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THE RHODOPHYTIN AND CHONDRIOL NATURAL PRODUCTS; STRUCTURES OF SEVERAL NEW ACETYLENES FROM *LAURENCIA*, AND A REASSIGNMENT OF STRUCTURE FOR *cis*-RHODOPHYTIN

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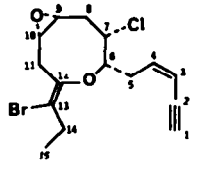
Abstract—The structures of five new halogenated vinyl acetylenes are described which are natural products from various species of the red seaweed *Laurencia*. The structure of epoxyrhodophytin (1) was determined by spectral, chemical, and X-ray diffraction analyses. The structures of *trans*-rhodophytin (5) and *trans*-chondriol (8) are based on chemical and spectral comparisons with the previously reported compounds *cis*-rhodophytin (4) and *cis*-chondriol (7). The structures of *cis*-chondrin (14) and *trans*-chondrin (15) were secured by synthesis from *cis*- and *trans*-chondriol, respectively. The reactivity of these enol-ethers to various conditions of catalytic hydrogenation has been examined in detail. Hydrogenation yields an unexpected and facile incorporation of oxygen into the reaction products. Based upon these studies, and upon combustion analysis, the structure of rhodophytin has been revised as the vinyl ether rather than the vinyl peroxide originally proposed.

Our chemical studies of the marine red alga *Laurencia* (Rhodomelaceae, Rhodophyta) have been concerned with assessing the diversity of halogen-based secondary metabolite biosynthesis in this genus. As part of this program we have described the structures of several halogenated and non-halogenated sesquiterpenoids[2] and diterpenoids[3] which have been important in understanding terpenoid biogenesis in this alga. In addition, we have been actively investigating several non-terpenoid C_{15} acetylene-containing compounds known to be characteristic components of many *Laurencia* species. In this paper we wish to describe in detail the structures of five new halogenated vinyl acetylene compounds which are related to the previously described natural products, chondriol[4] and rhodophytin.[5] We have also reinvestigated the structure and chemistry of rhodophytin and have reassigned this compound as a vinyl ether rather than the previously proposed vinyl peroxide.[5]

Epoxyrhodophytin. Epoxyrhodophytin (1) was isolated, as an oil, by silica gel chromatography of the chloroform-methanol extracts of an undescribed *Laurencia* species collected at Coyote Bay, Baja California, Mexico (April, 1975).[6,7] The IR spectrum (thin film) of 1 showed absorptions attributable to a terminal acetylene function (3300 and 2100 cm^{-1}) and an intense hydroxyl absorption which spanned the spectrum from 3800 to 3000 cm^{-1}. When 1 was rigorously dried under high vacuum, and the IR spectrum recorded in CCl_4 solution, the OH absorptions diaappeared, indicating 1 to be very hydroscopic. When placed in anhydrous ethanol and stored at −20°, 1 crystallised; m.p. 54–55°. High resolution mass spectral analysis of 1 indicated an elemental composition of $C_{15}H_{18}BrClO_2$ for the molecular ion at *m/e* 334 ($^{79}Br^{35}Cl$).

The ^1H NMR spectrum of 1 (Table 1) presented signals which could be assigned to a *cis* ene-yne function, an α-chlorine proton, an α-ether proton, two α-epoxide protons and an isolated Et group. The ^{13}C NMR spectrum of 1 (Table 2) revealed that, in addition to the acetylene carbons (88.6d and 80.0s), two double bonds were also present in the molecule, one disubstituted (139.8d and 111.2d) and one tetrasubstituted (147.3s and 117.5s). Based on mass spectral and ^{13}C NMR data, epoxyrhodophytin was shown to contain two rings, one of which was an epoxide (^{13}C NMR; 51.6d and 53.2d). Spectral comparisons of epoxyrhodophytin with the previously described vinyl acetylenes, rhodophytin and chondriol, served as a basis for the preliminary structure proposal of 1.



