First Total Synthesis of (–)-Caulerpenynol

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General Experimental Methods.

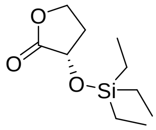
All reactions sensitive to oxygen and moisture were carried out in oven-dried glassware under a slight positive pressure of argon unless otherwise noted.

^{1}H NMR and ^{13}C NMR spectra were recorded on a AC300 or AC500 using the deuterated solvent as internal deuterium lock. Chemical shift data are given in units δ relative to residual protic solvent where δ (chloroform) = 7.26 ppm and δ (benzene) = 7.16 ppm. The multiplicity of a signal is indicated as: br - broad, s - singlet, d - doublet, t - triplet, q - quartet, m - multiplet, dd - doublet of doublets, dt - doublet of triplets, etc. Coupling constants (*J*) are quoted in Hz and recorded to the nearest 0.1 Hz. ^{13}C NMR Spectra were recorded on a AC300 or AC500 spectrometer using the deuterated solvent as internal deuterium lock. Chemical shift data are given in units δ relative to residual protic solvent where δ (chloroform) = 77.16 ppm and δ (benzene) = 128.06 ppm. NMR Spectra were assigned using information ascertained from DEPT, HMQC and NOE experiments.

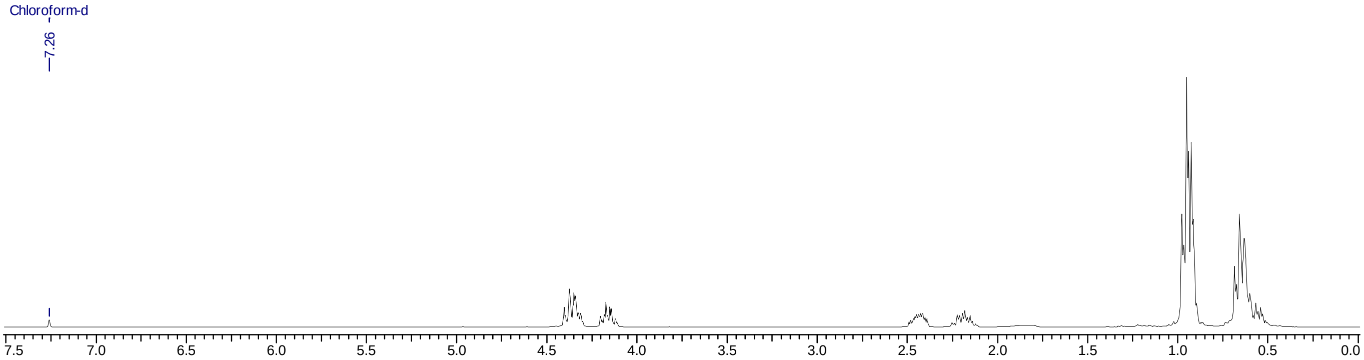
Reagents and solvents were commercial grades and were used as supplied. Dichloromethane, hexane, *N*,*N*dimethylformamide and toluene were distilled from calcium hydride and stored over molecular sieves 4 Å. THF and diethyl ether were distilled from sodium benzophenone prior to use. Triethyl and Pyridine were distilled from KOH prior to use.

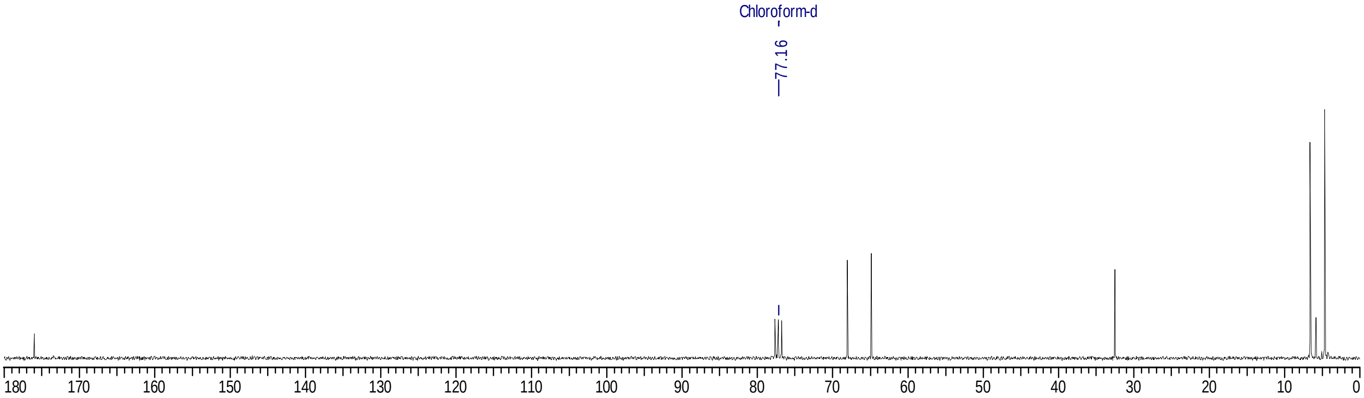
Mass spectra (MS) were performed with a triple quadrupole system with a pneumatically assisted electrospray interface. High resolution mass spectra (HRMS) have been performed using a mass spectrometer equipped with a pneumatically assisted atmospheric pressure ionization. The sample was ionized in positive mode electrospray in the following conditions: electrospray voltage (ISV): 5500 V; orifice voltage (OR): 70 V; nebulising gas flow pressure (air): 0.6 psi. The mass spectrum was obtained using a time of flight analyzer (TOF). The measure was realized in triplicate. The sample was dissolved in methanol (500 μL) then diluted (dilution factor 4/10000) in a methanolic solution of ammonium acetate (3 mM). The sample solution was infused in the ionization source at a 5 μL/min flow rate.

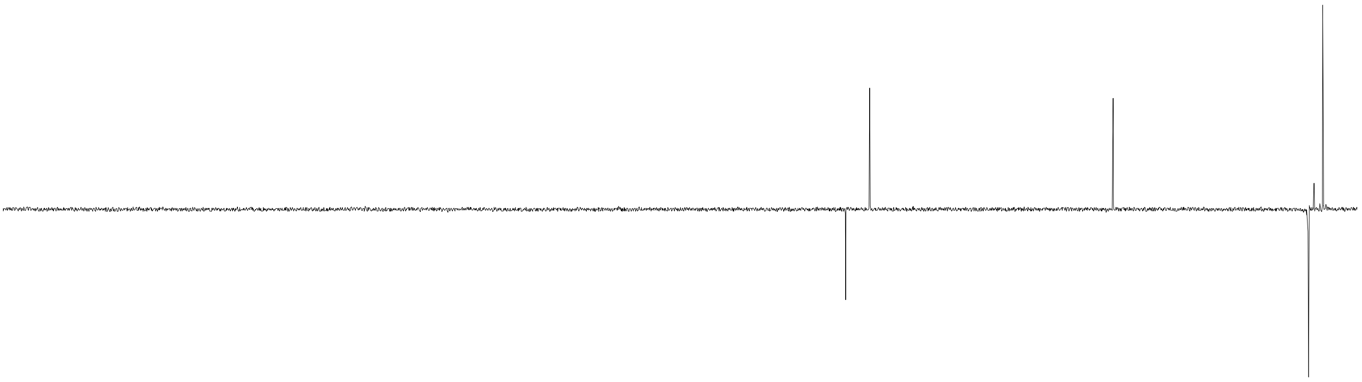
Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F254. Flash column chromatography was performed on Merck Kieselgel 60 (230–400 mesh).

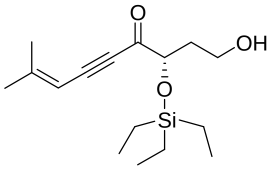


(*S*)-3-Triethylsilanyloxy-dihydro-furan-2-one (7). To a stirred solution of alcohol **6** (2.5 g, 24.48 mmol) in DMF (23 mL) was added imidazol (3.67 g, 53.87 mmol), DMAP (299 mg, 2.45 mmol) and TESCl (4.98 mL, 29.38 mmol). The solution was stirred at room temperature for 5 hours then quenched with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with saturated aqueous NaCl solution, dried over Na_2SO_4 then concentrated under vacuum. The crude product was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-Et_2O, 7/3 to 6/4) to give **7** (5.3 g) in quantitative yield. $[\alpha]^{22}_{D}$ −36.3 (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.60-0.69 (6H, m, 3 x $CH_{2,}$), 0.90-0.98 (9H, m, 3 x CH_3), 2.11-2.25 (1H, m, CH_2), 2.39-2.49 (1H, m, CH_2), 4.11-4.20 (1H, m, CH_2), 4.30-4.40 (2H, m, CH_2 and CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.7 (3 x CH_2), 6.6 (3 x CH_3), 32.5 (CH_2), 64.8 (CH_2), 68.00 (CH), 176.00 (C); HRMS (ESI) calcd for $C_{10}H_{24}NO_3Si$ $[M+NH_4]^+$: 234.1519 found 234.1515

