Total Synthesis of (3*R*,9*R*,10*R*)-Panaxytriol via Tandem Metathesis and Metallotropic [1,3]-Shift as a Key Step

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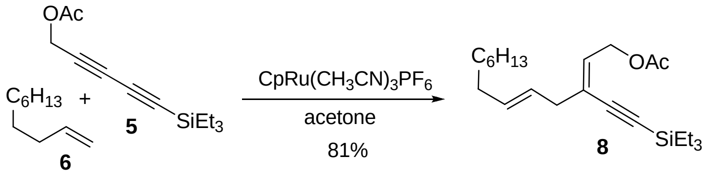
Supporting Information

Materials and Methods

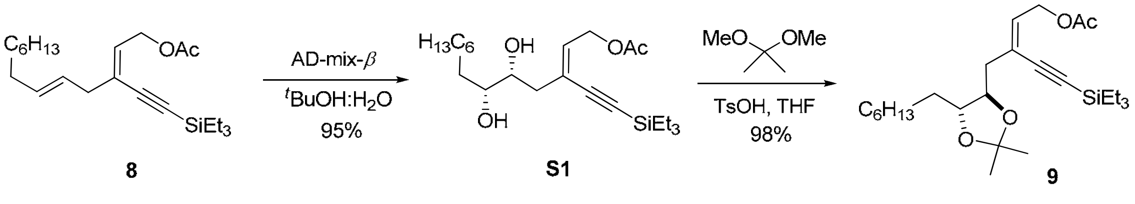
^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury plus 300 or a Bruker AC-300 spectrometer. Tetramethylsilane (TMS) served as an internal standard ($\delta = 0$) for ^{1}H NMR and $CDCl_3$ was used as an internal standard ($\delta = 77.23$) for ^{13}C NMR. Flasks were oven-dried overnight and cooled under a stream of nitrogen. All reagents were purchased from Aldrich Chemical Company except for the catalyst $RuCp(CH_3CN)_3PF_6$, which was purchased from Strem Chemicals. THF was distilled from sodium/benzophenone and dichloromethane was distilled from CaH_2. Flash chromatography was performed using silica gel 60 Å (32-63 mesh) from Sorbent Technologies. Reactions were monitored by thin layer chromatography (TLC) using 0.25 mm E. Merck pre-coated silica gel 60 (particle size 0.040–0.063 mm).

Experimental Procedures and Characterization information for compounds



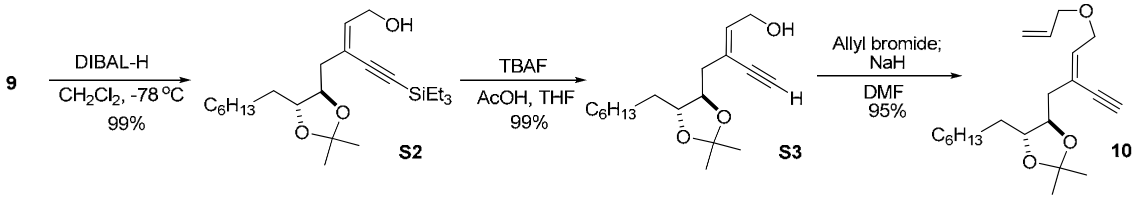
See: Cho, E. J.; Lee, D. J. Am. Chem. Soc. ***2007****, 129, 6692-6693.*

To a stirred solution of diyne **5** (35 mg, 0.15 mmol) and 1-decene **6** (42 mg, 0.30 mmol) in acetone (1.5 ml) under a nitrogen atmosphere was added $RuCp(CH_3CN)_3PF_6$ (7 mg, 0.016 mmol). The reaction was stirred at room temperature for 5 min, after which time the solvent was removed in vacuo and the residue was purified by silica gel chromatography giving the Alder ene product **8** (45 mg, 81%) as a light brown oil. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.81 (t, J = 6.8 Hz, 1H), 5.52 (dt, J = 15.3, 6.1 Hz, 1H), 5.42 (dt, J = 15.3, 6.1 Hz, 1H), 4.81 (d, J = 6.8 Hz, 2H), 2.84 (d, J = 6.1 Hz, 2H), 2.06 (s, 3H), 2.01 (dt, J = 6.1, 6.1 Hz, 2H), 1.38-1.22 (m, 10H), 1.03 (t, J = 8.0 Hz, 9H), 0.88 (t, J = 6.7 Hz, 3H), 0.62 (q, J = 8.0 Hz, 6H); **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.04, 133.78, 130.74, 127.57, 125.75, 103.34, 98.22, 63.33, 40.27, 32.75, 32.06, 29.58, 29.38, 22.89, 21.12, 14.29, 7.67, 4.59**; IR (neat)** ν_{max} = 2926, 2143, 1746, 1229 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{23}H_{40}O_2SiNa$ [M^++Na] 399.2695, found 399.2707.



To a solution of *tert*-butyl alcohol and water (20 mL:20 mL) were added AD-mix-β (4.00 g) and methanesulfonamide (278 mg, 2.92 mmol). The mixture was then cooled to 0 °C whereupon some of the dissolved salts precipitated. 1.10 g of olefin **8** was added, and the heterogeneous slurry was stirred vigorously at 0 °C until TLC indicated complete consumption of starting material. While the mixture was stirred at 0 °C, solid sodium sulfite was added and the mixture was allowed to warm to room temperature and stirred for additional 1 h. The organic layer was extracted with dichloromethane and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel) to give colorless product **S1** (1.14g, 95%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.92 (t, J = 6.8 Hz, 1H), 4.82 (d, J = 6.8 Hz, 2H), 3.81-3.74 (m, 1H), 3.52-3.45 (m, 1H), 2.45-2.23 (m, 4H), 2.07 (s, 3H), 1.53-1.24 (m, 12H), 1.00 (t, J = 8.0 Hz, 9H), 0.88 (t, J = 6.8 Hz, 3H), 0.63 (q, J = 8.0 Hz, 6H); **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.05, 134.14, 124.16, 102.69, 100.22, 73.64, 72.42, 63.09, 41.77, 33.88, 32.01, 29.84, 29.45, 25.78, 22.85, 21.08, 14.27, 7.67, 4.49**; IR (neat)** ν_{max} = 3245, 2930, 2142, 1746, 1233 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{23}H_{42}O_4SiNa$ [M^++Na] 433.2750, found 433.2737; $[\alpha]_D^{21}$ +5.19 (*c* 1.35, $CHCl_3$).

To a stirred solution of **S1** (2.0 g, 4.87 mmol) in THF were added 2,2-dimethoxypropane (3.0 mL, 24.4 mL) and toluenesulfonic acid (catalytic amount). The reaction was stirred at room temperature until TLC indicated complete consumption of starting material. The reaction mixture was then neutralized with small amount of triethylamine and concentrated under reduced pressure. The crude material was purified by flash chromatography (silica gel) to give pale yellow oil **9** (2.15g, 98%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.93 (t, J = 6.6 Hz, 1H), 4.81 (d, J = 6.6 Hz, 2H), 3.94 (ddd, J = 7.3, 7.1, 5.0 Hz, 1H), 3.69 (ddd, J = 7.3, 7.0, 4.0 Hz, 1H), 2.41 (AB of ABX, J_{AB} = 14.0, J_{AX} = 7.1, J_{BX} = 5.0, Hz, 2H), 2.06 (s, 3H), 1.58-1.44 (m, 3H), 1.39 (s, 3H), 1.38 (s, 3H), 1.28 (m, 9H), 1.01 (t, J = 8.0 Hz, 9H), 0.88 (t, J = 6.7 Hz, 3H), 0.63 (q, J = 8.0 Hz, 6H); **^{13}C NMR (75 MHz, $CDCl_3$)** δ 170.94, 133.35, 124.01, 108.38, 102.75, 99.83, 80.88, 78.83, 63.08, 40.87, 33.25, 32.02, 29.96, 29.41, 27.50, 27.41, 26.22, 22.84, 21.05, 14.26, 7.66, 4.52**; IR (neat)** ν_{max} = 2933, 2143, 1747, 1230 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{26}H_{46}O_4SiNa$ [M^++Na] 473.3063, found 473.3045; $[\alpha]_D^{21}$ +22.20 (*c* 1.22, $CHCl_3$).

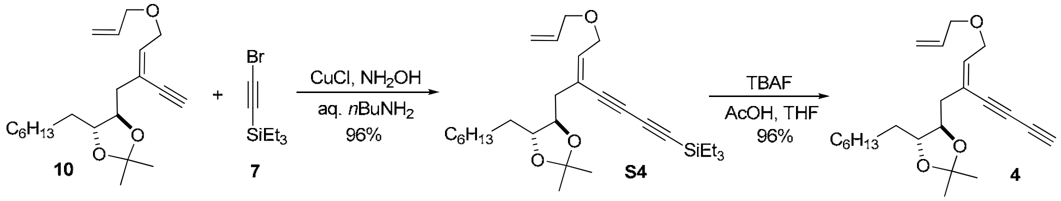


To a solution of acetate **9** (2.0 g, 4.44 mmol) in dry dichloromethane under N_2 was slowly added DIBAL-H (0.95 mL, 5.32 mmol) at -78 °C. After approximately 30 min, the reaction quenched with 10% aqueous KOH solution. The organic material was extracted with dichloromethane and dried with $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel) to give pale yellow oil **S2** (1.80 g, 99%).

^{1}H NMR (300 MHz, CDCl$_3$) δ 6.01 (tt, *J* = 6.4, 1.0 Hz, 1H), 4.44-4.32 (m, 2H), 3.95 (ddd, *J* = 7.8, 7.3, 4.9 Hz, 1H), 3.69 (ddd, *J* = 7.8, 6.8, 4.4 Hz, 1H), 2.38 (AB of ABX, J_{AB} = 14.0, J_{AX} = 7.3, J_{BX} = 4.9, Hz, 2H), 2.02 (s, 1H), 1.59-1.45 (m, 3H), 1.39 (s, 3H), 1.38 (s, 3H) 1.28 (m, 9H), 1.00 (t, *J* = 7.8 Hz, 9H), 0.88 (t, *J* = 6.7 Hz, 3H), 0.62 (q, *J* = 7.8 Hz, 6H); **^{13}C NMR (75 MHz, CDCl$_3$)** δ 138.91, 121.40, 108.41, 103.31, 98.91, 80.90, 78.93, 61.60, 40.90, 33.23, 32.02, 29.96, 29.41, 27.50, 27.43, 26.20, 22.85, 14.26, 7.70, 4.55; **IR (neat)** ν_{max} = 3442, 2932, 2141, 1238 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{24}H_{44}O_3SiNa$ [M$^+$+Na] 431.2957, found 431.2972; $[\alpha]_D^{21}$ +10.99 (*c* 1.16, CHCl$_3$).

