A New Construction of 2-Alkoxypyrans by an Acylation-Reductive Cyclization Sequence

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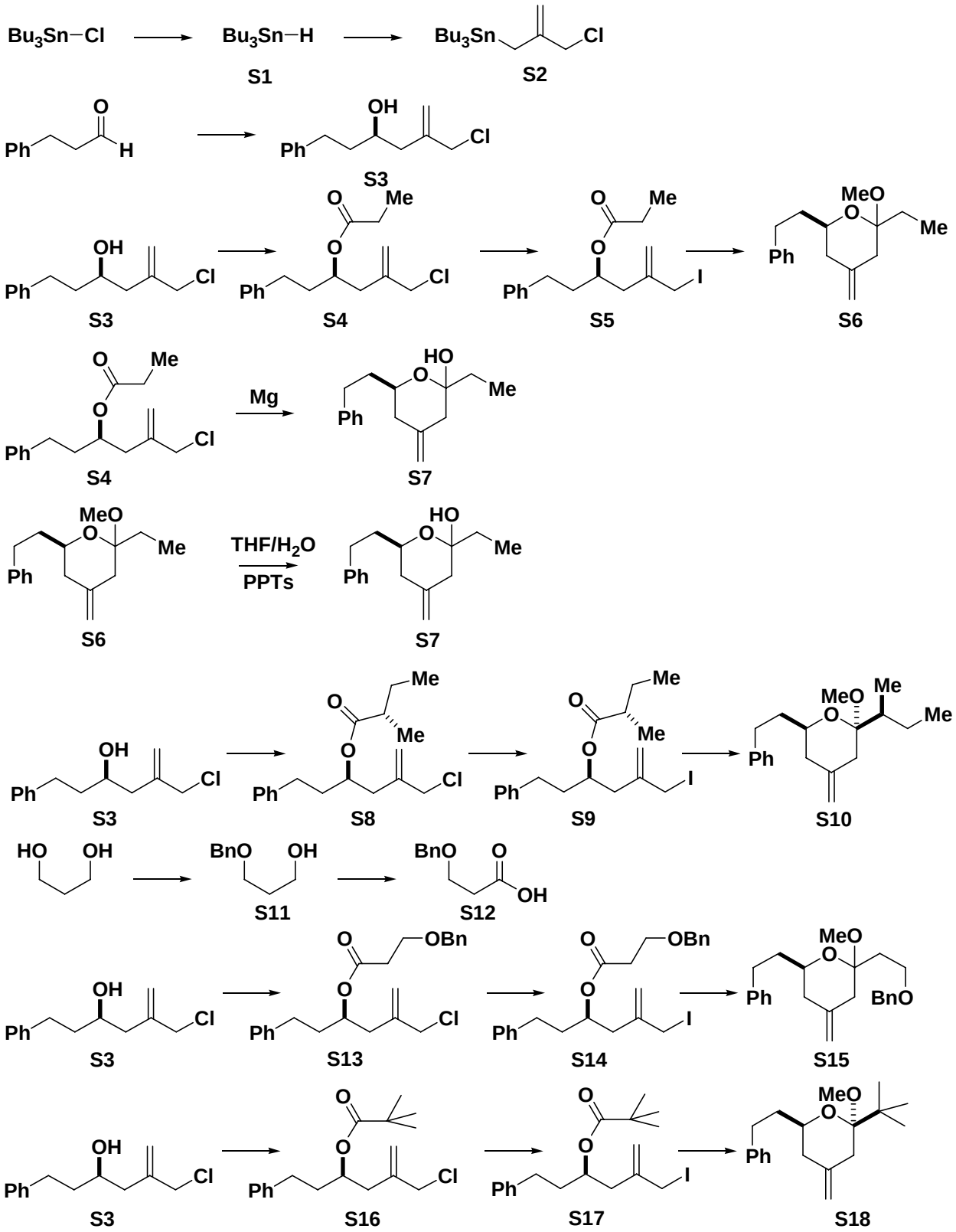
General Experimental Procedures, Materials, and Instrumentation: Solvents were purified according to the guidelines in *Purification of Common Laboratory Chemicals*.[1] Diisopropylamine, triethylamine, pyridine, Hünig's base, EtOAc and CH_2Cl_2 were distilled from CaH_2. The titer of *n*-butyllithium was determined by the method of Eastham and Watson.[2] All other reagents were used without further purification. Yields were calculated for material judged homogenous by thin layer chromatography and nuclear magnetic resonance (NMR). Thin layer chromatography was performed on Merck Kieselgel 60 F_{254} plates eluting with the solvent indicated, visualized by a 254 nm UV lamp, and stained with an ethanolic solution of 12-molybdophosphoric acid or 4-anisaldehyde solution. Glassware for reactions was oven dried at 125 °C and cooled under a dry atmosphere prior to use. Liquid reagents and solvents were introduced by oven dried syringes through septum-sealed flasks under a nitrogen atmosphere. Column flash chromatography was performed with Silicycle Grade 70 – 230 mesh, 60 – 200 μm, 60 Å silica gel, slurry packed with 1% EtOAc/hexanes in glass columns. Preparative thin layer chromatography was performed on Analtech Inc. Silica Gel GF 20 cm × 20 cm × 2000 μm plates or on Merck Kieselgel 60 F_{254} 20 cm × 20 cm × 250 μm plates. Nuclear magnetic resonance spectra were acquired on a Varian VXR-500 spectrometer or a Varian Inova-500 spectrometer 500 MHz for ^1H and 125 MHz for ^{13}C. Prior to use, $CDCl_3$ was filtered through a plug of Fisher Scientific 80 – 200 mesh Alumina Adsorption stored at 110 ºC. Chemical shifts for proton nuclear magnetic resonance (^1H NMR) spectra are reported in parts per million relative to the signal of tetramethylsilane at 0 ppm, relative to the signal of residual $CHCl_3$ at 7.27 ppm, or relative to the signal of residual C_6D_5H at 7.16 ppm. Chemicals shifts for carbon nuclear magnetic resonance

(^{13}C NMR and DEPT) spectra are reported in parts per million relative to the signal of tetramethylsilane at 0 ppm, relative to the center line of the $CDCl_3$ triplet at 77.23 ppm, or relative to the center line of the C_6D_6 triplet at 128.62 ppm. Chemical shifts of the unprotonated carbons ('C') for DEPT spectra were obtained by comparison with the ^{13}C NMR spectrum. The abbreviations s, bs, d, dd, ddd, dddd, t, td, tt, q, dq, dqd, ddq, qdd, qq, and m stand for the resonance multiplicity singlet, broad singlet, doublet, doublet of doublets, doublet of doublet of doublets, doublet of doublet of doublet of doublets, triplet, triplet of doublets, triplet of triplets, quartet, doublet of quartets, doublet of quartet of doublets, doublet of doublet of quartets, quartet of doublet of doublets, quartet of quartets, and multiplet, respectively. IR spectra were obtained from a Mattson FT-IR GL-3020 spectrometer, a Perkin Elmer FT-IR Paragon 1000 PC spectrometer, or a Bruker Tensor 27 FT-IR spectrometer. Melting points were obtained using a Mel-Temp electrochemical melting point apparatus and are uncorrected. Optical rotations were obtained on a Perkin Elmer Model 343 polarimeter (Na D line) using a microcell with 1 dm path length. Specific rotations ($[\alpha]_D^{20}$, Unit: °cm^2/g) are based on the equation $\alpha = (100\cdot\alpha)/(l\cdot c)$ and are reported as unitless numbers where the concentration c is in g/l00 mL and the path length l is in decimeters. Elemental analyses were performed by Atlantic Microlabs, Inc., Norcross, GA. Mass spectrometry was performed at the mass spectrometry facility of the Department of Chemistry at The University of Utah on a Finnigan MAT 95 double focusing high resolution mass spectrometer or at the mass spectrometry facility of the Department of Chemistry at the University of California, Riverside on an Agilent LCTOF mass spectrometer. Glassware for reactions was oven dried at 125 °C and cooled under a dry atmosphere prior to use. Liquid reagents and

solvents were introduced by oven dried syringes through septum-sealed flasks under a nitrogen atmosphere. Compounds were named using AutoNom 2000 for the MDL ISIS^{Tm}/Draw 2.5.

Compounds and Numbering in Supporting Information:



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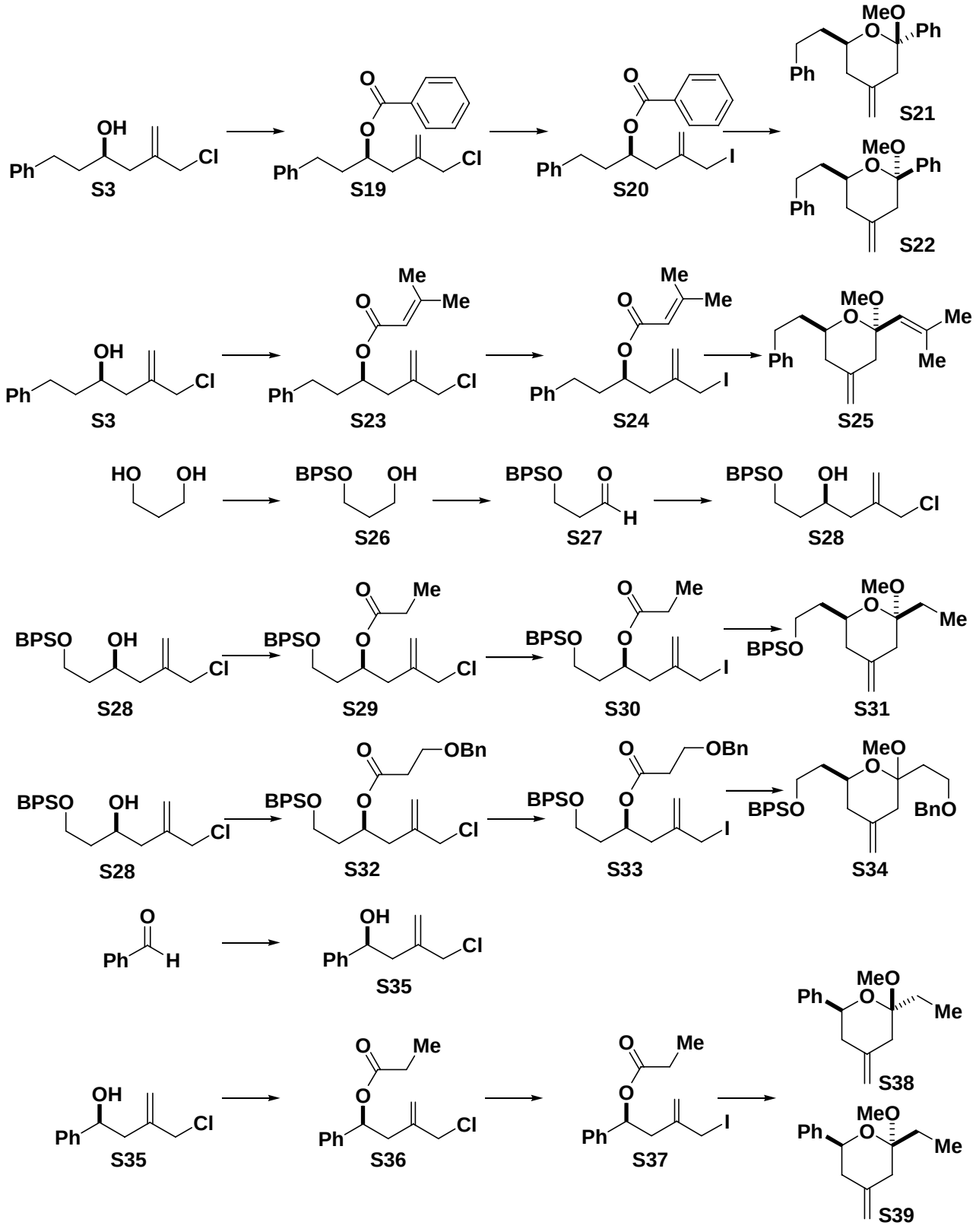

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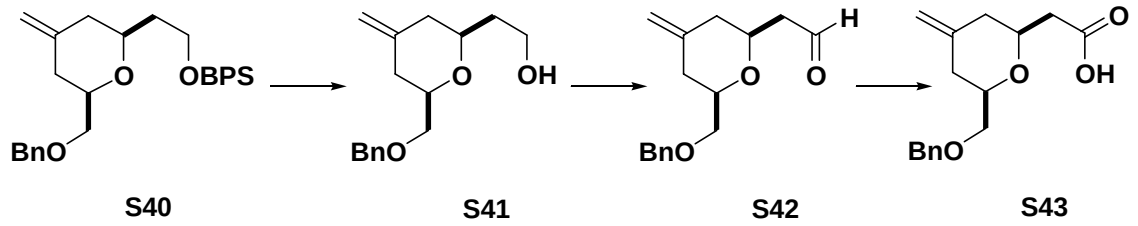
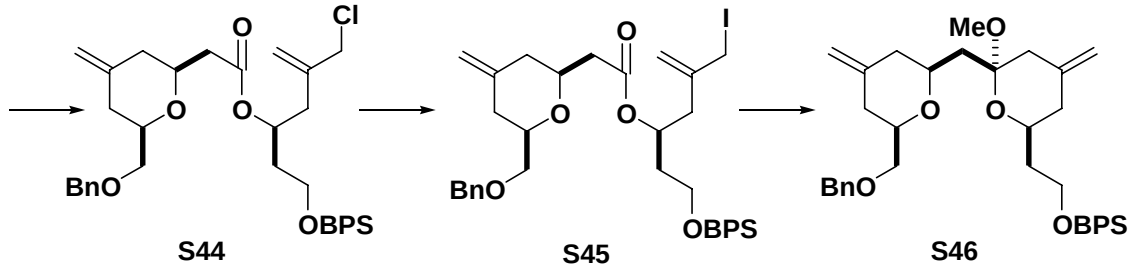
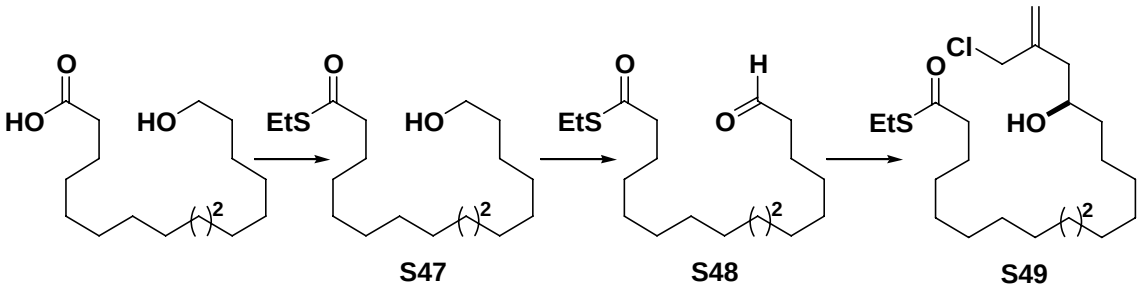
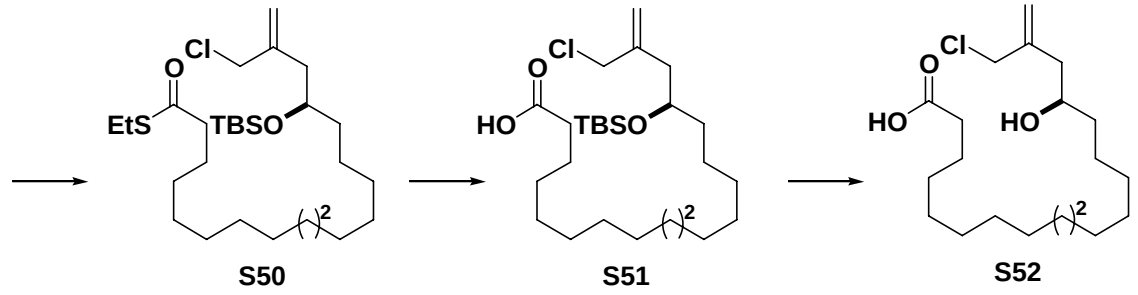
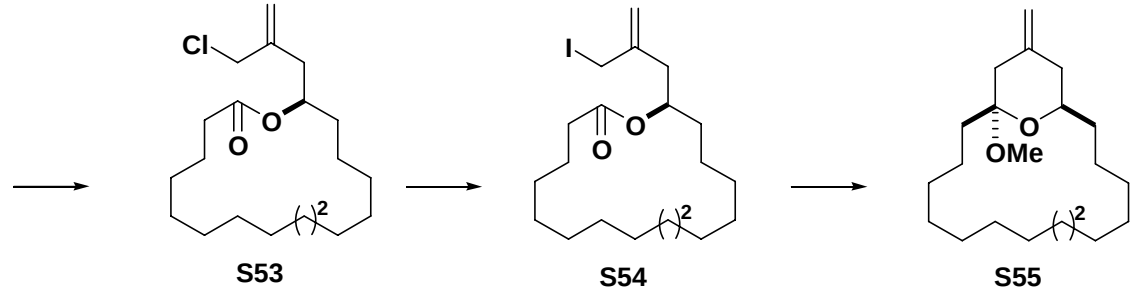


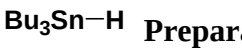




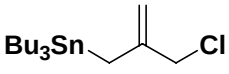




Experimental Procedures and Analytical Data:



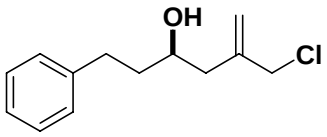
Preparation of tributyltin hydride S1.[3, 4] A stirring solution of $LiAlH_4$ (28.0 g, 737 mmol, 2.00 eq) and Et_2O (1000 mL, 0.2 M) in a 2000 mL three-neck round-bottom flask equipped with an efficient reflux condenser, mechanical stirrer and 500 mL addition funnel was heated at reflux. Using the addition funnel, Bu_3SnCl (100 mL, 367 mmol, 1.00 eq) was slowly added over a period of 45 min. After completion of the addition the mixture was kept at reflux for 1.5 h, cooled to room temperature and filtered through a plug of Celite®. The filtrate was cooled to 0 ºC and $Na_2SO_4 \bullet 12H_2O$ was slowly added in portions until the evolution of gas subsides. The mixture was filtered through a plug with each a 2 cm layer of $MgSO_4$, Celite® and sand, and the filtrate was concentrated under reduced pressure. The residue was purified by distillation from a 500 mL round-bottom flask with boiling chips using a distillation head with a 3 × 10 cm Vigreux-column giving Bu_3SnH **S1** (91 g, 313 mmol, 85%) as a clear colorless liquid: bp 70 ºC / 0.20 torr; 500 MHz ^{1}H NMR (C_6D_6) δ 5.09 – 5.05 (m, 1H), 1.60 – 1.53 (m, 6H), 1.39 – 1.31 (m, 6H), 0.97 – 0.89 (m, 15H); 125 MHz ^{13}C NMR (C_6D_6) δ 30.9 (3), 28.1 (3), 14.5 (3), 9.0 (3).



Preparation of tributyl-(2-chloromethyl-allyl)-stannane S2.[5] To a solution of (*i*-Pr)$_2$NH (11.5 mL, 82.1 mmol, 1.00 eq) and THF (191 mL, 0.43 M relative to (*i*-Pr)$_2$NH in a 500 mL round-bottom flask at 0 ºC was added *n*-BuLi (2.60 M solution in hexanes, 31.6 mL, 82.1 mmol, 1.00 eq). After 30 min Bu_3SnH **S1** (19.9 mL, 73.9 mmol, 0.90 eq) was slowly added. After 30 min this solution was cooled to -78 ºC and

then added to a mixture of 3-chloro-2-chloromethyl-1-propene (10.3 g, 82.1 mmol, 1.00 eq), TBAI (97 mg, 0.26 mmol, 3.2×10^{-3} eq) and hexanes (342 mL, 0.24 M relative to the dichloride) in a 1000 mL round-bottom flask at -78 ºC. After 2.5 h the murky solution was added to a vigorously stirred mixture of pH 7 sodium potassium phosphate buffer (0.05 M, 400 mL) and CH_2Cl_2 (200 mL). The organic phase was washed with water (2 × 100 mL), brine (50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by fractional distillation using a 250 mL round-bottom flask with boiling chips using a distillation head with a 2 × 7 cm column to give tributyl-(2-chloromethyl-allyl)-stannane **S2** (20 g, 53 mmol, 64%) as a clear colorless liquid: bp 100 ºC, 0.25 mm Hg; 500 MHz ^{1}H NMR ($CDCl_3$) δ 4.85 (d, J = 0.9 Hz, 1H), 4.72 (d, J = 0.9 Hz, 1H), 3.97 (s, 2H), 1.91 (s, 2H), 1.53 – 1.47 (m, 6H), 1.35 – 1.30 (m, 6H), 0.95 – 0.88 (m, 15H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 145.9, 110.1, 50.4, 29.3 (3), 27.6 (3), 16.1, 13.9 (3), 9.9 (3).

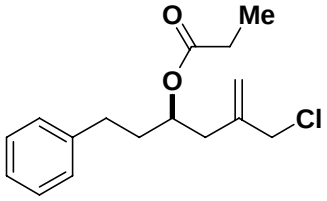
Representative Procedure for the Catalytic Asymmetric Allylation:



Preparation of (*R*)-5-chloromethyl-1-phenyl-hex-5-en-3-ol S3.[5] To a 50 mL round-bottom flask were added oven dried 4Å molecular sieves (890 mg, 400 mg/mmol of aldehyde), (*S*)-BINOL (140 mg, 0.489 mmol, 0.22 eq), CH_2Cl_2 (8.90 mL, 0.25 M), titanium(IV) isopropoxide (1.00 M solution in CH_2Cl_2, 245 µL, 245 µmol, 0.11 eq) and trifluoroacetic acid (freshly prepared 0.10 M solution in CH_2Cl_2, 78 µL, 7.7 µmol, 3.5×10^{-3} eq). The flask was equipped with a reflux condenser, and the red-brown mixture was heated at 40 °C. After 2 h the mixture was cooled to room

temperature and the reflux condenser exchanged for a rubber septum. Hydrocinnamaldehyde (293 μL, 2.23 mmol, 1.00 eq) was added, the mixture stirred for 30 min and then cooled to -78 °C. Tributyl-(2-chloromethyl-allyl)-stannane **S2** (959 μL, 2.89 mmol, 1.30 eq) was added, the mixture stirred for 30 min and the flask placed in a freezer at -20 °C. After 72 h the mixture was removed from the freezer, and a saturated aqueous $NaHCO_3$ solution (15 mL) was added. The mixture was stirred for 30 min, allowed to settle and then filtered through a plug of Celite®. The organic phase was diluted with CH_2Cl_2 (50 mL) and washed with water (2 × 25 mL) and brine (20 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography on a 4.5 × 18 cm silica gel column eluting with a solvent gradient from 2.5% (600 mL) through 5% (1500 mL), 7.5% (1000 mL) and 10% EtOAc/hexanes (1000 mL). The eluant was collected in 30 mL portions and the product containing fractions (30 to 67) were concentrated and combined to give alcohol **S3** (435 mg, 1.94 mmol, 87%) as a clear colorless liquid. The ratio of enantiomers was determined to be *er* > 99 : 1 (using BF_3•OEt_2, *er* = 48 : 52) by HPLC analysis using a Daicel Chiralcel OD-H silica column, eluting with a mobile phase of 6% 2-propanol/hexanes and a flow rate of 0.5 mL/min, which gave the retention times for the minor and major enantiomers of 20.1 and 30.1 min, respectively, detecting with a Rainin Dynamax Refractive Index Detector Model RI-1: R_f 0.36 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +6.1 (*c* = 1.065, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.33 – 7.20 (m, 5H), 5.29 (s, 1H), 5.10, (s, 1H), 4.11 (d, *J* = 12.0 Hz, 1H), 4.07 (d, *J* = 12.0 Hz, 1H), 3.84 (bs, 1H), 2.85 (m, 1H), 2.73 (m, 1H), 2.49 (dd, *J* = 14.5, 3.1 Hz, 1H), 2.28 (dd, *J* = 14.5, 9.0 Hz, 1H), 1.88 – 1.78 (m, 2H), 1.67 (s, 1H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.4, 142.0, 128.7 (2), 128.6

(2), 126.1, 117.9, 69.1, 48.4, 41.8, 39.1, 32.3; 125 MHz DEPT ($CDCl_3$) δ CH_2: 117.9, 48.4, 41.8, 39.1, 32.3. CH: 128.7 (2), 128.6 (2), 126.1, 69.1. C: 142.4, 142.0; IR (neat) 3562, 3406 (broad), 1643, 1602, 1495, 1453, 1258, 1074, 1053, 1030, 912, 748, 699 cm^{-1}; Anal. Calcd for $C_{13}H_{17}ClO$: C, 69.48; H, 7.62. Found: C, 69.39; H, 7.55.

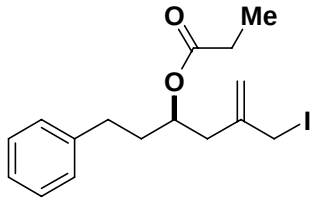


Preparation of propionic acid-(*R*)-3-chloromethyl-1-phenethyl-but-3-enyl ester S4. To stirring solution of alcohol **S3** (87.1 mg, 0.388 mmol, 1.00 eq) and CH_2Cl_2 (2.0 mL, 0.20 M) in a 15 mL round-bottom flask at 0 ºC were added pyridine (110 µL, 1.36 mmol, 3.50 eq), DMAP (5.0 mg, 3.9 µmol, 0.10 eq) and propionyl chloride (101 µL, 1.16 mmol, 3.00 eq). After 18 h the solution was added to a mixture of pH 7 sodium potassium phosphate buffer (20 mL) and CH_2Cl_2 (40 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography on a 4.5 × 17 cm silica gel column eluting with a solvent mixture of 3% EtOAc/hexanes (200 mL). The eluant was collected in 10 mL portions and the product containing fractions (2 to 10) were combined and concentrated to give ester **S4** (108 mg, 0.385 mmol, 99%) as a clear colorless liquid: R_f 0.78 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +7.6 (*c* = 1.135, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.31 – 7.18 (m, 5H), 5.19 (s, 1H), 5.16 – 5.10 (m, 1H), 5.00 (s, 1H), 4.12 (d, *J* = 11.8 Hz, 1H), 4.02 (d, *J* = 11.8 Hz, 1H), 2.72 – 2.61 (m, 2H), 2.57 (dd, *J* = 14.4, 4.1 Hz, 1H), 2.40 (dd, *J* = 14.6, 8.6 Hz, 1H), 2.30 (q, *J* = 7.7 Hz, 2H), 1.98 – 1.86 (m, 2H), 1.14 (t, *J* = 7.7 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 174.3, 141.5, 141.5,

128.6 (2), 128.5 (2), 126.2, 117.9, 71.3, 48.2, 38.4, 36.1, 32.0, 27.9, 9.4; 125 MHz DEPT ($CDCl_3$) δ CH_3: 9.4. CH_2: 117.9, 48.2, 38.4, 36.1, 32.0, 27.9. CH: 128.6 (2), 128.5 (2), 126.2, 71.3. C: 174.3, 141.5, 141.5; IR (neat) 3027, 2981, 2941, 1732, 1650, 1495, 1454, 1338, 1275, 1185, 1081, 1029, 912, 749, 699, 605 cm^{-1}; Anal. Calcd for $C_{16}H_{21}ClO_2$: C, 68.44; H, 7.54. Found: C, 68.72; H, 7.65.

Representative Procedure for the Finkelstein Reaction.

Chromatographic properties for the described allyl iodides were found to be identical to their respective allyl chlorides.



Preparation of propionic acid-(*R*)-3-iodoethyl-1-phenethyl-but-3-enyl ester S5. To a stirring solution of the ester **S4** (116.9 mg, 0.416 mmol, 1.00 eq) and acetone (4.2 mL, 0.10 M) in a 25 mL round-bottom flask at room temperature was added NaI (1.25 g, 8.32 mmol, 20 eq). The mixture was kept at room temperature in the dark for 24 h and then diluted with Et_2O (15 mL). The mixture was filtered through a plug of Celite®, the filtrate was diluted with Et_2O (50 mL) and filtered through the same plug of Celite®. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography on a 1.5 × 18 cm silica gel column eluting with a solvent gradient of 2.5% (100 mL) through 5% EtOAc/hexanes (100 mL). The eluant was collected in 10 mL portions and the product containing fractions (6 to 12) were combined and concentrated to give iodide **S5** (145 mg, 0.390 mmol, 94%) as a clear slightly yellow oil: R_f 0.68 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +22.9 (*c* = 1.015, $CHCl_3$); 500

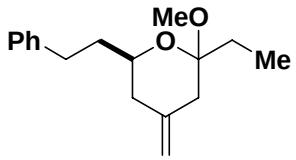
MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.18 (m, 5H), 5.30 (s, 1H), 5.14 – 5.09 (m, 1H), 4.95 (s, 1H), 4.02 (d, *J* = 9.4 Hz, 1H), 3.93 (d, *J* = 9.4 Hz, 1H), 2.73 – 2.63 (m, 3H), 2.43 (dd, *J* = 14.6, 8.6 Hz, 1H), 2.31 (q, *J* = 7.7 Hz, 2H), 1.98 – 1.86 (m, 2H), 1.15 (t, *J* = 7.7 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 174.3, 142.9, 141.5, 128.7 (2), 128.5 (2), 126.2, 117.0, 71.3, 39.4, 36.1, 32.1, 28.0, 10.6, 9.5; 125 MHz DEPT ($CDCl_3$) δ CH_3: 9.5. CH_2: 117.1, 39.5, 36.1, 32.1, 28.0, 10.6. CH: 128.7 (2), 128.5 (2), 126.3, 71.4. C: 174.3, 142.9, 141.5; IR (neat) 3083, 3026, 2978, 2940, 2861, 1732, 1634, 1602, 1495, 1454, 1432, 1273, 1185, 1080, 1028, 909, 748, 699 cm^{-1}; Anal. Calcd for $C_{16}H_{21}IO_2$: C, 51.63; H, 5.69. Found: C, 51.67; H, 5.71.

Preparation of 0.1 M SmI_2 Stock Solution. Flask preparation: To a mixture of samarium chips (242 mg, 1.61 mmol, 1.07 eq) and THF (60 mL) in a new 100 mL, 14/20 round-bottom flask with a new stir bar and a 14/20 rubber septum at room temperature was added CH_2I_2 (121 μL, 1.50 mmol, 1.00 eq). The rubber septum was sealed with Parafilm® and an upside-down 19/22 rubber septum. After 24 h the deep purple solution was discarded, and the flask was washed with water and acetone, and then dried.

The pretreated 100 mL round-bottom flask with stir bar and a rubber septum containing samarium chips (726 mg, 4.83 mmol, 1.07 eq) was evacuated and then purged with dry nitrogen. This procedure was repeated three times, and then THF (45.0 mL, 0.10 M) was added followed by CH_2I_2 (363 μL, 4.51 mmol, 1.00 eq). The 14/20 rubber septum was sealed with Parafilm®, an upside-down 19/22 rubber septum and again Parafilm®. After 24 h the deep purple mixture could be used as a 0.10 M SmI_2 stock-

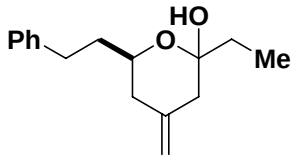
solution and stored under nitrogen in the dark at room temperature for up to 3 months without noticeable loss of activity.

Representative Procedure for the SmI_2 Promoted Cyclization:



Preparation of (6*R*)-2-ethyl-2-methoxy-4-methylene-6-phenethyl-tetrahydro-pyran S6. To a stirring solution of the iodide **S5** (80.0 mg, 0.215 mmol, 1.00 eq) and THF (2.2 mL, 0.10 M) in a 25 mL round-bottom flask at 0 ºC was added SmI_2 (0.10 M solution in THF, 6.5 mL, 0.65 mmol, 3.0 eq). After 10 min additional SmI_2 (0.10 M solution in THF, 4.3 mL, 0.43 mmol, 2.0 eq) was added, and the deep purple color of the reaction mixture persisted; TLC analysis showed consumption of the iodide starting material. The solution was added to a mixture of pH 7 sodium potassium phosphate (20 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with water (2 × 20 mL), brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure at room temperature. The residue was transferred into a 15 mL round-bottom flask and dissolved in a 1 : 1 mixture of CH_2Cl_2 and MeOH (7.2 mL, 0.03 M). The solution was cooled to 0 ºC and CSA (0.05 M solution in CH_2Cl_2, 129 µL, 6.5 µmol, 0.03 eq) was added. After 1 h the solution was added to a mixture of a saturated aqueous $NaHCO_3$ solution (20 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with water (2 × 20 mL), brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure at room temperature. The residue was purified by flash chromatography on a 1.5 × 20 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (250 mL). The eluant was collected in 10 mL portions and the

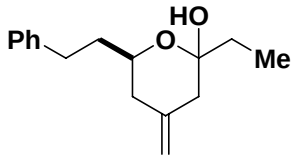
product containing fractions (3 to 6) were combined and concentrated to give 2-methoxypyran **S6** (55.0 mg, 0.211 mmol, 98%) as a clear colorless liquid consisting of a 1:1 mixture of anomers: R_f 0.79 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +12.4 (*c* = 1.015, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.18 (m, 10H), 4.85 – 4.79 (m, 4H), 3.67 – 3.61 (m, 1H), 3.54 – 3.49 (m, 1H), 3.22 (s, 3H), 3.15 (s, 3H), 3.00 – 2.86 (m, 1H), 2.75 – 2.62 (m, 3H), 2.49 (d, *J* = 13.7 Hz, 1H), 2.42 (d, *J* = 13.7 Hz, 1H), 2.29 – 2.23 (m, 2H), 2.15 – 2.08 (m, 2H), 2.01 – 1.72 (m, 7H), 1.62 – 1.49 (m, 3H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.93 (t, *J* = 7.7 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.5 (2), 142.3 (2), 128.8, 128.6 (3), 128.5 (2), 128.4 (2), 126.1, 126.0, 110.3, 110.2, 101.1, 100.4, 72.3, 70.5, 47.9, 47.8, 42.2, 41.6, 40.1, 38.7, 37.9, 37.8, 32.1, 29.9, 29.1, 28.9, 10.2, 7.9; 125 MHz DEPT ($CDCl_3$) δ CH_3: 47.9, 47.8, 10.2, 7.9. CH_2: 110.3, 110.2, 42.2, 41.6, 40.1, 39.7, 37.9, 37.8, 32.1, 29.9, 29.1, 28.9. CH: 128.8, 128.6, 128.6 (2), 128.5 (2), 128.4 (2), 126.1, 126.0, 72.3, 70.5. C: 142.5 (2), 142.3 (2), 101.1, 100.4; IR (neat) 3072, 3026, 2941, 2898, 2826, 1738, 1656, 1563, 1495, 1455, 1322, 1173, 1116, 1080, 1057, 1034, 884, 750, 698, 655 cm^{-1}; Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.15; H, 9.34.



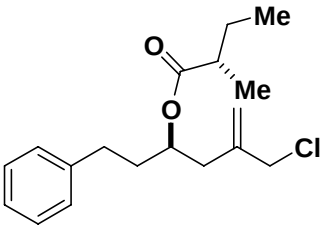
Preparation of racemic 2-ethyl-4-methylene-6-phenethyl-tetrahydro-pyran-2-ol S7. To a 15 mL round bottom flask with racemic chloride **S4** (100 mg, 0.356 mmol, 1.00 eq), magnesium turnings (52.0 mg, 2.14 mmol, 6.00 eq) and Et_2O (3.6 mL, 0.10 M) at room temperature was added 1,2-dibromoethane (30.7 μL, 0.356 mmol, 1.00 eq). After 15 min additional 1,2-dibromoethane (16.0 μL, 0.180 mmol,

0.50 eq) was added and the mixture then heated to 35 ºC. After 18 h the mixture was cooled to room temperature and diluted with a saturated aqueous solution of $NaHCO_3$ (5 mL) and Et_2O (50 mL). The organic phase was washed with water (2 × 10 mL), brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure at room temperature. The residue was purified by flash chromatography on a 1.5 × 20 cm silica gel column eluting with a solvent mixture of 1% (100 mL) through 5% (100 mL) and 7.5% EtOAc/hexanes (300 mL). The eluant was collected in 10 mL portions and the product containing fractions (41 to 46) were combined and concentrated to give hydroxy lactol **S7** (16.0 mg, 65.0 μmol, 18%) as a clear colorless oil consisting of a 2:1 mixture of anomers: R_f 0.45 (25% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.17 (m, 10H), 5.11 (s, 1H), 4.98 (s, 1H), 4.89 – 4.88 (m, 1H), 4.84 – 4.83 (m, 1H), 3.81 – 3.76 (m, 1H), 3.67 – 3.61 (m, 1H), 3.23 (d, *J* = 15.9 Hz, 1H), 3.15 (d, *J* = 15.9 Hz, 1H), 2.86 – 2.76 (m, 2H), 2.73 – 2.65 (m, 2H), 2.50 (d, *J* = 7.3 Hz, 1H), 2.47 (d, *J* = 7.3 Hz, 1H), 2.43 (d, *J* = 3.0 Hz, 1H), 2.33 – 2.24 (m, 5H), 2.16 (dd, *J* = 14.1, 9.9 Hz, 1H), 2.00 – 1.94 (m, 1H), 1.91 – 1.70 (m, 6H), 1.06 (dd, *J* = 7.3, 7.3 Hz, 3H), 1.03 (dd, *J* = 7.3, 7.3 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.4, 142.3, 142.3, 139.8, 128.7 (4), 128.6 (2), 128.5 (2), 126.0, 126.0, 118.3, 111.5, 97.7 (2), 70.2, 68.3, 50.0, 45.4, 43.2, 40.4, 38.9, 37.8, 35.9, 35.0, 32.3, 31.9, 8.0, 7.6; IR (neat) 3447 (bs), 3063, 3026, 2941, 1713, 1682, 1654, 1603, 1558, 1540, 1496, 1455, 1433, 1413, 1379, 1336, 1311, 1282, 1260, 1221, 1154, 1085, 1040, 993, 947 cm^{-1}; HRMS (APCI) Calcd for $C_{16}H_{21}O$ *m/z* (M-OH): 229.1592. Found: 229.1591; HRMS (APCI) Calcd for $C_{16}H_{22}NaO_2$ *m/z* (M+Na): 269.1517. Found: 269.1518.

Hydrolysis of a 2-Methoxypyran with Water and PPTs:

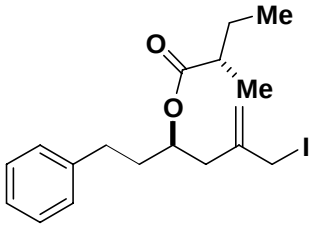


Preparation of racemic 2-ethyl-4-methylene-6-phenethyl-tetrahydro-pyran-2-ol S7. To a 5 mL vial with racemic 2-methoxypyran **S6** (14.8 mg, 56.8 μmol, 1.00 eq) and a 4:1 solution of THF and water (560 μL, 0.10 M) at room temperature was added PPTs (84.0 μL, 8.52 μmol, 0.30 eq). After 24 h, a 4:1 solution of THF and water (1.20 mL) was added and the solution stirred for an additional 24 h. The mixture was diluted with a mixture of 25% EtOAc and hexanes (50 mL) and pH 7 phosphate buffer (0.05 M aqueous solution, 10 mL). The organic phase was washed with water (2 × 20 mL), brine (15 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure at room temperature. The residue was purified by preparative TLC (20 cm × 20 cm × 250 μm) using a mobile phase of 25% EtOAc/hexanes. A suspension of the product containing silica gel and a solution of 1:4 MeOH/EtOAc (100 mL) was vigorously stirred for 40 min, filtered and concentrated under reduced pressure. Any remaining silica gel was removed by filtration of the residue through a 0.5 × 1.0 cm silica gel column eluting with 80% EtOAc/hexanes (10 mL). The eluant was concentrated under reduced pressure to give lactol **S7** (10.2 mg, 41.4 μmol, 73%) as a clear colorless oil consisting of a mixture of anomers. The spectroscopic data for lactol **S7** were identical to those for the lactol obtained from the cyclization of racemic chloride **S4** using Mg turnings.



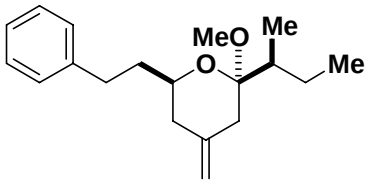
Preparation of (*S*)-2-methyl-butyric acid (*R*)-3-chloromethyl-1-phenethyl-but-3-enyl ester S8. To a stirring solution of alcohol **S3** (100 mg, 0.445 mmol, 1.00 eq) and ethanol-free $CHCl_3$ (4.40 mL, 0.10 M) in a 15 mL round-bottom flask at room temperature were added (*S*)-(+)-2-methylbutyric acid (58.0 μL, 0.534 mmol, 1.20 eq), DMAP (5.5 mg, 44 μmol, 0.10 eq), DMAP•HCl (7.1 mg, 45 μmol, 0.10 eq) and EDCI (213 mg, 1.11 mmol, 2.50 eq). The mixture was heated to 45 ºC and after 12 h additional (*S*)-(+)-2-methylbutyric acid (58.0 μL, 0.534 mmol, 1.20 eq) and EDCI (213 mg, 1.11 mmol, 2.50 eq) were added. After 18 h the mixture was added to pH 7 sodium potassium phosphate buffer (0.05 M, 20 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (300 mL). The eluant was collected in 30 mL portions and the product containing fractions (3 to 9) were combined and concentrated; remaining volatiles were removed under vacuum (0.025 mm Hg) to give ester **S8** (125 mg, 0.405 mmol, 91%) as a clear colorless oil: R_f 0.78 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +28.1 (*c* = 1.125, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.29 (m, 2H), 7.22 – 7.18 (m, 3H), 5.19 (s, 1H), 5.14 (dddd, *J* = 8.3, 8.3, 4.3, 4.3 Hz, 1H), 5.01 (d, *J* = 1.3 Hz, 1H), 4.15 (dd, *J* = 11.1, 0.9 Hz, 1H), 4.03 (d, *J* = 11.6 Hz, 1H), 2.73 – 2.60 (m, 2H), 2.57 (dd, *J* = 14.4, 3.6 Hz, 1H), 2.42 (dd, *J* = 14.6, 8.6 Hz, 1H), 2.36 (qdd, *J* = 6.9, 6.9, 6.9 Hz, 1H), 1.96 – 1.87 (m, 2H), 1.70 (dqd, *J* = 13.9, 7.5, 6.9 Hz, 1H), 1.48 (dqd, *J* = 13.7, 7.3, 6.9 Hz, 1H),

1.14 (d, *J* = 6.9 Hz, 3H), 0.94 (dd, *J* = 7.5, 7.5 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 176.6, 141.6, 141.5, 128.7 (2), 128.5 (2), 126.2, 117.9, 70.9, 48.2, 41.6, 38.5, 36.4, 32.0, 27.0, 17.1, 12.0; 125 MHz DEPT ($CDCl_3$) δ CH_3: 17.1, 12.0. CH_2: 117.9, 48.1, 38.5, 36.4, 32.0, 27.0. CH: 128.7 (2), 128.5 (2), 126.2, 70.9, 41.6. C: 176.6, 141.6, 141.5; IR (neat) 3085, 3063, 3027, 2966, 2935, 2877, 1729, 1646, 1603, 1496, 1455, 1381, 1297, 1261, 1239, 1153, 1078, 1029, 912, 750, 700 cm^{-1}; Anal. Calcd for $C_{18}H_{25}ClO_2$: C, 70.00; H, 8.16. Found: C, 70.29; H, 8.25.



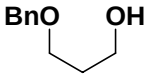
Preparation of (*S*)-2-methyl-butyric acid (*R*)-3-iodomethyl-1-phenethyl-but-3-enyl ester S9. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S8** (105 mg, 0.520 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 5% EtOAc/hexanes (200 mL). The eluant was collected in 10 mL portions and the product containing fractions (3 to 4) were combined and concentrated to give iodide **S9** (135 mg, 0.337 mmol, 99%) as a clear colorless oil: R_f 0.78 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +14.4 (*c* = 1.150, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.29 (m, 2H), 7.22 – 7.18 (m, 3H), 5.30 (s, 1H), 5.12 (dddd, *J* = 8.4, 8.4, 4.3, 4.3 Hz, 1H), 4.95 (s, 1H), 4.02 (d, *J* = 9.4 Hz, 1H), 3.93 (d, *J* = 9.4 Hz, 1H), 2.73 – 2.61 (m, 3H), 2.45 (dd, *J* = 14.6, 8.6 Hz, 1H), 2.37 (dddd, *J* = 13.8, 6.9, 6.9, 6.9 Hz, 1H), 1.96 – 1.87 (m, 2H), 1.70 (dqd, *J* = 13.9, 7.3, 7.1 Hz, 1H), 1.53 – 1.44 (m,

1H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.94 (dd, *J* = 7.7, 7.3 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 176.5, 142.9, 141.5, 128.7 (2), 128.5 (2), 126.2, 117.0, 70.9, 41.6, 39.4, 36.3, 32.0, 27.0, 17.1, 12.0, 10.6; 125 MHz DEPT ($CDCl_3$) δ CH_3: 17.1, 12.0. CH_2: 117.0, 39.4, 36.3, 32.0, 27.0, 10.6. CH: 128.7 (2), 128.5 (2), 126.2, 70.9, 41.6. C: 176.5, 142.9, 141.5; IR (neat) 3084, 3062, 2965, 2933, 2875, 1729, 1496, 1455, 1434, 1381, 1261, 1238, 1183, 1154, 1077, 1028, 909, 748, 699 cm^{-1}; HRMS (CI) Calcd for $C_{18}H_{26}IO_2$ (M+H): 401.0978. Found: 401.0985.



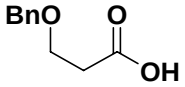
Preparation of (2*R*,6*R*)-2-((*S*)-sec-butyl)-2-methoxy-4-methylene-6-phenethyl-tetrahydro-pyran S10. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S9** (63.0 mg, 0.157 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (200 mL). The eluant was collected in 10 mL portions and the product containing fractions (3 to 6) were combined and concentrated to give methyl 2-methoxypyran **S10** (45.1 mg, 0.156 mmol, quant.) as a clear colorless oil consisting of a single anomer: R_f 0.91 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -10.4 (*c* = 1.350, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.29 (m, 2H), 7.23 – 7.20 (m, 3H), 4.85 (s, 1H), 4.82 (s, 1H), 3.44 – 3.40 (m, 1H), 3.22 (s, 3H), 2.71 (ddd, *J* = 13.0, 13.0, 5.6 Hz, 1H), 2.64 (ddd, *J* = 13.1, 13.1, 4.7 Hz, 1H), 2.47 (d, *J* = 13.3 Hz, 1H), 2.27 (d, *J* = 11.6 Hz, 1H), 2.24 (ddd, *J* = 13.2, 13.2, 4.7 Hz, 1H), 2.08 (ddd, *J* = 13.2, 13.2, 4.7 Hz, 1H), 1.97 (dd, *J* = 12.6, 12.6

Hz, 1H), 1.91 (ddd, *J* = 12.6, 12.6, 5.6 Hz, 1H), 1.75 – 1.65 (m, 1H), 1.55 – 1.47 (m, 1H), 1.20 – 1.11 (m, 1H), 0.95 – 0.91 (m, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.6, 142.3, 128.6 (2), 128.4 (2), 126.0, 110.4, 100.4, 74.5, 48.0, 42.2, 39.8, 38.0, 36.5, 30.1, 25.3, 14.8, 11.9; 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.0, 14.8, 11.9. CH_2: 110.4, 42.2, 38.0, 36.6, 30.1, 25.3. CH: 128.6 (2), 128.5 (2), 126.1, 74.5, 39.8. C: 142.6, 142.3, 100.4; IR (neat) 3064, 3027, 2959, 2932, 2876, 2827, 1732, 1656, 1604, 1496, 1455, 1380, 1349, 1326, 1266, 1233, 1192, 1174, 1147, 1117, 1073, 1051, 1031, 942, 885, 789, 749, 699, 642 cm^{-1}; HRMS (EI) Calcd for $C_{19}H_{28}O_2$ *m/z* (M): 288.2089. Found: 288.2091; LRMS (EI) Calcd for $C_{18}H_{25}O$ *m/z* (M-MeO): 257.2. Found: 257.2; LRMS (EI) Calcd for $C_{18}H_{24}O$ *m/z* (M-MeOH): 256.2. Found: 256.1.



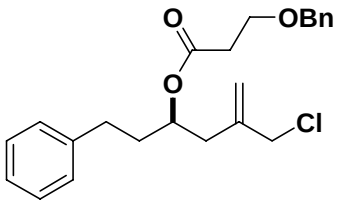
Preparation of 3-benzyloxy-propan-1-ol S11.[6] To a 500 mL round-bottom flask with 1,3-propanediol (14.5 mL, 200 mmol, 1.00 eq) and DMSO (200 mL, 1.00 M) at room temperature was slowly added washed and dried NaH (2.40 g, 100 mmol, 0.50 eq). After 30 min, benzyl chloride (11.5 mL, 100 mmol, 0.50 eq) and TBAI (740 mg, 2.00 mmol, 0.01 eq) were added. After an additional 2 h, water (50 mL) and a mixture of 15% EtOAc/hexanes (30 mL) were added. The aqueous phase was extracted with Et_2O (100, 200, 500 mL) and the combined organic phase washed brine (80 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was distilled from a 50 mL round-bottom flask through a 1.5 × 7 cm column to give benzylether **S11** (9.81 g, 59.0 mmol, 30%) as a clear colorless liquid: bp 90 – 100 ºC at 0.25 mm Hg, high-vacuum pump, pressure adjusted with dry nitrogen; R_f 0.16 (25% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.39 – 7.28 (m, 5H), 4.53 (s, 2H), 3.78 (t,

J = 5.6 Hz, 2H), 3.65 (t, *J* = 6.0 Hz, 2H), 2.61 (s, 1H), 1.88 (tt, *J* = 6.0, 5.6 Hz, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 138.2, 128.6 (2), 127.8, 127.8 (2), 73.4, 69.3, 61.7, 32.3;; IR (neat) 3390, 3090, 3059, 3030, 2925, 2864, 1961, 1876, 1814, 1496, 1476, 1454, 1416, 1365, 1313, 1259, 1243, 1205, 1095, 1075, 1027, 972, 946, 920, 737, 698 cm^{-1}.



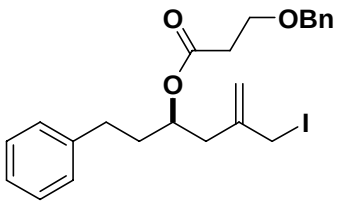
Preparation of 3-benzyloxy-propionic acid S12.[7] The Jones Reagent was prepared by adding CrO_3 (25 g, 0.157 mmol) to a stirring solution of water (50 mL) and H_2SO_4 (conc., 25 mL) in a 250 mL graduated cylinder at 0 ºC; the volume was adjusted to 125 mL with water (ca. 60 mL) to give Jones' reagent (1.26 M). To a solution of 3-benzyloxy-propan-1-ol **S11** (3.00 g, 18.1 mmol, 1.00 eq) and acetone (120 mL, 0.15 M) in a 500 mL round-bottom flask at 0 ºC was added Jones' reagent (1.26 M solution, 14.3 mL, 18.1 mmol, 1.00 eq). After 1 h the mixture was filtered through a plug of Celite®, the filtrate was concentrated under reduced pressure and the residue diluted with EtOAc (200 mL). The mixture was washed with water (3 × 100 mL), brine (50 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography using a 3.5 × 18 cm silica gel column eluting with a solvent gradient from 5% (500 mL) through 10% (250 mL) and 15% EtOAc/hexanes (500 mL) and then 0.5 % AcOH/EtOAc (300 mL). The eluant was collected in 30 mL portions and the product containing fractions (28 to 46) were combined and concentrated to give acid **S12** (2.95 g, 16.4 mmol, 91%) as a white solid: R_f 0.62 (20 : 10 : 1 = toluene : dioxane : AcOH); mp 30 ºC; 500 MHz ^{1}H NMR ($CDCl_3$) δ 11.17 (bs, 1H), 7.30 – 7.19 (m, 5H), 4.49 (s, 2H), 3.69 (t, *J* = 6.4 Hz, 2H), 2.61 (t, *J* = 6.4 Hz, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 177.7, 138.0, 128.7 (2), 128.0, 127.9 (2), 73.4, 65.4, 35.1; 125 MHz

DEPT ($CDCl_3$) δ CH_2: 73.4, 65.4, 35.1. CH: 128.7 (2), 128.0, 127.9 (2). C: 177.7, 138.0; IR (neat) 3087, 3063, 3031, 2920, 2874, 2715, 1714, 1453, 1424, 1364, 1262, 1237, 1199, 1103, 1070, 1028, 740, 698 cm^{-1}.



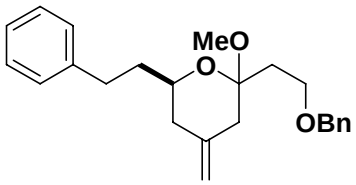
Preparation of 3-benzyloxy-propionic acid (*R*)-3-chloromethyl-1-phenethyl-but-3-enyl ester S13. To a stirring solution of alcohol **S3** (100 mg, 0.445 mmol, 1.00 eq) and ethanol-free $CHCl_3$ (4.40 mL, 0.10 M) in a 25 mL round-bottom flask at room temperature were added 3-benzyloxy-propionic acid **S12** (96.0 mg, 0.534 mmol, 1.20 eq), DMAP (5.5 mg, 44 μmol, 0.10 eq), DMAP•HCl (7.1 mg, 45 μmol, 0.10 eq) and DCC (230 mg, 1.11 mmol, 2.50 eq). The mixture was then diluted with ethanol-free $CHCl_3$ (4.0 mL). After 24 h the mixture was added to a saturated aqueous NH_4Cl solution (10 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with pH 7 sodium potassium phosphate buffer (0.05 M, 20 mL), water (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent gradient from 2.5% (100 mL) through 5% (200 mL) and 10% EtOAc/hexanes (100 mL). The eluant was collected in 10 mL portions and the product containing fractions (10 to 38) were combined and concentrated to give ester **S13** (157 mg, 0.406 mmol, 91%) as a clear colorless oil: R_f 0.58 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +9.8 (*c* = 1.060, $CHCl_3$); 500 MHz ^1H NMR ($CDCl_3$) δ 7.34 – 7.33 (m, 4H), 7.30 – 7.27 (m, 3H), 7.20 – 7.16 (m, 3H), 5.31 – 5.14 (m, 1H), 5.17 (s, 1H), 5.00 (s, 1H), 4.55 (s, 2H),

4.12 (d, *J* = 12.0 Hz, 1H), 4.01 (d, *J* = 11.6 Hz, 1H), 3.77 – 3.75 (m, 2H), 2.74 – 2.59 (m, 4H), 2.56 (dd, *J* = 14.8, 4.1 Hz, 1H), 2.42 (dd, *J* = 14.8, 8.4 Hz, 1H), 1.99 – 1.87 (m, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 171.5, 141.5, 141.4, 138.2, 128.7 (2), 128.6 (2), 128.5 (2), 127.9 (3), 126.2, 118.0, 73.3, 71.8, 65.9, 48.2, 38.3, 36.1, 35.6, 32.0; 125 MHz DEPT ($CDCl_3$) δ CH_2: 118.0, 73.3, 65.9, 48.2, 38.3, 36.1, 35.5, 31.9. CH: 128.6 (2), 128.6 (2), 128.5 (2), 127.8 (3), 126.2, 71.7. C: 171.5, 141.5, 141.4, 138.2; IR (neat) 3085, 3063, 3028, 2952, 2925, 2864, 1733, 1646, 1603, 1496, 1454, 1365, 1256, 1181, 1104, 1070, 1029, 913, 747, 699 cm^{-1}; Anal. Calcd for $C_{23}H_{27}ClO_3$: C, 71.40; H, 7.03. Found: C, 71.46; H, 7.17.



Preparation of 3-benzyloxy-propionic acid (*R*)-3-iodomethyl-1-phenethyl-but-3-enyl ester S14. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S13** (140 mg, 0.362 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 2.5 × 18 cm silica gel column eluting with a solvent mixture of 5% EtOAc/hexanes (100 mL). The eluant was collected in 10 mL portions and the product containing fractions (1 to 3) were combined and concentrated to give iodide **S14** (173 mg, 0.362 mmol, quant.) as a clear colorless oil: R_f 0.65 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +14.1 (*c* = 1.075, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.35 – 7.34 (m, 4H), 7.32 – 7.28 (m, 3H), 7.22 – 7.17 (m, 3H), 5.27 (s, 1H), 5.15 (dddd, *J* = 7.9, 7.9, 4.7, 4.7 Hz, 1H), 4.94 (s, 1H), 4.55 (s, 2H), 3.99 (d, *J* = 9.4 Hz, 1H), 3.91 (d, *J* = 9.4 Hz, 1H), 3.78 – 3.75

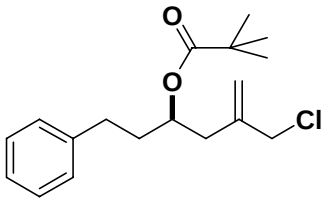
(m, 2H), 2.73 – 2.60 (m, 5H), 2.46 (dd, *J* = 14.8, 8.4 Hz, 1H), 1.96 – 1.90 (m, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 171.4, 142.8, 141.5, 138.2, 128.6 (2), 128.6 (2), 128.5 (2), 127.9 (3), 126.2, 117.1, 73.3, 71.8, 65.9, 39.3, 36.0, 35.6, 31.9, 10.7; 125 MHz DEPT ($CDCl_3$) δ CH_2: 117.1, 73.3, 65.9, 39.3, 36.0, 35.6, 32.0, 10.7. CH: 128.7 (2), 128.6 (2), 128.5 (2), 127.9 (3), 126.2, 71.8. C: 171.4, 142.8, 141.5, 138.2; IR (neat) 3084, 3062, 3027, 2952, 2922, 2863, 1732, 1635, 1603, 1496, 1454, 1431, 1365, 1252, 1181, 1104, 1070, 1028, 910, 740, 699 cm^{-1}; Anal. Calcd for $C_{23}H_{27}IO_3$: C, 57.75; H, 5.69. Found: C, 58.14; H, 5.58.



Preparation of (6*R*)-2-(2-benzyloxy-ethyl)-2-methoxy-4-methylene-6-phenethyl-tetrahydro-pyran S15. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S14** (57.0 mg, 0.119 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 25 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (200 mL). The eluant was collected in 10 mL portions and the product containing fractions (4 to 6) were combined and concentrated to give 2-methoxypyran **S15** (42.3 mg, 0.115 mmol, 97%) as a clear colorless oil consisting of a inseparable 3:1 mixture of anomers: R_f 0.60 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -7.7 (*c* = 1.250, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.37 – 7.34 (m, 4H major, 4H minor), 7.32 – 7.28 (m, 4H major, 4H minor), 7.23 – 7.19 (m, 2H major, 2H minor), 4.84 – 4.83 (m, 1H major), 4.82 – 4.81 (m, 1H major), 4.82 – 4.80 (m, 1H minor), 4.77 – 4.76 (m, 1H

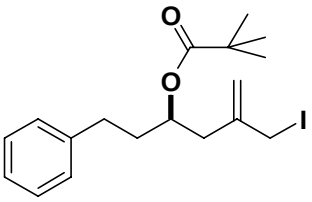
minor), 4.54 – 4.53 (m, 1H minor), 4.51 (s, 2H major, 2H minor), 3.85 – 3.80 (m, 1H major), 3.70 – 3.58 (m, 2H major, 2H minor), 3.18 (s, 3H major), 3.15 (s, 3H minor), 2.87 (ddd, J = 13.8, 10.4, 5.6 Hz, 1H minor), 2.73 – 2.60 (m, 2H major, 1H minor), 2.50 – 2.47 (m, 1H major), 2.41 – 2.38 (m, 1H minor), 2.29 – 2.22 (m, 1H major, 1H minor), 2.16 – 1.96 (m, 3H major, 3H minor), 1.91 – 1.78 (m, 3H major, 3H minor); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.4 (1 minor), 142.2 (1 major), 142.0 (1 minor), 141.9 (1 major), 138.6 (1 major, 1 minor), 128.6 (2 major, 2 minor), 128.6 (2 major, 2 major), 128.5 (1 minor), 128.4 (2 major, 1 minor), 127.9 (1 major, 1 minor), 127.8 (1 major, 1 minor), 127.8 (1 major, 1 minor), 126.1 (1 major), 126.0 (1 minor), 110.6 (1 major), 110.4 (1 minor), 100.4 (1 major), 99.9 (1 minor), 73.3 (1 major, 1 minor), 70.5 (1 minor), 67.9 (1 major), 66.9 (1 major), 66.1 (1 minor), 48.1 (1minor), 47.9 (1 major), 42.8 (1 minor), 42.2 (1 major), 40.2 (1 major), 39.9 (1 minor), 37.8 (1 major, 1 minor), 36.3 (1 major), 36.1 (1 minor), 32.0 (1 minor), 29.9 (1 major); 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.1 (1 minor), 47.9 (1 major). CH_2: 110.6 (1 major), 110.4 (1 minor), 73.3 (1 major, 1 minor), 66.9 (1 major), 66.1 (1 minor), 42.8 (1 minor), 42.2 (1 major), 40.2 (1 major), 39.9 (1 minor), 37.8 (1 major, 1 minor), 36.3 (1 major), 36.1 (1 minor), 32.0 (1 minor), 29.9 (1 major). CH: 128.6 (2 major, 2 minor), 128.6 (2 major, 2 minor), 128.5 (1 minor), 128.4 (2 major, 1 minor), 127.9 (1 major, 1 minor), 127.8 (1 major, 1 minor), 127.8 (1 major, 1 minor), 126.1 (1 major), 126.0 (1 minor), 70.5 (1 minor), 67.9 (1 major). C: 142.4 (1 minor), 142.2 (1 major), 142.0 (1 minor), 141.9 (1 major), 138.6 (1 major, 1 minor), 100.4 (1 major), 99.9 (1 minor); IR (neat) 3063, 3027, 2946, 2961, 1680, 1656, 1581, 1496, 1454, 1363, 1327, 1153, 1101, 1030, 698 cm^{-1}; HRMS (EI) Calcd for $C_{24}H_{30}O_3$ *m/z*

(M): 366.2195. Found: 366.2194; LRMS (EI) Calcd for $C_{23}H_{26}O_2$ *m/z* (M-MeOH): 334.4. Found: 334.3.



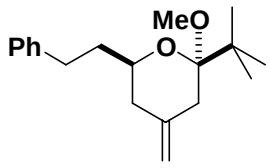
Preparation of 2,2-dimethyl-propionic acid (*R*)-3-chloromethyl-1-phenethyl-but-3-enyl ester S16. To a stirring solution of alcohol **S3** (150 mg, 0.670 mmol, 1.00 eq) and CH_2Cl_2 (3.30 mL, 0.10 M) in a 15 mL round-bottom flask at 0 ºC were added pyridine (190 µL, 2.34 mmol, 3.50 eq), DMAP (8.0 mg, 67 µmol, 0.10 eq) and trimethylacetyl chloride (248 µL, 2.01 mmol, 3.00 eq). After 20 h the solution was added to a mixture of pH 7 sodium potassium phosphate buffer (0.05 M, 20 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (600 mL). The eluant was collected in 30 mL portions and the product containing fractions (7 to 9) were combined and concentrated; remaining volatiles were removed under vacuum (0.025 mm Hg) to give ester **S16** (208 mg, 0.673 mmol, quant.) as a clear colorless oil: R_f 0.77 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +6.5 (*c* = 1.015, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.29 (m, 2H), 7.23 – 7.18 (m, 3H), 5.20 (s, 1H), 5.11 (dddd, *J* = 8.2, 8.2, 4.3, 3.9 Hz, 1H), 5.00 (d, *J* = 1.3 Hz, 1H), 4.15 (dd, *J* = 11.8, 1.3 Hz, 1H), 4.04 (d, *J* = 11.6 Hz, 1H), 2.72 – 2.60 (m, 2H), 2.58 (dd, *J* = 15.0, 4.3 Hz, 1H), 2.42 (dd, *J* = 14.8, 8.8 Hz, 1H), 1.98 – 1.87 (m, 2H), 1.22 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 178.3, 141.6, 141.5, 128.7 (2),

128.5 (2), 126.2, 117.9, 70.8, 48.1, 39.1, 38.4, 36.4, 32.0, 27.5 (3); 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.5 (3). CH_2: 117.9, 48.1, 38.4, 36.4, 32.0. CH: 128.7 (2), 128.5 (2), 126.2, 70.8. C: 178.3, 141.6, 141.5, 39.4; IR (neat) 3084, 3063, 3027, 2999, 2933, 2870, 1724, 1496, 1479, 1454, 1396, 1367, 1282, 1261, 1159, 1033, 911, 749, 699 cm^{-1}; Anal. Calcd for $C_{18}H_{25}ClO_2$: C, 70.00; H, 8.16. Found: C, 70.22; H, 8.19.



