(1:1:1:1) system, a major low R_f spot for the desired pentatriacose hCG (111–145)M peptide and a minor mid R_f streak for impurities. Amino acid analyses of the desalted peptide (6B), listed in Table III, were almost acceptable for the pentatriacosa peptide.

The material was then chromatographed on a 58 × 2.0 cm column of Sephadex LH-20, eluted with *n*-BuOH-H_2O (6:100) in 7-mL fractions with detection of the peptide by a UV monitor at 256 nm (Phe), to give a single symmetrical peak. Lyophilization of tubes 14–16, corresponding to the top of the peptide peak, gave 225.5 mg (7B) of white solid which on TLC showed primarily the low R_f spot for the pentatriacosa peptide contaminated by only a small amount of the higher R_f impurity.

Since the hentriacosa peptide hCG (117–147)C eluted in the lower phase of the 4:1:5 system partition column, it was decided to use a different partition system for the pentatriacosa peptide hCG (111–145)M. Fraction 7B was partitioned on a 57 × 2.0 cm column of Sephadex G-25 eluted with upper and then lower phase of the system 0.1 N HOAc–*n*–BuOH–Pyr (11:5:3), in 5.5-mL fractions with detection of the peptide by Folin–Lowry. No peak appeared in the upper-phase eluent, but there was a sharp, symmetrical peak at the beginning of the lower-phase elution. Lyophilization of tubes 43 and 44, corresponding to the top of this peak, gave 74.7 mg (8B) of white solid which now showed only the one low R_f spot on TLC for the desired pentatriacosa peptide.

A further purification of 50 mg of fraction 8B was carried out by ion-exchange chromatography on a 28 × 1.5 cm -52 column eluted in 25-mL fractions with 1 to 500 mM ammonium acetate buffer gradient, pH 6.4. A single, symmetrical peak was detected by the UV monitor at 256 nm and by Folin–Lowry at 660 nm. Lyophilization of tube 2, corresponding to the top of this peak, gave 27.6 mg (9A) of purified hCG (111–145)M, which gave the amino acid analysis of ratios listed in Table II.

9A (5.76 mg) was further purified by preparative thin layer electrophoresis on cellulose plates (160 μ thick, Eastman chromagram sheet) at 500 V in pyridine acetate buffer of pH 6.5 to give 2.0 mg of pentatricosa hCG (111–145)M (10A; IBR 12755). The amino acid analytical ratios are in Table II. Two separate purifications in the same manner of 8.97 mg of (9A) and 12.87 mg of (9A) gave 3.6 mg (10B; IBR 13202) and 5.5 mg (10C, IBR 13669) of pentatriacosa hCG (111–145)M. The amino acid analytical results are in Table II.

The purified hCG (111–145)M showed one spot by electrophoresis moving toward the cathode in pyridine acetate buffers of pH 3.6 and pH 6.5.

Acknowledgment. Appreciation is expressed to the Population Council, the Robert A. Welch Foundation, and the John A. Hartford Foundation for their respective support of this research.

Registry No.—Boc-Pro, 15761-39-4; Boc-Gln, 4530-20-5; (hCG 117–147)C, 63215-95-2; (hCG 111–145)M, 63301-41-7.

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Metabolites of the Red Alga *Laurencia subopposita*

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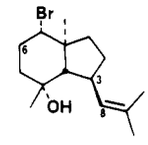
The red alga *Laurencia subopposita* contains a variety of secondary metabolites, some of which have previously been described from other sources. We have previously reported that the major metabolite was oppositol (1). The antibiotic activity of the alga was due to 7-hydroxylaurene (2) and 10-bromo-7-hydroxylaurene (3). Laurene (4), isoprelaurefucin (6), laurefucin (7), acetyllaurefucin (8), and oplopanone (19) have all been described previously. Two epimeric diols 13 and 14 were shown to be related to oppositol (1). A diol 21 having the germacrane skeleton rearranged on dehydration to give 8(15)-dehydrooplopanone (26). Two aromadendrene alcohols 27 and 29 were isolated. The optical enantiomer of 1-hydroxylalloaromadendrene (27) was synthesized by oxidation of alloaromadendrene (28) with selenium dioxide.

Red algae of the genus *Laurencia* have proved to be a most prolific source of halogenated metabolites of three major classes, sesquiterpenes, diterpenes, and acetylenes.[1] The halogenated sesquiterpenes may be further subdivided into three groups: the aromatic compounds, the chamigrenes and their precursors and rearrangement products, and the oppositol–eudesmane group. Although it is not uncommon to find representatives of more than one group in a *Laurenica* species, the structural elucidations have generally been described separately. In this paper we wish to present an account of the diversity of chemical structures which may be found in *Laurencia subopposita*.

We have previously reported that the major metabolite of *Laurencia subopposita* (J. G. Agardh) Setchell was oppositol (1), a sesquiterpene having a previously undescribed carbon skeleton.[2] On reinvestigation of the metabolites of *L. subopposita*, we found that oppositol (1) was not an antibiotic, as had been previously stated. The mild antibiotic activity of oppositol (1) had been due to the presence of traces of 7-hydroxylaurene (2) and/or 10-bromo-7-hydroxylaurene (3).

Hexane, ether, and acetone extracts of powdered, air-dried



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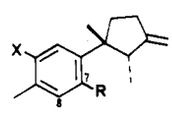
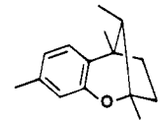


2 R = OH X = H
3 R = OH X = Br
4 R = H X = H



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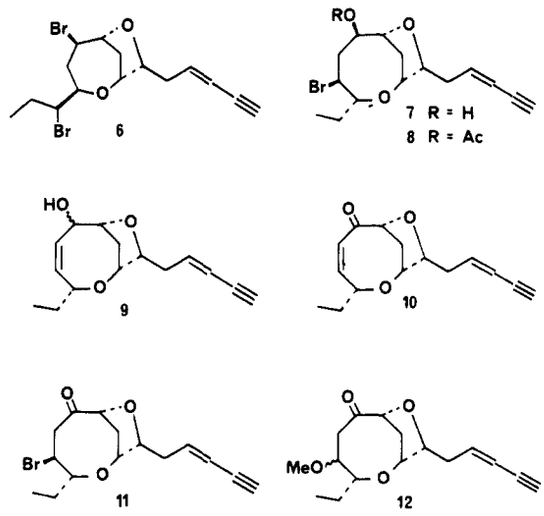
Laurencia subopposita were combined to yield a viscous oil (2.3% dry weight) which showed antibiotic activity against *Staphylococcus aureus*. The oil was chromatographed on Florisil, using a solvent gradient of increasing polarity from petroleum ether to methanol. Selected fractions were rechromatographed to obtain individual compounds, of which oppositol (1) (0.11% dry weight) was again the major metabolite.

The least polar sesquiterpene metabolite was laurene (4), whose spectral properties were identical with those reported.[3] The antibiotic activity of *L. subopposita* was due to two phenols, 7-hydroxylaurene (2) and 10-bromo-7-hydroxylaurene (3). The spectral data of our sample of 10-bromo-7-hydroxylaurene (3) were nearly identical with those recently reported by Kazlauskas et al.[4] for allolaurinterol,[5] isolated from *Laurencia filiformis*. The major antibiotic from *L. subopposita* was 7-hydroxylaurene (2) (0.013% dry weight). The ^{1}H NMR spectrum of 7-hydroxylaurene (2) showed signals due to an aromatic methyl group at δ 2.19, three aromatic protons at 6.36 (s), 6.56 (d, J = 7 Hz) and 6.93 (d, J = 7 Hz) and a hydroxyl proton at 4.76 (s). The remaining signals, at δ 0.67 (d, 3H, J = 7 Hz) due to the secondary methyl group, 1.30 (s, 3H) due to the tertiary methyl group, 2.95 (q, J = 7 Hz), and 4.82 and 4.92 due to the exocyclic methylene protons, were remarkably similar to the signals for the nonaromatic portion of laurene (4). Irradiation of the methyl doublet at δ 0.67 caused the methine quartet at 2.95 to collapse to a singlet, indicating that the methine proton was not coupled to other protons. The chemical shift of the secondary methyl signal at δ 0.67 suggested that the methyl group was in the deshielding region of the aromatic ring and hence the two groups must be *cis* with respect to the cyclopentane ring.[3] Since 7-hydroxylaurene (2) underwent a slow isomerization to a cyclic ether 5, the phenolic hydroxyl group must be at C-7, rather than C-8. The formation of the cyclic ether 5 from the phenol 2 parallels the reported isomerization of bromophenol 3 to a cyclic ether.[4]