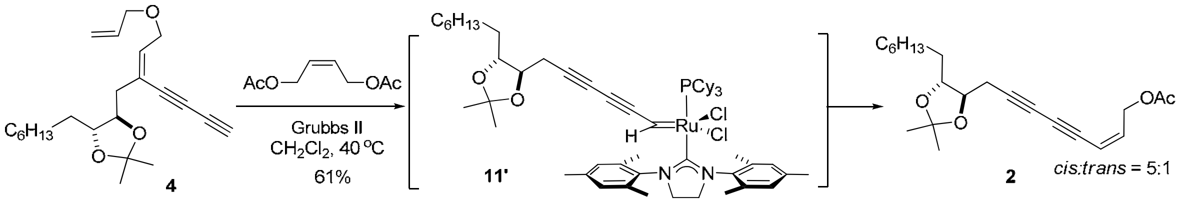
To a solution of silane **S2** (1.75 g, 4.28 mmol) in THF under N_2 were added a small amount of acetic acid and *n*-BuN$_4$F (4.50 mL, 1.0 M solution in THF) at room temperature. After approximately 25 min, the reaction was quenched with saturated aqueous NH$_4$Cl, extracted with ethyl ether, and the extracts were dried over MgSO$_4$. After filtration, the solvent was removed and the crude material was purified by flash chromatography (silica gel) to afford **S3** as a pale yellow oil (1.25 g, 99%). **^{1}H NMR (300 MHz, CDCl$_3$)** δ 6.08 (t, *J* = 6.6 Hz, 1H), 4.38 (d, *J* = 6.6 Hz, 2H), 3.90 (ddd, *J* = 7.8, 7.4, 5.0 Hz, 1H), 3.72-3.65 (m, 1H), 3.22 (s, 1H), 2.40 (AB of ABX, J_{AB} = 14.3, J_{AX} = 7.4, J_{BX} = 5.0, Hz, 2H), 1.74 (broad s, 1H), 1.58-1.43 (m, 3H), 1.39 (s, 3H), 1.38 (s, 3H) 1.28 (m, 9H), 0.88 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR (75 MHz, CDCl$_3$)** δ 139.80, 120.50, 108.50, 83.74, 80.94, 78.81, 61.41, 40.75, 33.18, 32.01, 29.88, 29.39, 27.58, 27.46, 26.26, 22.86, 14.30; **IR (neat)** ν_{max} = 3312, 2929, 2902 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{18}H_{30}O_3Na$ [M$^+$+Na] 317.2093, found 317.2080; $[\alpha]_D^{21}$ +23.50 (*c* 0.88, CHCl$_3$).

To a solution of allylic alcohol **S3** (1.20 g, 4.08 mmol) in DMF was added allyl bromide (0.99 g, 8.15 mmol) at room temperature and then NaH (196 mmg, 4.89 mmol) was subsequently added (Addition of NaH before allyl bromide generated a tetrahydrofuran derivative as a major side product). After two hours, the reaction was complete as indicated by TLC. The solution was quenched with saturated NH$_4$Cl solution. The organic material was extracted with ethyl ether. The ether layer was washed with brine solution and dried with MgSO$_4$. After filtration, the solvent was removed under reduced pressure and the crude material was purified by flash chromatography to give colorless oil **10** (1.30 g, 95%). **^{1}H NMR (300 MHz, CDCl$_3$)** δ 6.03 (t, *J* = 6.4 Hz, 1H), 5.92 (ddt, *J* = 17.2, 10.5, 5.7 Hz, 1H), 5.32 (ddt, *J* = 17.2, 1.6, 1.6 Hz, 1H), 5.19 (ddt, *J* = 10.5 , 1.6, 1.4 Hz, 1H), 4.24 (d, *J* = 6.4 Hz, 2H), 3.99 (ddd, *J* = 5.7, 1.6, 1.4 Hz, 2H), 3.90 (ddd, *J* = 7.6, 7.2, 5.0 Hz, 1H), 3.72-3.66 (m, 1H), 3.20 (s, 1H), 2.41 (AB of ABX, J_{AB} = 14.0, J_{AX} = 7.2, J_{BX} = 5.0, Hz, 2H), 1.55-1.43 (m, 3H), 1.39 (s, 3H), 1.38 (s, 3H) 1.28 (m, 9H), 0.88 (t, *J* = 6.7 Hz, 3H); **^{13}C NMR (75 MHz, CDCl$_3$)** δ 137.74, 134.80, 121.06, 117.33, 108.36, 83.62, 81.06, 80.95, 78.78, 71.44, 68.42, 40.80, 33.22, 31.97, 29.84, 29.35, 27.55, 27.43, 26.24, 22.81, 14.26; **IR (neat)** ν_{max} = 2930, 2094, 1064 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{21}H_{34}O_3$ [M$^+$] 334.2508, found 334.2521; $[\alpha]_D^{21}$ +26.24 (*c* 1.01, CHCl$_3$).

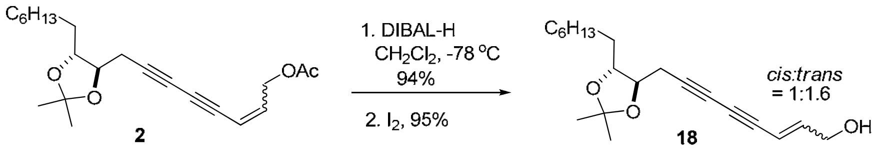


Copper(I) chloride (77 mg, 0.78 mmol) was added to a stirred solution of *n*-BuNH$_2$ (9 mL) and distilled water (21 mL) at 0 ^{o}C to result in a deep blue solution. A few crystals of NH$_2$OH·HCl were added to get a colorless solution, which is indicative of the presence of the required Cu(I) salt. To this solution, was added alkyne **10** in CH$_2$Cl$_2$ (1.30 g, 3.89 mmol) upon which was a yellow suspension formed. Then a freshly prepared bromoalkyne **7** (1.28 g, 5.84 mmol) was slowly added under a flow of N$_2$ in order to prevent the solution from turning to green or blue (NH$_2$OH·HCl can be added as necessary throughout the reaction). The reaction mixture was allowed to warm up to room temperature. After stirring for 5~10 minutes, the brownish orange colored solution was extracted twice with CH$_2$Cl$_2$, dried over magnesium sulfate, and concentrated under vacuum. Purification by flash chromatography on silica gel (hexane/ethyl ether) afforded the product **S4** (1.77 g, 96%). **^{1}H NMR (300 MHz, CDCl$_3$)** δ 6.12 (t, *J* = 6.6 Hz, 1H), 5.92 (ddt, *J* = 17.3, 10.2, 5.6 Hz, 1H), 5.30 (ddt, *J* = 17.3, 1.6, 1.5 Hz, 1H), 5.20 (ddt, *J* = 10.2 , 1.6, 1.3 Hz, 1H), 4.24 (d, *J* = 6.4 Hz, 2H), 3.99 (ddd, *J* = 5.6, 1.5, 1.3 Hz, 2H), 3.88-3.81 (m, 1H), 3.72-3.65 (m, 1H), 2.41 (AB of ABX, J_{AB} = 14.3, J_{AX} = 6.9, J_{BX} = 5.1, Hz, 2H), 1.55-1.47 (m, 3H), 1.38 (s, 3H), 1.37 (s, 3H) 1.28 (m, 9H), 1.01 (t, *J* = 7.8 Hz, 9H), 0.88 (t, *J* = 6.6 Hz, 3H), 0.65 (q, *J* = 7.8 Hz, 6H); **^{13}C NMR (75 MHz, CDCl$_3$)** δ 140.64, 134.72, 120.53, 117.50, 108.41, 90.38, 88.58, 80.93, 80.40, 78.87, 73.50, 71.56, 68.56, 40.44, 33.23, 32.00, 29.88, 29.39, 27.58, 27.43, 26.30, 22.85, 14.28, 7.54, 4.36; **IR (neat)** ν_{max} = 2932, 2196, 2099, 1089 cm^{-1}; **HRMS *m/z* (ESI)** calc. for C$_{29}$H$_{48}$O$_3$SiNa [M$^+$+Na] 495.3270, found 495.3274; $[\alpha]_D^{21}$ +21.71 (*c* 0.88, CHCl$_3$).

To a solution of silane **S4** (1.77 g, 3.74 mmol) in THF under N$_2$ were added a small amount of acetic acid and *n*-BuN$_4$F (3.93 mL, 1.0 M solution in THF) at room temperature. After approx. 10 min, the reaction was complete as indicated by TLC. The solution was quenched with saturated NH$_4$Cl solution. The organic material was extracted with ethyl ether and dried with MgSO$_4$. After filtration, the solvent was removed under reduced pressure and the crude material was purified by flash chromatography on silica gel to afford the desilylated product **4** as a pale yellow oil (1.29 g, 96%). **^{1}H NMR (300 MHz, CDCl$_3$)** δ 6.16 (t, *J* = 6.6 Hz, 1H), 5.92 (ddt, *J* = 17.2, 10.2, 5.7 Hz, 1H), 5.30 (ddt, *J* = 17.2, 1.4, 1.4 Hz, 1H), 5.21 (ddt, *J* = 10.2 , 1.4, 1.4 Hz, 1H), 4.24 (d, *J* = 6.6 Hz, 2H), 3.99 (ddd, *J* = 5.7, 1.4, 1.4 Hz, 2H), 3.88-3.81 (m, 1H), 3.71-3.65 (m, 1H), 2.54 (s, 1H), 2.41 (AB of ABX, J_{AB} = 14.4, J_{AX} = 6.9, J_{BX} = 5.7, Hz, 2H), 1.58-1.46 (m, 3H), 1.39 (s, 3H), 1.38 (s, 3H) 1.28 (m, 9H), 0.88 (t, *J* = 6.7 Hz, 3H); **^{13}C NMR (75 MHz, CDCl$_3$)** δ 141.26, 134.67, 120.25, 117.65, 108.53, 80.90, 79.44, 78.88, 72.95, 72.88, 71.65, 68.49, 67.96, 40.33, 33.23, 32.01, 29.88, 29.40, 27.59, 27.46, 26.30, 22.87, 14.31; **IR (neat)** ν_{max} = 2930, 2857, 2202, 1085 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{23}H_{34}O_3Na$ [M$^+$+Na] 381.2406, found 381.2406; $[\alpha]_D^{21}$ +27.36 (*c* 1.59, $CHCl_3$).