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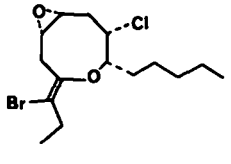

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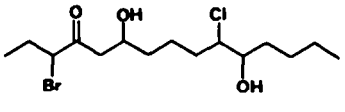

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Table 1. ^{1}H NMR assignments for the rhodophytin and chondriol natural products[a]

Proton(s) at Carbon No.	1	4	5	7[c]	8[b]	14	15
1	3.11d (2)	3.05d (2)	2.71d (2)	3.23d (2)	2.57d (2)	3.07d (2)	2.74d (2)
3	5.77dd (12,2)	5.53d (10)	5.59d (15)	5.63d (10)	5.48dd (15,2)	5.57d (10)	5.53dd (15,2)
4	6.02ddd (12,8,8)	6.00ddd (10,8,8)	6.16ddd (15,7,7)	6.13ddd (10,8,8)	6.14ddd (15,7,7)	6.05ddd (12,8,8)	6.15ddd (15,7,7)
5	2.6m	2.66m	2.66m	2.72m	2.77m	2.48m	2.50m
6	4.20ddd (7,7,2)	4.38ddd (7,7,2)	4.36ddd (7,7,2)	4.17m	4.77dd (12,5)	4.09m	4.05m
7	4.07ddd (12,6,2)	3.89ddd (12,6,2)	3.91ddd (12,6,2)	3.83m	3.25dd (14,5)	3.77dd (8,4)	3.78dd (8,4)
8	2.6m	2.66m 3.09m	2.66m 3.20m	2.72m 3.09m	2.77m 2.98m	2.48m	2.50m
9	3.02m	5.53m	5.59m	5.93m	5.07m	5.81m	5.80m
10	3.02m	5.73m	5.77m	5.93m	5.64m	5.81m	5.80m
11		3.76dd (18,4) 2.83bd (18)	3.82dd (18,4) 2.89bd (18)	5.10d (4)	5.40bd (4)	5.00d (4)	4.99d (4)
14	2.11m	2.60m	2.66m		2.02m		
15	1.11t (7)	1.03t (7)	1.11t (7)	1.10t (7)	1.14t (7)	1.05t (7)	1.05t (7)

[a] All spectra were recorded at 220 MHz in CCl_4 solution, except where noted. Chemical shifts are reported in PPM relative to TMS(0).

[b] Recorded in d_6-benzene solution.

[c] Recorded in $CDCl_3$ solution.

Table 2. ^{13}C NMR assignments for the rhodophytin and chondriol natural products[a,b]

Carbon	1	4	5	7	8	14	15
1	88.6	83.1	77.6	83.1	77.1	88.2	80.8
2	80.0	80.1	82.1	80.3	82.5	80.0	81.7
3	111.7	111.2	112.5	110.6	111.8	111.0	112.1
4	139.8	140.6	141.1	140.9	141.0	139.6	140.0
5	35.0	34.4	37.0	34.3	36.8	32.6	35.0
6	77.5	76.3	76.0	73.6	73.1	81.1	77.1
7	63.3	64.0	63.8	63.3	63.3	66.0	65.9
8	32.8	32.9	32.8	32.9	32.8	23.1	23.0
9	51.6	124.6	124.5	124.4	124.3	125.7	125.5
10	53.2	130.9	130.9	134.7	134.8	125.7	125.6
11	34.8	33.3	33.2	68.2	68.2	68.3	68.2
12	147.3	149.2	149.1	150.6	150.8	145.0	145.5
13	117.5	112.8	113.0	112.8	112.6	111.3	111.9
14	27.4	27.7	27.7	28.0	28.1	26.8	26.5
15	12.8	12.8	12.8	12.5	12.6	13.1	12.9

[a] All spectra taken at 20 MHz in benzene-d_6 and reported in PPM relative to TMS

