Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Total Synthesis of Spirastrellolide A Methyl Ester. Part 1: Synthesis of an Advanced C17–C40 *Bis*-Spiroacetal Subunit

Ian Paterson, Edward A. Anderson, Stephen M. Dalby, Jong Ho Lim, Julien Genovino, Philip Maltas, and Christian Moessner*

University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, United Kingdom
Fax: (+44) 1223-336362
E-mail: ip100@cam.ac.uk

The following data is included as supporting information:
Characterisation data for compound **8, 10, 11, 29, and 3**
^{1}H NMR and ^{13}C NMR spectra for compound **8 and 10** ($CDCl_3$)
^{1}H NMR and ^{13}C NMR spectra for compound **11, 29 and 3** (C_6D_6)

NMR spectra were recorded in deuterated benzene (C_6D_6) or deuterated chloroform ($CDCl_3$). Signal positions (δ) are given in parts per million from tetramethylsilane (δ 0) and were measured relative to the signal of the solvent in which the sample was analyzed (C_6D_6: δ 7.15, ^{1}H NMR; δ 128.0, ^{13}C NMR; $CDCl_3$: δ 7.26, ^{1}H NMR; δ 77.0, ^{13}C NMR). Coupling constants (*J* values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. ^{1}H NMR spectral data are reported in the order: integration, multiplicity (br, broad; s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; m, multiplet), coupling constant, and assignment. Infra-red spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer fitted with a universal ATR sampling accessory. Wavelengths of maximum absorbance (ν_{max}) are quoted in cm^{-1}. High and low resolution mass spectra were recorded by the EPSRC Mass Spectrometry service, Swansea, UK and by the Departmental Mass Spectrometry Service (Cambridge University Chemical Laboratories), using chemical ionization (CI), electron impact (EI) or electron spray ionization (ESI) techniques. The parent ion $[M]^+$ or $[M+H]^+$, $[M+NH_4]^+$, $[M+Na]^+$ is quoted. Optical rotations were measured on a Perkin Elmer 241 polarimeter at the sodium D-line (589 nm) and are reported as follows: $[\alpha]_D^{20}$ concentration (c in g / 100 mL) and solvent. Analytical thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 F254 plates with visualization by ultraviolet light (254 nm) and potassium permanganate or phosphomolybdic acid / cerium sulphate dips.

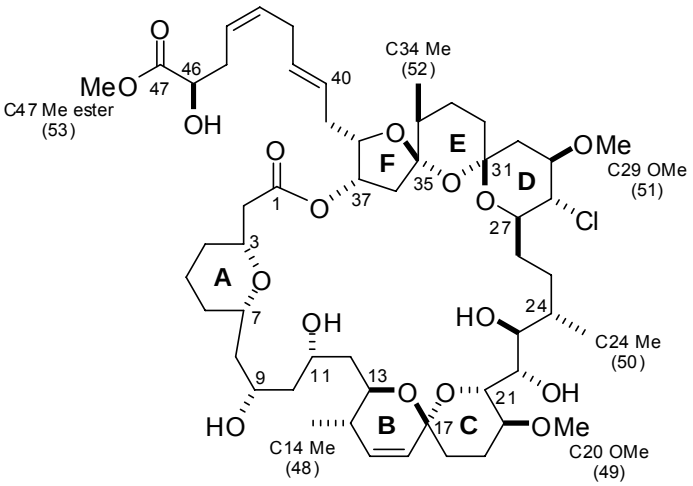
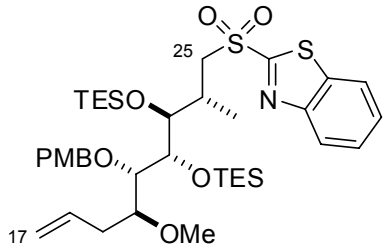


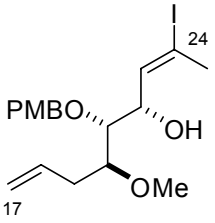
Figure 1: Numbering system for spirastrellolide A methyl ester (**2**)

2-((2*R*,3*S*,4*R*,5*S*,6*S*)-6-methoxy-5-(4-methoxybenzyloxy)-2-methyl-3,4-*bis*(triethylsilyloxy)non-8-enylsulfonyl)benzo[d]thiazole (8)



R$_f$ 0.30 (Et_2O / PE 40-60, 1:3); **$[\alpha]_D^{20}$** = −18.8 (*c* 1.25, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2955, 2877, 1614, 1514, 1459, 1318, 1247, 1147, 1092, 729; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 8.20 (1H, d, *J* = 7.7 Hz, ArH), 8.01 (1H, d, *J* = 7.8 Hz, ArH), 7.60 (2H, dt, *J* = 21.4, 7.1, 7.1 Hz, ArH), 7.20 (2H, d, *J* = 8.6 Hz, ArH), 6.84 (2H, d, *J* = 8.6 Hz, ArH), 5.80 (1H, dd, *J* = 17.1, 10.2 Hz, H_{18}), 5.04 (1H, d, *J* = 5.0 Hz, H_{17}), 5.02 (1H, s, H_{17}), 4.54 (1H, d, *J* = 15.6 Hz, H_{25}), 4.52 (1H, d, *J* = 11.3 Hz, C$\underline{H}_a$H$_b$Ar), 4.41 (1H, d, *J* = 11.3 Hz, CH$_a$$\underline{H}_b$Ar), 3.80 (3H, s, ArOMe), 3.76 (1H, dd, *J* = 7.5, 1.8 Hz, H_{22}), 3.60 (1H, m, H_{23}), 3.36 (1H, dd, *J* = 7.5, 3.5 Hz, H_{21}), 3.31 (1H, dd, J = 10.9, 1.6 Hz, H_{25}), 3.29 (3H, s, OMe), 3.24-3.20 (1H, m, H20), 2.71-2.63 (1H, m, H24), 2.42-2.34 (1H, m, H19), 2.23-2.16 (1H, m, H19), 1.29 (3H, d, *J* = 6.8 Hz, Me_{24}), 0.96 (9H, t, *J* = 8.0 Hz, Si($CH_2C\underline{H}_3$)$_3$), 0.84 (9H, t, *J* = 8.0 Hz, Si($CH_2C\underline{H}_3$)$_3$), 0.63 (6H, q, *J* = 8.0 Hz, Si($C\underline{H}_2CH_3$)$_3$), 0.53 (6H, q, *J* = 8.0 Hz, Si($C\underline{H}_2CH_3$)$_3$); **^{13}C NMR** (127.5 MHz, $CDCl_3$) δ_C 167.2, 158.8, 152.8, 136.9, 135.1, 131.0, 129.0, 127.8, 127.4, 125.4, 122.3, 116.8, 113.5, 82.0, 79.3, 78.7, 73.4, 57.7, 57.3, 55.2, 34.4, 30.0, 19.6, 7.0, 7.0, 5.1, 5.1; **HRMS** (ES$^+$) calcd for $C_{38}H_{65}O_7N_2S_2Si_2$ $[M+NH_4]^+$ 781.3766, found 781.3759.

