Notes

Chlorinated Acetylenes from the San Diego Sponge *Haliclona lunisimilis*

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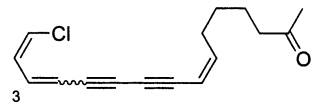
The sponge *Haliclona lunisimilis* from Point Loma, California, contained six known chlorinated acetylenes, previously isolated from the dorid nudibranch *Diaulula sandiegensis*, and three new metabolites, (1*Z*,3*Z*)-1-chlorohexadeca-1,3-diene-5,7-diyne-14-ol, (1*Z*,3*E*,9*Z*)-15-acetoxy-1-chlorohexadeca-5,7-diyne-1,3,9-triene, and (1*Z*,3*E*)-14-acetoxy-1-chlorohexadeca-1,3-diene-5,7-diyne. The structures of the new compounds were elucidated by interpretation of spectroscopic data. The relationship between the sponge metabolites and the nudibranch metabolites is discussed.

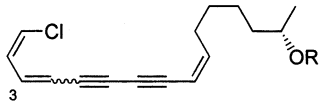
In 1981, we reported the isolation of nine chlorinated acetylenes (**1**−**9**) from the dorid nudibranch *Diaulula sandiegensis* that had been collected off Point Loma, San Diego, at a depth of −15 m.[1] On the basis of the known feeding preferences of dorid nudibranchs, we suspected that the chlorinated acetylenes had been produced by a sponge and concentrated by the nudibranch for use in a defensive secretion.[2−4] For nearly 20 years we searched sporadically for the source of these metabolites, without success, presumably because the nudibranchs were consuming the majority of the chlorinated acetylene-producing sponges in the area. From approximately the same location at Pt. Loma (−15 m), we recently collected specimens of *Haliclona lunisimilis* that contained six of the chlorinated acetylenes (**3**−**7**, **9**) found previously in *D. sandiegensis*, together with three new chlorinated acetylenes (**10**−**12**).

The ethyl acetate-soluble fraction from a methanolic extract of the sponge *H. lunisimilis* was dissolved in toluene and rapidly filtered through a short column of silica gel. The resulting yellow oil was fractionated by preparative and semipreparative HPLC to obtain the known metabolites (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**3**), (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**4**), (1*E*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**5**), (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-14-ol (**6**), (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-14-ol (**7**), and (1*Z*,3*E*)-1-chlorohexadeca-1,3-diene-5,7-diyne-14-ol (**9**), together with three new metabolites, (1*Z*,3*Z*)-1-chlorohexadeca-1,3-diene-5,7-diyne-14-ol (**10**), (1*Z*,3*E*,9*Z*)-15-acetoxy-1-chlorohexadeca-5,7-diyne-1,3,9-triene (**11**), and (1*Z*,3*E*)-14-acetoxy-1-chlorohexadeca-1,3-diene-5,7-diyne (**12**). The optical rotations and ^{13}C NMR spectra of the known acetylenes **3**−**7** and **9** are reported for the first time.

(1*Z*,3*Z*)-1-Chlorohexadeca-1,3-diene-5,7-diyne-14-ol (**10**) was isolated as a pale yellow oil, $[\alpha]_D$ −9.7 (*c* 1.6, CH_2Cl_2). The molecular formula, $C_{16}H_{21}ClO$, was determined by high-resolution mass measurement of the M^+ ion at *m/z* 264.1280 (Δ −0.1 mmu), which is isomeric with that of (1*Z*,3*E*)-1-chlorohexadeca-1,3-diene-5,7-diyne-14-ol (**9**). The

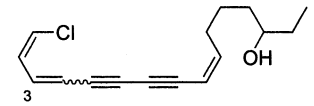


1 (3*E*)
2 (3*Z*)

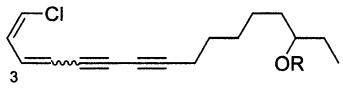


3 (3*E*), R = H
4 (3*Z*), R = H
11 (3*E*), R = Ac

5 R_1 = H, R_2 = OH
8 R_1 = OH, R_2 = H



6 (3*E*)
7 (3*Z*)



