Studies towards the synthesis of tedanolide C. Construction of the C13-*epi* C1–C15 fragment

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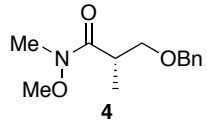
1. General Experimental Methods

Unless otherwise noted, reactions were conducted in oven-dried glassware under inert atmosphere of N_2 with anhydrous solvents. The solvents and reagents were dried and purified when necessary according to standard procedures. Commercially available reagents were used as received. Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel 60 F_{254} plates and analyzed by UV (254 nm) and stained with phosphomolybdic acid and *p*-anisaldehyde; R_f values are approximate. Specific rotations ($[\alpha]_D$) were determined at 20 °C on a Perkin-Elmer 241 MC polarimeter. **IR** spectra (Attenuated Total Reflectance, ATR) were recorded on a Nicolet 6700 FT-IR Thermo Scientific spectrometer and only the more representative frequencies (ν) are reported in cm^{-1}. **^{1}H NMR** (400 MHz) and **^{13}C NMR** (100.6 MHz) spectra were recorded on a Varian Mercury 400. **^{1}H NMR** (500 MHz) and **^{13}C NMR** (125 MHz) spectra were recorded on a Bruker DMX 500. Chemical shifts (δ) are quoted in ppm and referenced to internal TMS (δ 0.00 for ^{1}H NMR) or $CDCl_3$ (δ 77.0 for ^{13}C NMR); coupling constants (*J*) are quoted in Hz; data are reported as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet (and their corresponding combinations); where necessary, 2D techniques (NOESY, COSY, HSQC) were also used to assist on structure elucidation. High resolution mass spectra (**HRMS**) were obtained with an Agilent 1100 spectrometer by the Unitat d'Espectrometria de Masses (CCiTUB), Universitat de Barcelona. Column chromatographies were carried under low pressure (flash) conditions and performed on SDS silica gel 60 (35–70 μm). **HPLC** analyses were carried out with a silica Tracer Spherisorb S3W (N4184) column using isocratic conditions (0.9 mL ·min^{-1}) at room temperature.

2. Synthesis of the *northern* fragment

(*S*)-3-Benzyloxy-2,*N*-dimethyl-*N*-methoxypropanamide (4).



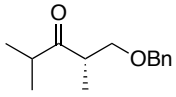
4

Neat TMSOTf (0.20 mL, 1.1 mmol) was added dropwise to a solution of methyl (*S*)-3-hydroxy-2-methylpropanoate (1.87 g, 15.8 mmol) and benzyl 2,2,2-trichloroacetimidate (3.25 mL, 17.4 mmol) in 2:1 cyclohexane/CH_2Cl_2 (90 mL) at room temperature and the resulting milky suspension was stirred for 15 h at room temperature. It was filtered through a cotton plug eluting with hexane (200 mL) and the organic solution was washed with sat $NaHCO_3$ (30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (85:15 hexanes/EtOAc) to afford 3.01 g (14.5 mmol, 91% yield) of methyl (*S*)-3-benzyloxy-2-methylpropanoate as a colourless oil. R_f

(85:15 hexanes/EtOAc) 0.30. **[α]$_D$** +10.6 (c 1.2, $CHCl_3$) [lit.[1] **[α]$_D$** +12.1 (c 10, $CHCl_3$)]. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (5H, br s, ArH), 4.52 (2H, s, $PhCH_2O$), 3.69 (3H, s, OCH_3), 3.67 (1H, dd, *J* = 9.1, 7.4 Hz, $BnOCH_xH_y$), 3.49 (1H, dd, *J* = 9.1, 6.0 Hz, $BnOCH_xH_y$), 2.90–2.70 (1H, m, $CHCH_3$), 1.18 (3H, d, *J* = 7.0 Hz, $CHCH_3$).

A 2 M solution of *i*-PrMgCl in Et_2O (16 mL, 32 mmol) was slowly added for 30 min to a mixture of (*S*)-3-benzyloxy-2-methylpropanoate (2.11 g, 10.1 mmol) and MeONH(Me)·HCl (1.60 g, 16 mmol)[2] in THF (17 mL) at –15 °C and the reacting mixture was stirred for 30 min at –15 °C. Then, it was partitioned with sat NH_4Cl (20 mL) and Et_2O (20 mL). The aqueous layer was extracted with Et_2O (2 × 20 mL) and the combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was filtered through a short pad of silica (Et_2O) to afford 2.18 g (9.2 mmol, 90% yield) of (*S*)-3-benzyloxy-2,*N*-dimethyl-*N*-methoxypropanamide (**4**) as a yellowish oil. ***R$_f$*** (97:3 CH_2Cl_2/MeOH) 0.60. **[α]$_D$** +4.8 (c 1.61, $CHCl_3$) [lit.[1] **[α]$_D$** +5.0 (c 3.9, $CHCl_3$)]. **IR** (ATR) ν 3031, 2937, 2862, 1662, 1454, 1387, 1102. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (5H, br s, ArH), 4.55 (1H, d, *J* = 12.2 Hz, $PhCH_xH_y$), 4.48 (1H, d, *J* = 12.2 Hz, $PhCH_xH_y$), 3.72 (1H, dd, *J* = 9.2, 8.8 Hz, $BnOCH_xH_y$), 3.69 (3H, s, OCH_3), 3.43 (1H, dd, *J* = 9.2, 6.0 Hz, $BnOCH_xH_y$), 3.32–3.24 (1H, m, $CHCH_3$), 3.21 (3H, s, NCH_3), 1.11 (3H, d, *J* = 6.8 Hz, $CHCH_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 175.9, 138.4, 128.3, 127.5, 127.4, 73.2, 72.6, 61.5, 35.8, 32.1, 14.2.

(*S*)-1-Benzyloxy-2,4-dimethyl-3-pentanone (2).

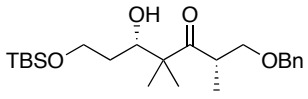


2

A 0.7 M solution of *i*-PrLi in pentane (20.5 mL, 14.4 mmol) was slowly added to a solution of **4** (1.70 g, 7.2 mmol) in THF (20 mL) at 0 °C and the reacting mixture was stirred for 1 h at 0 °C. It was quenched with sat NH_4Cl (20 mL) and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. Purification of the resulting oil by column chromatography (90:10 hexanes/EtOAc) afforded 520 mg (2.4 mmol, 33% yield) of (*S*)-1-benzyloxy-2,4-dimethyl-3-pentanone (**2**) as a colourless oil. ***R$_f$*** (90:10 hexanes/EtOAc) 0.45. **[α]$_D$** +28.2 (c 1.20, $CHCl_3$). **IR** (ATR) ν 2970, 2933, 2873, 1713, 1454, 1363, 1101, 1027. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35–7.25 (5H, m, ArH), 4.49 (1H, d, *J* = 12.0 Hz, $PhCH_xH_y$), 4.45 (1H, d, *J* = 12.0 Hz, $PhCH_xH_y$), 3.63 (1H, dd, *J* = 8.9, 8.2 Hz, $BnOCH_xH_y$), 3.43 (1H, dd, *J* = 8.9, 5.6 Hz, $BnOCH_xH_y$), 3.12–3.04 (1H, m, $CHCH_3$), 2.81–2.70 (1H, m, $CH(CH_3)_2$), 1.09 (3H, d, *J* = 6.9 Hz, $BnOCH_2CHCH_3$), 1.09 (3H, d, *J* = 7.0 Hz, $CHCH_3$), 1.05 (3H, d, *J* = 7.0 Hz, $CHCH_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 217.0 (C), 138.2 (C), 128.3 (CH), 127.5 (2 × CH), 73.2 (CH_2), 72.7 (CH_2), 44.4 (CH), 40.5 (CH), 18.1 (CH_3), 17.9 (CH_3), 14.0 (CH_3).

[1] I. Paterson, R. D. Norcross, R. A. Ward, P. Romea and M. A. Lister, *J. Am. Chem. Soc.*, 1994, **116**, 11287.
[2] This material was kept under vacuum for one day before using.

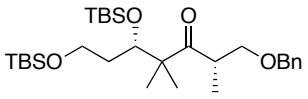
(2*S*,5*S*)-1-Benzyloxy-7-*tert*-butyldimethylsilyloxy-5-hydroxy-2,4,4-trimethyl-3-heptanone (5).



5

Neat $TiCl_4$ (0.33 mL, 3.0 mmol) was carefully added to a solution of ketone **2** (661 mg, 3.0 mmol) in CH_2Cl_2 (12 mL) at –78 °C. The orange solution was stirred for 3 min and treated with DIPEA (0.58 mL, 3.3 mmol) and the resulting dark red solution was stirred for 30 min at –78 °C. Then, $TiCl_4$ (0.33 mL, 3.0 mmol) was dropwise added and, 10 min later, a solution of 3-*tert*-butyldimethylsilyloxypropanal (675 mg, 3.6 mmol) in CH_2Cl_2 (1.5 & 1.5 mL) was added via cannula. The reaction mixture was stirred for 30 min at –78 °C and was carefully quenched with sat NH_4Cl (15 mL). It was diluted with Et_2O (60 mL) and the organic layer was washed with water (100 mL), sat $NaHCO_3$ (100 mL) and brine (100 mL). The aqueous layers were extracted with Et_2O (2 × 100 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography (70:30 hexanes/EtOAc) to afford 1.030 g (2.52 mmol, 84% yield) of (2*S*,5*S*)-1-benzyloxy-7-*tert*-butyldimethylsilyloxy-5-hydroxy-2,4,4-trimethyl-3-heptanone (**5**) as a colourless oil. R_f (70:30 hexanes/EtOAc) 0.70. **HPLC** (97:3 hexanes/EtOAc) t_R 7.5 min. **[α]$_D$** –20.4 (c 1.00, $CHCl_3$). **IR** (ATR) ν 3469, 2954, 2928, 2856, 1708, 1469, 1251, 1082. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36–7.23 (5H, m, Ar$\underline{H}$), 4.48 (1H, d, *J* = 11.9 Hz, PhC$\underline{H}_x$H$_y$), 4.43 (1H, d, *J* = 11.9 Hz, PhCH$_x\underline{H}_y$), 4.05 (1H, ddd, *J* = 10.5, 4.2, 1.7 Hz, C$\underline{H}$OH), 3.75–3.69 (3H, m, BnOC$\underline{H}_x$H$_y$ & SiOC$\underline{H}_2$), 3.51 (1H, dd, *J* = 4.2, 1.1 Hz, O$\underline{H}$), 3.50–3.39 (1H, m, BnOCH$_2$C$\underline{H}$), 3.36 (1H, dd, *J* = 8.3, 4.6 Hz, BnOCH$_x\underline{H}_y$), 1.68–1.57 (1H, m, SiOCH$_2$C$\underline{H}_x$H$_y$), 1.52–1.40 (1H, m, SiOCH$_2$CH$_x\underline{H}_y$), 1.12 (3H, s, CC$\underline{H}_3$), 1.09 (3H, s, CC$\underline{H}_3$), 1.00 (3H, d, *J* = 6.8 Hz, CHC$\underline{H}_3$), 0.91 (9H, s, SiC(C$\underline{H}_3$)$_3$), 0.06 (3H, s, SiC$\underline{H}_3$), 0.06 (3H, s, SiC$\underline{H}_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 218.1 (C), 137.3 (C), 128.4 (CH), 127.8 (CH), 127.8 (CH), 73.7 (CH_2), 73.5 (CH_2), 72.7 (CH), 61.1 (CH_2), 53.3 (C), 40.3 (CH), 33.4 (CH_2), 25.9 (CH_3), 21.0 (CH_3), 18.3 (C), 17.4 (CH_3), 15.5 (CH_3), –5.4 (CH_3), –5.4 (CH_3). **HRMS** (+ESI) *m/z* calcd. for $C_{23}H_{41}O_4Si$ $[M+H]^+$: 409.2769, found: 409.2766.

(2*S*,5*S*)-1-Benzyloxy-5,7-di-*tert*-butyldimethylsilyloxy-2,4,4-trimethyl-3-heptanone (8).

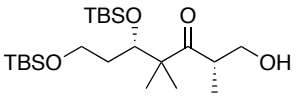


8

A solution of aldol **5** (392 mg, 0.96 mmol), TBSOTf (0.45 mL, 2.0 mmol), and 2,6-lutidine (0.57 mL, 4.8 mmol) in CH_2Cl_2 (12 mL) was stirred at 0 °C for 2 h. The reaction was quenched by addition of sat NH_4Cl (15 mL) and stirred vigorously for 5 min. The resulting mixture was partitioned with CH_2Cl_2 (50 mL) and brine (50 mL). The aqueous layer was further extracted with CH_2Cl_2 (50 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. The resultant oil was purifed by column chromatography (90:10 hexanes/EtOAc) to afford 456 mg (0.87 mmol, 89% yield) of (2*S*,5*S*)-1-benzyloxy-5,7-di-*tert*-butyldimethylsilyloxy-2,4,4-trimethyl-3-heptanone (**8**) as a colourless oil. R_f (90:10 hexanes/EtOAc) 0.60. **[α]$_D$** +2.4 (c 1.20, $CHCl_3$). **IR** (ATR) ν 2954, 2928, 2855,

1701, 1471, 1360, 1252, 1093. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35–7.26 (5H, m, ArH), 4.48 (1H, d, *J* = 12.0 Hz, PhCH$_x$H$_y$), 4.42 (1H, d, *J* = 12.0 Hz, PhCH$_x$H$_y$), 4.06 (1H, dd, *J* = 7.9, 2.7 Hz, SiOCH), 3.70–3.55 (3H, m, BnOCH$_x$H$_y$ & SiOCH$_2$), 3.40–3.30 (2H, m, BnOCH$_x$H$_y$CH), 1.61–1.45 (2H, m, SiOCHCH$_2$), 1.13 (3H, s, CCH$_3$), 1.10 (3H, s, CCH$_3$), 1.04 (3H, d, *J* = 6.6 Hz, CHCH$_3$), 0.89 (9H, s, SiC(CH$_3$)$_3$), 0.88 (9H, s, SiC(CH$_3$)$_3$), 0.11 (3H, s, SiCH$_3$), 0.06 (3H, s, SiCH$_3$), 0.02 (6H, s, 2 × SiCH$_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 217.2 (C), 138.3 (C), 128.3 (CH), 127.5 (CH), 127.5 (CH), 73.3 (CH_2), 73.3 (CH_2), 72.6 (CH), 60.4 (CH_2), 53.9 (C), 41.4 (CH), 37.5 (CH_2), 26.1 (CH_3), 26.0 (CH_3), 22.6 (CH_3), 19.1 (CH_3), 18.4 (C), 18.3 (C), 15.4 (CH_3), –3.7 (CH_3), –4.0 (CH_3), –5.3 (CH_3), –5.3 (CH_3). **HRMS** (+ESI) *m/z* calcd. for $C_{29}H_{55}O_4Si_2$ $[M+H]^+$: 523.3633, found: 523.3632.

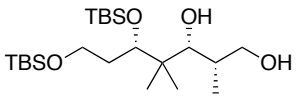
(2*S*,5*S*)-5,7-Di-*tert*-butyldimethylsilyloxy-1-hydroxy-2,4,4-trimethyl-3-heptanone (9).



9

A mixture of protected aldol adduct **8** (357 mg, 0.68 mmol) and $Pd(OH)_2/C$ (235 mg, 50 mol%) in THF (20 mL) was stirred at room temperature under a H_2 atmosphere (balloon) for 50 min. The reaction mixture was filtered through a pad of Celite® and eluted with CH_2Cl_2. The solvent was evaporated and the resulting oil was purified by column chromatography (90:10 hexanes/EtOAc) to afford 259 mg (0.6 mmol, 88% yield) of (2*S*,5*S*)-5,7-di-*tert*-butyldimethylsilyloxy-1-hydroxy-2,4,4-trimethyl-3-heptanone (**9**) as a colourless oil. R_f (90:10 hexanes/EtOAc) 0.20. **$[\alpha]_D$** –8.3 (*c* 1.85, $CHCl_3$). **IR** (ATR) ν 3446, 2957, 2928, 2900, 2858, 1696, 1471, 1387, 1253, 1079. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.02 (1H, dd, *J* = 7.8, 2.5 Hz, SiOCH), 3.79–3.56 (4H, m, HOCH$_2$ & SiOCH$_2$), 3.26 (1H, qd, *J* = 7.0, 4.3 Hz, CHCH$_3$), 2.29 (1H, t, *J* = 5.7 Hz, OH), 1.70–1.56 (1H, m, SiOCH$_2$CH$_x$H$_y$), 1.56–1.43 (1H, m , SiOCH$_2$CH$_x$H$_y$), 1.16 (3H, s CCH$_3$), 1.13 (3H, s CCH$_3$), 1.09 (3H, d, *J* = 7.0 Hz, CHCH$_3$), 0.90 (9H, s, SiC(CH$_3$)$_3$), 0.89 (9H, s, SiC(CH$_3$)$_3$), 0.12 (3H, s, SiCH$_3$), 0.08 (3H, s, SiCH$_3$), 0.04 (3H, s, SiCH$_3$), 0.03 (3H, s, SiCH$_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 219.8 (C), 73.6 (CH), 65.3 (CH_2), 60.2 (CH_2), 53.8 (C), 43.1 (CH), 37.5 (CH_2), 26.1 (CH_3), 25.9 (CH_3), 22.6 (CH_3), 19.8 (CH_3), 18.4 (C), 18.3 (C) 14.8 (CH_3), –3.7 (CH_3), –4.0 (CH_3), –5.3 (CH_3), –5.3 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{22}H_{49}O_4Si_2$ $[M+H]^+$: 433.3164, found: 433.3155.

(2*S*,3*R*,5*S*)-5,7-Di-*tert*-butyldimethylsilyloxy-2,4,4-trimethyl-1,3-heptandiol (10).

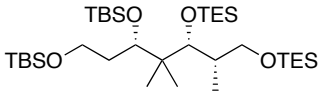


10

A mixture of $(Me_4N)HB(OAc)_3$ (1.79 g, 6.8 mmol) in 1:1 AcOH/CH_3CN (6 mL) was stirred at room temperature until it became a clear solution (*ca* 15 min). It was cooled at 0 °C and a solution of hydroxy ketone **9** (255 mg, 0.6 mmol) in CH_3CN (3 mL) was added dropwise. The resultant mixture was stirred for 10 min at 0 °C, 7 h at room temperature, and cooled again at 0 °C. The reaction was then quenched with a 1 M solution of Rochelle salt (2.5 mL), stirred for 1 h at room temperature and carefully partitioned with EtOAc (15 mL) and sat $NaHCO_3$ (10 mL). The aqueous layer was extracted

with EtOAc (2 × 35 mL) and the combined organic extracts were washed with $NaHCO_3$ (35 mL), brine (35 mL), dried ($MgSO_4$), and concentrated . The resulting oil was purified by column chromatography (from 9:1 to 7:3 hexanes/EtOAc) to afford 237 mg (0.55 mmol, 93% yield) of a 92:8 diastereomeric mixture of (2*S*,3*R*,5*S*)-5,7-di-*tert*-butyldimethylsilyloxy-2,4,4-trimethyl-1,3-heptandiol (**10**) as a colourless oil. R_f (70:30 hexanes/EtOAc) 0.45. $[\alpha]_D$ +1.4 (*c* 1.35, $CHCl_3$). **IR** (ATR) ν 3367, 2954, 2928, 2883, 2856, 1471, 1388, 1253, 1080. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.79–3.62 (5H, m, 5 × C$\underline{H}$O), 3.59 (1H, dd, *J* = 10.3, 5.2 Hz, $CH_x\underline{H}_y$OH), 2.05–1.95 (1H, m, SiOCH_2C$\underline{H}_x$H$_y$), 1.94–1.85 (1H, m, C$\underline{H}$CH_2OH), 1.54 (1H, ddd, *J* = 14.5, 10.0, 4.8 Hz, SiOCH_2C$H_x\underline{H}_y$), 1.05 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$), 0.95 (3H, s, CC$\underline{H}_3$), 0.90 (18H, s, 2 × OSiC(C$\underline{H}_3$)$_3$), 0.81 (3H, s, CC$\underline{H}_3$), 0.09 (6H, s, 2 × SiC$\underline{H}_3$), 0.07 (6H, s, 2 × SiC$\underline{H}_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 77.7 (CH), 77.3 (CH), 70.0 (CH_2), 61.5 (CH_2), 43.0 (C), 36.6 (CH_2), 35.7 (CH), 26.0 (CH_3), 26.0 (CH_3), 20.0 (CH_3), 18.9 (CH_3), 18.3 (C), 18.3 (C), 11.3 (CH_3), –3.6 (CH_3), –4.3 (CH_3), –5.3 (CH_3), –5.4 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{22}H_{51}O_4Si_2$ $[M+H]^+$: 435.3320, found: 435.3326.

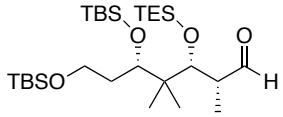
(2*S*,3*R*,5*S*)-5,7-Di-*tert*-butyldimethylsilyloxy-1,3-ditriethylsililoxy-2,4,4-trimethylheptane (11).



11

A mixture of diol **10** (100 mg, 0.23 mmol), 2,6-lutidine (161 μL, 1.4 mmol), and TESOTf (208 μL, 0.9 mmol) in CH_2Cl_2 (2.5 mL) was stirred at 0 °C for 2 h. The reaction was quenched by the addition of sat NH_4Cl (5 mL) and diluted with CH_2Cl_2 (40 mL). The organic layer was washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The resulting oil was purified by column chromatography (95:5 hexanes/EtOAc) to afford 136 mg (0.205 mmol, 89% yield) of (2*S*,3*R*,5*S*)-5,7-di-*tert*-butyldimethylsilyloxy-1,3-ditriethylsilyloxy-2,4,4-trimethylheptane (**11**) as a cololurless oil. R_f (95:5 hexanes/EtOAc) 0.65. $[\alpha]_D$ –3.9 (*c* 0.60, $CHCl_3$). **IR** (ATR) ν 2953, 2929, 2877, 2857, 1471, 1462, 1386, 1252, 1077, 1002. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.81 (1H, s, TESOC$\underline{H}$), 3.71 (1H, td, *J* = 9.1, 4.9 Hz, TBSOC$\underline{H}_x$H$_y$), 3.65–3.54 (2H, m, TBSOC$\underline{H}$ & TBSOC$H_x\underline{H}_y$), 3.38 (1H, t, *J* = 9.1 Hz, C$\underline{H}_x$H$_y$OTES), 3.31 (1H, dd, *J* = 9.1, 7.1 Hz, $CH_x\underline{H}_y$OTES), 2.22–2.10 (1H, m, C$\underline{H}$CH$_3$), 1.97–1.86 (1H, m, TBSOCHC$\underline{H}_x$H$_y$), 1.69–1.59 (1H, m, TBSOCHC$H_x\underline{H}_y$), 1.00–0.93 (18H, m, 2 × Si(CH_2C$\underline{H}_3$)$_3$), 0.89 (18H, s, 2 × SiC(C$\underline{H}_3$)$_3$), 0.85 (6H, s, C(C$\underline{H}_3$)$_2$), 0.81 (3H, d, *J* = 6.7 Hz, CHC$\underline{H}_3$), 0.63 (6H, q, *J* = 8.0 Hz, Si(C$\underline{H}_2$CH$_3$)$_3$), 0.59 (6H, q, *J* = 7.9 Hz, Si(C$\underline{H}_2$CH$_3$)$_3$), 0.06 (3H, s, SiC$\underline{H}_3$), 0.05 (3H, s, SiC$\underline{H}_3$), 0.04 (6H, s, 2 × SiCH$_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 75.8 (CH), 75.2 (CH), 67.1 (CH_2), 61.3 (CH_2), 44.2 (C), 37.1 (CH), 36.2 (CH_2), 26.2 (CH_3), 26.0 (CH_3), 24.5 (CH_3), 20.0 (CH_3), 18.4 (C), 18.3 (C), 11.7 (CH_3), 7.2 (CH_3), 6.8 (CH_3), 5.7 (CH_2), 4.5 (CH_2), –3.5 (CH_3), –3.8 (CH_3), –5.3 (2 × CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{28}H_{65}O_4Si_3$ $[M–TES]^+$: 549.4185, found: 549.4181.

(2*R*,3*R*,5*S*)-5,7-Di-*tert*-butyldimethylsilyloxy-2,4,4-trimethyl-3-triethylsilyloxyheptanal (12).

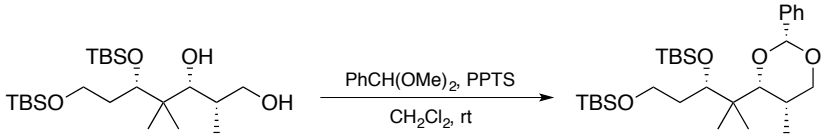


12

DMSO (30 μL, 0.42 mmol) was added dopwise to a solution of oxalyl chloride (19 μL, 0.21 mmol) in CH_2Cl_2 (1 mL) at –78 °C and the resultant mixture was stirred for 30 min at –78 °C. Then, a solution of **11** (32 mg, 48 μmol) in CH_2Cl_2 (1 mL) was added and stirring continued for 10 min at –78 °C and 2 h at –40 °C. It was cooled again at –78 °C and Et_3N (100 μL, 0.72 mmol) was added. The reaction mixture was stirred for 5 min at –78 °C and at room temperature for 2 h.

The mixture was partitioned with CH_2Cl_2 (5 mL) and water (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic extracts were washed with water (2 × 10 mL), dried ($MgSO_4$), and concentrated. The resulting oil was filtered through a short pad of silica (95:5 hexanes/EtOAc) to afford 22 mg (40 μmol, 83% yield) of (2*R*,3*R*,5*S*)-5,7-di-*tert*-butyldimethylsilyloxy-2,4,4-trimethyl-3-triethylsilyloxyheptanal (**12**) as a colourless oil, which was used without further purification. R_f (95:5 hexanes/EtOAc) 0.60. $[\alpha]_D$ –7.4 (*c* 0.60, $CHCl_3$). **IR** (ATR) ν 2954, 2929, 2878, 2857, 1724, 1471, 1462, 1253, 1091, 1070, 1002. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.66 (1H, s, C<u>H</u>O), 4.35 (1H, d, *J* = 1.6 Hz, TESOC<u>H</u>), 3.75–3.56 (3H, m, TBSOC<u>H</u>$_2$ & TBSOC<u>H</u>), 2.97 (1H, qd, *J* = 7.1, 1.6 Hz, C<u>H</u>CH$_3$), 2.01–1.88 (1H, m, TBSOCH$_2$C<u>H</u>$_x$H$_y$), 1.56– 1.48 (1H, m, TBSOCH$_2$CH$_x$<u>H</u>$_y$), 1.16 (3H, d, *J* = 7.1 Hz, CHC<u>H</u>$_3$), 0.94 (9H, t, *J* = 7.9 Hz, OSi(CH$_2$C<u>H</u>$_3$)$_3$), 0.91 (3H, s, CC<u>H</u>$_3$), 0.89 (12H, s, CC<u>H</u>$_3$ & SiC(C<u>H</u>$_3$)$_3$), 0.88 (9H, s, SiC(C<u>H</u>$_3$)$_3$), 0.57 (6H, q, *J* = 7.9 Hz, Si(C<u>H</u>$_2$CH$_3$)$_3$), 0.08 (3H, s, SiC<u>H</u>$_3$), 0.05 (9H, s, 3 × SiC<u>H</u>$_3$). **HRMS** (+ESI) *m/z* calcd for $C_{28}H_{66}NO_4Si_3$ $[M+NH_4]^+$: 564.4294, found: 564.4284.

Proof of the stereochemistry of diol 10

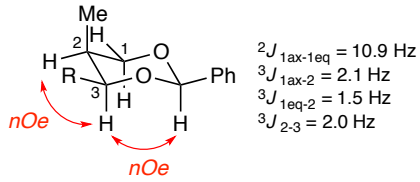


10 **25**

A mixture of diol **10** (15 mg, 34 μmol), $PhCH(OMe)_2$ (13 μL, 90 μmol) and PPTS (a crystal) in CH_2Cl_2 (0.7 mL) was stirred for 1 h at room temperature. The reacting mixture was partitioned with CH_2Cl_2 (2 mL) and sat $NaHCO_3$ (2 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water (15 mL) and brine (15 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (from 90:10 to 80:20 hexanes/EtOAc) to afford 15 mg (29 μmol, 83% yield) of (2*R*,4*R*,5*S*)-4-[(3*S*)-3,5-di-*tert*-butyldimethylsilyloxy-2-methyl-2-pentyl]-5-methyl-2-phenyl-1,3-dioxane (**25**) as a colourless oil. R_f (90:10 hexanes/EtOAc) 0.65. **IR** (ATR) ν 2954, 2927, 2855, 1471, 1462, 1386, 1251, 1113, 1082, 1005. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53–7.47 (2H, m, Ar<u>H</u>), 7.39–7.27 (3H, m, Ar<u>H</u>), 5.52 (1H, s, C<u>H</u>Ph), 4.08 (1H, dd, *J* = 10.9, 2.1 Hz, CHC<u>H</u>$_x$H$_y$O), 4.04 (1H, d, *J* = 2.0 Hz, CHC<u>H</u>O), 3.96 (1H, dd, *J* = 10.9, 1.5 Hz, CHCH$_x$<u>H</u>$_y$O), 3.68 (1H, ddd, *J* = 10.0, 7.7, 4.8 Hz, TBSOC<u>H</u>$_x$H$_y$), 3.62–3.54 (2H, m, TBSOCH$_x$<u>H</u>$_y$CH$_2$C<u>H</u>), 1.98

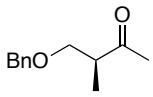
(1H, dtd, *J* = 14.5, 7.7, 2.8 Hz, TBSOCH$_2$CH$_x$H$_y$), 1.79–1.66 (1H, m, CHCH$_3$), 1.63–1.50 (1H, m, TBSOCH$_2$CH$_x$H$_y$), 1.28 (3H, d, *J* = 6.8 Hz, CHCH$_3$), 1.01 (3H, s, CCH$_3$), 0.93 (3H, s, CCH$_3$), 0.92 (9H, s, SiC(CH$_3$)$_3$), 0.87 (9H, s, SiC(CH$_3$)$_3$), 0.09 (3H, s, SiCH$_3$), 0.07 (3H, s, SiCH$_3$), 0.02 (3H, s, SiCH$_3$), 0.01 (3H, s, SiCH$_3$). **^{13}C NMR** (100.6 MHz, CDCl$_3$) δ 139.4 (C), 128.4 (CH), 128.1 (CH), 126.0 (CH), 101.8 (CH), 81.5 (CH), 76.3 (2 × CH$_2$), 61.0 (CH$_2$), 42.3 (C), 37.0 (CH$_2$), 31.2 (CH), 26.2 (CH$_3$), 25.9 (CH$_3$), 21.5 (CH$_3$), 21.1 (CH$_3$), 18.5 (C), 18.2 (C), 14.1 (CH$_3$), –3.5 (CH$_3$), –4.0 (CH$_3$), –5.2 (CH$_3$), –5.3 (CH$_3$).