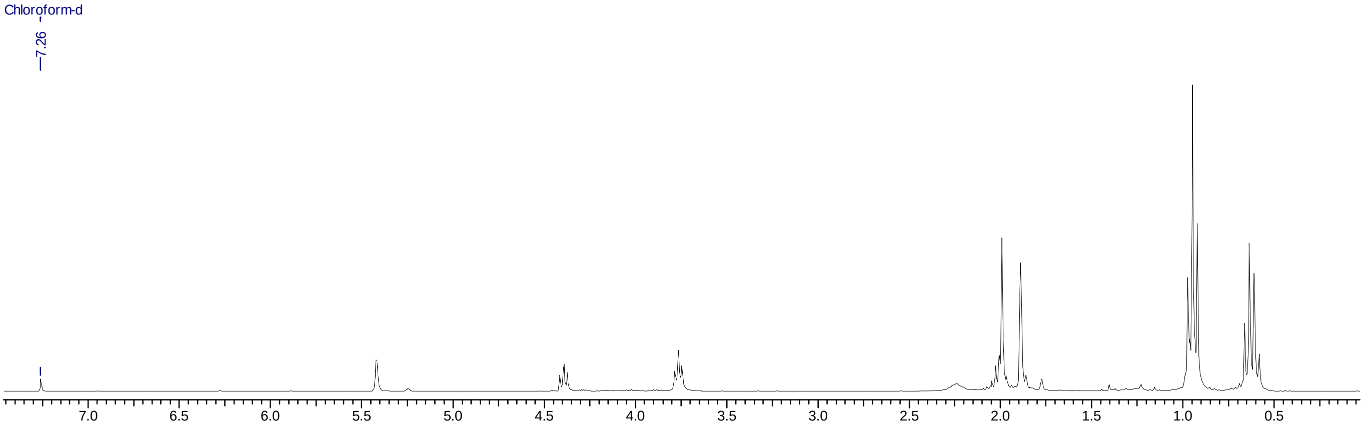


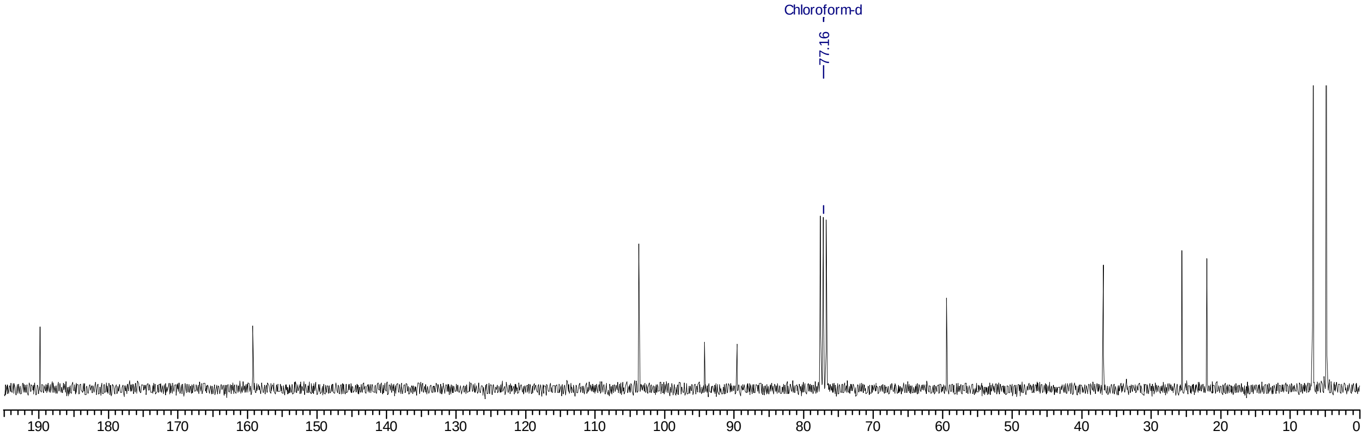


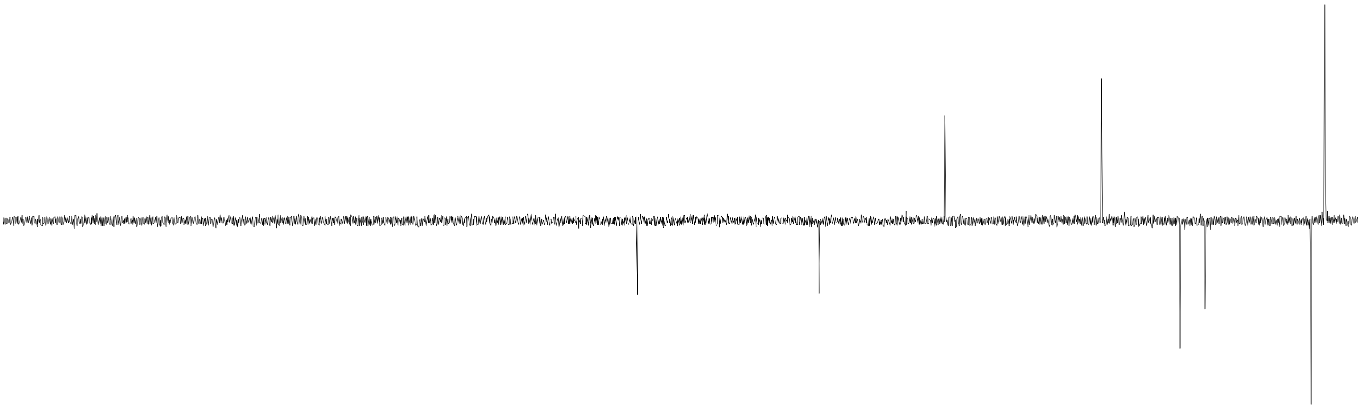


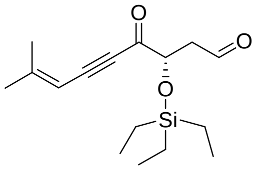


(*S*)-1-Hydroxy-8-methyl-3-(triethylsilyloxy)non-7-en-5-yn-4-one (8). To a solution of 1,1-dibromo-4-methylpent-1,3-diene (7.31 g, 30.46 mmol) in THF (130 mL) was added dropwise, at –78 °C, *n*-butyllithium (2.5 M, 24.4 mL, 61 mmol). The solution was stirred at –78 °C for 1.5 h. then transferred *via* canula to the lactone **7** (6 g, 27.73 mmol) in THF (130 mL) at –78 °C. After warming to -20 °C, the mixture was quenched with a 9/1 mixture of saturated aqueous NH_4Cl solution and aqueous 33% NH_4OH solution. The aqueous phase was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered then concentrated under vacuum. The crude alcohol was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-Et_2O, 7/3 to 6/4) to give **8** (5.04 g) in 61% yield. $[\alpha]^{22}_{D}$ –56.3 (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.63 (6H, q, *J* = 7.9 Hz, 3 x CH_2), 0.95 (9H, t, *J* = 7.9 Hz, 3 x CH_3), 1.89 (3H, br s, CH_3), 1.99 (3H, br s, CH_3), 1.97-2.05 (2H, m, CH_2), 2.24 (1H, m, OH), 3.76 (2H, t, *J* = 5.6 Hz, CH_2), 4.39 (1H, br dd, *J* = 5.1 and 6.8 Hz, CH), 5.42 (1H, br s, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.8 (3 x CH_2), 6.8 (3 x CH_3), 22.0 (CH_3), 25.6 (CH_3), 36.9 (CH_2), 59.4 (CH_2), 77.5 (CH, C3), 89.6 (C), 94.3 (C), 103.7 (CH), 159.2 (C), 189.8 (C); HRMS (ESI) calcd for $C_{16}H_{29}O_3Si$ $[M+H]^+$: 297.1880 found 297.1879

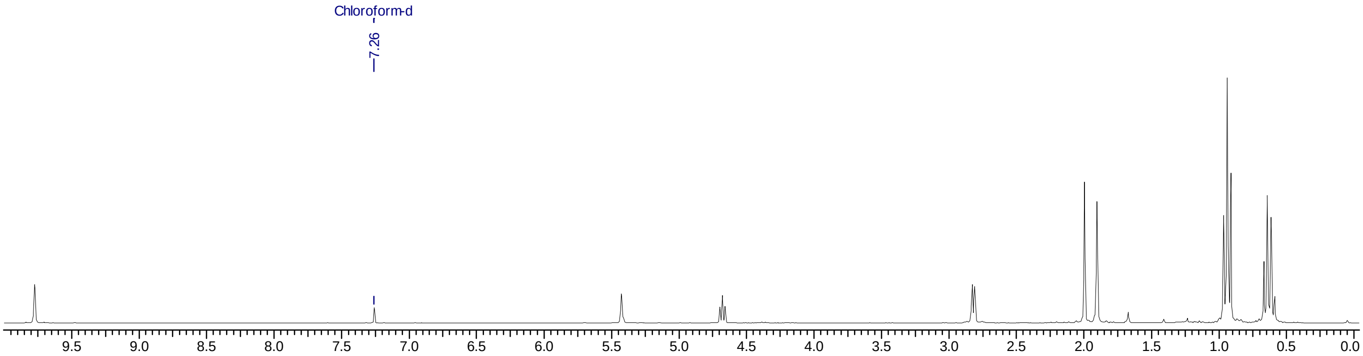


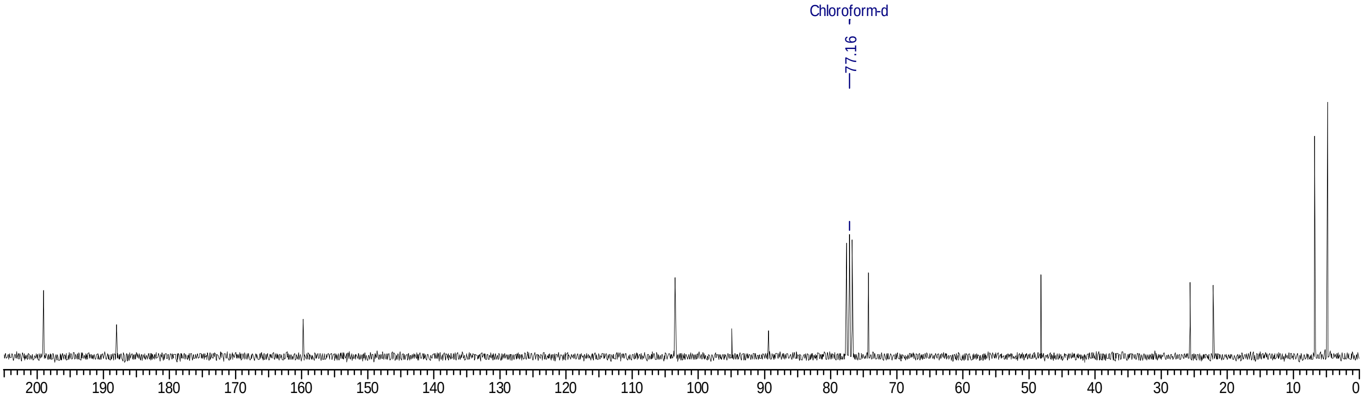


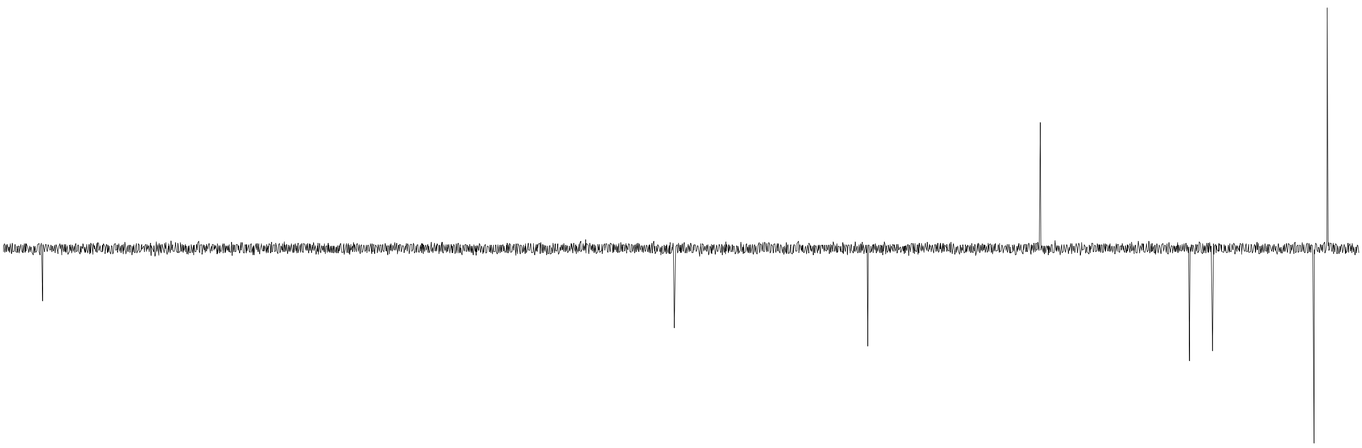


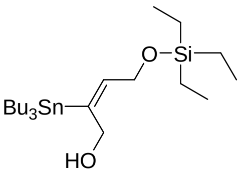


(*S*)-8-Methyl-4-oxo-3-(triethylsilyloxy)non-7-en-5-ynal (9). To a stirred solution of alcohol **8** (1.5 g, 5.06 mmol) in DCM (45 mL) was added at 0°C Dess-Martin périodinane (2.55 g, 6.04 mmol). The mixture was stirred at r.t. and followed by TLC. After disappearance of starting material (2 hours), the solution was poured into a saturated aqueous $Na_2S_2O_3$ / $NaHCO_3$ solution (255 mL, 1/1). After stirring for 10 mn, the layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 then concentrated under vacuum. The crude aldehyde was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-Et_2O, 8/2) to give **9** (1.27 g) in 85% yield. $[\alpha]^{20}_{D}$ –46.4 (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.63 (6H, q, *J* = 8.0 Hz, 3 x CH_2), 0.94 (9H, t, *J* = 8.0 Hz, 3 x CH_3), 1.91 (3H, s, CH_3), 2.00 (3H, s, CH_3), 2.80-2.83 (2H, m, CH_2), 4.68 (1H, br t, *J* = 5.8 Hz, CH), 5.43 (1H, br s, CH), 9.78 (1H, br t, *J* = 1.4 Hz, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.8 (3 x CH_2), 6.8 (3 x CH_3), 22.1 (CH_3), 25.6 (CH_3), 48.2 (CH_2), 74.3 (CH), 89.4 (C), 95.0 (C), 103.6 (CH), 159.8 (C), 188.0 (C), 199.08 (CH); m/z (ESI+) 295 $[M+H]^+$; HRMS (ESI) calcd for $C_{16}H_{27}O_3Si$ $[M+H]^+$: 295.1723 found 295.1723

