Supporting Information

Synthesis and Structural Revision of Symbiodinolide C23-C34 Fragment

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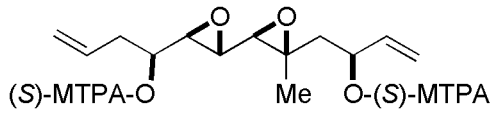
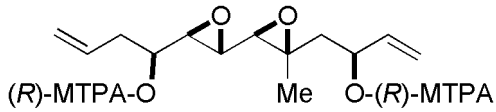
General method. Reagents were used as received from commercial suppliers unless otherwise indicated. All reactions were carried out under an atmosphere of N_2 or Ar. All reaction solvents were purchased as dehydrated solvents and stored with active molecular sieves 4A under Ar prior to use for reactions. All solvents for work-up procedure were used as received. All inorganic salt solutions are aqueous unless otherwise stated. “Brine” refers to saturated aqueous NaCl solution. “Concentration” refers to removal of solvent under reduced pressure (10-100 mmHg) with a rotary evaporator, followed by a period under high vacuum (< 0.1 mmHg) unless otherwise indicated. Chemical shifts in nuclear magnetic resonance (NMR) data are indicated in parts per million (ppm) downfield from tetramethylsilane (TMS, $\delta = 0.00$) with residual undeuterated solvent peaks as internal reference, for ^{1}H NMR $CHCl_3$ (7.26), CHD_2OD (3.31) or C_6HD_5 (7.16) and deuterated solvent peaks shifts for ^{13}C NMR $CDCl_3$ (77.2), CD_3OD (49.0), C_6D_6 (128.1). Multiplicities are reported as s (singlet), d (doublet), t (triplet), q (quantet), m (multiplet), br (broad) or combinations of those. Coupling constants (J) are in hertz.



(*S*)-**3** (proposed structure)

Bis-*(S)*-MTPA ester (*S*)-**3** (proposed structure)

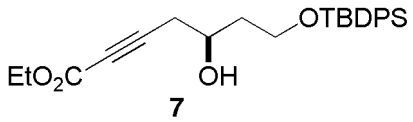
To a mixture of diepoxide **2** (0.3 mg, 1.25 μmol) and DMAP (0.9 mg, 7.50 μmol) in CH_2Cl_2 (0.2 mL) were added Et_3N (0.1 mL, 0.72 mmol) and *(R)*-MTPA-Cl (1.0 μL, 5.00 μmol) at 0 °C. The reaction mixture was stirred at room temperature for 30 min and then quenched with MeOH at 0 °C. After evaporation of the solvent, the residue was purified by column chromatography (silica gel, EtOAc/hexane = 1:30) to afford bis-*(S)*-MTPA ester (*S*)-**3** (0.8 mg, 95%) as a light yellow oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52-7.48 (m, 4 H), 7.41-7.38 (m, 6 H), 5.86-5.80 (m, 1 H), 5.69-5.62 (m, 1 H), 5.61-5.58 (m, 1 H), 5.39 (d, *J* = 17.2 Hz, 1 H), 5.30 (d, *J* = 10.3 Hz, 1 H), 5.13-5.10 (m, 1 H), 5.08 (dd, *J* = 16.5, 1.4 Hz, 1 H), 5.07 (d, *J* = 9.6 Hz, 1 H), 3.52 (s, 3 H), 3.50 (s, 3 H), 3.01 (dd, *J* = 4.1, 2.1 Hz, 1 H), 2.83 (dd, *J* = 4.8, 2.1 Hz, 1 H), 2.61 (d, *J* = 4.8 Hz, 1 H), 2.53-2.49 (m, 1 H), 2.45-2.40 (m, 1 H), 1.97 (dd, *J* = 15.1, 4.8 Hz, 1 H), 1.80 (dd, *J* = 15.1, 8.3 Hz, 1 H), 1.27 (s, 3 H).



(*R*)-**3** (proposed structure)

Bis-*(R)*-MTPA ester (*R*)-**3** (proposed structure)

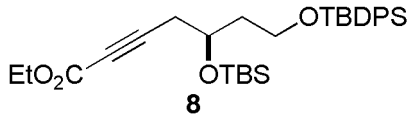
To a mixture of diepoxide **2** (0.3 mg, 1.25 μmol) and DMAP (0.9 mg, 7.50 μmol) in CH_2Cl_2 (0.2 mL) were added Et_3N (0.1 mL, 0.72 mmol) and *(S)*-MTPA-Cl (1.0 μL, 5.00 μmol) at 0 °C. The reaction mixture was stirred at room temperature for 30 min and then quenched with MeOH at 0 °C. After evaporation of the solvent, the residue was purified by column chromatography (silica gel, EtOAc/hexane = 1:30) to afford bis-*(R)*-MTPA ester (*R*)-**3** (0.8 mg, 95%) as a light yellow oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52-7.49 (m, 4 H), 7.42-7.37 (m, 6 H), 5.79-5.72 (m, 2 H), 5.57-5.53 (m, 1 H), 5.31 (d, *J* = 17.2 Hz, 1 H), 5.25 (d, *J* = 10.3 Hz, 1 H), 5.17 (dd, *J* = 17.2, 1.4 Hz, 1 H), 5.15 (d, *J* = 9.6 Hz, 1 H), 5.10-5.07 (m, 1 H), 3.51 (s, 3 H), 3.49 (s, 3 H), 2.94 (dd, *J* = 4.8, 2.1 Hz, 1 H), 2.80 (dd, *J* = 4.8, 2.1 Hz, 1 H), 2.59 (d, *J* = 4.8 Hz, 1 H), 2.57-2.54 (m, 1 H), 2.50-2.44 (m, 1 H), 2.00 (dd, *J* = 14.4, 4.8 Hz, 1 H), 1.85 (dd, *J* = 14.4, 8.3 Hz, 1 H), 1.32 (s, 3 H).



7

Acetylenic alcohol **7**

To a solution of ethyl propiolate (7.9 mL, 78.0 mmol) in THF (140 mL) was added *n*-BuLi (1.59 M solution in hexane, 49 mL, 78.0 mmol) at -78 °C, and the mixture was stirred for 10 min. To the resulting solution were added boron trifluoride etherate (9.8 mL, 78.0 mmol) and a solution of epoxide **6** (15.0 g, 45.9 mmol) in THF, and the mixture was stirred for 1 h at -78 °C. The reaction was quenched by adding saturated aqueous NH_4Cl, and then the resulting mixture was extracted with Et_2O. The extract was washed successively with water and brine, and dried over Na_2SO_4. Concentration and column chromatography (silica gel, EtOAc/hexane = 0:1, 1:40, 1:20) gave acetylenic alcohol **7** (9.55 g, 49%) and recovered epoxide **6** (5.00 g, 33%) as a light yellow oil, respectively. Acetylenic alcohol **7**: $[\alpha]_D^{25}$ -0.8 (*c* 0.83, $CHCl_3$); IR (neat) 3451, 2956, 2929, 2857, 2237, 1710, 1427, 1252, 1110, 1074 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.67-7.66 (m, 4 H), 7.46-7.44 (m, 2 H), 7.42-7.39 (m, 4 H), 4.21 (q, *J* = 6.9 Hz, 2 H), 4.16-4.12 (m, 1 H), 3.92-3.84 (m, 2 H), 2.60 (dd, *J* = 17.2, 6.2 Hz, 1 H), 2.54 (dd, *J* = 17.2, 6.9 Hz, 1 H), 1.86-1.78 (m, 2 H), 1.30 (t, *J* = 6.9 Hz, 3 H), 1.05 (s, 9 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.8, 135.7, 133.0, 132.9, 130.1, 128.0, 85.8, 75.0, 69.7, 63.0, 62.0, 35.5, 27.5, 27.0, 19.1, 14.2; HRMS (FAB) calcd for $C_{25}H_{33}O_4Si$ $(M+H)^+$ 425.2149, found 425.2151.

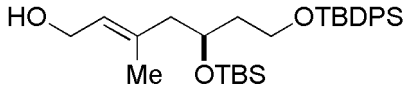


8

Silyl ether **8**

To a solution of acetylenic alcohol **7** (9.50 g, 22.4 mmol) in CH_2Cl_2 (90 mL) were added 2,6-lutidine (5.2 mL, 44.8 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (7.2 mL, 31.3 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and then quenched by addition of MeOH. After the solution was stirred for 5 min at room temperature, the organic layer was washed with water and brine, and dried over Na_2SO_4. Concentration and column chromatography (silica gel, EtOAc/hexane = 1:50) afforded silyl ether **8** (12.1 g, quant.) as a light yellow oil: $[\alpha]_D^{25}$ +13.9 (*c* 0.50, $CHCl_3$); IR (neat) 2953, 2929, 2857, 2237, 1714, 1472, 1427, 1251, 1112

cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.67-7.65 (m, 4 H), 7.44-7.41 (m, 2 H), 7.40-7.37 (m, 4 H), 4.22 (q, *J* = 6.9 Hz, 2 H), 4.14-4.10 (m, 1 H), 3.77-3.70 (m, 2 H), 2.53 (dd, *J* = 17.2, 6.2 Hz, 1 H), 2.48 (dd, *J* = 17.2, 6.2 Hz, 1 H), 1.85-1.79 (m, 1 H), 1.78-1.73 (m, 1 H), 1.30 (t, *J* = 6.9 Hz, 3 H), 1.05 (s, 9 H), 0.86 (s, 9 H), 0.10 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.9, 135.7, 135.7, 133.9, 133.9, 129.8, 129.8, 127.8, 127.7, 86.8, 74.8, 67.7, 61.9, 60.4, 39.8, 28.0, 27.0, 25.9, 19.3, 18.2, 14.2, -4.5, -4.6; HRMS (FAB) calcd for $C_{31}H_{47}O_4Si_2$ $(M+H)^+$ 539.3013, found 539.3016.



10

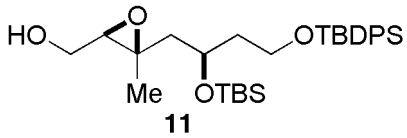
Allylic alcohol **10**

To a solution of NaOMe (61 mg, 1.1 mmol) in MeOH (56 mL) were added PhSH (2.7 mL, 26.9 mmol) and alkyne **8** (12.1 g, 22.4 mmol). After stirring for 14 h at room temperature, the mixture was filtered through a silica gel pad and washed with Et_2O. Concentration and short column chromatography (silica gel, hexane) afforded the corresponding (*Z*)-thioether (12.6 g) as yellow oil, which was used in the next reaction without further purification.

To a suspension of CuI (5.2 g, 27.2 mmol) in THF (77 mL) was added MeMgBr (3.0 M solution in Et_2O, 8.4 mL, 25.2 mmol) dropwise at -78 °C. The reaction mixture was warmed to room temperature and then cooled back to -78 °C. To the resulting mixture was added the (*Z*)-thioether (12.6 g) obtained above in THF (30 mL). The solution was warmed to 0 °C and stirred for 1 h. After saturated aqueous NH_4Cl was added, the mixture was diluted with Et_2O and dried over Na_2SO_4. The solution was filtered through a silica gel pad and washed with Et_2O. Concentration and short column chromatography (silica gel, hexane) afforded α,β-unsaturated ester **9** (7.80 g), which was used in the next reaction without further purification.

To a solution of α,β-unsaturated ester **9** (7.80 g) obtained above in CH_2Cl_2 (70 mL) was added DIBALH (1.0 M solution in hexane, 34.4 mL, 35.1 mmol) dropwise at -78 °C. After stirring for 2 h, the solution was poured directly into a stirring mixture of a saturated sodium potassium tartrate aqueous solution and MeOH. The mixture was stirred for 30 min, and diluted with Et_2O. The organic layer was washed with brine and dried over Na_2SO_4. Concentration and column chromatography (silica gel, EtOAc/hexane = 1:50) afforded allylic alcohol **10** (7.10 g, 61% in 3 steps) as a light

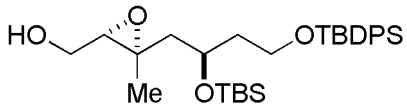
yellow oil: $[\alpha]_D^{24}$ +11.3 (*c* 1.00, $CHCl_3$); IR (neat) 3338, 2956, 2929, 2857, 1472, 1428, 1254, 1111 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.66-7.64 (m, 4 H), 7.43-7.41 (m, 2 H), 7.39-7.36 (m, 4 H), 5.39 (t, *J* = 6.9 Hz, 1 H), 4.16-4.10 (m, 2 H), 4.06-4.02 (m, 1 H), 3.76-3.68 (m, 2 H), 2.19 (dd, *J* = 13.1, 6.2 Hz, 1 H), 2.13 (dd, *J* = 13.1, 6.2 Hz, 1 H), 1.70-1.65 (m, 1 H), 1.67 (s, 3 H), 1.63-1.57 (m, 1 H), 1.04 (s, 9 H), 0.84 (s, 9 H), 0.02 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.9, 135.7, 134.1, 134.1, 129.7, 129.7, 127.8, 126.5, 67.9, 60.9, 59.5, 48.1, 39.9, 27.0, 26.0, 19.3, 18.2, 17.0, -4.3, -4.5; HRMS (FAB) calcd for $C_{30}H_{49}O_3Si_2$ $(M+H)^+$ 513.3220, found 513.3210.



11

Epoxy alcohol **11**

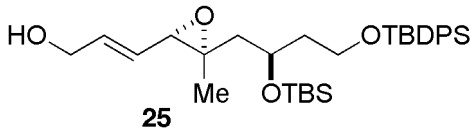
To a suspension of powdered molecular sieves 4A (300 mg) in CH_2Cl_2 (2 mL) at 0 °C were added D-(-)-diethyltartrate (50 μL, 0.292 mmol) and titanium(IV) isopropoxide (57 μL, 0.195 mmol). After 5 min, the mixture was cooled to -25 °C and *tert*-butyl hydroperoxide (5.0-6.0 M solution in decane, 177 μL, 0.885-1.06 mmol) was added dropwise. The reaction mixture was stirred at -30 °C for 20 min and a solution of allylic alcohol **10** (250 mg, 0.487 mmol) in CH_2Cl_2 (1 mL) was added. Stirring was continued at -30 °C for 4 h before the reaction was quenched by addition of water. The mixture was vigorously stirred for 30 min and 30% aqueous solution of NaOH was added. The mixture was allowed to warm to room temperature and stirred for further 1 h. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extract was dried over $MgSO_4$ and concentrated. Purification of the residue by column chromatography (silica gel, EtOAc/hexane = 1:20, 1:15, 1:10) afforded epoxy alcohol **11** (230 mg, 89%, dr = 12:1) as a light yellow oil: $[\alpha]_D^{24}$ +16.6 (*c* 0.71, $CHCl_3$); IR (neat) 3463, 2954, 2929, 2858, 1472, 1428, 1254, 1111 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.66-7.64 (m, 4 H), 7.44-7.41 (m, 2 H), 7.39-7.36 (m, 4 H), 4.09-4.04 (m, 1 H), 3.79-3.75 (m, 2 H), 3.73-3.69 (m, 1 H), 3.65 (dd, *J* = 11.7, 6.9 Hz, 1 H), 2.92 (dd, *J* = 6.9, 4.1 Hz, 1 H), 2.01 (dd, *J* = 13.8, 5.5 Hz, 1 H), 1.76-1.71 (m, 1 H), 1.63-1.58 (m, 1 H), 1.46 (dd, *J* = 13.8, 7.6 Hz, 1 H), 1.30 (s, 3 H), 1.05 (s, 9 H), 0.85 (s, 9 H), 0.07 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.7, 134.0, 134.0, 129.8, 129.8, 127.8, 127.8, 66.9, 63.2, 61.4, 60.6, 59.6, 49.8, 39.9, 27.0, 26.0, 19.3, 18.1, 17.8, -4.2, -4.5; HRMS (FAB) calcd for $C_{30}H_{49}O_4Si_2$ $(M+H)^+$ 529.3169, found 529.3192.



23

Epoxy alcohol **23**

To a suspension of powdered molecular sieves 4A (1.5 g) in CH_2Cl_2 (40 mL) were added L-(+)-diethyltartrate (1.5 mL, 8.77 mmol) and titanium(IV) isopropoxide (1.5 mL, 5.26 mmol) at 0 °C. After 5 min, the mixture was cooled to -25 °C and *tert*-butyl hydroperoxide (5.0-6.0 M solution in decane, 4.8 mL, 24.0-28.8 mmol) was added dropwise. The reaction mixture was stirred at -30 °C for 20 min and a solution of allylic alcohol **10** (4.50 g, 8.77 mmol) in CH_2Cl_2 (20 mL) was added. Stirring was continued at -30 °C for 4 h before the reaction was quenched by addition of water. The mixture was vigorously stirred for 30 min and 30% aqueous solution of NaOH was added. The mixture was allowed to warm to room temperature and stirred for further 1 h. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extract was dried over $MgSO_4$ and concentrated. Purification of the residue by column chromatography (silica gel, EtOAc/hexane = 1:50, 1:20) afforded epoxy alcohol **23** (3.90 g, 84%, dr = 20:1) as a light yellow oil: $[\alpha]_D^{24}$ -2.2 (*c* 0.50, $CHCl_3$); IR (neat) 3452, 2953, 2929, 2857, 1472, 1428, 1388, 1254, 1111 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.66-7.63 (m, 4 H), 7.44-7.41 (m, 2 H), 7.39-7.35 (m, 4 H), 4.15-4.10 (m, 1 H), 3.89-3.86 (m, 1 H), 3.74-3.62 (m, 3 H), 2.98 (dd, *J* = 6.9, 4.1 Hz, 1 H), 1.87 (dd, *J* = 13.8, 4.8 Hz, 1 H), 1.79-1.70 (m, 2 H), 1.67 (brs, 1 H), 1.52 (dd, *J* = 13.8, 7.6 Hz, 1 H), 1.32 (s, 3 H), 1.05 (s, 9 H), 0.85 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.7, 133.9, 129.8, 129.8, 127.8, 127.8, 66.9, 63.6, 61.4, 60.7, 59.9, 46.4, 40.6, 27.0, 26.0, 19.3, 18.1, 17.4, -4.2, -4.2; HRMS (FAB) calcd for $C_{30}H_{49}O_4Si_2$ $(M+H)^+$ 529.3170, found 529.3165.



25

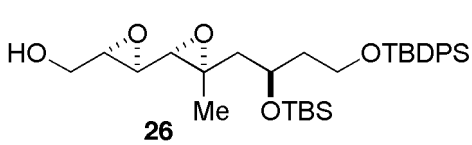
Allylic alcohol **25**

To a solution of oxalyl chloride (65 μL, 0.756 mmol) in CH_2Cl_2 (2.5 mL) was added DMSO (0.11 mL, 1.51 mmol) dropwise at -78 °C. After 30 min, epoxy alcohol **23** (200 mg, 0.378 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise. The mixture was stirred at -78 °C for 2 h before Et_3N (0.32 mL, 2.27 mmol) was added slowly. The mixture was

stirred for 1 h at -78 °C. The reaction was quenched with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2. The combined organic phase was washed with water and brine, and dried over $MgSO_4$. Concentration and short column chromatography (silica gel, EtOAc/hexane = 1:40, 1:20) afforded the corresponding aldehyde (199 mg) as a yellow oil, which was used immediately in the next reaction without further purification.

To a stirred suspension of LiCl (19 mg 0.454 mmol) and the aldehyde (199 mg) obtained above in CH_3CN (3.0 mL) was added trimethyl phosphonoacetate (73 μL, 0.454 mmol). The mixture was cooled to 0 °C and DBU (68 μL, 0.454 mmol) was added. The mixture was stirred for 20 min at 0 °C and then allowed to reach room temperature for 20 min. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with Et_2O. The organic layer was washed successively with water and brine, and dried over Na_2SO_4. Concentration and short column chromatography (silica gel, EtOAc/hexane = 0:1, 1:30) afforded the corresponding α,β-unsaturated ester **24** (175 mg) as a light yellow oil, which was used in the next reaction without further purification.

To a solution of the α,β-unsaturated ester **24** (175 mg) obtained above in CH_2Cl_2 (2.5 mL) was added DIBALH (1.0 M solution in hexane, 0.74 mL, 0.75 mmol) dropwise at -78 °C. After stirring for 30 min at -78 °C, the solution was poured directly into a stirring mixture of saturated sodium potassium tartrate aqueous solution and MeOH. The aqueous layer was extracted with EtOAc. The organic layer was washed with brine and dried over Na_2SO_4. Concentration and column chromatography (silica gel, EtOAc/hexane = 1:12) afforded allylic alcohol **25** (136 mg, 65% in 3 steps) as a light yellow oil: $[\alpha]_D^{23}$ +1.5 (*c* 1.33, $CHCl_3$); IR (neat) 3423, 2952, 2929, 2857, 1472, 1428, 1388, 1255, 1111 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.67-7.65 (m, 4 H), 7.44-7.41 (m, 2 H), 7.39-7.37 (m, 4 H), 6.03 (dt, *J* = 15.8, 4.8 Hz, 1 H), 5.62 (ddt, *J* = 15.8, 7.6, 1.4 Hz, 1 H), 4.19 (brd, *J* = 4.8 Hz, 2 H), 4.16-4.12 (m, 1 H), 3.75-3.67 (m, 2 H), 3.24 (d, *J* = 7.6 Hz, 1 H), 1.91 (dd, *J* = 13.8, 4.8 Hz, 1 H), 1.80-1.70 (m, 2 H), 1.53 (dd, *J* = 13.8, 7.6 Hz, 1 H), 1.30 (s, 3 H), 1.05 (s, 9 H), 0.85 (s, 9 H), 0.04 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.7, 133.9, 129.8, 129.8, 127.8, 127.8, 126.5, 67.0, 63.4, 63.1, 61.3, 60.7, 46.4, 40.8, 27.0, 26.0, 19.3, 18.1, 17.2, -4.1, -4.3; HRMS (FAB) calcd for $C_{32}H_{51}O_4Si_2$ $(M+H)^+$ 555.3326, found 555.3324.



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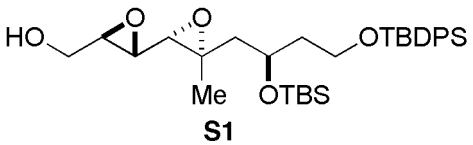
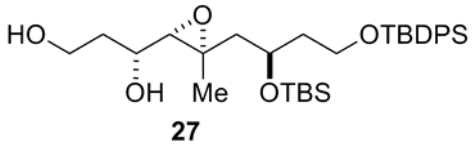


S1

Epoxy alcohols **26** and **S1**

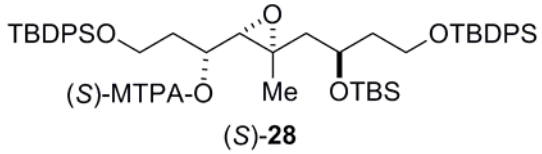
To a solution of allylic alcohol **25** (550 mg, 0.991 mmol) in CH_2Cl_2 (15 mL) was added *m*CPBA (555 mg, 2.48 mmol) at 0 °C. After stirring at room temperature for 7 h, to the solution were added dimethylsulfide and saturated aqueous $NaHCO_3$ at 0 °C. After stirring for 10 min, the aqueous layer was extracted with Et_2O. The organic layer was washed with water and brine, and dried over $MgSO_4$. Concentration and column chromatography (silica gel, EtOAc/hexane = 1:9) afforded epoxy alcohol **26** (244 mg, 43%) and its 27,28-epimer **S1** (244 mg, 43%) as a light yellow oil, respectively. Epoxy alcohol **26**: $[\alpha]_D^{24}$ -21.5 (*c* 1.00, $CHCl_3$); IR (neat) 3438, 2953, 2930, 2856, 2359, 1471, 1428, 1387, 1255, 1110 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.66-7.64 (m, 4 H), 7.43-7.41 (m, 2 H), 7.39-7.37 (m, 4 H), 4.16-4.12 (m, 1 H), 3.97 (ddd, *J* = 13.1, 4.8, 2.1 Hz, 1 H), 3.73-3.65 (m, 3 H), 3.12 (dd, *J* = 4.1, 2.1 Hz, 1 H), 3.00 (dd, *J* = 6.2, 2.1 Hz, 1 H), 2.62 (d, *J* = 6.2 Hz, 1 H), 1.87 (dd, *J* = 14.4, 4.8 Hz, 1 H), 1.79-1.68 (m, 2 H), 1.50 (dd, *J* = 14.4, 7.6 Hz, 1 H), 1.42 (s, 3 H), 1.05 (s, 9 H), 0.86 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.7, 133.9, 133.9, 129.8, 129.8, 127.8, 127.8, 66.9, 62.5, 60.7, 60.6, 59.7, 55.8, 52.9, 46.0, 40.6, 27.0, 26.0, 19.3, 18.1, 17.8, -4.1, -4.3; HRMS (FAB) calcd for $C_{32}H_{51}O_5Si_2$ $(M+H)^+$ 571.3275, found 571.3267. Epoxy alcohol **S1**: $[\alpha]_D^{21}$ +12.3 (*c* 0.83, $CHCl_3$); IR (neat) 3432, 2955, 2929, 2857, 1472, 1428, 1389, 1255, 1111 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.67-7.64 (m, 4 H), 7.44-7.36 (m, 6 H), 4.17-4.13 (m, 1 H), 3.97 (dd, *J* = 12.6, 2.3 Hz, 1 H), 3.75-3.66 (m, 3 H), 3.19-3.17 (m, 1 H), 3.02 (dd, *J* = 5.7, 2.3 Hz, 1 H), 2.70 (d, *J* = 5.7 Hz, 1 H), 1.84 (dd, *J* = 13.8, 4.6 Hz, 1 H), 1.77-1.73 (m, 2 H), 1.61-1.55 (m, 2 H), 1.40 (s, 3 H), 1.05 (s, 9 H), 0.86 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.7, 133.9, 129.8, 129.8, 127.8, 127.8, 66.7, 61.3, 60.9, 60.6, 59.8, 57.0, 52.6, 45.8, 40.6, 27.0, 26.0, 19.3, 18.1, 17.5, -4.2, -4.3; HRMS (FAB) calcd for $C_{32}H_{51}O_5Si_2$ $(M+H)^+$ 571.3275, found 571.3267.



27

Diol **27**

To a solution of epoxy alcohol **26** (14.0 mg, 24.5 μmol) in THF (0.5 mL) was added sodium bis(2-methoxyethoxy)aluminum hydride solution (65% in toluene, 50 μL, 0.161 mmol) at 0 °C. After stirring for 4 h at room temperature, the solution was then poured into the saturated sodium potassium tartrate aqueous solution at 0 °C and stirred for 30 min. The aqueous layer was extracted with Et_2O and successively washed with water and brine, dried over Na_2SO_4, and concentrated. Purification of the residue by preparative TLC (silica, EtOAc/hexanes = 1:5) afforded diol **27** (8.8 mg, 63%) as a light yellow oil.

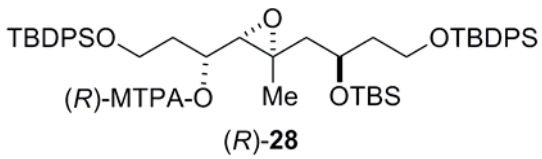


(*S*)-**28**

(S)-MTPA ester (*S*)-**28**

To a mixture of diol **27** (4.0 mg, 6.98 μmol) and DMAP (1.2 mg, 10.5 μmol) in CH_2Cl_2 (0.5 mL) were added imidazole (0.7 mg, 10.5 μmol) and *tert*-butyl(chloro)diphenylsilane (2.7 μL, 10.5 μmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 h and then quenched with saturated aqueous $NaHCO_3$. The mixture was extracted with Et_2O. The extract was washed successively with water and brine, and dried over Na_2SO_4. Concentration gave the corresponding mono-TBDPS ether, which was used immediately in the next step without further purification.

To a mixture of alcohol obtained above (3.0 mg) and DMAP (2.5 mg, 20.5 μmol) in CH_2Cl_2 (0.5 mL) were added Et_3N (2.8 μL, 20.5 μmol) and *(R)*-MTPA-Cl (3.8 μL, 20.5 μmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 h and then quenched with MeOH at 0 °C. After evaporation of the solvent, the residue was purified by column chromatography (silica gel, EtOAc/hexanes = 1:30) to afford *(S)*-MTPA ester (*S*)-**28** (3.0 mg, 42%) as a light yellow oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.85 (m, 2 H), 7.81-7.77 (m, 6 H), 7.75-7.73 (m, 2 H), 7.32-7.22 (m, 13 H), 7.08-7.05 (m, 2 H), 5.75-5.70 (m, 1 H), 4.21-4.16 (m, 1 H), 3.86-3.73 (m, 3 H), 3.69-3.65 (m, 1 H), 3.45 (s, 3 H), 2.66 (d, *J* = 8.6 Hz, 1 H), 1.97-1.90 (m, 1 H), 1.80-1.73 (m, 3 H), 1.70 (dd, *J* = 14.3, 5.2 Hz, 1 H), 1.55 (dd, *J* = 14.3, 6.9 Hz, 1 H), 1.47 (s, 3 H), 1.19 (s, 9 H), 1.17 (s, 9 H), 0.95 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H).

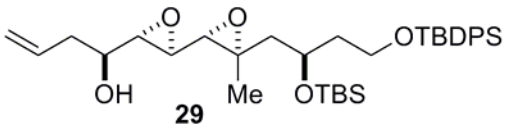


(*R*)-**28**

(R)-MTPA ester (*R*)-**28**

To a mixture of diol **27** (4.0 mg, 6.98 μmol) and DMAP (1.2 mg, 10.5 μmol) in CH_2Cl_2 (0.5 mL) were added imidazole (0.7 mg, 10.5 μmol) and *tert*-butyl(chloro)diphenylsilane (2.7 μL, 10.5 μmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 h and then quenched with saturated aqueous $NaHCO_3$. The mixture was extracted with Et_2O. The extract was washed successively with water and brine, and dried over Na_2SO_4. Concentration gave the corresponding mono-TBDPS ether, which was used immediately in the next step without further purification.

To a mixture of alcohol (3.0 mg, 3.70 μmol) and DMAP (2.5 mg, 20.5 μmol) in CH_2Cl_2 (0.5 mL) were added Et_3N (2.8 μL, 20.5 μmol) and *(S)*-MTPA-Cl (3.8 μL, 20.5 μmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 h and then quenched with MeOH at 0 °C. After evaporation of the solvent, the residue was purified by column chromatography (silica gel, EtOAc/hexanes = 1:30) to afford *(R)*-MTPA ester (*R*)-**28** (3.0 mg, 42%) as a light yellow oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76-7.71 (m, 8 H), 7.67-7.65 (m, 2 H), 7.24-7.16 (m, 12 H), 7.07-7.04 (m, 2 H), 6.99-6.97 (m, 1 H), 5.69-5.66 (m, 1 H), 4.16-4.12 (m, 1 H), 3.80-3.76 (m, 1 H), 3.74-3.70 (m, 1 H), 3.59-3.55 (m, 4 H), 3.51-3.48 (m, 1 H), 2.65 (d, *J* = 8.9 Hz, 1 H), 1.90-1.85 (m, 1 H), 1.75-1.70 (m, 1 H), 1.67 (dd, *J* = 14.4, 5.5 Hz, 1 H), 1.64-1.57 (m, 2 H), 1.52 (dd, *J* = 14.4, 6.9 Hz, 1 H), 1.40 (s, 3 H), 1.12 (s, 9 H), 1.12 (s, 9 H), 0.88 (s, 9 H), 0.08 (s, 3 H), 0.03 (s, 3 H).

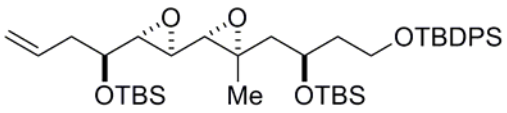


29

Homoallylic alcohol **29**

To a solution of oxalyl chloride (0.11 mL, 1.34 mmol) in CH_2Cl_2 (8.0 mL) was added DMSO (0.14 mL, 2.01 mmol) dropwise at -78 °C. After 30 min, alcohol **26** (382 mg, 0.669 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise. The mixture was stirred at -78 °C for 2 h before Et_3N (0.56 mL, 4.01 mmol) was added slowly. The mixture was stirred for an additional 1 h at -78 °C. The reaction was quenched with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2. The combined organic phase was washed with water and brine, and dried over $MgSO_4$. Concentration and short column chromatography (silica gel, EtOAc/hexane = 1:40, 1:20) afforded the corresponding aldehyde (332 mg) as a yellow oil, which was used immediately in the next reaction without further purification.

To a mixture of the aldehyde (332 mg) obtained above and powdered molecular sieves 4A (75 mg) in toluene (5.5 mL) was added (*R*,*R*)-tartrate allylboronate (0.20 mL, 0.791 mmol) at -78 °C. The reaction was stirred for 1 h at -78 °C. Saturated aqueous $NaHCO_3$ was added, the mixture was stirred for 30 min, and then the organic phase was separated. The aqueous phase was extracted with Et_2O. The combined organic extract was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel, EtOAc/hexane = 1:20, 1:10) to afford homoallylic alcohol **29** (295 mg, 72% in 2 steps) and its 26-epimer (59.0 mg, 14% in 2 steps) as a yellow oil, respectively. Homoallylic alcohol **29**: $[\alpha]_D^{23}$ -12.4 (*c* 1.33, $CHCl_3$); IR (neat) 3458, 2955, 2929, 2856, 1472, 1427, 1388, 1254, 1109 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.66-7.64 (m, 4 H), 7.44-7.41 (m, 2 H), 7.39-7.36 (m, 4 H), 5.89-5.82 (m, 1 H), 5.17 (dd, *J* = 17.2, 1.4 Hz, 1 H), 5.14 (dd, *J* = 10.3, 1.4 Hz, 1 H), 4.16-4.12 (m, 1 H), 3.92-3.86 (m, 1 H), 3.73-3.66 (m, 2 H), 3.05 (dd, *J* = 5.5, 2.8 Hz, 1 H), 3.00 (dd, *J* = 5.5, 2.8 Hz, 1 H), 2.63 (d, *J* = 5.5 Hz, 1 H), 2.43-2.39 (m, 1 H), 2.32-2.27 (m, 1 H), 1.89 (brs, 1 H), 1.82 (dd, *J* = 14.4, 5.5 Hz, 1 H), 1.77-1.68 (m, 2 H), 1.56 (dd, *J* = 14.4, 6.2 Hz, 1 H), 1.43 (s, 3 H), 1.05 (s, 9 H), 0.86 (s, 9 H), 0.07 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.7, 133.9, 133.9, 133.5, 129.8, 129.8, 127.8, 127.8, 118.6, 67.7, 66.7, 62.2, 60.7, 59.5, 57.4, 52.5, 46.0, 40.4, 38.1, 27.0, 26.0, 19.3, 18.1, -4.1, -4.4; HRMS (FAB) calcd for $C_{35}H_{55}O_5Si_2$ $(M+H)^+$ 611.3588, found 611.3572.