^{1}H NMR Analyses and NOESY studies indicated the stereochemistry shown below



3. Synthesis of the *southern* fragment

(*S*)-4-Benzyloxy-3-methyl-2-butanone (3).

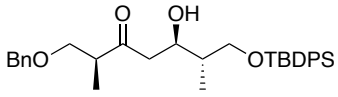


3

A 1.4 M solution of MeMgCl in toluene/THF (11.2 mL, 15.8 mmol) was slowly added to a solution of **4** (1.864 g, 7.8 mmol)in THF (30 mL) at 0 °C and the resulting mixture was stirred for 2 h at 0 °C. It was quenched with sat NH$_4$Cl (20 mL) and the mixture was stirred vigorously for 10 min at room temperature. The aqueous layer was extracted with Et$_2$O (3 × 40 mL) and the combined organic extracts were washed with brine (40 mL), dried (MgSO$_4$), and concentrated. The residue was purified by column chromatography (90:10 hexanes/EtOAc) to afford 1.298 g (6.75 mmol, 86% yield) of (*S*)-4-benzyloxy-3-methyl-2-butanone (**3**) as a colourless oil. R_f (90:10 hexanes/EtOAc) 0.20. **[α]$_D$** +22.3 (c 1.25, CHCl$_3$) [lit.[3] **[α]$_D$** +16.6 (c 8.70, CHCl$_3$)]. **IR** (ATR) ν 2860, 1715, 1454, 1360, 1179, 1098. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.35–7.25 (5H, m, ArH), 4.50 (1H, d, *J* = 12.1 Hz, PhCH$_x$H$_y$), 4.49 (1H, d, *J* = 12.1 Hz, PhCH$_x$H$_y$), 3.63 (1H, dd, *J* = 9.2, 7.6 Hz, BnOCH$_x$H$_y$), 3.48 (1H, dd, *J* = 9.2, 5.5 Hz, BnOCH$_x$H$_y$), 2.90–2.82 (1H, m, CHCH$_3$), 2.18 (3H, s, COCH$_3$), 1.10 (3H, d, *J* = 7.1 Hz, CHCH$_3$). **^{13}C NMR** (100.6 MHz, CDCl$_3$) δ 211.0 (C), 138.0 (C), 128.3 (CH), 127.6 (CH), 127.5 (CH), 73.2 (CH$_2$), 72.0 (CH$_2$), 47.1 (CH), 28.9 (CH$_3$), 13.3 (CH$_3$).

[3] I. Paterson, J. M. Goodman and M. Isaka, *Tetrahedron Lett.*, 1989, **30**, 7121.

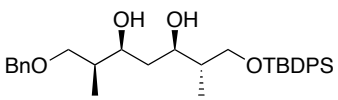
(2*S*,5*R*,6*S*)-1-Benzyloxy-7-*tert*-butyldiphenylsilyloxy-5-hydroxy-2,6-dimethyl-3-heptanone (14).



14

Neat $TiCl_4$ (0.4 mL, 3.6 mmol) was added dropwise to a solution of ketone **3** (688 mg, 3.6 mmol) in CH_2Cl_2 (13 mL) at –78 °C and the resulting yellow mixture was stirred for 3 min. Then, *i*-Pr_2NEt (0.7 mL, 4.0 mmol) was carefully added, and the ensuing dark red solution was stirred for 30 min at –78 °C followed by addition of neat $TiCl_4$ (0.4 mL, 3.6 mmol). After stirring for 10 min, a solution of (*S*)-3-*tert*-butyldiphenylsilyloxy-2-methylpropanal[4] (1.3 g, 4.0 mmol) in CH_2Cl_2 (2.5 & 2.5 mL) was slowly added, and the reaction mixture was stirred for 30 min at –78 °C. The mixture was quenched by addition of sat NH_4Cl (20 mL), diluted with Et_2O (100 mL), and washed with H_2O (75 mL), sat $NaHCO_3$ (75 mL), and brine (75 mL). The aqueous layers were extracted with Et_2O (2 × 100 mL), and the combined organic extracts were dried ($MgSO_4$), and concentrated. The resulting oil was analyzed by HPLC and NMR and purified by column chromatography (from 95:5 to 70:30 hexanes/EtOAc) to afford 1.474 g (2.84 mmol, 79% yield) of (2*S*,5*R*,6*S*)-1-benzyloxy-7-*tert*-butyldiphenylsilyloxy-5-hydroxy-2,6-dimethyl-3-heptanone (**14**) as a colourless oil. R_f (70:30 hexanes/EtOAc) 0.50. **HPLC** (hexane/*i*-PrOH 95:5) t_R 8.7 min. $[\alpha]_D$ +24.0 (c 1.3, $CHCl_3$). **IR** (ATR) ν 3497, 3070, 2961, 2931, 2858, 1709, 1472, 1428, 1112. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68–7.65 (4H, m, ArH), 7.44–7.25 (11H, m, ArH), 4.49 (1H, d, *J* = 12.1 Hz, PhCH$_x$H$_y$), 4.45 (1H, d, *J* = 12.1 Hz, PhCH$_x$H$_y$), 4.17–4.11 (1H, m, CHOH), 3.71 (1H, dd, *J* = 10.2, 5.0 Hz, CH$_x$H$_y$OTBDPS), 3.66 (1H, dd, *J* = 10.2, 6.1Hz, CH$_x$H$_y$OTBDPS), 3.62 (1H, dd, *J* = 9.0, 8.0Hz, BnOCH$_x$H$_y$), 3.51 (1H d, *J* = 3.3Hz, OH), 3.47 (1H, dd, *J* = 9.0, 5.3 Hz, BnOCH$_x$H$_y$), 2.95–2.87 (1H, m, BnOCH$_2$CH), 2.73–2.62 (1H, m, COCH$_2$), 1.85–1.75 (1H, m, CHCH$_2$OTBDPS), 1.07 (3H, d, *J* = 7.0 Hz, BnOCH$_2$CHCH$_3$), 1.05 (9H, s, SiC(CH$_3$)$_3$), 0.88 (3H, d, *J* = 7.0 Hz, CH$_3$CHCH$_2$OTBDPS). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 213.9 (C), 137.9 (C), 135.6 (C), 133.3 (C), 129.7 (CH), 128.4 (CH), 127.7 (CH), 127.6 (CH), 73.3 (CH_2), 72.1 (CH_2), 70.3 (CH), 66.7 (CH_2), 46.9 (CH), 46.8 (CH_2), 40.2 (CH), 26.9 (CH_3), 19.2 (C), 13.3 (2 × CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{32}H_{43}O_4Si$ $[M+H]^+$: 519.2925, found 519.2925.

(2*S*,3*S*,5*R*,6*S*)-1-Benzyloxy-7-*tert*-butyldiphenylsilyloxy-2,6-dimethyl-3,5-heptandiol (15).



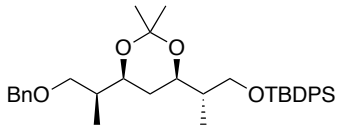
15

A 1 M solution of DIBALH in toluene (5.7 mL, 5.7 mmol) was added to a solution of aldol **14** (1.18 g, 2.3 mmol) in THF (45 mL) at –78 °C. After stirring for 2.5 h, the reaction was carefully quenched with a 1 M solution of Rochelle salt (30 mL) and the resulting mixture was stirred for 30 min at room temperature. The aqueous layer was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), and concentrated. The residue was purified

[4] This aldehyde was prepared according to R. W. Roush, A. D. Palkowitz and K. Ando, *J. Am. Chem. Soc.*, 1990, **112**, 6348.

by column chromatography (from 90:10 to 70:30 hexanes/EtOAc) to afford 211 mg (0.41 mmol, 17%) of the *anti* 1,3-diol isomer and 942 mg (1.81 mmol, 80% yield) of the desired *syn* 1,3-diol (2*S*,3*S*,5*R*,6*S*)-1-benzyloxy-7-*tert*-butyldiphenylsilyloxy-2,6-dimethyl-3,5-heptandiol (**15**) as a colourless oil. R_f (70:30 hexanes/EtOAc) 0.45. $[\alpha]_D$ +6.3 (*c* 0.70, $CHCl_3$). **IR** (ATR) ν 3432, 2959, 2930, 2856, 1454, 1427, 1104. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69–7.64 (4H, m, ArH), 7.48–7.28 (11H, m, ArH), 4.54 (1H, d, *J* = 12.0 Hz, PhCH$_x$H$_y$), 4.50 (1H, d, *J* = 12.0 Hz, PhCH$_x$H$_y$), 4.04 (1H, dt, *J* = 9.5, 2.7 Hz, BnOCH$_2$CHCHOH), 3.89 (1H, ddd, *J* = 9.6, 6.5, 2.7 Hz, HOCHCHCH$_2$OTBDPS), 3.74 (1H, dd, *J* = 10.3, 4.6 Hz, CH$_x$H$_y$OTBDPS), 3.63 (1H, dd, *J* = 10.3, 7.1 Hz, CH$_x$H$_y$OTBDPS), 3.56 (1H, dd, *J* = 9.0, 6.8 Hz, BnOCH$_x$H$_y$), 3.47 (1H, dd, *J* = 9.0, 5.3 Hz, BnOCH$_x$H$_y$), 1.94–1.84 (1H, m, BnOCH$_2$CH), 1.83–1.74 (1H, m, CHCH$_2$OTBDPS), 1.66–1.47 (2H, m, OCHCH$_2$CHO), 1.05 (9H, s, SiC(CH$_3$)$_3$), 0.95 (3H, d, *J* = 7.0 Hz, BnOCH$_2$CHCH$_3$), 0.85 (3H, d, *J* = 7.0 Hz, CH$_3$CHCH$_2$OTBDPS). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 138.3 (C), 135.6 (CH), 135.6 (CH), 133.0 (C), 133.0 (C), 129.8 (CH), 129.8 (CH), 128.4 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 77.0 (CH), 74.2 (CH), 73.9 (CH_2), 73.4 (CH_2), 68.1 (CH_2), 40.7 (CH), 39.0 (CH), 37.4 (CH_2), 26.8 (CH_3), 19.1 (C), 13.2 (CH_3), 11.3 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{32}H_{45}O_4Si$ $[M+H]^+$: 521.3082, found: 521.3084.

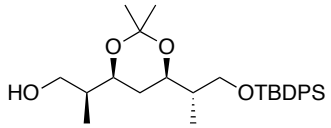
(2*S*,3*S*,5*R*,6*S*)-1-Benzyloxy-7-*tert*-butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethylheptane (16).



16

A mixture of diol **15** (1.04 g, 2.0 mmol) and a few crystals of PPTS in 1:1 CH_2Cl_2/$Me_2C(OMe)_2$ (20 mL) was stirred at room temperature for 16 h. The volatiles were removed *in vacuo* and the residue was purified by column chromatography (from 95:5 to 90:10 hexanes/EtOAc) to afford 1.008 g (1.79 mmol, 90% yield) of (2*S*,3*S*,5*R*,6*S*)-1-benzyloxy-7-*tert*-butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethylheptane (**16**) as a colourless oil. R_f (90:10 hexanes/EtOAc) 0.55. $[\alpha]_D$ +11.8 (*c* 0.90, $CHCl_3$). **IR** (ATR) ν 2930, 2856, 1427, 1378, 1105. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72–7.63 (4H, m, ArH), 7.47–7.26 (11H, m, ArH), 4.51 (1H, d, *J* = 12.1 Hz, PhCH$_x$H$_y$), 4.48 (1H, d, *J* = 12.1 Hz, PhCH$_x$H$_y$), 3.95–3.86 (2H, m, OCHCH$_2$CHO), 3.81 (1H, dd, *J* = 9.7, 4.6 Hz, SiOCH$_x$H$_y$), 3.54 (1H, dd, *J* = 9.7, 4.0 Hz, SiOCH$_x$H$_y$), 3.47 (1H, dd, *J* = 9.0, 6.4 Hz, BnOCH$_x$H$_y$), 3.34 (1H, dd, *J* = 9.0, 5.9 Hz, BnOCH$_x$H$_y$), 1.85–1.75 (1H, m, BnOCH$_2$CH), 1.73–1.61 (1H, m, SiOCH$_2$CH), 1.42–1.37 (1H, m, OCHCH$_x$H$_y$CHO), 1.40 (3H, s, CCH$_3$), 1.34 (3H, s, CCH$_3$), 1.29–1.17 (1H, m, OCHCH$_x$H$_y$CHO), 1.04 (9H, s, SiC(CH$_3$)$_3$), 0.95 (6H, d, *J* = 6.9 Hz, 2 × CHCH$_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 138.7 (C), 135.6 (CH), 135.6 (CH), 134.0 (C), 133.9 (C), 129.5 (CH), 129.4 (CH), 128.3 (CH), 127.6 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 98.3 (C), 73.1 (CH_2), 72.3 (CH_2), 69.6 (CH), 69.5 (CH), 64.6 (CH_2), 41.0 (CH), 38.7 (CH), 31.3 (CH_2), 30.2 (CH_3), 26.8 (CH_3), 19.9 (CH_3), 19.3 (C), 12.7 (CH_3), 12.2 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{35}H_{49}O_4Si$ $[M+H]^+$: 561.3395, found 561.3386.

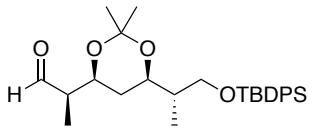
(2*S*,3*S*,5*R*,6*S*)-7-*tert*-Butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethyl-1-heptanol (17).



17

A mixture of **16** (700 mg, 1.25 mmol) and $Pd(OH)_2/C$ (449 mg, 50 mol%) in EtOH (35 mL) was stirred for 3 h at room temperature under a H_2 atmosphere (balloon). The resulting suspension was filtered (CH_2Cl_2) through Celite® and concentrated to produce 590 mg of (2*S*,3*S*,5*R*,6*S*)-7-*tert*-Butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethyl-1-heptanol (**17**) as a colourless oil, which was used without further purification. R_f (70:30 hexanes/EtOAc) 0.35. $[\alpha]_D$ +6.1 (*c* 0.75, $CHCl_3$). **IR** (ATR) ν 3463, 2988, 2967, 2929, 2900, 1380, 1216, 1076. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72–7.64 (4H, m, ArH), 7.45–7.33 (6H, m, ArH), 4.04 (1H, dt, *J* = 8.2, 3.9 Hz, $HOCH_2CHCHO$), 3.99–3.92 (1H, m, $OCHCHCH_2OTBDPS$), 3.82 (1H, dd, *J* = 9.8, 4.5 Hz, $CH_xH_yOTBDPS$), 3.75–3.67 (1H, m, $HOCH_xH_y$), 3.63–3.57 (1H, m, $HOCH_xH_y$), 3.55 (1H, dd, *J* = 9.8, 4.2 Hz, $CH_xH_yOTBDPS$), 2.75 (1H, s, OH), 1.96–1.85 (1H, m, $HOCH_2CH$), 1.78–1.63 (1H, m, $CHCH_2OTBDPS$), 1.42 (3H, s, CCH_3), 1.38–1.37 (2H, m, $OCHCH_2$), 1.36 (3H, s, CCH_3), 1.05 (9H, s, $SiC(CH_3)_3$), 0.97 (3H, d, *J* = 7.0 Hz, $CH_3CHCH_2OTBDPS$), 0.90 (3H, d, *J* = 7.2 Hz, $HOCH_2CHCH_3$). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 135.6 (CH), 135.6 (CH), 133.9 (C), 133.8 (C), 129.5 (CH), 129.5 (CH), 127.6 (CH), 127.5 (CH), 98.5 (C), 73.0 (CH), 69.4 (CH), 66.0 (CH_2), 64.5 (CH_2), 40.9 (CH), 38.8 (CH), 30.2 (CH_3), 29.1 (CH_2), 26.8 (CH_3), 19.6 (CH_3), 19.3 (C), 12.7 (CH_3), 11.6 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{28}H_{43}O_4Si$ $[M+H]^+$: 471.2925, found: 471.2925.

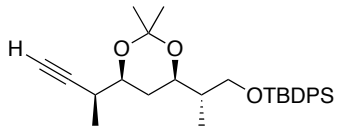
(2*R*,3*S*,5*R*,6*S*)-7-*tert*-Butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethylheptanal (18).



18

A mixture of alcohol **17** (590 mg, 1.25 mmol) and Dess-Martin periodinane (1.09 g, 2.5 mmol) in CH_2Cl_2 (20 mL) was stirred at room temperature for 1 h. Then, it was treated with sat $NaHCO_3$ (10 mL) and sat $Na_2S_2O_3$ (10 mL) and the resultant mixture was stirred vigorously for 15 min. The aqueous layer was extracted with Et_2O (2 × 30 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated to provide 570 mg of (2*R*,3*S*,5*R*,6*S*)-7-*tert*-butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethylheptanal (**18**) as a yellowish oil, which was used without further purification. R_f (90:10 hexanes/EtOAc) 0.35. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.75 (1H, d, *J* = 1.1 Hz, CHO), 7.71–7.65 (4H, m, ArH), 7.47–7.32 (6H, m, ArH), 4.22 (1H, ddd, *J* = 11.8, 4.8, 2.5 Hz, $OHCCHCHO$), 3.97 (1H, ddd, *J* = 11.0, 7.6, 2.3 Hz, $CHCHCH_2OTBDPS$), 3.82 (1H, dd, *J* = 9.8, 4.5 Hz, $CH_xH_yOTBDPS$), 3.53 (1H, dd, *J* = 9.8, 4.3 Hz, $CH_xH_yOTBDPS$), 2.51–2.36 (1H, m, $OHCCH$), 1.77–1.62 (1H, m, $CHCH_2OTBDPS$), 1.51–1.44 (2H, m, $OCHCH_2$), 1.43 (3H, s, CCH_3), 1.35 (3H, s, CCH_3), 1.10 (3H, d, *J* = 7.1 Hz, $OHCCHCH_3$), 1.05 (9H, s, $SiC(CH_3)_3$), 0.95 (3H, d, *J* = 7.0 Hz, $CH_3CHCH_2OTBDPS$).

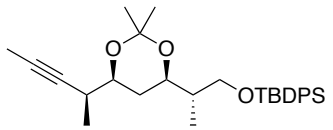
(2*S*,3*R*,5*S*,6*S*)-1-*tert*-Butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethyl-7-octyne (20)



20

A freshly prepared 3 M solution of MeONa in MeOH (833 μL, 2.5 mmol) was added to a solution of the Ohira-Bestmann reagent (480 mg, 2.5 mmol) in THF (10 mL) at –78 °C. The solution was stirred for 15 min at –78 °C and a solution of the previously prepared aldehyde **18** (570 mg) in THF (8 mL) was dropwise added. After 5 min at –78 °C, the resultant mixture was stirred for 1 h at –40 °C. The reaction was quenched by addition of sat NH_4Cl (2 mL) and further diluted with water (20 mL). The aqueous layer was extracted with Et_2O (2 × 20 mL) and the combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (97:3 hexanes/EtOAc) to afford 400 mg (0.86 mmol, 69% yield over three steps) of (2*S*,3*R*,5*S*,6*S*)-1-*tert*-butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethyl-7-octyne (**20**) as a colourless oil. R_f (90:10 hexanes/EtOAc) 0.60. **[α]D** –3.6 (*c* 1.9, $CHCl_3$). **IR** (ATR) ν 3308, 2961, 2931, 2857, 1428, 1215, 1105. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72–7.63 (4H, m, ArH), 7.46–7.33 (6H, m, ArH), 3.95 (1H, ddd, *J* = 11.5, 7.6, 2.3 Hz, CHCHCH$_2$OTBDPS), 3.83 (1H, dd, *J* = 9.7, 4.5 Hz, CH$_x$H$_y$OTBDPS), 3.64 (1H, ddd, *J* = 11.5, 7.9, 2.3 Hz, HCCCHCHO), 3.56 (1H, dd, *J* = 9.7, 4.2 Hz, CH$_x$H$_y$OTBDPS), 2.49–2.42 (1H, m, CCCH), 2.09 (1H, d, *J* = 2.4 Hz, HCC), 1.87 (1H, dt, *J* = 12.7, 2.4 Hz, OCHCH$_x$H$_y$), 1.76–1.67 (1H, m, CHCH$_2$OTBDPS), 1.41 (3H, s, CCH$_3$), 1.37 (3H, s, CCH$_3$), 1.23–1.16 (1H, m, OCHCH$_x$H$_y$), 1.22 (3H, d, *J* = 6.9 Hz, CCCHCH$_3$), 1.04 (9H, s, SiC(CH$_3$)$_3$), 0.98 (3H, d, *J* = 7.0 Hz, CH$_3$CHCH$_2$OTBDPS). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 135.6 (CH), 135.6 (CH), 134.0 (C), 133.9 (C), 129.5 (CH), 129.5 (CH), 127.6 (CH), 127.5 (CH), 98.6 (C), 85.7 (C), 72.2 (CH), 70.2 (CH), 69.4 (CH), 64.5 (CH_2), 40.9 (CH), 32.3 (CH), 31.9 (CH_2), 30.1 (CH_3), 26.8 (CH_3), 19.8 (CH_3), 19.3 (C), 17.1 (CH_3), 12.6 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{29}H_{41}O_3Si$ $[M+H]^+$: 465.2819, found: 465.2812.

(2*S*,3*R*,5*S*,6*S*)-1-*tert*-Butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethyl-7-nonyne (21).

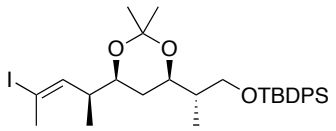


21

A mixture of alkyne **20** (80 mg, 0.18 mmol) and a 1.6 M solution of *n*-BuLi in hexanes (131 μL, 0.21 mmol) in THF (10 mL) was stirred for 30 min at –78 °C. Then, MeI (55 μL, 0.88 mmol) was added and the resulting solution was stirred for 4 h at room temperature. The reaction was quenched by addition of sat NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (2 × 20 mL) and the combined extracts were washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated. The resiude was purified by column chromatography (from 95:5 to 90:10 hexanes/EtOAc) to afford 72 mg (0.15 mmol, 87% yield) of (2*S*,3*R*,5*S*,6*S*)-1-*tert*-butyldiphenylsilyloxy-3,5-isopropilidendioxy-2,6-dimethyl-7-nonyne (**21**) as a colourless oil. R_f(90:10 hexanes/EtOAc) 0.60. **[α]D** –5.8 (*c* 1.10, $CHCl_3$). **IR** (ATR) ν

2992, 1960, 2930, 2856, 1427, 1379, 1200, 1110. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70–7.64 (4H, m, ArH), 7.46–7.30 (6H, m, ArH), 3.94 (1H, ddd, *J* = 11.4, 7.8, 2.5 Hz, CHCHCH$_2$OTBDPS), 3.83 (1H, dd, *J* = 9.7, 4.4 Hz, CH$_x$H$_y$OTBDPS), 3.62–3.52 (1H, m, CCCHCH), 3.56 (1H, dd, *J* = 9.7, 4.6 Hz, CH$_x$H$_y$OTBDPS), 2.42–2.32 (1H, m, CCCH), 1.87 (1H, dt, *J* = 12.8, 2.4 Hz, OCHCH$_x$H$_y$), 1.79 (3H, d, *J* = 1.2 Hz, CH$_3$CC), 1.74–1.66 (1H, m, CHCH$_2$OTBDPS), 1.40 (3H, s, CCH$_3$), 1.37 (3H, s, CCH$_3$), 1.21–1.13 (1H, m, OCHCH$_x$H$_y$), 1.17 (3H, d, *J* = 7.1 Hz, CCCHCH$_3$), 1.05 (9H, s, SiC(CH$_3$)$_3$), 0.99 (3H, d, *J* = 6.9 Hz, CH$_3$CHCH2OTBDPS). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 135.6 (CH), 135.6 (CH), 134.0 (C), 133.9 (C), 129.5 (CH), 129.5 (CH), 127.6 (CH), 127.5 (CH), 98.5 (C), 80.4 (C), 77.6 (C), 72.7 (CH), 69.4 (CH), 64.6 (CH_2), 40.9 (CH), 32.6 (CH), 32.1 (CH_2), 30.2 (CH_3), 26.8 (CH_3), 19.8 (CH_3), 19.3 (C), 17.6 (CH_3), 12.7 (CH_3), 3.6 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{30}H_{43}O_3Si$ $[M+H]^+$: 479.2976, found: 479.2972.

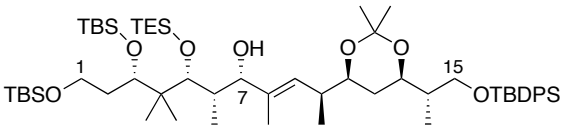
(2*S*,3*R*,5*S*,6*S*,7*E*)-1-*tert*-Butyldiphenylsilyloxy-8-iodo-3,5-isopropilidendioxy-2,6-dimethyl-7-nonene (22).



22

A mixture of **21** (71 mg, 0.15 mmol) and Cp_2ZrHCl (101 mg, 0.40 mmol) in THF (3 mL) was heated for 30 min at 40 °C protected from light. It was cooled at room temperature and a iodine solution (76 mg, 0.30 mmol) en THF (1.5 mL) was added. The resulting mixture was stirred for 30 min at room temperature and cooled to 0 °C. Then, the reaction was quenched by addition of sat $Na_2S_2O_3$ (3 mL) and was partitioned between water (20 mL) and CH_2Cl_2 (20 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were washed with 1 M HCl (20 mL), sat $NaHCO_3$ (20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated. The resultant oil was purified by column chromatography (90:10 hexanes/EtOAc) to afford 80 mg (0.13 mmol, 89% yield) of (2*S*,3*R*,5*S*,6*S*,7*E*)-1-*tert*-butyldiphenylsilyloxy-8-iodo-3,5-isopropilidendioxy-2,6-dimethyl-7-nonene (**22**) as a yellowish oil. ***R*$_f$** (90:10 hexanes/EtOAc) 0.60. **[α]$_D$** −14.8 (*c* 0.80, $CHCl_3$). **IR** (ATR) ν 2954, 2929, 3071, 3050, 2993, 2959, 2930, 2857, 1472, 1427, 1378, 1215, 1110. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70–7.64 (4H, m, ArH), 7.48–7.32 (6H, m, ArH), 5.97 (1H, dq, *J* = 10.1, 1.5 Hz, C=CH), 3.89 (1H, ddd, *J* = 11.5, 7.4, 2.3 Hz, OCHCHCH$_2$OTBDPS), 3.81 (1H, dd, *J* = 9.8, 4.6 Hz, CH$_x$H$_y$OTBDPS), 3.54 (1H, dd, *J* = 9.8, 4.4 Hz, CH$_x$H$_y$OTBDPS), 3.51 (1H, ddd, *J* = 11.5, 7.5, 2.6 Hz, =CHCHCH), 2.38 (3H, d, *J* = 1.5 Hz, CH$_3$C(I)=), 2.43–2.33 (1H, m, =CHCH), 1.74–1.63 (1H, m, CHCH$_2$OTBDPS), 1.49 (1H, dt, *J* = 12.7, 2.4 Hz, OCHCH$_x$H$_y$), 1.39 (3H, s, CCH$_3$), 1.36 (3H, s, CCH$_3$), 1.05 (9H, s, SiC(CH$_3$)$_3$), 1.07–1.04 (1H, m, OCHCH$_x$H$_y$) 0.99 (3H, d, *J* = 6.7 Hz, C=CHCHCH$_3$), 0.95 (3H, d, *J* = 7.0 Hz, CH$_3$CHCH$_2$OTBDPS). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 142.9 (CH), 135.6 (CH), 135.6 (CH), 134.0 (C), 133.8 (C), 129.5 (CH), 129.5 (CH), 127.6 (CH), 127.5 (CH), 98.4 (C), 94.5 (C), 72.2 (CH), 69.4 (CH), 64.5 (CH_2), 41.5 (CH), 40.9 (CH), 31.9 (CH_2), 30.3 (CH_3), 30.2 (CH_3), 28.1 (CH_3), 26.8 (CH_3), 19.8 (CH_3), 19.3 (C), 16.1 (CH_3), 12.7 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{30}H_{44}IO_3Si$ $[M+H]^+$: 607.2099, found: 607.2104.