Laurencia subopposita contains eight acetylenes, which were isolated as four pairs of geometrical isomers. The geometrical isomers about the Δ^3 olefinic bond were inseparable by column chromatography but could be distinguished by the characteristic signals in the ^{1}H NMR spectra and, in some cases, could be estimated by VPC analysis. Since most of the acetylenes had been described previously, we did not attempt to separate the mixtures of geometrical isomers. The major acetylenic metabolites were a 1:2 mixture of *cis*- and *trans*-isoprelaurefucin (6) (0.1% dry weight), the trans isomer of which had previously been isolated from *L. nipponica*.[6] A 1:1 mixture of *cis*- and *trans*-acetyllaurefucin (8) (0.016% dry weight) and a 1:3 mixture of *cis*- and *trans*-laurefucin (7) (0.019% dry weight) were also obtained.[7] Each of the pairs of acetylenes had spectral characteristics appropriate for a mixture of geometrical isomers about the Δ^3 olefinic bond. Although very complex, the ^{1}H NMR spectra of the mixtures provided the most diagnostic information. In each case, the spectra were identical with those of a pure geometrical isomer except for the signals due to the acetylenic and olefinic protons. The signals due to the acetylenic proton were at δ ~2.8 in the cis isomers and at δ ~3.1 in the trans isomers. The olefinic signals for cis and trans isomers usually overlapped but could be clearly identified due to the difference between cis (J = 11 Hz) and trans (J = 16 Hz) coupling constants.

The only undescribed acetylenes were a 1:1 mixture of *cis*- and *trans*-dehydrobromolaurefucin (9) (0.03% dry weight). The GC–mass spectra of the two isomers were almost identical, as expected, each showing a molecular ion at m/e 248, corresponding to the molecular formula $C_{15}H_{20}O_3$. Examination of the ^{1}H NMR spectrum suggested that the alcohol 9 was related to laurefucin (7) by loss of hydrogen bromide.



The ^{1}H NMR spectrum of 9 contained signals at δ 5.03 (bd, J = 13 Hz) due to the α-hydroxy proton, 5.59 (bt, J = 12, 13 Hz) and 5.41 (bd, J = 12 Hz) due to the olefinic protons in the ring, and four signals between 3.88 and 4.19 due to the protons adjacent to ether oxygens. The allylic alcohol 9 was oxidized with chromic oxide to an α,β-unsaturated ketone 10 (IR 1680 cm^{-1}). The ^{1}H NMR spectrum of 10 contained two signals at δ 5.81 (bd, J = 12 Hz) and 6.14 (d, J = 12 Hz) due to the olefinic protons in the ring. Oxidation of laurefucin 7 with Jones reagent gave a bromoketone 11 (IR 1720 cm^{-1}). Treatment of the bromoketone 11 with potassium hydroxide in methanol did not give the expected α,β-unsaturated ketone 10 but resulted instead in the formation of a β-methoxyketone 12. Treatment of the bromoketone 11 with stronger bases such as potassium *tert*-butoxide in *tert*-butyl alcohol resulted in decomposition of the molecule. However the α,β-unsaturated ketone 10 was converted into the same β-methoxy ketone 12 by treatment with potassium hydroxide in methanol. This sequence of reactions indicated that the allylic alcohol 9 had the gross structure shown. The stereochemistry was defined at all centers except the carbon bearing hydroxyl.

The most interesting compounds to be isolated from *L. subopposita* were oppositol (1), two related diols 13 and 14,

13 R = H 14
15 R = Ac 16
19 R = PhCO

and a series of nonhalogenated sesquiterpenes. The diols 13 and 14 were shown to be epimers, but the relative configurations at the epimeric center in the side chain could not be conclusively defined. The more polar diol 13 (0.015% dry weight), mp 123–124 °C, $[\alpha]^{20}_D$ +10°, had the molecular formula $C_{15}H_{25}O_2Br$. The ^{1}H NMR spectrum of 13 contained a signal due to an α-bromo proton at δ 3.96 (dd, 1H, J = 4, 12 Hz) and two methyl signals at 1.19 and 1.41 (CH_3-C-OH) reminiscent of signals in oppositol (1). Perhaps the most unusual and characteristic signal in the ^{1}H NMR spectra of op-

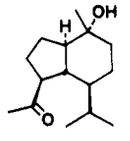
positol (1) and related compounds was a quartet of doublets (J = 12, 12, 12, 4 Hz) which was cleanly separated from all other signals. This signal, which was at δ 2.33 in the diol **13** and 2.28 in oppositol (1), was due to the axial proton at C-6, which was shifted downfield from a normal cyclohexane position by a 1,2 interaction with bromine and a 1,3-diaxial interaction with hydroxyl. The side chain of **13** gave rise to ^{1}H NMR signals at δ 1.74 (s, 3H), 4.11 (d, 1H, J = 7 Hz) and 4.86 (s, 2H). The ^{1}H NMR spectrum of the corresponding acetate **15** contained two signals at δ 4.99 and 5.04 due to the methylene protons, 5.44 (d, J = 5 Hz) due to the methine proton, 2.04 for the acetoxy protons, and 1.78 due to the vinyl methyl group. The change in chemical shift of the methine and methylene protons on acetylation implied the presence of an allylic alcohol moiety.

The less polar diol **14** (~0.008% dry weight) was isolated as an inseparable mixture with oplopanone (**20**). The two compounds were separated by acetylation of the mixture, since only the diol **14** reacted, allowing isolation of the monoacetate **16**, which was then treated with lithium aluminium hydride in ether at −78 °C to regenerate the diol. Neither the diol **14** nor the corresponding acetate **16** gave a molecular ion in the mass spectrum; the molecular formula $C_{15}H_{25}O_2Br$ was determined by high resolution mass measurement on the m/e 316 peak $(M - CH_2CO)^+$ of the monoacetate. The ^{1}H NMR spectrum of the diol **14**, with signals at δ 1.18 (s, 3H), 1.34 (s, 3H), 1.75 (s, 3H), 2.35 (qd, 1H, J = 12, 12, 12, 4 Hz), 4.06 (dd, 1H, J = 12, 4 Hz), 4.41 (bs, 1H), 4.89 (s, 1H), 5.01 (s, 1H), suggested that the diols **13** and **14** might have the same gross structure. The ^{1}H NMR spectrum of the monoacetate **16** was very similar to that of the monoacetate **15**, the major difference being that the allylic α-acetoxy proton in **16** appeared as a broad singlet at δ 5.48, while the equivalent proton in **15** appeared as a doublet at 5.44 (J = 5 Hz). These data suggested that the diols **13** and **14** were epimers at either C-3 or C-8. Oxidation of either diol with Jones reagent gave the same α,β-unsaturated ketone **17** (IR 1675 cm^{-1}). The ^{1}H NMR spectrum of **17** contained signals at δ 6.05 and 5.84 due to methylene protons β to the ketone, 1.91 due to the vinyl methyl and 3.77 (dt, 1H, J = 4, 11, 11 Hz) due to an α-keto proton which was trans to the bridgehead proton and shifted downfield by 1,3-diaxial interaction with the hydroxyl. The two diols must therefore be epimeric at C-8.

The gross structures of the epimeric diols were confirmed by ozonolysis of the ketone **17** to an acid, which was esterified with diazomethane to obtain the methyl ester **18**, identical in all respects with the methyl ester obtained from oppositol (**1**) by ozonolysis followed by methylation.