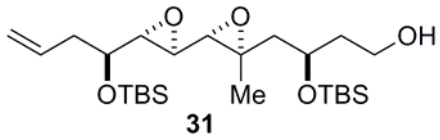


30

Silyl ether **30**

To a mixture of alcohol **29** (23.0 mg, 37.6 μmol) and 2,6-lutidine (18 μL, 0.151 mmol) in CH_2Cl_2 (0.5 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (26 μL, 0.113 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 20 min, then quenched by the addition of MeOH. The mixture was diluted with Et_2O and extracted. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography (silica gel, EtOAc/hexane = 1:40) afforded silyl ether **30** (27.0 mg, 99%) as a yellow oil: $[\alpha]_D^{23}$ -5.7 (*c* 0.42, $CHCl_3$); IR (neat) 2952, 2929, 2858, 2359, 1472, 1427, 1388, 1360, 1254, 1111 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.66-7.63 (m, 4 H), 7.43-7.41 (m, 2 H), 7.39-7.36 (m, 4 H), 5.88-5.81 (m, 1 H), 5.10 (dd, *J* = 17.2, 1.4 Hz, 1 H), 5.07 (d, *J* = 10.3 Hz, 1 H), 4.15-4.11 (m, 1 H), 3.79-3.77 (m, 1 H),

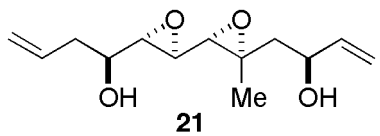
3.72-3.65 (m, 2 H), 2.96 (dd, *J* = 5.5, 2.1 Hz, 1 H), 2.88 (dd, *J* = 4.8, 2.1 Hz, 1 H), 2.63 (d, *J* = 4.8 Hz, 1 H), 2.39-2.35 (m, 1 H), 2.32-2.27 (m, 1 H), 1.81 (dd, *J* = 14.4, 5.5 Hz, 1 H), 1.74-1.71 (m, 2 H), 1.48 (dd, *J* = 14.4, 6.2 Hz, 1 H), 1.42 (s, 3 H), 1.05 (s, 9 H), 0.87 (s, 9 H), 0.86 (s, 9 H), 0.07 (s, 3 H), 0.05 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.7, 134.0, 133.9, 129.8, 129.7, 127.8, 127.8, 117.8, 69.9, 66.8, 62.3, 60.7, 59.6, 57.5, 52.6, 46.0, 40.3, 40.0, 27.0, 26.0, 25.9, 19.3, 18.3, 18.1, -4.1, -4.4, -4.4, -4.7; HRMS (FAB) calcd for $C_{41}H_{69}O_5Si_3$ $(M+H)^+$ 725.4453, found 725.4422.



31

Alcohol **31**

To a solution of TBDPS ether **30** (10.0 mg, 13.8 μmol) in MeOH (0.5 mL) was added NH_4F (10.0 mg, 0.276 mmol). After stirring for 9 h at room temperature, the reaction mixture was quenched by the addition of a saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O and the organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography (silica gel, EtOAc/hexanes = 1:30, 1:10) afforded alcohol **31** (5.2 mg, 77%) as a yellow oil: $[\alpha]_D^{24}$ -1.8 (*c* 0.10, $CHCl_3$); IR (neat) 2952, 2928, 2855, 1470, 1253, 1106 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.89-5.83 (m, 1 H), 5.12 (dd, *J* = 17.2, 2.1 Hz, 1 H), 5.09 (d, *J* = 10.3 Hz, 1 H), 4.20-4.16 (m, 1 H), 3.80-3.78 (m, 2 H), 3.75-3.70 (m, 1 H), 2.95 (dd, *J* = 5.5, 2.1 Hz, 1 H), 2.90 (dd, *J* = 4.1, 2.1 Hz, 1 H), 2.63 (d, *J* = 5.5 Hz, 1 H), 2.41-2.37 (m, 1 H), 2.33-2.29 (m, 1 H), 2.13 (brs, 1 H), 1.91-1.86 (m, 1 H), 1.83 (dd, *J* = 14.4, 5.5 Hz, 1 H), 1.76-1.71 (m, 2 H), 1.42 (s, 3 H), 0.90 (s, 9 H), 0.87 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 133.9, 117.9, 69.8, 68.5, 62.2, 59.8, 59.2, 57.6, 52.5, 45.3, 40.0, 38.7, 26.0, 25.9, 18.3, 18.1, 17.9, -4.3, -4.5, -4.6, -4.7; HRMS (FAB) calcd for $C_{25}H_{51}O_5Si_2$ $(M+H)^+$ 487.3275, found 487.3284.



21

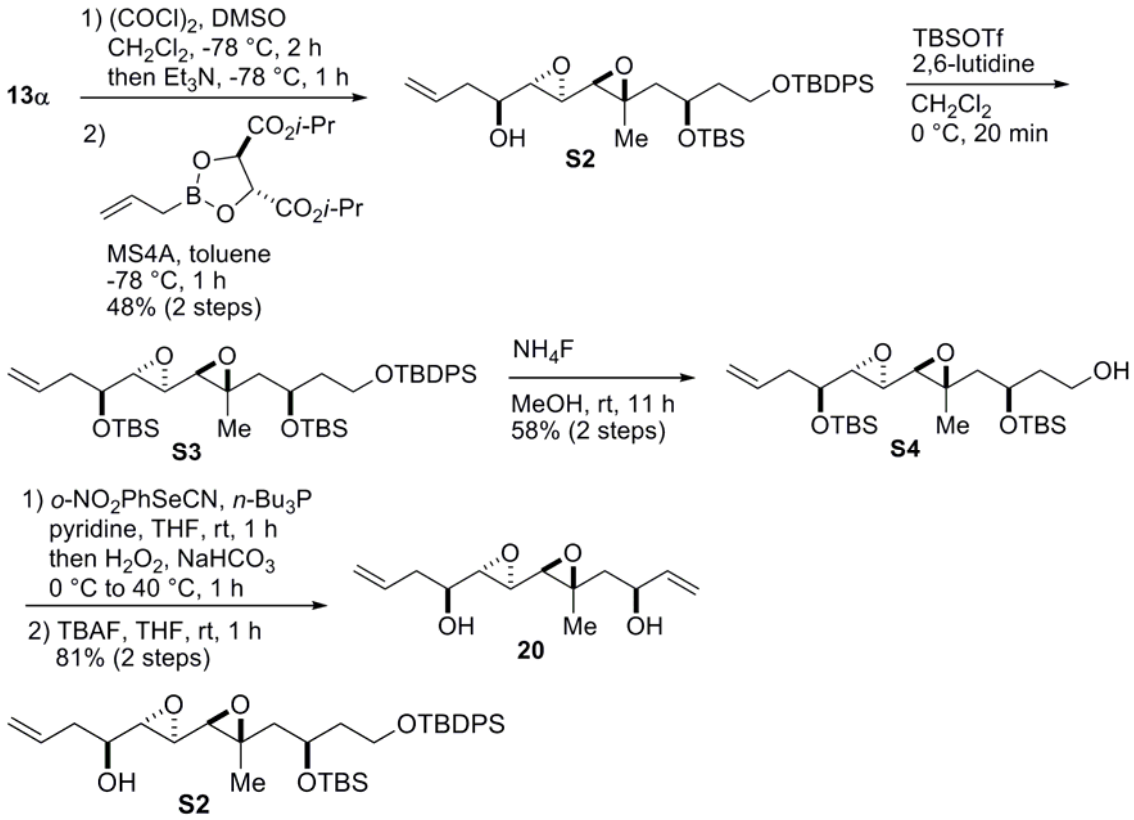
Diepoxide **21**

To a mixture of alcohol **31** (7.5 mg, 15.4 μmol) and *o*-nitrophenyl selenocyanate (44.0 mg, 0.195 mmol) in THF (0.4 mL) were added pyridine (16 μL, 0.195 mmol) and tributylphosphine (48 μL, 0.195 mmol). The mixture was stirred for 1 h at room

temperature. To the resulting mixture were added $NaHCO_3$ (4.8 mg, 57 μmol) and 30% H_2O_2 (100 μL) at 0 °C. The stirring was continued for 40 min at 40 °C. The mixture was diluted with Et_2O, then washed with water, saturated aqueous Na_2CO_3, and brine. Concentration and short column chromatography (silica gel, EtOAc/hexane = 1:50) gave alkene **32** (5.0 mg), which was used in the next reaction without further purification.

To a mixture of diene **32** (5.0 mg) obtained above in THF was added TBAF (1.0 M solution in THF, 0.21 mL, 0.21 mmol), and the mixture was stirred for 1 h at room temperature. The mixture was diluted with Et_2O, then washed with water and brine. Concentration and column chromatography (silica gel, EtOAc/hexane = 1:10, 1:1) gave diepoxide **21** (2.5 mg, 68% in 2 steps) as a yellow oil.

Scheme S1. Synthesis of **20**

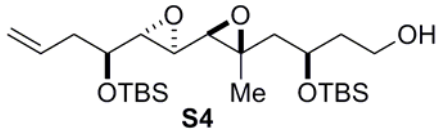


Homoallylic alcohol **S2**

To a solution of oxalyl chloride (17 μL, 0.196 mmol) in CH_2Cl_2 (0.5 mL) was added DMSO (28 μL, 0.378 mmol) dropwise at -78 °C. After 30 min, alcohol **13α** (14.0 mg, 24.5 μmol) in CH_2Cl_2 (0.5 mL) was added dropwise. The mixture was stirred at -78 °C for 2 h before Et_3N (70 μL, 0.490 mmol) was added slowly. The mixture was stirred for

an additional 1 h at -78 °C. The reaction was quenched with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2. The combined organic phase was washed with water and brine, and dried over $MgSO_4$. Concentration and short column chromatography (silica gel, EtOAc/hexane = 1:40, 1:20) afforded the corresponding aldehyde (9.0 mg) as a yellow oil, which was used immediately in the next reaction without further purification.

To a mixture of aldehyde (9.0 mg) obtained above and powdered molecular sieves 4A (12 mg) in toluene (1.2 mL) was added (*R*,*R*)-tartrate allylboronate (6.0 μL, 22.0 μmol) at -78 °C. The reaction was stirred for 1 h at -78 °C. Saturated aqueous $NaHCO_3$ was added, the mixture was stirred for 30 min, and then the organic phase was separated. The aqueous phase was extracted with Et_2O. The combined organic extract was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel, EtOAc/hexane = 1:20) to afford homoallylic alcohol **S2** (7.2 mg, 48% in 2 steps) and its 26-epimer (1.4 mg, 9% in 2 steps) as a yellow oil, respectively. Homoallylic alcohol **S2**: $[\alpha]_D^{21}$ +5.2 (*c* 0.13, $CHCl_3$); IR (neat) 3453, 2955, 2930, 2857, 1472, 1428, 1388, 1255, 1111 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.66-7.64 (m, 4 H), 7.43-7.41 (m, 2 H), 7.39-7.37 (m, 4 H), 5.91-5.83 (m, 1 H), 5.21-5.16 (m, 2 H), 4.11-4.07 (m, 1 H), 3.89-3.87 (m, 1 H), 3.77-3.73 (m, 1 H), 3.71-3.67 (m, 1 H), 3.08-3.07 (m, 1 H), 3.04 (dd, *J* = 5.5, 2.1 Hz, 1 H), 2.66 (d, *J* = 5.5 Hz, 1 H), 2.43-2.39 (m, 1 H), 2.34-2.29 (m, 1 H), 1.95 (dd, *J* = 13.8, 5.5 Hz, 1 H), 1.81-1.73 (m, 1 H), 1.65-1.60 (m, 1 H), 1.52 (dd, *J* = 13.8, 7.6 Hz, 1 H), 1.41 (s, 3 H), 1.05 (s, 9 H), 0.85 (s, 9 H), 0.07 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.6, 133.9, 133.8, 133.5, 133.3, 129.7, 129.7, 127.8, 127.7, 118.5, 68.2, 66.9, 60.9, 60.5, 59.9, 59.1, 52.4, 46.0, 39.8, 38.2, 27.0, 25.9, 19.2, 18.0, 18.0, -4.3, -4.5; HRMS (FAB) calcd for $C_{35}H_{55}O_5Si_2$ $(M+H)^+$ 611.3588, found 611.3592.



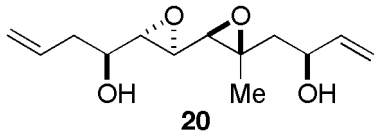
S4

Alcohol **S4**

To a mixture of homoallylic alcohol **S2** (15.0 mg, 24.6 μmol) and 2,6-lutidine (8.6 μL, 73.6 μmol) in CH_2Cl_2 (0.5 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (17.0 μL, 73.6 μmol) at 0 °C. The reaction mixture was stirred at 0 °C for 20 min, then quenched by the addition of MeOH. The mixture was diluted with Et_2O and extracted. The organic layer was washed with water and brine, dried over

Na_2SO_4, and concentrated. Purification by column chromatography (silica gel, EtOAc/hexane = 1:40) afforded silyl ether **S3** (16.0 mg) as a light yellow oil, which was used in the next reaction without further purification.

To a solution of TBDPS ether **S3** (16.0 mg) obtained above in MeOH (0.5 mL) was added NH_4F (16.4 mg, 0.442 mmol). After stirring for 11 h at room temperature, the reaction mixture was quenched by the addition of a saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O and the organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography (silica gel, EtOAc/hexane = 1:30, 1:15) afforded alcohol **S4** (7.0 mg, 58% in 2 steps) as a yellow oil: $[\alpha]_D^{21}$ -1.5 (*c* 0.13, $CHCl_3$); IR (neat) 3459, 2957, 2928, 2857, 1728, 1460, 1379, 1270, 1122, 1071 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.88-5.81 (m, 1 H), 5.13-5.08 (m, 2 H), 4.07-4.03 (m, 1 H), 3.80-3.71 (m, 3 H), 2.97 (dd, *J* = 4.0, 2.2 Hz, 1 H), 2.88 (dd, *J* = 6.2, 2.2 Hz, 1 H), 2.57 (d, *J* = 6.2 Hz, 1 H), 2.39-2.29 (m, 2 H), 2.05 (dd, *J* = 13.9, 4.4 Hz, 1 H), 1.93-1.87 (m, 1 H), 1.68-1.63 (m, 2 H), 1.42 (s, 3 H), 0.89 (s, 9 H), 0.87 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H), 0.04 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 134.0, 117.9, 70.2, 69.2, 61.5, 60.2, 59.7, 59.3, 52.8, 45.6, 40.0, 38.4, 29.9, 25.9, 18.3, 18.0, -4.3, -4.4, -4.6, -4.7; HRMS (FAB) calcd for $C_{25}H_{51}O_5Si_2$ $(M+H)^+$ 487.3275, found 487.3296.



20

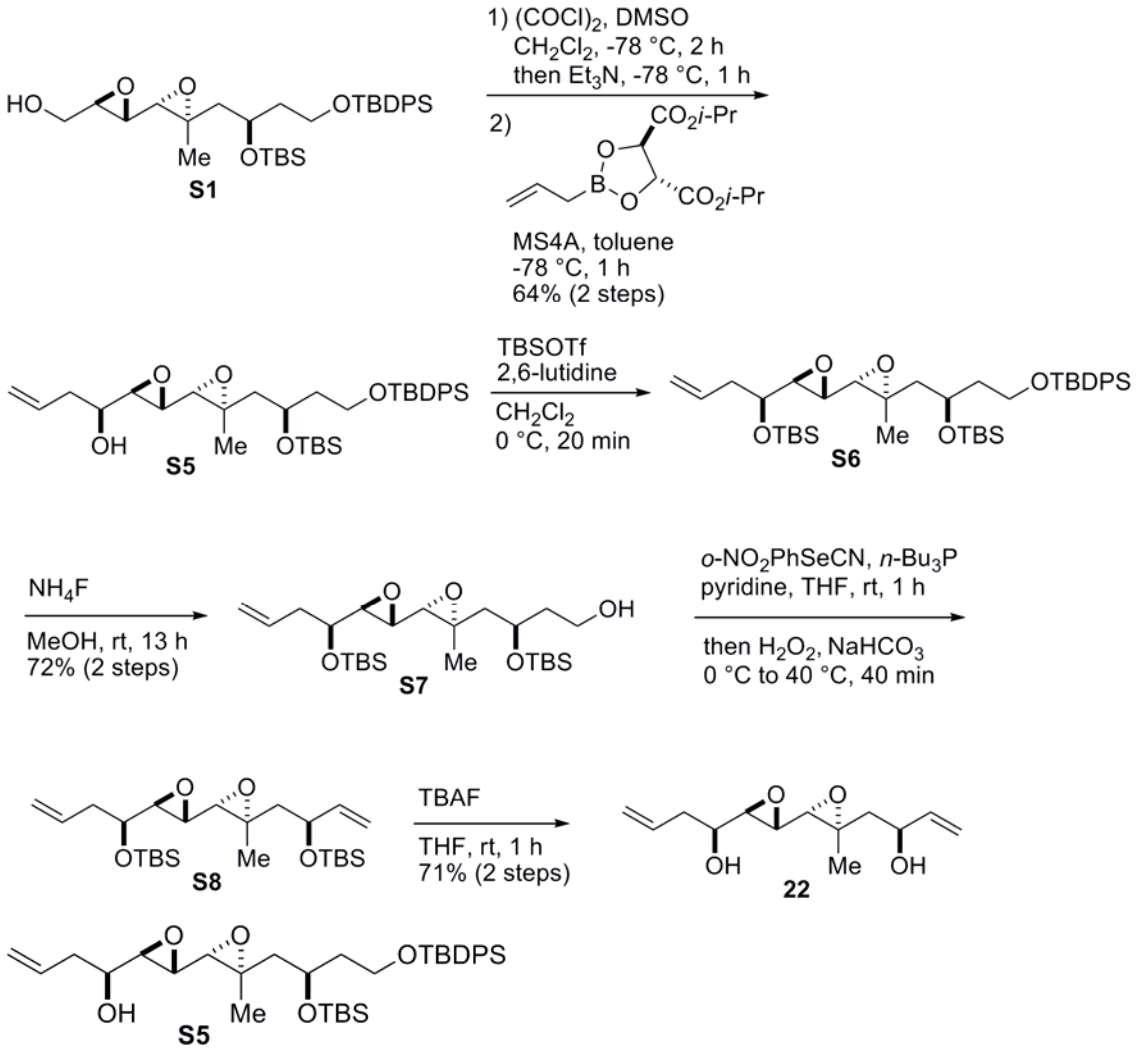
Diepoxide **20**

To a mixture of alcohol **S4** (3.0 mg, 6.16 μmol) and *o*-nitrophenyl selenocyanate (5.6 mg, 24.6 μmol) in THF (0.4 mL) were added pyridine (2.0 μL, 24.6 μmol) and tributylphosphine (6.0 μL, 24.6 μmol). The mixture was stirred for 1 h at room temperature. To the resulting mixture were added $NaHCO_3$ (2.0 mg, 23.8 μmol) and 30% H_2O_2 (100 μL) at 0 °C. The stirring was continued for 1 h at 40 °C. The mixture was diluted with Et_2O, then washed with water, saturated aqueous Na_2CO_3, and brine. Concentration and short column chromatography (silica gel, EtOAc/hexane = 1:50) gave the corresponding diene (2.4 mg), which was used in the next reaction without further purification.

To a solution of diene (2.4 mg) obtained above in THF was added TBAF (1.0 M solution in THF, 0.102 mL, 0.102 mmol), and the mixture was stirred for 1 h at room

temperature. The mixture was diluted with Et_2O, then washed with water and brine. Concentration and column chromatography (silica gel, EtOAc/hexane = 1:10, 1:1) gave diepoxide **20** (1.2 mg, 81% in 2 steps) as a colorless oil.

Scheme S2. Synthesis of **22**

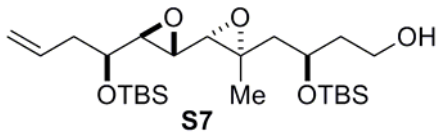


Homoallylic alcohol **S5**

To a solution of oxalyl chloride (0.11 mL, 1.34 mmol) in CH_2Cl_2 (8.0 mL) was added DMSO (0.14 mL, 2.01 mmol) dropwise at -78 °C. After 30 min, alcohol **S1** (191 mg, 0.335 mmol) in CH_2Cl_2 (2.0 mL) was added dropwise. The mixture was stirred at -78 °C for 2 h before Et_3N (0.56 mL, 4.01 mmol) was added slowly. The mixture was stirred for an additional 1 h at -78 °C. The reaction was quenched with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2. The combined organic phase was washed with water and brine, and dried over $MgSO_4$. Concentration and short column

chromatography (silica gel, EtOAc/hexane = 1:40, 1:20) afforded the corresponding aldehyde (166 mg) as a yellow oil, which was used immediately in the next reaction without further purification.

To a mixture of the aldehyde (166 mg) obtained above and powdered molecular sieves 4A (75 mg) in toluene (5.5 mL) was added (*R*,*R*)-tartrate allylboronate (0.20 mL, 0.791 mmol) at -78 °C. The reaction was stirred for 1 h at -78 °C. Saturated aqueous $NaHCO_3$ was added, the mixture was stirred for 30 min, and then the organic phase was separated. The aqueous phase was extracted with Et_2O. The combined organic extract was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel, EtOAc/hexane = 1:20, 1:10) to afford homoallylic alcohol **S5** (131 mg, 64% in 2 steps) and its 26-epimer (24.5 mg, 14% in 2 steps) as a yellow oil, respectively. Homoallylic alcohol **S5**: $[\alpha]_D^{21}$ +1.7 (*c* 1.60, $CHCl_3$); IR (neat) 3444, 2955, 2929, 2857, 1472, 1428, 1388, 1255, 1112 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.67-7.64 (m, 4 H), 7.44-7.41 (m, 2 H), 7.39-7.36 (m, 4 H), 5.89-5.82 (m, 1 H), 5.20-5.16 (m, 2 H), 4.16-4.12 (m, 1 H), 3.74-3.65 (m, 3 H), 3.06 (dd, *J* = 4.1, 2.1 Hz, 1 H), 2.99 (dd, *J* = 5.5, 2.1 Hz, 1 H), 2.67 (d, *J* = 5.5 Hz, 1 H), 2.43-2.37 (m, 2 H), 1.82 (dd, *J* = 13.8, 4.8 Hz, 1 H), 1.75-1.72 (m, 2 H), 1.58 (dd, *J* = 13.8, 6.9 Hz, 1 H), 1.40 (s, 3 H), 1.05 (s, 9 H), 0.86 (s, 9 H), 0.09 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.7, 133.9, 133.3, 129.8, 127.8, 127.8, 118.9, 69.3, 66.7, 61.3, 60.6, 59.8, 59.5, 53.2, 45.8, 40.5, 39.3, 27.0, 26.0, 19.3, 18.1, 17.6, -4.2, -4.4; HRMS (FAB) calcd for $C_{35}H_{55}O_5Si_2$ $(M+H)^+$ 611.3588, found 611.3572.

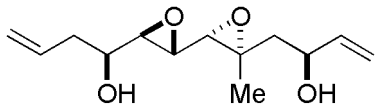


S7

Alcohol **S7**

To a mixture of homoallylic alcohol **S5** (14.0 mg, 22.9 μmol) and 2,6-lutidine (12.9 μL, 0.111 mmol) in CH_2Cl_2 (0.5 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (25.5 μL, 0.111 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 20 min, then quenched by the addition of MeOH. The mixture was diluted with Et_2O and extracted. The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography (silica gel, EtOAc/hexane = 1:40) afforded silyl ether **S6** (15.0 mg) as a yellow oil, which was used in the next reaction without further purification.

To a solution of TBDPS ether **S6** (15.0 mg) obtained above in MeOH (0.8 mL) was added NH_4F (15.3 mg, 0.414 mmol). After stirring for 13 h at room temperature, the reaction mixture was quenched by the addition of a saturated aqueous $NaHCO_3$. The aqueous layer was extracted with Et_2O and the organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography (silica gel, EtOAc/hexanes = 1:30, 1:10) afforded alcohol **S7** (8.0 mg, 72% in 2 steps) as a yellow oil: $[\alpha]_D^{21}$ -4.5 (*c* 0.13, $CHCl_3$); IR (neat) 2952, 2927, 2856, 1734, 1717, 1458, 1253, 1113, 1071 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 5.88-5.79 (m, 1 H), 5.12-5.07 (m, 2 H), 4.21-4.17 (m, 1 H), 3.82-3.78 (m, 1 H), 3.75-3.71 (m, 1 H), 3.46-3.42 (m, 1 H), 3.01 (dd, *J* = 6.2, 2.1 Hz, 1 H), 2.79 (dd, *J* = 6.2, 2.1 Hz, 1 H), 2.57 (d, *J* = 6.2 Hz, 1 H), 2.35-2.29 (m, 2 H), 1.94-1.85 (m, 2 H), 1.77-1.68 (m, 2 H), 1.41 (s, 3 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H), 0.09 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 134.0, 117.9, 72.9, 68.6, 61.4, 60.7, 59.8, 59.3, 53.1, 45.1, 39.7, 38.6, 29.8, 25.9, 22.8, 18.0, 17.4, -4.4, -4.5, -4.7; HRMS (FAB) calcd for $C_{25}H_{51}O_5Si_2$ $(M+H)^+$ 487.3275, found 487.3269.

