Supporting Information

Stereoselective Formation of Tetrahydrofuran Rings via [3 + 2] Annulation: Total Synthesis of Plakortone L

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Materials and Methods.

All experiments were performed in well-dried glassware fitted with rubber septa under argon atmosphere. Solvents and commercially available chemicals were purified by standard methods or used as purchased. Analytical TLC was performed on silica gel plates 60 F_{254} (Merck Co.). Flash column chromatography was performed on silica gel 60A (Kanto Co.). Optical rotations were measured on a JASCO DIP-1000 polarimeter. IR spectra were recorded on a JASCO FTIR-4100A spectrometer as thin film. NMR spectra were recorded on a JEOL JNM-ECX-500II spectrometer in $CDCl_3$ with TMS as the internal standard.

Aldehyde **2**,[1] methallyl ether **3**,[2] and phosphonium bromide **17**[3] were prepared according to the literature methods.

References

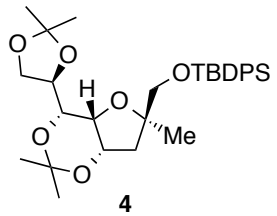
(1) Yadav, J. S.; Rao, B. M.; Sanjeevarao, K.; Reddy, B. V. S. *Synlett* **2008**, 1039-1041.

(2) Waser, J.; Gaspar, B.; Nambu, H.; Carreira, E. M. *J. Am. Chem. Soc.* **2006**, *128*, 11693-11712.

(3) Garnier, J.-M.; Robin, S.; Guillot, R.; Rousseau, G. *Tetrahedron: Asymmetry.* **2007**, *18*, 1434-1442.

Experimental Procedures

Tetrahyderofuran **4**: [3 + 2] annulation of aldehyde **2** with methallyl ether **3**

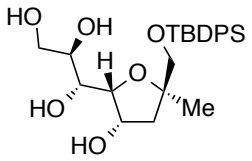


4

To a solution of aldehyde **2** (4.87 g, 21.2 mmol) and methallyl ether **3** (7.92 g, 25.4 mmol) in CH_2Cl_2 (200 mL) at –78 °C under Ar was added $BF_3 \cdot OEt_2$ (3.3 ml, 23.3 mmol) dropwise. The reaction mixture was stirred at –78 °C for 6 h, and then quenched with Et_3N (5 ml). The mixture was warmed to room temperature, poured into saturated aqueous $NaHCO_3$ (100 ml). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 ml). The combined organic layers were dried over $MgSO_4$,

filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 9:1) to afford tetrahydrofuran derivative **4** (8.59 g, 75%) as a white crystalline: $[\alpha]_D^{30}$ –19.7 (c 0.26, $CHCl_3$); IR (KBr) 2927, 2854, 1382, 1218, 1156, 1120, 1069, 836, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.04 (s, 9H), 1.30 (s, 3H), 1.35 (s, 3H), 1.36 (s, 3H), 1.41 (s, 3H), 1.44 (s, 3H), 1.56 (s, 3H), 1.76 (d, *J* = 13.3 Hz, 1H), 2.44 (dd, *J* = 13.3, 4.6 Hz, 1H), 3.43 (d, *J* = 10.1 Hz, 1H), 3.60 (d, *J* = 10.1 Hz, 1H), 3.86 (dd, *J* = 6.9, 2.3 Hz, 1H), 3.96 (dd, *J* = 2.3, 2.3 Hz, 1H), 4.00 (dd, *J* = 8.7, 5.5 Hz, 1H), 4.10 (dd, *J* = 8.7, 6.4 Hz, 1H), 4.38 (ddd, *J* = 6.9, 6.4, 5.5 Hz, 1H), 4.42 (dd, *J* = 4.6, 2.3 Hz, 1H), 7.36–7.42 (m, 6H), 7.69–7.76 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1, 19.4, 24.5, 25.5, 26.8, 26.8, 29.6, 40.4, 66.8, 70.1, 70.4, 72.7, 73.9, 75.0, 83.2, 97.7, 108.7, 127.6, 127.6, 129.5, 129.6, 133.4, 133.6, 135.7, 135.8.