9 (3*E*), R = H
10 (3*Z*), R = H
12 (3*E*), R = Ac

IR spectrum contained bands at 3385 (hydroxyl) and 2228 cm^{-1} (acetylene). The UV spectrum showed absorptions at 318 (ε 40 600), 300 (ε 40 000), 243 (ε 38 200), and 233 (ε 16 700) nm, similar to those recorded for compound **9**. The ^{13}C NMR spectrum contained four olefinic signals, four acetylenic signals, a −CHOH− signal, five methylene signals, and a methyl signal. The two olefin and two

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acetylene groups account for all six unsaturation equivalents required by the molecular formula. The COSY spectrum showed that the terminal methyl signal at δ 0.83 (3H, t, $J = 7$ Hz) was coupled to a methylene signal at ca. 1.25 ppm, which was in turn coupled to a signal at δ 3.18 (1H, quintet, $J = 6$ Hz). This placed the hydroxyl group at C-14 and was confirmed by HMBC correlations from the methyl signal to signals at δ 30.8 (C-15) and 72.0 (C-14). Since the ^{1}H and ^{13}C NMR spectra rule out the presence of a terminal acetylene, the other end of the molecule must be occupied by a chlorovinyl group. The coupling constants of the olefinic signals in the ^{1}H NMR spectrum of **10** were difficult to determine because the H-2 and H-3 signals were at almost the same chemical shift, a feature of other 1*Z*,3*Z* isomers,[1] and gave rise to second-order spectra. By recording the ^{1}H spectra in different solvents and at both 300 and 400 MHz, we were able to obtain the approximate chemical shifts and coupling constants using the NMR-Simul simulation program. The coupling constants, $J_{1,2} = 6.5$ Hz and $J_{3,4} < 10$ Hz, that were obtained in this manner were appropriate for the 1*Z*,3*Z* isomer. The HMBC data confirmed the assignment of the two acetylene groups (C-5 to C-8) adjacent to the olefins and a linear chain of methylene groups from C-9 to C-13, completing the structural elucidation of (1*Z*,3*Z*)-1-chlorohexadeca-1,3-diene-5,7-diyne-14-ol (**10**).

(1*Z*,3*E*,9*Z*)-15-Acetoxy-1-chlorohexadeca-5,7-diyne-1,3,9-triene (**11**) was obtained in about 90% purity as a yellow oil, $[\alpha]_D$ +8.4. The molecular formula, $C_{18}H_{21}ClO_2$, was determined by high-resolution mass measurement of the $[M + NH_4]^+$ ion at *m*/*z* 322.1574 (Δ +0.1 mmu). The IR spectrum contained bands at 2195 (acetylene) and 1730 cm^{-1} (ester). The UV spectrum showed absorptions at 345 (ϵ 43 400), 322 (ϵ 54 300), 303 (ϵ 43 200), 271 (ϵ 36 300), and 256 nm (ϵ 36 600), which are similar to those reported for the 1-chloro-5,7-diyne-1,3,9-trienes.[1] The ^{1}H NMR spectrum (benzene-d_6) contained a methyl signal at δ 1.05 (3H, d, $J = 6$ Hz), which was coupled to a signal at 4.91 (1H, sextet, $J = 6$ Hz), and a second methyl signal at 1.70 (3H, s), which was assigned to an acetate group. The signals at δ 4.91 and 1.70 both showed HMBC correlations to an ester carbonyl signal at δ 169.6, indicating the presence of a 15-acetoxy group. Comparison of the ^{1}H NMR spectrum and particularly the coupling constants of the olefinic protons with those of alcohols **3**, **4**, and **5** clearly indicated the 1*Z*,3*E*,9*Z* geometry. The structure was confirmed by acetylation of alcohol **3** to obtain (1*Z*,3*E*,9*Z*)-15-acetoxy-1-chlorohexadeca-5,7-diyne-1,3,9-triene (**11**).