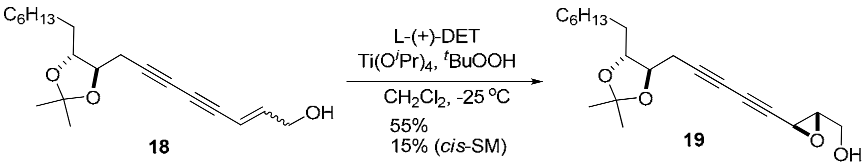


The endiyne **4** (180 mg, 0.50 mmol) was added to a solution of alkene **4** (173 mg, 1.0 mmol) in dry dichloromethane (10 mL) under a N_2 atmosphere. Grubbs second generation catalyst (30 mg, 0.035 mmol) was added and the reaction was heated to 40 °C. The reaction was monitored by TLC until complete consumption of starting endiyne. After the reaction was complete, the solvent was removed in vacuo and the crude material was purified by silica gel chromatography to give compound **2** (110 mg, 61% yield) together with ruthenium alkylidene complex **11'**. **Compound 2: ^{1}H NMR (300 MHz, $CDCl_3$) *cis*** δ 6.14 (dt, *J* = 11.0, 6.6 Hz, 1H), 5.68 (dd, *J* = 11.0, 1.0 Hz, 1H), 4.82 (dd, *J* = 6.6, 1.0 Hz, 2H), 3.85-3.71 (m, 2H), 2.67-2.64 (m, 2H), 2.08 (s, 3H), 1.64-1.46 (m, 3H), 1.40 (s, 6H) 1.33-1.28 (m, 9H), 0.88 (t, *J* = 6.8 Hz, 3H); ***trans*** δ 6.28 (dt, *J* = 15.9, 5.8 Hz, 1H), 5.76 (dd, *J* = 15.9, 1.0 Hz, 1H), 4.61 (dd, *J* = 5.8, 1.0 Hz, 2H), 3.85-3.71 (m, 2H), 2.65 (d, *J* = 4.4 Hz, 2H), 2.08 (s, 3H), 1.64-1.46 (m, 3H), 1.40 (s, 6H) 1.33-1.28 (m, 9H), 0.88 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$) *cis*** δ 170.83, 140.09, 111.76, 108.89, 81.64, 80.66, 78.34, 70.78, 67.08, 63.79, 62.52, 33.09, 31.97, 29.80, 29.32, 27.61, 27.22, 26.13, 24.07, 22.83, 20.97, 14.27; ***trans*** δ 170.54, 139.81, 112.15, 108.86, 80.66, 80.12, 78.34, 75.60, 73.11, 67.28, 63.79, 33.09, 31.97, 29.80, 29.32, 27.61, 27.22, 26.13, 24.02, 22.83, 20.94, 14.27; **IR (neat)** ν_{max} = 2931, 2236, 1746, 1229 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{22}H_{32}O_4Na$ [M$^+$+Na] 383.2198, found 383.2195. **Compound 11': ^{1}H NMR (300 MHz, $CDCl_3$)** δ 18.54 (s, 1H), 6.96 (broad s, 2H), 6.92 (broad s, 2H), 3.93 (m, 4H), 3.87-3.75 (m, 2H), 2.58 (s, 6H), 2.44 (d, *J* = 5.2 H z, 2H), 2.40 (s, 6H), 2.31 (s, 3H), 2.29 (s, 3H), 2.26-2.19 (m, 3H), 1.42 (s, 3H), 1.41 (s, 3H), 1.60-0.86 (m, 45H); **^{31}P NMR ($CDCl_3$)** δ 30.14; **HRMS *m/z* (FAB)** calc. for $C_{57}H_{87}O_2N_2Cl_2PRu$ [M$^+$+1] 1034.493, found 1034.4937.

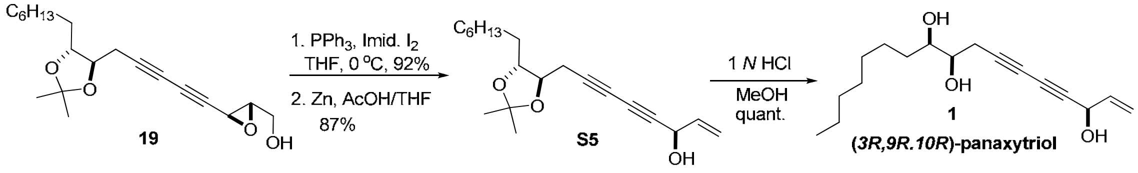


To a stirred solution of the acetate **2** (0.35 g, 0.97 mmol) in dry dichloromethane under N_2 atmosphere was slowly added DIBAL-H (0.21 mL, 1.17 mmol) in dichloromethane (0.2 mL) at -78

^{o}C. After approx. 20 min, the reaction quenched with 10% aqueous KOH solution. The organic material was extracted with dichloromethane and dried with $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel) to give the allylic alcohol **18** (0.29 g, 94%). Subsequently, 0.1 equiv of iodine was added to a solution of **18** in $CHCl_3$ at room temperature. After 30 min, the solution was poured into aqueous solution of $Na_2S_2O_3$ and extracted with dichloromethane. The organic phase was dried with $MgSO_4$, and the solvent was removed under reduced pressure and the crude material was purified by flash chromatography (silica gel) to give a mixture of (*E*)- and (*Z*)-**18** (275 mg, 95%). **^{1}H NMR (300 MHz, $CDCl_3$)** (*Z*)-**18** δ 6.23 (dt, *J* = 10.9, 6.5 Hz, 1H), 5.60 (dt, *J* = 10.9, 1.1 Hz, 1H), 4.42 (dd, *J* = 6.5, 1.1 Hz, 2H), 3.82 (ddd, *J* = 7.8, 7.1, 4.1 Hz, 1H), 3.74 (dt, *J* = 7.8, 5.3 Hz, 1H), 2.73-2.59 (m, 2H), 1.66 (broad s, 1H), 1.64-1.47 (m, 3H), 1.41 (s, 6H) 1.35-1.25 (m, 9H), 0.88 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$)** (*Z*)-**18** δ 145.54, 109.64, 108.94, 81.26, 80.68, 79.90, 78.39, 71.37, 67.14, 61.35, 33.12, 31.99, 29.85, 29.35, 27.63, 27.25, 26.17, 24.09, 22.86, 14.30; **IR (neat)** ν_{max} = 3418, 2930, 2237, 1378 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{20}H_{30}O_3$ [M$^+$] 318.2195, found 318.2199; $[\alpha]_D^{21}$ +43.41 (*c* 0.36, $CHCl_3$).

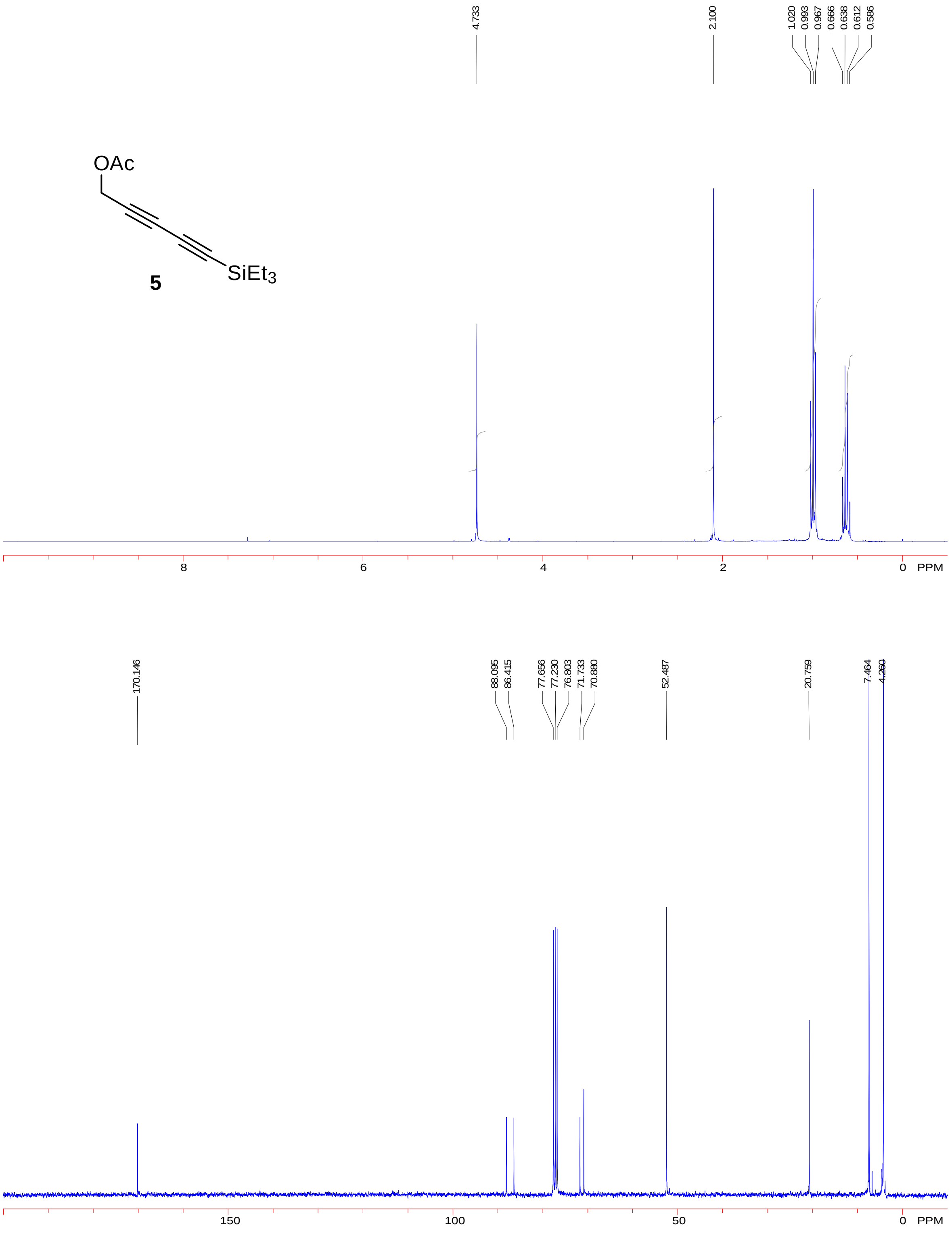


Titanium(IV) isopropoxide (35mg, 0.14 mmol) was slowly added to a mixture of L-(+)-diethyltartrate (29 mg, 0.14 mmol) and powdered activated molecular sieves (4Å, 30 mg) in CH_2Cl_2 (1 mL) at -25 ^{o}C. The mixture was allowed to stand at -25 ^{o}C for 1 h, and compound **18** (30 mg, 0.094 mmol, *trans*:*cis*=1.6:1) in CH_2Cl_2 (0.5 mL) was added. The reaction mixture was stirred at -20 ^{o}C for an additional 20 min, and a decane solution of *ter*-butyl hydroperoxide (5.5 M, 0.05 mL) was added slowly. The reaction mixture was maintained at -25 ^{o}C for an additional 16 h, quenched with 10% aqueous tartaric acid (1.5 mL) and stirred at the same temperature for 30 min and at room temperature for 1 h. It was then extracted with CH_2Cl_2, and the organic extract was dried and concentrated under reduced pressure. The residue was purified by silicagel chromatography to give compound **19** (17.4 mg, 55% and 15% of *cis*-starting material recovered). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.95 (d, *J* = 12.9 Hz, 1H), 3.83-3.69 (m, 3H), 3.51 (d, *J* = 2.0 Hz, 1H), 3.34 (dt, *J* = 3.0, 2.3 Hz, 1H), 2.60 (AB of ABX, J_{AB} = 16.3, J_{AX} = 4.2, J_{BX} = 3.7, Hz, 2H), 1.65 (broad s, 1H), 1.61-1.47 (m, 3H), 1.40 (s, 6H) 1.34-1.25 (m, 9H), 0.89 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$)** δ 108.95, 80.60, 78.22, 76.92, 72.28, 69.24, 66.68, 60.25, 60.09, 42.81, 33.07, 31.98, 29.82, 29.35, 27.61, 27.24, 26.15, 23.70, 22.85, 14.30; **IR (neat)** ν_{max} = 3419, 2929, 2257 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{20}H_{30}O_4Na$ [M$^+$+Na] 357.2042, found 357.2039; $[\alpha]_D^{21}$ +6.03 (*c* 0.63, $CHCl_3$).