The relative configurations of the diols **13** and **14** have been determined by two methods, neither of which can be regarded as conclusive. The diol **13** was converted into the corresponding benzoate **19**. According to Brewster's rule, comparison of the optical rotation of the benzoate **19**, $[\alpha]^{20}_D$ −17°, with that of the diol **13**, $[\alpha]^{20}_D$ +10°, suggested the configuration shown.[8] The coupling constant of the α-hydroxy proton in each diol indicated that the side chain adopted a fairly rigid conformation in solution. We performed lanthanide-induced shift experiments on both acetates **15** and **16**. In each case we were able to determine a position for the europium atom in which it must be associated with the tertiary alcohol functionality. In each complex, the α-acetoxy proton was directed toward the tertiary alcohol and the "best fit" for the shifts of the acetoxy methyl signal and the signals due to the isopropylidene group occurred with the configurations shown.

The remaining metabolites were all nonhalogenated sesquiterpenes. We identified oplopanone (**20**), previously isolated from *Oplopanax japonicus*, by comparison of physical data with literature values[9] and confirmed the assignment by showing that the melting point (93–94 °C) was undepressed on admixture with an authentic sample. The most polar metabolite that we isolated was a diol **21**, mp 118–120 °C, $[\alpha]^{20}_D$ +55°, having a molecular formula $C_{15}H_{26}O_2$. The infrared spectrum showed a strong hydroxyl band at 3600 cm^{-1} and bands at 1382 and 1367 cm^{-1} due to a gem-dimethyl group. The ^{1}H NMR spectrum contained signals at δ 0.85 (d, 3H, J = 7 Hz) and 0.91 (d, 3H, J = 7 Hz) due to an isopropyl group, 1.26 (s, 3H) due to methyl on a carbon atom bearing hydroxyl, 3.96 (dd, 1H, J = 3, 10 Hz) due to an α-hydroxy proton, 4.94 (bs, 1H) and 5.14 (bd, 1H) due to the exocyclic methylene protons, and 5.24 (d, 1H, J = 16 Hz) and 5.29 (dd, J = 16, 9 Hz) due to a trans olefinic bond which has only one proton on an adjacent carbon atom. The ^{13}C NMR spectrum confirmed the presence of a disubstituted olefin (δ 137.6 and 129.9), an exocyclic methylene (151.0 and 111.4), a secondary alcohol, (78.7), a tertiary alcohol (72.3), and no other tetrasubstituted carbons. The diol **21**, having three degrees of unsaturation, must contain a single ring. Since the UV spectrum showed only end absorption, the trans-disubstituted olefinic bond must be in a side chain or medium-sized ring and must be between the tertiary alcohol carbon and a carbon bearing only one hydrogen. Spin decoupling experiments revealed that both methyl doublets were collapsed to singlets upon irradiation at δ 1.52, while the olefinic signals were not affected, and that the secondary hydroxyl group was not on a carbon atom adjacent to the trans-disubstituted olefinic bond. Assuming that the isopropyl group must be adjacent to a chiral center for the ^{1}H NMR signals of the methyl groups to have different chemical shifts, and assuming an isoprenoid skeleton, we found only three reasonable gross structures, **22**, **23**, and **24**.



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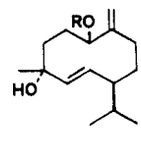
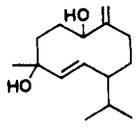


21 R = H
25 R = Ac



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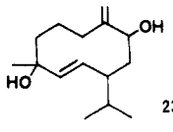

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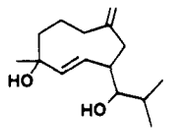

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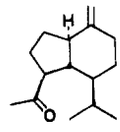
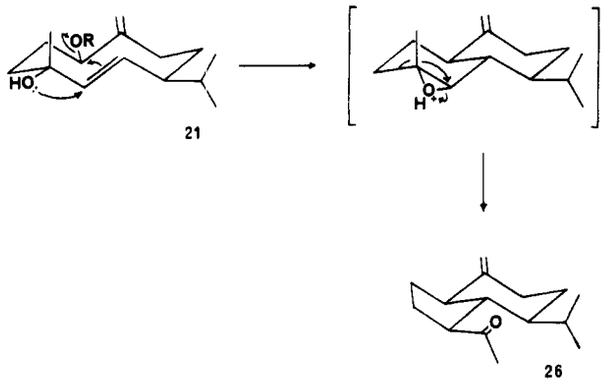


26

In the corresponding acetate **25**, the ^{1}H NMR signals of all the olefinic protons were shifted downfield [δ 5.00 (bs), 5.20 (bs) and 5.35 (d, 2H, J = 6 Hz)], while the isopropyl methyl signals (0.83 and 0.88) were scarcely shifted, indicating a preference for structure **22**.

Dehydration of the diol **21** with phosgene in pyridine or Moffatt oxidation conditions[10] gave a ketone **26** (IR 1710 cm^{-1}, no hydroxyl band) in quantitative yield. The ^{1}H NMR spectrum contained signals due to an exocyclic methylene (δ 4.51 and 4.61), a methyl ketone (2.09) and an isopropyl group [0.89 (d, 3H, J = 7 Hz) and 0.64 (d, 3H, J = 7 Hz)]. An identical product could be obtained by dehydration of oplopanone **20** with phosphorus oxychloride in pyridine. The formation of 8(15)-dehydrooplopanone **26** from the diol **21** can be explained only if the diol has the structure shown. Assuming a concerted reaction mechanism for dehydration and ring formation (Scheme I), we can derive the most likely relative configuration for the diol **21**. An alternative configuration at

Scheme I. Proposed Mechanism for the Conversion of Diol 21 to 8(15)-Dehydrooplopanone (26)

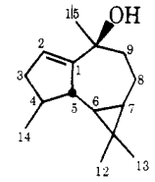


the tertiary alcohol carbon is possible, but we prefer the configuration shown.

The remaining two compounds were isomeric tertiary alcohols having the aromadendrene skeleton. 1-Hydroxyalloaromadendrene (**27**), isolated as an oil, had the molecular formula $C_{15}H_{24}O$. The ^1H NMR spectrum contained signals at δ 0.22 (dd, 1H, J = 9, 12 Hz) and 0.56 (m, 1H) due to two cyclopropyl protons, 0.98 (d, 3H, J = 6 Hz), 0.99 (s, 3H) and 1.02 (s, 3H) due to methyl groups, and 4.89 and 5.03 due to methylene protons. This ^1H NMR spectrum closely resembles that expected from a sesquiterpene of the aromadendrene group. The infrared spectrum indicated the presence of a hydroxyl group (3420 cm^{-1}) which must be tertiary and which must be adjacent to the exocyclic methylene group, since in the ^1H NMR spectrum neither of the cyclopropane protons appeared as a doublet and the exocyclic methylene protons were well separated in chemical shift. Treatment of an authentic sample of alloaromadendrene (**28**) with selenium dioxide in aqueous ethanol at 70 °C yielded a mixture of products from which was isolated a single tertiary alcohol, 1-hydroxyalloaromadendrene (**27**), identical with the natural product in all respects except that the optical rotations were of opposite signs. An LIS study of 1-hydroxyalloaromadendrene (**27**) showed that the proton experiencing the greatest induced shift was coupled to the high-field cyclopropane proton, which appeared as a double doublet, and to a proton which was, in turn, coupled to the secondary methyl group. These data indicated a cis-fused bicyclic ring system for 1-hydroxyalloaromadendrene (**27**).