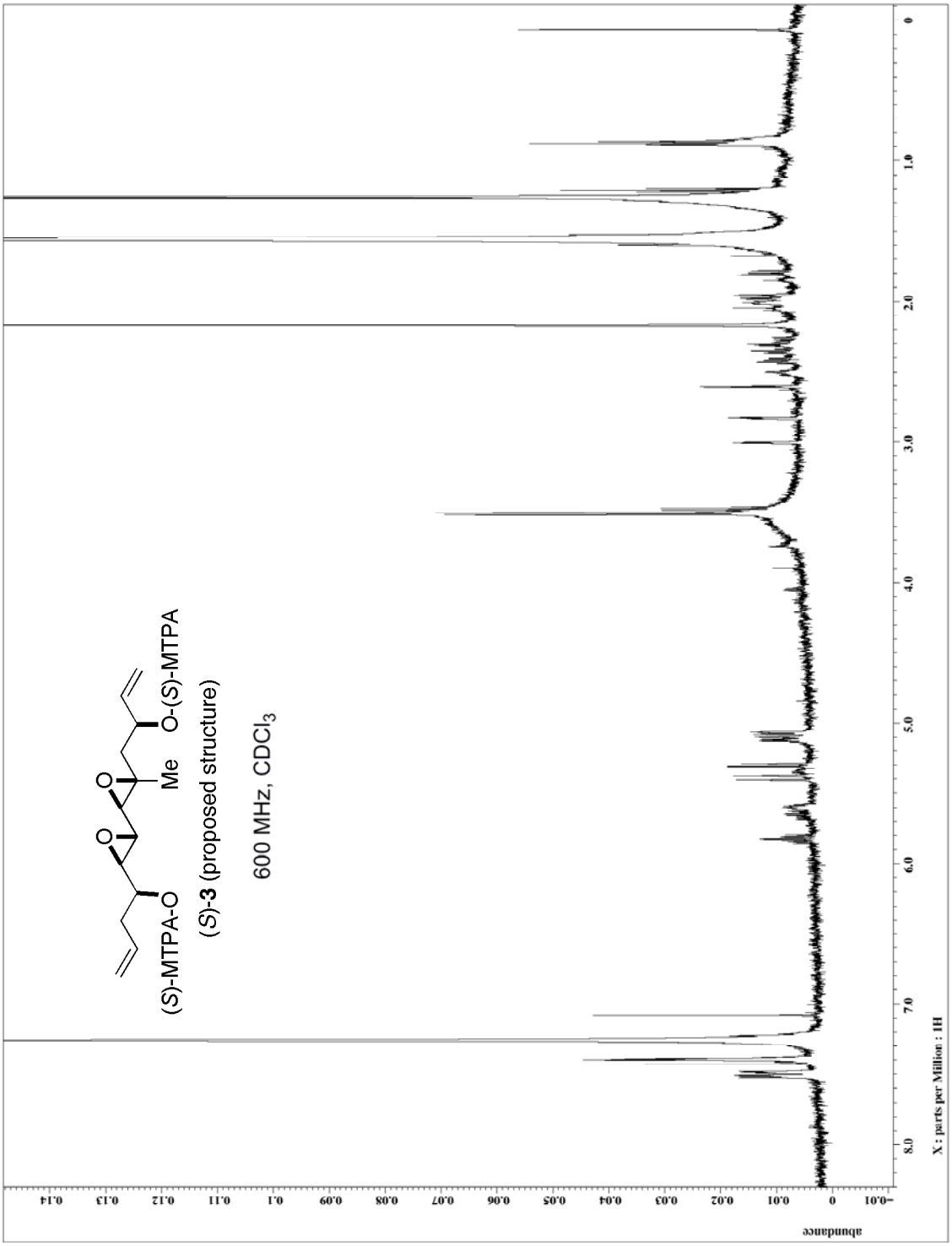


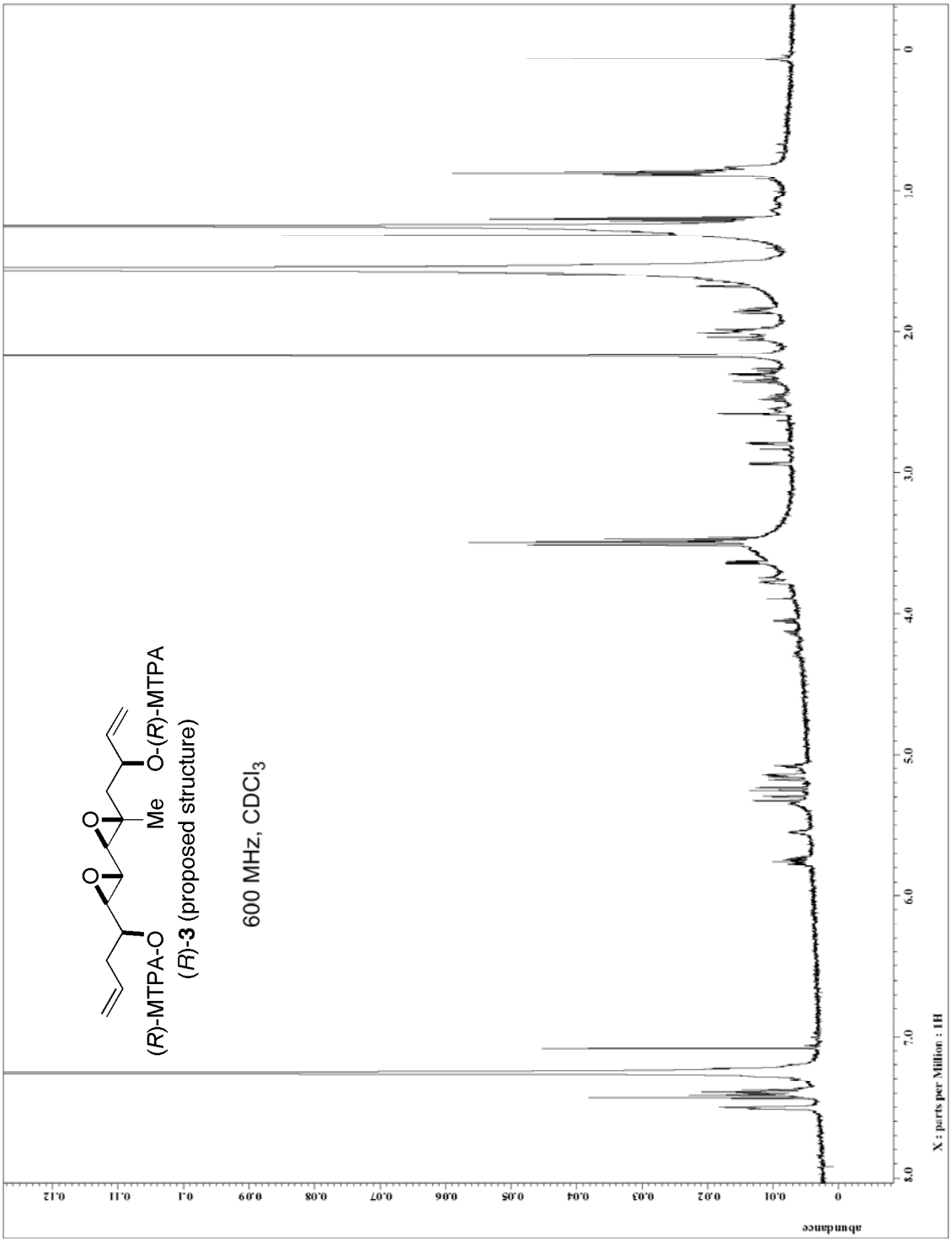
22

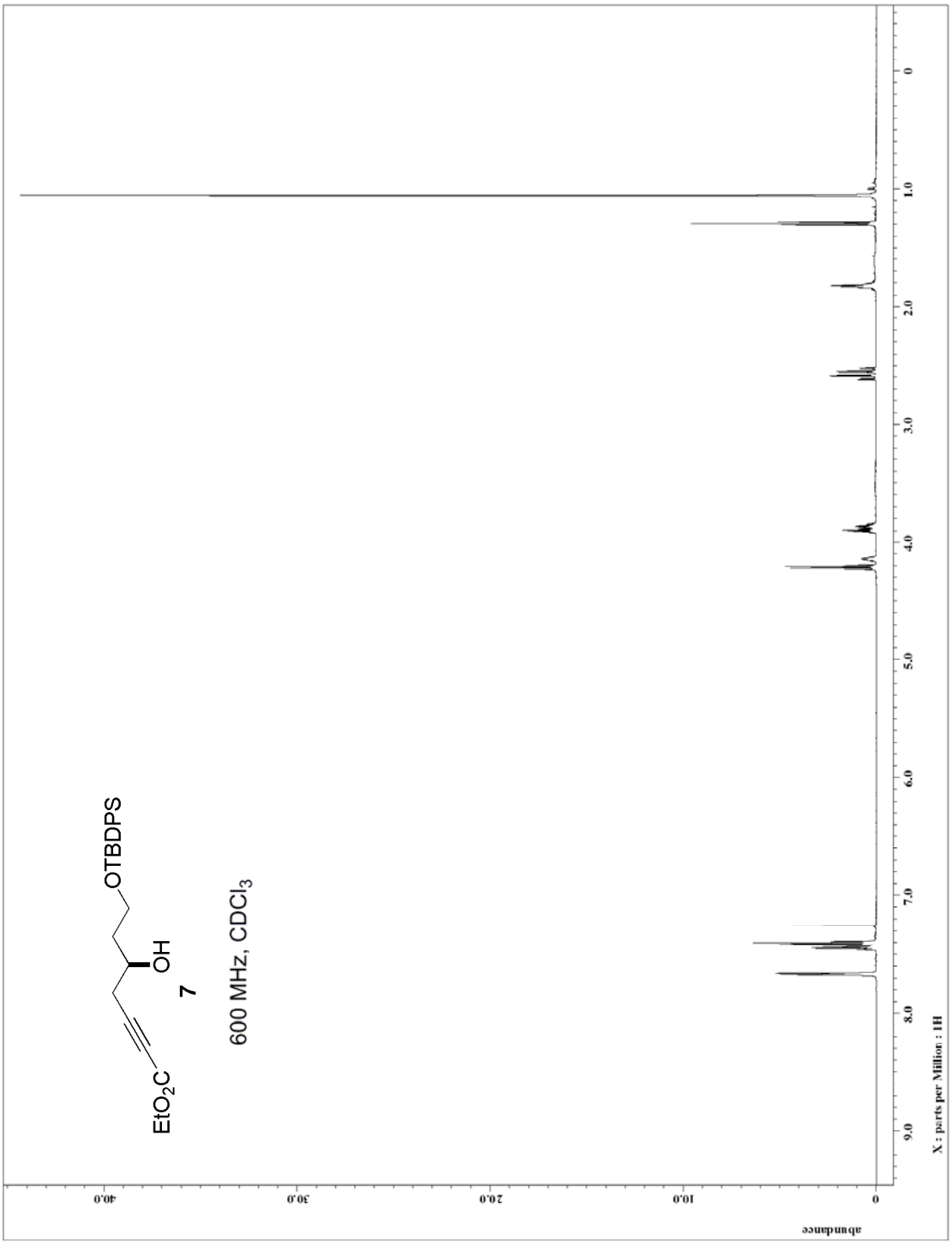
Diepoxide **22**

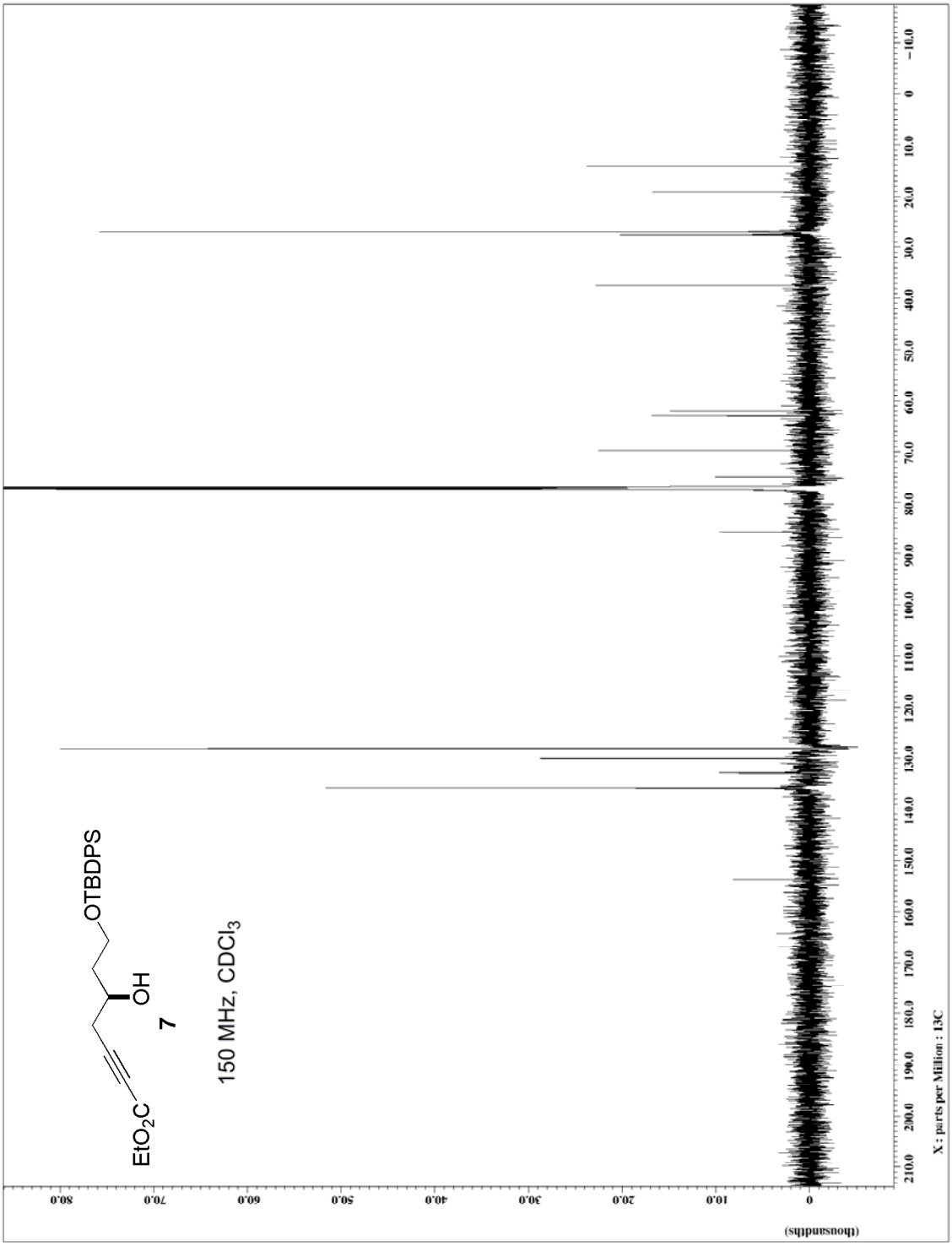
To a mixture of alcohol **S7** (4.0 mg, 8.21 μmol) and *o*-nitrophenyl selenocyanate (7.6 mg, 33.5 μmol) in THF (0.5 mL) were added pyridine (4.0 μL, 49.6 μmol) and tributylphosphine (8.3 μL, 33.5 μmol). The mixture was stirred for 1 h at room temperature. To the resulting mixture were added $NaHCO_3$ (2.0 mg, 23.8 μmol) and 30% H_2O_2 (300 μL) at 0 °C. The stirring was continued for 40 min at 40 °C. The mixture was diluted with Et_2O, then washed with water, saturated aqueous Na_2CO_3, and brine. Concentration and short column chromatography (silica gel, EtOAc/hexane = 1:50) gave diene **S8** (3.0 mg), which was used in the next reaction without further purification.

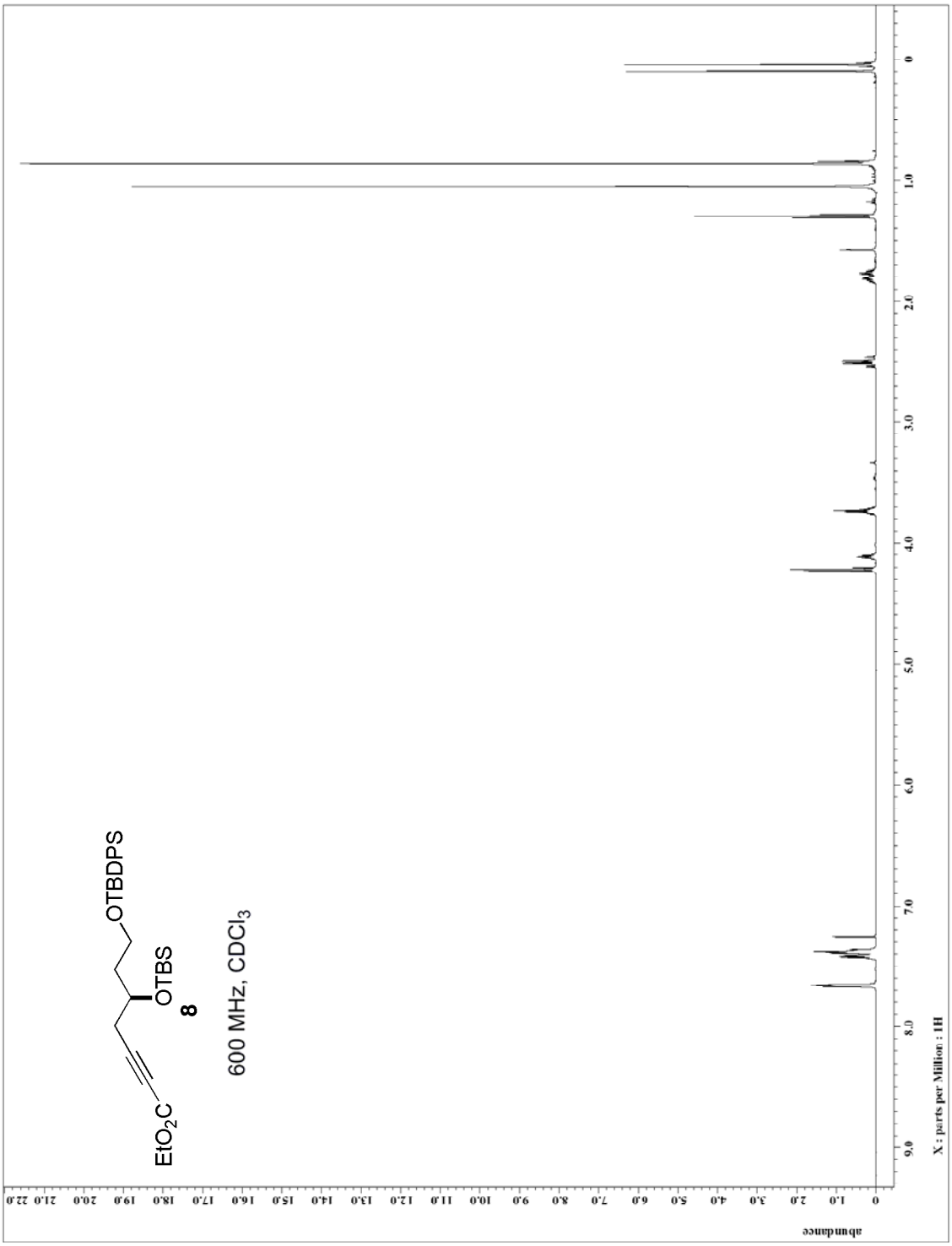
To a mixture of diene **S8** (3.0 mg) obtained above in THF was added TBAF (1.0 M solution in THF, 0.128 mL, 0.128 mmol), and the mixture was stirred for 1 h at room temperature. The mixture was diluted with Et_2O, then washed with water and brine. Concentration and column chromatography (silica gel, EtOAc/hexane = 1:10, 1:1) gave diepoxide **22** (1.4 mg, 71% in 2 steps) as a yellow oil.


(S)-MTPA-O
Me
O-(S)-MTPA
(S)-3 (proposed structure)
600 MHz, CDCl3
abundance
X : parts per Million : 1H


(R)-MTPA-O
Me
O-(R)-MTPA
(R)-3 (proposed structure)
600 MHz, CDCl3
abundance
X : parts per Million : 1H


OTBDPS
OH
EtO2C
7
600 MHz, CDCl3
abundance
X : parts per Million : 1H


OTBDPS
OH
7
EtO2C
150 MHz, CDCl3
(thousandths)
X : parts per Million : 13C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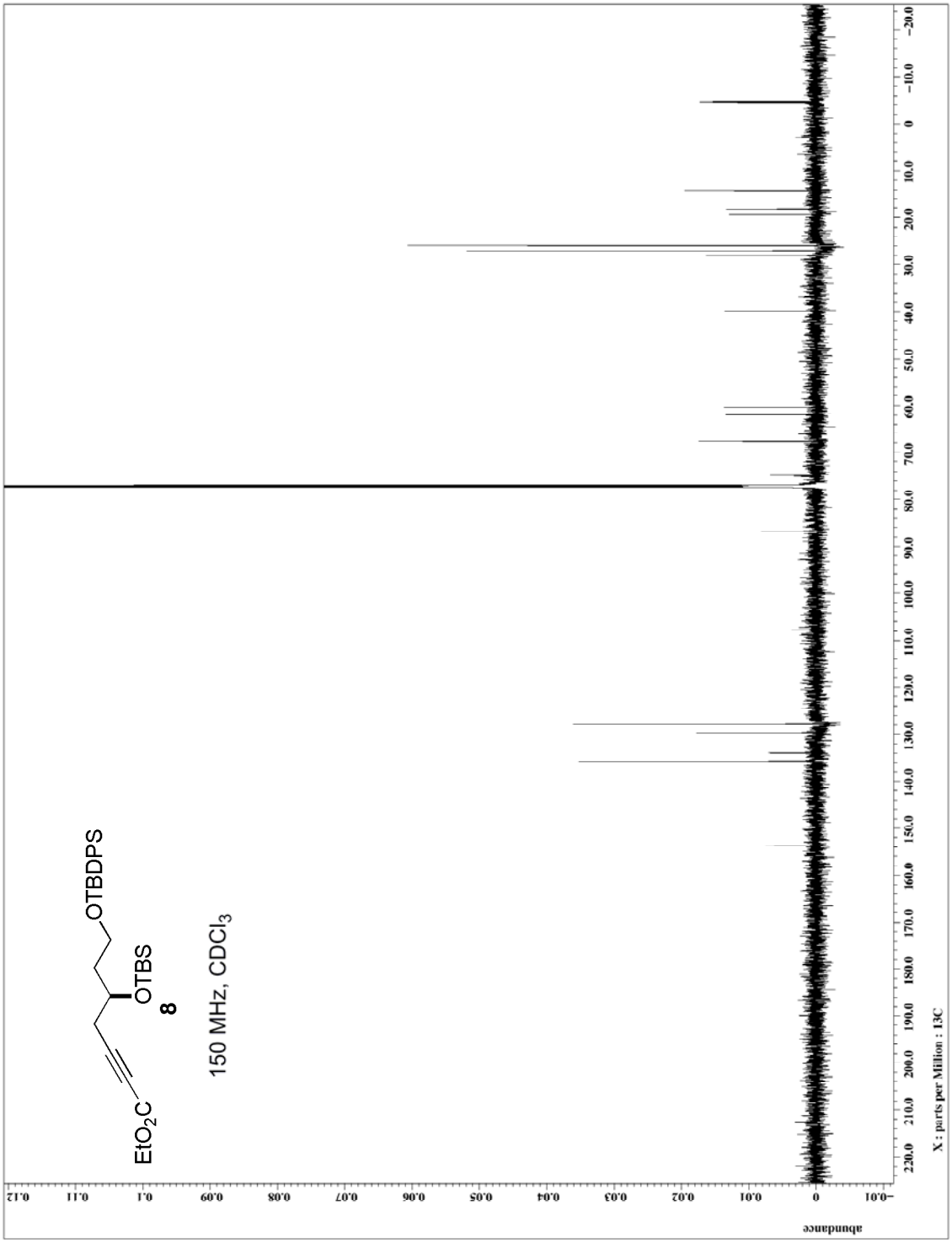
OTBS
8
EtO2C
600 MHz, CDCl3
abundance
X : parts per Million : 1H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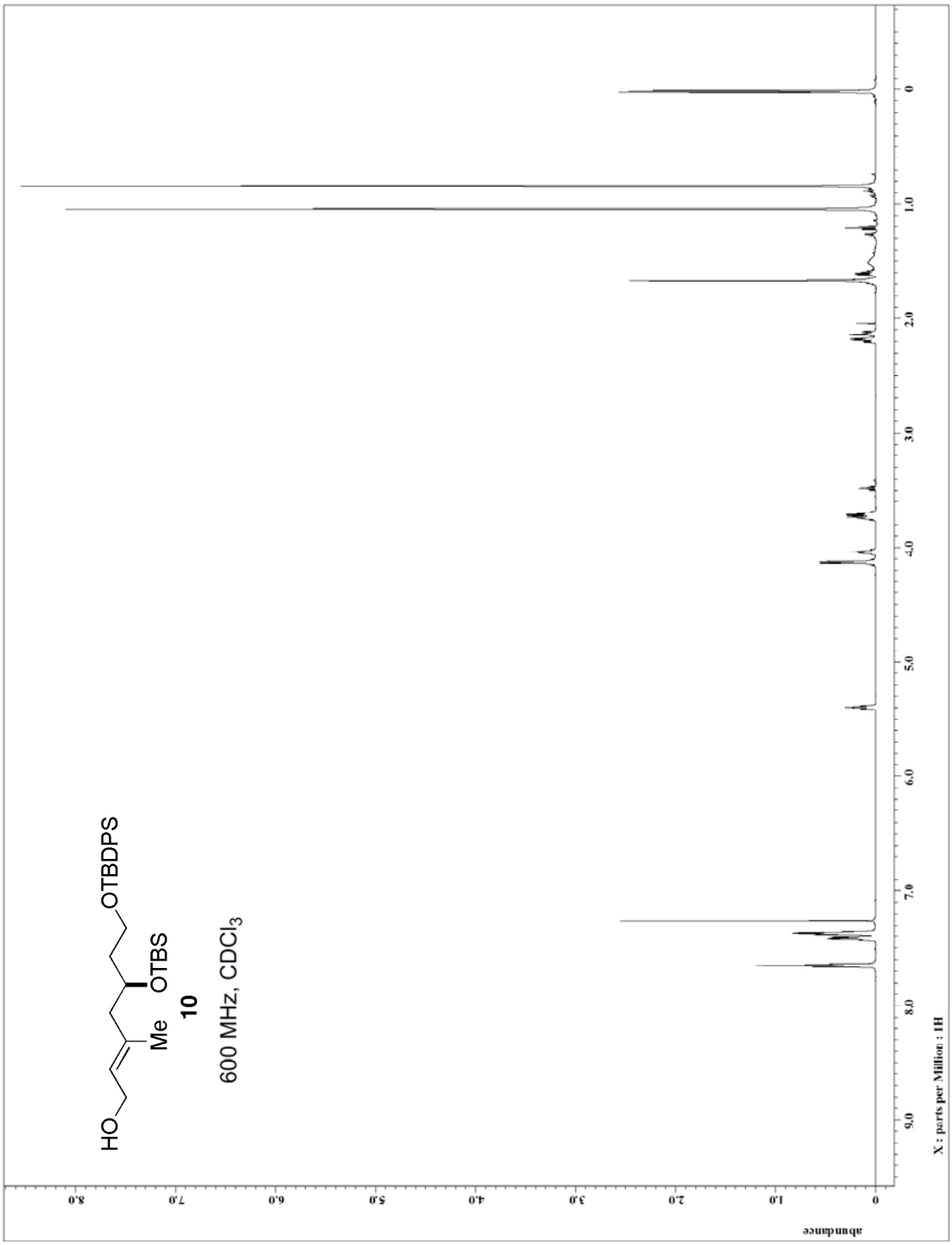
OTBS
EtO2C
8
150 MHz, CDCl3
abundance
X : parts per Million : 13C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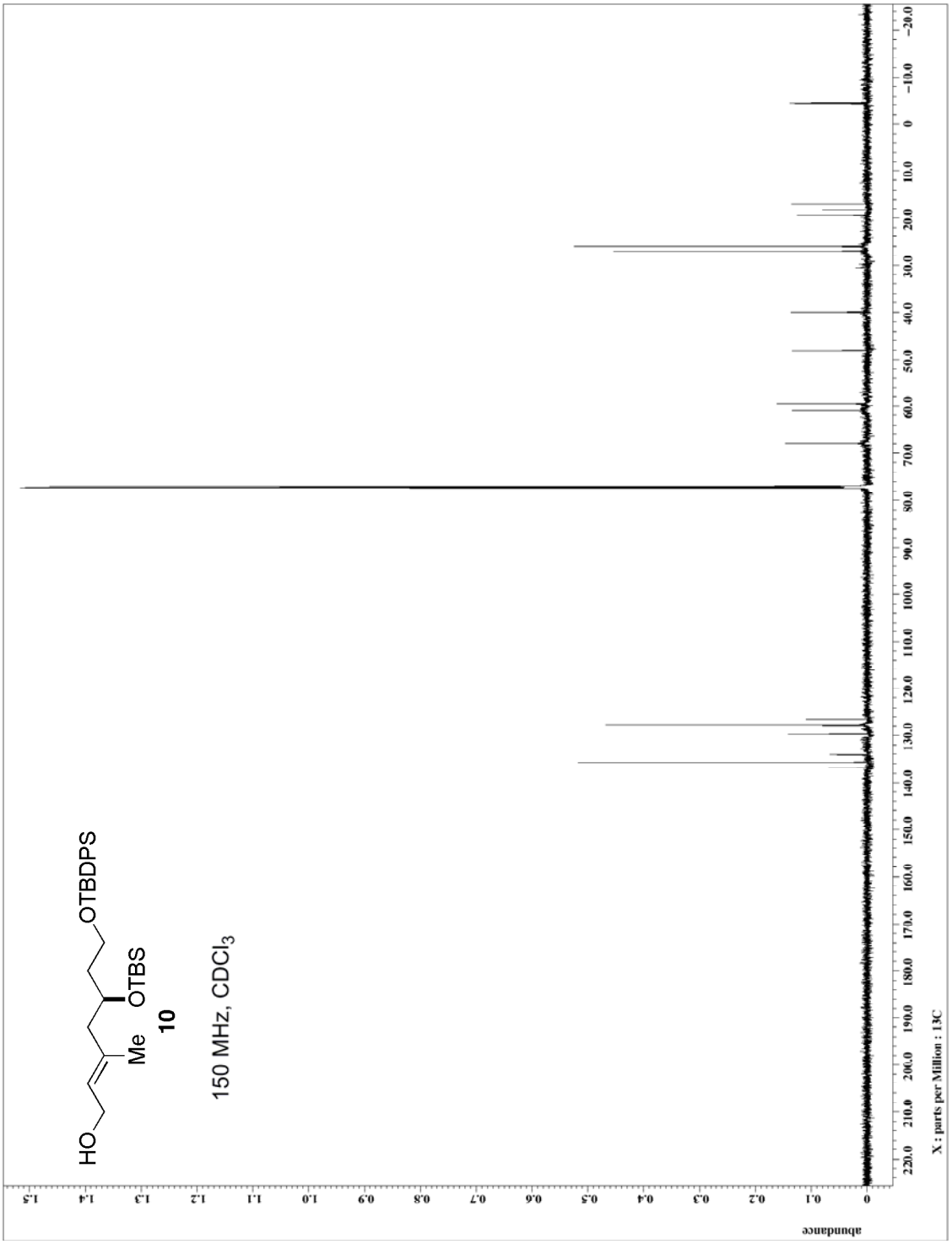
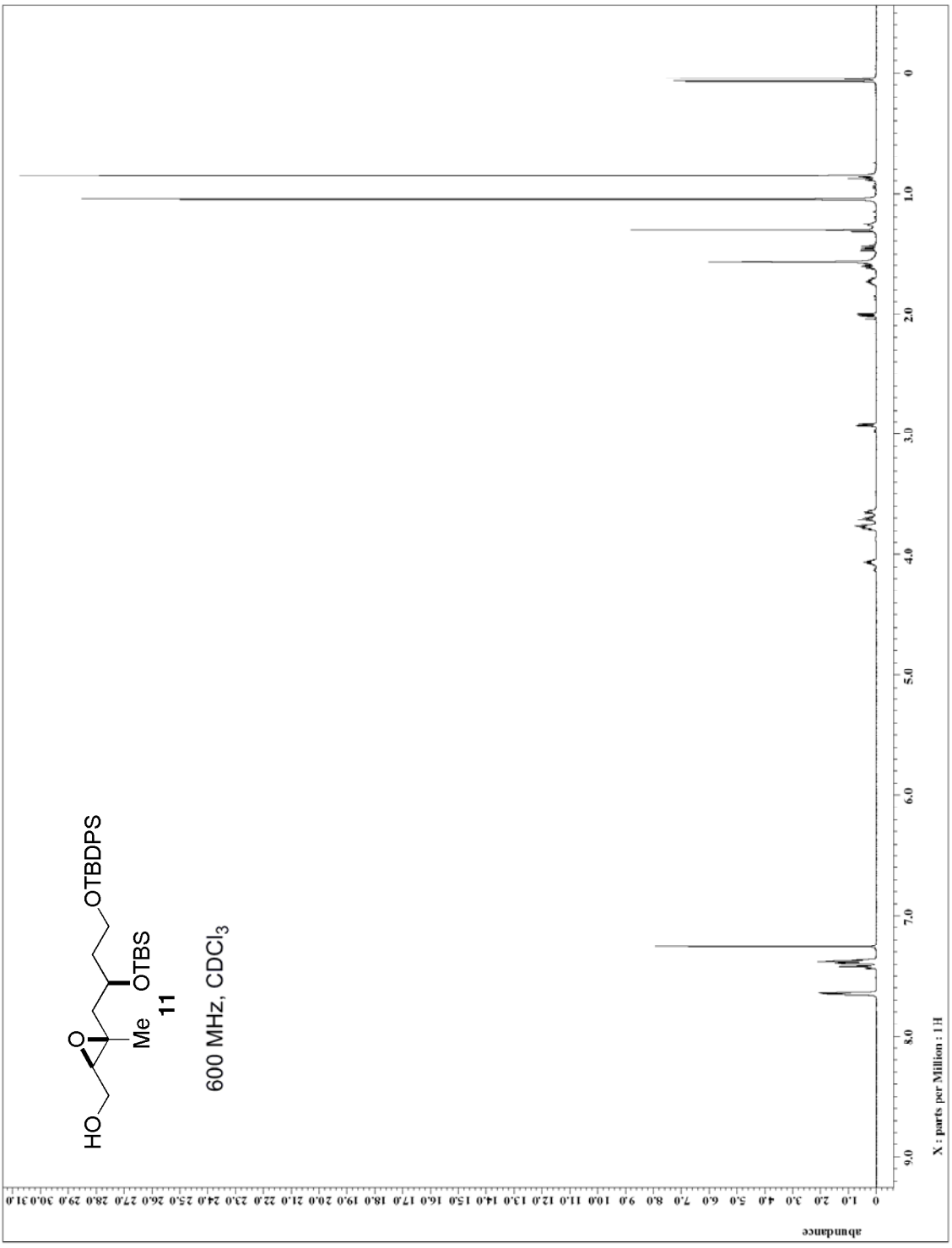
OTBS
Me
HO
10
600 MHz, CDCl3
abundance
X : parts per Million : 1H


HO
Me
OTBS
OTBDPS
10
150 MHz, CDCl3
abundance
X : parts per Million : 13C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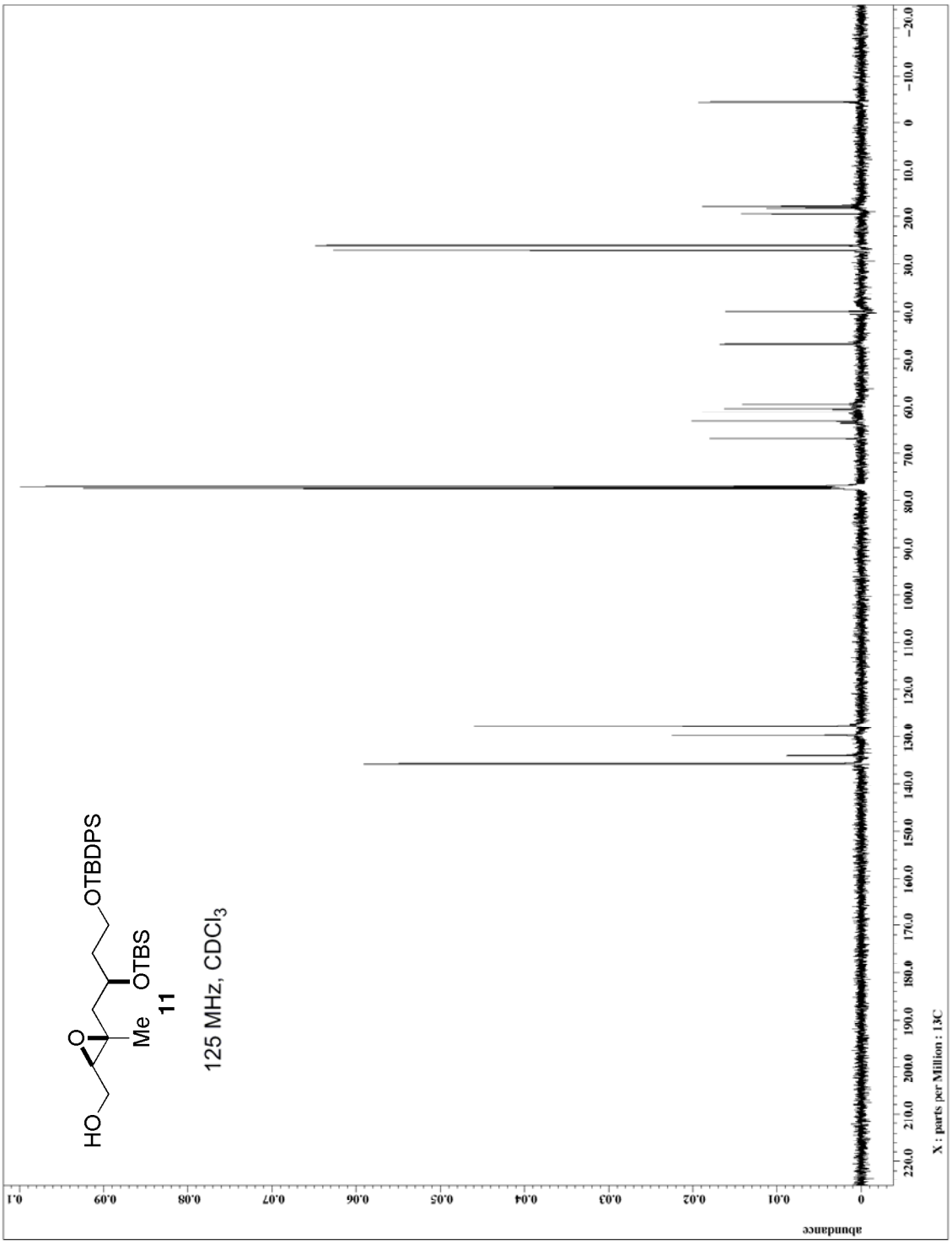
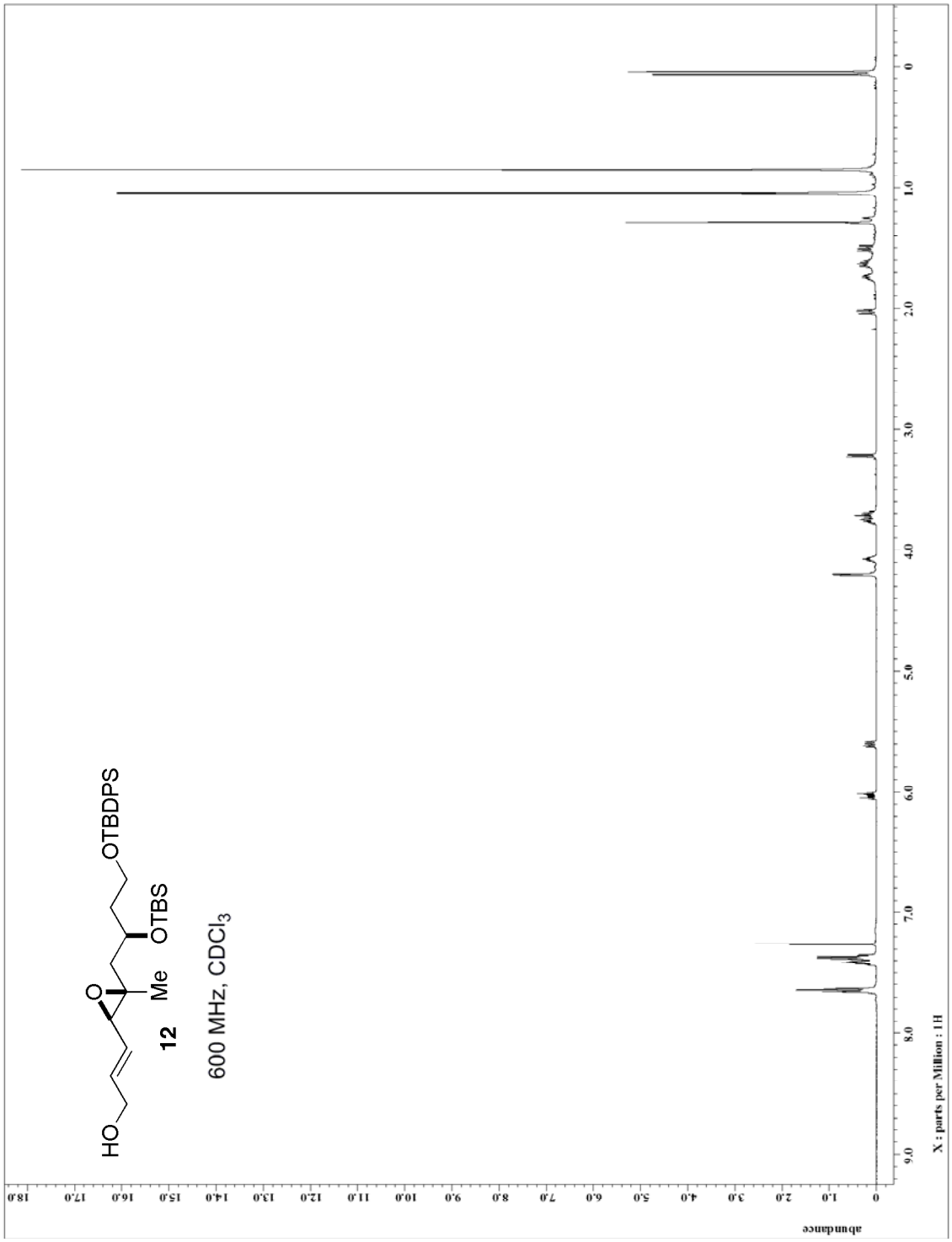
OTBS
Me
O
HO
11
600 MHz, CDCl3
abundance
X : parts per Million : 1 H