4. Coupling of the *northern* and the *southern* fragment



24

Via transmetallation with $ZnMe_2$

A mixture of **22** (25 mg, 40 μmol) and a 1.7 M solution of *tert*-BuLi in pentane (46 μL, 80 μmol) in Et_2O (0.7 mL) was stirred at –78 °C for 1 h. A 2 M solution of $ZnMe_2$ in toluene (33 μL, 40 μmol) was added and the resultant mixture was stirred for 15 min. Finally, a solution of aldehyde **12** (20 mg, 36.5 μmol) in Et_2O (2 × 0.4 mL) was carefully added and the resultant mixture was further stirred for 2 h at –78 °C. The reaction was quenched with water (1 mL) and the mixture was partitioned with Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (from 80:20 hexanes/CH_2Cl_2 to CH_2Cl_2) to afford 26 mg (25 μmol, 70% yield) of a 60:40 mixture of (3*S*,5*R*,6*R*,7*S*,8*E*,10*S*,11*S*,13*R*,14*S*)-1,3-bis-*tert*-butyldimethylsilyloxy-15-*tert*-butyldiphenylsilyloxy-5-trietylsilyloxy-11,13-isopropilidendioxy-4,4,6,8,10,14-hexamethyl-8-pentadecen-7-ol (**24**) and the C-7 epimer (***epi*-24**).

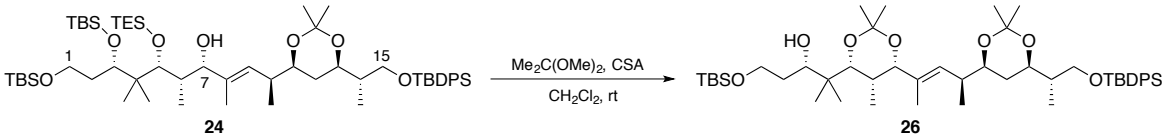
Via alkenyl lithium

A mixture of **22** (38 mg, 60 μmol) and a 1.7 M solution of *n*-BuLi in pentane (67 μL, 0.11 mmol) in Et_2O (1 mL) was stirred at –78 °C for 1 h. Then, a solution of aldehyde **12** (17 mg, 30 μmol) in Et_2O (2 × 0.5 mL) was carefully added and the resultant mixture was further stirred for 2 h at –78 °C. The reaction was quenched with methanol (1 mL) and sat $NaHCO_3$ (1 mL) and the mixture was partitioned with Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (10 mL) and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (from 75:25 hexanes/CH_2Cl_2 to CH_2Cl_2) to afford 24 mg (23 μmol, 76% yield) of a 60:40 mixture of (3*S*,5*R*,6*R*,7*S*,8*E*,10*S*,11*S*,13*R*,14*S*)-15-*tert*-butyldiphenylsilyloxy-1,3-bis-*tert*-butyldimethylsilyloxy-5-trietylsilyloxy-11,13-isopropilidendioxy-4,4,6,8,10,14-hexamethyl-8-pentadecen-7-ol (**24**) and the C-7 epimer (***epi*-24**).

Further purification permitted to isolate 10 mg of pure **24** as a colourless oil. $\boldsymbol{R_f}$(CH_2Cl_2) 0.80. $\boldsymbol{[\alpha]_D}$ +6.6 (*c* 0.50, $CHCl_3$). **IR** (ATR) ν 2955, 2928, 2856, 1461, 1379, 1361, 1253, 1087, 1002. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72–7.62 (4H, m, ArH), 7.46–7.32 (6H, m, ArH), 5.25 (1H, d, *J* = 9.7 Hz, C=CH), 3.91 (1H, d, *J* = 3.1 Hz, TESOCH), 3.86 (1H, ddd, *J* = 11.5, 7.7, 2.2 Hz, OCHCHCH$_2$OTBDPS), 3.81 (1H, dd, *J* = 9.7, 4.6 Hz, CH$_x$H$_y$OTBDPS), 3.77–3.71 (2H, m, TBSOCH$_x$H$_y$ & CHOH), 3.74 (1H, s, OH), 3.69 (1H, dd, *J* = 8.7, 1.9 Hz, TBSOCH), 3.66–3.60 (1H, m, C=CHCHCH), 3.58–3.52 (1H, m, TBSOCH$_x$H$_y$), 3.55 (1H, dd, *J* = 9.7, 4.0 Hz, CH$_x$H$_y$OTBDPS), 2.47–2.35 (1H, m, C=CHCH), 2.23–2.12 (1H, m, TESOCHCH), 2.05–1.95 (1H, m, TBSOCH$_2$CH$_x$H$_y$), 1.68–1.61 (1H, m, CHCH$_2$OTBDPS), 1.58 (3H, d, *J* = 0.9 Hz, C(CH$_3$)=CH), 1.56–1.50 (1H, m, C=CHCHCHCH$_x$H$_y$), 1.40 (3H, s, O$_2$CCH$_3$), 1.37 (3H, s, O$_2$CCH$_3$), 1.33–1.27 (1H, m, TBSOCH$_2$CH$_x$H$_y$),

1.04 (9H, s, $SiPh_2C(C\underline{H}_3)_3$), 1.05–1.00 (4H, m, $C{=}CHCH(C\underline{H}_3)CHCH_x\underline{H}_y$), 1.00 (9H, t, *J* = 8.0 Hz, $Si(CH_2C\underline{H}_3)_3$), 0.95 (3H, d, *J* = 6.9 Hz, $C\underline{H}_3CHCH_2OTBDPS$), 0.89 (9H, s, $SiMe_2C(C\underline{H}_3)_3$), 0.89 (9H, s, $SiMe_2C(C\underline{H}_3)_3$), 0.85 (3H, s, $CC\underline{H}_3$), 0.84 (3H, s, $CC\underline{H}_3$), 0.77 (3H, d, *J* = 7.0 Hz, $TESOCHCHC\underline{H}_3$), 0.73–0.67 (6H, m, $Si(C\underline{H}_2CH_3)_3$), 0.07 (3H, s, $SiC\underline{H}_3$), 0.05 (3H, s, $SiC\underline{H}_3$), 0.04 (3H, s, $SiC\underline{H}_3$), 0.04 (3H, s, $SiC\underline{H}_3$). **^{13}C NMR** (125.0 MHz, $CDCl_3$) δ 136.7 (C), 135.6 (CH), 135.6 (CH), 134.0 (C), 133.9 (C), 129.5 (CH), 129.4 (CH), 127.6 (CH), 127.5 (CH), 127.1 (CH), 98.3 (C), 80.7 (CH), 80.3 (CH), 74.5 (CH), 73.2 (CH), 69.5 (CH), 64.6 (CH_2), 61.3 (CH_2), 45.0 (C), 41.1 (CH), 38.4 (CH), 36.0 (CH), 32.7 (CH_2), 31.9 (CH_2), 30.2 (CH_3), 29.7 (CH_3), 26.8 (CH_3), 26.2 (CH_3), 26.0 (CH_3), 19.8 (CH_3), 19.5 (CH_3), 19.3 (CH_3), 18.5 (C), 18.3 (C), 16.9 (CH_3), 14.2 (CH_3), 14.1 (C), 12.9 (CH_3), 8.1 (CH_3), 7.3 (CH_3), 5.8 (CH_2), –3.4 (CH_3), –3.6 (CH_3), –5.3 (CH_3), –5.3 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{58}H_{110}NO_7Si_4$ $[M+NH_4]^+$: 1044.7354, found: 1044.7351.

Proof of the stereochemistry of 24



24 **26**

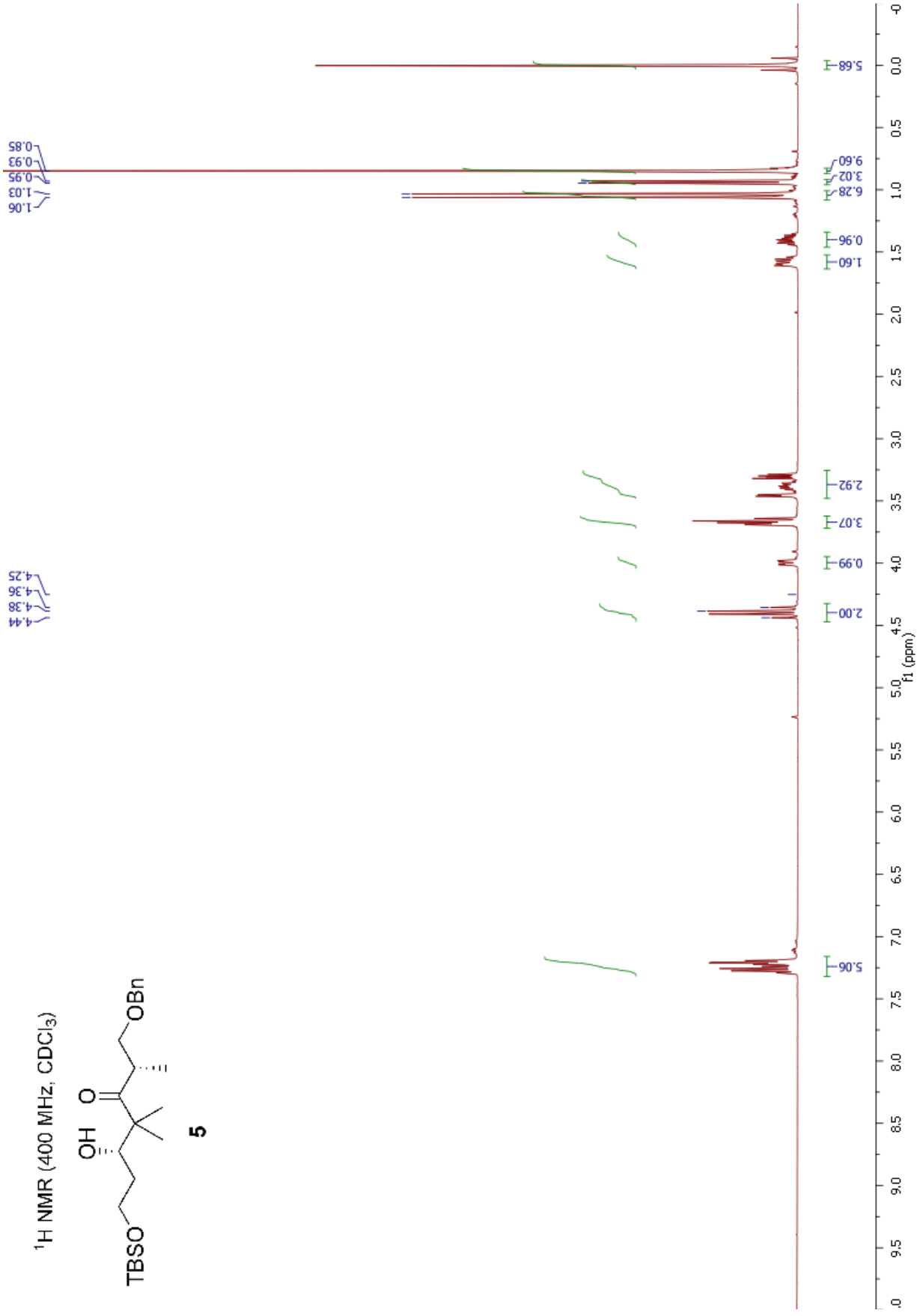
A mixture of **24** (13 mg, 13 μmol), 2,2-dimethoxypropane (10 μL, 80 μmol) and a crystal of CSA in DMF (0.2 mL) was stirred at room temperature for 3 h. The reaction mixture was partitioned with sat $NaHCO_3$ (10 mL) and hexane (10 mL). The aqueous layer was extracted with hexane (4 × 10 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (from 95:5 to 70:30 hexanes/EtOAc) to afford 4 mg (4.2 μmol, 32% yield) of a highly sensitive (3*S*,5*R*,6*R*,7*S*,8*E*,10*S*,11*S*,13*R*,14*S*)-1-*tert*-butyldimethylsilyloxy-5,7,11,13-bis(isopropilidendioxy)-15-*tert*-butyldiphenylsilyloxy-4,4,6,8,10,14-hexamethyl-8-pentadecen-3-ol (**26**) as a colourless oil. R_f(hexanes/EtOAc) 0.35. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77–7.59 (4H, m, Ar$\underline{H}$), 7.52–7.30 (6H, m, Ar$\underline{H}$), 5.20 (1H, broad d, *J* = 10.0 Hz, C=C$\underline{H}$), 4.18 (1H, m, CH=CC$\underline{H}$), 4.08 (1H, d, *J* = 1.7 Hz, CH=CCHCHC$\underline{H}$), 3.87 (1H, ddd, *J* = 11.5, 7.5, 2.2 Hz, C$\underline{H}$CHCH$_2$OTBDPS), 3.80 (1H, dd, *J* = 9.7, 4.7 Hz, C$\underline{H}_x$H$_y$OTBDPS), 3.75 (1H, ddd, *J* = 10.3, 7.4, 5.0 Hz, TBSOC$\underline{H}_x$H$_y$), 3.70–3.60 (1H, m, TBSOCH$_x\underline{H}_y$), 3.55 (1H, dd, *J* = 9.7, 4.1 Hz, CH$_x\underline{H}_y$OTBDPS), 3.52 (1H, d, *J* = 2.5 Hz, C=CHCHC$\underline{H}$), 3.49 (1H, dd, *J* = 7.3, 2.9 Hz, C$\underline{H}$OH), 2.47–2.31 (1H, m, C=CHC$\underline{H}$), 2.10–1.92 (2H, m, TBSOCH$_2$C$\underline{H}_x$H$_y$ & C=CHCHCHC$\underline{H}_x$H$_y$), 1.78–1.61 (3H, m, TBSOCH$_2$CH$_x\underline{H}_y$, CH=CCHC$\underline{H}$ & C$\underline{H}$CH$_2$OTBDPS), 1.52 (3H, d, *J* = 1.6 Hz, CH=CC$\underline{H}_3$), 1.41 (3H, s, O$_2$CC$\underline{H}_3$), 1.41 (3H, s, O$_2$CC$\underline{H}_3$), 1.40 (3H, s, O$_2$CC$\underline{H}_3$), 1.38 (3H, s, O$_2$CC$\underline{H}_3$), 1.36–1.28 (1H, m, C=CHCHCHCH$_x\underline{H}_y$), 1.04 (9H, s, SiC(C$\underline{H}_3$)$_3$), 0.99 (3H, d, *J* = 6.6 Hz, C=CHCHC$\underline{H}_3$), 0.94 (3H, d, *J* = 7.0 Hz, C$\underline{H}_3$CHCH$_2$OTBDPS), 0.93 (9H, s, SiC(C$\underline{H}_3$)$_3$), 0.89 (3H, s, CC$\underline{H}_3$), 0.87 (3H, s, CC$\underline{H}_3$), 0.76 (3H, d, *J* = 6.7 Hz, CH=CCHCHC$\underline{H}_3$), 0.11 (3H, s, SiC$\underline{H}_3$), 0.09 (3H, s, SiC$\underline{H}_3$). **^{13}C NMR** (125.0 MHz, $CDCl_3$) δ 135.6 (CH), 135.6 (CH), 134.0 (C), 133.9 (C), 130.0 (C), 129.5 (CH), 129.4 (CH), 127.6 (CH), 127.5 (CH), 126.2 (CH), 98.7 (C), 98.3 (C), 77.4 (CH), 77.4 (CH), 74.1 (CH), 73.4 (CH), 69.6 (CH), 64.6 (CH_2), 61.1 (CH_2), 42.0 (C),

41.0 (CH), 38.5 (CH), 36.9 (CH_2), 32.6 (CH), 30.3 (CH_3), 30.0 (CH_3), 27.2 (CH_2), 26.8 (CH_3), 26.2 (CH_3), 22.3 (CH_3), 20.9 (CH_3), 19.9 (CH_3), 19.6 (CH_3), 19.3 (C), 18.5 (C), 17.3 (CH_3), 13.9 (CH_3), 12.7 (CH_3), 7.3 (CH_3), –3.5 (CH_3), –3.9 (CH_3). **HRMS** (+ESI) *m/z* calcd for $C_{49}H_{86}NO_7Si_2$ $[M+NH_4]^+$: 856.5937, found: 856.5936.

The configuration of the C7 stereocentre has been assigned according to diagnostic peaks in ^{13}C NMR. Indeed, $O_2\underline{C}Me_2$ quaternary carbon atoms at 98.7 and 98.3 ppm indicate that both acetonides come from 1,3-*syn* diols.[5]

11. ^1H and ^{13}C Spectra of new compounds

[5] For a full account of such an analysis, see: (*a*) S. D. Rychnovsky and D. J. Skalitzky, *Tetrahedron Lett.*, 1990, **31**, 945; (*b*) D. A. Evans, D. L. Rieger and J. R. Gage, *Tetrahedron Lett.*, 1990, **31**, 7099; (*c*) S. D. Rychnovsky, B. Rogers and G. Yang, *J. Org. Chem.,* 1993, **58**, 3511.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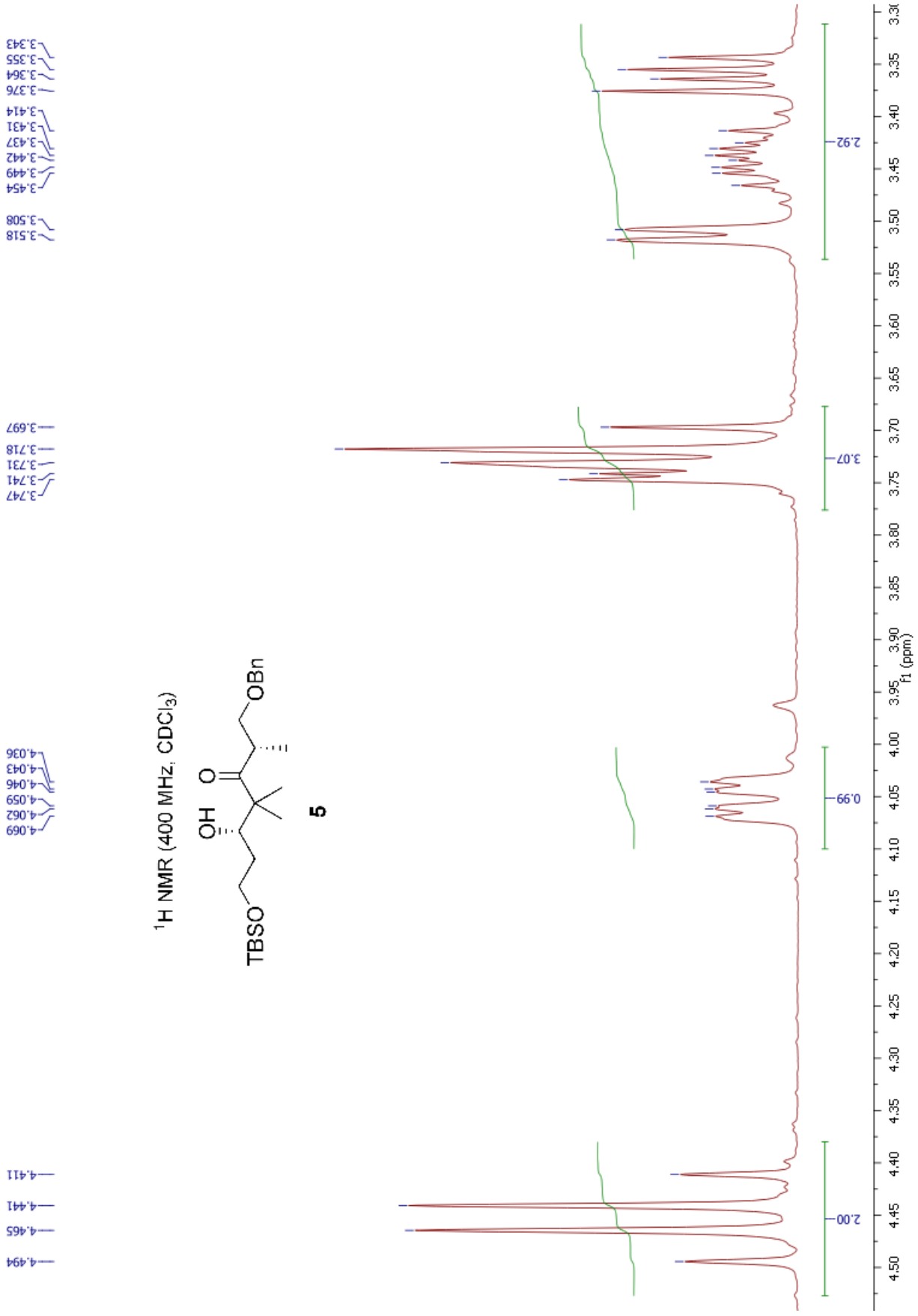
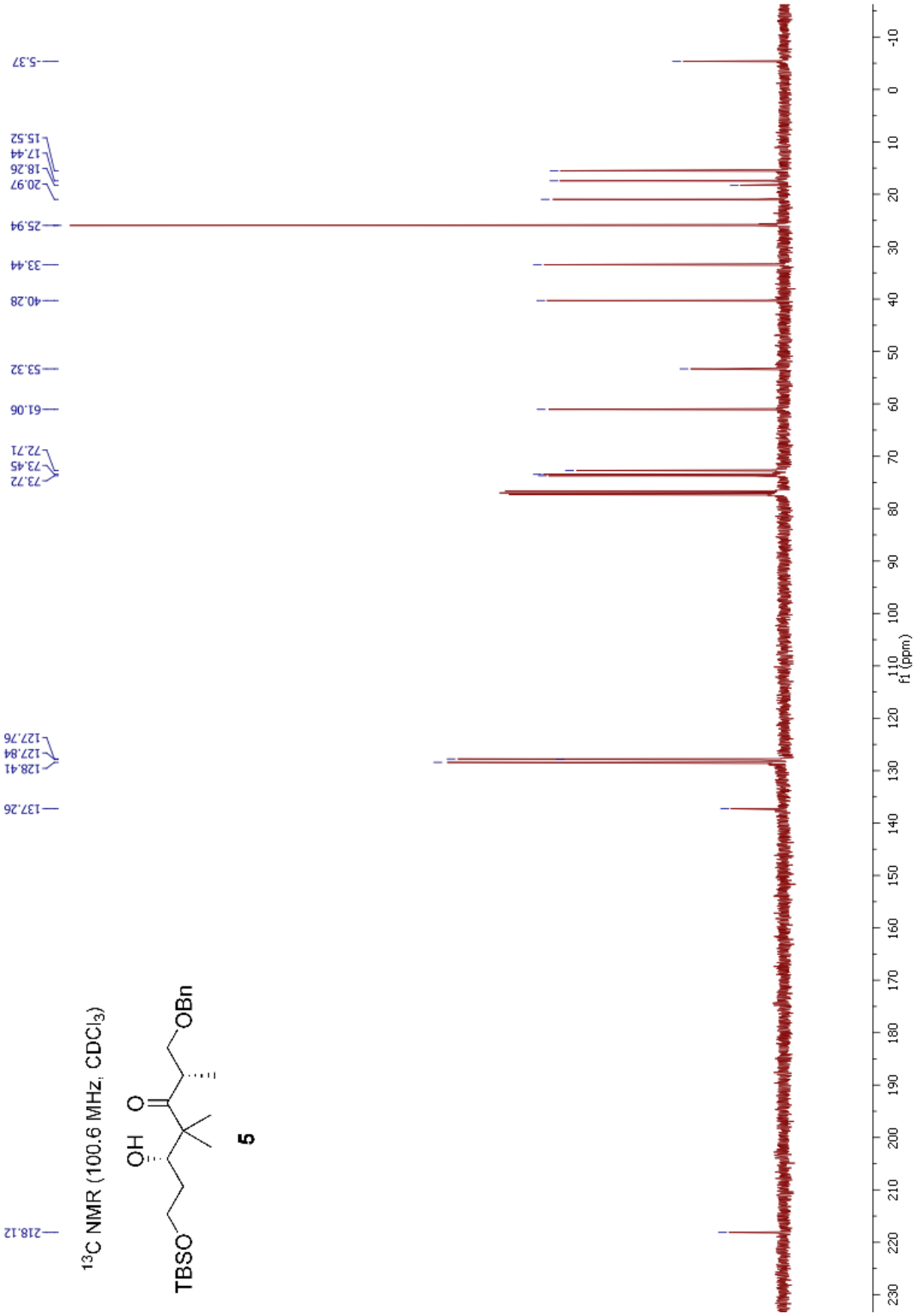
TBSO
OH
O
OBn
5
0.85
0.93
0.95
1.03
1.06
4.25
4.36
4.38
4.44
5.68
9.60
3.02
6.28
0.96
1.60
2.92
3.07
0.99
2.00
5.06
f1 (ppm)


