Chlorinated Acetylenes from the Nudibranch *Diaulula sandiegensis*

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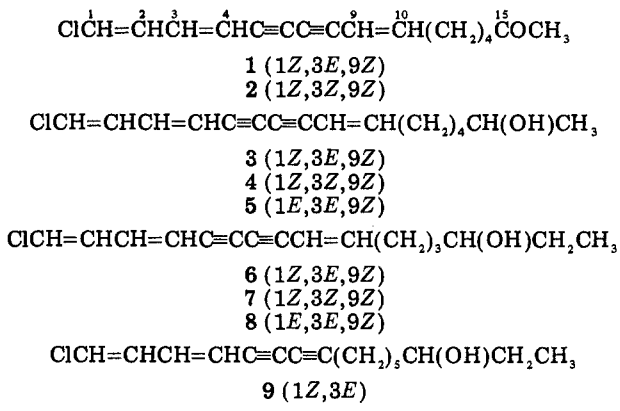
The nudibranch mollusc *Diaulula sandiegensis* contained nine chlorinated acetylenes, **1**–**9**, all of which were relatively unstable when purified. The nine metabolites were identified as (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-one (**1**), (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-one (**2**), (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (**3**), (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (**4**), (1*E*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (**5**), (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**6**), (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**7**), (1*E*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**8**), and (1*Z*,3*E*)-1-chlorohexadeca-1,3-diene-5,7-diyn-14-ol (**9**) by analysis of spectral data. The chlorinated acetylenes **1**–**9** are believed to be involved in the chemical defense mechanism of the nudibranch.

An unusually diverse array of secondary metabolites has been isolated from opisthobranch molluscs.[1] The secondary metabolites, often obtained from dietary sources,[2] are believed to be involved in chemical defense mechanisms.[3,4] Dorid nudibranchs, of which *Diaulula sandiegensis* is an example, are known to feed exclusively on sponges[5] and in some cases the metabolites of a nudibranch have been traced to a particular sponge.[1,4]

Although acetylenes are commonly encountered as metabolites of the Compositae,[6] they are relatively rare metabolites of marine organisms. Acetylenes have been isolated from green algae,[7] red algae,[8] and the sea hares that eat red algae.[9] Marine sponges are known to contain acetylenic compounds including steroids,[10] carotenoids,[11] polyacetylenes,[12] and brominated acetylenes.[13] In this paper, we report the isolation and structural elucidation of nine chlorinated acetylenes from the nudibranch *Diaulula sandiegensis*.

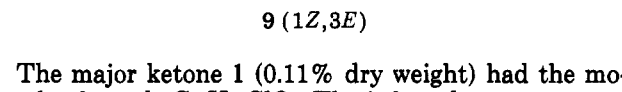
The nudibranchs were collected by hand, using SCUBA (−15 m) at Point Loma, San Diego, CA, and stored in methanol at −5 °C for 2 weeks. The hexane-soluble material from the methanol extract was chromatographed on Partisil, using 20% ether in dichloromethane as eluant, to obtain seven fractions, three of which contained the chlorinated acetylenes. The least polar of these fractions was rechromatographed on Partisil-ODS, using 32% water in methanol as eluant, to separate the ketones **1** and **2**. Rechromatography of the two more polar fractions under identical conditions gave pure samples of the alcohols **3**–**9**. Once separated, each of the chlorinated acetylenes was stored at −70 °C in the dark under a nitrogen atmosphere.



1 (1*Z*,3*E*,9*Z*)
2 (1*Z*,3*Z*,9*Z*)

3 (1*Z*,3*E*,9*Z*)
4 (1*Z*,3*Z*,9*Z*)
5 (1*E*,3*E*,9*Z*)

6 (1*Z*,3*E*,9*Z*)
7 (1*Z*,3*Z*,9*Z*)
8 (1*E*,3*E*,9*Z*)



9 (1*Z*,3*E*)