(1*Z*,3*E*)-14-Acetoxy-1-chlorohexadeca-1,3-diene-5,7-diyne (**12**) was obtained in about 90% purity as a pale yellow oil, $[\alpha]_D$ +13.6. The molecular formula, $C_{18}H_{23}ClO_2$, was determined by high-resolution mass measurement of the $[M + NH_4]^+$ ion at *m*/*z* 324.1721 (Δ −0.9 mmu). The IR spectrum contained bands at 2225 (acetylene) and 1730 cm^{-1} (ester). The UV spectrum showed absorptions at 319 (ϵ 40 200), 300 (ϵ 38 700), 240 (ϵ 24 600), and 225 nm (ϵ 21 000), which are similar to those reported for the 1-chloro-1,3-diene-5,7-diynes.[1] The ^{1}H NMR spectrum (benzene-d_6) contained a methyl signal at δ 0.81 (3H, t, $J = 7$ Hz) that was coupled to a methylene signal at 1.40 (2H, m), which was in turn coupled to a signal at 4.89 (1H, pentet, $J = 6$ Hz). A methyl signal at 1.74 (3H, s) was assigned to an acetate group. HMBC correlations from the signals at δ 1.74 and 4.89 to the ester carbonyl signal at δ 169.8 indicated a 14-acetoxy group. Comparison of the NMR spectra with those of **9** and **10** suggested that **12** contained a (1*Z*,3*E*)-1-chloro-1,3-diene-5,7-diyne moiety. The structure was confirmed by acetylation of alcohol **9** to obtain (1*Z*,3*E*)-14-acetoxy-1-chlorohexadeca-1,3-diene-5,7-diyne (**12**).

We did not previously have the opportunity to determine the absolute stereochemistry of any of the chlorinated acetylenes. We therefore chose to establish the absolute stereochemistry of the major metabolite using two methods. Catalytic hydrogenation of chlorinated acetylene **3** gave (*S*)-2-hexadecanol, $[\alpha]_D$ +12.1 (lit.[5] $[\alpha]_D$ +5.6), in 60% yield after chromatography.[6] Since the magnitude of the optical rotation was not identical to that in the literature, we decided to confirm the absolute stereochemistry of **3** by using Mosher's method. The (*R*)- and (*S*)-MTPA esters of **3** were prepared using (*S*)- and (*R*)-α-MTPA chlorides in dry pyridine. Analysis of the $\Delta\delta$ values confirmed the *S* absolute stereochemistry. Since all of the alcohols in this series gave optical rotations of the same sign (−ve), we consider it most likely that the *S* absolute stereochemistry prevails for all alcohols in this series.[6] Interestingly, acetylation of alcohols **3** and **9** caused the sign of the optical rotation to change from negative in alcohols **3** and **9** to positive in acetates **11** and **12**.

It is interesting that ketones **1** and **2**, which are the major metabolites of the dorid nudibranch *D. sandiegensis*, were not found in the sponge *H. lunisimilis*, which contained all but one of the other metabolites found in the nudibranch. This suggests that the ketones **1** and **2** are synthesized by the nudibranch from the corresponding alcohols **3** and **4**, which are found in the sponge. Oxidation or reduction of dietary metabolites by opistobranch molluscs for the purpose of increasing their defensive properties is not an isolated phenomenon.[7−9]

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Rudolph Research Autopol 3 polarimeter. Infrared spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer, and ultraviolet spectra were recorded on a Varian Cary 50 Bio spectrophotometer. ^{13}C NMR spectra were recorded on a 400 MHz Varian Inova spectrometer, and ^{1}H NMR and two-dimensional spectra were recorded on a 300 MHz Varian Gemini spectrometer. Additional ^{1}H NMR spectra were recorded on a 400 MHz Varian Inova spectrometer as noted. Spectra are reported using residual solvent as an internal reference. High-resolution mass measurements were recorded on a VG 7070 mass spectrometer at the UC Riverside Mass Spectrometry Facility. All solvents were distilled from glass prior to use.

Animal Material. The sponge *Haliclona lunisimilis* de Laubenfels, 1930 was collected by hand using scuba (−15 m) at Point Loma, San Diego, CA. A voucher cup of the specimen has been deposited in the Scripps Institution of Oceanography Benthic Invertebrate Collection (SIO BIC; no. P1183). The sponge matches the description by de Laubenfels 1932 and was identified through comparison with a specimen in the SIO BIC (no. 79-267). This taxonomic assignment is according to the current literature available for the poriferan order Haplosclerida, which has recently been revised.[10] Due to the changes in the order, many of the Halosclerid sponges from the coast of California may also need revision.