^{1}H NMR (400 MHz, CDCl$_3$)
OBn
OH
O
TBSO
5
f1 (ppm)
2.92
3.07
0.99
2.00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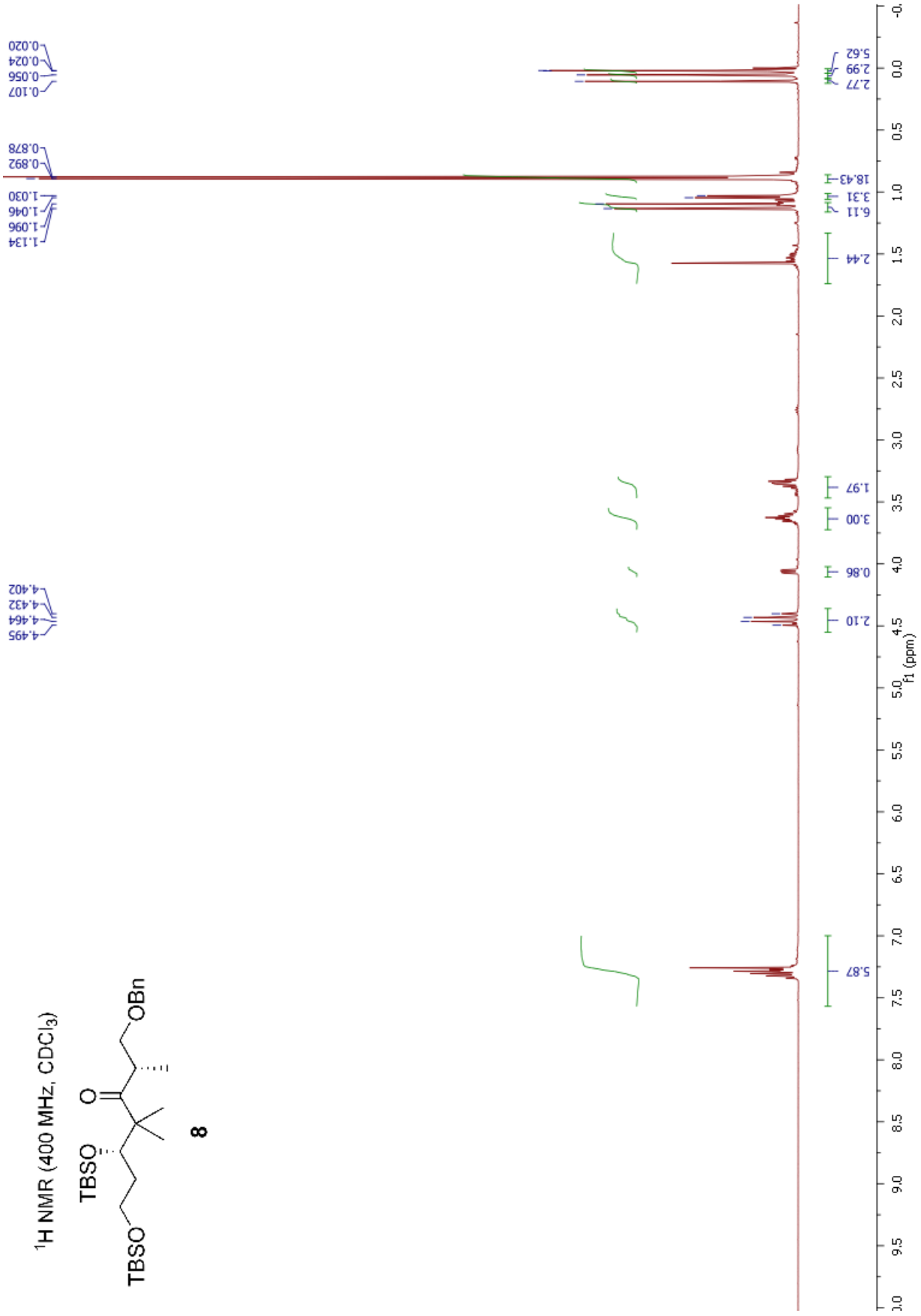
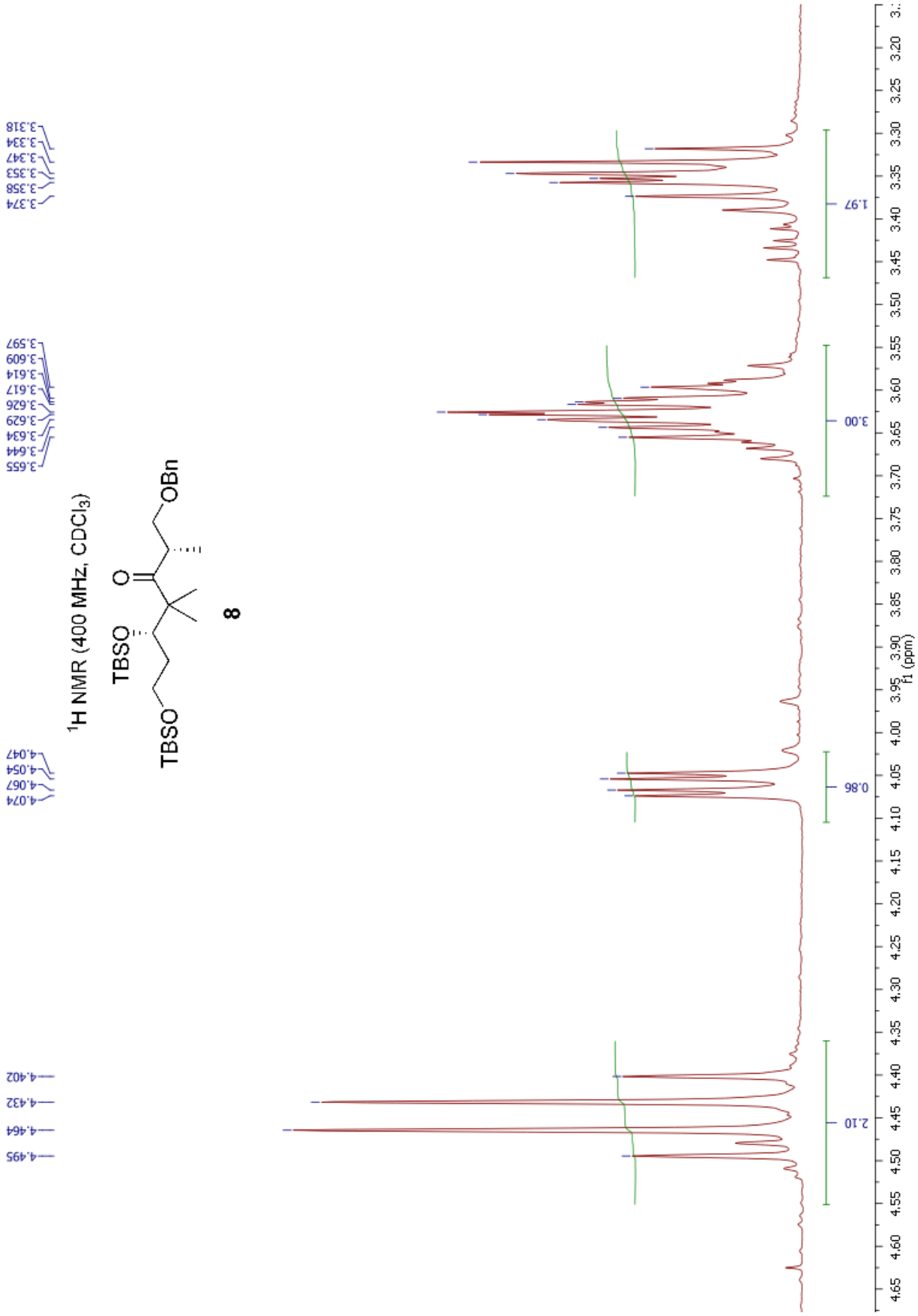
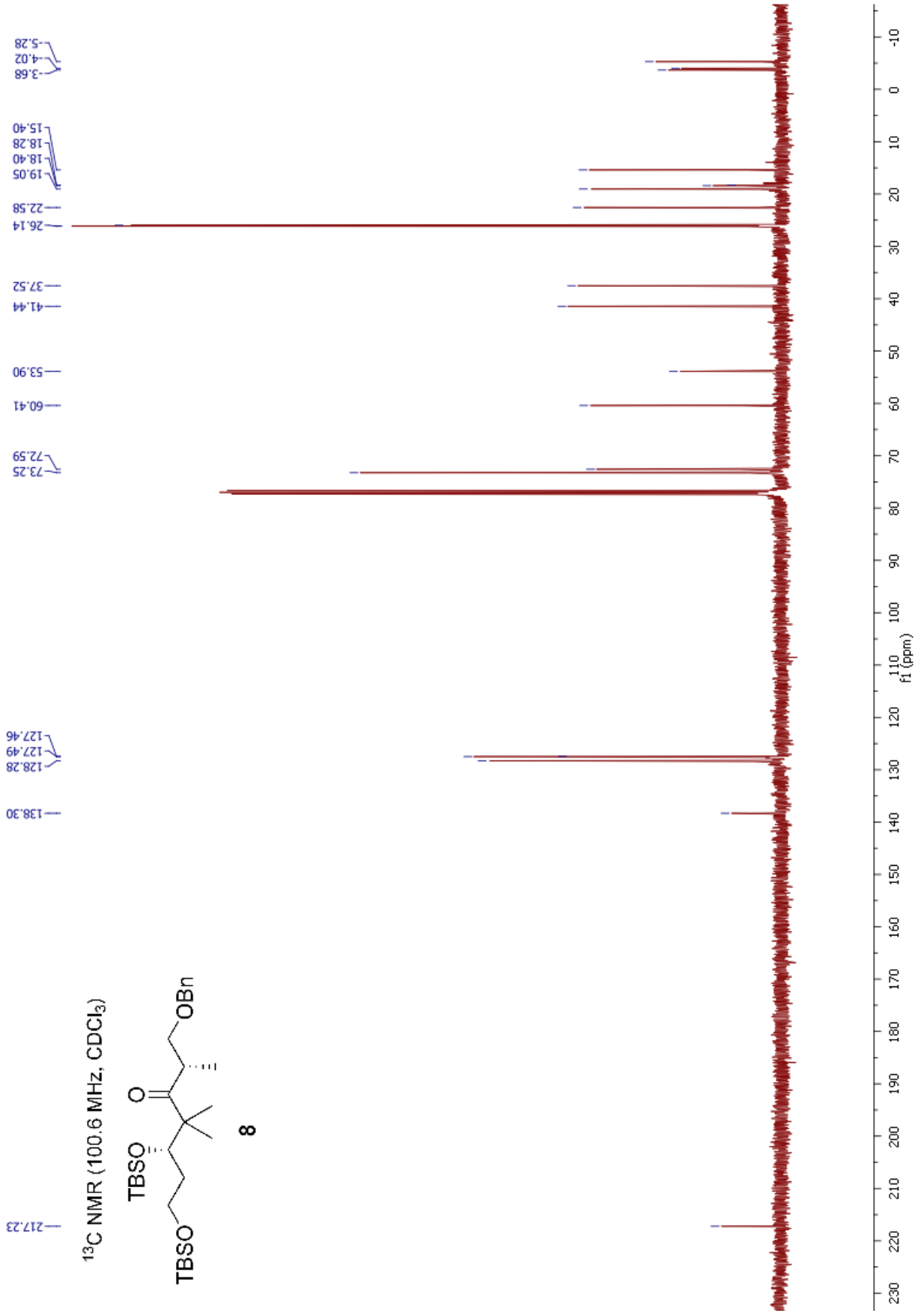
15.52
17.44
18.26
20.97
25.94
33.44
40.28
53.32
61.06
72.71
73.45
73.72
127.76
127.84
128.41
137.26
218.12
^{13}C NMR (100.6 MHz, $CDCl_3$)
TBSO
OH
O
OBn
5
f1 (ppm)


0.020
0.024
0.056
0.107
0.878
0.892
1.030
1.046
1.096
1.134
4.402
4.432
4.464
4.495
5.62
2.99
2.77
18.43
3.31
6.11
2.44
1.97
3.00
0.86
2.10
5.87
f1 (ppm)
^{1}H NMR (400 MHz, $CDCl_3$)
TBSO
O
OBn
TBSO
8


^{1}H NMR (400 MHz, $CDCl_3$)
TBSO
O
OBn
TBSO
8
4.495
4.464
4.432
4.402
4.074
4.067
4.054
4.047
3.655
3.644
3.634
3.629
3.626
3.617
3.614
3.609
3.597
3.374
3.358
3.353
3.347
3.334
3.318
2.10
0.86
3.00
1.97
f1 (ppm)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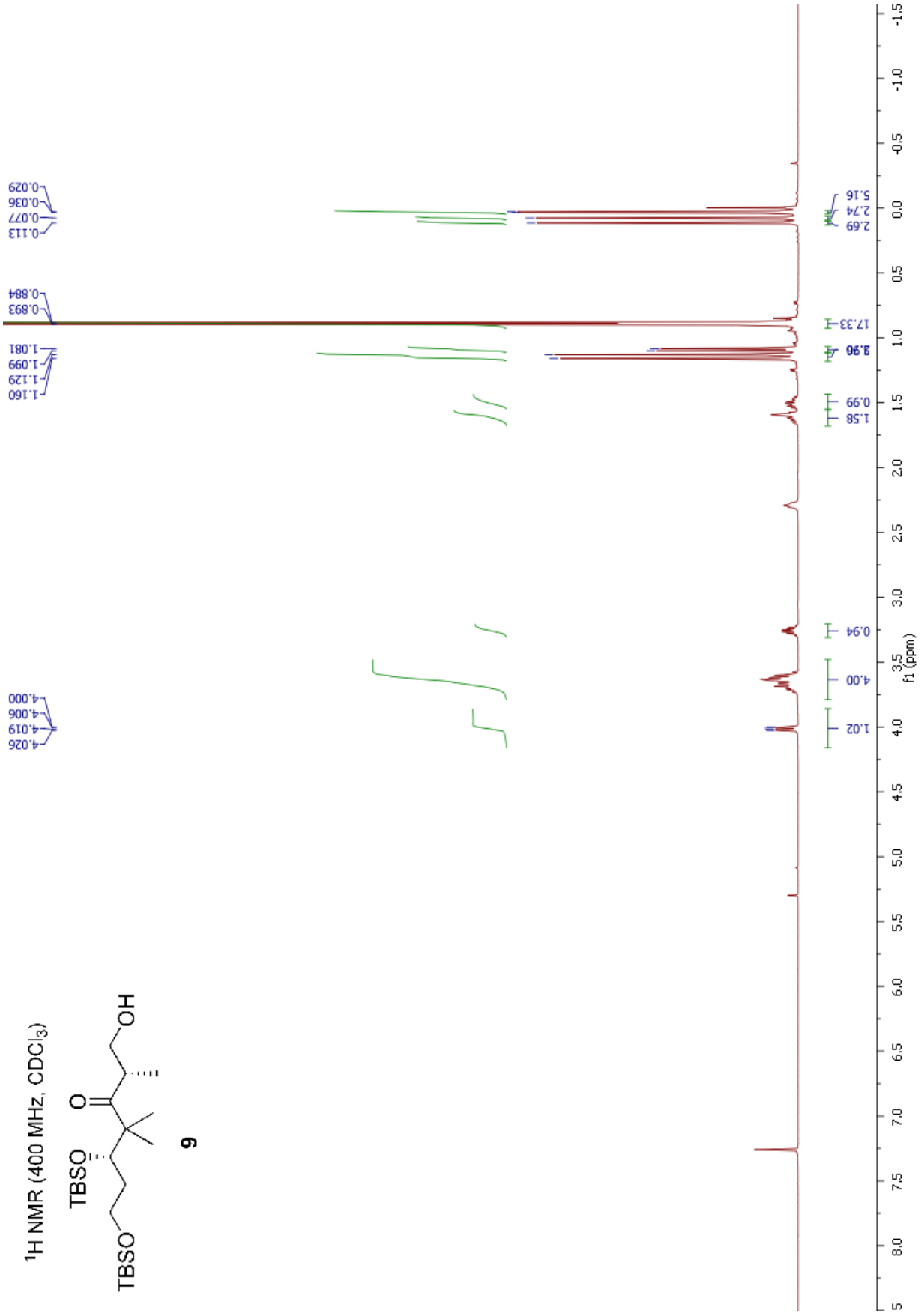
-4.02
-3.68
15.40
18.28
18.40
19.05
22.58
26.14
37.52
41.44
53.90
60.41
72.59
73.25
127.46
127.49
128.28
138.30
217.23
f1 (ppm)
^{13}C NMR (100.6 MHz, $CDCl_3$)
TBSO
O
OBn
TBSO
8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0.077
0.113
0.884
0.893
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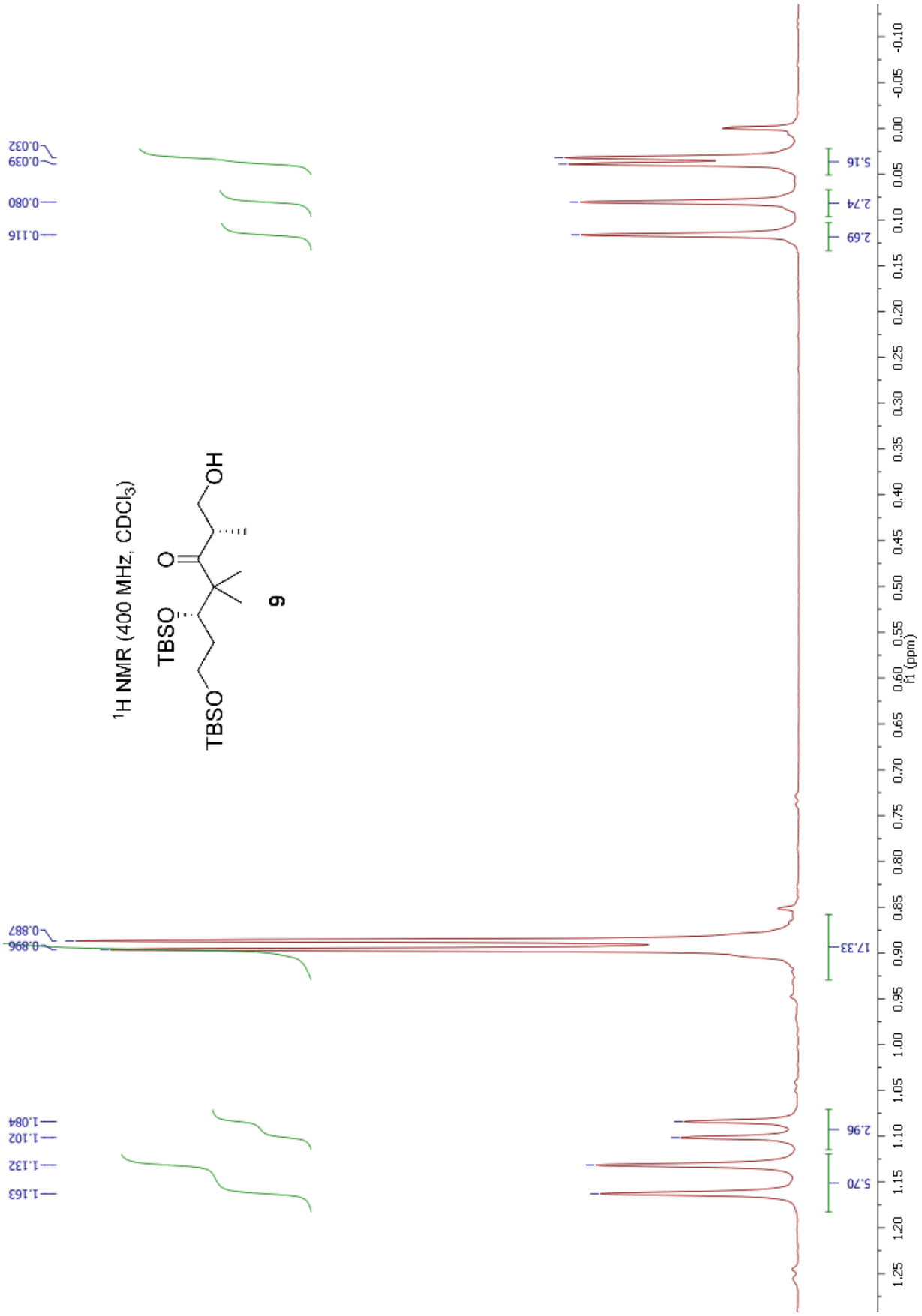
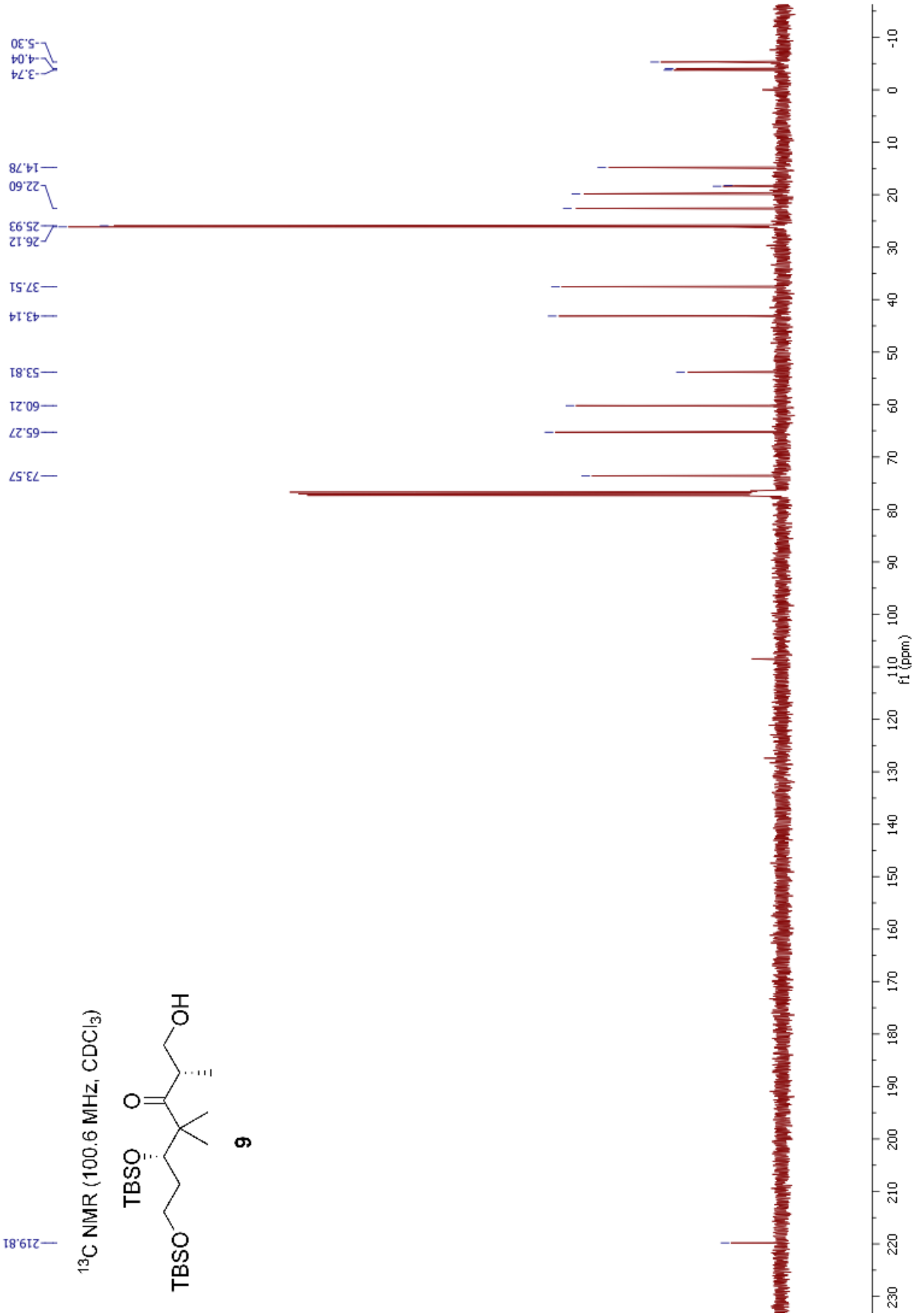
1.099
1.129
1.160
4.000
4.006
4.019
4.026
5.16
2.74
2.69
17.33
8.96
0.99
1.58
0.94
4.00
1.02
f1 (ppm)
^{1}H NMR (400 MHz, $CDCl_3$)
TBSO
O
OH
TBSO
9


^{1}H NMR (400 MHz, $CDCl_3$)
TBSO
O
OH
TBSO
9
0.032
0.039
0.080
0.116
0.887
0.896
1.084
1.102
1.132
1.163
5.16
2.74
2.69
17.33
2.96
5.70
f1 (ppm)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TBSO
O
OH
TBSO
9
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-4.04
-3.74
14.78
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26.12
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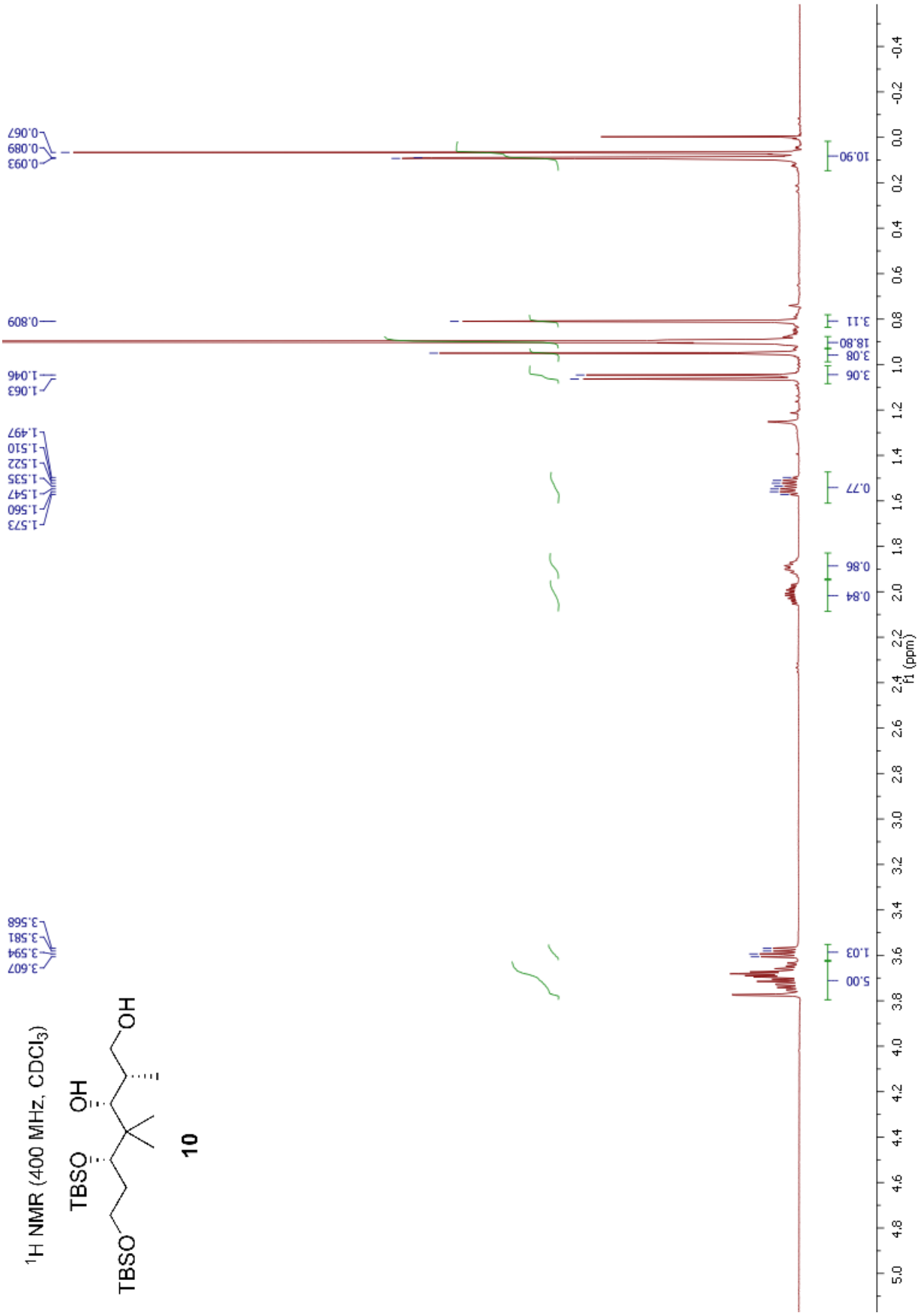
43.14
53.81
60.21
65.27
73.57
219.81
f1 (ppm)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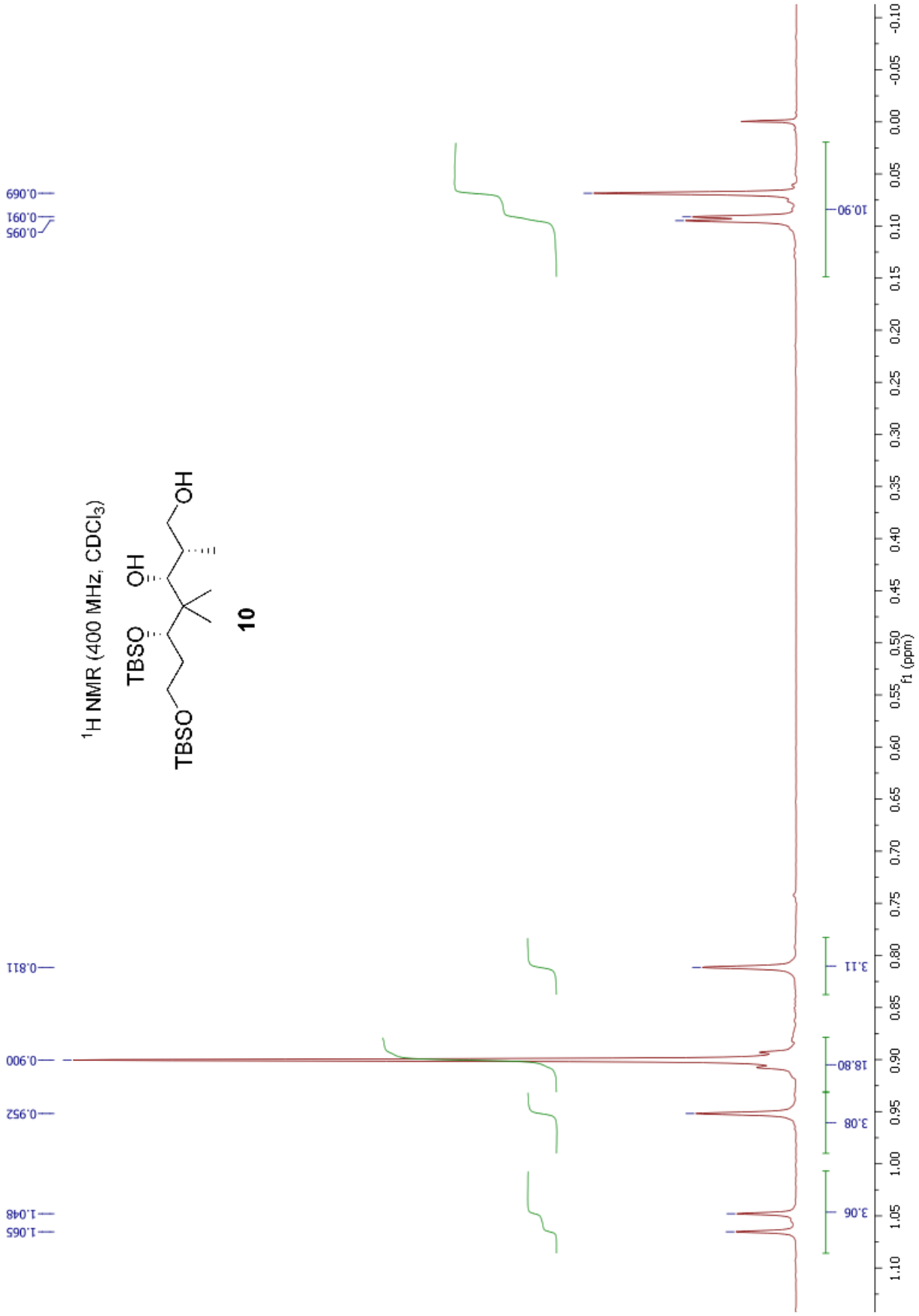
0.089
0.093
0.809
1.046
1.063
1.497
1.510
1.522
1.535
1.547
1.560
1.573
3.568
3.581
3.594
3.607
10.90
3.11
18.80
3.08
3.06
0.77
0.86
0.84
1.03
5.00
f1 (ppm)
^{1}H NMR (400 MHz, $CDCl_3$)
TBSO
OH
TBSO
OH
10