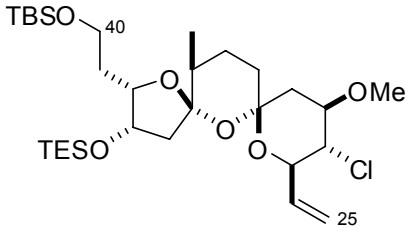
(4*S*,5*R*,6*S*,E)-2-iodo-6-methoxy-5-(4-methoxybenzyloxy)nona-2,8-dien-4-ol (10)



R$_f$ 0.14 (EtOAc / PE 40-60, 1:8); **$[\alpha]_D^{20}$** = −6.7 (*c* 1.15, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3478, 2932, 1638, 1612, 1514, 1463, 1248, 1174, 1098, 1034, 822; **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 7.25 (2H, d, *J* = 8.8 Hz, ArH), 6.90 (2H, d, *J* = 8.8 Hz, ArH), 6.23 (1H, dq, *J* = 8.6, 1.5 Hz, H_{23}), 5.82 (1H, ddt, *J* = 17.1, 10.4, 7.2 Hz, H_{18}), 5.13-5.08 (2H, m, 2 x H_{17}), 4.62 (1H, d, *J* = 11.0 Hz, C$\underline{H}_a$H$_b$Ar), 4.52 (1H, d, *J* = 11.0 Hz, C$\underline{H}_a$H$_b$Ar), 4.45 (1H, m, H_{21}), 3.82 (3H, s, ArOMe), 3.43-3.38 (2H, m, H_{20}, H_{22}), 3.42 (3H, s, OMe_{20}), 3.04 (1H, d, *J* = 6.2 Hz, OH), 2.47-2.34 (2H,

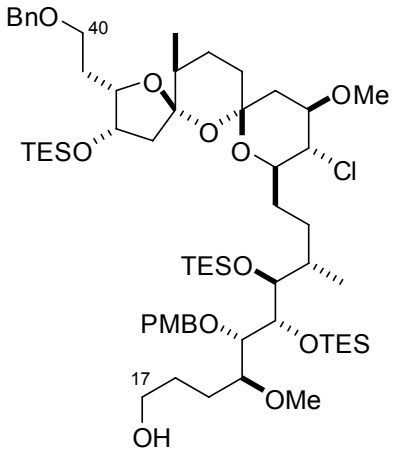
m, 2 x H_{19}), 2.44 (3H, d, *J* = 1.5 Hz, Me_{24}); **^{13}C NMR** (127.5 MHz, $CDCl_3$) δ_C 159.5, 141.0, 134.2, 129.8, 129.7, 117.6, 114.0, 98.5, 81.0, 80.7, 73.5, 68.8, 57.9, 55.3, 34.4, 28.6; **HRMS** (ES^+) calcd for $C_{18}H_{25}IO_4Na$ $[M+Na]^+$ 455.0695, found 455.0709.

Alkene 11



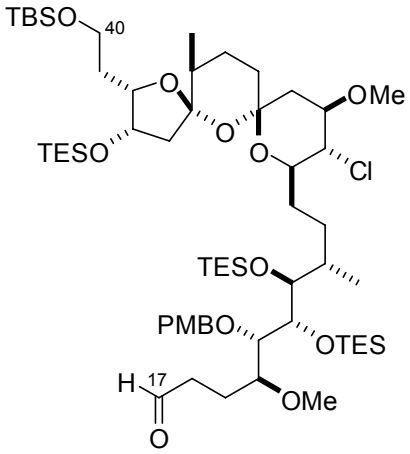
R_f 0.61 (EtOAc / PE 40-60, 1:4); **$[\alpha]_D^{20}$** = −4.4 (*c* 0.50, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2955, 2878, 1462, 1380, 1254, 1083, 975, 929, 835, 776, 729; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 6.30 (1H, ddd, *J* = 17.1, 10.7, 4.7 Hz, H_{26}), 5.73 (1H, d, *J* = 17.1 Hz, H_{25}), 5.21 (1H, d, *J* = 10.7 Hz, H_{25}), 4.48 (1H, m, H_{27}), 4.23 (1H, m, H_{38}), 4.16 (1H, m, H_{37}), 3.93-3.77 (3H, m, 2 x H_{40}, H_{29}), 3.63 (1H, dd, *J* = 10.1, 9.9 Hz, H_{28}), 3.31 (3H, s, OMe_{29}), 2.19 (1H, dd, *J* = 14.1, 2.5 Hz, H_{36}), 2.11 (2H, m, H_{33eq}, H_{30eq}), 2.02 (1H, m, H_{39}), 1.97 (1H, dd, *J* = 14.2, 2.5 Hz, H_{36}), 1.91 (1H, m, H_{39}), 1.71 (1H, dt, *J* = 13.2, 3.1 Hz, H_{32eq}), 1.51 (1H, m, H_{34}), 1.34 (2H, m, H_{32ax}, H_{30ax}), 1.21 (1H, m, H_{33ax}), 1.03 (3H, d, *J* = 6.7 Hz, Me_{34}), 1.01 (9H, s, ^{t}BuSi), 0.97 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.54 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.13 (3H, s, SiMe), 0.11 (3H, s, SiMe); **^{13}C NMR** (127.5 MHz, C_6D_6) δ_C 135.4, 116.7, 108.8, 97.6, 80.7, 79.4, 73.3, 72.4, 64.7, 61.3, 57.3, 49.0, 43.2, 37.8, 36.0, 33.1, 26.0, 23.9, 18.3, 16.5, 6.9, 4.9, −5.2, −5.3; **HRMS** (ES^+) calcd for $C_{30}H_{57}ClO_6Si_2$ $[M+Na]^+$ 627.3280, found 627.3271.