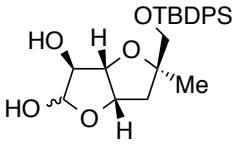
Tetraol **7**



7

To a solution of compound **4** (8.52 g, 15.8 mmol) in MeCN (220 ml) was added $Zn(NO_3)_2 \cdot 6H_2O$ (23.8 g, 80 mmol), and the reaction mixture was stirred at 50 °C for 5 h. After removal of the solvent under reduced pressure, a saturated aqueous solution of $NaHCO_3$ was added to the residue and extracted with AcOEt (3 x 100 ml). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1:2) to afford tetraol **7** (5.66 g, 78%) as a white crystalline: $[\alpha]_D^{26}$ –5.8 (c 1.19, $CHCl_3$); IR (KBr) 3418(br), 2931, 2854, 1425, 1113, 821, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (s , 9H), 1.33 (s, 3H), 1.79 (dd, *J* = 13.3, 2.3 Hz, 1H), 2.24 (s, 1H), 2.44 (dd, *J* = 13.3, 6.0 Hz, 1H), 2.82 (d, *J* = 4.6 Hz, 1H), 3.01 (d, *J* = 6.4 Hz, 1H), 3.45 (d, *J* = 10.5 Hz, 1H), 3.48 (d, *J* = 3.7 Hz, 1H), 3.56 (d, *J* = 10.5 Hz, 1H), 3.73—3.82 (m, 3H), 3.97 (ddd, *J* = 6.2, 6.2, 3.7 Hz, 1H), 4.11 (dd, *J* = 3.7, 3.7 Hz, 1H), 4.55 (ddd, *J* = 6.0, 3.7, 2.3 Hz, 1H), 7.37–7.45 (m, 6H), 7.64–7.68 (m, 4H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2, 24.7, 26.8, 42.8, 63.6, 70.1, 71.3, 72.6, 74.6, 82.1, 83.4, 127.7(x2), 129.7(x2), 133.2(x2), 135.6, 135.6.

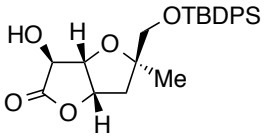
Lactol **8**



8

To a solution of compound **7** (5.32 g, 11.6 mmol) in CH_2Cl_2 (125 ml) at 0 °C was added aqueous solution (50 ml) of $NaIO_4$ (2.74 g, 12.7 mmol) dropwise over 2 h. The reaction mixture was stirred at 0 °C for 4 h. After addition of water (100 ml), the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 ml). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1:1) to afford lactol **8** (4.43 g, 92%, ca. 2:1 anomeric mixture) as a colorless oil: IR (neat) 3429(br), 2932, 2854, 1429, 1109, 1062, 825, 709 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ1.05 (s, 9H), 1.23 (s, 2H, major), 1.31 (s, 1H, minor), 1.64 (br, 0.7H, major), 1.87 (d, *J* = 13.8 Hz, 0.7H, major), 1.92 (br, 0.3H, minor), 2.04 (br, 0.3 H, minor), 2.07 (d, *J* = 14.2 Hz, 0.3H, minor), 2.36 (dd, *J* = 5.0, 13.8 Hz, 0.7H, major), 2.48 (dd, *J* = 6.9, 14.2 Hz, 0.3H, minor), 2.69 (br, 0.7H, major), 3.35 (d, *J* = 10.1 Hz, 1H), 3.53 (d, *J* = 10.5 Hz, 1H), 3.73 (br, 0.7H, major), 4.19 (t, *J* = 4.6 Hz, 0.7H, major), 4.27 (d, *J* = 4.6 Hz, 0.3H, minor), 4.45 (d, *J* = 4.1 Hz, 0.3H, minor), 4.56 (d, *J* = 3.7 Hz, 0.7H, major), 4.94–4.98 (m, 1H), 5.21 (d, *J* = 10.5 Hz, 0.3H, minor), 5.56 (dd, *J* = 3.7, 7.3 Hz, 0.7H, major), 7.36–7.44 (m, 6H), 7.64–7.68 (m, 4H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2, 24.0, 24.2, 26.8, 40.5, 41.9, 70.4, 76.1, 79.0, 83.3, 85.8, 86.5, 87.0, 88.4, 89.0, 98.4, 104.8, 127.7, 127.8, 129.7, 129.8, 129.9, 132.9, 133.1, 133.2, 135.5, 135.6, 135.7.