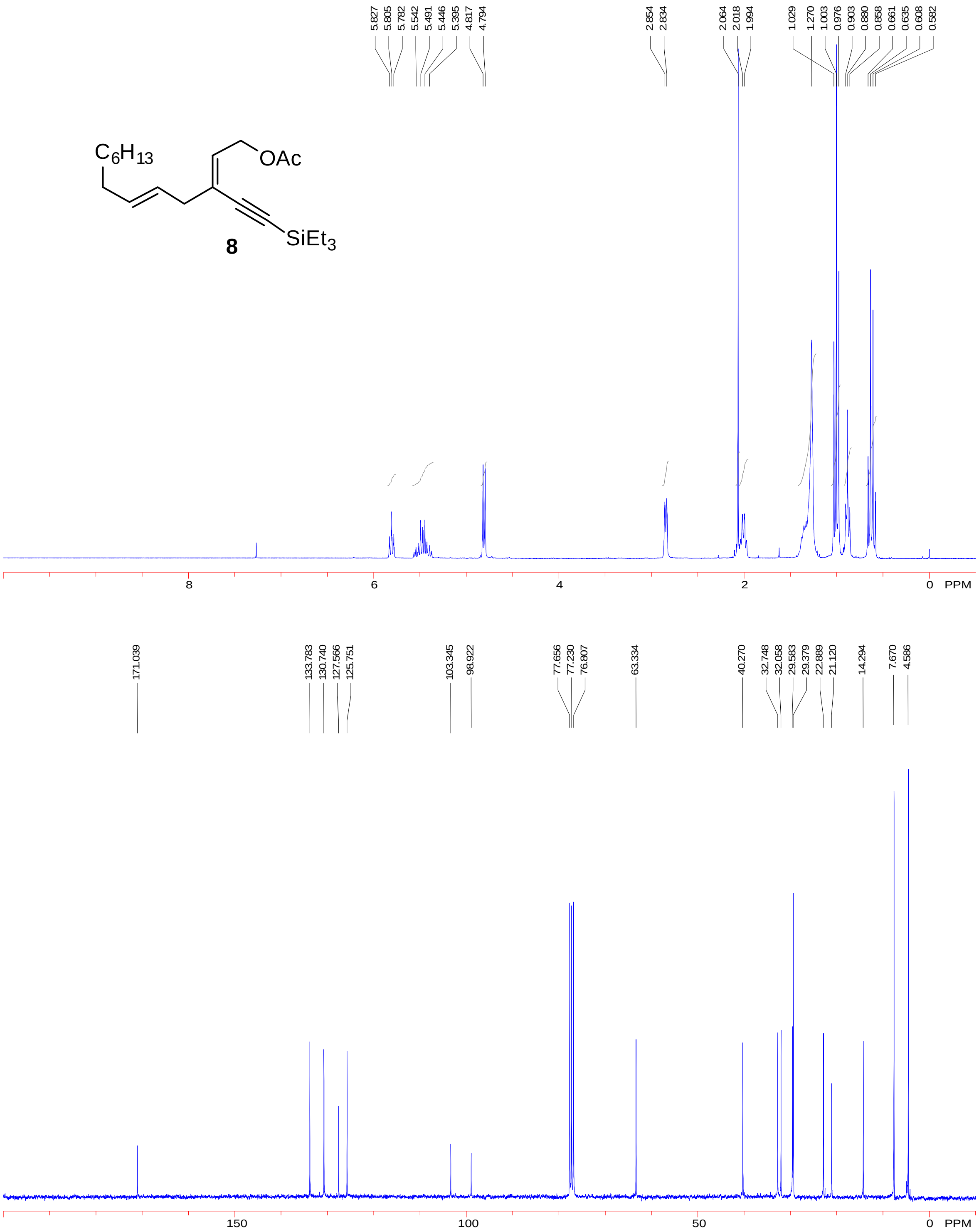
To a solution of epoxy alcohol **19** (18 mg, 0.054 mmol) in THF were added PPh_3, imidazole and iodine at 0 °C. After approx. 10 min, the reaction was complete as indicated by TLC. The solution was quenched and washed with saturated aqueous $Na_2S_2O_3$ solution. The organic material was extracted with ethyl ether and dried with $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the crude material was purified by flash chromatography on silica gel to give the corresponding allylic iodide (22 mg, 92%). Subsequently, Zn dust was added to a solution of the iodide (20 mg, 0.045 mmol) in acetic acid and THF at room temperature. After two hours the reaction was complete as indicated by TLC. The solution was quenched with water. Organic material was extracted with ethyl ether. The ether layer was washed successively with brine solution and dried with $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the crude material was purified by flash chromatography to give colorless oil **S5** (12.5 mg, 87%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.95 (ddd, *J* = 17.0, 10.2, 5.4 Hz, 1H), 5.47 (d, *J* = 17.0 Hz, 1H), 5.26 (d, *J* = 10.2 Hz, 1H), 4.92 (dd, *J* = 5.4, 5.4 Hz, 1H), 3.81 (ddd, *J* = 7.7, 7.5, 4.4 Hz, 1H), 3.73 (ddd, *J* = 7.7, 5.4, 5.1 Hz, 1H), 2.68-2.54 (m, 2H), 1.91 (d, *J* = 6.6 Hz, 1H), 1.63-1.54 (m, 3H), 1.40 (s, 6H) 1.34-1.25 (m, 9H), 0.88 (t, *J* = 6.6 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$)** δ 136.28, 117.34, 108.94, 80.69, 78.34, 74.84, 71.22, 68.19, 66.65, 63.73, 33.13, 32.01, 29.85, 29.37, 27.64, 27.27, 26.18, 23.81, 22.86, 14.31; **IR (neat)** ν_{max} = 3424, 2929, 1378 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{20}H_{30}O_3Na$ $[M^+ + Na]$ 341.2093, found 341.2089; $[\alpha]_D^{21}$ -9.33 (*c* 0.30, $CHCl_3$).

To a solution of acetonide **S5** (4 mg, 0.013 mmol) in MeOH was added aqueous 1 *N* HCl solution at room temperature. After two hours the reaction was complete as indicated by TLC. The solution was diluted with water. Organic material was extracted with ethyl acetate and dried with $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the crude material was purified by flash chromatography to give (3*R*,9*R*,10*R*)-panaxytriol **1** (3.5 mg, quantitative yield). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.95 (ddd, *J* = 17.0, 10.1, 5.3 Hz, 1H), 5.47 (ddd, *J* = 17.0, 1.4, 1.2 Hz, 1H), 5.26 (d, *J* = 10.2, 1.2, 1.1 Hz, 1H), 4.93 (dd, *J* = 5.4, 5.3 Hz, 1H), 3.69-3.56 (m, 2H), 2.59 (d, *J* = 5.5 Hz, 2H), 2.37(d, *J* = 5.4 Hz, 1H), 2.00 (d, *J* = 4.9 Hz, 1H), 1.60 (broad s, 1H), 1.54-1.44 (m, 3H), 1.36-1.24 (m, 9H), 0.88 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR (75 MHz, $CDCl_3$)** δ 136.26, 117.39, 78.34, 74.98, 73.31, 72.35, 71.14, 66.74, 63.73, 33.81, 32.02, 29.75, 29.42, 25.79, 25.22, 22.86, 14.30; **IR (neat)** ν_{max} = 3333, 2926, 2855, 2256, 2234 cm^{-1}; **HRMS *m/z* (ESI)** calc. for $C_{17}H_{26}O_3Na$ $[M^+ + Na]$ 301.1780, found 301.1794; $[\alpha]_D^{21}$ -13.89 (*c* 0.18, $CHCl_3$).