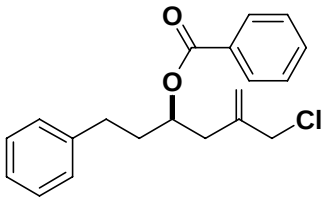
Preparation of (*R*)-3-iodomethyl-1-phenethyl-but-3-enyl ester S17. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S16** (160 mg, 0.520 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 2.5 × 18 cm silica gel column eluting with a solvent mixture of 5% EtOAc/hexanes (500 mL). The eluant was collected in 30 mL portions and the product containing fractions (3 to 6) were combined and concentrated to give iodide **S17** (206 mg, 0.515 mmol, 99%) as a clear colorless oil: R_f 0.78 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +19.2 (*c* = 0.955, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.29 (m, 2H), 7.23 – 7.18 (m, 3H), 5.30 (s, 1H), 5.09 (dddd, *J* = 8.2, 8.2, 4.5, 4.5 Hz, 1H), 4.95 (d, *J* = 0.9 Hz, 1H), 4.01 (d, *J* = 9.4 Hz, 1H), 3.93 (d, *J* = 9.8 Hz, 1H), 2.72 – 2.61 (m, 3H), 2.45 (dd, *J* = 14.8, 8.8 Hz, 1H), 1.98 – 1.87 (m, 2H), 1.22 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 178.2, 142.9, 141.6, 128.7 (2), 128.5 (2), 126.2, 117.0, 70.9, 39.4, 39.1, 36.4, 32.0, 27.5 (3), 10.5; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.5 (3). CH_2: 117.0, 39.4, 36.4, 32.0, 10.5. CH: 128.7 (2), 128.5 (2), 126.3, 70.9. C: 178.2, 142.9, 141.6, 39.1; IR (neat) 3084, 3062, 3026, 2967, 2958, 2931, 2868, 1723, 1495, 1478,

1454, 1433, 1396, 1366, 1281, 1157, 1032, 908, 753, 699 cm^{-1}; Anal. Calcd for $C_{18}H_{25}IO_2$: C, 54.01; H, 6.29. Found: C, 54.27; H, 6.21.



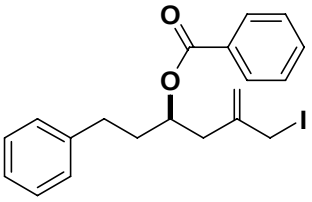
Preparation of (2*R*,6*R*)-2-*tert*-butyl-2-methoxy-4-methylene-6-phenethyl-tetrahydro-pyran S18. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S17** (80.0 mg, 0.200 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (200 mL). The eluant was collected in 10 mL portions and the product containing fractions (4 to 5) were combined and concentrated to give 2-methoxypyran **S18** (53.8 mg, 0.187 mmol, 93%) as a clear colorless oil consisting of a single anomer: R_f 0.77 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -15.3 (*c* = 1.030, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.32 – 7.11 (m, 5H), 4.85 (d, *J* = 2.2 Hz, 1H), 4.83 (d, *J* = 1.7 Hz, 1H), 3.29 (dd, *J* = 11.8, 2.6 Hz, 1H), 3.22 (s, 3H), 2.71 (ddd, *J* = 13.1, 13.1, 5.6 Hz, 1H), 2.64 (ddd, *J* = 13.1, 13.0, 5.1 Hz, 1H), 2.45 (dd, *J* = 13.3, 0.9 Hz, 1H), 2.27 – 2.22 (m, 2H), 2.09 – 1.71 (m, 2H), 1.23 – 1.22 (m, 1H), 0.95 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 143.0, 142.4, 128.6 (2), 128.5 (2), 126.1, 110.2, 100.4, 77.9, 48.0, 42.1, 38.1, 34.3, 34.2, 30.2, 26.0 (3); 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.0, 16.0 (3). CH_2: 110.3, 42.1, 38.1, 34.3, 30.2. CH: 128.6 (2), 128.5 (2), 126.1, 77.9. C: 143.0, 142.4, 100.4, 34.2; IR (neat) 3065, 3025, 2958, 2870, 1724, 1659, 1603, 1577, 1478, 1456, 1392, 1364, 1285, 1218, 1147,

1105, 1028, 933, 888 cm^{-1}; HRMS (CI) Calcd for $C_{19}H_{29}O_2$ *m/z* (M+H): 289.2168. Found: 289.21731; LRMS (CI) Calcd for $C_{18}H_{25}O$ *m/z* (M-MeO): 257.2. Found: 257.3.



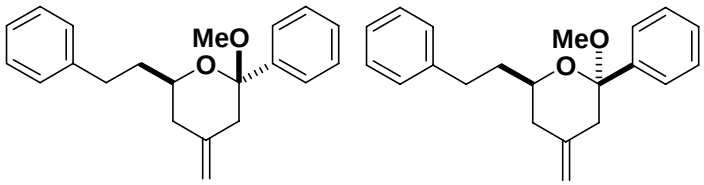
Preparation of benzoic acid (*R*)-3-chloromethyl-1-phenethyl-but-3-enyl ester S19. To a solution of alcohol **S3** (150 mg, 0.670 mmol, 1.00 eq) and CH_2Cl_2 (3.30 mL, 0.20 M) in a 15 mL round-bottom flask at 0 ºC were added pyridine (190 µL, 2.34 mmol, 3.50 eq), DMAP (8.0 mg, 67 µmol, 0.10 eq) and benzoyl chloride (233 µL, 2.01 mmol, 3.00 eq). After 18 h the solution was added to a mixture of pH 7 sodium potassium phosphate buffer (0.05 M, 20 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 15 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (200 mL). The eluant was collected in 30 mL portions and the product containing fractions (7 to 10) were combined and concentrated to give ester **S19** (221 mg, 0.672 mmol, quant.) as a clear colorless oil: R_f 0.73 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +9.8 (*c* = 1.130, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 8.06 – 8.04 (m, 2H), 7.61 – 7.57 (m, 1H), 7.49 – 7.46 (m, 2H), 7.31 – 7.27 (m, 2H), 7.21 – 7.19 (m, 3H), 5.41 – 5.37 (m, 1H), 5.19 (s, 1H), 5.05 (s, 1H), 4.19 (d, *J* = 6.0 Hz, 1H), 4.07 (d, *J* = 6.0 Hz, 1H), 2.82 – 2.72 (m, 2H), 2.69 (dd, *J* = 14.6, 4.3 Hz, 1H), 2.60 (dd, *J* = 14.6, 8.1 Hz, 1H), 2.15 – 2.01 (m, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 166.4, 141.5, 141.4, 133.2, 130.5, 129.8 (2), 128.7 (2), 128.6 (2), 128.5 (2), 126.2, 118.2, 72.3, 48.3, 38.4, 36.3, 32.0; 125 MHz

DEPT ($CDCl_3$) δ CH_2: 118.2, 48.3, 38.4, 36.3, 32.0. CH: 133.2, 129.8 (2), 128.7 (2), 128.6 (2), 128.5 (2), 126.2, 72.3. C: 166.4, 141.5, 141.4, 130.5; IR (neat) 3084, 3062, 3027, 3002, 2953, 2926, 2861, 1789, 1715, 1645, 1601, 1584, 1495, 1451, 1358, 1313, 1272, 1175, 1112, 1069, 1026, 914, 749, 711, 667 cm^{-1}; Anal. Calcd for $C_{20}H_{21}ClO_2$: C, 73.05; H, 6.44. Found: C, 73.25; H, 6.47.



Preparation of (*R*)-3-iodomethyl-1-phenethyl-but-3-enyl ester S20. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S19** (199 mg, 0.607 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 2.5 × 18 cm silica gel column eluting with a solvent gradient from 2.5% (300 mL) through 5% EtOAc/hexanes (300 mL). The eluant was collected in 30 mL portions and the product containing fractions (5 to 13) were combined and concentrated to give iodide **S20** (254 mg, 0.604 mmol, quant.) as a clear colorless oil: R_f 0.70 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +10.4 (*c* = 0.955, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 8.07 – 8.04 (m, 2H), 7.61 – 7.57 (m, 1H), 7.49 – 7.46 (m, 2H), 7.32 – 7.28 (m, 2H), 7.22 – 7.19 (m, 3H), 5.38 (dddd, *J* = 8.4, 8.4, 4.3, 4.3 Hz, 1H), 5.30 (s, 1H), 5.00 (s, 1H), 4.06 (d, *J* = 9.4 Hz, 1H), 3.97 (d, *J* = 9.4 Hz, 1H), 2.83 – 2.72 (m, 3H), 2.63 (dd, *J* = 14.6, 8.6 Hz, 1H), 2.15 – 2.00 (m, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 166.3, 142.7, 141.4, 133.2, 130.5, 129.8 (2), 128.7 (2), 128.6 (2), 128.5 (2), 126.2, 117.2, 72.3, 39.5, 36.2, 23.0, 10.6; 125 MHz DEPT ($CDCl_3$) δ CH_2: 117.2, 39.5, 36.2, 32.0, 10.6. CH: 133.2, 129.8 (2), 128.7 (2), 128.6 (2), 128.5 (2), 126.2 72.3. C:

166.3, 142.7, 141.4, 130.5; IR (neat) 3084, 3061, 3026, 2953, 2927, 2860, 1819, 1713, 1634, 1602, 1584, 1494, 1451, 1432, 1399, 1357, 1313, 1272, 1218, 1175, 1157, 1113, 1069, 1025, 991, 910, 851, 752, 711 cm^{-1}; Anal. Calcd for $C_{20}H_{21}IO_2$: C, 57.16; H, 5.04. Found: C, 57.42; H, 4.98.

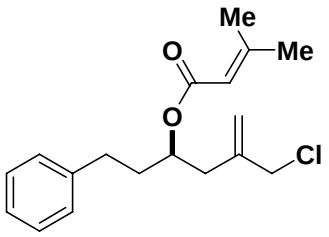


Preparation of (2*S*,6*R*)-2-methoxy-4-methylene-6-phenethyl-2-phenyl-tetrahydro-pyran S21 and (2*R*,6*R*)-2-methoxy-4-methylene-6-phenethyl-2-phenyl-tetrahydro-pyran S22. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S20** (90.0 mg, 0.214 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 0.5% EtOAc/hexanes (300 mL). The eluant was collected in 10 mL portions and the product containing fractions (6 to 7 for the (2*S*)-isomer **S21**, and 9 to 12 for the (2*R*)-isomer **S22**) were each combined and concentrated to give (2*S*)-2-methoxypyran **S21** (6.1 mg, 20 μmol, 9%) and (2*R*)-2-methoxypyran **S22** (55.2 mg, 0.179 mmol, 84%) as clear slightly yellow oils (93% combined yield): (2*S*,6*R*)-2-Methoxy-4-methylene-6-phenethyl-2-phenyl-tetrahydro-pyran **S21**: R_f 0.77 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +32.7 (*c* = 0.420, $CHCl_3$); 500 MHz ^1H NMR ($CDCl_3$) δ 7.57 – 7.55 (m, 2H), 7.41 – 7.38 (m, 2H), 7.34 -7.20 (m, 6H), 4.89 (s, 1H), 4.86 (s, 1H), 3.87 – 3.83 (m, 1H), 3.02 – 2.94 (m, 1H), 2.97 (s, 3H), 2.80 – 2.73 (m, 1H), 2.66 (d, *J* = 14.1 Hz, 1H), 2.36 (d, *J* = 13.3 Hz, 1H), 2.26 (d, *J* = 14.2 Hz, 1H), 2.13 – 1.94 (m, 3H); 125

MHz ^{13}C NMR ($CDCl_3$) δ 142.5, 142.5, 142.1, 128.6 (2), 128.6 (2), 128.4 (2), 128.0, 126.2 (2), 126.0, 110.5, 100.7, 70.7, 49.6, 46.8, 39.8, 38.0, 32.1; 125 MHz DEPT ($CDCl_3$) δ CH_3: 49.6. CH_2: 110.5, 46.8, 39.8, 38.0, 32.1. CH: 128.6 (2), 128.6 (2), 128.4 (2), 128.0, 126.2 (2), 126.0, 70.7. C: 142.5, 142.5, 142.1, 100.7; IR (neat) 3084, 3062, 3027, 2982, 2941, 2861, 2828, 1717, 1657, 1622, 1603, 1575, 1495, 1449, 1435, 1418, 1373, 1323, 1272, 1229, 1203, 1140, 1112, 1086, 1043, 1016, 888, 762, 754, 700, 637 cm^{-1}; HRMS (EI) Calcd for $C_{21}H_{24}O_2$ *m/z* (M): 308.1776. Found: 308.1774; LRMS (EI) Calcd for $C_{20}H_{21}O$ *m/z* (M-MeO): 277.2. Found: 277.2; LRMS (EI) Calcd for $C_{20}H_{20}O$ *m/z* (M-MeOH): 276.2. Found: 276.1.

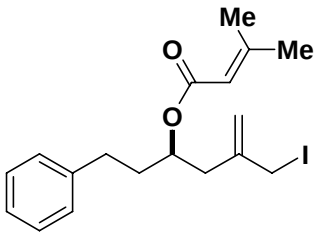
(2*R*,6*R*)-2-Methoxy-4-methylene-6-phenethyl-2-phenyl-tetrahydro-pyran **S22**: R_f 0.73 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -54.3 (*c* = 0.700, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.43 – 7.41 (m, 2H), 7.39 – 7.36 (m, 2H), 7.33 – 7.29 (m, 3H), 7.25 – 7.20 (m, 3H), 4.94 (d, *J* = 1.7 Hz, 1H), 4.91 (s, 1H), 4.68 (dd, *J* = 11.5, 2.6 Hz, 1H), 3.27 (s, 3H), 2.79 (ddd, *J* = 13.7, 13.1, 5.6 Hz, 1H), 2.72 (ddd, *J* = 13.7, 13.1, 5.2 Hz, 1H), 2.57 (d, *J* = 13.7 Hz, 1H), 2.52 – 2.50 (m, 1H), 2.42 (d, *J* = 13.3 Hz, 1H), 2.29 (dd, *J* = 12.7, 12.7 Hz, 1H), 2.16 (ddd, *J* = 13.1, 13.1, 5.1 Hz, 1H), 2.05 (ddd, *J* = 11.6, 11.3, 5.6 Hz, 1H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.4, 142.1, 141.8, 128.7 (2), 128.6 (2), 128.5 (2), 127.8, 126.2 (2), 126.1, 111.0, 101.0, 73.1, 48.2, 42.2, 41.9, 37.9, 30.1; 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.2. CH_2: 111.0, 42.2, 41.9, 37.9, 30.1. CH: 128.7 (2), 128.6 (2), 128.5 (2), 127.8, 126.2 (2), 126.1, 73.1. C: 142.4, 142.1, 141.8, 101.0; IR (neat) 3084, 3064, 3027, 2982, 2955, 2900, 2827, 1657, 1603, 1496, 1454, 1418, 1362, 1326, 1312, 1269, 1233, 1221, 1186, 1172, 1145, 1117, 1073, 1044, 1013, 991, 883, 872, 824, 787, 753, 698, 648 cm^{-1}; LRMS (EI) Calcd for $C_{21}H_{24}O_2$ *m/z* (M): 308.2. Found: 308.2; LRMS (EI) Calcd for $C_{20}H_{21}O$

m/z (M-MeO): 277.2. Found: 277.2; LRMS (EI) Calcd for $C_{20}H_{20}O$ *m/z* (M-MeOH): 276.2. Found: 276.1.



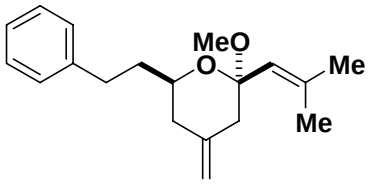
Preparation of 3-methyl-but-2-enoic acid (*R*)-3-chloromethyl-1-phenethyl-but-3-enyl ester S23. To a stirring solution of alcohol **S3** (150 mg, 0.670 mmol, 1.00 eq) and CH_2Cl_2 (3.30 mL, 0.20 M) in a 15 mL round-bottom-flask at 0 ºC were added pyridine (190 µL, 2.34 mmol, 3.50 eq), DMAP (8.0 mg, 67 µmol, 0.10 eq) and 3,3-dimethylacryloyl chloride (224 µL, 2.01 mmol, 3.00 eq). After 36 h the solution was added to a mixture of pH 7 sodium potassium phosphate buffer (0.05 M, 20 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 15 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (200 mL). The eluant was collected in 30 mL portions and the product containing fractions (6 to 9) were combined and concentrated to give ester **S23** (156 mg, 0.508 mmol, 76%) as a clear colorless oil: R_f 0.82 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +3.0 (*c* = 0.910, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.30 – 7.26 (m, 2H), 7.21 – 7.17 (m, 3H), 5.67 – 5.66 (m, 1H), 5.19 (s, 1H), 5.14 (dddd, *J* = 7.8, 7.7, 4.9, 4.7 Hz, 1H), 5.01 (s, 1H), 4.14 (d, *J* = 12.0 Hz, 1H), 4.04 (d, *J* = 11.6 Hz, 1H), 2.74 – 2.61 (m, 2H), 2.55 (dd, *J* = 14.6, 4.3 Hz, 1H), 2.53 (dd, *J* = 14.6, 8.1 Hz, 1H), 2.17 (d, *J* = 1.3 Hz, 3H), 1.94 – 1.90 (m, 2H), 1.91 (d, *J* = 1.3 Hz,

3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 166.4, 157.2, 141.7, 141.6, 128.6 (2), 128.5 (2), 126.1, 117.8, 116.2, 70.5, 48.3, 38.5, 36.3, 32.0, 27.6, 20.5; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.6, 20.5. CH_2: 117.8, 48.3, 38.5, 36.3, 32.0. CH: 128.6 (2), 128.5 (2), 126.1, 116.2, 70.5. C: 166.4, 157.2, 141.7, 141.6; IR (neat) 3084, 3062, 3027, 2937, 2917, 2861, 1714, 1651, 1603, 1495, 1446, 1379, 1345, 1262, 1227, 1146, 1076, 1030, 997, 977, 912, 850, 749, 699, 669 cm^{-1}; Anal. Calcd for $C_{18}H_{23}ClO_2$: C, 70.46; H, 7.56. Found: C, 70.67; H, 7.55.



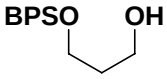
Preparation of 3-methyl-but-2-enoic acid (*R*)-3-iodomethyl-1-phenethyl-but-3-enyl ester S24. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S23** (84.0 mg, 0.270 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (150 mL). The eluant was collected in 10 mL portions and the product containing fractions (4 to 7) were combined and concentrated to give iodide **S24** (106 mg, 0.266 mmol, 99%) as a clear colorless oil: R_f 0.73 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +6.1 (*c* = 1.035, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.31 – 7.28 (m, 2H), 7.21 – 7.19 (m, 3H), 5.69 – 5.68 (m, 1H), 5.30 (s, 1H), 5.14 (dddd, *J* = 7.8, 7.7, 4.7, 4.7 Hz, 1H), 4.96 (s, 1H), 4.03 (d, *J* = 9.4 Hz, 1H), 3.94 (d, *J* = 9.4 Hz, 1H), 2.75 – 2.62 (m, 3H), 2.47 (dd, *J* = 14.8, 8.6 Hz, 1H), 2.18 (d, *J* = 0.9 Hz, 3H), 1.96 – 1.88 (m, 2H), 1.92 (d, *J* = 1.3 Hz, 3H);

125 MHz ^{13}C NMR ($CDCl_3$) δ 166.4, 157.2, 143.0, 141.7, 128.6 (2), 128.5 (2), 126.1, 117.0, 116.2, 70.6, 39.4, 36.3, 32.0, 27.6, 20.5, 10.9; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.6, 20.5. CH_2: 117.0, 39.4, 36.3, 32.0, 10.9. CH: 128.6 (2), 128.5 (2), 126.1, 116.2, 70.6. C: 166.4, 157.2, 143.0, 141.7; IR (neat) 3083, 3061, 3026, 3001, 2936, 2916, 2860, 1713, 1650, 1603, 1584, 1495, 1452, 1444, 1379, 1345, 1308, 1271, 1227, 1146, 1113, 1076, 1029, 978, 908, 850, 750, 699 cm^{-1}; Anal. Calcd for $C_{18}H_{23}IO_2$: C, 54.28; H, 5.82. Found: C, 54.60; H, 5.84.



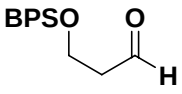
Preparation of (2*R*,6*R*)-2-methoxy-4-methylene-2-(2-methyl-propenyl)-6-phenethyl-tetrahydro-pyran S25. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S24** (104 mg, 0.261 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent gradient from 2.5% (50 mL) through 5% EtOAc/hexanes (150 mL). The eluant was collected in 10 mL portions and the product containing fractions (4 to 9) were combined and concentrated to give 2-methoxypyran **S25** (53.3 mg, 0.186 mmol, 71%) as a clear slightly yellow oil: R_f 0.85 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -51.9 (*c* = 1.065, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.23 – 7.17 (m, 3H), 5.24 – 5.22 (m, 1H), 4.86 – 4.83 (m, 2H), 4.41 – 4.36 (m, 1H), 3.26 (s, 3H), 2.75 – 2.61 (m, 2H), 2.51 – 2.47 (m, 1H), 2.27 – 2.20 (m, 2H), 2.18 – 2.05 (m, 2H), 1.95 – 1.88 (m, 1H), 1.76 (s, 3H), 1.73 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.0, 141.8, 136.2, 128.6 (2), 128.4 (2), 126.1, 125.7,

110.6, 100.7, 68.4, 48.1, 41.9, 40.3, 37.7, 29.8, 26.1, 18.6; 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.1, 26.1, 18.6. CH_2: 110.6, 41.9, 40.3, 37.7, 29.8. CH: 128.6 (2), 128.4 (2), 126.1, 125.7, 68.4. C: 142.0, 141.8, 136.2, 100.7; IR (neat) 3072, 3026, 2941, 2827, 1716, 1657, 1604, 1496, 1454, 1418, 1376, 1325, 1269, 1230, 1183, 1146, 1116, 1074, 1042, 1005, 980, 940, 887, 821, 781, 750, 700 cm^{-1}; LRMS (EI) Calcd for $C_{19}H_{26}O_2$ *m/z* (M): 286.2. Found: 286.2; HRMS (EI) Calcd for $C_{18}H_{22}O$ *m/z* (M-MeOH): 254.1671. Found: 254.1667.



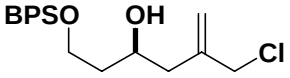
Preparation of 3-(*tert*-butyl-diphenyl-silanyloxy)-propan-1-ol S26.[8] To a stirring solution of BPSCl (59.1 mL, 227 mmol, 1.00 eq) and CH_2Cl_2 (1350 mL, 0.17 M) in a 2000 mL round-bottom flask at room temperature were added 1,3-propanediol (82.1 mL, 1.14 mol, 5.00 eq), triethylamine (63.3 mL, 454 mmol, 2.00 eq), and DMAP (1.39 g, 11.4 mmol, 0.05 eq). After 36 h the mixture was diluted with a mixture of 50% EtOAc/hexanes (100 mL) and washed with water (250, 250 and 500 mL) and brine (100 mL), dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography on a 7.5 × 28 cm silica gel column eluting with a solvent gradient from 3% (4000 mL) through 5% (1000 mL) and 20% (4000 mL) EtOAc/hexanes. The eluant was first collected in 180, 30 mL fractions and then in two 2000 mL round-bottom flasks. The product containing fractions (141 to 180) and the contents of the two 2000 mL round-bottom flasks were combined and concentrated under reduced pressure to give alcohol **S26** (63.2 g, 201 mmol, 89% yield) as a white crystalline solid: R_f 0.25 (25% EtOAc/hexanes); mp 39 °C; 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.72 – 7.68 (m, 4H), 7.49 – 7.27 (m, 6H), 3.87 (t, *J* = 5.6 Hz, 4H), 2.43 (bs, 1H), 1.83 (tt, *J* = 5.6, 5.6 Hz, 2H), 1.07

(s, 9H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 135.8 (4), 133.4 (2), 130.0 (2), 128.0 (4), 63.6, 62.2, 34.4, 27.0 (3), 19.3; IR ($CHCl_3$) 3422 (bs), 3071, 3050, 3012, 2931, 2858, 1471, 1427, 1390, 1361, 1216, 1110, 966, 822, 756, 703, 612 cm^{-1}.



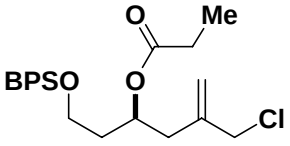
Preparation of 3-(*tert*-butyl-diphenyl-silanyloxy)-propionaldehyde S27.[9] To a solution of oxalyl chloride (26.3 mL, 301 mmol, 1.50 eq) and CH_2Cl_2 (2000 mL, 0.10 M) in a 3000 mL three-neck round-bottom flask equipped with a mechanical stirrer at -78 °C was slowly added a solution of dimethyl sulfoxide (42.8 mL, 603 mmol, 3.00 eq) in CH_2Cl_2 (56 mL). After 1 h, a solution of alcohol **S26** (63.2 g, 201 mmol, 1.00 eq) in CH_2Cl_2 (100 mL) was added via cannula, followed, after 1 h, by slow addition of triethylamine (140 mL, 1.00 mol). After 1 h the cold bath was removed and the mixture warmed to -20 °C over a period of 40 min and pH 7 phosphate buffer (0.05 M aqueous solution, 400 mL) was added. The mixture was warmed to room temperature, the organic phase separated and the solvent removed under reduced pressure. The residue was diluted with 15% EtOAc/hexanes (500 mL), and extracted with water (2 × 200 mL) and brine (50 mL). The organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by flash chromatography on a 7.5 × 28 cm silica gel column eluting with a solvent gradient from 2% (1000 mL) through 5% (1000 mL), 10% (1000 mL), 15% (1000 mL) and 20% (1000 mL) EtOAc/hexanes and the eluant collected in 1000 mL fractions. The product containing fractions (3 to 5) were combined and concentrated under reduced pressure to give aldehyde **S27** (60.6 g, 194 mmol, 97% yield) as a clear colorless oil: R_f 0.56 (25% EtOAc/hexanes); 300 MHz ^{1}H NMR ($CDCl_3$) δ

9.86 (t, *J* = 2.2 Hz, 1H), 7.75 – 7.71 (m, 4H), 7.51 – 7.41 (m, 6H), 4.08 (t, *J* = 6.1 Hz, 2H), 2.65 (td, *J* = 6.0, 2.2 Hz, 2H), 1.10 (s, 9H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 202.0, 135.7 (4), 133.4 (2), 130.0 (2), 128.0 (4), 58.4, 46.5, 26.9 (3), 19.3; IR (neat) 3050, 2932, 2858, 1727, 1471, 1390, 1256, 1110, 972, 823, 705, 509 cm^{-1}.



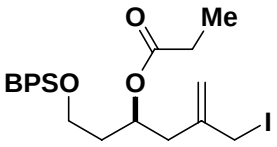
Preparation of (*S*)-1-(*tert*-butyl-diphenyl-silanyloxy)-5-chloromethyl-hex-5-en-3-ol S28. The crude reaction mixture was obtained by following the general procedure for the CAA using BPS aldehyde **S27** (1.00 g, 3.20 mmol) and was purified by flash chromatography using a 3 × 18 cm silica gel column eluting with a solvent gradient of 2.5% (1000 mL) through 5% (1000 mL) and 7.5% EtOAc/hexanes (750 mL). The eluant was collected in 30 mL portions and the product containing fractions (45 to 80) were combined and concentrated to give alcohol **S28** (1.07 g, 2.65 mmol, 83%) as a clear colorless oil. The ratio of enantiomers was determined to be *er* > 99 : 1 (using BF_3•OEt_2, *er* = 50 : 50) by HPLC analysis using a Daicel Chiralcel OD-H silica column, eluting with a mobile phase of 1% 2-propanol/hexanes and a flow rate of 0.5 mL/min, which gave the retention times for the major and minor enantiomers of 19.2 and 20.8 min, respectively, detecting with a Rainin Dynamax Refractive Index Detector Model RI-1: R_f 0.46 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -6.19 (*c* = 1.030, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.71 – 7.69 (m, 4H), 7.48 – 7.40 (m, 6H), 5.27 (s, 1H), 5.09 (d, *J* = 1.3 Hz, 1H), 4.18 – 4.12 (m, 3H), 3.94 – 3.86 (m, 2H), 3.28 (s, 1H), 2.44 – 2.35 (m, 2H), 1.81 – 1.69 (m, 2H), 1.08 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.6, 135.8 (2), 135.7 (2), 133.2, 133.1, 130.1, 130.1, 128.0 (2), 128.0 (2), 117.3, 69.9, 63.5, 48.6, 41.5, 38.5, 27.0

(3), 19.2; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.1 (3). CH_2: 117.3, 63.5, 48.6, 41.5, 38.5. CH: 135.8 (2), 135.8 (2), 130.1, 130.1, 128.1 (4), 69.9. C: 142.6, 133.2, 133.1, 19.2; IR (neat) 3500 (bs), 3071, 3050, 2953, 2931, 2858, 1471, 1427, 1390, 1111, 1082, 910, 736, 702 cm^{-1}; Anal. Calcd for $C_{23}H_{31}ClO_2Si$: C, 68.54; H, 7.75. Found: C, 68.60; H, 7.69.



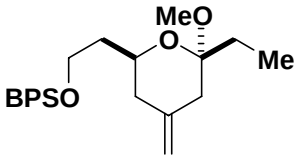
Preparation of propionic acid (*S*)-1-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-3-chloromethyl-but-3-enyl ester S29. To a stirring solution of alcohol **S28** (182 mg, 0.452 mmol, 1.00 eq) and CH_2Cl_2 (2.3 mL, 0.20 M) in a 15 mL round-bottom flask at 0 ºC were added pyridine (128 µL, 1.58 mmol, 3.50 eq), DMAP (6.0 mg, 45 µmol, 0.10 eq) and propionyl chloride (118 µL, 1.36 mmol, 3.00 eq). After 3 h the solution was added to a mixture of pH 7 sodium potassium phosphate buffer (0.05 M, 20 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent gradient from 2.5% (300 mL) through 5% EtOAc/hexanes (300 mL). The eluant was collected in 30 mL portions and the product containing fractions (5 to 12) were combined and concentrated to give ester **S29** (206 mg, 0.450 mmol, quant.) as a clear colorless oil: R_f 0.65 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +11.3 (*c* = 1.120, $CHCl_3$); 500 MHz ^1H NMR ($CDCl_3$) δ 7.68 – 7.65 (m, 4H), 7.45 – 7.38 (m, 6H), 5.29 (dddd, *J* = 8.3, 8.3, 4.3, 4.3 Hz, 1H), 5.19 (s, 1H), 4.99 (s, 1H), 4.10 (d, *J* = 11.7 Hz, 1H), 4.04 (d, *J* = 11.6 Hz, 1H), 3.72 – 3.66 (m, 2H), 2.56 (dd, *J* = 14.6, 4.7 Hz, 1H), 2.39 (dd, *J* = 15.0, 8.1 Hz, 1H), 2.27 – 2.19 (m, 2H), 1.90 – 1.78 (m, 2H), 1.09 (dd, *J* = 8.6, 7.7 Hz, 3H),

1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 174.1, 141.7, 135.8 (2), 135.8 (2), 133.9, 133.8, 129.9 (2), 127.9 (4), 117.7, 69.0, 60.3, 48.2, 38.6, 37.1, 27.9, 27.0 (3), 19.4, 9.4; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.0 (3), 9.4. CH_2: 117.7, 60.3, 48.2, 28.5, 37.0, 27.9. CH: 135.8 (2), 135.8 (2), 129.9 (2), 127.9 (4), 69.0. C: 174.1, 141.7, 133.9, 133.8, 19.4; IR (neat) 3071, 3049, 2957, 2931, 2881, 2858, 1735, 1473, 1462, 1427, 1361, 1186, 1111, 1006, 822, 739, 702 cm^{-1}; Anal. Calcd for $C_{26}H_{35}ClO_3Si$: C, 68.02; H, 7.68. Found: C, 68.15; H, 7.66.



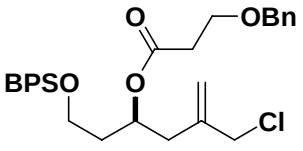
Preparation of (*S*)-1-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-3-iodomethyl-but-3-enyl ester S30. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S29** (107 mg, 0.234 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (250 mL). The eluant was collected in 10 mL portions and the product containing fractions (4 to 7) were combined and concentrated to give iodide **S30** (86.9 mg, 0.233 mmol, quant.) as a clear colorless oil: R_f 0.82 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +23.9 (*c* = 1.040, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.69 – 7.66 (m, 4H), 7.46 – 7.38 (m, 6H), 5.31 – 5.26 (m, 1H), 5.29 (s, 1H), 4.94 (s, 1H), 4.04 (d, *J* = 9.4 Hz, 1H), 3.94 (d, *J* = 9.4 Hz, 1H), 3.71 – 3.68 (m, 2H), 2.63 (dd, *J* = 14.8, 4.5 Hz, 1H), 2.43 (dd, *J* = 14.6, 8.2 Hz, 1H), 2.26 – 2.21 (m, 2H), 1.90 – 1.78 (m, 2H), 1.09 (dd, *J* = 7.7, 7.3 Hz, 3H), 1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 174.0, 143.1, 135.8 (2), 135.8 (2), 133.9, 133.7, 129.8 (2), 127.9 (4), 116.9, 69.0, 60.2, 39.5, 37.0, 27.9, 27.0 (3), 19.3, 10.6, 9.4;

125 MHz DEPT ($CDCl_3$) δ CH_3: 27.0 (3), 9.4. CH_2: 116.9, 60.2, 39.5, 37.0, 27.9, 10.6. CH: 135.8 (2), 135.8 (2), 129.8 (2), 127.9 (4), 69.0. C: 174.0, 143.1, 133.9, 133.7, 19.3; IR (neat) 3070, 3048, 2957, 2931, 2879, 2857, 1735, 1427, 1184, 1158, 1111, 1089, 1006, 738, 702 cm^{-1}; Anal. Calcd for $C_{26}H_{35}IO_3Si$: C, 56.72; H, 6.41. Found: C, 56.99; H, 6.49.



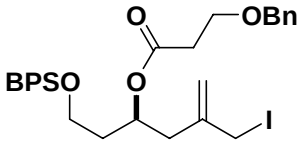
Preparation of *tert*-butyl-[2-((2*S*,6*S*)-6-ethyl-6-methoxy-4-methylene-tetrahydro-pyran-2-yl)-ethoxy]-diphenyl-silane S31. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S30** (70.0 mg, 0.127 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (250 mL). The eluant was collected in 10 mL portions and the product containing fractions (8 to 11) were combined and concentrated to give 2-methoxypyran **S31** (55.3 mg, 0.126 mmol, 99%) as a clear colorless oil consisting of a single anomer: R_f 0.69 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +19.4 (*c* = 1.010, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.69 – 7.67 (m, 4H), 7.45 – 7.38 (m, 6H), 4.82 – 4.81 (m, 1H), 4.80 – 4.79 (m, 1H), 3.90 – 3.81 (m, 2H), 3.79 – 3.75 (m, 1H), 3.13 (s, 3H), 2.40 (dd, *J* = 13.7, 1.3 Hz, 1H), 2.25 (ddd, *J* = 13.3, 1.9, 1.9 Hz, 1H), 2.12 – 2.09 (m, 1H), 1.96 – 1.91 (m, 1H), 1.85 – 1.69 (m, 3H), 1.50 (dddd, *J* = 15.4, 7.7, 7.7, 7.7 Hz, 1H), 1.06 (s, 9H), 0.89 (dd, *J* = 7.7, 7.7 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.3, 135.8 (4), 134.2 (2), 129.8 (2), 127.8 (4), 110.2, 101.0, 67.7, 60.5, 47.8, 41.6, 40.2, 39.2, 28.8,

27.0 (3), 19.4, 7.9; 125 MHz DEPT ($CDCl_3$) δ CH_3: 47.8, 27.0 (3), 7.9. CH_2: 110.2, 60.5, 41.5, 40.2, 39.2, 28.8. CH: 135.7 (4), 129.8 (2), 127.8 (4), 67.7. C: 142.3, 134.2 (2), 101.0, 19.4; IR (neat) 3071, 3049, 2940, 2884, 2857, 2827, 1471, 1427, 1148, 1110, 1084, 1065, 1033, 887, 822, 736, 701 cm^{-1}; Anal. Calcd for $C_{27}H_{38}O_3Si$: C, 73.92; H, 8.73. Found: C, 73.82; H, 8.80.



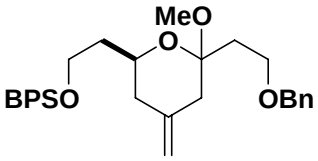
Preparation of 3-benzyloxy-propionic acid (*S*)-1-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-3-chloromethyl-but-3-enyl ester S32. To a stirring solution of alcohol **S28** (100 mg, 0.248 mmol, 1.00 eq) and ethanol-free $CHCl_3$ (2.5 mL, 0.10 M) in a 15 mL round-bottom flask at room temperature were added 3-benzyloxy-propionic acid **S12** (54.0 mg, 0.298 mmol, 1.20 eq), DMAP (3.1 mg, 25 μmol, 0.10 eq), DMAP•HCl (4.0 mg, 25 μmol, 0.10 eq) and DCC (128 mg, 0.620 mmol, 2.50 eq). The mixture was then diluted with ethanol-free $CHCl_3$ (2.0 mL). After 14 h the mixture was added to a saturated aqueous NH_4Cl solution (10 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with pH 7 sodium potassium phosphate buffer (0.05 M, 20 mL), water (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent gradient from 2.5% (100 mL) through 5% (100 mL) and 10% EtOAc/hexanes (200 mL). The eluant was collected in 10 mL portions and the product containing fractions (19 to 33) were combined and concentrated to give ester **S32** (131 mg, 0.232 mmol, 94%) as a clear colorless oil: R_f 0.69 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +10.3 (*c* = 0.990, $CHCl_3$); 500 MHz ^1H NMR ($CDCl_3$) δ 7.68 – 7.65 (m, 4H), 7.45 – 7.27

(m, 11H), 5.32 (dddd, *J* = 7.8, 7.8, 4.9, 4.7 Hz, 1H), 5.16 (d, *J* = 0.9 Hz, 1H), 4.99 (d, *J* = 0.9 Hz, 1H), 4.51 (d, *J* = 14.6 Hz, 1H), 4.48 (d, *J* = 15.8 Hz, 1H), 4.12 (dd, *J* = 12.0, 0.9 Hz, 1H), 4.02 (d, *J* = 12.0 Hz, 1H), 3.72 – 3.68 (m, 4H), 2.58 – 2.49 (m, 3H), 2.41 (dd, *J* = 14.6, 8.1 Hz, 1H), 1.90 – 1.79 (m, 2H), 1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 171.2, 141.5, 138.3, 135.8 (2), 135.8 (2), 133.9, 133.7, 129.9 (2), 128.6 (2), 127.9 (7), 117.8, 73.3, 69.6, 65.8, 60.2, 48.2, 38.4, 37.0, 35.4, 27.0 (3), 19.3; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.0 (3). CH_2: 117.8, 73.3, 65.8, 60.2, 48.2, 38.4, 37.0, 35.5. CH: 135.8 (2), 135.8 (2), 129.9 (2), 128.6 (2), 127.9 (7), 69.6. C: 171.2, 141.5, 138.3, 133.9, 133.7, 19.3; IR (neat) 3070, 3031, 2957, 2930, 2858, 1736, 1472, 1428, 1363, 1257, 1182, 1111, 1008, 823, 738, 702, 613 cm^{-1}; Anal. Calcd for $C_{33}H_{41}ClO_4Si$: C, 70.12; H, 7.31. Found: C, 70.05; H, 7.43.



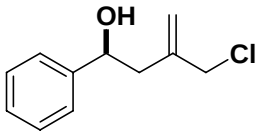
Preparation of (*S*)-1-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-3-iodomethyl-but-3-enyl ester S33. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S32** (110 mg, 0.195 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 27 cm silica gel column eluting with a solvent gradient from 2.5% (400 mL) through 5% EtOAc/hexanes (100 mL). The eluant was collected in 10 mL portions and the product containing fractions (13 to 35) were combined and concentrated to give iodide **S33** (127 mg, 0.193 mmol, 99%) as a clear colorless oil: R_f 0.62 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +20.9 (*c* = 1.070, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.68 – 7.66 (m, 4H), 7.44 – 7.29 (m, 11H), 5.34 – 5.29 (m, 1H), 5.26 (s, 1H), 4.93 (s, 1H), 4.49

(s, 2H), 4.00 (d, *J* = 9.4 Hz, 1H), 3.91 (d, *J* = 9.9 Hz, 1H), 3.72 – 3.68 (m, 4H), 2.62 (dd, *J* = 14.6, 4.7 Hz, 1H), 2.56 – 2.52 (m, 2H), 2.45 (dd, *J* = 15.0, 8.1 Hz, 1H), 1.86 – 1.80 (m, 2H), 1.07 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 171.1, 143.0, 138.3, 135.8 (2), 135.8 (2), 133.9, 133.7, 129.9 (2), 128.6 (2), 127.9 (5), 127.9 (2), 117.0, 73.3, 69.7, 65.9, 60.2, 39.4, 37.0, 35.5, 27.1 (3), 19.4, 10.7; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.1 (3). CH_2: 117.0, 73.3, 65.8, 60.2, 39.4, 37.0, 35.5, 10.7. CH: 135.8 (2), 135.8 (2), 129.9 (2), 128.6 (2), 127.9 (7), 69.7. C: 171.1, 143.0, 138.3, 133.9, 133.7, 19.4; IR (neat) 3069, 3048, 3030, 2957, 2930, 2857, 1735, 1472, 1454, 1428, 1362, 1253, 1181, 1159, 1111, 1028, 1008, 909, 823, 738, 702, 613 cm^{-1}; Anal. Calcd for $C_{33}H_{41}IO_4Si$: C, 60.36; H, 6.29. Found: C, 60.25; H, 6.20.



Preparation of {2-[(2*S*)-6-(2-benzyloxy-ethyl)-6-methoxy-4-methylene-tetrahydro-pyran-2-yl]-ethoxy}-tert-butyl-diphenyl-silane S34. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S33** (79.0 mg, 0.120 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 25 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (500 mL). The eluant was collected in 10 mL portions and the product containing fractions (15 to 40) were combined and concentrated to give 2-methoxypyran **S34** (56.4 mg, 0.104 mmol, 96%) as a clear colorless oil consisting of an inseparable 1:1 mixture of anomers: R_f 0.77 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +0.8 (*c* = 1.300, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.71 – 7.66 (m, 8H), 7.45 – 7.28

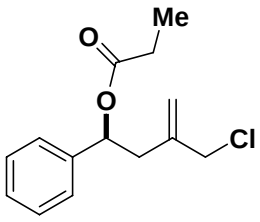
(m, 22H), 4.81 – 4.72 (m, 4H), 4.57 – 4.49 (m, 4H), 3.90 – 3.70 (m, 6H), 3.67 – 3.62 (m, 1H), 3.60 – 3.53 (m, 3H), 3.14 (s, 3H), 3.01 (s, 3H), 2.40 – 2.32 (m, 2H), 2.28 – 2.17 (m, 4H), 2.11 – 2.04 (m, 2H), 1.98 – 1.87 (m, 4H), 1.82 – 1.69 (m, 4H), 1.07 (s, 9H), 1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.0 (2), 142.0, 138.6, 135.8 (2), 135.4 (4), 135.0 (2), 134.1, 134.0, 129.9 (6), 128.6 (4), 127.9 (4), 127.9 (2), 127.8 (8), 110.4 (2), 99.7 (2), 73.2, 67.7, 67.6 (2), 66.9, 66.2, 60.5, 59.8, 48.1, 47.9, 42.9, 42.8, 40.1, 40.0, 39.1, 38.9, 36.2, 36.1, 27.0 (3), 26.8 (3), 19.4, 19.3; 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.1, 47.9, 27.1 (3), 26.8 (3). CH_2: 110.3 (2), 73.2, 67.5, 66.9, 66.1, 60.5, 59.8, 42.9, 42.8, 40.0, 40.0, 39.1, 38.8, 36.2, 36.0. CH: 135.8 (2), 135.8 (2), 135.0 (2), 129.9 (2), 129.8 (2), 129.8 (2), 128.6 (4), 127.9 (4), 127.9 (2), 127.8 (2), 127.8 (2), 127.8 (2), 127.7 (2), 67.7, 67.6. C: 142.0 (2), 142.0, 138.6, 135.4 (2), 134.1, 134.0, 99.7 (2), 19.4, 19.3; IR (neat) 3071, 3049, 3030, 2955, 2933, 2890, 2857, 2741, 1960, 1889, 1823, 1737, 1657, 1589, 1472, 1462, 1428, 1362, 1330, 1307, 1251, 1221, 1111, 1030, 999, 941, 888, 823, 737, 702, 613 cm^{-1}; HRMS (EI) Calcd for $C_{34}H_{44}O_4Si$ *m/z* (M): 544.3009. Found: 544.3002; LRMS (EI) Calcd for $C_{33}H_{40}O_3Si$ *m/z* (M-MeOH): 511.2. Found: 511.1.



Preparation of (*S*)-3-chloromethyl-1-phenyl-but-3-en-1-ol S35.[5]

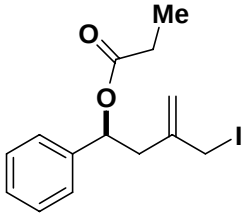
The crude reaction mixture was obtained by following the general procedure for the CAA using benzaldehyde (323 µl, 3.18 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 3.5 × 18 cm silica gel column eluting with a solvent gradient from 1% (300 mL) through 5% (500 mL), 7.5% (500 mL) and 10% EtOAc/hexanes (1000 mL). The eluant was collected in 30 mL portions and the product

containing fractions (37 to 65) were combined and concentrated to give alcohol **S35** (613 mg, 3.12 mmol, 98%) as a clear colorless oil. The ratio of enantiomers was determined to be *er* = 98:2 (using (*R*)-BITIP *er* = 4:96) by HPLC analysis using a Daicel Chiralcel OD-H silica column, eluting with a mobile phase of 20% 2-propanol/hexanes and a flow rate of 0.45 mL/min, which gave the retention times for the major and minor enantiomers of 11.4 and 12.8 min, respectively, detecting with a Rainin Dynamax Refractive Index Detector Model RI-1: R_f 0.38 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -42.9 (*c* = 1.190, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.40 – 7.36 (m, 3H), 7.33 – 7.30 (m, 2H), 5.29 (s, 1H), 5.11 (d, *J* = 0.9 Hz, 1H), 4.89 (dd, *J* = 9.0, 4.3 Hz, 1H), 4.10 (dd, *J* = 11.8, 0.9 Hz, 1H), 4.07 (dd, *J* = 11.8, 0.9 Hz, 1H), 2.66 (dd, *J* = 14.6, 0.9 Hz, 1H), 2.59 (dd, *J* = 14.4, 0.8 Hz, 1H), 2.13 (s, 1H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 144.0, 142.1, 128.7 (2), 128.0, 125.9 (2), 118.0, 72.7, 48.4, 43.3; 125 MHz DEPT ($CDCl_3$) δ CH_2: 118.0, 48.4, 43.3. CH: 128.7 (2), 128.0, 125.9 (2), 72.7. C: 144.0, 142.1; IR (neat) 3550, 3392 (bs), 3084, 3063, 3030, 2947, 2920, 1645, 1603, 1493, 1453, 1401, 1360, 1309, 1258, 1201, 1081, 1052, 1018, 914, 885, 857, 757, 701, 673, 631 cm^{-1}; Anal. Calcd for $C_{11}H_{13}OCl$: C, 67.18; H, 6.66. Found: C, 67.13; H, 6.60.



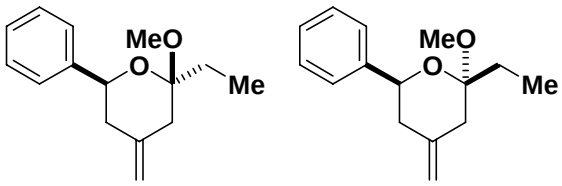
Preparation of propionic acid (*S*)-3-chloromethyl-1-phenyl-but-3-enyl ester S36. To a stirring solution of alcohol **S35** (120 mg, 0.610 mmol, 1.00 eq) and CH_2Cl_2 (3.1 mL, 0.10 M) in a 15 mL round-bottom flask at 0 ºC were added pyridine (173 μL, 2.14 mmol, 3.50 eq), DMAP (7.5 mg, 61 μmol, 0.10 eq) and propionyl chloride

(159 μL, 1.83 mmol, 3.00 eq). The reaction was warmed to 4 ºC, and after 12 h the solution was added to a mixture of pH 7 sodium potassium phosphate buffer (0.05 M, 20 mL) and CH_2Cl_2 (50 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 15 cm silica gel column eluting with a solvent mixture of 3% EtOAc/hexanes (300 mL). The eluant was collected in 30 mL portions and the product containing fractions (5 to 9) were combined and concentrated to give ester **S36** (142 mg, 0.562 mmol, 92%) as a clear colorless oil: R_f 0.80 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -55.3 (*c* = 1.130, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.38 – 7.30 (m, 5H), 5.98 (dd, *J* = 7.7, 6.0 Hz, 1H), 5.21 (s, 1H), 5.02 (s, 1H), 4.06 (d, *J* = 12.0 Hz, 1H), 4.01 (d, *J* = 12.0 Hz, 1H), 2.75 – 2.73 (m, 2H), 2.36 (dq, *J* = 15.0, 7.7 Hz, 1H), 2.35 (dq, *J* = 15.0, 7.3 Hz, 1H), 1.14 (d, *J* = 7.7, 7.3 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 173.7, 141.1, 140.3, 128.7 (2), 128.3, 126.6 (2), 118.2, 73.7, 46.3, 40.3, 27.9, 9.3; 125 MHz DEPT ($CDCl_3$) δ CH_3: 9.3. CH_2: 118.2, 48.3, 40.3, 27.9. CH: 128.7 (2), 128.3, 126.6 (2), 73.3. C: 173.7, 141.1, 140.3; IR (neat) 3086, 3066, 3034, 2983, 2942, 2882, 1739, 1647, 1495, 1455, 1434, 1359, 1331, 1262, 1184, 1081, 1011, 914, 753, 700, 676 cm^{-1}; Anal. Calcd for $C_{14}H_{17}ClO_2$: C, 66.53; H, 6.78. Found: C, 66.63; H, 6.81.



Preparation of (*S*)-3-iodomethyl-1-phenyl-but-3-enyl ester S37. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S36** (120 mg, 0.475 mmol, 1.00 eq) as starting material

and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 5% EtOAc/hexanes (200 mL). The eluant was collected in 10 mL portions and the product containing fractions (2 to 5) were combined and concentrated to give iodide **S37** (161 mg, 0.467 mmol, 98%) as a clear colorless oil: R_f 0.65 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -13.7 (*c* = 1.030, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.38 – 7.30 (m, 5H), 5.96 (dd, *J* = 8.2, 6.0 Hz, 1H), 5.31 (s, 1H), 4.96 (s, 1H), 3.90 (s, 2H), 2.79 – 2.77 (m, 2H), 2.36 (dq, *J* = 15.0, 7.7 Hz, 1H), 2.35 (dq, *J* = 15.0, 7.7 Hz, 1H), 1.14 (dd, *J* = 7.7, 7.7 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 173.7, 142.5, 140.3, 128.7 (2), 128.3, 126.6 (2), 117.3, 73.8, 41.5, 28.0, 10.6, 9.3; 125 MHz DEPT ($CDCl_3$) δ CH_3: 9.3. CH_2: 117.3, 41.5, 28.0, 10.6. CH: 128.7 (2), 128.3, 126.6 (2), 73.8. C: 173.3, 142.5, 140.5; IR (neat) 3064, 3033, 2981, 2941, 2881, 1738, 1635, 1495, 1455, 1428, 1358, 1331, 1273, 1176, 1081, 1066, 1004, 911, 758, 699 cm^{-1}; Anal. Calcd for $C_{14}H_{17}IO_2$: C,48.85; H, 4.98. Found: C, 49.08; H, 5.01.

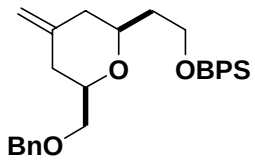


Preparation of (2*R*,6*S*)-2-ethyl-2-methoxy-4-methylene-6-phenyl-tetrahydro-pyran S38 and (2*S*,6*S*)-2-ethyl-2-methoxy-4-methylene-6-phenyl-tetrahydro-pyran S39. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S37** (59.1 mg, 0.171 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 1% EtOAc/hexanes (200 mL). The eluant was collected in 10 mL portions and the

product containing fractions (4 to 6 for the (2*R*)-isomer **S38**, and 7 to 13 for the (2*S*)-isomer **S39**) were each combined and concentrated to give (2*R*)-2-methoxypyran **S38** (14.3 mg, 61.6 μmol, 36%) and (2*S*)-2-methoxypyran **S39** (23.0 mg, 99.0 μmol, 58%) as clear slightly yellow oils (94% combined yield): (2*R*,6*S*)-2-ethyl-2-methoxy-4-methylene-6-phenyl-tetrahydro-pyran **S38**: R_f 0.81 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -48.2 (*c* = 0.610, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.57 – 7.55 (m, 2H), 7.40 – 7.36 (m, 2H), 7.33 – 7.29 (m, 1H), 4.87 (d, *J* = 1.7 Hz, 1H), 4.85 (d, *J* = 1.7 Hz, 1H), 3.72 – 3.67 (m, 1H), 2.97 (s, 3H), 2.65 (d, *J* = 13.7 Hz, 1H), 2.32 (d, *J* = 13.3 Hz, 1H), 2.24 (d, *J* = 13.7 Hz, 1H), 2.07 – 2.02 (m, 1H), 1.77 – 1.61 (m, 2H), 1.07 (dd, *J* = 7.7, 7.3 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.7, 142.4, 128.3 (2), 127.9, 126.2 (2), 110.2, 100.5, 72.4, 49.5, 46.8, 39.4, 29.2, 10.2; 125 MHz DEPT ($CDCl_3$) δ CH_3: 49.5, 10.2. CH_2: 110.2, 46.8, 39.4, 29.2. CH: 128.3 (2), 127.9, 126.2 (2), 72.4. C: 142.7, 142.4, 100.5; IR (neat) 3073, 3030, 2960, 2938, 2856, 2829, 1743, 1658, 1492, 1463, 1449, 1419, 1323, 1228, 1199, 1176, 1149, 1133, 1118, 1078, 1041, 1018, 978, 757, 700, 675, 636 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{20}O_2$ *m/z* (M): 232.1463. Found: 232.1752; HRMS (EI) Calcd for $C_{14}H_{17}O$ *m/z* (M-MeO): 201.1279. Found: 201.1373; HRMS (EI) Calcd for $C_{14}H_{16}O$ *m/z* (M-MeOH): 200.1201. Found: 200.1284.

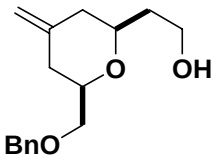
(2*S*,6*S*)-2-ethyl-2-methoxy-4-methylene-6-phenyl-tetrahydro-pyran **S39**: R_f 0.73 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +68.1 (*c* = 1.370, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.43 – 7.41 (m, 2H), 7.39 – 7.36 (m, 2H), 7.31 – 7.27 (m, 1H), 4.90 (d, *J* = 0.7 Hz, 1H), 4.88 (d, *J* = 0.6 Hz, 1H), 4.62 (d, *J* = 9.9 Hz, 1H), 3.21 (s, 3H), 2.50 (s, 1H), 2.47 (s, 1H), 2.30 – 2.24 (m, 2H), 1.89 (dq, *J* = 14.4, 7.7 Hz, 1H), 1.69 (dq, *J* = 14.4, 7.7 Hz, 1H), 0.97 (dd, *J* = 7.7, 7.7 Hz, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 142.5, 142.1, 128.6 (2), 127.8, 126.3

(2), 110.7, 101.7, 73.1, 48.0, 42.1, 41.3, 28.9, 8.0; 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.0, 8.0. CH_2: 110.7, 42.1, 41.3, 28.9. CH: 128.6 (2), 127.8, 126.3 (2), 73.1. C: 142.5, 142.1, 101.7; IR (neat) 3072, 3030, 2971, 2943, 2899, 2828, 1739, 1655, 1496, 1455, 1437, 1419, 1340, 1320, 1299, 1226, 1175, 1143, 1068, 1049, 1026, 989, 960, 879, 830, 754, 698, 656 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{20}O_2$ *m/z* (M): 232.1463. Found: 232.1752; HRMS (EI) Calcd for $C_{14}H_{17}O$ *m/z* (M-MeO): 201.1279. Found: 201.1373; HRMS (EI) Calcd for $C_{14}H_{16}O$ *m/z* (M-MeOH): 200.1201. Found: 200.1284.



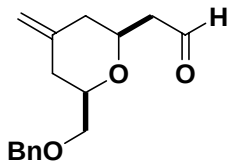
Spectroscopic data for [2-((2*S*,6*R*)-6-benzyloxymethyl-4-methylene-tetrahydro-pyran-2-yl)-ethoxy]-*tert*-butyl-diphenyl-silane S40.[10] R_f 0.77 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +3.1 (*c* = 1.100, $CHCl_3$, *er* = 96:4); 500 MHz ^1H NMR ($CDCl_3$) δ 7.69 – 7.67 (m, 4H), 7.44 – 7.28 (m, 11H), 4.76 – 4.75 (m, 2H), 4.58 (s, 2H), 3.86 (ddd, *J* = 10.1, 7.9, 5.6 Hz, 1H), 3.77 (ddd, *J* = 10.5, 5.6, 5.6 Hz, 1H), 3.58 – 3.49 (m, 3H), 3.49 – 3.45 (m, 1H), 2.29 – 2.24 (m, 2H), 2.05 (dd, *J* = 12.0, 12.0 Hz, 1H), 1.97 (dd, *J* = 12.0, 12.0 Hz, 1H), 1.91 – 1.85 (m, 1H), 1.81 – 1.74 (m, 1H), 1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 144.6, 138.6, 135.8 (4), 134.2, 134.1, 129.7 (2), 128.6 (2), 127.9 (2), 127.8 (4), 127.8, 109.0, 77.7, 75.7, 73.6, 73.4, 60.6, 41.1, 39.3, 37.7, 27.1 (3), 19.4; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.1 (3). CH_2: 109.0, 73.6, 73.4, 60.6, 40.0, 39.3, 37.7. CH: 135.8 (4), 129.7 (2), 128.6 (2), 127.9 (2), 127.8 (4), 127.8, 77.7, 75.7. C: 144.6, 138.6, 134.2, 134.1, 19.4; IR (neat) 3070, 3049, 3030, 2998, 2939, 2932, 2889, 2857,

1652, 1589, 1472, 1453, 1428, 1389, 1361, 1327, 1309, 1247, 1174, 1112, 1029, 1007, 998, 957, 940, 891, 823, 737, 701, 614 cm^{-1}.



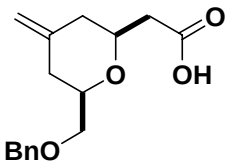
Preparation of 2-((2*S*,6*R*)-6-benzyloxymethyl-4-methylene-tetrahydro-pyran-2-yl)-ethanol S41.[10] To stirring solution of pyran **S40** (300 mg, 0.599 mmol, 1.00 eq) and THF (40 mL, 15 mM), in a 100 mL round-bottom flask at room temperature was added TBAF (659 μL, 0.659 mmol 1.10 eq). After 4h the solution was added to a mixture of a saturated aqueous $NaHCO_3$ solution (50 mL) and CH_2Cl_2 (200 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent gradient from 15% (300 mL) through 50% EtOAc/hexanes (900 mL). The eluant was collected in 30 mL portions and the product containing fractions (13 to 19) were combined and concentrated to give alcohol **S41** (108 mg, 0.412 mmol, 69%) as a clear colorless oil: R_f 0.09 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -1.6 (*c* = 1.060, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.38 – 7.33 (m, 4H), 7.31 – 7.27 (m, 1H), 4.76 (s, 2H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 3.84 – 3.80 (m, 2H), 3.62 – 3.55 (m, 2H), 3.51 (dd, *J* = 10.1, 6.2 Hz, 1H), 3.46 (dd, *J* = 8.9, 4.3 Hz, 1H), 2.94 (bs, 1H), 2.24 – 2.20 (m, 2H), 2.10 – 2.00 (m, 2H), 1.89 – 1.82 (m, 1H), 1.77 – 1.71 (m, 1H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 143.5, 138.3, 128.6 (2), 127.9 (2), 127.9, 109.7, 79.5, 77.7, 73.7, 73.3, 61.8, 40.9, 38.0, 37.2; 125 MHz DEPT ($CDCl_3$) δ CH_2: 109.6, 73.6, 73.3, 61.8, 40.9, 38.0,

37.2. CH: 128.6 (2), 127.9 (2), 127.9, 79.4, 77.7. C: 143.5, 138.3; IR (neat) 3435 (bs), 3070, 3030, 2979, 2941, 2888, 2862, 1652, 1497, 1454, 1426, 1366, 1327, 1310, 1262, 1241, 1205, 1172, 1097, 1055, 1028, 999, 972, 941, 892, 738, 698, 659, 609 cm^{-1}.



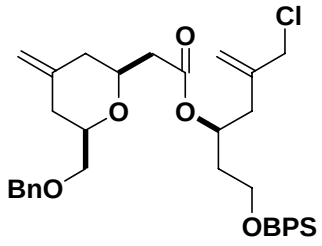
Preparation of ((2*S*,6*R*)-6-benzyloxymethyl-4-methylene-tetrahydro-pyran-2-yl)-acetaldehyde S42.[10] To a stirring solution of alcohol **S41** (110 mg, 0.419 mmol, 1.00 eq) and CH_2Cl_2 (4.20 mL, 0.10 M) in a 20 mL round-bottom flask at -10 ºC were added Hünig's base (512 µL, 2.94 mmol, 7.00 eq), DMSO (298 µL, 4.19 mmol, 10.0 eq) and SO_3•py (267 mg, 1.68 mmol, 4.00 eq). After 1 h the mixture was added to pH 7 sodium potassium phosphate buffer (0.05M, 30 mL) and CH_2Cl_2 (100 mL). The organic phase was washed with water (2 × 30 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent mixture of 10% EtOAc/hexanes (900 mL). The eluant was collected in 30 mL portions and the product containing fractions (7 to 14) were combined and concentrated to give aldehyde **S42** (106 mg, 0.407 mmol, 97%) as a clear colorless oil: R_f 0.39 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ -2.6 (*c* = 1.030, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 9.82 (dd, *J* = 2.2, 2.2. Hz, 1H), 7.38 – 7.33 (m, 4H), 7.31 – 7.27 (m, 1H), 4.80 – 4.79 (m, 2H), 4.58 (s, 2H), 3.87 (dddd, *J* = 11.3, 7.5, 4.9, 2.6 Hz, 1H), 3.62 – 3.57 (m, 1H), 3.53 (dd, *J* = 10.3, 5.5 Hz, 1H), 3.48 (dd, *J* = 10.3, 4.3 Hz, 1H), 2.70 (ddd, *J* = 16.4, 7.6, 2.6 Hz, 1H), 2.55 (ddd, *J* = 16.5, 4.9, 1.9 Hz, 1H), 2.31 – 2.24 (m, 2H), 2.00 – 2.01 (m, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 201.1, 143.1, 138.4, 128.6 (2), 127.9 (2), 127.8, 110.0, 78.0, 73.8,

73.6, 73.1, 49.8, 40.6, 37.1; 125 MHz DEPT ($CDCl_3$) δ CH_2: 110.0, 73.6, 73.1, 49.8, 40.6, 37.1. CH: 201.1, 128.6 (2), 127.9 (2), 127.8, 78.0, 73.8. C: 143.1, 138.4; IR (neat) 3071, 3030, 3006, 2981, 2893, 2860, 1726, 1653, 1497, 1454, 1422, 1382, 1363, 1323, 1310, 1205, 1172, 1106, 1048, 1029, 896, 738, 699, 668, 606 cm^{-1}; HRMS (CI) Calcd for $C_{16}H_{21}O_3$ *m/z* (M+H): 261.1491. Found: 261.1481; HRMS (CI) Calcd for $C_{16}H_{20}O_3$ *m/z* (M): 260.1412. Found: 260.1416.



