Supporting Information

for

Macrocyclic polyenynes: A stereoselective route to vinyl-ether-containing skipped diene systems

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Detailed experimental procedures, characterisation data and ^{1}H and ^{13}C NMR spectra for all compounds.

1. General Experimental Details

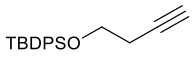
Reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros Organics or Fluorochem and used as received unless otherwise noted. Dry dichloromethane, THF, hexane, acetonitrile, toluene and diethyl ether were obtained from a Pure Solv MD-7 solvent machine and stored under nitrogen. Dry DMF was purchased from Acros Organics (<50 ppm water) and degassed by nitrogen bubbling and sonication prior to use. TMEDA was purified by distillation from KOH and stored under nitrogen. Petrol refers to the fraction of petroleum ether boiling in the range 40–60 °C.

Dess–Martin periodinane (DMP)[1] and Pd(Br)(*N*-Succ)($AsPh_3$)$_2$ (AsCat)[2] were synthesised using literature procedures.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Jeol ECX400 or Jeol ECS400 spectrometer operating at 400 and 100 MHz respectively, on a Bruker AV500 operating at 500 and 125 MHz respectively, or on a Bruker AV700 operating at 700 and 175 MHz respectively. ^{19}F and ^{31}P NMR spectra were recorded on a Jeol ECX400 spectrometer at 376 MHz and 162 MHz respectively; ^{119}Sn spectra were recorded on a Bruker AV500 spectrometer at 187 MHz. TLC analysis was carried out using Merck 5554 aluminium backed silica plates. Preparatory TLC was carried out using Analtech UNIPLATE glass-backed silica plates. Flash column chromatography was performed using Merck 60 silica gel (particle size 40–63 μm). Electrospray ionisation (ESI) mass spectrometry was performed on a Bruker daltronics micrOTOF spectrometer; electron impact (EI) and atmospheric pressure chemical ionisation (APCI) were performed on a Waters GCT Premier mass spectrometer. Less than 5 ppm error was recorded for all HRMS samples. Infrared (IR) spectroscopy was performed on a PerkinElmer Spectrum Two spectrometer using an UATR attachment. Melting point analyses were performed on a Stuart SMP3 melting point apparatus, using a temperature ramp of 3 °C/minute.

2. Experimental Procedures and Characterisation Data

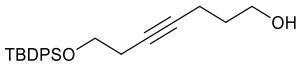
(But-3-ynyloxy)*tert*-butyldiphenylsilane (3)[3]



To a stirred solution of 3-butyn-1-ol (2.5 g, 35.7 mmol) and imidazole (2.55 g, 35.7 mmol) in CH_2Cl_2 (200 mL) was added dropwise *tert*-butyldiphenylchlorosilane (9.27 mL, 35.7 mmol). The resulting mixture was stirred for 24 h at RT, before being filtered through a short plug of silica gel, eluting with CH_2Cl_2. The solution was concentrated *in vacuo* to afford the *title compound* as a colourless oil (10.85 g, 99%).

R_f 0.54 (ether/petrol, 1:9, *v*/*v*); IR (thin film)/cm^{-1} 3309w, 3072w, 2931m, 2858m, 1473m, 1428m, 1384w, 1106s, 1008w, 918m, 823m, 799w, 737m, 700s, 613s, 503s, 488s; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.66 (m, 4H), 7.45–7.35 (m, 6H), 3.79 (t, *J* = 7.1 Hz, 2H), 2.45 (td, *J* = 7.1, 2.7 Hz, 2H), 1.95 (t, *J* = 2.7 Hz, 1H), 1.06 (s, 9H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 133.7, 129.8, 127.8, 81.6, 69.5, 62.4, 26.9, 22.7, 19.3; MS (APCI$^+$) *m*/*z* (rel. %) 309 ([M+H]$^+$, 100); HRMS (APCI$^+$) 309.1661 [M+H]$^+$, $C_{20}H_{25}OSi$ requires 309.1669.

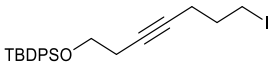
7-(*tert*-Butyldiphenylsilyloxy)hept-4-yn-1-ol (5)[4]



To a solution of alkyne **3** (5 g, 16.2 mmol) in dry THF (30 mL) was added dropwise *n*-butyllithium (2.0 M in hexanes, 8.1 mL, 16.2 mmol) at −78 °C. The reaction mixture was stirred for 25 min before the addition of BF_3•Et_2O (2.0 mL, 16.2 mmol), and the resulting solution stirred for a further 15 mins. After this time trimethylene oxide (526 µL, 8.1 mmol) was added dropwise and the reaction mixture maintained at −78 °C for a further 2 h. After this time, the cooling was removed and the reaction immediately quenched with sat. aq. NH_4Cl (60 mL). The layers were separated and the aqueous layer extracted with ether (3 × 60 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. Purification by flash chromatography (SiO_2, petrol/ether, 9:1 → 1:1, *v*/*v*) afforded the *title compound* as a colourless oil (2.71 g, 91%).

R_f 0.25 (ether/petrol, 1:1, *v*/*v*); IR (thin film)/cm^{-1} 2245br, 3071w, 2931m, 2858m, 1473m, 1428m, 1389w, 1361w, 1101s, 1057m, 916w, 823m, 738m, 701s, 688m, 614m, 505s, 490m; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.66 (m, 4H), 7.46–7.35 (m, 6H), 3.75 (t, *J* = 7.1 Hz, 2H), 3.72 (t, *J* = 6.2 Hz, 2H), 2.42 (tt, *J* = 7.1, 2.4 Hz, 2H), 2.26 (tt, *J* = 6.9, 2.4 Hz, 2H), 1.71 (tt, *J* = 6.9, 6.2 Hz, 2H), 1.05 (s, 9H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 133.8, 129.8, 127.8, 80.7, 77.9, 63.0, 62.1, 31.6, 26.9, 23.0, 19.3, 15.5; MS (ESI$^+$) *m*/*z* (rel. %) 389 ([M+H]$^+$, 100); HRMS (ESI$^+$) 389.1906 [M+H]$^+$, $C_{23}H_{30}NaO_2Si$ requires 389.1907.

7-(*tert*-Butyldiphenylsilyloxy)-1-iodohept-4-yne (6)

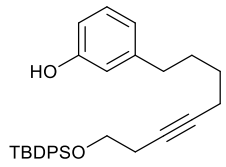


To a solution of triphenylphosphine (3.83 g, 14.6 mmol) and imidazole (1.98 g, 29.1 mmol) in CH_2Cl_2 (60 mL) was added iodine (3.71 g, 14.6 mmol) in one portion, and the resulting mixture stirred at RT for 1.5 h. After this time, a solution of alcohol **5** (4.85 g, 13.2 mmol) in CH_2Cl_2 (40 mL) was added and the reaction mixture was stirred for a further 3 h, at which point the reaction was quenched by the addition of 10% aq. $Na_2S_2O_3$ (50 mL). The layers were separated, and

the aqueous layer extracted with CH_2Cl_2 (2 ×20 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. Purification by flash chromatography (SiO_2, petrol/ether, 19:1, *v*/*v*) afforded the *title compound* as a colourless oil (5.53 g, 88%).

R_f 0.50 (ether/petrol, 1:9, *v*/*v*); IR (thin film)/cm^{-1} 3070w, 2931m, 2857m, 1472w, 1428m, 1221w, 1111s, 823m, 738m, 701s, 614m, 505s, 490m; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.66 (m, 4H), 7.46–7.36 (m, 6H), 3.74 (t, *J* = 7.0 Hz, 2H), 3.27 (t, *J* = 6.8 Hz, 2H), 2.41 (tt, *J* = 7.0, 2.4 Hz, 2H), 2.27 (tt, *J* = 6.7, 2.4 Hz, 2H), 1.94 (p, *J* = 6.7 Hz, 2H), 1.06 (s, 9H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 133.8, 129.8, 127.8, 79.2, 78.5, 62.9, 32.5, 26.9, 23.0, 19.9, 19.4, 5.8; MS (ESI$^+$) *m*/*z* (rel. %) 477 ([M+H]$^+$, 10), 494 ([M+NH_4]$^+$, 100); HRMS (ESI$^+$) 477.1100 [M+H]$^+$, $C_{23}H_{30}IO_4Si$ requires 477.1105.

3-([8-*tert*-Butyldiphenylsilyl]oct-5-ynyl)phenol (8)

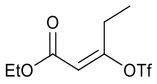


To a suspension of potassium *tert*-butoxide (1.10 g, 9.8 mmol) and dry TMEDA (1.47 mL, 9.8 mmol) in dry hexane (21 mL) at −78 °C was added dropwise *n*-butyllithium (2.0 M in hexanes, 4.87 mL, 9.8 mmol), and the mixture was stirred for 15 min. After this time, *m*-cresol (410 µL, 3.9 mmol) was added, and the reaction mixture was warmed to −20 °C and stirred at this temperature for 3.5 h. The cooling bath was then removed, dry THF (5 mL) added, and the reaction cooled to −78 °C before a solution of iodide **6** (2.8 g, 5.9 mmol) in dry THF (8 mL) was added. The resulting mixture was stirred at −78 °C for 20 h before being quenched with brine (20 mL) and 6 M aq. HCl (5 mL). The layers were separated, and the aqueous layer extracted with ether (4 × 30 mL). The combined organic layers were washed with water (5 mL), dried ($MgSO_4$) and evaporated. Flash chromatography (SiO_2, petrol/EtOAc, 19:1 → 17:3, *v*/*v*) and drying *in vacuo* afforded the *title compound* as a colourless oil (1.27 g, 71%).

R_f 0.46 (ether/petrol, 1:1, *v*/*v*); IR (thin film)/cm^{-1} 3397br, 2928s, 2856m, 1589m, 1456m, 1428m, 1155w, 1111s, 823w, 738m, 701s, 613m, 505s; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.66 (m, 4H), 7.45–7.33 (m, 6H), 7.12 (td, *J* = 7.4, 1.2 Hz, 1H), 6.73 (dt, *J* = 7.7, 1.2 Hz, 1H), 6.67–6.60 (m, 2H), 4.59 (br s, 1H), 3.76 (t, *J* = 7.1 Hz, 2H), 2.55 (t, *J* = 7.6 Hz, 2H), 2.42 (tt, *J* = 7.1, 2.4 Hz, 2H), 2.14 (tt, *J* = 7.0, 2.4 Hz, 2H), 1.68 (tt, *J* = 9.0, 6.7 Hz, 2H), 1.49 (p, *J* = 7.2 Hz, 2H), 1.05 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 144.5, 135.7, 133.9, 129.8, 129.6, 127.8, 121.1, 115.4, 112.7, 81.3, 77.3, 63.1, 35.4, 30.4, 28.6, 26.9, 23.1, 19.4, 18.8; MS (ESI$^+$)

m/*z* (rel. %) 457 ([M+H]$^+$, 5), 474 ([M+NH$_4$]$^+$, 100), 479 ([M+Na]$^+$, 80), 495 ([M+K]$^+$, 40); HRMS (ESI$^+$) 479.2381 [M+Na]$^+$, $C_{30}H_{36}NaO_2Si$ requires 479.2377.

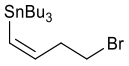
Ethyl (*E*)-3-(trifluoromethylsulfonyloxy)pent-2-enoate (10)[5]



To a solution of ethyl propionylacetate (3.31 g, 23.0 mmol) in hexane (116 mL) was added water (29 mL), and the resulting biphasic mixture was cooled to 5 °C with rapid stirring. Tetramethylammonium hydroxide (25 wt% aq., 41.9 mL, 115 mmol) was added and the biphasic mixture was vigorously stirred for *ca*. 10 min, followed by dropwise addition of triflic anhydride (9.7 mL, 57.4 mmol). After 20 mins, the reaction mixture was diluted with water (120 mL) and the layers separated. The aqueous layer was extracted with ethyl acetate (2 × 100 mL), and the combined organic layers were washed with water (100 mL), brine (100 mL), dried over $MgSO_4$ and evaporated. Flash chromatography (SiO_2, petrol/ether, 19:1, *v*/*v*) afforded the *title compound* as a colourless oil (4.04 g, 63%).

R_f 0.70 (ether/petrol, 1:1, *v*/*v*); IR ($CHCl_3$)/cm^{-1} 2926m, 2855w, 1729m, 1666w, 1425m, 1374w, 1246m, 1214s, 1143s, 1112m, 1026m, 963s, 881w, 855m; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.94 (q, *J* = 7.5 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 164.2, 120.1 (q, $^1J_{C–F}$ = 320.1 Hz), 112.2, 61.3, 25.2, 14.2, 10.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.9; MS (ESI$^+$) *m*/*z* (rel. %) 277 ([M+H]$^+$, 100); HRMS (ESI$^+$) 277.0357 [M+H]$^+$, $C_8H_{12}F_3O_5S$ requires 277.0352.

(*Z*)-1-Tri-*n*-butylstannyl-4-bromobut-1-ene (13)

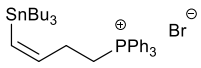


To a solution of 4-bromo-1-butyne (2.87 g, 21.6 mmol) in dry THF (150 mL) at −78 °C was added dropwise *n*-butyllithium (2.0 M in hexanes, 10.7 mL, 21.6 mmol), and the resulting solution was stirred for 10 min before dropwise addition of tributyltin chloride (7.71 g, 23.7 mmol) with the use of a syringe pump over 30 min. After stirring for an additional 5 min, the cooling was removed and the reaction mixture stirred for 1 h at RT. The resulting solution was then diluted with ether (50 mL) and washed with brine (2 × 20 mL). The combined aqueous layers were re-extracted with ether (30 mL), and the combined organic layers dried over $MgSO_4$ and evaporated to afford a yellow oil which was used directly without further purification.

Diisobutylaluminium hydride (1.0 M in hexane, 26.5 mL, 26.5 mmol) was added dropwise to a solution of zirconocene dichloride (8.4 g, 28.7 mmol) in dry THF (50 mL) at 0 °C. The reaction mixture was then stirred for 10 min at 0 °C during which time an off-white suspension formed. A solution of the crude intermediate stannane was then added in dry THF (10 mL), with additional dry THF (15 mL) used to rinse the flask and ensure quantitative transfer. The cooling was then removed, and the reaction mixture rapidly became a homogenous red solution. After stirring for 1 h, the reaction was quenched with water (1.2 mL) and diluted with *n*-pentane (60 mL), leading to the disappearance of the red colour and formation of a yellow solution containing a white precipitate. The reaction mixture was filtered through a Celite plug which was washed copiously with hexane. Evaporation of the filtrate and flash chromatography (SiO_2, petrol) afforded the *title compound* as a colourless oil (5.1 g, 55% over two steps).

R_f 0.43 (petrol); IR (thin film)/cm^{-1} 2957s, 2924s, 2871m, 2853m, 1599w, 1464m, 1418w, 1374w, 1340w, 1296w, 1264m, 1205w, 1072w, 1000w, 961w, 874w, 692m, 626w, 598w; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (dt, J = 12.5, 6.9 Hz, $^3J_{^{119}Sn-H}$ = 135.9 Hz, $^3J_{^{117}Sn-H}$ = 130.0 Hz, 1H), 6.02 (dt, J = 12.5, 1.1 Hz, $^2J_{^{119}Sn-H}$ = 67.4 Hz, $^2J_{^{117}Sn-H}$ = 64.7 Hz, 1H), 3.38 (t, J = 7.2 Hz, 2H), 2.59 (qd, J = 7.1, 1.1 Hz, 2H), 1.54–1.44 (m, 6H), 1.37–1.25 (m, 6H), 0.96–0.90 (m, 6H), 0.89 (t, J = 7.3 Hz, 9H); ^{13}C NMR (101 MHz, C_6D_6) δ 144.9, 132.7, 40.0, 32.3, 29.3 ($^3J_{Sn-C}$ = 20.6 Hz), 27.5 ($^2J_{^{119}Sn-C}$ = 57.5 Hz, $^2J_{^{117}Sn-C}$ = 54.7 Hz), 13.9, 10.4 ($^1J_{^{119}Sn-C}$ = 341.4 Hz, $^1J_{^{117}Sn-C}$ = 326.7 Hz); MS (EI$^+$) *m*/*z* (rel. %) 423 ([M−H]$^+$, 100), 367 ([M−Bu]$^+$, 90), 311 ([M−2Bu+H]$^+$, 95), 255 ([M−3Bu+2H]$^+$, 50); HRMS (EI$^+$) 423.0701 [M−H]$^+$, $C_{16}H_{32}BrSn$ requires 423.0709.