[b] Assignments were aided by off-resonance decoupling of each compound

Catalytic hydrogenation of 1 over Pd–C for 30 min in anhydrous diethyl ether gave the hexahydro derivative 2 (90% yield). In compound 2, the vinyl acetylene function has been saturated, but the tetrasubstituted double bond was left intact, as evidenced by ^{13}C NMR singlets at 147.8 and 116.5 ppm, IR absorption at 1650 cm^{-1} and UV absorption at λ_{max} (Et_2O) 227 nm (ϵ = 5700). When 1 or 2 was subjected to the above conditions of catalytic hydrogenation for longer periods of time (8 hr), a new product, 3, could be isolated in 20% yield. The ^{13}C NMR spectrum of 3 showed the presence of a CO group (207.0), two OH-bearing carbons (74.4 and 70.1), a carbon-bearing Cl (67.3), a carbon-bearing Br (60.0), two Me groups (14.2 and 13.7 ppm) and eight methylene groups. The ^1H NMR spectrum of 3 also substantiated its structure. Compound 3 is a product of hydrogenation, epoxide hydrogenolysis and, presumably, vinyl ether hydrolysis. Since this hydrogenation was performed under anhydrous conditions, the source of oxygen incorporation into 3 is unknown. The reactivity noted here is in direct analogy with the hydrogenation product obtained from rhodophytin, which was previously proposed to be a vinyl peroxide. To determine whether 1 was a vinyl ether or vinyl peroxide, analytical combustion analysis was performed. The combustion data showed that 1 consisted of 52.45%C and 5.20% H thus indicating the vinyl ether (calculated %C 52.12, %H 5.24). Further, to provide stereochemical information and to confirm the assignment of 1 as a vinyl ether, a single crystal X-ray diffraction experiment was performed and the proposed structure fully confirmed as shown in Fig. 1 (see Experimental for details).

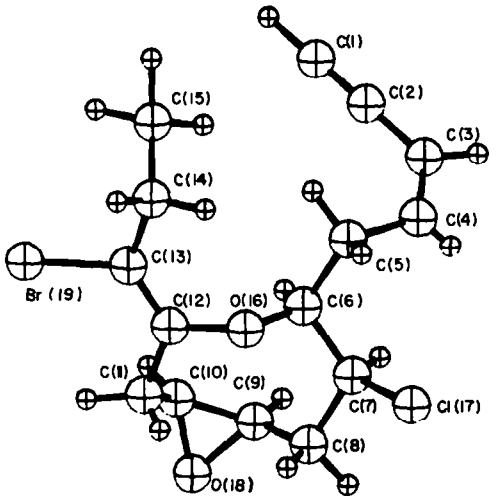
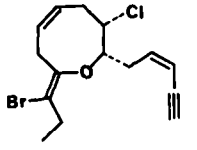


Fig. 1. The final X-ray model for epoxyrhodophytin (1). The absolute stereochemistry at C-6 is R, and bond angles and distances agree well with generally accepted values.

Based on the unexpected and facile oxygen incorporation during catalytic hydrogenation, we felt it was important to reinvestigate the structures of rhodophytin, chondriol and other enol ethers of this type. Fortuitously, an undescribed *Laurencia* sp.,[6,7] collected in San Carlos Bay, Guaymas, Mexico, yielded both *cis*- and *trans*-rhodophytin (4, 5), *cis*- and *trans*-chondriol (7, 8), and *cis*- and *trans*-chondrin (14, 15) in amounts sufficient to allow the following studies.

Cis- *and* trans-*rhodophytin.* Open column silica gel chromatography of the chloroform–methanol extract of the fresh alga yielded a fraction (20% benzene–petroleum ether) which contained a mixture of the *cis* and *trans* double bond isomers of rhodophytin. High pressure liquid chromatography (HPLC) of this mixture (μ-porasil, 0.25% diethyl ether–petroleum ether) give *cis*-rhodophytin (4) as the less polar constituent and *trans*-rhodophytin (5) as the more polar constituent in a 1:5 ratio. The ^1H NMR (Table 1), ^{13}C NMR (Table 2) and IR spectra of 4 indicated it to be identical with the compound previously proposed to be a vinyl peroxide. *Trans*-rhodophytin (5) showed NMR characteristics (Tables 1 and 2) consistent with its assignment as the *trans* double bond isomer. The mass spectra of both 4 and 5 showed the highest mass fragment at *m/e* 328/330/332 for $C_{15}H_{18}BrClO$.



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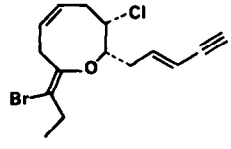

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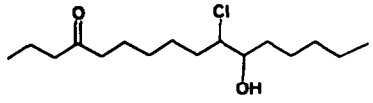