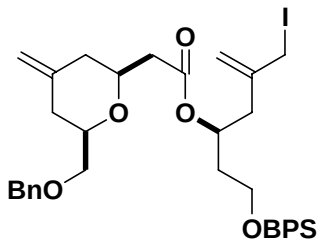
Preparation of ((2*S*,6*R*)-6-benzyloxymethyl-4-methylene-tetrahydro-pyran-2-yl)-acetic acid S43. To a stirring solution of aldehyde **S42** (100 mg, 0.384 mmol, 1.00 eq) in *t*-butanol (5.80 mL, 66 mM) and 2-methyl-2-butene (5.80 mL, 66 mM) in a 100 mL round-bottom flask at -5 ºC was added KH_2PO_4 (1.25 M solution, 1.6 mL, 0.25 M) and then $NaClO_2$ (139 mg, 1.54 mmol, 4.00 eq). After 4 h the mixture was added to water (20 mL) and acidified with HCl (2.0 M solution) to pH 3. The mixture was extracted with Et_2O (3 × 100 mL), the organic phase dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent gradient from 3% (300 mL) through 6% MeOH/CH_2Cl_2 (500 mL). The eluant was collected in 30 mL portions and the product containing fractions (3 to 12) were combined and concentrated to give acid **S43** (99.7 mg, 0.361 mmol, 94%) as a clear colorless oil: R_f 0.09 (25% EtOAc/hexanes); R_f 0.60 (10% MeOH/CH_2Cl_2); $[\alpha]_D^{20}$ +3.4 (*c* = 0.886, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 10.4 (bs, 1H), 7.30 – 7.26 (m, 4H), 7.23 – 7.20 (m, 1H), 4.74 – 4.72

(m, 2H), 4.53 (d, *J* = 12.4 Hz, 1H), 4.50 (d, *J* = 12.4 Hz, 1H), 3.71 (dddd, *J* = 11.6, 7.7, 5.4, 2.6 Hz, 1H), 3.58 – 3.53 (m, 1H), 3.47 (dd, *J* = 10.3, 6.0 Hz, 1H), 3.42 (dd, *J* = 10.3, 4.3 Hz, 1H), 2.61 (dd, *J* = 15.7, 7.7 Hz, 1H), 2.47 (dd, *J* = 15.9, 5.2 Hz, 1H), 2.27 – 2.24 (m, 1H), 2.20 – 2.16 (m, 1H), 2.02 – 1.93 (m, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 175.6, 142.7, 138.3, 128.6 (2), 127.9 (2), 127.8, 110.3, 78.0, 74.7, 73.6, 72.9, 41.1, 40.2, 36.9; 125 MHz DEPT ($CDCl_3$) δ CH_2: 110.3, 73.6, 72.9, 41.1, 40.2, 36.9. CH: 128.6 (2), 127.9 (2), 127.8, 78.0, 74.7. C: 175.6, 142.7, 138.3; IR (neat) 3166, 3069, 3031, 2981, 2940, 2894, 2866, 2703, 2688, 2653, 1732, 1713, 1652, 1497, 1454, 1422, 1363, 1328, 1292, 1261, 1208, 1162, 1102, 1075, 1028, 947, 896, 738, 698, 651, 608 cm^{-1}; HRMS (CI) Calcd for $C_{16}H_{21}O_4$ *m/z* (M+H): 277.3355. Found: 277.1422.



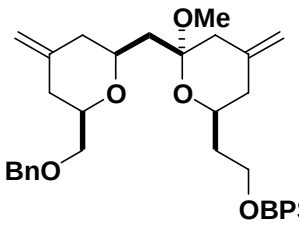
Preparation of ((2*S*,6*R*)-6-benzyloxymethyl-4-methylene-tetrahydro-pyran-2-yl)-acetic acid (*S*)-1-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-3-chloromethyl-but-3-enyl ester S44. To a stirring solution of alcohol **S28** (54.0 mg, 0.135 mmol, 1.00 eq), acid **S43** (41.0 mg, 0.148 mmol, 1.10 eq) and THF (2.10 mL, 0.20 M) in a 5 mL vial at room temperature was added DMAP (1.6 mg, 13 µL, 0.10 eq), DMAP•HCl (2.1 mg, 13 µL, 0.10 eq) and EDCI (65 mg, 0.337 mmol, 2.50 eq), and the mixture was heated to 50 ºC. After 36 h the mixture was cooled to room temperature and added to a mixture of a saturated aqueous NH_4Cl solution (20 mL) and CH_2Cl_2 (70 mL). The organic phase was washed with water (2 × 20 mL) and brine (20 mL), dried over

Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent gradient from 5% (300 mL) through 10% EtOAc/hexanes (300 mL). The eluant was collected in 30 mL portions and the product containing fractions (7 to 13) were combined and concentrated to give ester **S44** (75.7 mg, 0.115 mmol, 85%) as a clear colorless oil: R_f 0.79 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +4.8 (*c* = 1.060, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.68 – 7.64 (m, 4H), 7.45 – 7.26 (m, 11H), 5.35 – 5.28 (m, 1H), 5.16 (s, 1H), 4.98 (s, 1H), 4.77 (d, *J* = 1.7 Hz, 1H), 4.74 (d, *J* = 1.7 Hz, 1H), 4.53 (s, 2H), 4.11 (d, *J* = 11.6 Hz, 1H), 4.00 (d, *J* = 12.0 Hz, 1H), 3.73 – 3.65 (m, 3H), 3.54 – 3.46 (m, 2H), 3.42 (dd, *J* = 10.7, 4.5 Hz, 1H), 2.60 – 2.52 (m, 2H), 2.42 – 2.35 (m, 2H), 2.29 – 2.23 (m, 2H), 2.03 (dd, *J* = 12.2, 12.2 Hz, 1H), 1.95 (dd, *J* = 12.2, 12.2 Hz, 1H), 1.84 – 1.78 (m, 2H), 1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 170.5, 143.4, 141.6, 138.5, 135.8 (2), 135.8 (2), 133.9, 133.7, 129.9 (2), 128.6 (2), 127.9 (6), 127.8, 117.7, 109.8, 77.7, 75.1, 73.6, 73.1, 69.6, 60.3, 48.2, 41.7, 40.5, 38.4, 37.3, 37.1, 27.0 (3), 19.3; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.0 (3). CH_2: 117.7, 109.8, 73.6, 73.1, 60.3, 48.2, 41.7, 40.4, 38.4, 37.3, 37.1. CH: 135.8 (2), 135.8 (2), 129.9 (2), 128.6 (2), 127.9 (6), 127.8, 77.7, 75.1, 69.9. C: 170.5, 143.4, 141.6, 138.5, 133.9, 133.7, 19.3; IR (neat) 3071, 3030, 2956, 2931, 2892, 2858, 1737, 1653, 1589, 1472, 1453, 1428, 1390, 1362, 1328, 1259, 1217, 1155, 1111, 1029, 1008, 975, 897, 823, 738, 702, 668, 614 cm^{-1}; HRMS (CI) Calcd for $C_{39}H_{50}ClO_5Si$ *m/z* (M+H): 661.3116. Found: 661.3105.



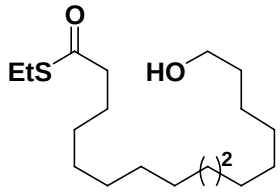
Preparation of ((2*S*,6*R*)-6-benzyloxymethyl-4-methylene-tetrahydro-pyran-2-yl)-acetic acid (*S*)-1-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-3-iodomethyl-but-3-enyl ester S45. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using ester **S44** (40.0 mg, 60.0 μmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent gradient from 2.5% (50 mL) through 5% EtOAc/hexanes (150 mL). The eluant was collected in 10 mL portions and the product containing fractions (7 to 13) were combined and concentrated to give iodide **S45** (44.8 mg, 59.5 μmol, 99%) as a clear colorless oil: R_f 0.85 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +11.4 (*c* = 1.516, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.68 – 7.65 (m, 4H), 7.45 – 7.26 (m, 11H), 5.32 – 5.27 (m, 1H), 5.26 (s, 1H), 4.93 (s, 1H), 4.77 (d, *J* = 1.7 Hz, 1H), 4.74 (d, *J* = 1.7 Hz, 1H), 4.54 (s, 2H), 3.99 (d, *J* = 9.4 Hz, 1H), 3.90 (d, *J* = 9.4 Hz, 1H), 3.73 – 3.67 (m, 3H), 3.54 – 3.46 (m, 2H), 3.42 (dd, *J* = 9.6, 4.3 Hz, 1H), 2.64 – 2.55 (m, 2H), 2.44 (dd, *J* = 14.8, 8.6 Hz, 1H), 2.38 (dd, *J* = 15.2, 6.2 Hz, 1H), 2.30 – 2.24 (m, 2H), 2.03 (dd, *J* = 12.6, 12.6 Hz, 1H), 1.95 (dd, *J* = 12.4, 12.4 Hz, 1H), 1.85 – 1.80 (m, 2H), 1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 170.5, 143.4, 143.0, 138.5, 135.8 (2), 135.8 (2), 133.8, 133.7, 129.9 (2), 128.6 (2), 127.9 (6), 127.8, 116.9, 109.8, 77.7, 75.1, 73.6, 73.1, 69.6, 60.3, 41.8, 40.5, 39.4, 37.3, 37.1, 27.1 (3), 19.4, 10.6; 125 MHz DEPT ($CDCl_3$) δ CH_3: 27.1 (3). CH_2: 116.9, 109.8, 73.6, 73.1, 60.3, 41.8, 40.5, 39.4, 37.3, 37.1, 10.6. CH: 135.8 (2), 135.8 (2), 129.9 (2), 128.6 (2), 127.9 (6), 127.8, 77.7, 75.1, 69.6. C:

170.5, 143.4, 143.0, 138.5, 133.8, 133.7, 19.4; IR (neat) 3070, 3030, 2955, 2931, 2891, 2857, 1737, 1652, 1634, 1589, 1472, 1428, 1389, 1362, 1328, 1259, 1217, 1191, 1156, 1111, 1028, 998, 973, 904, 823, 738, 702, 614 cm^{-1}; HRMS (CI) Calcd for $C_{39}H_{50}IO_5Si$ *m/z* (M+H): 753.2472. Found: 753.2487.

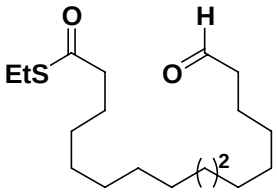


Preparation of {2-[(2*S*,6*R*)-6-((2*S*,6*R*)-6-benzyloxymethyl-4-methylene-tetrahydro-pyran-2-ylmethyl)-6-methoxy-4-methylene-tetrahydro-pyran-2-yl]-ethoxy}-*tert*-butyl-diphenyl-silane S46. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S45** (20.9 mg, 27.7 μmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 5% EtOAc/hexanes (250 mL). The eluant was collected in 10 mL portions and the product containing fractions (8 to 16) were combined and concentrated to give 2-methoxypyran **S46** (16.1 mg, 25.1 μmol, 91%) as a clear colorless and viscous oil: R_f 0.65 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +15.1 (*c* = 0.780, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.70 – 7.66 (m, 4H), 7.45 – 7.28 (m, 11H), 4.81 – 4.72 (m, 4H), 4.58 (s, 2H), 3.88 – 3.74 (m, 3H), 3.56 – 3.49 (m, 4H), 3.16 (s, 3H), 2.49 (d, *J* = 14.1 Hz, 1H), 2.33 (d, *J* = 13.7 Hz, 1H), 2.26 – 2.20 (m, 3H), 2.07 – 2.00 (m, 2H), 1.94 – 1.88 (m, 2H), 1.82 (dd, *J* = 14.6, 3.4 Hz, 1H), 1.79 – 1.68 (m, 2H), 1.06 (s, 9H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 144.5, 142.4, 138.6, 135.8 (3), 134.2 (2), 129.8 (2), 128.6 (3), 127.9, 127.8 (4), 127.8, 127.7, 110.1, 109.2, 99.8, 77.5, 75.2, 73.6, 73.5, 67.8, 60.6, 48.1, 42.6, 42.5, 42.0, 39.9,

39.2, 37.3, 27.1 (3), 19.4; 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.2, 27.1 (3). CH_2: 110.1, 109.3, 73.6, 73.5, 60.6, 42.6, 42.5, 42.0, 39.9, 39.2, 37.3. CH: 135.8 (3), 129.8 (2), 128.6 (3), 127.9, 127.9 (4), 127.8, 127.7, 77.5, 75.2, 67.8. C: 144.5, 142.4, 138.6, 134.2 (2), 99.8, 19.4; 500 MHz ^{1}H NMR (C_6D_6) δ 7.79 – 7.78 (m, 2H), 7.31 – 7.09 (m, 13H), 4.85 (s, 1H), 4.84 (s, 1H), 4.72 (s, 2H), 4.39 (d, *J* = 12.0 Hz, 1H), 4.34 (d, *J* = 12.0 Hz, 1H), 3.95 – 3.91 (m, 2H), 3.86 – 3.81 (m, 1H), 3.64 – 3.60 (m, 1H), 3.54 – 3.53 (m, 1H), 3.46 (dd, *J* = 9.9, 6.4 Hz, 1H), 3.31 (dd, *J* = 10.3, 4.3 Hz, 1H), 3.15 (s, 3H), 2.63 (d, *J* = 13.7 Hz, 1H), 2.50 (d, *J* = 13.7 Hz, 1H), 2.21 – 2.08 (m, 3H), 2.03 – 1.87 (m, 4H), 1.83 – 1.79 (m, 2H), 1.75 – 1.69 (m, 1H), 1.18 (s, 9H); 125 MHz ^{13}C NMR (C_6D_6) δ 145.3, 143.0, 139.8, 136.5 (3), 134.9, 134.9, 130.5 (2), 129.1, 128.9 (5), 128.5 (2), 128.3, 128.1, 110.7, 109.7, 100.6, 78.3, 75.7, 74.3, 73.9, 68.5, 61.5, 48.2, 43.5, 43.4, 42.7, 40.8, 40.0, 38.1, 27.7 (3), 20.0; 125 MHz DEPT (C_6D_6) δ CH_3: 48.2, 27.7 (3). CH_2: 110.7, 109.7, 74.3, 73.9, 61.5, 43.5, 43.4, 42.7, 40.8, 40.0, 38.1. CH: 136.6 (3), 130.5 (2), 129.1, 128.9 (5), 128.6 (2), 128.3, 128.2, 78.3, 75.7, 68.5. C: 145.3, 143.0, 139.8, 134.9, 134.9, 100.6, 20.0; IR (neat) 3071, 2951, 2932, 2892, 2857, 1738, 1652, 1471, 1455, 1428, 1389, 1362, 1331, 1311, 1224, 1179, 1111, 1029, 1008, 950, 890, 823, 737, 701, 613 cm^{-1}; HRMS (EI) Calcd for $C_{39}H_{49}O_4Si$ *m/z* (M-MeO): 609.3400. Found: 609.3333; HRMS (EI) Calcd for $C_{39}H_{48}O_4Si$ *m/z* (M-MeOH): 608.3297. Found: 608.3322; LRMS (EI) Calcd for $C_{35}H_{39}O_4Si$ *m/z* (M-MeOH-*t*Bu): 551.3. Found: 551.2; LRMS (EI) Calcd for $C_{32}H_{41}O_4Si$ *m/z* (M-MeOH-Bn): 517.3. Found: 551.2.

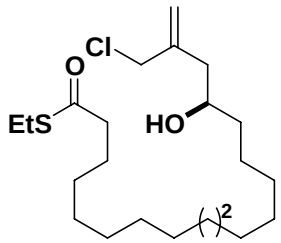


Preparation of 16-hydroxy-hexadecanethioic acid *S*-ethyl ester S47.[11] To a stirring solution of 16-hydroxyhexadecanoic acid (500 mg, 1.84 mmol, 1.00 eq) and CH_2Cl_2 (1.8 mL, 1.0 M) in a 50 mL round-bottom flask at 0 ºC was added DMAP (22.0 mg, 0.184 mmol, 0.10 eq), ethane thiol (544 µL, 7.34 mmol, 4.00 eq) and DCC (757 mg, 3.67 mmol, 2.00 eq) and the ice bath was allowed to expire over a period of 10 h. The mixture was then diluted with CH_2Cl_2 (50 mL) and filtered through a plug of silica gel. The organic phase was washed with water (2 × 30 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and silica gel (ca. 1 g) was added. The mixture was carefully concentrated under reduced pressure and the residue purified by flash chromatography on a 3.5 × 18 cm silica gel column eluting with a solvent gradient from 10% (500 mL) through 15% (500 mL) and 20% EtOAc/hexanes (500 mL). The eluant was collected in 30 mL portions and the product containing fractions (20 to 40) were combined and concentrated to give ester **S47** (508 mg, 1.61 mmol, 87%) as a white crystalline solid: R_f 0.39 (25% EtOAc/hexanes); mp 59 ºC; 500 MHz ^{1}H NMR ($CDCl_3$) δ 3.67 – 3.63 (m, 2H), 2.87 (q, *J* = 7.3 Hz, 2H), 2.54 (t, *J* = 7.3 Hz, 2H), 1.69 – 1.62 (m, 2H), 1.60 – 1.55 (m, 2H), 1.34 – 1.24 (m, 26H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 200.1, 63.3, 44.4, 33.0, 29.8 (4), 29.8 (3), 29.6, 29.5, 29.2, 26.0, 25.9, 23.4, 15.0; 125 MHz DEPT ($CDCl_3$) δ CH_3: 15.0. CH_2: 63.3, 44.4, 33.0, 29.8 (7), 29.6, 29.5, 29.2, 26.0, 25.9, 23.4. C: 200.1; IR (neat) 3228 (bs), 2917, 2849, 1692, 1462, 1404, 1058, 1024, 978, 959, 769, 728, 719, 613 cm^{-1}.



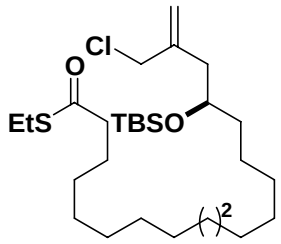
Preparation of 16-oxo-hexadecanethioic acid *S*-ethyl ester S48.

To a solution of ester **S47** (400 mg, 1.26 mmol, 1.00 eq) and CH_2Cl_2 (13 mL, 0.10 M) in a 50 mL round-bottom flask at -10 ºC was added Hünig's base (1.55 mL, 8.86 mmol, 7.00 eq), DMSO (897 µL, 12.6 mmol, 10.0 eq) and SO_3•py (805 mg, 5.06 mmol, 4.00 eq). After 2 h the mixture was added to pH 7 sodium phosphate buffer (0.05 M, 40 mL) and CH_2Cl_2 (100 mL). The organic phase was washed with water (2 × 30 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 3.5 × 15 cm silica gel column eluting with a solvent mixture of 10% EtOAc/hexanes (500 mL). The eluant was collected in 30 mL portions and the product containing fractions (5 to 10) were combined and concentrated to give aldehyde **S48** (382 mg, 1.22 mmol, 96%) as a white crystalline solid: R_f 0.86 (25% EtOAc/hexanes); mp 41 ºC; 500 MHz ^{1}H NMR ($CDCl_3$) δ 9.77 (d, *J* = 2.2 Hz, 1H), 2.87 (q, *J* = 7.3 Hz, 2H), 2.53 (t, *J* = 7.3 Hz, 2H), 2.42 (td, *J* = 7.3, 2.1 Hz, 2H), 1.68 – 1.60 (m, 4H), 1.32 – 1.23 (m, 23H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 203.2, 200.0, 44.3, 44.1, 29.8 (2), 29.8 (2), 29.6 (2), 29.5, 29.5, 29.4, 29.2, 25.9, 23.4, 22.3, 15.0; 125 MHz DEPT ($CDCl_3$) δ CH_3: 15.0. CH_2: 44.3, 44.1, 29.8 (2), 29.8 (2), 29.6 (2), 29.6, 29.5, 29.4, 29.2, 25.9, 23.4, 22.3. CH: 203.2. C: 200.0; IR (neat) 2916, 2849, 2740, 1714, 1692, 1471, 1462, 1405, 1374, 1357, 1328, 1279, 1264, 1235, 1189, 1087, 1058, 1039, 1015, 984, 961, 897, 770, 726, 719, 699, 657 cm^{-1}; HRMS (CI) Calcd for $C_{18}H_{35}O_2S$ *m/z* (M+H): 315.2358. Found: 315.2353.



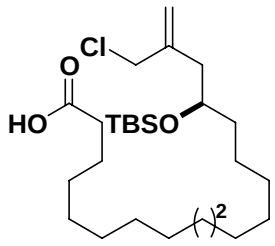
Preparation of (*R*)-18-chloromethyl-16-hydroxy-nonadec-18-enethioic acid *S*-ethyl ester S49. The crude reaction mixture was obtained by following the general procedure for the CAA using aldehyde **S48** (270 mg, 0.858 mmol, 1.00 eq) as starting material and was purified by flash chromatography using a 3.5 × 15 cm silica gel column eluting with a solvent gradient from 7.5% (1000 mL) through 10% EtOAc/hexanes (1000 mL). The eluant was collected in 30 mL portions and the product containing fractions (31 to 57) were combined and concentrated to give alcohol **S49** (288 mg, 0.711 mmol, 83%) as a clear colorless oil. The ratio of enantiomers was determined to be *er* > 97 : 3 by HPLC analysis using a Daicel Chiralcel OD-H silica column, eluting with a mobile phase of 5% 2-propanol/hexanes and a flow rate of 0.45 mL/min, which gave the retention times for the major and minor enantiomers of 13.8 and 14.9 min, respectively, detecting with a Rainin Dynamax Refractive Index Detector Model RI-1: R_f 0.52 (25% EtOAc/hexanes); R_f 0.48 (20% acetone/hexanes); $[\alpha]_D^{20}$ +0.8 (*c* = 0.990, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 5.27 (s, 1H), 5.09 (s, 1H), 4.12 (d, *J* = 11.6 Hz, 1H), 4.08 (d, *J* = 11.6 Hz, 1H), 3.82 – 3.78 (m, 1H), 2.87 (q, *J* = 7.3 Hz, 2H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.46 (dd, *J* = 14.6, 3.3 Hz, 1H), 2.21 (dd, *J* = 14.6, 9.4 Hz, 1H), 1.69 – 162 (m, 2H), 1.60 – 1.58 (m, 1H), 1.52 – 1.44 (m, 3H), 1.33 – 1.23 (m, 24H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 200.1, 142.7, 117.6, 69.8, 48.4, 44.3, 41.7, 37.6, 29.8 (4), 29.8 (3), 29.6, 29.5, 29.2, 25.9 (2), 23.4, 15.0; 125 MHz DEPT ($CDCl_3$) δ CH_3: 15.0. CH_2: 117.6, 48.4,

44.3, 41.7, 37.6, 29.8 (4), 29.8 (3), 29.6, 29.5, 29.2, 25.9 (2), 23.4. CH: 69.8. C: 200.1, 142.7; IR (neat) 3509, 3389, 3359, 3330, 2917, 2849, 1689, 1675, 1468, 1408, 1376, 1262, 1119, 1092, 1070, 1038, 1009, 959, 905, 868, 768, 748, 719 cm^{-1}; HRMS (CI) Calcd for $C_{22}H_{42}ClO_2S$ *m/z* (M+H): 405.2594. Found: 405.2601.



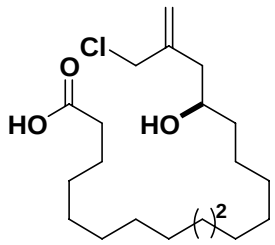
Preparation of (*R*)-16-(*tert*-butyl-dimethyl-silanyloxy)-18-chloromethyl-nonadec-18-enethioic acid *S*-ethyl ester S50. To a stirring solution of alcohol **S49** (160 mg, 0.395 mmol, 1.00 eq) and DMF (2.6 mL, 0.15 M) in a 15 mL round-bottom flask at 0 ºC was added imidazole (67.2 mg, 0.987 mmol, 2.50 eq), DMAP (8.9 mg, 79 μmol, 0.10 eq) and TBSCl (143 mg, 0.948 mmol, 2.40 eq) and the ice bath was allowed to expire over a period of 14 h. The solution was then added to a mixture of a saturated aqueous $NaHCO_3$ solution (30 mL) and CH_2Cl_2 (100 mL). The organic phase was washed with water (2 × 30 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 15 cm silica gel column eluting with a solvent mixture of 5% EtOAc/hexanes (600 mL). The eluant was collected in 30 mL portions and the product containing fractions (4 to 5) were combined and concentrated to give ester **S50** (205 mg, 0.395 mmol, quant.) as a clear colorless liquid: R_f 0.92 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +2.5 (*c* = 1.010, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 5.20 (s, 1H), 4.99 (s, 1H), 4.12 (d, *J* = 11.6 Hz, 1H), 4.06 (d, *J* = 12.0 Hz, 1H), 3.81 (dddd, *J* = 6.0, 6.0, 6.0, 5.6, Hz, 1H), 2.87 (q, *J* =

7.7 Hz, 2H), 2.53 (t, *J* = 7.7 Hz, 2H), 2.37 (dd, *J* = 13.9, 6.0 Hz, 1H), 2.29 (dd, *J* = 13.7, 6.0 Hz, 1H), 1.69 – 1.63 (m, 2H), 1.44 – 1.41 (m, 2H), 1.34 – 1.24 (m, 25H), 0.89 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 200.0, 142.8, 117.2, 71.4, 49.0, 44.4, 40.9, 37.2, 30.0, 29.9 (4), 29.8 (2), 29.7, 29.5, 29.2, 26.1 (3), 25.9, 25.5, 23.4, 18.3, 15.0, -4.2, -4.3; 125 MHz DEPT ($CDCl_3$) δ CH_3: 26.1 (3), 15.0, -4.2, -4.3. CH_2: 117.2, 49.0, 44.4, 40.9, 37.2, 30.0, 29.9 (4), 29.8 (2), 29.6, 29.5, 29.2, 25.9, 25.5, 23.4. CH: 71.3. C: 200.0, 142.8, 18.3; IR (neat) 2928, 2855, 1732, 1694, 1645, 1471, 1463, 1435, 1412, 1388, 1372, 1361, 1256, 1059, 1005, 968, 939, 908, 836, 809, 775, 752, 722, 665 cm^{-1}; HRMS (CI) Calcd for $C_{28}H_{56}ClO_2SSi$ *m/z* (M+H): 519.3459. Found: 519.3453; LRMS (CI) Calcd for $C_{24}H_{49}O_2SSi$ *m/z* (M-C_4H_6Cl): 429.3. Found: 429.2; LRMS (CI) Calcd for $C_{22}H_{39}OS$ *m/z* (M-Cl-TBSO-H): 351.3. Found: 351.1.



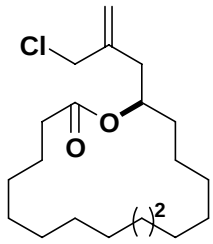
Preparation of (*R*)-17-(*tert*-butyl-dimethyl-silanyloxy)-19-chloromethyl-icos-19-en-2-one S51. To a stirring solution of ester **S50** (450 mg, 0.866 mmol, 1.00 eq) and a 4:1 mixture of THF and water (84 mL, 0.01 M) in a 500 mL round-bottom flask at 0 ºC was added $LiOH•H_2O$ (354 mg, 8.44 mmol, 9.7 eq) and H_2O_2 (30% solution, 1.91 mL, 16.9 mmol, 19.5 eq). After 30 min the mixture was diluted with Et_2O (150 mL) and brine (50 mL). An aqueous solution of HCl (2 M) was added dropwise until reaching pH 2. The aqueous phase was extracted with Et_2O (2 × 50 mL) and the combined organic phase was washed with brine (10 mL), dried over Na_2SO_4, filtered and

concentrated under reduced pressure. The residue was purified by flash chromatography on a 2.5 × 18 cm silica gel column eluting with a solvent gradient from 5:95 EtOAc/hexanes (300 mL), 1:15:84 MeOH/EtOAc/hexanes (300 mL) through 2:15:83 MeOH/EtOAc/hexanes (300 mL). The eluant was collected in 30 mL portions and the product containing fractions (12 to 29) were combined and concentrated to give acid **S51** (396 mg, 0.832 mmol, 96%) as a clear colorless oil: R_f 0.69 (10% MeOH/CH_2Cl_2); $[\alpha]_D^{20}$ +1.5 (*c* = 1.194, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 5.20 (s, 1H), 4.99 (s, 1H), 4.11 (d, *J* = 11.6 Hz, 1H), 4.06 (d, *J* = 11.6 Hz, 1H), 3.82 (dddd, *J* = 6.0, 6.0, 6.0, 5.7 Hz, 1H), 2.39 – 2.34 (m, 3H), 2.30 (dd, *J* = 14.2, 6.0 Hz, 1H), 1.67 – 1.61 (m, 2H), 1.45 – 1.41 (m, 2H), 1.38 – 1.23 (m, 22H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), $C_1OO\mathit{H}$ not detected; 125 MHz ^{13}C NMR ($CDCl_3$) δ 179.4, 142.9, 117.2, 71.4, 49.0, 41.0, 37.2, 34.2, 30.0 (2), 29.9 (4), 29.7, 29.5, 29.3, 26.1 (3), 25.5, 25.0, 23.0, 18.3, -4.2, -4.3; 125 MHz DEPT ($CDCl_3$) δ CH_3: 26.1 (3), -4.2, -4.3. CH_2: 117.2, 49.0, 41.0, 37.2, 34.2, 30.0 (2), 29.9 (4), 29.7, 29.5, 29.3, 25.5, 25.0, 23.0. CH: 71.4. C: 179.4, 142.9, 18.3; IR (neat) 3081, 2926, 2855, 2737, 2709, 2681, 1738, 1712, 1463, 1447, 1435, 1412, 1387, 1361, 1256, 1174, 1093, 1076, 1006, 939, 908, 836, 809, 775, 751, 663 cm^{-1}; HRMS (CI) Calcd for $C_{26}H_{52}ClO_3Si$ *m/z* (M+H): 475.3374. Found: 475.3367; LRMS (CI) Calcd for $C_{22}H_{45}O_3Si$ *m/z* (M-C_4H_6Cl): 385.3. Found: 385.2; LRMS (CI) Calcd for $C_{20}H_{35}O_2$ *m/z* (M-Cl-TBSO-H): 307.3. Found: 307.2.



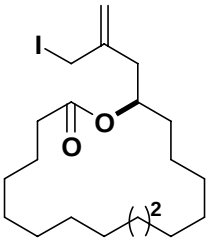
Preparation of (*R*)-18-chloromethyl-16-hydroxy-nonadec-18-enoic acid S52. To a 100 mL round-bottom flask containing acid **S51** (120 mg, 0.253 mmol, 1.00 eq) at room temperature was added a 3:1:1 solution of AcOH/THF/H_2O (26 mL, 0.01 M). After 36 h the solution was diluted with Et_2O (300 mL) and hexanes (30 mL), and the organic phase was washed with brine (2 × 15 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on a 1.5 × 18 cm silica gel column eluting with a solvent gradient from 1:15:84 MeOH/EtOAc/hexanes (200 mL) through 2:15:83 MeOH/EtOAc/hexanes (100 mL). The eluant was collected in 30 mL portions and the product containing fractions (6 to 12) were combined and concentrated to give *seco*-acid **S52** (83.3 mg, 0.231 mmol, 91%) as a white solid: R_f 0.68 (10% MeOH/CH_2Cl_2); mp 42 ºC; $[\alpha]_D^{20}$ +2.4 (*c* = 0.420, C_6H_6); 500 MHz ^{1}H NMR ($CDCl_3$) δ 5.28 (s, 1H), 5.09 (s, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 4.08 (d, *J* = 12.0 Hz, 1H), 3.81 (dddd, *J* = 12.0, 6.0, 3.4, 3.4 Hz, 1H), 2.46 (dd, *J* = 14.6, 3.4 Hz, 1H), 2.36 (d, *J* = 10.7 Hz, 1H), 2.35 (d, *J* = 7.7 Hz, 1H), 2.22 (dd, *J* = 14.6, 9.4 Hz, 1H), 1.67 – 1.61 (m, 2H), 1.52 – 1.44 (m, 3H), 1.37 – 1.27 (m, 21H), $C_1OO\mathit{H}$ and $C_{16}O\mathit{H}$ not observed; 125 MHz ^{13}C NMR ($CDCl_3$) δ 178.9 (bs), 142.7, 117.6, 69.9, 48.4, 41.7, 37.6, 34.0, 29.8, 29.8 (5), 29.7, 29.6, 29.4, 29.3, 25.9, 24.9; 125 MHz DEPT ($CDCl_3$) δ CH_2: 117.6, 48.5, 41.7, 37.6, 34.1, 29.8 (6), 29.7, 29.6, 29.4, 29.3, 25.9, 24.9. CH: 69.9. C: 178.9, 142.7; 500 MHz ^{1}H NMR (C_6D_6) δ 5.29 (s, 1H), 5.15 (s, 1H), 4.13 (d, *J* = 11.6 Hz, 1H), 4.08 (d, *J* = 12.0 Hz, 1H), 3.90 – 3.86 (m, 1H), 2.56 (dd, *J* = 14.4,

3.2 Hz, 1H), 2.45 (t, *J* = 6.4 Hz, 2H), 2.36 (dd, *J* = 14.6, 9.0 Hz, 1H), 1.88 – 1.81 (m, 2H), 1.79 - 1.50 (m, 24H), $C_1OO\mathit{H}$ and $C_{16}O\mathit{H}$ not observed; 125 MHz ^{13}C NMR (C_6D_6) δ 179.8, 143.4, 128.7, 117.1, 70.1, 48.7, 42.1, 38.1, 34.5, 30.5 (5), 30.3, 30.1, 29.9, 29.7, 26.4, 25.4; 125 MHz DEPT (C_6D_6) δ CH_2: 128.7, 117.1, 48.7, 42.1, 38.1, 34.5, 30.4 (5), 30.3, 30.1, 29.9, 29.7, 26.4, 25.4. CH: 70.1. C: 179.8, 143.4; IR (neat) 3347, 3243, 2917, 2849, 2673 (bs), 1704, 1470, 1434, 1411, 1338, 1259, 1204, 1121, 1089, 1068, 923, 870, 857, 753, 719, 683 cm^{-1}; HRMS (CI) Calcd for $C_{20}H_{38}ClO_3$ *m/z* (M+H): 361.2509. Found: 361.2494.

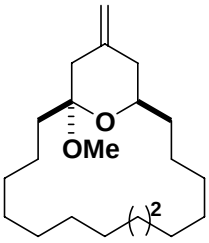


Preparation of (*R*)-17-(2-chloromethyl-allyl)-oxacycloheptadecan-2-one S53. To a stirring solution of *seco*-acid **S52** (38.8 mg, 107 μmol, 1.00 eq) and THF (3.6 mL, 0.03 M) in a 50 mL pear-shaped flask at 0 ºC were added Et_3N (39.0 μL, 0.279 mmol, 2.60 eq) and 2,4,5-trichlorobenzoyl chloride (22.0 μL, 140 μmol, 1.30 eq). After 5 min the mixture was warmed to room temperature. After 3 h, TLC analysis showed consumption of the *seco*-acid starting material (mixed anhydride R_f 0.23 (25% EtOAc/hexanes) and a 3:1 mixture of toluene and THF (25 mL) was added. The mixture was transferred into a gas-tight glass-syringe and diluted with a 3:1 mixture of toluene and THF to a total volume of 50 mL. The mixture was added by syringe pump over a period of 12 h to a solution of DMAP (263 mg, 2.15 mmol, 20.0 eq) and toluene (72.0 mL, 1.50 mM) in a 500 mL round-bottom flask at 45 ºC; during the addition the tip of the

hypodermic needle was adjusted to barely maintain contact with the surface of the reaction mixture. After the addition was complete the residue was washed into the reaction mixture with a 3:1 mixture of toluene and THF (20 mL), and the temperature maintained at 45 ºC for an additional 2 h. The organic phase was then diluted with 15% EtOAc/hexanes (300 mL), washed with water (3 × 100 mL) and brine (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on a 1.5 × 18 cm silica gel column eluting with a solvent gradient from 1% (100 mL) through 5% EtOAc/hexanes (100 mL). The eluant was collected in 10 mL portions and the product containing fractions (5 to 10) were combined and concentrated to give macrolactone **S53** (33.9 mg, 98.9 mmol, 92%) as a clear colorless oil: R_f 0.92 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +18.3 (*c* = 1.480, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 5.17 (s, 1H), 5.14 – 5.09 (m, 1H), 4.99 (s, 1H), 4.16 (d, *J* = 12.0 Hz, 1H), 4.03 (d, *J* = 12.0 Hz, 1H), 2.48 (dd, *J* = 14.6, 4.7 Hz, 1H), 2.37 (dd, *J* = 15.0, 8.6 Hz, 1H), 2.33 – 2.25 (m, 2H), 1.74 – 1.68 (m, 1H), 1.59 – 1.55 (m, 4H), 1.40 – 1.23 (m, 21H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 173.8, 141.8, 117.6, 71.7, 48.3, 38.9, 34.7 (2), 28.5, 28.5, 28.4, 27.9, 27.8, 27.2, 27.1 (2), 27.1, 26.8, 25.1, 25.0; 125 MHz DEPT ($CDCl_3$) δ CH_2: 117.6, 48.2, 38.9, 34.7 (2), 28.5, 28.4, 28.4, 27.9, 27.8, 27.2, 27.1 (2), 27.0, 26.8, 25.1, 25.0. CH: 71.7. C: 173.8, 141.8; IR (neat) 2928, 2857, 1732, 1646, 1580, 1459, 1372, 1251, 1181, 1109, 1061, 912, 752, 678 cm^{-1}; HRMS (CI) Calcd for $C_{20}H_{36}ClO_2$ *m/z* (M+H): 343.2404. Found: 343.2408; LRMS (CI) Calcd for $C_{20}H_{35}O_2$ *m/z* (M-Cl): 307.3. Found: 307.2.



Preparation of (*R*)-17-(2-iodomethyl-allyl)-oxacycloheptadecan-2-one S54. The crude reaction mixture was obtained by following the general procedure for the Finkelstein reaction using macrolactone **S53** (14.0 mg, 40.8 μmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent gradient from 2.5% (50 mL) through 5% EtOAc/hexanes (150 mL). The eluant was collected in 10 mL portions and the product containing fractions (3 to 6) were combined and concentrated to give iodide **S54** (17.2 mg, 39.6 μmol, 97%) as a clear colorless oil: R_f 0.91 (25% EtOAc/hexanes); $[\alpha]_D^{20}$ +34.6 (*c* = 0.905, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 5.28 (s, 1H), 5.12 – 5.07 (m, 1H), 4.94 (s, 1H), 4.03 (d, *J* = 9.4 Hz, 1H), 3.93 (d, *J* = 9.4 Hz, 1H), 2.55 (dd, *J* = 14.6, 4.7 Hz, 1H), 2.40 (dd, *J* = 14.6, 8.6 Hz, 1H), 2.35 – 2.25 (m, 2H), 1.74 – 1.68 (m, 1H), 1.59 – 1.55 (m, 4H), 1.40 – 1.24 (m, 21H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 173.8, 143.2, 116.8, 71.8, 39.9, 34.7, 34.6, 28.5, 28.4, 28.4, 27.9, 27.8, 27.2, 27.1 (2), 27.1, 26.8, 25.1, 25.0, 10.7; 125 MHz DEPT ($CDCl_3$) δ CH_2: 116.8, 39.9, 34.7, 34.7, 28.5, 28.5, 28.4, 27.9, 27.8, 27.2, 27.1 (2), 27.1, 26.8, 25.1, 25.0, 10.5. CH: 71.8. C: 173.8, 143.2; IR (neat) 2927, 2856, 1732, 1460, 1440, 1372, 1349, 1238, 1160, 1111, 1061, 906, 717 cm^{-1}; HRMS (CI) Calcd for $C_{20}H_{36}IO_2$ *m/z* (M+H): 435.1760. Found: 435.1777; LRMS (CI) Calcd for $C_{20}H_{36}O_2$ *m/z* (M+H-I): 307.3. Found: 307.2



Preparation of (1*S*,16*R*)-1-methoxy-18-methylene-20-oxa-bicyclo[14.3.1]icosane S55. The crude reaction mixture was obtained by following the general procedure for the SmI_2 promoted cyclization using iodide **S54** (11.2 mg, 25.8 μmol, 1.00 eq) as starting material and was purified by flash chromatography using a 1.5 × 18 cm silica gel column eluting with a solvent mixture of 2.5% EtOAc/hexanes (150 mL). The eluant was collected in 10 mL portions and the product containing fractions (3 to 4) were combined and concentrated to give 2-methoxypyran **S55** (7.3 mg, 22.6 μmol, 88%) as a clear colorless and viscous oil: $[\alpha]_D^{20}$ -6.3 (*c* = 0.410, $CHCl_3$); R_f 0.82 (25% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 4.79 (d, *J* = 2.2 Hz, 1H), 4.75 (d, *J* = 1.7 Hz, 1H), 3.61 – 3.55 (m, 1H), 3.19 (s, 3H), 2.31 – 2.27 (m, 1H), 2.22 – 2.18 (m, 1H), 2.14 – 2.11 (m, 1H), 2.01 – 1.94 (m, 1H), 1.85 – 1.80 (m, 1H), 1.52 – 1.28 (m, 27H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 143.1, 109.7, 100.8, 71.2, 48.0, 41.2, 39.7, 35.9, 35.6, 28.6, 28.4, 28.3, 28.0, 27.9, 27.8, 27.6, 27.6, 27.4, 27.3, 24.4, 23.2; 125 MHz DEPT ($CDCl_3$) δ CH_3: 48.0. CH_2: 109.7, 41.2, 39.6, 35.9, 35.5, 28.5, 28.3, 28.2, 27.9, 27.9, 27.7, 27.6, 27.5, 27.4, 27.3, 24.3, 23.1. CH: 71.2. C: 143.1, 100.8; IR (neat) 2927, 2856, 1737, 1682, 1657, 1645, 1581, 1459, 1380, 1351, 1327, 1229, 1218, 1164, 1140, 1086, 1051, 1011, 886 cm^{-1}; HRMS (EI) Calcd for $C_{21}H_{38}O_2$ m/z (M): 322.2872. Found: 322.2860. LRMS (EI) Calcd for $C_{20}H_{35}O$ m/z (M-MeO): 291.3. Found: 291.3. LRMS (EI) Calcd for $C_{20}H_{34}O$ m/z (M-MeOH): 290.3. Found: 290.3.

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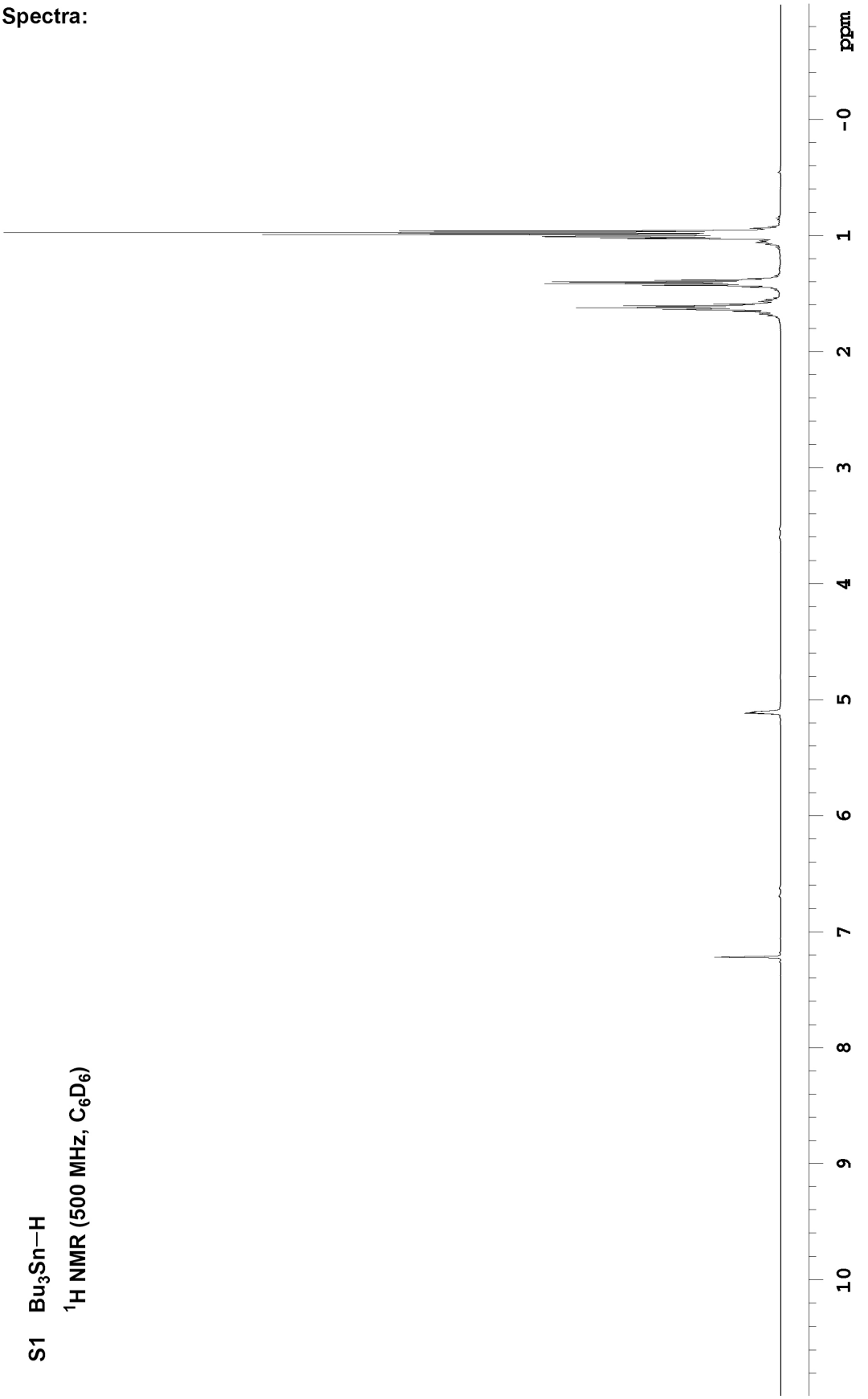
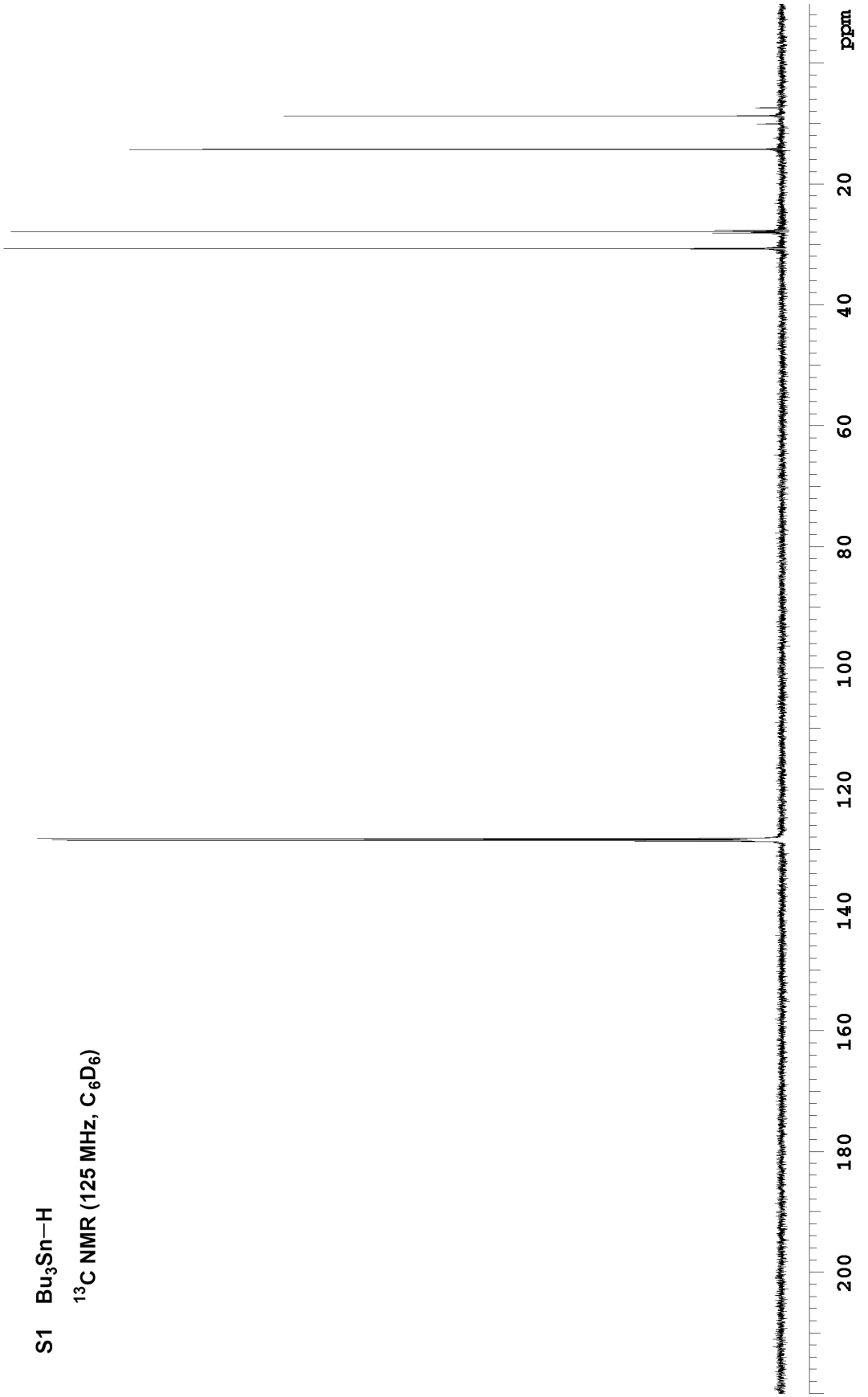
NMR Spectra:



S1 Bu_3Sn-H

^1H NMR (500 MHz, C_6D_6)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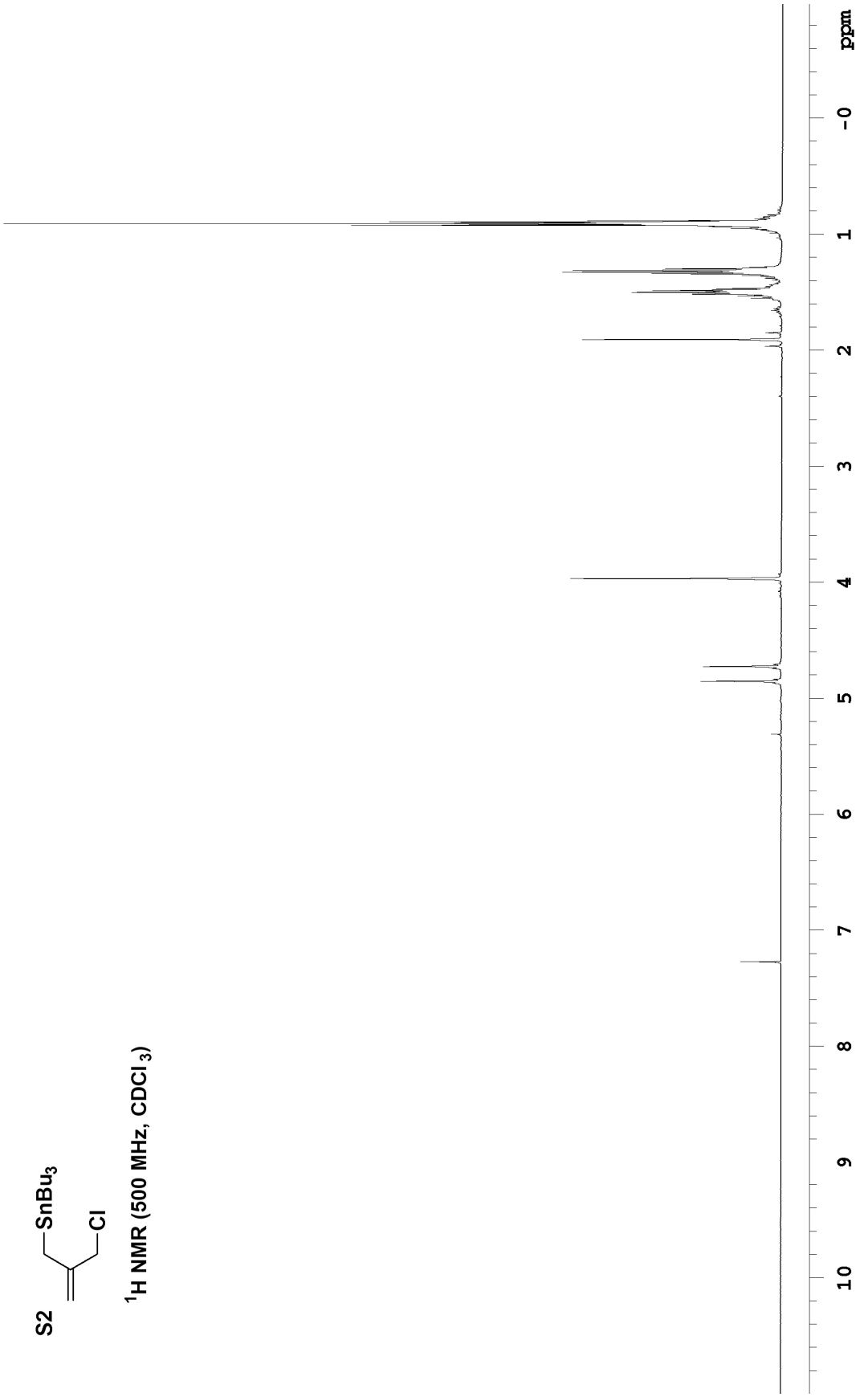
160
140
120
100
80
60
40
20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SnBu3
Cl
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ppm
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8
7
6
5
4
3
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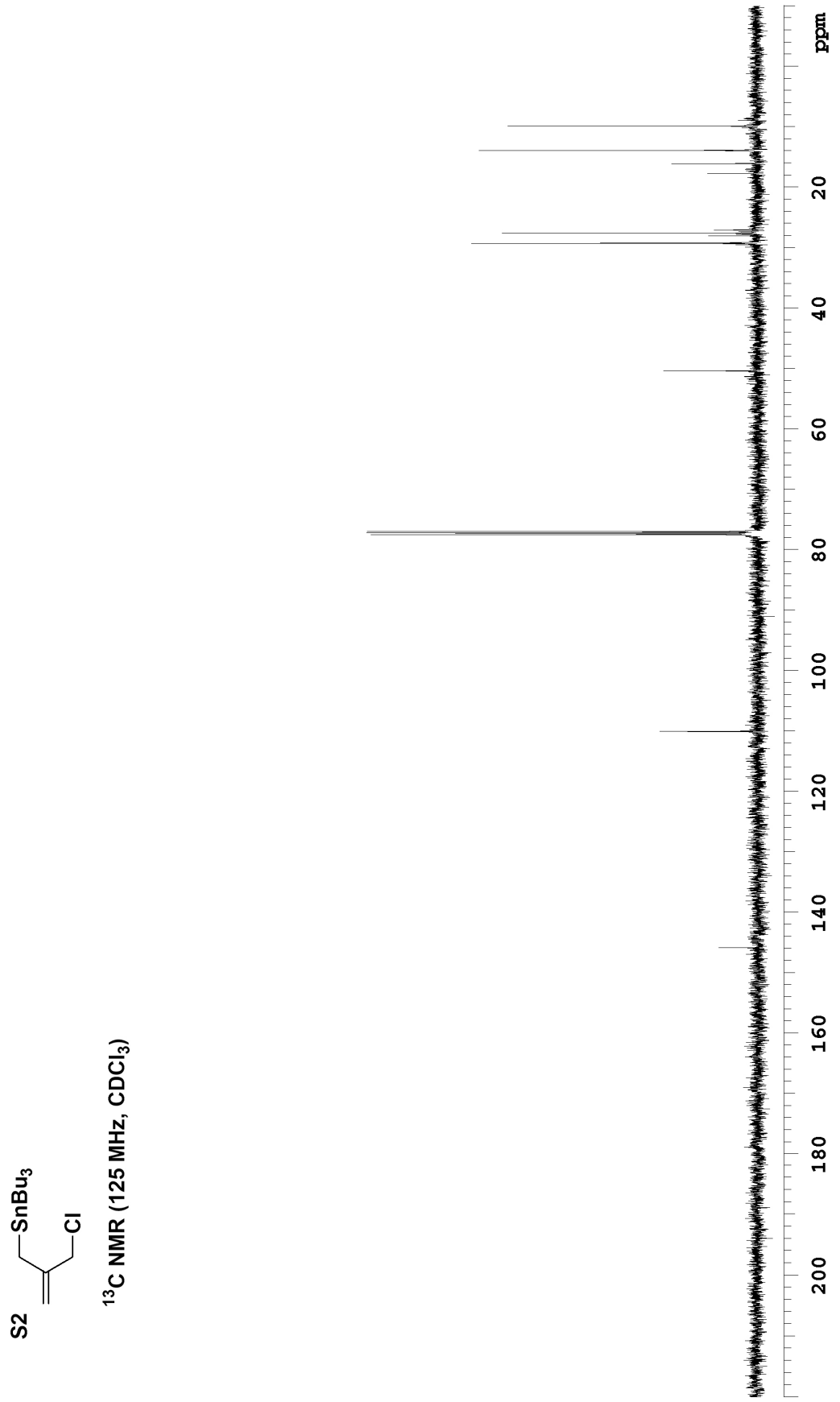
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Cl
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ppm
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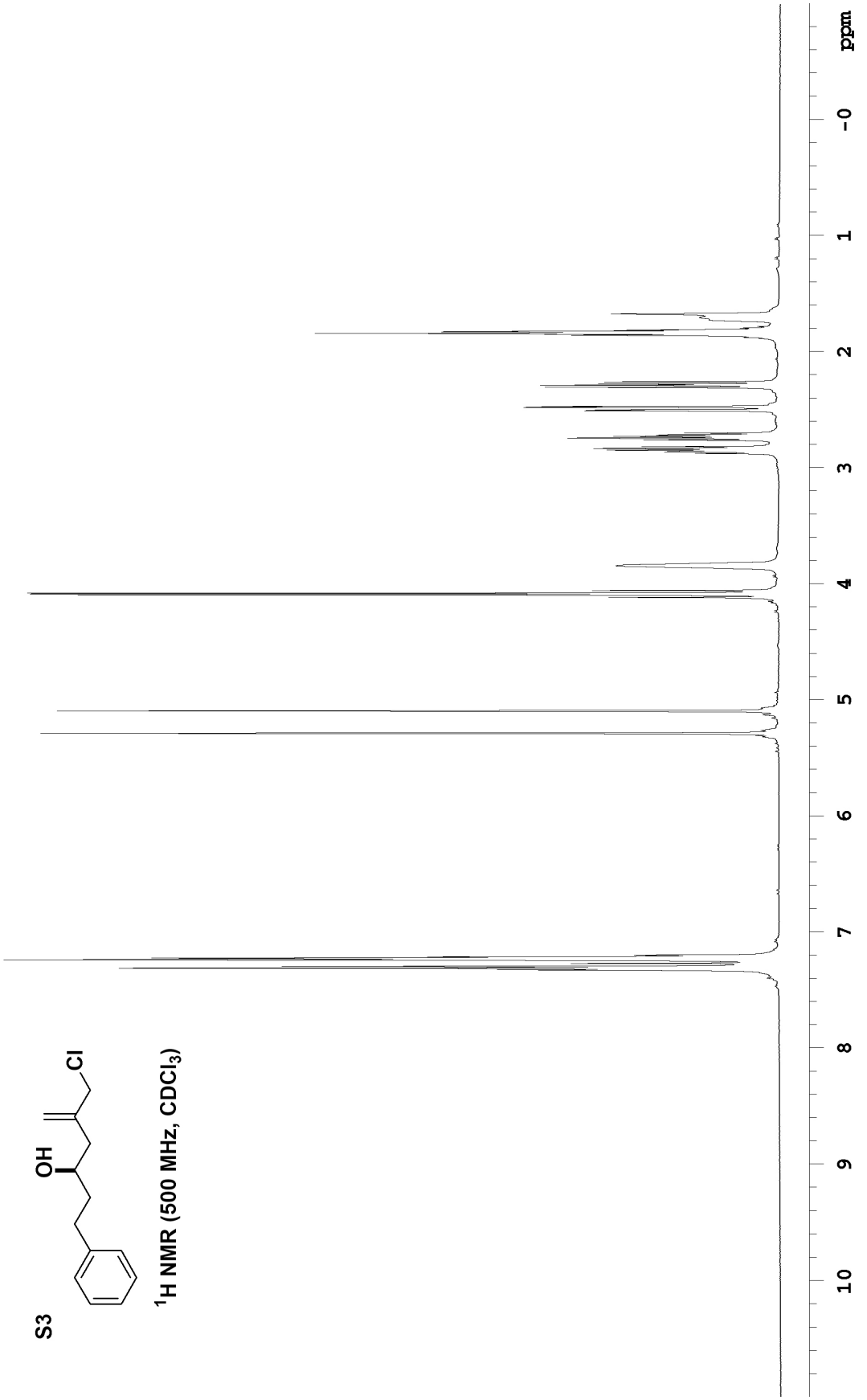
180
160
140
120
100
80
60
40
20


ppm
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9
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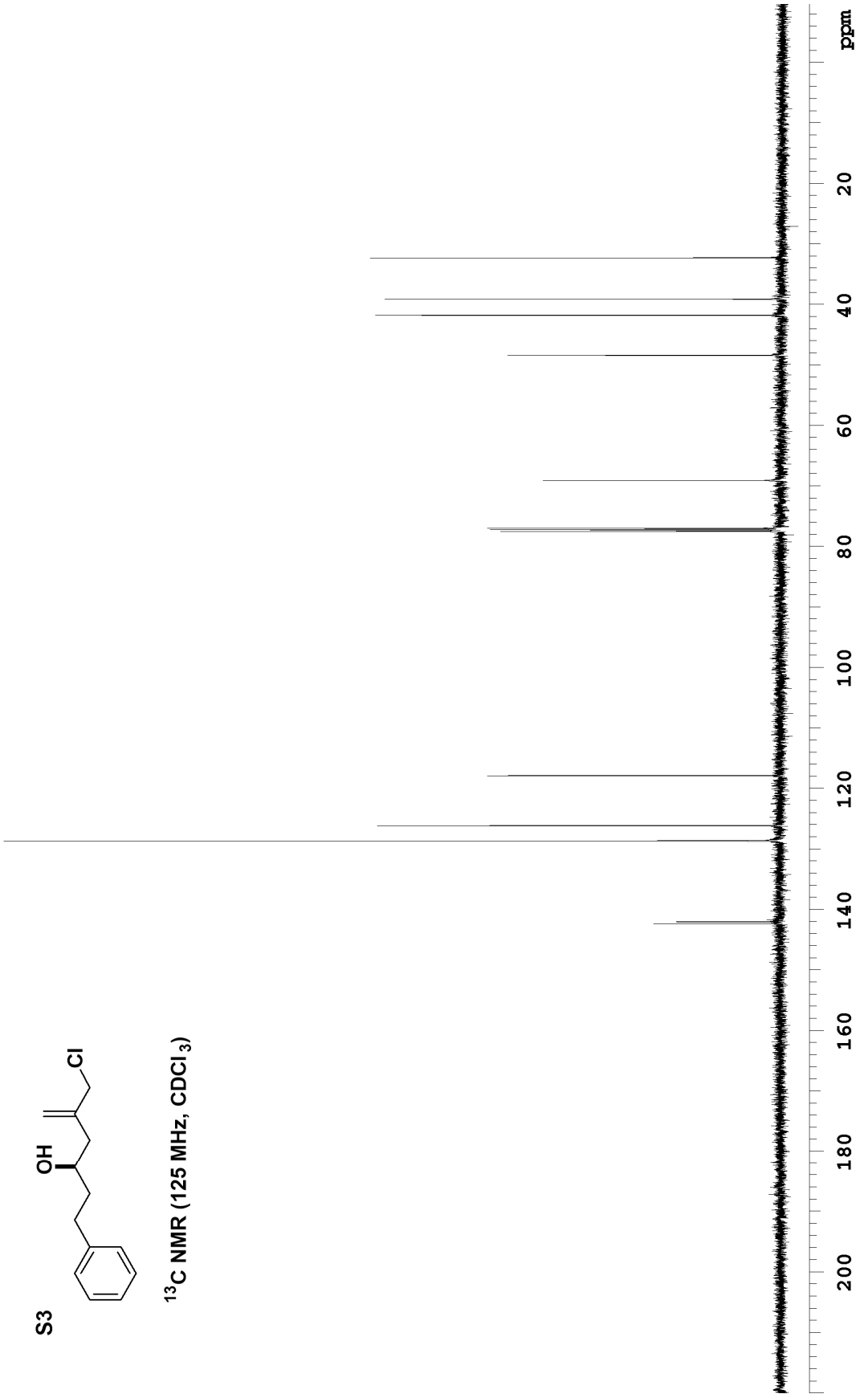
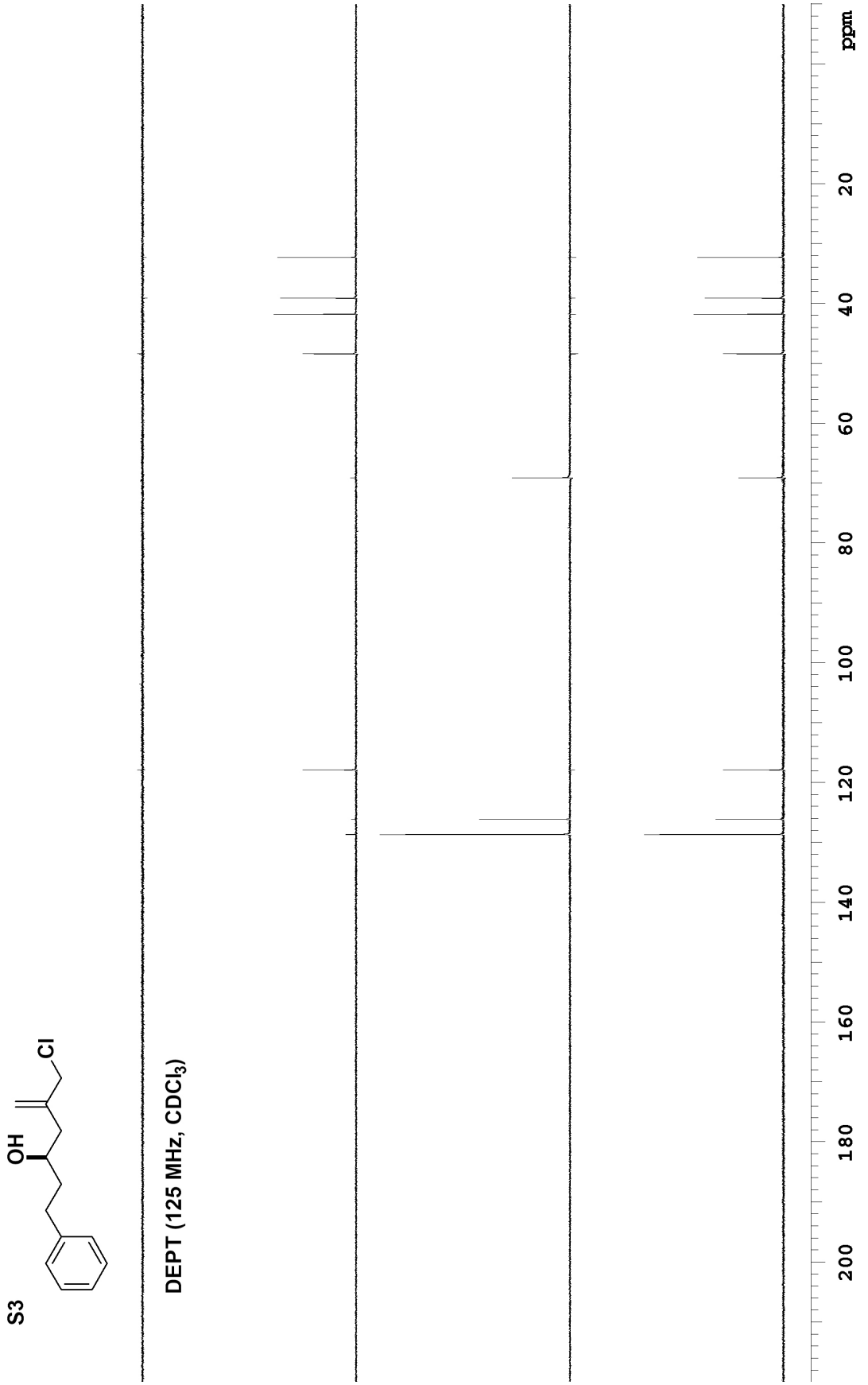
7
6
5
4
3
2
1
-0
OH
Cl
S3
^{1}H NMR (500 MHz, $CDCl_3$)