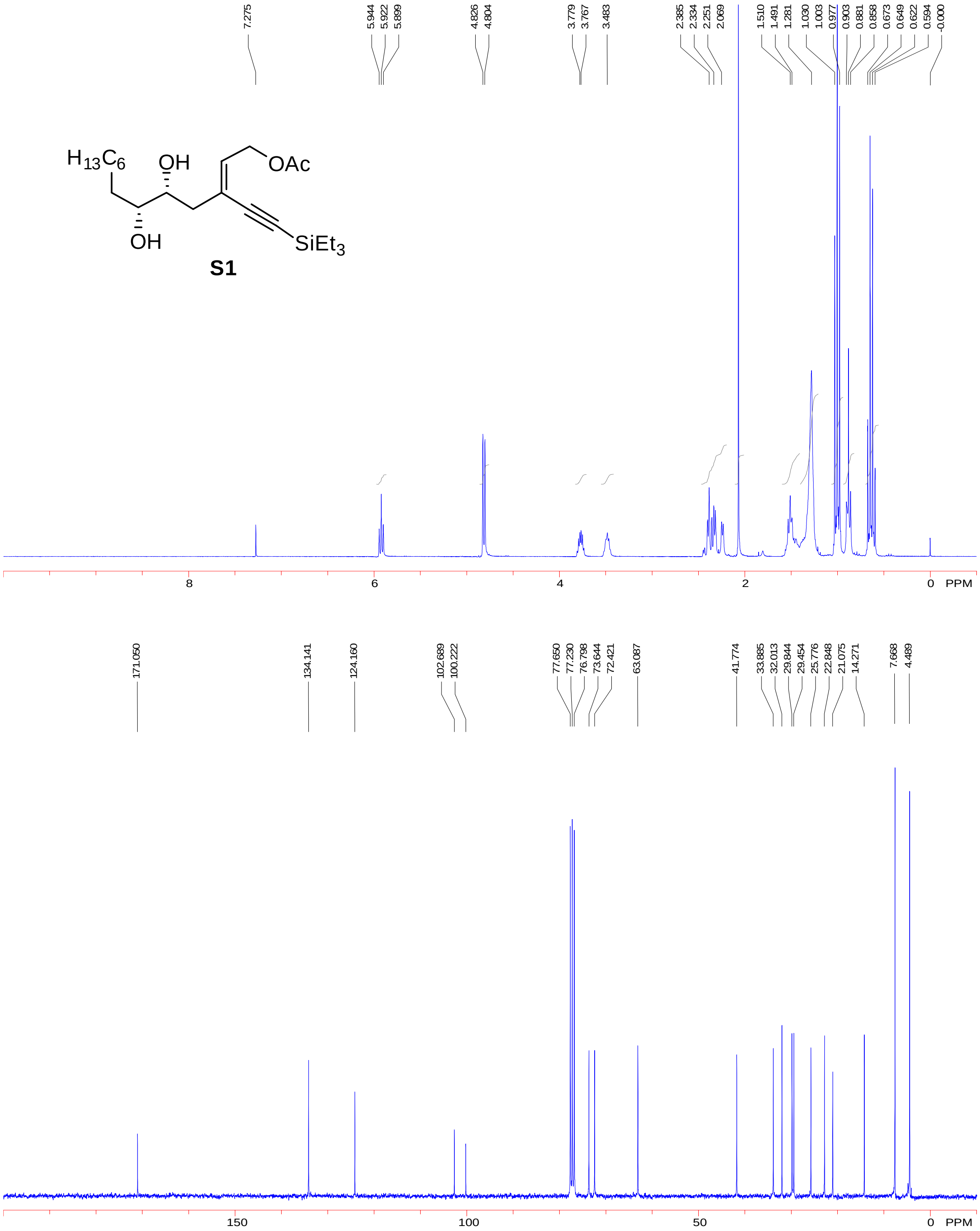
^{1}H NMR and ^{13}C NMR of **5**

See: Cho, E. J.; Lee, D. J. Am. Chem. Soc. ***2007****, 129, 6692-6693.*

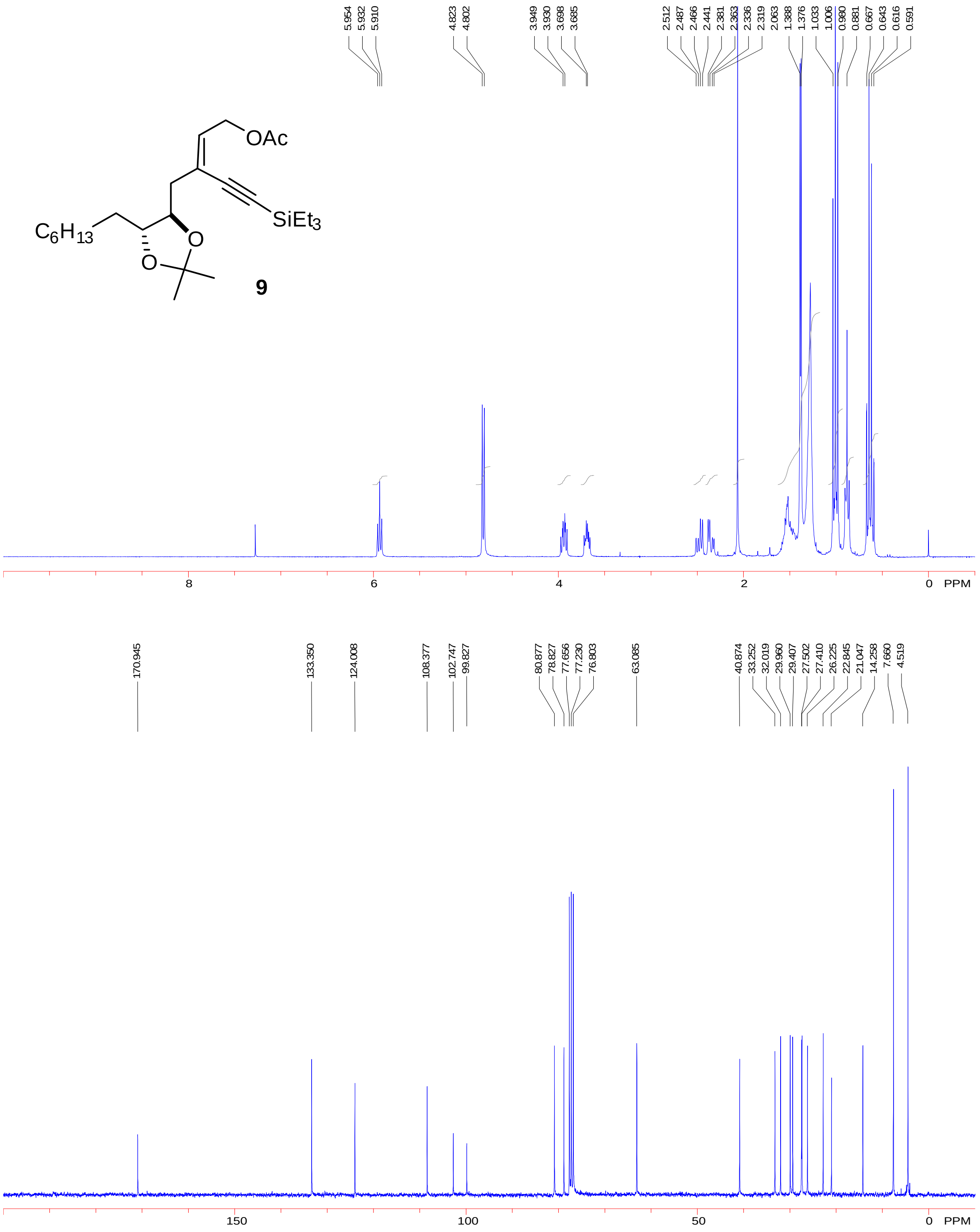


^{1}H NMR and ^{13}C NMR of **8**

See: Cho, E. J.; Lee, D. J. Am. Chem. Soc. ***2007****, 129, 6692-6693.*