(*Z*)-4-Tri-*n*-butylstannylbut-3-enylphosphonium bromide (14)

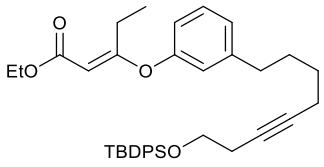


A solution of stannane **13** (1.23 g, 2.9 mmol) in dry toluene/MeCN (1:1, 16 mL) was added to a Schlenk tube containing triphenylphosphine (3.80 g, 14.5 mmol) and NaI (43.5 mg, 0.29 mmol). The resulting solution was heated to 80 °C and stirred for 4 days. After this time, the reaction mixture was cooled to RT and the solvent removed *in vacuo*. The residue was taken up in *n*-pentane, and CH_2Cl_2 added until the slurry became a clear solution; *n*-pentane was then added, and the resulting precipitate collected by filtration and dried *in vacuo*, affording the *title compound* as a white solid (1.39 g, 70%).

M.P. 122 °C; R_f 0.18 (EtOAc/petrol, 1:1, *v*/*v*); IR (ATR)/cm^{-1} 2956m, 2922m, 2852m, 1587m, 1485m, 1436s, 1376w, 1317w, 1190w, 1111s, 1072m, 996m, 874w, 747s, 724s, 690s, 596m,

525s, 505s, 496s; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.86 (m, 6H), 7.83–7.76 (m, 3H), 7.75–7.67 (m, 6H), 6.90 (dt, J = 12.8, 6.5 Hz, $^3J_{^{119}Sn-H}$ = 68.4 Hz, $^3J_{^{117}Sn-H}$ = 65.3 Hz, 1H), 5.92 (dt, J = 12.4, 1.2 Hz, $^2J_{Sn-H}$= 33.2 Hz, 1H), 4.07–3.93 (m, 2H), 2.37–2.25 (m, 2H). 1.36–1.25 (m, 6H), 1.23–1.10 (m, 6H), 0.81 (t, J = 7.2 Hz, 9H), 0.66–0.58 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.3 (d, J_{C-P} = 17.8 Hz), 135.2 (d, J_{C-P} = 3.0 Hz), 133.9 (d, J_{C-P} = 10.0 Hz), 131.3 (d, J_{C-P} = 2.1 Hz), 130.7, (d, J_{C-P} = 12.6 Hz), 118.3 (d, J_{C-P} = 85.6 Hz), 29.6 (d, J_{C-P} = 3.7 Hz), 29.2 ($^3J_{Sn-C}$ = 20.5 Hz), 27.3 ($^2J_{Sn-C}$ = 55.3 Hz), 22.9 (d, J_{C-P} = 48.1 Hz), 13.8, 10.1 ($^1J_{^{119}Sn-C}$ = 340.5 Hz, $^1J_{^{117}Sn-C}$ = 323.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) 24.5; MS (ESI$^+$) *m*/*z* (rel. %) 607 ([M−Br]$^+$, 100); HRMS (ESI$^+$) 607.2533 [M−Br]$^+$, $C_{34}H_{48}PSn$ requires 607.2516.

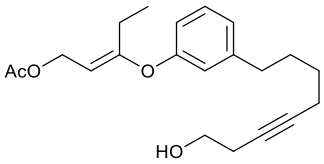
Ethyl (*E*)-3-(3-[8-*tert*-butyldiphenylsilyloxyoct-5-ynyl]phenoxy)pent-2-enoate (15)



An oven-dried Schlenk tube containing a stirrer bar was charged with K_3PO_4 (110 mg, 0.52 mmol), followed by a solution of triflate **10** (72 mg, 0.26 mmol) in dry toluene (1 mL), a premixed solution of $Pd_3(OAc)_6$ (1.5 mg, 2.2 µmol) and XPhos (6.2 mg, 0.013 mmol, Pd:L ratio = 1:2) in dry toluene (1 mL) and a solution of phenol **8** (142 mg, 0.31 mmol) in dry toluene (1 mL). The resulting suspension was heated to 100 °C for 2 h. The reaction mixture was then cooled to RT, filtered through a pad of Celite and evaporated. Flash chromatography (SiO_2, petrol/ether, 19:1→7:3, *v*/*v*) afforded the *title compound* as a colourless oil (127 mg, 84%).

R_f 0.59 (ether/petrol, 2:3, *v*/*v*); IR (thin film)/cm^{-1} 2932m, 2858m, 1712s, 1632s, 1608w, 1584w, 1485w, 1463w, 1428m, 1377m, 1242m, 1223m, 1182w, 1128s, 1112s, 1046s, 999w, 917w, 823m, 738m, 701s, 613m, 505s, 490m; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72–7.67 (m, 4H), 7.46–7.36 (m, 6H), 7.32–7.21 (m, 1H), 7.02 (dt, J = 7.7, 1.5 Hz, 1H), 6.88–6.78 (m, 2H), 4.79 (s, 1H), 4.09 (q, J = 7.1 Hz, 2H), 3.76 (t, J = 7.1 Hz, 2H), 2.95 (q, J = 7.5 Hz, 2H), 2.64–2.58 (m, 2H), 2.44 (tt, J = 7.1, 2.4 Hz, 2H), 2.17 (tt, J = 7.0, 2.4 Hz, 2H), 1.76–1.66 (m, 2H), 1.56–1.46 (m, 2H), 1.29 (t, J = 7.5 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 167.6, 153.6, 144.9, 135.7, 133.9, 129.8, 129.7, 127.8, 125.8, 121.5, 118.9, 95.1, 81.1, 77.4, 63.0, 59.6, 35.3, 30.4, 28.6, 26.9, 25.1, 23.1, 19.3, 18.7, 14.4, 12.0; MS (ESI$^+$) *m*/*z* (rel. %) 583 ([M+H]$^+$, 5), 600 ([M+NH_4]$^+$, 80), 605 ([M+Na]$^+$, 100), 621 ([M+K]$^+$, 5); HRMS (ESI$^+$) 605.3063 [M+Na]$^+$, $C_{37}H_{46}NaO_4Si$ requires 605.3058.

(*E*)-3-(3-[8-Hydroxyoct-5-ynyl]phenoxy)pent-2-enyl acetate (16)



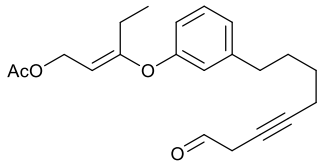
Diisobutylaluminium hydride (1.0 M in hexane, 2.1 mL, 2.1 mmol) was added to a solution of ester **15** (589 mg, 1.01 mmol) in dry ether (20 mL) at −78 °C. After stirring for 2 h, the reaction mixture was poured onto a vigorously stirred mixture of ether (30 mL) and 1.1 M aq. Rochelle's salt (30 mL) and stirred for a further 1 h. The layers were separated, and the aqueous layer extracted with ether (2 × 30 mL). The combined organic layers were then dried over Na_2SO_4 and evaporated.

The crude residue was dissolved in CH_2Cl_2 (20 mL), and acetic anhydride (0.19 mL, 2.02 mmol), triethylamine (0.20 mL, 1.41 mmol) and DMAP (17.1 mg, 0.14 mmol) were added. The resulting solution was stirred at ambient temperature for 17 h before being quenched with sat. aq. NH_4Cl (20 mL), the layers separated and the aqueous layer extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with water (25 mL) and brine (25 mL), dried over $MgSO_4$ and evaporated.

The crude residue was dissolved in dry THF (30 mL), TBAF (1 M in THF, 1.10 mL, 1.10 mmol) was added dropwise, and the resulting solution stirred at RT for 1 h. After this time, the reaction mixture was diluted with ether (30 mL) and washed with sat. aq. NH_4Cl (40 mL). The layers were separated and aqueous layer extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. Purification by flash chromatography (SiO_2, petrol/EtOAc, 3:1, *v*/*v*) afforded the *title compound* as a yellow oil (292 mg, 84% over three steps).

R_f 0.13 (EtOAc/petrol, 1:3, *v*/*v*); IR (thin film)/cm^{-1} 3443br, 2937m, 2860w, 1737s, 1664m, 1606w, 1585m, 1485m, 1442m, 1365m, 1303w, 1230s, 1181s, 1151m, 1053s, 1021s, 970m, 946m, 850w, 801m, 697m; ^{1}H NMR (400 MHz, C_6D_6) δ 7.04 (t, *J* = 7.8 Hz, 1H), 6.89 (t, *J* = 2.0 Hz, 1H), 6.85 (ddd, *J* = 8.1, 2.4, 1.0 Hz, 1H), 6.76 (dt, *J* = 7.6, 1.3 Hz, 1H), 4.84 (t, *J* = 8.1 Hz, 1H), 4.52 (d, *J* = 8.1 Hz, 2H), 3.43 (t, *J* = 6.5 Hz, 2H), 2.36–2.28 (m, 4H), 2.19 (tt, *J* = 6.6, 2.4 Hz, 2H), 1.99 (tt, *J* = 7.1, 2.4 Hz, 2H), 1.63 (s, 3H), 1.52 (tt, *J* = 9.2, 6.8 Hz, 2H), 1.39–1.27 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, C_6D_6) δ 170.3, 164.0, 155.6, 144.7, 129.8, 124.5, 121.3, 118.6, 99.7, 82.0, 77.4, 61.6, 60.6, 35.4, 30.6, 28.7, 23.5, 23.4, 20.6, 18.9, 12.6; MS (ESI$^+$) *m*/*z* (rel. %) 307 ([M−AcOH+Na]$^+$, 75), 367 ([M+Na]$^+$, 100), 383 ([M+K]$^+$, 10); HRMS (ESI$^+$) 367.1878 [M+Na]$^+$, $C_{21}H_{28}NaO_4$ requires 367.1880.

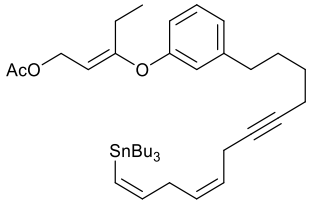
(*E*)-3-(3-[(8-formyl)oct-5-ynyl]phenoxy)pent-2-enyl acetate (17)



To a solution of alcohol **16** (114 mg, 0.33 mmol) in dry CH_2Cl_2 (3 mL) at 0 °C was added Dess–Martin periodinane (350 mg, 0.83 mmol). The resulting suspension was stirred for 5 min before the cooling was removed and the reaction stirred for a further 1.5 h at ambient temperature, after which time TLC analysis indicated that the reaction was complete. The solution was cooled to −15 °C, diluted with hexane (4 mL), and filtered through a short plug of silica, eluting with ether/pentane (4:1, *v*/*v*). The resulting clear solution was evaporated, affording the *title compound* as a yellow oil (97 mg, 86%).

R_f 0.49 (EtOAc/petrol, 2:3, *v*/*v*); IR (thin film)/cm^{-1} 2939m, 2864w, 1735s, 1663w, 1604w, 1585w, 1485w, 1444w, 1365w, 1232s, 1182m, 1149w, 1052w, 1020m; ^{1}H NMR (500 MHz, C_6D_6) δ 9.08 (t, *J* = 1.7 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 6.90 (t, *J* = 2.0 Hz, 1H), 6.85 (ddd, *J* = 8.0, 2.4, 1.0 Hz, 1H), 6.79–6.75 (m, 1H), 4.85 (t, *J* = 8.0 Hz, 1H), 4.52 (d, *J* = 8.0 Hz, 2H), 2.58 (td, *J* = 2.4, 1.7 Hz, 2H), 2.35–2.28 (m, 4H), 1.95 (tt, *J* = 7.1, 2.4 Hz, 2H), 1.63 (s, 3H), 1.57–1.45 (m, 2H), 1.40–1.27 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 194.0, 170.1, 163.9, 155.7, 144.6, 129.8, 124.5, 121.2, 118.6, 99.8, 85.6, 71.3, 60.6, 35.4, 34.4, 30.5, 28.5, 23.4, 20.6, 18.8, 12.6; MS (ESI$^+$) *m*/*z* (rel. %) 397 ([M+MeOH+Na]$^+$, 100), 365 ([M+Na]$^+$, 45), 315 ([M+MeOH−OAc]$^+$, 10) 283 ([M−OAc]$^+$, 20); HRMS (ESI$^+$) 365.1739 [M+Na]$^+$, $C_{21}H_{26}NaO_4$ requires 365.1723.

(2*E*, 7*Z*, 10*Z*)-3-(3-[(12-tributylstannyl)dodeca-7,10-dien-5-ynyl]phenoxy)pent-2-enyl acetate (18)

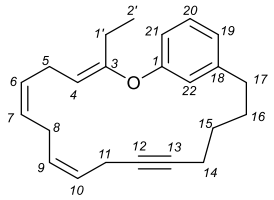


To a solution of phosphonium salt **14** (410 mg, 0.60 mmol) in dry THF (1 mL) at −78 °C was added dropwise NaHMDS (1 M in THF, 0.57 mL, 0.57 mmol). The resulting orange solution was warmed to 0 °C for 10 min, before being cooled once again to −78 °C. A solution of aldehyde **17** (97 mg, 0.28 mmol) in dry THF (0.5 mL) was added *via* cannula. An additional portion of dry THF (1 mL) was used to ensure quantitative transfer. The resulting solution was

warmed to RT and stirred for 3 h. After this time, the reaction was diluted with ether (4 mL) and quenched with water (2 mL) and brine (2 mL). The layers were separated and the aqueous layer extracted with ether (3 × 5 mL), and the combined organic layers dried over $MgSO_4$ and evaporated. Purification by flash chromatography (SiO_2, petrol/ether/triethylamine, 88:10:2, *v*/*v*) afforded the *title compound* as a yellow oil (81.7 mg, 43%).

R_f 0.32 (ether/petrol/triethylamine, 8:90:2, *v*/*v*); IR (thin film)/cm^{-1} 2956m, 2926s, 2856m, 1739s, 1664w, 1586m, 1485w, 1464w, 1229s, 1182s, 1151w, 1055w, 1019m, 970w, 876w, 801w, 696m, 606w; ^{1}H NMR (400 MHz, C_6D_6) δ 7.04 (t, *J* = 7.8 Hz, 1H), 6.89 (t, *J* = 2.0 Hz, 1H), 6.85 (ddd, *J* = 8.0, 2.5, 1.0 Hz, 1H), 6.77 (dt, *J* = 7.7, 1.4 Hz, 1H), 6.56 (dt, *J* = 12.3, 1.2 Hz, 1H), 6.02 (dt, *J* = 12.3, 1.2 Hz, 1H), 5.62 (dtt, *J* = 10.2, 6.8, 1.6 Hz, 1H), 5.50 (dtt, *J* = 10.2, 7.0, 1.5 Hz, 1H), 4.84 (t, *J* = 8.1 Hz, 1H), 4.53 (d, *J* = 8.1 Hz, 2H), 3.00–2.94 (m, 2H), 2.88 (tt, *J* = 7.1, 1.4 Hz, 2H), 2.37–2.28 (m, 4H), 2.04 (tt, *J* = 7.1, 2.5 Hz, 2H), 1.64 (s, 3H), 1.63–1.50 (m, 8H), 1.43–1.32 (m, 8H), 1.16 (t, *J* = 7.5 Hz, 3H), 1.04–0.98 (m, 6H), 0.94 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.1, 163.9, 155.6, 146.9, 144.7, 129.8, 129.1, 129.0, 126.5, 124.5, 121.3, 118.5, 99.8, 80.3, 78.6, 60.6, 35.5, 35.4, 30.7, 29.7 ($^3J_{Sn-C}$ = 20.7 Hz), 28.9, 27.8 ($^2J_{Sn-C}$ = 54.4 Hz), 23.4, 20.6, 19.0, 17.9, 14.0, 12.6, 10.6 ($^1J_{^{119}Sn-C}$ = 339.5 Hz, $^1J_{^{117}Sn-C}$ = 323.9 Hz); ^{119}Sn NMR (186 MHz, C_6D_6) –60.6; MS (ESI$^+$) *m*/*z* (rel. %) 693 ([M+Na]$^+$, 100); HRMS (ESI$^+$) 693.3276 [M+Na]$^+$, $C_{37}H_{58}NaO_3Sn$ requires 693.3307.