S3

^{13}C NMR (125 MHz, $CDCl_3$)


S3
OH
Cl
DEPT (125 MHz, CDCl3)
ppm
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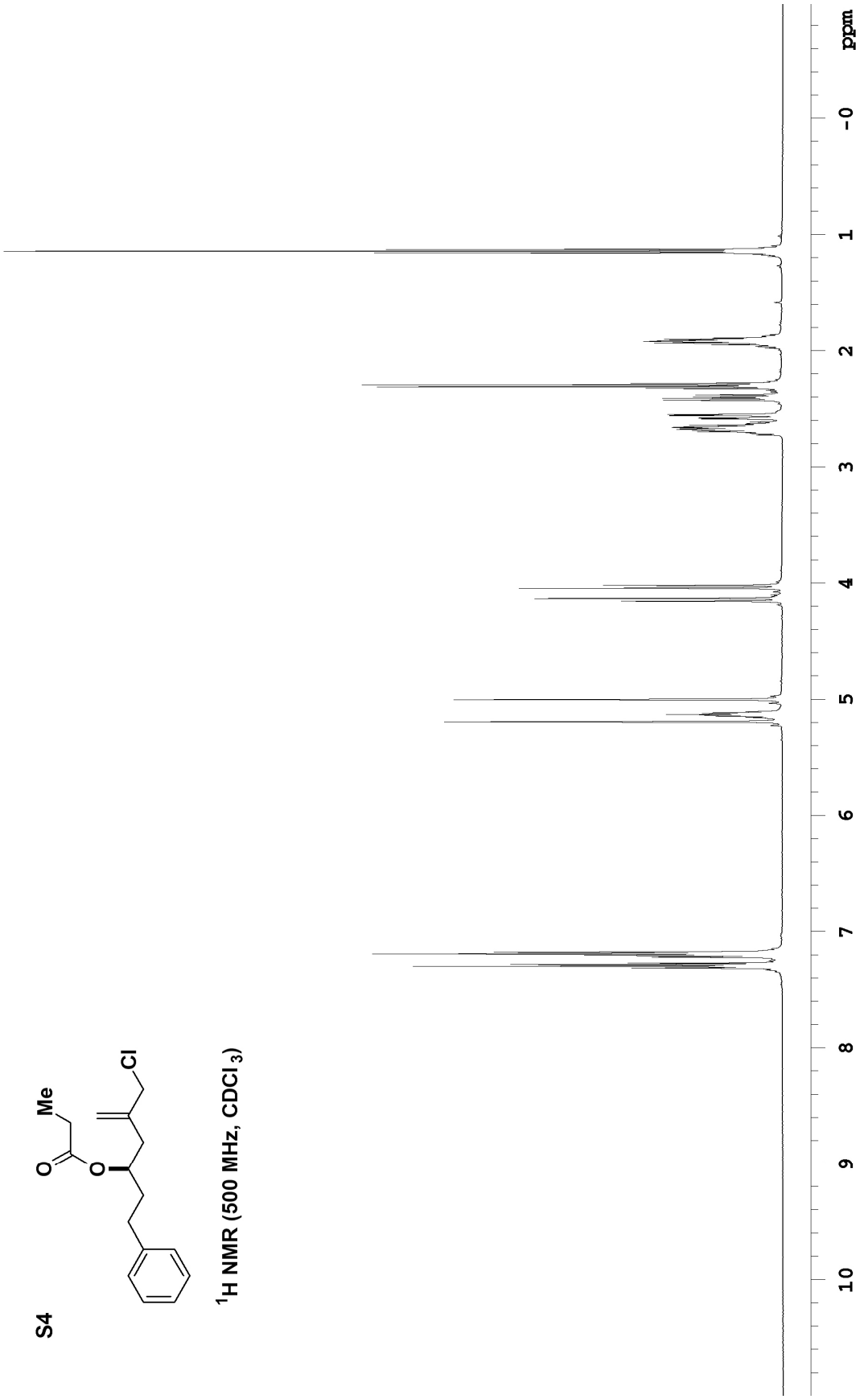
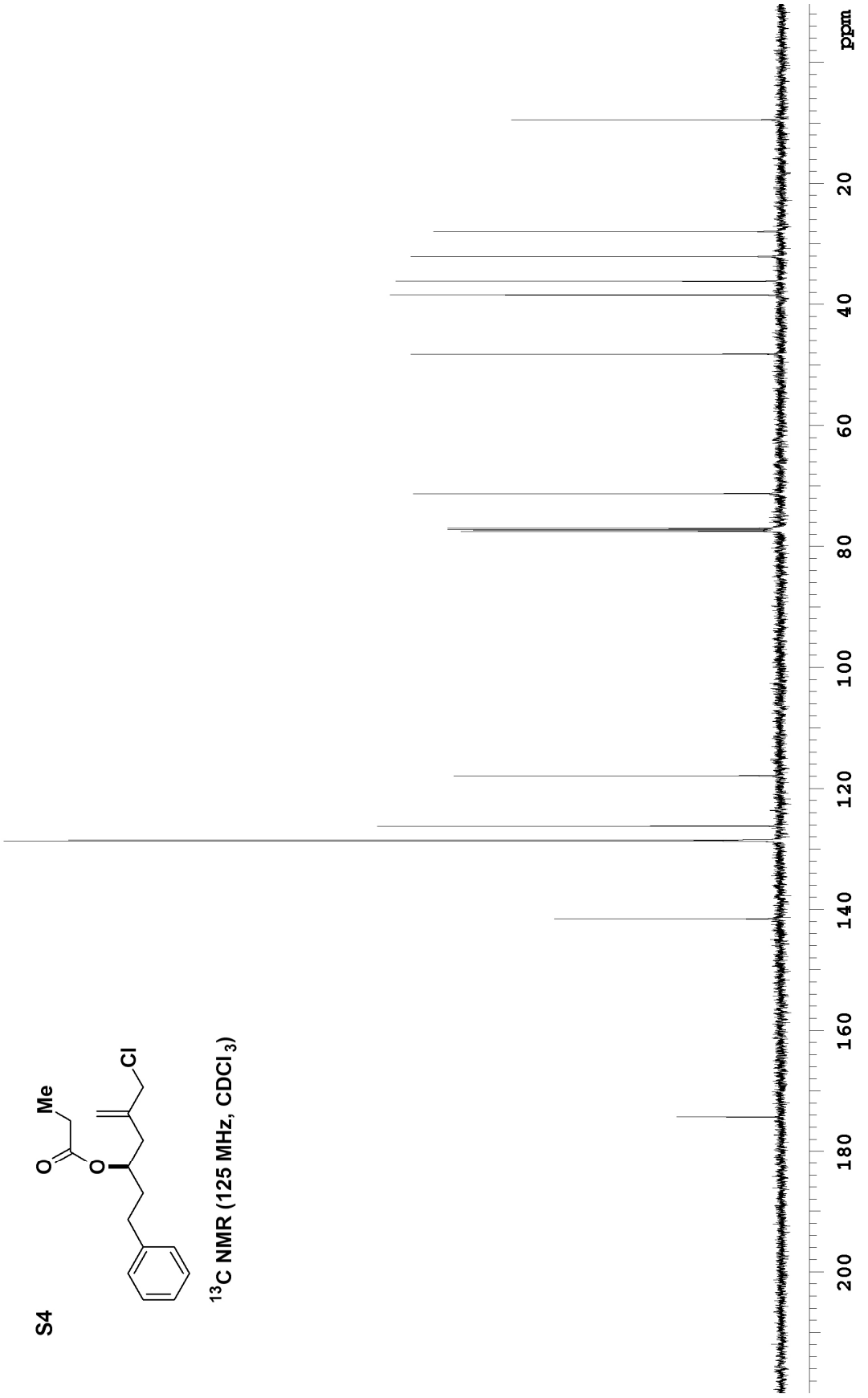
180
160
140
120
100
80
60
40
20



S4

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


S4
Me
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O
Cl
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ppm
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160
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80
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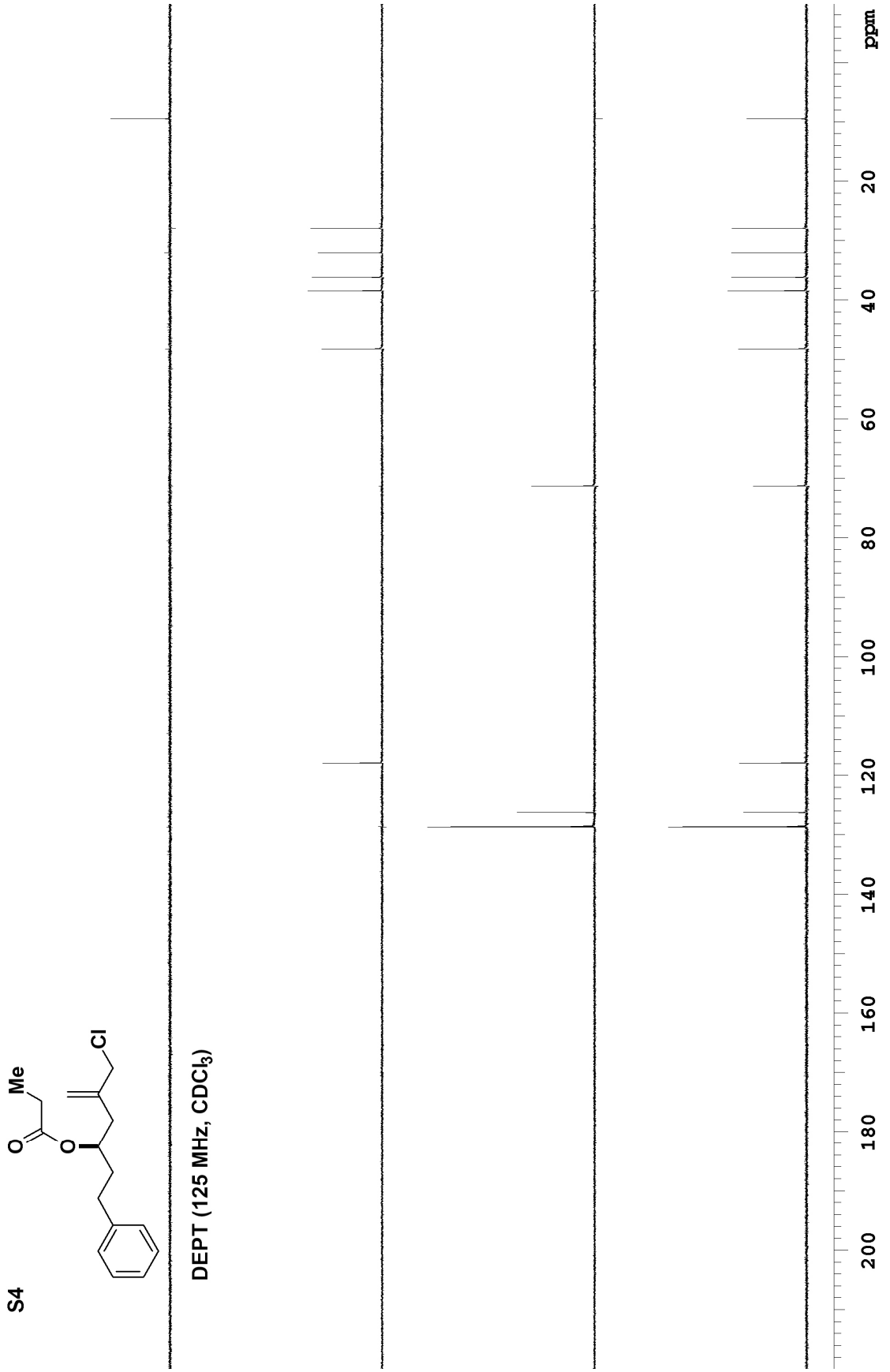
40
20


S4
Me
O
O
Cl
DEPT (125 MHz, CDCl3)
ppm
200
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160
140
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100
80
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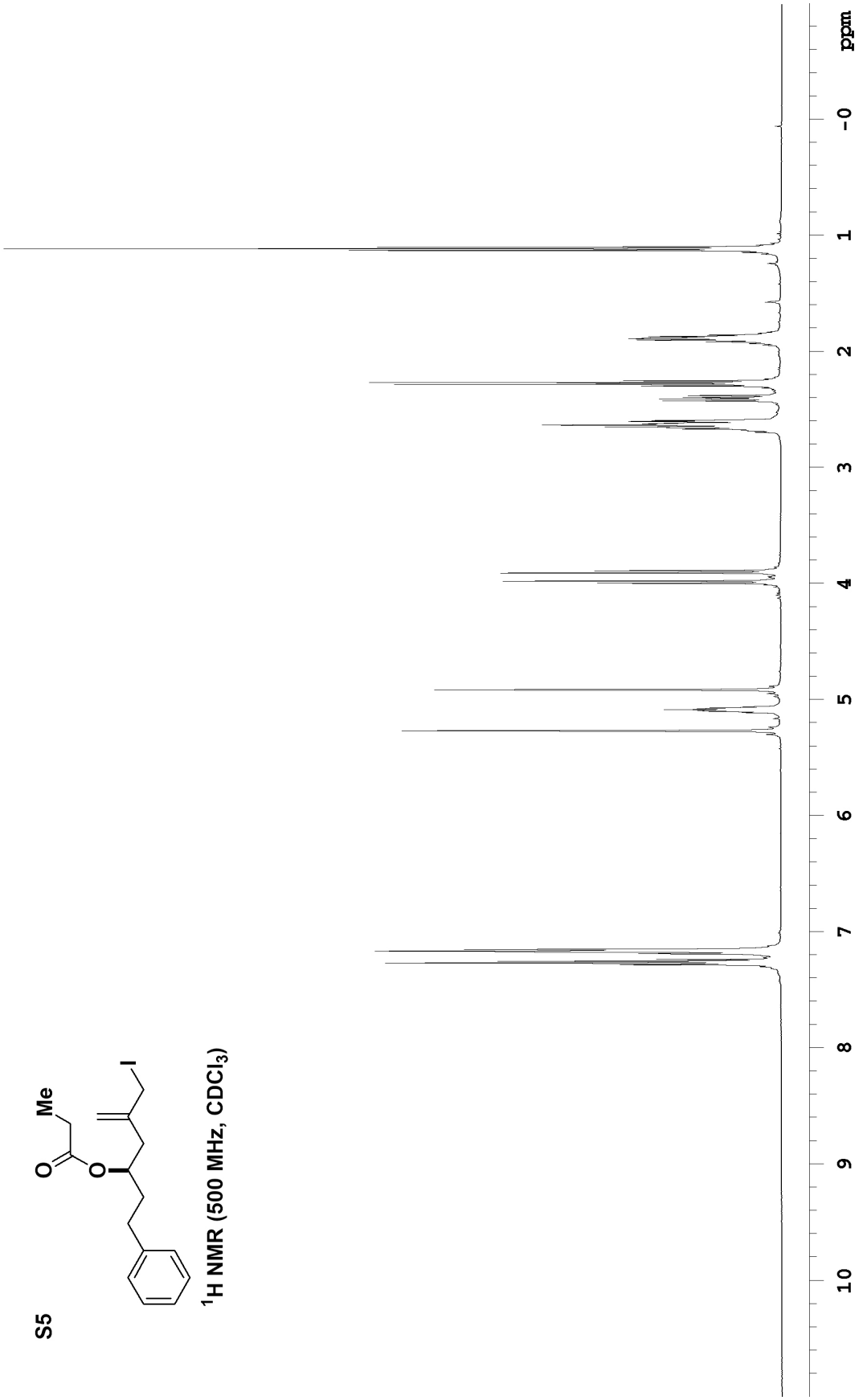
S5
Me
O
O
I
^{1}H NMR (500 MHz, CDCl$_3$)
ppm
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9
8
7
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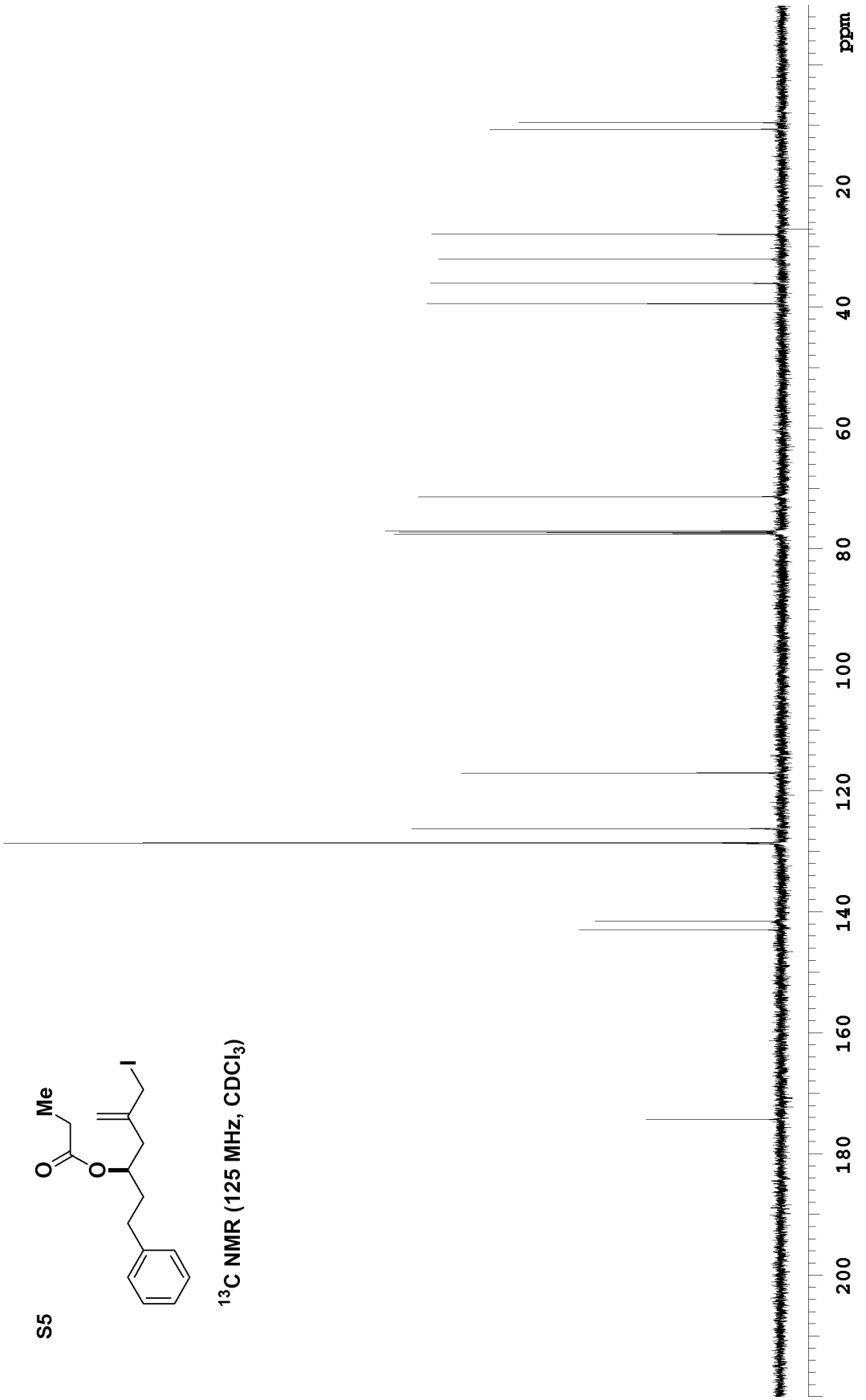
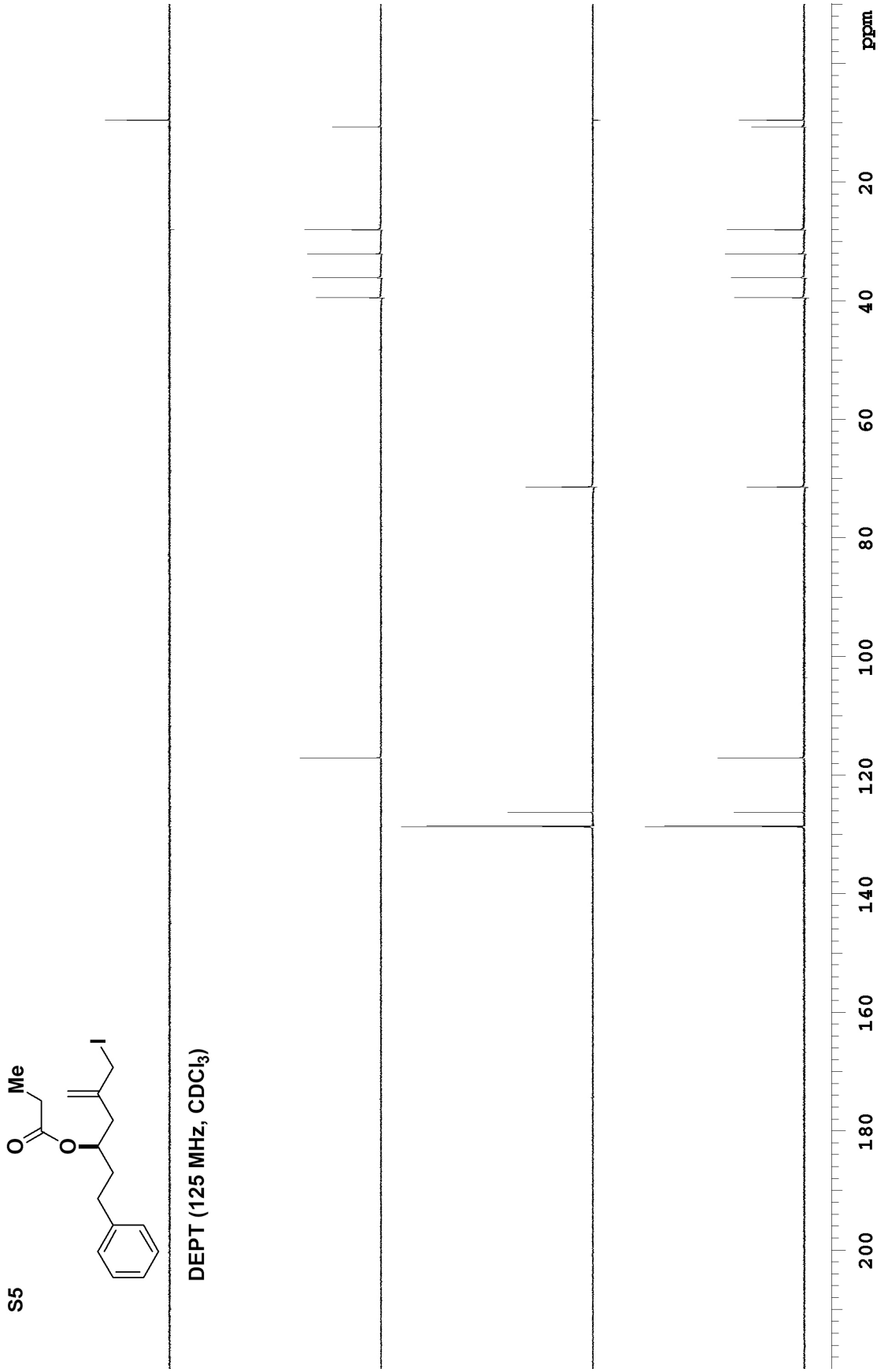
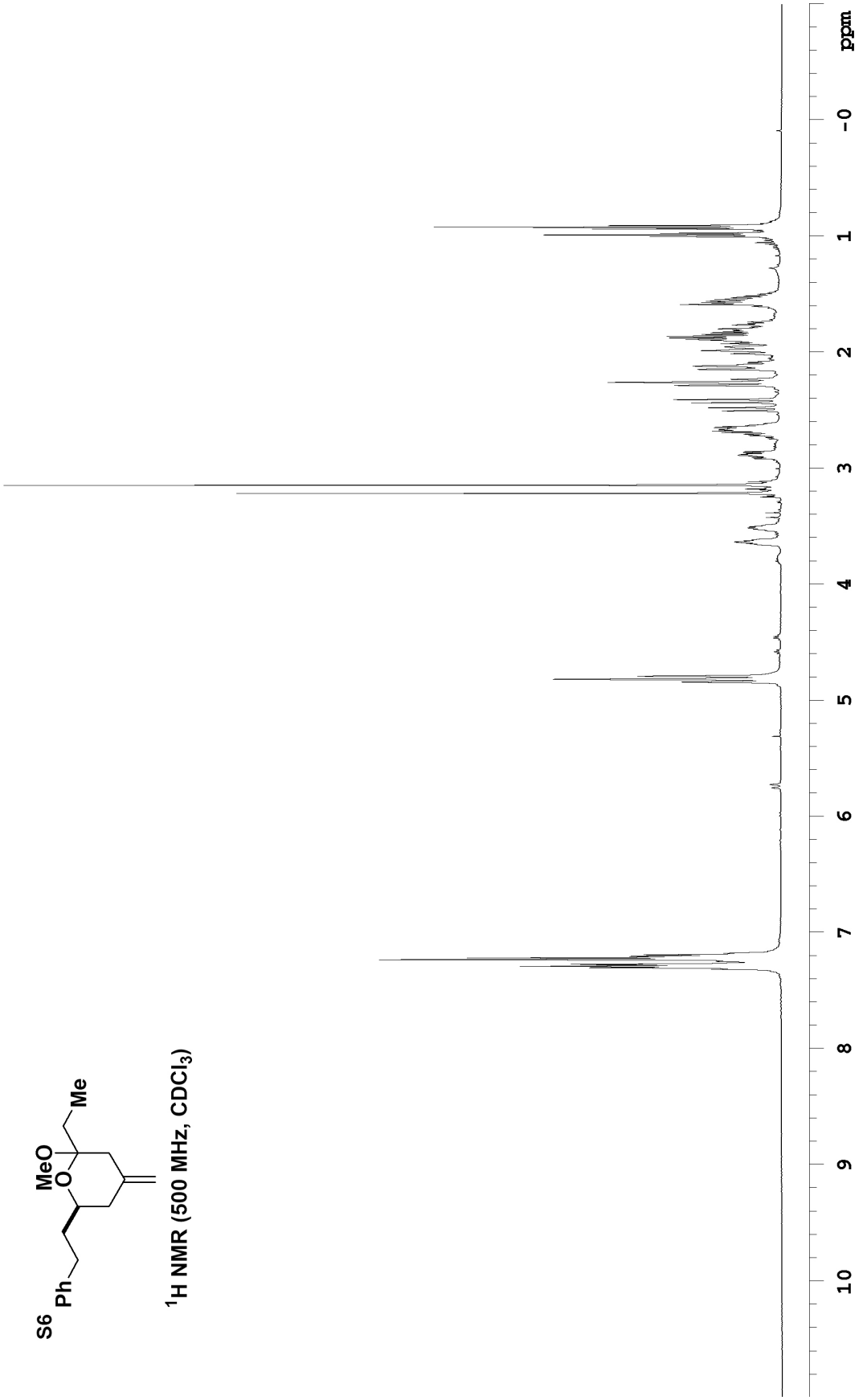
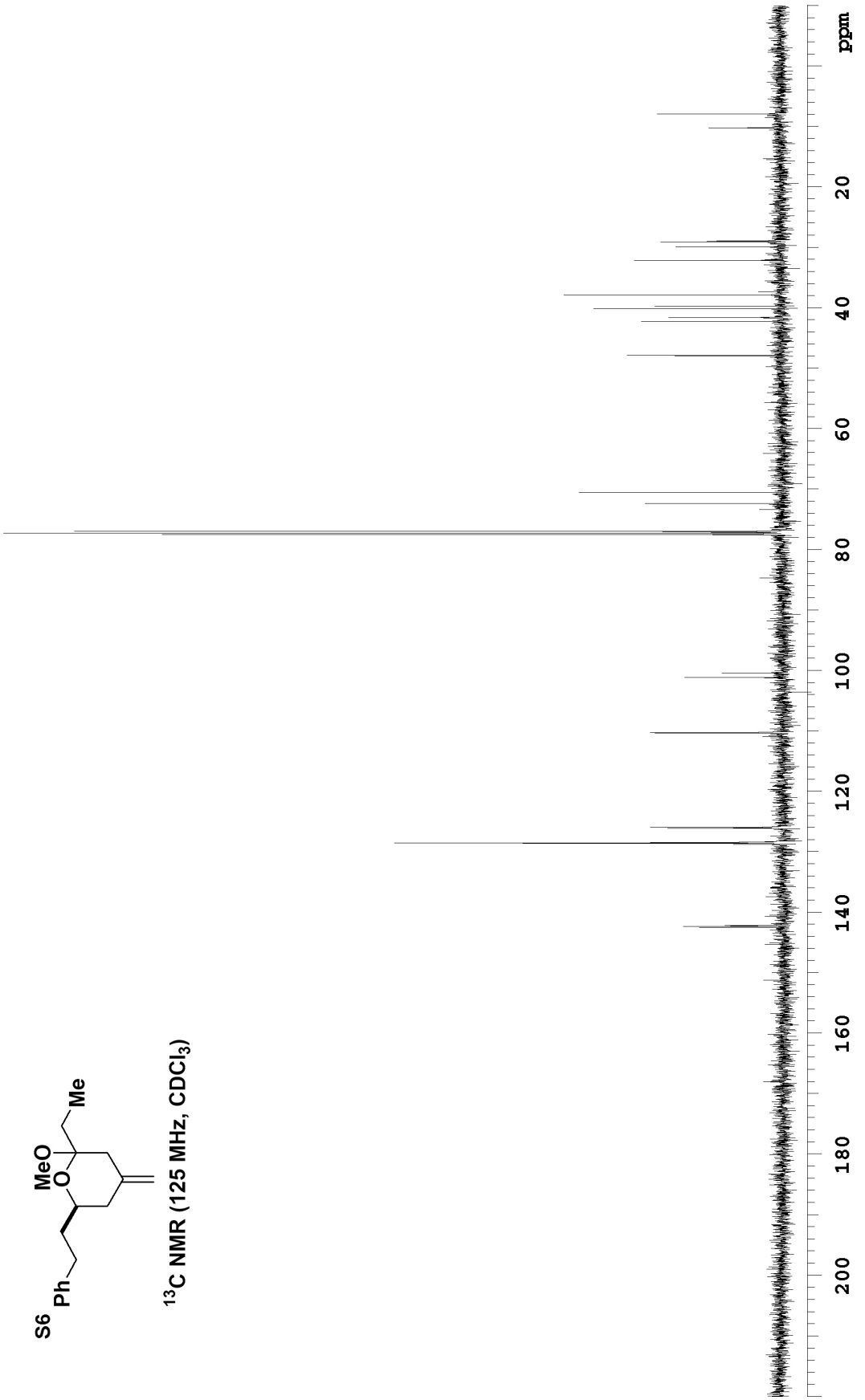
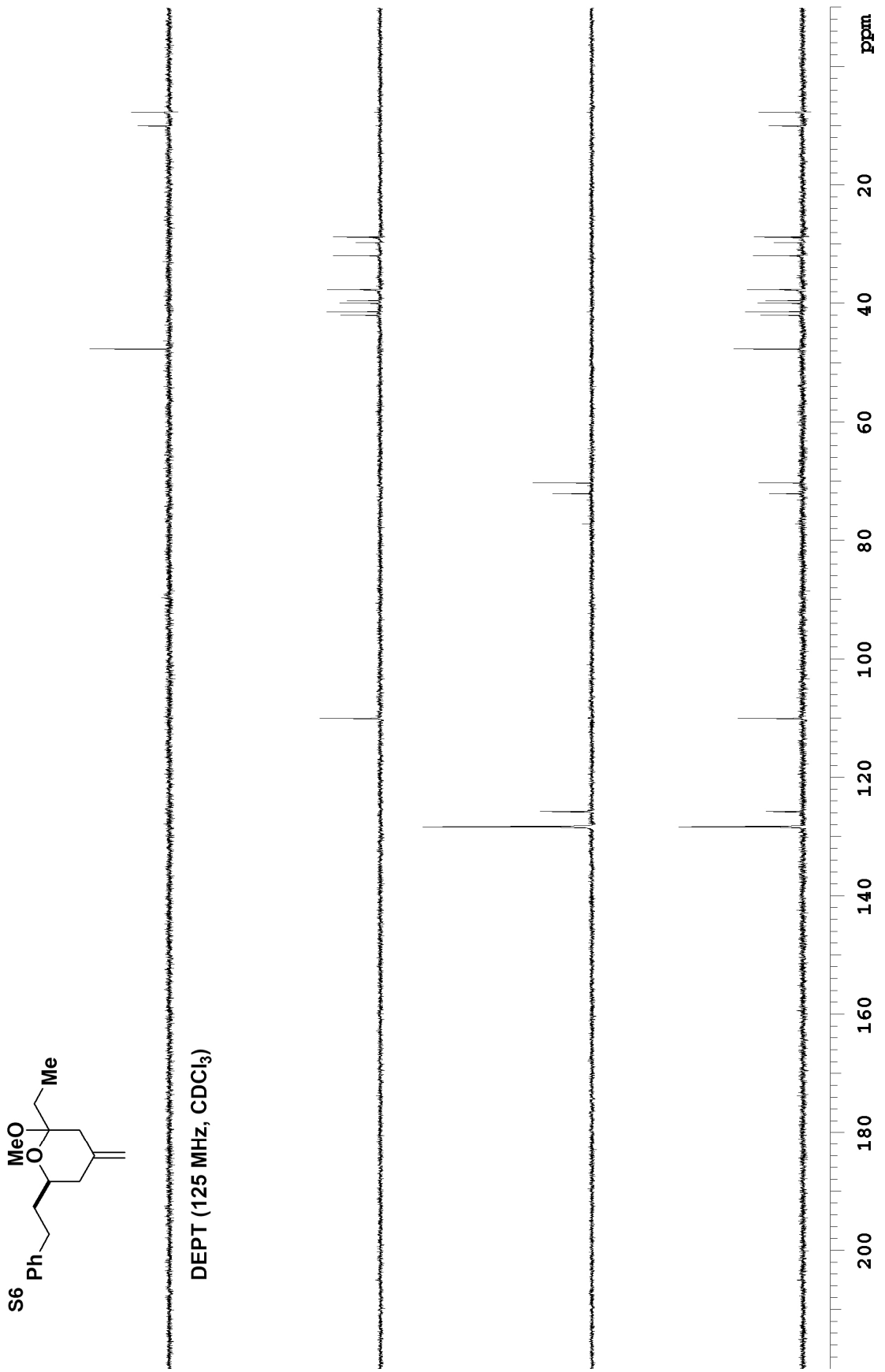
2
1
0

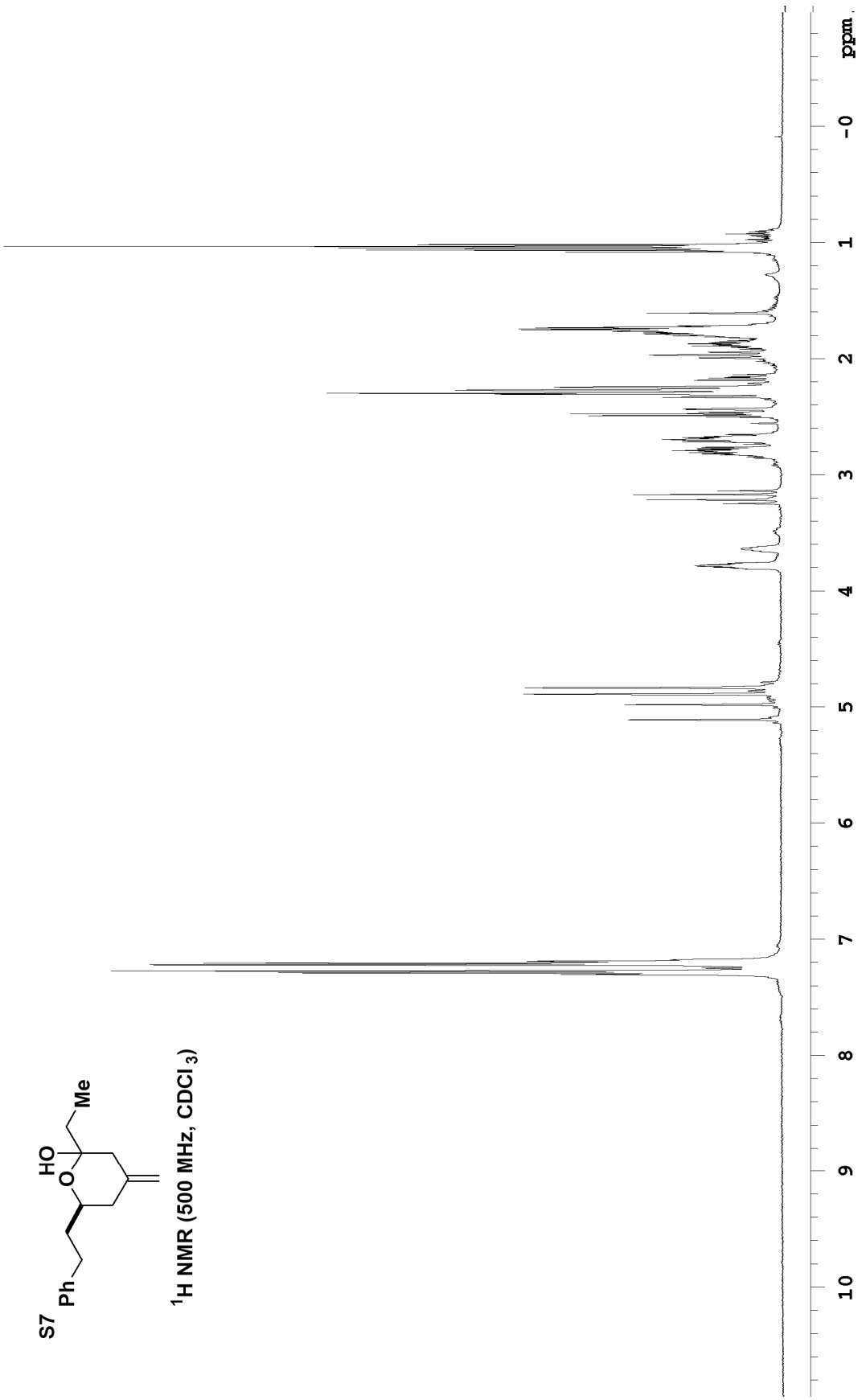

S5
Me
O
O
I
^{13}C NMR (125 MHz, CDCl$_3$)
ppm
200
180
160
140
120
100
80
60
40
20

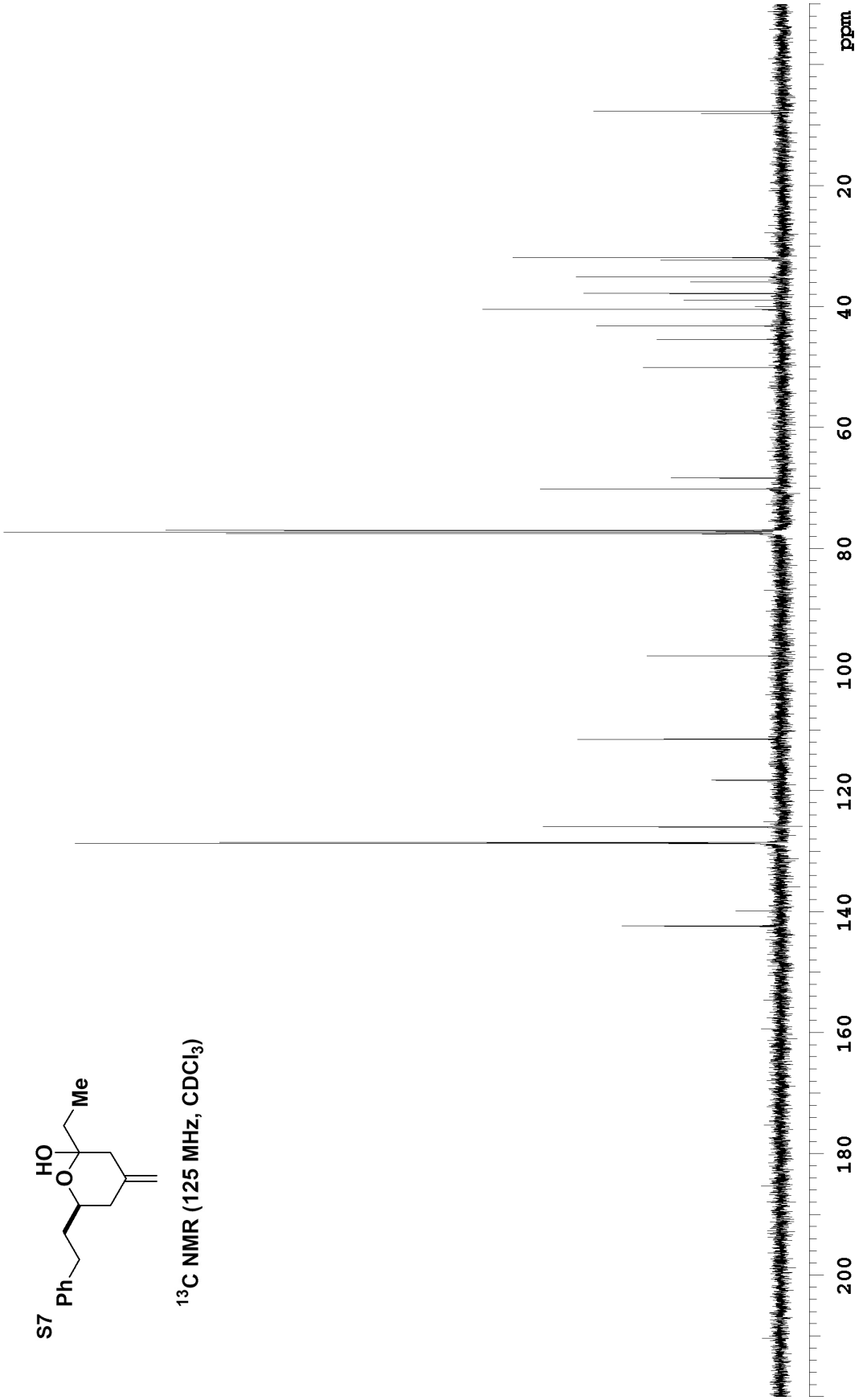

S5
DEPT (125 MHz, $CDCl_3$)
Me
O
O
I
ppm
20
40
60
80
100
120
140
160
180
200

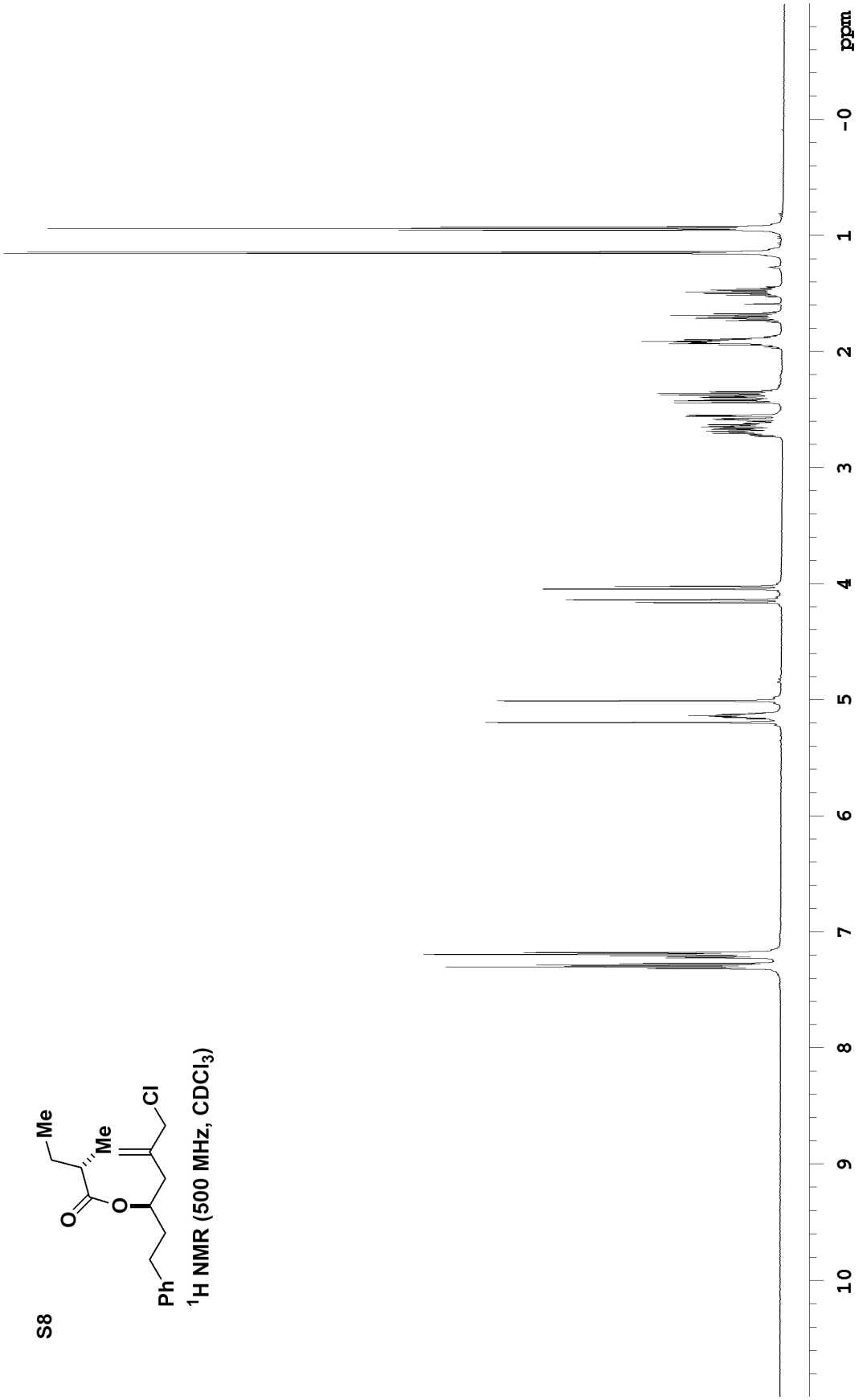

ppm
10
9
8
7
6
5
4
3
2
1
-0
MeO
Me
O
Ph
S6
^{1}H NMR (500 MHz, $CDCl_3$)

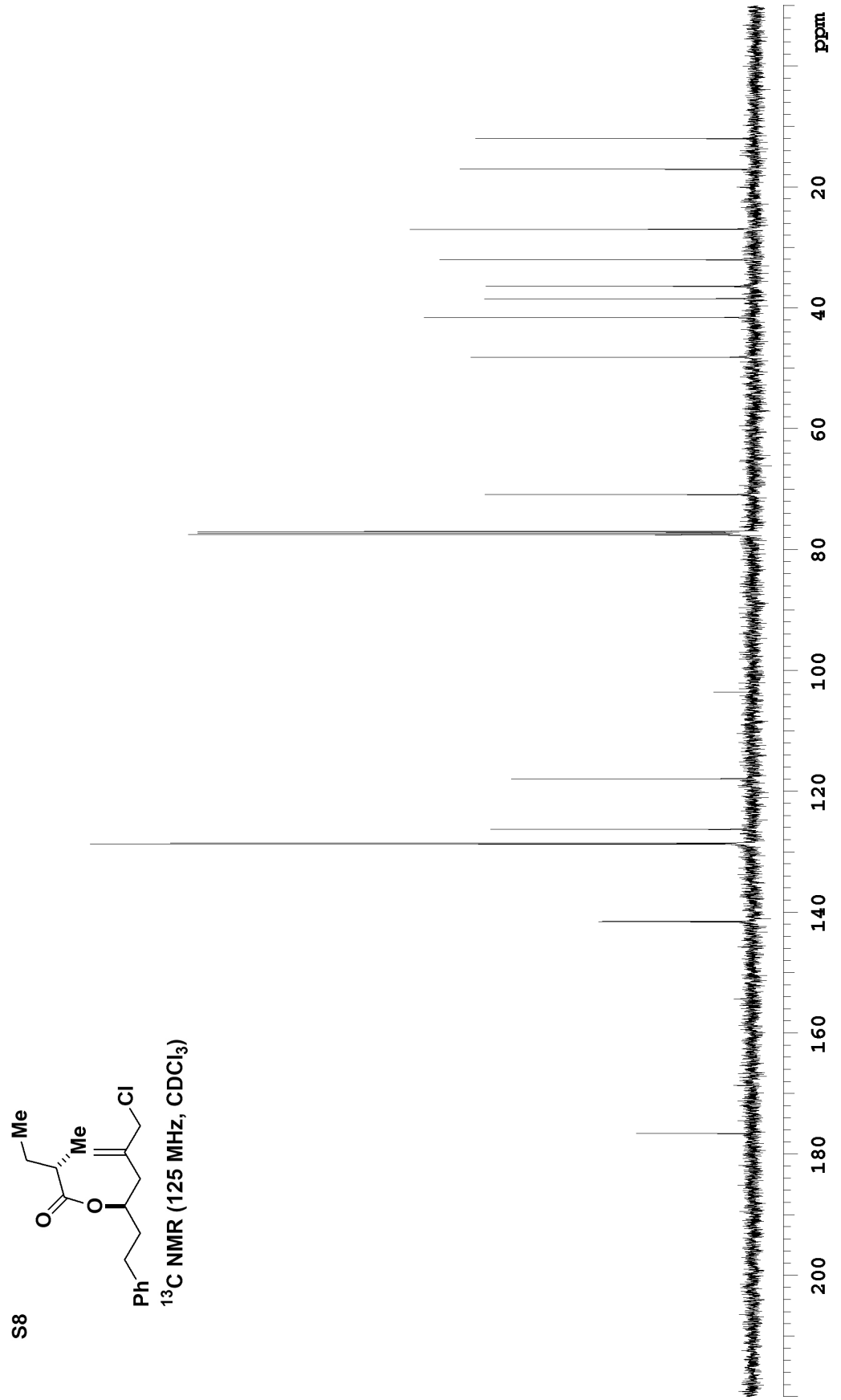

ppm
20
40
60
80
100
120
140
160
180
200
MeO
Me
O
Ph
S6
^{13}C NMR (125 MHz, CDCl$_3$)

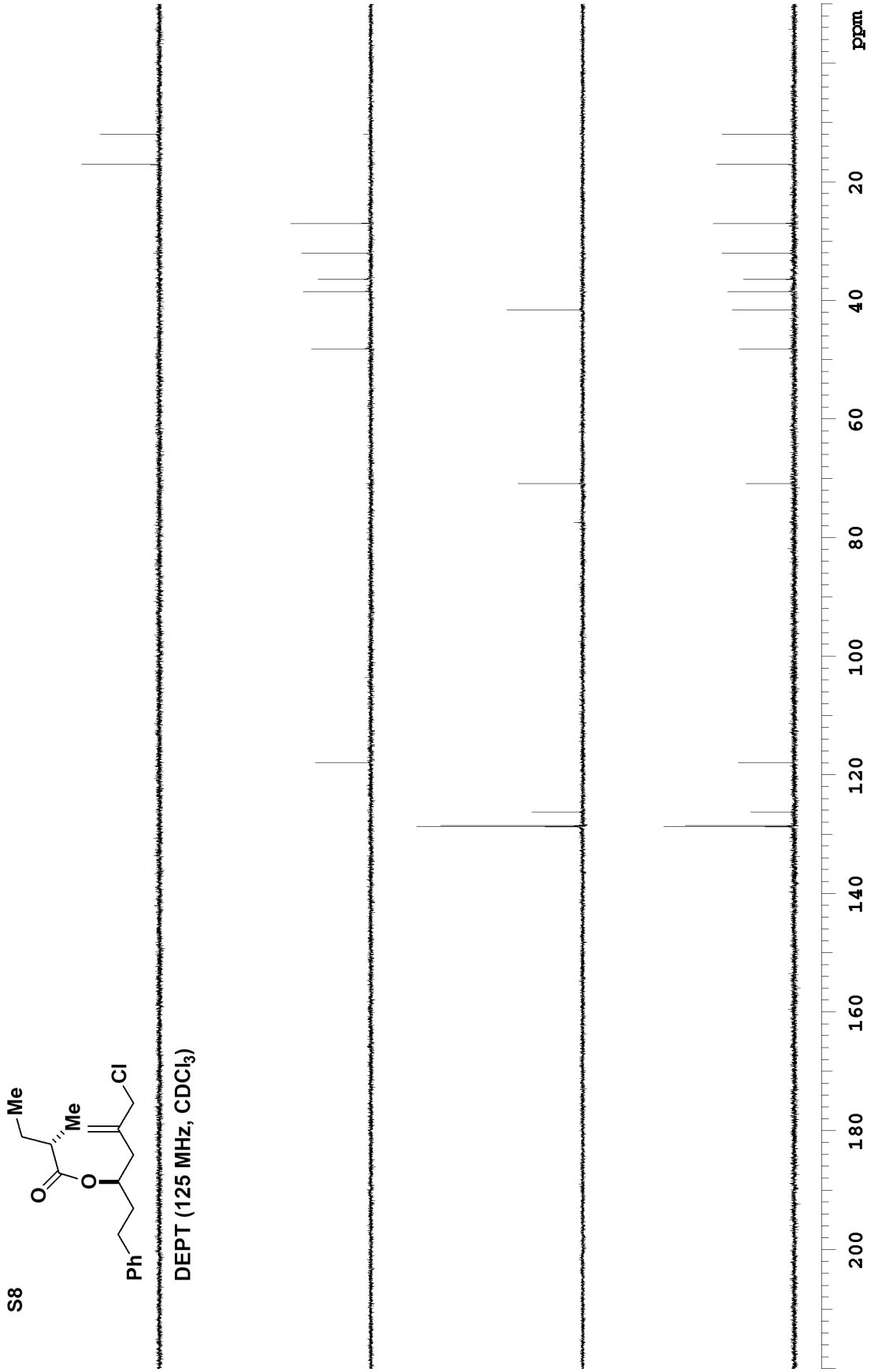

S6
Ph
MeO
O
Me
DEPT (125 MHz, CDCl3)
ppm
20
40
60
80
100
120
140
160
180
200

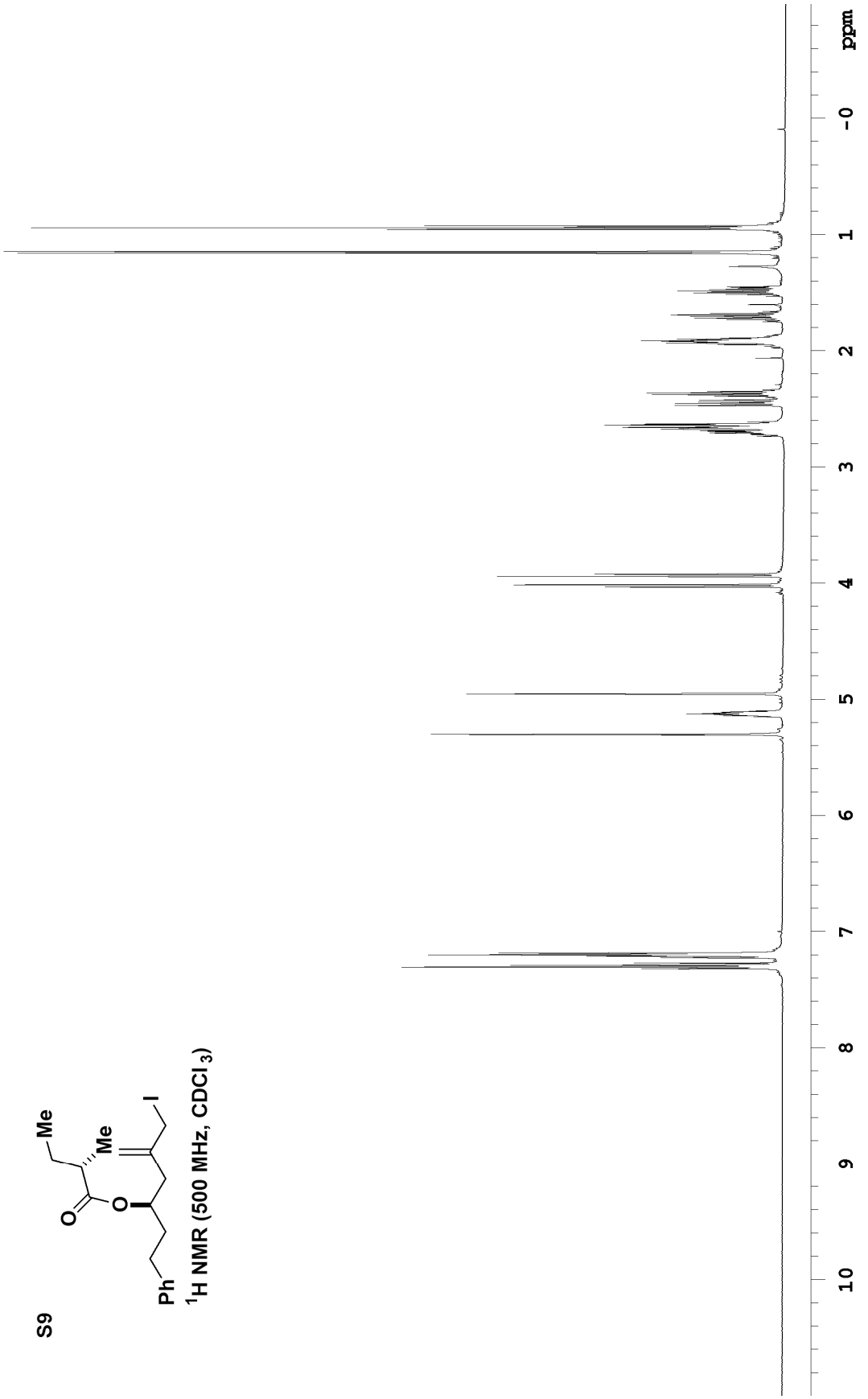

S7
Ph
HO
O
Me
^{1}H NMR (500 MHz, CDCl$_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
20
40
60
80
100
120
140
160
180
200
HO
O
Me
Ph
S7
^{13}C NMR (125 MHz, $CDCl_3$)


ppm
10
9
8
7
6
5
4
3
2
1
-0
S8
Me
Me
O
O
Cl
Ph
^{1}H NMR (500 MHz, $CDCl_3$)