Extraction and Isolation. The sponge (500 g wet wt) was twice extracted with methanol (2 × 500 mL), and the combined extracts were concentrated under vacuum to obtain an aqueous suspension that was extracted with ethyl acetate (2 × 200 mL) to obtain a brown oil (1.1 g). A toluene solution of the oil was rapidly filtered through a short column of silica gel using additional toluene. Evaporation of the solvent gave a yellow oil (500 mg) that was subjected to HPLC on a preparative silica column using a gradient of 10%−25% acetone in hexane to obtain 10 fractions. Fraction 10 contained only the known

compound (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**3**, 17.4 mg, 3.48 × 10^{-3}% wet wt).[1] Fraction 8 was purified by HPLC on silica using 10% acetone in hexane to obtain the known compounds (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**4**, 6.2 mg, 1.24 × 10^{-3}% wet wt) and (1*E*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**5**, 1.8 mg, 3.6 × 10^{-4}% wet wt). Fraction 6 was rechromatographed under the same conditions to obtain (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-14-ol (**6**, 5.0 mg, 1.0 × 10^{-3}% wet wt) and (1*Z*,3*E*)-1-chlorohexadeca-1,3-diene-5,7-diyne-14-ol (**9**, 7.6 mg, 1.52 × 10^{-3}% wet wt). Fraction 5 was rechromatographed using the same conditions to obtain (1*Z*,3*Z*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-14-ol (**7**, 6.0 mg, 1.2 × 10^{-3}% wet wt) and (1*Z*,3*Z*)-1-chlorohexadeca-1,3-diene-5,7-diyne-14-ol (**10**, 3.3 mg, 6.6 × 10^{-4}% wet wt, ca. 90% pure). Fraction 4 was rechromatographed by HPLC on silica using 5% acetone in hexane to obtain (1*Z*,3*E*,9*Z*)-15-acetoxy-1-chlorohexadeca-5,7-diyne-1,3,9-triene (**11**, 5.5 mg, 1.1 × 10^{-3}% wet wt) and (1*Z*,3*E*)-14-acetoxy-1-chlorohexadeca-1,3-diene-5,7-diyne (**12**, 2.6 mg, 5.2 × 10^{-4}% wet wt). All fractions were stored in the dark in acetone under nitrogen at −10 °C. All known compounds were identified by comparison of their UV and ^{1}H NMR data with those recorded previously.

(1*Z*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (3): $[\alpha]_D$ −6.8 (*c* 1.0, CH_2Cl_2); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.7 (C-10), 137.7 (C-3), 129.4 (C-2), 122.3 (C-1), 113.9 (C-4), 108.3 (C-9), 81.5 (C-6 or C-7), 81.4 (C-6 or C-7), 78.4 (C-5 or C-8), 78.0 (C-5 or C-8), 67.3 (C-15), 39.9 (C-14), 31.5 (C-11), 29.5 (C-12), 26.1 (C-13), 24.0 (C-16).

(1*Z*,3*Z*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (4): $[\alpha]_D$ −5.1 (*c* 1.0, CH_2Cl_2); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.8 (C-10), 136.2 (C-3), 127.3 (C-2), 124.0 (C-1), 111.8 (C-4), 108.3 (C-9), 82.1 (C-6 or C-7), 81.9 (C-6 or C-7), 79.1 (C-5 or C-8), 77.7 (C-5 or C-8), 67.2 (C-15), 39.9 (C-14), 31.6 (C-11), 29.5 (C-12), 26.1 (C-13), 24.1 (C-16).

(1*E*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (5): $[\alpha]_D$ −4.8 (*c* 1.8, CH_2Cl_2); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.5 (C-10), 141.2 (C-3), 133.6 (C-2), 125.6 (C-1), 111.4 (C-4), 108.3 (C-9), 81.6 (C-6 or C-7), 80.8 (C-6 or C-7), 78.1 (C-5 or C-8), 77.4 (C-5 or C-8), 67.2 (C-15), 39.3 (C-14), 31.5 (C-11), 29.5 (C-12), 26.2 (C-13), 24.0 (C-16).