^{1}H NMR (400 MHz, $CDCl_3$)
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OH
TBSO
OH
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0.091
0.095
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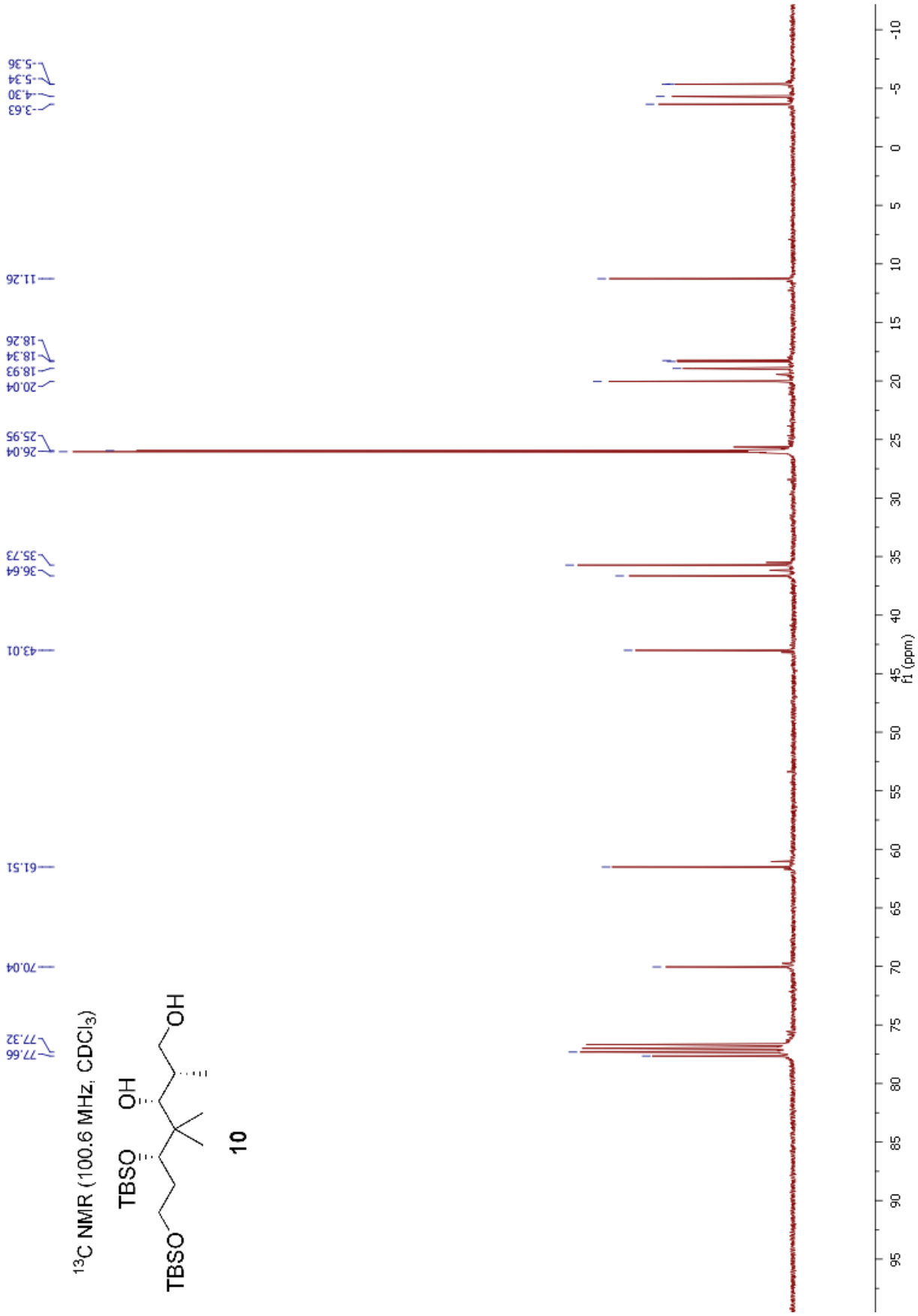
0.952
1.048
1.065
10.90
3.11
18.80
3.08
3.06
f1 (ppm)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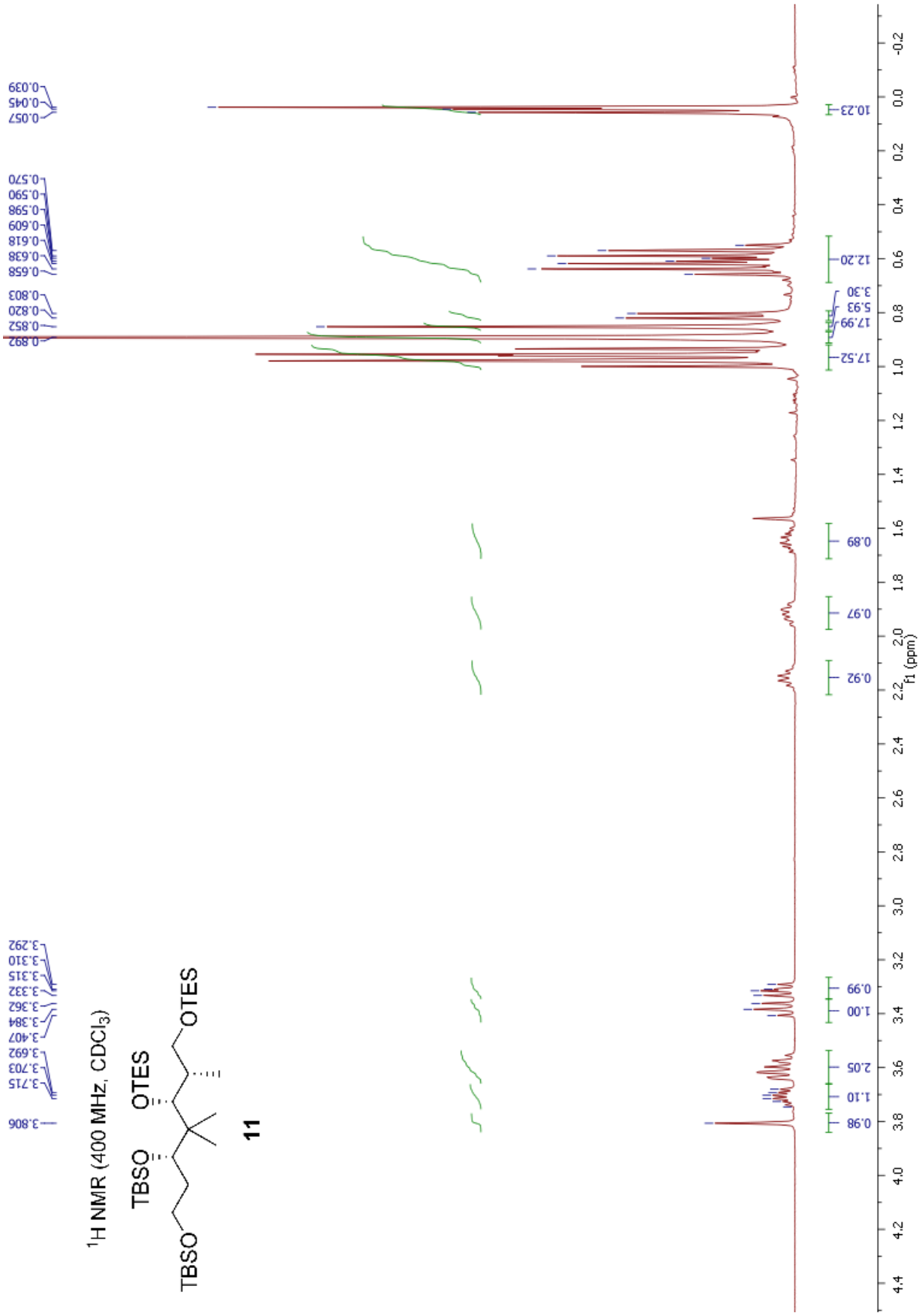
-4.30
-5.34
-5.36
11.26
18.26
18.34
18.93
20.04
25.95
26.04
35.73
36.64
43.01
61.51
70.04
77.32
77.66
f1 (ppm)
^{13}C NMR (100.6 MHz, $CDCl_3$)
TBSO
OH
TBSO
OH
10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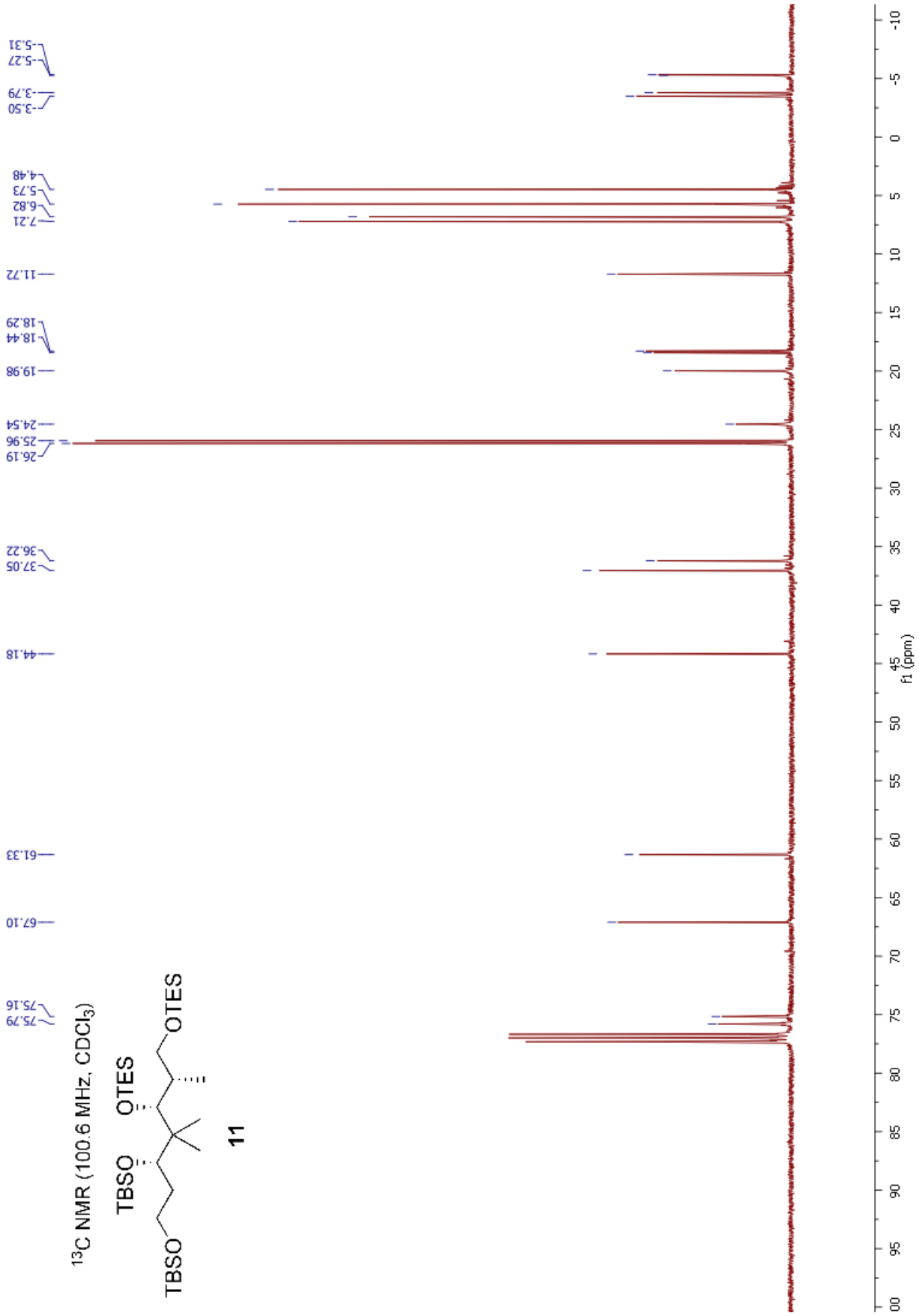
TBSO
OTES
OTES
TBSO
11
f1 (ppm)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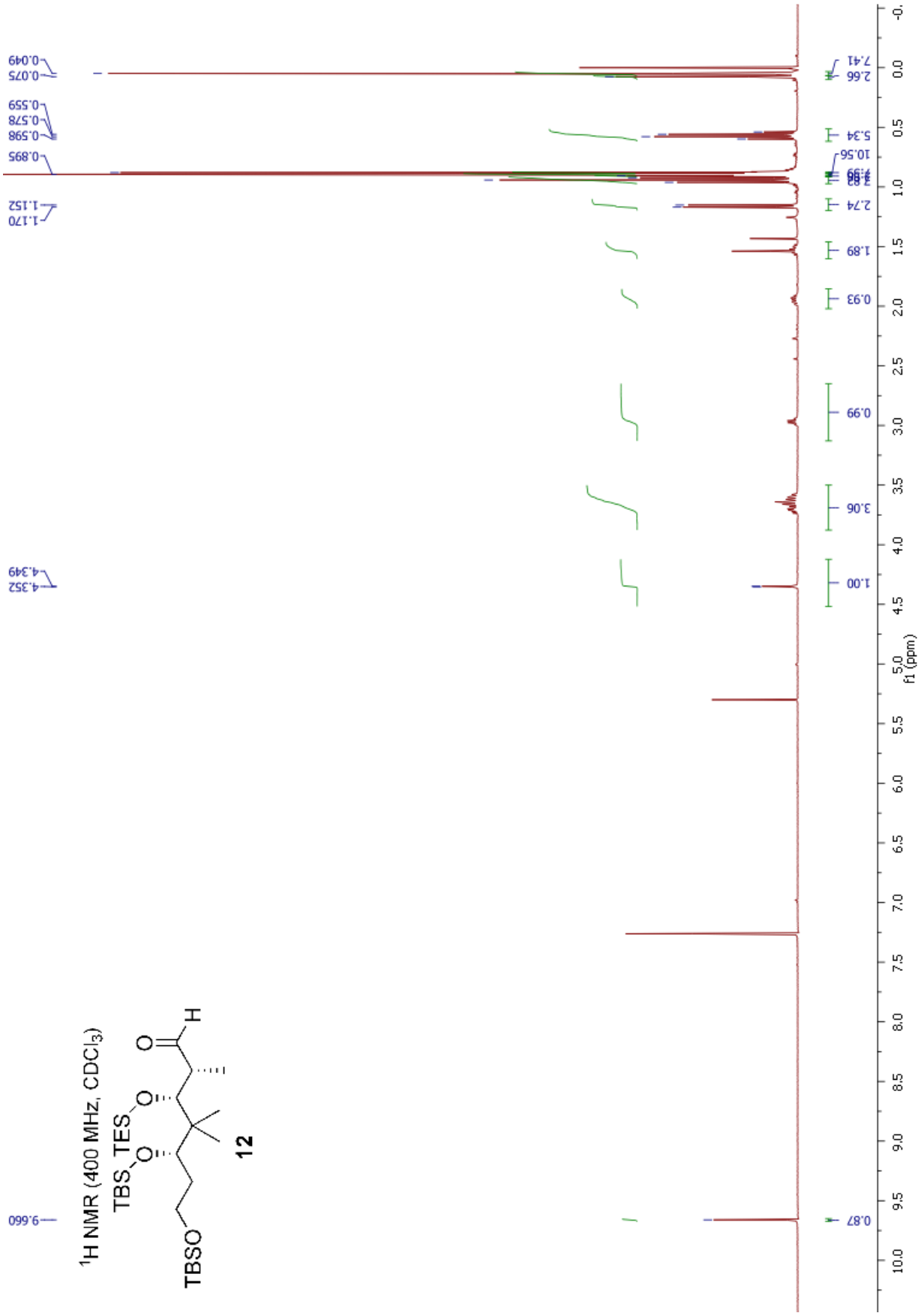
-3.79
-3.50
4.48
5.73
6.82
7.21
11.72
18.29
18.44
19.98
24.54
25.96
26.19
36.22
37.05
44.18
61.33
67.10
75.16
75.79
f1 (ppm)
^{13}C NMR (100.6 MHz, $CDCl_3$)
TBSO
OTES
OTES
TBSO
11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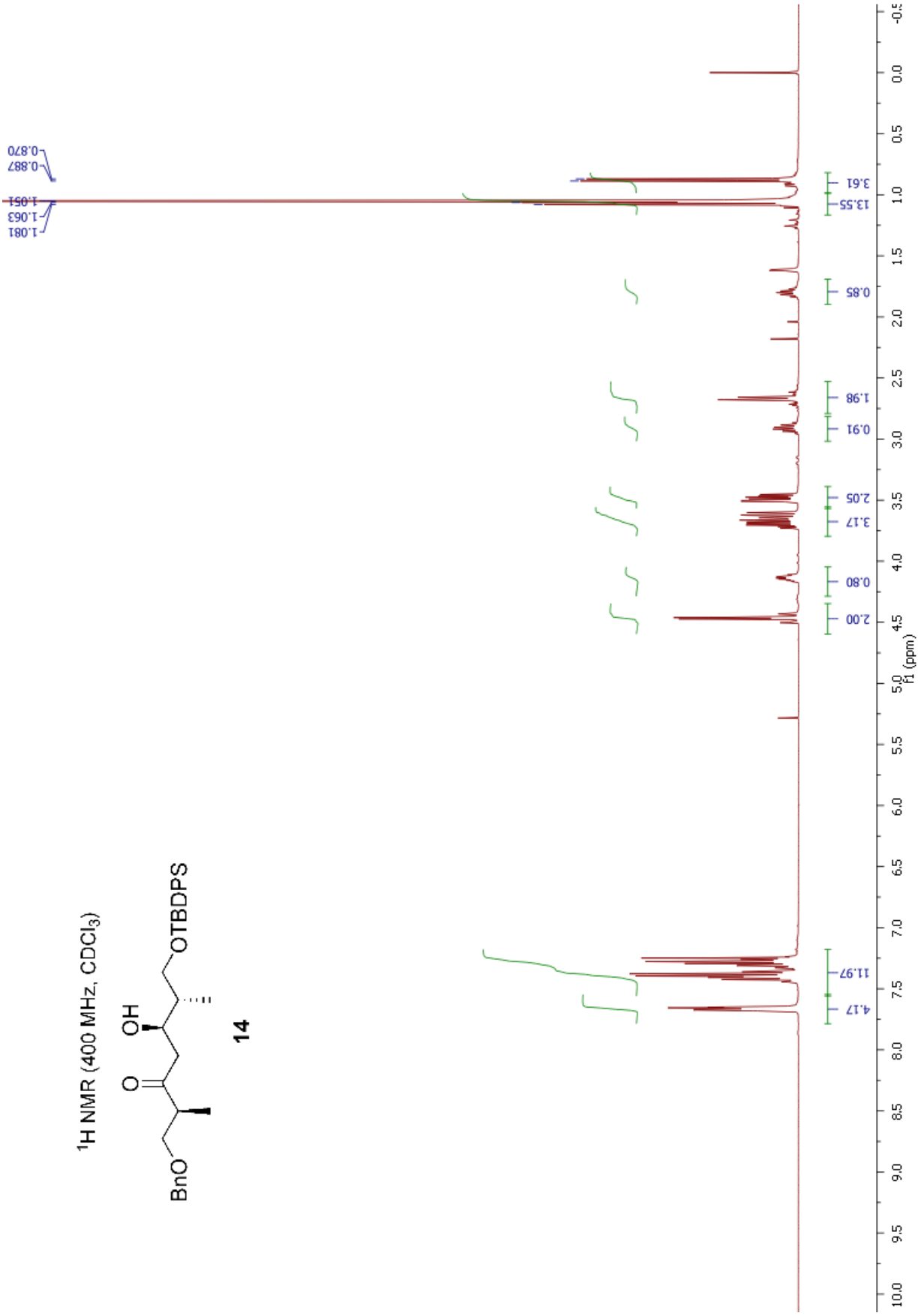
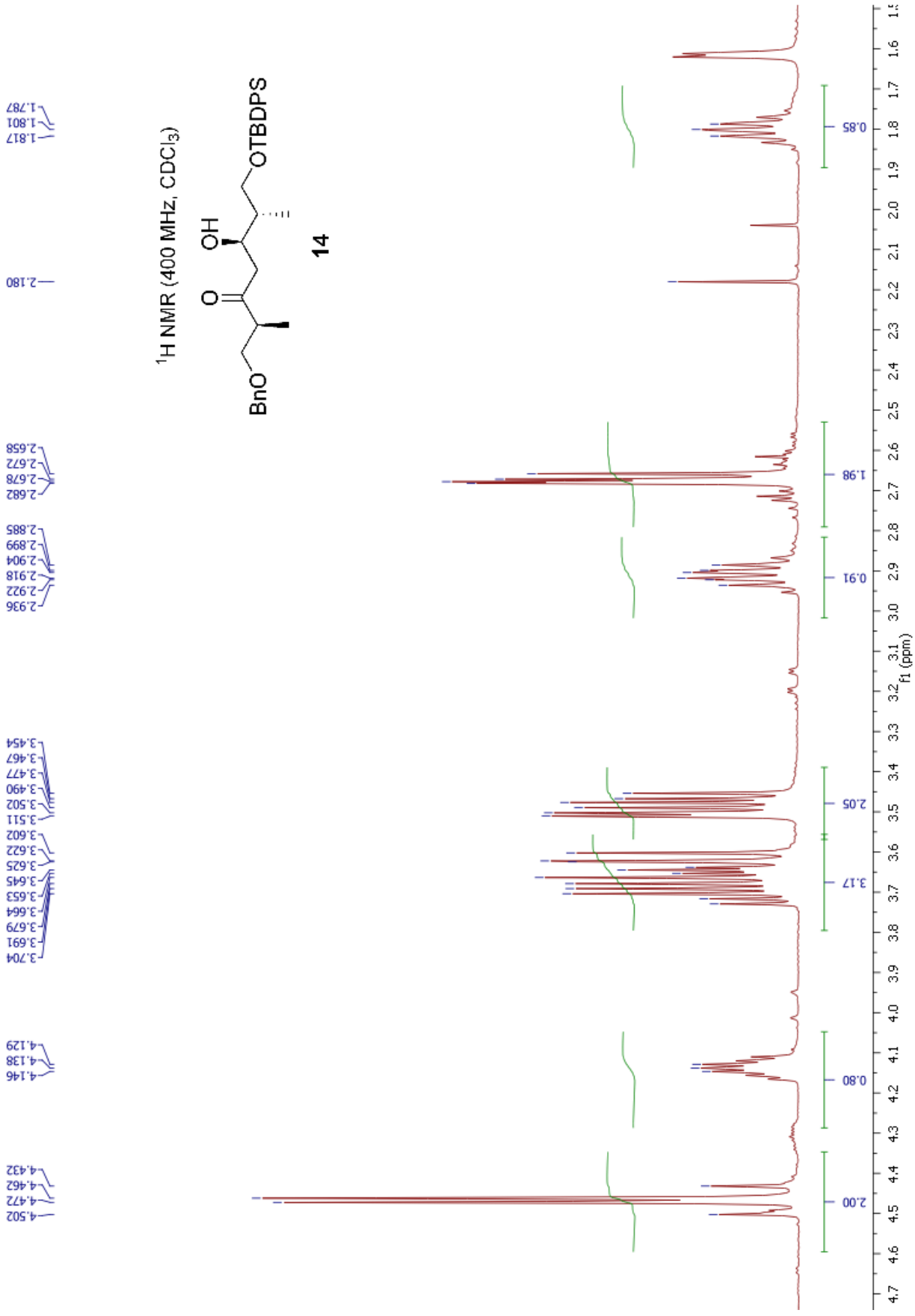
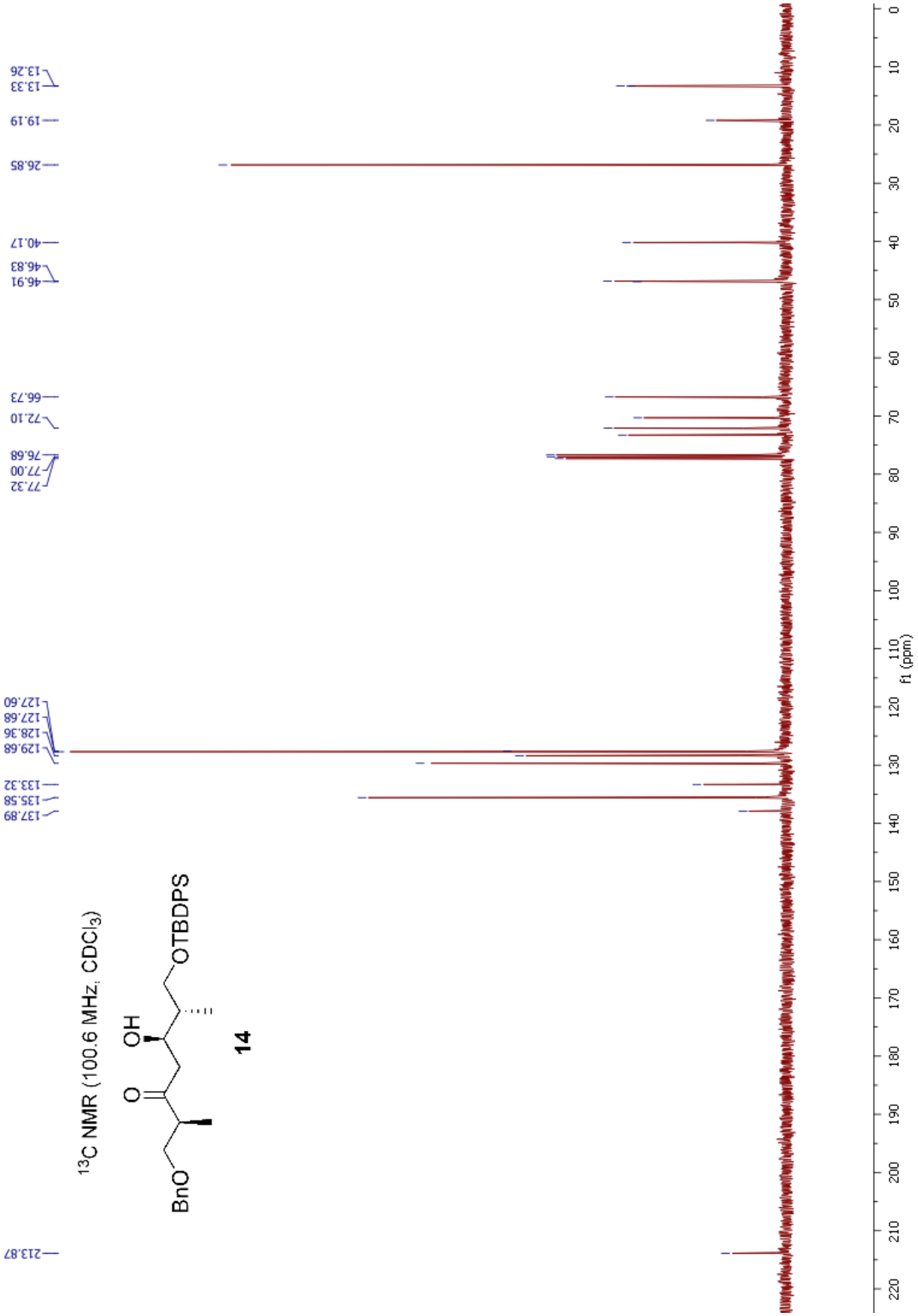
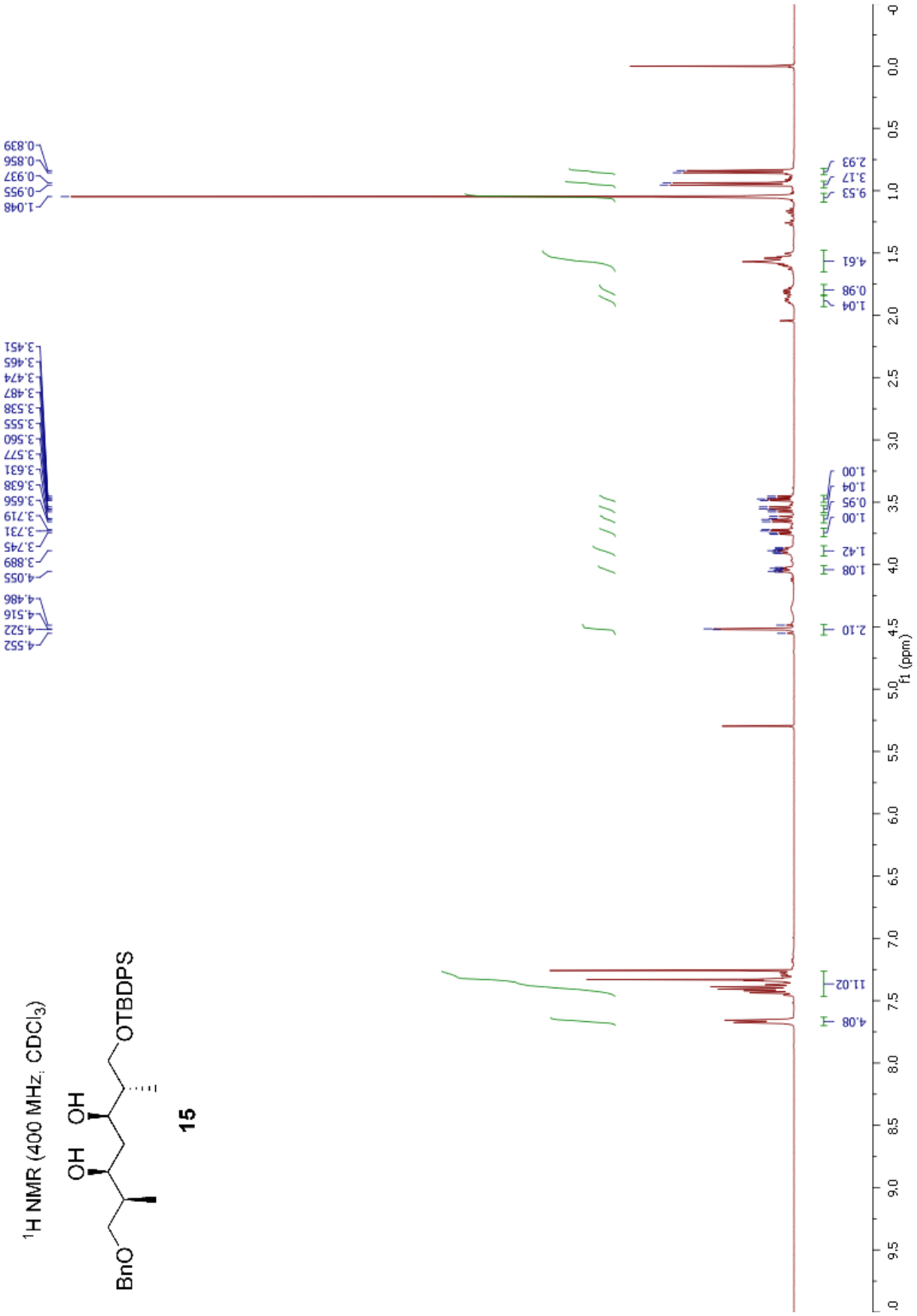
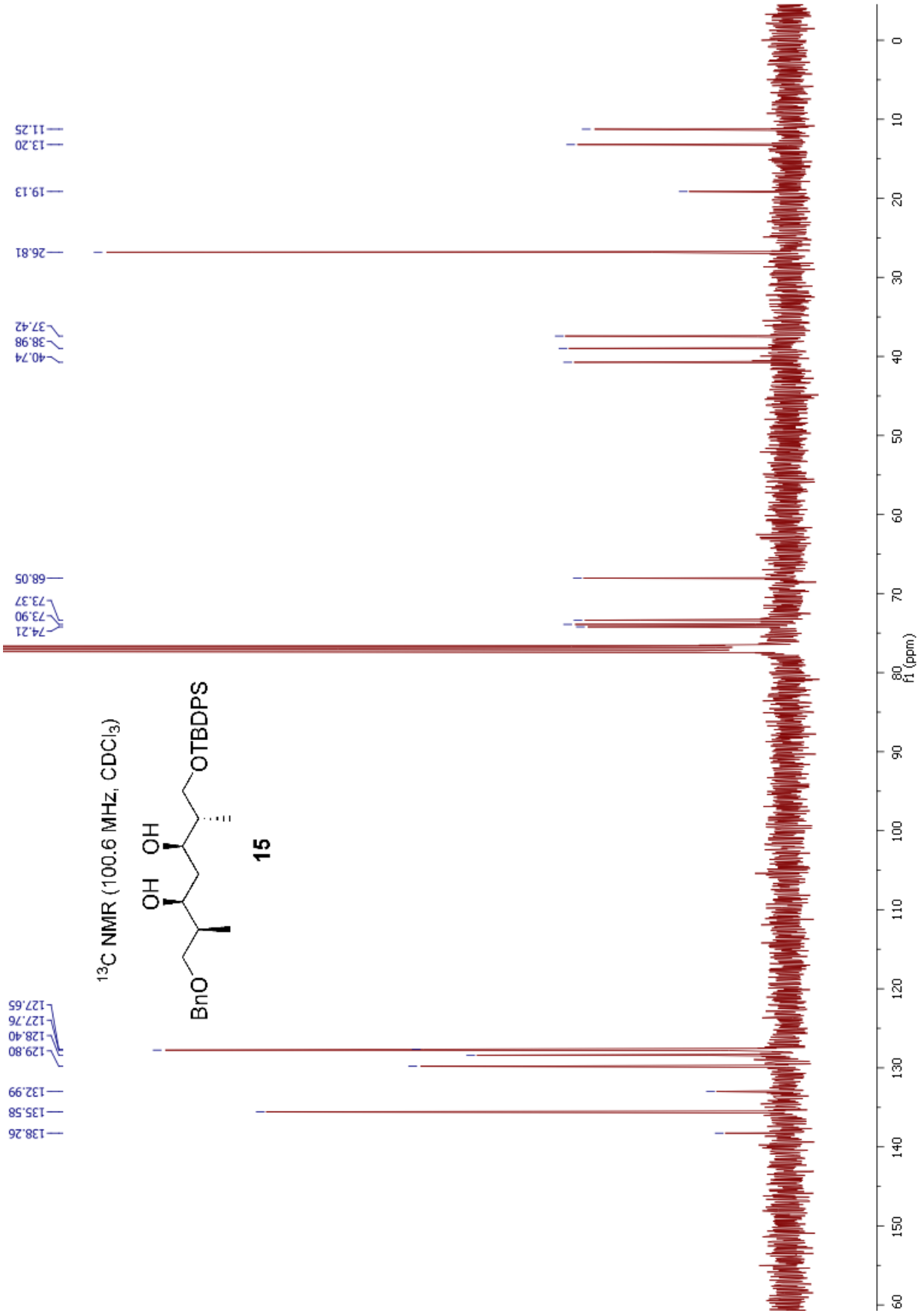
0.075
0.559
0.578
0.598
0.895
1.152
1.170
4.349
4.352
9.660
7.41
2.66
5.34
10.56
3.88
2.74
1.89
0.93
0.99
3.06
1.00
0.87
f1 (ppm)
^{1}H NMR (400 MHz, $CDCl_3$)
TBS, TES
TBSO
12