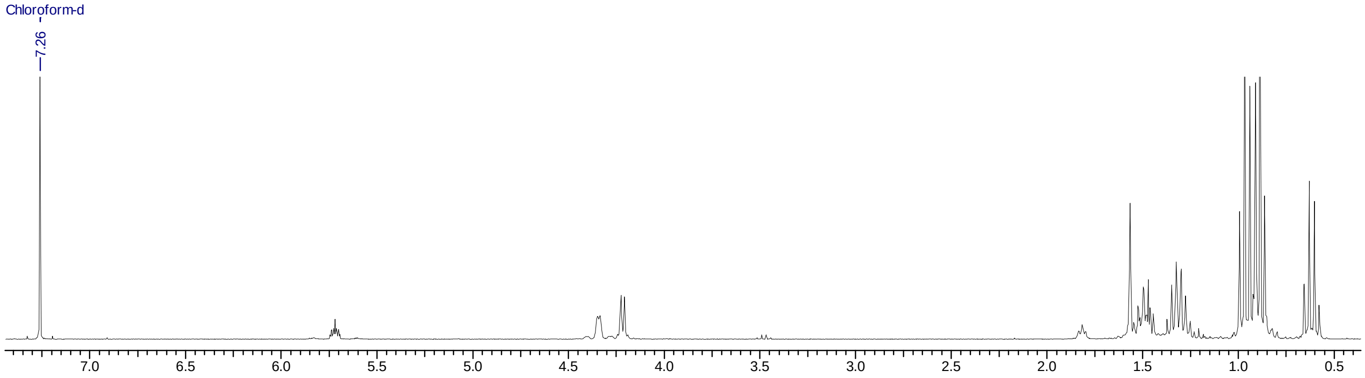


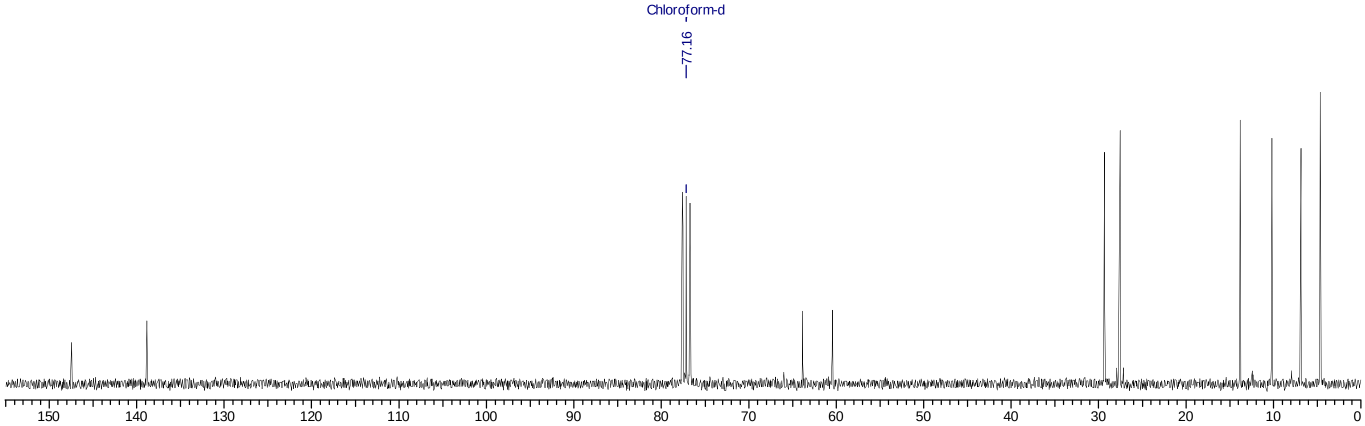


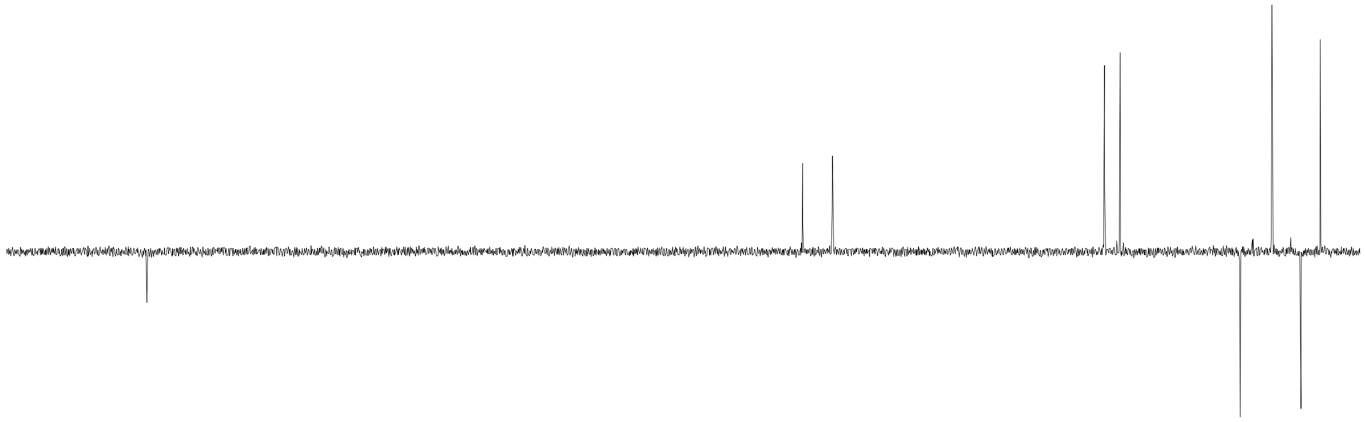


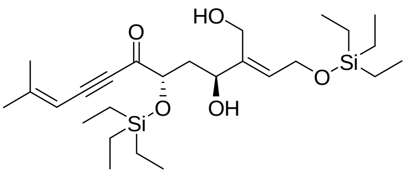


(*E*)-4-Triethylsilyloxy-2-tributylstannyl but-2-en-1-ol (10). To a solution of (*E*)-2-tributylstannylbut-2-en-1-ol (9.66 g, 25.61 mmol) in THF (105 mL) at -20 °C was added NEt_3 (7.13 mL, 51.22 mmol) and triethylsilylchloride (4.33 mL, 25.61 mmol). The solution was stirred at -20 °C and followed by TLC. After disappearance of starting material (4 hours) the reaction was quenched with water and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered and concentrated under vacuum. The crude alcohol was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-Et_2O, 9/1) to give **10** (6.62 g) in 53% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 0.62 (6H, q, J = 7.7 Hz, 3 x CH_2), 0.86-0.99 (24H, m, 6 x CH_3, 3 x CH_2), 1.25-1.37 (6H, m, 6 x CH_2), 1.44-1.55 (6H, m, 6 x CH_2), 1.82 (1H, br t, J = 5.4 Hz, OH), 4.22 (2H, br d, J = 5.5 Hz, $^4J_{Sn,H}$ = 16 Hz, CH_2), 4.34 (2H, m, $^3J_{Sn,H}$ = 37 Hz, CH_2), 5.72 (1H, br t, J = 5.4 Hz, $^3J_{Sn,H}$ = 69 Hz, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.6 (3 x CH_2), 6.9 (3 x CH_3), 7.9 ($^1J_{Sn\text{-}C}$ = 332 Hz, 3 x CH_2), 13.8 (3 x CH_2), 27.2 ($^3J_{Sn\text{-}C}$ = 58 Hz, 3 x CH_2), 29.3 ($^2J_{Sn\text{-}C}$ = 19 Hz, 3 x CH_2), 60.5 (CH_2), 63.8 ($^2J_{Sn\text{-}C}$ = 24 Hz, CH_2), 138.9 ($^2J_{Sn\text{-}C}$ = 19 Hz, CH), 147.5 (C); HRMS (ESI) calcd for $C_{22}H_{49}O_2SiSn$ $[M+H]^+$: 493.2522 found 493.2534

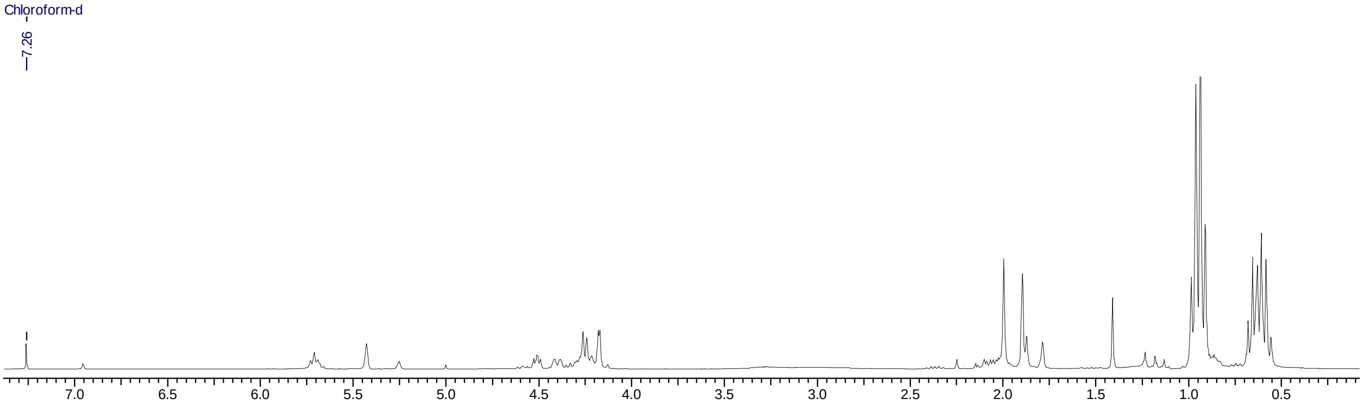


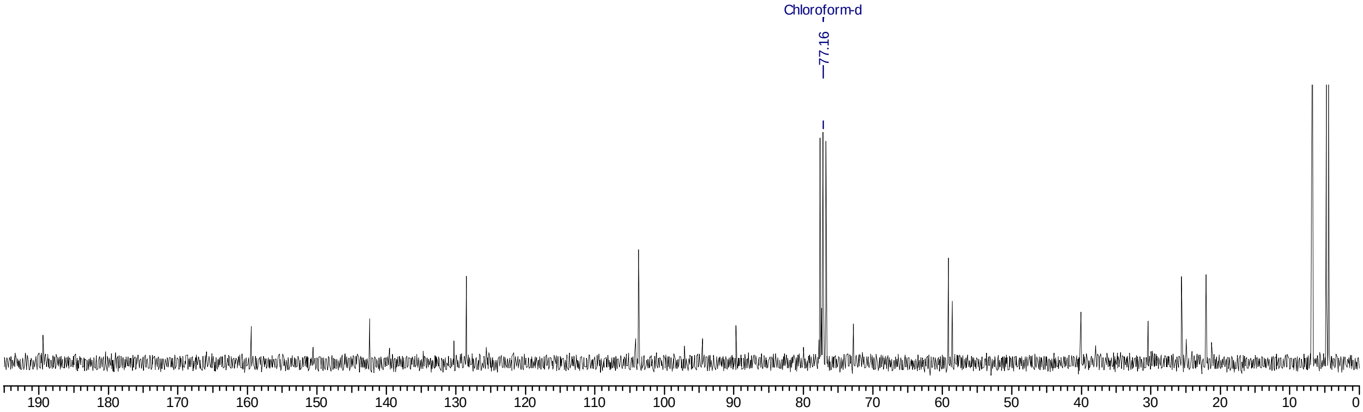


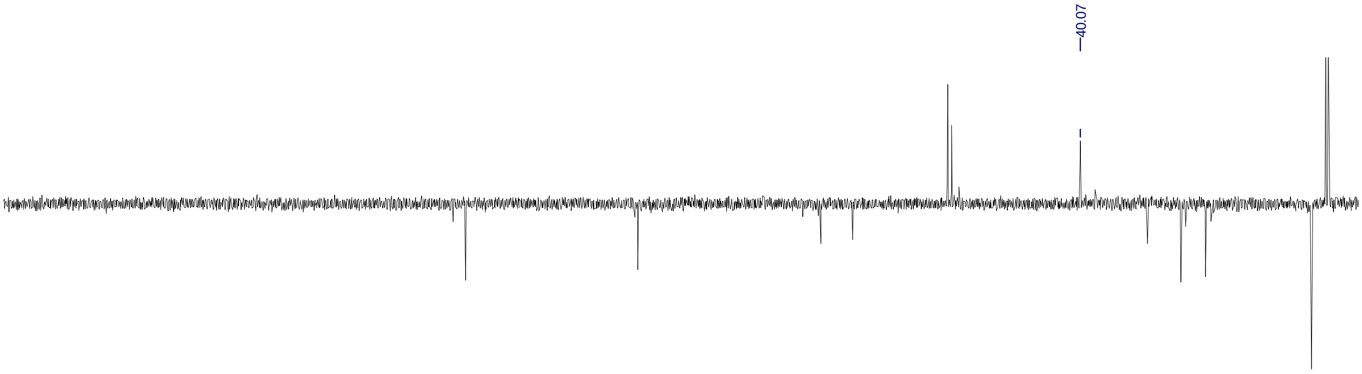


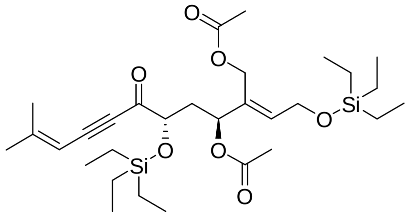


(7*S*,9*S*,*E*)-9-Hydroxy-10-(hydroxymethyl)-2-methyl-7,12-bis(triethylsilyloxy)dodeca-2,10-dien-4-yn-6-one (11). To a solution of vinyl tin **10** (1.08 g, 2.21 mmol) in THF (31 mL) at –78 °C was added dropwise MeLi.LiBr (2.0 mL, 4.41 mmol, 2.2 M in Et_2O). The reaction mixture was warmed to –35 °C. The mixture was then cooled to –78°C and aldehyde **9** (620 mg, 2.1 mmol) diluted in minimum of THF was added dropwise at -78°C. The solution was kept at –78 °C for 1h and quenched with a 9/1 mixture of saturated aqueous NH_4Cl solution and aqueous 33% NH_4OH solution. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography (SiO_2, 3% NEt_3, petroleum ether-Et_2O, 6/4) to give a 7/3 separable mixture of diastereomers **11** (444 mg) in 43% yield. Major diastereomer **11**: $[\alpha]^{21}_{D}$ –32.8 (*c* 1, $CHCl_3$); ^1H NMR of (300 MHz, $CDCl_3$) δ 0.55-0.68 (12H, m, 6 x CH_2), 0.91-0.99 (18H, m, 6 x CH_3), 1.90 (3H, s, CH_3), 2.00 (3H, s, CH_3), 2.00-2.15 (2H,m, CH_2), 4.17 (2H,br d, *J* = 2.5 Hz, CH_2), 4.25 (2H,d, *J* = 5.6 Hz, CH_2), 4.41 (1H,d, *J* = 9.2 Hz, CH), 4.51 (1H, br dd, *J* = 4.3 and 6.6 Hz, CH), 5.43 (1H, br s, CH), 5.71 (1H, t, *J* = 5.6 Hz, CH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 4.4 (CH_2), 4.8 (CH_2), 6.8 (3 x CH_3), 22.0 (CH_3), 25.6 (CH_3), 40.1 (CH_2), 58.6 (CH_2), 59.1 (CH_2), 72.8 (CH), 77.4 (CH), 89.7 (C), 94.5 (C), 103.7 (CH), 128.5 (CH), 142.4 (C), 159.4 (C), 189.4 (C); m/z (ESI+) 514 $[M+NH_4]^+$; HRMS (ESI) calcd for $C_{26}H_{52}NO_5Si_2$ $[M+NH_4]^+$: 514.3378 found 514.3378