Lactone **9**

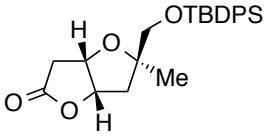


9

To a solution of compound **8** (5.75 g, 13.4 mmol) in CH_2Cl_2 (85 ml) at 0 °C under Ar was added a solution of NIS (7.77 g, 34.5 mmol) and Bu_4NI (5.65 g, 15.3 mmol) in CH_2Cl_2 (60 ml). The reaction mixture was stirred at room temperature for 21 h. The mixture was poured into a saturated aqueous solution of $Na_2S_2O_3$ and extracted with CH_2Cl_2 (3 x 50

ml). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1:1) to afford lactone **9** (5.68 g, 99%) as a colorless oil: $[a]_D^{30}$ –45.3 (c 1.86, $CHCl_3$); IR (neat) 3426(br), 2934, 2862, 1786, 1425, 1185, 1108, 1065, 825, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.06 (s, 9H), 1.21 (s, 3H), 2.05 (dd, *J* = 14.2, 1.8 Hz, 1H), 2.56 (dd, *J* = 14.2, 6.4 Hz, 1H), 3.25 (br, 1H) , 3.39 (d, *J* = 10.5 Hz, 1H), 3.60 (d, *J* = 10.5 Hz, 1H), 4.34 (d, *J* = 1.8 Hz, 1H), 4.68 (dd, *J* = 4.1, 1.8 Hz, 1H), 5.30 (ddd, *J* = 6.4, 4.1, 1.8 Hz, 1H), 7.37-7.45 (m, 6H), 7.64-7.68 (m, 4H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1, 24.2, 26.8, 39.4, 53.4, 70.4, 73.6, 84.8, 85.5, 86.3, 127.8, 129.8, 129.9, 132.8, 132.8, 135.5, 135.5, 176.7.

Lactone **5** :Barton-McCombie deoxygenation



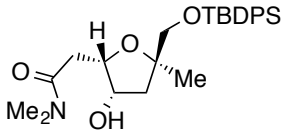
5

To a solution of compound **9** (2.12 g, 4.97 mmol) in MeCN (48 ml) at 0 °C under Ar was added N,N-dimethyl-4-aminopyridine (1.22 g, 9.94 mmol) and phenyl chlorothionoformate (1.05 g, 5.67 mmol). The reaction mixture was stirred at 0 °C for 40 min. The mixture was poured into a saturated aqueous solution of $NaHCO_3$ and extracted with AcOEt (3 x 50 ml). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 9:1) to afford lactone **10** (2.45 g, 84%) as a pale yellow oil: IR (neat) 2931, 2854, 1793, 1487, 1425, 1283, 1182, 1109, 1069, 822, 739, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.06 (s, 9H), 1.26 (s, 3H), 2.11 (dd, *J* = 14.2, 1.8 Hz, 1H), 2.67 (dd, *J* = 14.2, 6.9 Hz, 1H), 3.41 (d, *J* = 10.5 Hz, 1H), 3.66 (d, *J* = 10.5 Hz, 1H), 5.01 (dd, *J* = 4.6, 0.9 Hz, 1H), 5.38 (ddd, *J* = 6.9, 4.6, 1.8 Hz, 1H), 5.68 (d, *J* = 0.9 Hz, 1H), 7.08-7.10 (m, 2H), 7.30-7.45 (m, 9H) 7.64-7.67 (m, 4H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.2, 19.1, 21.0, 24.0, 26.8, 39.8, 60.4, 70.9, 80.3, 82.6, 85.5, 86.9, 121.6, 126.9, 127.9, 129.7, 129.9, 132.6, 132.7, 135.5, 153.5, 170.6, 193.3.

To a solution of compound **10** (2.84 g, 5.04 mmol) and Bu3SnH (5.09 g, 17.5 mmol) in toluene (40 ml) at reflex under Ar was added a solution of AIBN (0.17 g, 1.0 mmol) in toluene (6 ml). The reaction mixture was stirred at reflux for 30 min and cooled to room

temperature. The mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 14:1) to afford lactone **5** (2.01 g, 97%) as a white crystalline: $[a]_D^{26}$ –22.6 (c 0.54, $CHCl_3$); IR (KBr) 2964, 2934, 2856, 1778, 1429, 1164, 1113, 1094, 1065, 825, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.05 (s, 9H), 1.23 (s, 3H), 2.08 (d, *J* = 14.7 Hz, 1H), 2.57 (dd, *J* = 14.7, 6.4 Hz, 1H), 2.70 (d, *J* = 2.9 Hz, 2H), 3.40 (d, *J* = 10.5 Hz, 1H), 3.61 (d, *J* = 10.5 Hz, 1H), 4.85 (ddd, *J* = 4.6, 2.9, 2.9 Hz, 1H), 5.08 (dd, *J* = 6.4, 4.6 Hz, 1H), 7.37-7.46 (m, 6H), 7.63-7.66 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.2, 24.4, 26.8, 37.5, 39.9, 70.6, 79.3, 85.9, 86.3, 127.7, 127.8, 129.8, 129.9, 132.9, 133.0, 135.5, 135.5, 175.8.