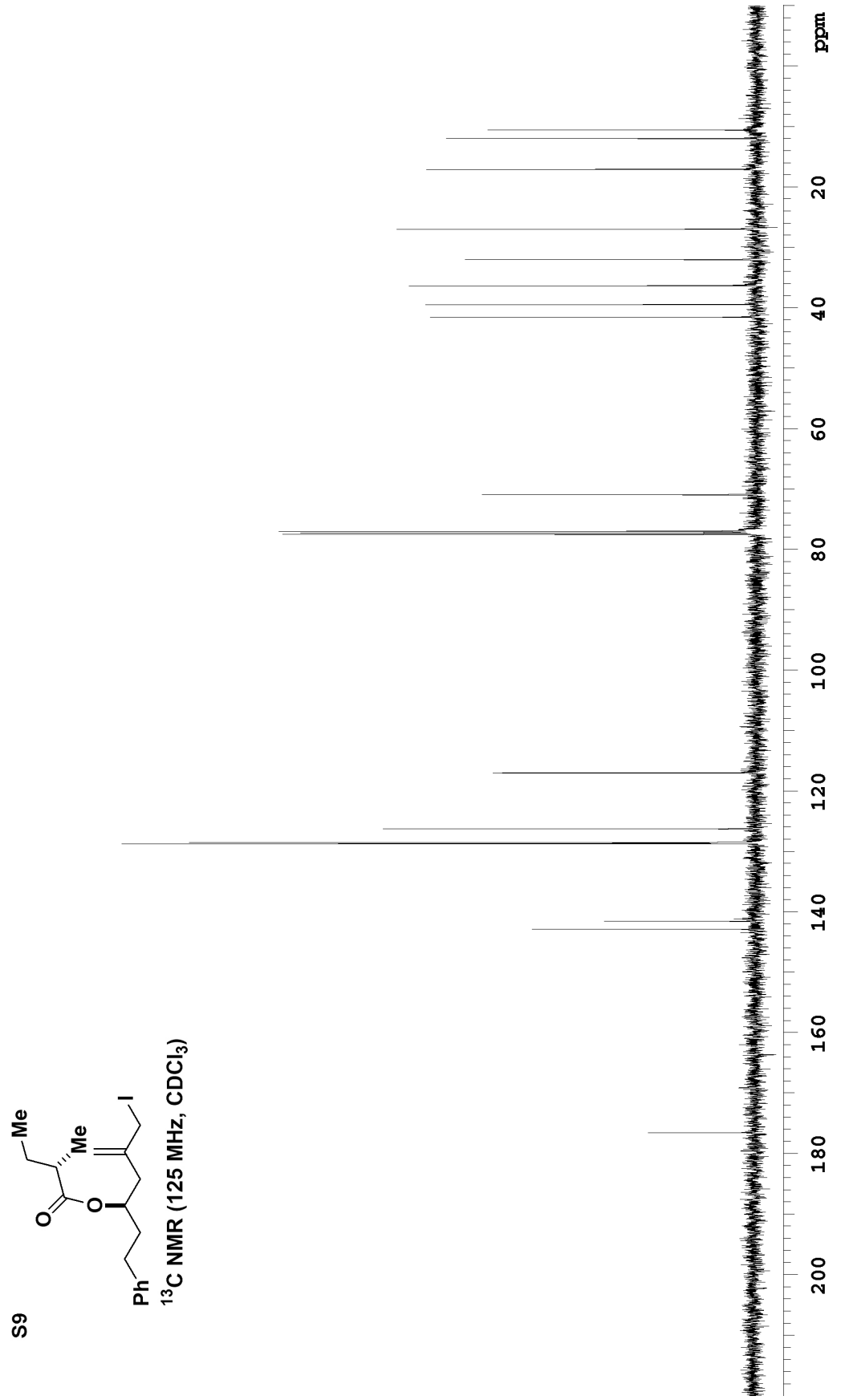

S8
^{13}C NMR (125 MHz, $CDCl_3$)
Me
Me
O
O
Cl
Ph
ppm
200
180
160
140
120
100
80
60
40
20

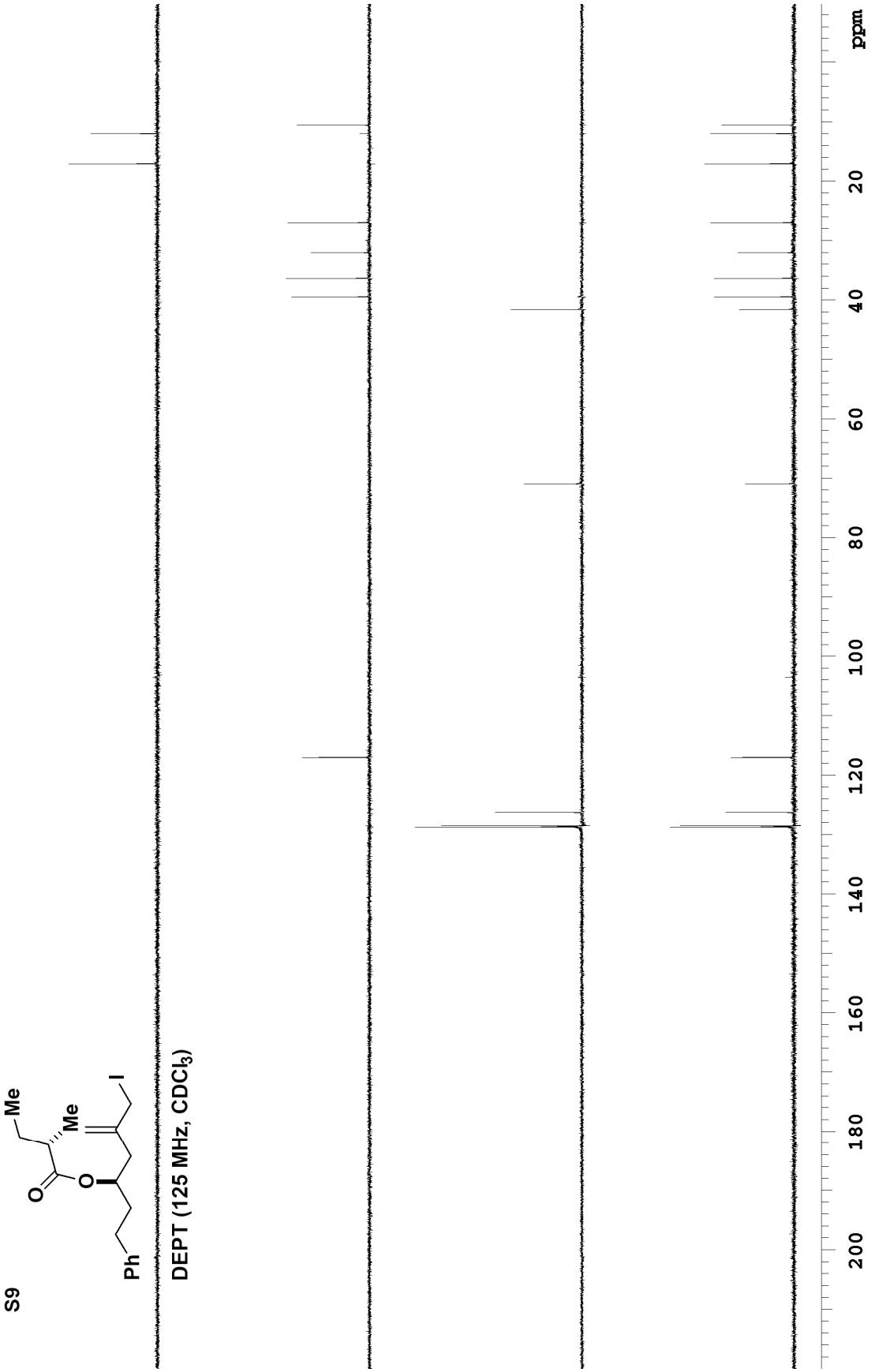

S8
Me
Me
Cl
O
O
Ph
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

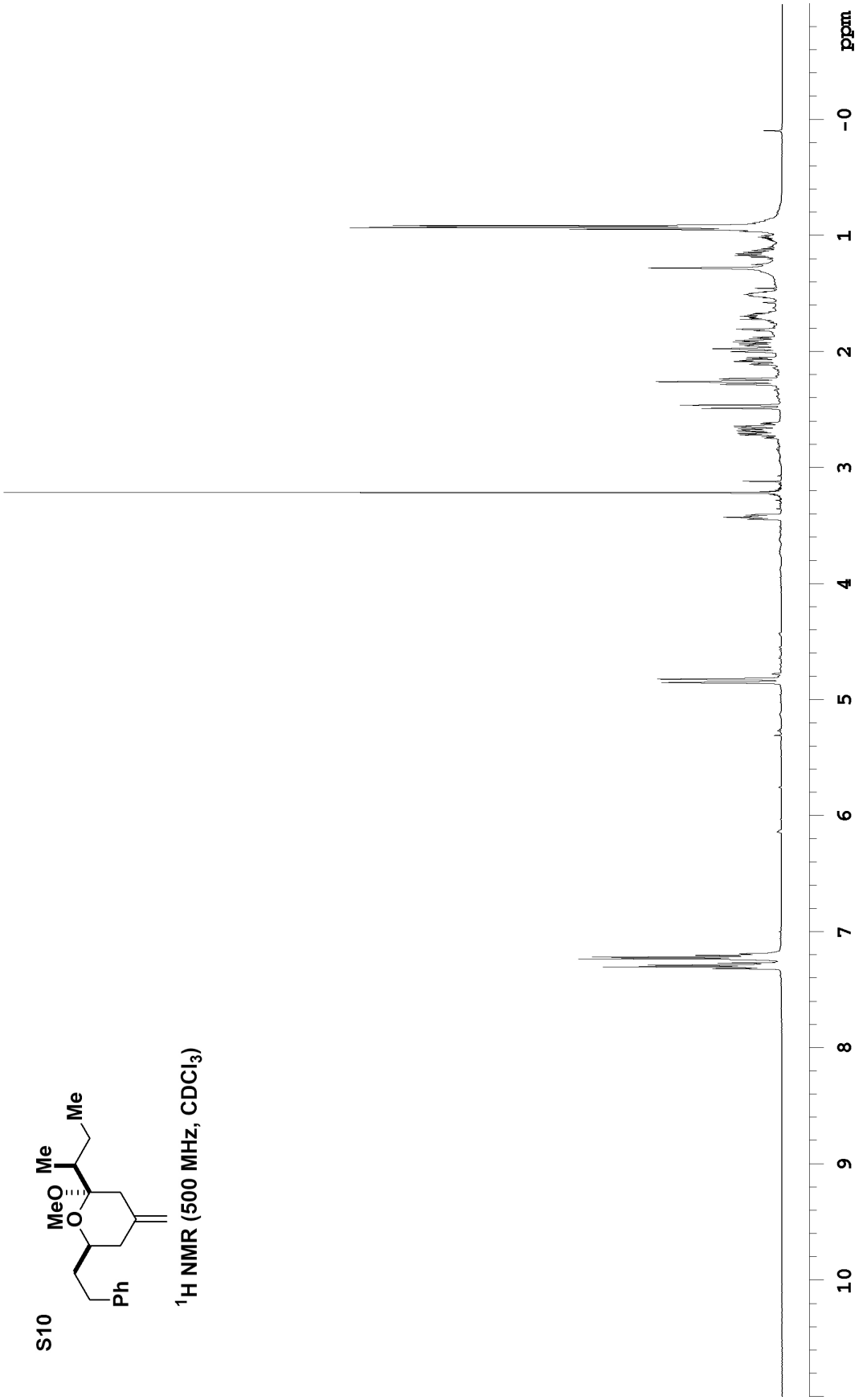


S9

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

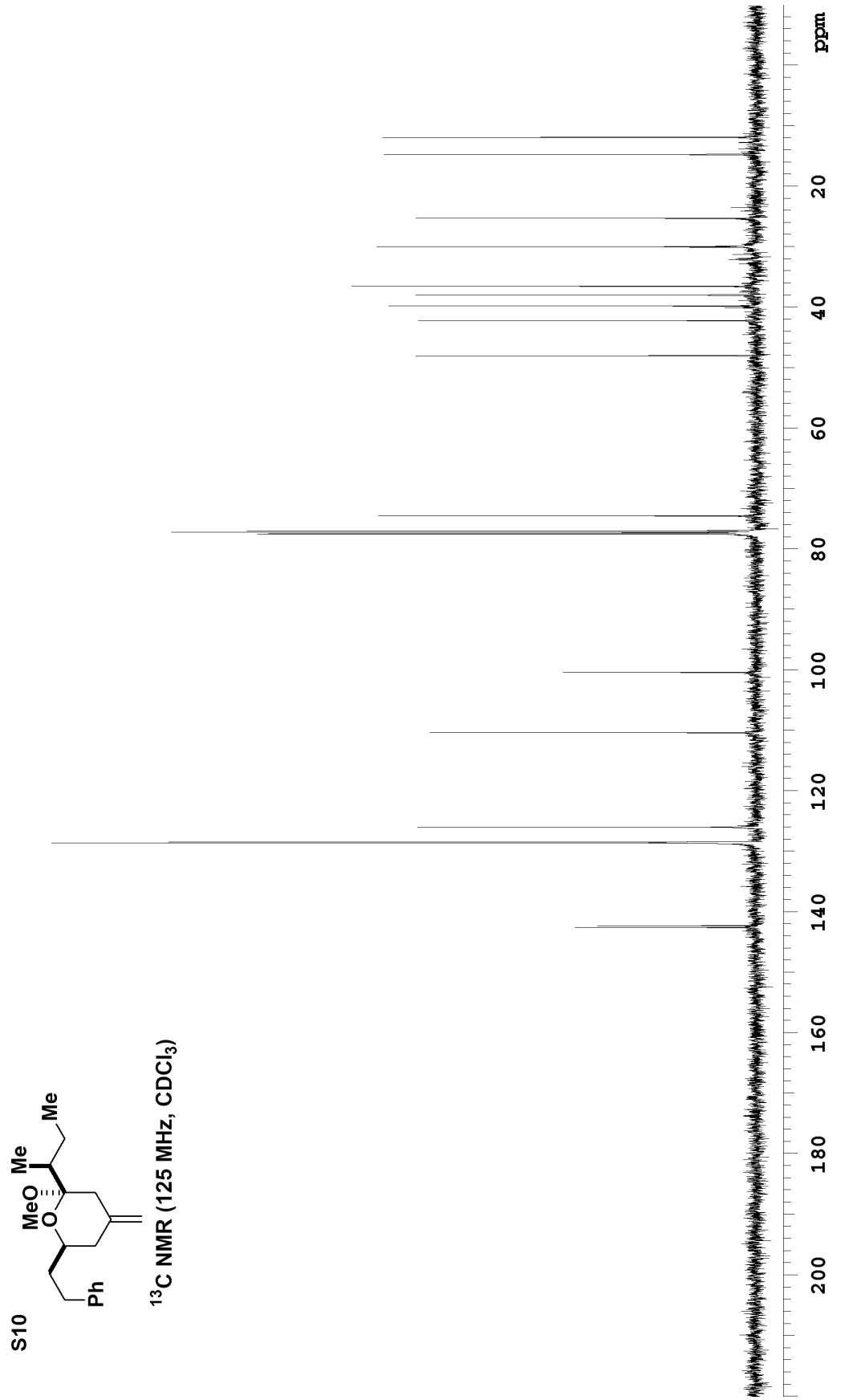

S9
^{13}C NMR (125 MHz, CDCl$_3$)
Me
Me
O
O
I
Ph
ppm
200
180
160
140
120
100
80
60
40
20

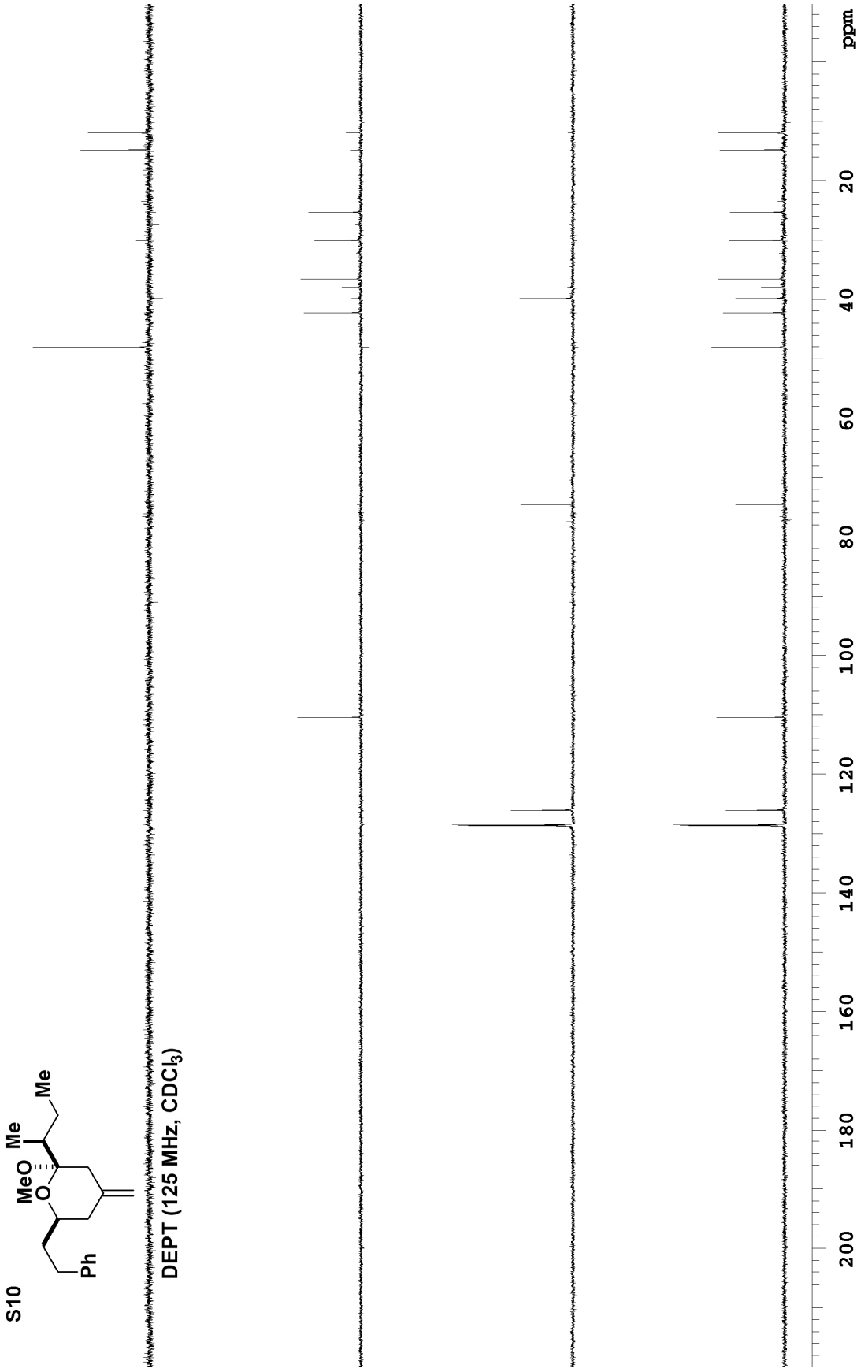

S9
Me
Me
O
O
I
Ph
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

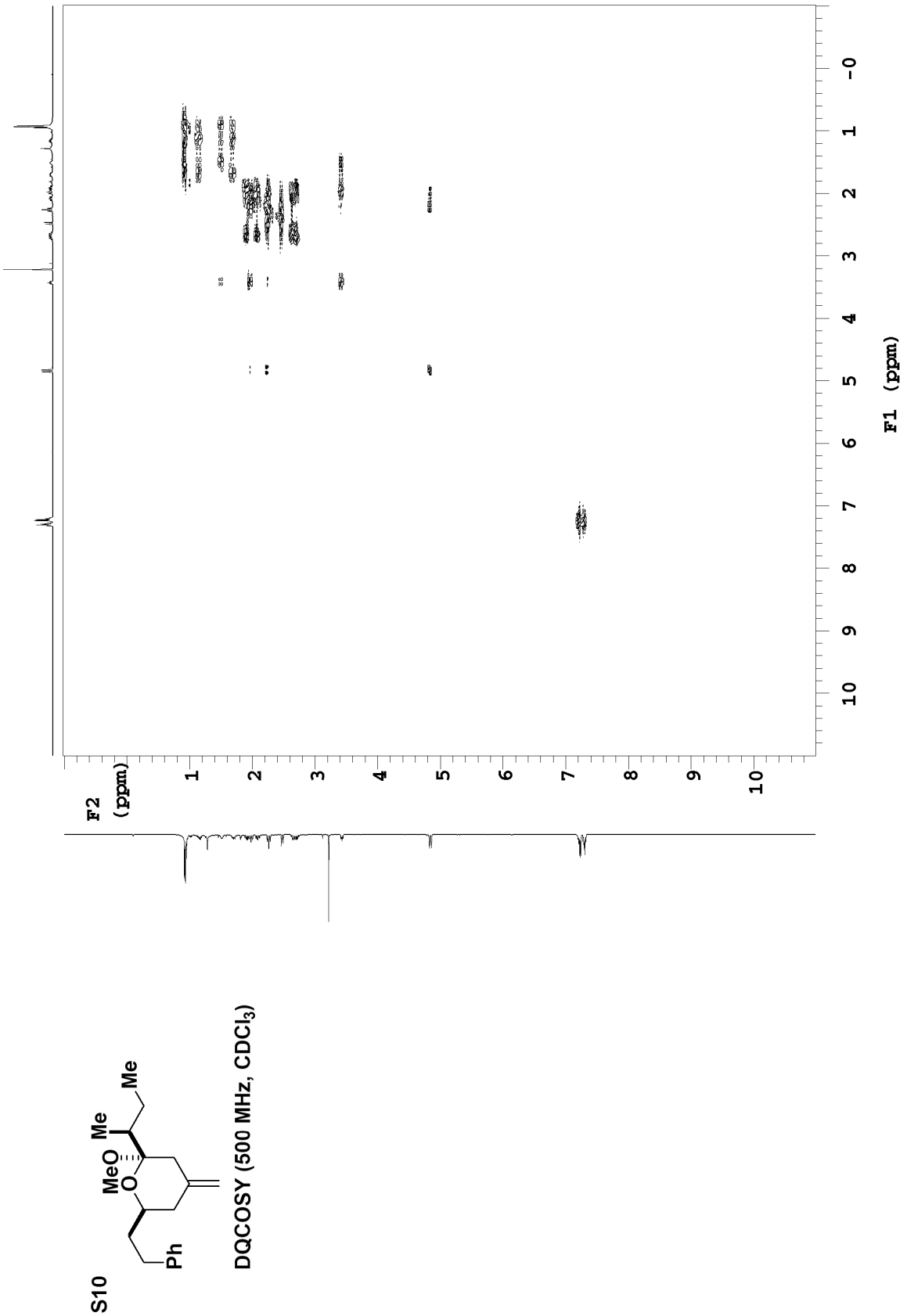


S10

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

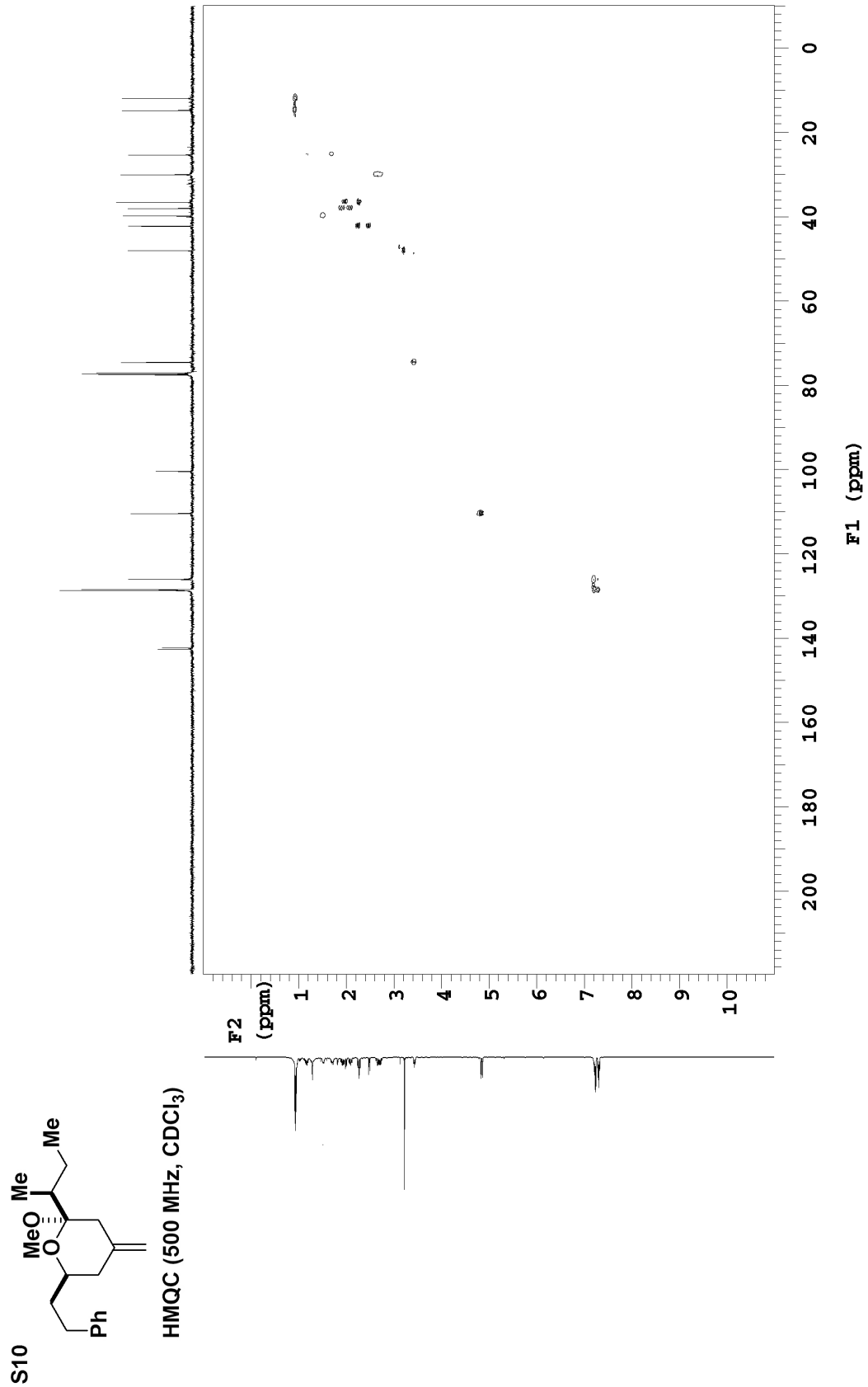

S10
MeO
Me
Me
O
Ph
^{13}C NMR (125 MHz, CDCl$_3$)
ppm
200
180
160
140
120
100
80
60
40
20

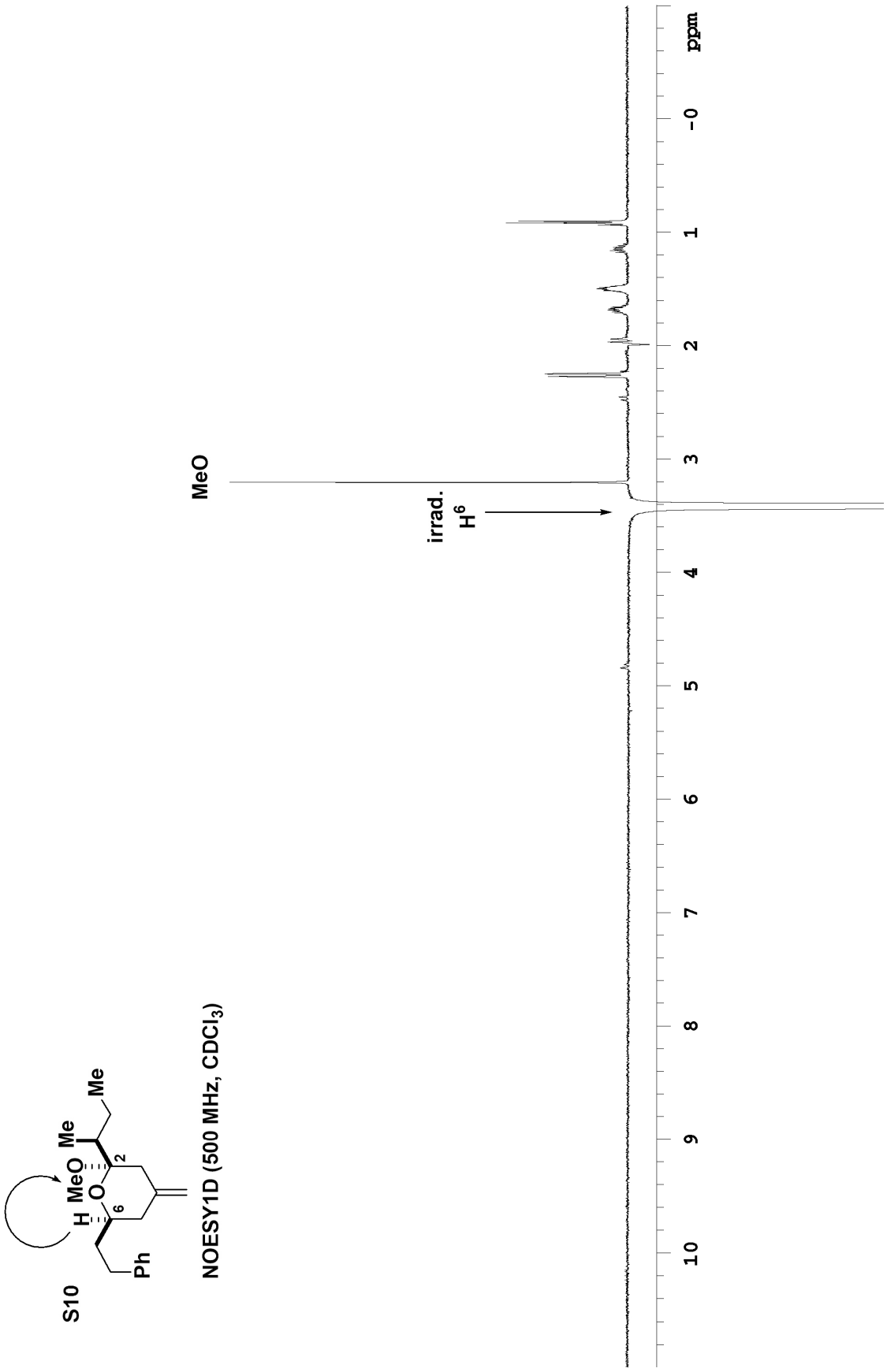

S10
Me
Me
MeO
O
Ph
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

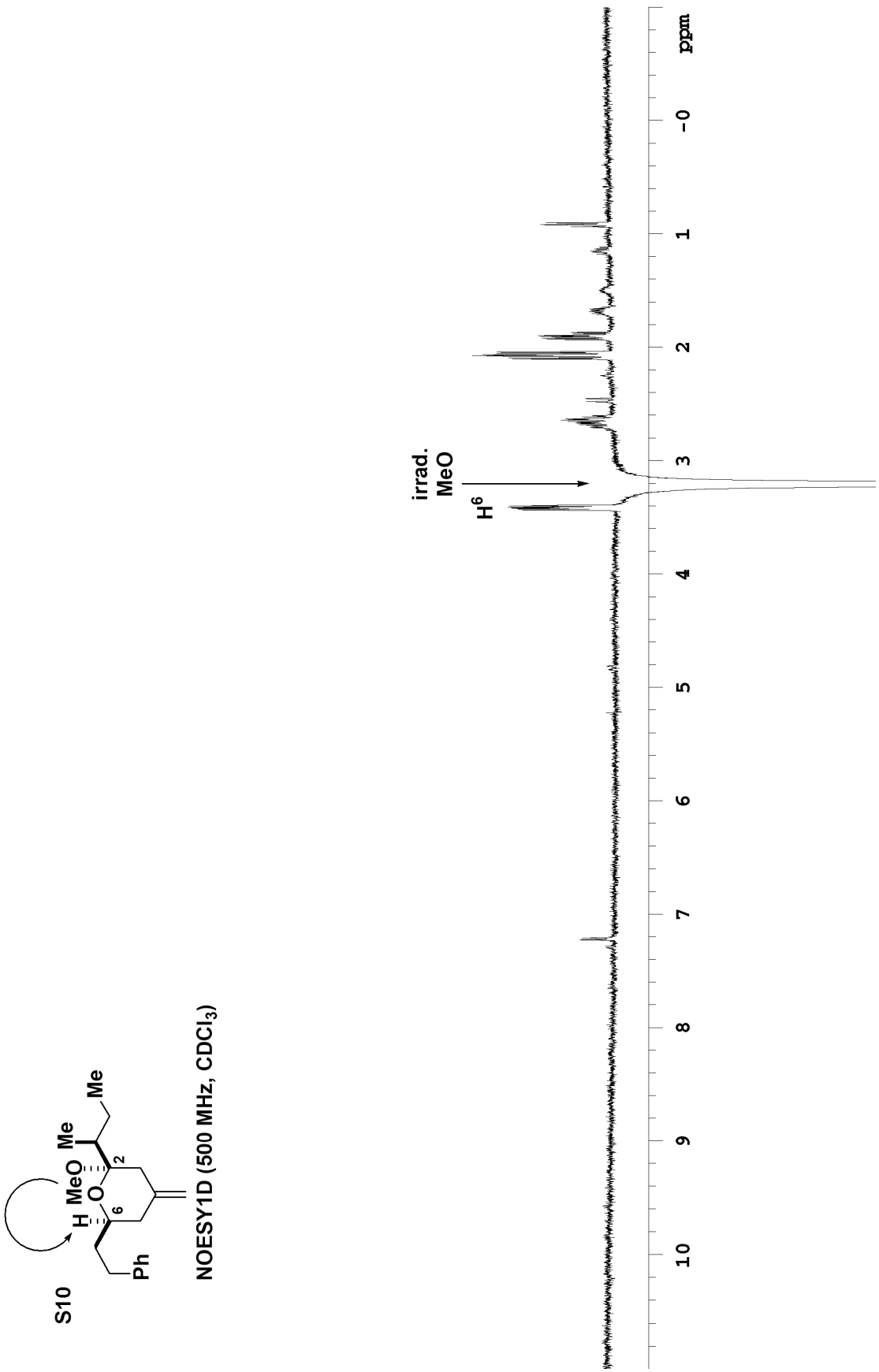


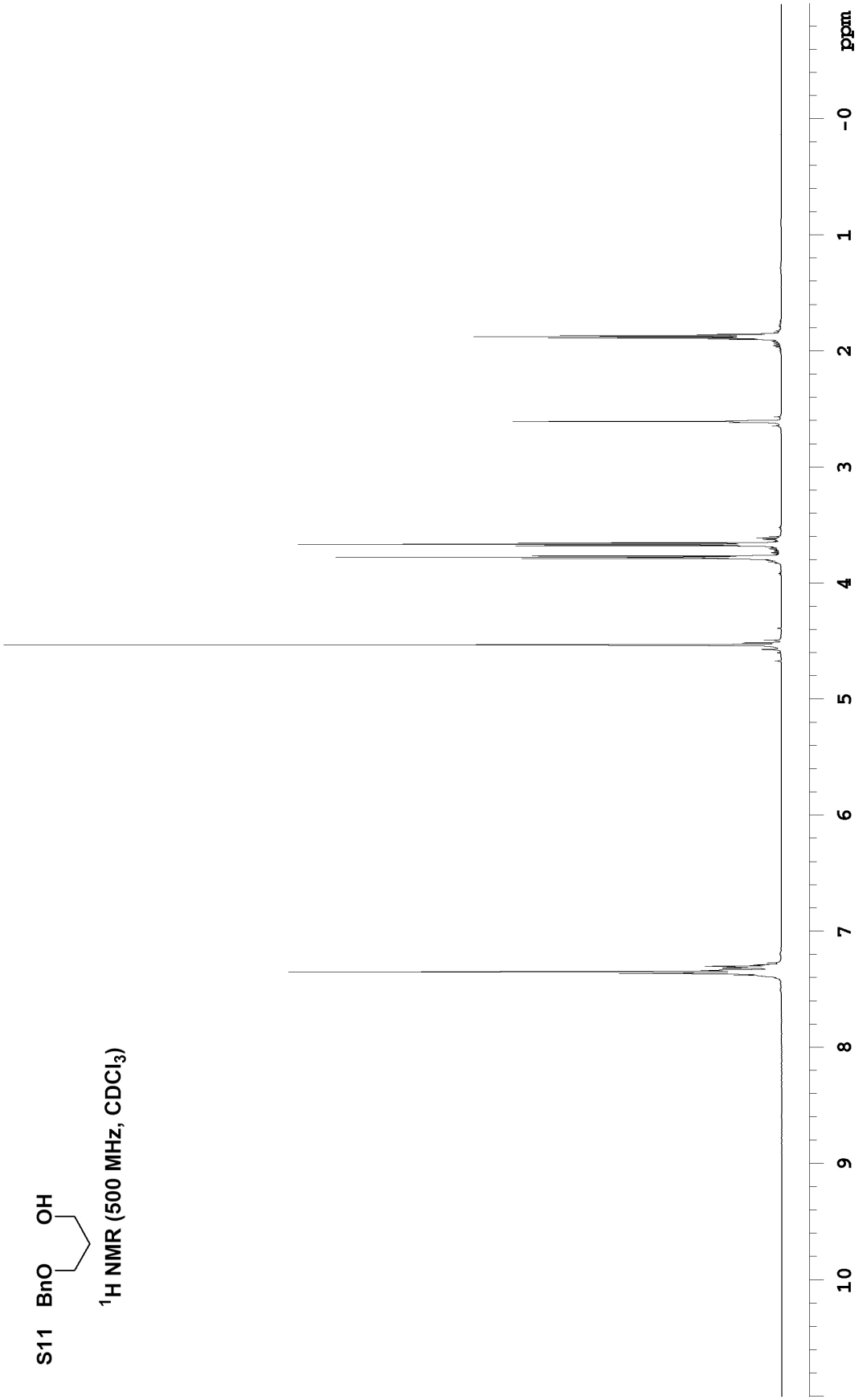
S10

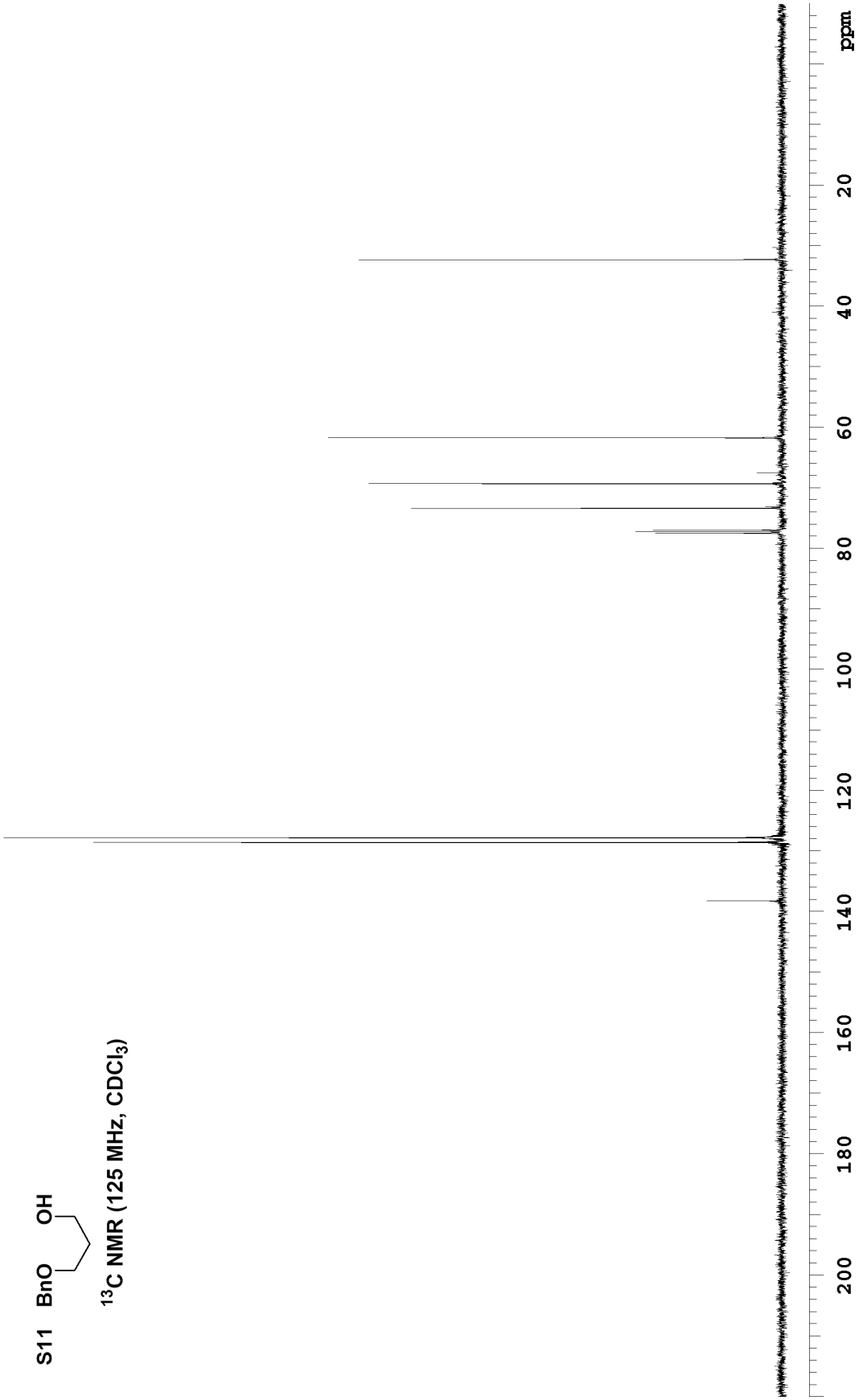
DQCOSY (500 MHz, $CDCl_3$)

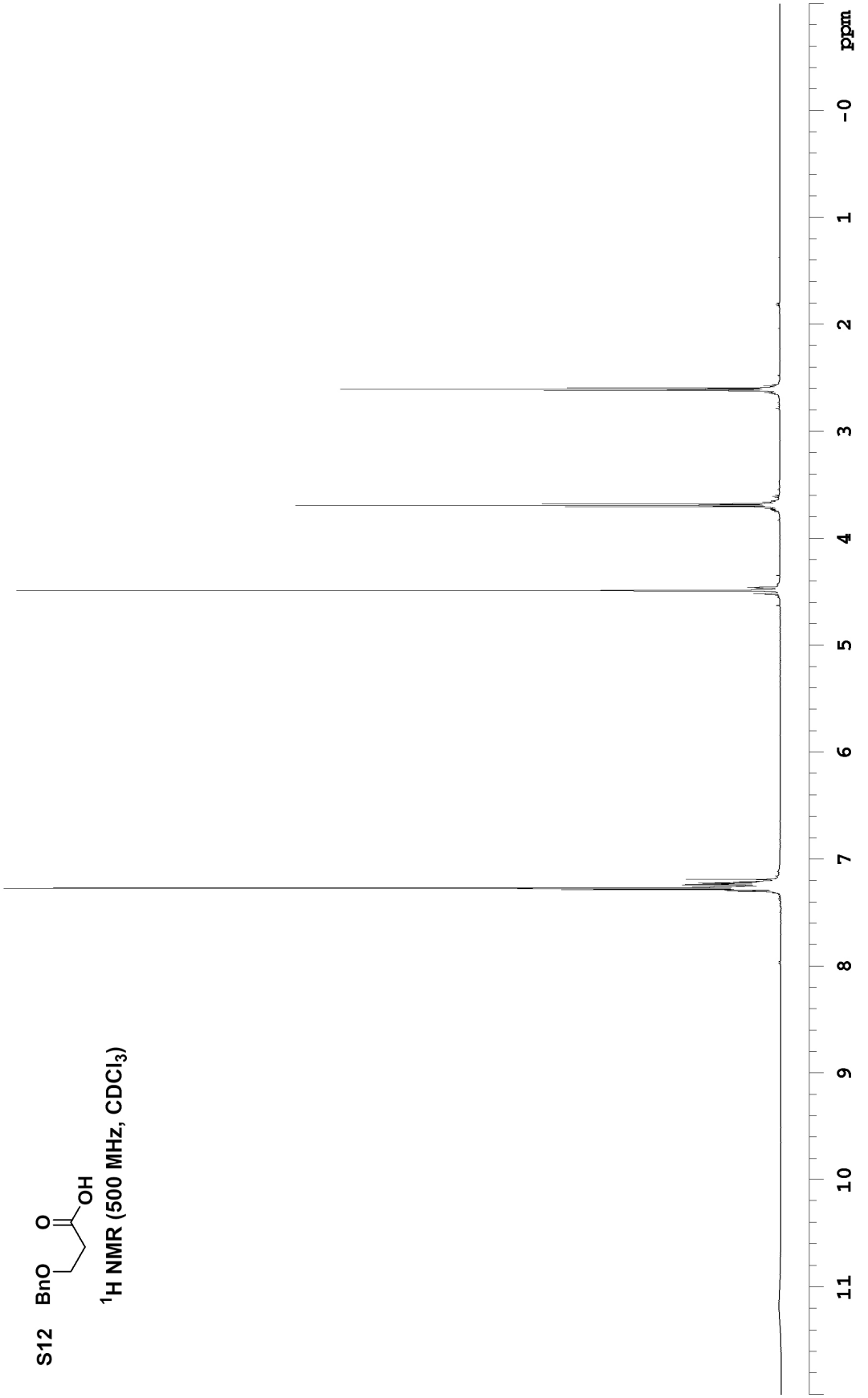

S10
HMQC (500 MHz, $CDCl_3$)
F2 (ppm)
F1 (ppm)
Me
Me
MeO
O
Ph

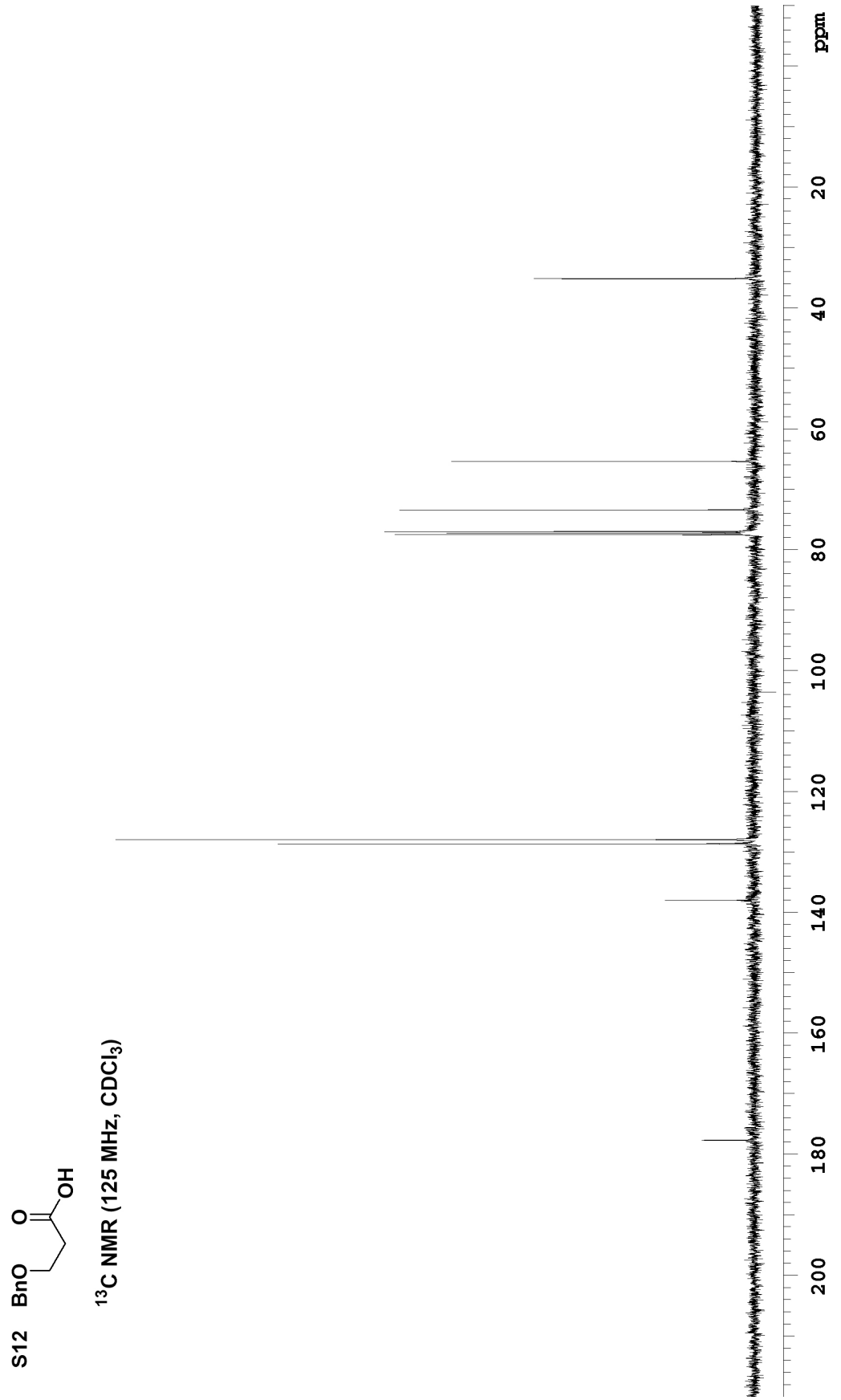

MeO
irrad.
H6
ppm
-0
1
2
3
4
5
6
7
8
9
10
Me
Me
MeO
O
H
2
6
Ph
S10
NOESY1D (500 MHz, CDCl3)

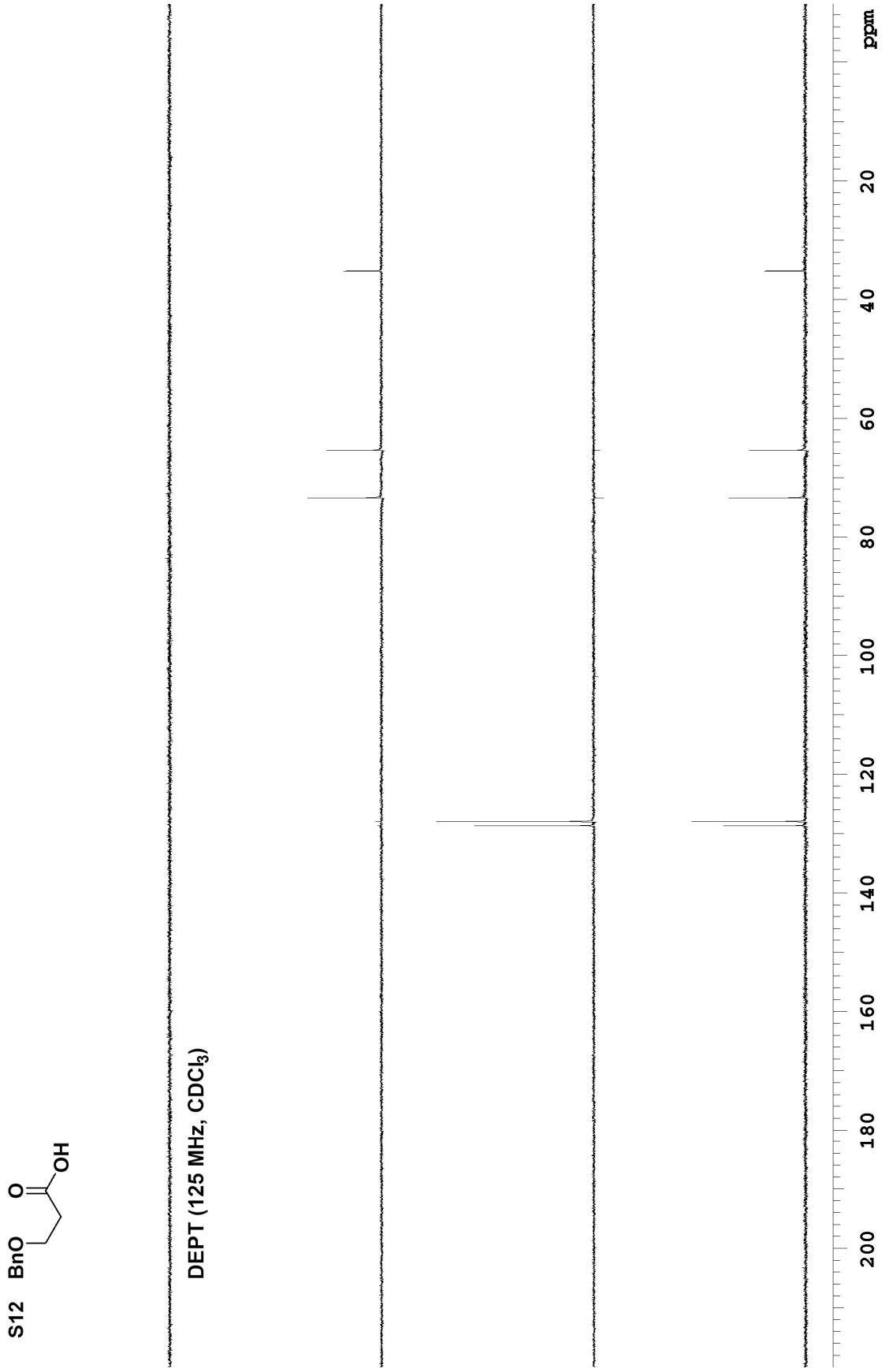

irrad.
MeO
H6
ppm
10
9
8
7
6
5
4
3
2
1
-0
S10
Me
Me
MeO
H
O
2
6
Ph
NOESY1D (500 MHz, CDCl3)

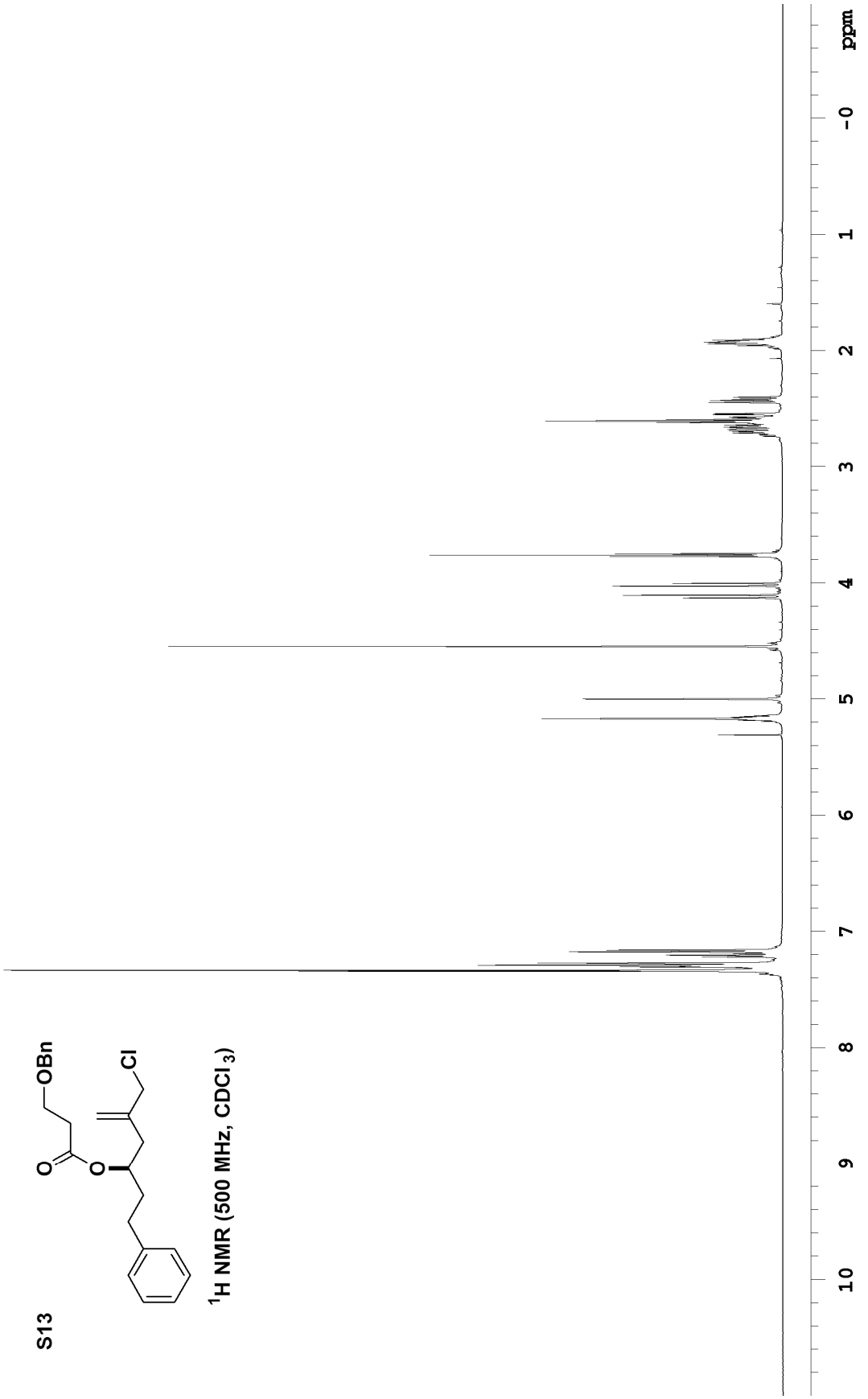

S11
BnO
OH
^{1}H NMR (500 MHz, $CDCl_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0

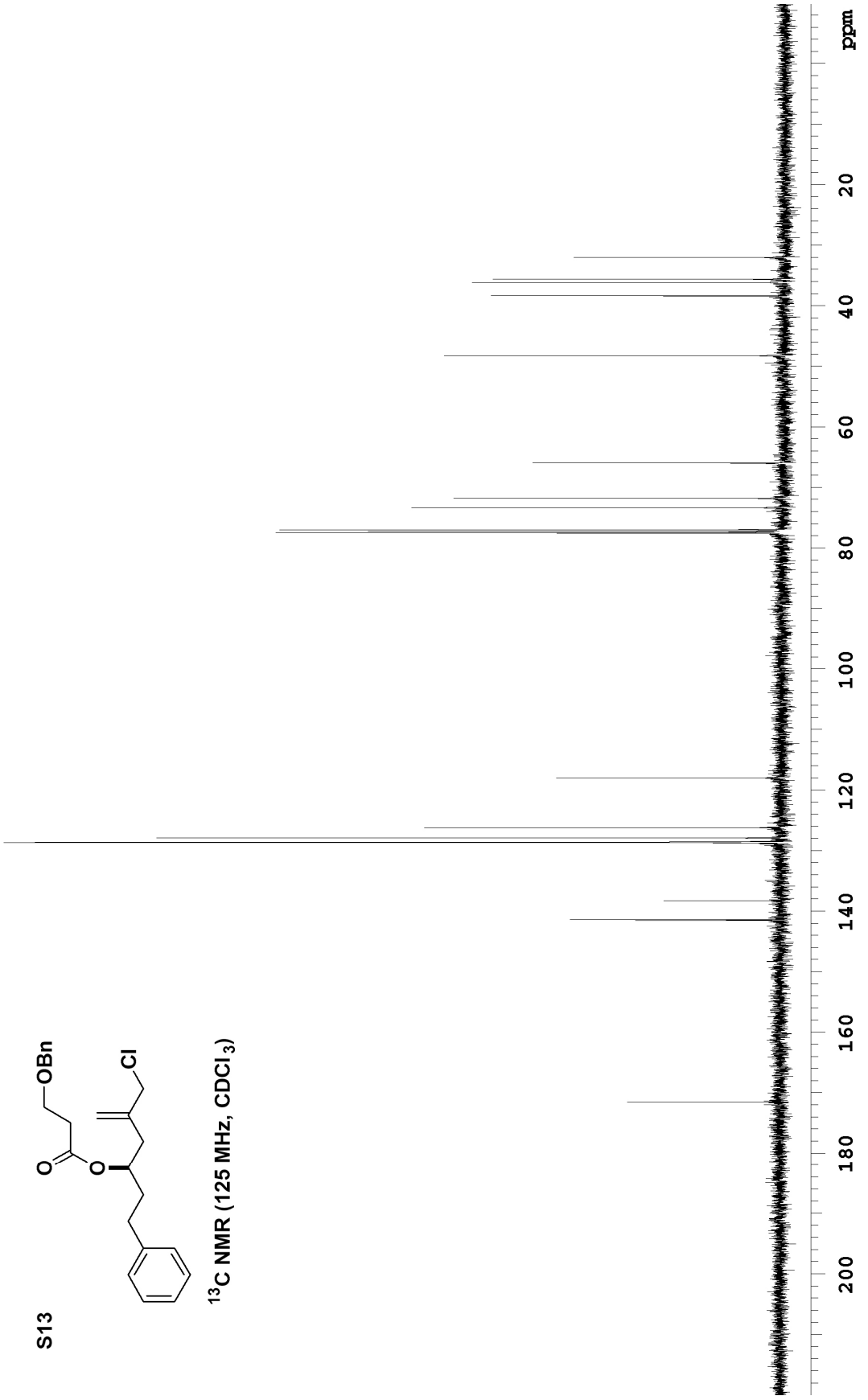

S11
BnO
OH
^{13}C NMR (125 MHz, $CDCl_3$)
ppm
200
180
160
140
120
100
80
60
40
20

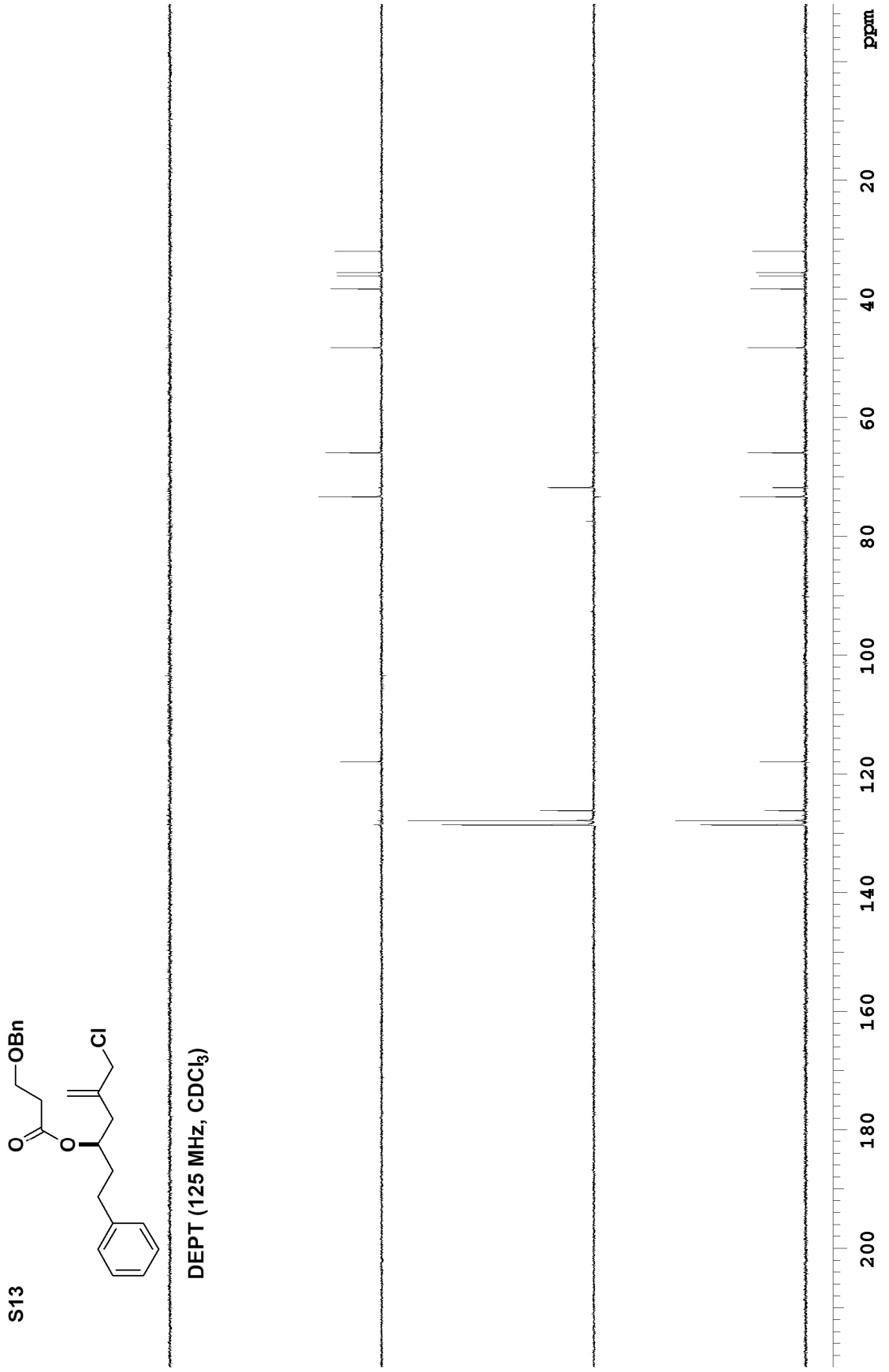

S12
BnO
O
OH
^{1}H NMR (500 MHz, CDCl$_3$)
ppm
-0
1
2
3
4
5
6
7
8
9
10
11

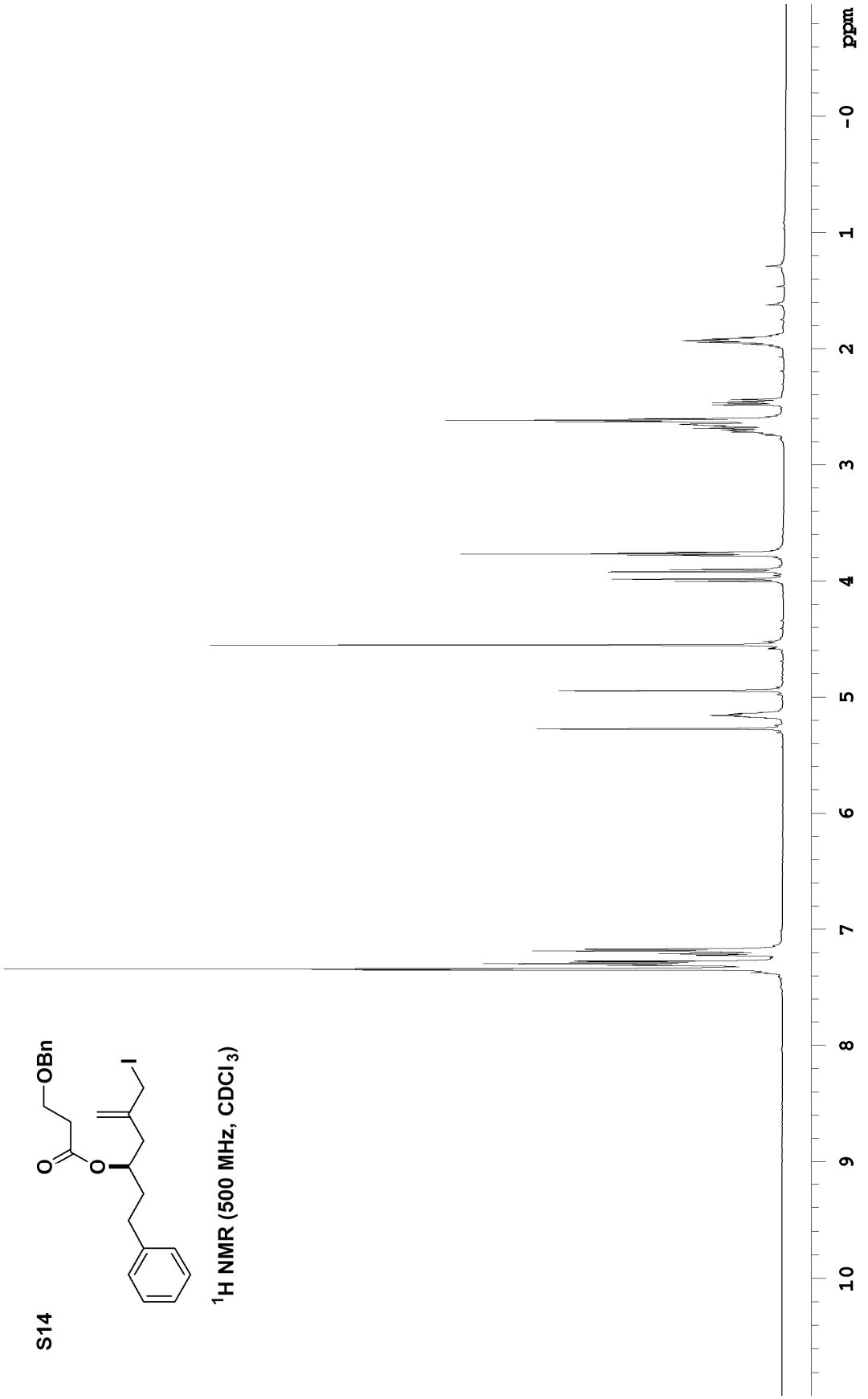

S12
BnO
O
OH
^{13}C NMR (125 MHz, $CDCl_3$)
ppm
200
180
160
140
120
100
80
60
40
20