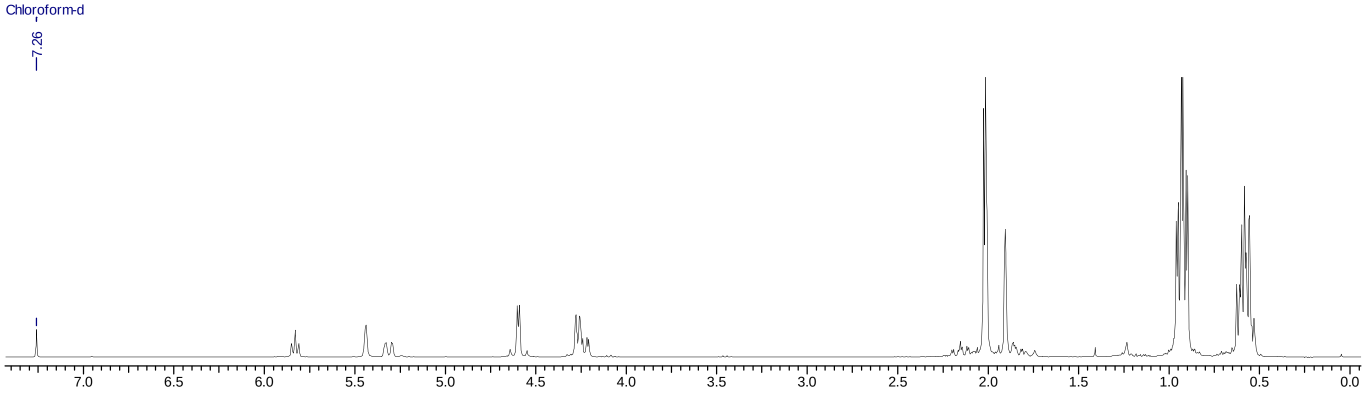


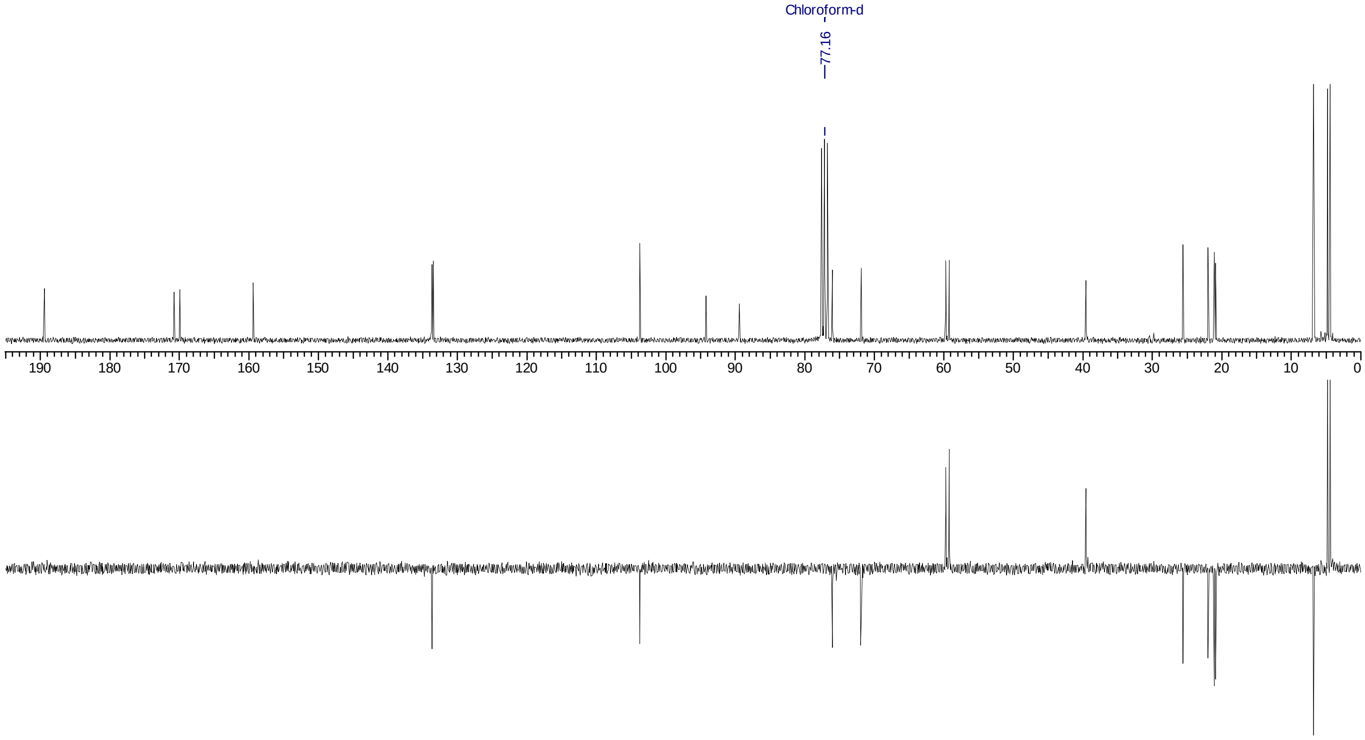


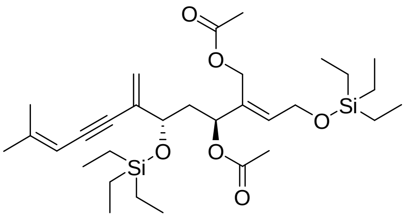




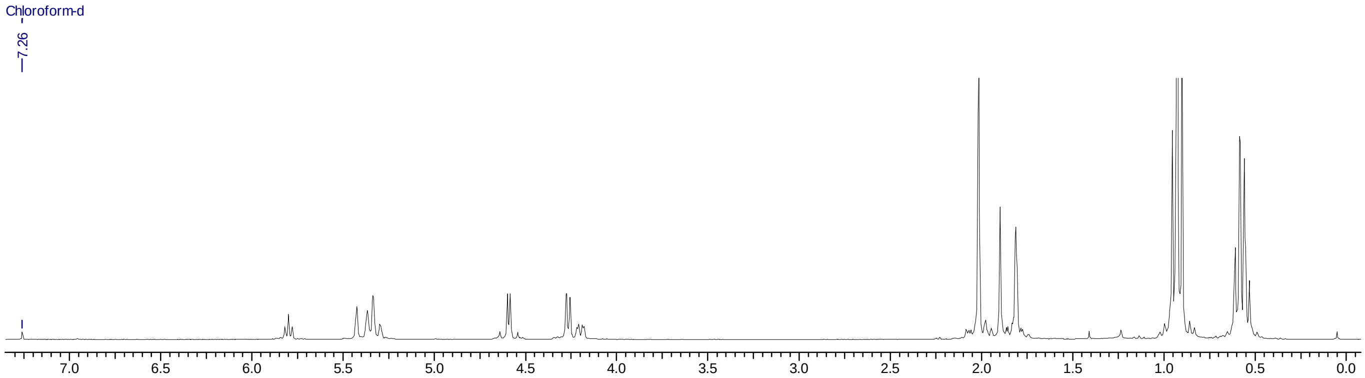
(3*S*,5*S*,*E*)-10-Methyl-6-oxo-5-(triethylsilyloxy)-2-(2-(triethylsilyloxy)ethylidene)undec-9-en-7-yne-1,3-diyl diacetate (12). A solution of diol **11** (70 mg, 0.141 mmol), acetic anhydride (53 µL, 0.563 mmol) and DMAP (1.7 mg, 0.014 mmol) in pyridine (2 mL) was stirred at r.t. After disappearance of starting material (4 hours), the mixture was quenched with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with diethyl ether and the organic layers were washed with saturated aqueous $CuSO_4$ solution and water, dried over $MgSO_4$ then concentrated under vacuum. The crude product was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-Et_2O, 85/15) to give **12** (66 mg) in 81% yield. $[\alpha]^{19}_{D}$ –31.5 (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.53-0.63 (12H, m, 6 x CH_2), 0.92 (9H, t, *J* = 7.9 Hz, 3 x CH_3), 0.93 (9H, t, *J* = 7.9 Hz, 3 x CH_3), 1.74-1.87 (1H, m, CH_2), 1.91 (3H, s, CH_3), 2.01-2.02 (9H, m, 3 x CH_3), 2.06-2.20 (1H, m, CH_2), 4.23 (1H, dd, *J* = 9.8 and 2.8 Hz, CH), 4.27 (2H, d, *J* = 5.9 Hz, CH_2), 4.57 (1H, d, *J* = 12.7 Hz, CH_2), 4.62 (1H, d, *J* = 12.7 Hz, CH_2), 5.31 (1H, br dd, *J* = 10.6 and 1.9 Hz, CH), 5.44 (1H, br s, CH), 5.83 (1H, t, *J* = 5.9 Hz, CH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 4.5 (CH_2), 4.8 (CH_2), 6.8 (3 x CH_3), 20.9 (CH_3), 21.1 (CH_3), 22.0 (CH_3), 25.6 (CH_3), 39.6 (CH_2), 59.2 (CH_2), 59.7 (CH_2), 71.9 (CH), 76.0 (CH), 89.4 (C), 94.2 (C), 103.7 (CH), 133.4 (C), 133.7 (CH), 159.3 (C), 169.9 (C), 170.7 (C), 189.4 (C); m/z (ESI+) 598 $[M+NH_4]^+$; HRMS (ESI) calcd for $C_{30}H_{56}NO_7Si_2$ $[M+NH_4]^+$: 598.3589 found 598.3584

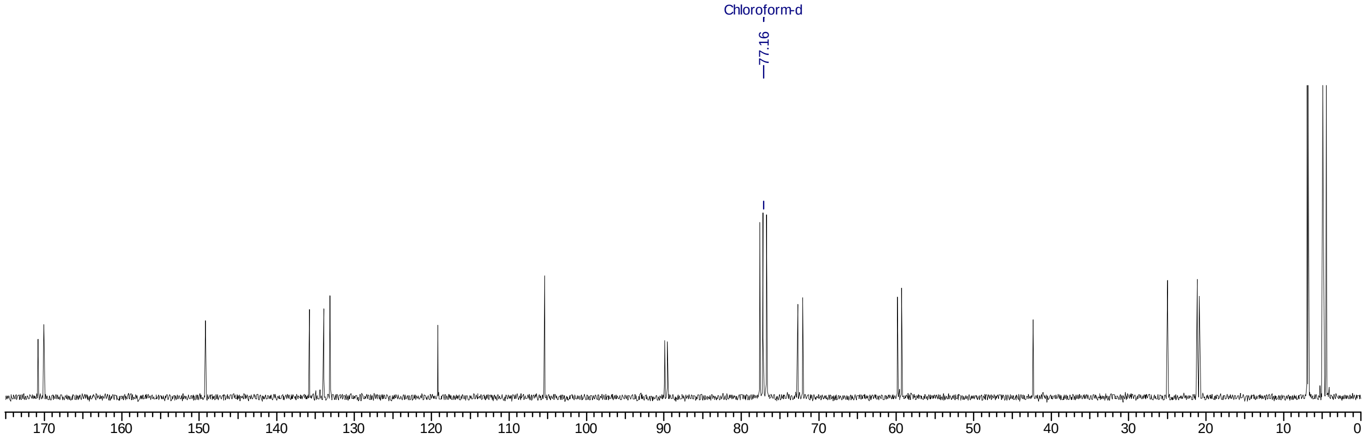


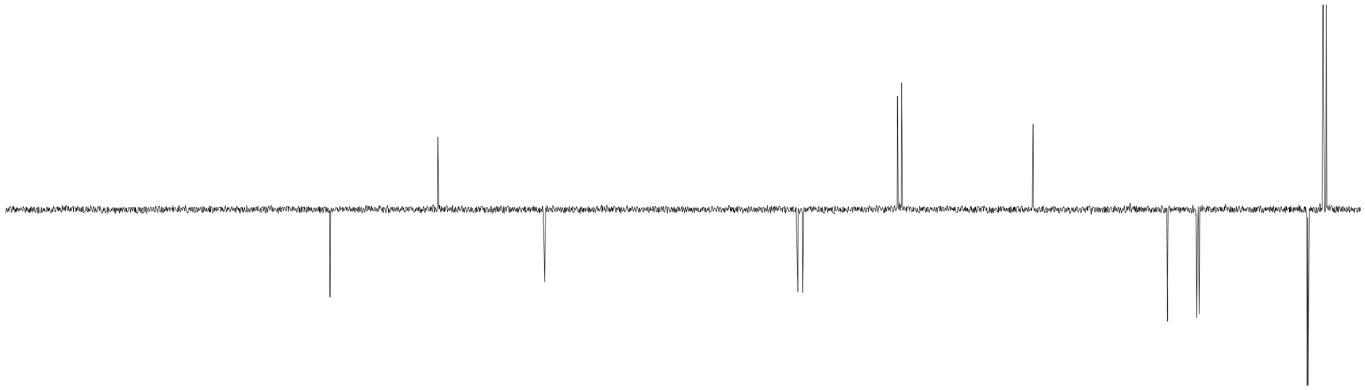


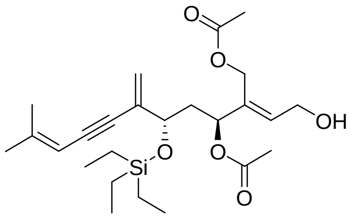


(3*S*,5*S*,*E*)-10-Methyl-6-oxo-5-(triethylsilyloxy)-2-(2-(triethylsilyloxy)ethylidene)undec-9-en-7-yne-1,3-diyl diacetate (13). To a stirred solution of CH_3PPh_3Br (307 mg, 8.59 mmol) in THF (0.7 mL) was added *t*-BuOK (77 mg, 0.69 mmol) in THF (0.7 mL). The solution was stirred at 0°C for 30 mn then cooled to -78°C. The ketone **12** (100 mg, 0.172 mmol) diluted in THF (1 mL) was then added. The solution was warmed up to 0°C then quenched with water. The aqueous layer was extracted with Et_2O and the combined organic layers were dried over Na_2SO_4 then concentrated under vacuum. The crude product was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-Et_2O, 9/1) to give **13** (52 mg) in 53% yield. $[\alpha]^{19}_{D}$ –34.0 (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.57 (12H, q, *J* = 8.12 Hz, 6 x CH_2), 0.93 (9H, t, *J* = 8.1 Hz, 6 x CH_3), 1.74-1.87 (1H, m, CH_2), 1.81 (3H, s, CH_3), 1.90 (3H, s, CH_3), 1.95-2.08 (1H, m, CH_2), 2.01 (6H, m, 2 x CH_3), 4.20 (2H, dd, *J* = 9.1 and 2.7 Hz, CH), 4.27 (2H, d, *J* = 6.0 Hz, CH_2), 4.56 (1H, d, *J* = 12.5 Hz, CH_2), 4.62 (1H, d, *J* = 12.5 Hz, CH_2), 5.29-5.37 (3H, m, CH_2 and 2 x CH), 5.43 (1H, br s, CH_2), 5.80 (1H, t, *J* = 6.0 Hz, CH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 4.5 (3 x CH_2), 4.9 (3 x CH_2), 6.8 (3 x CH_3), 6.9 (3 x CH_3), 20.9 (CH_3), 21.1 (CH_3), 21.2 (CH_3), 25.0 (CH_3), 42.32 (CH_2), 59.3 (CH_2), 59.8 (CH_2), 72.0 (CH), 72.7 (CH), 89.5 (C), 89.9 (C), 105.4 (CH), 119.1 (CH_2), 133.1 (CH), 133.9 (C), 135.7 (C), 149.2 (C), 170.0 (C), 170.8 (C); m/z (ESI+) 596 $[M+NH_4]^+$; HRMS (ESI) calcd for $C_{31}H_{58}NO_6Si_2$ $[M+NH_4]^+$: 596.3797 found 596.3790