The major ketone **1** (0.11% dry weight) had the molecular formula $C_{16}H_{17}ClO$. The infrared spectrum contained an acetylenic band at 2200 cm^{-1} and a carbonyl band at 1710 cm^{-1}. The ultraviolet spectrum [342 nm (ε 19 500), 319.5 (26 800), 300 (19 500), 269 (18 700), 254 (18 900)] was similar to that of trideca-4,6-diyne-2,8,10-triene,[6] with a small bathychromic shift due to substitution by chlorine. The ^1H NMR spectrum contained signals due to a 1,4-substituted 1,3-diene system at δ 5.81 (dd, 1 H, J = 16, 1 Hz), 6.10 (dd, 1 H, J = 7, 1 Hz), 6.37 (ddd, 1 H, J = 11, 7, 1 Hz), and 7.04 (ddd, 1 H, J = 16, 11, 1 Hz). The small coupling constant (J = 7 Hz) between the signals at δ 6.10 and 6.39 indicated that the diene consisted of a (*Z*)-vinyl chloride[14] conjugated to an (*E*)-olefin adjacent to the two acetylene groups. The ^1H NMR signals at δ 5.53 (d, 1 H, J = 10 Hz) and 6.06 (dt, 1 H, J = 10, 7, 7 Hz) showed that the remaining olefin in the conjugated system had the *Z* geometry. The position of the carbonyl group was defined by the presence of a signal at δ 2.06 (s, 3 H) due to a methyl ketone. Other ^1H NMR signals are assigned in Table I. The major ketone was therefore (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-one (**1**).

The minor ketone **2** (0.06% dry weight) had the molecular formula $C_{16}H_{17}ClO$, isomeric with ketone **1**. The major features of the infrared and ultraviolet spectra of ketones **1** and **2** were identical. The ^1H NMR spectrum of ketone **2** was almost identical with that of ketone **1** (Table I) with the exception of the signals associated with the terminal diene. In solvents such as carbon tetrachloride and benzene-d_6, the signals for the protons at C-2 and C-3 occur at the same chemical shift, giving rise to virtual coupling. In order to determine the geometry about the diene system, the ^1H NMR spectrum was measured in acetone-d_6 solution to obtain signals at δ 5.91 (d, 1 H, J = 10 Hz), 6.52 (d, 1 H, J = 6.5 Hz), 6.93 (dd, 1 H, J =

(1) Faulkner, D. J.; Ireland, C. In "Marine Natural Products Chemistry"; Faulkner, D. J., Fenical, W. H., Eds.; Plenum Press: New York, 1977; pp 23–34.
(2) Stallard, M O.; Faulkner, D. J. *Comp. Biochem. Physiol.* **1974**, *49B*, 37.
(3) Ireland, C.; Faulkner, D. J. *Bioorg. Chem.* **1978**, *7*, 125.
(4) Hagadone, M. R.; Burreson, B. J.; Scheuer, P. J.; Finer, J. S.; Clardy, J. *Helv. Chim. Acta* **1979**, *62*, 2484.
(5) Young, D. J. *Malacologia* **1970**, *9*, 421. Bloom, S. A. *Veliger* **1974**, *14*, 158. McBeth, J. W. *Ibid.* **1978**, *18*, 289.
(6) Bohlmann, F.; Burkhardt, T.; Zdero, C. "Naturally Occurring Acetylenes"; Academic Press: New York, 1973.
(7) Amico, V.; Oriente, G.; Piatelli, M.; Trignali, C.; Fattorusso, E.; Magno, S.; Mayol, L. *Tetrahedron Lett.* **1978**, 3953.
(8) Moore, R. E. In "Marine Natural Products Chemical and Biological Perspectives"; Scheuer, P. J., Ed.; Academic Press: New York, 1978; Vol. I, Chapter 2. Paul, V. J.; Fenical, W. *Tetrahedron Lett.* **1980**, *21*, 3327.
(9) McDonald, F. J.; Campbell, D. C.; Vanderah, D. J.; Schmitz, F. J.; Washecheck, D. M.; Burks, J. E.; van der Helm, D. *J. Org. Chem.* **1975**, *40*, 665. Vanderah, D. J.; Schmitz, F. J. *Ibid.* **1976**, *41*, 3480.
(10) Steiner, E.; Djerassi, C.; Fattorusso, E.; Magno, S.; Mayol, L.; Santacroce, C.; Sica, D. *Helv. Chim. Acta* **1977**, *60*, 475.
(11) Hamasaki, T.; Okukado, N.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1884.
(12) Rotem, M.; Kashman, Y. *Tetrahedron Lett.* **1979**, 3193.
(13) Cimino, C.; De Stefano, S. *Tetrahedron Lett.* **1977**, 1325. Schmitz, F. J.; Gopichand, Y. *Ibid.* **1978**, 3637.