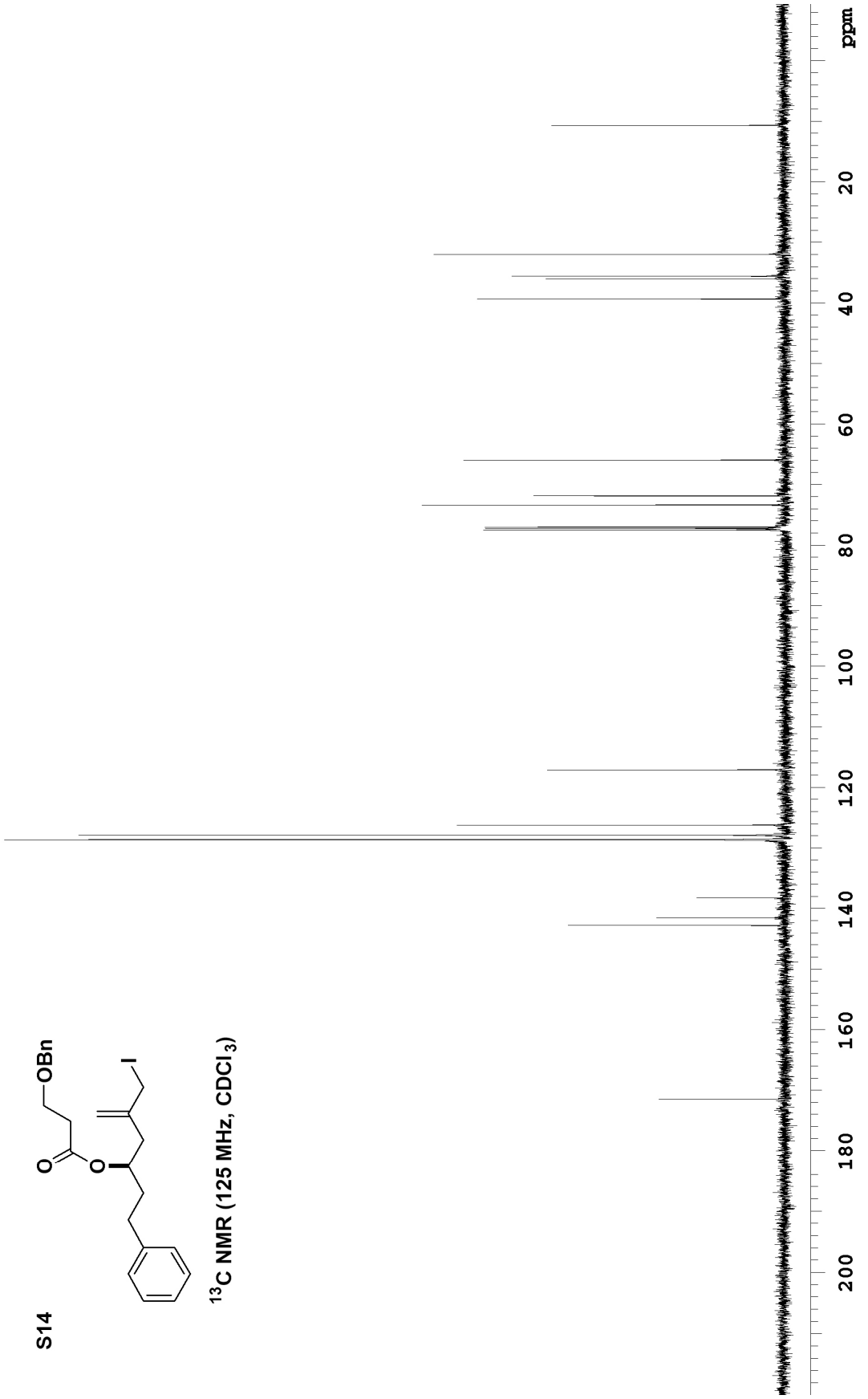

S12
BnO
O
OH
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

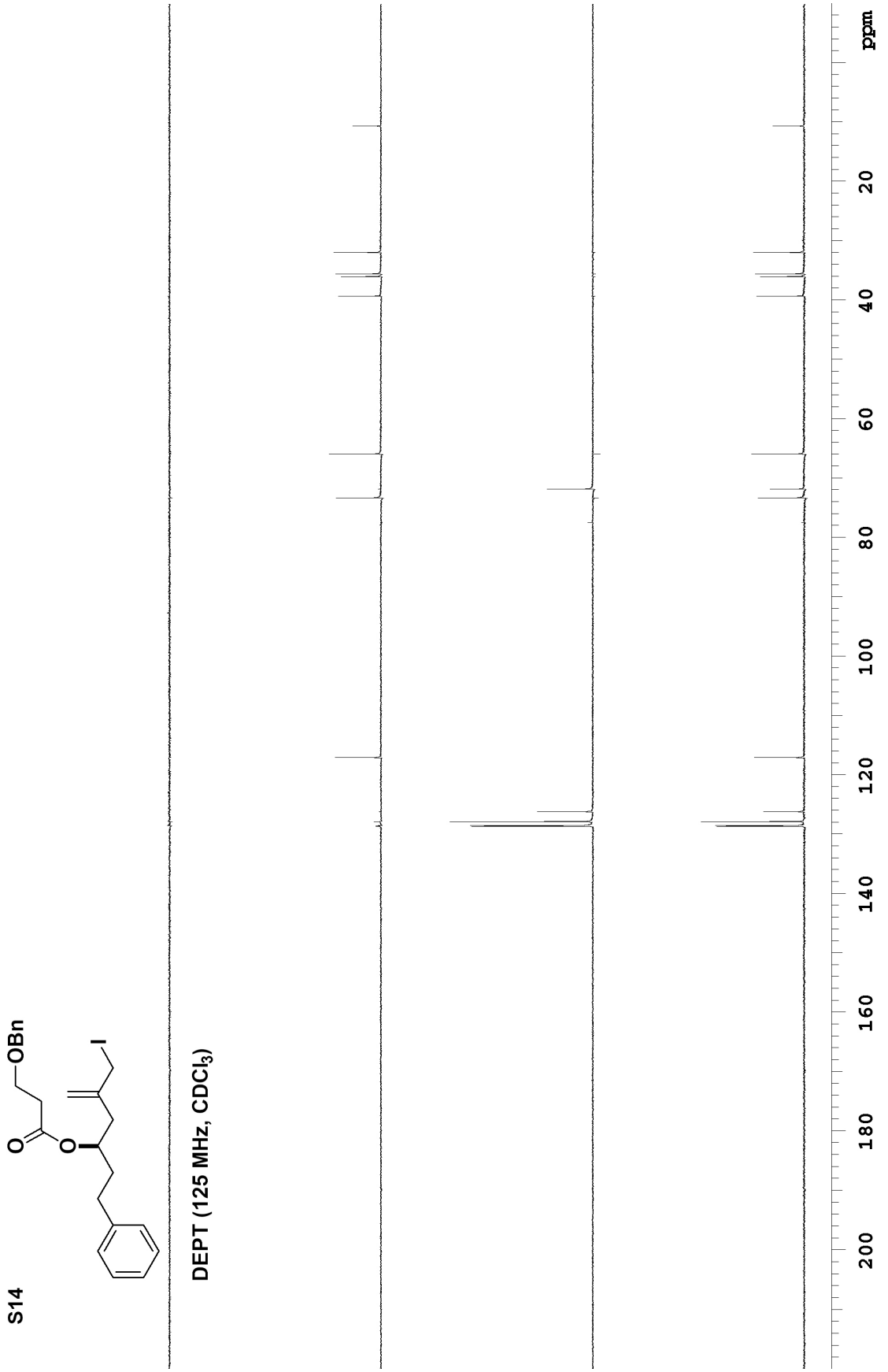

S13
OBn
O
O
Cl
^{1}H NMR (500 MHz, CDCl$_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0

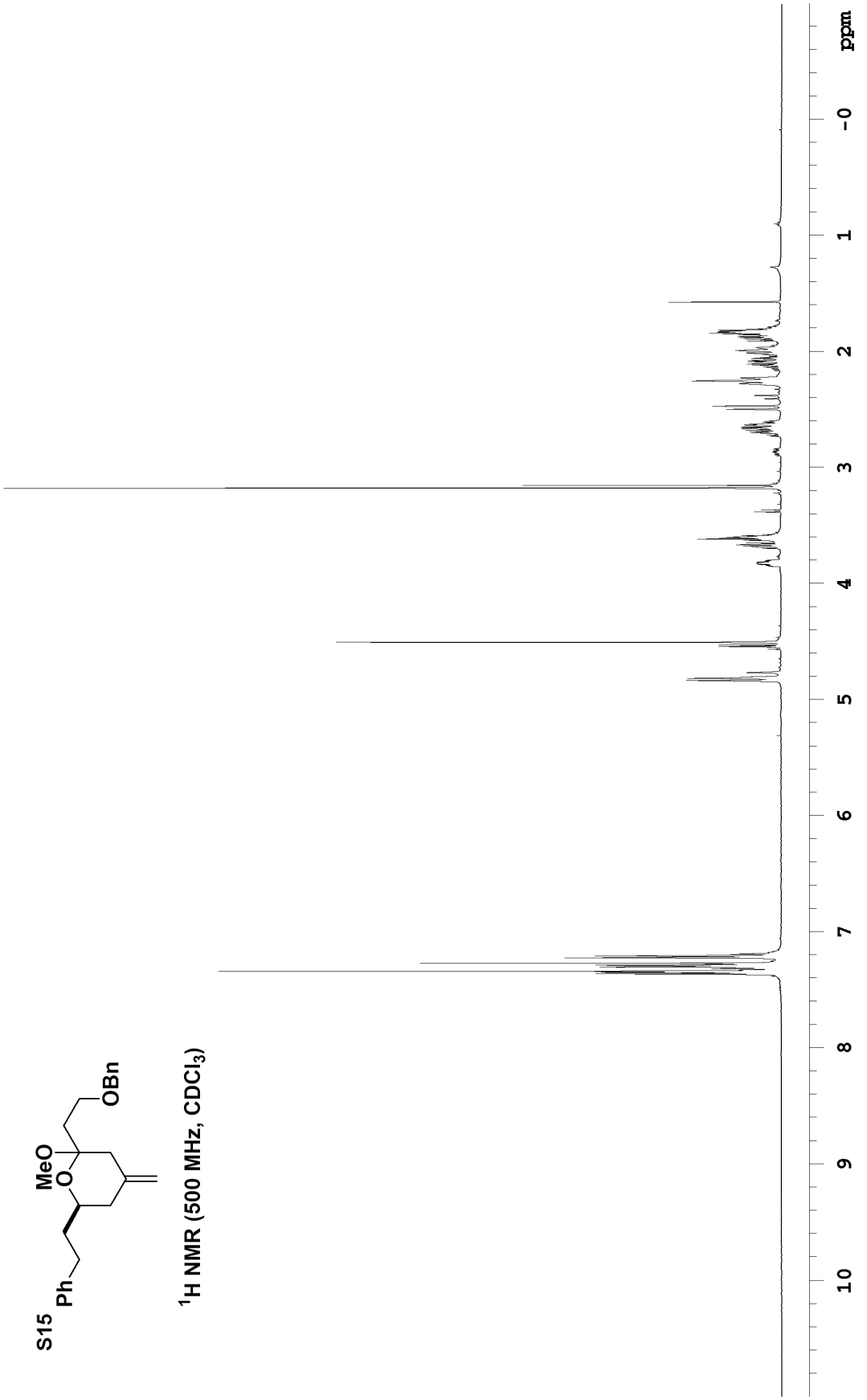

S13
^{13}C NMR (125 MHz, CDCl$_3$)
OBn
O
O
Cl
ppm
200
180
160
140
120
100
80
60
40
20

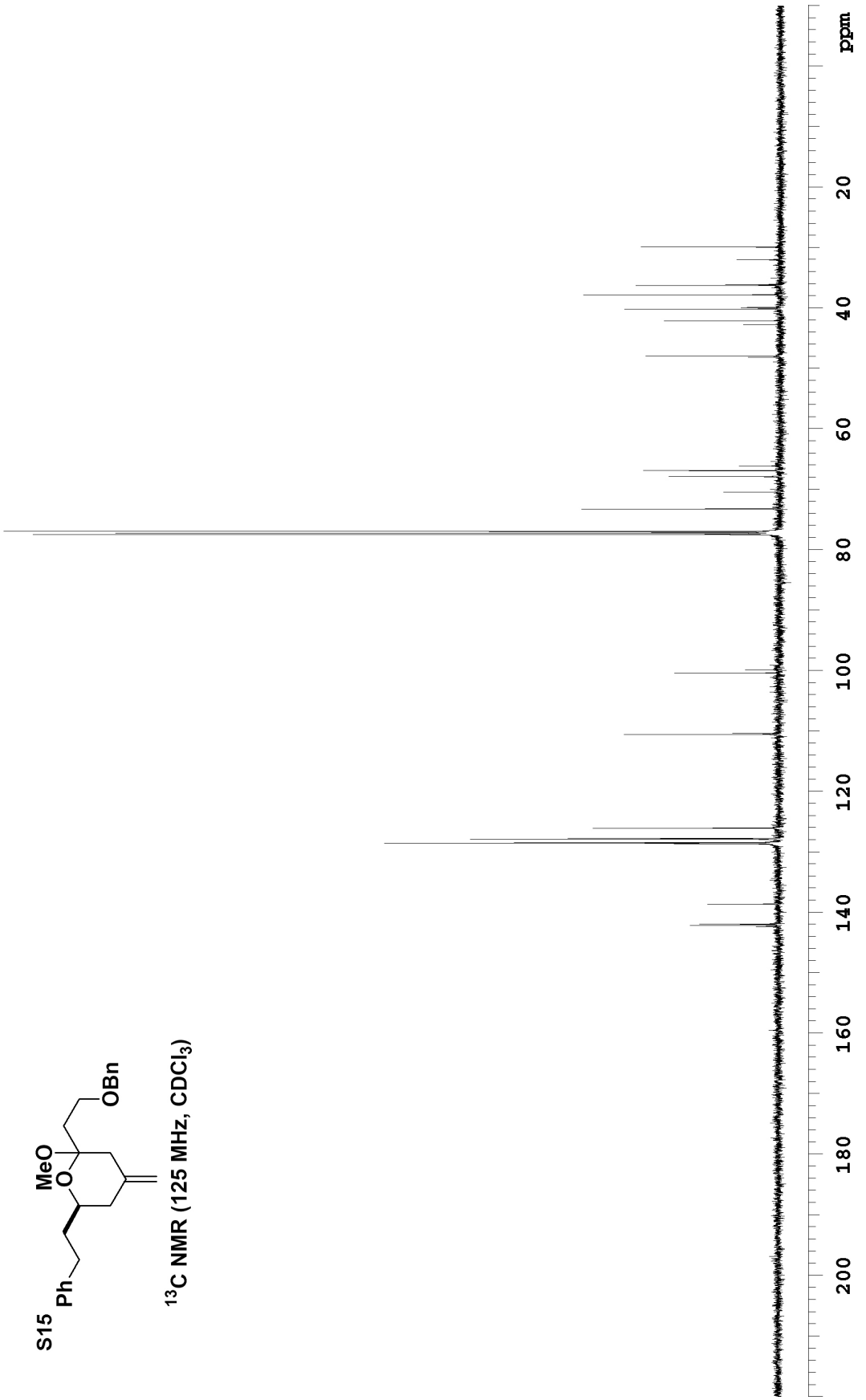

S13
OBn
O
O
Cl
DEPT (125 MHz, $CDCl_3$)
ppm
200
180
160
140
120
100
80
60
40
20

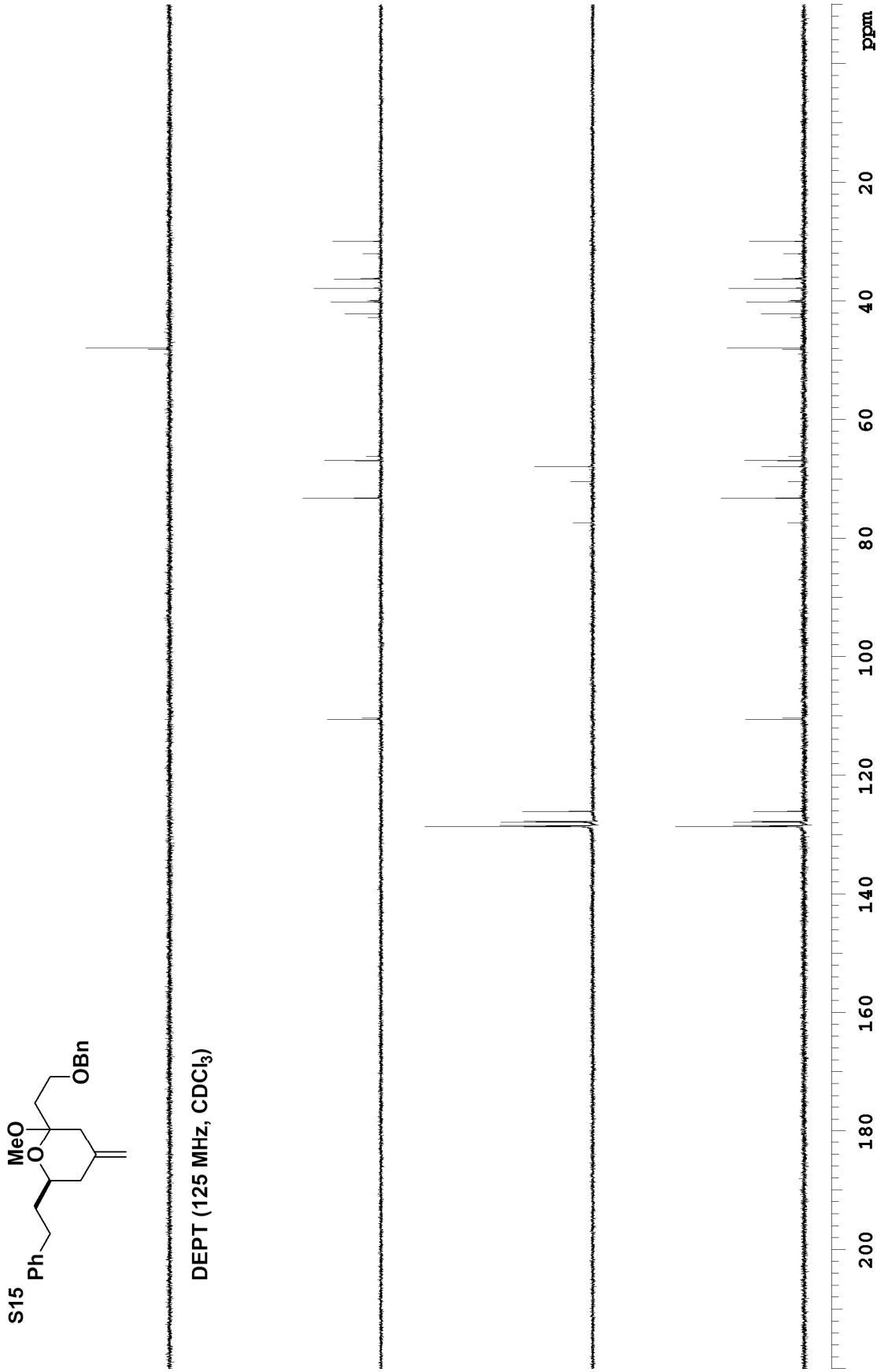

S14
OBn
O
O
I
^{1}H NMR (500 MHz, CDCl$_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0

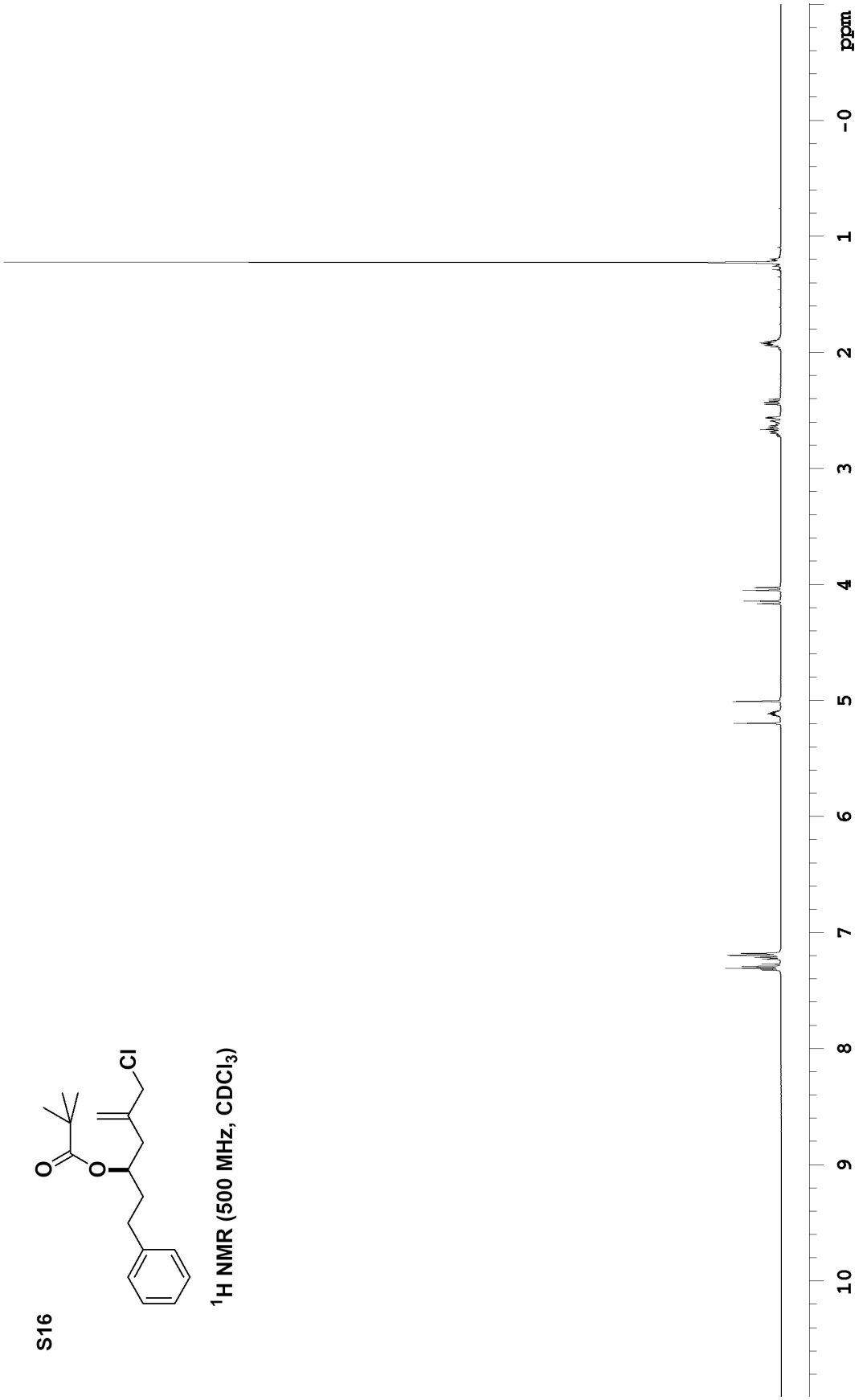

S14
OBn
O
O
I
^{13}C NMR (125 MHz, CDCl$_3$)
ppm
200
180
160
140
120
100
80
60
40
20

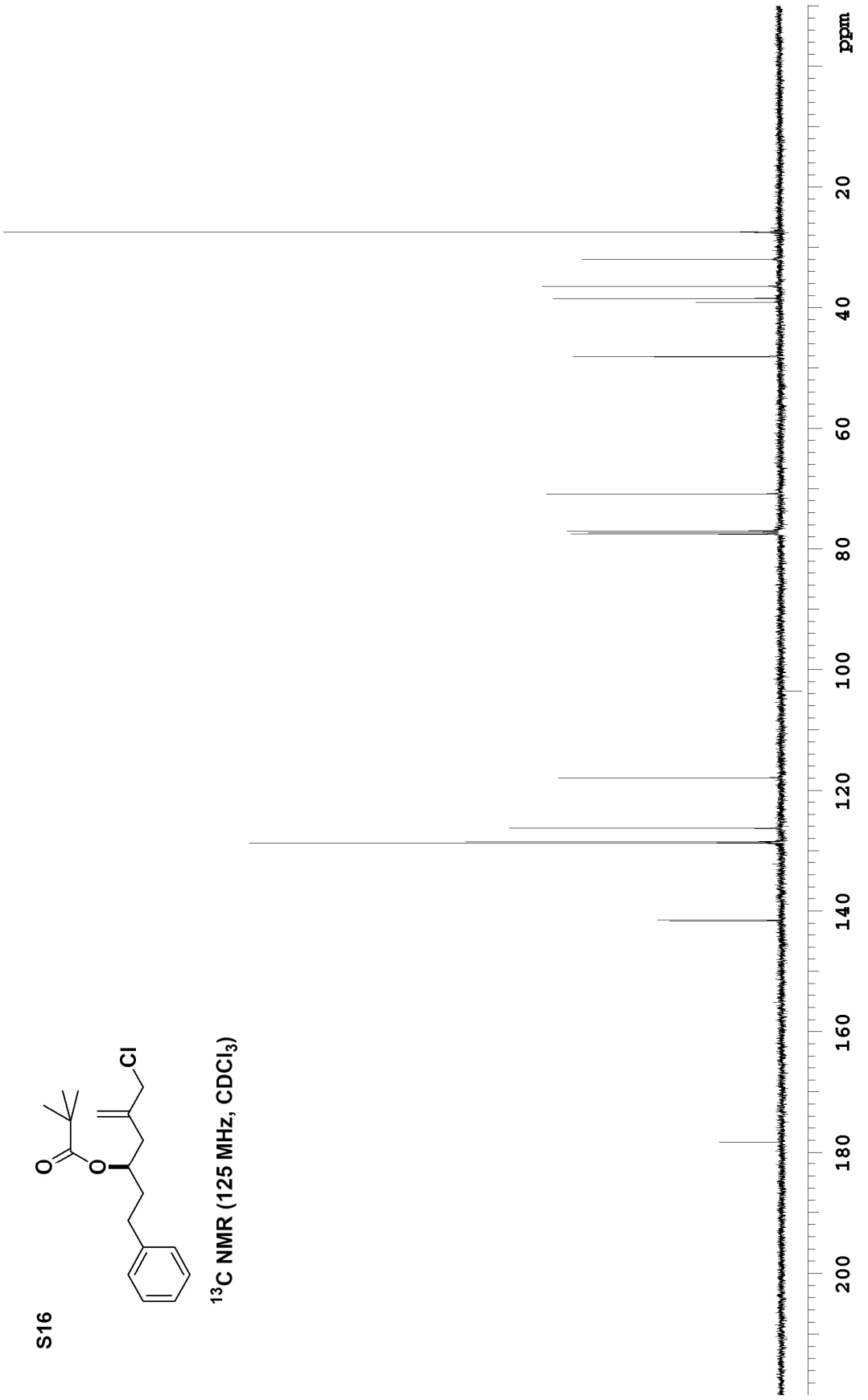

S14
OBn
O
O
I
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

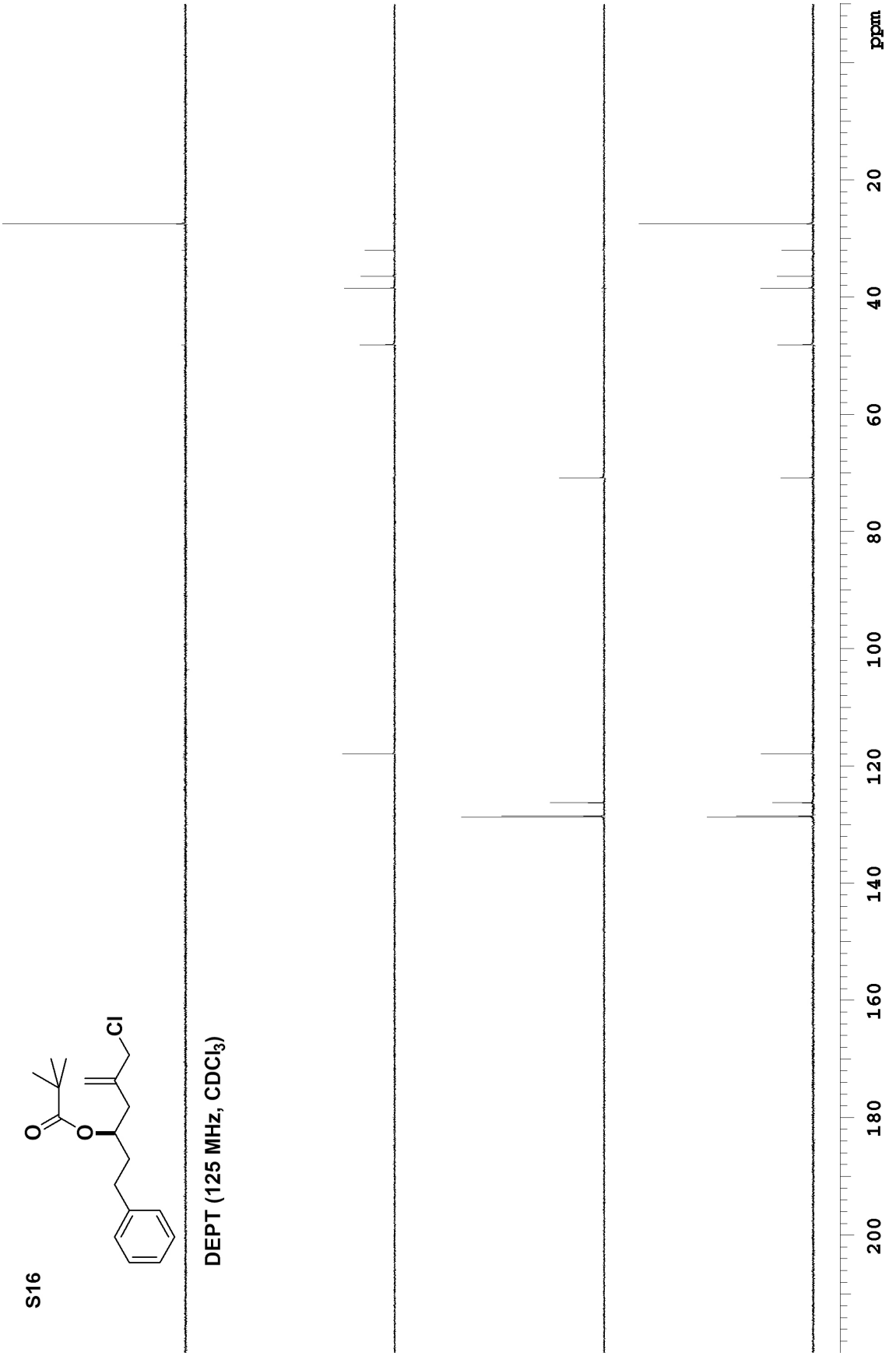

S15
Ph
O
MeO
OBn
^{1}H NMR (500 MHz, $CDCl_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0

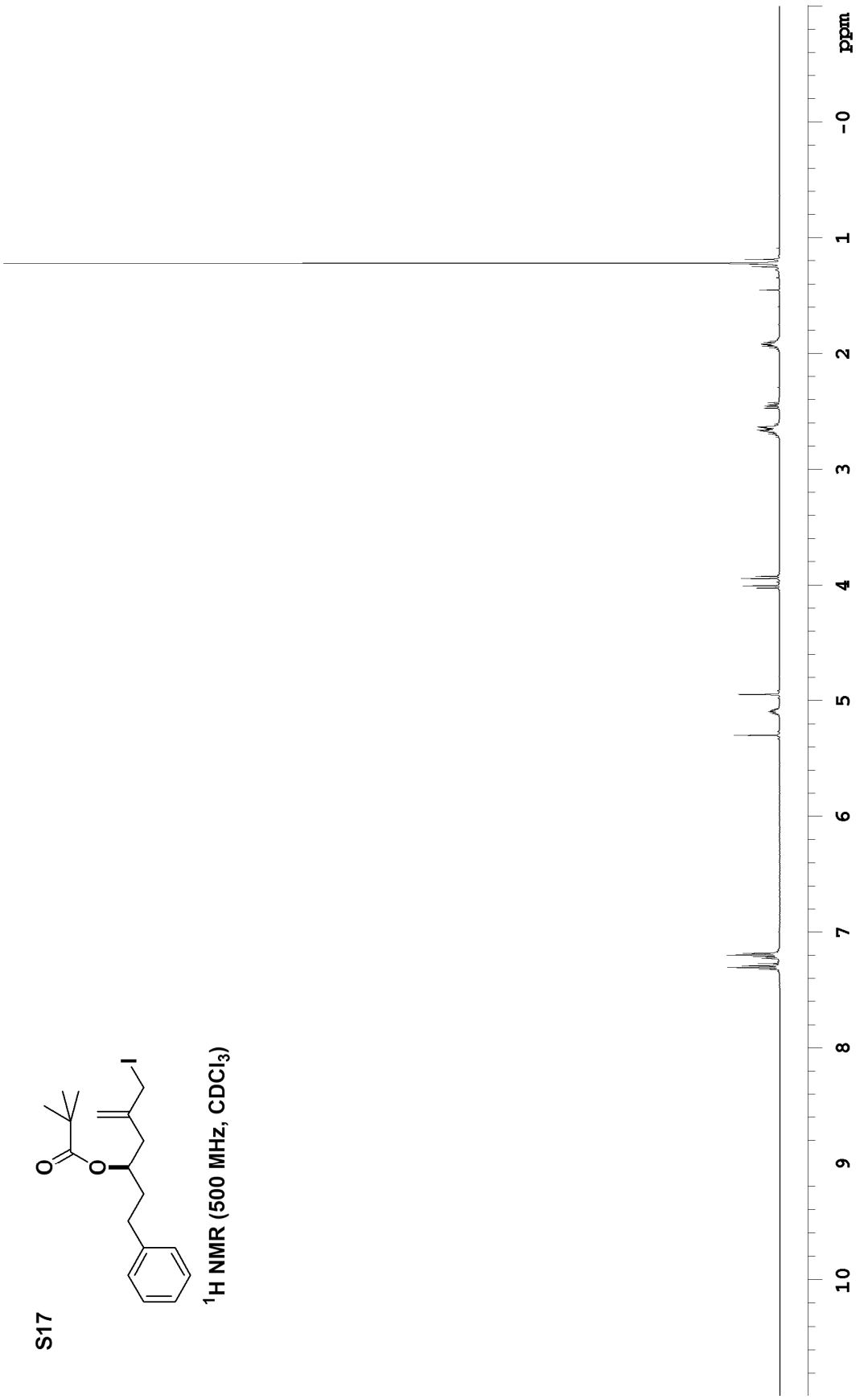

ppm
200
180
160
140
120
100
80
60
40
20
S15
Ph
O
MeO
OBn
^{13}C NMR (125 MHz, $CDCl_3$)

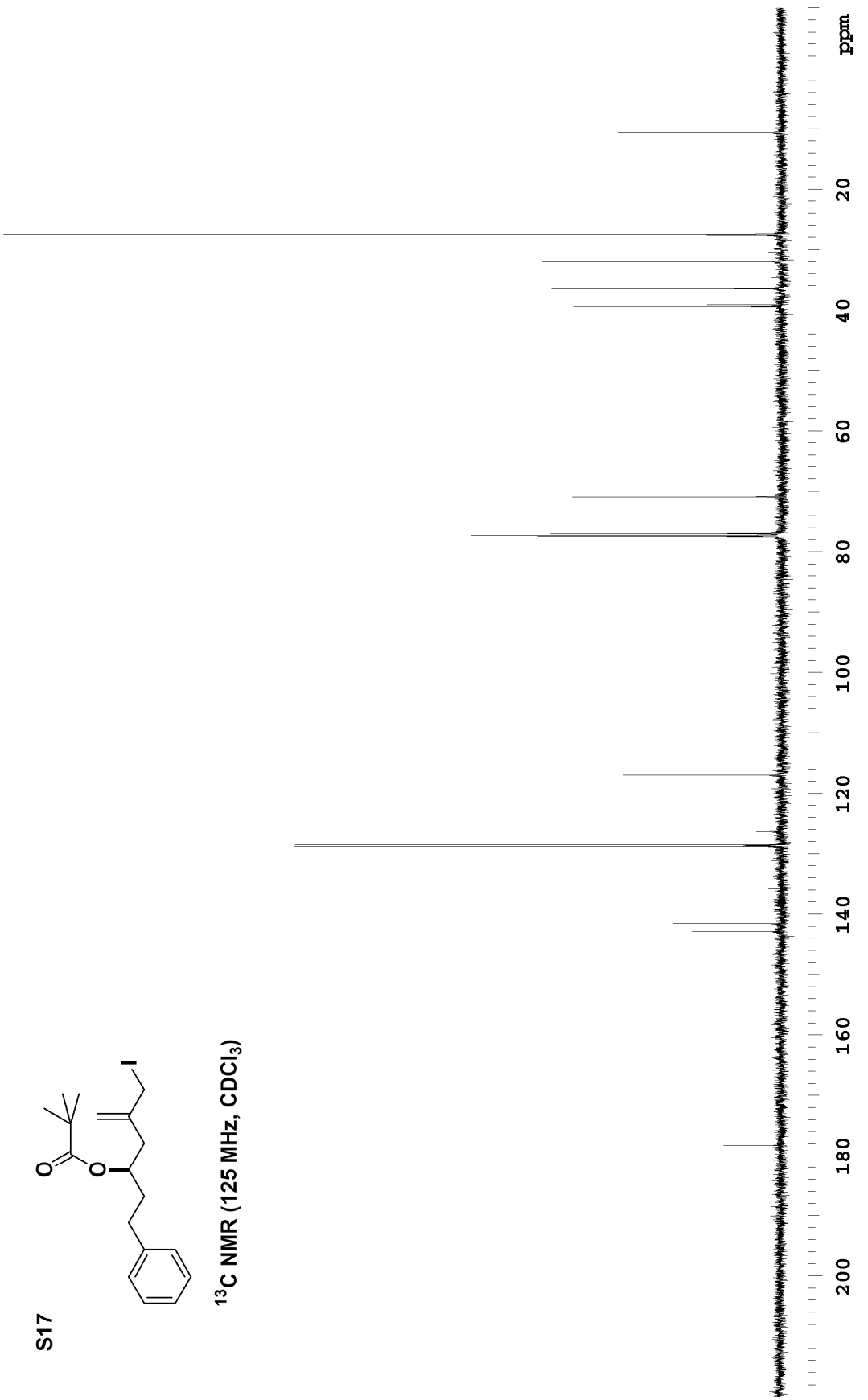

S15
Ph
MeO
O
OBn
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

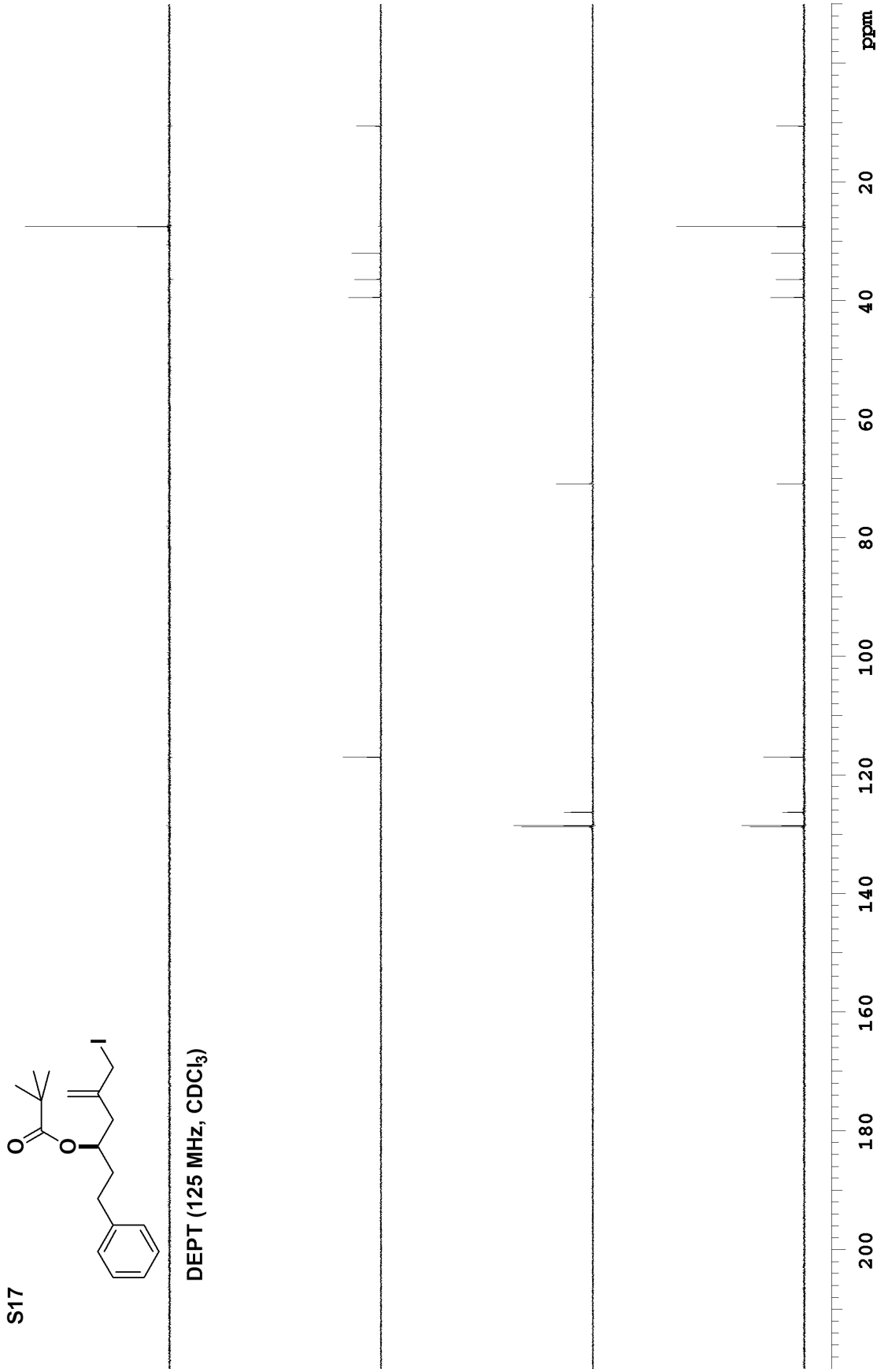

S16
O
O
Cl
^{1}H NMR (500 MHz, $CDCl_3$)
ppm
10
9
8
7
6
5
4
3
2
1
-0

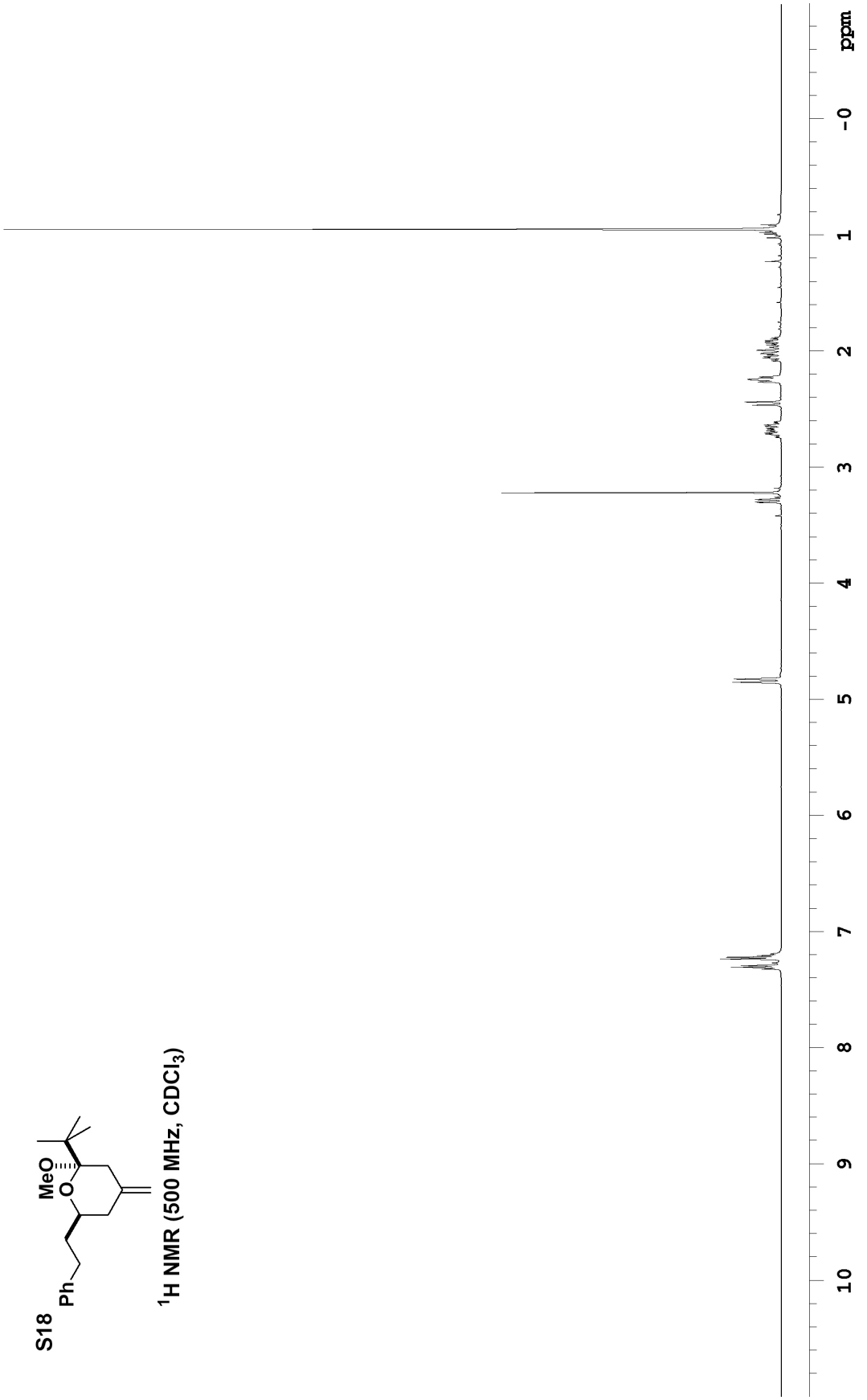

S16
Cl
O
O
^{13}C NMR (125 MHz, $CDCl_3$)
ppm
200
180
160
140
120
100
80
60
40
20


S16
DEPT (125 MHz, $CDCl_3$)
Cl
O
O
ppm
20
40
60
80
100
120
140
160
180
200


S17
^{1}H NMR (500 MHz, $CDCl_3$)
O
O
I
ppm
10
9
8
7
6
5
4
3
2
1
0

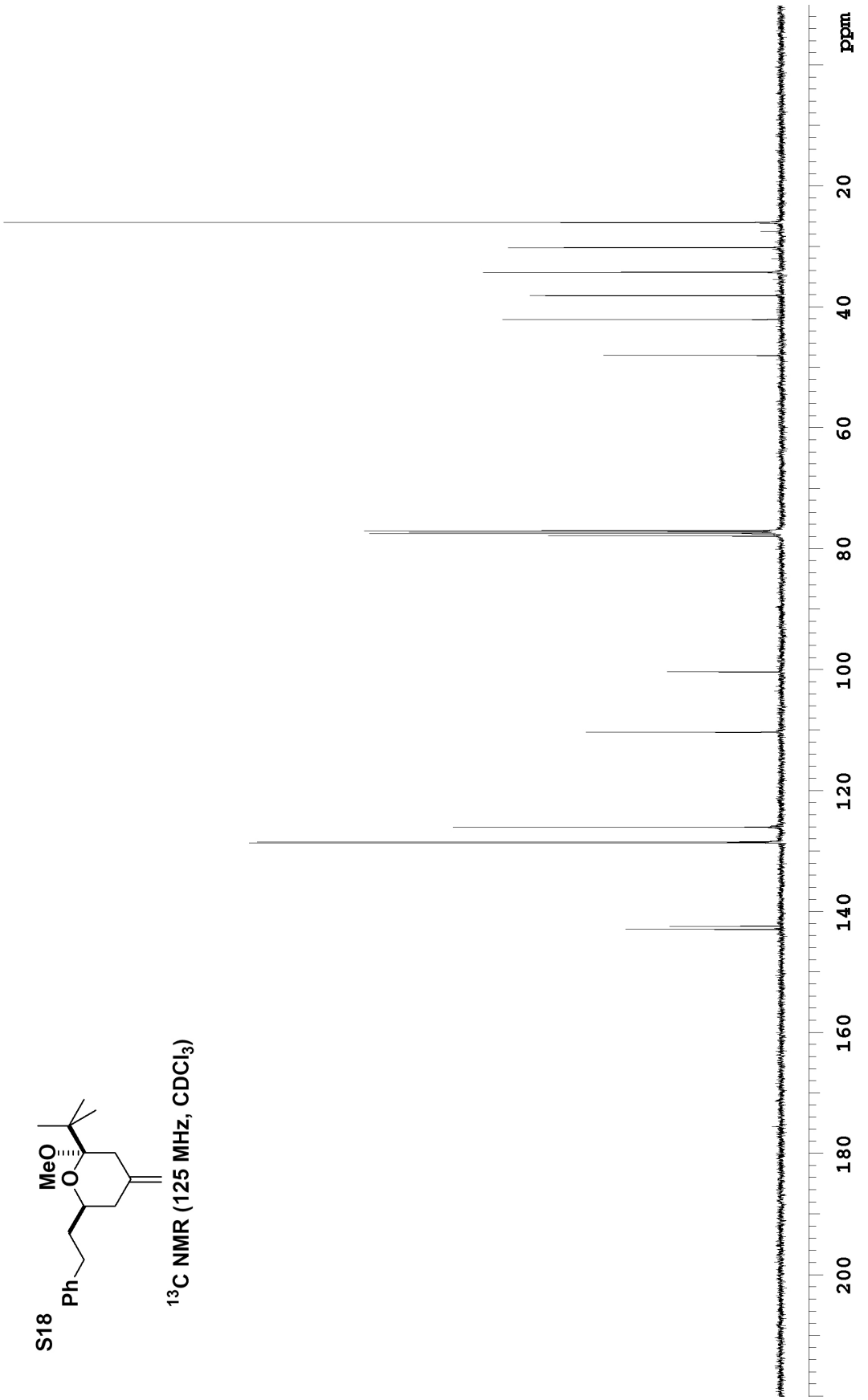

S17
^{13}C NMR (125 MHz, CDCl$_3$)
ppm
200
180
160
140
120
100
80
60
40
20


S17
DEPT (125 MHz, $CDCl_3$)
O
O
I
ppm
20
40
60
80
100
120
140
160
180
200



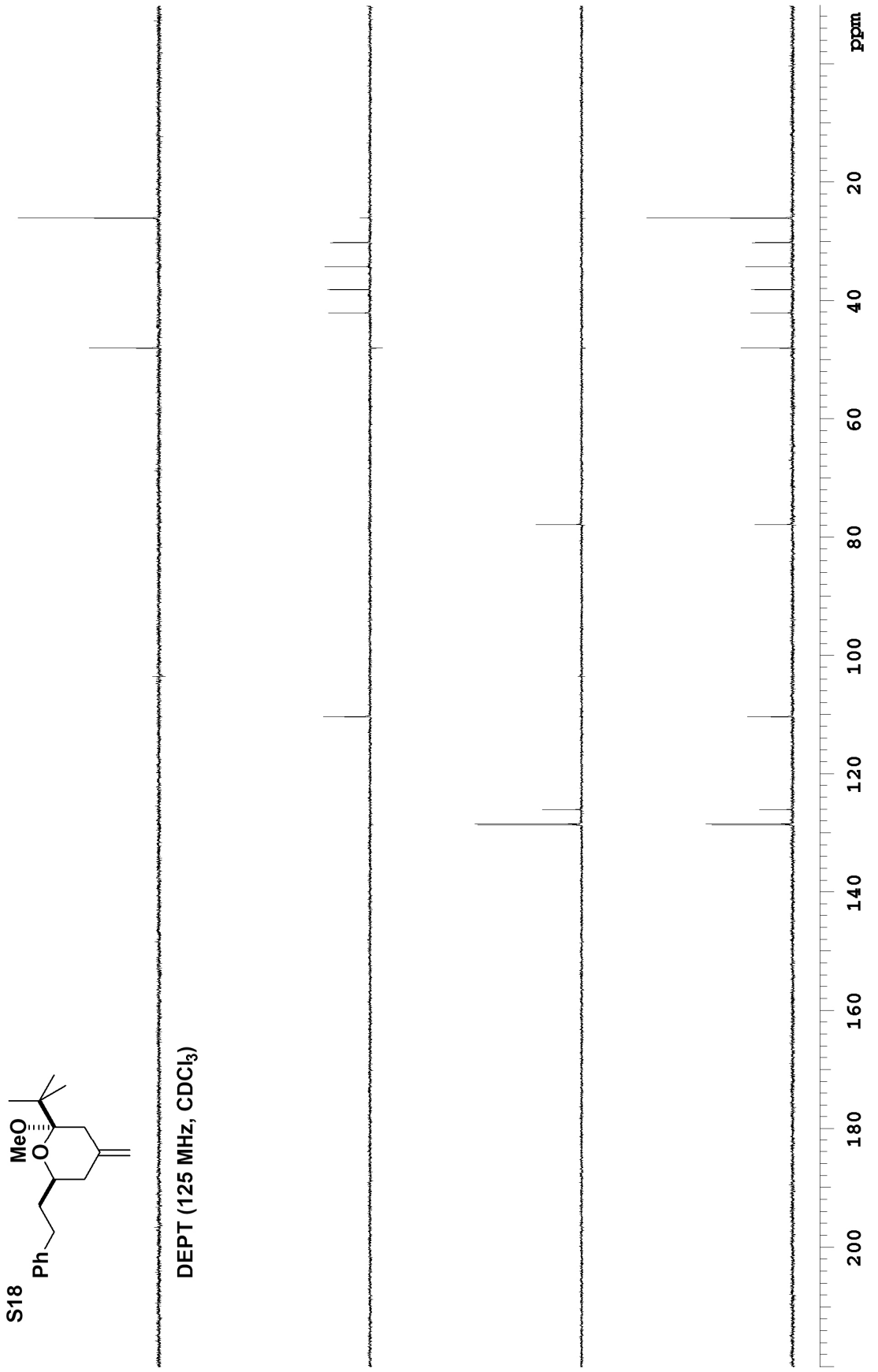
S18

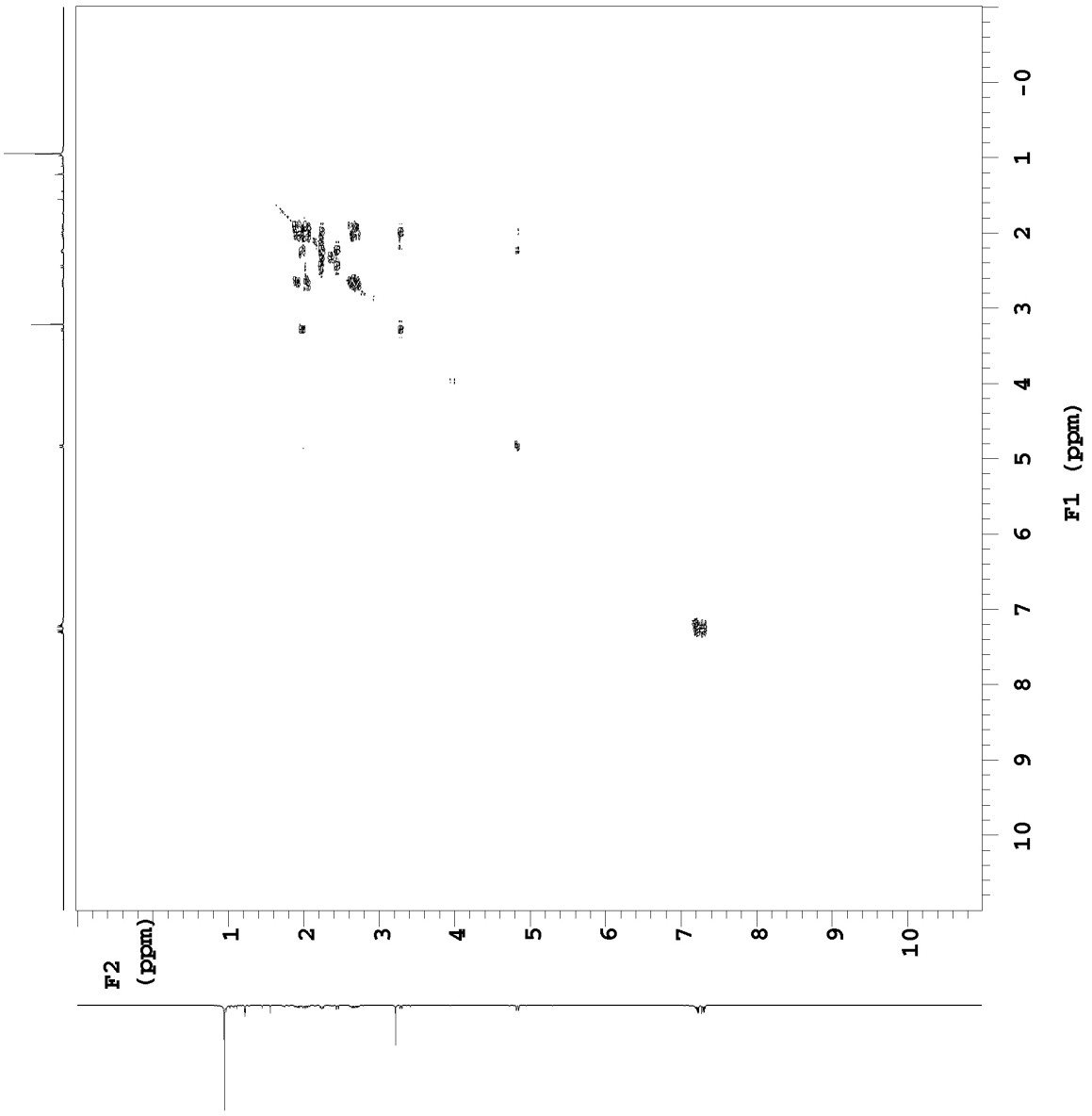
^{1}H NMR (500 MHz, $CDCl_3$)

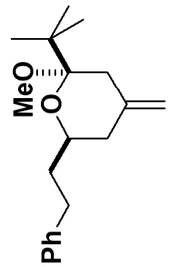


S18

^{13}C NMR (125 MHz, $CDCl_3$)