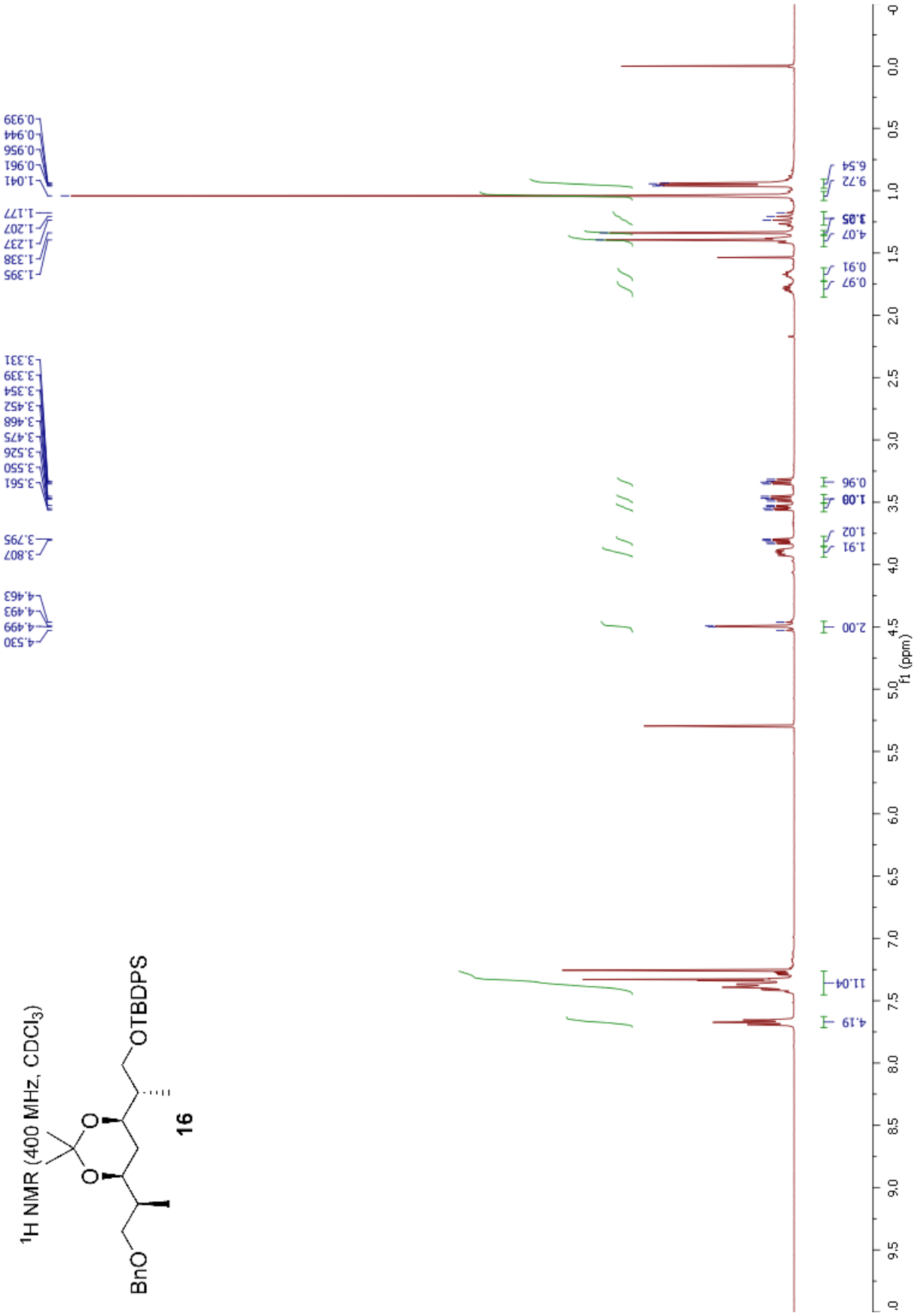

0.870
0.887
1.051
1.063
1.081
3.61
13.55
0.85
1.98
0.91
2.05
3.17
0.80
2.00
11.97
4.17
f1 (ppm)
^{1}H NMR (400 MHz, CDCl$_3$)
OTBDPS
OH
O
BnO
14

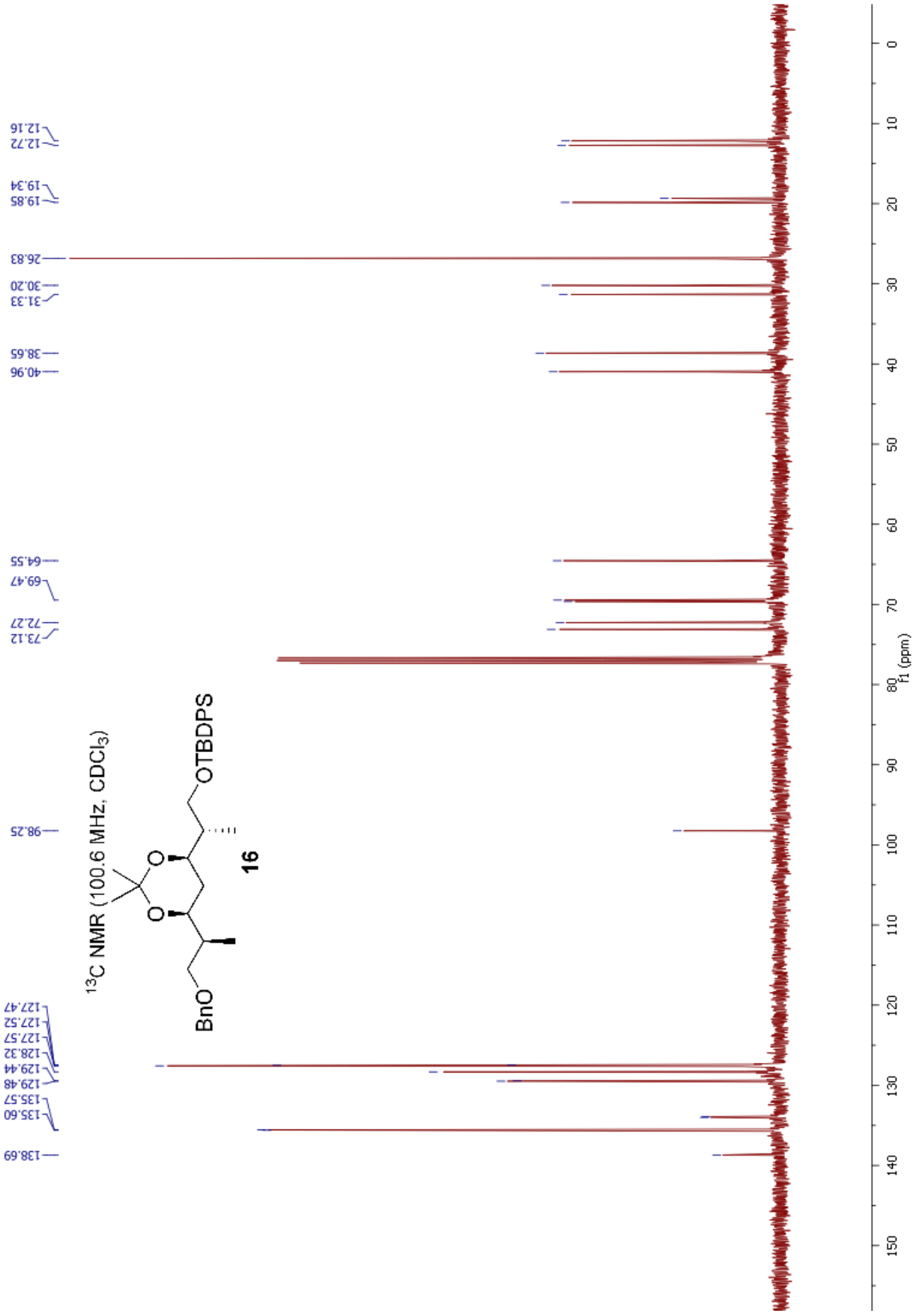

^{1}H NMR (400 MHz, $CDCl_3$)
OTBDPS
OH
O
BnO
14
f1 (ppm)
0.85
1.98
0.91
2.05
3.17
0.80
2.00

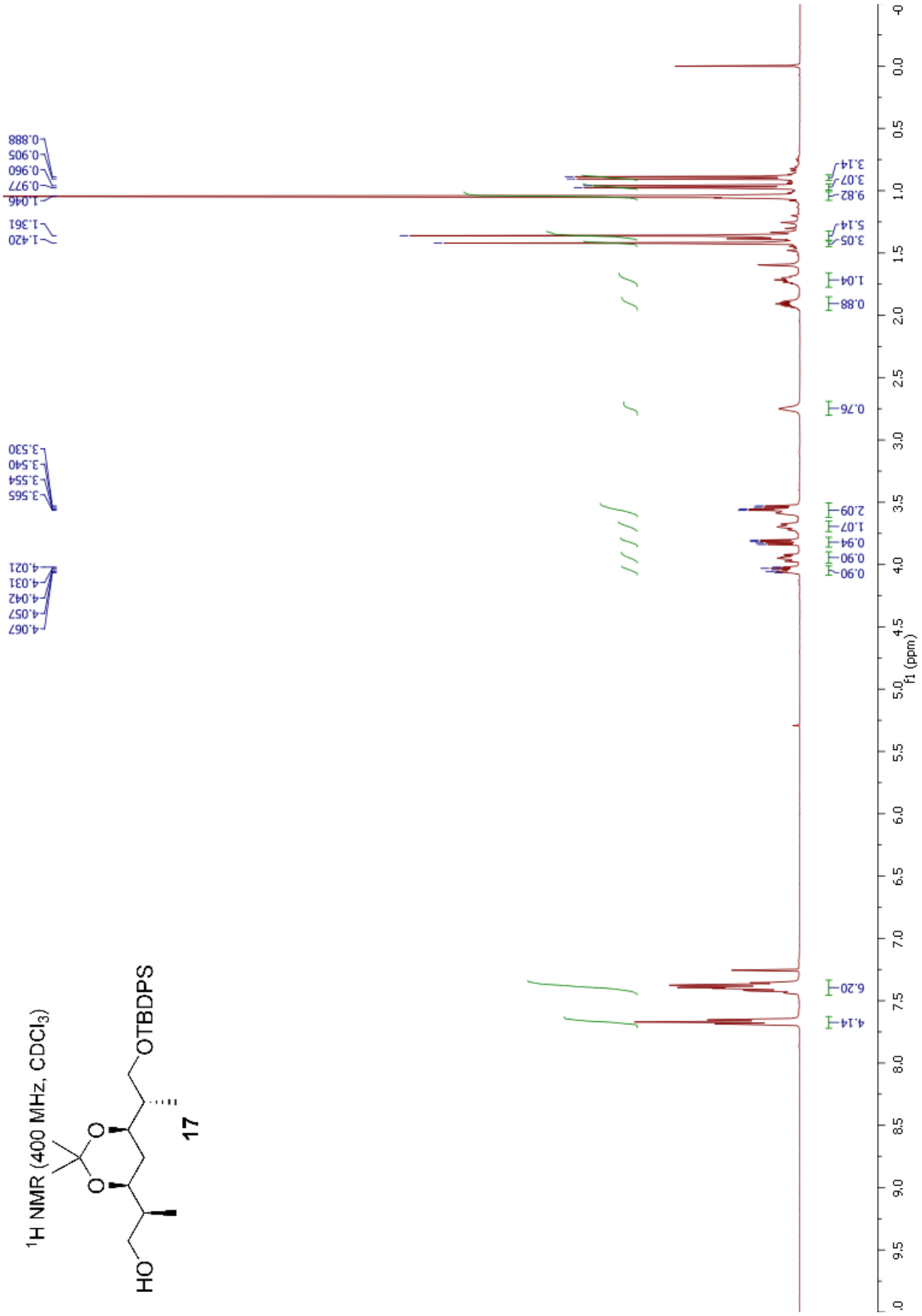

^{13}C NMR (100.6 MHz, $CDCl_3$)
14
OTBDPS
OH
O
BnO
13.26
13.33
19.19
26.85
40.17
46.83
46.91
66.73
72.10
76.68
77.00
77.32
127.60
127.68
128.36
129.68
133.32
135.58
137.89
213.87
f1 (ppm)

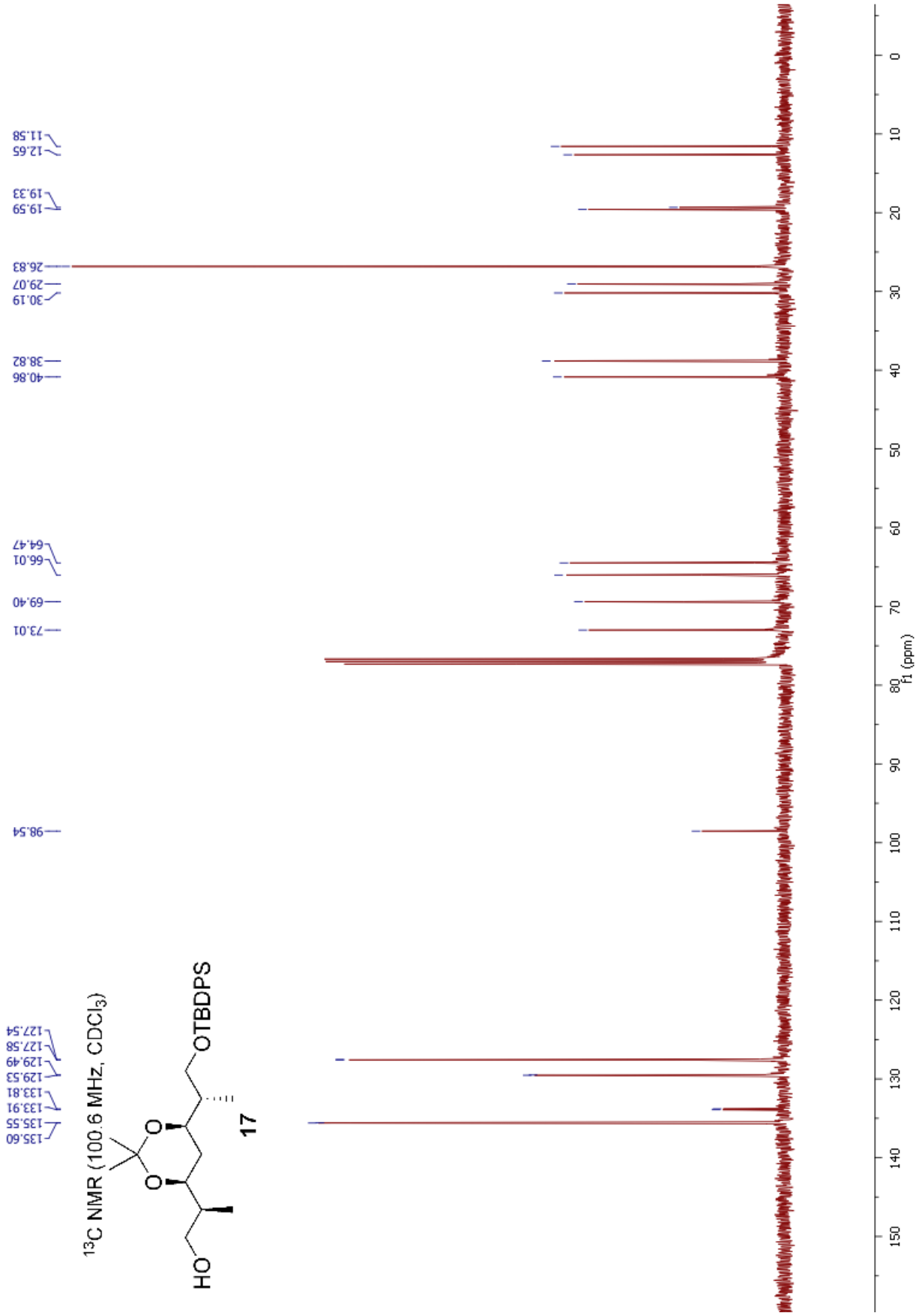

^{1}H NMR (400 MHz, $CDCl_3$)
BnO
OH
OH
OTBDPS
15
f1 (ppm)

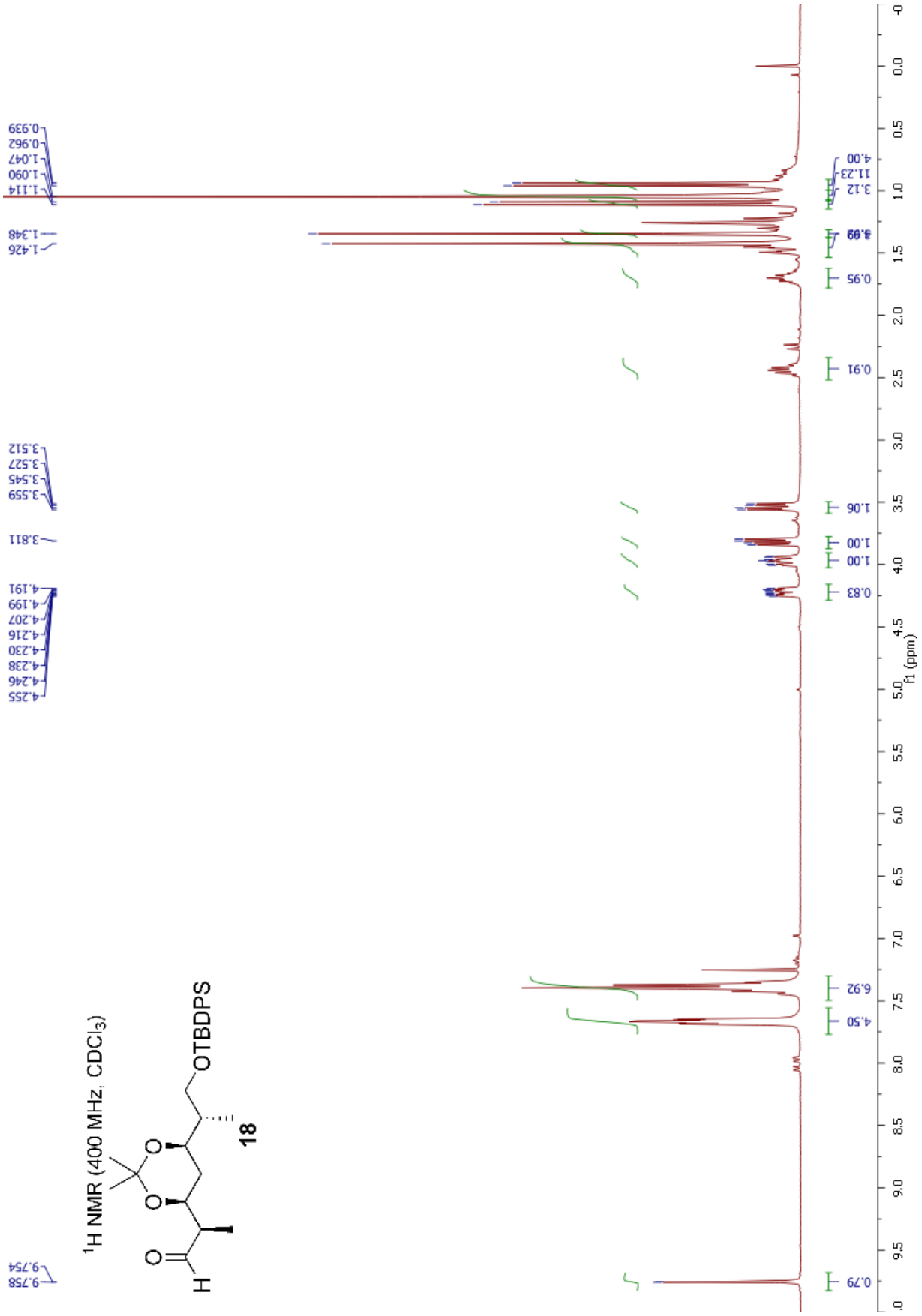

^{13}C NMR (100.6 MHz, $CDCl_3$)
OH
OH
OTBDPS
BnO
15
11.25
13.20
19.13
26.81
37.42
38.98
40.74
68.05
73.37
73.90
74.21
127.65
127.76
128.40
129.80
132.99
135.58
138.26
f1 (ppm)

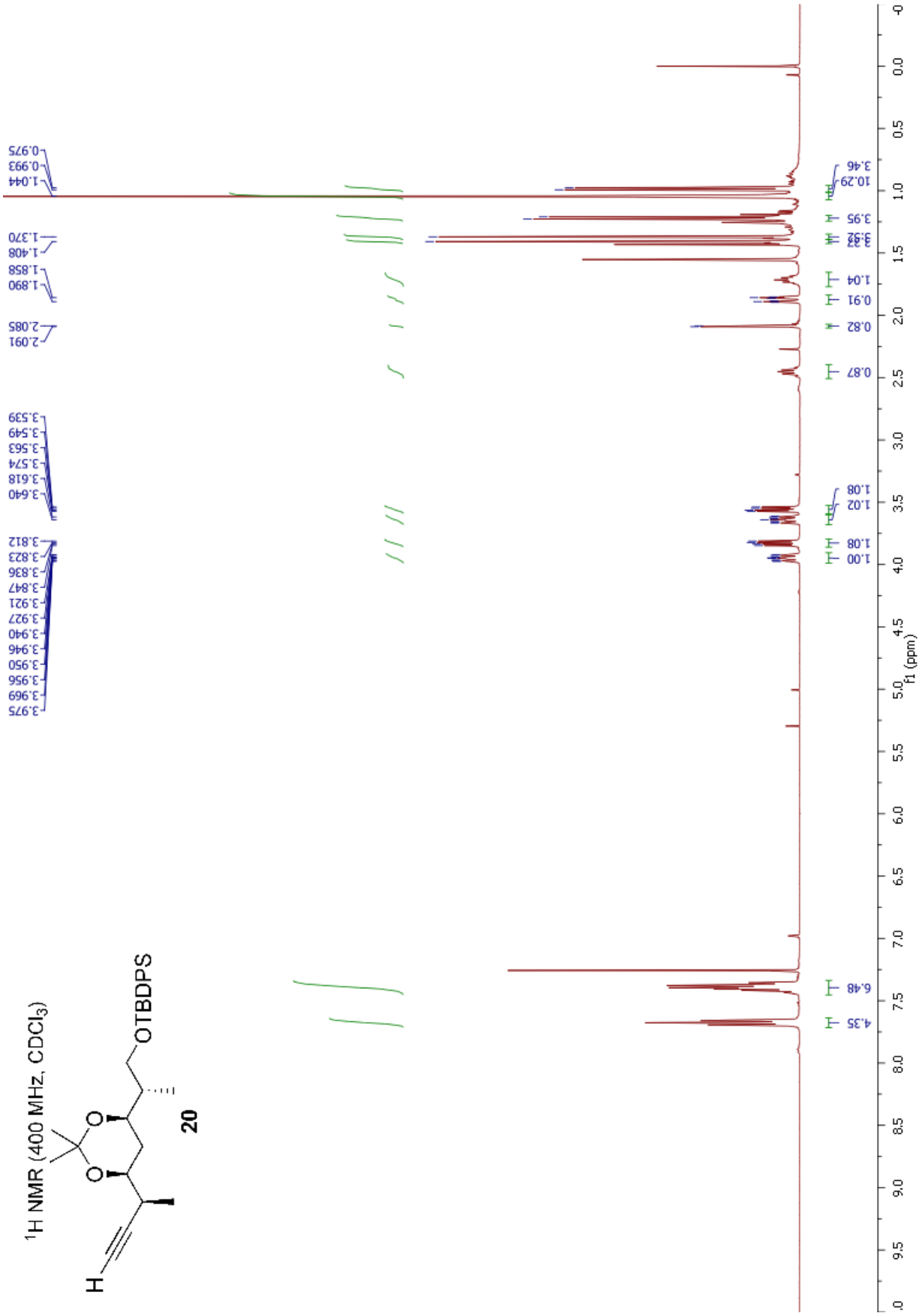

0.939
0.944
0.956
0.961
1.041
1.177
1.207
1.237
1.338
1.395
3.331
3.339
3.354
3.452
3.468
3.475
3.526
3.550
3.561
3.795
3.807
4.463
4.493
4.499
4.530
6.54
9.72
3.85
4.07
0.91
0.97
0.96
1.00
1.91
1.02
2.00
11.04
4.19
f1 (ppm)
^{1}H NMR (400 MHz, $CDCl_3$)
OTBDPS
BnO
16