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Table I. ^{1}H NMR Chemical Shift Data

H at C no.	1	2	3	5	6	7	8	8	9
1	6.10	6.22	6.08	6.21	6.33	6.08	6.22	6.34	6.05
2	6.37	6.90	6.36	6.90	6.49	6.36	6.90	6.50	6.32
3	7.04	6.90	7.06	6.90	6.60	7.08	6.90	6.61	7.03
4	5.81	5.71	5.81	5.71	5.68	5.80	5.71	5.68	5.72
9	5.53	5.56	5.54	5.56	5.53	5.55	5.56	5.53	2.35
10	6.06	6.08	6.06	6.06	6.07	6.06	6.08	6.07	1.59
11	2.38	2.38	2.36	2.36	2.36	2.36	2.37	2.37	~1.4
12	1.43	1.43	~1.4	~1.4	~1.4	~1.4	~1.4	~1.4	~1.4
13	1.59	1.59	~1.4	~1.4	~1.4	~1.4	~1.4	~1.4	~1.4
14	2.38	2.38	~1.4	~1.4	~1.4	3.46	3.46	3.46	3.43
15			3.69	3.69	3.69	1.4	1.4	1.4	1.4
16	2.06	2.06	1.14	1.14	1.13	0.94	0.94	0.93	0.93

10, 6.5 Hz), and 7.00 (t, 1 H, J = 10 Hz). The minor ketone was assigned the structure (1Z,3Z,9Z)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-one (**2**).

Both ketones were quite unstable, particularly when exposed to light. The only successful transformations were those involving reduction of ketones **1** and **2**. Catalytic hydrogenation of both ketones **1** and **2** gave 2-hexadecanone. Reduction of ketones **1** and **2** with sodium borohydride in ethanol gave the alcohols **3** and **4**, respectively. The alcohols were identical in all respects with the natural products (1Z,3E,9Z)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (**3**, 0.04% dry weight) and (1Z,3Z,9Z)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (**4**, 0.03% dry weight).

Among the minor products was the alcohol **5** (0.01% dry weight) that had the same molecular formula ($C_{16}H_{19}ClO$) as the alcohols **3** and **4**. The ultraviolet spectrum of alcohol **5** was almost identical with those of compounds **1**–**4** and the infrared spectrum contained bands at 3450 (hydroxyl) and 2200 cm^{-1} (acetylene). The ^{1}H NMR spectrum of alcohol **5** was almost identical with those of alcohols **3** and **4** with the exception of the signals associated with the terminal diene moiety at δ 5.68 (d, 1 H, J = 15 Hz), 6.33 (d, 1 H, J = 13 Hz), 6.49 (dd, 1 H, J = 13, 11 Hz), and 6.60 (dd, 1 H, J = 15, 11 Hz). Since the coupling constant (J = 13 Hz) between the signals at δ 6.33 and 6.49 is a typical value for trans protons on a vinyl chloride,[14] the alcohol **5** was assigned the structure (1E,3E,9Z)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol.