HO
O
Me
OTBS
OTBDPS
11
125 MHz, CDCl3
abundance
X : parts per Million : 13C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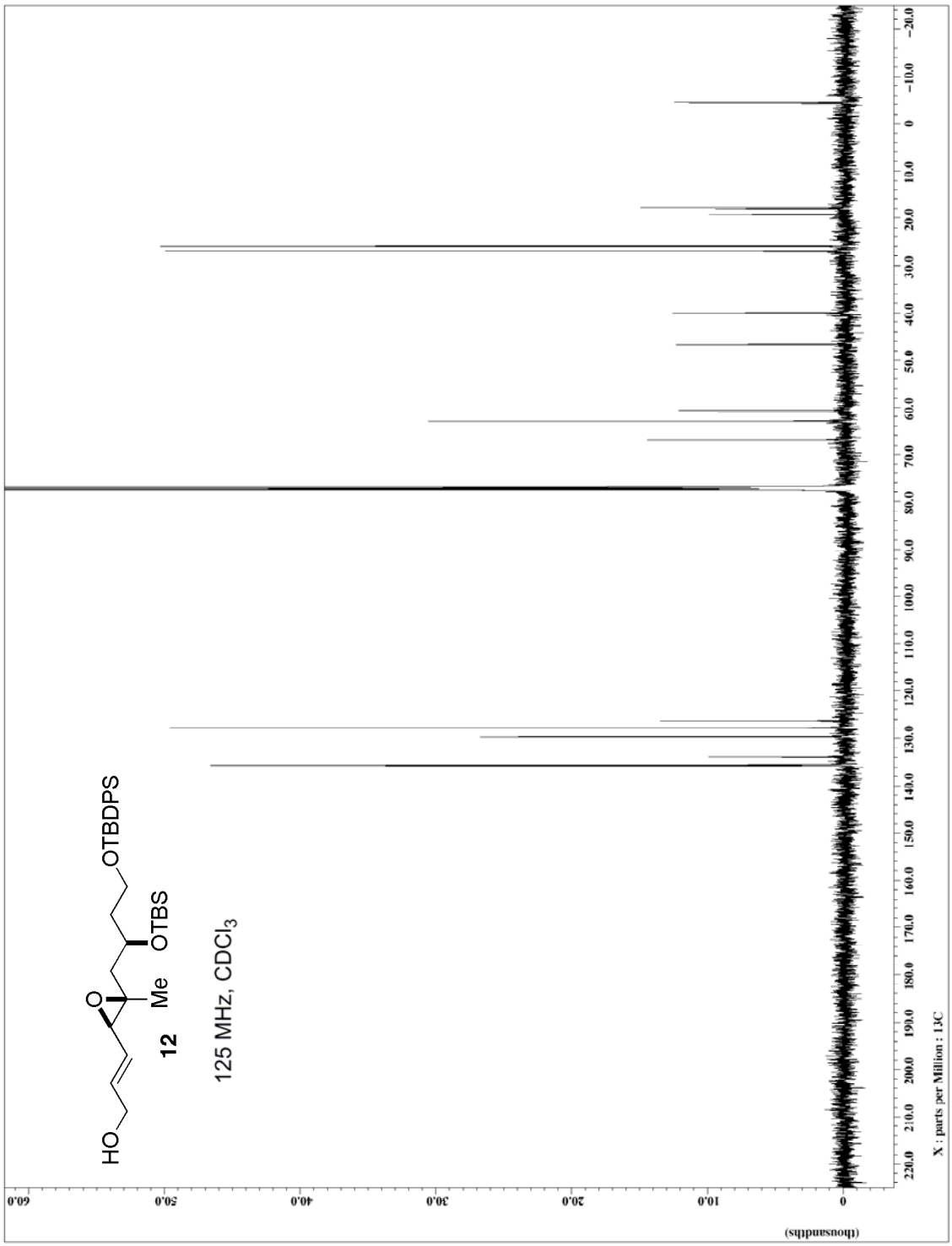
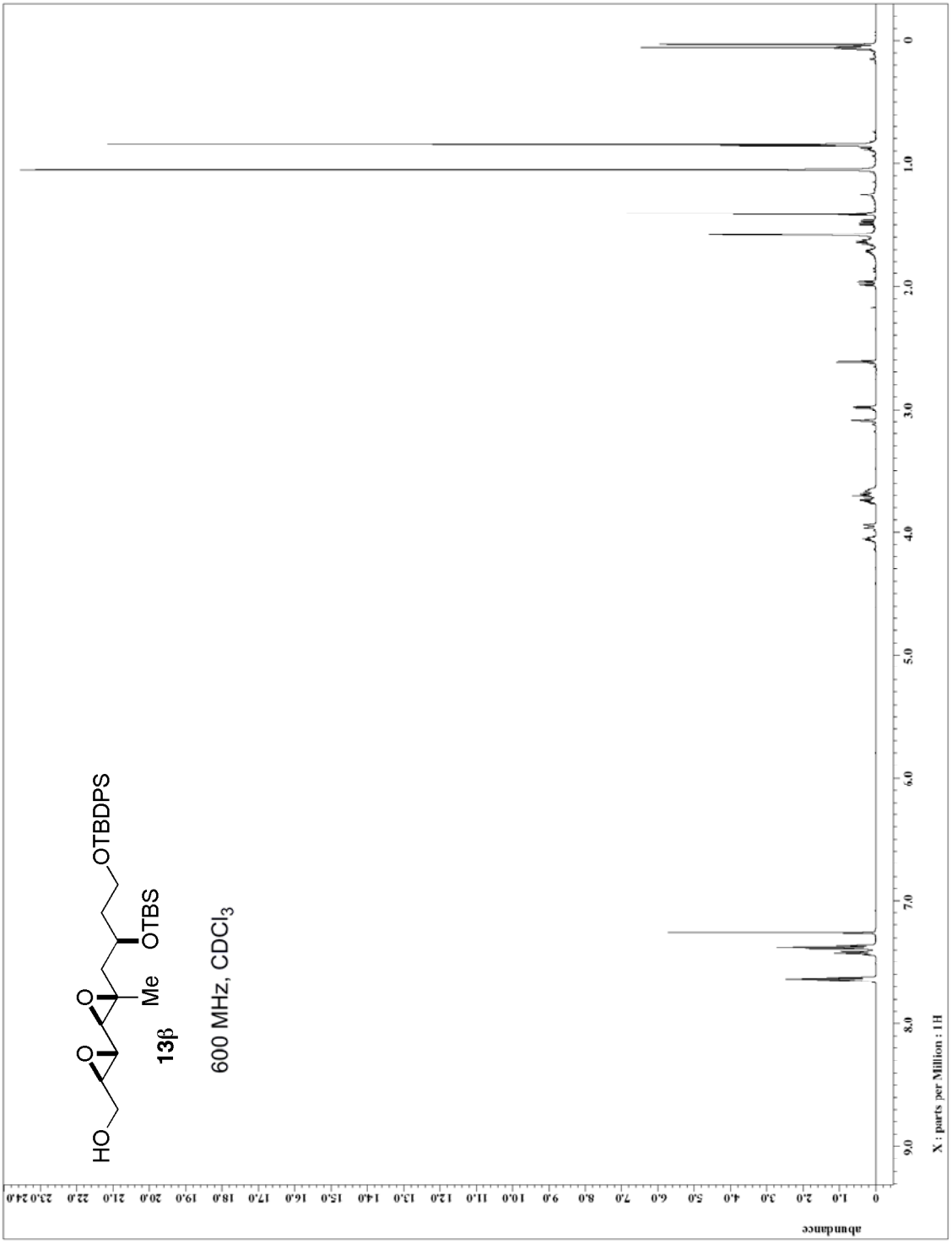
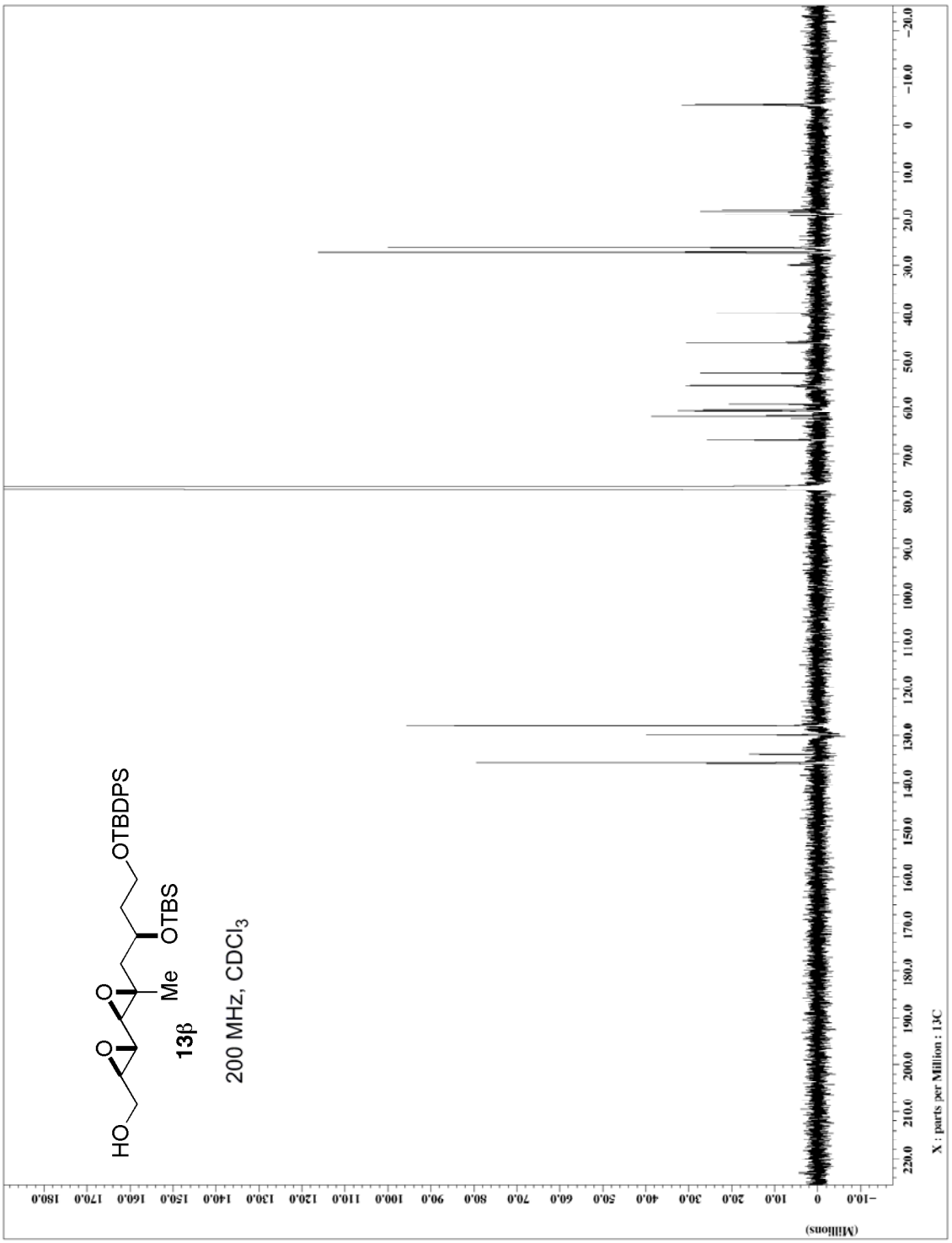
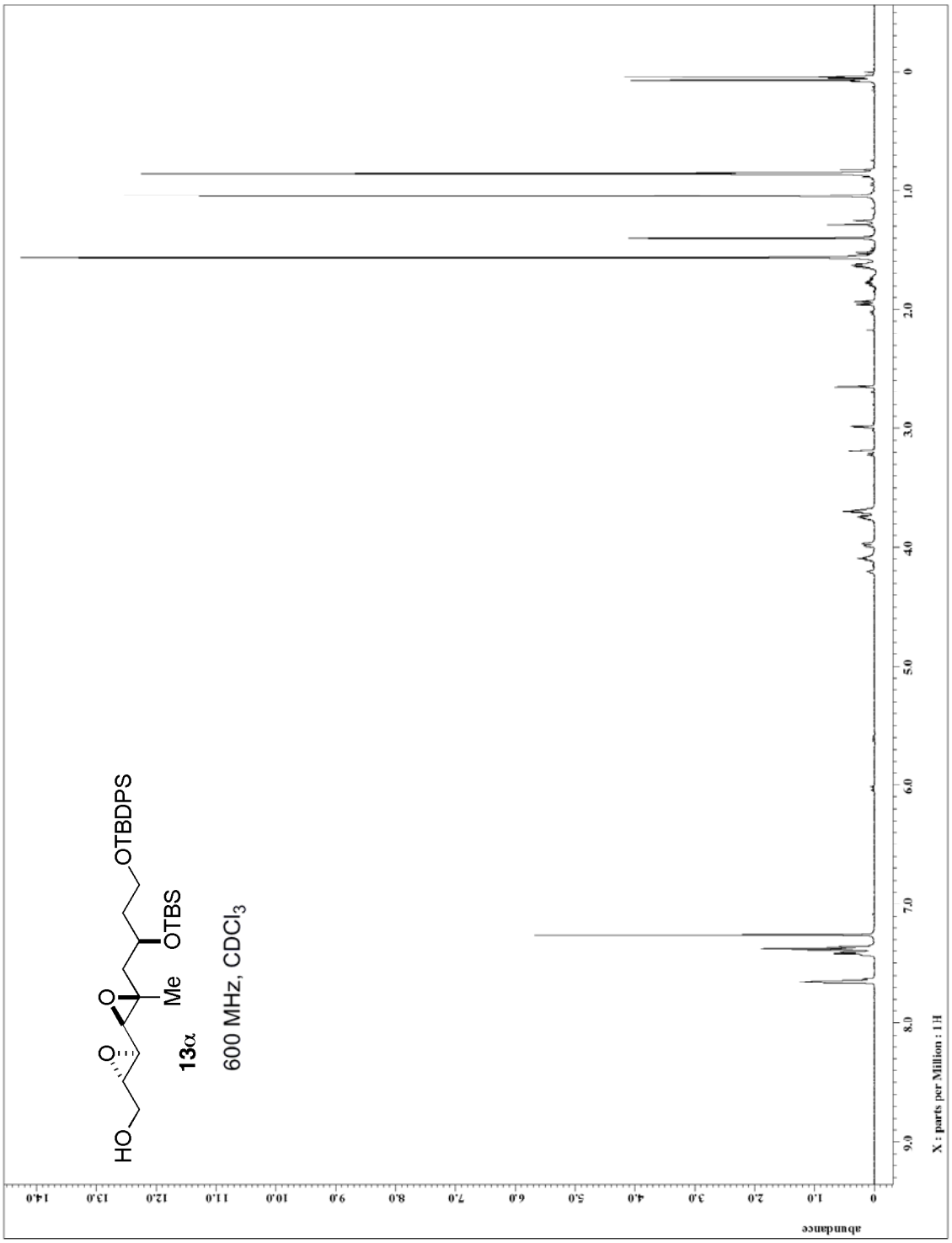
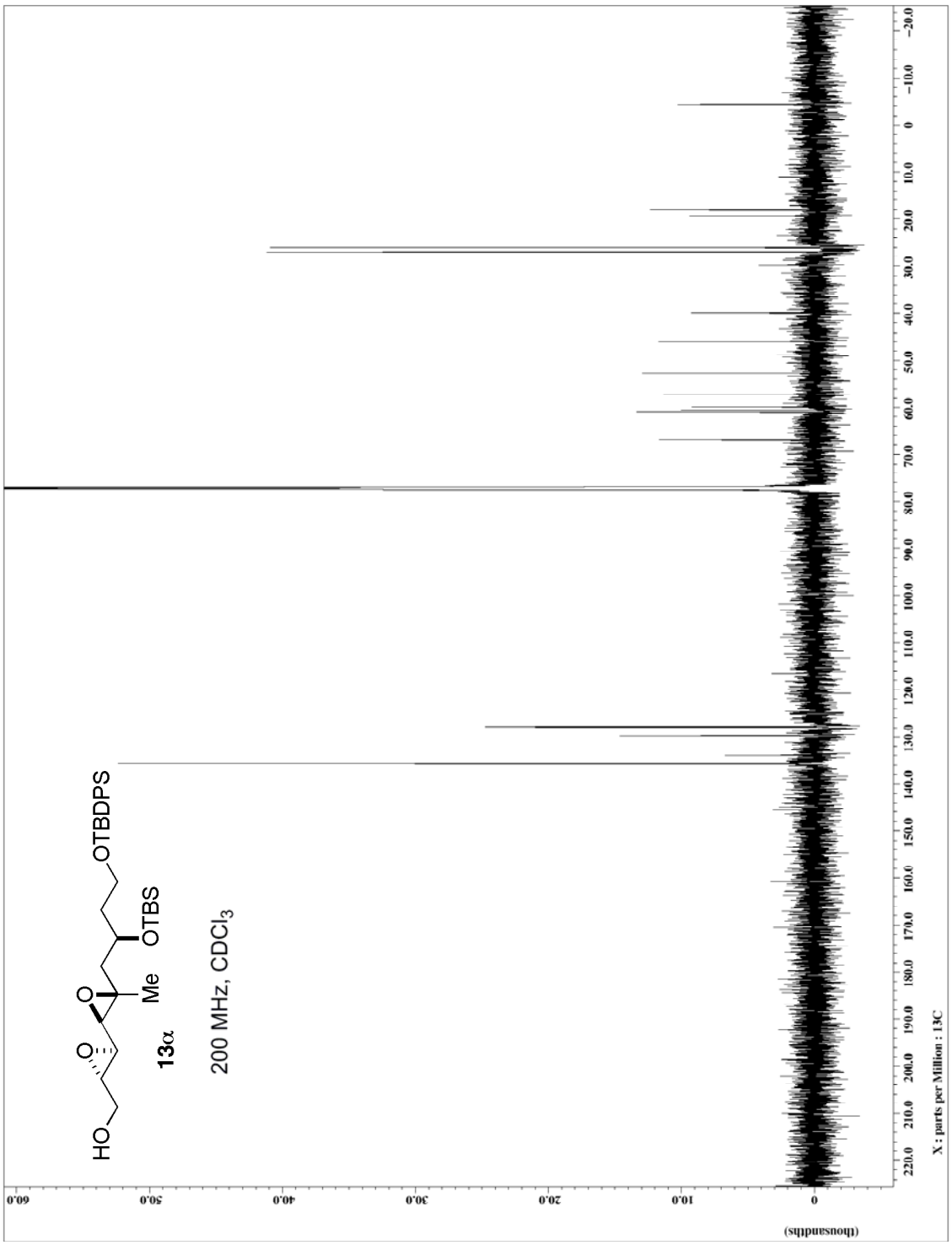
OTBS
Me
12
600 MHz, CDCl3
HO
abundance
X : parts per Million : 1H

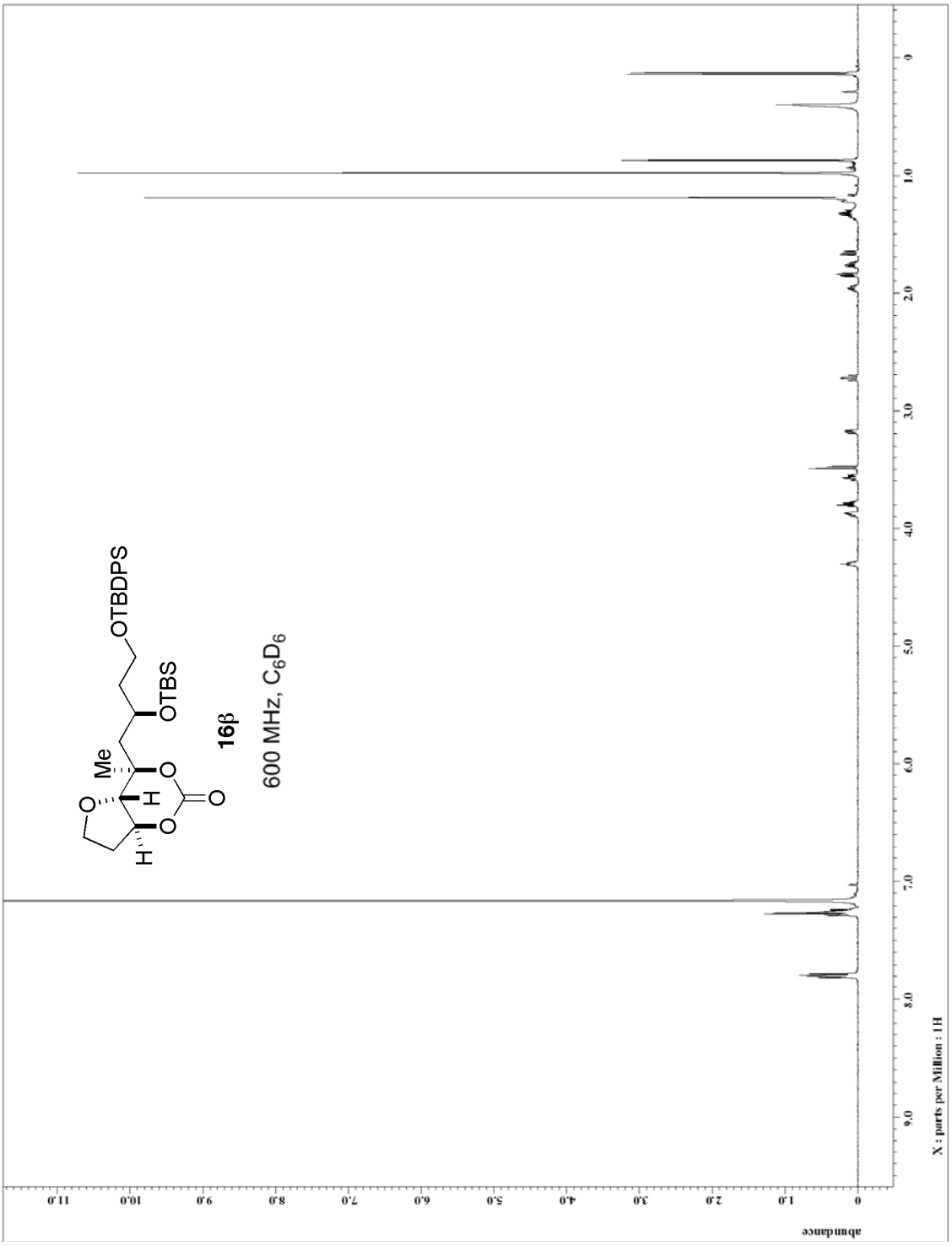

HO
O
Me
OTBS
OTBDPS
12
125 MHz, CDCl3
(thousandths)
X : parts per Million : 13C

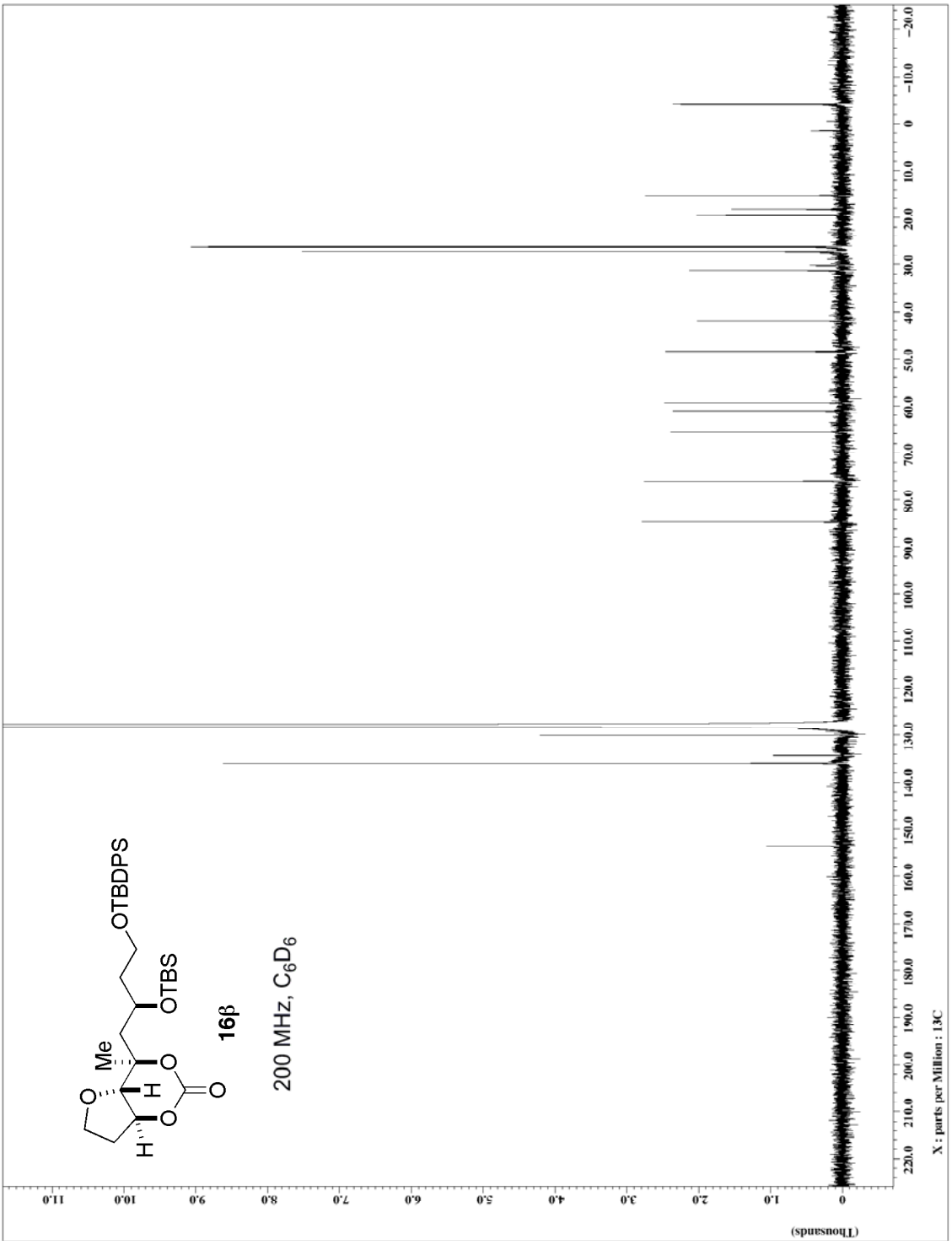

HO
O
O
Me
OTBS
OTBDPS
13β
600 MHz, CDCl3
abundance
X : parts per Million : 1H

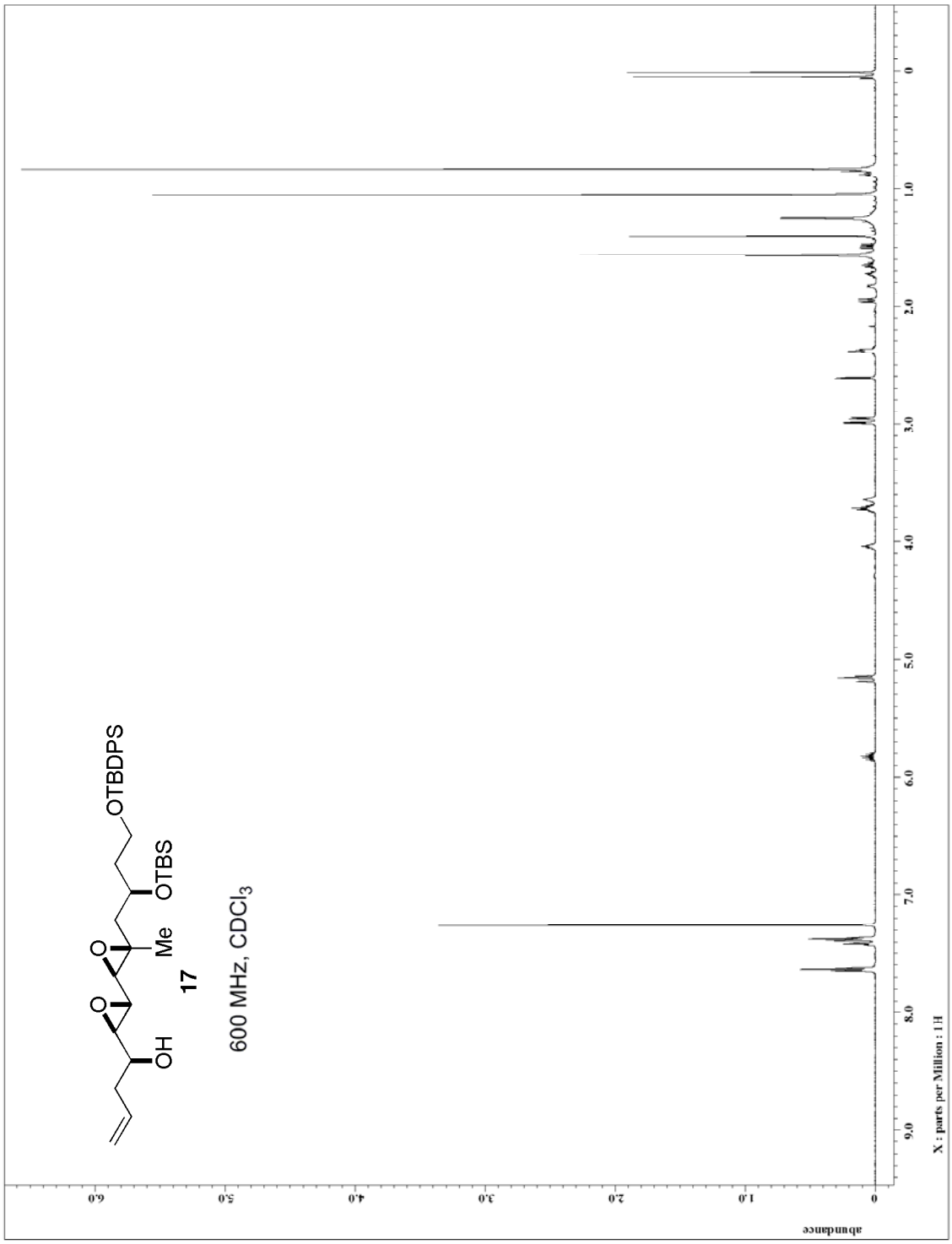

HO
O
O
Me
OTBS
OTBDPS
13β
200 MHz, CDCl3
X : parts per Million : 13C
(Millions)