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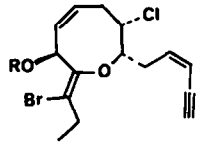
Catalytic hydrogen atom of 4 or 5 over Pd–C in anhydrous diethyl ether gave 7-chloro-6-hydroxypentadecane-12-one (6) in approximately 40% yield. Since two O atoms are clearly present in 6, the question arises as to whether two oxygens are present in the natural products, or if oxygen incorporation has taken place during hydrogenation, as is found with the conversion of 1 to 3. To determine the number of oxygens in 4 and 5, analytical combustion analysis data were necessary. Since more of the *trans* isomer was available, it was subjected to repeated HPLC (μ-porasil, 0.25% diethyl ether–petroleum ether) until it appeared as a clear mobile oil and its ^1H NMR (220 MHz) illustrated no signs of impurities. Combustion analysis of 5 gave 54.55% C and 5.89% H. Calculations for the vinyl ether formula ($C_{15}H_{18}BrClO$) gave 54.65% C and 5.50% H which is acceptable with the observed values. Therefore, *trans*-rhodophytin (5) and correspondingly *cis*-rhodophytin (4) must be reassigned as vinyl ethers and not vinyl peroxides.[8] However, the source of oxygen incorporation during anhydrous conditions of hydrogenation is unknown. In an effort to understand this oxygen incorporation, we investigated the structures and chemistries of other natural products related to rhodophytin.

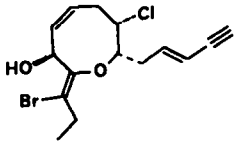
Cis *and* trans-*chondriol.* Column chromatography fractions eluted with 70% benzene–petroleum ether contained *cis*-chondriol (7) and *trans*-chondriol (8), and were further separated by HPLC (μ-porasil, 6% diethyl ether–petroleum ether). The samples of *cis*-chondriol isolated here were found to be identical with that previously described as determined by ^1H NMR (Table 1) and ^{13}C NMR (Table 2). Compound 8 illustrated ^1H NMR bands for a *trans*-di-substituted olefin [δ 5.48 dd (J = 15, 2); 6.14 ddd (J = 15, 7, 7)], which suggested it to be the C-3, C-4 double bond isomer of 7. Catalytic hydrogenation of 7 and 8 under anhydrous conditions gave complex mix-

tures. However, when *cis*-chondriol acetate (9) was hydrogenated in the presence of 10% Pd–C in anhydrous diethyl ether with a catalytic amount of potassium tertiary butoxide, the hexahydro derivative 10 was obtained. Further hydrogenation of 10 in the absence of base again produced complex mixtures.

In an attempt to relate *cis*-chondriol (7) and *cis*-rhodophytin (4), 7 was treated with methanesulfonylchloride in pyridine. However, the mesylate could not be isolated but instead the dehydration products 11 and 12 were obtained. Compound 12 is the dehydro analog of isorhodophytin (13), which is produced when 4 is exposed to unpurified carbon tetrachloride. Catalytic hydrogenation of 12 and 13 again gave unresolvable mixtures.



7 R=H
9 R=Ac



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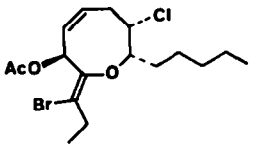

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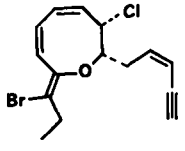

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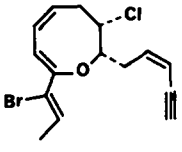

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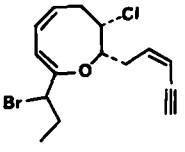

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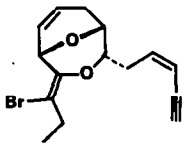

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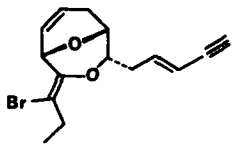

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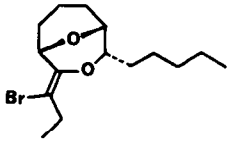

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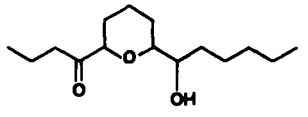

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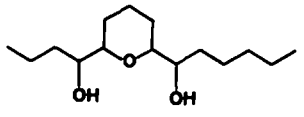