The three isomeric alcohols **6** (0.05% dry weight), **7** (0.02% dry weight), and **8** (0.015% dry weight) all had the molecular formula $C_{16}H_{19}ClO$. The ultraviolet and infrared spectra were similar to those of alcohols **3**–**5**. The ^{1}H NMR spectra (Table I) indicated that the alcohols **6**–**8** were known geometrical isomers about the terminal diene functionality. The ^{1}H NMR spectra of the alcohols **6**–**8** each contained a methyl signal at δ 0.94 (t, 3 H, J = 7 Hz) and an α-hydroxy proton signal at 3.46 (m, 1 H), indicating that the hydroxyl group must be at C-13 or C-14 in these alcohols. Oxidation of the alcohols **6** and **7** with pyridinium chlorochromate in dichloromethane solution gave the ketones **10** and **11**, respectively. The ^{1}H NMR spectra of

$$ClCH{=}CHCH{=}CHC{\equiv}CC{\equiv}CCH{=}CH(CH_2)_3COCH_2CH_3$$

10 (1Z,3E,9Z)
11 (1Z,3Z,9Z)

both ketones **10** and **11** contained a methyl signal at δ 1.02 (t, 3 H, J = 7 Hz) coupled to a methylene signal at δ 2.34 (q, 2 H, J = 7 Hz) which must be adjacent to the carbonyl group. The three alcohols have therefore been assigned the structures (1Z,3E,9Z)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**6**), (1Z,3Z,9Z)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**7**), and, by analogy, (1E,3E,9Z)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**8**).

The remaining alcohol **9** (0.06% dry weight) had the molecular formula $C_{16}H_{21}ClO$. The infrared spectrum contained bands at 3450 (hydroxyl) and 2200 cm^{-1} (acetylene). The ultraviolet spectrum [316 nm (ϵ 39 600), 296 (37 500), 238 (34 700), and 229 (17 700)] differed from those of compounds **1**–**8** and suggested that alcohol **9** contained a conjugated diene–diyne system.[6] The ^{1}H NMR spectrum (Table I) of alcohol **9** contained signals at δ 5.72 (dd, 1 H, J = 16, 1 Hz), 6.05 (dd, 1 H, J = 7, 1 Hz), 6.32 (ddd, 1 H, J = 11, 7, 1 Hz), and 7.03 (ddd, 1 H, J = 16, 11, 1 Hz) due to the terminal (1Z,3E)-diene system but lacked the signals expected for a (9Z)-olefin. The position of the alcohol group was determined by oxidation of alcohol **9** with pyridinium chlorochromate in dichloromethane to obtain the ketone **12**. The ^{1}H NMR spectrum of the ketone **12**

$$ClCH{=}CHCH{=}CHC{\equiv}CC{\equiv}C(CH_2)_5COCH_2CH_3$$

12 (1Z,3E)

contained a methyl signal at δ 1.02 (t, 3 H, J = 7 Hz) coupled to a methylene signal at δ 2.34 (multiplicity obscured), indicating that the alcohol **9** contained a hydroxyl group at C-14. The alcohol **9** was therefore (1Z,3E)-1-chlorohexadeca-1,3-diene-5,7-diyn-14-ol.

During the collection of *Diaulula sandiegensis*, the nudibranch was observed to feed on a variety of sponges. None of these sponges contained the chlorinated acetylenes **1**–**9** or an obvious precursor. Examination of the stomach contents of representative samples of *D. sandiegensis* revealed that the nudibranch must have eaten other common sponges[15] but, again, none of these sponges contained the chlorinated acetylenes. There is a body of circumstantial evidence to support the hypothesis that the chlorinated acetylenes are involved in a chemical defense mechanism. The ease with which the acetylenes are leached from the nudibranch suggests that the compounds are stored in the skin rather than in an internal organ. The ketone **1** exhibited mild antimicrobial activity against several bacteria and a yeast but this activity is a poor indicator of the type of activity (antifeedant, toxicity, etc.) required for an effective chemical defense mechanism. Although we have been unable to perform toxicity assays on these compounds due to their instability, closely related acetylenes are often highly toxic to fish and invertebrates.[16]

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 137 spectrophotometer. Ultraviolet spectra were recorded on a Cary 219 spectrophotometer. ^{1}H NMR spectra were recorded on a 360-MHz spectrometer constructed from an Oxford narrow-bore magnet

(14) Laszlo, P.; Schleyer, P. R. *Bull. Soc. Chim. Fr.* **1964**, 87.

(15) Thompson, J. E., unpublished data.