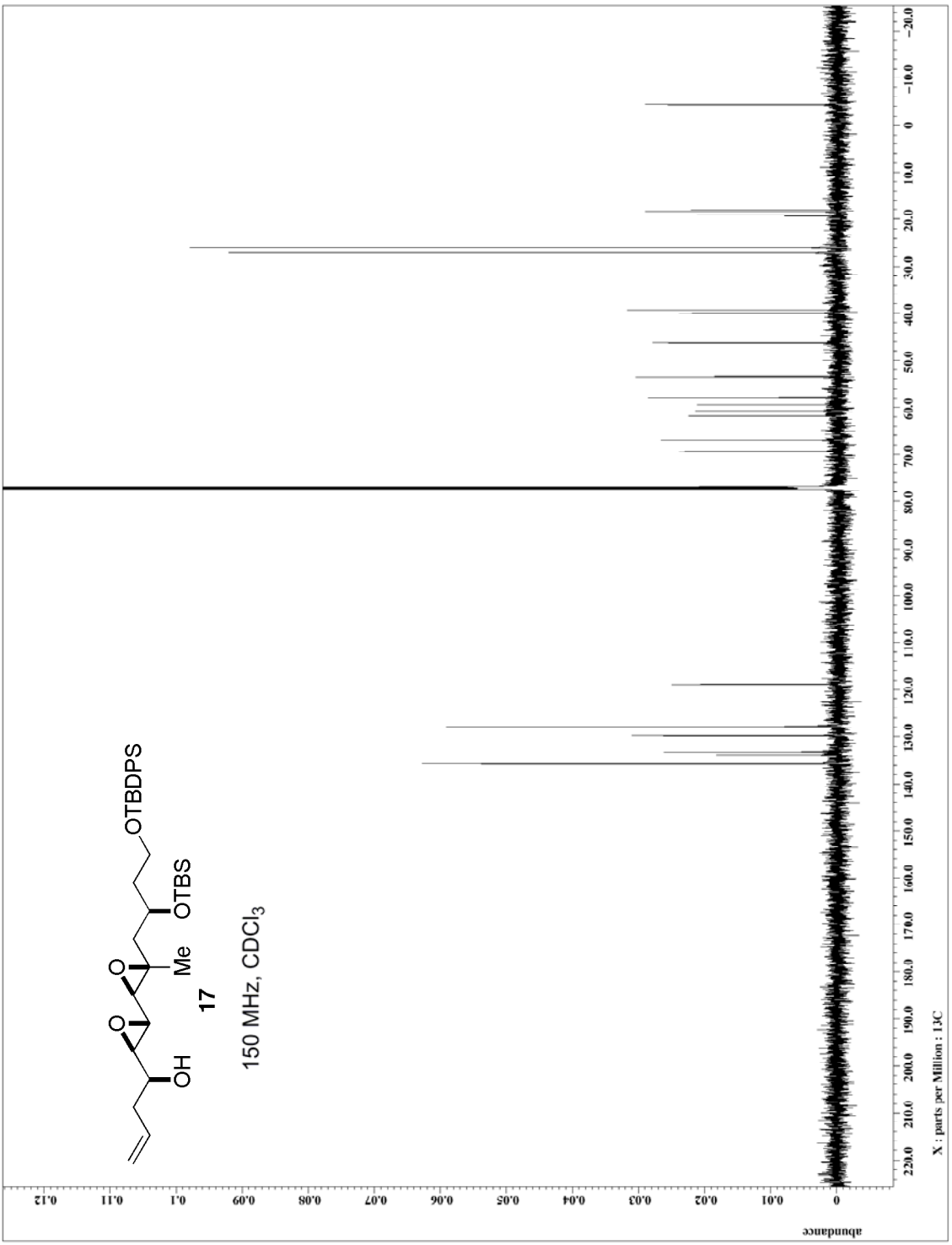

OTBDPS
OTBS
Me
HO
13α
600 MHz, CDCl3
abundance
X : parts per Million : 1H

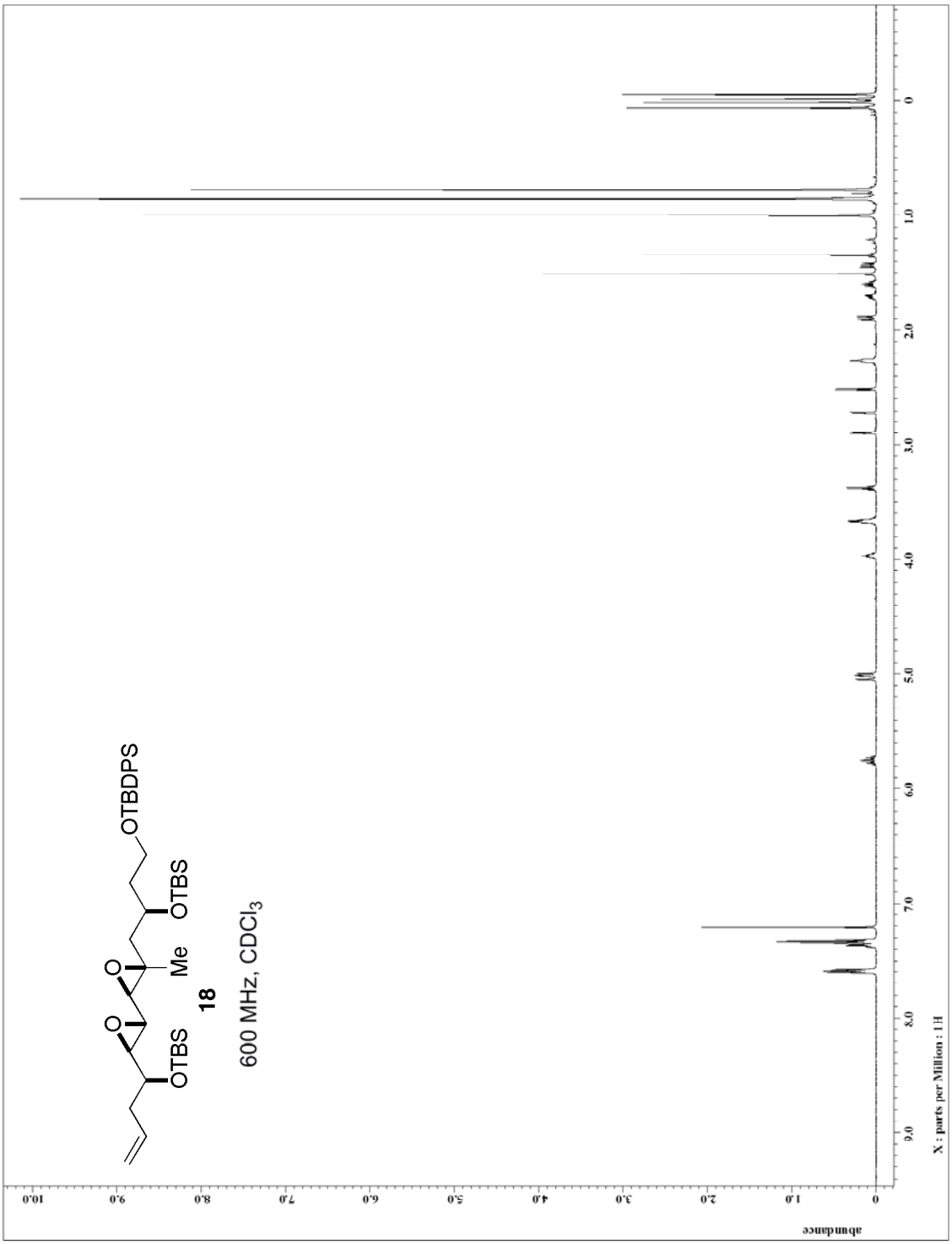

HO
O
O
Me
OTBS
OTBDPS
13α
200 MHz, CDCl3
(thousandths)
X : parts per Million : 13C

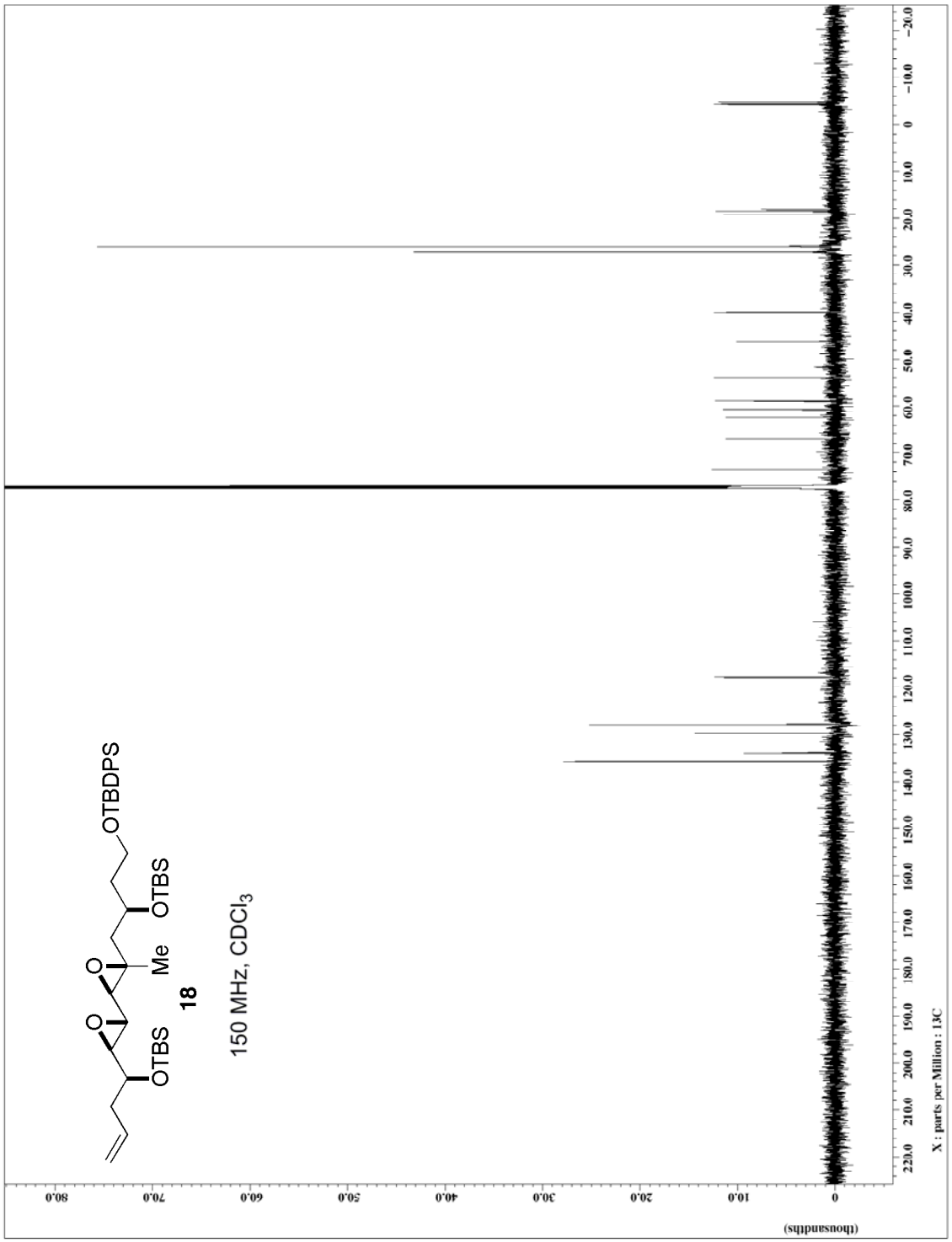

OTBDPS
OTBS
Me
16β
600 MHz, C6D6
abundance
X : parts per Million : 1H

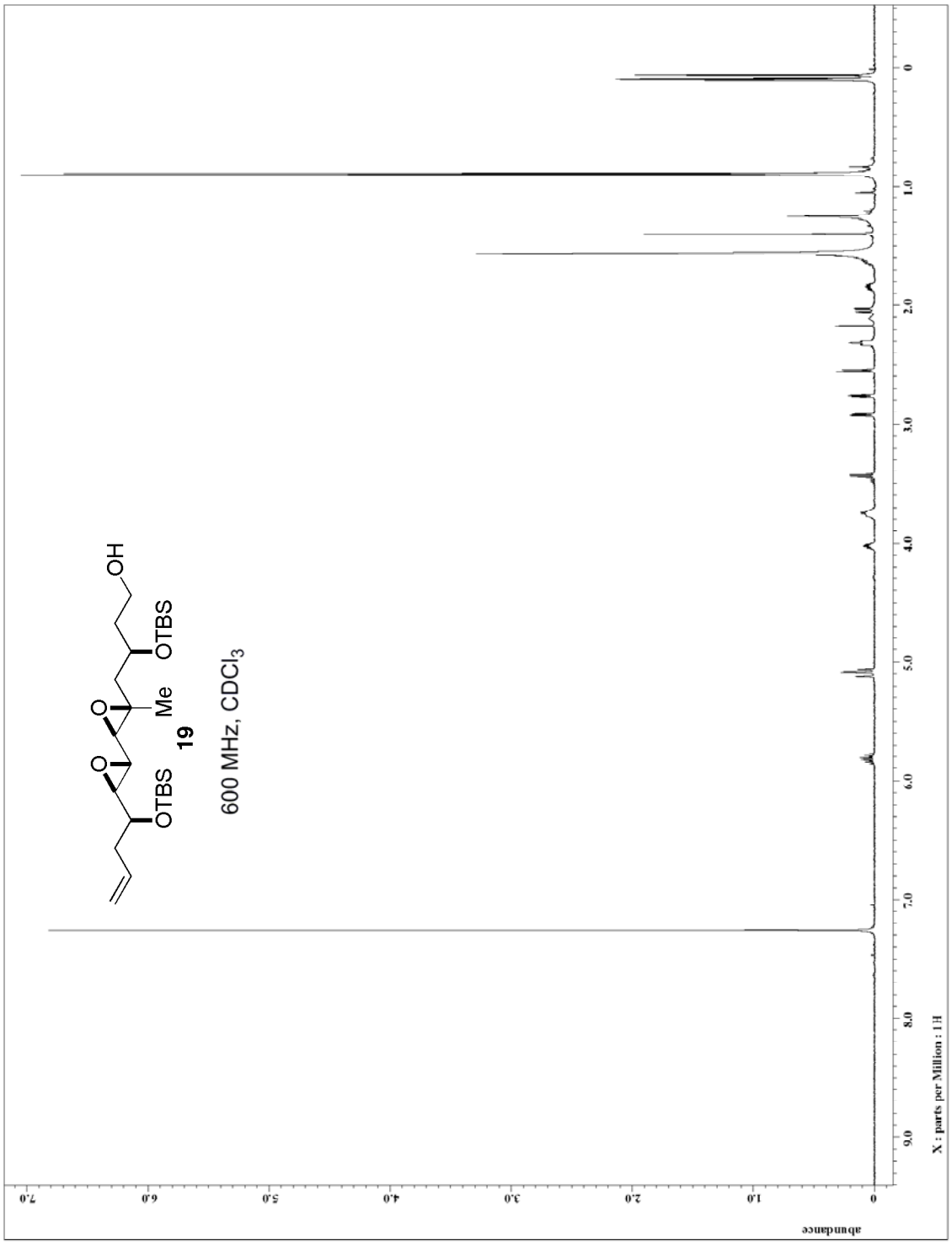

OTBDPS
OTBS
Me
H
H
O
O
O
O
O
16β
200 MHz, C6D6
(Thousands)
X : parts per Million : 13C