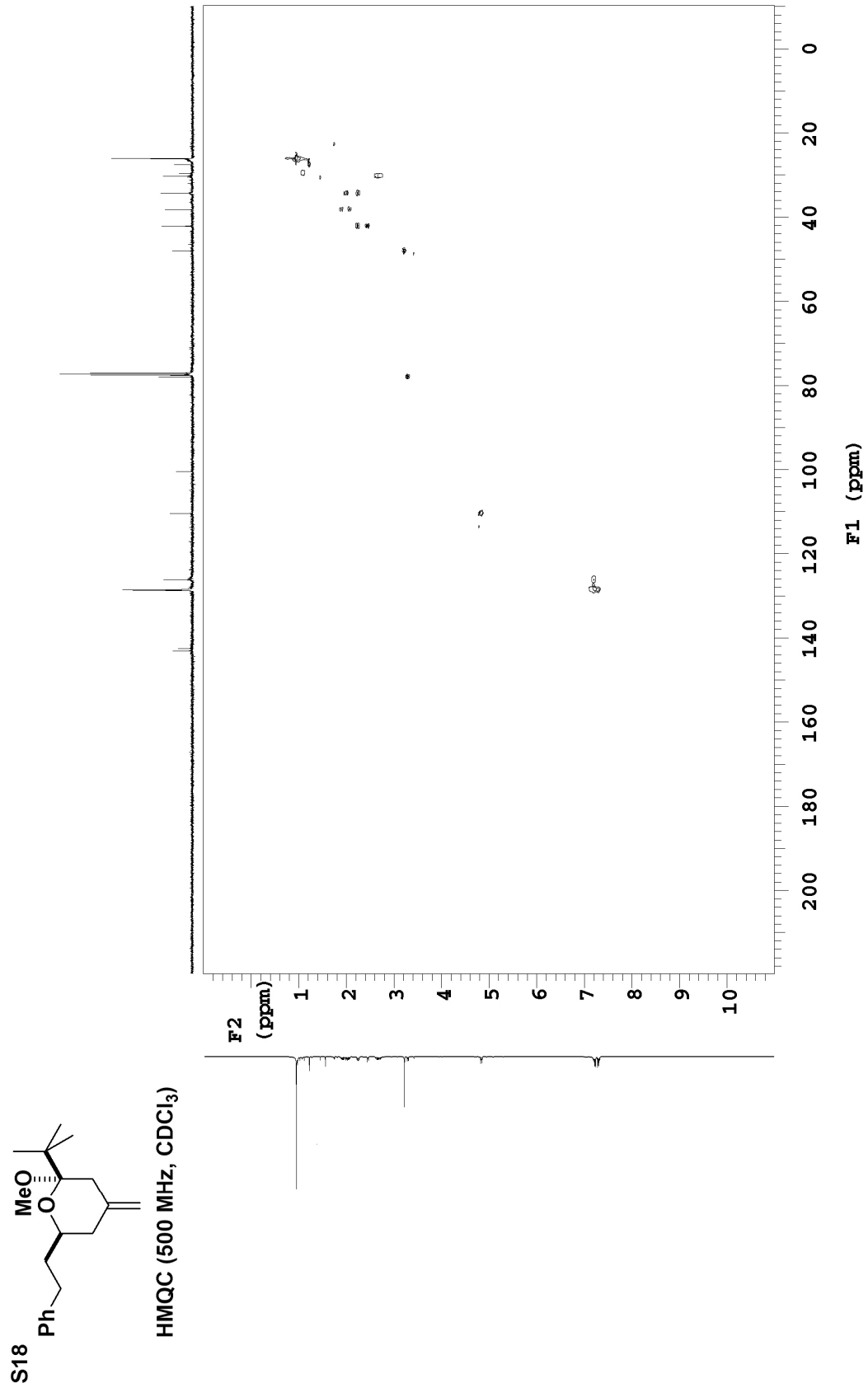

S18
MeO
O
Ph
DEPT (125 MHz, $CDCl_3$)
ppm
20
40
60
80
100
120
140
160
180
200

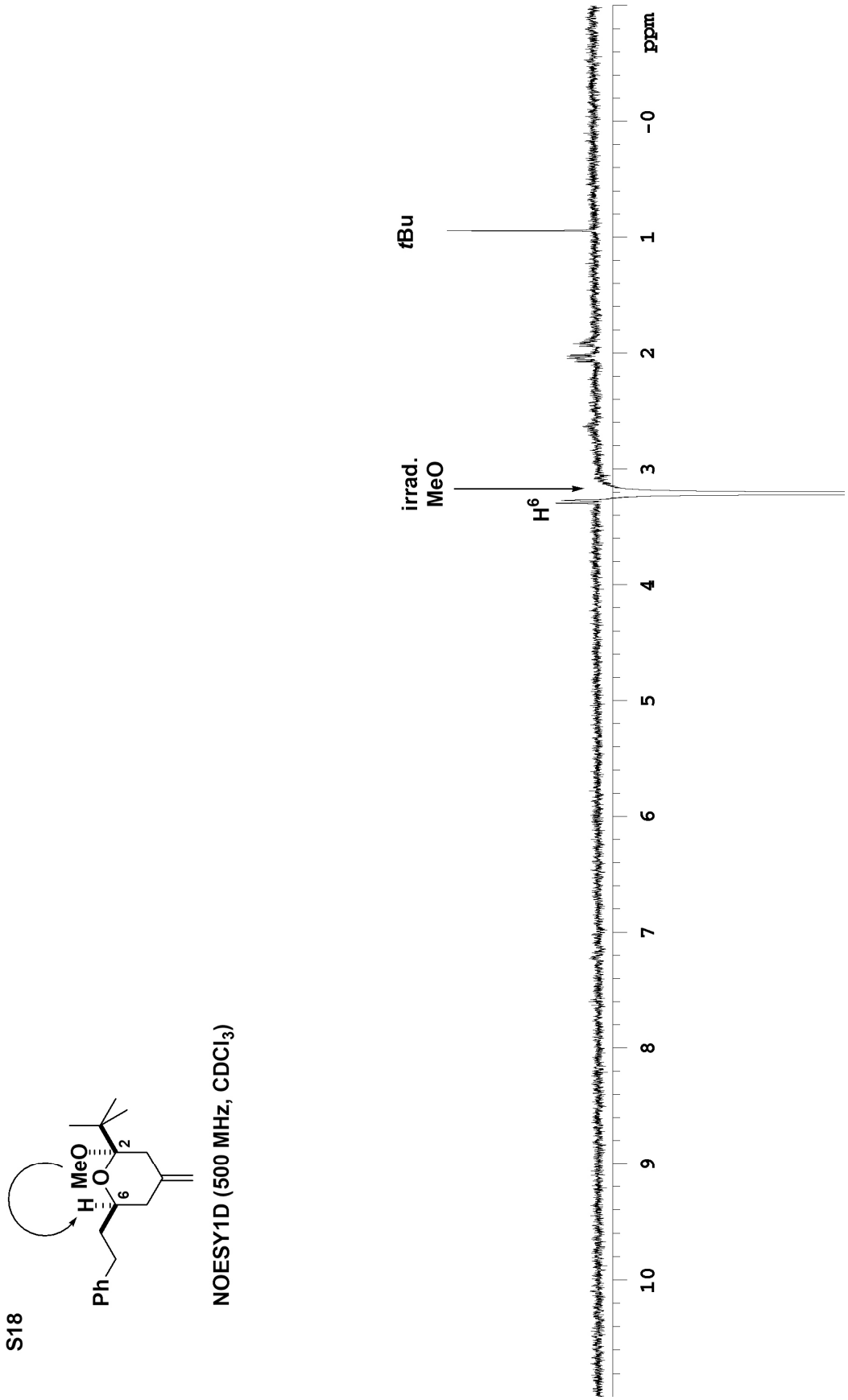


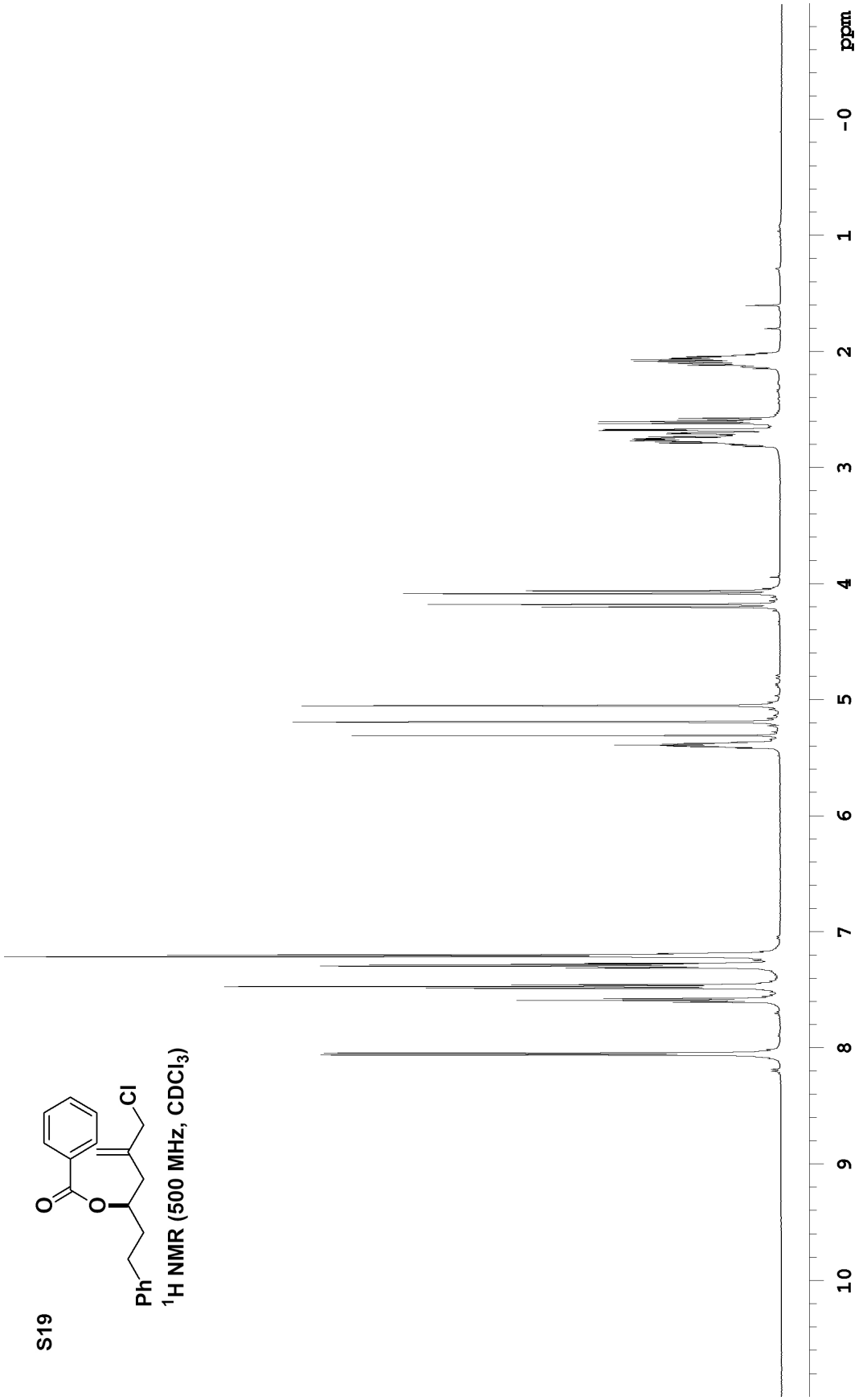


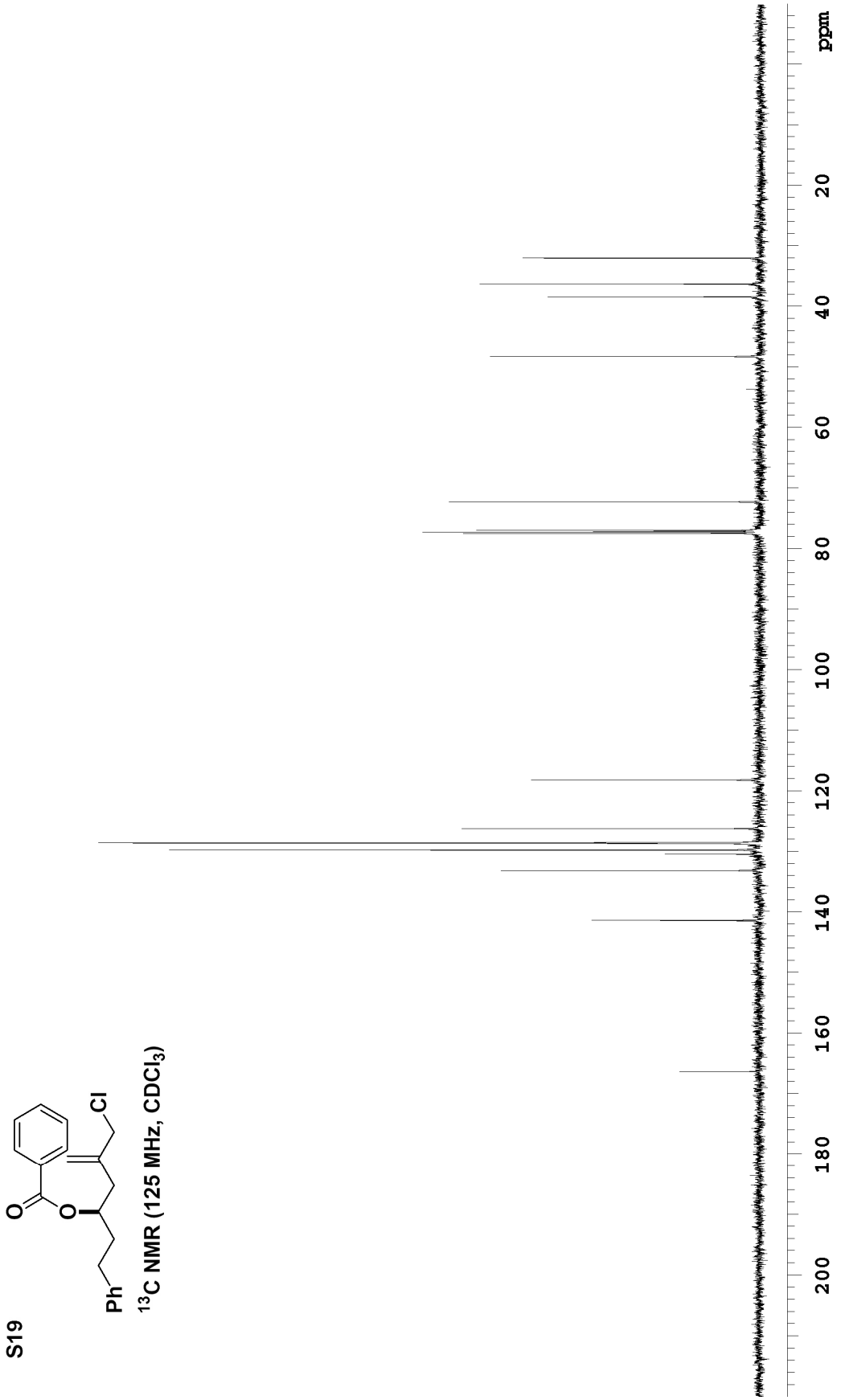
S18

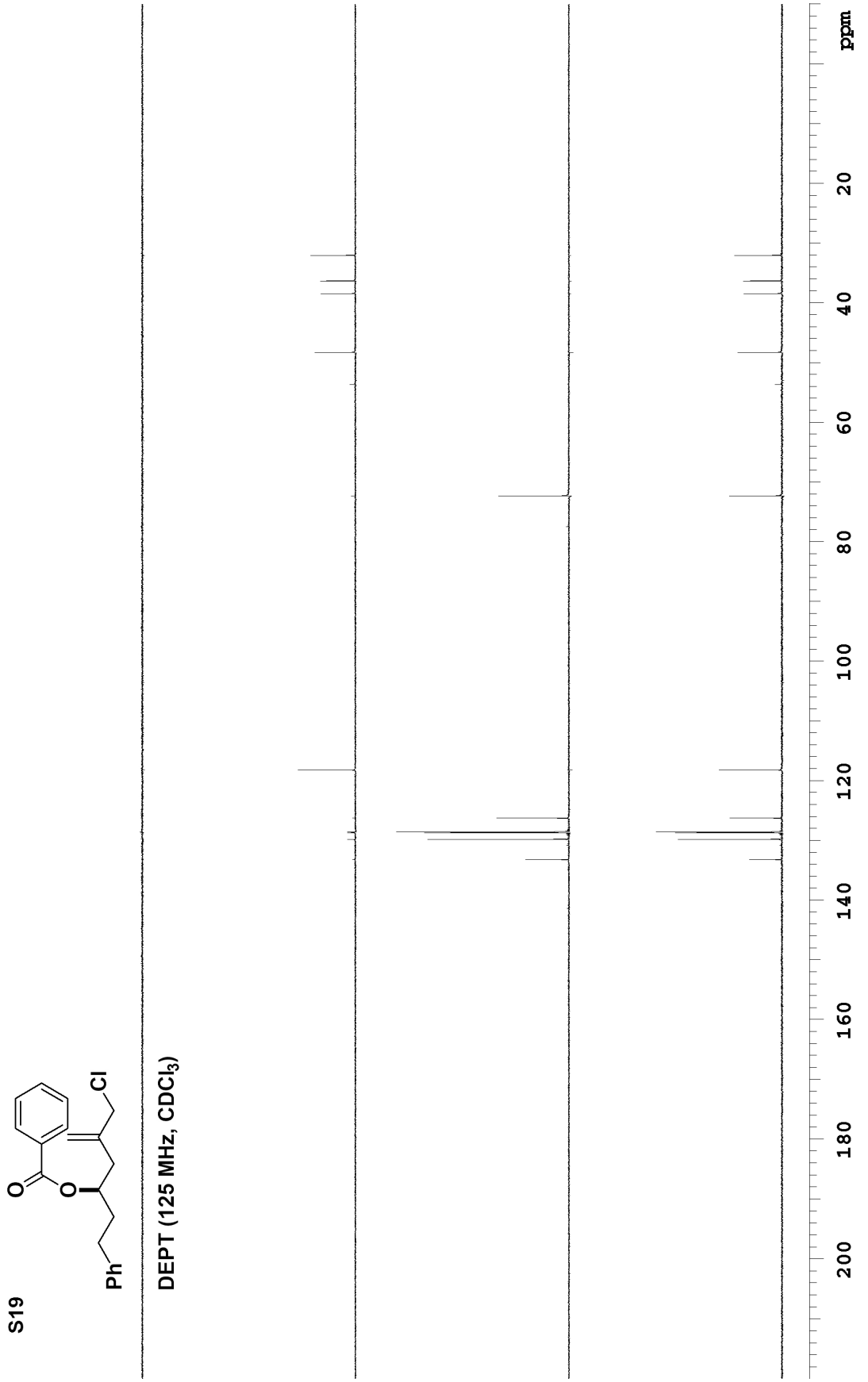
DQCOSY (500 MHz, $CDCl_3$)

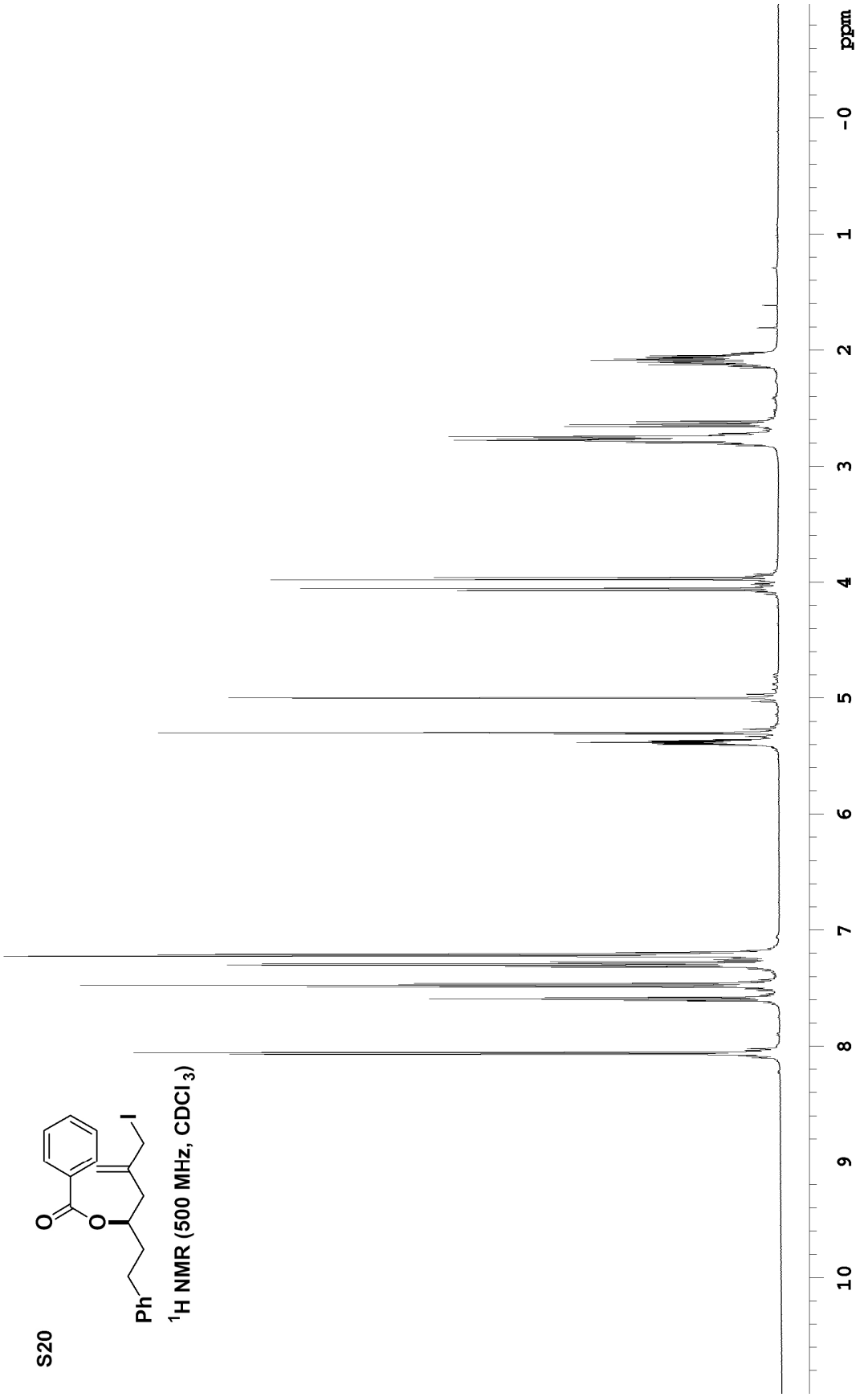

S18
MeO
O
Ph
HMQC (500 MHz, CDCl3)
F2 (ppm)
1
2
3
4
5
6
7
8
9
10
F1 (ppm)
0
20
40
60
80
100
120
140
160
180
200

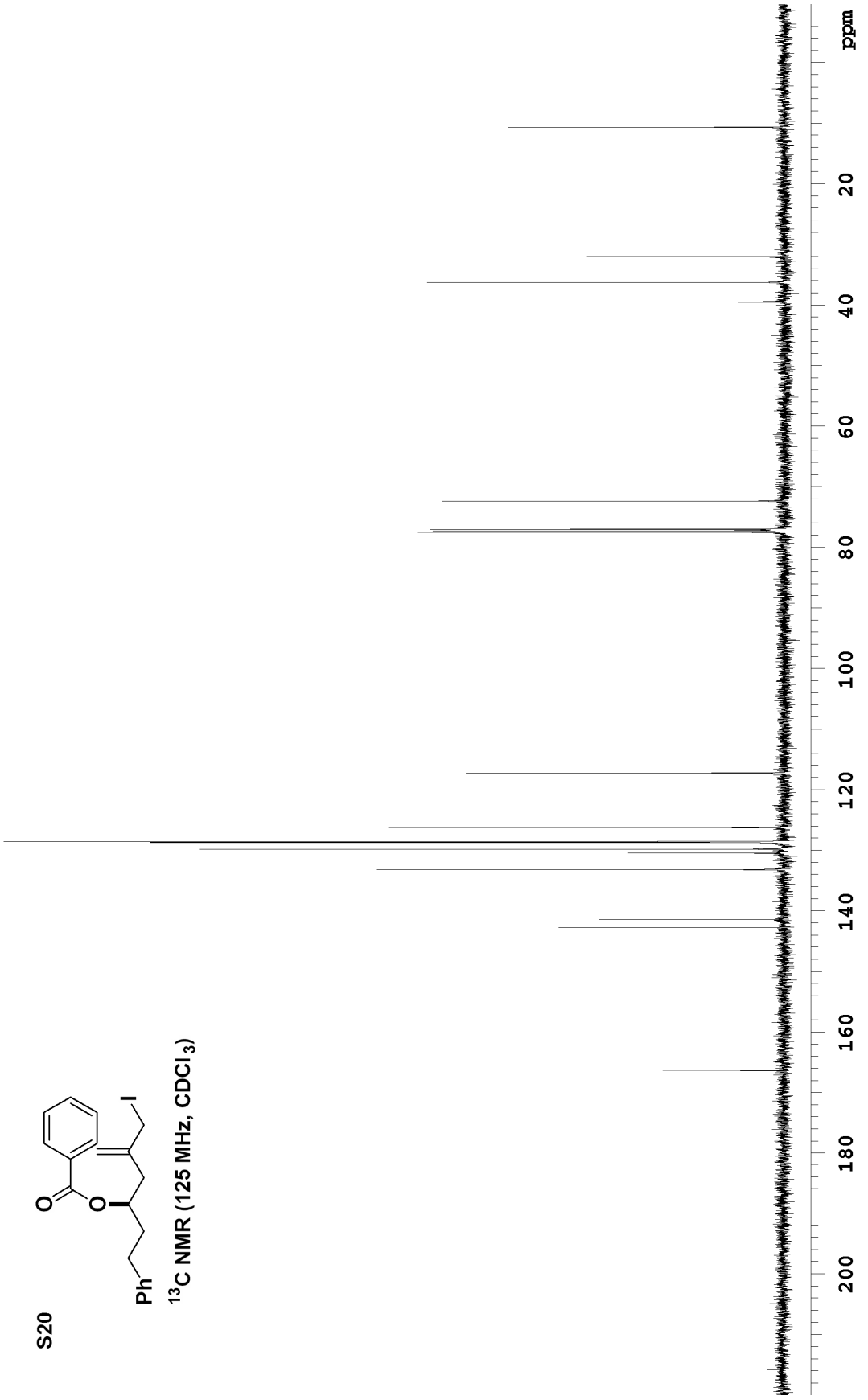

S18
NOESY1D (500 MHz, CDCl3)
MeO
H
O
2
6
Ph
tBu
irrad.
MeO
H6
ppm
10
9
8
7
6
5
4
3
2
1
-0

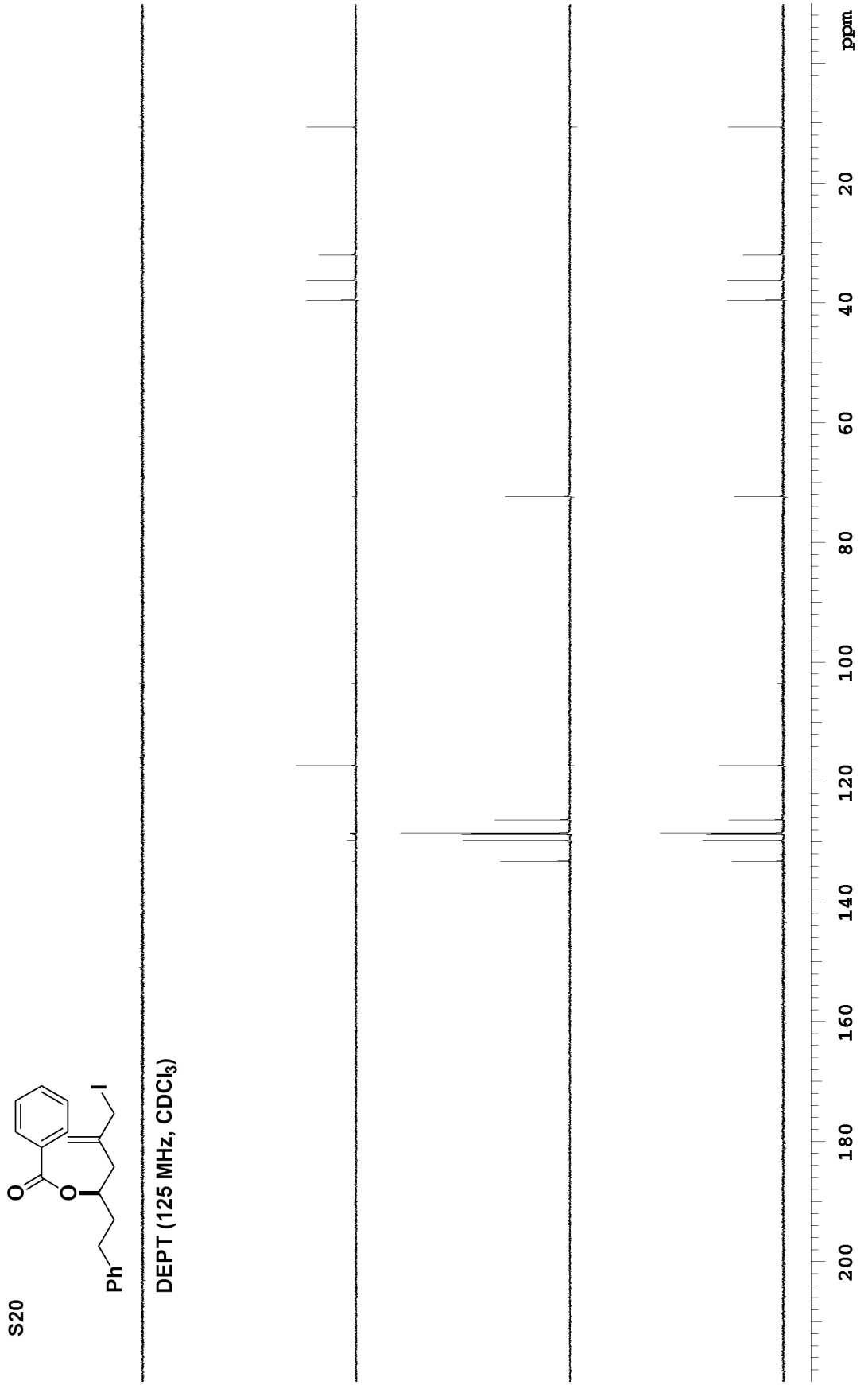

S19
Ph
Cl
O
O
^{1}H NMR (500 MHz, $CDCl_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0

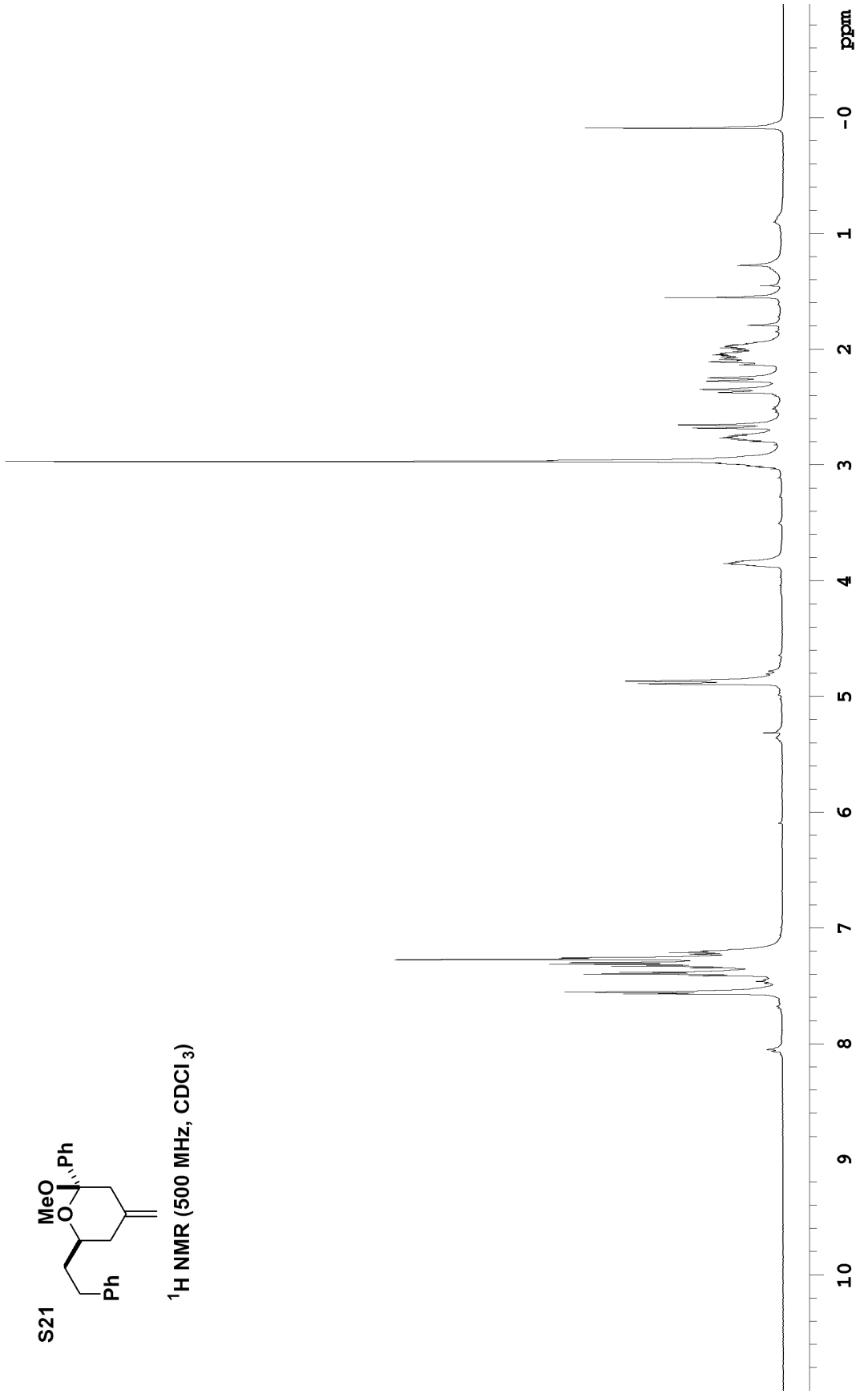

S19
^{13}C NMR (125 MHz, $CDCl_3$)
Cl
O
O
Ph
ppm
200
180
160
140
120
100
80
60
40
20

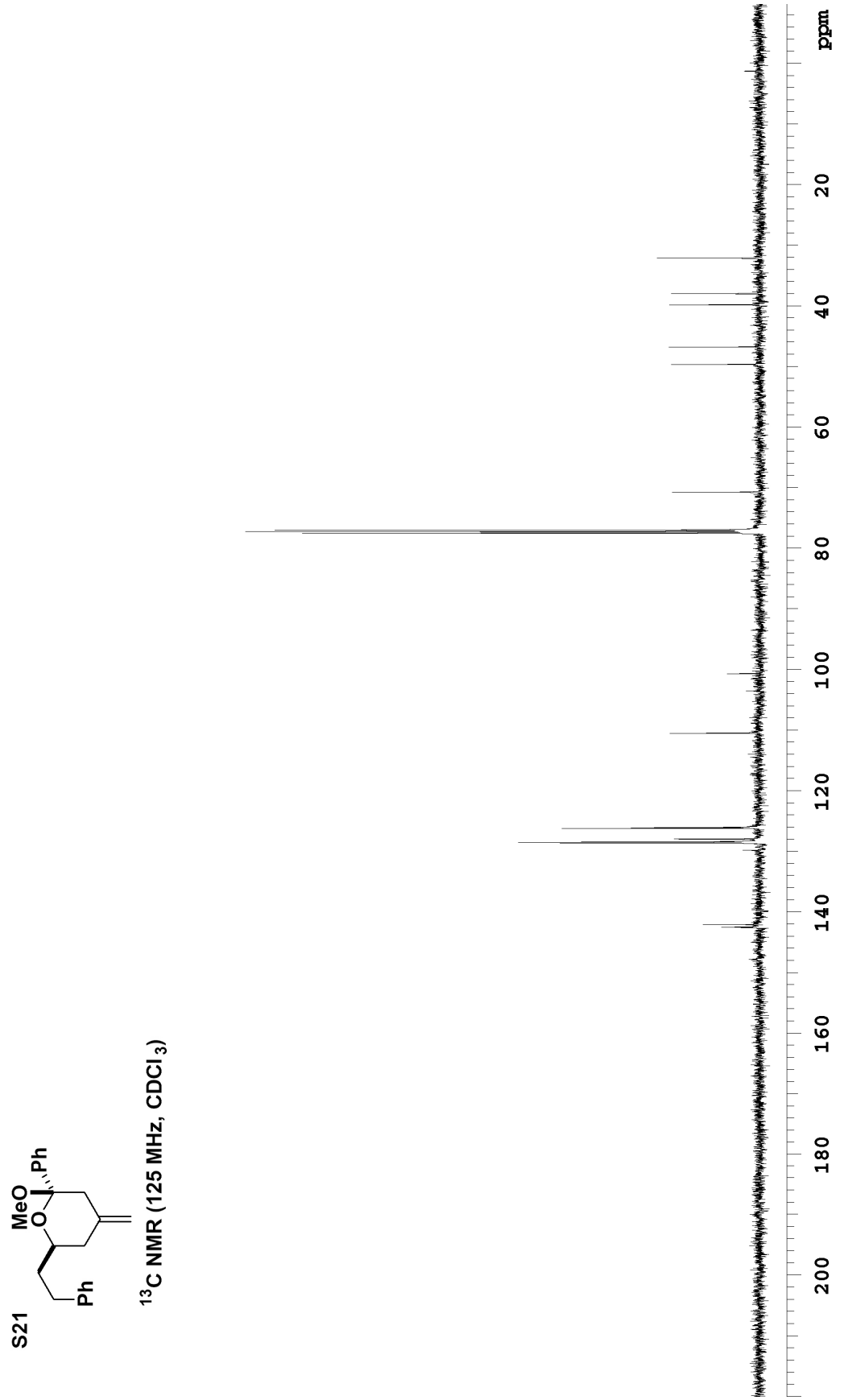

S19
Ph
O
O
Cl
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

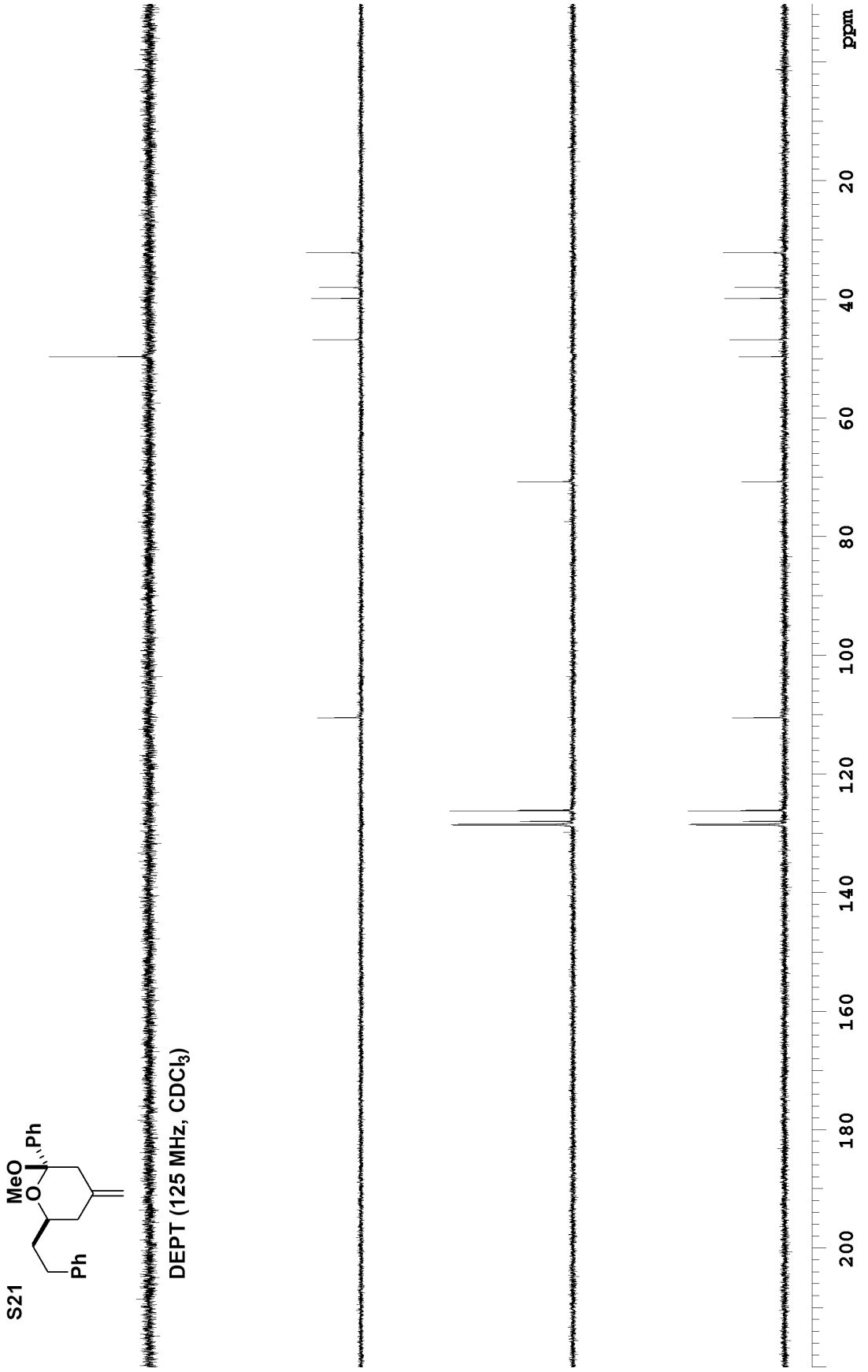

S20
^{1}H NMR (500 MHz, CDCl$_3$)
O
O
I
Ph
ppm
10
9
8
7
6
5
4
3
2
1
-0

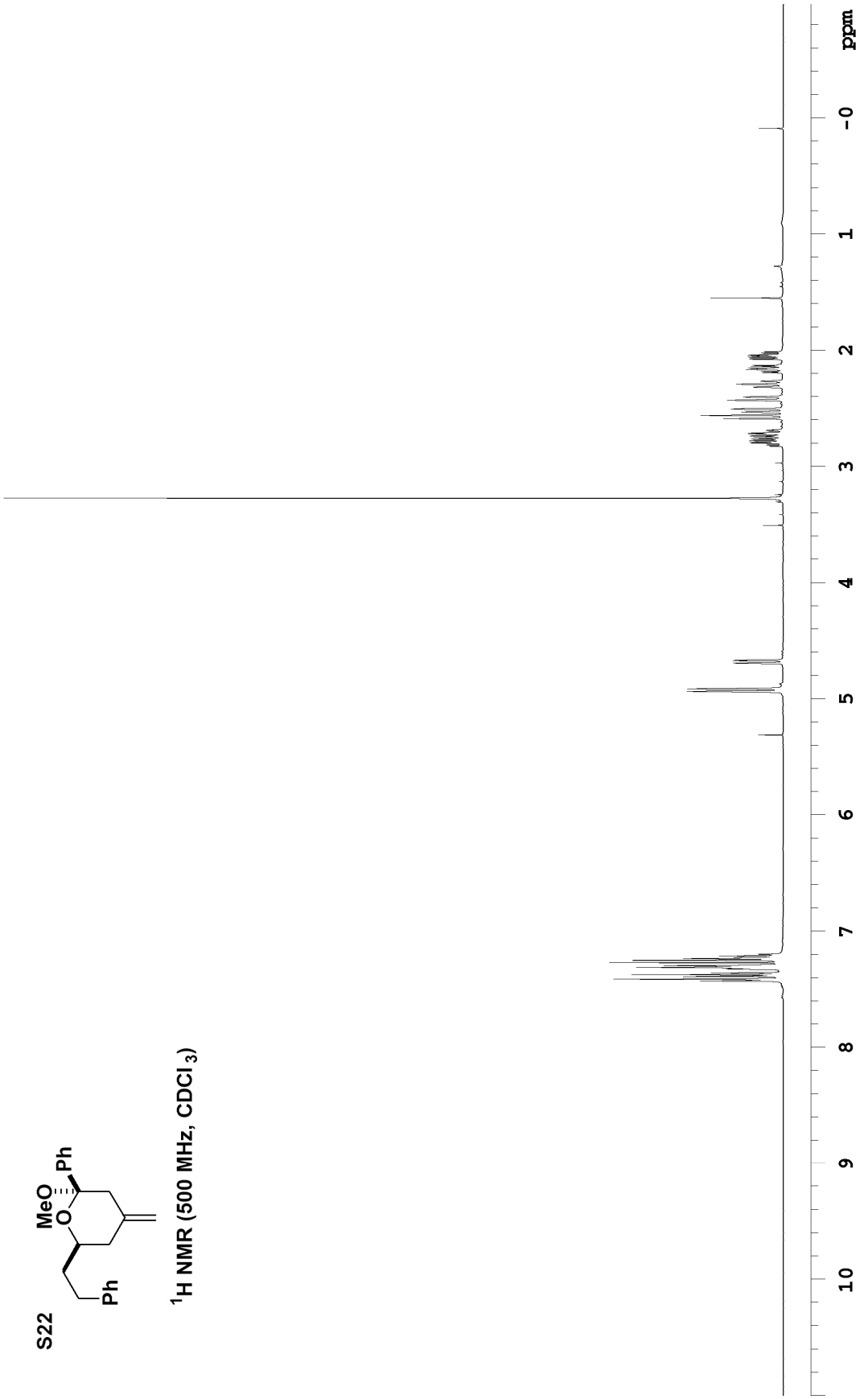

S20
^{13}C NMR (125 MHz, CDCl$_3$)
O
O
I
Ph
ppm
200
180
160
140
120
100
80
60
40
20

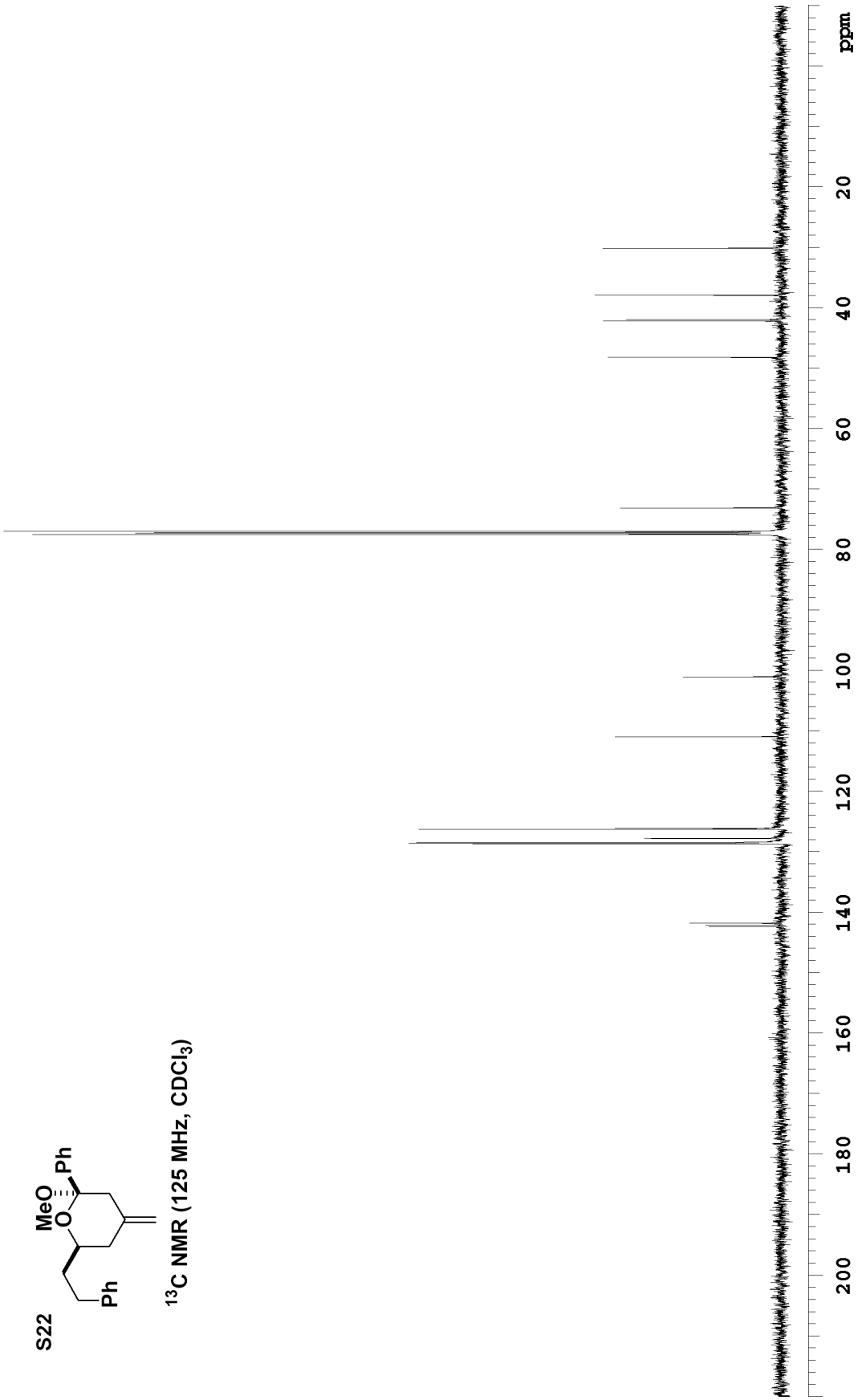

S20
DEPT (125 MHz, $CDCl_3$)
ppm
200
180
160
140
120
100
80
60
40
20

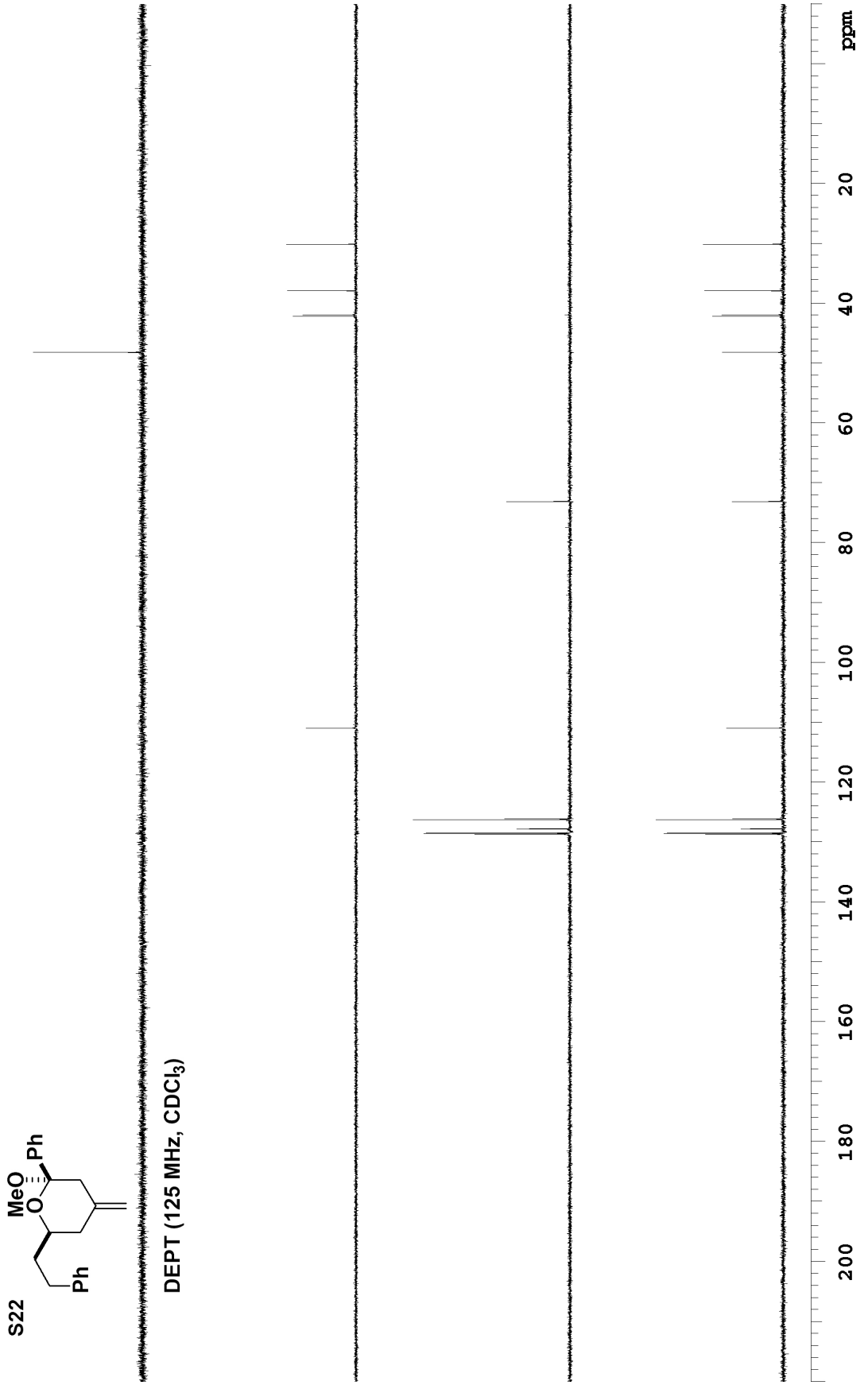

MeO
O
Ph
Ph
S21
^{1}H NMR (500 MHz, CDCl$_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0

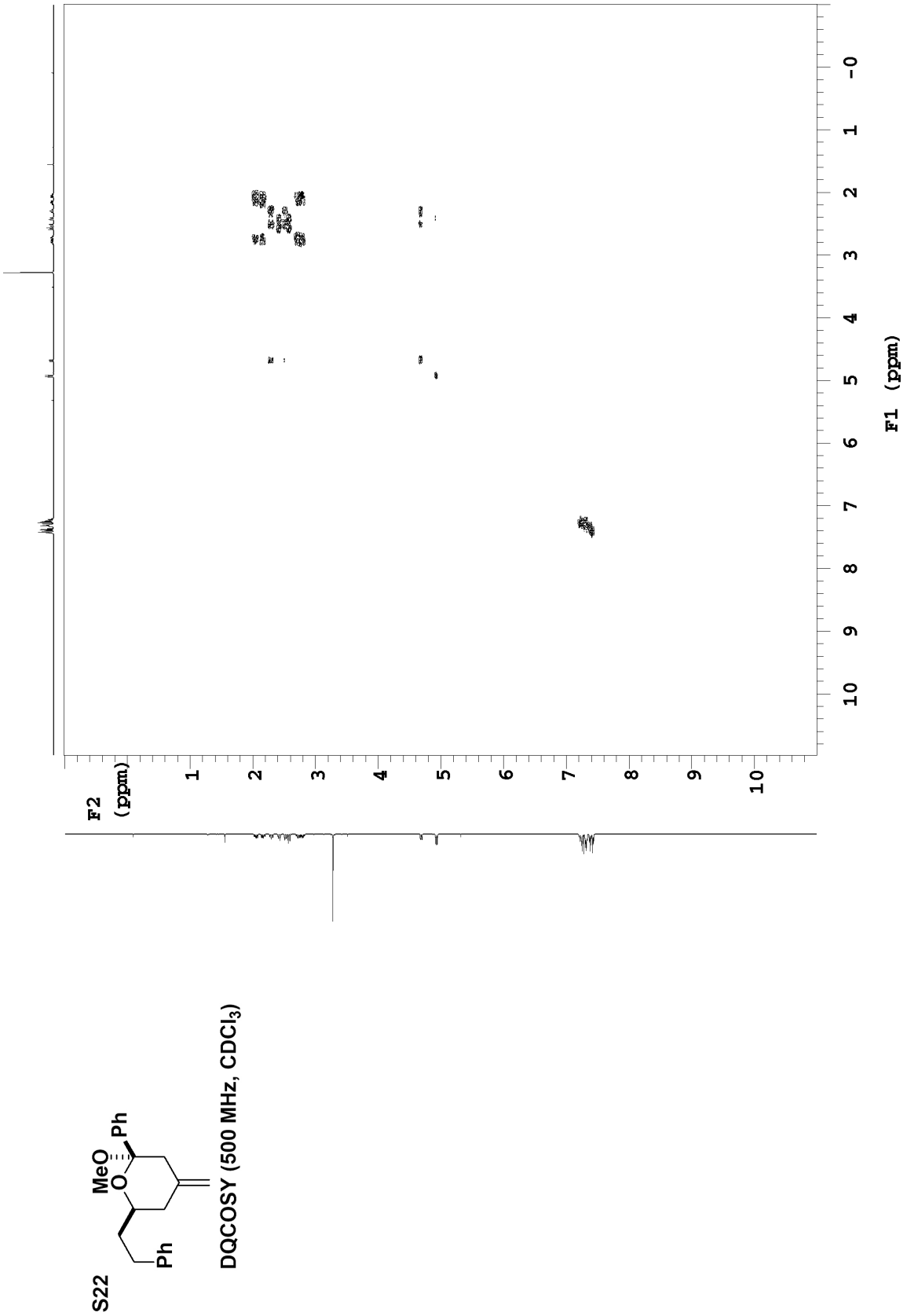

MeO
O
Ph
Ph
S21
^{13}C NMR (125 MHz, CDCl$_3$)
ppm
200
180
160
140
120
100
80
60
40
20


S21
MeO
O
Ph
Ph
DEPT (125 MHz, CDCl3)
200
180
160
140
120
100
80
60
40
20
ppm


S22
MeO
O
Ph
Ph
^{1}H NMR (500 MHz, CDCl$_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0

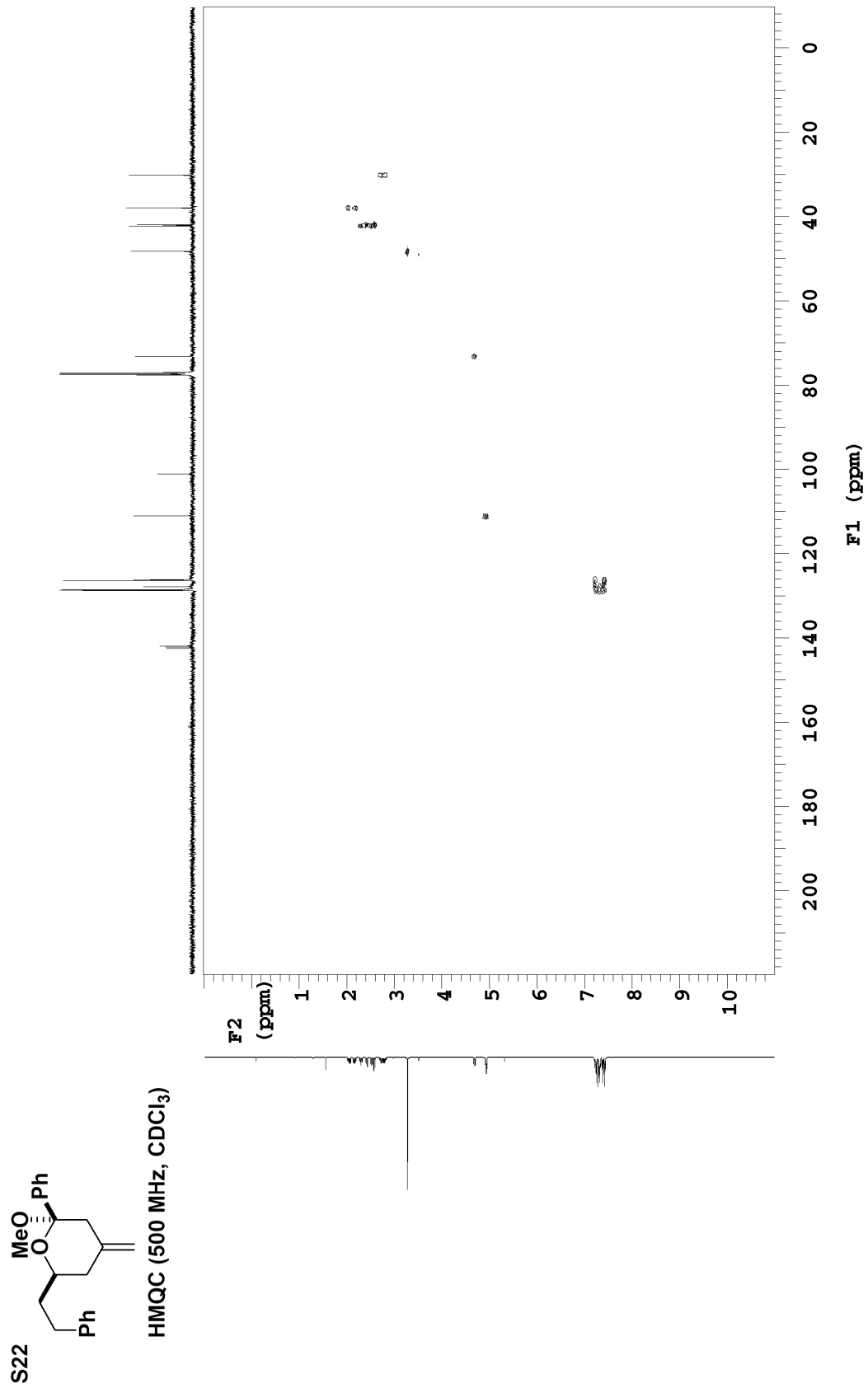

ppm
20
40
60
80
100
120
140
160
180
200
MeO
O
Ph
Ph
S22
^{13}C NMR (125 MHz, $CDCl_3$)

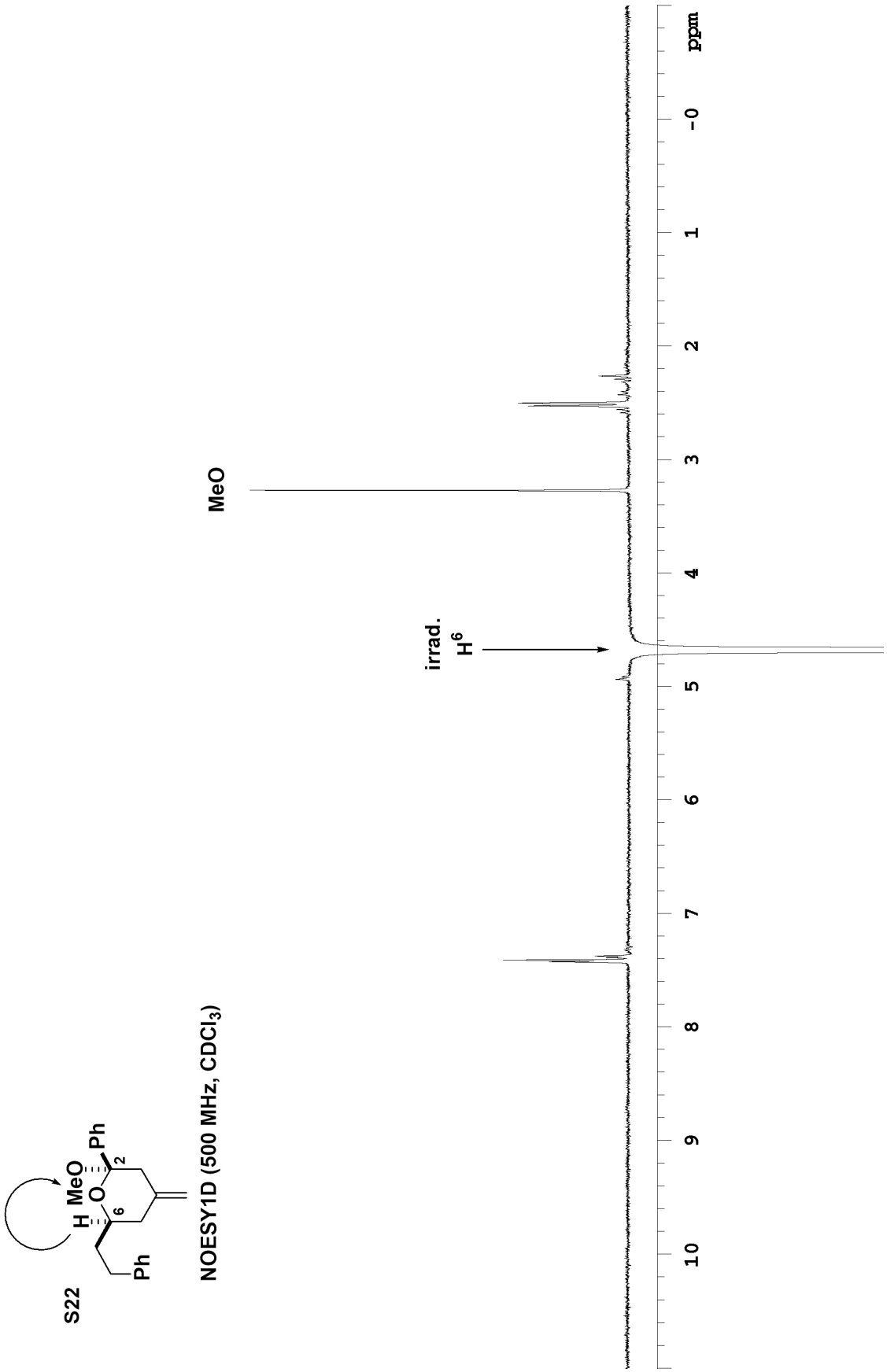

S22
MeO
Ph
Ph
O
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

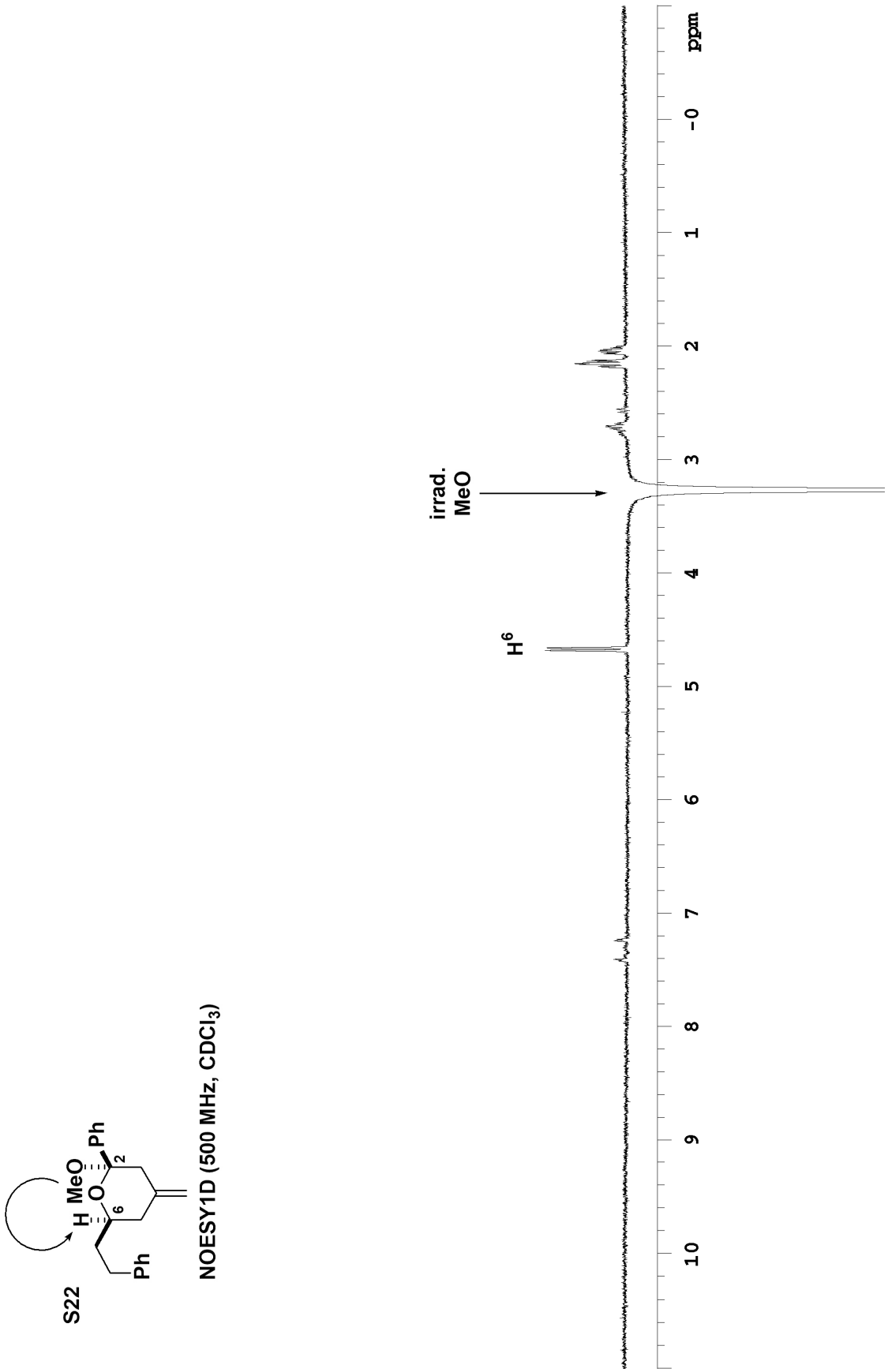


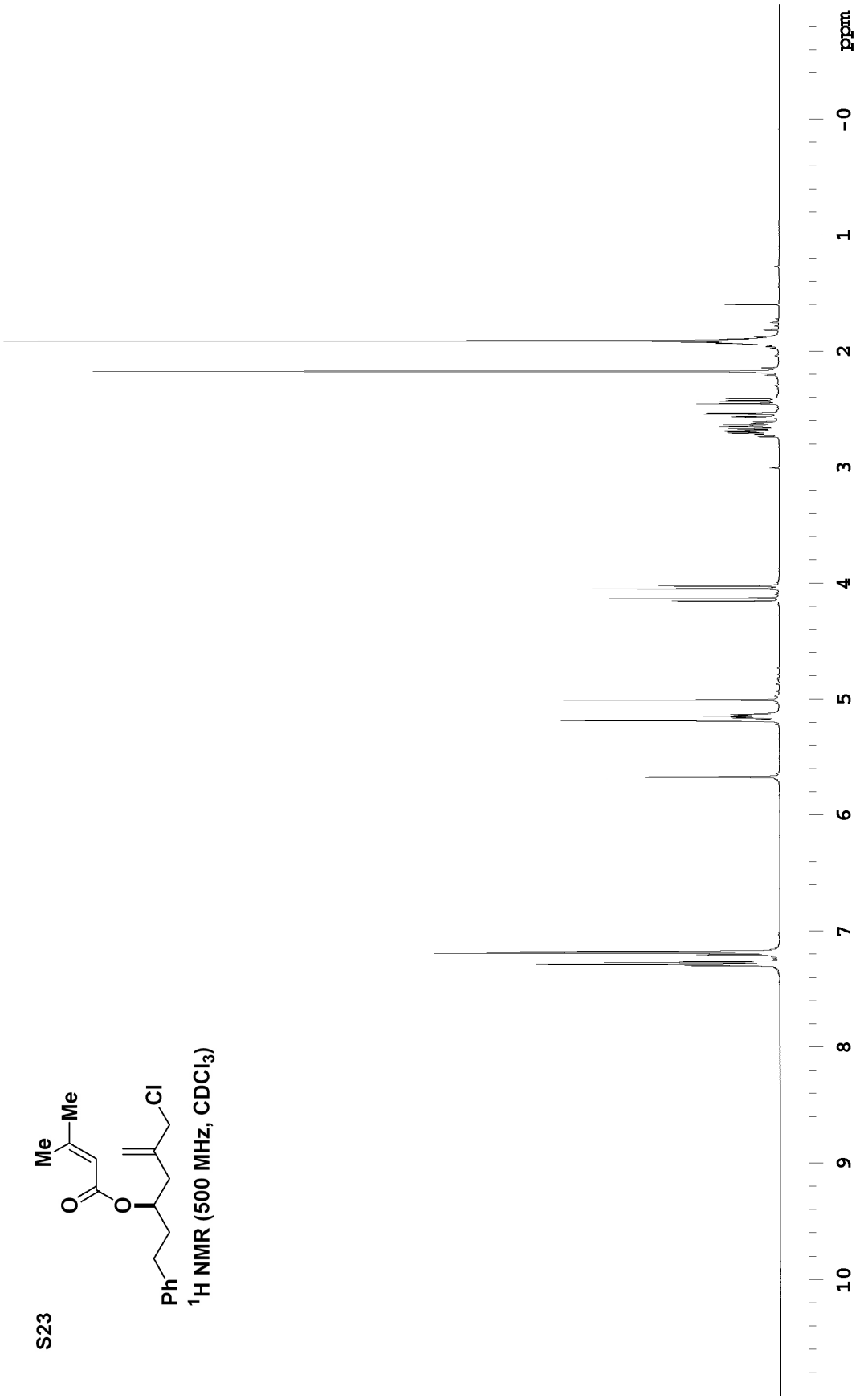
DQCOSY (500 MHz, $CDCl_3$)