(1*Z*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-triene-14-ol (6): $[\alpha]_D$ −13.0 (*c* 1.0, CH_2Cl_2); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.8 (C-10), 137.7 (C-3), 129.5 (C-2), 122.4 (C-1), 113.9 (C-4), 108.3 (C-9), 81.5 (C-7 or C-6), 81.4 (C-6 or C-7), 78.4 (C-5), 72.3 (C-8), 65.6 (C-14), 37.3 (C-13), 31.6 (C-11), 31.1 (C-15), 25.7 (C-12), 10.4 (C-16).

(1*Z*,3*Z*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-triene-14-ol (7): $[\alpha]_D$ −18.1 (*c* 1.1, CH_2Cl_2); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.9 (C-10), 136.2 (C-3), 127.2 (C-2), 124.0 (C-1), 111.8 (C-4), 108.3 (C-9), 82.1 (C-6 or C-7), 79.1 (C-6 or C-7), 77.7 (C-5), 72.4 (C-8), 65.4 (C-14), 37.6 (C-13), 31.6 (C-11), 31.1 (C-15), 25.6 (C-12), 10.4 (C-16).

(1*Z*,3*E*)-1-Chlorohexadeca-1,3-diene-5,7-diyne-14-ol (9): $[\alpha]_D$ −14.9 (*c* 1.0, CH_2Cl_2); ^{13}C NMR (100 MHz, acetone-d_6) δ 137.4 (C-3), 128.5 (C-2), 121.9 (C-1), 114.2 (C-4), 87.6 (C-6), 79.2 (C-8), 74.4 (C-5), 72.5 (C-14), 65.6 (C-7), 37.7 (C-13), 31.1 (C-15), 29.6 (C-11), 28.9 (C-10), 25.9 (C-12), 19.8 (C-9), 10.4 (C-16).

(1*Z*,3*Z*)-1-Chlorohexadeca-1,3-diene-5,7-diyne-14-ol (10): yellow oil; $[\alpha]_D$ −9.7 (*c* 1.6, CH_2Cl_2); IR (CH_2Cl_2) 3385, 2228, 1315 cm^{-1}; UV (CH_2Cl_2) 318 (ϵ 40 600), 300 (ϵ 40 000), 243 (ϵ 38 200), and 233 nm (ϵ 16 700); ^{1}H NMR (300 MHz, benzene-d_6) δ 0.83 (3H, t, *J* = 7 Hz, H-16), 1.15−1.17 (4H, m, H-11, H-13), 1.19 (2H, m, H-12), 1.24−1.26 (4H, m, H-10, H-15), 1.98 (2H, t, *J* = 7 Hz, H-9), 3.18 (1H, quintet, *J* = 6 Hz, H-14), 5.23 (1H, br d, *J* = 7.5 Hz, H-4), 5.54 (1H, br d, *J* = 6.5 Hz, H-1), 6.64 (1H, dd, *J* = 11, 6.5 Hz, H-2), 6.67 (1H, dd, *J* = 11, 7.5 Hz, H-3); (400 MHz, acetone-d_6) δ 0.83 (3H, t, *J* = 7 Hz, H-16), 1.15−1.17 (4H, m, H-11, H-13), 1.19 (2H, m, H-12), 1.24−1.26 (4H, m, H-10, H-15), 2.50 (2H, t, *J* = 7 Hz, H-9), 3.20 (1H, quintet, *J* = 6 Hz, H-14), 5.81 (1H, br d, *J* = 9.5 Hz, H-4), 6.48 (1H, br d, *J* = 6.5 Hz, H-1), 6.89 (1H, dd, *J* = 11, 6.5 Hz, H-2), 6.95 (1H, dd, *J* = 11, 9.5 Hz, H-3); ^{13}C NMR (100 MHz, benzene-d_6) δ 135.5 (C-3), 126.9 (C-2), 123.1 (C-1), 111.6 (C-4), 87.8 (C-6), 82.2 (C-8), 72.0 (C-14), 71.5 (C-5), 64.9 (C-7), 37.3 (C-13), 30.8 (C-15), 29.3 (C-11), 28.6 (C-10), 25.6 (C-12), 19.9 (C-9), 10.3 (C-16); HRMS, M^+ *m*/*z* 264.1280 (calcd for $C_{16}H_{21}ClO$, 264.1281).