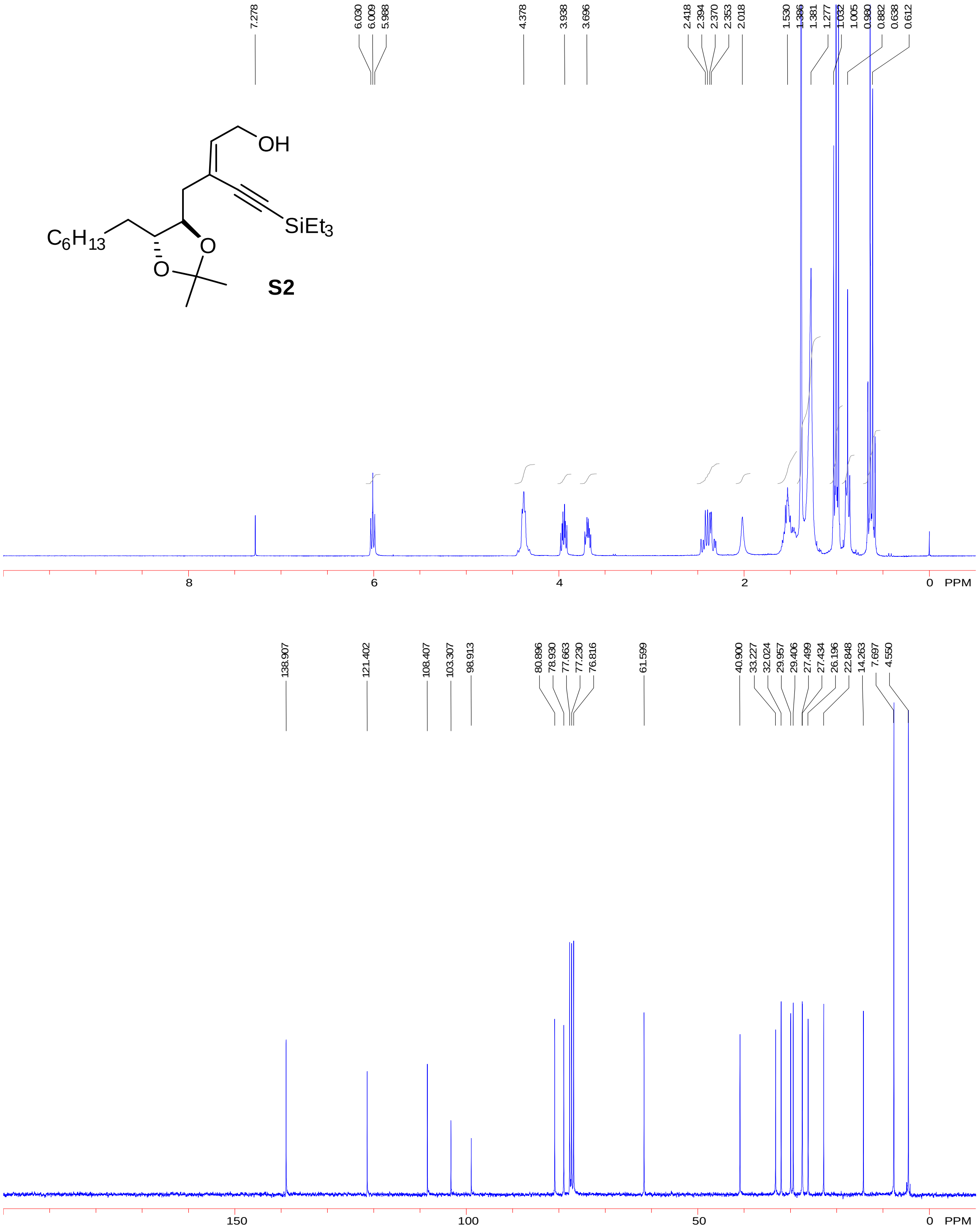


^{1}H NMR and ^{13}C NMR of **S1**

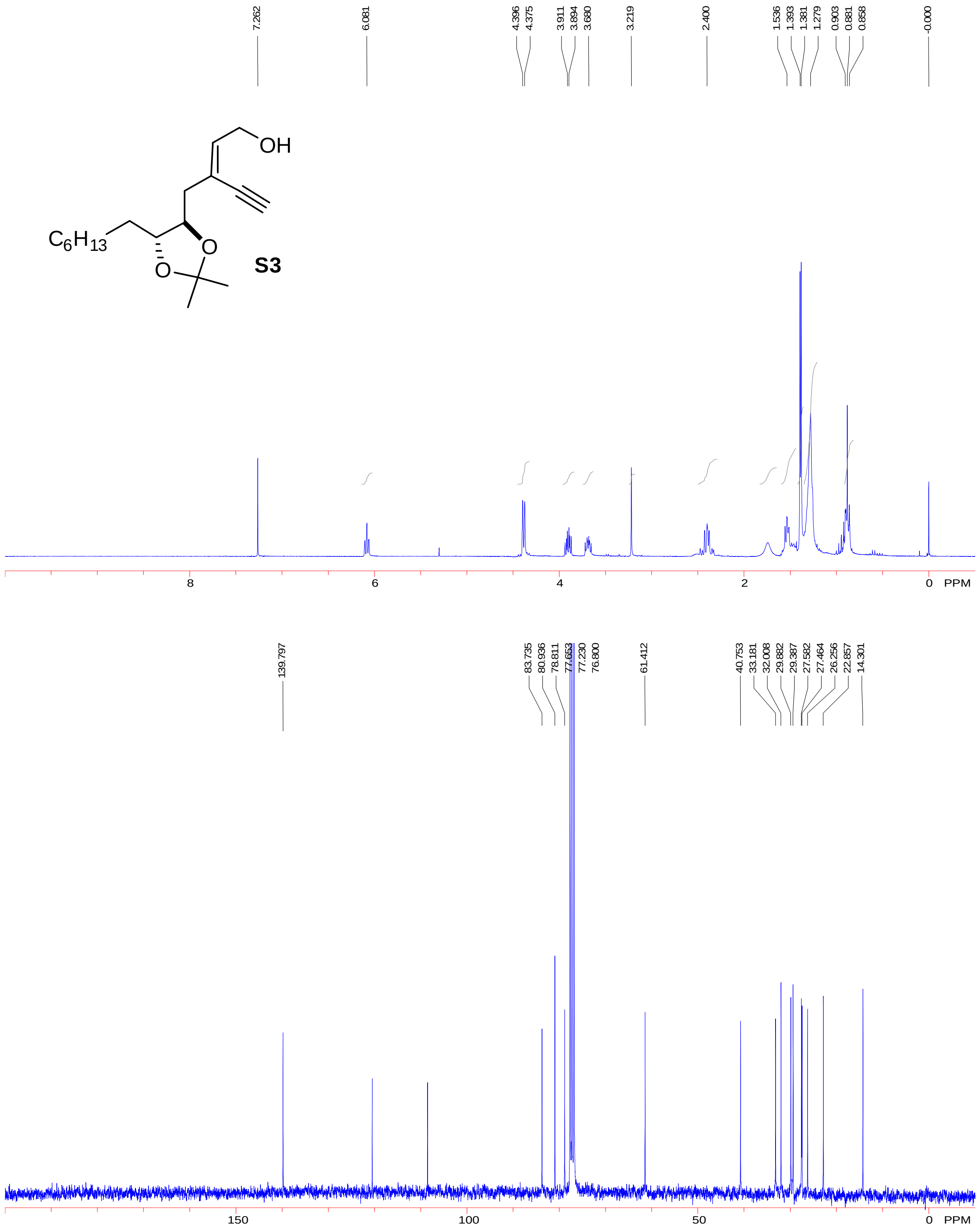


9

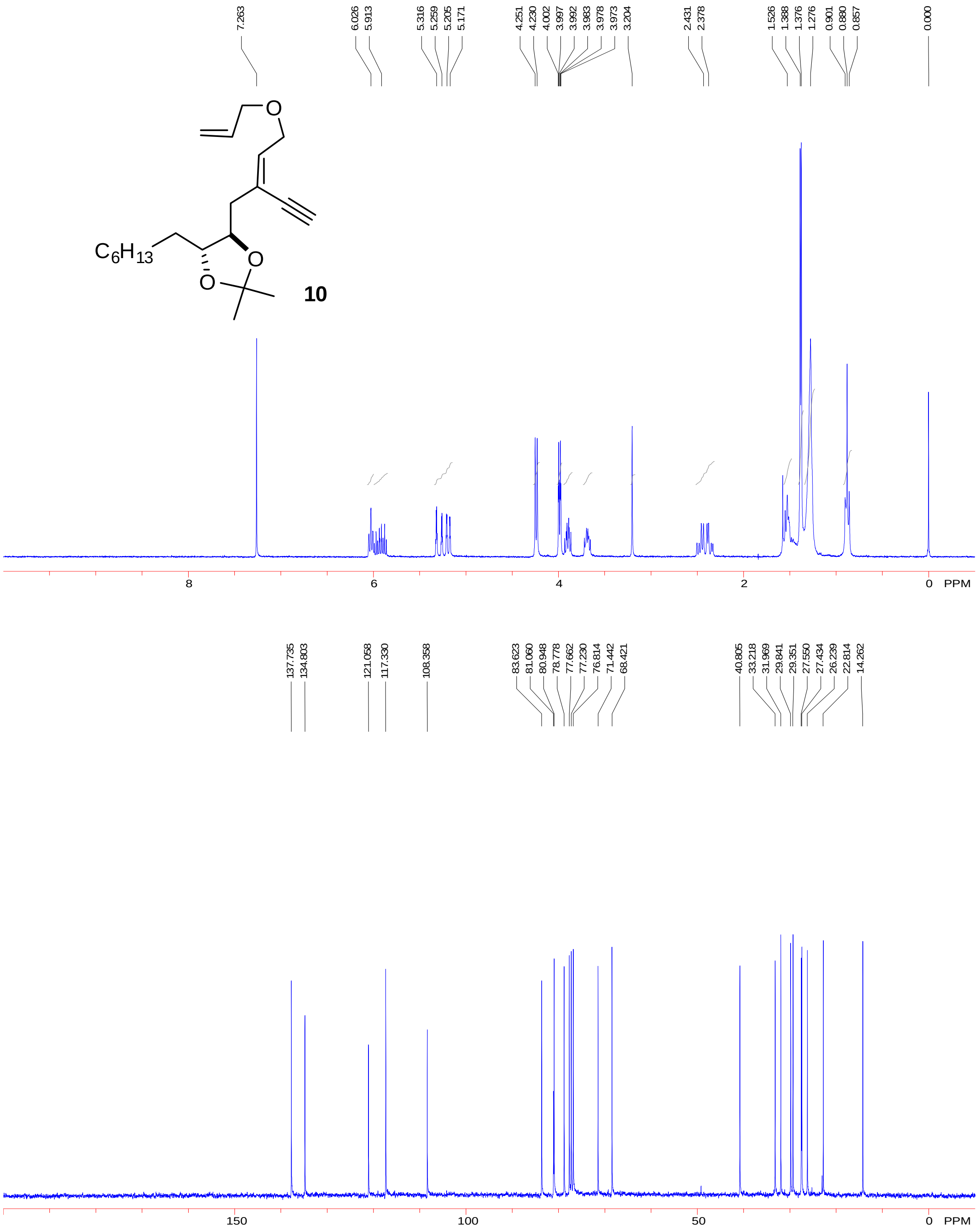
^{1}H NMR and ^{13}C NMR of **9**



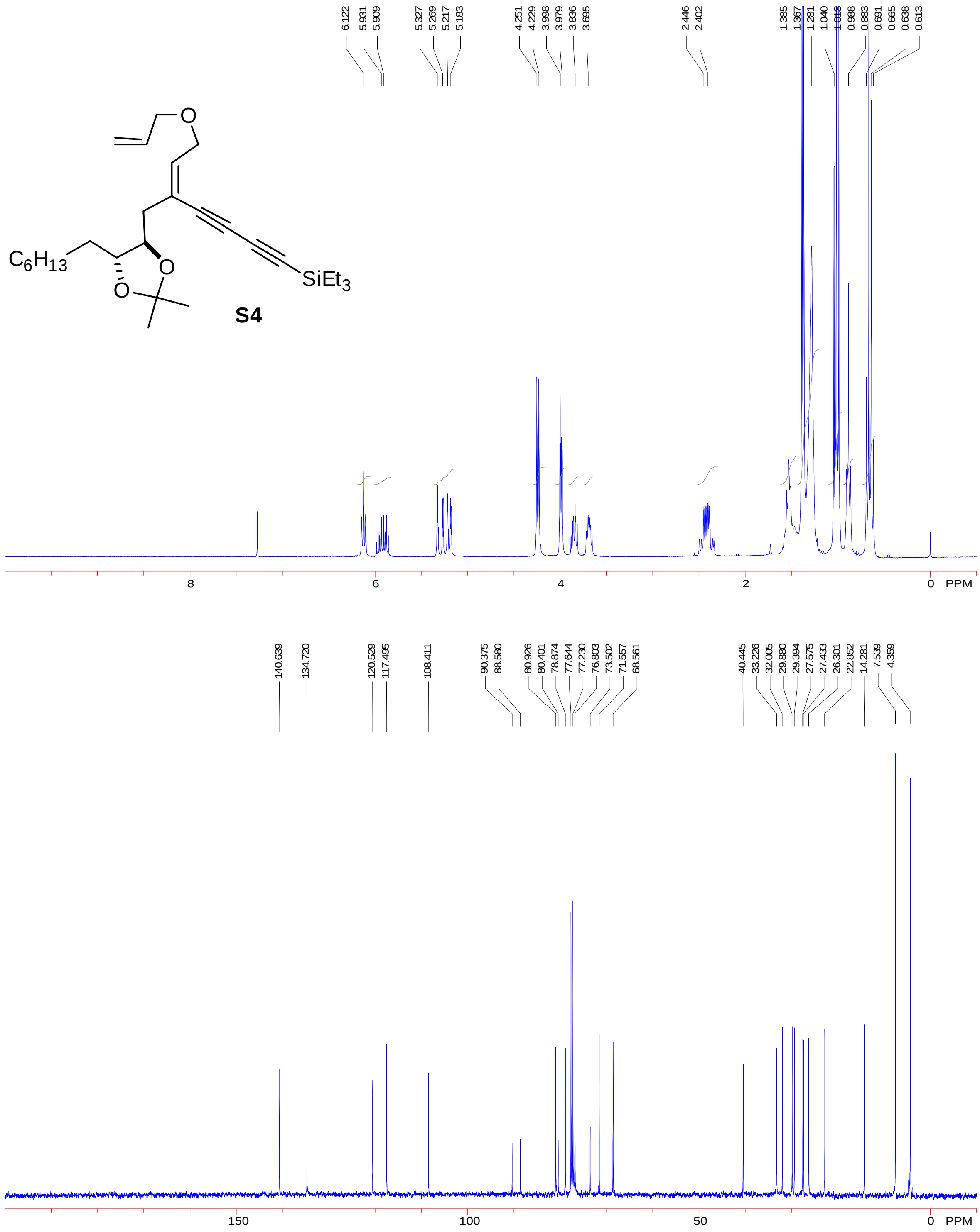
^{1}H NMR and ^{13}C NMR of **S2**



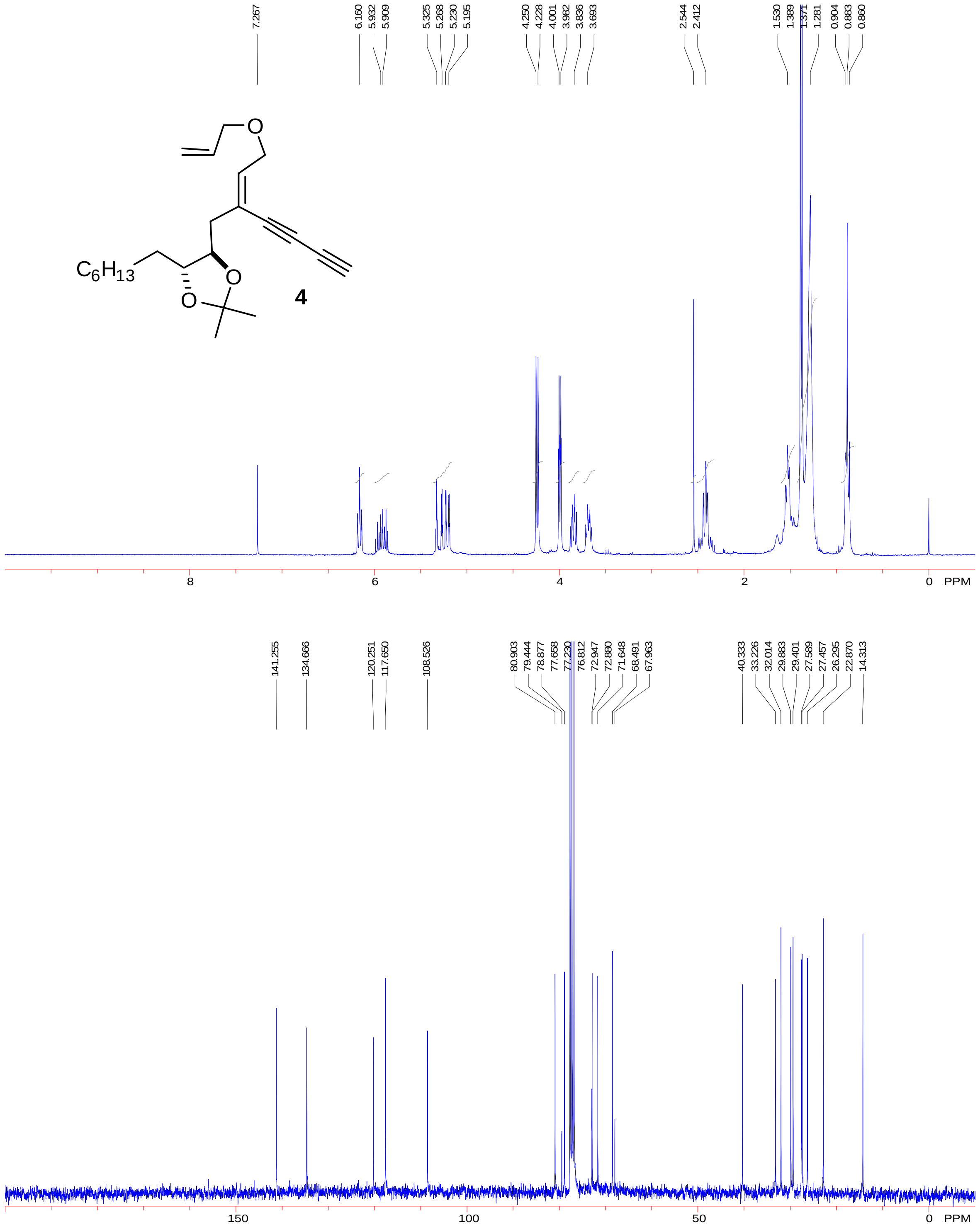