(16) Towers, G. H. N. In "Progress in Phytochemistry"; Reinhold, L., Harbone, J. B., Swain, T., Eds.; Pergamon Press: Oxford, 1978; Vol. 6, pp 183–202.

and a Nicolet Fourier transform system by Dr. John M. Wright for the UCSD NMR Facility; all chemical shifts are reported with respect to Me_4Si (δ 0). Low-resolution mass spectra were recorded on a Hewlett-Packard 5930A mass spectrometer. High-resolution mass measurements were supplied by Professor A. Burlingame, U. C. Berkeley. Melting points were recorded on a Fisher-Johns apparatus and are reported uncorrected. All solvents were distilled from glass prior to use.

Collection and Extraction. Specimens of *Diaulula sandiegensis* were collected by hand, using SCUBA (−15 m) at Point Loma, San Diego, in Aug 1980. Forty-one animals (11.7 g dry weight) were steeped in methanol (150 mL) in the dark at −5 °C for 2 weeks. After filtration, the methanolic extract was evaporated under vacuum to obtain an aqueous suspension that was extracted with hexane (4 × 100 mL), ethyl acetate (3 × 100 mL), and 2:1 chloroform–2-propanol (3 × 100 mL). The extracts were evaporated under vacuum and the residues were examined by TLC and ^1H NMR spectroscopy.

The hexane-soluble material (390 mg, 2.9% dry weight) was dissolved in ether and filtered through a short column of silica gel. The ether was evaporated to obtain an oil that was chromatographed by LC on Partisil, using 20% ether in dichloromethane as eluant to obtain seven fractions. Fraction 2 was rechromatographed on Partisil-ODS, using 32% aqueous methanol as eluant, to obtain (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-one (**1**, 13.7 mg, 0.11% dry weight) and (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-one (**2**, 6.9 mg 0.06% dry weight). Fraction 4 was rechromatographed, using the same conditions, to obtain (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**6**, 6.3 mg, 0.05% dry weight), (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**7**, 2.9 mg, 0.02% dry weight), (1*E*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (**8**, 1.8 mg, 0.015% dry weight), and (1*Z*,3*E*)-1-chlorohexadeca-1,3-diene-5,7-diyn-14-ol (**9**, 7.4 mg, 0.06% dry weight). Fraction 6 was rechromatographed under the same conditions to obtain (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (**3**, 5.1 mg, 0.04% dry weight), (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (**4**, 3.6 mg, 0.03% dry weight), and (1*E*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (**5**, 0.7 mg, 0.01% dry weight). The pure compounds were stored in the dark under nitrogen at −78 °C.

(1*Z*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-trien-15-one (1): IR (film) 2200, 1710 cm^{-1}; UV (C_5H_{12}) 342 nm (ϵ 19 500), 319.5 (26 800), 300 (19 500), 269 (18 700), 254 (18 900); ^1H NMR (CCl_4) δ 1.43 (m, 2 H), 1.59 (m, 2 H), 2.06 (s, 3 H), 2.38 (m, 4 H), 5.53 (d, 1 H, J = 10 Hz), 5.81 (dd, 1 H, J = 16, 1 Hz), 6.06 (dt, 1 H, J = 10, 7, 7 Hz), 610 (dd, 1 H, J = 7, 1 Hz), 6.37 (ddd, 1 H, J = 11, 7, 1 Hz), 7.04 (ddd, 1 H, J = 16, 11, 1 Hz); high-resolution mass spectrum, found m/z 260.0968 ($C_{16}H_{17}{}^{35}ClO$ requires 260.0967).

(1*Z*,3*Z*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-trien-15-one (2): IR (film) 2200, 1710 cm^{-1}; UV (C_5H_{12}) 341 nm (ϵ 17 200), 319 (23 500), 299 (17 500), 269 (18 700), 255 (19 250); ^1H NMR (CCl_4) δ 1.43 (m, 2 H), 1.59 (m, 2 H), 2.06 (s, 3 H), 2.38 (m, 4 H), 5.56 (d, 1 H, J = 10 Hz), 5.71 (m, 1 H), 6.08 (dt, 1 H, J = 10, 7, 7 Hz), 6.22 (m, 1 H), 6.90 (m, 2 H); ^1H NMR (acetone-d_6) δ 1.44 (m, 2 H), 1.59 (m, 2 H), 2.09 (s, 3 H), 2.35 (m, 2 H), 2.49 (t, 2 H, J = 7 Hz), 5.69 (d, 1 H, J = 10 Hz), 5.91 (d, 1 H, J = 10 Hz), 6.25 (dt, 1 H, J = 10, 7 Hz), 6.52 (d, 1 H, J = 6.5 Hz), 6.93 (dd, 1 H, J = 10, 6.5 Hz), 7.00 (t, 1 H, J = 10 Hz); high-resolution mass spectrum, found m/z 260.0964 ($C_{16}H_{17}{}^{35}ClO$ requires 260.0967).