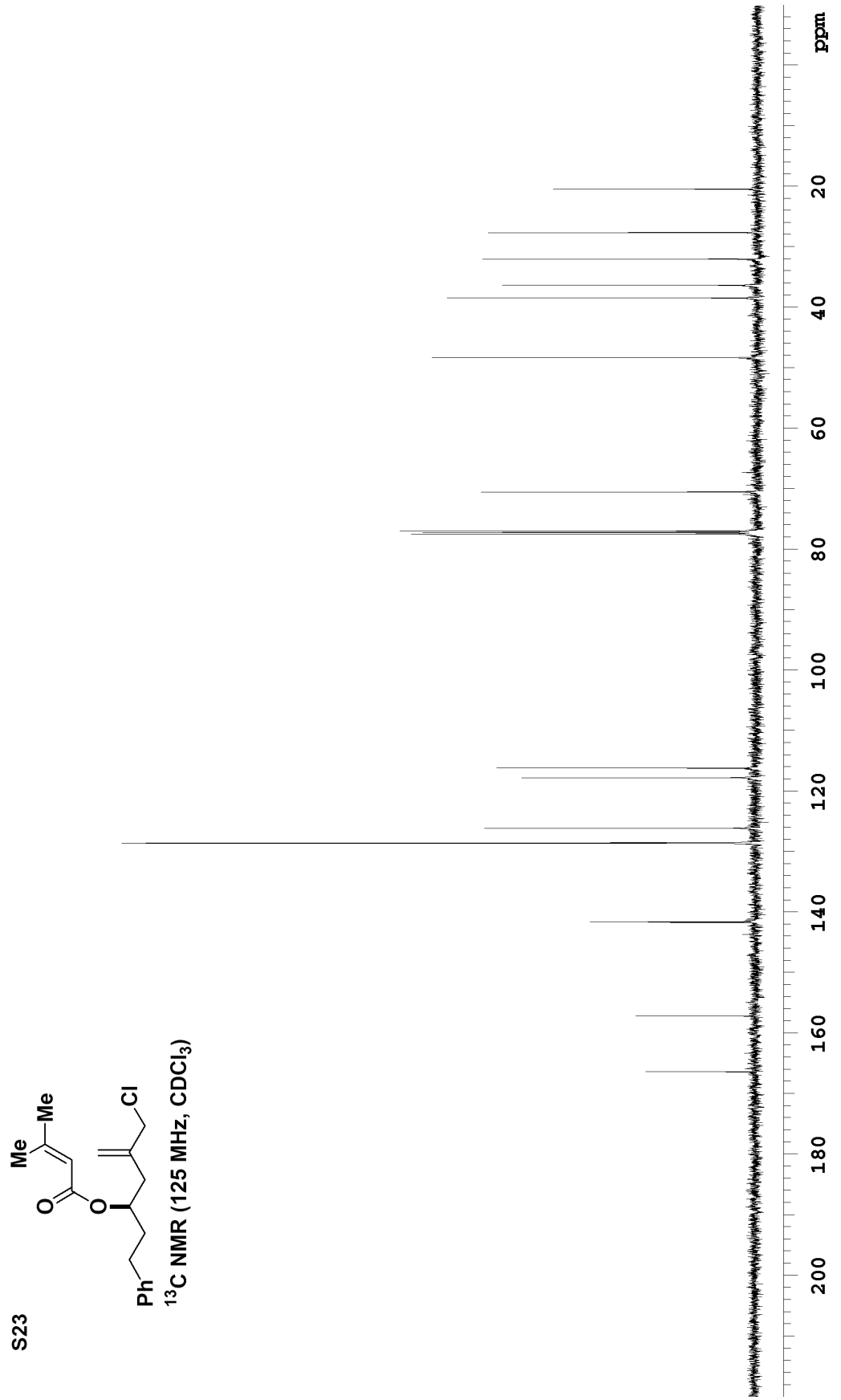
S22

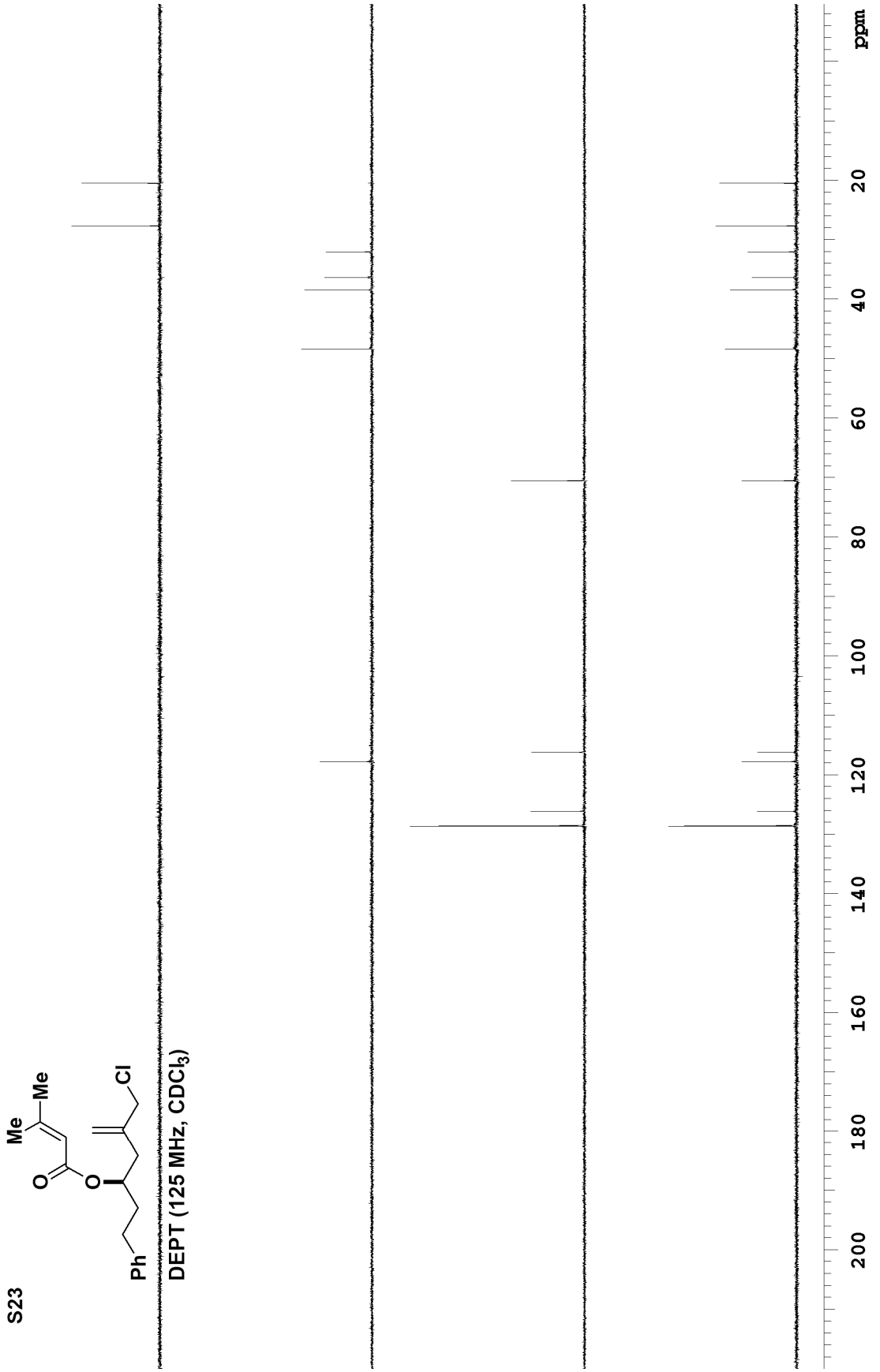

S22
HMQC (500 MHz, CDCl3)
MeO
Ph
O
Ph
F2 (ppm)
F1 (ppm)

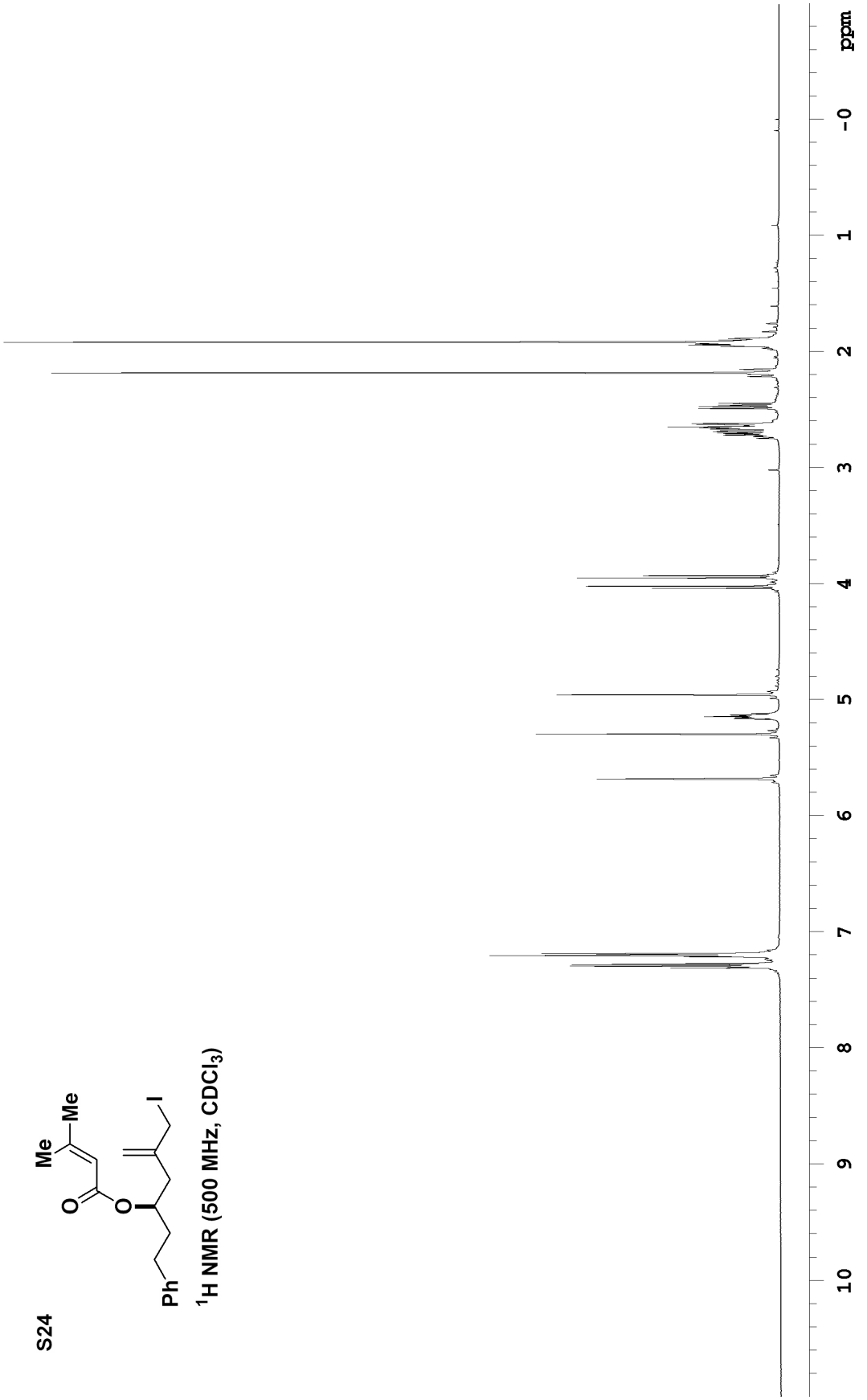

S22
NOESY1D (500 MHz, CDCl3)
MeO
irrad.
H6
ppm
-0
1
2
3
4
5
6
7
8
9
10

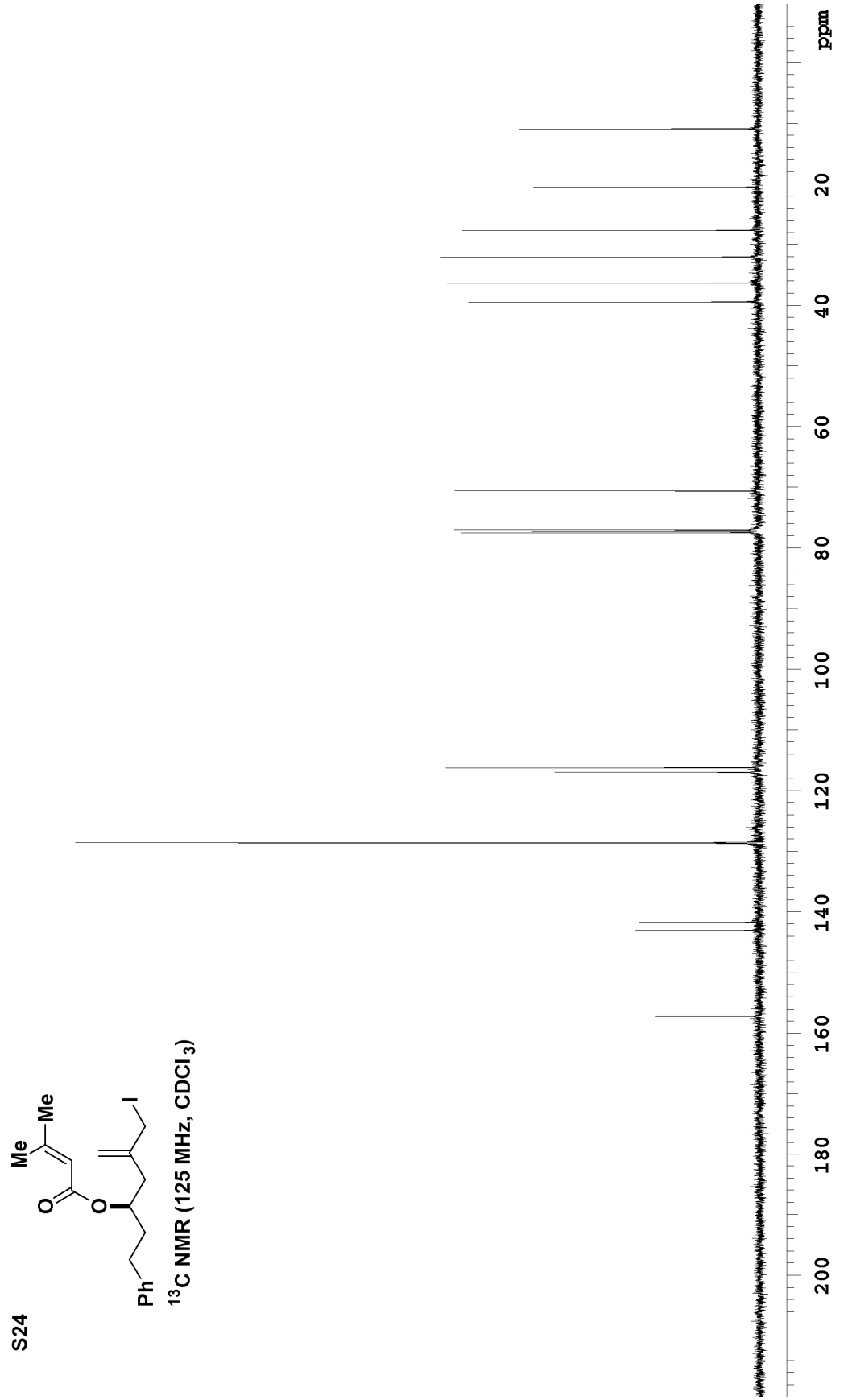

S22
H
MeO
O
Ph
Ph
2
6
NOESY1D (500 MHz, CDCl3)
irrad.
MeO
H6
ppm
-0
1
2
3
4
5
6
7
8
9
10

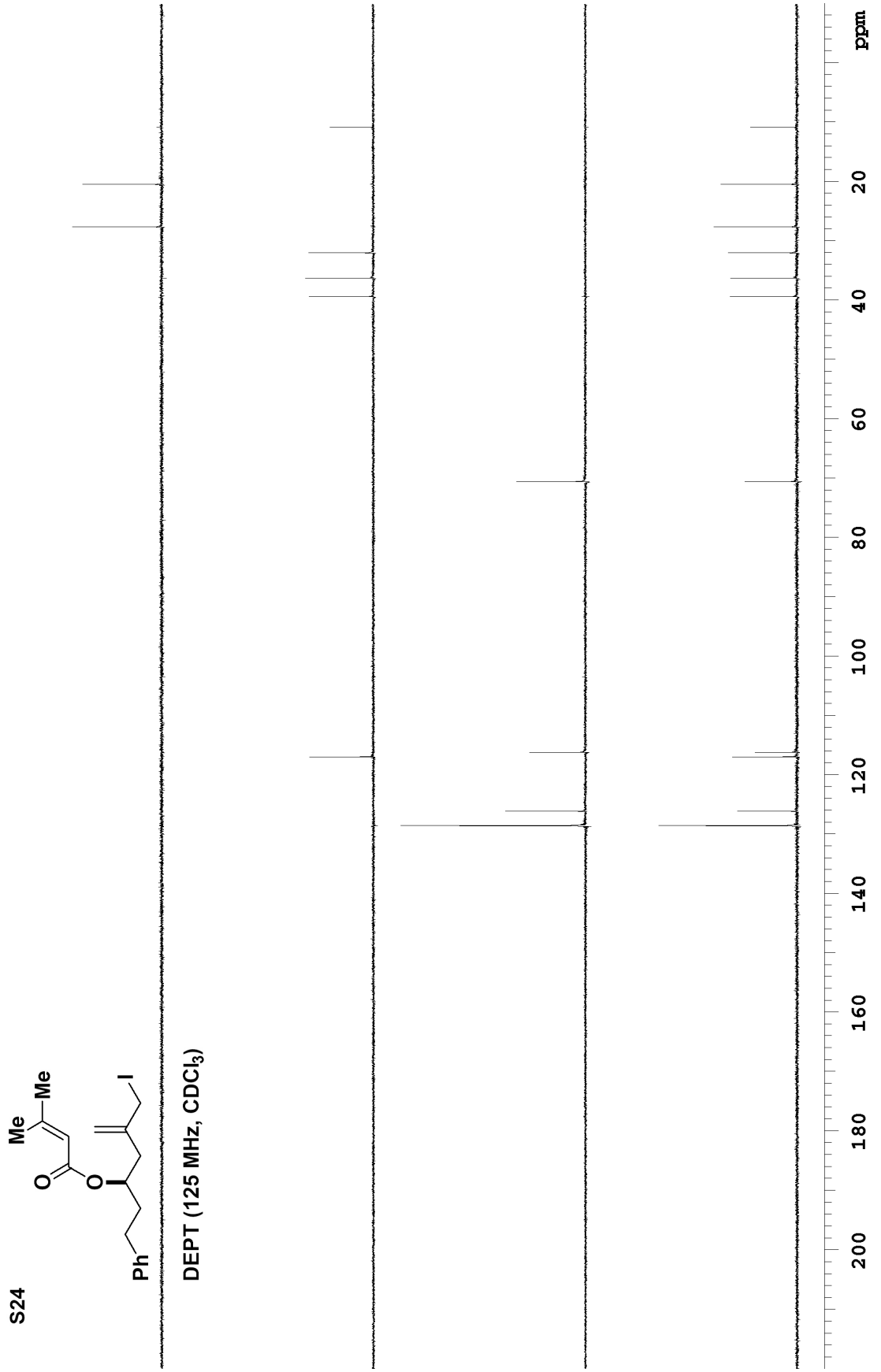

S23
Me
Me
O
O
Cl
Ph
^{1}H NMR (500 MHz, $CDCl_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0

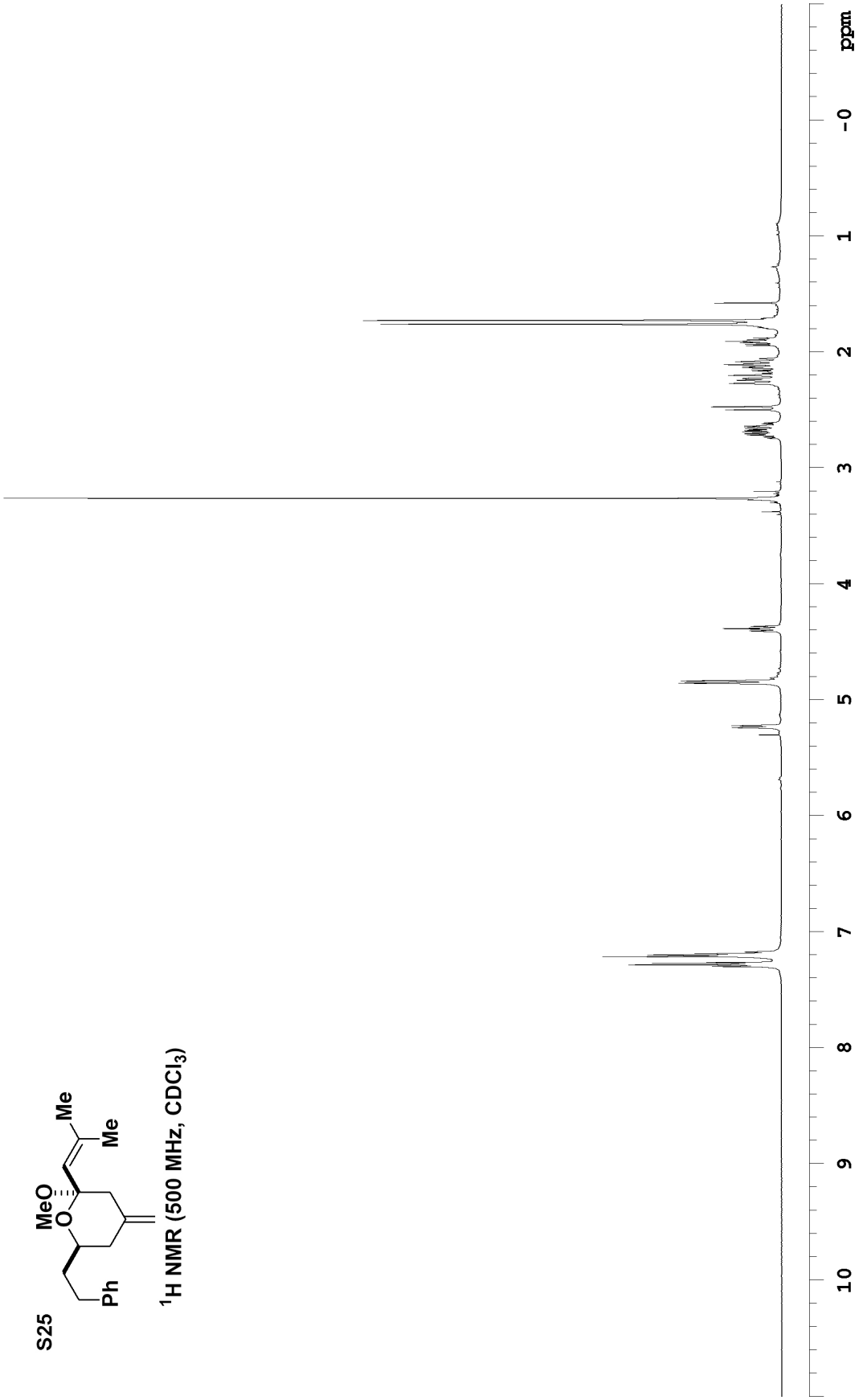

S23
^{13}C NMR (125 MHz, CDCl$_3$)
Me
Me
O
O
Cl
Ph
ppm
20
40
60
80
100
120
140
160
180
200

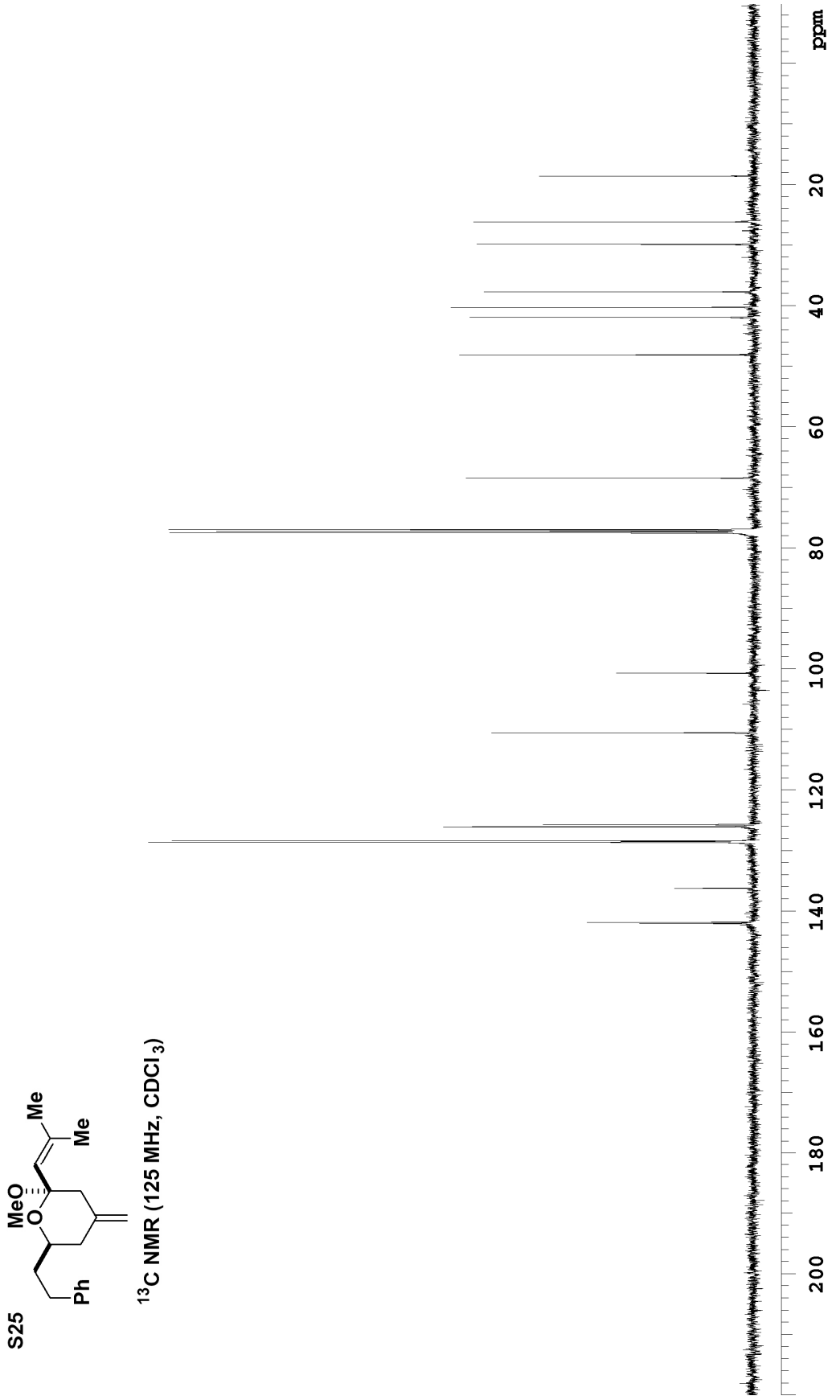

S23
DEPT (125 MHz, $CDCl_3$)
Me
Me
O
O
Cl
Ph
ppm
200
180
160
140
120
100
80
60
40
20

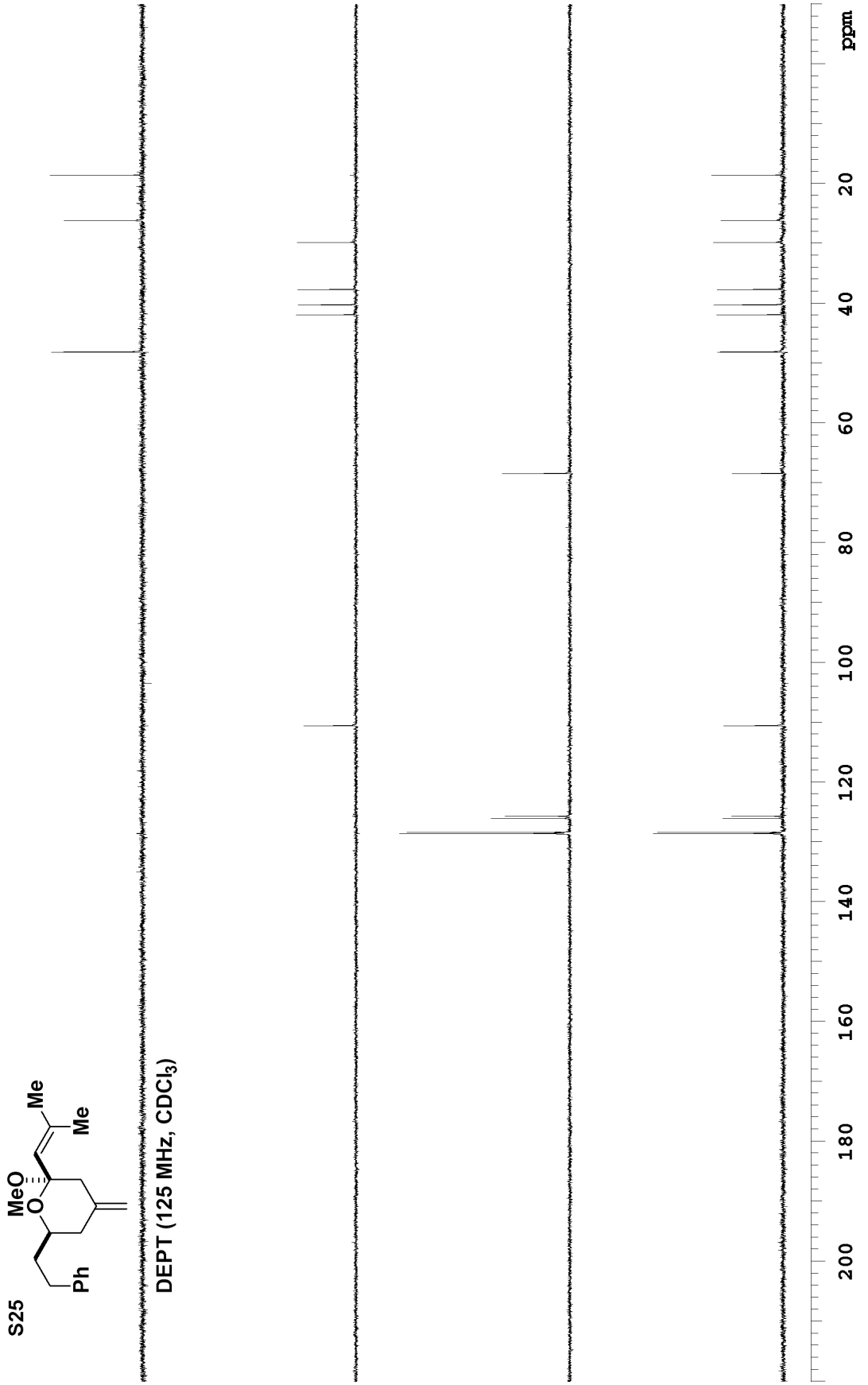

S24
Me
Me
O
O
I
Ph
^{1}H NMR (500 MHz, $CDCl_3$)
ppm
10
9
8
7
6
5
4
3
2
1
-0

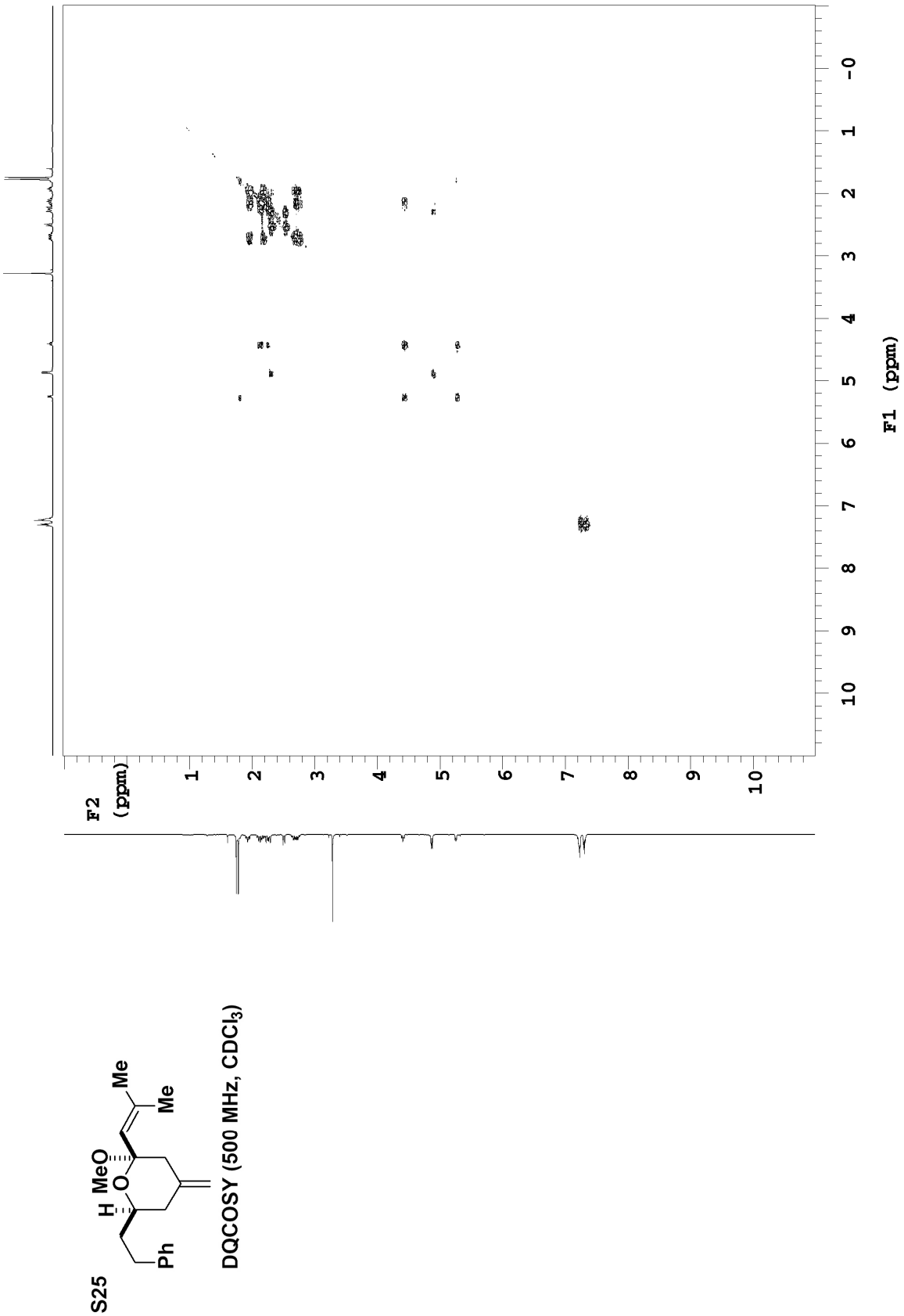

S24
^{13}C NMR (125 MHz, CDCl$_3$)
Me
Me
O
O
I
Ph
ppm
200
180
160
140
120
100
80
60
40
20


S24
DEPT (125 MHz, $CDCl_3$)
Me
Me
O
O
I
Ph
ppm
200
180
160
140
120
100
80
60
40
20


ppm
10
9
8
7
6
5
4
3
2
1
-0
MeO
O
Me
Me
Ph
S25
^{1}H NMR (500 MHz, $CDCl_3$)

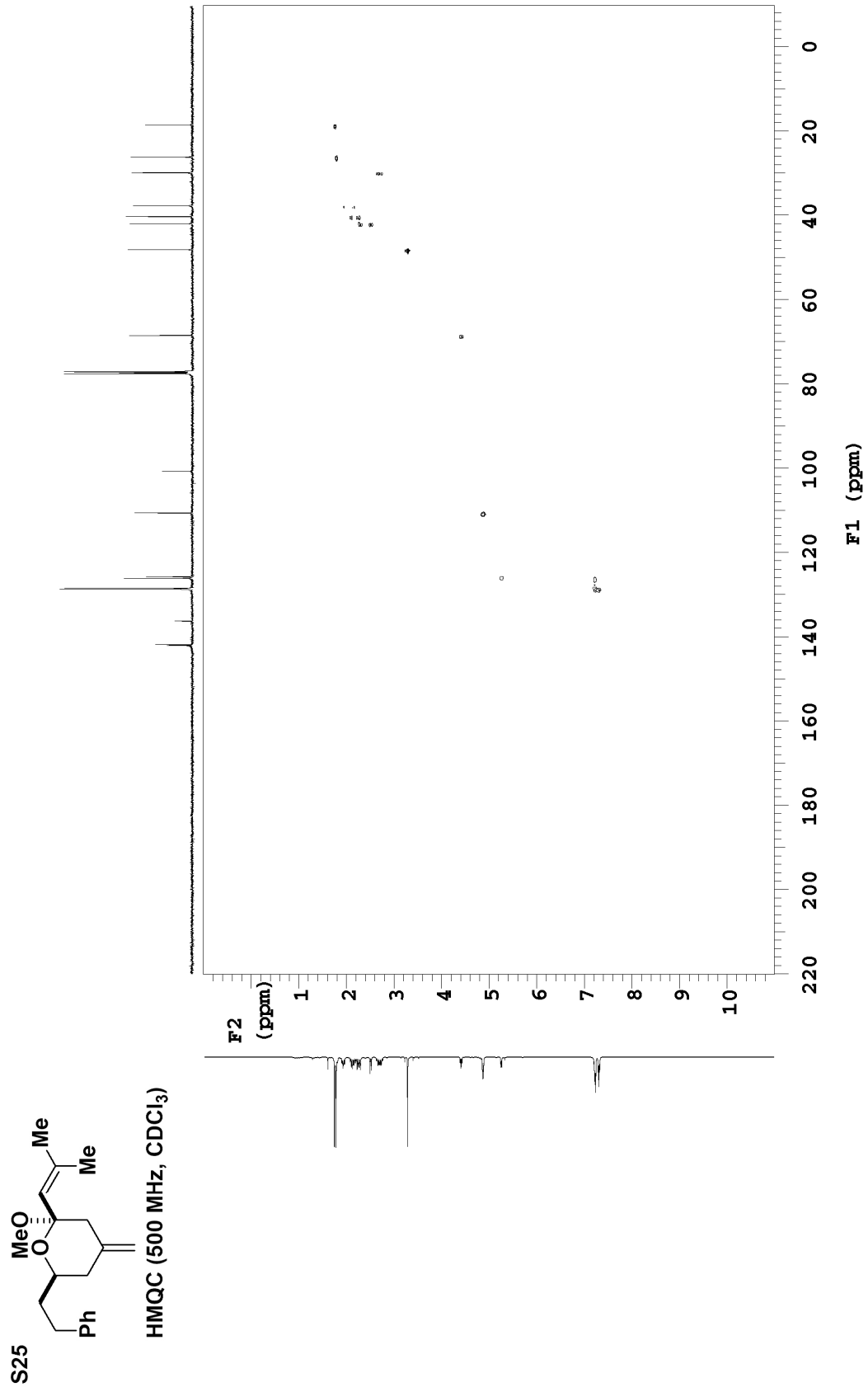

S25
Me
Me
MeO
O
Ph
^{13}C NMR (125 MHz, CDCl$_3$)
ppm
200
180
160
140
120
100
80
60
40
20

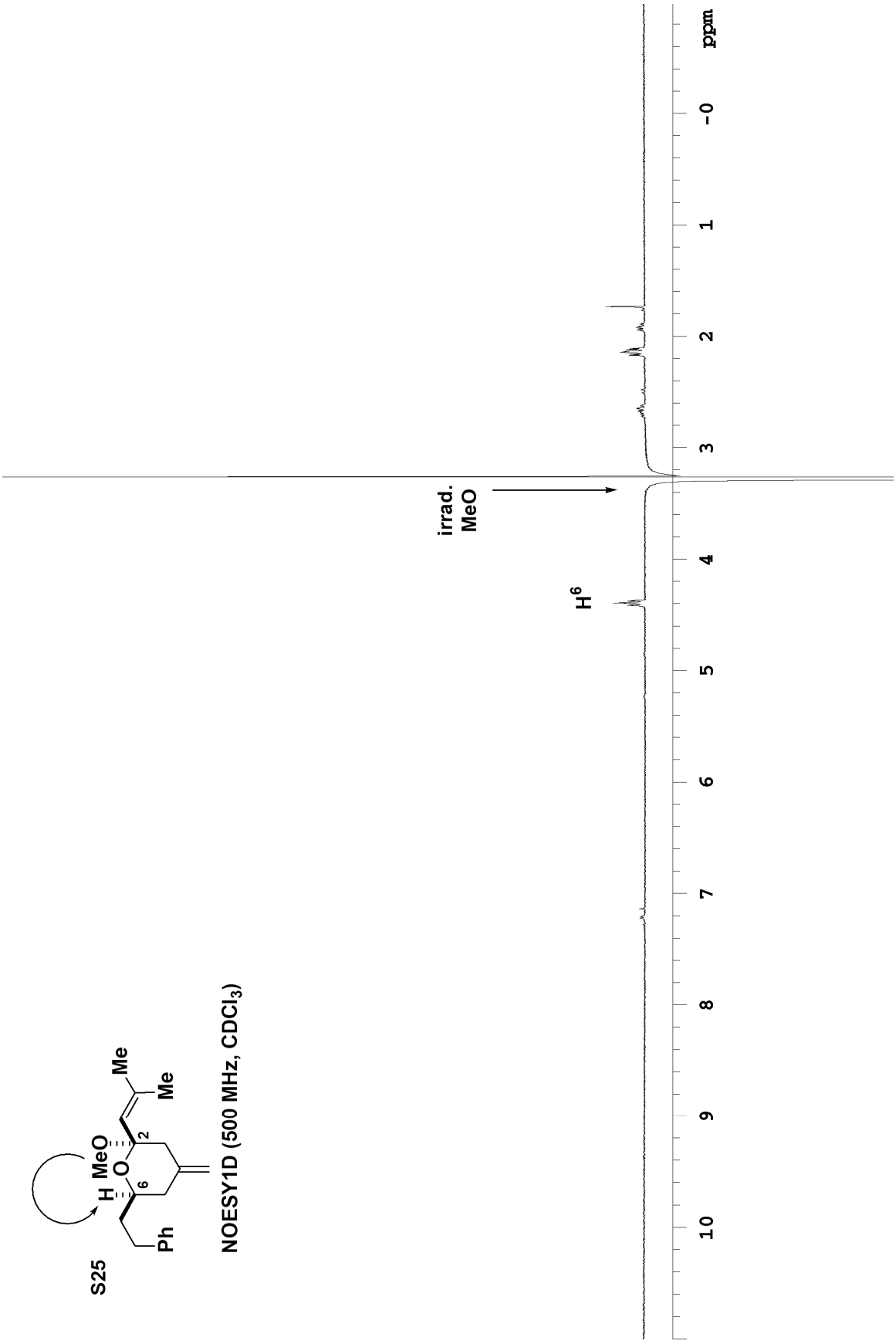

S25
Me
Me
MeO
O
Ph
DEPT (125 MHz, CDCl3)
ppm
200
180
160
140
120
100
80
60
40
20

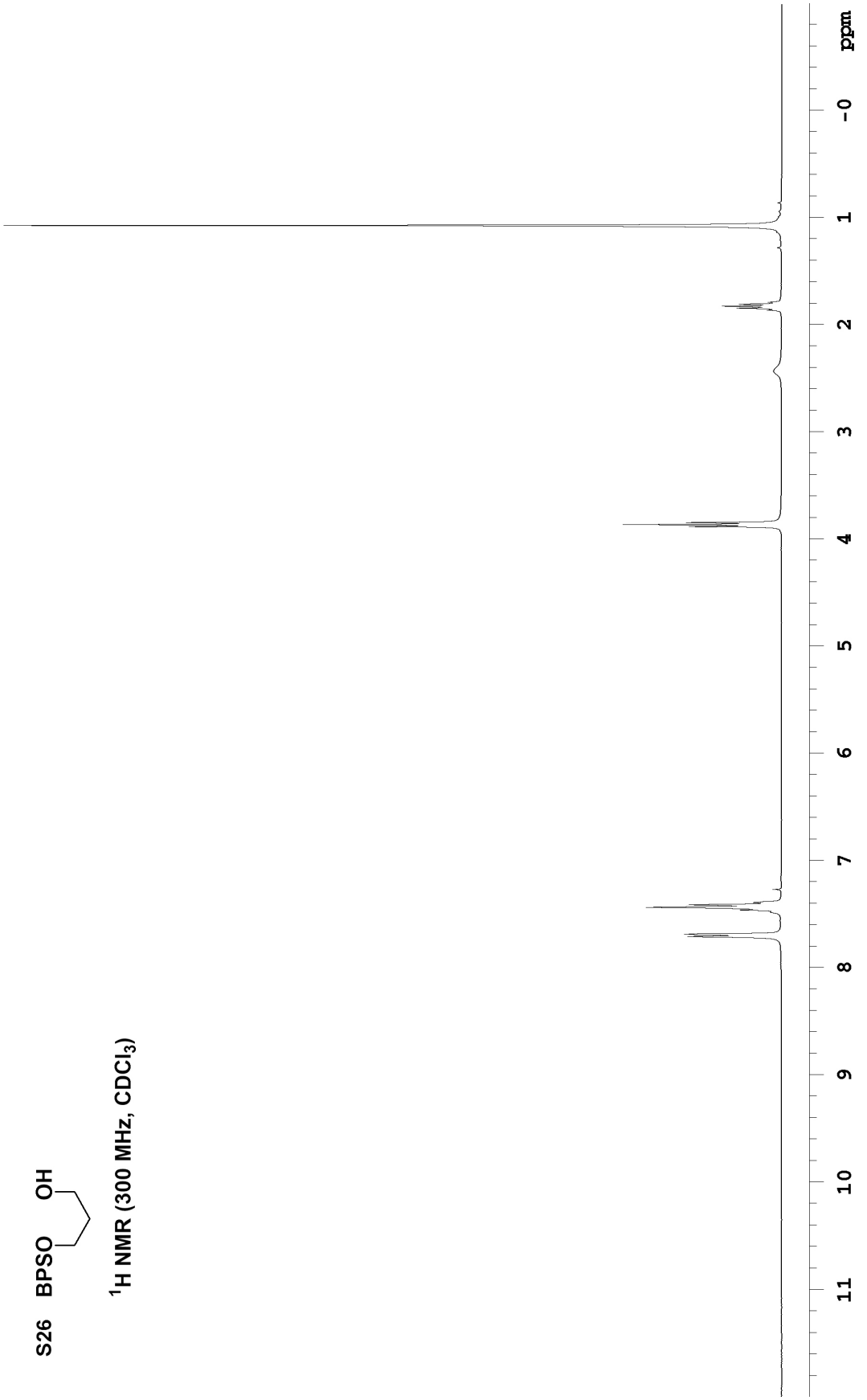


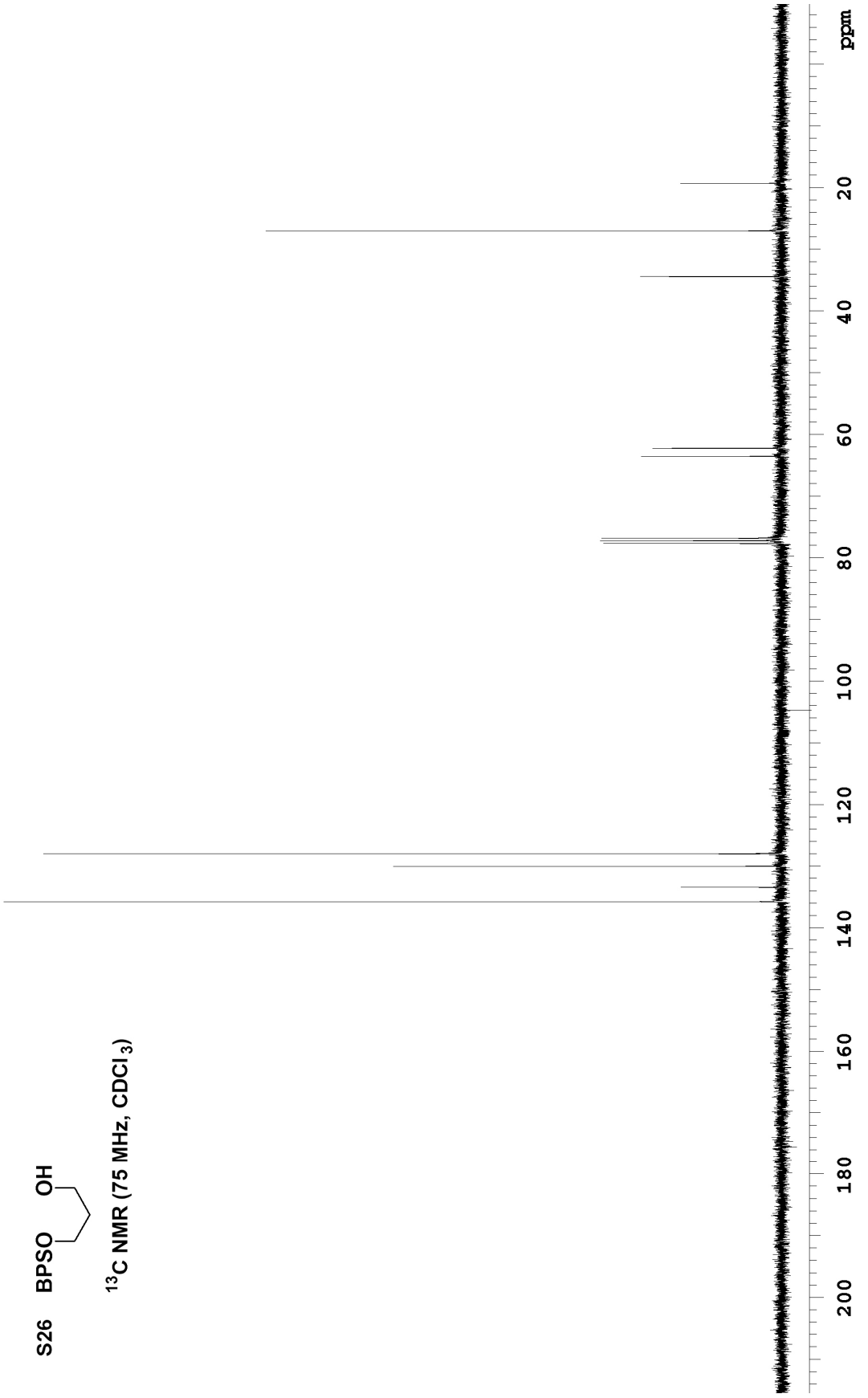
S25

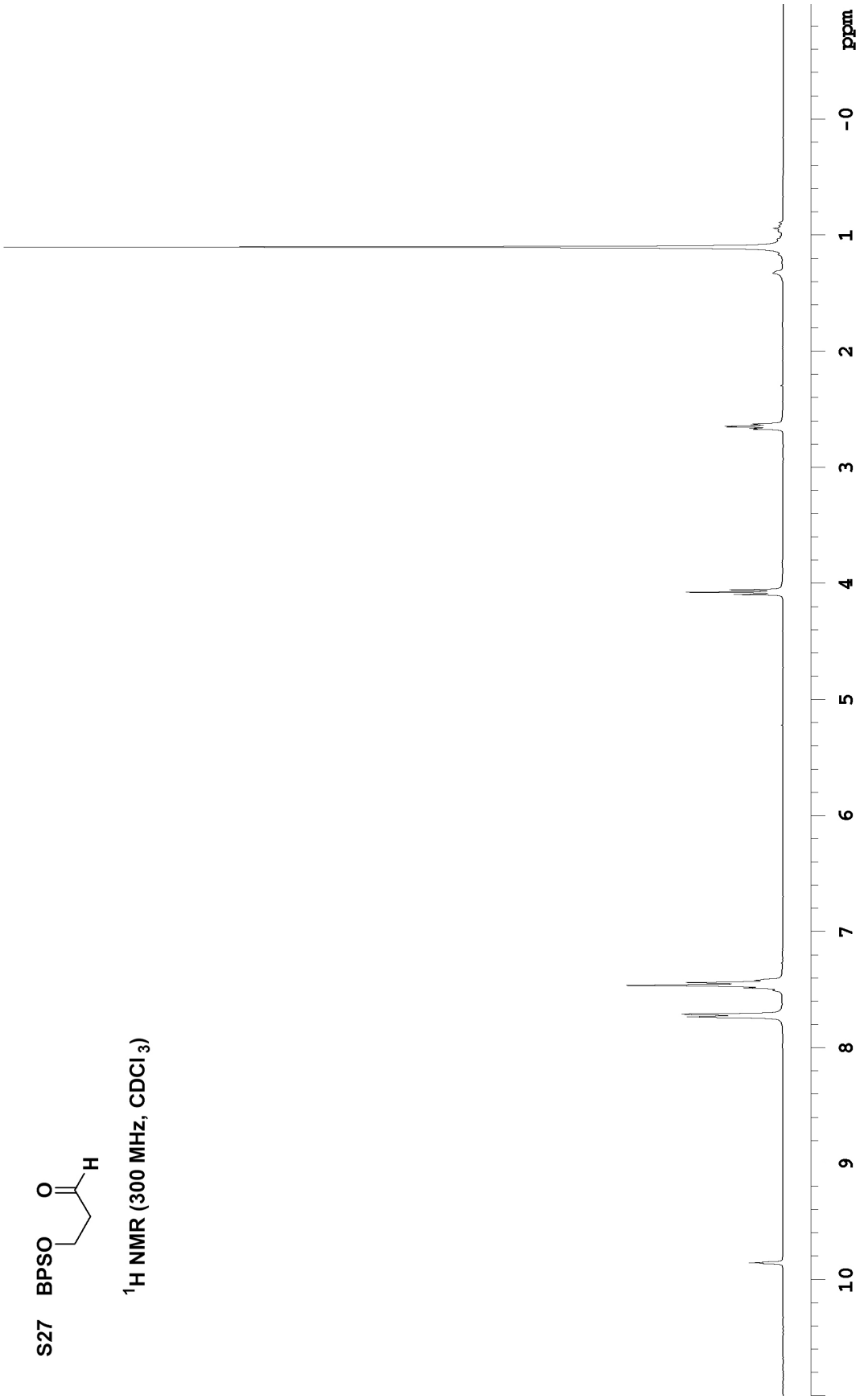
DQCOSY (500 MHz, $CDCl_3$)

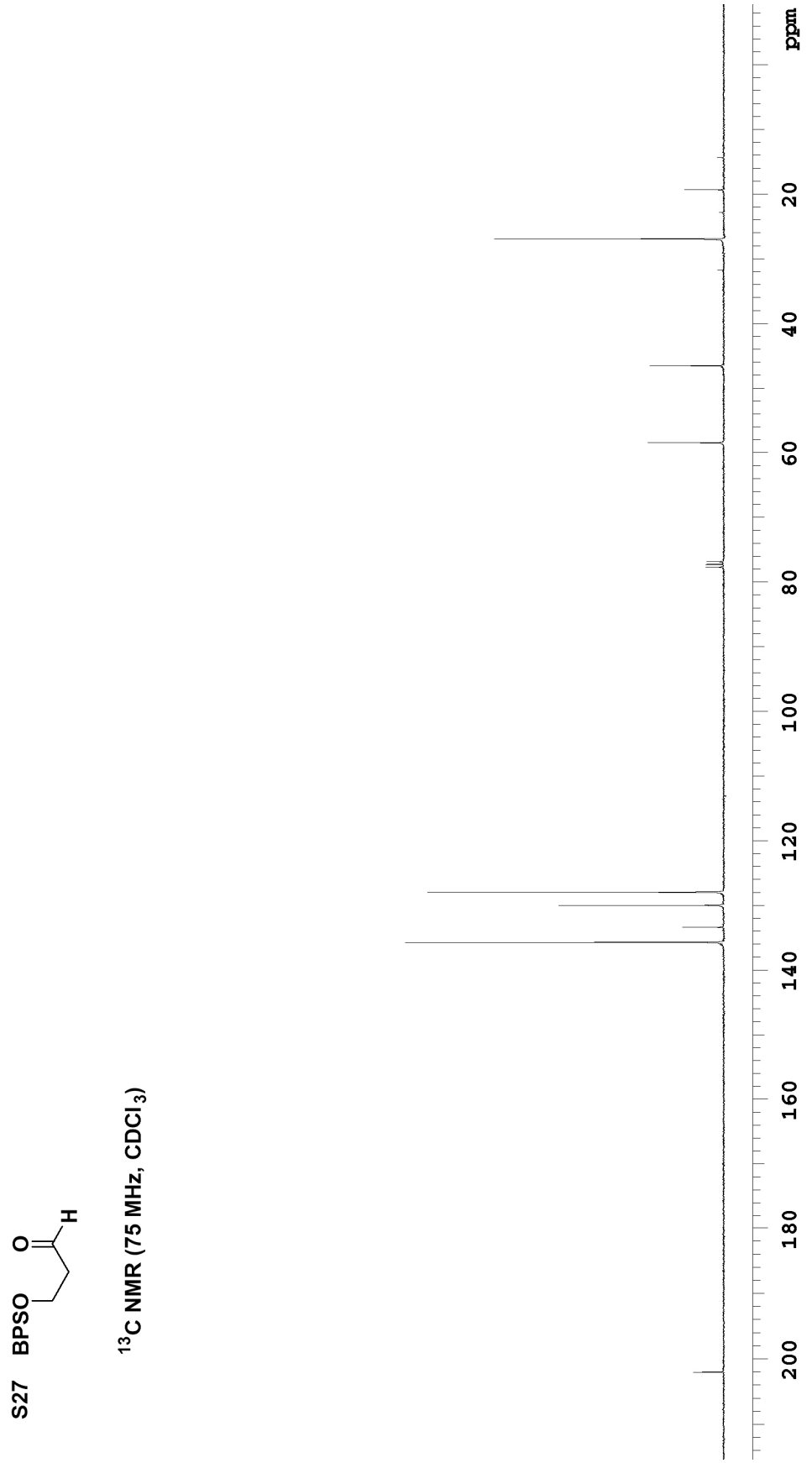

S25
HMQC (500 MHz, CDCl3)
MeO
Me
Me
Ph
O
F2 (ppm)
F1 (ppm)


ppm
-0
1
2
3
4
5
6
7
8
9
10
irrad.
MeO
H6
NOESY1D (500 MHz, CDCl3)
S25
H
MeO
O
2
6
Me
Me
Ph


S26 BPSO OH
^{1}H NMR (300 MHz, $CDCl_3$)
ppm
-0
1
2
3
4
5
6
7
8
9
10
11


S26 BPSO OH
^{13}C NMR (75 MHz, CDCl$_3$)
ppm
20
40
60
80
100
120
140
160
180
200


S27
BPSO
O
H
^{1}H NMR (300 MHz, CDCl$_3$)
ppm
10
9
8
7
6
5
4
3
2
1
0


S27 BPSO
O
H
^{13}C NMR (75 MHz, $CDCl_3$)
ppm
200
180
160
140
120
100
80
60
40
20