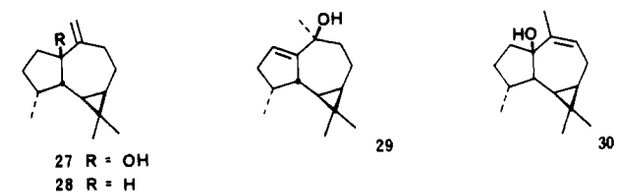
The second aromadendrene alcohol (**29**) (IR 3460 cm^{-1}) was isolated as an oil of molecular formula $C_{15}H_{24}O$.[11] The ^1H NMR spectrum contained signals at δ 0.44 (t, 1H, J = 9 Hz) and 0.53 (m, (m, 1H) due to the cyclopropyl protons, 1.02 (s, 3H), 1.06 (s, 3H), 1.07 (d, 3H, J = 7 Hz) and 1.45 (s, 3H) due to methyl groups and at 5.52 (bs, 1H) due to a vinyl proton. Assuming the aromadendrene skeleton, both the isomers **29** and **30** were compatible with the spectral data. The observation that the vinyl proton appeared as a broad singlet strongly suggested that the double bond was in a five-membered ring. In addition, the chemical shift of the methyl singlet at δ 1.45 was outside the normal range for a vinyl methyl. An LIS study of the alcohol **29** indicated that the alcohol had the gross structure and stereochemistry shown. After addition of 0.6 equivalents of $Eu(fod)_3$, each proton was observed as a separate signal and the coupling constants were measured (Table I). We were able to find a position for the europium ion such that a graph of log $\Delta\delta$ against log r_{meas} gave a line of slope −3 (r_{meas} is the distance between the europium ion and a proton measured using a Dreiding model; $\Delta\delta$ is the shift induced by 1 equiv of $Eu(fod)_3$ obtained by graphical extrapolation.) The structural assignment can be explained on the basis of two observations: the second largest induced shift was experienced by the methyl singlet originally at δ 1.45 and the next largest

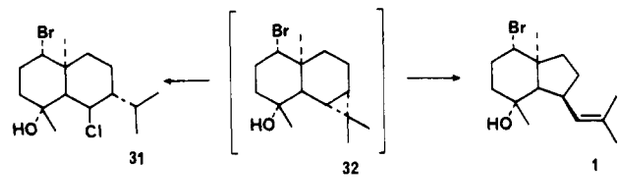
Table I. ^1H NMR Data for the Alcohol 29. Chemical Shifts (δ), Induced Shifts ($\Delta\delta$), Multiplicities, and Coupling Constants

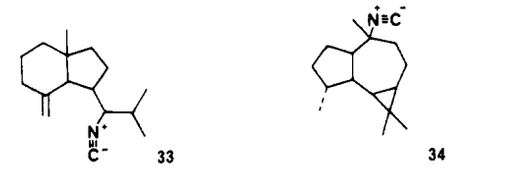


H at C-	δ, ppm	$\Delta\delta$, ppm	Multiplicity and coupling constants, Hz	
2	5.52	2.91	bs(dd)	J = 3, 1
3(α)	2.24	0.95	ddd	J = 15, 8, 3
3(β)	2.02	1.36	ddd	J = 15, 9, 1
4	2.32	1.73	m	J = 9, 8, 8, 7, 7, 7
5	2.47	4.64	t	J = 8, 8
6	0.44	2.50	t	J = 9, 8
7	0.53	2.05	m	J = 11, 9, 5
8(α)	1.88	1.91	dt	J = 13, 6, 5
8(β)	1.55	4.59	m	J = 13, 12, 11
9(α)	1.72	3.41	t	J = 14, 12
9(β)	1.72	5.91	dd	J = 14, 6
12	1.02	0.64	s	
13	1.06	0.64	s	
14	1.07	0.73	d	J = 7
15	1.45	5.23	s	

induced shift was recorded for a proton originally at 2.47 (t, J = 8 Hz) which was coupled to a proton at 0.44 (dd, J = 8, 9 Hz) and a proton at 2.32 which was, in turn, coupled to the







methyl doublet at 1.07. Thus the hydroxyl group must be on the same face as the bridgehead proton and on the carbon bearing methyl. The small induced shifts of the cyclopropyl protons suggest that they are on the opposite face of the seven-membered ring to the hydroxyl.

We have described the major compounds from our collection of *L. subopposita*. Analysis of a second sample of *L. subopposita* by thin layer chromatography suggested a very similar composition. We have found that it was well worth the effort to examine the minor constituents and particularly the nonhalogenated sesquiterpenes. Kazlauskas et al.[4] have

speculated that oppositol (1) might be formed in vivo from a eudesmane precursor such as heterocladol (31). We believe that the coexistence of cyclopropane-containing sesquiterpenes with oppositol (1) suggests a cyclopropane-containing precursor (32) for both heterocladol (31) and oppositol (1). It is interesting to note that the only other compound having the oppositol skeleton, axionitrile-1 (33), was found together with an aromadendrane derivative, axisonitrile-2 (34), in *Axinella cannabina*,[12] suggesting a similar biogenetic relationship.

Experimental Section

^{1}H NMR spectra were recorded on a Varian HR-220 spectrometer, ^{13}C NMR spectra were recorded on a Varian CFT-20 spectrometer, infrared spectra were recorded on a Perkin-Elmer Model 700 spectrophotometer, and optical rotations were measured on a Perkin-Elmer Model 141 polarimeter, using a 10-cm microcell. Low resolution mass spectra were recorded on a Hewlett-Packard 5930A mass spectrometer. High resolution mass measurements were supplied by the Analytical Facility at California Institute of Technology. Melting points were measured on a Fisher-Johns apparatus and are reported uncorrected. All solvents used were either spectral grade or distilled from glass prior to use.

Collection, Extraction, and Chromatographic Separation. *Laurencia subopposita* was collected at low tide in La Jolla in May 1975, air-dried, and ground in a Wiley mill to a 1 mm particle size. The dried alga (1 kg) was extracted in a Soxhlet apparatus for 24 h each with hexane (2 L), diethyl ether (2 L), and acetone (2 L). The combined extracts were evaporated to leave a dark green viscous oil (22.5 g, 2.3% dry weight). When assayed for antimicrobial activity, the crude extract inhibited the growth of *Staphylococcus aureus*.

The crude extract (22.5 g) was added as a concentrated petroleum ether solution to a column (75 × 5 cm) containing Florisil (750 g) in petroleum ether. Elution with a solvent gradient of increasing polarity from petroleum ether through benzene, ethyl acetate, acetone, and methanol led to 36 fractions (500 mL). Antimicrobial screening of the individual fractions indicated that only fraction 13 was active against *S. aureus*.

Laurene (4). Fractions 3 and 4 were combined (500 mg) and rechromatographed on a column (20 × 2 cm) containing 10% $AgNO_3$ on silica gel (40 g) in hexane. Elution with hexane allowed isolation of a mobile oil (110 mg, 0.011% dry weight) having spectral properties identical to those reported[3] for laurene (4).

7-Hydroxylaurene (2) and 10-Bromo-7-hydroxylaurene (3). Fraction 13 (625 mg) was rechromatographed on a column (30 × 1.5 cm) of silica gel (25 g) in 10% benzene in petroleum ether, yielding a mixture of phenols (160 mg) which was separated by HPLC on a Porasil A column (4 ft × 3/8 in.) using 15% diethyl ether in petroleum ether as an eluent to obtain 7-hydroxylaurene (2) (125 mg, 0.013%) and 10-bromo-7-hydroxylaurene (3) (25 mg, 0.0025%). Antimicrobial testing showed that each of these two substances (100 μg) inhibited the growth of *S. aureus*.

7-Hydroxylaurene (2). $[\alpha]^{20}_D$ + 45° (2.5, $CHCl_3$); IR ($CHcl_3$) 3650, 2990, 1660, 1620, 1575 cm^{-1}; NMR (CCl_4) δ 6.93 (d, 1H, J = 7 Hz), 6.56 (d, 1H, J = 7 Hz), 6.36 (s, 1H), 4.92 (s, 1H), 4.82 (s, 1H), 4.76 (s, 1H), 2.95 (q, 1H, J = 7 Hz), 2.19 (s, 3H), 1.30 (s, 3H), 0.67 (d, 3H, J = 7 Hz); mass spectrum *m/e* (relative intensity) 216 (26), 201 (74), 187 (26) 159 (38), 145, (20), 121 (40), 69 (55), 57 (60), 55 (70), 43 (92), 41 (100); high resolution mass measurement, observed 216.152, $C_{15}H_{20}O$ requires 216.151.

