FACS-I diffractometer (Cu Kα, λ = 1.54178 Å, graphite monochromator) to be a = 10.060 (5), b = 6.127 (4), c = 16.037 (6) Å, β = 96.02 (2)°, ρc = 1.53 g/ml, and Z = 2. Intensity data were collected using a scintillation counter with pulse-height analyzer, θ–2θ scan, 2°/min scan rate, 10-s background counts, attenuators when the count rate exceeded 10^4 counts/s, and a 2° scan range with a dispersion factor allowing for α_1–α_2 splitting at large 2θ values. Of 1620 independent reflections measured, 1591 > $3\sigma(I)$ were considered observed. Lorentz and polarization corrections were applied, but no correction was made for absorption. No significant decrease was observed in the intensities of standards.

The structure was solved using MULTAN.[17] The first E map revealed Br and seven other atoms. The rest of the nonhydrogen atoms were located by difference synthesis. The structure was refined by full matrix least-squares techniques to a final R of 0.053. Anisotropic thermal parameters were assumed for nonhydrogen atoms, and all hydrogen atoms were located and included in the refinement. The scattering factors used were those of Hanson et al.[18] Anomalous scattering factors were used for bromine, but the absolute configuration was not determined and is assumed to be as established earlier.[14] The refinement was based on F_o, the quantity minimized being $\Sigma w(F_o - F_c)^2$. The weighting scheme used was based on counter statistics,[19] with p = 0.04.

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Registry No.—**7**, 58934-07-9; **8**, 34294-03-6; *N*-bromoacetamide, 79-15-2.

Supplementary Material Available. A table of temperature factors (1 page). Ordering information is given on any current masthead page.

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Some Chemical Constituents of the Digestive Gland of the Sea Hare *Aplysia californica*

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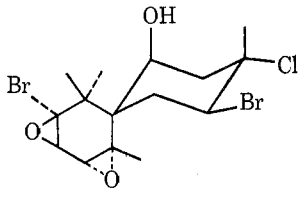
The digestive gland of the sea hare *Aplysia californica* contains halogenated metabolites which are obtained from its algal diet. We have isolated three halogenated sesquiterpenes, prepacifenol epoxide (**1**), the diol **5**, and the epoxide **6**, and two halogenated monoterpenes **7** and **11**, which had not been isolated from algae. The structure of the epoxide **6** was elucidated by single-crystal x-ray diffraction analysis, and the remaining four compounds by chemical and spectroscopic techniques.

We previously reported[2] that the chemical constituents of the digestive gland of the herbivorous opisthobranch mollusc *Aplysia californica* (Cooper) were identical with metabolites of the red algae which form a major portion of the sea hare's diet. In a few instances we were able to demonstrate that chemical transformations had occurred within the digestive gland.[3] We found that the sea hare obtained halogenated sesquiterpenes from *Laurencia* sp. and halogenated monoterpenes from *Plocamium* sp. The mixture of halogenated monoterpenes in *Aplysia* was so complex that we chose to investigate these metabolites from *P. cartilagineum*[4] and *P. violaceum*[5] separately. In recent studies of the chemical constituents of the digestive gland of *Aplysia*, we found compounds which have not been detected in local red algae. We wish to report the structural elucidations of three sesquiterpenes and two monoterpenes.

During 1973 and 1974, we made three collections of *Aplysia californica* at three locations in the vicinity of La Jolla, Calif. Each collection of *Aplysia* was investigated separately, resulting in three digestive gland extracts having different compositions. In the first collection, the major constituents were sesquiterpenes, while the two later collections each contained a different monoterpene as the major component.