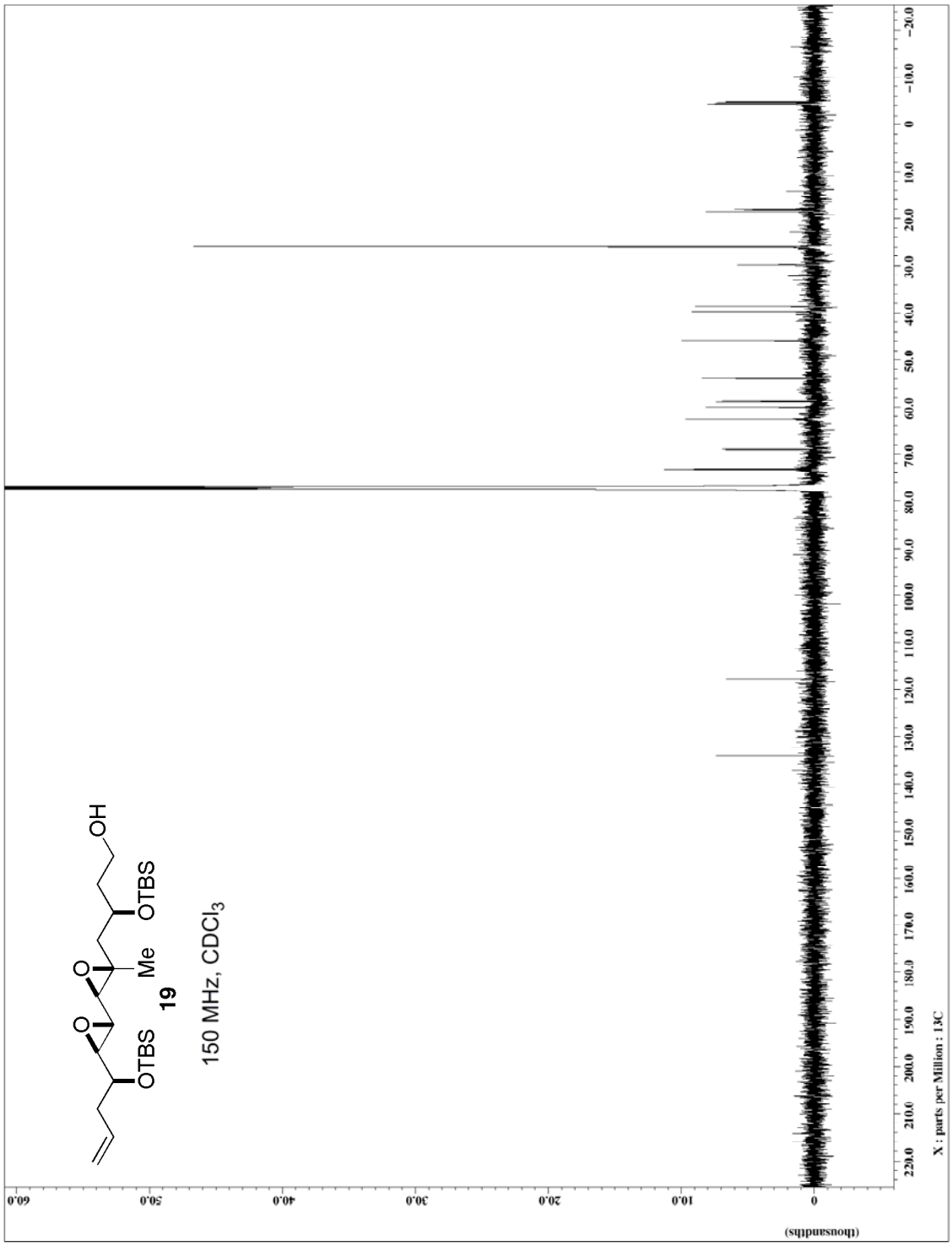

OTBDPS
OTBS
Me
OH
17
600 MHz, CDCl3
abundance
X : parts per Million : 1H

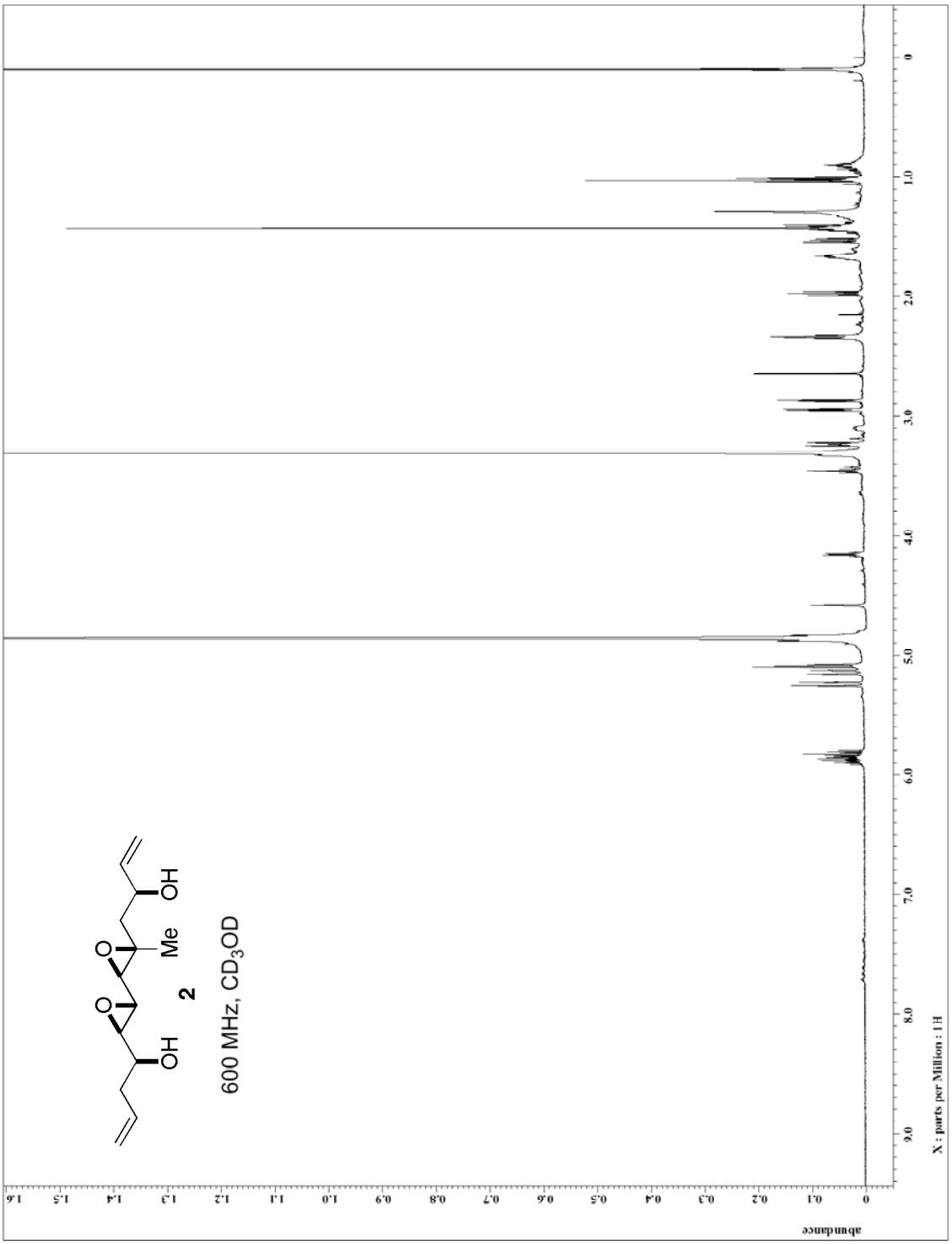

OTBDPS
OTBS
Me
OH
17
150 MHz, CDCl3
abundance
X : parts per Million : 13C

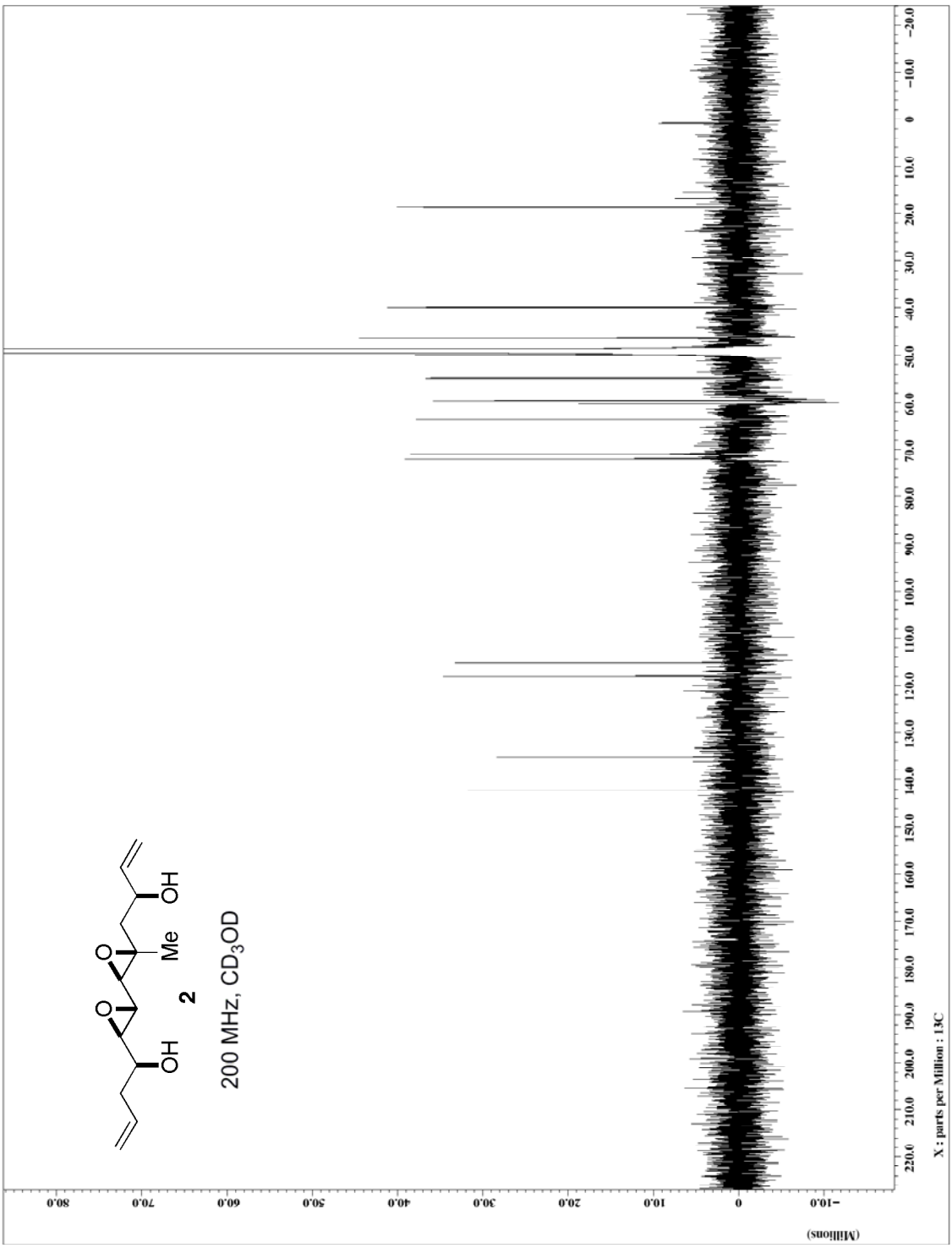

OTBDPS
OTBS
Me
OTBS
18
600 MHz, CDCl3
abundance
X : parts per Million : 1H

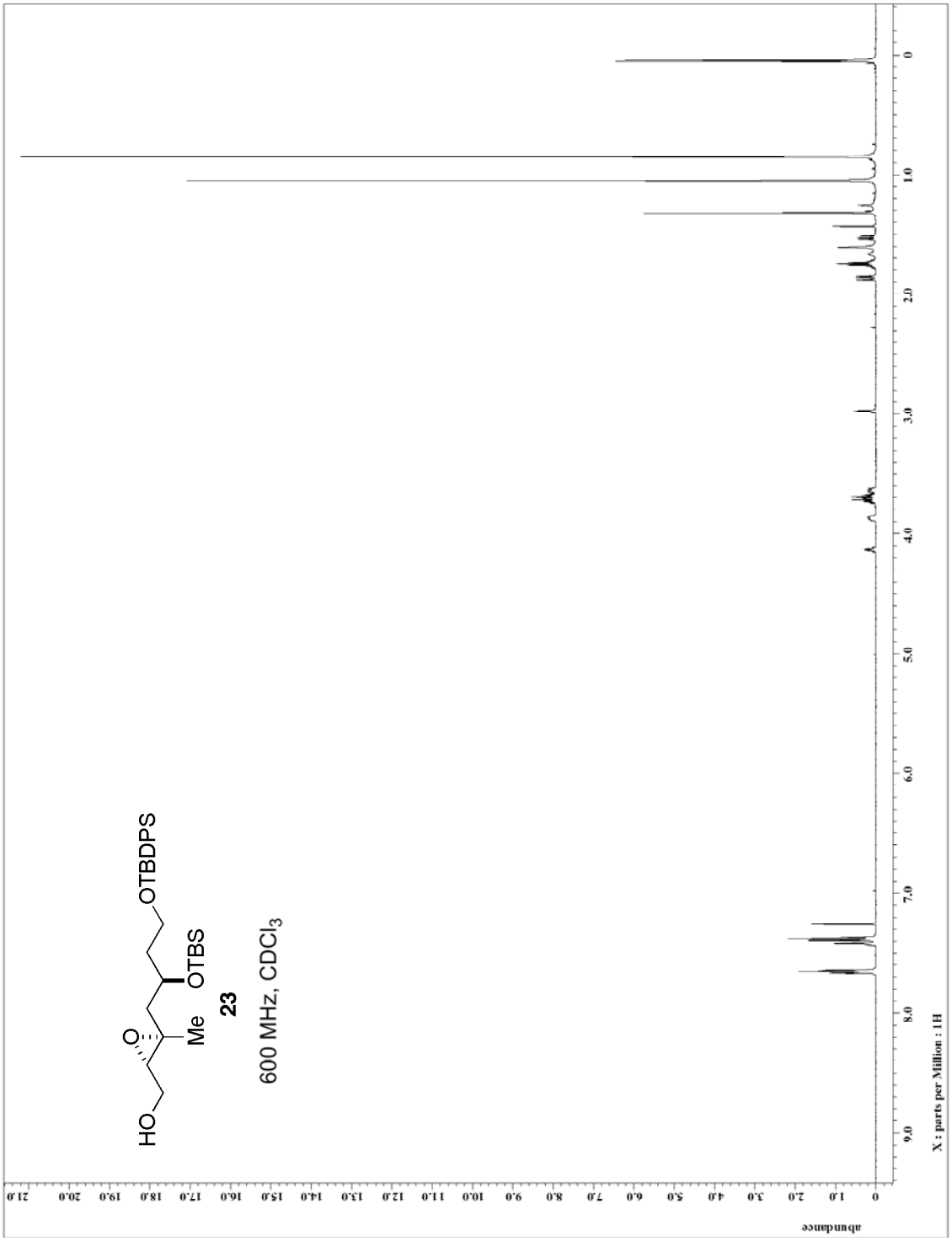

OTBDPS
OTBS
Me
OTBS
18
150 MHz, CDCl3
(thousandths)
X : parts per Million : 13C

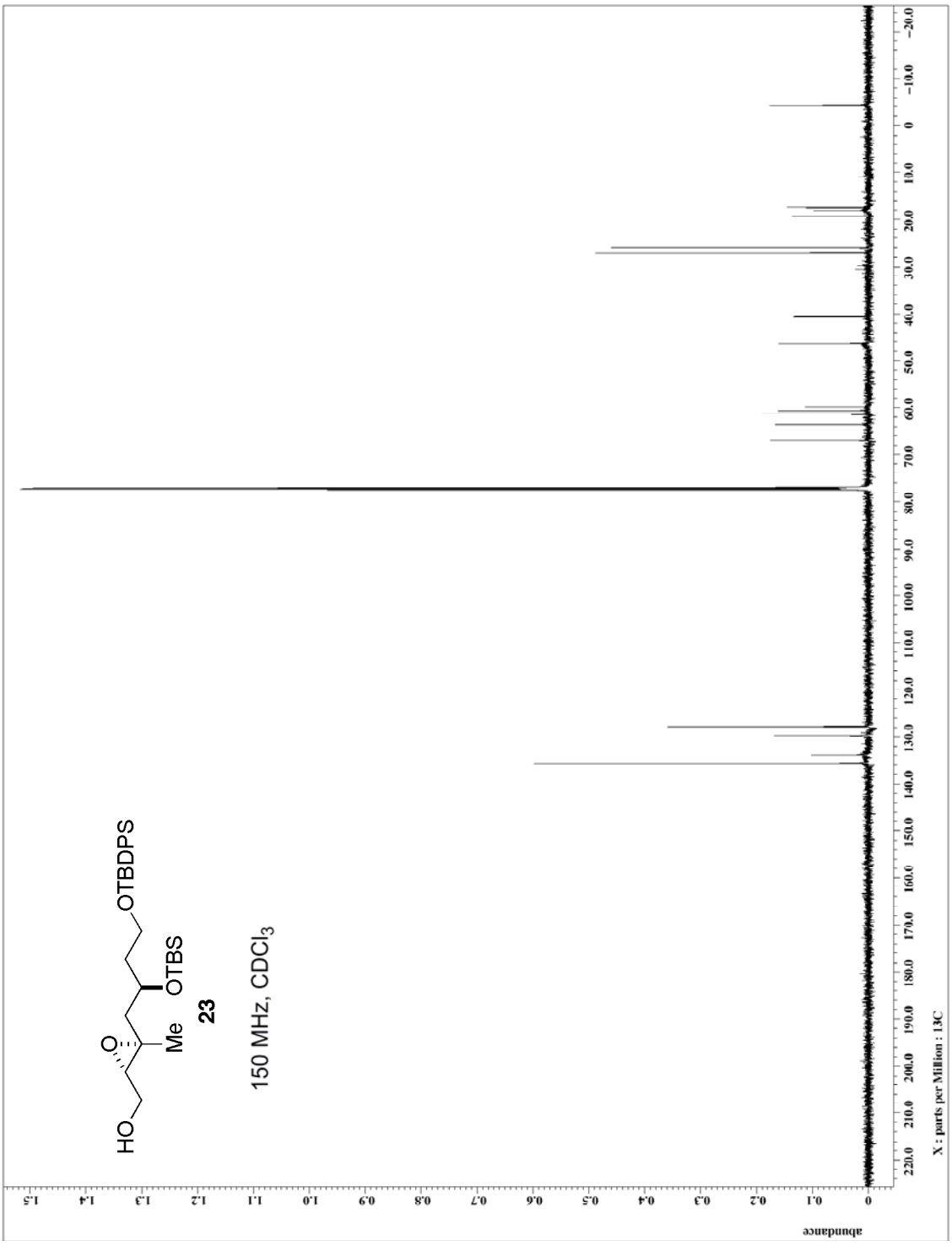

OH
OTBS
Me
OTBS
19
600 MHz, CDCl3
abundance
X : parts per Million : 1 H

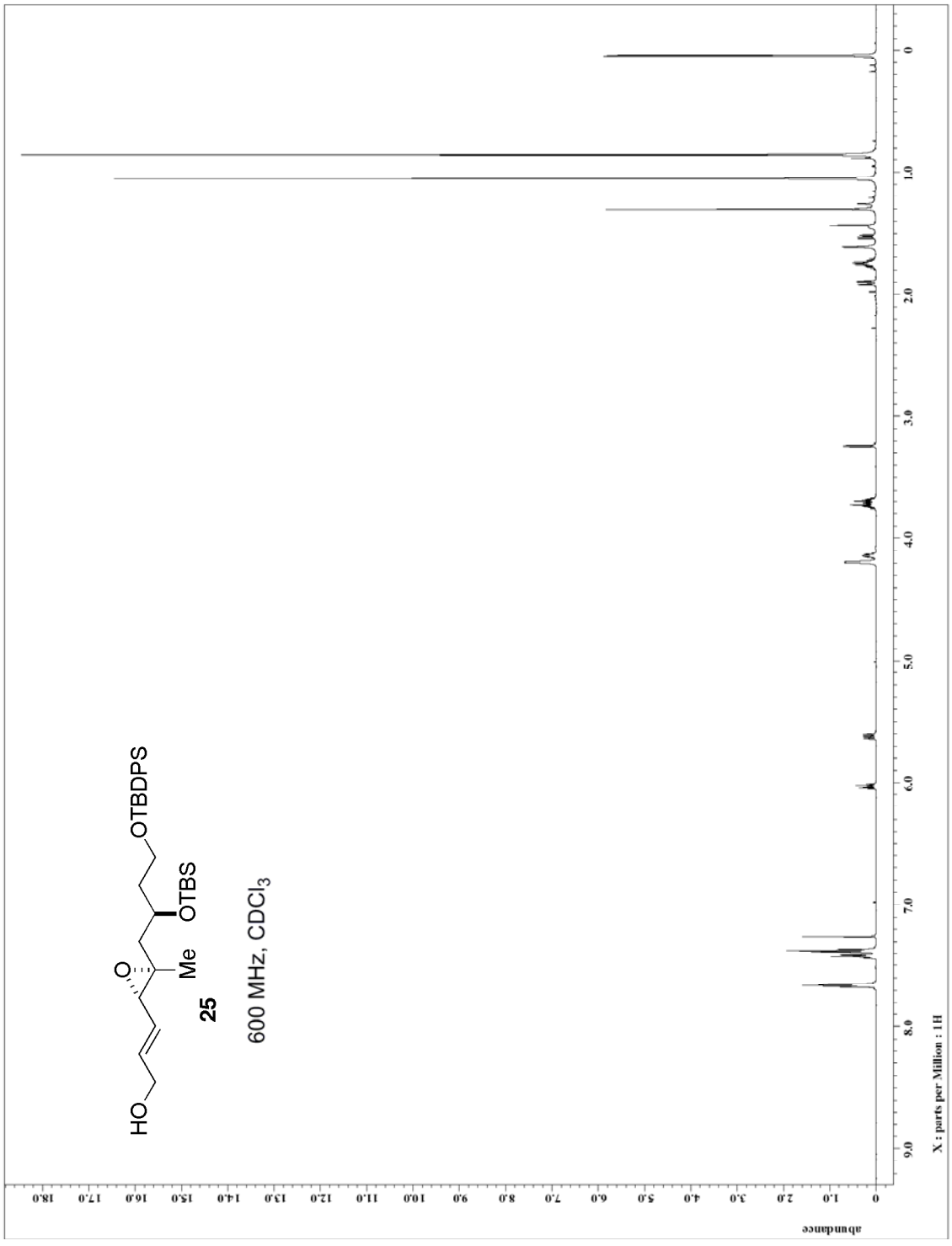

OH
OTBS
Me
OTBS
19
150 MHz, $CDCl_3$
(thousandths)
X : parts per Million : 13C

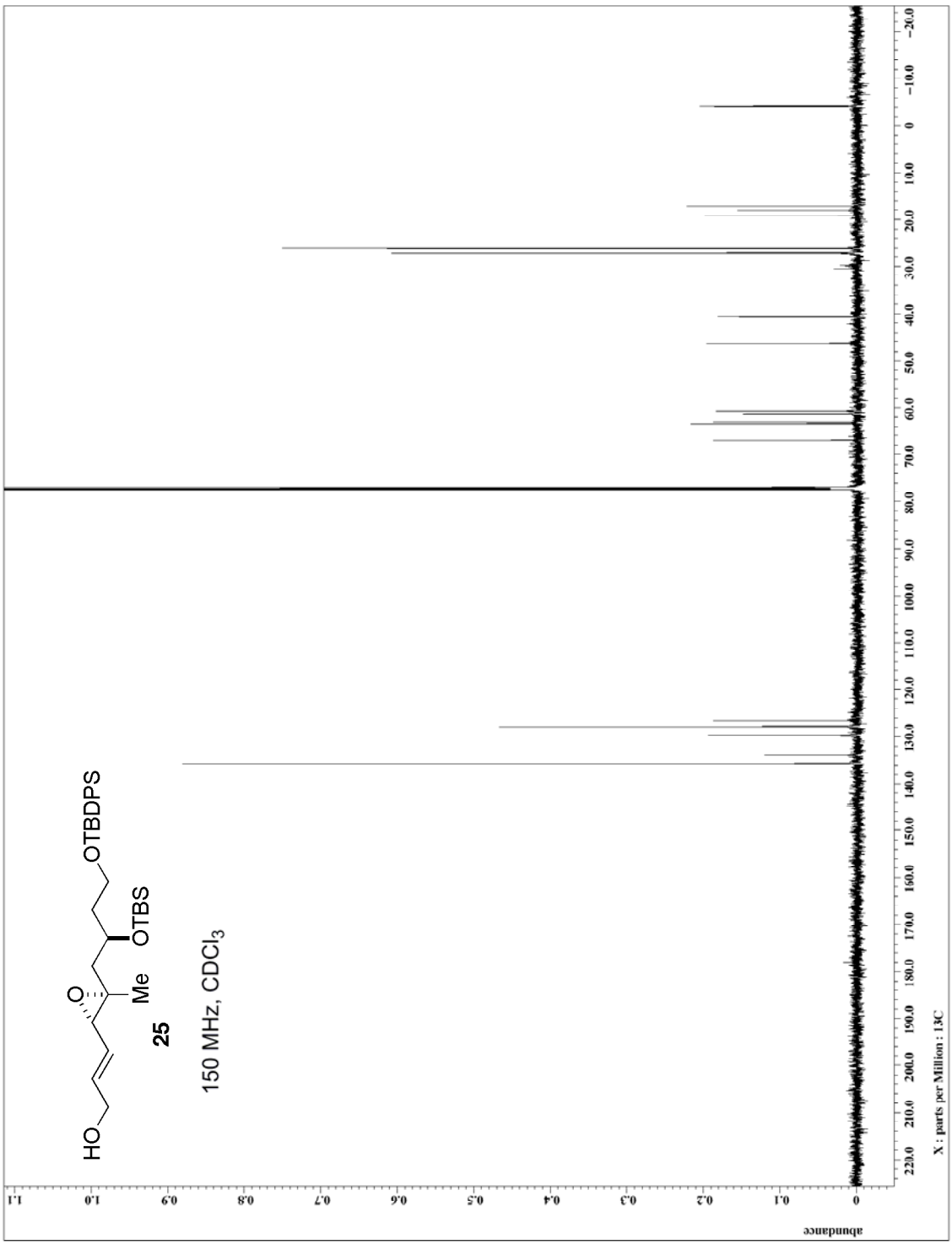

OH
O
O
Me
OH
2
600 MHz, CD3OD
X : parts per Million : 1H
abundance

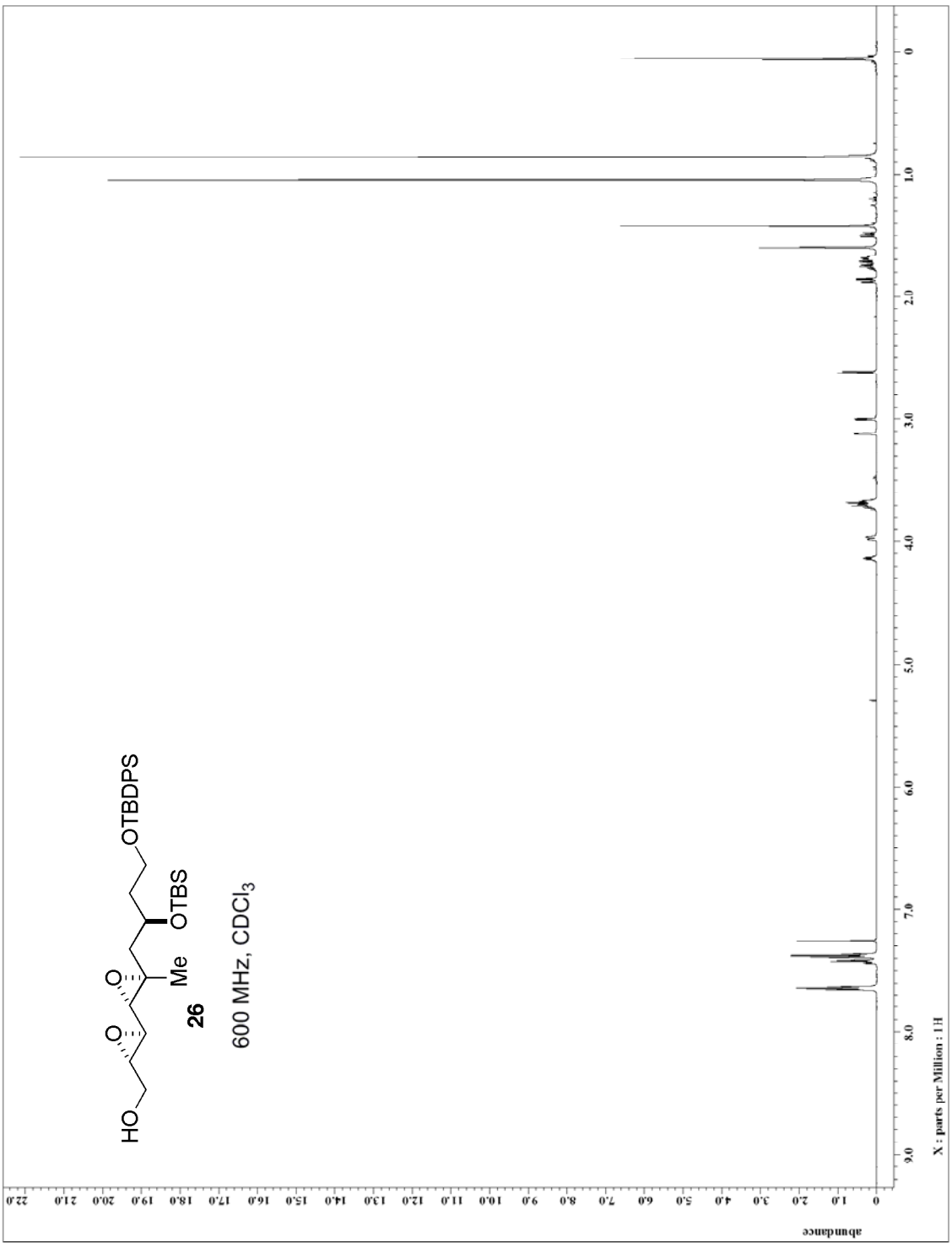

OH
O
O
Me
OH
2
200 MHz, CD3OD
X : parts per Million : 13C

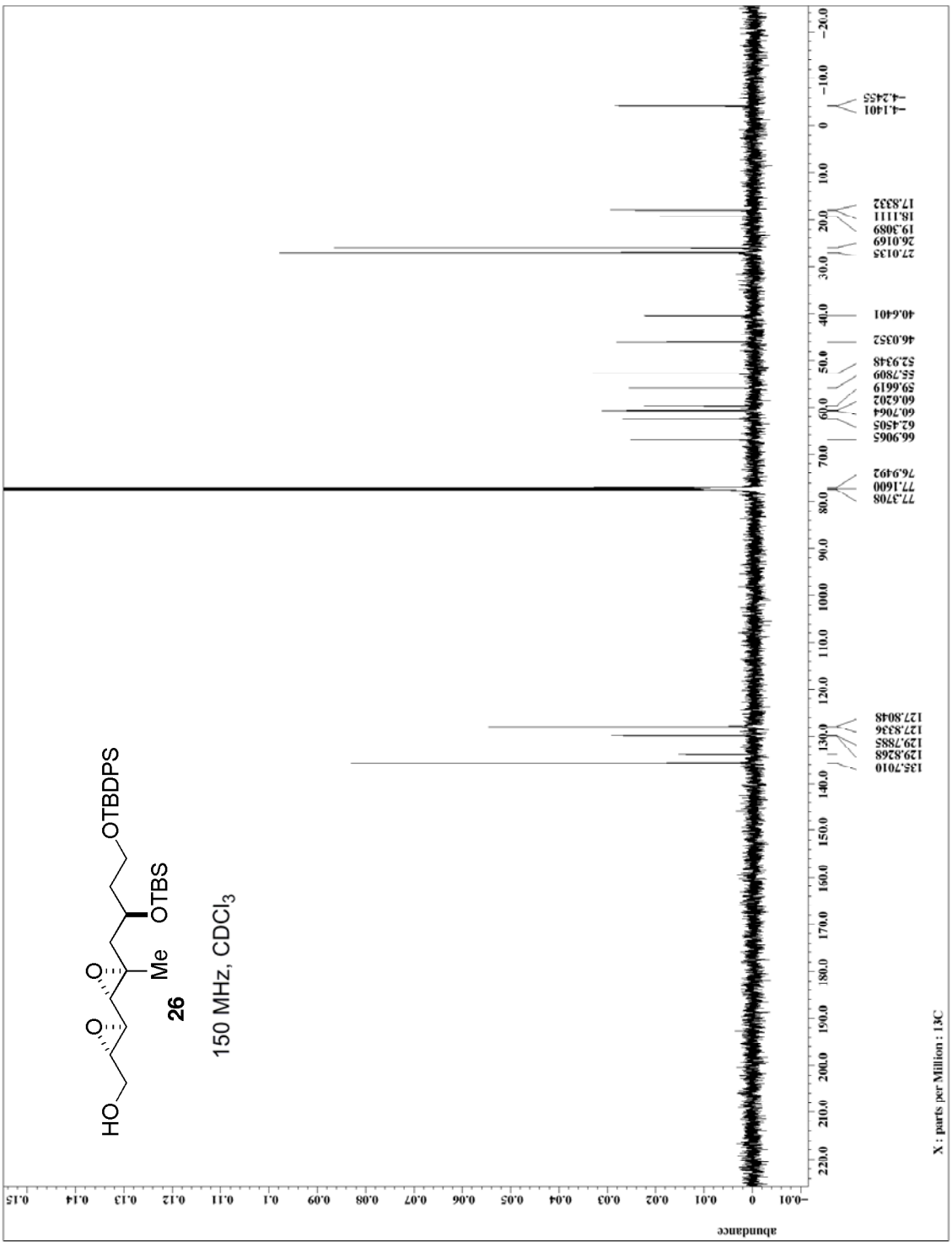

OTBDPS
OTBS
Me
O
HO
23
600 MHz, CDCl3
abundance
X : parts per Million : 1H

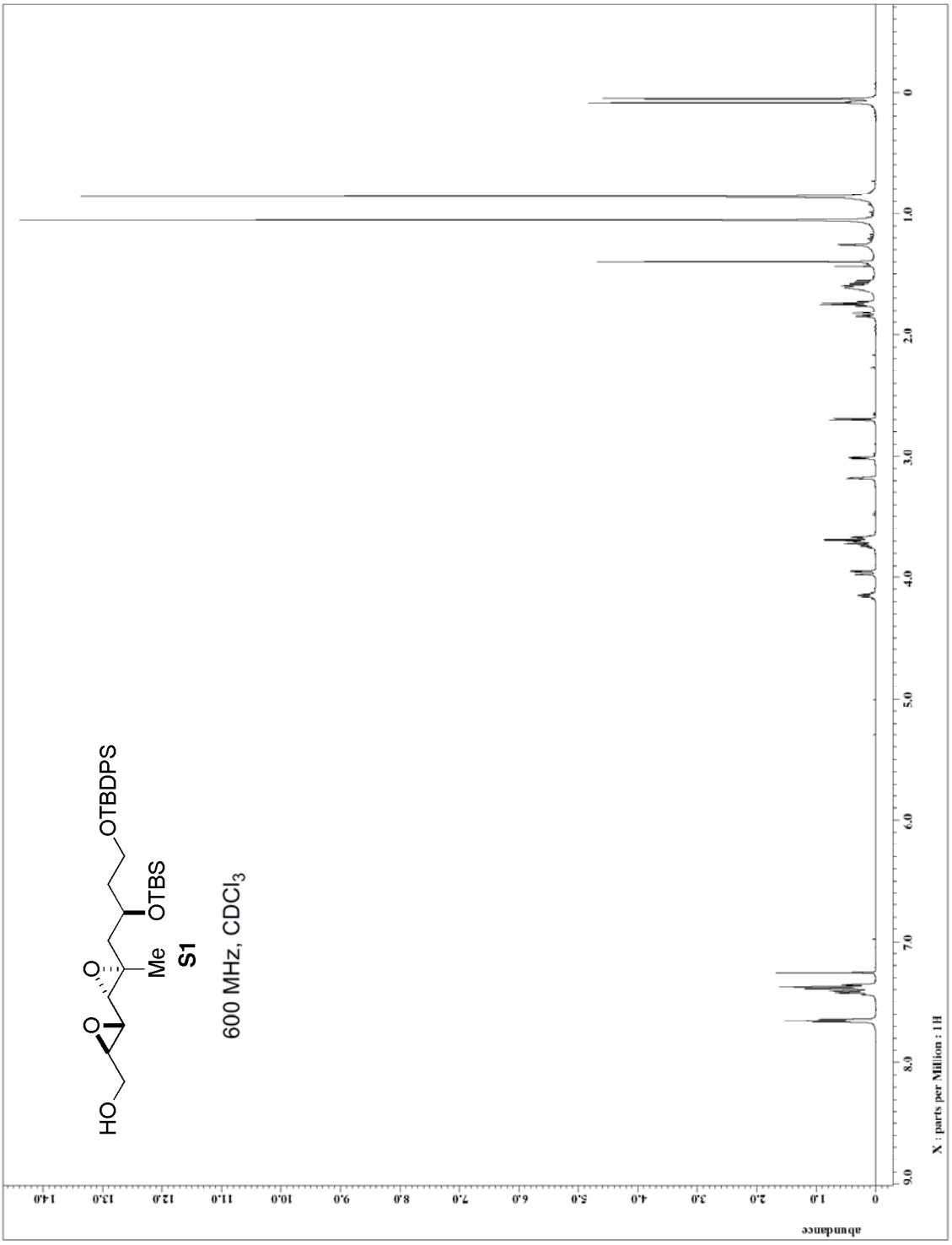

HO
O
Me
OTBS
OTBDPS
23
150 MHz, CDCl3
abundance
X : parts per Million : 13C

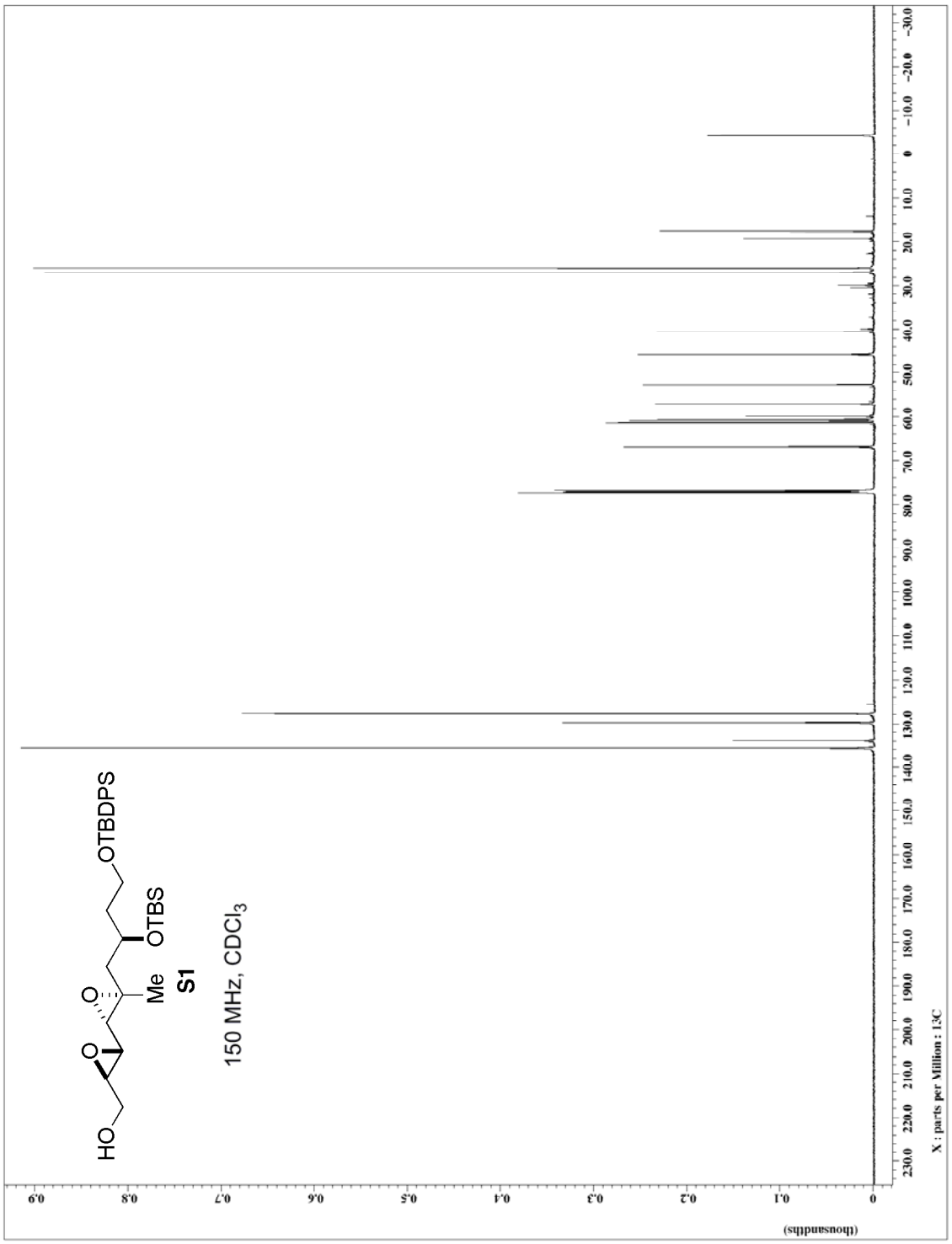

HO
O
Me
OTBS
OTBDPS
25
600 MHz, CDCl3
abundance
X : parts per Million : 1 H

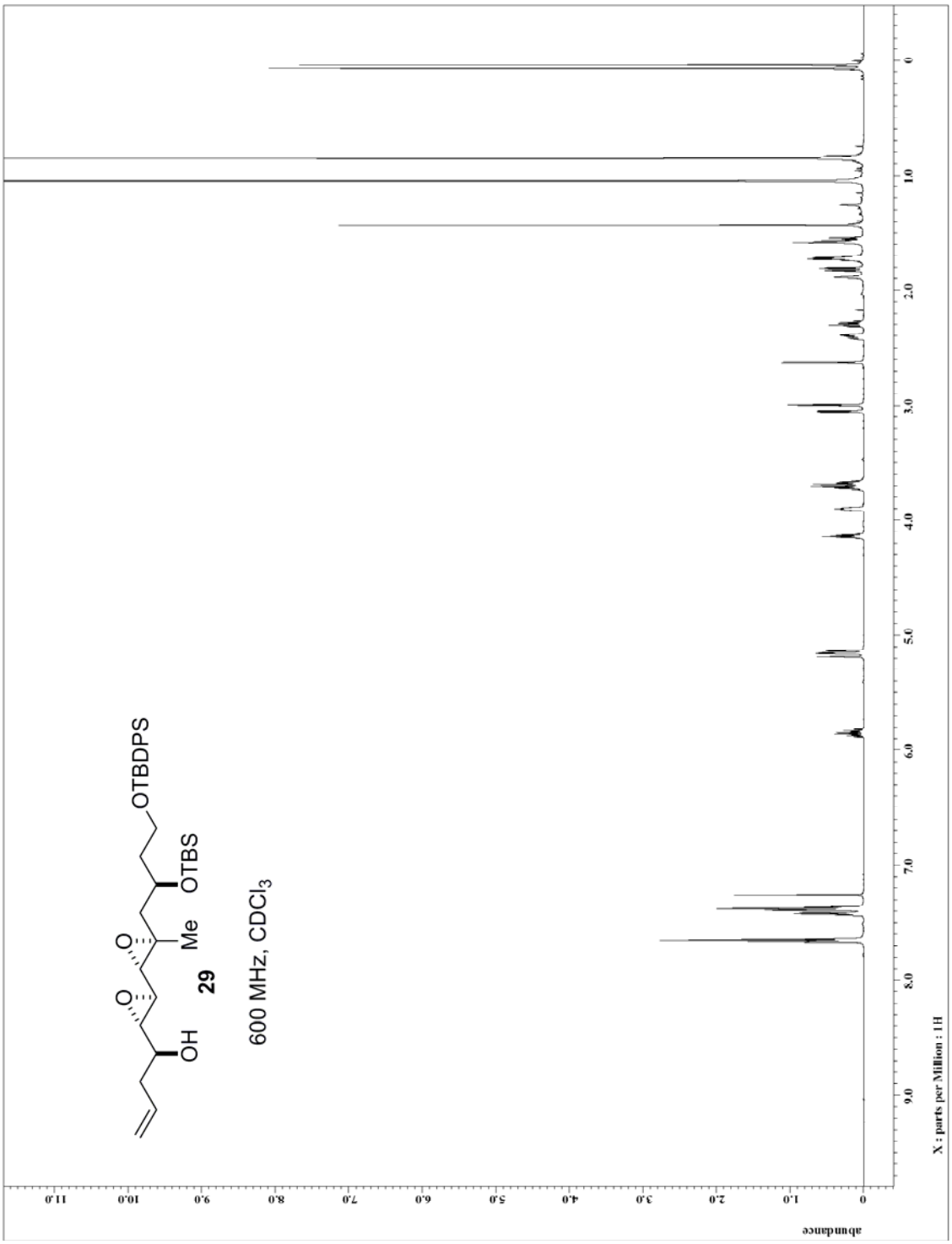

HO
OTBDPS
OTBS
Me
O
25
150 MHz, CDCl3
abundance
X : parts per Million : 13C

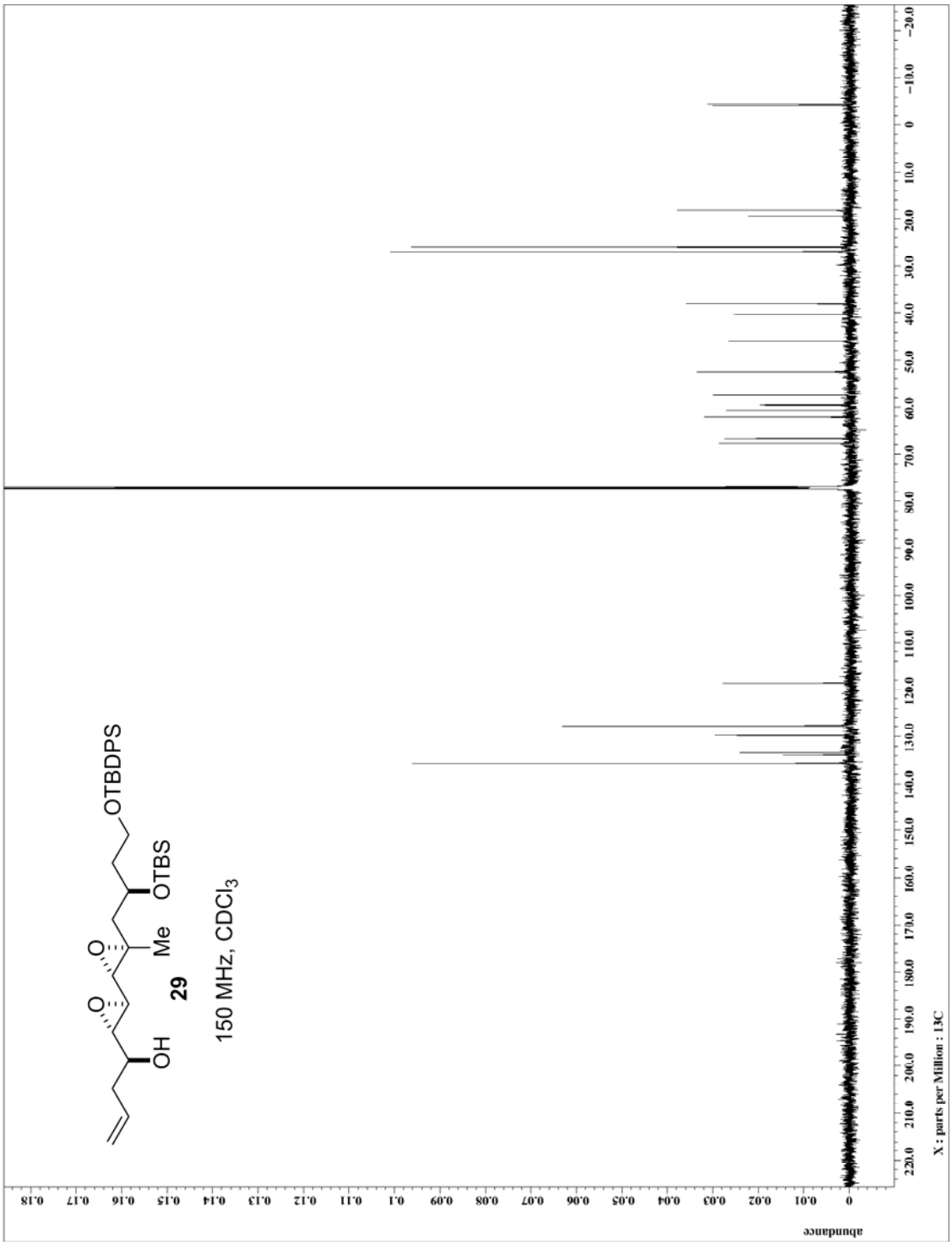

HO
O
O
Me
OTBS
OTBDPS
26
600 MHz, CDCl3
abundance
X : parts per Million : 1H

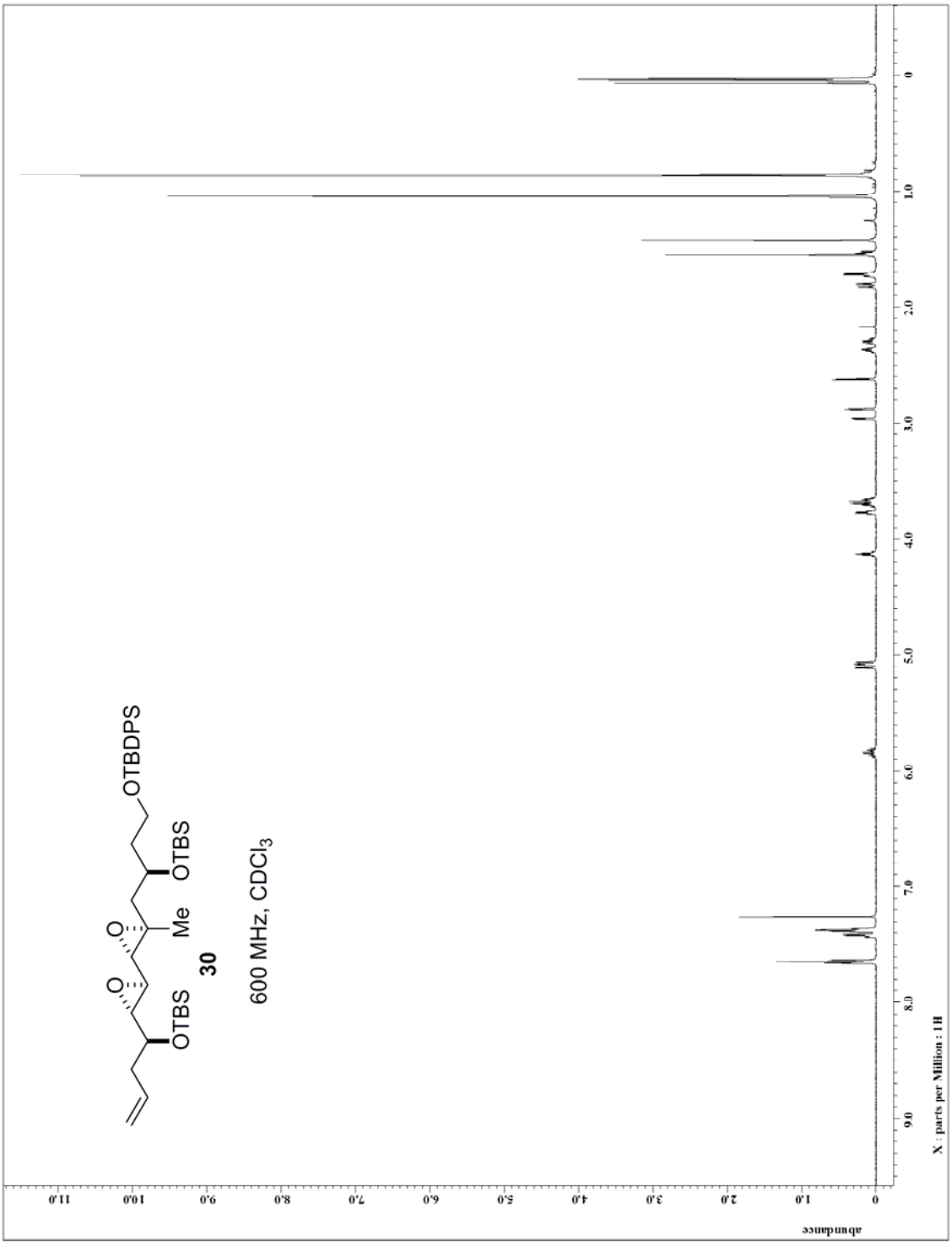

OTBDPS
OTBS
Me
O
O
HO
26
150 MHz, CDCl3
abundance
X : parts per Million : 13C
135.7010
129.8268
129.7885
127.8336
127.8048
77.3708
77.1600
76.9492
66.9065
62.4505
60.7064
60.6202
59.6619
55.7809
52.9348
46.0352
40.6401
27.0135
26.0169
19.3089
18.1111
17.8332
-4.1401
-4.2455