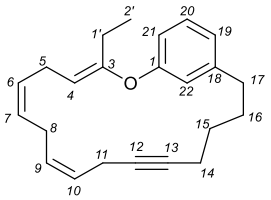
(3*E*,6*Z*,9*Z*)-3-Ethyl-2-oxabicyclo[16.3.1]docosa-1(22),3,6,9,18,20-hexaen-12-yne (1)



LiCl (15.1 mg, 0.36 mmol) was placed with a stirrer bar in a Schlenk tube and dried under vacuum with vigorous heating (approx. 10 min). Dry DMF (1.8 mL) was added and stirred until the LiCl had dissolved. The resulting solution was added *via* cannula to another Schlenk tube containing stannane **18** (24.0 mg, 35.8 μmol) and Pd(Br)(*N*-Succ)($AsPh_3$)$_2$ (AsCat, 3.2 mg, 3.6 μmol). The resulting solution was stirred at 25 °C (controlled using an oil bath) for 72 h. After this time, the reaction mixture was diluted with ether (3 mL) and washed with water (4 × 3 mL). The combined aqueous layers were then re-extracted with ether (3 × 3 mL), and the combined organics layers washed with brine (5 mL), dried over $MgSO_4$, and evaporated. Purification by preparatory thin layer chromatography (SiO_2, petrol/ether, 98:2, *v*/*v*) afforded the *title compound* as a colourless oil (5.0 mg, 44%).

R_f 0.49 (ether/petrol, 1:19, *v*/*v*); IR (thin film)/cm^{-1} 3018w, 2933s, 2857m, 1743w, 1669w, 1602w, 1588m, 1485m, 1443m, 1249s, 1155s, 1048w, 989w, 799w, 696m; ^{1}H NMR (700 MHz, $CDCl_3$) 7.20 (t, *J* = 7.7 Hz, 1H, H-20), 6.83–6.81 (m, 3H, H-19, 21, 22), 5.48–5.43 (m, 2H, H-9, 10), 5.43–5.38 (m, 2H, H-6, 7), 4.62 (t, *J* = 7.6 Hz, 1H, H-4), 2.89 (dt, *J* = 5.8, 2.3 Hz, 2H, H-11), 2.86 (t, *J* = 5.6 Hz, 2H, H-8), 2.81–2.78 (m, 2H, H-5), 2.58 (t, *J* = 7.5 Hz, 2H, H-17), 2.34 (q, *J* = 7.5 Hz, 2H, H-1′), 2.16 (tt, *J* = 7.0, 2.3 Hz, 2H, H-14), 1.71–1.64 (m, 2H, H-16), 1.48–1.41 (m, 2H, H-15), 1.16 (t, *J* = 7.5 Hz, 3H, H-2′); ^{13}C NMR (175 MHz, $CDCl_3$) 156.7 (C, C-1 + C-3), 143.9 (C, C-18), 130.0 (CH, C-10), 129.6 (CH, C-20), 128.6 (CH, C-6), 128.0 (CH, C-7), 124.7 (CH, C-9), 123.2 (CH, C-19), 118.7 (CH, C-22), 117.5 (CH, C-21), 106.7 (CH, C-4), 79.9 (C, C-13), 78.4 (C, C-12), 35.4 (CH_2, C-17), 30.5 (CH_2, C-16), 28.0 (CH_2, C-15), 25.6 (CH_2, C-8), 24.9 (CH_2, C-5), 22.6 (CH_2, C-1′), 18.7 (CH_2, C-14), 17.2 (CH_2, C-11), 12.3 (CH_3, C-2′); MS (APCI$^+$) *m*/*z* (rel. %) 338 ([M+NH_4]$^+$, 100), 321 ([M+H]$^+$, 20); HRMS (APCI$^+$) 321.2237 [M+H]$^+$, $C_{23}H_{29}O$ requires 321.2213.

3. Table of Correlations for compound 1



^{1}H NMR ($CDCl_3$, 700 MHz)							^{13}C NMR ($CDCl_3$, 175 MHz)	
No.	**δ / ppm**	**Integral**	**Multiplicity**	**COSY**	***J* / Hz**	**NOESY**	**δ / ppm**	**HMBC**
1	-	-	-	-	-	-	156.7	*4, 5, 20, 1', 2'*
3	-	-	-	-	-	-	156.7	
4	4.62	1H	t	*5*	7.6	*5*	106.5	*5, 1'*
5	2.81–2.78	2H	m	*4, 6/7*	-	*4, 6/7, 1'*	24.9	*6/7*
6	5.43–5.38	1H	m	*5, 8*	-	*4, 5, 8*	128.6	*5*
7		1H					128.0	*5, 8*
8	2.86	2H	t	*6/7, 9/10*	5.6	*6/7, 9/10*	25.6	*6/7*
9	5.48–5.43	1H	m	*8, 11*	-	*8, 11*	124.7	*8, 11*
10		1H					130.0	*11*
11	2.89	2H	dt	*9/10, 14*	5.8, 2.3	*9/10*	17.2	-
12	-	-	-	-	-	-	78.4	*14*
13	-	-	-	-	-	-	79.9	*14, 15*
14	2.16	2H	tt	*11, 15*	7.0, 2.3	*15, 16, 17*	18.7	*15, 16*
15	1.48–1.41	2H	m	*14, 16*	-	*14, 16, 17*	28.0	*14, 16, 17*
16	1.71–1.64	2H	m	*15, 17*	-	*14, 15, 17*	30.5	*14, 15, 17*
17	2.58	2H	t	*16*	7.5	*14, 15, 16 19/21/22*	35.4	*15, 16*
18	-	-	-	-	-	-	143.9	*16, 17, 20*
19	6.83–6.81	1H	m	*17, 20*	-	*16,17, 20*	123.2	*17, 20, 21/22*
20	7.20	1H	t	*19/21/22*	7.7	*19/21/22*	129.6	*19/21/22*
21	6.83–6.81	1H	m	*17, 20*	-	*16, 17, 20*	117.5	*19/22*
22		1H					118.7	*17, 19/21*
1'	2.34	2H	q	*2'*	7.5	*5, 2'*	22.6	*5, 2'*
2'	1.16	3H	t	*1'*	7.5	*1'*	12.3	*1'*

4. References

1. (a) M. Frigerio; M. Santagostino; S. Sputore, *J. Org. Chem.*, 1999, **64**, 4537–4538; (b) R. E. Ireland; L. Liu, *J. Org. Chem.*, 1993, **58**, 2899–2899.

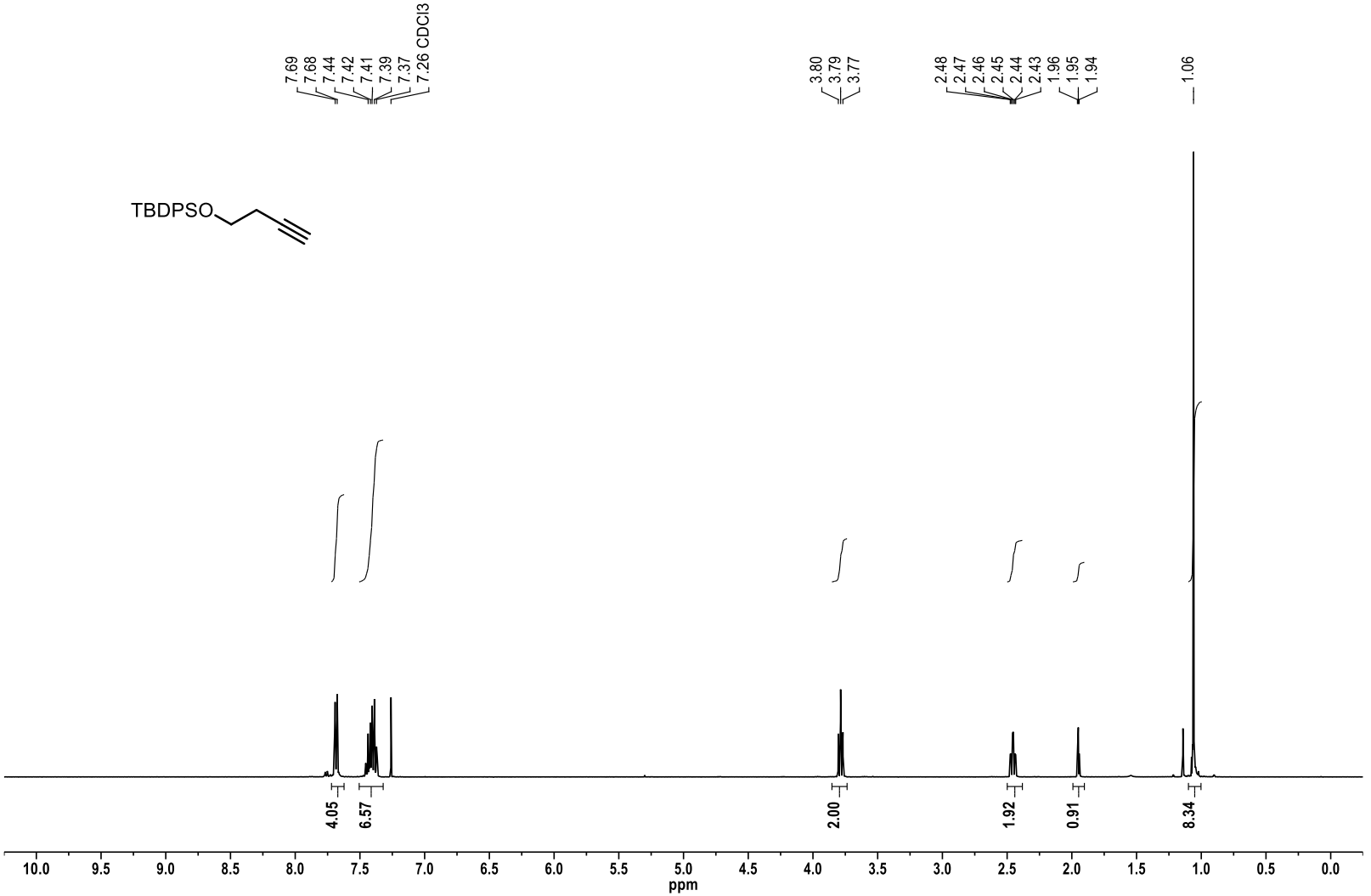
2. T. O. Ronson; J. R. Carney; A. C. Whitwood; R. J. K. Taylor; I. J. S. Fairlamb, *Chem. Commun.*, 2015, **51**, 3466–3469.

3. Y. Wang; W.-M. Dai, *Eur. J. Org. Chem.*, 2014, **2014**, 323–330.

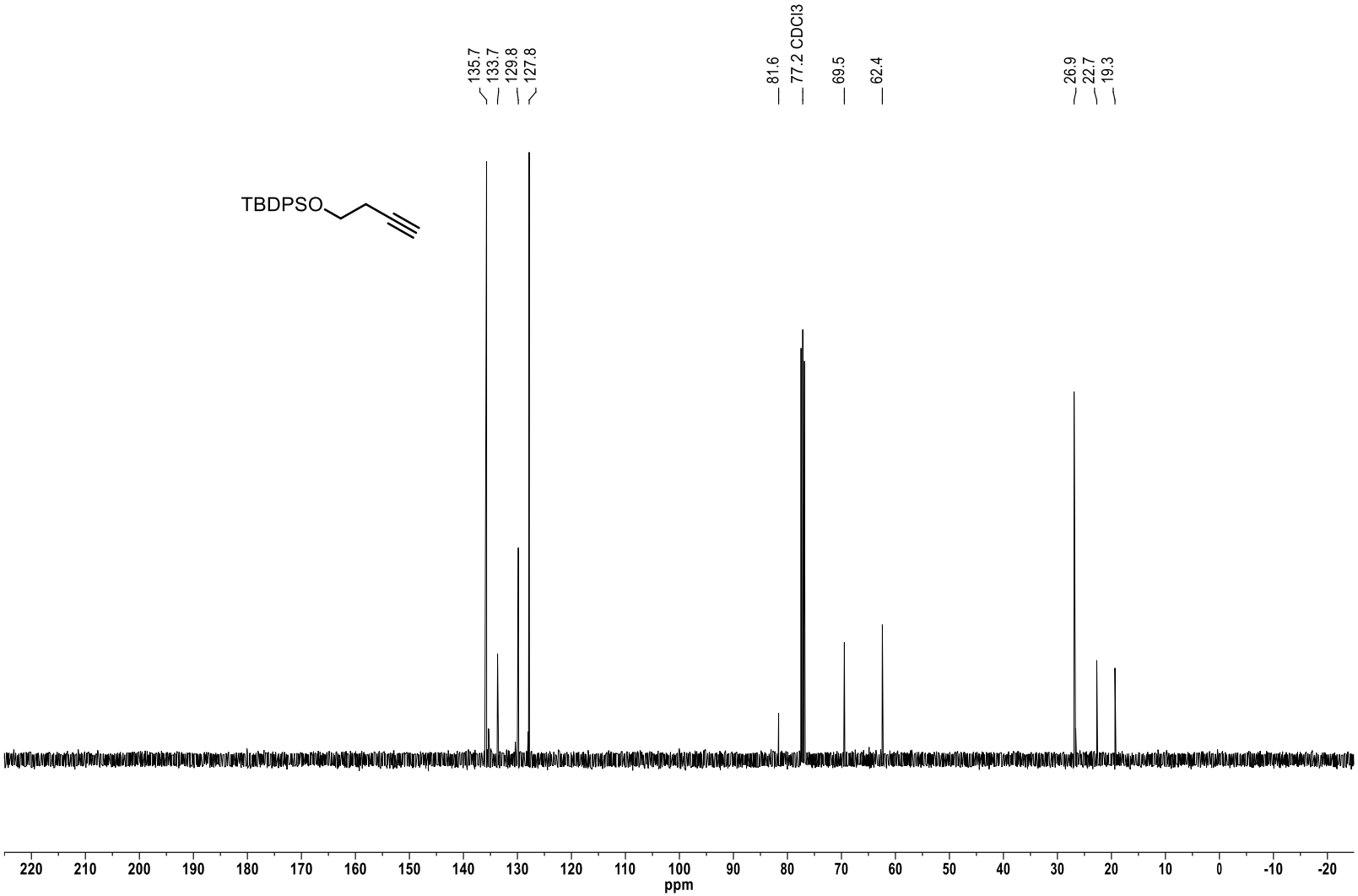
4. G. Dayaker; T. Durand; L. Balas, *Chem. Eur. J.*, 2014, **20**, 2879–2887.