A group of 50 *Aplysia* were collected at Sunset Cliffs, San Diego, Calif., during August 1973, and the digestive glands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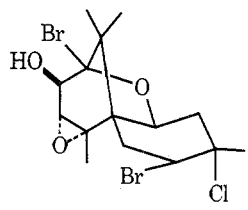
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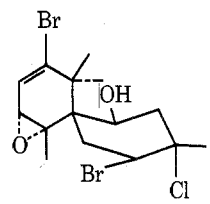
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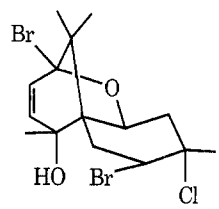
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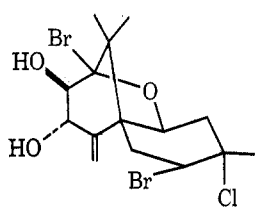
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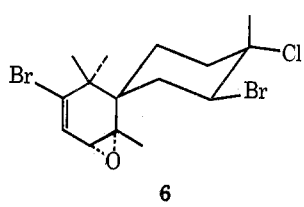
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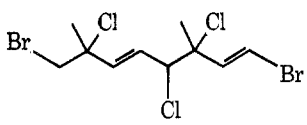
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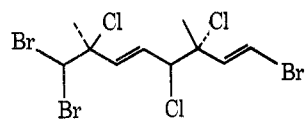
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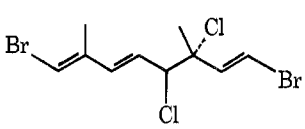
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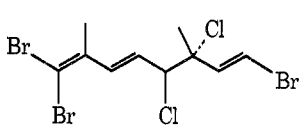
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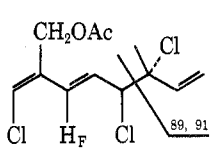
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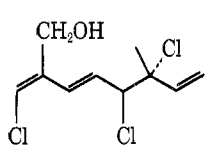
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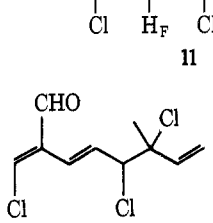
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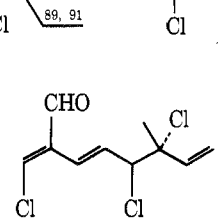
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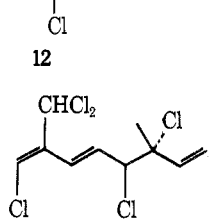
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were excised and homogenized in acetone. Chromatography of the ether-soluble material on silica gel led to the isolation of three undescribed crystalline halogenated sesquiterpenes. Prepacifenol epoxide (1),[6] mp 98–99 °C (1% of ether-soluble material), was shown to be an isomer of johnstonol (2), which had previously been isolated from *A. californica* and *L. johnstonii*.[7] The NMR spectrum (220 MHz, $CDCl_3$, Me_4Si) of 1 contained signals for four methyl groups at δ 0.95, 1.50, 1.54, and 1.86, two α-epoxy protons at 3.00 and 3.58, one proton α to hydroxyl at 4.00, and an α-bromo proton at 4.64 ppm. The presence of the hydroxyl group was indicated by a band at 3500 cm^{-1} in the infrared spectrum and a signal in the NMR spectrum at 1.95 ppm which disappeared on D_2O treatment. Comparison of the NMR spectrum with those of johnstonol (2) and prepacifenol (3) led to the suggestion of the diepoxide structure for prepacifenol epoxide (1).

Some details of the stereochemistry of prepacifenol epoxide (1) could be deduced from the coupling constants observed in the NMR spectrum. The absence of coupling between the two α-epoxy protons indicated that the epoxide rings were trans to one another. The coupling constants for the proton α to bromine (J = 13.5, 4.0 Hz) and the proton α to hydroxyl (J = 3.5, 3.5 Hz) suggested an equatorial bromine and an axial hydroxyl. This is precisely the stereochemistry which is required if prepacifenol epoxide (1) is to be a precursor to johnstonol (2) in the same way that prepacifenol (3) is related to pacifenol (4).[8]

The structure of prepacifenol (3) had been confirmed by its conversion to pacifenol (4) under mild acid catalysis. In similar manner, prepacifenol epoxide (1) was converted into johnstonol (2) in high yield by treatment with a catalytic quantity of oxalic acid in refluxing methanol for 24 h.

When treated with p-toluenesulfonic acid in benzene, prepacifenol epoxide (1) was converted into the diol 5 in quantitative yield. We had previously encountered the diol 5, mp 172–173 °C, as the most polar product from the chromatography of the ether-soluble material from *Aplysia* (0.05% of ether-soluble material). The diol 5 had also been obtained by Sims et al.[7] by treatment of johnstonol (2) with hydrogen bromide in acetic acid. All spectral data which we have recorded for the diol 5 are completely in accord with the structure proposed by Sims et al.

A third sesquiterpene was obtained from *Aplysia* in low yield (0.1% of ether-soluble material). The epoxide 6, mp 124–125 °C, has the molecular formula $C_{15}H_{21}OBr_2Cl$. The NMR spectrum of 6, which contained an α-epoxy proton at δ 2.95 (J = 3 Hz) coupled to an olefinic proton at 6.23 and an α-bromo proton at 4.68 ppm, was almost identical with the published spectral data for prepacifenol (3). These data, considered in conjunction with the ir spectrum, which lacks a hydroxyl band, strongly suggested that the epoxide 6 differed from prepacifenol (3) only by the absence of the hydroxyl function. Confirmation of this assignment was provided by single-crystal x-ray structure determination.