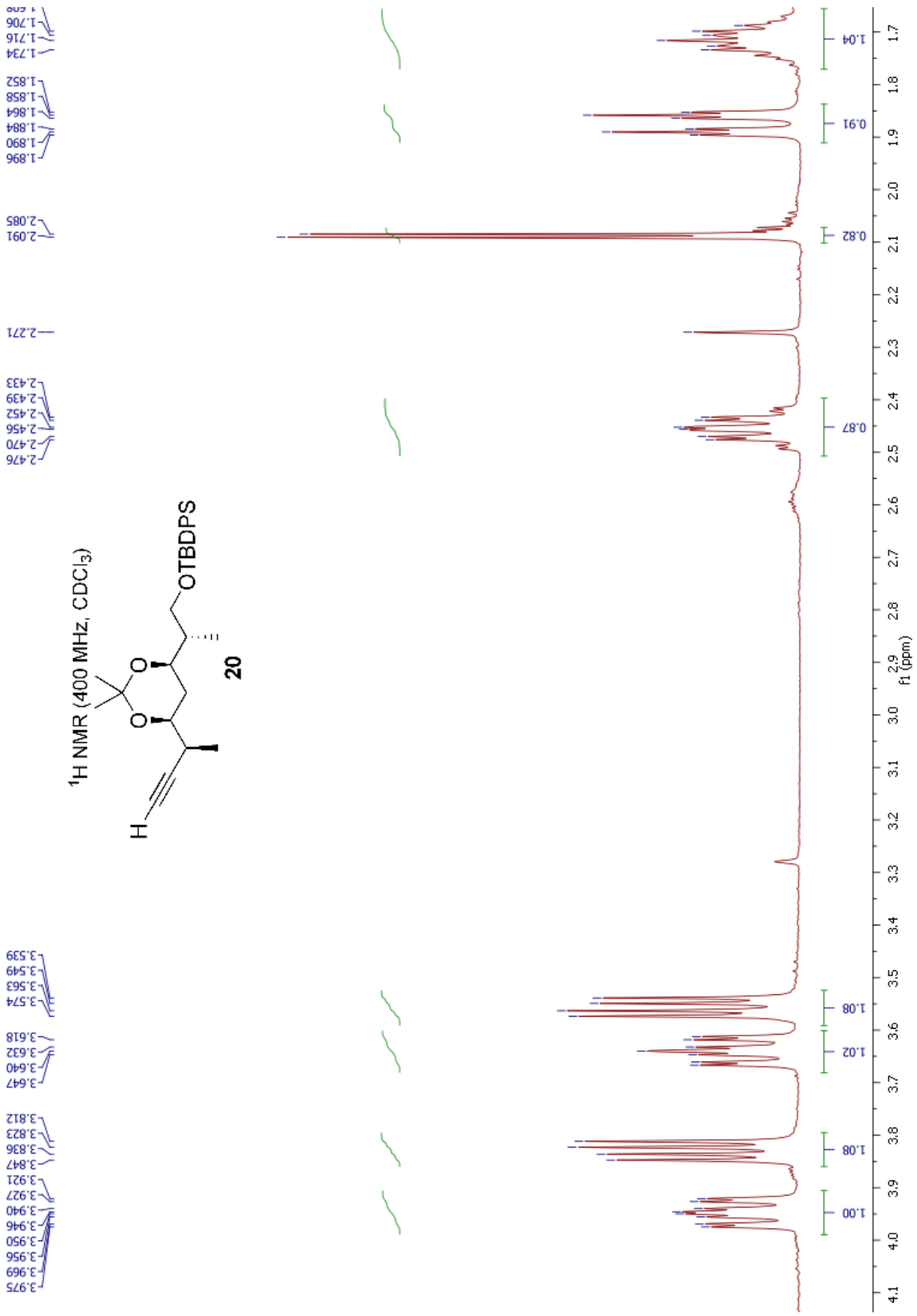

^{13}C NMR (100.6 MHz, CDCl$_3$)
OTBDPS
BnO
16
12.16
12.72
19.34
19.85
26.83
30.20
31.33
38.65
40.96
64.55
69.47
72.27
73.12
98.25
127.47
127.52
127.57
128.32
129.44
129.48
135.57
135.60
138.69
f1 (ppm)

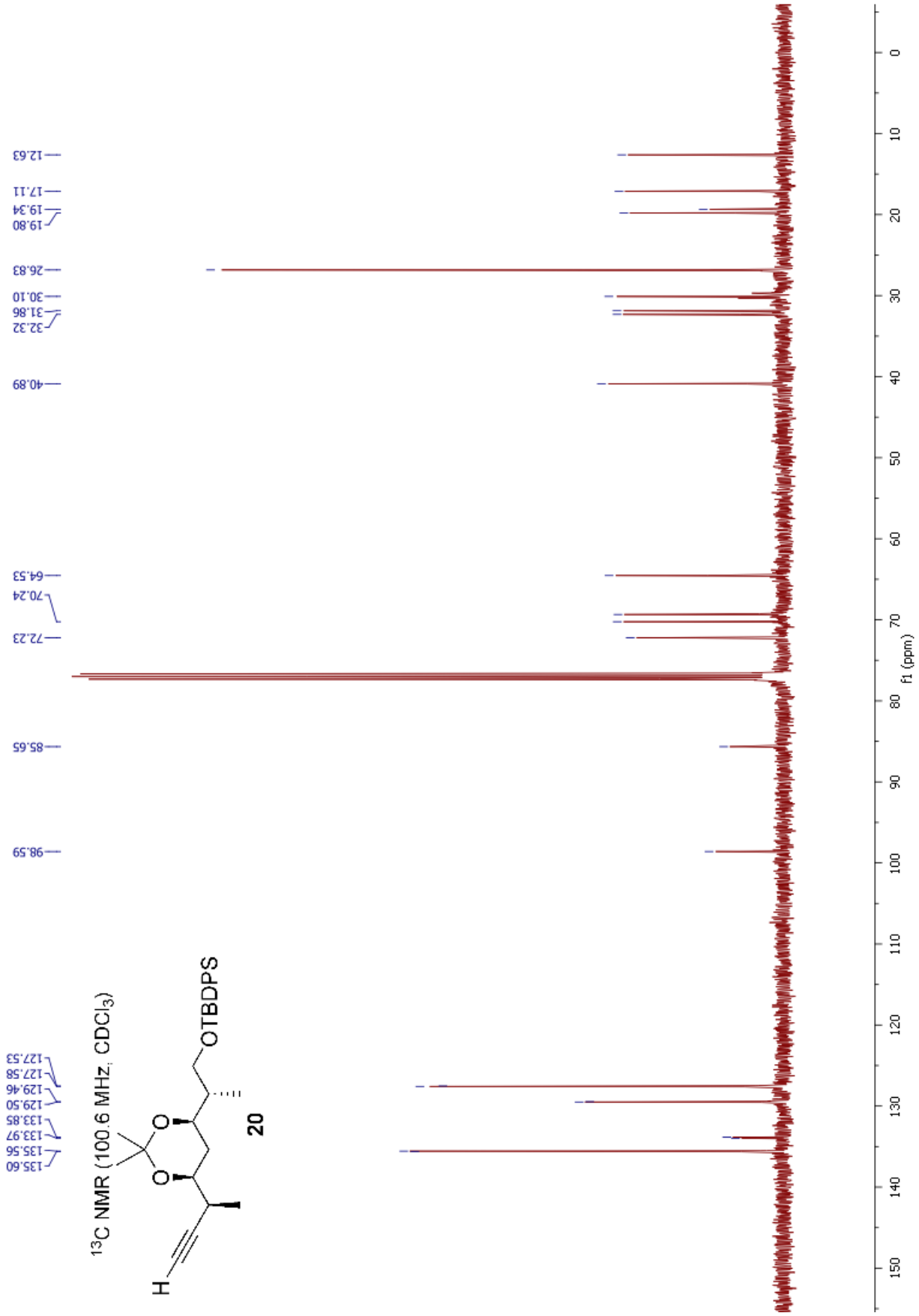

0.888
0.905
0.960
0.977
1.046
1.361
1.420
3.530
3.540
3.554
3.565
4.021
4.031
4.042
4.057
4.067
3.14
3.07
9.82
5.14
3.05
1.04
0.88
0.76
2.09
1.07
0.94
0.90
0.90
6.20
4.14
f1 (ppm)
^{1}H NMR (400 MHz, CDCl$_3$)
OTBDPS
HO
17

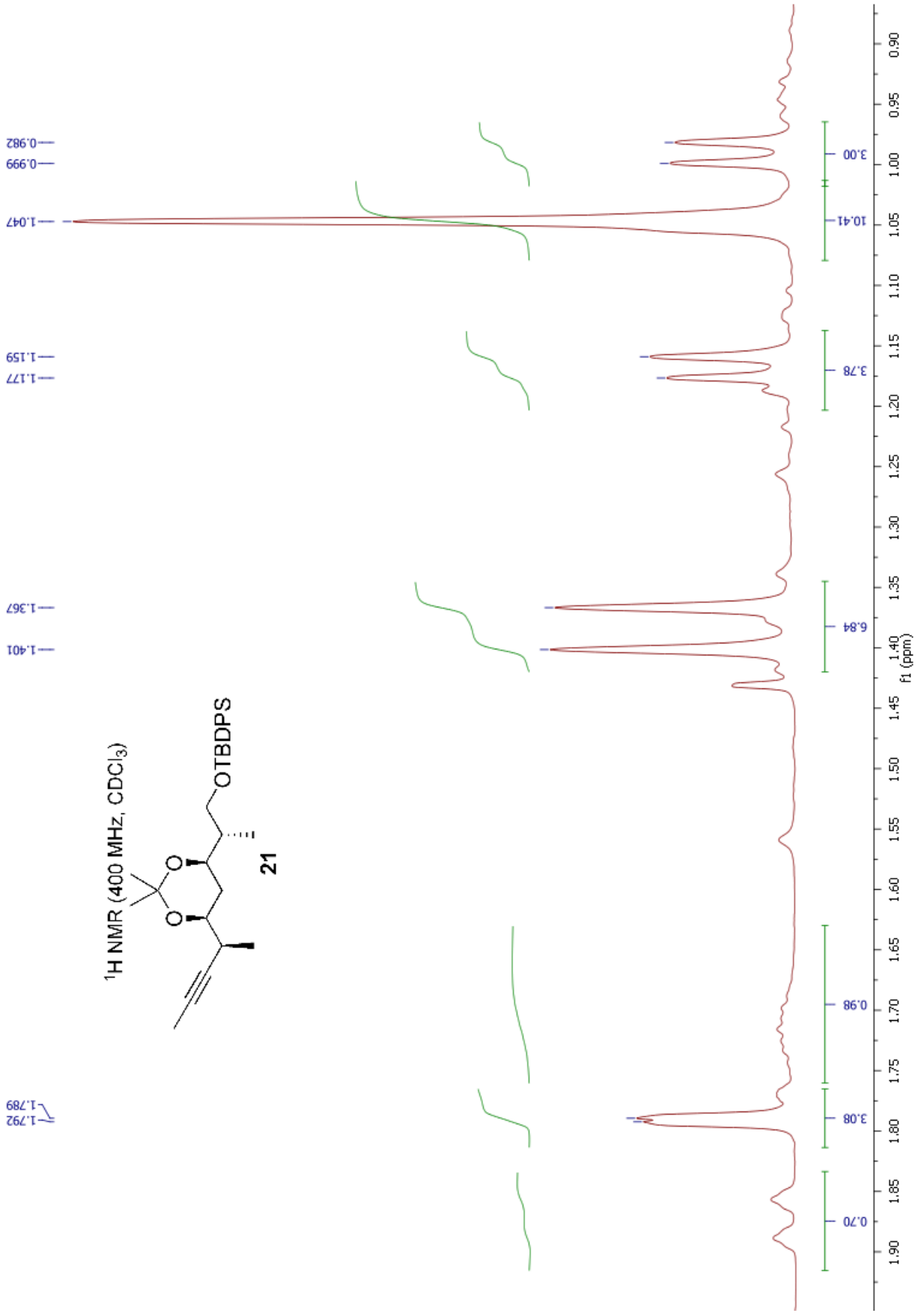

11.58
12.65
19.33
19.59
26.83
29.07
30.19
38.82
40.86
64.47
66.01
69.40
73.01
98.54
127.54
127.58
129.49
129.53
133.81
133.91
135.55
135.60
^{13}C NMR (100.6 MHz, $CDCl_3$)
OTBDPS
HO
O
O
17
f1 (ppm)

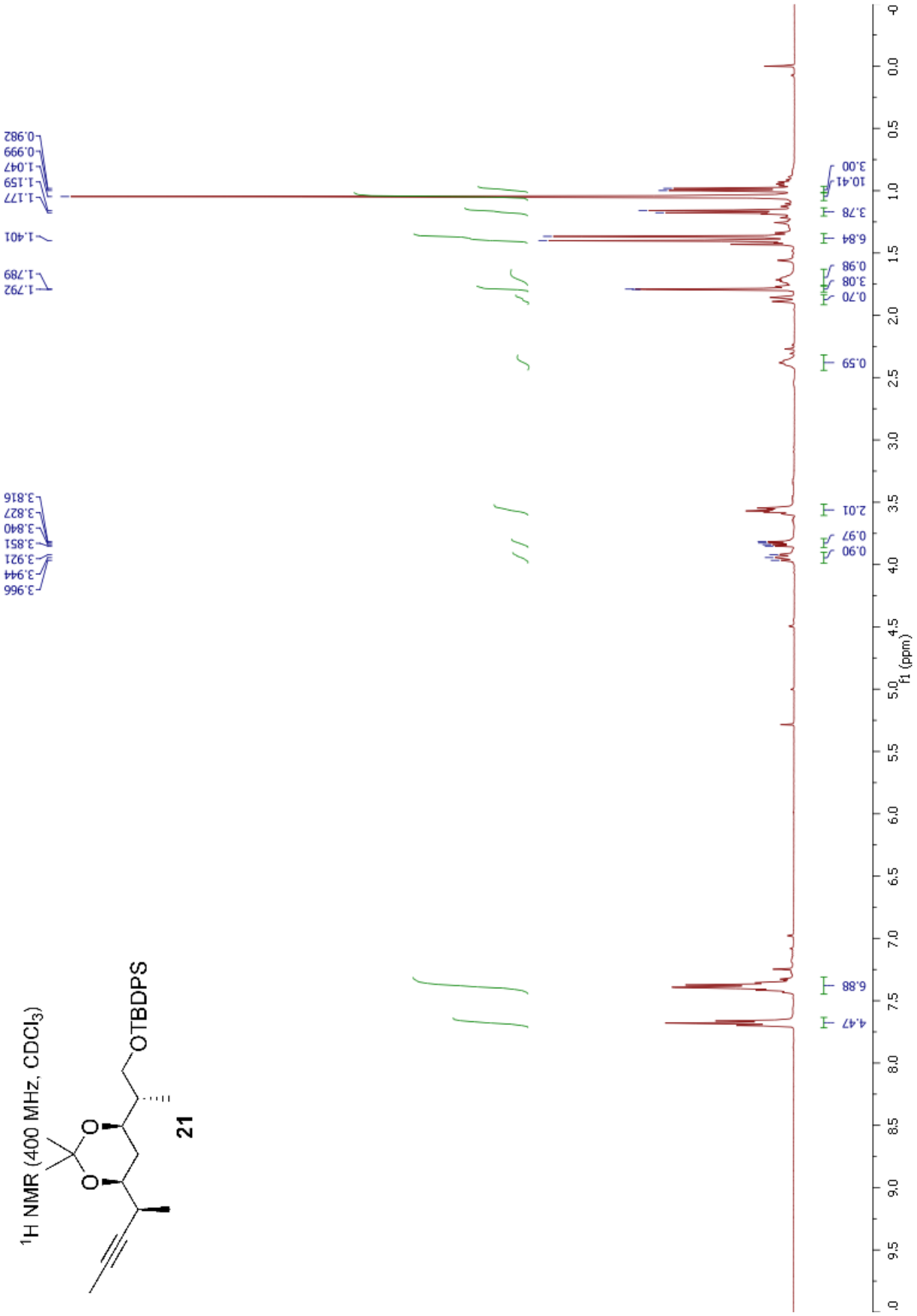

^{1}H NMR (400 MHz, $CDCl_3$)
OTBDPS
18
f1 (ppm)

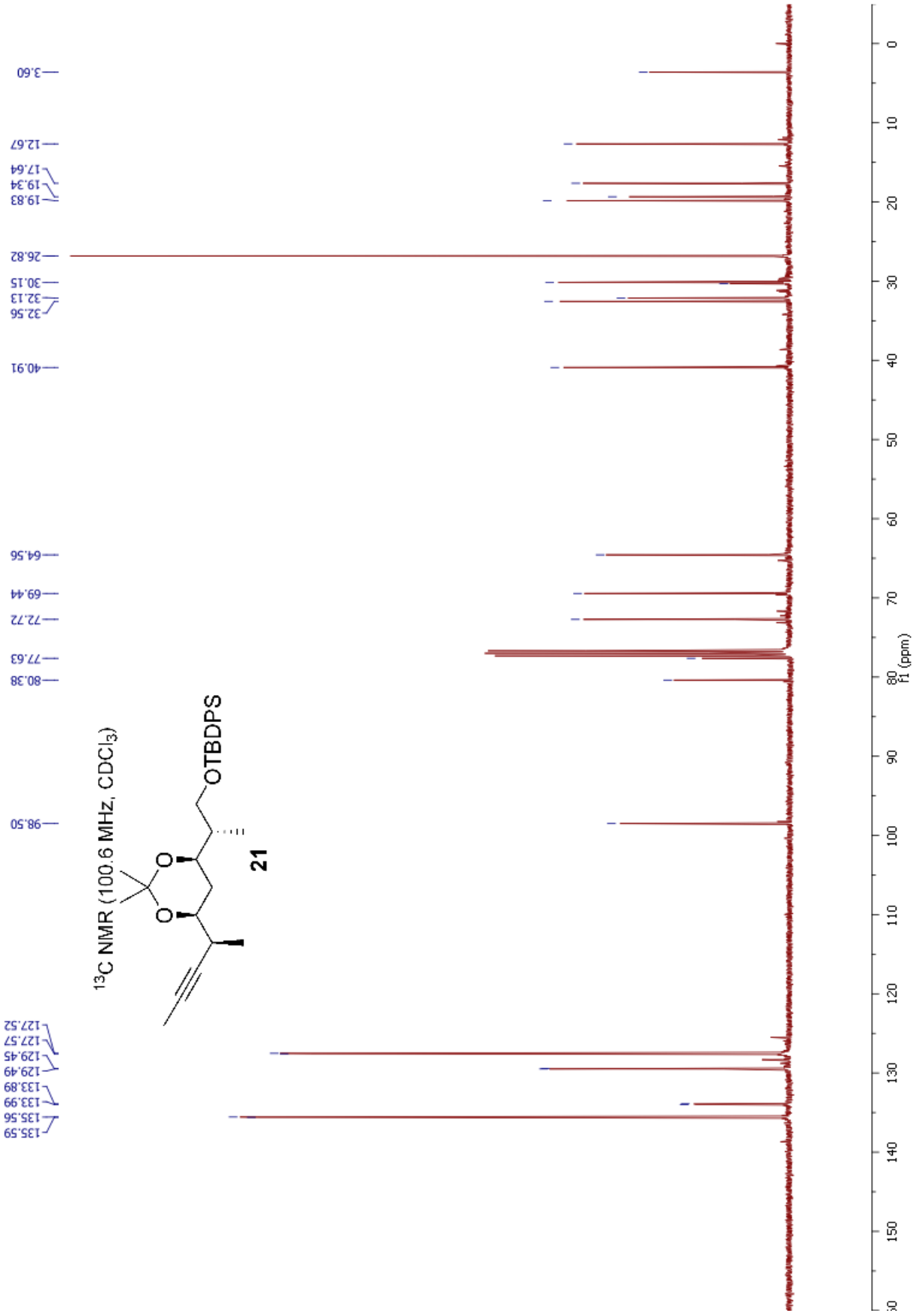

0.975
0.993
1.044
1.370
1.408
1.858
1.890
2.085
2.091
3.539
3.549
3.563
3.574
3.618
3.640
3.812
3.823
3.836
3.847
3.921
3.927
3.940
3.946
3.950
3.956
3.969
3.975
3.46
10.29
3.95
3.92
3.87
1.04
0.91
0.82
0.87
1.08
1.02
1.08
1.00
6.48
4.35
f1 (ppm)
^{1}H NMR (400 MHz, $CDCl_3$)
OTBDPS
O
O
H
20

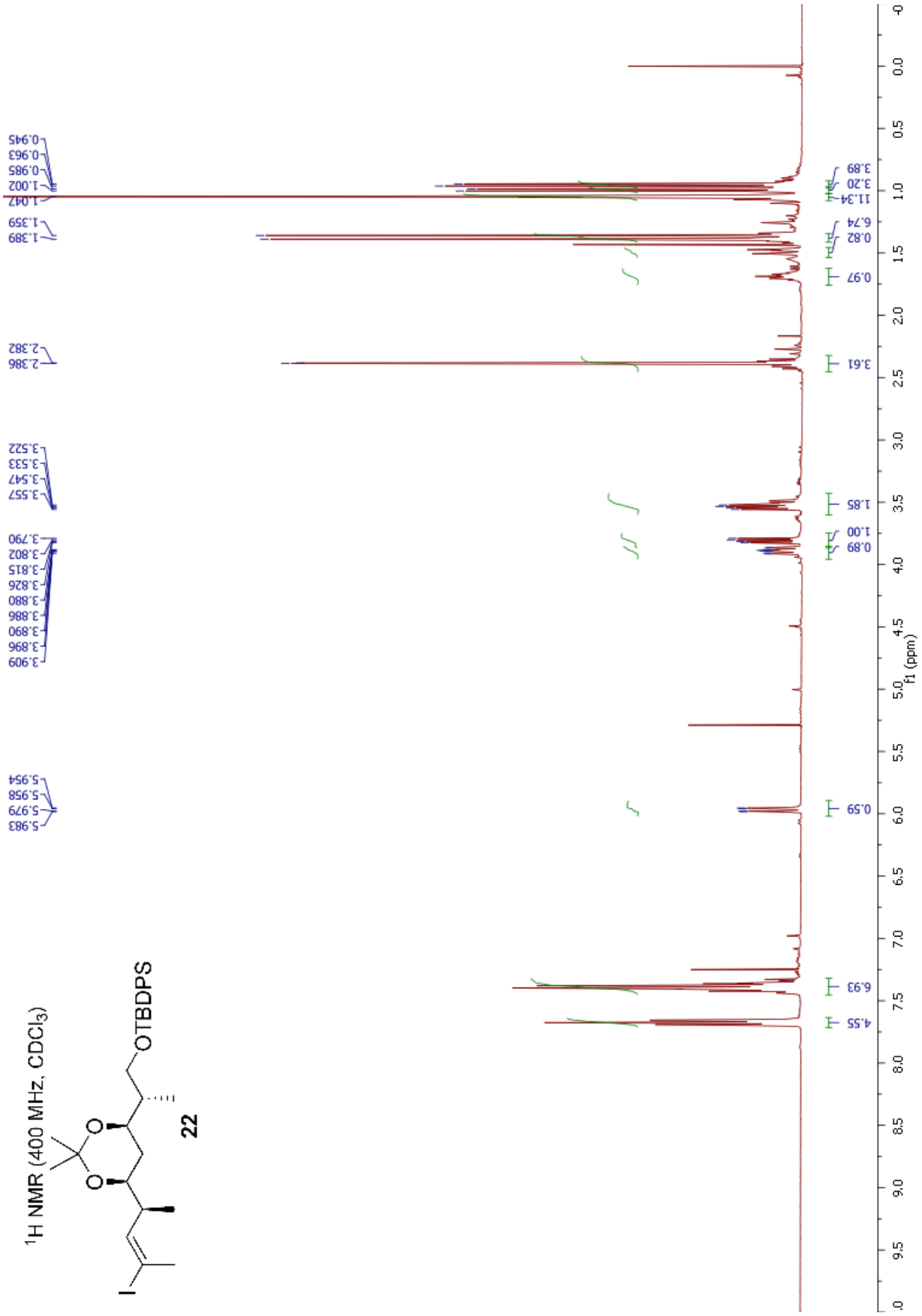

^{1}H NMR (400 MHz, CDCl$_3$)
OTBDPS
O
O
H
20
1.734
1.716
1.706
1.852
1.858
1.864
1.884
1.890
1.896
2.085
2.091
2.271
2.433
2.439
2.452
2.456
2.470
2.476
3.539
3.549
3.563
3.574
3.618
3.632
3.640
3.647
3.812
3.823
3.836
3.847
3.921
3.927
3.940
3.946
3.950
3.956
3.969
3.975
1.04
0.91
0.82
0.87
1.08
1.02
1.08
1.00
f1 (ppm)

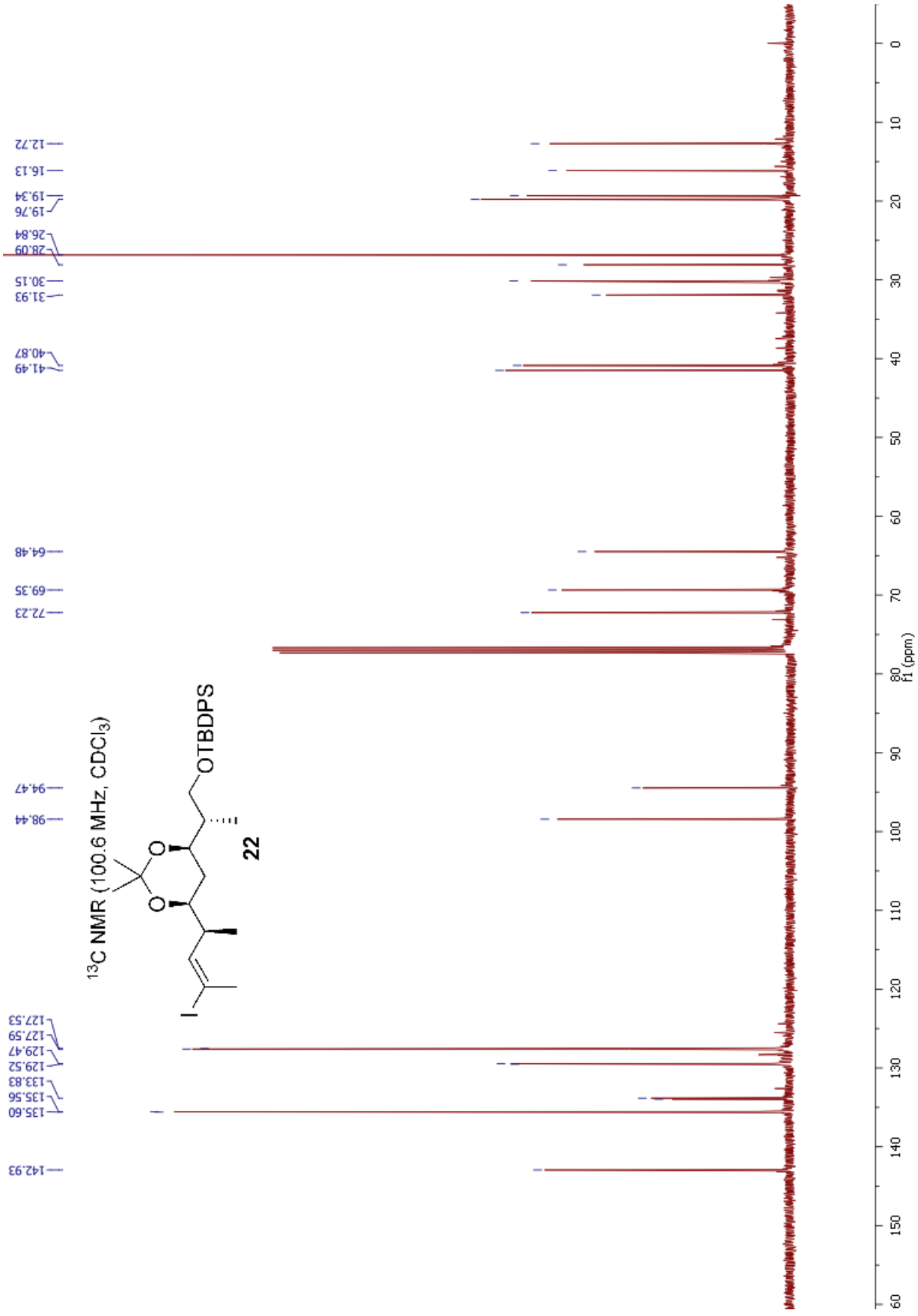

12.63
17.11
19.34
19.80
26.83
30.10
31.86
32.32
40.89
64.53
70.24
72.23
85.65
98.59
127.53
127.58
129.46
129.50
133.85
133.97
135.56
135.60
^{13}C NMR (100.6 MHz, CDCl$_3$)
OTBDPS
O
O
H
20
f1 (ppm)