5. D. Babinski; O. Soltani; D. E. Frantz, *Org. Lett.*, 2008, **10**, 2901–2904.

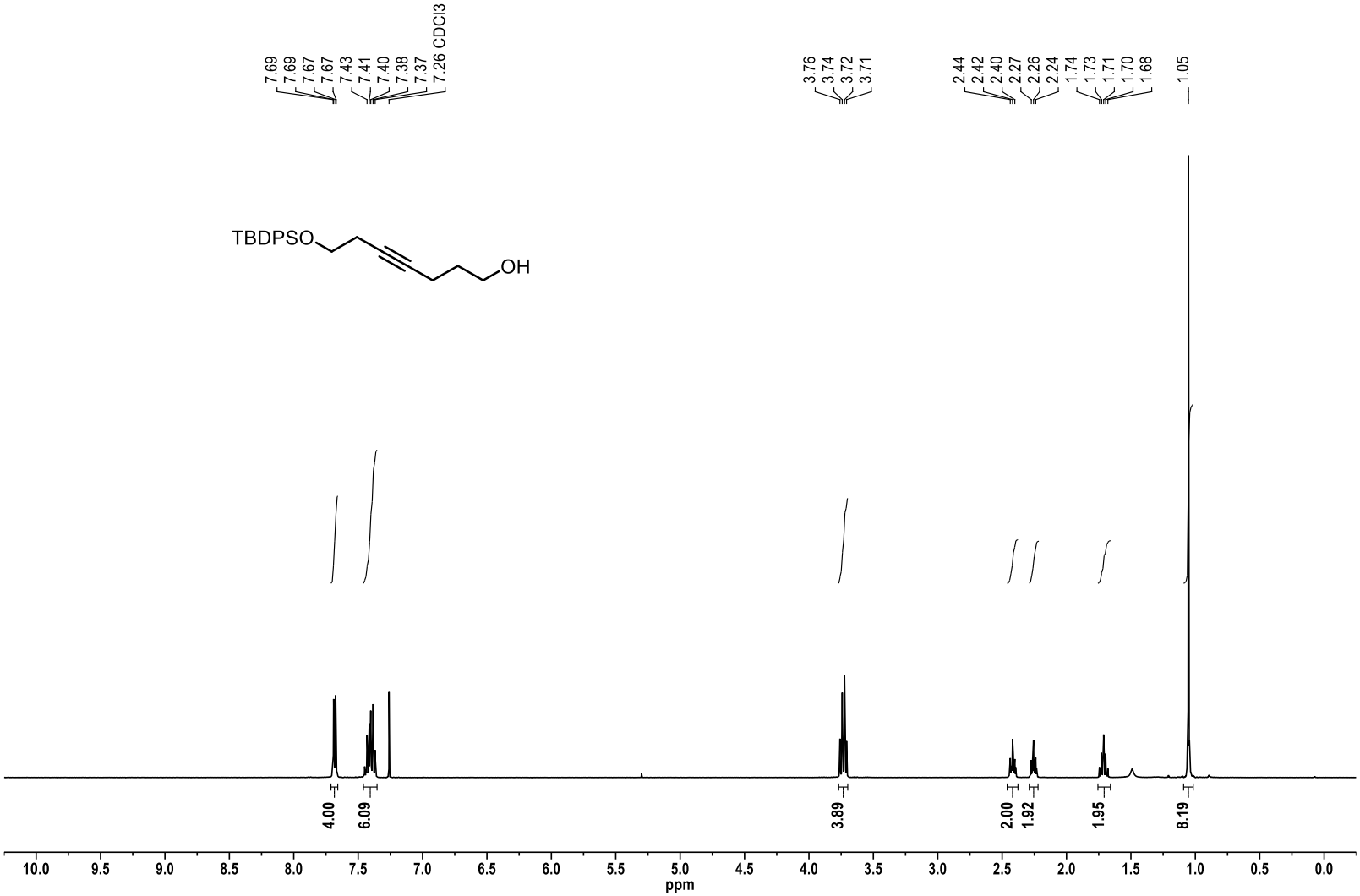
^{1}H NMR spectrum of compound **3** (400 MHz, $CDCl_3$)



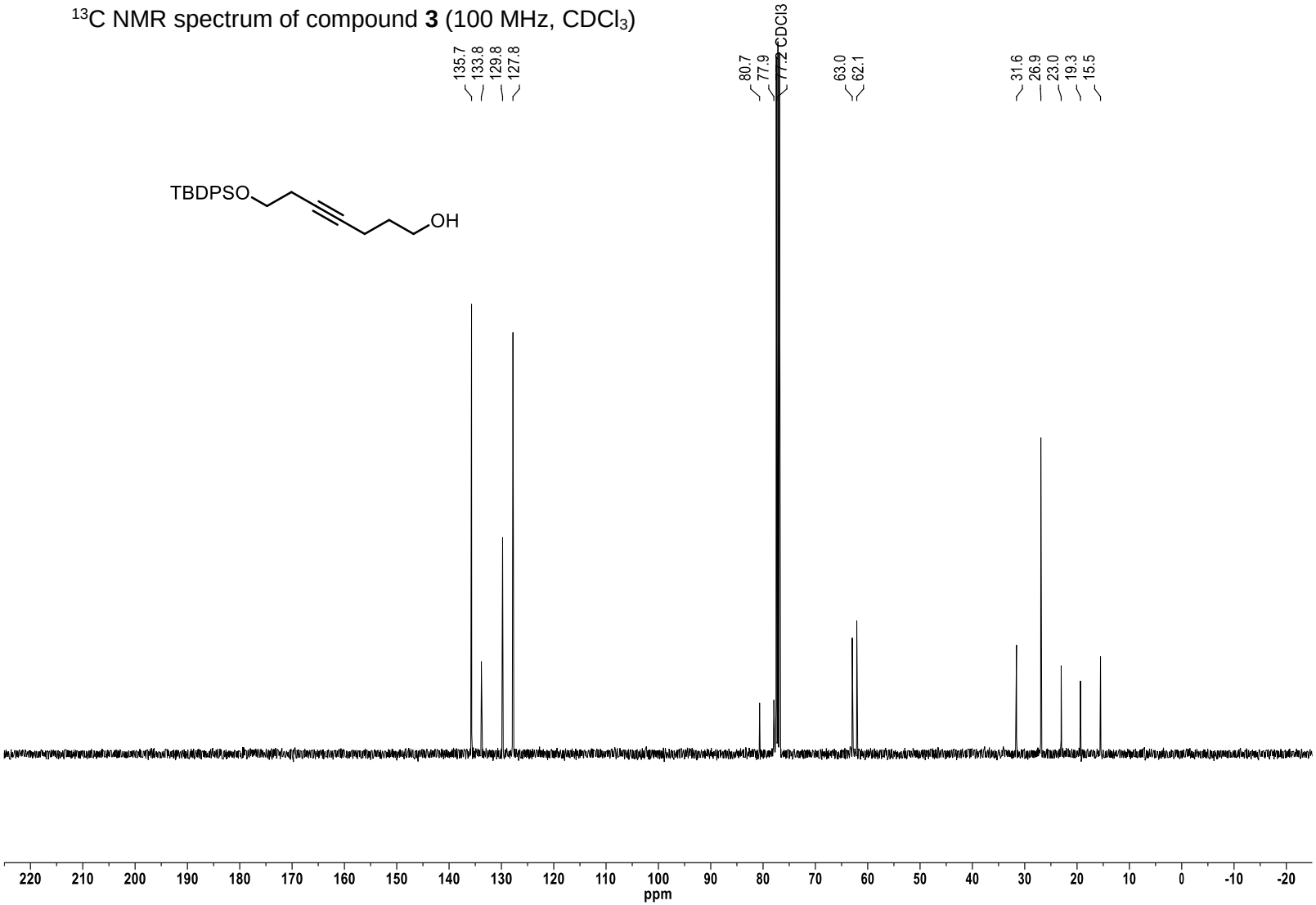
^{13}C NMR spectrum of compound **3** (100 MHz, $CDCl_3$)



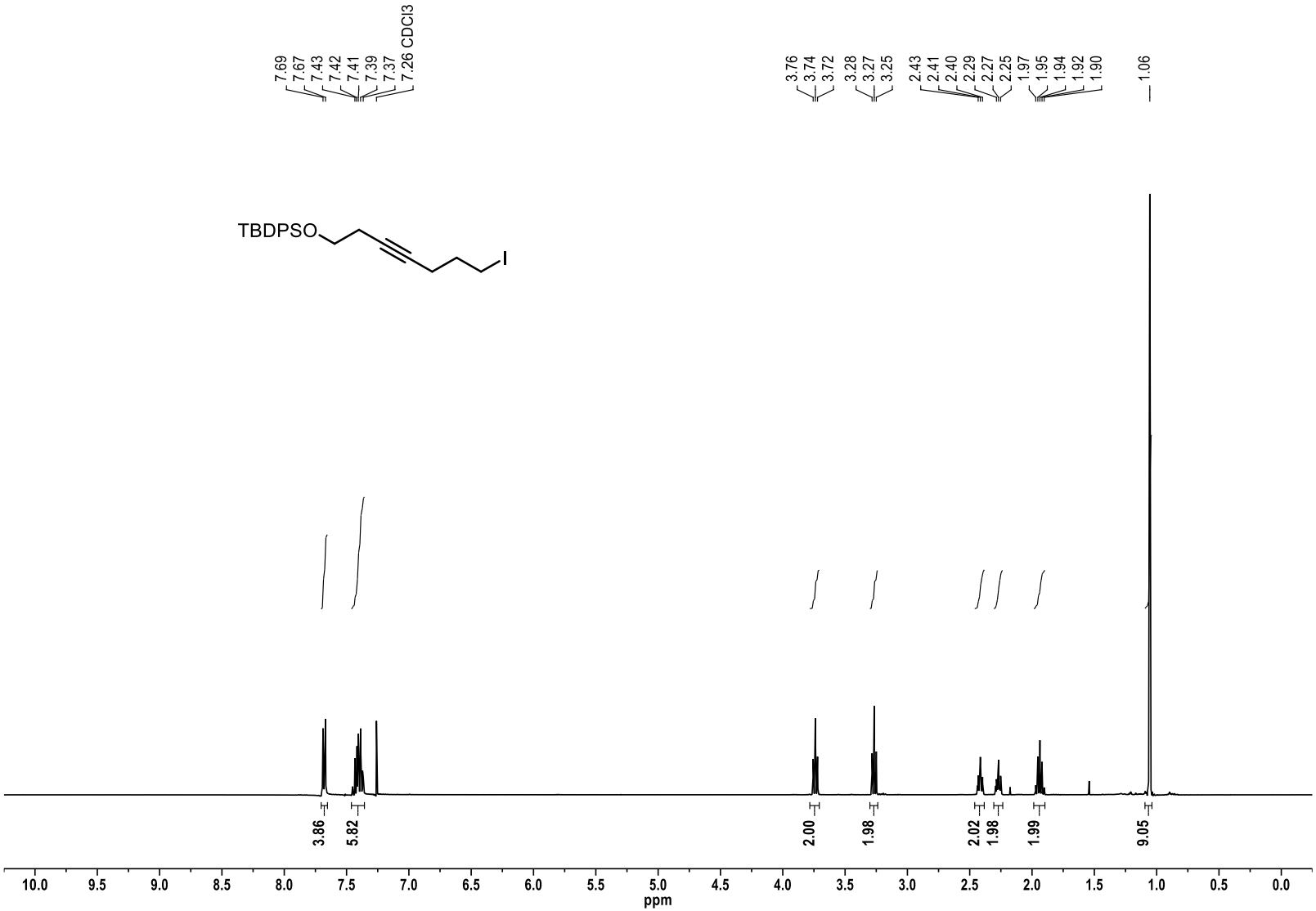
^{1}H NMR spectrum of compound **5** (400 MHz, $CDCl_3$)



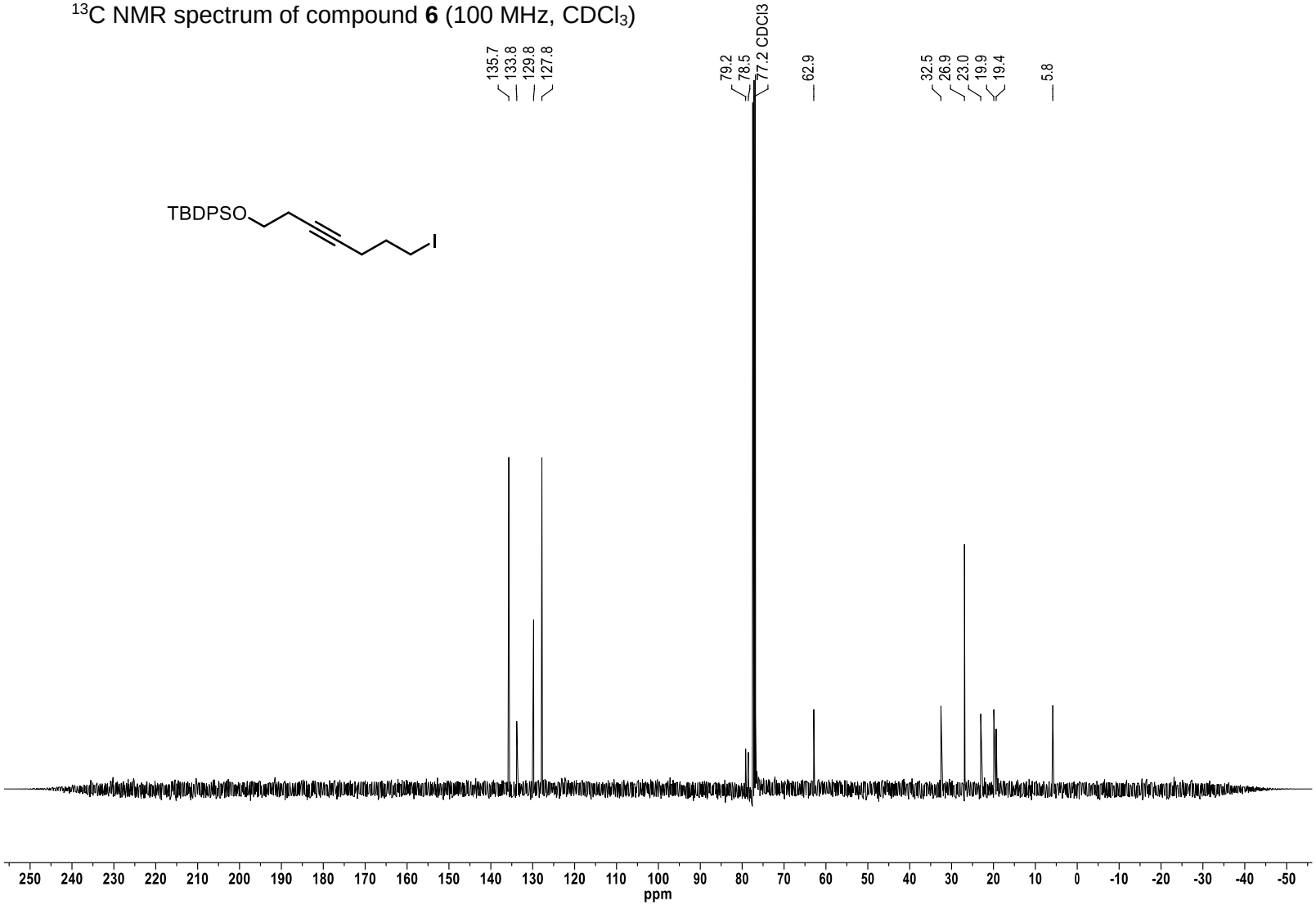
^{13}C NMR spectrum of compound **3** (100 MHz, $CDCl_3$)