The epoxide crystallized in space group $P2_12_12_1$ with one molecule per asymmetric unit and unit cell axes a = 12.10 (1) Å, b = 11.593 (6) Å, and c = 11.64 (1) Å. The calculated density of the crystals is 1.59 g/cm^3 with one molecule of $C_{15}H_{21}OBr_2Cl$ per asymmetric unit. A total of 1344 reflections with $\theta < 57°$ were measured on a Syntex $P2_1$ four-circle automated diffractometer using Cu Kα radiation (λ = 1.5418 A) and an ω-scan technique with a minimum scan speed of 2°/min. Of these, 1285 of the reflections were judged observed using the criteria [$F_o \geq 3\sigma(F_o)$].

The Patterson map calculated from the data was easily deconvoluted to give the fractional coordinates of the two bromine atoms.[9] Two subsequent electron density map calculations served to locate all remaining nonhydrogen atoms. Refinement of the structure proceeded routinely, giving a final residual index of 0.085. Anisotropic temperature factors were assigned to all nonhydrogen atoms. Included in the final model were 11 nonmethyl hydrogens. These were assigned isotropic temperature factors, and both their positions and temperature factors were held fixed during refinement.

In order to determine the absolute configuration of the molecule, the model was also refined using a complete data set of Friedel pairs and correcting for anomalous scattering by the bromines and chlorines. The original model refined to a residual index of 0.085 while its mirror image refined to a significantly higher residual, 0.088, a statistically significant difference.[10] Figure 1 shows a computer-generated drawing of 6. In general, bond distances and angles agree well with generally accepted values.[11]

A second batch of 24 *Aplysia* was collected at Cardiff, 15 miles north of La Jolla, Calif., in June 1974. The ether-soluble

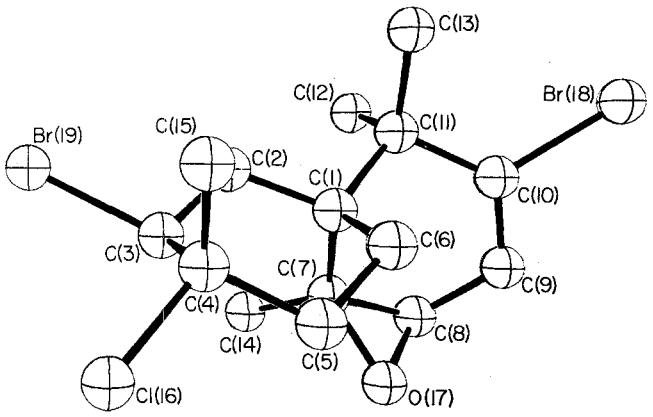

Figure 1. A computer-generated perspective drawing of **6**. Hydrogen atoms are omitted for clarity.

material from this sample contained a previously undescribed halogenated monoterpene as the major component (7.5% of ether-soluble material). The monoterpene **7**, obtained as an oil which crystallized from ethanol at −10 °C, had the molecular formula $C_{10}H_{13}Br_2Cl_3$. The mass spectrum did not exhibit a molecular ion, the highest peaks being a cluster at *m/e* 361, 363, 365, 367 due to the $M^+ - Cl$ ion. The mass spectrum also contained a $(C_4H_5BrCl)\cdot^+$ cluster at *m/e* 167, 169, 171, identical with the base peak of the known monoterpene **8**[12] and assigned to the ion indicated (Figure 2). The NMR spectrum contained two methyl singlets at δ 1.78 and 1.83, an AB quartet at 6.36 and 6.51 (J = 13 Hz) assigned to the vinyl bromide group, an AMX system at 4.54 (J = 8 Hz), 5.89 (J = 16 Hz), and 6.00 (J = 16, 8 Hz) assigned to a –CH=CHCHCl– group, and a two-proton singlet at 3.65 ppm. The NMR spectrum of the monoterpene **7** was remarkably similar to that of monoterpene **8**, with the notable exception that a one-proton singlet at 5.76 ppm had been replaced by a two-proton singlet at 3.65 ppm. We therefore propose that monoterpene **7** differs from the known monoterpene **8** by replacement of the $-CHBr_2$ group by a $-CH_2Br$ group. The coupling constants exhibited by the vinyl protons indicated that both olefinic bonds were trans.