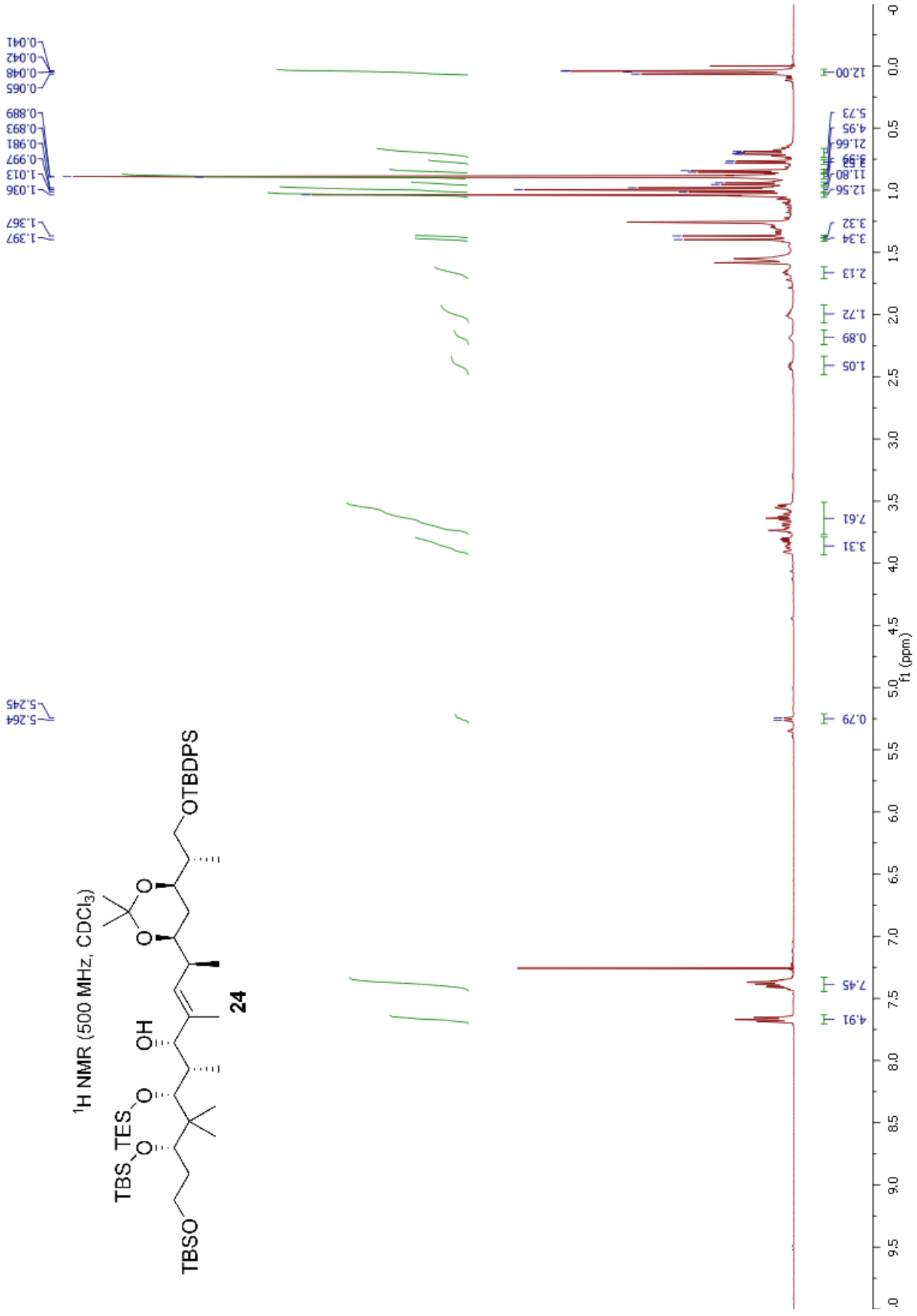

0.982
0.999
1.047
1.159
1.177
1.367
1.401
1.789
1.792
3.00
10.41
3.78
6.84
0.98
3.08
0.70
0.90
0.95
1.00
1.05
1.10
1.15
1.20
1.25
1.30
1.35
1.40
1.45
1.50
1.55
1.60
1.65
1.70
1.75
1.80
1.85
1.90
f1 (ppm)
^{1}H NMR (400 MHz, CDCl$_3$)
OTBDPS
21

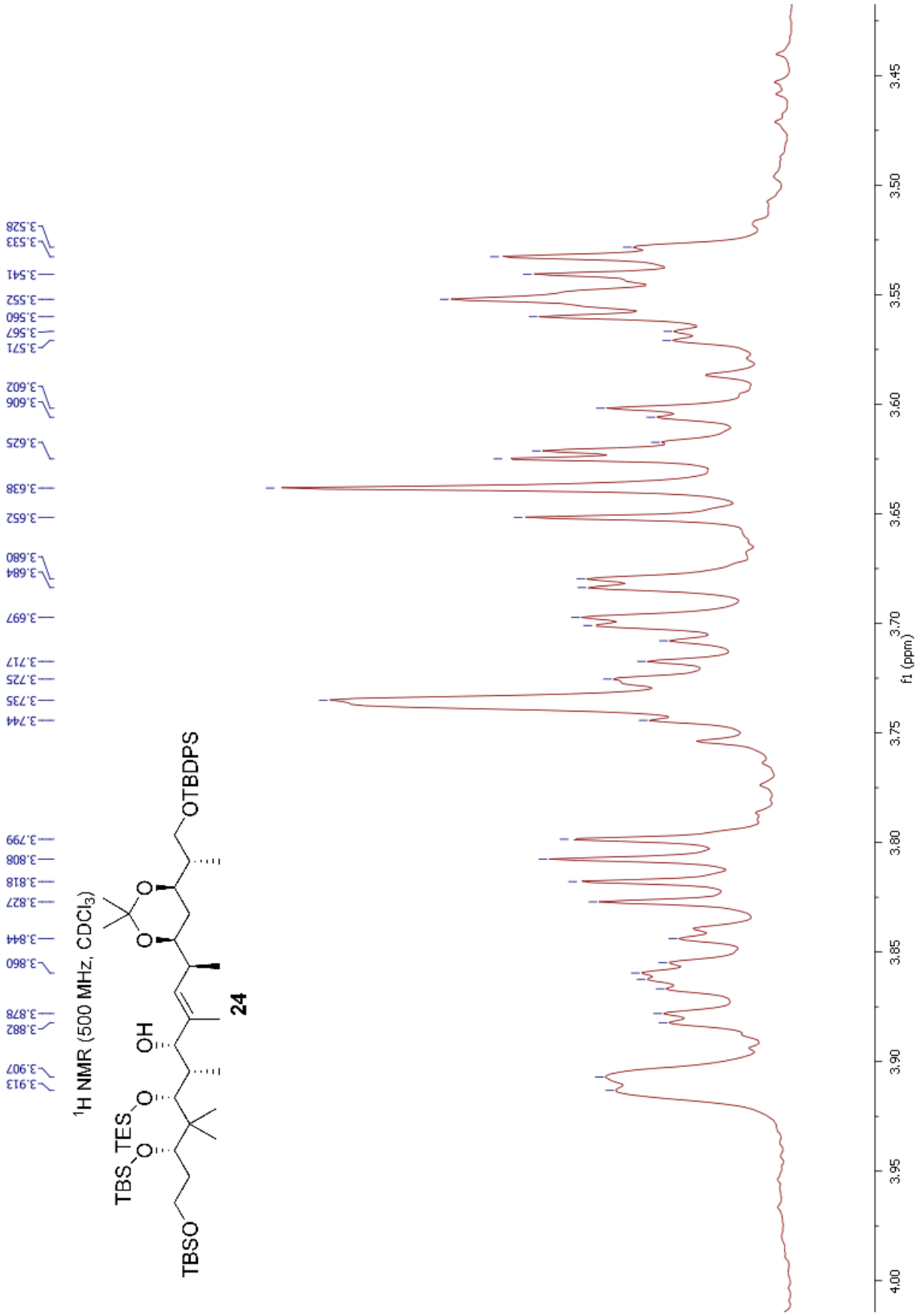

0.982
0.999
1.047
1.159
1.177
1.401
1.789
1.792
3.816
3.827
3.840
3.851
3.921
3.944
3.966
3.00
10.41
3.78
6.84
0.98
3.08
0.70
0.59
2.01
0.97
0.90
6.88
4.47
f1 (ppm)
^{1}H NMR (400 MHz, $CDCl_3$)
OTBDPS
21

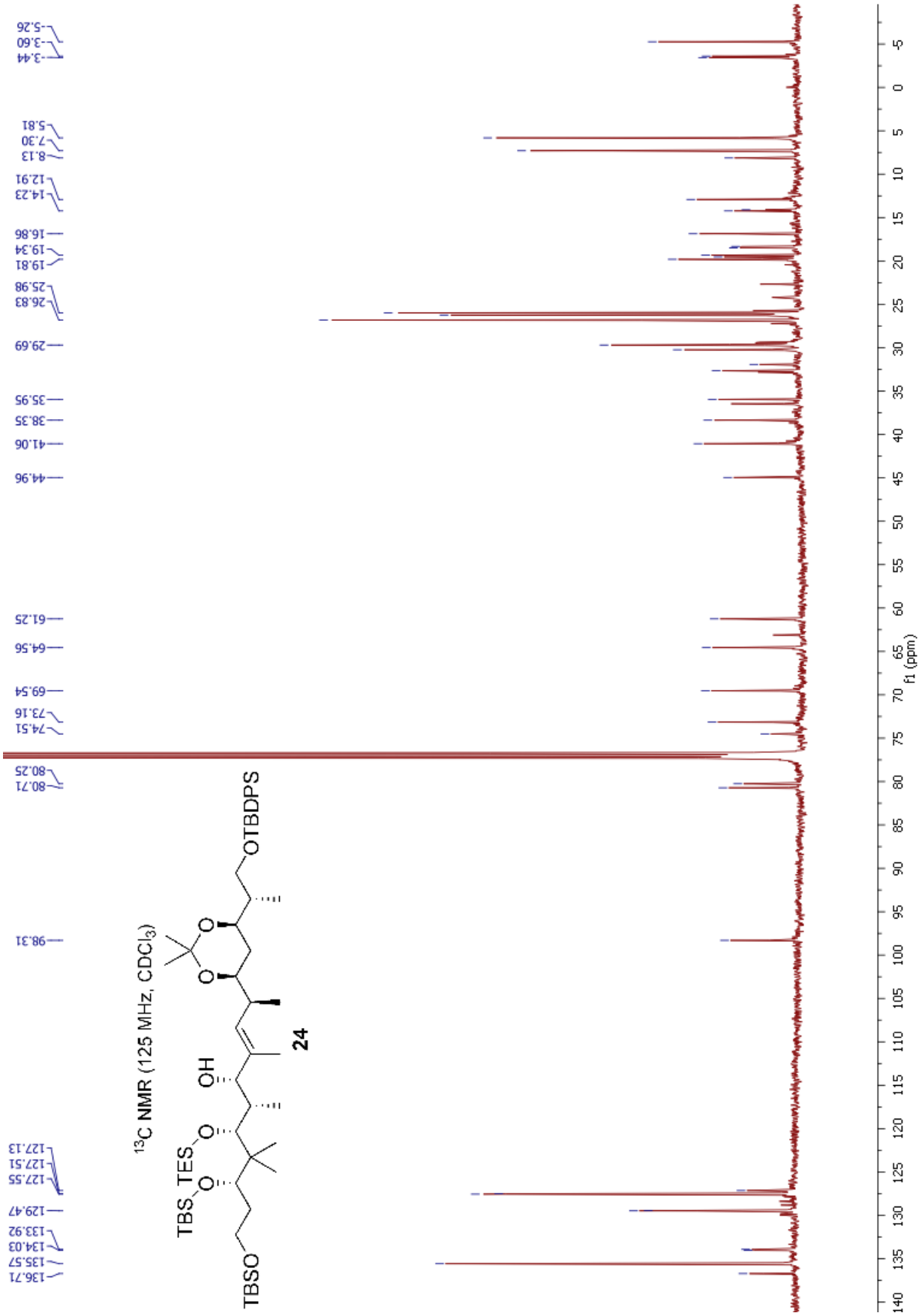

^{13}C NMR (100.6 MHz, $CDCl_3$)
OTBDPS
21
3.60
12.67
17.64
19.34
19.83
26.82
30.15
32.13
32.56
40.91
64.56
69.44
72.72
77.63
80.38
98.50
127.52
127.57
129.45
129.49
133.89
133.99
135.56
135.59
f1 (ppm)

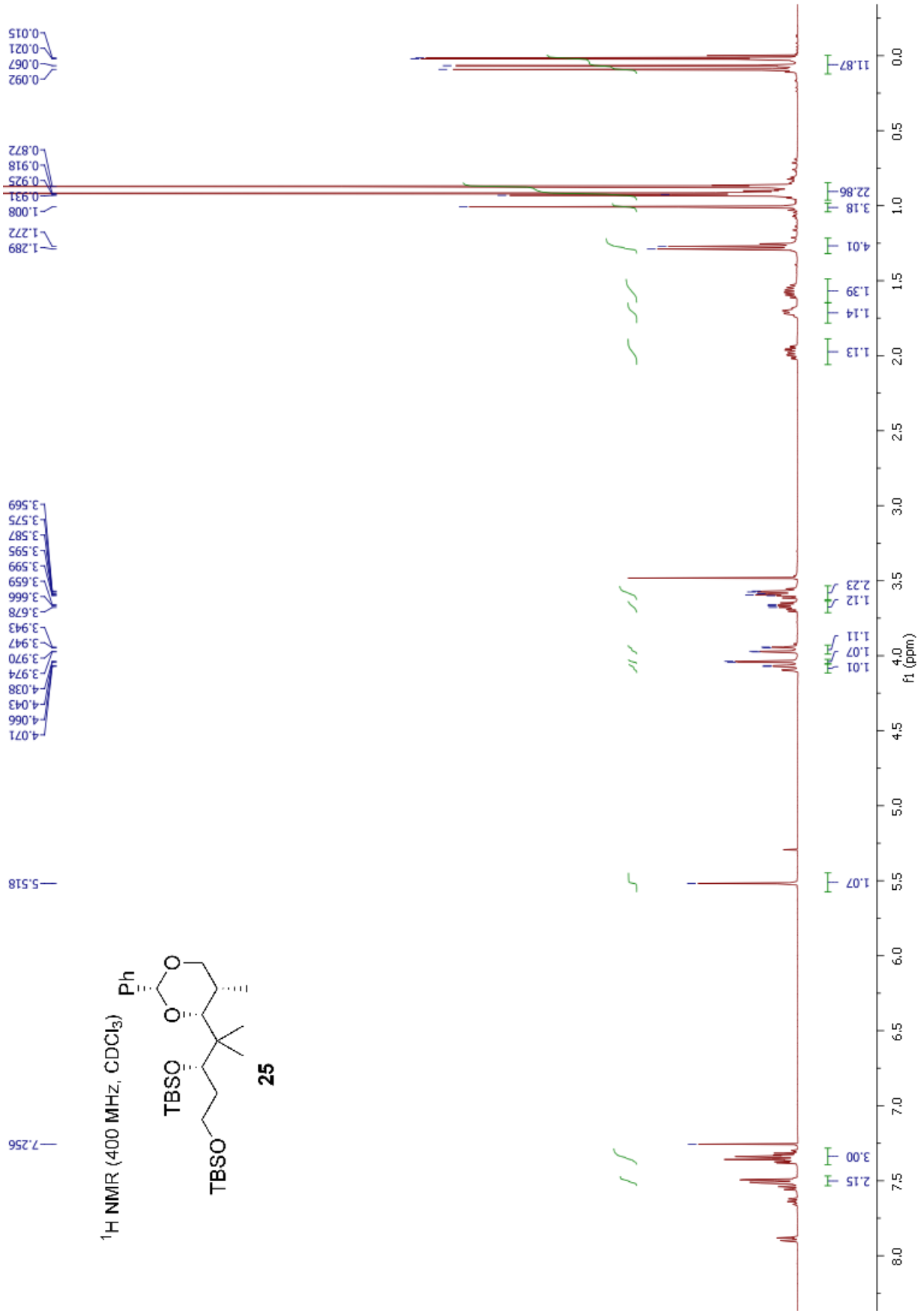

^{1}H NMR (400 MHz, $CDCl_3$)
OTBDPS
22
f1 (ppm)

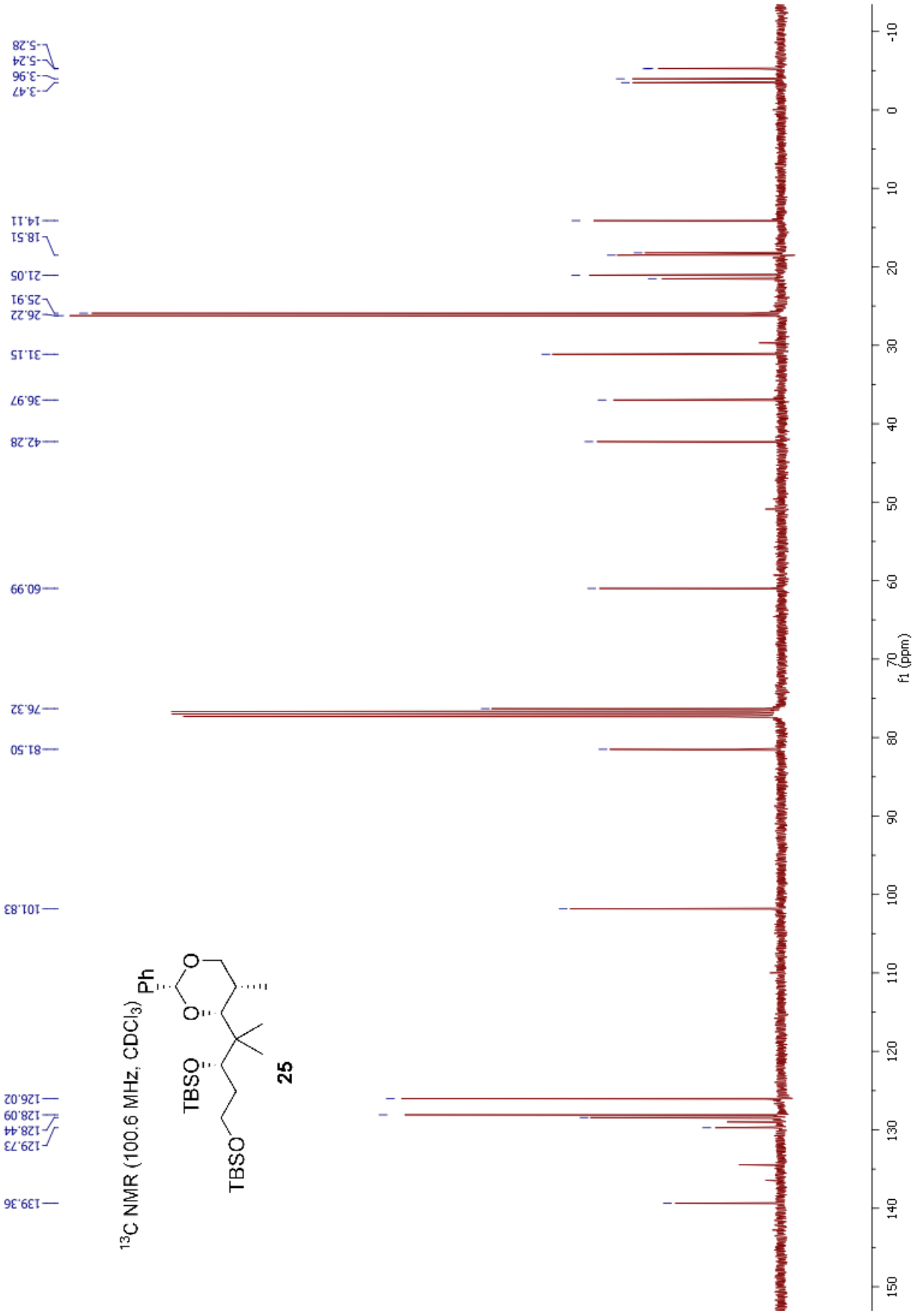

^{13}C NMR (100.6 MHz, $CDCl_3$)
OTBDPS
22
I
12.72
16.13
19.34
19.76
26.84
28.09
30.15
31.93
40.87
41.49
64.48
69.35
72.23
94.47
98.44
127.53
127.59
129.47
129.52
133.83
135.56
135.60
142.93
f1 (ppm)

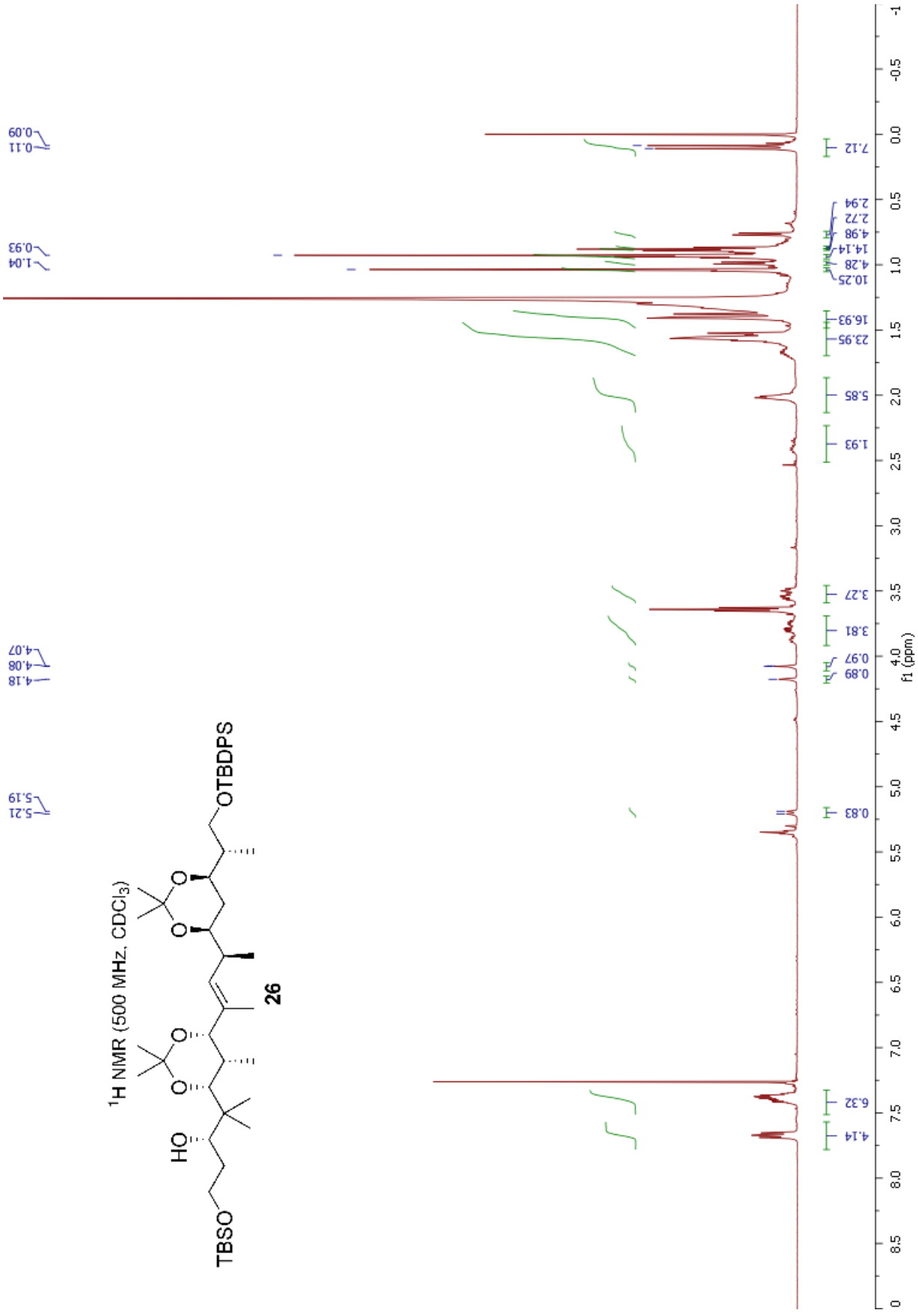

0.041
0.042
0.048
0.065
0.889
0.893
0.981
0.997
1.013
1.036
1.367
1.397
5.245
5.264
12.00
5.73
4.95
21.66
3.99
3.58
11.80
12.56
3.34
3.32
2.13
1.72
0.89
1.05
7.61
3.31
0.79
7.45
4.91
f1 (ppm)
^{1}H NMR (500 MHz, CDCl$_3$)
TBS
TES
OH
OTBDPS
TBSO
24

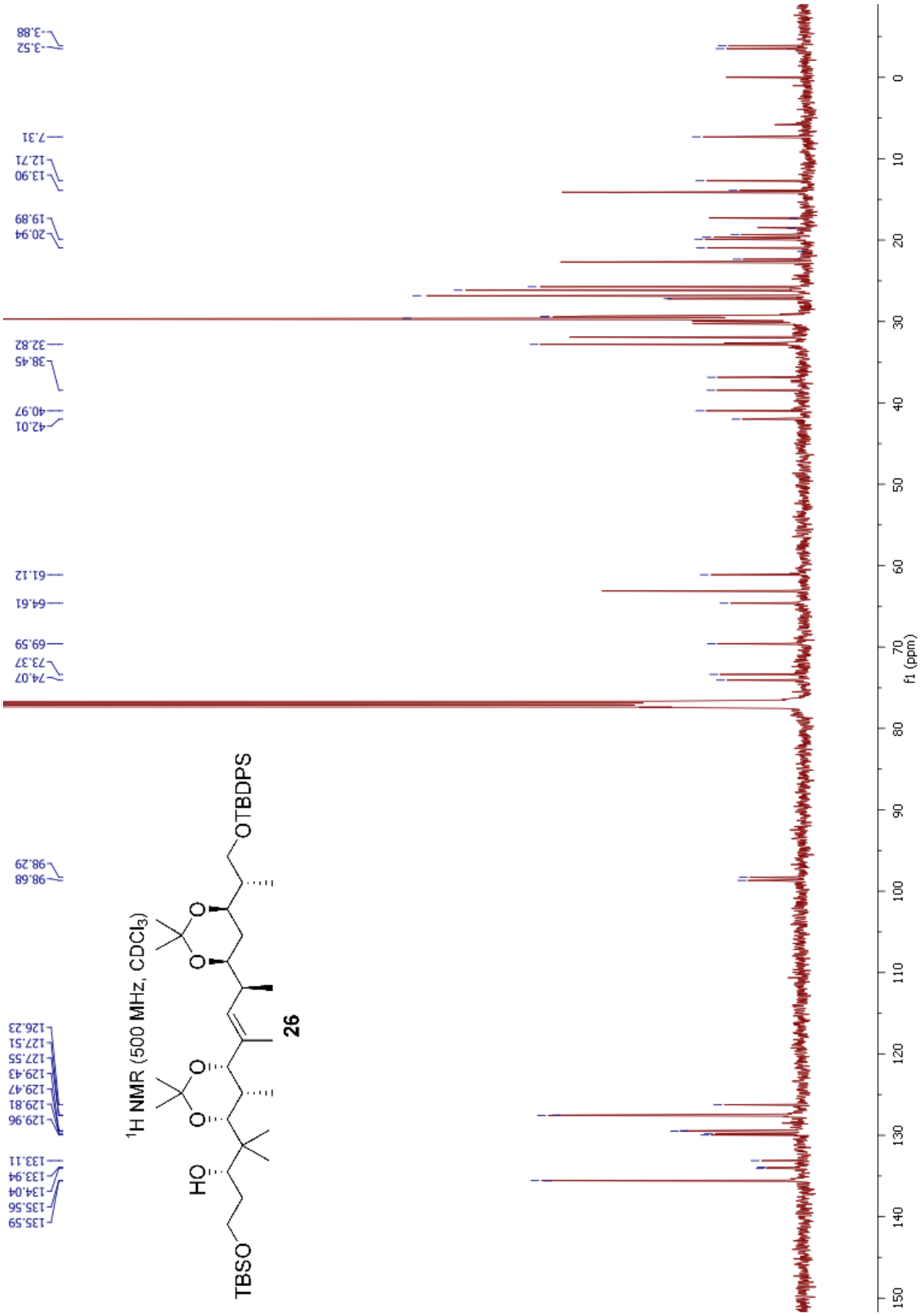

3.528
3.533
3.541
3.552
3.560
3.567
3.571
3.602
3.606
3.625
3.638
3.652
3.680
3.684
3.697
3.717
3.725
3.735
3.744
3.799
3.808
3.818
3.827
3.844
3.860
3.878
3.882
3.907
3.913
^{1}H NMR (500 MHz, $CDCl_3$)
TBSO
TBS
TES
OH
OTBDPS
24
3.45
3.50
3.55
3.60
3.65
3.70
3.75
3.80
3.85
3.90
3.95
4.00
f1 (ppm)


^{13}C NMR (125 MHz, CDCl$_3$)
TBSO
TBS
TES
OH
OTBDPS
24
f1 (ppm)


^{1}H NMR (400 MHz, CDCl$_3$)
Ph
O
O
TBSO
TBSO
25
f1 (ppm)


-5.28
-5.24
-3.96
-3.47
14.11
18.51
21.05
25.91
26.22
31.15
36.97
42.28
60.99
76.32
81.50
101.83
126.02
128.09
128.44
129.73
139.36
^{13}C NMR (100.6 MHz, CDCl$_3$)
TBSO
TBSO
Ph
O
O
25
f1 (ppm)


^{1}H NMR (500 MHz, $CDCl_3$)
26
OTBDPS
TBSO
HO
O
O
O
O
0.09
0.11
0.93
1.04
4.07
4.08
4.18
5.19
5.21
7.12
2.72
2.94
4.28
4.98
10.25
14.14
16.93
23.95
5.85
1.93
3.27
3.81
0.89
0.97
0.83
6.32
4.14
f1 (ppm)


-3.88
-3.52
7.31
12.71
13.90
19.89
20.94
32.82
38.45
40.97
42.01
61.12
64.61
69.59
73.37
74.07
98.29
98.68
126.23
127.51
127.55
129.43
129.47
129.81
129.96
133.11
133.94
134.04
135.56
135.59
f1 (ppm)
^{1}H NMR (500 MHz, CDCl$_3$)
OTBDPS
TBSO
HO
26