10-Bromo-7-hydroxylaurene (3). IR ($CHCl_3$) 3690, 2990, 1660, 1610 cm^{-1}; NMR (CCl_4) δ 7.27 (s, 1H), 6.60 (s, 1H), 5.00 (s, 1H), 4.98 (s, 1H), 4.90 (s, 1H), 2.99 (q, 1H, J = Hz), 2.28 (s, 3H), 1.21 (s, 3H), 0.73 (d, 3H, J = 7 Hz); mass spectrum *m/e* (relative intensity) 294, 296 (1:1) (10), 279, 281 (26), 237,239 (9) 201 (24), 159 (21), 69 (80), 57 (65), 55 (70), 43 (90), 41 (100).

Isoprelaurefucin (6). Fractions 14 and 15 were combined (2.0 g) and rechromatographed on a column (40 × 2.5 cm) containing silica gel (100 g) in 10% benzene in petroleum ether. Elution with a solvent gradient of increasing polarity from 10% benzene in petroleum ether to dichloromethane allowed isolation of an oil (1.04 g) with spectral characteristics appropriate for a mixture (1:2) of *cis:trans*-isoprelaurefucin (6).

Oppositol (1). Fraction 16 (1.40 g) was rechromatographed on a column (30 × 1.5 cm) containing silica gel (25 g) in 15% diethyl ether in petroleum ether, which allowed isolation of oppositol (1) (1.14 g, 0.11%) identical in every respect with an authentic sample. ^{13}C NMR ($CDCl_3$) 132.0 (d), 128.7 (s), 71.6 (s), 63.3 (d), 60.7 (d), 47.7 (s), 42.0 (t), 40.4 (t), 36.4 (d), 31.2 (t), 30.6 (q), 28.5 (t), 25.7 (q), 18.0 (q), 16.3 (q) ppm.

1-Hydroxyalloaromedendrene (27) and 10β-hydroxy-Δ$^{1(2)}$-aromadendrene (29). Fractions 17 and 18 were combined (1.02 g) and rechromatographed on a column of silica gel (50 g) in 15% diethyl ether in petroleum ether. Elution allowed isolation of an oil (530 mg) which was purified further by HPLC on a μ-C18 column (2 ft × 1/4 in.) using 30% water in acetonitrile as an eluent. This yielded an oil (95 mg) which was rechromatographed on a column (20 × 1 cm) containing 10% $AgNO_3$ on silica gel (15 g) in 30% diethyl ether in hexane to yield 1-hydroxyalloaromadendrene (27) (35 mg, 0.0035%) and 10β-hydroxy-Δ$^{1(2)}$-aromadendrene (29) (25 mg, 0.0025%).

1-Hydroxyalloaromadendrene (27). $[\alpha]^{20}_D$ +99° (1.0, $CHCl_3$); IR (neat) 3410, 2960, 1460, 1390 cm^{-1}; NMR ($CDCl_3$) δ 5.03 (s, 1H), 4.89 (s, 1H), 2.63 (m, 2H), 2.34 (m, 2H), 1.02 (s, 3H), 0.99 (s, 3H), 0.98 (d, 3H, J = 6 Hz), 0.56 (m, 1H), 0.22 (dd, 1H, J = 9, 12 Hz); mass spectrum *m/e* (relative intensity) 220 (1), 205 (1), 202 (1), 191 (1), 187 (2), 177 (3), 163 (4), 159 (4), 107 (15), 91 (20), 79 (30), 67 (32), 55 (42), 43 (48), 41 (100); high resolution mass measurement, observed 220.181, $C_{15}H_{24}O$ requires 220.183.

10β-Hydroxy-Δ$^{1(2)}$-aromadendrene (29). $[\alpha]^{20}_D$ −46° (1.0, $CHCl_3$); IR (neat) 3460, 2950, 1460, 1390 cm^{-}; NMR ($CDCl_3$) δ 5.52 (bs, 1H), 1.45 (s, 3H), 1.07 (d, 3H, J = 7 Hz), 1.06 (s, 3H), 1.02 (s, 3H), 0.53 (m, 1H), 0.44 (t, 1H, J = 9 Hz); NMR ($CDCl_3$, 0.6 equivalent Eu(fod)$_3$) δ 7.24 (bs, 1H), 5.32 (dd, 1H, J = 14, 6 Hz), 5.06 (t, 1H, J = 8 Hz), 4.46 (s, 3H), 4.33 (ddd = 1H, J = 11, 12, 13, Hz), 3.52 (dd, 1H, J = 12, 14 Hz), 3.30 (m, 1H, J = 7, 7, 7, 8, 8, 9 Hz), 2.78 (m, 3H), 1.60 (d, 3H, J = 7 Hz), 1.50 (m, 2H), 1.40 (s, 6H); mass spectrum *m/e* (relative intensity) 220 (2), 205 (1), 202 (2), 187 (2), 177 (2), 159 (20), 105 (30), 91 (45), 81 (35), 79 (40), 77 (40), 67 (40), 55 (60), 43 (100); high resolution mass measurement, observed 220.181, $C_{15}H_{24}O$ requires 220.183.

Acetyllaurefucin (8). Fractions 21, 22, and 23 were combined (1.42 g) and rechromatographed on a column (40 × 2.5 cm) containing silica gel (100 g) in 25% diethyl ether in petroleum ether. Elution led to an oil (530 mg) which was purified further on a column (30 × 1.5 cm) containing silica gel (25 g) in chloroform, which allowed isolation of an oil (160 mg) having spectral characteristics appropriate for a mixture (1:1) of *cis:trans*-acetyllaurefucin (8). A mixture of sterols (750 mg) was also isolated from these fractions.

Diol Acetate 16 and Oplopanone (20). Fractions 24, 25, and 26 were combined (1350 mg) and rechromatographed on a column (40 × 2 cm) containing silica gel (60 g) in 1:1 diethyl ether–petroleum ether, which led to two interesting components. The least polar (410 mg) was further purified on a column (30 × 1 cm) containing silica gel (20 g) in 25% diethyl ether in petroleum ether to yield an oil (270 mg). This material was treated with acetic anhydride (2 mL) and pyridine (2 mL) at 25 °C for 16 h, and the volatile liquids were evaporated to leave an oil (300 mg) which was chromatographed by preparative tlc on three silica gel plates (20 × 20 × 0.15 cm) using 25% ethyl acetate in chloroform as an eluent to yield the diol acetate 16 (120 mg, 0.012%) as an oil. The more polar component (100 mg) was purified by preparative tlc on a silica gel plate (20 × 20 × 0.15 cm) using diethyl ether as an eluent. Isolation of a band (R_F = 0.4) led to a solid (35 mg, 0.0035%) which was recrystallized from 25% diethyl ether in hexane to yield oplopanone (20): mp 93–94 °C, $[\alpha]^{20}_D$ +13° (1.0, $CHCl_3$), which proved to be identical in all respects with an authentic sample.

Diol Acetate 16. IR ($CHCl_3$) 3700, 3000, 1738, 1460, 1380 cm^{-1}; NMR ($CDCl_3$) δ 5.48 (s, 1H), 4.84 (s, 1H), 4.81 (s, 1H), 3.97 (dd, 1H, J = 4, 13 Hz), 2.59 (m, 1H), 2.35 (m, 1H), 2.10 (s, 3H), 1.76 (s, 3H), 1.27 (s, 3H), 1.18 (s, 3H); mass spectrum *m/e* (relative intensity) 316,318 (1:1) (1), 298,300 (25), 265,267 (7), 257,259 (16), 219 (35), 201 (48), 177 (68), 159 (65), 147 (25), 145 (50), 135 (100), 119 (60), 107 (85), 105 (65), 97 (55), 95 (60), 81 (62), 71 (50), 69 (45), 57 (30), 55 (37); high resolution mass measurement, observed 316.102, $C_{15}H_{25}O_2Br$ requires 316.104.