Despite the persuasive arguments of analogy, it was difficult to assign specific locations for the halogen atoms.[13] However, comparison of the mass spectra of monoterpenes **7** and **8** revealed that the major peaks in both spectra can be rationalized using identical mechanisms (Figure 2) only when the halogen atoms of **7** are arranged as shown. In particular, the peaks at *m/e* 115, 117 in the spectrum of **7**, corresponding to peaks at *m/e* 193, 195, 197 in the spectrum of **8**, strongly suggest that there is a bromine atom at C-8, rather than at C-4 or C-7. The monoterpenes **9** and **10**, which are related to **7** and **8**, respectively, by loss of the C-8 hydrogen and the C-7 chlorine, have been isolated from *P. cartilagineum*.[4]

Two large *Aplysia* were collected at Casa Cove, La Jolla, Calif., in July 1974. The major component (16% of ether-soluble material) of the digestive gland extract was a halogenated monoterpene acetate **11** (ir 1740 cm^{-1}). The mass spectrum exhibited a strong cluster at *m/e* 89, 91, which has been assigned to $(C_4H_6Cl)^+$ ion indicated. The uv absorption at 259 nm was indicative of a halogenated diene system similar to that found in a number of the metabolites of *Plocamium cartilagineum*. The NMR spectrum contained a methyl singlet at δ 1.72, an acetoxy singlet at 2.00, the three signals of a vinyl group at 5.23, 5.36, and 6.02, an AMX system at 4.50 (J = 9 Hz), 6.02 (J = 9, 16 Hz), and 6.68 (J = 16 Hz), an AB quartet at 4.67 and 4.74 (J = 13 Hz) due to the nonequivalent protons of the $-CH_2OAc$ group, and a one-proton singlet at 6.36 ppm. The spectral data allow only one gross structure to be assigned to the acetate **11**.

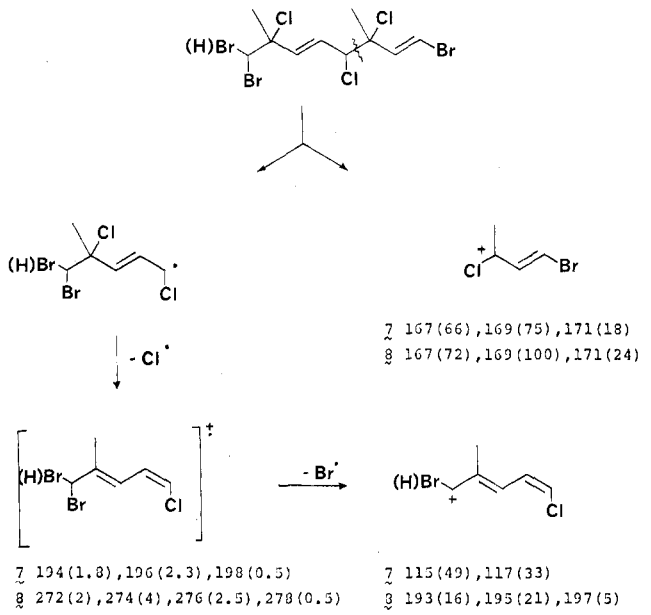

Figure 2. Mass spectral fragmentation of monoterpenes **7** and **8**.

Hydrolysis of the acetate **11** with 0.16% methanolic potassium hydroxide solution gave the corresponding alcohol **12** (ir 3600 cm^{-1}) in good yield. The NMR spectrum of the alcohol **12** was similar to that of the acetate **11**, except that the signals at δ 4.67 and 4.74 were replaced by a two-proton singlet at 4.31 ppm and the acetoxy singlet was absent.

The assignment of the stereochemistry of **11** and **12** depends on the empirical rules developed for the assignment of stereochemistry for *Plocamium cartilagineum* metabolites using NMR spectral data.[4] The chemical shifts of the methyl signals suggested the erythro configuration at carbons 3 and 4. The chemical shifts of proton H_f (δ 6.68 and 6.70 ppm) indicated that the 7,8 double bond has the *E* geometry.