(1*Z*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (3): IR (film) 3450, 2200 cm^{-1}; UV (C_5H_{12}) 342 nm (ϵ 22 700), 320 (29 150), 300 (20 500), 269 (20 900), 254 (21 950); ^1H NMR (CCl_4) δ 1.14 (d, 3 H, J = 7 Hz), 1.42 (m, 6 H), 2.36 (m, 2 H), 3.69 (m, 1 H), 5.54 (d, 1 H, J = 10 Hz), 5.81 (dd, 1 H, J = 16, 1 Hz), 6.06 (dt, 1 H, J = 10, 7, 7 Hz), 6.08 (dd, 1 H, J = 7, 1 Hz), 6.36 (ddd, 1 H, J = 11, 7, 1 Hz), 7.06 (ddd, 1 H, J = 16, 11, 1 Hz); high-resolution mass spectrum, found m/z 262.1102 ($C_{16}H_{19}{}^{35}ClO$ requires 262.1124).

(1*Z*,3*Z*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (4): IR (film) 3450, 2200 cm^{-1}; UV (C_5H_{12}) 341 nm (ϵ 16 300), 318 (23 600), 299 (17 350), 270 (17 700), 255 (17 350); ^1H NMR (CCl_4) δ 1.14 (d, 3 H, J = 7 Hz), 1.42 (m, 6 H), 2.36 (m, 2 H) 3.69 (m, 1 H), 5.56 (d, 1 H, J = 10 Hz), 5.71 (m, 1 H), 6.06 (dt, 1 H, J = 10, 7, 7 Hz), 6.21 (m, 1 H), 6.90 (m, 2 H); high-resolution mass spectrum, found m/z 262.1112 ($C_{16}H_{19}{}^{35}ClO$ requires 262.1124).

(1*E*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-trien-15-ol (5): IR (film) 3450, 2200 cm^{-1}; UV (C_5H_{12}) 340 nm (ϵ 27 400), 318 (35 800), 299 (25 600), 268 (26 800), 252 (28 250); ^1H NMR (CCl_4) δ 1.13 (d, 3 H, J = 7 Hz), 2.36 (m, 2 H), 3.69 (m, 1 H), 5.53 (d, 1 H, J = 10 Hz), 5.68 (d, 1 H, J = 15 Hz), 6.07 (dt, 1 H, J = 10, 7 Hz), 6.33 (d, 1 H, J = 13 Hz), 6.49 (dd, 1 H, J = 13, 11 Hz), 6.60 (dd, 1 H, J = 15, 11 Hz); high-resolution mass spectrum, found m/z 262.1139 ($C_{16}H_{19}{}^{35}ClO$ requires 262.1124).

(1*Z*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (6): IR (film) 3450, 2200 cm^{-1}; UV (C_5H_{12}) 342 nm (ϵ 20 500), 319 (31 000), 300 (25 300), 269 (21 200), 254 (20 500); ^1H NMR (CCl_4) δ 0.94 (t, 3 H, J = 7 Hz), 2.36 (m, 2 H), 3.46 (m, 1 H), 5.55 (d, 1 H, J = 10 Hz), 5.80 (d, 1 H, J = 16 Hz), 6.06 (dt, 1 H, J = 10, 7 Hz), 6.08 (d, 1 H, J = 7 Hz), 6.36 (dd, 1 H, J = 11, 7 Hz), 7.08 (dd, 1 H, J = 16, 11 Hz); high-resolution mass spectrum, found m/z 262.1146 ($C_{16}H_{19}{}^{35}ClO$ requires 262.1124).