(1*Z*,3*E*,9*Z*)-15-Acetoxy-1-chlorohexadeca-5,7-diyne-1,3,9-triene (11): pale yellow oil; $[\alpha]_D$ +8.4 (*c* 2.7, CH_2Cl_2); IR (CH_2Cl_2) 2195, 1730, 1605, 1245 cm^{-1}; UV (CH_2Cl_2) 345 (ϵ 43 400), 322 (ϵ 54 300), 303 (ϵ 43 200), 271 (ϵ 36 300), and 256 nm (ϵ 36 600); ^{1}H NMR (300 MHz, benzene-d_6) δ 1.05 (3H, d, *J* = 6 Hz, H-16), 1.15−1.20 (4H, m, H-12, H-13), 1.38 (2H, m, H-14), 1.70 (3H, s, −OAc), 2.20 (2H, q, *J* = 7 Hz, H-11), 4.91 (1H, sextet, *J* = 6 Hz, H-15), 5.32 (1H, d, *J* = 15 Hz, H-4), 5.38 (1H, d, *J* = 11 Hz, H-9), 5.40 (1H, br d, *J* = 9 Hz, H-1), 5.53 (1H, dd, *J* = 10, 9 Hz, H-2), 5.65 (1H, dt, *J* = 11, 7 Hz, H-10), 7.05 (1H, dd, *J* = 15, 10 Hz, H-3); ^{13}C NMR (100 MHz, benzene-d_6) δ 169.6 (−O*C*OCH$_3$), 148.4 (C-10), 137.0 (C-1), 128.7 (C-3), 121.3 (C-2), 113.4 (C-9), 108.4 (C-4), 81.7 (C-7), 81.4 (C-6), 79.3 (C-5), 79.0 (C-8), 70.6 (C-15), 36.1 (C-14), 30.9 (C-11), 28.9 (C-12), 25.4 (C-13), 20.9 (−OCO*C*H$_3$), 20.0 (C-16); HRMS, $[M + NH_4]^+$ *m*/*z* 322.1575 (calcd for $C_{18}H_{25}ClNO_2$, 322.1574).

(1*Z*,3*E*)-14-Acetoxy-1-chlorohexadeca-1,3-diene-5,7-diyne (12): pale yellow oil; $[\alpha]_D$ +13.6 (*c* 1.3, CH_2Cl_2); IR (CH_2Cl_2) 2225, 1730, 1245 cm^{-1}; UV (CH_2Cl_2) 319 (ϵ 40 200), 300 (ϵ 38 700), 240 (ϵ 24 600), and 225 nm (ϵ 21 000); ^{1}H NMR (300 MHz, benzene-d_6) δ 0.81 (3H, t, *J* = 7 Hz, H-16), 1.08−1.14 (4H, m, H-11, H-12), 1.20 (2H, m, H-10), 1.33 (2H, m, H-13), 1.40 (2H, m, H-15), 1.74 (3H, s, −OAc), 1.94 (2H, t, *J* = 7 Hz, H-9), 4.89 (1H, quintet, *J* = 6 Hz, H-14), 5.33 (1H, br d, *J* = 15 Hz, H-4), 5.40 (1H, br d, *J* = 7.5 Hz, H-1), 5.58 (1H, dd, *J* = 10, 7.5 Hz, H-2), 7.06 (1H, dd, *J* = 15, 10 Hz, H-3); ^{13}C NMR (100 MHz, benzene-d_6) δ 169.8 (−O*C*OCH$_3$), 137.1 (C-3), 128.9 (C-2), 121.0 (C-1), 113.9 (C-4), 87.1 (C-6), 80.1 (C-8), 75.1 (C-14), 74.7 (C-5), 66.6 (C-7), 34.0 (C-13), 29.1 (C-10), 28.5 (C-11), 27.6 (C-15), 25.4 (C-12), 21.0 (−OCO*C*H$_3$), 19.9 (C-9), 10.0 (C-16); HRMS, $[M + NH_4]^+$ *m*/*z* 324.1721 (calcd for $C_{18}H_{27}ClNO_2$, 324.1730).