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Cis- *and* trans-*Chondrin*. Column chromatography fractions which were eluted with 50% benzene–petroleum ether contained the *cis* and *trans* double bond isomers of a new vinyl acetylene compound. HPLC separation (μ-porasil, 6% diethyl ether–petroleum ether) gave pure samples of each isomer and were given the name *cis*-chondrin (14) and *trans*-chondrin (15). The ^{1}H NMR (Table 1) and ^{13}C NMR (Table 2) spectra of 14 and 15 indicated that each contained a tetrasubstituted double bond, two disubstituted double bonds and a terminal acetylene function, in analogy with other compounds of this class. The IR spectra of 14 and 15 were devoid of OH or CO absorptions. Low resolution mass spectral analysis suggested a molecular formula of $C_{15}H_{17}BrO_2$ for each isomer. Treatment of *cis*-chondriol (7) and *trans*-chondriol (8) with refluxing 10% methanolic potassium hydroxide for 1 hr gave 14 and 15, respectively. Since the structure of *cis*-chondriol was rigorously determined by X-ray methods,[4] the structures of 14 and 15 are also secured.

Catalytic hydrogenation of 14 and 15 in the presence of 10% Pd–C, anhydrous diethyl ether and a catalytic amount of potassium tertiary butoxide gave the common octahydro derivative 16 (90% yield), as determined by ^{1}H and ^{13}C NMR analysis. Hydrogenation of 14, 15 or 16 under the above conditions in the absence of base gave a new product, 17, in approximately 60% yield. Compound 17 is a result of hydrogenation, bromine hydrogenolysis and vinyl ether hydrolysis, in analogy with the reactivity of epoxyrhodophytin and *cis* and *trans*-rhodophytin. The addition of base to these hydrogenations appears to quench any HBr formed from hydrogenolysis, but in the absence of base, HBr production may be autocatalytic. Hydrogenolysis followed by HBr production seems to be an important factor in the incorporation of oxygen into the final products. To investigate the possible mechanisms by which oxygen is incorporated during hydrogenation, the chondrin isomers were studied.

Even though anhydrous solvents were used during hydrogenation, it seemed likely that a lack of totally anhydrous conditions might be the source of oxygen incorporation. Therefore great care was exercised in running a totally anhydrous and oxygen-free hydrogenation. Commercial anhydrous ether was further dried over LAH. The hydrogenation was conducted in a dry box under an anhydrous nitrogen atmosphere. The hydrogen used was of the extra dry quality (Mallinckrodt) and passed over anhydrous $CaSO_4$ before use. Catalytic hydrogenation of 14 under these conditions gave 17 as the only isolable product in 55% yield. The same reaction was repeated using anhydrous pentane as the solvent, but 17 was again the only product isolated. The use of other catalysts was also investigated (platinum on carbon and ruthenium on carbon) with the same result.

Since water had been rigorously excluded and net incorporation of water observed, the possibility existed that a decomposition reaction had taken place, perhaps at the catalyst surface, which produced water. Decomposition of the natural products to produce water would account for the consistently low yields of these reactions. In an effort to study the role of water in these hydrogenations, $H_2{}^{18}O$ (95% ^{18}O) was added to the hydrogenation reaction of 14 under $H_2{}^{16}O$ anhydrous conditions. The only isolable product was 17 in 69.5%

yield. Mass spectral analysis of 17 and the LAH reduction product 18 failed to exhibit ^{18}O incorporation. Since these compounds have been shown to be ethers and not peroxides, the oxygen incorporation during hydrogenation appears to be due to disproportionation reactions which do not involve the intermediacy of water.

EXPERIMENTAL

^1H NMR spectra were recorded on a Varian HR-220 spectrometer, ^{13}C NMR spectra were recorded on a Varian CFT-20 spectrometer, and IR spectra were recorded on a Perkin–Elmer model 137 spectrophotometer. Low resolution mass spectra were obtained on a Hewlett–Packard 5930A mass spectrometer and high resolution mass spectra were obtained through the Department of Chemistry, UCLA.

Isolation of epoxyrhodophytin (1). Crude extract (30.0 g) obtained from the 1:1 $CHCl_3$–MeOH extraction of 3 kg fresh *Laurencia* (Coyote Bay, Mexico), was applied to a column containing 300 g of silica gel (Grace Chemical). The column was eluted with a solvent gradient system from petroleum ether to benzene to diethyl ether. Compound 1 was obtained in fractions eluted with 50% benzene–petroleum ether. Repeated silica gel chromatography of these fractions gave pure samples of 1: High resolution mass spectrum M^+ *m/e* 344.0180 for $C_{15}H_{18}BrClO_2$ (Calc. 344.0179); IR spectrum (CCl_4) γ3300, 2950, 2120, 1650, 1450, 1380, 1200, 1100; UV (Et_2O) λ_{max} 223,230 nm. Fraction eluted with 20% benzene–petroleum ether also contained samples of *cis*-rhodophytin (4).