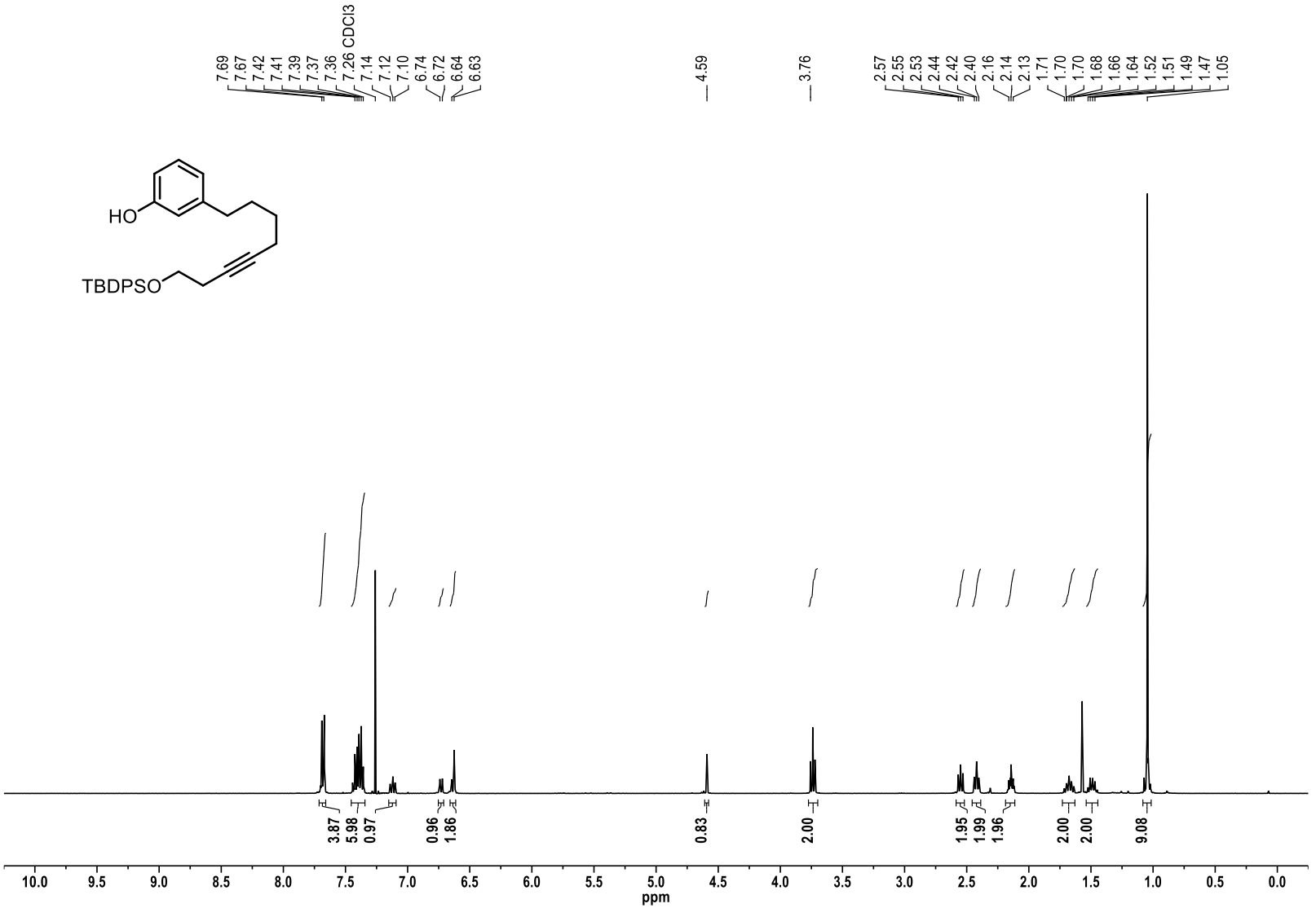
^{1}H NMR spectrum of compound **6** (400 MHz, $CDCl_3$)



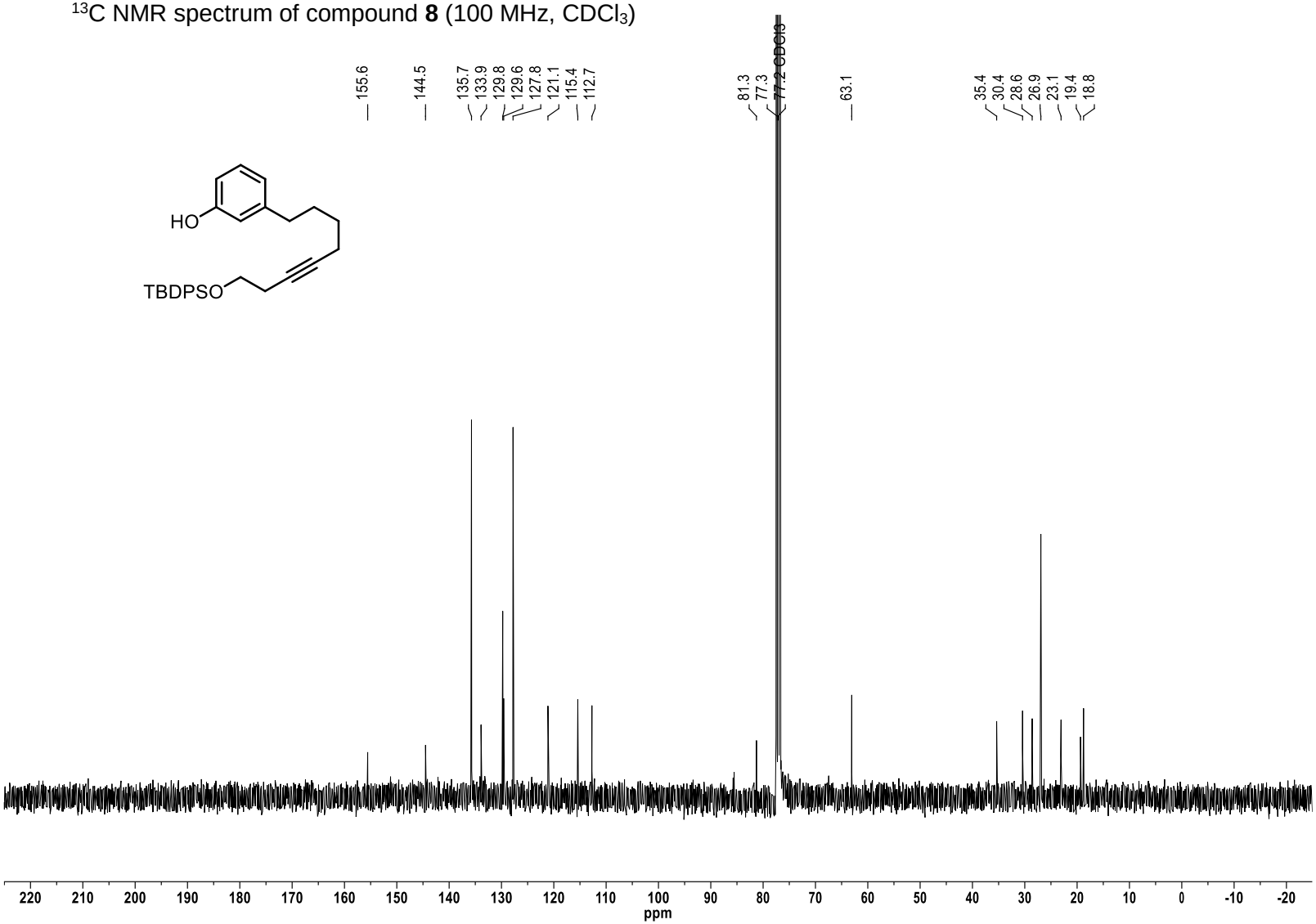
^{13}C NMR spectrum of compound **6** (100 MHz, $CDCl_3$)



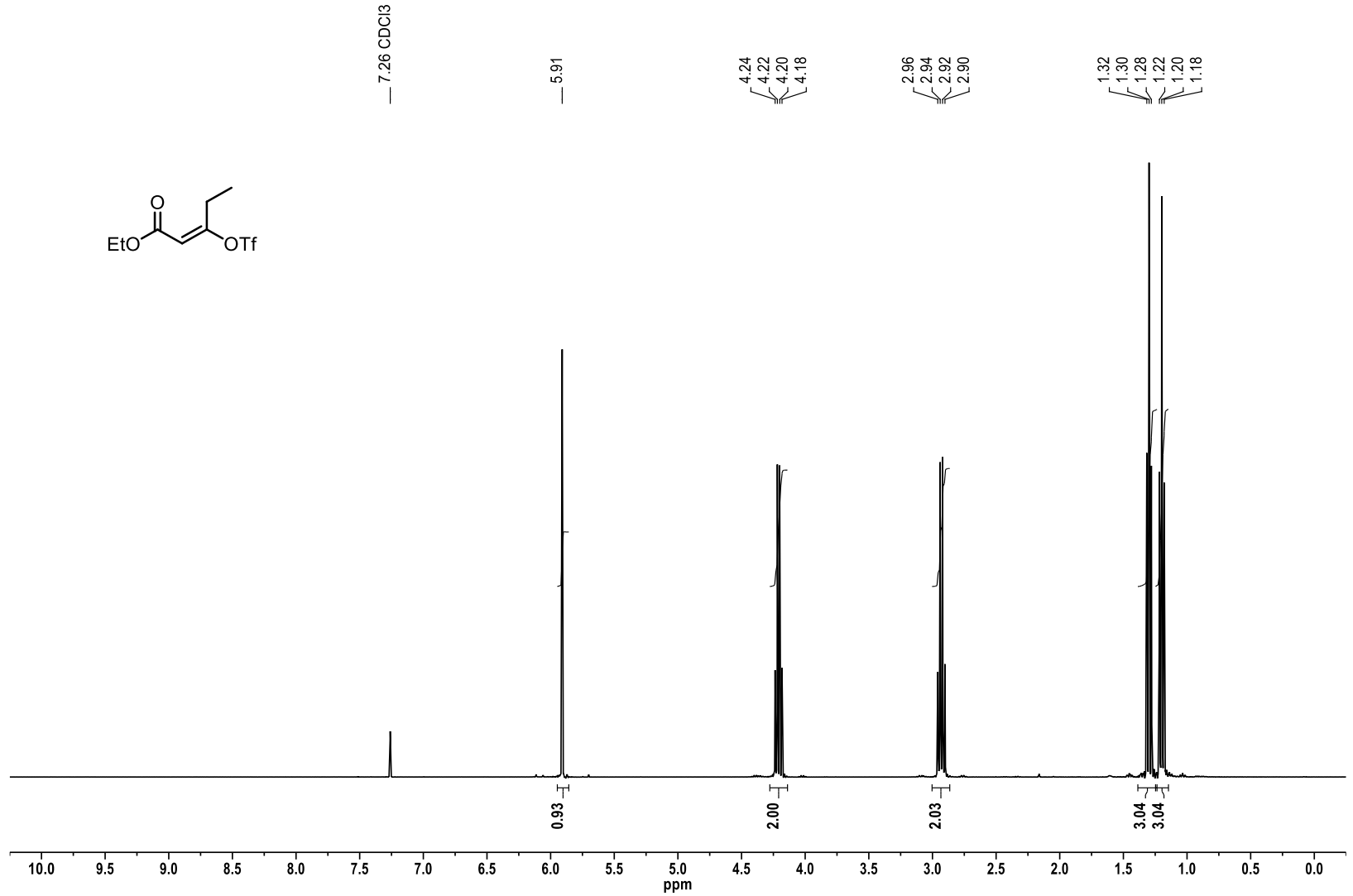
^{1}H NMR spectrum of compound **8** (400 MHz, $CDCl_3$)



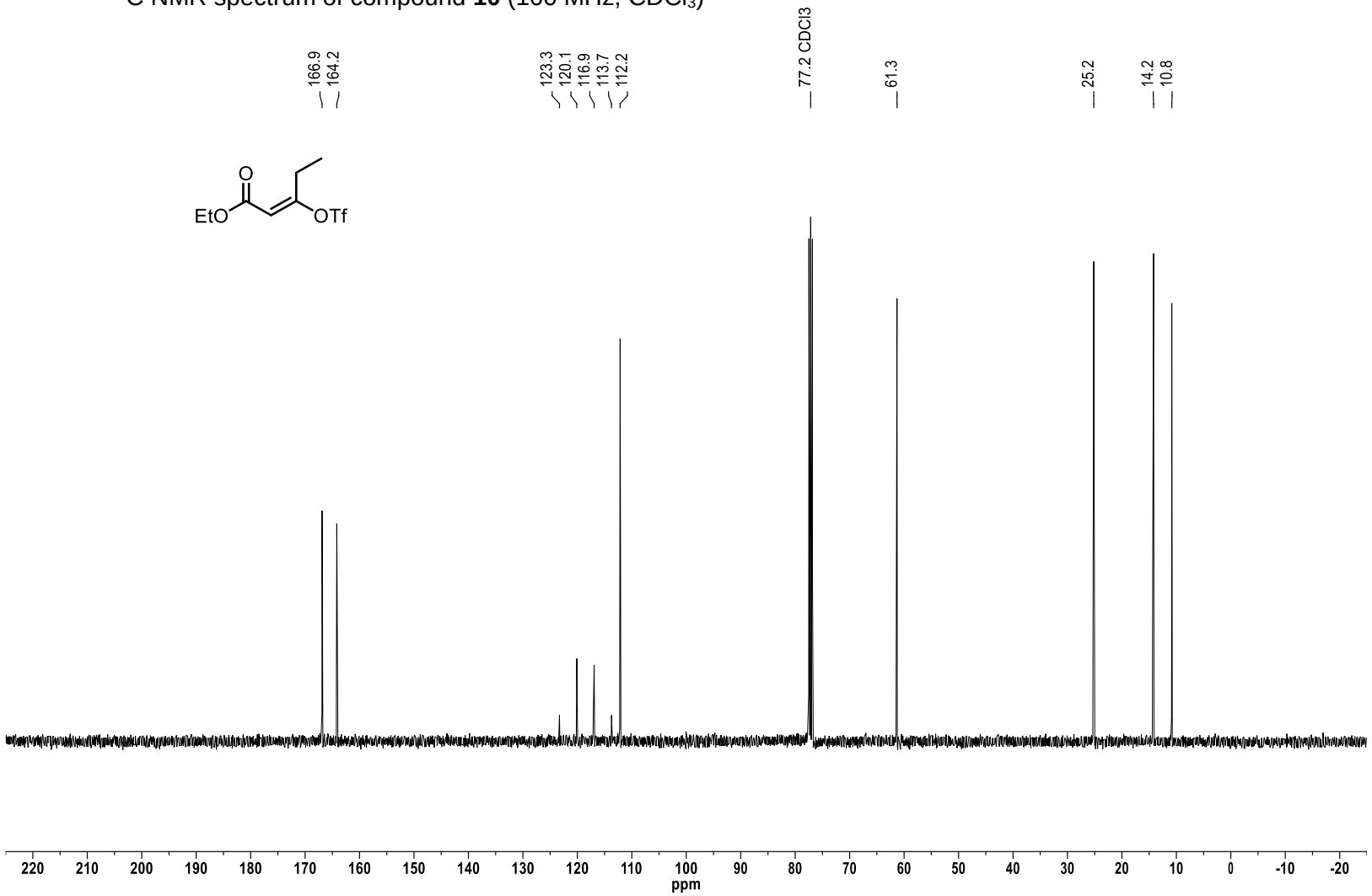
^{13}C NMR spectrum of compound **8** (100 MHz, $CDCl_3$)



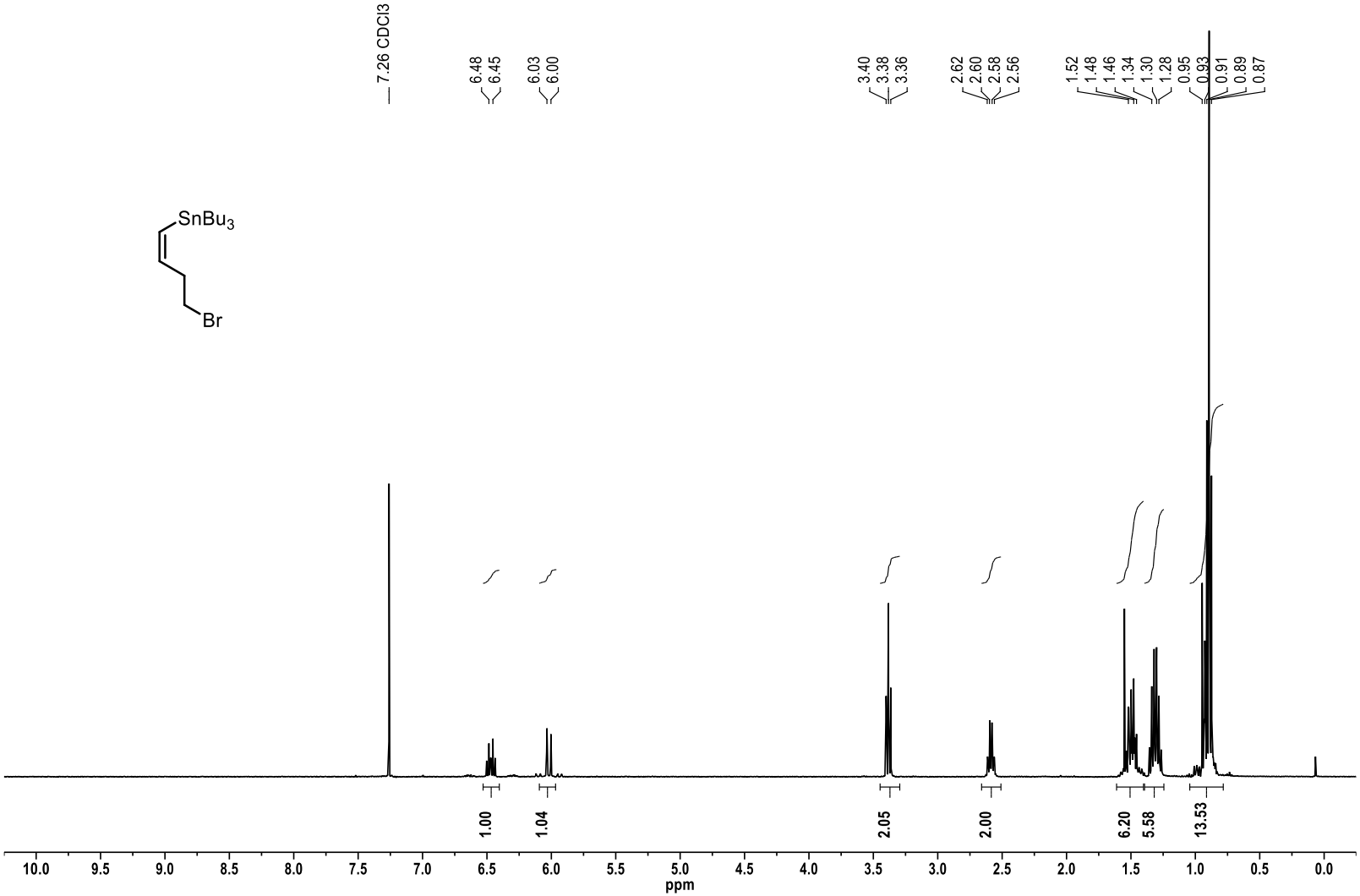
^{1}H NMR spectrum of compound **10** (400 MHz, $CDCl_3$)