Alcohol 29



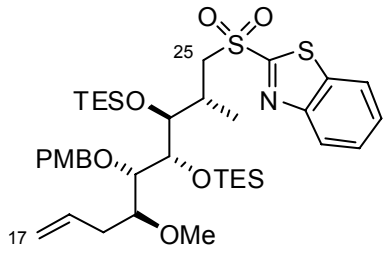
R_f 0.14 (EtOAc / PE 40-60, 1:4); **$[\alpha]_D^{20}$** = +7.9 (*c* 0.62, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3452, 2952, 2876, 1612, 1514, 1457, 1381, 1246, 1170, 1081, 1014, 976, 739; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 7.45 (2H, d, *J* = 8.6 Hz, ArH), 7.40 (2H, d, *J* = 7.4 Hz, ArH), 7.23 (2H, app t, *J* = 7.7 Hz, ArH), 7.10 (1H, app t, *J* = 7.4, Hz, ArH), 6.84 (2H, d, *J* = 8.6 Hz, ArH), 4.96 (1H, d, *J* = 11.0 Hz, $C\underline{H}_aH_bAr$), 4.83 (1H, d, *J* = 11.0 Hz, $CH_a\underline{H}_bAr$), 4.55 (1H, d, *J* = 12.0 Hz, $C\underline{H}_cH_dAr$), 4.46 (1H, d, *J* = 12.0 Hz, $CH_c\underline{H}_dAr$), 4.35 (1H, ddd, *J* = 6.3, 4.4, 0.5 Hz, H_{38}), 4.22 (1H, m, H_{27}), 4.15 (1H, m, H_{37}), 4.03 (1H, dd, *J* = 7.5, 1.2 Hz, H_{22}), 4.01 (1H, dd, *J* = 7.5, 2.0 Hz, H_{21}), 3.93 (1H, m, H_{28}), 3.91 (1H, m, H_{29}), 3.74-3.69 (2H, m, H_{40}, H_{23}), 3.66 (1H, m, H_{40}), 3.59 (1H, m, H_{20}), 3.57-3.49 (2H, m, 2 x H_{17}), 3.34 (3H, s, ArOMe), 3.31 (3H, s, OMe_{20}), 3.30 (3H, s, OMe_{29}), 2.33-2.28 (2H, m, 2 x H_{26}), 2.24-2.12 (5H, m, 2 x H_{39}, H_{36}, H_{33}, H_{30}), 2.11-2.00 (3H, m, H_{25}, 2 x H_{19}), 1.97 (1H, dd, *J* = 14.1, 2.9 Hz, H_{36}), 1.89-1.69 (4H, m, H_{32}, H_{24}, 2 x H_{18}), 1.54 (1H, m, H_{34}), 1.46-1.24 (4H, m, H_{33}, H_{32}, H_{30}, H_{25}), 1.17 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.13 (3H, d, *J* = 6.7 Hz, Me_{24}), 1.08 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.06 (3H, d, *J* = 6.4 Hz, Me_{34}), 0.95 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.91 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.90 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.52 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$); **^{13}C NMR** (127.5 MHz, C_6D_6) δ_C 159.3, 139.0, 132.0, 129.3, 128.4, 113.7, 108.5, 97.5, 82.5, 82.2, 80.8, 80.0, 79.5, 76.1, 74.2, 73.0, 72.1, 67.9, 63.8, 62.5, 57.3, 56.8, 54.5, 48.9, 43.5, 37.8, 36.8, 36.2, 30.2, 30.0, 29.7, 29.6, 26.7, 26.3, 24.0, 17.7, 16.5, 7.5, 7.3, 6.9, 5.9, 5.7, 5.6, 4.9; **HRMS** (ES^+) calcd for $C_{61}H_{107}ClO_{12}Si_3Na$ $[M+Na]^+$ 1173.6694, found 1173.6651.

Aldehyde 3



R_f 0.40 (EtOAc / PE 40-60, 1:6); **$[\alpha]_D^{20}$** = +9.2 (*c* 0.40, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2955, 2878, 1727, 1614, 1514, 1460, 1382, 1248, 1100, 1009, 977, 836, 740; **^{1}H NMR** (500 MHz, C_6D_6) δ_H 9.52 (1H, s, H_{17}), 7.43 (2H, d, *J* = 8.6 Hz, ArH), 6.85 (2H, d, *J* = 8.6 Hz, ArH), 4.90 (1H, d, *J* = 11.0 Hz, $C\underline{H}_aH_bAr$), 4.82 (1H, d, *J* = 10.9 Hz, $CH_a\underline{H}_bAr$), 4.36 (1H, m, H_{38}), 4.29 (1H, m, H_{37}), 4.19 (1H, m, H_{27}), 4.02 (1H, dd, *J* = 7.3, 1.0 Hz, H_{22}), 3.96-3.89 (5H, m, 2 x H_{40}, H_{29}, H_{28}, H_{21}), 3.73 (1H, dd, *J* = 7.7, 1.0 Hz, H_{23}), 3.52 (1H, m, *J* = 8.9, 2.4 Hz, H_{20}), 3.34 (3H, s, ArOMe), 3.31 (3H, s, OMe), 3.23 (3H, s, OMe), 2.37-2.13 (8H, m, H_{39}, H_{36}, H_{33}, H_{30}, H_{26}, H_{25}, 2 x H_{18}), 2.12-2.00 (3H, m, H_{39}, H_{19}, H_{26}), 1.99 (1H, dd, *J* = 14.0, 2.7 Hz, H_{36}), 1.93-1.83 (2H, m, H_{24}, H_{19}), 1.80 (1H, dt, *J* = 13.2, 3.2 Hz, H_{32}), 1.54 (1H, m, H_{34}), 1.46-1.23 (4H, m, H_{33}, H_{32}, H_{30}, H_{25}), 1.16 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.19 (3H, d, *J* = 6.9 Hz, Me_{24}), 1.09 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 1.06 (3H, d, *J* = 7.0 Hz, Me_{34}), 1.05 (9H, s, ^{t}BuSi), 0.98 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.89 (6H, qd, *J* = 8.0, 3.2 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.77 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.57 (6H, q, *J* = 8.0 Hz, $Si(C\underline{H}_2CH_3)_3$), 0.19 (3H, s, SiMe), 0.17 (3H, s, SiMe); **^{13}C NMR** (127.5 MHz, C_6D_6) δ_C 200.4, 159.4, 131.7, 129.3, 113.7, 108.5, 97.5, 82.0, 81.5, 80.5, 80.0, 79.5, 75.9, 74.3, 72.9, 72.2, 65.7, 63.6, 60.9, 57.3, 56.7, 54.5, 48.9, 43.5, 40.4, 37.8, 36.8, 36.2, 33.1, 29.5, 26.2, 26.0, 24.0, 22.9, 18.3, 17.9, 16.5, 15.3, 7.4, 7.3, 6.9, 5.7, 5.5, 5.0, −5.1, −5.2; **HRMS** (ES^+) calcd for $C_{60}H_{113}ClO_{12}Si_4Na$ $[M+Na]^+$ 1195.6895, found 1195.6924.