While this research was in progress, the gross structure of cartilagineal (**13**), a metabolite of *Plocamium cartilagineum*, was described.[14] We therefore oxidized the alcohol **12** with manganese dioxide in hexane to obtain the corresponding aldehyde **14**. Owing to fairly rapid decomposition[15] of this sample, we were unable to arrange a direct comparison with cartilagineal. The NMR spectrum of the aldehyde **14** contained a methyl singlet at δ 1.74, three signals of the vinyl group at 5.24, 5.40, and 6.05, an AMX system at 4.46 (J = 9 Hz), 6.49 (J = 15 Hz), and 7.11 (J = 9, 15 Hz), a vinyl proton singlet at 7.02, and an aldehyde proton at 9.52 ppm. The chemical shift (9.04 ppm) of the aldehyde proton in cartilagineal (**13**) differs substantially from that of the aldehyde proton in **14**, indicating that the aldehyde **14** could be a stereoisomer of cartilagineal, but it should be noted that the spectra were recorded in different solvents.

Although the new compounds described in this paper are closely related to known algal metabolites, they have not been found in specimens of *Laurencia* and *Plocamium* collected locally. Over 200 samples of *Plocamium cartilagineum* have been collected from various depths and locations. Although all samples contained **8**, examination of the gas–liquid chromatography traces and selected GC–mass spectral analyses did not reveal the presence of **7** and **11**. The close relationships between **7** and **8** and between **11** and cartilagineal (**13**) and the pentachloro monoterpene **15**, found in *P. cartilagineum*,[4] coupled with the failure to locate the compounds in *P. cartilagineum*, may indicate transformations within the digestive gland. More likely, however, is the possibility of an undiscovered source of halogenated monoterpenes among the red algae which abound in the La Jolla region or the presence of different chemical strains of *P. cartilagineum*.

The isolation of the chamigrenes **1**, **5**, and **6** from *Aplysia* but not from local[16] *Laurencia* species shows the value of studying a herbivore rather than the algal species that comprise its diet. The extract from which these compounds were isolated also contained very much larger quantities of pacifenol (**4**) and johnstonol (**2**). In order to have obtained similar quantities of pacifenol (**4**) and johnstonol (**2**) from plant sources, we would have had to expend considerably greater effort. The chamigrenes which occur in small quantities in *Aplysia* could very easily be overlooked when studying a *Laurencia* species.

We wish to suggest that the epoxide **6** is the biosynthetic precursor of prepacifenol (**3**) and is the missing link between the more simple halogenated chamigrenes[17] and pacifenol (**4**) and johnstonol (**2**). Prepacifenol epoxide **1** is the obligatory precursor to johnstonol (**2**). We were rather surprised to find prepacifenol epoxide (**1**) in the digestive gland extract, since the compound is very sensitive to acid-catalyzed conversion to johnstonol (**2**). It is not possible to determine whether the conversion of prepacifenol epoxide (**1**) first to johnstonol (**2**) and then to the diol **5** is simply a chemical reaction controlled by the pH of the digestive gland or is an enzyme-controlled reaction. We have some preliminary evidence that the more polar diol **5** can be transported to the skin of *Aplysia*, where it may be employed as a chemical deterrent.[18]

Experimental Section

Commercially available chemicals were used without further purification unless otherwise stated. All solvents were either spectral grade or redistilled prior to use. Melting points were measured on a Fisher-Johns apparatus and are uncorrected. NMR spectra were recorded on Varian HR-220 or EM-360 spectrometers; chemical shifts are expressed as values in parts per million relative to tetramethylsilane (0). Infrared spectra were recorded on a Perkin-Elmer 700 spectrometer. Gas chromatographic analyses were performed on a Hewlett-Packard 402 instrument. Mass spectra were recorded on a Hewlett-Packard 5930A mass spectrometer. High-resolution mass spectra were measured by Beth Irwin, Department of Chemistry, UCLA.

Collections. *Aplysia californica* were collected intertidally from three different habitats: (1) Sunset Cliffs, August 1973, (2) Cardiff, June 1974, (3) Casa Cove, July 1974. The organisms from the different locations were extracted separately.

Typical Extraction. The *Aplysia* were anesthetized by injection of 10 ml of a saturated magnesium chloride solution 2 cm behind the rhinophores. The *Aplysia* were dissected to remove the digestive gland. The digestive glands were homogenized in acetone in a Waring blender and the resulting suspension was filtered through a pad of Celite to remove the solids. The solids were rehomogenized in acetone and allowed to stand for 18 h. The second suspension was filtered and both extracts were combined. The solvent was evaporated in vacuo, and the residue was partitioned between ether and water. The ether solution was dried over anhydrous sodium sulfate and the solvent removed to obtain a black oil.