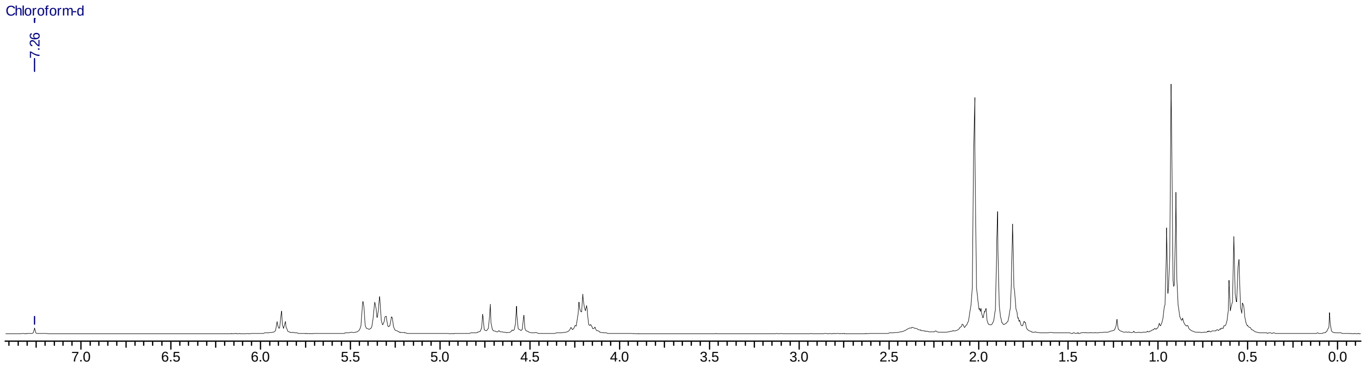


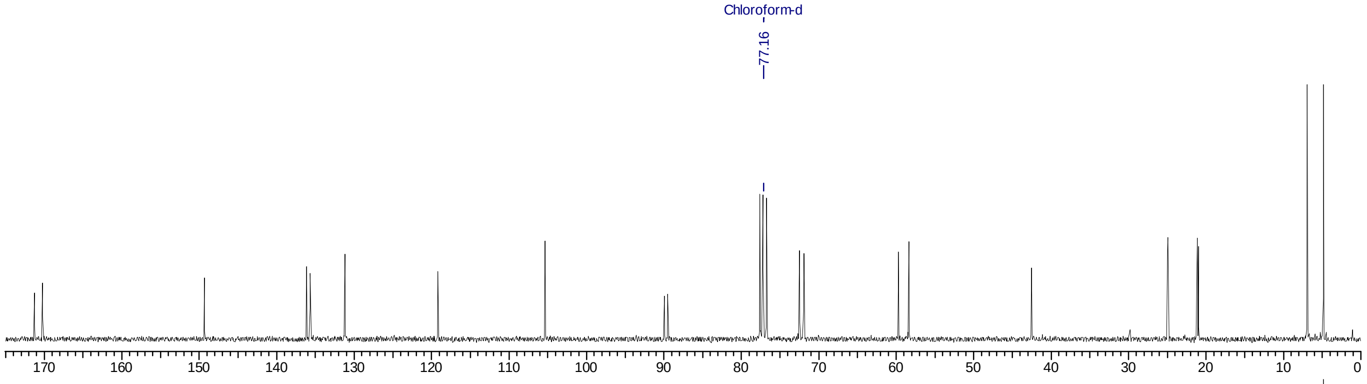


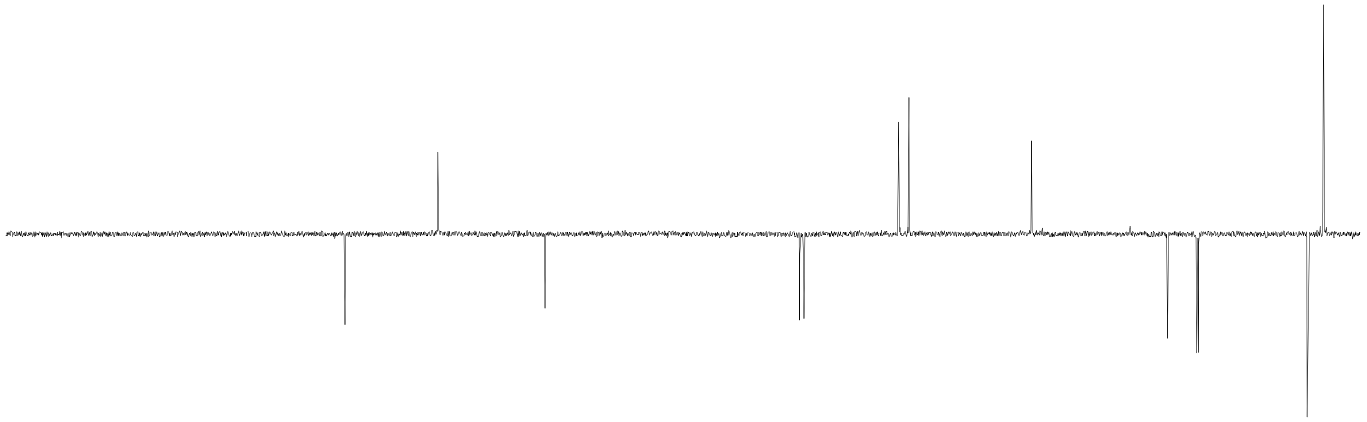


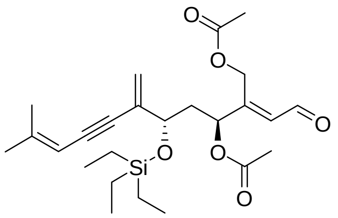


(3*S*,5*S*,*E*)-2-(2-hydroxyethylidene)-10-methyl-6-methylene-5-(triethylsilyloxy)undec-9-en-7-yne-1,3-diyl diacetate (14). To a stirred solution of **13** (89 mg, 0.154 mmol) in THF (7 mL) was added a mixture of H_2O (700 μL) and AcOH (1.4 mL) dropwise. The mixture was warmed to 40°C and stirred for 12 hours. The mixture was then cooled to 0°C and poured slowly into a suspension of 3g of $NaHCO_3$ in 20 mL of water. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 then concentrated under vacuum. The crude product was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-EtOAc, 1/1) to give **14** (63 mg) in 88% yield. $[\alpha]^{18}_{D}$ –36.9 (*c* 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.52-0.60 (6H, m, 3 x CH_2), 0.93 (9H, t, *J* = 7.9 Hz, 3 x CH_3), 1.74-1.87 (1H, m, CH_2), 1.81 (3H, s, CH_3), 1.90 (3H, s, CH_3), 1.96-2.09 (1H, m, CH_2), 2.02 (6H, br s, 2 x CH_3), 2.37 (1H, m, OH), 4.14-4.27 (3H, m, CH and CH_2), 4.55 (1H, d, *J* = 12.5 Hz, CH_2), 4.74 (1H, d, *J* = 12.5 Hz, CH_2), 5.28 (1H, dd, *J* = 10.4 and 1.8 Hz, CH), 5.34 (1H, br s, CH_2), 5.36 (1H, br s, CH), 5.43 (1H, br s, CH_2), 5.88 (1H, t, *J* = 6.8 Hz, CH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 4.9 (3 x CH_2), 6.9 (3 x CH_3), 21.0 (CH_3), 21.1 (CH_3), 21.2 (CH_3), 25.0 (CH_3), 42.5 (CH_2), 58.4 (CH_2), 59.7 (CH_2), 71.9 (CH), 72.5 (CH), 89.5 (C), 89.9 (C), 105.3 (CH), 119.1 (CH_2), 131.2 (CH), 135.6 (C), 136.1 (C), 149.3 (C), 170.2 (C), 171.2 (C); m/z (ESI+) 482 $[M+NH_4]^+$; HRMS (ESI) calcd for $C_{25}H_{44}NO_6Si$ $[M+NH_4]^+$: 482.2932 found 482.2929

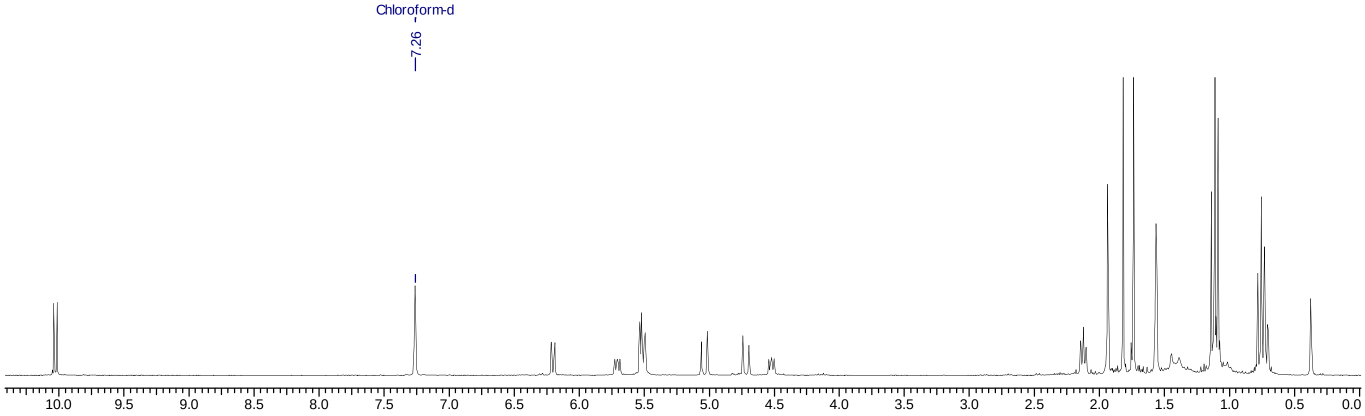


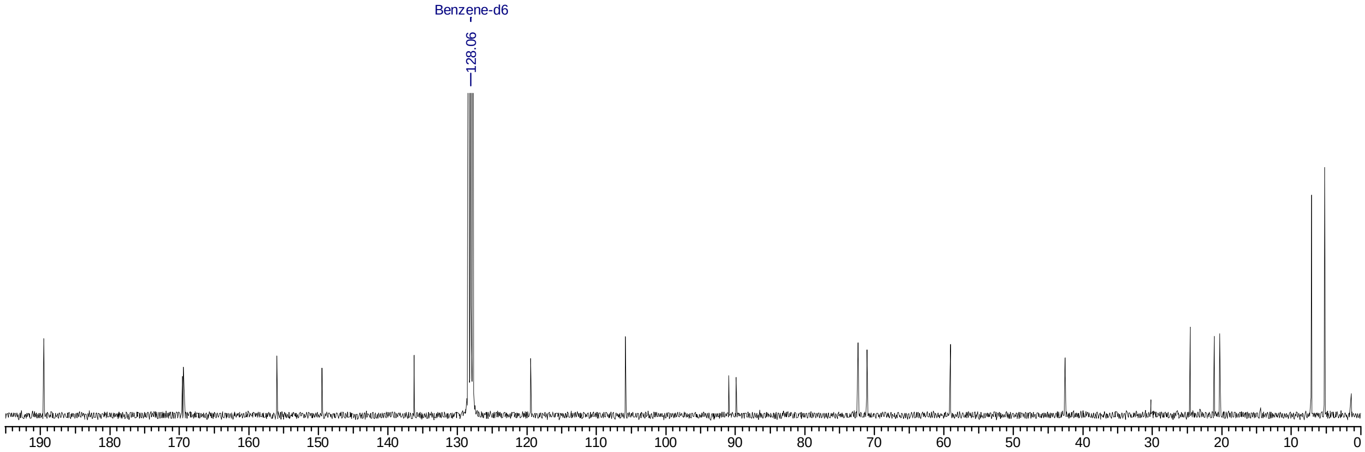


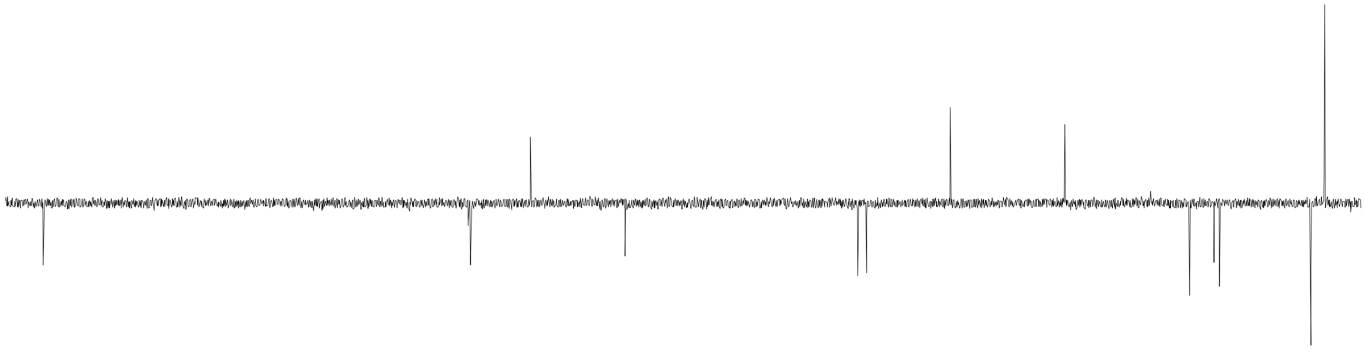


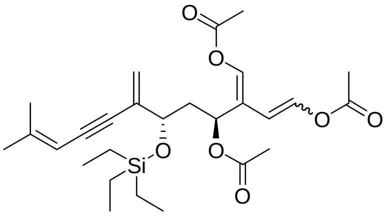


(3*S*,5*S*,*E*)-10-Methyl-6-methylene-2-(2-oxoethylidene)-5-(triethylsilyloxy)undec-9-en-7-yne-1,3-diyl diacetate (15). To a stirred solution of alcohol **14** (58 mg, 0.125 mmol) in DCM (4 mL) was added at 0°C Dess-Martin periodinane (63 mg, 0.15 mmol). The mixture was stirred at r.t. and followed by TLC. After disappearance of starting material (2 hours), the solution was poured into a saturated aqueous $Na_2S_2O_3$ / $NaHCO_3$ solution (7 mL, 1/1). After stirring for 10 mn, the layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 then concentrated under vacuum. The crude aldehyde was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-EtOAc, 7/3) to give **15** (51 mg) in 89 % yield. $[\alpha]^{19}_{D}$ −18.7 (*c* 1, DCM); ^{1}H NMR (300 MHz, C_6D_6) δ 0.60-0.68 (6H, m, 3 x CH_2), 1.01 (9H, t, *J* = 7.9 Hz, 3 x CH_3), 1.46 (3H, br s, CH_3), 1.64 (3H, s, CH_3), 1.72 (3H, s, CH_3), 1.84 (3H, br s, CH_3), 2.00-2.04 (2H, m, CH_2), 4.40-4.44 (1H, m, CH), 4.62 (1H, d, *J* = 13.6 Hz, C*H*$_2$), 4.93 (1H, d, *J* = 13.6 Hz, C*H*$_2$), 5.39-5.44 (3H, m, CH and CH_2), 5.58-5.62 (1H, m, CH), 6.10 (1H, br d, *J* = 7.4 Hz, CH), 9.93 (1H, d, *J* = 7.4 Hz, CH); ^{13}C NMR (C_6D_6, 75 MHz) δ 5.2 (3 x CH_2), 7.1 (3x CH_3), 20.2 (CH_3), 20.3 (CH_3), 21.1 (CH_3), 24.6 (CH_3), 42.5 (CH_2), 59.0 (CH_2), 71.1 (CH), 72.3 (CH), 89.9 (C), 90.9 (C), 105.8 (CH), 119.4 (CH_2), 128.1 (CH), 135.2 (C), 149.4 (C), 156.0 (C), 19.4 (C), 169.6 (C), 189.5 (CH); m/z (ESI+) 480 $[M+NH_4]^+$; HRMS (ESI) calcd for $C_{25}H_{42}NO_6Si$ $[M+NH_4]^+$: 480.2775 found 480.2774