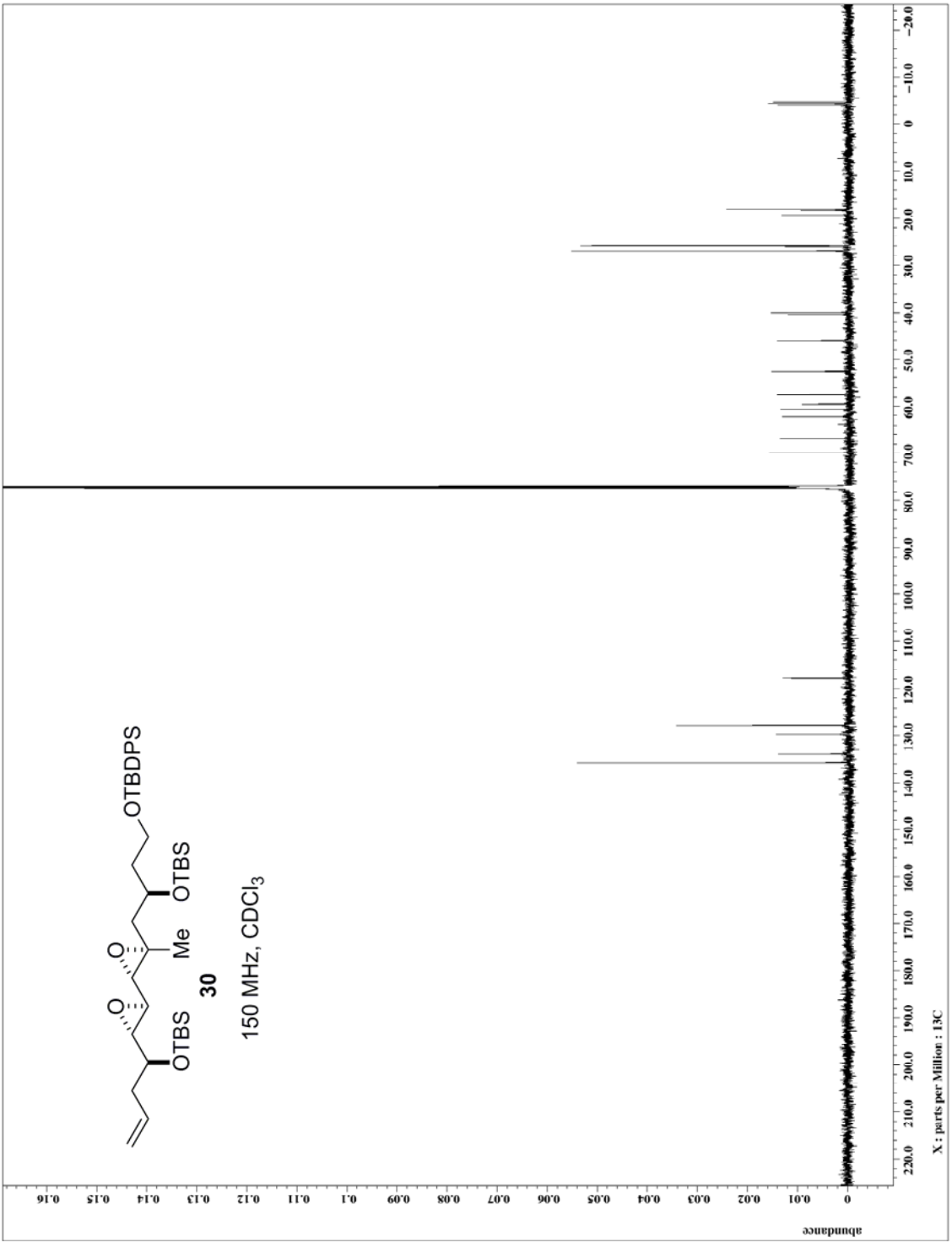

OTBDPS
OTBS
Me
O
O
HO
S1
600 MHz, CDCl3
abundance
X : parts per Million : 1H

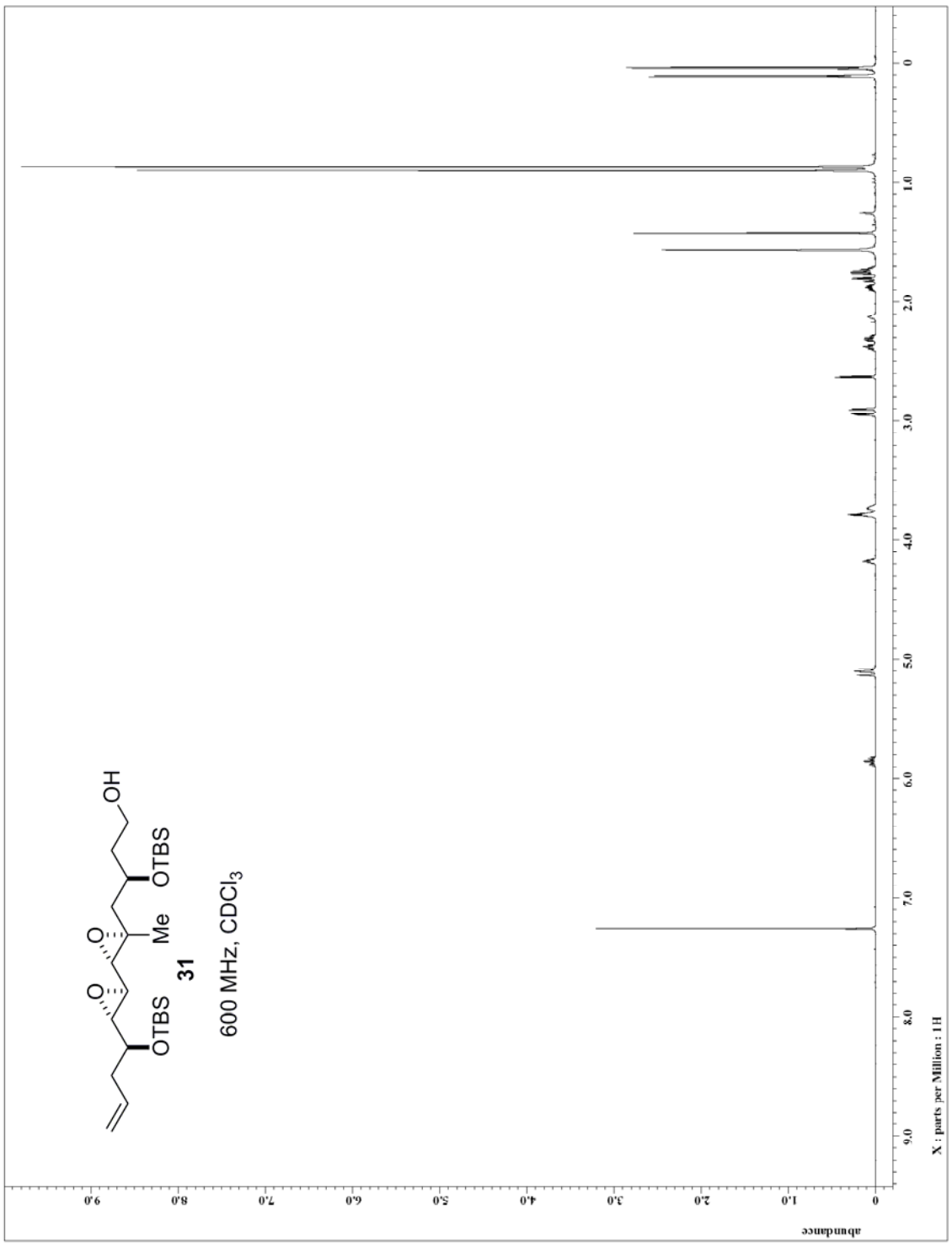

HO
O
O
Me
OTBS
OTBDPS
S1
150 MHz, CDCl3
(thousandths)
X : parts per Million : 13C

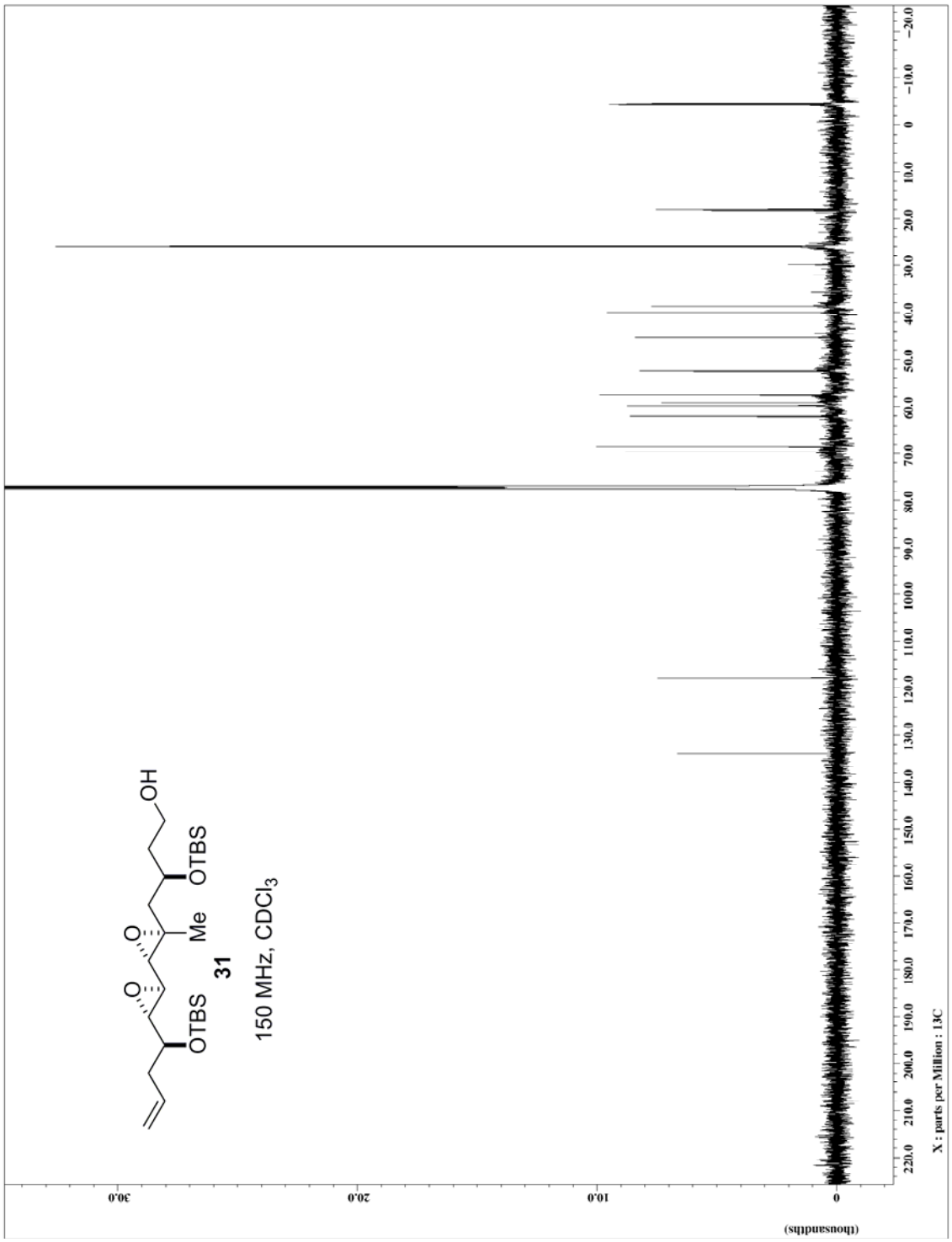

OTBDPS
OTBS
Me
OH
29
600 MHz, CDCl3
abundance
X : parts per Million : 1H

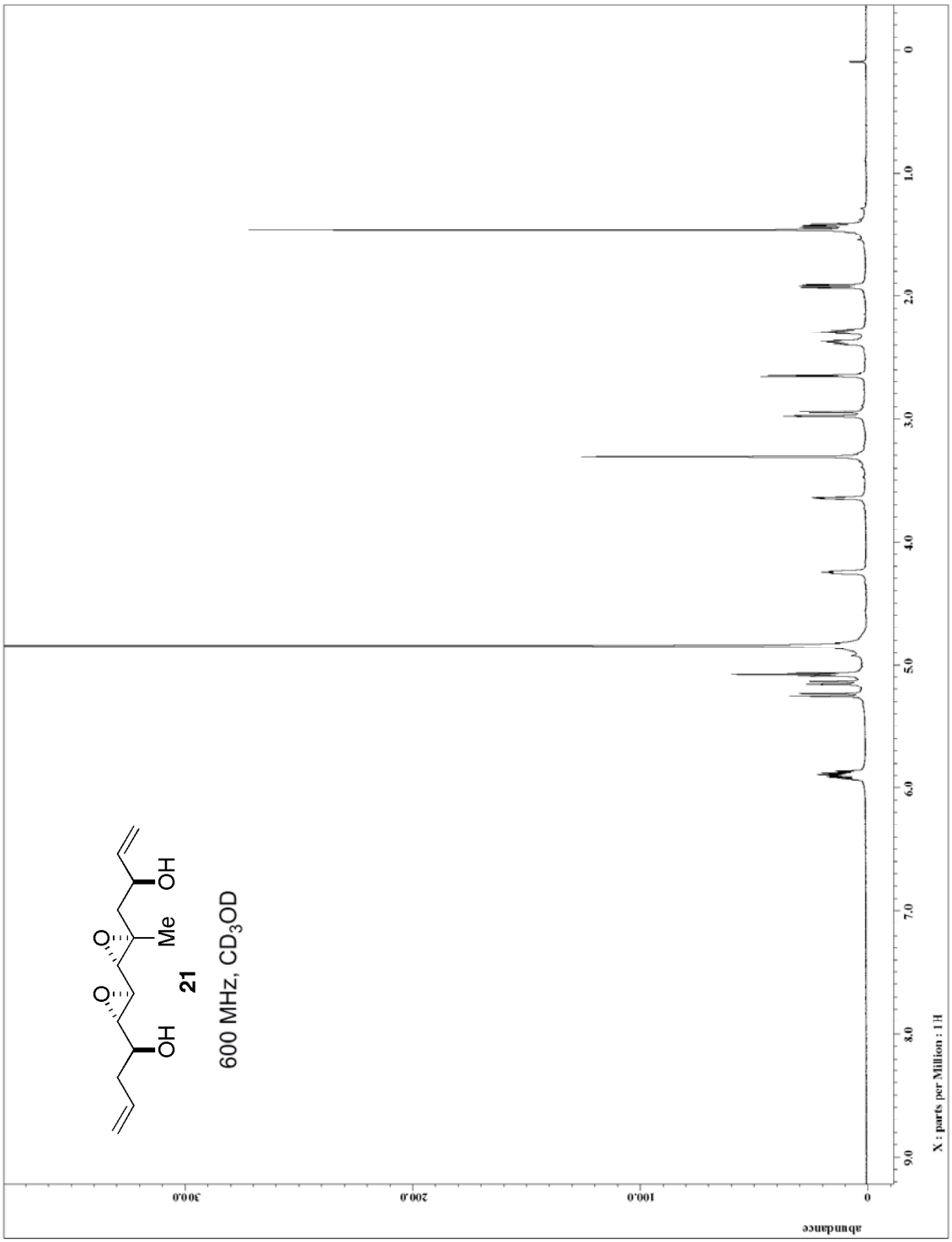

OTBDPS
OTBS
Me
O
O
OH
29
150 MHz, CDCl3
abundance
X : parts per Million : 13C

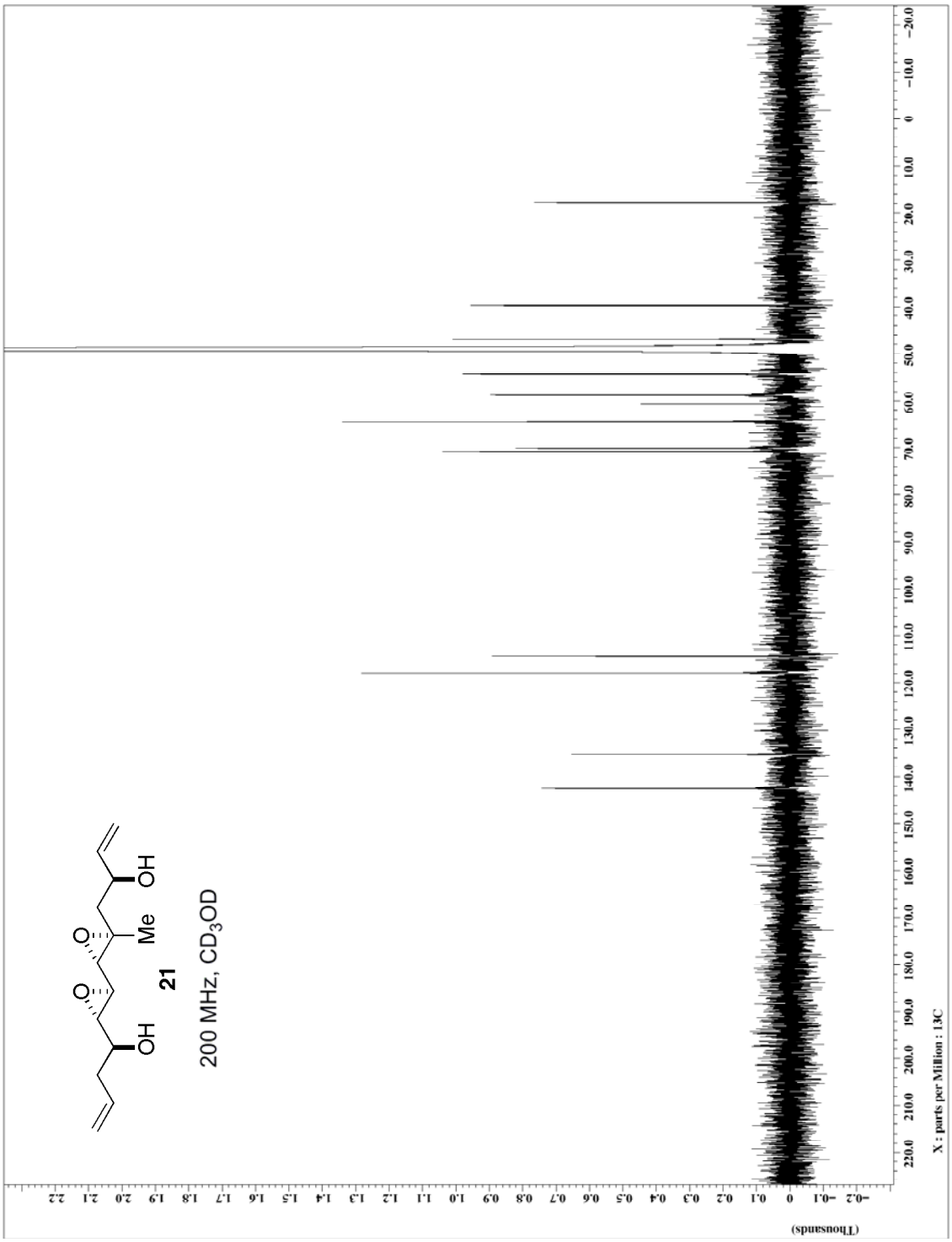

OTBDPS
OTBS
Me
OTBS
30
600 MHz, CDCl3
abundance
X : parts per Million : 1H

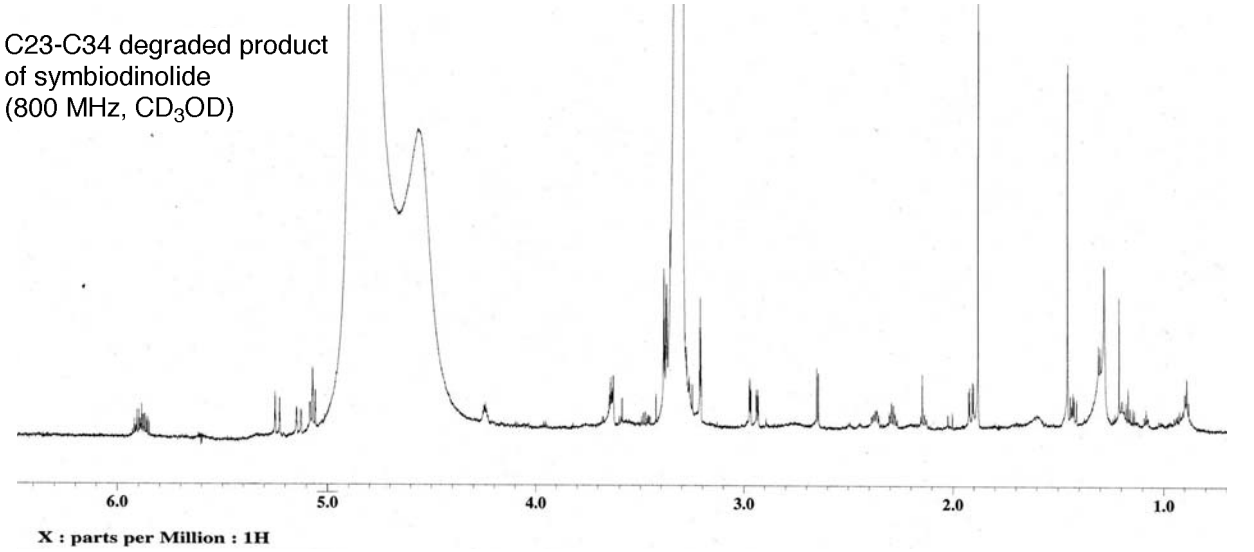

OTBDPS
OTBS
Me
OTBS
30
150 MHz, CDCl3
abundance
X : parts per Million : 13C

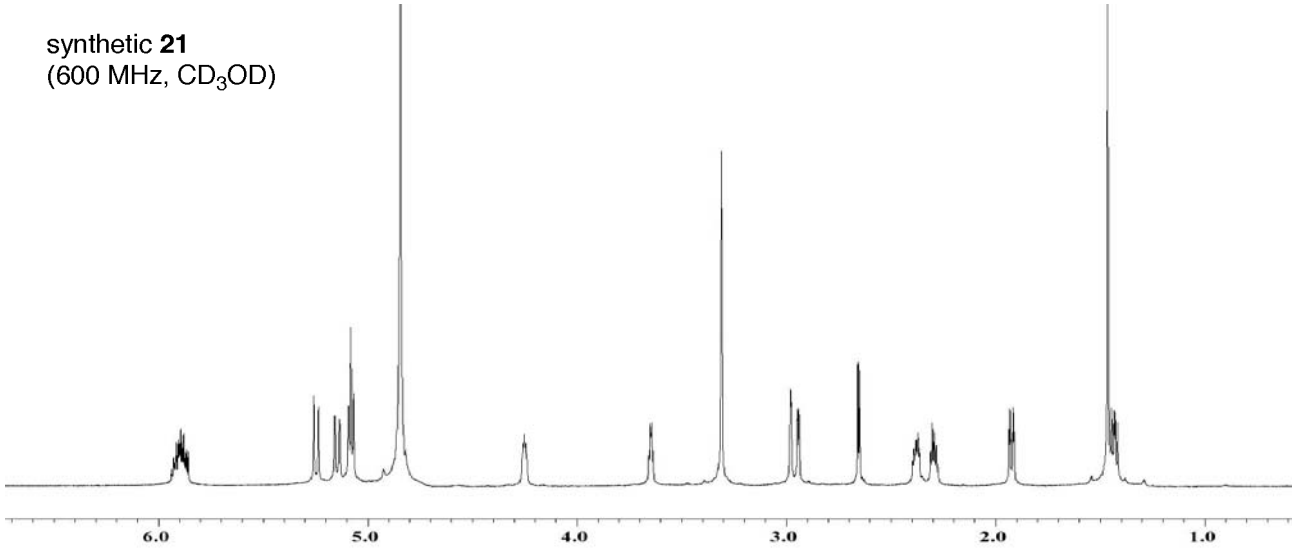

OH
OTBS
Me
OTBS
31
600 MHz, CDCl3
abundance
X : parts per Million : 1 H

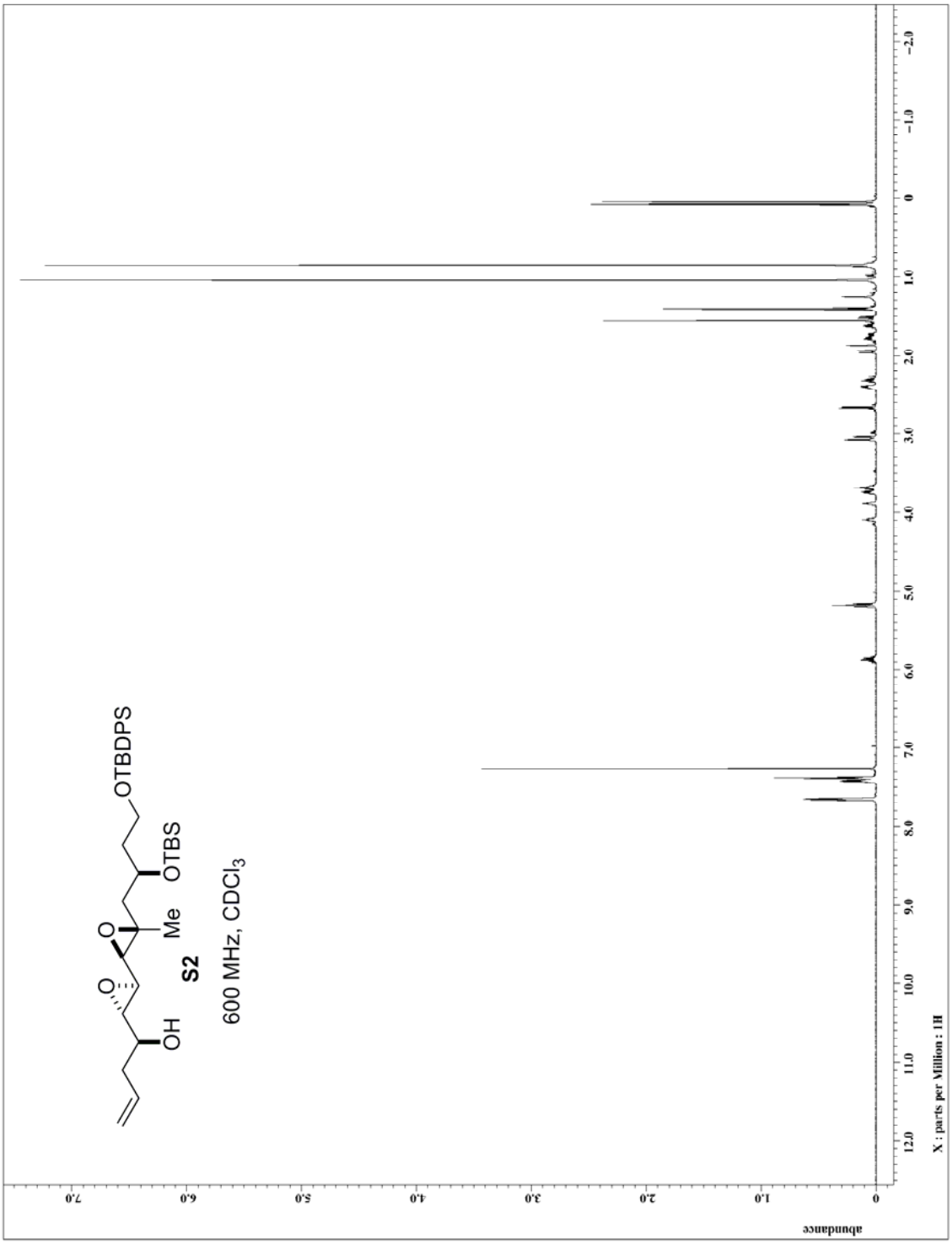

OH
OTBS
Me
OTBS
31
150 MHz, CDCl3
(thousandths)
30.0
20.0
10.0
0
X : parts per Million : 13C
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0

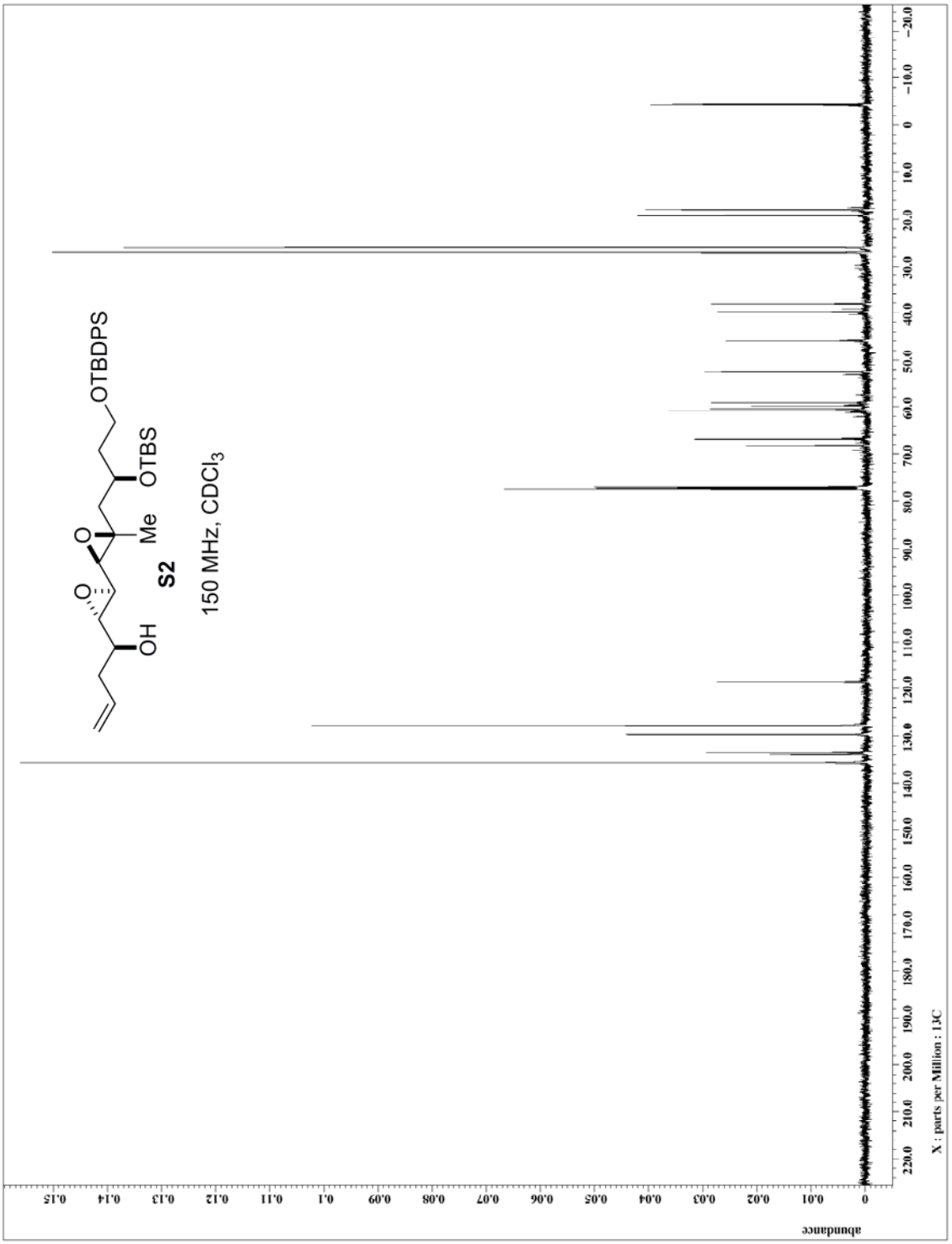

OH
Me
OH
21
600 MHz, CD3OD
X : parts per Million : 1H
abundance

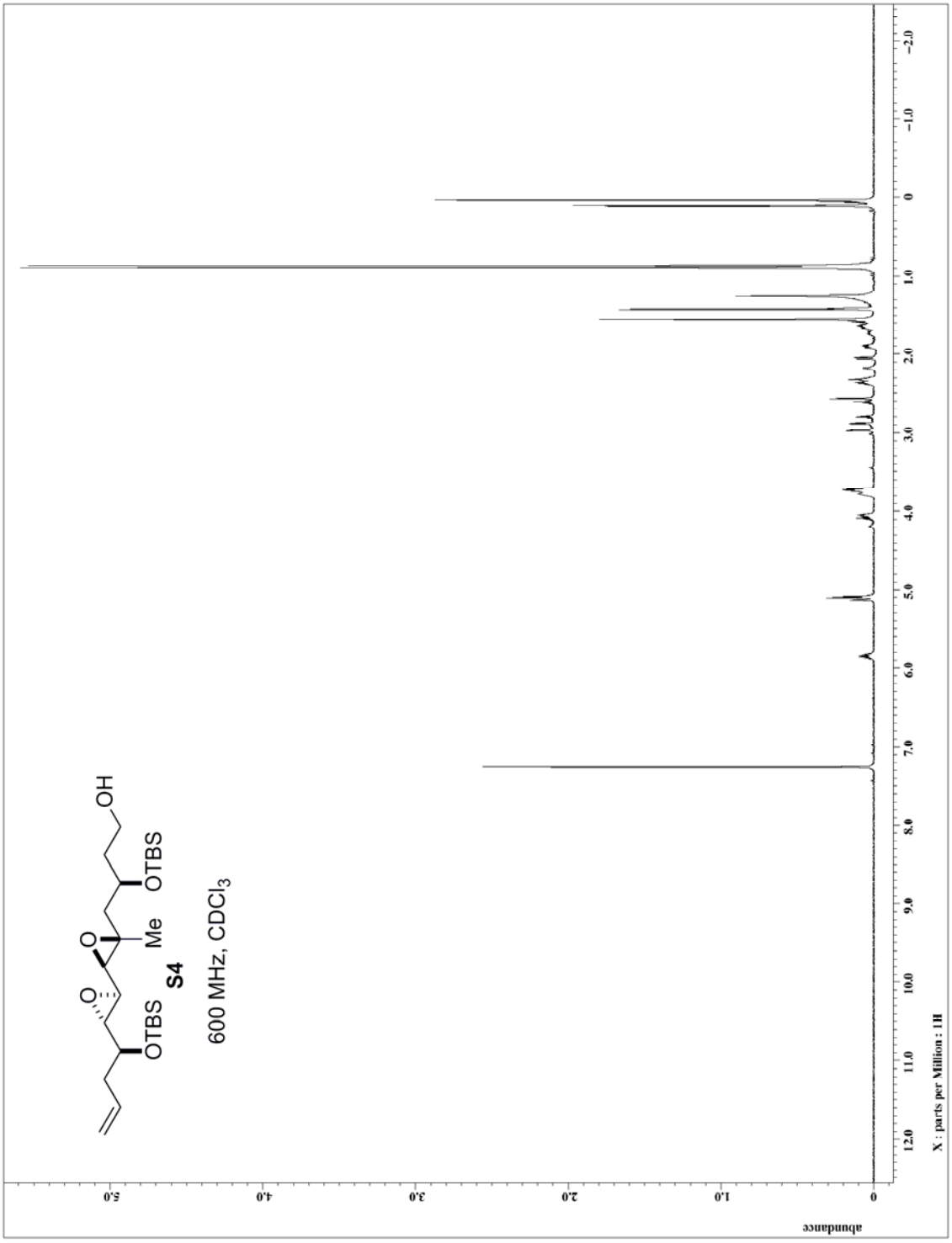

OH
O
O
Me
OH
21
200 MHz, CD3OD
(Thousands)
X : parts per Million : 13C

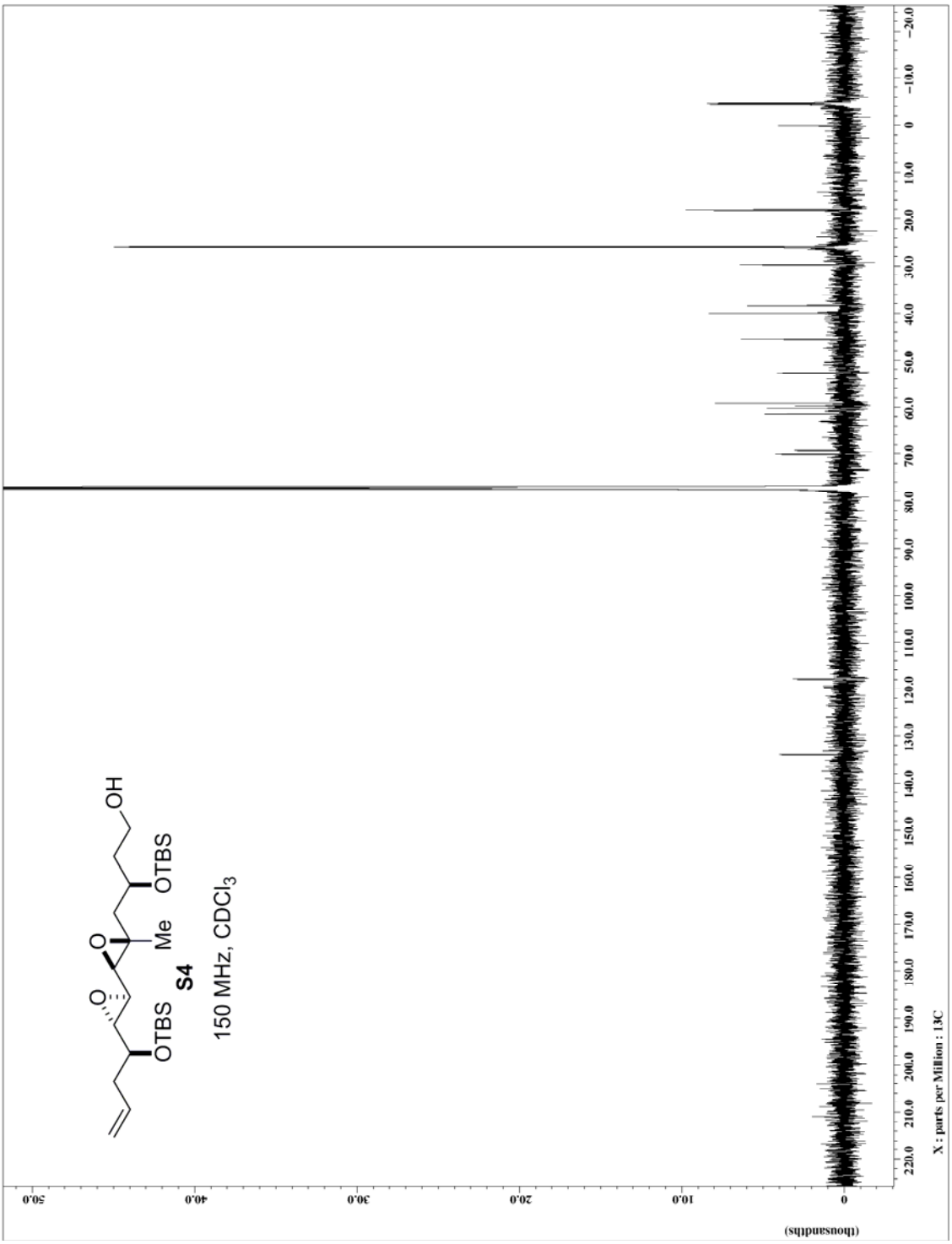

C23-C34 degraded product
of symbiodinolide
(800 MHz, CD3OD)
6.0
5.0
4.0
3.0
2.0
1.0
X : parts per Million : 1H