^{1}H NMR and ^{13}C NMR of **S3**



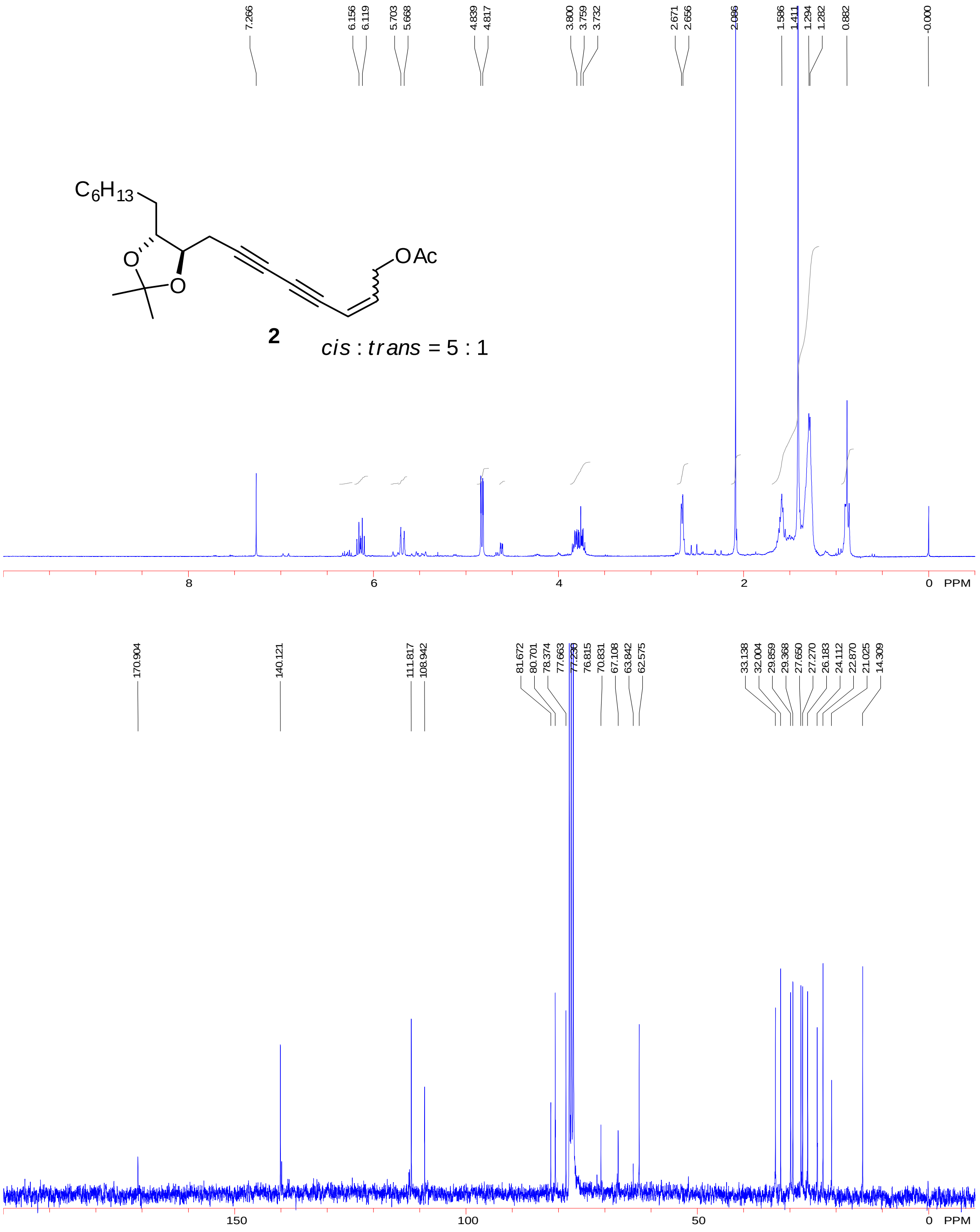
^{1}H NMR and ^{13}C NMR of **10**



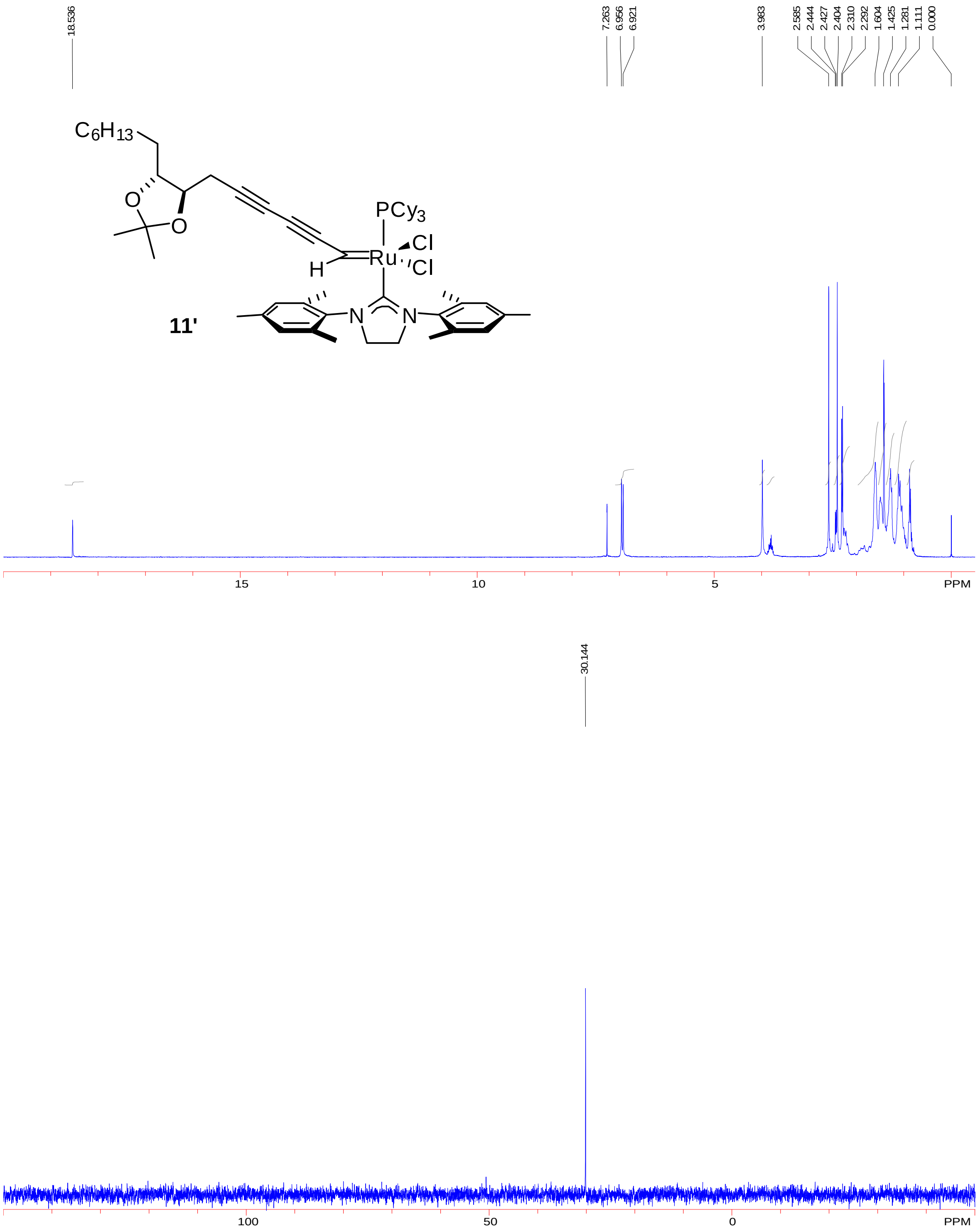
^{1}H NMR and ^{13}C NMR of **S4**



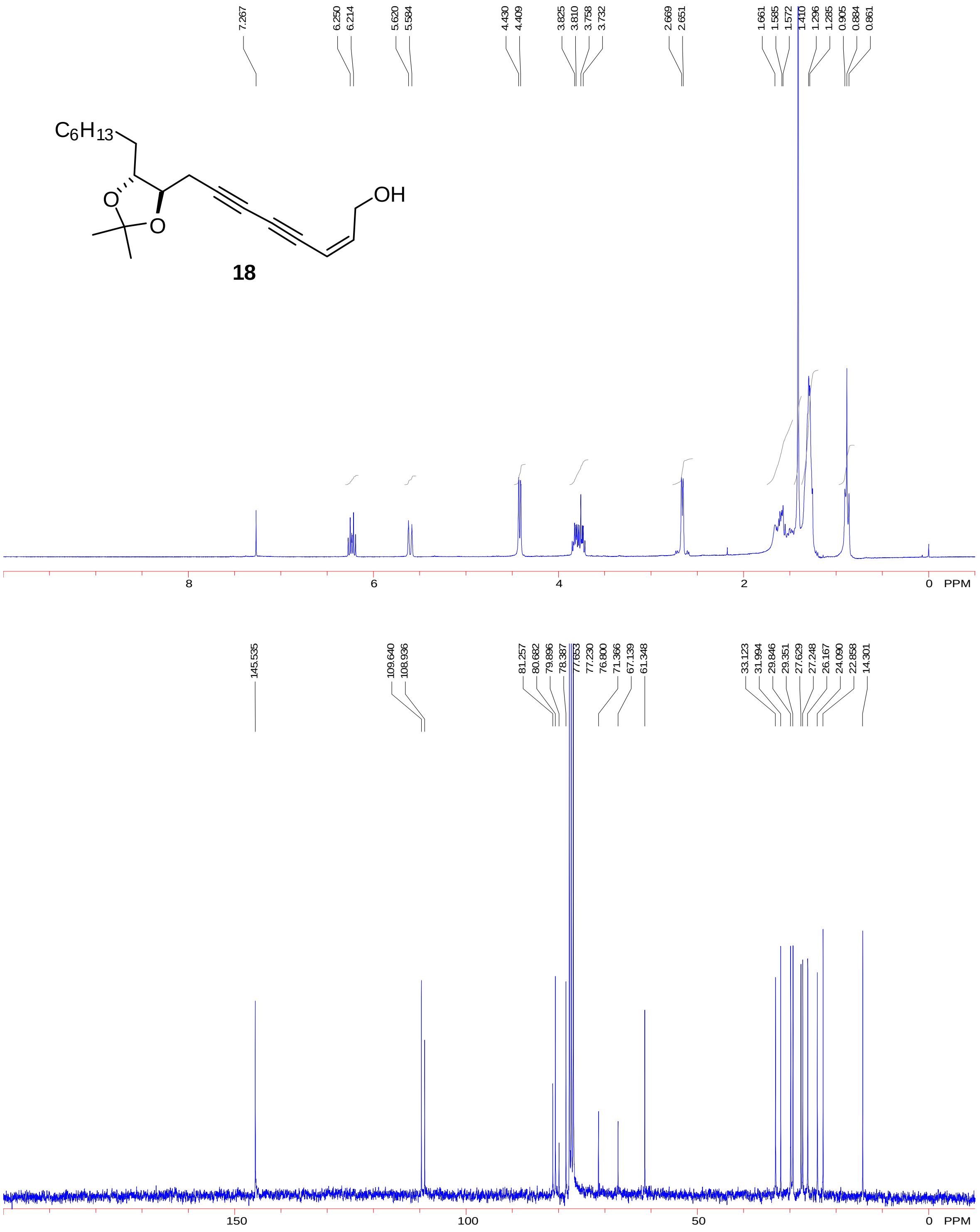
^{1}H NMR and ^{13}C NMR of **4**



^{1}H NMR and ^{13}C NMR of **2**

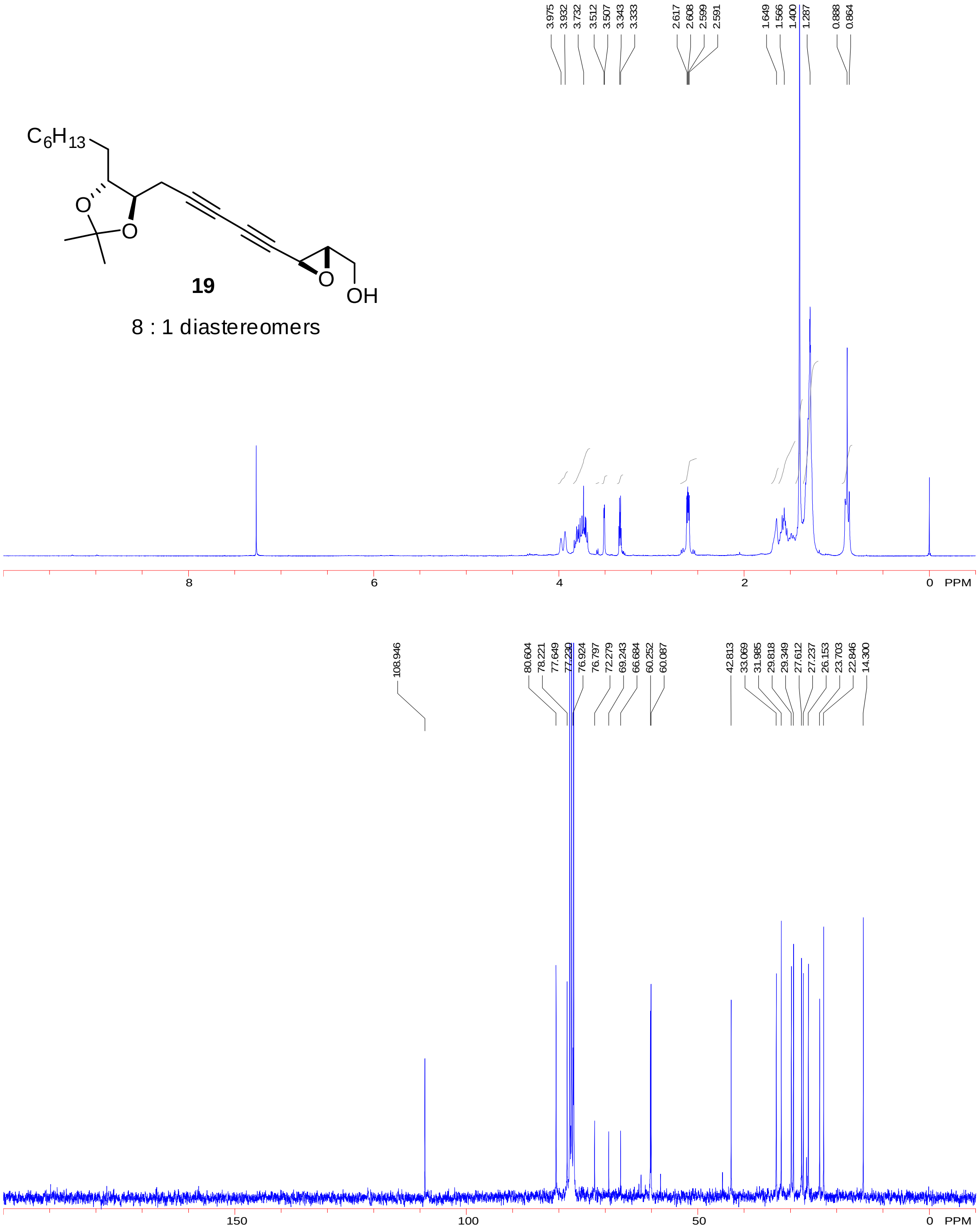