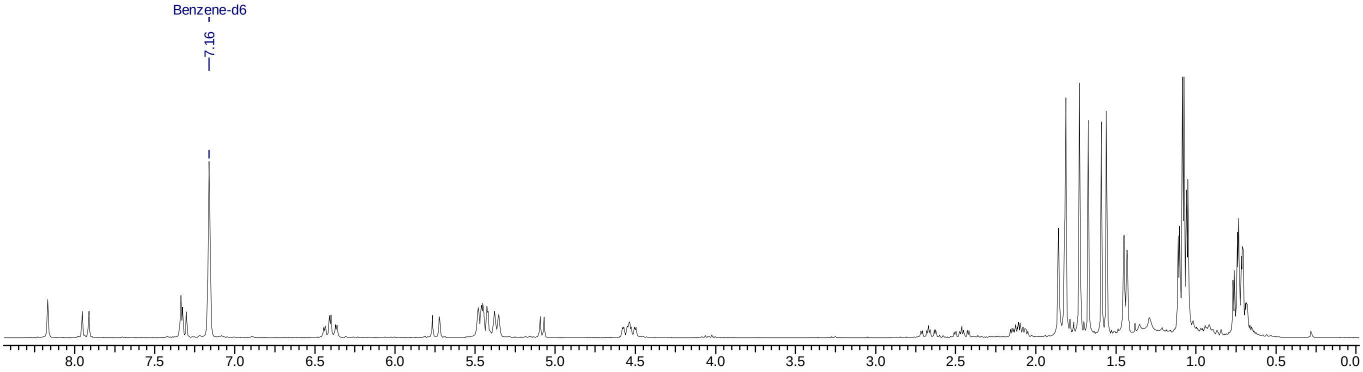


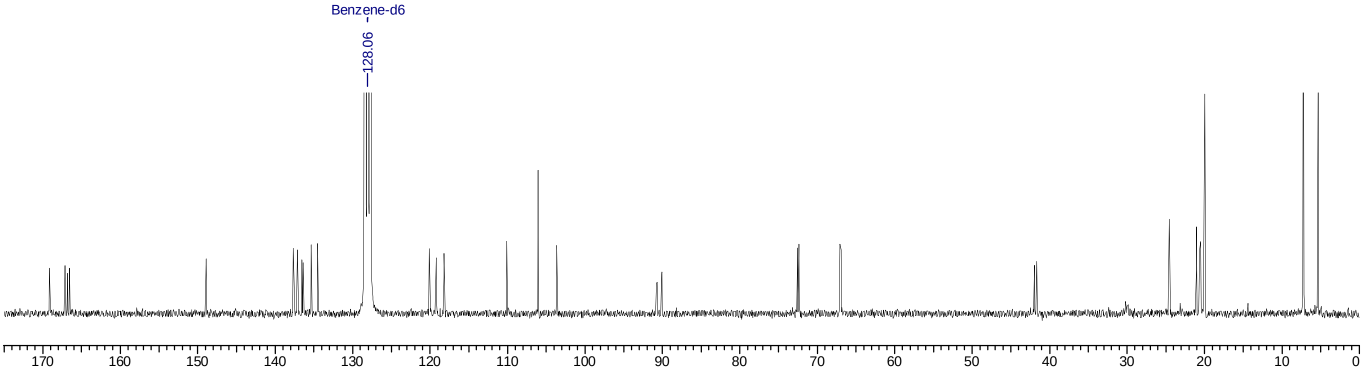


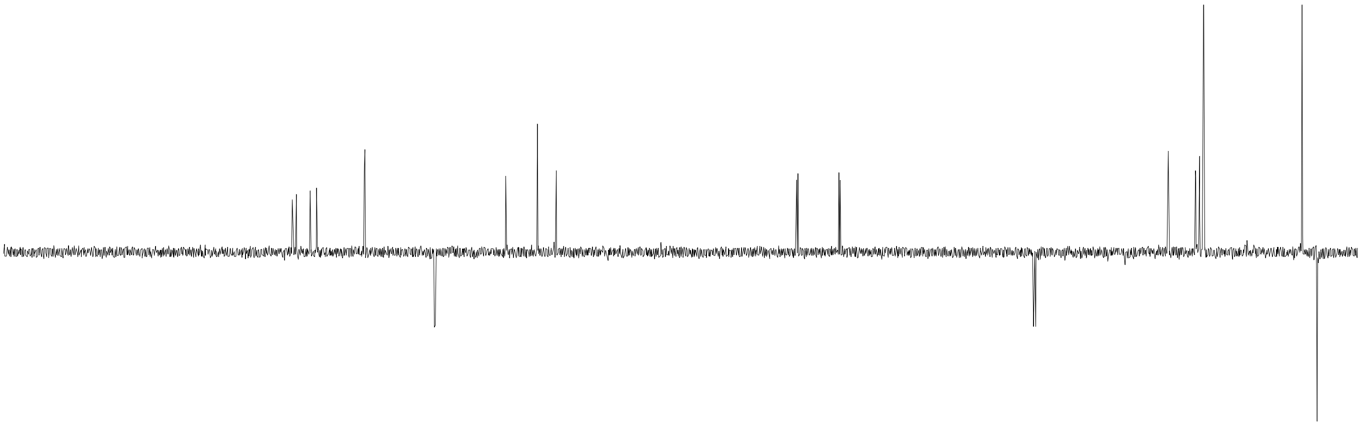


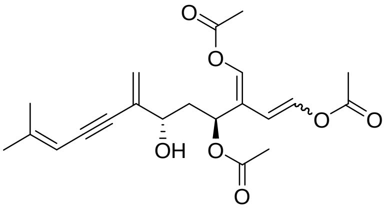


(3*S*,5*S*,*Z*)-2-(2-Acetoxyvinyl)-10-methyl-6-methylene-5-(triethylsilyloxy)undeca-1,9-dien-7-yne-1,3-diyl diacetate (16). In a dry Schlenk tube, a solution of **15** (50 mg, 0.108 mmol), DMAP (13 mg, 0.108 mmol), NEt_3 (0.67 mL) and acetic anhydride (30 µL, 0.324 mmol) was stirred under argon at 80°C and monitored by TLC. After disappearance of the starting material (3 hours), the mixture was concentrated under vacuum. The crude product was then purified by flash chromatography (SiO_2, 3% NEt_3, petroleum ether-EtOAc, 7/3) to give a 53/47 mixture (40 mg) of **16** and *iso*-**16** in 89 % yield. ^{1}H NMR (300 MHz, C_6D_6) δ 0.68-0.77 (12H, m, 6 x CH_2), 1.05-1.11 (18H, m, 6 x CH_3), 1.43 (3H, br s, CH_3), 1.45 (3H, br s, CH_3), 1.56 (3H, s, CH_3), 1.59 (3H, s, CH_3), 1.67 (3H, s, CH_3), 1.73 (6H, br s, 2 x CH_3), 1.81 (6H, br s, 2 x CH_3), 1.86 (3H, br s, CH_3), 2.00-2.16 (2H, m, 2 x $C\mathit{H}_2$), 2.42-2.51 (1H, m, $C\mathit{H}_2$), 2.62-2.72 (1H, m, $C\mathit{H}_2$), 4.50-4.58 (2H, m, 2 x CH), 5.08 (1H, d, *J* = 7.4 Hz, CH), 5.35-5.48 (6H, m, 6 x CH), 5.74 (1H, d, *J* = 12.7 Hz, CH), 6.36-6.44 (2H, m, 2 x CH_2), 7.31 (1H, d, *J* = 7.4 Hz, CH), 7.34 (1H, s, CH), 6.10 (1H, br d, *J* = 7.4 Hz, CH), 7.93 (1H, d, *J* = 12.7 Hz, CH), 8.17 (1H, s, CH); ^{13}C NMR (C_6D_6, 75 MHz) δ 5.3_2 (3 x CH_2), 5.3_4 (3 x CH_2), 7.3 (6 x CH_3), 20.0 (3 x CH_3), 20.1 (CH_3), 20.5 (CH_3), 20.7 (CH_3), 21.0 (CH_3), 21.1 (CH_3), 24.6 (2 x CH_3), 41.7 (CH_2), 42.0 (CH_2), 67.0 (CH), 67.2 (CH), 72.5 (CH), 72.6 (CH), 90.1_1 (C), 90.1_4 (C), 90.7 (C), 90.8 (C), 103.7 (CH), 106.1 (CH), 110.2 (CH), 118.2 (C), 119.2 (CH_2), 119.3 (CH_2), 120.1 (C), 128.4 (CH), 134.6 (CH), 135.3 (CH), 136.4 (C), 136.6 (C), 137.2 (CH), 137.7 (CH), 148.9 (C), 149.0 (C), 166.6 (C), 166.8 (C), 166.9 (C), 167.2 (C), 169.1 (C), 169.2 (C); m/z (ESI+) 522 $[M+NH_4]^+$; HRMS (ESI) calcd for $C_{27}H_{44}NO_7Si$ $[M+NH_4]^+$: 522.2881 found 522.2880





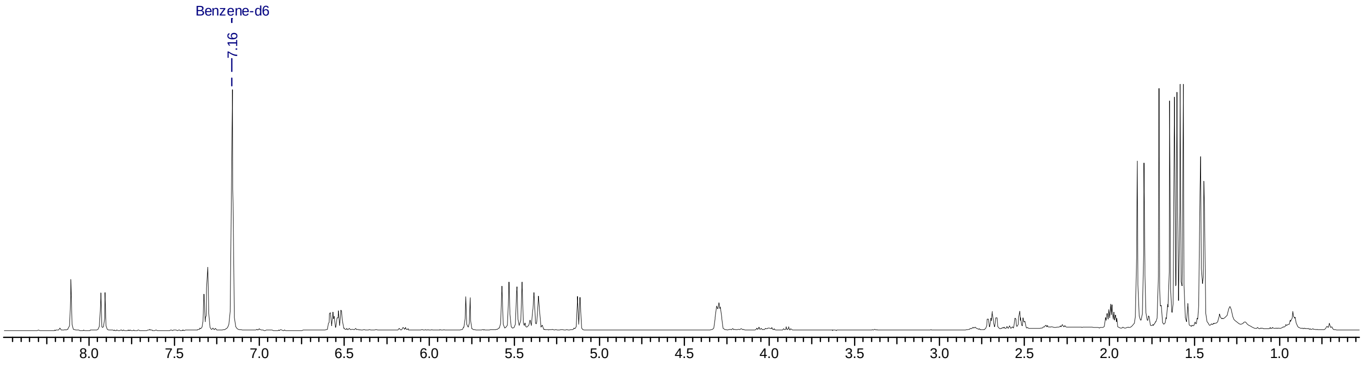


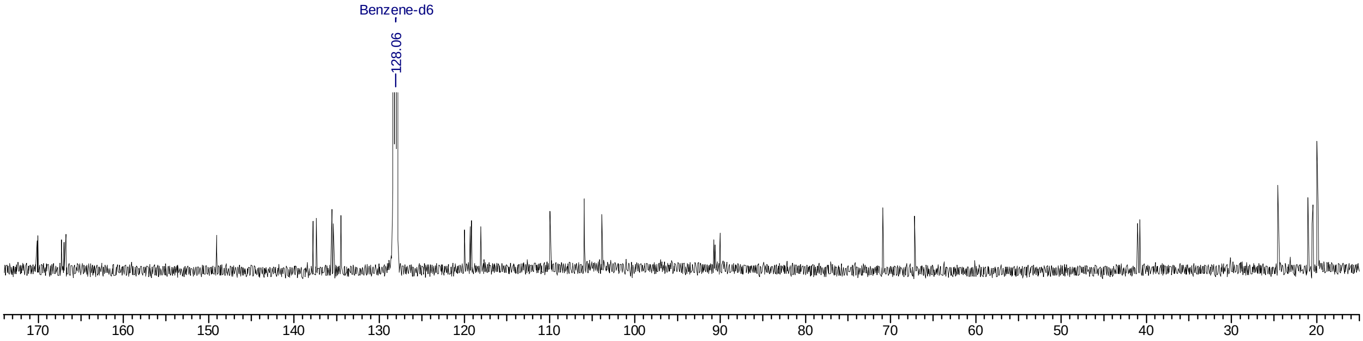


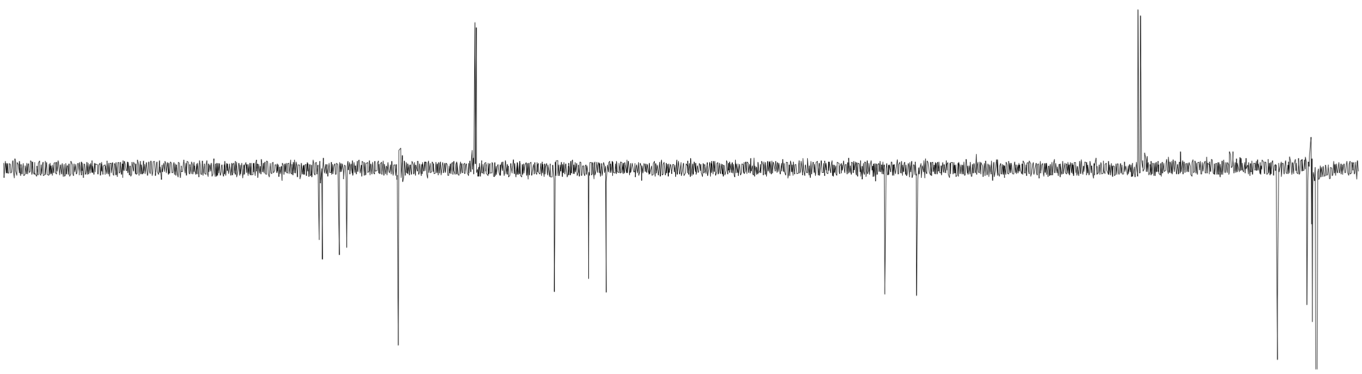
Caulerpenynol (2). To a stirred solution of **16** (20 mg, 0.0396 mmol) in THF (640 μL) was added a mixture of 2 mL of AcOH and 1 mL of H_2O. The solution was then heated at 45°C and followed by TLC. After disappearance of the starting material (2 hours) the mixture was poured into a aqueous solution of $NaHCO_3$ (3 g). The aqueous layer was extracted with EtOAc. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4 then concentrated under vacuum. The crude product was purified by column of chromatography (SiO_2, 3% NEt_3, petroleum ether-EtOAc, 1/1) to give a 52/48 mixture of **2** and *iso*-**2** (12.5 mg) in 81 % yield separable by HPLC.[1]

