (47), 147 (30), 121 (80).

Luzonensol acetate (8): colorless oil, $[\alpha]^{25}_D$ −13.04° (*c* 0.23, $CHCl_3$); IR (KBr) ν_{max} 2750, 1730, 1375, 1240, 960, 910 cm^{-1}; ^{1}H and ^{13}C NMR data (see Tables 1 and 2); LR EIMS (70 eV) *m*/*z* 364 (5), 362 (7, M^+ − AcOH), 201 (58), 121 (60), 107 (32).

Luzonensin (9): colorless oil, $[\alpha]^{25}_D$ +3.0° (*c* 0.16, $CHCl_3$); IR (film) ν_{max} 3087, 2971, 1646, 1433, 1369, 987, 898 cm^{-1}; ^{1}H and ^{13}C NMR data (see Tables 1 and 2); LR EIMS (70 eV) *m*/*z* 284 (11), 282 (13, M^+), 281 (100), 201 (47), 147 (30), 121 (80), 81 (100).

(3*Z*,6*E*)-1-Bromo-2-hydroxy-3,7,11-trimethyldodeca-3,6,10-triene (10): colorless oil, $[\alpha]^{25}_D$ +2.9° (*c* 0.17, $CHCl_3$); IR (film) ν_{max} 3417, 2923, 1650, 1068, 993 cm^{-1}; ^{1}H and ^{13}C NMR data (see Tables 1 and 2); LR EIMS (70 eV) *m*/*z* 300 (8), 298 (8, M^+), 240 (5), 121 (100), 105 (15), 93 (17).

3-Bromobarekoxide (11): colorless crystals (recrystallized from CCl_4), mp 165 °C, $[\alpha]^{27}_D$ +6.18° (*c* 0.3, $CHCl_3$); IR (KBr) ν_{max} 2950, 2850, 1450, 1375, 1260, 1150, 870, 775 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.98 (dd, 13.0, 4.5 Hz, H-3), 2.70 (dd, 7.5, 7.5 Hz, H-14), 2.18 (dq, 12.5, 3.5 Hz, H-2), 2.07 (m, H-2), 2.00 (m, H-12), 1.85 (dd, 14.0, 14.0 Hz, H-15), 1.80 (dt, 13.0, 3.5 Hz, H-1), 1.70, (m, H-11), 1.60, (m, H-7), 1.50 (m, H-6), 1.50 (m, H-7), 1.50 (m, H-11), 1.35 (m, H-12), 1.32 (s, H-16), 1.25 (m, H-6), 1.20 (dd, 14.0, 7.5 Hz, H-15), 1.05 (s, H-19), 1.02 (s, H-17), 1.00 (br dd, 13.0, 3.5 Hz, H-1), 0.93 (s, H-18), 0.90 (dd, 11.5, 3.0 Hz, H-5), 0.87 (s, H-20), 0.82, (br d, 10.0 Hz, H-9); ^{13}C NMR ($CDCl_3$) δ 69.52 (d), 64.28 (d), 60.52 (s), 60.45 (d), 56.77 (d), 47.07 (t), 44.04 (t), 41.68 (t), 39.80 (s), 38.82 (s), 37.32 (t), 35.9 (t), 31.00 (t), 30.50 (q), 22.42 (q), 21.10 (t), 19.97 (t), 19.55 (q), 18.13 (q), 15.93 (q); LR EIMS (70 eV) *m*/*z* 370 (4), 368 (40, M^+), 289 (45), 271 (35), 137 (65), 123 (86), 95 (75), 81 (70), 69 (100).

Conversion of 3-Bromobarekoxide (11) to Barekoxide (13). To a solution of **11** (6 mg) in DMSO (0.2 mL) was added tributyltin hydride (50 mL) and α,α-azobisisobutyronitrile (3 mg). The mixture was stirred for 24 h under N_2 and subsequently extracted with hexane. Purification by HPLC (AcOEt−hexane, 1:10) gave **13** (4.2 mg, 88% yield): colorless crystals (recrystallized from hexane), mp 140 °C, $[\alpha]^{24}_D$ +5.28° (*c* 0.256, $CHCl_3$); IR (KBr) ν_{max} 1950, 1850, 1475, 1375, 965, 875 cm^{-1}; ^{1}H NMR (C_6D_6) δ 2.55 (t, 7.5 Hz, H-14), 1.88 (dd, 14.0, 8.0 Hz, H-12), 1.71 (dd, 13.5, 6.0 Hz, H-15), 1.58 (m, H-1), 1.55 (m, H-6), 1.55 (m, H-2), 1.50 (m, H-11), 1.42 (br t, 13.0 Hz, H-12), 1.35 (m, H-2), 1.33 (m, H-3), 1.29 (m, H-7), 1.25 (m, H-15), 1.25 (m, H-6), 1.22 (s, H-16), 1.15 (m, H-11), 1.10 (m, H-3), 1.02 (m, H-7), 0.86 (s, H-17), 0.84 (s, H-18), 0.80 (s, H-19), 0.70 (s, H-20), 0.60 (br d, 11.5 Hz, H-5), 0.56 (m, H-1), 0.56 (m, H-9); ^{13}C NMR (C_6D_6) δ 64.51 (d, C-9), 60.02 (d, C-14), 59.87 (s, C-13), 56.26 (d, C-5), 47.99 (t, C-15), 44.23 (t, C-7), 42.11 (t, C-3), 40.27 (t, C-1), 38.96 (s, C-10), 37.74 (s, C-8), 36.64 (t, C-12), 33.57 (s, C-4), 33.57 (q, C-18), 22.70 (q, C-16), 21.77 (q, C-19), 20.38 (t, C-11), 19.79 (q, C-17), 19.16 (t, C-2), 18.85 (t, C-6), 16.20 (q, C-20); LR EIMS (70 eV) *m*/*z* 290 (55, M^+), 275 (20), 257 (205), 191 (45), 138 (75), 123 (100), 109 (90), 95 (77), 81 (88), 69 (80), 55 (75).

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