Diol 13 and Laurefucin (7). Fractions 27 and 28 were combined (1200 mg) and rechromatographed on a column (30 × 2 cm) containing silica gel (50 g) in 25% diethyl ether in chloroform, which allowed isolation of two components. The least polar had spectral characteristics appropriate for a mixture (1:3) of *cis:trans*-laurefucin (190 mg, 0.019%). The more polar component (150 mg) was recrystallized from 20% diethyl ether in hexane to yield the diol 13, mp 123–124 °C, $[\alpha]^{20}_D$ +10° (2.5, $CHCl_3$); IR ($CHCl_3$) 3630, 3450, 2960, 1650, 1460, 1375 cm^{-1}; NMR ($CDCl_3$) δ 4.86 (s, 2H), 4.11 (d, 1H, J = 7 Hz), 3.96 (dd, 1H, J = 4, 12 Hz), 2.33 (m, 1H), 1.74 (s, 3H), 1.41 (s, 3H), 1.19 (s, 3H); mass spectrum *m/e* (relative intensity) 301,303 (1:1) (2), 283,285 (3), 245, 247 (2), 228 (4), 219 (3), 203 (4), 201 (2), 185 (6), 177 (8), 165 (13), 159 (13), 147 (48), 135 (27), 121 (27), 119 (34), 107 (96), 105 (66), 93

(81), 91 (75), 81 (99), 79 (74), 71 (100), 69 (95), 57 (50), 55 (80), 43 (95). Anal. Found: C, 56.51; H, 7.88; Br, 24.96; $C_{15}H_{25}O_2Br$ requires C, 56.78; H, 7.94; Br, 25.19.

Dehydrobromolaurefucin (9) and 7β,10α-Dihydroxy-3β-isopropyl-10-methyl-6-methylene-*trans*-cyclodecene (21). Fractions 29 and 30 were combined (1.64 g) and rechromatographed on a column (30 × 2.5 cm) containing silica gel (80 g) in 30% diethyl ether in chloroform. Elution with a solvent gradient of increasing polarity from 30% diethyl ether in chloroform to diethyl ether led to two interesting components. The least polar (670 mg) was rechromatographed on a column (20 × 2 cm) containing silica gel (30 g) in diethyl ether, which allowed isolation of an oil (300 mg, 0.03%) containing a mixture (1:1) of *cis*:*trans* dehydrobromolaurefucin (**9**):λ_{max} (MeOH) 224 nm; IR ($CHCl_3$) 3500, 3350, 2960, 1660 cm^{-1}; NMR ($CDCl_3$) δ 6.29 (m, 0.5 H), 6.15 (m, 0.5 H), 5.64 (m, 1H), 5.59 (m, 1H), 5.41 (bd, 1H, J = 12 Hz), 5.03 (bd, 1H, J = 13 Hz), 4.19 (m, 1H), 4.03 (bs, 1H), 3.90 (m, 2H), 3.13 (d, 0.5 H, J = 2 Hz), 2.83 (d, 0.5 H, J = 2 Hz), 0.95 (t, 3H, J = 7 Hz); mass spectrum m/e (relative intensity) 248 (1), 233 (0.5), 230 (0.5), 219 (4), 201 (3), 191 (6), 133 (25), 105 (90), 83 (100), 79 (95), 77 (90), 65 (90); high resolution mass measurement, observed 248.140, $C_{15}H_{20}O_3$ requires 248.141. The more polar solid component was recrystallized from diethyl ether to yield **7β,10α-dihydroxy-3β-isopropyl-10β-methyl-6-methylene-*trans*-cyclodecene (21)** (220 mg, 0.022%): mp 118–120 °C; $[\alpha]^{20}_D$ +55° (2.5, $CHCl_3$); IR ($CHCl_3$) 3600, 3430, 2950, 1530, 1440, 1382, 1367 cm^{-1}; NMR ($CDCl_3$) δ 5.27 (m, 2H), 5.14 (s, 1H), 4.94 (s, 1H), 3.96 (dd, 1H, J = 3, 10 Hz), 2.27 (m, 1H), 1.26 (s, 3H), 0.91 (d, 3H, J = 7 Hz), 0.85 (d, 3H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) 151.0 (s), 137.6 (d), 129.9 (d), 111.4 (t), 78.7 (d), 72.3 (s), 49.9 (d), 38.6 (d), 32.4 (t), 29.9 (t), 29.5 (q), 28.3 (t, 2C) 20.6 (q, 2C); mass spectrum m/e (relative intensity) 238 (1), 220 (7), 205 (5), 202 (6), 177 (35), 135 (35), 119 (40), 109 (53), 107 (68), 97 (73), 81 (100), 41 (53). Anal. Found: C, 75.75; H, 11.18; $C_{15}H_{26}O_2$ requires C, 75.63; H, 10.92.

Isomerization of 7-Hydroxylaurene (2) to the Cyclic Ether 5. Storage of 7-hydroxylaurene (**2**) (125 mg) in diethyl ether solution (3 mL) at −20 °C for 12 months followed by preparative TLC on a silica gel plate (20 × 20 × 0.15 cm) using hexane as an eluent yielded a cyclic ether **5** (85 mg); IR (neat) 2850, 1516, 1570, 1170, 1110 cm^{-1}; NMR ($CDCl_3$) δ 7.00 (d, 1H, J = 7 Hz), 6.65 (d, 1H, J = 7 Hz), 6.55 (s, 1H), 2.24 (s, 3H), 2.1–1.5 (m, 4H), 1.49 (q, 1H, J = 7 Hz), 1.39 (s, 3H), 1.34 (s, 3H), 0.76 (d, 3H, J = 7 Hz); mass spectrum m/e (relative intensity) 216 (40), 201 (100), 187 (25), 173 (30), 159 (50), 145 (20), 115 (23), 93 (30), 91 (35), 79 (25), 77 (30), 69 (20), 67 (15), 65 (15), 57 (20), 55 (30). When tested for antimicrobial activity against *S. aureus*, this material showed no inhibitory capability.

Oxidation of Dehydrobromolaurefucin (9) to Ketone 10. Dehydrobromolaurefucin (**9**) (cis:trans, 1:1, 15 mg, 0.06 mmol) was dissolved in dichloromethane (4 mL) and stirred at 25 °C. A solution of the pyridine complex of chromic oxide (0.36 mmol) in dichloromethane (0.9 mL) was added dropwise, and the resulting mixture was stirred for 15 min at 25 °C. Water (5 mL) was added, and the organic material was extracted with dichloromethane (2 × 10 mL). The combined organic extracts were dried over sodium sulfate and the solvent evaporated to leave a brown oil (18 mg) which was purified by preparative tlc on silica gel (20 × 20 × 0.025 cm) using diethyl ether as an eluent to obtain the ketone **10** (mixture of cis:trans 1:1, 12 mg) as an oil: λ_{max} (MeOH) 223 nm; IR (neat) 3180, 2860, 1680, 1450, 1370, 1320 cm^{-1}; NMR ($CDCl_3$) δ 6.26 (m, 0.5 H), 6.14 (m, 0.5 H), 6.14 (d, 1H, J = 12 Hz), 5.81 (bd, 1H, J = 12 Hz), 5.65 (d, 0.5 H, J = 16 Hz), 5.57 (d, 0.5 H, J = 9 Hz), 4.27 (m, 2H), 3.98 (m, 2H), 3.12 (d, 0.5 H, J = 2 Hz), 2.95 (d, 0.5 H, J = 2 Hz), 2.0–2.5 (m, 3h), 2.02 (m, 1H), 1.66 (m, 2H), 0.97 (t, 3H, J = 7 Hz); mass spectrum m/e (relative intensity) 246 (1), 228 (1), 217 (3), 189 (3), 173 (4), 171 (4), 150 (6), 145 (9), 143 (10), 129 (30), 105 (90), 103 (40), 95 (60), 91 (55), 81 (100), 65 (45); high resolution mass measurement, observed 246.1258, $C_{15}H_{18}O_3$ requires 246.1251.