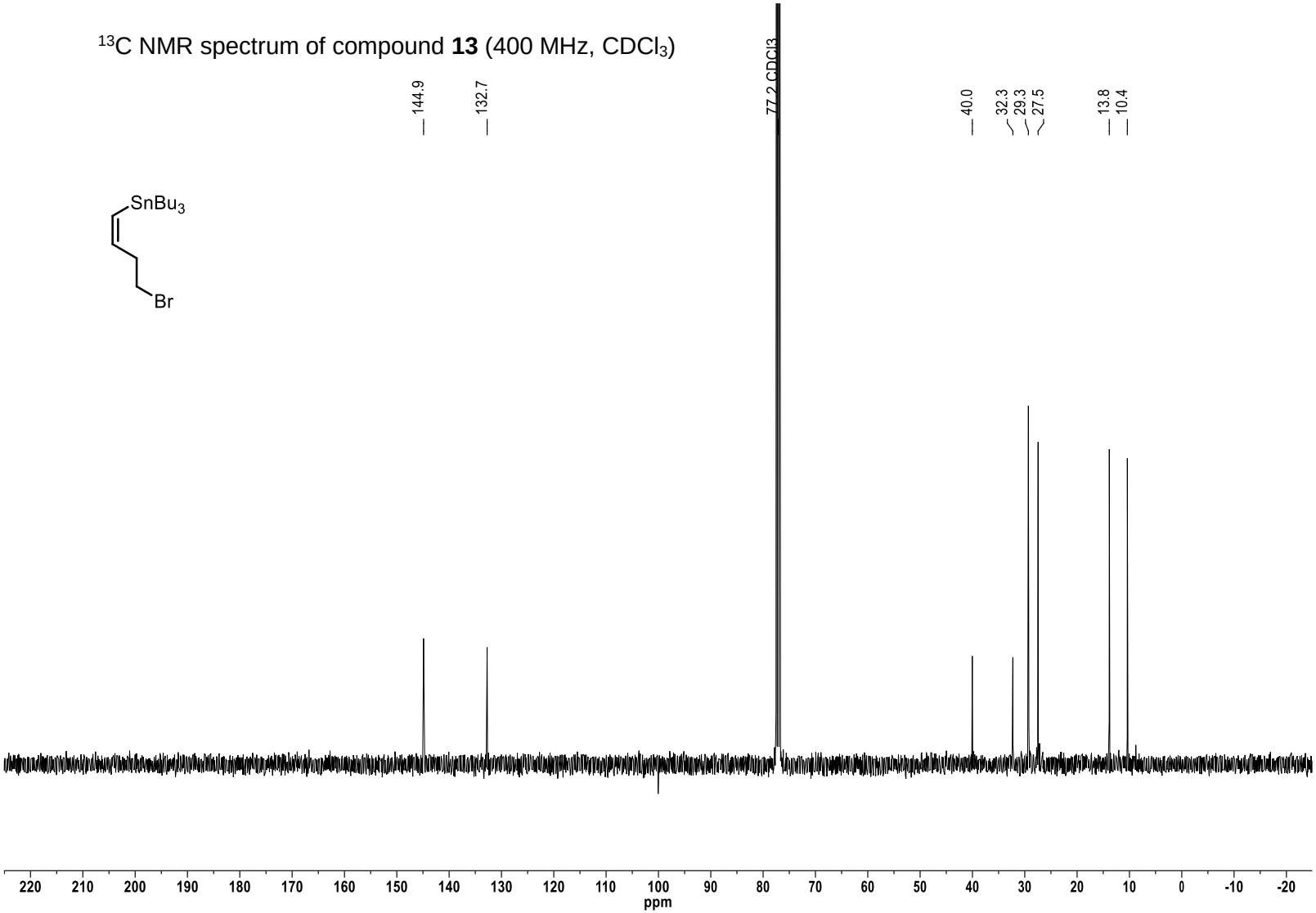
^{13}C NMR spectrum of compound **10** (100 MHz, $CDCl_3$)



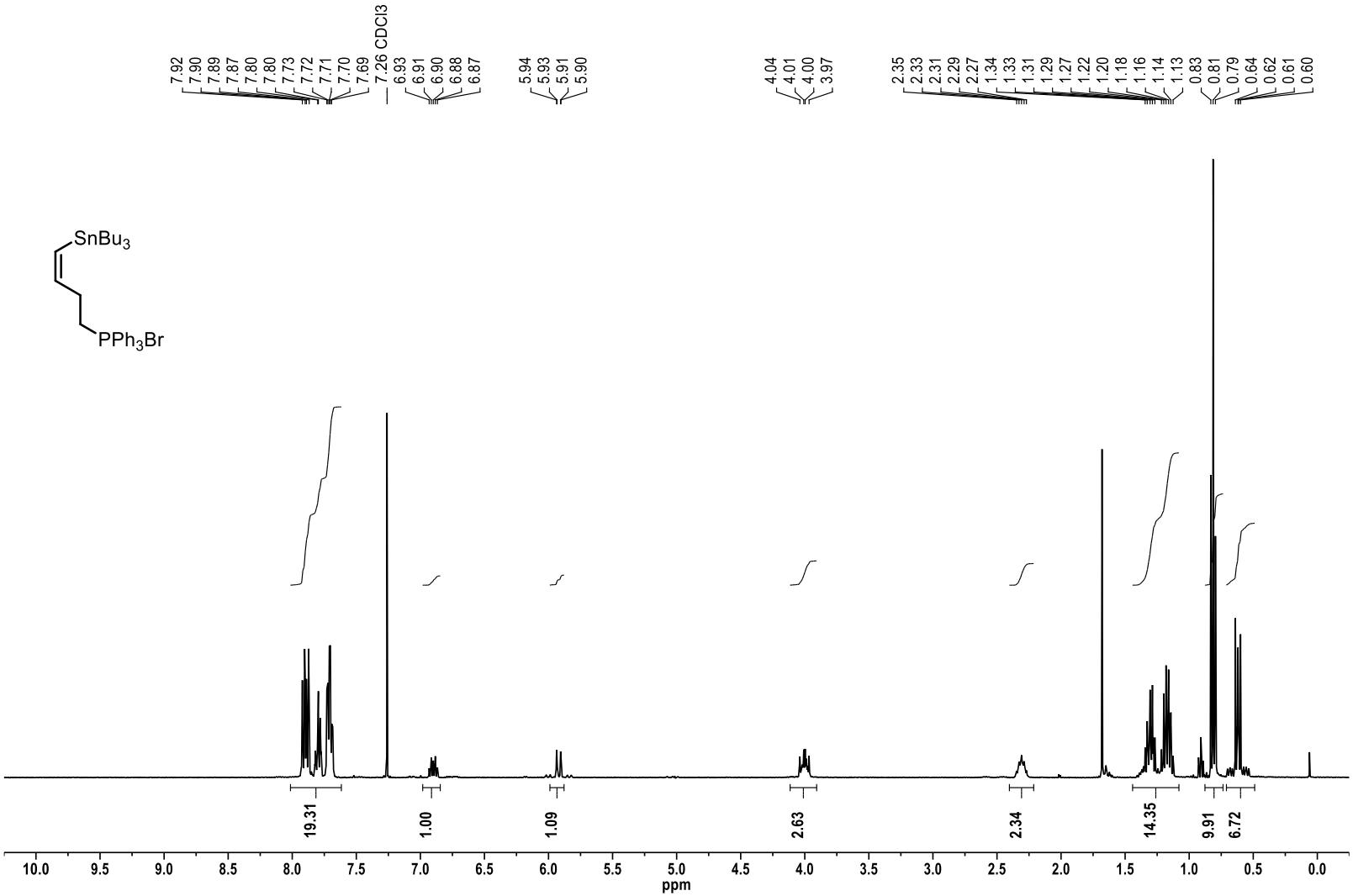
^{1}H NMR spectrum of compound **13** (400 MHz, $CDCl_3$)



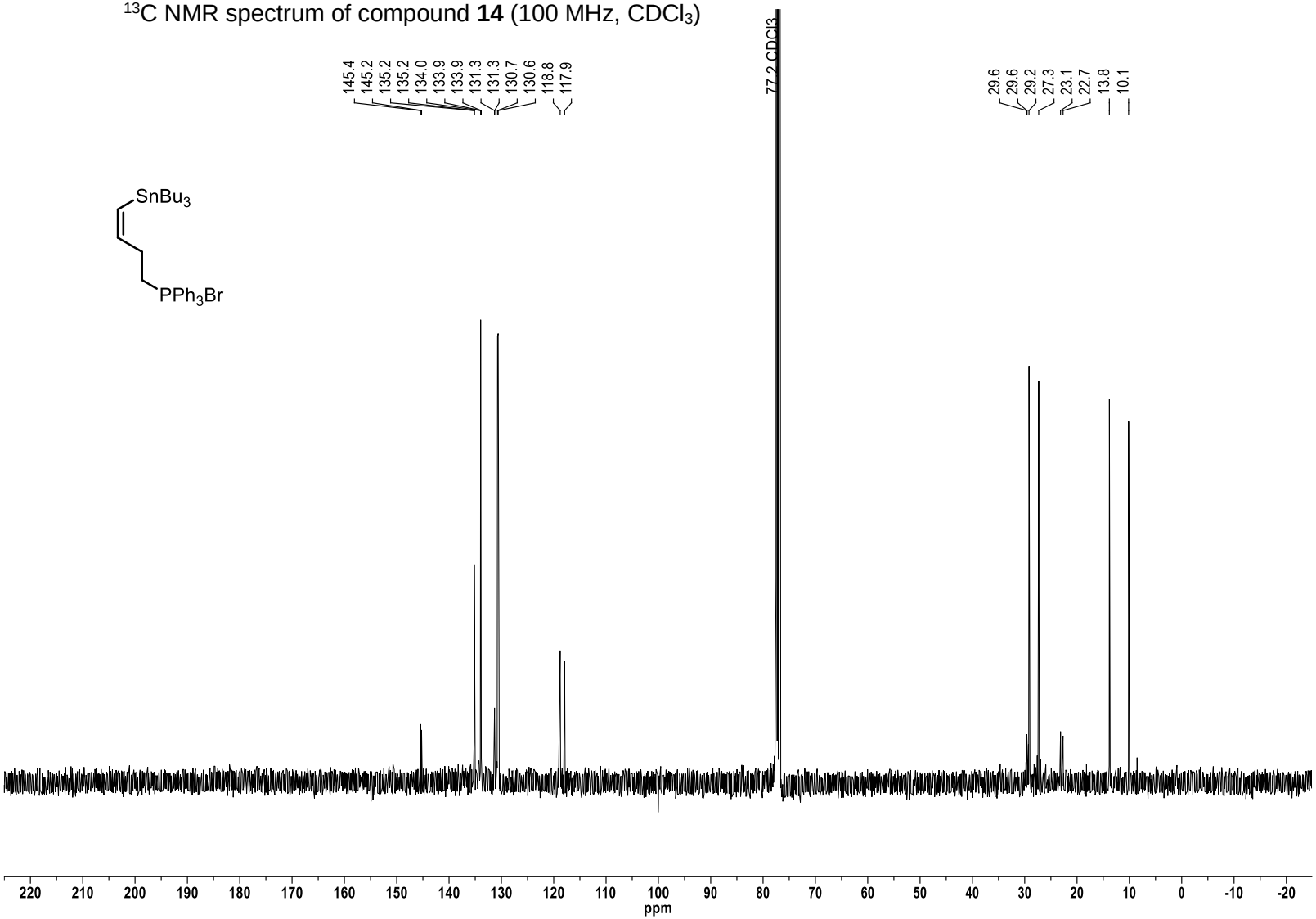
^{13}C NMR spectrum of compound **13** (400 MHz, $CDCl_3$)



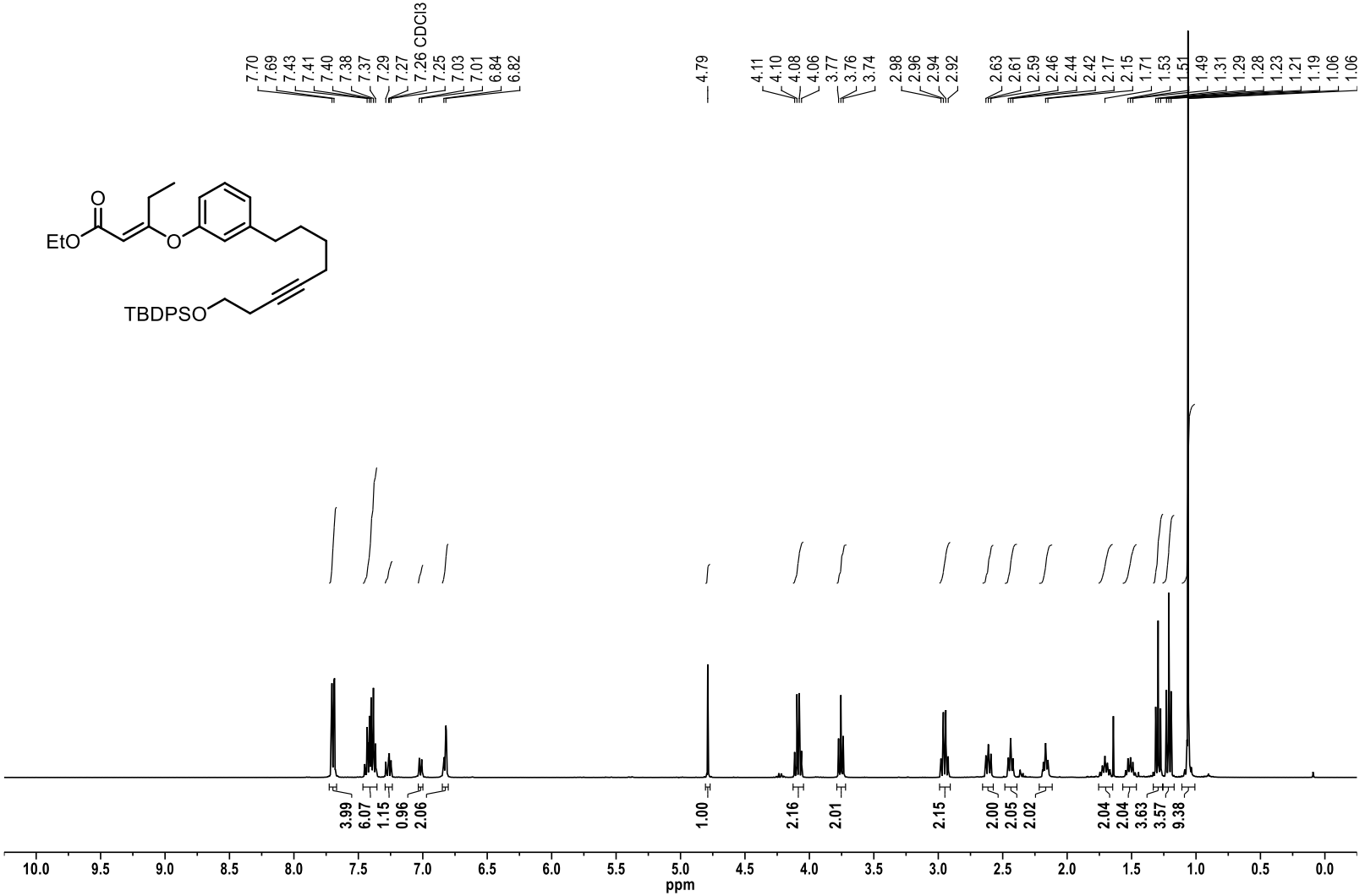
^{1}H NMR spectrum of compound **14** (400 MHz, $CDCl_3$)