Mixture of caulerpenynol 2 and *iso*-caulerpenynol *iso*-2

m/z (ESI+) 408 $[M+NH_4]^+$







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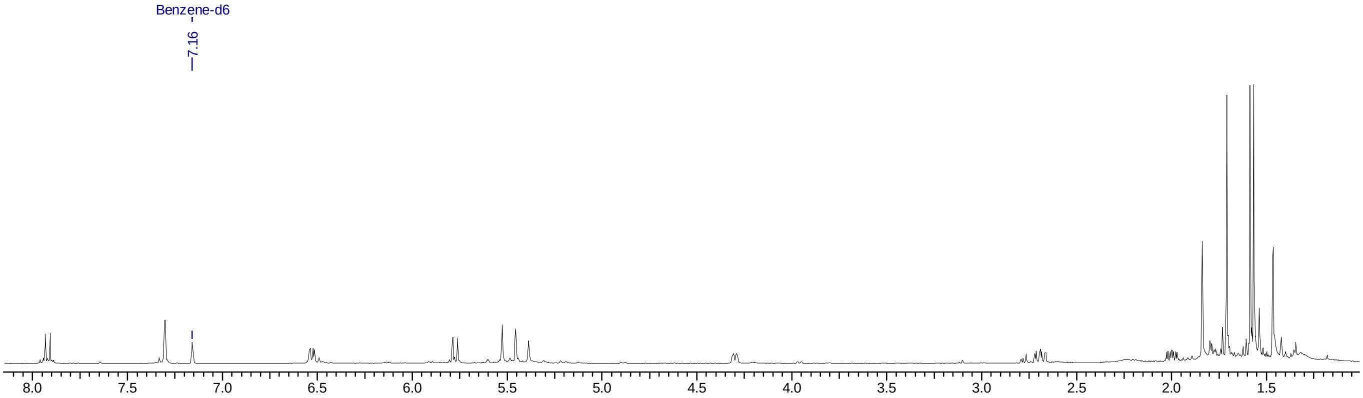
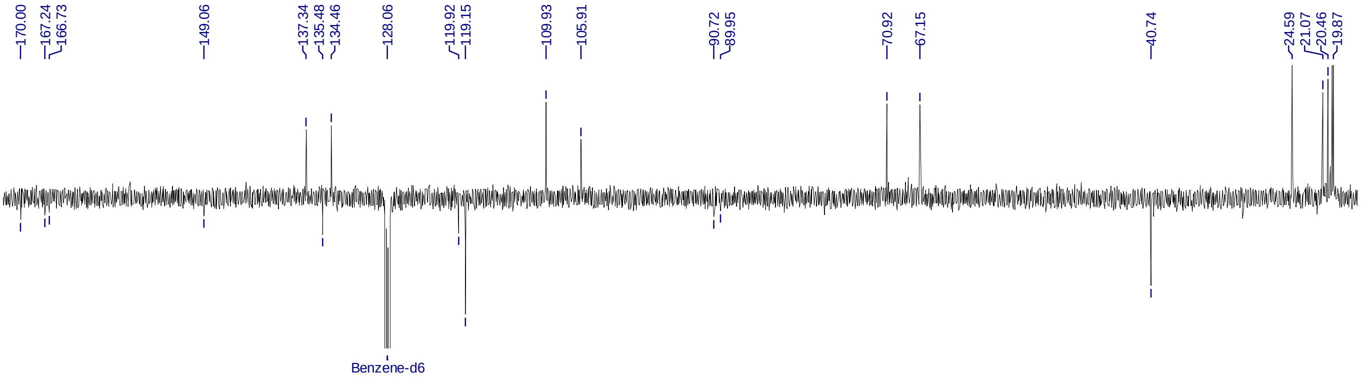
[1] Semi-preparative separations were performed by successive injections on a Knauer unit composed of a Smartline 1000 pump, a Smartline 3900 autosampler, a Smartline 2500 UV-detector and a valve to collect separately the different isomers. Chiralpak AD (250 x 10 mm) was used with hexane/ethanol (95/5) as mobile phase, 5 mL/min as flow-rate and UV at 220 nm.

Caulerpenynol 2

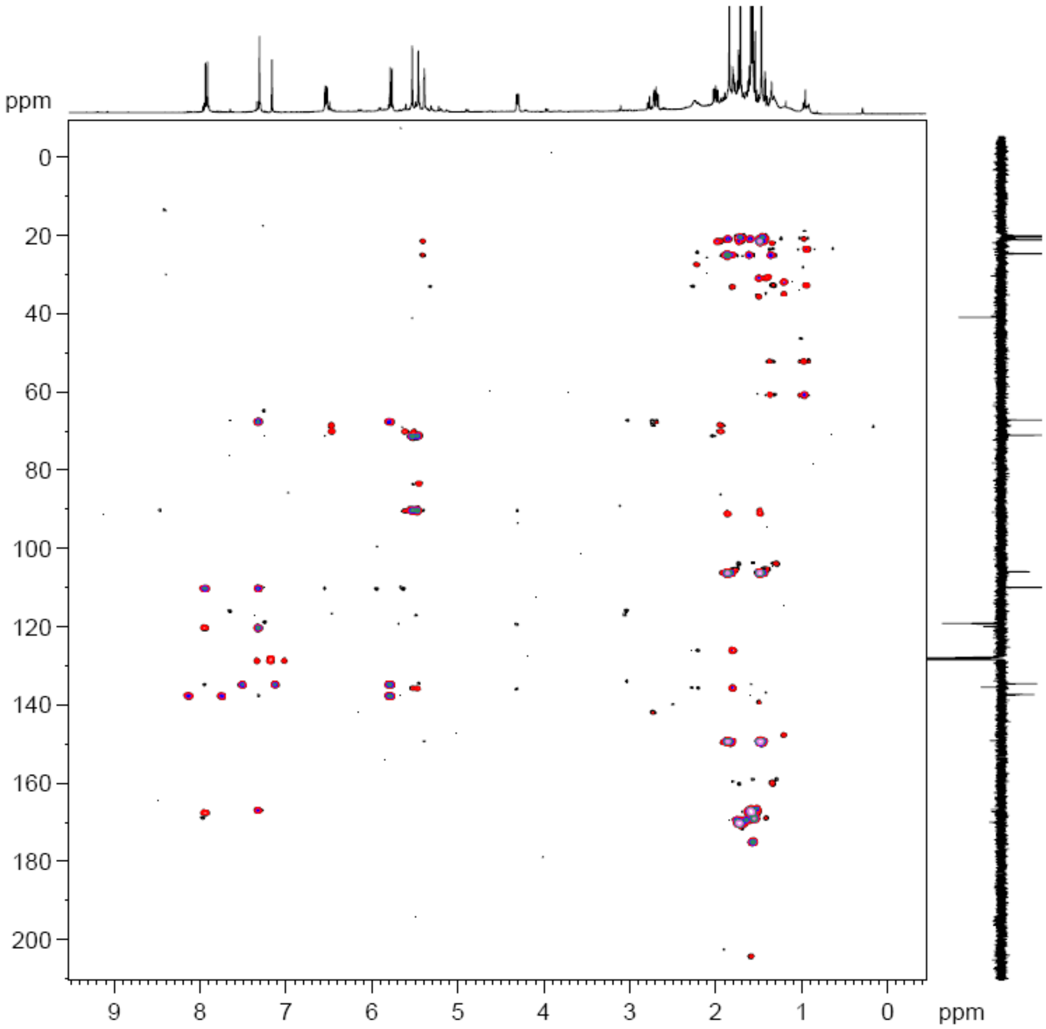
$[\alpha]^{25}_{D}$ –48.6 (*c* 0.105 in EtOH), (lit., $[\alpha]^{20}_{D}$ –53.7 (*c* 0.095 in EtOH) ^{1}H NMR (500 MHz, C_6D_6) 1.46 (3H, br s, CH_3), 1.57 (3H, s, CH_3), 1.59 (3H, s, CH_3), 1.71 (3H, s, CH_3), 1.84 (3H, br s, CH_3), 2.00 (1H, ddd, *J* = 14.5, 9.6 and 3.4 Hz, CH_2), 2.69 (1H, ddd, *J* = 14.5, 10.4 and 3.2 Hz, CH_2), 4.30 (1H, br d, *J* = 9.6 Hz, CH), 5.39 (1H, br s, CH), 5.46 (1H, br s, CH), 5.53 (1H, br s, CH), 5.77 (1H, d, *J* = 12.7 Hz, CH), 6.53 (1H, dd, *J* = 10.4 and 3.4 Hz, CH), 7.30 (1H, s, CH), 7.92 (1H, d, *J* = 12.7 Hz, CH); ^{13}C NMR (C_6D_6, 125 MHz) 19.87 (CH_3), 19.98 (CH_3), 20.46 (CH_3), 21.07 (CH_3), 24.59 (CH_3), 40.74 (CH_2), 67.15 (CH), 70.92 (CH), 89.95 (C), 90.72 (C), 105.91 (CH), 109.93 (CH), 119.15 (CH_2), 119.92 (C), 134.46 (CH), 135.48 (C), 137.34 (CH), 149.06 (C), 166.73 (C), 167.24 (C), 170.00 (C).



DEPTQ of 2



HMBC of 2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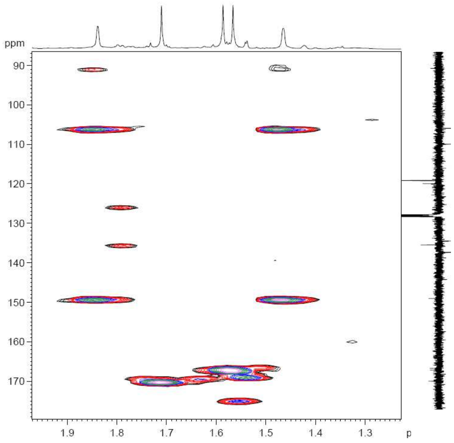
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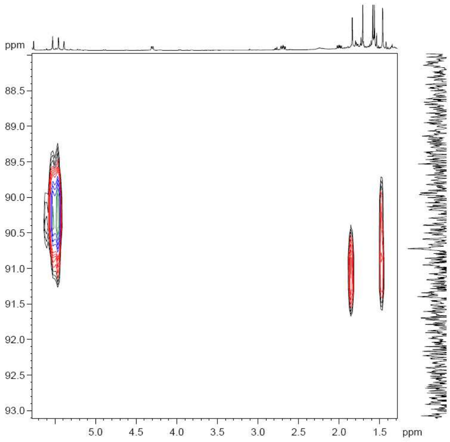
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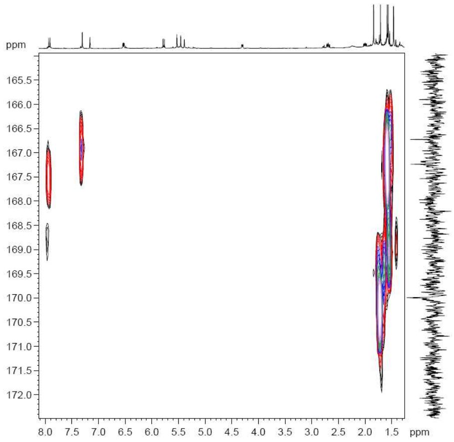
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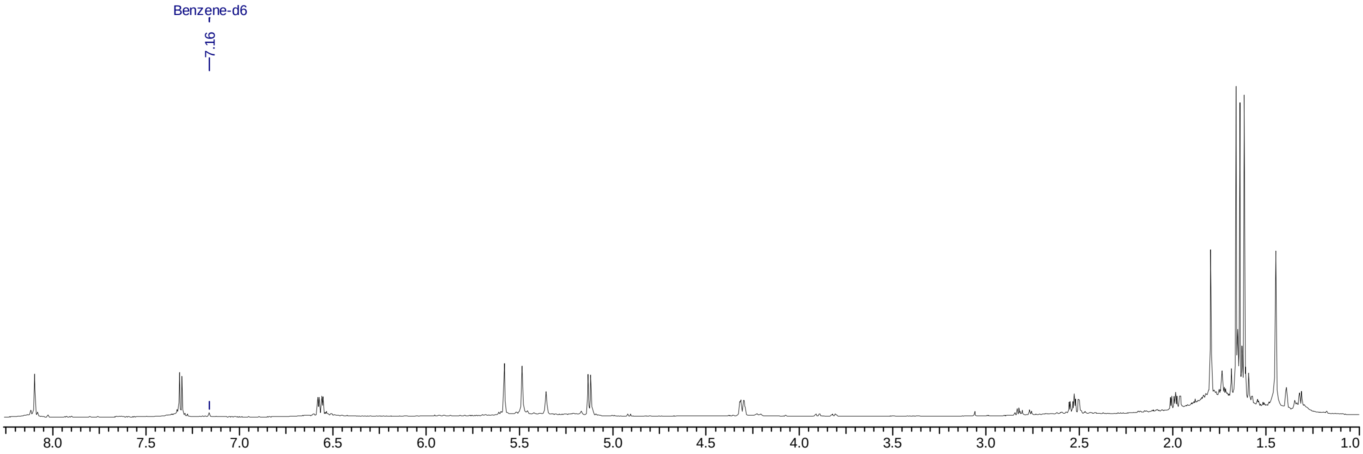
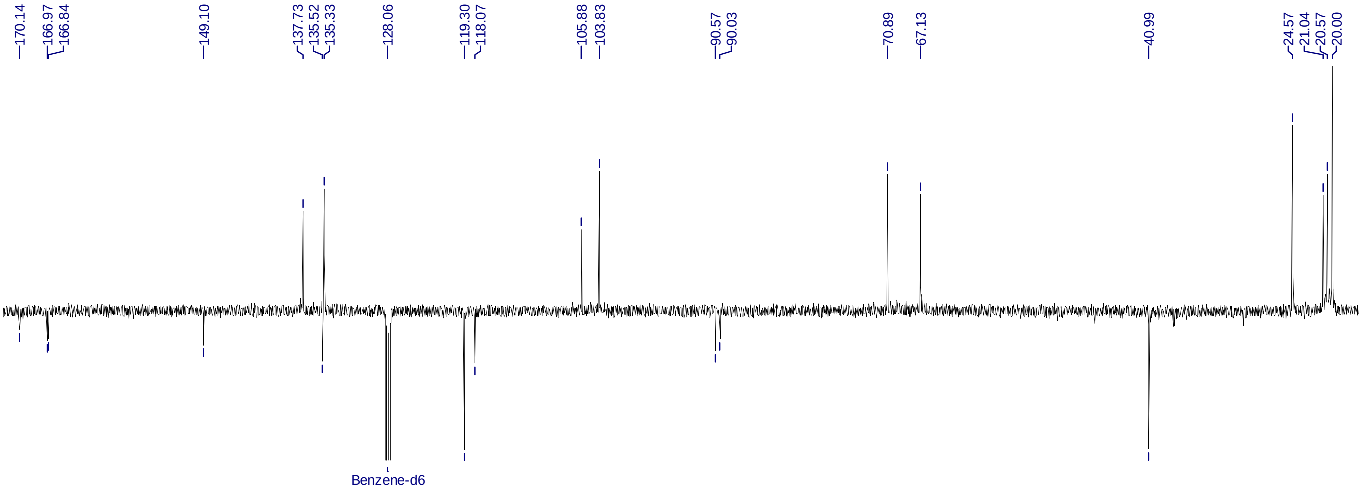
ppm