Oxidation of Laurefucin (7) to the Ketone 11. Laurefucin (**7**) (mixture cis:trans, 1:3, 15 mg, 0.05 mmol) was dissolved in dichloromethane (1 mL) and stirred at 25 °C. A solution of the pyridine complex of chromic oxide (0.3 mmol) in dichloromethane (0.8 mL) was added dropwise, and the resulting mixture was stirred for 30 min at 25 °C. Water (5 mL) was added, and the mixture was extracted with diethyl ether (3 × 10 mL). The combined organic extract was dried over magnesium sulfate and the solvent evaporated to obtain an oil (18 mg) which was purified by preparative tlc on a silica gel plate (20 × 20 × 0.025 cm) using diethyl ether as an eluent to yield the ketone **11** (mixture cis:trans, 1:3, 12 mg) as an oil: λ_{max} (MeOH) 224 nm; IR ($CHCl_3$) 3110, 2850, 1720, 1460, 1385; NMR ($CDCl_3$) δ 6.19 (m, 0.8 H), 6.05 (m, 0.2 H), 5.57 (d, 0.8 H, J = 16 Hz), 5.50 (bd, 0.2 H, J = 9 Hz), 4.28 (d, 1H, J = 8 Hz), 4.20 (bs, 1H), 3.95 (m, 2H), 3.61 (t, 1H, J = 9 Hz), 311 (d, 0.2 H, J = 2 Hz), 2.98 (m, 2H), 2.82 (d, 0.8 H, J = 2 Hz), 2.51 (m, 1H), 2.12 (m, 2H), 1.64 (m, 2H), 1.27 (m, 1H), 0.98 (t, 3H, J = 7 Hz); mass spectrum m/e (relative intensity) 326,328 (1:1) (0.1), 246 (1), 228 (2), 218 (1), 179 (3), 177 (3), 151 (10), 149 (11), 131 (20), 107 (30), 105 (40), 97 (15), 95 (15), 91 (30), 79 (35), 77 (35), 69 (100), 65 (30), 57 (20), 55 (50).

Treatment of Ketone 11 with Methanolic Potassium Hydroxide Solution. The ketone **11** (4 mg, 0.01 mmol, cis:trans, 1:3) was dissolved in methanolic potassium hydroxide solution (0.5 N, 1.0 mL) and the solution was stirred for 1 h at 25 °C. The solution was neutralized with 0.5 N hydrochloric acid solution and the product extracted with diethyl ether (3 × 10 mL). The combined extracts were dried over magnesium sulfate and the solvent evaporated to obtain an oil (3 mg) which was purified on preparative silica gel TLC using diethyl ether as eluent to give the ketone **12** (2 mg, cis:trans, 1:3): λ_{max} (MeOH) 224 nm; IR (neat) 3150, 2820, 1715; NMR ($CDCl_3$) δ 6.16 (m, 0.5 H), 6.04 (m, 0.5 H), 5.57 (d, 0.5 H, J = 15 Hz), 5.50 (d, 0.5 H, J = 9 Hz), 4.23 (m, 1H), 4.14 (bs, 1H), 3.93 (m, 1H), 3.36 (s, 3H), 3.30 (m, 2H), 3.08 (d, 0.5 H, J = 2 Hz), 2.91 (d, 0.5 H, J = 2 Hz), 2.9–2.5 (m, 4H), 2.06 (m, 1H), 1.82 (m, 2H), 1.44 (m, 1H), 0.95 (t, 1.5 H, J = 7 Hz), 0.94 (t, 1.5 H, J = 7 Hz); mass spectrum m/e (relative intensity) 278 (1), 260 (1), 246 (4), 231 (1), 217 (2), 213 (2), 202 (5), 191 (5), 145 (21), 133 (47), 131 (45), 105 (100), 91 (58), 79 (47), 77 (43), 71 (52), 69 (47), 65 (53); high resolution mass measurement, observed 278.1521, $C_{16}H_{22}O_4$ requires 278.1521.

Treatment of Ketone 10 with Methanolic Potassium Hydroxide Solution. The ketone **10** (10 mg, 0.04 mmol, cis:trans, 1:1) was dissolved in methanolic potassium hydroxide solution (0.5 N, 2.0 mL) and the solution was stirred for 1 h at 25 °C. The reaction was worked up according to the procedure above to obtain the ketone **12** (7 mg, cis:trans, 1:1), identical except for the cis:trans olefin ratios with the compound obtained above.

Acetylation of the Diol 13. The diol **13** (20 mg, 0.06 mmol) was dissolved in a mixture of acetic anhydride (1 mL) and pyridine (2 mL), and the resulting solution was stirred for 16 h at room temperature. The reagents were removed in vacuo, and the residue was purified on a silica gel plate (20 × 20 × 0.025 cm) using diethyl ether as eluent to obtain the acetate **15** (17 mg, 75% theoretical) as an oil: IR ($CHCl_3$) 2980, 1710, 1660, 1530, 1430, 1360 cm^{-1}; NMR ($CDCl_3$) δ 5.44 (d, 1H, J = 5 Hz), 5.04 (s, 1H), 4.99 (s, 1H), 3.97 (dd, 1H, J = 4, 12 Hz), 2.62 (m, 1H), 2.34 (m, 1H), 2.04 (s, 3H), 1.78 (s, 3H), 1.30 (s, 3H), 1.18 (s, 3H); mass spectrum m/e (relative intensity) 343,345 (1:1) (1), 316,318 (1), 298,300 (11), 283,285 (5), 265,267 (4), 245,247 (4), 227,229 (4), 219 (18), 201 (21), 177 (38), 159 (40), 147 (65), 135 (100), 114 (70), 107 (70), 95 (30), 93 (30), 81 (27), 72 (65).

Benzoylation of the Diol 13. The diol **13** (17 mg, 0.05 mmol) was dissolved in a mixture of benzoyl chloride (0.5 mL) and pyridine (1 mL) and the resulting solution treated according to the previous procedure (except 20% ether in hexane) to obtain the benzoate (12 mg, 53% theoretical), $[\alpha]^{20}_D$ −17° (c = 1.2, $CHCl_3$).

The Diol 14. A solution of the acetate **16** (20 mg, 0.06 mmol) in dry ether (1 mL) was added to a stirred suspension of lithium aluminium hydride (100 mg, 3 mmol) in dry ether (4 mL) at −78 °C. After 15 min, the reaction mixture was warmed to −5 °C and allowed to stir for an additional 15 min. Ethyl acetate (1 mL) was added cautiously, followed by water (0.3 mL), 3 N potassium hydroxide solution (0.3 mL) and water (1.0 mL). The precipitate was removed by filtration and washed with ether (3 × 10 mL). The combined extracts were dried over magnesium sulfate and the solvent evaporated to yield an oil (13 mg). The crude product was purified by TLC on a silica gel plate (20 × 20 × 0.025 cm) using ether as eluent to obtain the diol **14** (10 mg, 57% theoretical): IR (neat) 3200, 2800, 1640, 1380 cm^{-1}; NMR ($CDCl_3$) δ 5.01 (s, 1H), 4.89 (s, 1H), 4.41 (bs, 1H), 4.06 (dd, 1H, J = 4, 12 Hz), 2.53 (m, 1H), 2.35 (m, 1H), 1.75 (s, 3H), 1.34 (s, 3H), 1.18 (s, 3H); mass spectrum m/e (relative intensity) 298,300 (1:1) (3), 283,285 (2), 255,257 (3), 245,247 (4), 229 (14), 228 (14), 227 (14), 226 (10), 219 (30), 177 (13), 165 (25), 159 (16), 149 (86), 148 (91), 147 (100), 135 (21), 133 (27), 107 (94), 105 (51), 95 (37), 93 (42), 91 (36), 81 (40), 71 (46), 69 (37), 57 (19), 55 (26), 43 (39), 41 (18).