***Aplysia* Collected at Sunset Cliffs.** The digestive glands of 50 adult *Aplysia* were homogenized and extracted to obtain the ether-soluble oil (32 g). A portion of the oil (30 g) was applied to a 6 × 90 cm column of Silicar CC-7 prepared in distilled hexane. Material was eluted from the column with mixtures of hexane, benzene, and ether, allowing the polarity to gradually increase.

The Epoxide (6). The material (0.390 g) eluted with 40% benzene in hexane was rechromatographed on alumina plates (20 × 20 × 0.15 cm) prepared from EM aluminum oxide PF-254, type E. Development with 20% CH_2Cl_2 in hexane permitted resolution of two bands. The band of lower R_f yielded pure 7-chloro-3,7-dimethyl-1,4,6-tribromo-1-octen-3-ol[19] (330 mg). The more mobile band solidified on evaporation of solvent and was recrystallized from pentane to give colorless crystals of the epoxide (30 mg): mp 125 °C; NMR (CCl_4/Me_4Si) δ 1.17 (s, 3 H), 1.20 (s, 3 H), 1.61 (s, 3 H), 1.68 (s, 3 H), 2.05–2.50 (m, 6 H), 2.95 (d, 1 H, J = 3 Hz), 4.68 (dd, 1 H, J = 13, 5 Hz), 6.23 (d, 1 H, J = 3 Hz); mass spectrum m/e 410, 412, 414, 416 (M^+); high-resolution mass measurement M^+ 409.9648, $C_{15}H_{21}OBr_2{}^{79}Cl^{35}$ requires 409.9649.

Prepacifenol Epoxide (1). The material eluted with 50% benzene in hexane (0.5 g) was recrystallized from pentane to yield colorless crystals of prepacifenol epoxide (300 mg): mp 98 °C; ir (CCl_4) 3650 cm^{-1}; NMR (CCl_4/Me_4Si) δ 0.95 (s, 3 H), 1.50 (s, 3 H), 1.54 (s, 3 H), 1.86 (s, 3 H), 1.96 (d, 1 H, J = 6 Hz), 2.09 (d of dd, 1 H, J = 13.5, 4, 1.6 Hz), 2.45 (d, 2 H, J = 3.5 Hz), 2.50 (t, 1 H, J = 13.5 Hz), 3.00 (s, 1 H), 3.58 (s, 1 H), 4.00 (d of dd, 1 H, J = 6.0, 3.5, 1.6 Hz), 4.64 (dd, 1 H, J = 13.5, 4 Hz); mass spectrum m/e 442, 444, 446, 448 (M^+), 426, 428, 430, 432, ($M^+ - 0$), 424, 426, 428, 430 ($M^+ - H_2O$), 407, 409, 411 ($M^+ - Cl$); high-resolution mass measurement M^+ 441.9548, $C_{15}H_{21}O_3Br_2{}^{79}Cl^{35}$ requires 441.9547.

The Diol (5). The fraction eluted with ether (0.05 g) was rechromatographed on alumina plates (20 × 20 × 0.15 cm) prepared from EM aluminum oxide PF-254, type E. Development with ether allowed resolution of one major band. The solid obtained upon evaporation of solvent was recrystallized from carbon tetrachloride to yield the diol **5** (15 mg): mp 172–173 °C; NMR ($CDCl_3$/Me_4Si) δ 0.91 (s, 3 H), 1.39 (s, 3 H), 1.83 (s, 3 H), 4.29 (s, 1 H), 4.55 (dd, 1 H), 4.79 (s, 1 H), 5.07 (dd, 1 H), 5.39 (s, 1 H), 5.58 (s, 1 H).

Conversion of Prepacifenol Epoxide to Johnstonol. Prepacifenol epoxide (20 mg) was dissolved in anhydrous methanol (5 ml) under a nitrogen atmosphere. One crystal of oxalic acid was added, and the solution was refluxed for 24 h. After addition of water (5 ml) the solution was partitioned between ether and 5% sodium bicarbonate solution. The ether layer was dried over sodium sulfate and the solvent evaporated to yield a solid. The solid was recrystallized from carbon tetrachloride to give colorless needles that were identical in every respect with johnstonol.