^{1}H NMR and ^{31}P NMR of **11'**



18

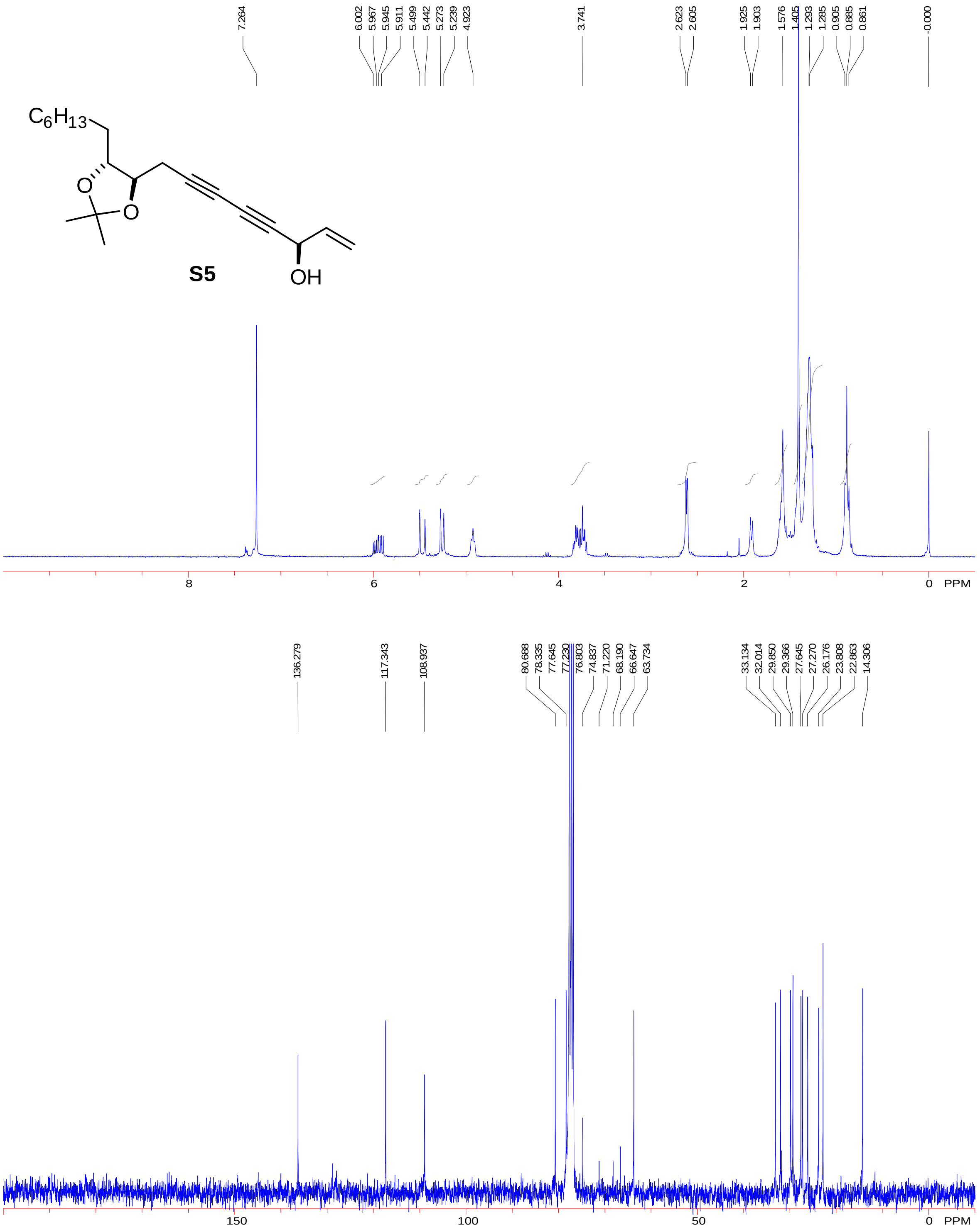
^{1}H NMR and ^{13}C NMR of *cis*-**18**



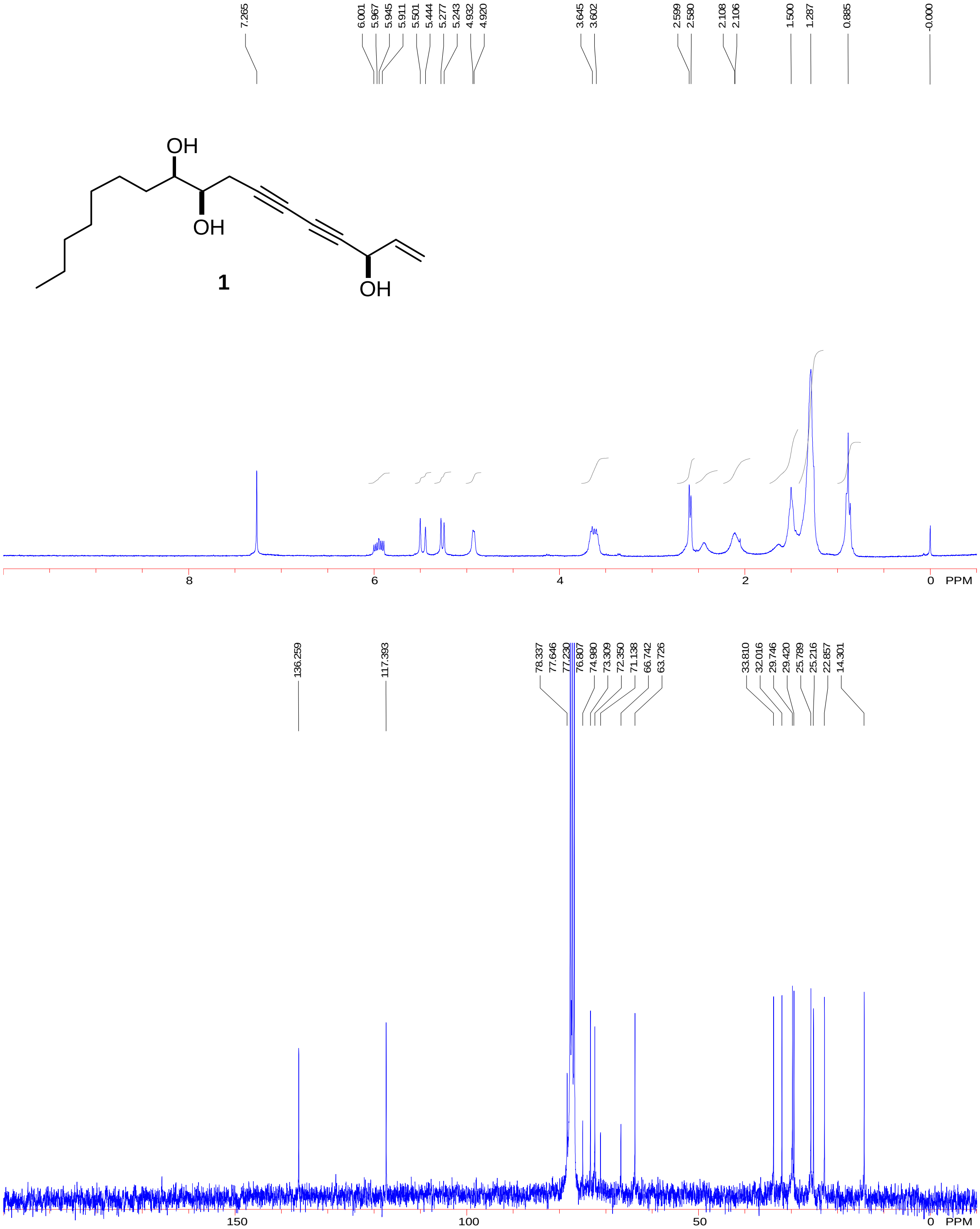
19

8 : 1 diastereomers

^{1}H NMR and ^{13}C NMR of **19**



^{1}H NMR and ^{13}C NMR of **S5**



^{1}H NMR and ^{13}C NMR of **1**