Oxidation of Diols 13 and 14 to the Ketone 17. Jones' reagent (40 μL, 0.04 mmmol of CrO_3) was added dropwise to a stirred solution of either diol **13** or **14** (10 mg, 0.04 mmol) in dry acetone (2 mL) at 0 °C. After 15 min, the reaction mixture was quenched with water (2 mL) and the organic material extracted with diethyl ether (3 × 10 mL). The combined extracts were dried over magnesium sulfate and the solvent evaporated to yield an oil (9 mg) which was purified on a silica gel plate (20 × 20 × 0.025 cm) using diethyl ether as eluent to obtain the ketone **17** (6 mg, 60% theoretical). Both alcohols **13** and **14** gave the same ketone **17**, having identical properties with the exception of the optical rotations, which were: $[\alpha]^{20}_D$ −71° (0.5, $CHCl_3$) from

13, $[\alpha]^{20}_D$ −53° (1.2, $CHCl_3$) from 14: IR ($CHCl_3$) 3650, 2980, 1675, 1635, 1460, 1380, 1330 cm^{-1}; λ_{max} 219 nm; NMR ($CDCl_3$) δ 6.05 (s, 1H), 5.84 (s, 1H), 4.11 (dd, 1H, J = 4, 12 Hz), 3.77 (dt, 1H, J = 4, 11, 11 Hz), 1.91 (s, 3H), 1.24 (s, 3H), 0.91 (s, 3H); mass spectrum *m/e* (relative intensity) 299,301 (1:1) (5), 296,298 (7), 245,247 (17), 227,229 (10), 226,228 (10), 217 (29), 165 (43), 147 (48), 123 (38), 107 (43), 69 (100); high resolution mass measurement, observed 301.0625, $C_{14}H_{20}O_2Br$ requires 301.0621.

Ozonolysis of Ketone 17. A stream of ozone in oxygen was bubbled through a solution of the ketone **17** (3 mg, 0.01 mmol) in methanol (3 mL) at −78 °C for 2 min. The resulting blue solution was warmed to room temperature and the solvent evaporated to yield a crystalline acid (2 mg), mp 152–153 °C. The acid was dissolved in dry ether and treated with an excess of a solution of diazomethane in ether at room temperature for 30 min. The solvent was evaporated to yield the methyl ester **18** (2 mg, 70% theoretical) as an oil: $[\alpha]^{20}_D$ −5° (1.9, $CHCl_3$)]; IR ($CHCl_3$) 3560, 2960, 1730, 1460, 1385 cm^{-1}; NMR ($CDCl_3$) δ 3.94 (dd, 1H, J = 4, 13 Hz), 3.62 (s, 3H), 2.92 (dt, 1H, J = 4, 12, 12 Hz), 1.11 (s, 3H), 1.00 (s, 3H); mass spectrum *m/e* (relative intensity) 289,291 (1:1) (7), 273,275 (2), 257,259 (7), 224 (17), 207 (8), 193 (11), 183 (42), 151 (57), 147 (52), 123 (100), 107, (67), 81 (70), 71 (45), 55 (52).

Ozonolysis of Oppositol (1). A stream of ozone in oxygen was bubbled through a solution of oppositol (**1**) (70 mg, 0.3 mmol) in methanol (25 mL) at −78 °C for 15 min. The resulting solution was warmed to room temperature under a stream of nitrogen and the solvent was evaporated to yield an oil. The oil was dissolved in chloroform (25 mL) and the acid extracted with 1 N sodium bicarbonate solution (3 × 25 mL). The extracts were acidified to pH 1 with 3 N hydrochloric acid and the acid extracted with chloroform (3 × 25 mL). The combined extracts were dried over sodium sulfate and the solvent evaporated to yield a crystalline acid, mp 152–153 °C. The methyl ester **18**, prepared as in the previous procedure, was identical in all respects with the material from ketone **17**.

Dehydration of Oplopanone (20). Phosphorus oxychloride (45 μL, 75 mg, 0.5 mmol) was added dropwise to a stirred solution of oplopanone (2.5 mg, 0.01 mmol) in dry pyridine (0.5 mL) at 0 °C. The reaction mixture was stirred at 25 °C for 24 h and quenched with water (1 mL). The organic material was extracted with ether (2 × 10 mL) and the combined extracts were washed with 3 N hydrochloric acid (3 × 10 mL). The extract was dried over magnesium sulfate and the solvent was evaporated to yield 8(15)-dehydrooplopanone (**26**) (2 mg, 87% theoretical) mp 67–68 °C; IR ($CHCl_3$) 2980, 1710, 1660, 1530, 1430, 1360 cm^{-1}; NMR ($CDCl_3$) δ 4.61 (s, 1H), 4.51 (s, 1H), 2.61 (m, 1H), 2.36 (m, 1H), 2.09 (s, 3H), 0.89 (d, 3H, J = 7 Hz), 0.64 (d, 3H, J = 7 Hz); mass spectrum *m/e* (relative intensity) 220 (17), 205 (4), 202 (2), 187 (4), 177 (100), 159 (7), 150 (15), 135 (42), 133 (35), 121 (50), 119 (35), 107 (78), 95 (75), 93 (67), 91 (60), 81 (75), 59 (80); high resolution mass measurement, observed 220.1817, $C_{15}H_{24}O$ requires 220.1821.

Dehydration of the Diol 21. (a) Dimethyl sulfoxide (170 μL), pyridine (3 μL), trifluoroacetic acid (2 μL), and dicyclohexylcarbodiimide (25 mg, 0.12 mmol) were added, in order, to a solution of the diol **21** (10 mg, 0.04 mmol) in dichloromethane (170 μL) and the mixture was allowed to stand at 25 °C for 24 h. The solvent was evaporated and the resulting brown oil chromatographed on a silica gel plate (20 × 20 × 0.025 cm) using 25% ether in hexane as eluent to obtain 8(15)-dehydrooplopanone (**26**) (7 mg, 75% theoretical), mp 67–68 °C. (b) A 12% solution of phosgene in benzene (5 mL) was added dropwise to a solution of the diol (10 mg, 0.004 mmol) in benzene (1 mL) containing pyridine (1.5 mL) and the reaction mixture was stirred for 2 h at 25 °C. The reaction mixture was poured onto ice (10 g) and the organic material extracted with ether (3 × 20 mL). The combined extracts were washed with 3 N nydrochloric acid (2 × 25 mL), dried over magnesium sulfate, and the solvent evaporated to obtain 8(15)-dehydrooplopanone (10 mg), identical in all respects with the authentic sample.

7-Acetoxy-10-hydroxy-3-isopropyl-10-methyl-6-methylene-*trans*-cyclodecene (25). The diol **21** (5 mg, 0.02 mmol) was dissolved in acetic anhydride (0.5 mL) and pyridine)1 mL), and the resulting solution was stirred for 16 h at 25 °C. The solvents were evaporated in vacuo and the resulting oil was purified on a silica gel plate (5 × 20 × 0.025 cm) using diethyl ether as eluent to obtain the monoacetate **25** (3 mg, 51% theoretical as an oil: NMR ($CDCl_3$) δ 5.35 (d, 2H, J = 6 Hz), 5.20 (s, 1H), 5.02 (dd, 1H, J = 8, 3 Hz), 5.00 (s, 1H), 1.98 (s, 3H), 1.28 (s, 3H), 0.88 (d, 3H, J = 7 Hz), 0.83 (d, 3H, J = 7 Hz); mass spectrum *m/e* (relative intensity) 238 (2), 220 (10), 205 (5), 202 (5), 177 (25), 162 (20), 159 (25), 119 (40), 107 (75), 43 (100).

Synthesis of 1-Hydroxyalloaromadendrene (27). Selenium dioxide (55 mg, 0.49 mmol) was added in a single portion to a solution of alloaromadendrene (100 mg, 0.46 mmol) in 95% ethanol (25 mL) at 70 °C. The reaction mixture was stirred for 2 h, then concentrated in vacuo to 10 ml. The product was partitioned between sodium bicarbonate solution (20 mL) and ether (3 × 50 mL). The combined ether extracts were dried over magnesium sulfate and the solvent evaporated to yield an oil (92 mg) which was purified on a silica gel plate (20 × 20 × 0.15 cm) using 35% ether in hexane as eluent to obtain 1-hydroxyalloaromadendrene (25 mg, 23% theoretical), identical in all respects except optical rotation, $[\alpha]^{20}_D$ −105° (1.7, $CHCl_3$), with the natural alcohol.

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