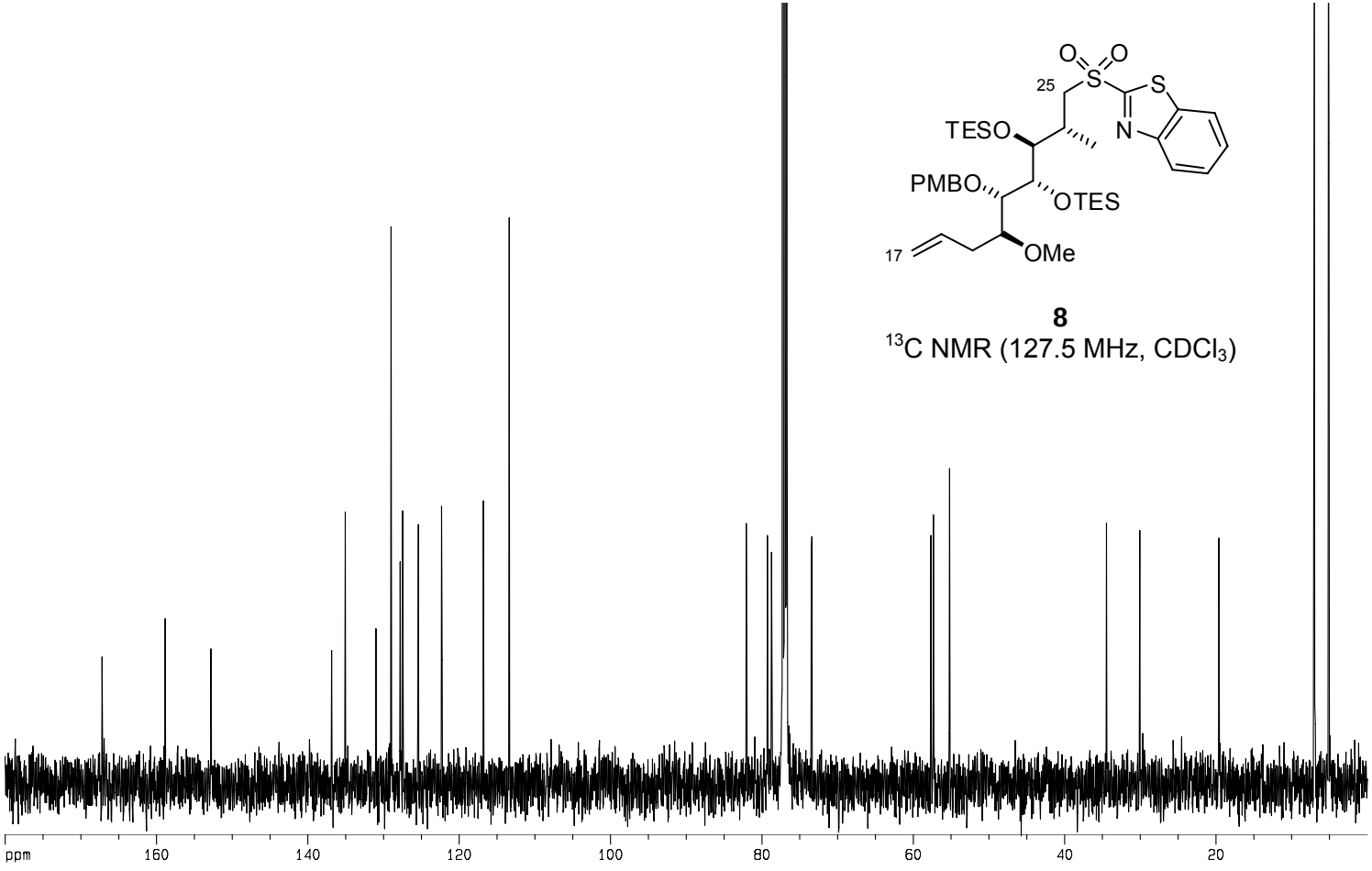
^{1}H NMR Spectrum for compound 8



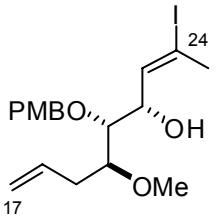
8

^{1}H NMR (500 MHz, $CDCl_3$)