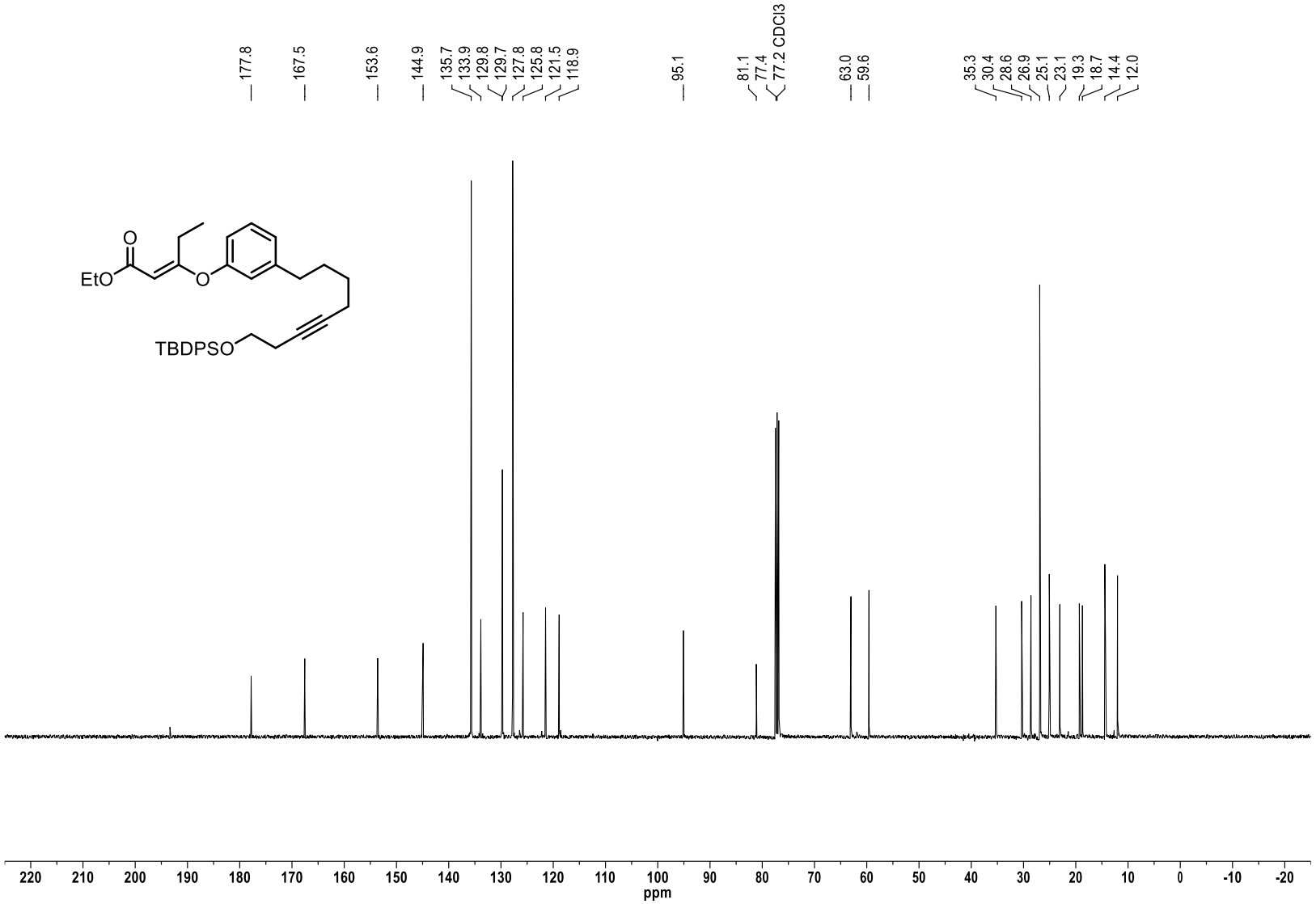
^{13}C NMR spectrum of compound **14** (100 MHz, $CDCl_3$)



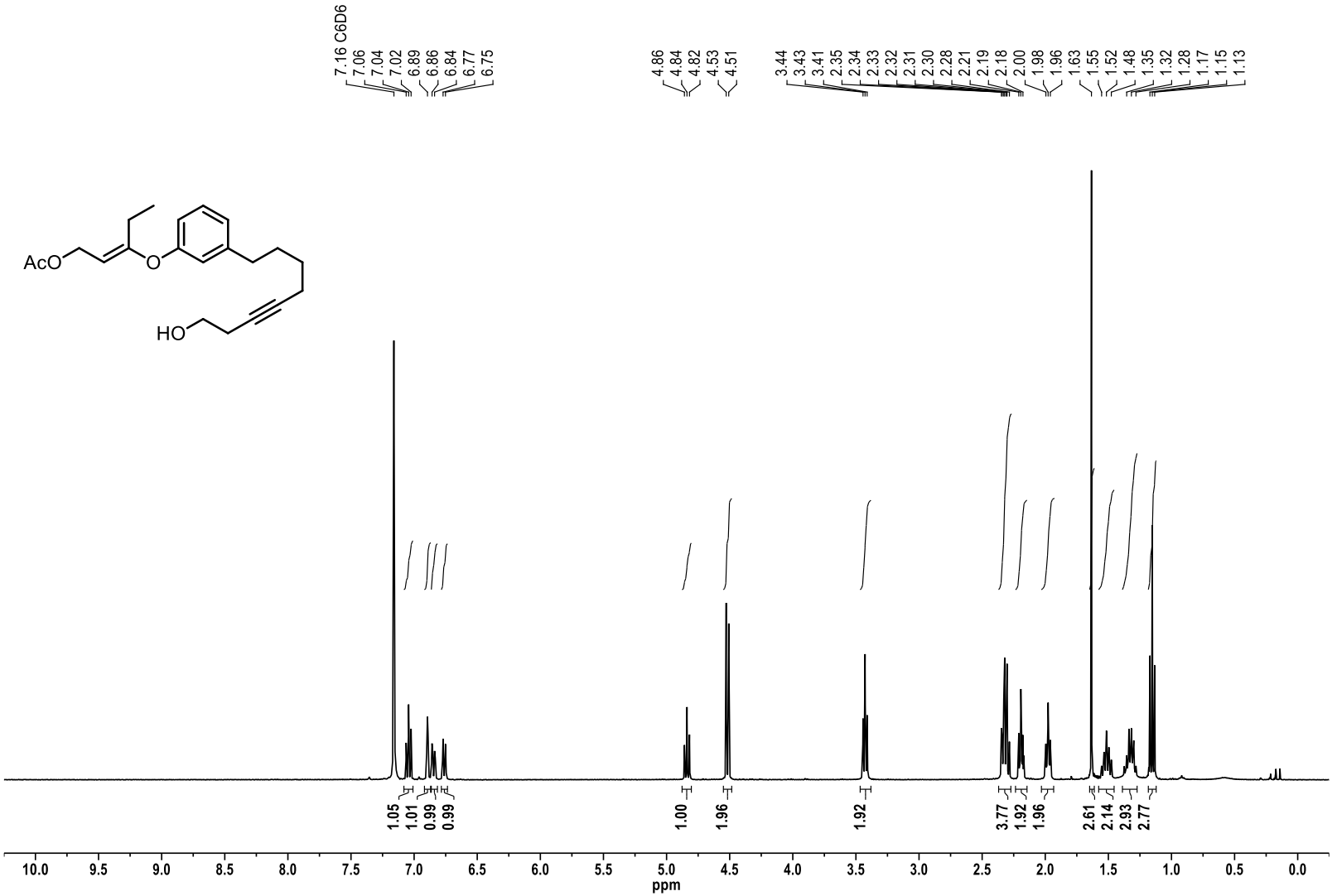
^{1}H NMR spectrum of compound **15** (400 MHz, $CDCl_3$)



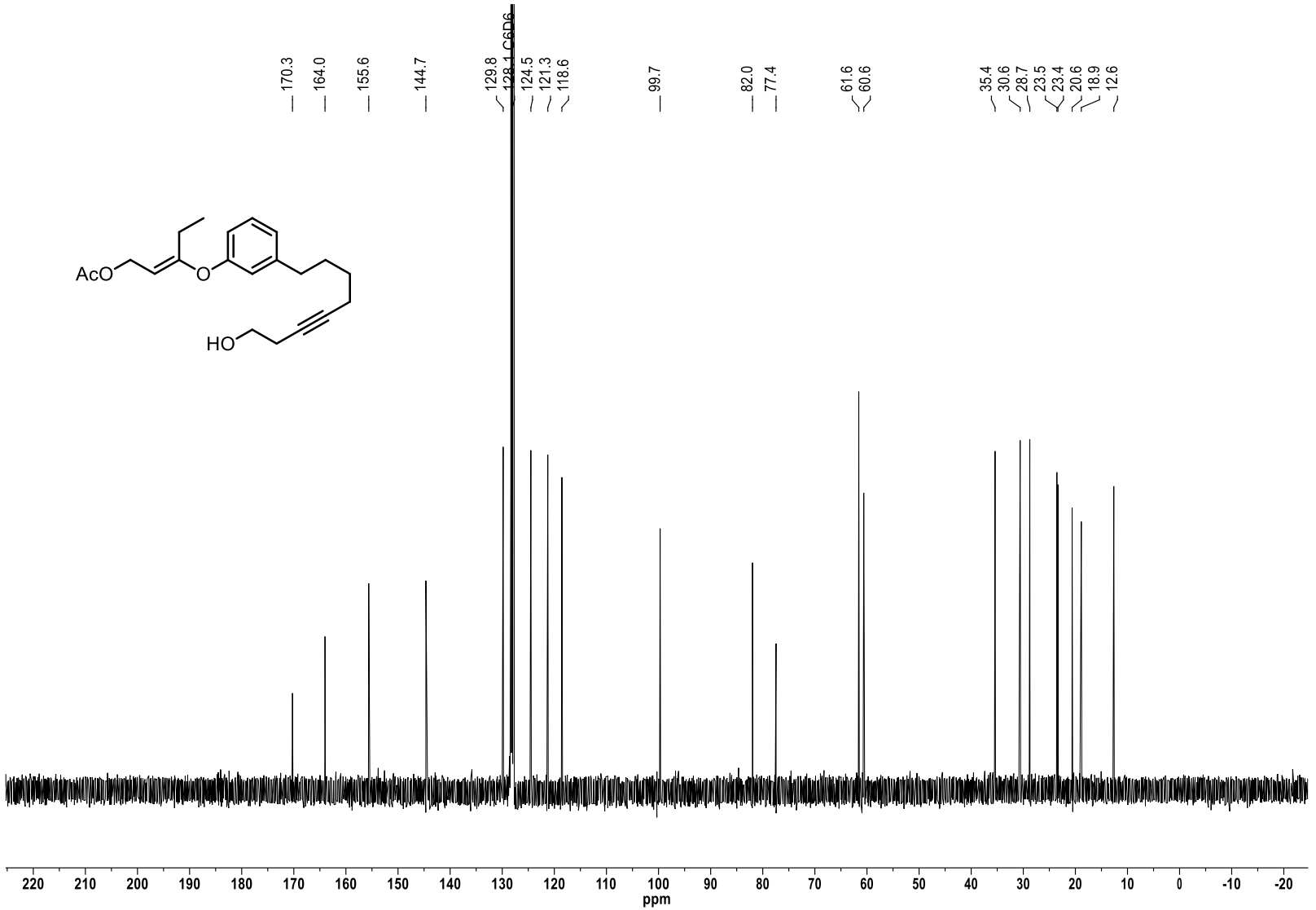
^{13}C NMR spectrum of compound **15** (100 MHz, $CDCl_3$)



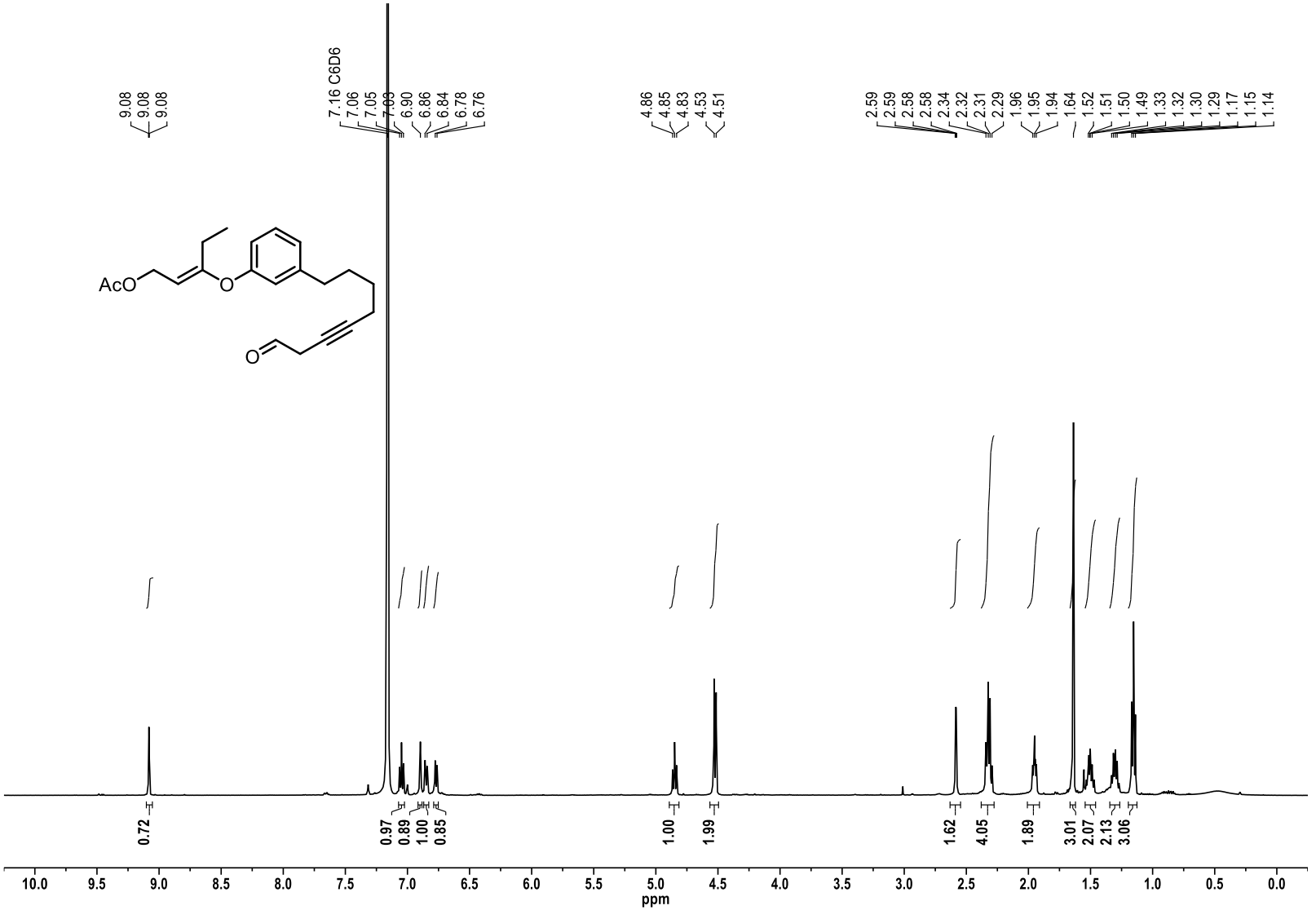
^{1}H NMR spectrum of compound **16** (400 MHz, C_6D_6)