Acetylation of Acetylenic Alcohols 3 and 9. (1*Z*,3*E*,9*Z*)-1-Chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**3**, 2.0 mg, 0.0076 mmol) and (1*Z*,3*E*)-1-chlorohexadeca-1,3-diene-5,7-diyne-14-ol (**9**, 2.0 mg, 0.0076 mmol) were each dissolved in pyridine (0.5 mL) containing acetic anhydride (0.1 mL). After 16 h, the reactions were quenched with cold water (10 mL). The resulting aqueous solutions were passed through short columns of HP-20SS resin, which were washed with water and eluted with acetone. Evaporation of the acetone fractions gave the acetates **11** (∼2 mg) and **12** (∼2 mg), respectively, which were identical in all respects, including optical rotations, to the natural products.

Catalytic Hydrogenation of Acetylenic Alcohol 3. A solution of (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**3**, 6.0 mg, 0.023 mmol) in methanol (1 mL) containing 10% palladium on charcoal catalyst (2.0 mg) was stirred under an atmosphere of hydrogen for 16 h. The solution was filtered to remove the catalyst, and the solvent was evaporated. The residual oil was chromatographed on a short column of silica gel to obtain 2-hexadecanol (3.3 mg, 60% yield): $[\alpha]_D$ +12.1 (*c* 1.3 CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, 3H, *J* = 7 Hz), 1.17 (d, 3H, *J* = 6 Hz), 1.22−1.28 (br, 26H), 1.40 (m, 2H), 1.52 (m, 2H), 3.77 (sextet, 1 H, *J* = 6 Hz); EIMS, *m*/*z* 225 $[M - OH]^+$.

Preparation of the (*R*)- and (*S*)-MTPA Esters of Acetylenic Alcohol 3. To solutions of (1*Z*,3*E*,9*Z*)-1-chlorohexadeca-5,7-diyne-1,3,9-triene-15-ol (**3**, 2.5 mg, 0.0095 mmol) in dry pyridine (75 μL) was added either (*R*)- or (*S*)-α-methoxy-α-trifluoromethylphenylacetyl chloride (10 μL, 5 molar excess). Each solution was capped and allowed to stand for 24 h, after which time 3-(dimethylamino)propylamine was added. The solutions were allowed to stand for a further 10 min, and the solvents were then evaporated under vacuum. The residues were dissolved in ether, and the resulting solutions were filtered through a silica plug to obtain the (*S*)- and (*R*)-MTPA esters, respectively.

(*S*)-MTPA ester of acetylenic alcohol 3: Selected ^{1}H NMR signals (400 MHz, acetone-d_6) δ 1.36 (d, 3H, *J* = 6 Hz,

H-16), 1.62 (m, 2H, H-14), 2.28 (q, 2H, $J = 7$ Hz, H-11), 5.17 (sextet, 1H, $J = 6$ Hz, H-15), 5.65 (d, 1H, $J = 11$ Hz, H-9), 6.17 (dt, 1H, $J = 11, 7$ Hz, H-10).

(*R*)-MTPA ester of acetylenic alcohol 3: Selected ^{1}H NMR signals (400 MHz, acetone-d_6) δ 1.27 (d, 3H, $J = 6$ Hz, H-16), 1.70 (m, 2H, H-14), 2.37 (q, 2H, $J = 7$ Hz, H-11), 5.17 (sextet, 1H, $J = 6$ Hz, H-15), 5.68 (d, 1H, $J = 11$ Hz, H-9), 6.23 (dt, 1H, $J = 11, 7$ Hz, H-10).

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Supporting Information Available: Copies of the ^{1}H and ^{13}C NMR spectra of the acetylenes **10**−**12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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