Conversion of Prepacifenol Epoxide to the Diol 5. A solution of *p*-toluenesulfonic acid (one crystal) in benzene (20 ml) was refluxed for 1 h in a Dean-Stark apparatus to remove any moisture. Prepacifenol epoxide (10 mg) was added, and refluxing was continued for 0.5 h. The cooled solution was washed with 5% sodium bicarbonate solution, dried over sodium sulfate, and evaporated to a solid. The solid was recrystallized from carbon tetrachloride to give the diol **5** as the only product.

Conversion of Johnstonol to the Diol 5. A solution of *p*-toluenesulfonic acid (1 mg) in benzene (20 ml) was refluxed for 1 h in a Dean-Stark apparatus. Johnstonol (30 mg) was added, and refluxing was continued for 0.5 h. The organic layer was washed with 5% sodium bicarbonate solution, dried over sodium sulfate, and evaporated to yield a solid. Recrystallization from carbon tetrachloride gave the diol **5** (28 mg).

***Aplysia* Collected at Cardiff.** The digestive glands of 24 adult *Aplysia* were homogenized and extracted as described previously to yield the ether-soluble oil (11 g). A portion of this oil (10 g) was applied to a 2.5 × 30 cm column of Silicar CC-7 prepared in distilled hexane. The material was eluted from the column with mixtures of hexane and benzene of increasing polarity.

***trans,trans*-1,8-Dibromo-3,7-dimethyl-3,4,7-trichloro-1,5-octadiene (7).** The material eluted with 40% benzene in hexane (1.3 g) was rechromatographed on alumina plates (20 × 20 × 0.15 cm) prepared from EM aluminum oxide PF-254, type E. Development with hexane gave a band at R_f 0.3. The resulting oil crystallized on standing and was recrystallized from MeOH to give needles of **7** (0.75 g): mp 20 °C; NMR (CCl_4/Me_4Si) δ 1.78 (s, 3 H), 1.83 (s, 3 H), 3.65 (s, 2 H), 4.54 (d, 1 H, J = 8 Hz), 5.89 (d, 1 H, J = 16 Hz), 6.00 (dd, 1 H, J = 16, 8 Hz), 6.36 (d, 1 H, J = 13 Hz), 6.51 (d, 1 H, J = 13 Hz); mass spectrum m/e 361, 363, 365, 367 ($M^+ - Cl$), 167, 169, 171 ($C_4H_5BrCl^+$), base peak 91 ($C_7H_7^+$); high-resolution mass measurement M^+ 360.8762, $C_{10}H_{13}Br_2{}^{79}Cl_2{}^{35}$ ($M^+ - Cl$) requires 360.8760. Anal. Cl/Br ratio 1.68, $C_{10}H_{13}Br_2Cl_3$ requires 1.5.

***Aplysia* Collected at Casa Cove.** The digestive glands of two adult *Aplysia* were homogenized and extracted in the manner described previously to yield an ether-soluble oil (6.89 g). A portion of this oil (6 g) was applied to a 2.5 × 30 cm column of Silicar CC-7 prepared in CCl_4. Three 200-ml fractions were collected.

7-Acetoxymethylene-3-methyl-3,4,8-trichloro-1,5,7-octatriene (11). The second and third fractions (2 g) were subjected to reverse phase high performance liquid chromatography, using a 4 ft × 0.375 in. o.d. column of Bondapak C_{18}/Porosil B (37–75 μ) with 60% CH_3CN/H_2O eluent. The resulting fractions were extracted with pentane. Combined pentane layers were dried over sodium sulfate and the solvent evaporated in vacuo to yield the acetate **11** (1.0 g): λ_{max} (CCl_4) 259 nm; ir 1740 cm^{-1}; NMR (CCl_4) δ 1.72 (s, 3 H), 2.0 (s, 3 H), 4.50 (d, 1 H, J = 9 Hz), 4.67 (d, 1 H, J = 13 Hz), 4.74 (d, 1 H, J = 13 Hz), 5.23 (d, 1 H, J = 10 Hz), 5.36 (d, 1 H, J = 17 Hz), 6.02 (dd, 1 H, J = 17, 10 Hz), 6.02 (dd, 1 H, J = 16, 9 Hz), 6.36 (s, 1 H), 6.68 (d, 1 H, J = 16 Hz); mass spectrum m/e 89, 91 ($C_4H_6Cl^+$), base peak 43 ($C_2H_3O^+$); high-resolution mass measurement M^+ 296.0138, $C_{12}H_{15}O_2Cl_3{}^{35}$ requires 296.013757.