^{13}C NMR Spectrum for compound 8

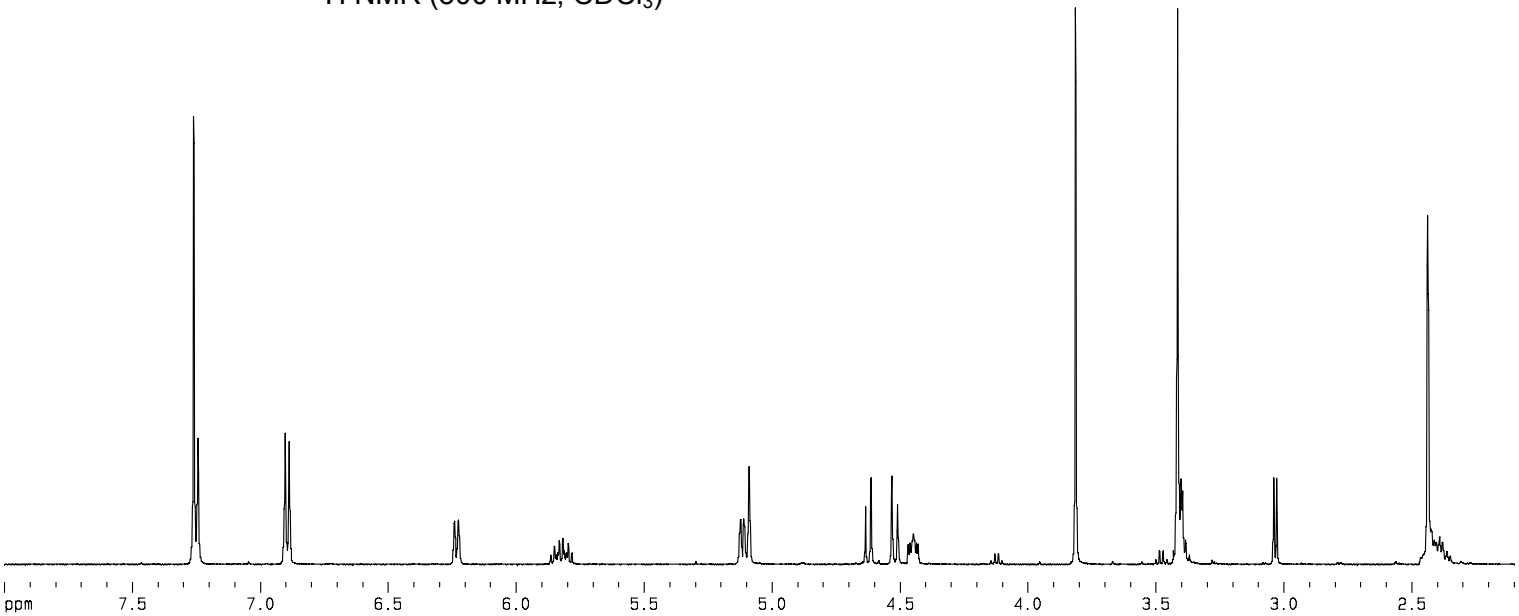


^{1}H NMR Spectrum for compound 10

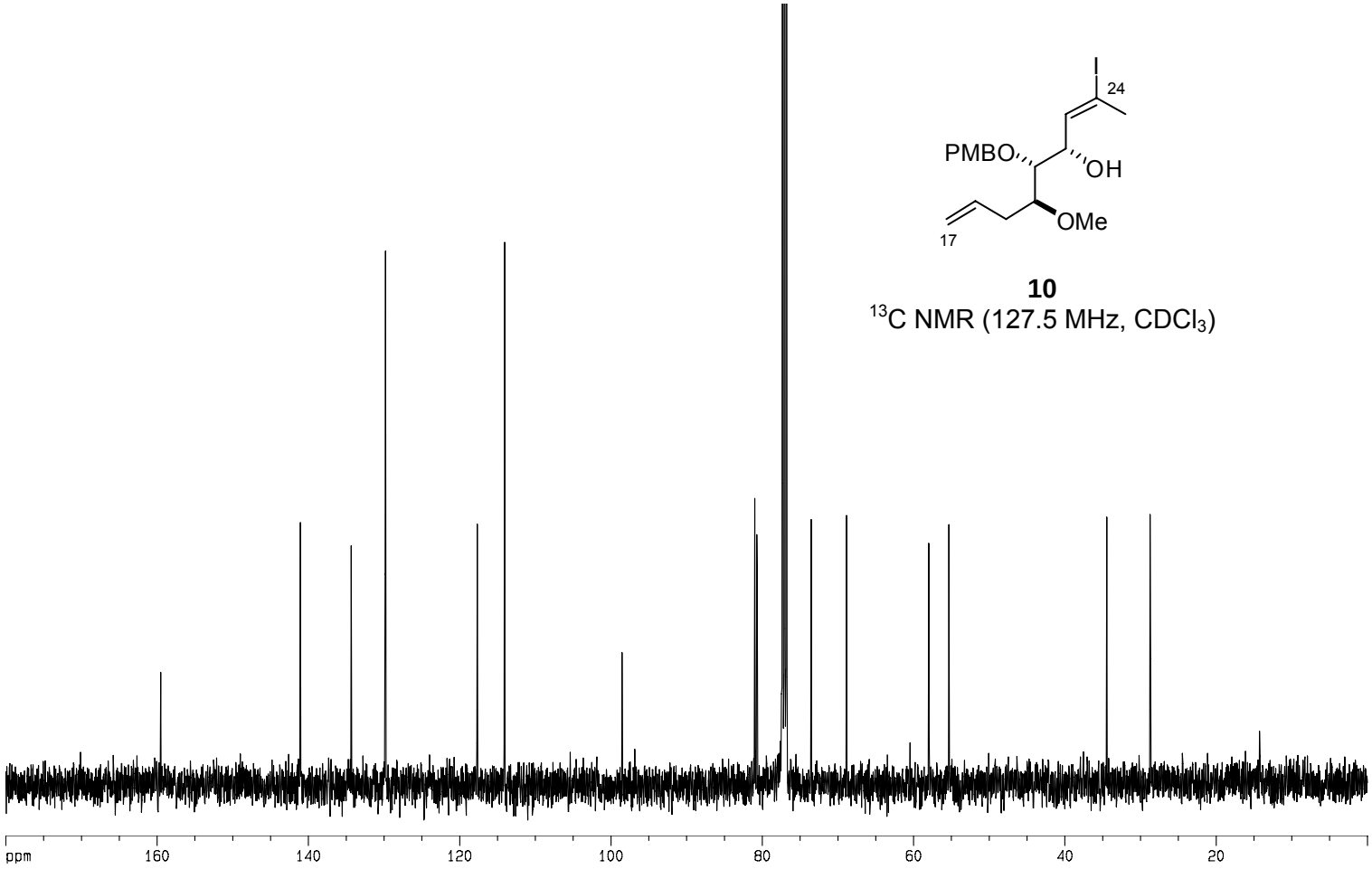


10

^{1}H NMR (500 MHz, $CDCl_3$)



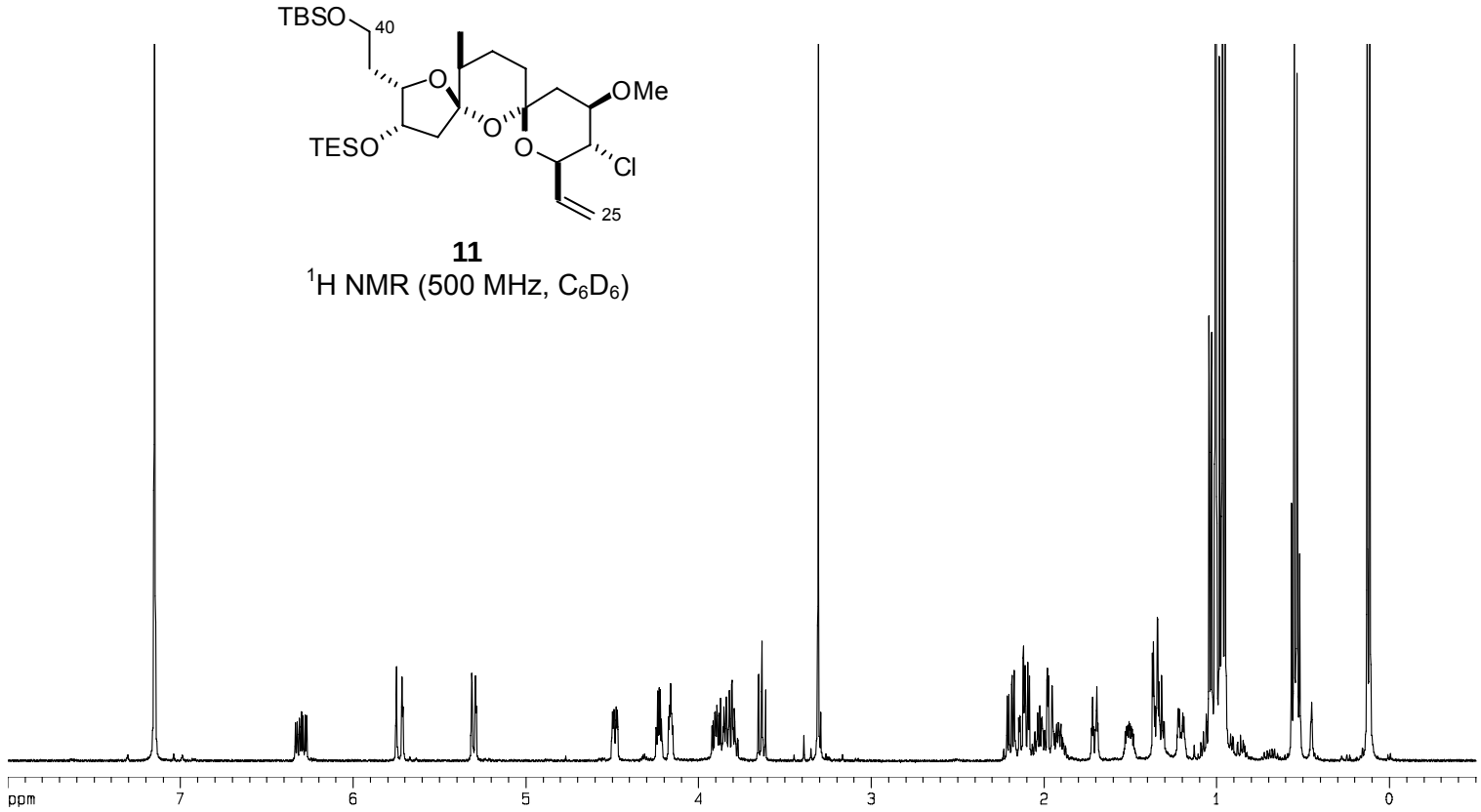
^{13}C NMR Spectrum for compound 10



10

^{13}C NMR (127.5 MHz, $CDCl_3$)