Iso-caulerpenynol _iso_-2

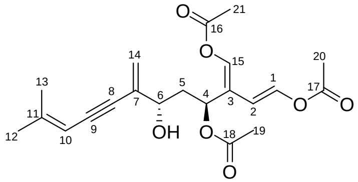
$[\alpha]^{25}_{D}$ −33.2 (*c* 0.295 in EtOH), ^{1}H NMR (500 MHz, C_6D_6) 1.45 (3H, br s, CH_3), 1.62 (3H, s, CH_3), 1.64 (3H, s, CH_3), 1.66 (3H, s, CH_3), 1.80 (3H, br s, CH_3), 1.98 (1H, ddd, *J* = 14.2, 9.6 and 3.4 Hz, CH_2), 2.53 (1H, ddd, *J* = 14.2, 10.4 and 3.0 Hz, CH_2), 4.30 (1H, br d, *J* = 9.6 Hz, CH), 5.12 (1H, d, *J* = 7.3 Hz, CH), 5.36 (1H, br s, CH), 5.48 (1H, br s, CH), 5.58 (1H, br s, CH), 6.57 (1H, dd, *J* = 10.4 and 3.4 Hz, CH), 7.31 (1H, d, *J* = 7.3 Hz, CH), 8.10 (1H, s, CH); ^{13}C NMR (C_6D_6, 125 MHz) 20.00 (CH_3), 20.57 (CH_3), 21.04 (CH_3), 24.57 (CH_3), 40.99 (CH_2), 67.13 (CH), 70.89 (CH), 90.03 (C), 90.57 (C), 103.83 (CH), 105.88 (CH), 118.07 (C), 119.30 (CH_2), 135.33 (CH), 135.52 (C), 137.73 (CH), 149.10 (C), 166.84 (C), 166.97 (C), 170.14 (C).



DEPTQ of iso-2

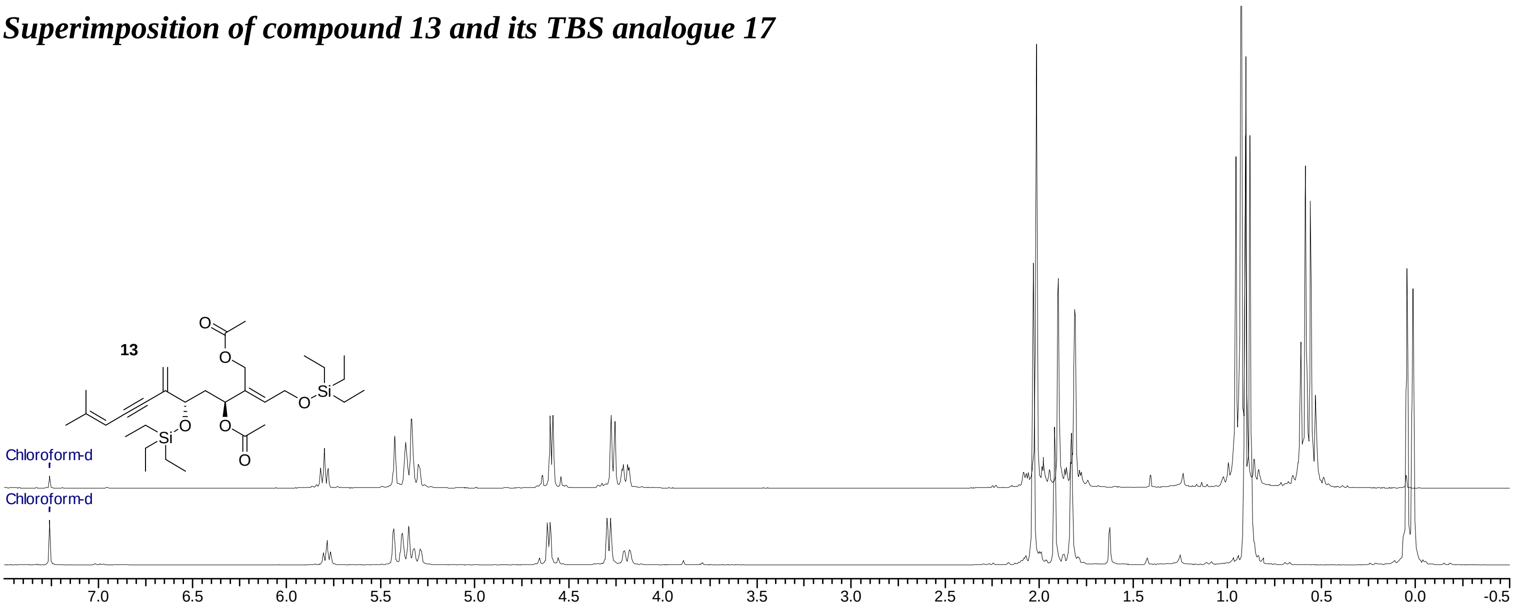


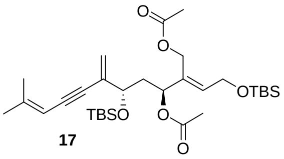
Comparison of ^{1}H NMR and ^{13}C NMR shifts of natural, synthetic caulerpenynol 2 and iso-caulerênynol iso-2



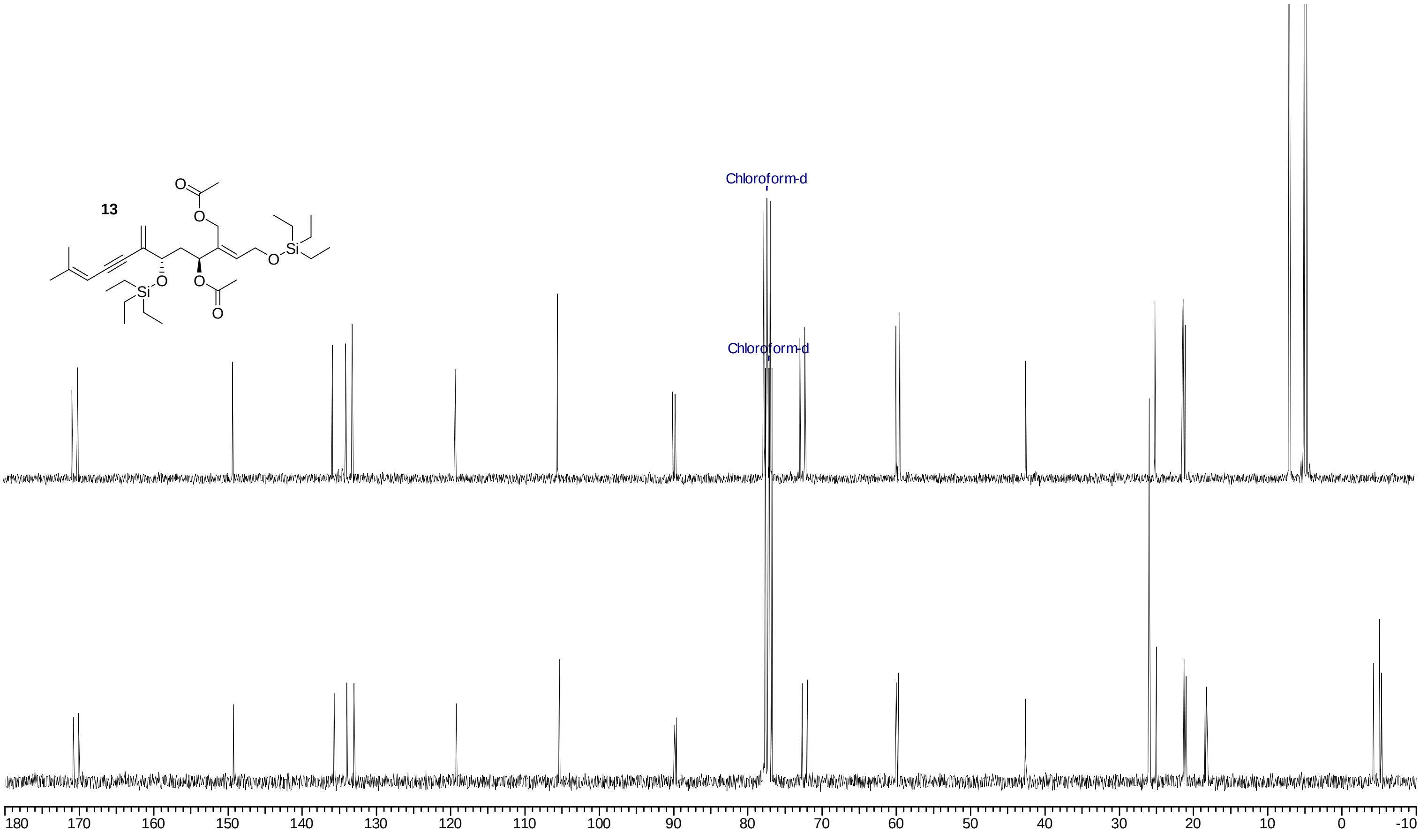
	^{1}H Natural Product	^{1}H Synthetic Compound 2	^{1}H Synthetic Compound *iso*-2	^{13}C Natural Product	^{13}C Synthetic Compound 2	^{13}C Synthetic Compound *iso*-2
12	1.46	1.46	1.45	24.57	24.59	24.57
20 (ou 21)	1.551	1.57	1.62	19.82	19.87	20.00 (x2)
21 (ou 20)	1.554	1.59	1.64	19.95	19.98	
19	1.69	1.71	1.66	20.42	20.46	20.57
13	1.84	1.84	1.80	21.04	21.07	21.04
5	2.00 ddd, *J* = 14.7, 9.3, 3.3 Hz	2.00 ddd, *J* = 14.5, 9.6, 3.4 Hz	1.98 ddd, *J* = 14.2, 9.6, 3.4 Hz	40.71	40.74	40.99
5’	2.68 ddd, *J* = 14.7, 10.5, 3.0 Hz	2.69 ddd, *J* = 14.5, 10.4, 3.2 Hz	2.53 ddd, *J* = 14.2, 10.4, 3.0 Hz			
6	4.27 br d, *J* = 9.3 Hz	4.30 br d, *J* = 9.6 Hz	4.30 br d, *J* = 9.6 Hz	70.88	70.92	70.89
10	5.38	5.39	5.36	105.87	105.91	105.88
14	5.45	5.46	5.48	119.12	119.15	119.30
14’	5.50	5.53	5.58			
2	5.77 d, *J* = 12.6 Hz	5.77 d, *J* = 12.7 Hz	5.12 d, *J* = 7.3 Hz	109.86	109.93	103.83
4	6.54 dd, *J* = 10.5 and 3.3 Hz	6.53 dd, *J* = 10.4 and 3.4 Hz	6.57 dd, *J* = 10.4 and 3.4 Hz	67.08	67.15	67.13
15	7.30	7.30	8.10	134.39	134.46	135.33
1	7.93 d, *J* = 12.6 Hz	7.92 d, *J* = 12.7 Hz	7.31 d, *J* = 7.3 Hz	137.29	137.34	137.73
3				119.85	119.92	118.07
7				135.36	135.48	135.52
8				90.69	90.72	90.57
9				89.87	89.95	90.03
11				149.04	149.06	149.10
17				166.62	166.73	166.84
18				169.91	170.00	170.14
16				167.15	167.24	166.97

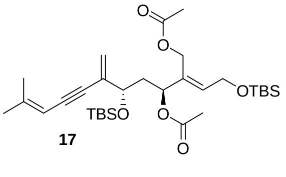
Superimposition of compound 13 and its TBS analogue 17





17





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