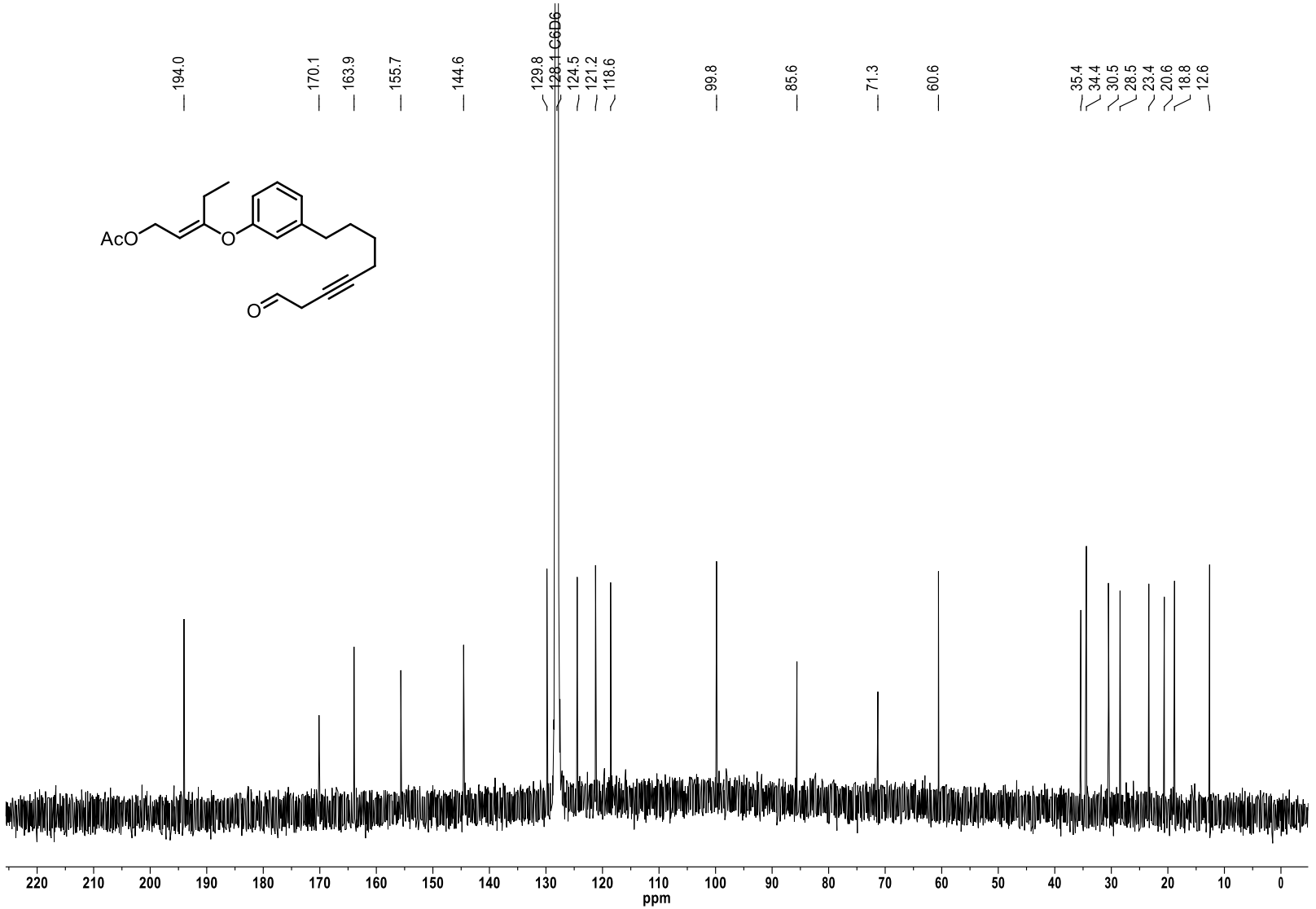
^{13}C NMR spectrum of compound **16** (100 MHz, C_6D_6)



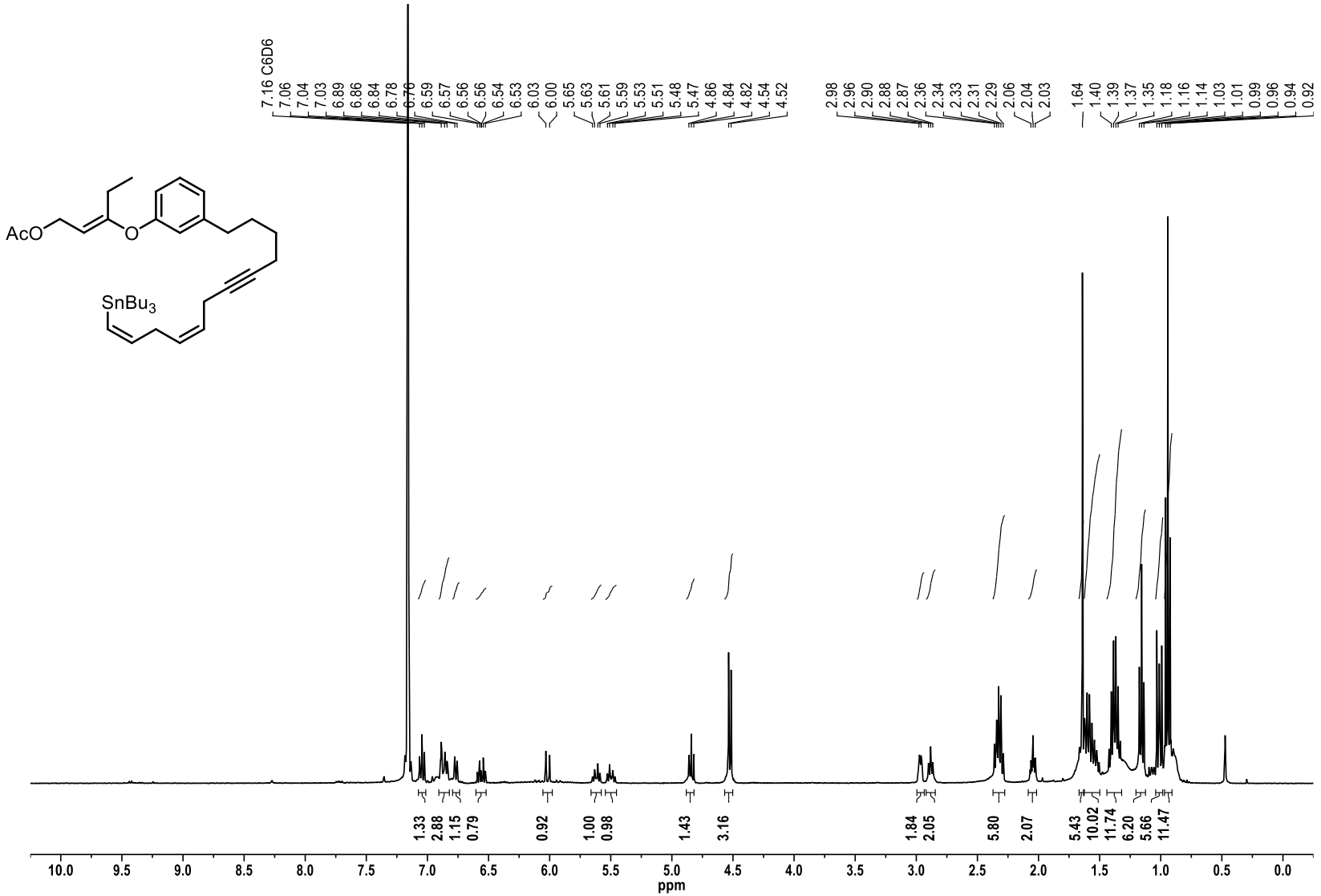
^{1}H NMR spectrum of compound **17** (500 MHz, C_6D_6)



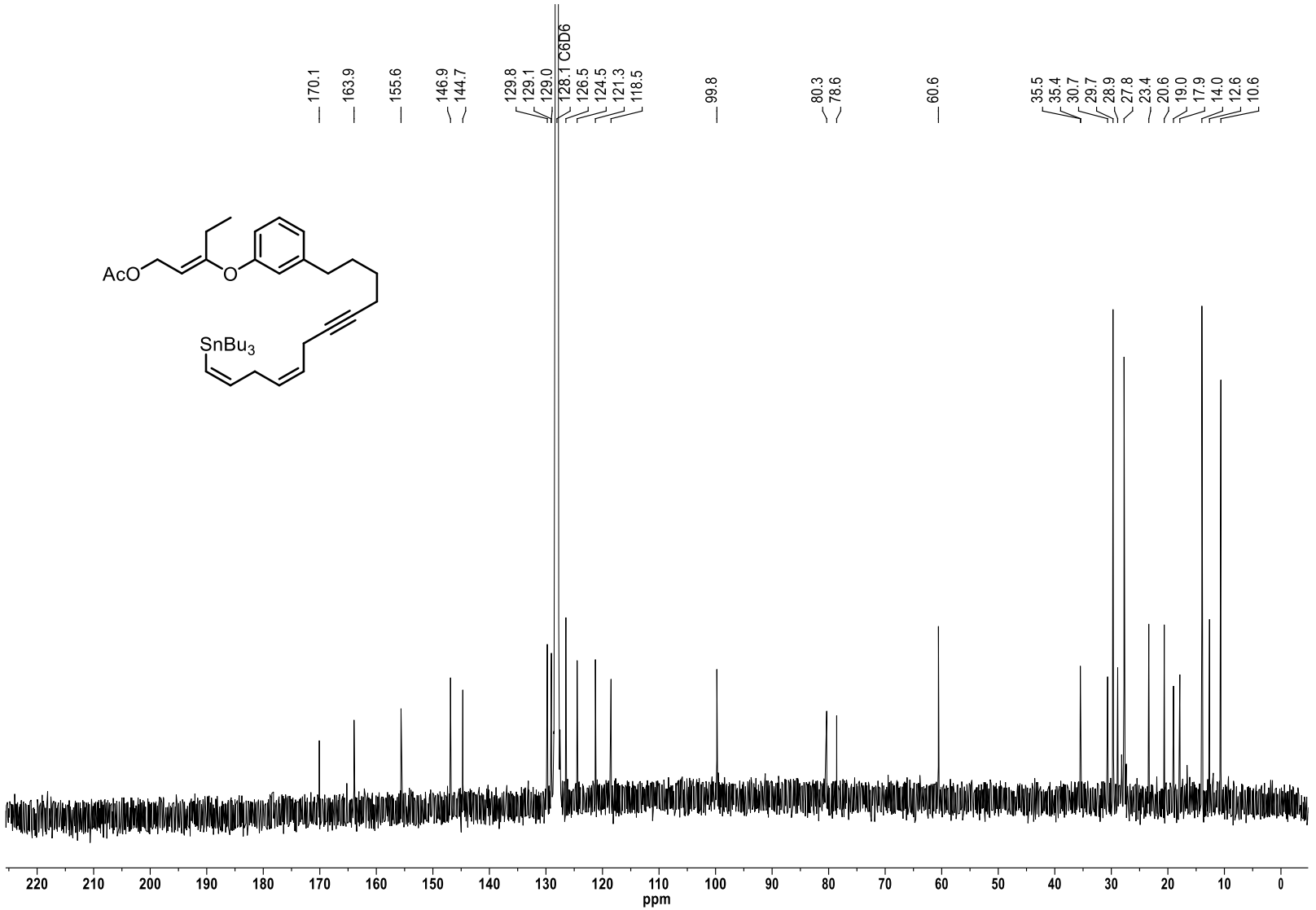
^{13}C NMR spectrum of compound **17** (125 MHz, C_6D_6)



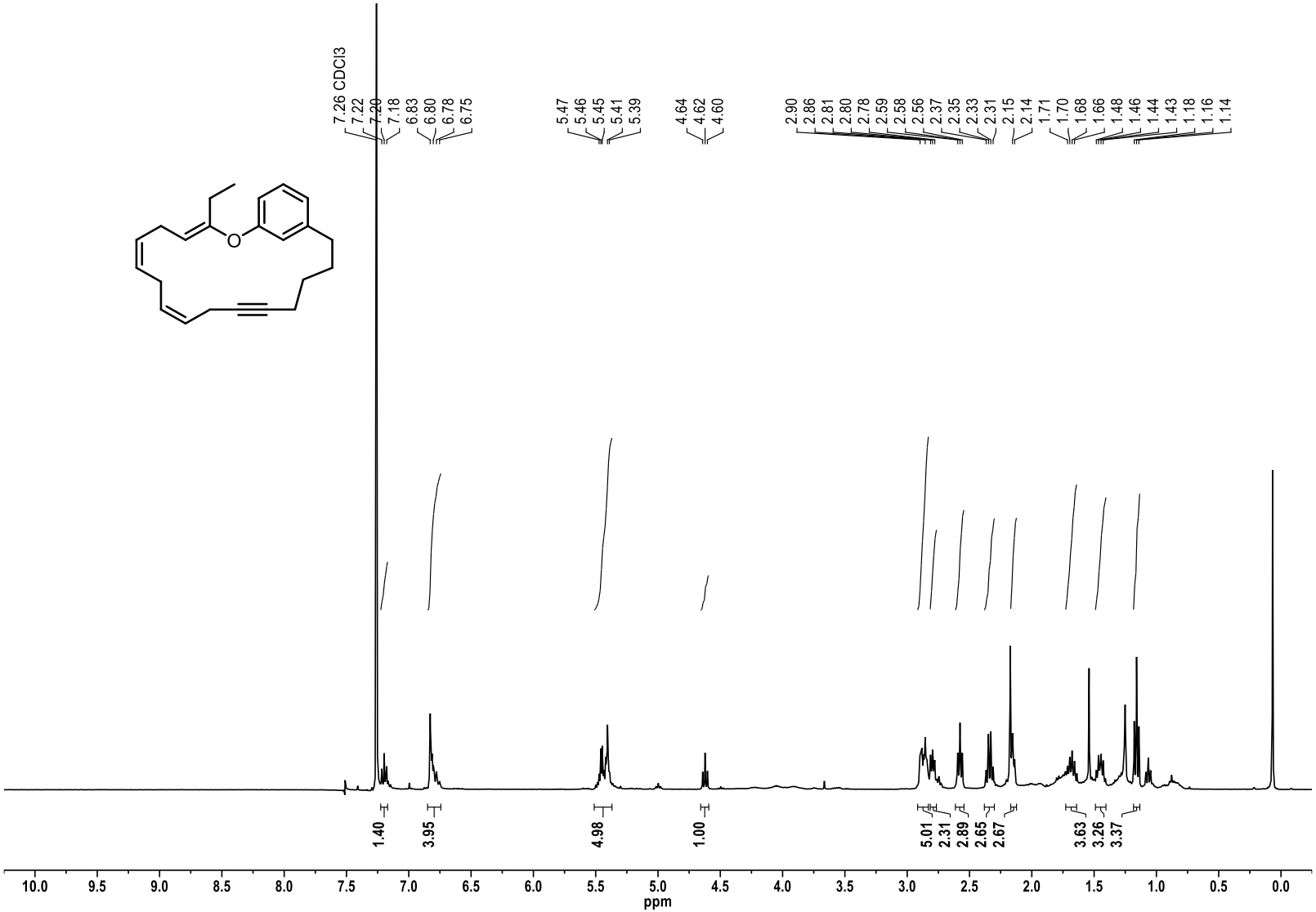
^{1}H NMR spectrum of compound **18** (400 MHz, C_6D_6)



^{1}H NMR spectrum of compound **18** (125 MHz, C_6D_6)



^{1}H NMR spectrum of compound **1** (400 MHz, $CDCl_3$)



^{1}H NMR spectrum of compound **1** (175 MHz, $CDCl_3$)