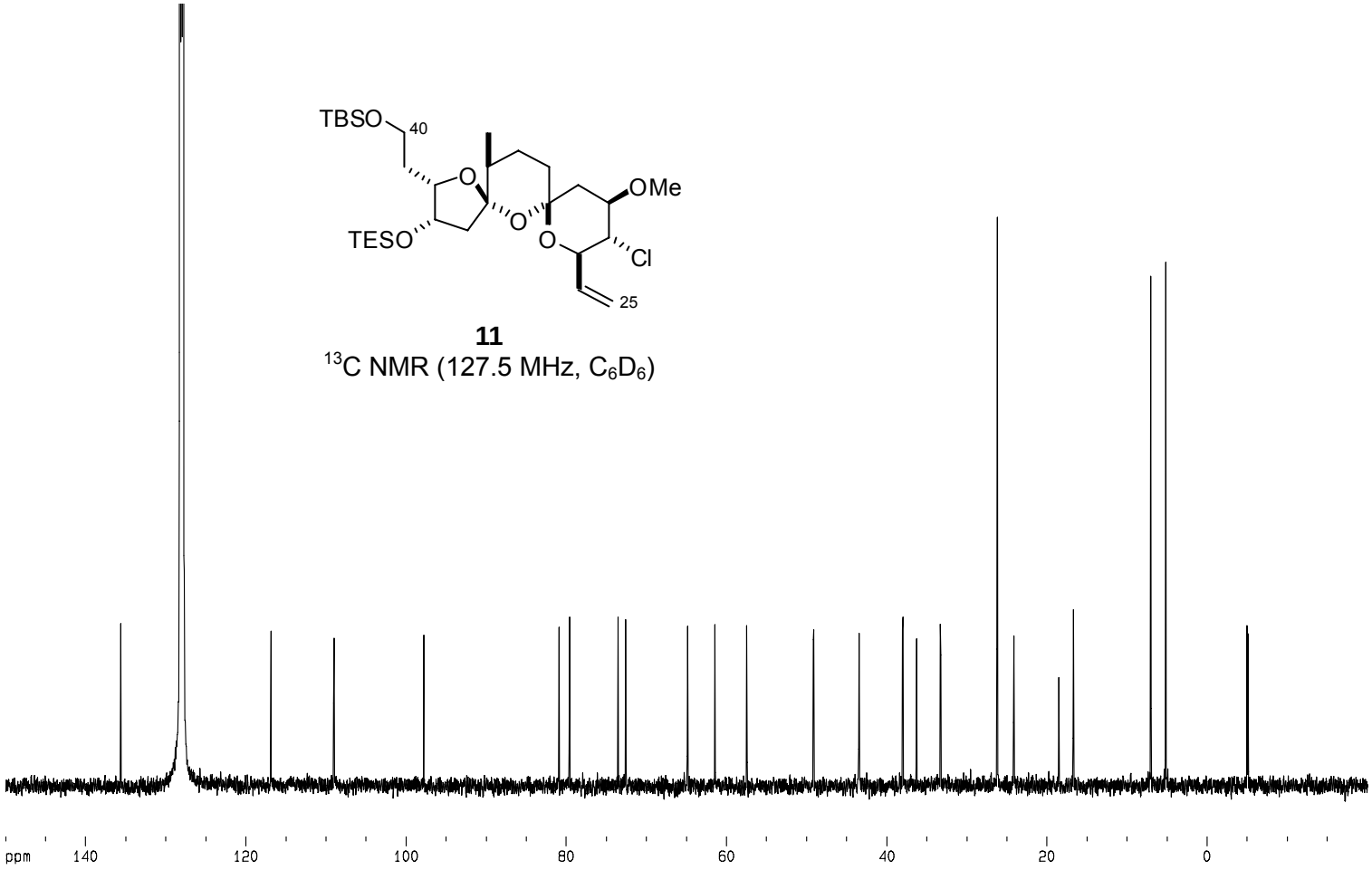
^{1}H NMR Spectrum for compound 11



11

^{1}H NMR (500 MHz, C_6D_6)