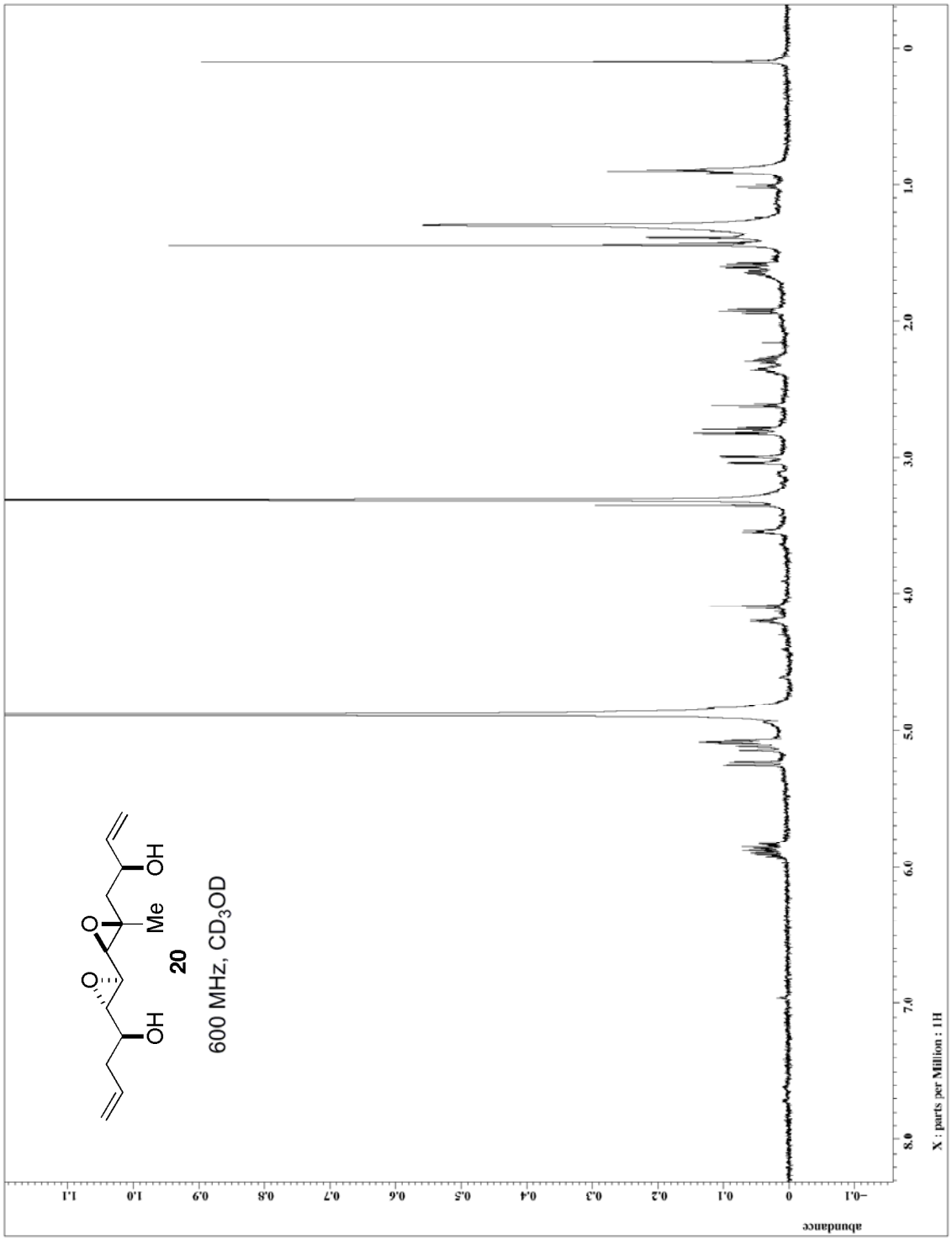

synthetic 21
(600 MHz, CD3OD)
6.0
5.0
4.0
3.0
2.0
1.0

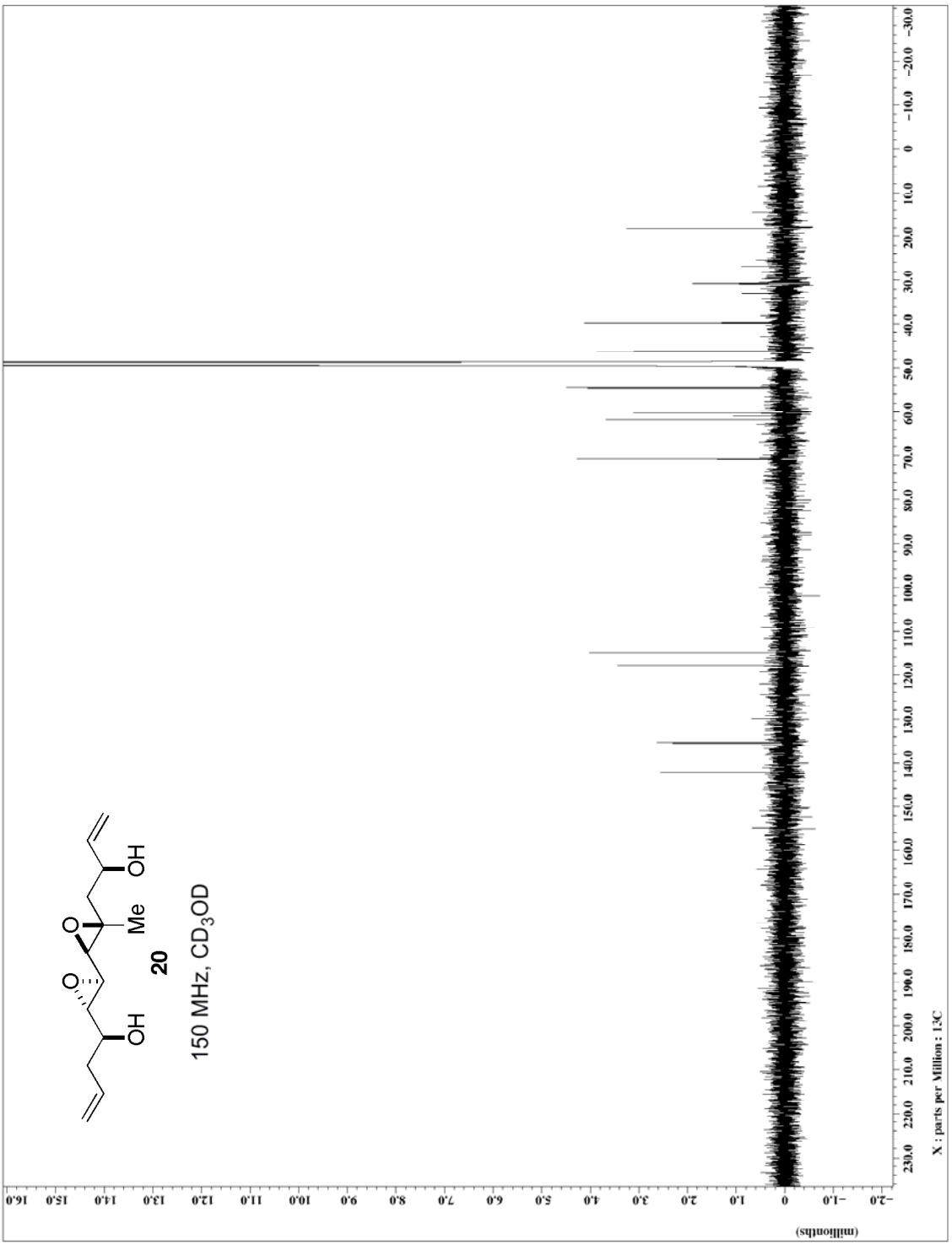

OTBDPS
OTBS
Me
OH
S2
600 MHz, CDCl3
abundance
X : parts per Million : 1H

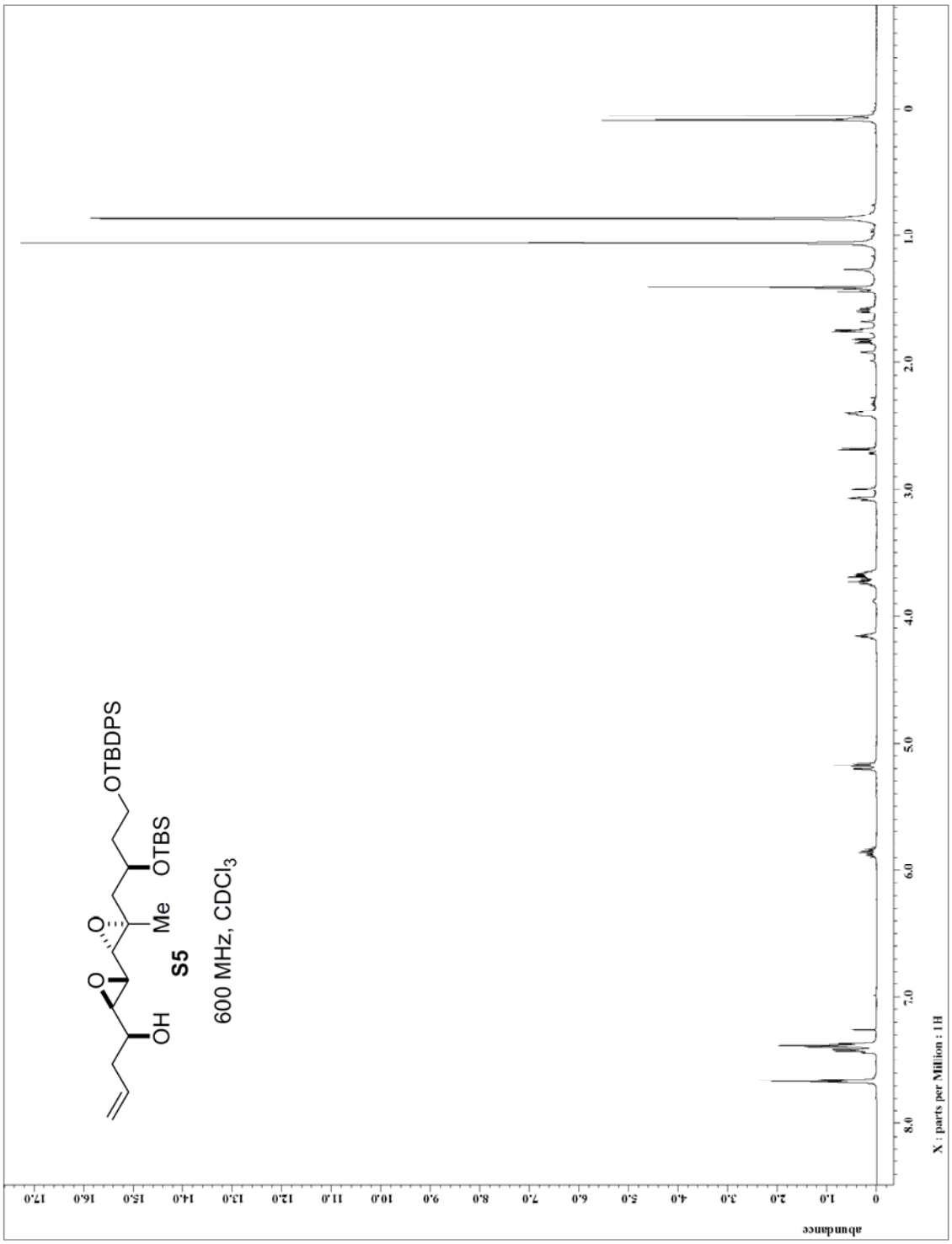

OTBDPS
OTBS
Me
OH
S2
150 MHz, CDCl3
abundance
X : parts per Million : 13C

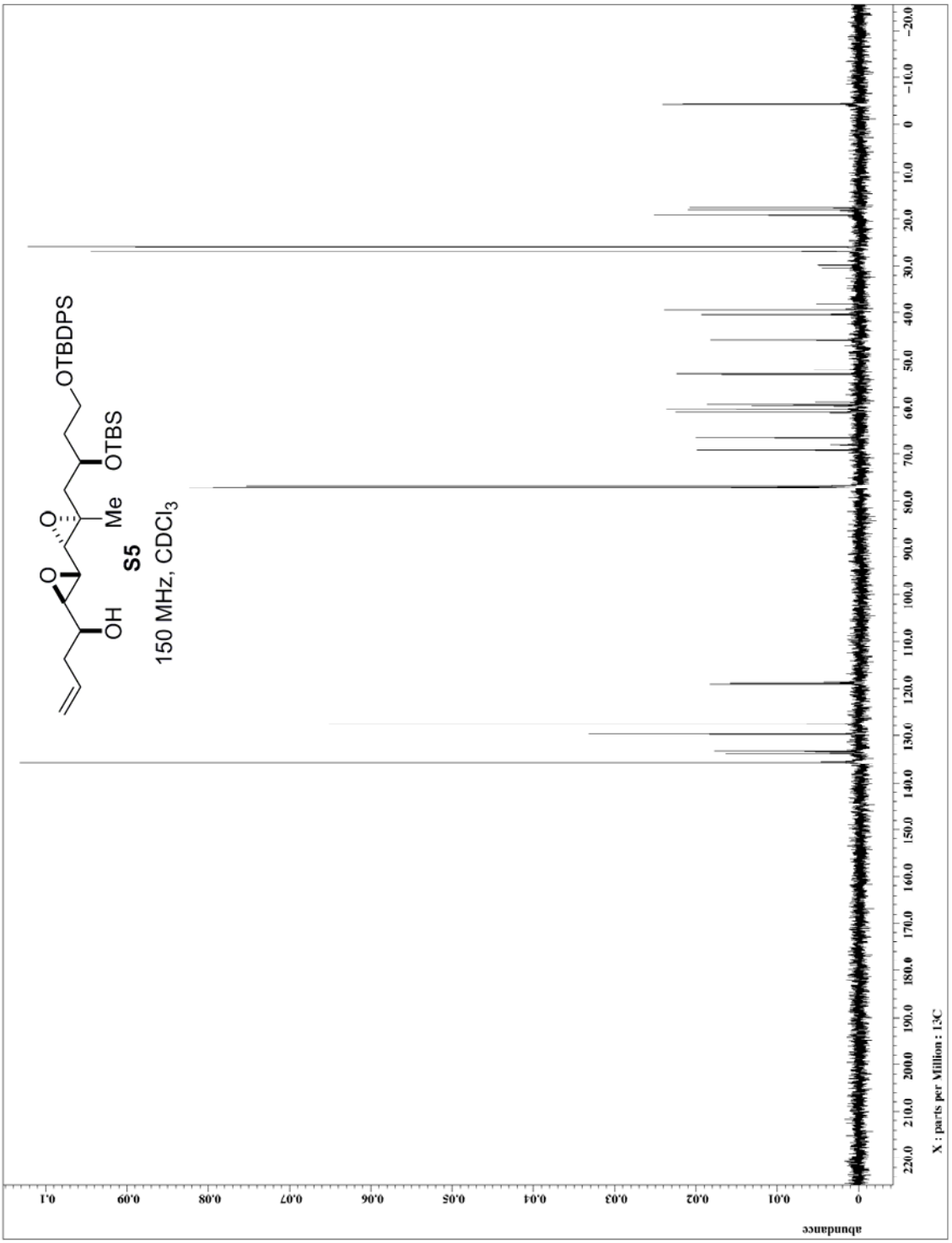

OH
OTBS
Me
OTBS
O
O
S4
600 MHz, CDCl3
abundance
X : parts per Million : 1H

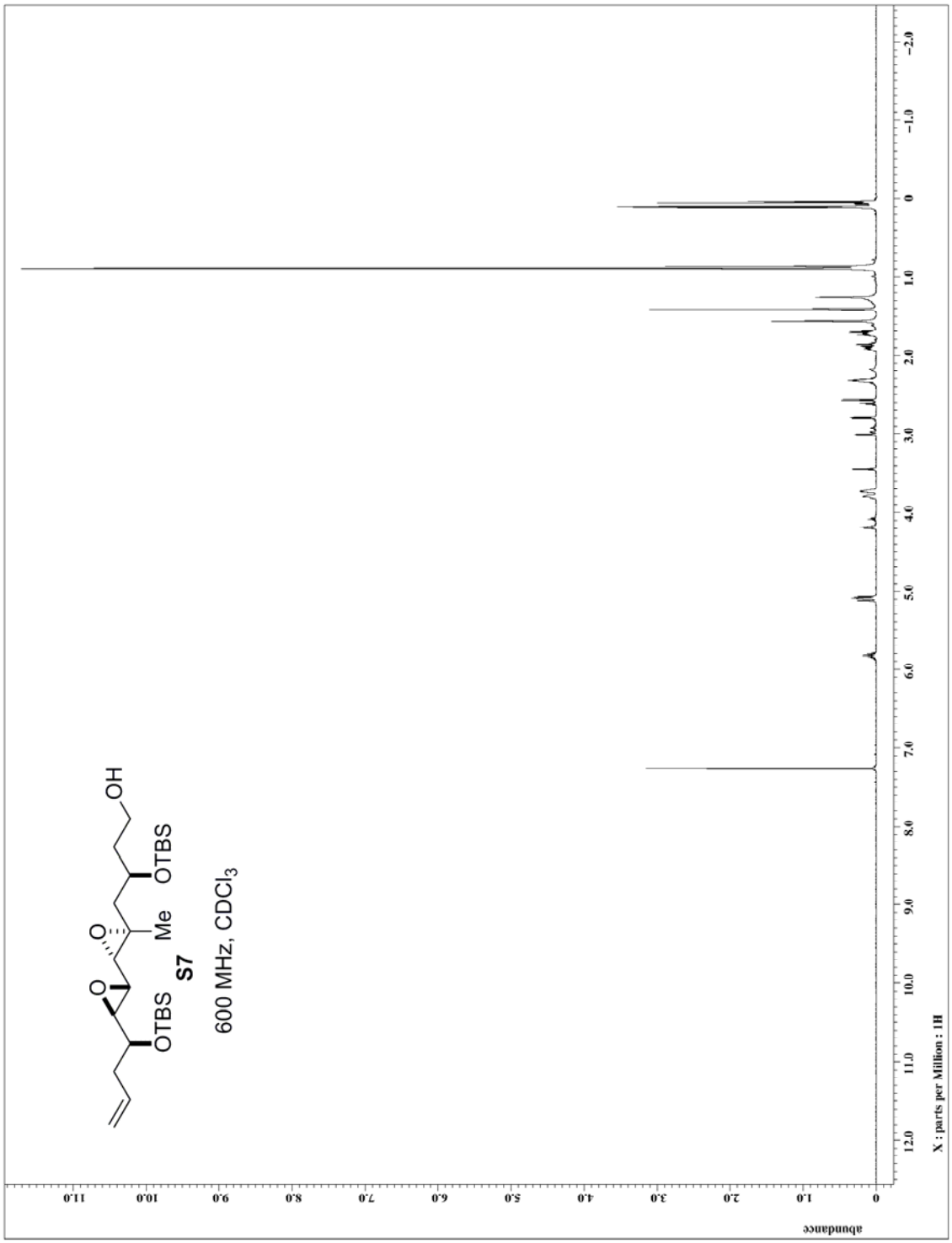

OH
OTBS
Me
OTBS
O
O
S4
150 MHz, $CDCl_3$
(thousandths)
X : parts per Million : 13C

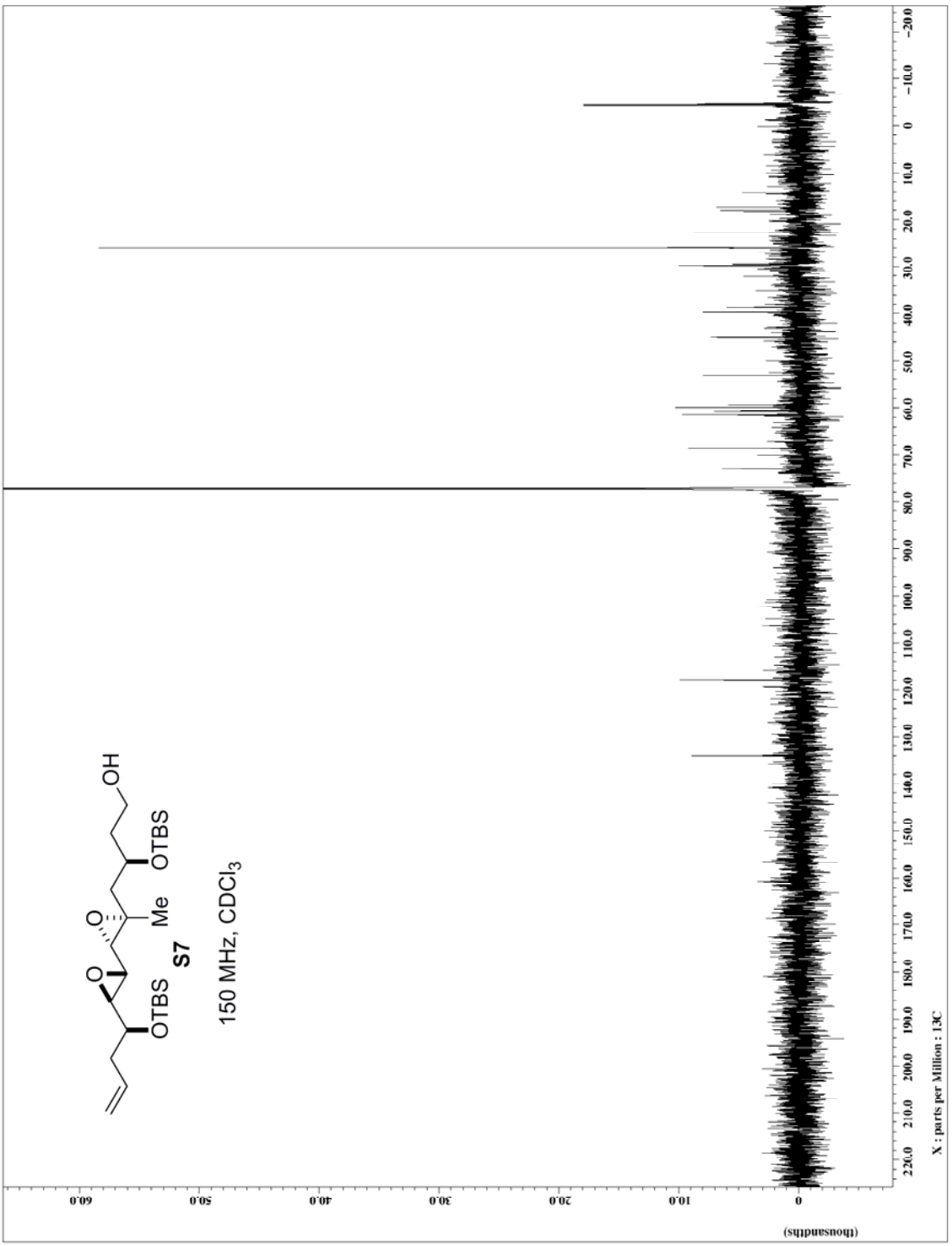

OH
Me
O
O
OH
20
600 MHz, CD3OD
abundance
X : parts per Million : 1H

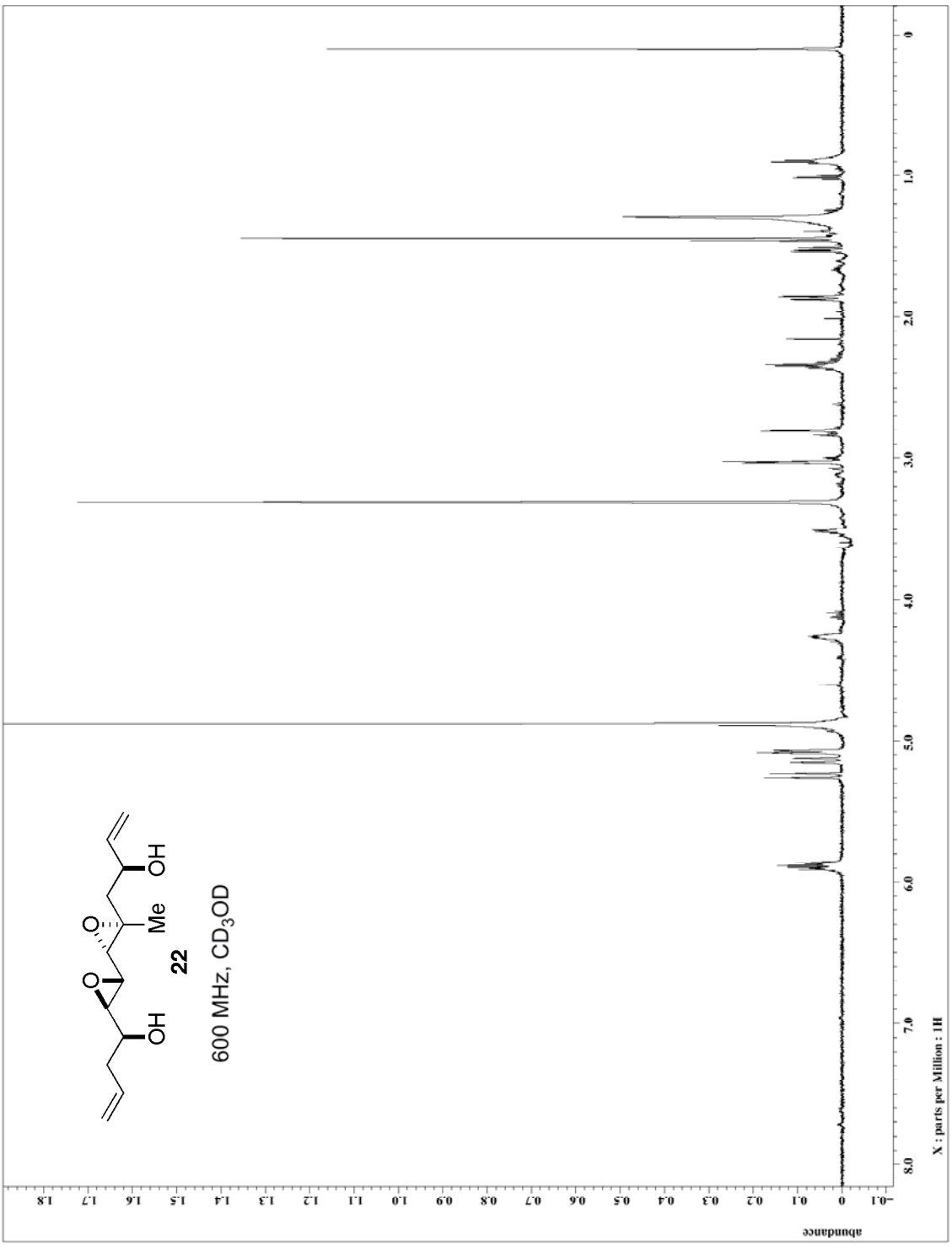

OH
Me
O
O
OH
20
150 MHz, CD3OD
X : parts per Million : 13C
(millionths)

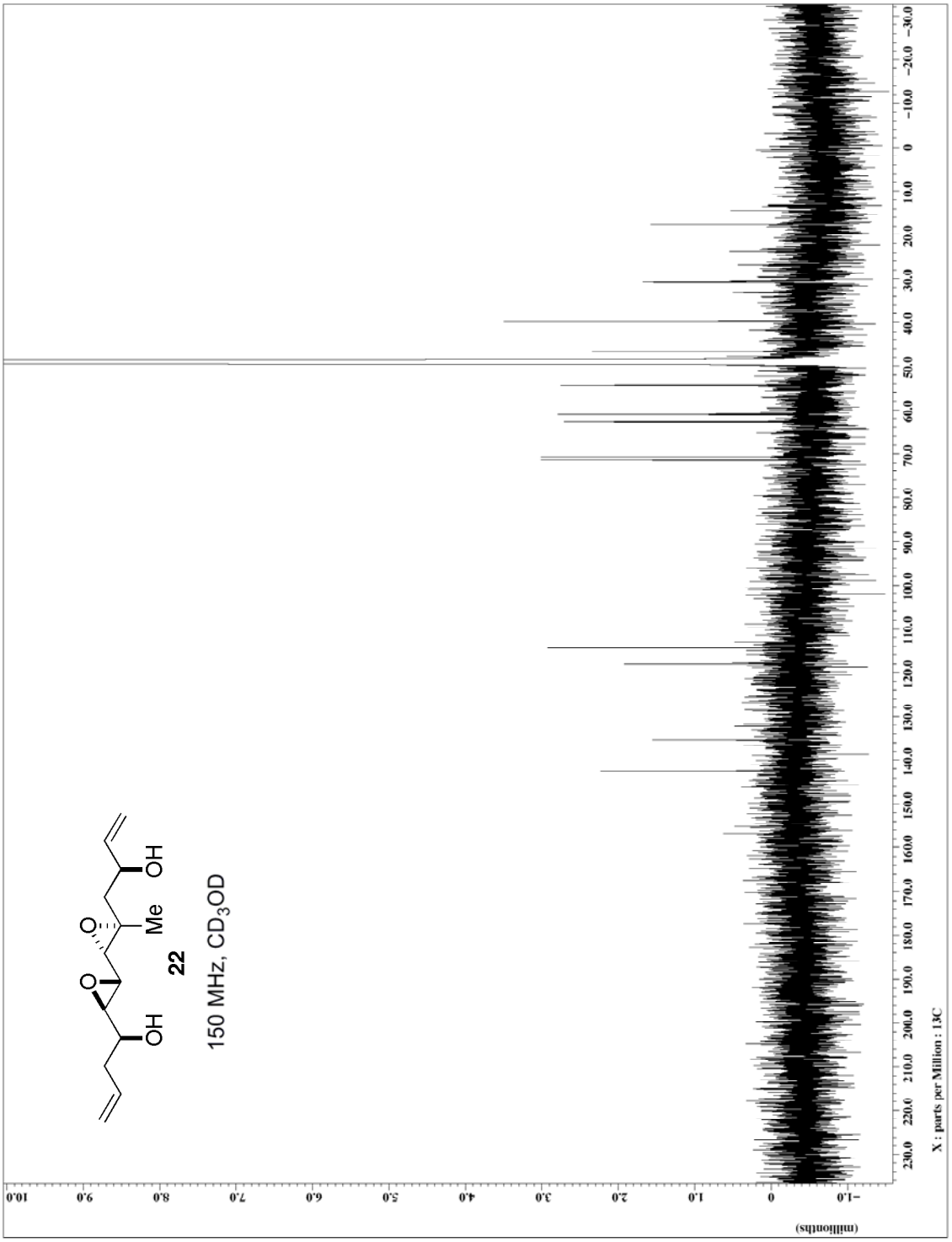

OTBDPS
OTBS
Me
OH
S5
600 MHz, CDCl3
abundance
X : parts per Million : 1H


OTBDPS
OTBS
Me
O
O
OH
S5
150 MHz, CDCl3
abundance
X : parts per Million : 13C


OH
OTBS
Me
OTBS
O
O
S7
600 MHz, CDCl3
abundance
X : parts per Million : 1H


OH
OTBS
Me
OTBS
O
O
S7
150 MHz, CDCl3
(thousandths)
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : 13C
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
-20.0


OH
O
O
Me
OH
22
600 MHz, CD3OD
abundance
X : parts per Million : 1H


OH
Me
O
O
OH
22
150 MHz, CD3OD
(millionths)
X : parts per Million : 13C