Catalytic hydrogenation method. Between 20 and 200 mg of each compound to be hydrogenated was dissolved in 30 mL of anhyd diethyl ether and added to a 50 ml Erlenmeyer suction flask containing a catalytic amount of 10% Pd–C (10 mg) and a magnetic stirring bar. The reaction vessel was fitted with a balloon and septum, purged with hydrogen and the balloon filled. After stirring at 25°, the hydrogen was removed, the soln filtered and the ether evaporated to give, after thick-layer silica gel chromatography (THLC), purified reaction products.

Catalytic Hydrogenation of 1. Catalytic of hydrogenation of 1 for 30 min gave the hexahydro derivative 2 in 90% yield after THLC (10% diethyl ether–petroleum ether) purification. IR spectrum ($CHCl_3$:) 2950, 1650, 1470, 1440, 1390, 1320, 1290, 1270, 1240, 1190, 1160, 1000, 970 cm^{-1}. Mass spectrum: M^+ *m/e* 350/352/354. Catalytic hydrogenation of 1 or 2 for 8 hr gave 3 in 20% isolated yield. ^1H NMR (220 MHz, benzene-d_6) δ4.34 (2H, m), 3.84 (1H, m), 3.36 (1H, m), 2.04 (1H, dd J = 16, 4), 0.87 (3H, t J = 7), 0.75 (3H, t J = 7). ^{13}C NMR (20 MHz, benzene-d_6) ppm 13.7, 14.2, 17.1, 22.9, 25.7, 32.0, 34.9, 41.1, 45.2, 47.8, 60.0, 67.3, 70.1, 74.4, 207.0.

X-ray crystallographic analysis of 1. Preliminary X-ray photographs revealed that epoxyrhodophytin belonged to the orthorhombic crystal class. Accurate diffractometer measured cell constants were a = 5.235(2), b = 9.555(5) and c = 32.210(15) Å in the unambigously determined space group $P2_12_12_1$. A rough density measurement suggested one molecule of $C_{15}H_{18}BrClO_2$ per asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer controlled four-circle diffractometer using graphite monochromated CuK_α (1.54178 Å) radiation and a variable speed ω-scan. Of the 1335 reflections surveyed in this manner, 1194 (89%) were judged observed [$F_o^2 \geq 3\sigma(F_o^2)$] after correction for Lorentz, polarization and background effects. The Patterson synthesis readily yielded a Br position but the placement of the Br at 1/4, 0, 3/4 led to pseudosymmetry problems. The Br only phased reflections of the hkl type if h + k = 2n and this C-centering generated additional false symmetry elements. The situation was not helped when a Cl position was deduced from the Patterson for the Cl sat at 0, 1/4, 1/2. Partial refinement of this model and careful inspection of the resulting electron density syntheses eventually led to a reasonable trial structure. Full matrix least-squares refinements with anisotropic temp. factors for the non-H atoms, isotropic temp. factors for hydrogens and anomalous scattering corrections for Br and Cl rapidly converged to the correct crystallographic residual of 0.059. The enantiomeric structure refined to a significantly higher 0.065.[10] A final difference synthesis showed no large residual electron density and there were no abnormally short intermolecular contacts. Further crystallographic details can be found in the Supplementary Material described at the end of this paper.

Collection, extraction and chromatographic separation. A taxonomically undescribed *Laurencia* was collected in San Carlos Bay (Guaymas, Mexico) in April of 1976.[7] The fresh algae (2.5 kg) were stored in methanol for two weeks then homogenized and extracted with chloroform–methanol (1:1) to yield a dark green oil (20 g). The crude extract was applied to a column containing 250 g of silica gel (Grace Chemical, grade 62). The column was eluted with a solvent gradient system of increasing polarity from petroleum ether to benzene to diethyl ether.