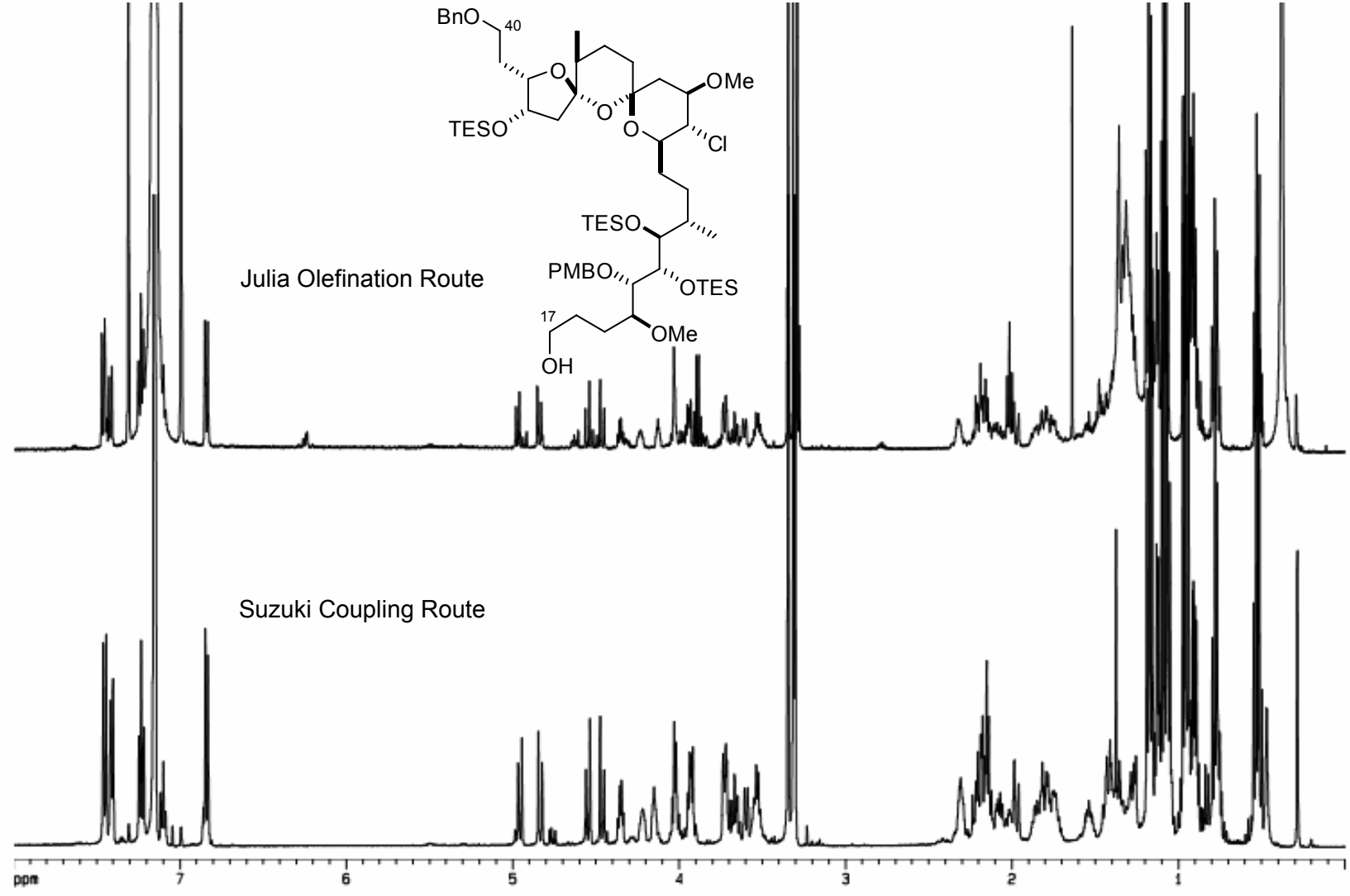
^{13}C NMR Spectrum for compound 11



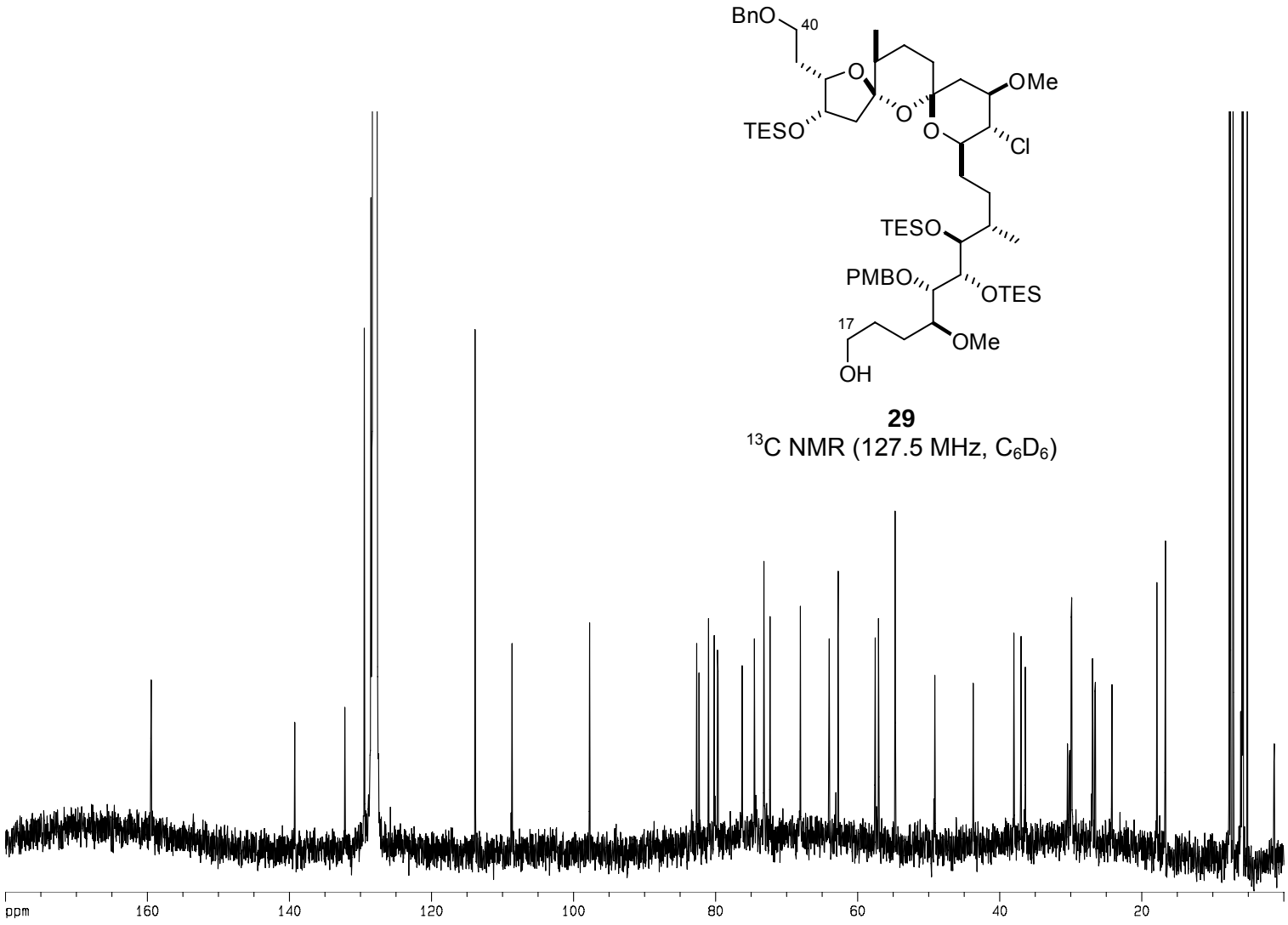
11

^{13}C NMR (127.5 MHz, C_6D_6)

^{1}H NMR Spectra for compound 29 (500 MHz, C_6D_6)