(1*Z*,3*Z*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (7): IR (film) 3450, 2200 cm^{-1}; UV (C_5H_{12}) 341 nm (ϵ 21 400), 319 (29 050), 300 (21 350), 269 (22 700), 254 (22 900); ^1H NMR (CCl_4) δ 0.94 (t, 3 H, J = 7 Hz), 2.37 (m, 2 H), 3.46 (m, 1 H), 5.56 (d, 1 H, J = 10 Hz), 5.71 (m, 1 H), 6.08 (dt, 1 H, J = 10, 7 Hz), 6.22 (m, 1 H), 6.90 (m, 2 H); ^1H NMR (acetone-d_6) δ 0.92 (t, 3 H, J = 7 Hz), 2.37 (m, 2 H), 2.91 (t, 2 H, J = 7 Hz), 3.48 (m, 1 H), 5.69 (d, 1 H, J = 10 Hz), 5.91 (d, 1 H, J = 10 Hz), 6.26 (dt, 1 H, J = 10, 7 Hz), 6.52 (d, 1 H, J = 6 Hz), 6.93 (dd, 1 H, J = 10, 6 Hz), 7.01 (t, 1 H, J = 10 Hz); high-resolution mass spectrum, found m/z 262.1135 ($C_{16}H_{19}{}^{35}ClO$ requires 262.1124).

(1*E*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-trien-14-ol (8): IR (film) 3450, 2200 cm^{-1}; UV (C_5H_{12}) 340 nm (ϵ 21 300), 318 (26 300), 299 (19 850), 268 (29 250), 253 (25 100); ^1H NMR (CCl_4) δ 0.93 (t, 3 H, J = 7 Hz), 2.37 (m, 2 H), 3.46 (m, 1 H), 5.53 (d, 1 H, J = 10 Hz), 5.68 (d, 1 H, J = 15 Hz), 6.07 (dt, 1 H, J = 10, 7 Hz), 6.34 (d, 1 H, J = 13 Hz), 6.50 (dd, 1 H, J = 13, 11 Hz), 6.61 (dd, 1 H, J = 15, 11 Hz); high-resolution mass spectrum, found m/z 262.1109 ($C_{16}H_{19}{}^{35}ClO$ requires 262.1124).

(1*Z*,3*E*)-1-Chlorohexadeca-1,3-diene-5,7-diyn-15-ol (9): IR (film) 3450, 2200 cm^{-1}; UV (C_5H_{12}) 316 nm (ϵ 39 600), 296 (37 450), 238 (39 700), 229 (17 700); ^1H NMR (CCl_4) δ 0.93 (t, 3 H, J = 7 Hz), 1.43 (m, 7 H), 1.59 (m, 2 H), 2.35 (t, 2 H, J = 7 Hz), 3.43 m, 1 H), 5.72 (dd, 1 H, J = 16, 1 Hz), 6.05 (dd, 1 H, J = 7, 1 Hz), 6.32 (ddd, 1 H, J = 11, 7, 1 Hz), 7.03 (ddd, 1 H, J = 16, 11, 1 Hz); high-resolution mass spectrum, found m/z 264.1272 ($C_{16}H_{21}{}^{35}ClO$ requires 264.1280).

Catalytic Hydrogenation of Ketones 1 and 2. A solution of the acetylene (1 mg, 0.004 mmol) in ether (3 mL) containing 10% palladium on charcoal catalyst (0.5 mg) was stirred under an atmosphere of hydrogen for 4 h. The catalyst was removed by filtration and the solvent evaporated to obtain 2-hexadecanone (0.9 mg, quantitative): mp 37–39 °C [lit.[17] mp 43 °C]; IR (film) 1710 cm^{-1}; ^1H NMR (CCl_4) δ 0.89 (t, 1 H, J = 7 Hz), 1.25 (br s, 22 H), 1.51 (m, 2 H), 2.04 (s, 3 H), 2.31 (t, 2 H, J = 7 Hz); mass spectrum, m/z 240.