7-Hydroxymethylene-3-methyl-3,4,8-trichloro-1,5,7-octa-

triene (12). The acetate (75 mg) was dissolved in anhydrous methanol (5 ml) under a nitrogen atmosphere. The solution was cooled to 0 °C using an alcohol–ice bath. Methanolic potassium hydroxide solution (1%, 1 ml) was added and the solution stirred for 1 h. The reaction mixture was poured into ether, then washed with 5% hydrochloric acid. The ether layer was dried over sodium sulfate to a residue. The residue was chromatographed on silica plates (20 × 20 × 0.15 cm) prepared from EM silica gel PF-254 which were developed with 25% ether in hexane to obtain the alcohol **12** (40 mg): R_f 0.25; λ_{max} (CCl_4) 260 nm; ir 3600 cm^{-1}; NMR (CCl_4/Me_4Si) δ 1.75 (s, 3 H), 4.31 (s, 2 H), 4.51 (d, 1 H, J = 9 Hz), 5.26 (d, 1 H, J = 10 Hz), 5.39 (d, 1 H, J = 17 Hz), 6.05 (dd, 1 H, J = 17, 10 Hz), 6.05 (dd, 1 H, J = 16, 9 Hz), 6.32 (s, 1 H), 6.70 (d, 1 H, J = 16 Hz); mass spectrum *m/e* 165, 167, 169 ($C_6H_7OCl_2^+$), base peak 129, 131 ($C_6H_6OCl^+$), 89, 91 ($C_4H_6Cl^+$); high-resolution mass measurement M^+ 254.0031, $C_{10}H_{13}OCl_3{}^{35}$ requires 254.0032.

7-Formyl-3-methyl-3,4,8-trichloro-1,5,7-octatriene (14). The alcohol (39 mg) and manganese dioxide were stirred in hexane at room temperature for 24 h. The solution was filtered through Whatman paper to remove solids. The hexane was evaporated in vacuo to a residue. The residue was chromatographed on silica plates (20 × 20 × 0.15 cm) prepared from EM silica gel PF-254. Development with 25% ether in hexane gave the pure aldehyde (15 mg): R_f 0.3; λ_{max} (CCl_4) 264 nm; NMR (CCl_4/Me_4Si) δ 1.74 (s, 3 H), 4.46 (d, 1 H, J = 9 Hz), 5.24 (d, 1 H, J = 10 Hz), 5.40 (d, 1 H, J = 16 Hz), 6.05 (dd, 1 H, J = 16, 10 Hz), 6.49 (dd, 1 H, J = 15, 2 Hz), 7.02 (s, 1 H), 7.11 (dd, 1 H, J = 15, 9 Hz), 9.52 (d, 1 H, J = 2 Hz); mass spectrum *m/e* 252, 254, 256, 258 (M^+), 217, 219, 221 (M^+ − Cl), 181, 183 ($C_{10}H_{10}OCl^+$), base peak 89, 91 ($C_4H_6OCl^+$); high-resolution mass measurement M^+ 251.9875, $C_{10}H_{11}OCl_3{}^{35}$ requires 251.9875.

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Supplementary Material Available. A listing of fractional coordinates, bond distances, bond angles, and observed and calculated structure factors (9 pages). Ordering information is given on any current masthead page.

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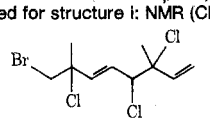

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Cyclic Polysulfides from the Red Alga *Chondria californica*

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The antibiotic activity of the red alga *Chondria californica* is due to a mixture of cyclic polysulfides and their oxidation products. We have identified 1,2,4-trithiolane, 1,2,4,6-tetrathiepane, 1,2,3,5,6-pentathiepane, 1-oxo-1,2,4-trithiolane, 4-oxo-1,2,4-trithiolane, 4-dioxo-1,2,4,6-tetrathiepane, and a 12-membered heterocycle containing eight sulfur atoms.

Cyclic polysulfides are relatively uncommon in nature, but those compounds which have been described have usually exhibited interesting biological activities.[1] Marine organisms have provided two interesting examples of cyclic disulfides. The annelid worm *Lumbriconereis heteropoda* contains nereistoxin (**1**), a simple compound having insecticidal activity.[2] Two brown algae of the genus *Dictyopteris* have been shown to contain a cyclic disulfide **2**, together with acyclic mono-, di-, and trisulfides.[3] Among examples of cyclic polysulfides attributed to terrestrial organisms are two antibiotics, 1,2,3,5,6-pentathiepane (lenthionine, **3**) and 1,2,4,6-tetra-