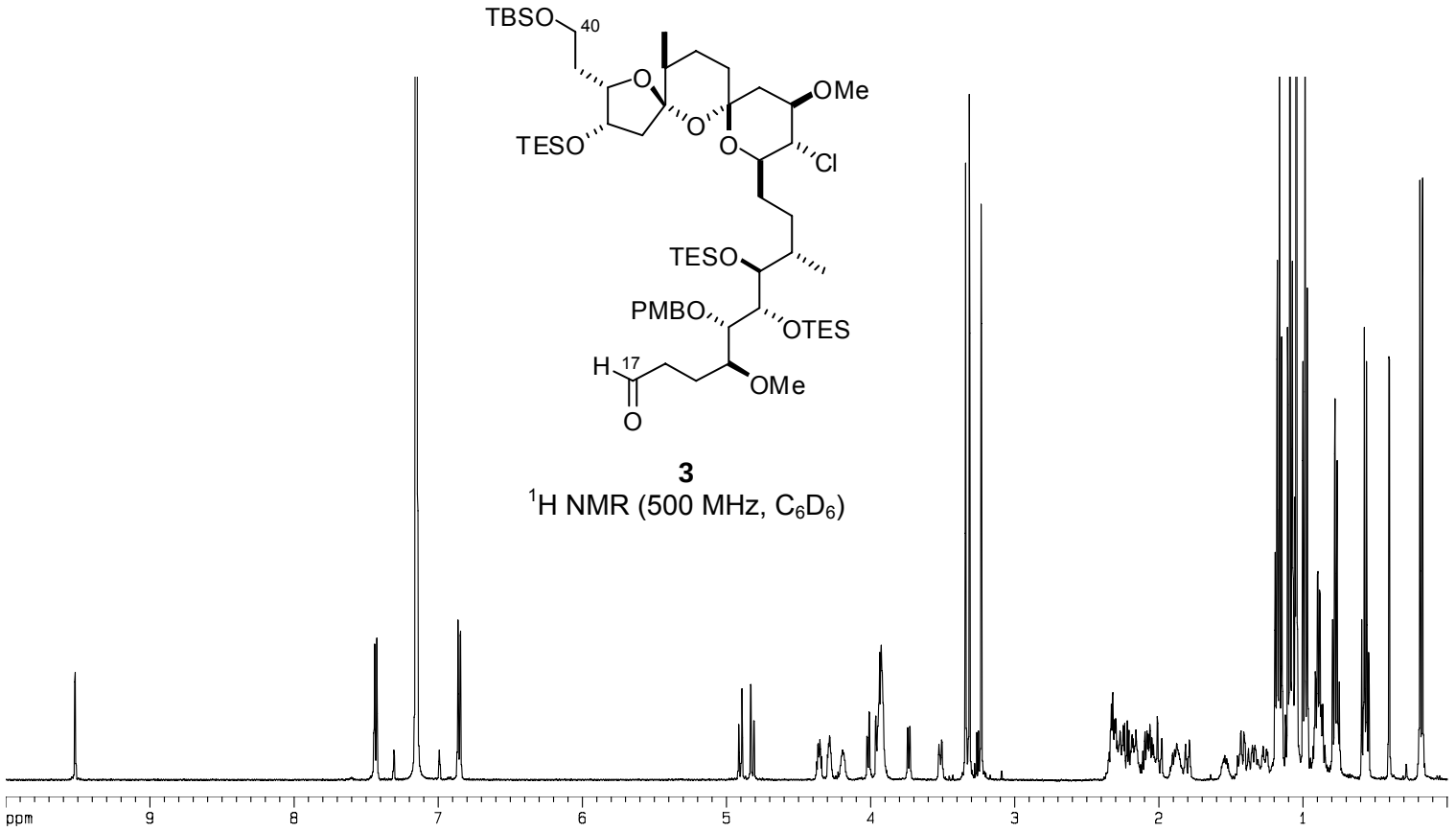
^{13}C NMR Spectrum for compound 29



29

^{13}C NMR (127.5 MHz, C_6D_6)

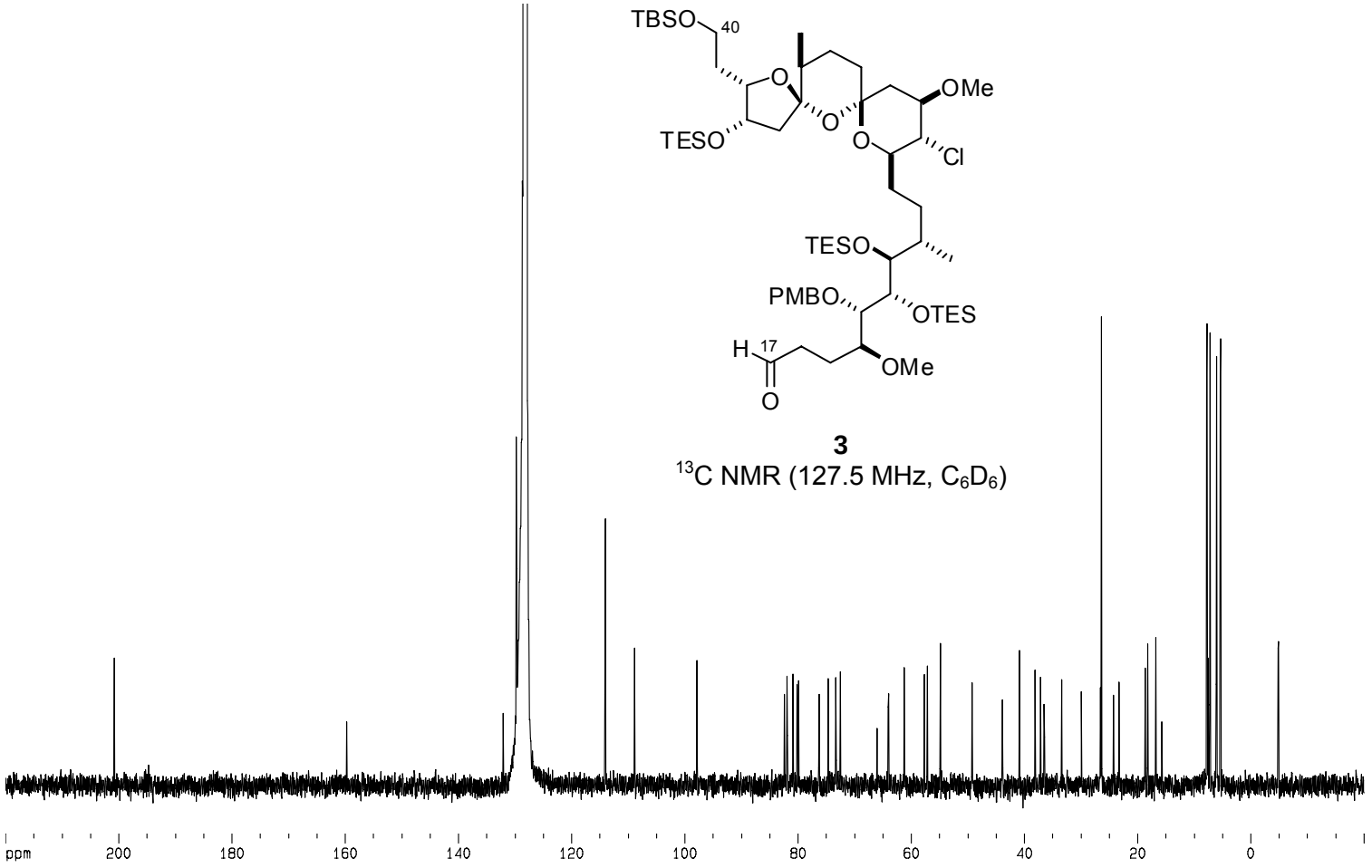
^{1}H NMR Spectrum for compound 3



3

^{1}H NMR (500 MHz, C_6D_6)

^{13}C NMR Spectrum for compound 3



3

^{13}C NMR (127.5 MHz, C_6D_6)