cis-*Rhodophytin* (4) *and* trans-*rhodophytin* (5). Four fractions which were eluted with 20% benzene-petroleum ether contained a mixture of 4 and 5. Subjection of this mixture to repeated HPLC (μ-porasil, 0.25% diethyl ether–petroleum ether) gave pure samples of 4 and 5 as clear mobile oils. For compound 4: Mass spectrum M^+ *m/e* 328/330/332; IR spectrum (film): 3300, 2950, 1650, 1450, 1420, 1240, 1170, 1100, 980 cm^{-1}. For compound 5: Mass spectrum M^+ *m/e* 328/330/332; IR spectrum (CCl_4): 3300, 3950, 1650, 1450, 1380, 1200, 1100 cm^{-1}. Catalytic hydrogenation of 4 and 5 as previously described gave 6 in 40% isolated yield. For compound 6: ^1H NMR (220 MHz, benzene-d_6) δ3.66 (1H, bs), 1.91 (4H, t), 1715, 1460, 1420, 1380, 1140 cm^{-1}; mass spectrum: M^+ *m/e* 276/278.

cis-*Chondriol* (7) *and* trans-*chondriol* (8). Three column chromatography fractions which were eluted with 70% benzene–petroleum ether contained a mixture of 7 and 8 as determined by ^1H NMR analysis. Separation of this mixture by HPLC (μ-porasil, 6% diethyl ether–peteoleum ether) gave pure samples of each isomer. For compound 7: Mass spectrum M^+ *m/e* 344/346/348; IR spectrum ($CHCl_3$): 3500, 3300, 2950, 2121, 1650, 1450, 1420, 1220, 1090, 1040 CM^{-1}. For compound 8: Mass spectrum M^+ *m/e* 344/346/348; IR spectrum ($CHCl_3$): 3500, 3300, 2950, 2100, 1650, 1450, 1420, 1200, 1100, 1050 cm^{-1}.

Catalytic hydrogenation of cis-*chondriol acetate* (9). 50 mg of 9 was hydrogenated as described previously except 10 mg of t-BuOK was added to the mixture. THLC purification gave 10 in 80% isolated yield. For compound 10: IR spectrum ($CHCl_3$): 2950, 1740, 1650, 1210, 1160 cm^{-1}; ^1H NMR (220 MHz, $CDCl_3$) δ 6.72 (1H, d J = 5), 5.89 (1H, dd J = 10, 5), 5.75 (1H, m), 4.75 (1H, m), 3.89 (1H, m), 3.14 (1H, m), 2.05 (3H, s), 1.09 (3H, t J = 7), 0.89 (3H, t J = 7); ^{13}C NMR (20 MHz, benzene-d_6) δ 147.7, 131.8, ~126.0, 114.8, 75.2, 69.9, 63.8, 33.7, 33.0, 32.1, 28.0, 26.0, 22.9, 14.2, 12.6 (15 of 17 bands were observed).

Treatment of 7 *with methanesulfonylchloride.* 100 mg of 8 was dissolved in pyridine (5 ml) and 1 equivalent methanesulfonylchloride was added drop-wise with stirring. After 2 hr the mixture had turned black and it was extracted with diethyl ether. The ether was washed with 5% HCl (3 × 50 ml) and distilled water (2 × 50 ml). The ether layer was dried ($MgSO_4$), evaporated and purified by silica gel column chromatography to give 11 (20 mg) and 12 (30 mg). For compound 11: ^1H NMR (220 MHz, $CDCl_3$) δ 6.55 (1H, d J = 12), 6.11 (1H, ddd J = 10, 8, 8), 5.68 (4H, m), 4.31 (1H, m), 3.98 (1H, m), 3.20 (1H, bs), 3.00 (1H, m), 1.66 (3H, m), 1.14 (3H, t J = 7). For compound 12: ^1H NMR (220 MHz, $CDCl_3$) 6.68 (1H, d J = 10), 6.02 (2H, m), 5.55 (3H, m), 5.03 (1H, m), 3.92 (1H, ddd J = 12, 4, 2), 3.16 (1H, s), 3.00 (2H, m), 2.68 (2H, m), 1.86 (3H, d J = 7); ^{13}C NMR (20 MHz, acetone-d_6) 141.1, 129.7 (2C), 123.0, 125.8, 112.0, 111.8, 103.3, 84.5, 78.6, 59.8, 36.1, 35.3, 17.9 ppm.

cis-*Chondrin* (14) *and* trans-*chondrin* (15). Compounds 14 and 15 were isolated as a mixture from column chromatography (50% benzene–petroleum ether elution) and were separated by HPLC (μ-porasil, 6% diethyl ether–petroleum ether). For compound 14: IR spectrum (film) γ3300, 2950, 1650, 1460, 1440, 1220, 1100, 1050, 980, 940, 860, 820 cm^{-1}; mass spectrum M^+ *m/e* 308/310/312. For compound 15: Mass spectrum M^+ *m/e* 308/310/312.