Reduction of Ketone 1 with Sodium Borohydride. Sodium borohydride (5 mg) was added to a stirred solution of the ketone **1** (1.8 mg, 0.007 mmol) in methanol (3 mL) at 0 °C. After a 5-min reaction time, the excess reagent was destroyed by addition of water (10 mL). The reaction mixture was extracted with hexane (3 × 7 mL), the combined extracts were dried over anhydrous sodium sulfate, and the solvent was evaporated to obtain the alcohol **3** (1.6 mg, 88% theoretical), identical in all respects with the natural product.

Reduction of Ketone 2 with Sodium Borohydride. By the experimental procedure described above, the ketone **2** (2 mg, 0.008 mmol) was reduced to the alcohol **4** (2 mg, quantitative), identical in all respects with the natural product.

Oxidation of Alcohol 6. A solution of pyridinium chlorochromate (10 mg) in dichloromethane (3 mL) was added to a stirred solution of the alcohol **6** (1.5 mg, 0.006 mmol) in dichloromethane (2 mL). The reaction mixture was stirred at room temperature for 1.5 h, then poured into water (20 mL), and extracted with ether (3 × 5 mL). The combined organic extracts were dried over anhydrous sodium sulfate and the solvent was

(17) "Dictionary of Organic Compounds", 4th ed.; Harris, G., Ed.; Eyre and Spottiswoode: London, 1965.

evaporated. The resulting oil was chromatographed by LC on Partisil, using 10% ether in dichloromethane, to obtain the ketone **10** (1.4 mg, 94% theoretical): IR (film) 2200, 1710 cm^{-1}, ^1H NMR (CCl_4) δ 1.02 (t, 3 H, J = 7 Hz), 1.71 (m, 2 H), 2.34 (m, 6 H), 5.56 (d, 1 H, J = 10 Hz), 5.81 (d, 1 H, J = 16 Hz), 6.06 (dt, 1 H, J = 10, 7, 7 Hz), 6.07 (d, 1 H, J = 7 Hz), 6.35 (dd, 1 H, J = 11, 7 Hz), 7.08 (dd, 1 H, J = 16, 11 Hz); mass spectrum, m/z 262/260, 233/231.

Oxidation of Alcohol 7. By the experimental procedure described above, the alcohol **7** (2.1 mg, 0.008 mmol) was oxidized to the ketone **11** (1.4 mg, 67% theoretical): IR (film) 2200, 1710 cm^{-1}; ^1H NMR (CCl_4) δ 1.02 (t, 3 H, J = 7 Hz), 1.71 (m, 2 H), 2.34 (m, 6 H), 5.56 (d, 1 H, J = 10 Hz), 5.71 (m, 1 H), 6.07 (dt, 1 H, J = 10, 7, 7 Hz), 6.22 (m, 1 H), 6.88 (m, 2 H); mass spectrum, m/z 262/260, 233/231.

Oxidation of Alcohol 9. By the experimental procedure described above, the alcohol **9** (2.9 mg, 0.011 mmol) was oxidized to the ketone **12** (2.6 mg, 90% theoretical): IR (film) 2200, 1710 cm^{-1}; ^1H NMR (CCl_4) δ 1.02 (t, 3 H, J = 7 Hz), 1.39 (m, 2 H), 1.57 (m, 4 H), 2.34 (m, 6 H), 5.72 (dd, 1 H, J = 16, 1 Hz), 6.05 (dd, 1 H, J = 7, 1 Hz), 6.33 (ddd, 1 H, J = 11, 7, 1 Hz), 7.03 (ddd, 1 H, J = 16, 11, 1 Hz); mass spectrum, m/z 264/262, 235/233.

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Registry No. **1**, 76480-28-9; **2**, 76480-29-0; **3**, 76480-30-3; **4**, 76480-31-4; **5**, 76480-32-5; **6**, 76480-33-6; **7**, 76480-34-7; **8**, 76480-35-8; **9**, 76480-36-9; **10**, 76480-37-0; **11**, 76480-38-1; **12**, 76480-39-2; 2-hexadecanone, 18787-63-8.