Catalytic hydrogenation of 14 *and* 15. Catalytic hydrogenation of 14 and 15 in the presence of t-BuOK for 8 hr gave the common intermediate 16 which was isolated in 90% yield by silica gel

THLC (10% diethyl ether–petroleum ether). For compound 16: Mass spectrum M^+ *m/e* 316/318/320; ^{1}H NMR (220 MHz, benzene-d_6) δ 4.77 (1H, bs), 3.84 (1H, m), 3.57 (1H, bs), 2.52 (2H, m), 1.05 (3H, t, J = 7 Hz) −0.89 (3H, t, J = 7 Hz); ^{13}C NMR (20 MHz, benzene-d_6) 147.8s, 109.6s, 80.2d, 69.4d, 67.5d, 31.8t, 31.8t, 28.8t, 26.4t, 25.3t, 24.5t, 22.6t, 17.4t, 14.0q, 13.2q. When 14, 14 or 16 where hydrogenated in the absence of base, 17 was obtained in 60% yield after THLC purification (50% diethyl ether–petroleum ether). For compound 17: Mass spectrum *m/e* 185 (M^+–C_4H_7O); IR spectrum (film): γ 3200, 2950, 1715, 1450, 1100, 1050, 940 cm^{-1}; ^{1}H NMR (220 MHz, $CDCl_3$) δ 3.86 (1H, dd, J = 12, 3 Hz), 3.50 (1H, m), 3.39 (1H, m), 2.55 (2H, T, J = 7), 0.94 (3H, t, J = 7), 0.91 (3H, t, J = 7): ^{13}C NMR (20 MHz, benzene-d_6) ppm 209.3s, 83.3d, 81.2d, 73.7d, 39.8t, 32.8t, 32.4t, 28.2t, 26.0t, 25.1t, 23.1t, 16.8t, 14.3q, 13.4q (only 14 C atoms observed).

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REFERENCES

[1]Present address: Department of Chemistry, San Fransico State University, 1600 Holloway Avenue, San Francisco, CA 94132, U.S.A.

[2]B. M. Howard and W. Fenical, *Tetrahedron Letters* 1687 (1975); *Ibid.* 41 (1976); *Ibid.* 2519 (1976).

[3]W. Fenical, B. Howard, K. B. Gifkins and J. Clardy, *Ibid.* 3983 (1975). B. M. Howard, W. Fenical, J. Finer, K. Hirotsu and J. Clardy, *J. Am. Chem. Soc.* **99**, 6440 (1977).

[4]W. Fenical, K. B. Gifkins and J. Clardy, *Tetrahedron Letters* 1507 (1974).

[5]W. Fenical, *J. Am. Chem. Soc.* **96**, 5580 (1974).

[6]For a previous report on the natural products chemistry of this alga, see B. M. Howard and W. Fenical, *J. Org. Chem.* **43**, 2518 (1977).

[7]A voucher specimen from this collection has been deposited in the National Herbarium, Smithsonian Institution, Washington, D.C.

[8]Compounds 4 and 5 as well as 1, 7, 8, 14 and 15 are exceedingly prone to decomposition in acid or on air oxidation, and this reactivity is responsible for the previously reported positive iodide-iodine peroxide tests.

[9]All crystallographic calculations were done on a Prime 400 computer operated by the Materials Science Center and the Department of Chemistry, Cornell University. The principal programs used were: REDUCE and UNIQUE, data reduction programs, M. E. Leonowicz, Cornell University, 1978; BLS, block diagonal least squares refinement, K. Hirotsu, Cornell University, 1978; ORFLS (modified), full matrix least squares, W. R. Busing, K. O. Martin and H. S. Levy, Oak Ridge, ORNL-TM-305; ORTEP, crystallographic illustration program, C. Johnson, Oak Ridge, ORNL-3794, BOND, structural parameters and erros, K. Hirotsu, Cornell University, 1978; MULTAN-76, direct methods and fast fourier transform, G. Germain, P. Main and M. Woolfson, University of York.

[10]W. C. Hamilton, *Acta Crystallogr.* **18**, 502 (1965).