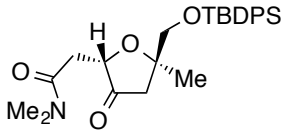
Hydroxy amide **11**



11

To a 1 M THF solution of Me_2NH (24.6 mmol, 24.6 ml) at –78 °C under Ar was added Me_3Al (1.4 M in hexane, 9.8 mmol, 7.0 ml). The resulting mixture was stirred at –78 °C for 30 min. A solution of lactone **5** (2.01 g, 4.90 mmol) in THF (12 ml) was added dropwise via cannula, and the solution was warmed to room temperature and stirred for 1.5 h. The reaction mixture was quenched by careful addition of 50 ml of CH_2Cl_2 and 100 ml of 0.1 M HCl solution and extracted with CH_2Cl_2 (3 x 20 ml). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1:1) to afford hydroxyl amide **11** (2.12 g, 95%) as a colorless oil: $[a]_D^{29}$ +5.5 (c 0.43, $CHCl_3$); IR (neat) 3418(br), 2934, 2858, 1626, 1429, 1113, 1051, 705 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.04 (s, 9H), 1.29 (s, 3H), 1.78 (dd, *J* = 13.3, 3.2 Hz, 1H), 2.48 (dd, *J* = 13.3, 6.4 Hz, 1H), 2.78 (dd, *J* = 14.2, 9.2 Hz, 1H), 2.84 (dd, *J* = 14.2, 4.1 Hz, 1H), 2.95 (s, 3H), 3.05 (s, 3H), 3.41 (d, *J* = 10.1 Hz, 1H), 3.52 (d, *J* = 10.1 Hz, 1H), 4.28 (ddd, *J* = 9.2, 4.1, 4.1 Hz, 1H), 4.50 (ddd, *J* = 6.4, 4.1, 3.2 Hz, 1H), 7.36-7.43 (m, 6H), 7.65-7.68 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.2, 25.0, 26.8, 34.2, 35.5, 37.9, 42.1, 70.4, 73.8, 79.8, 82.9, 127.6(x2), 129.6, 129.7, 133.4, 133.5, 135.6, 135.6, 171.8.

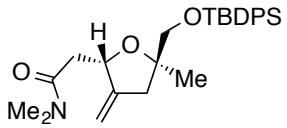
Keto amide **12**



12

To a solution of compound **11** (1.31 g, 2.88 mmol) and $NaHCO_3$ (484 mg, 5.76 mmol) in CH_2Cl_2 (32 ml) at 0 °C under Ar was added Dess-Martin periodinane (2.44 g, 5.76 mmol) portion-wise. The resulting mixture was stirred at room temperature for 2.5 h. The reaction mixture was filtered through a Celite bed and washed thoroughly with CH_2Cl_2 (2 x 20 ml). The filtrate was washed with an aqueous solution of $Na_2S_2O_3$ and a saturated aqueous solution of $NaHCO_3$ and dried over $MgSO_4$. The organic layer was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1:1) to afford keto amide **12** (1.25 g, 96%) as a colorless oil: $[a]_D^{33}$ –36.9 (c 0.43, $CHCl_3$); IR (neat) 2931, 2858, 1753, 1651, 1429, 1392, 1113, 1084, 825, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.01 (s, 9H), 1.31 (s, 3H), 2.67 (d, *J* = 17.4 Hz, 1H), 2.77 (dd, *J* = 17.0, 4.1 Hz, 1H), 2.81 (d, *J* = 17.4 Hz, 1H), 2.91 (s, 3H), 2.95 (dd, *J* = 17.0, 4.1 Hz, 1H), 2.98 (s, 3H), 3.46 (d, *J* = 10.5 Hz, 1H), 3.74 (d, *J* = 10.5 Hz, 1H), 4.47 (dd, *J* = 4.1, 4.1 Hz, 1H), 7.36-7.45 (m, 6H), 7.62-7.66 (m, 4H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.1, 23.7, 26.7, 35.5, 36.8, 37.3, 44.3, 72.1, 78.3, 81.1, 127.8(x2), 129.7, 129.8, 132.7, 132.9, 135.5, 135.6, 169.0, 216.7.

Methylene amide **13**

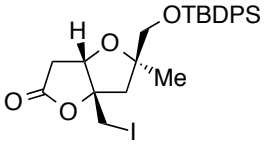


13

To a solution of methyltriphenylphosphonium bromide (2.36 g, 6.61 mmol) in THF (44 ml) at 0 °C under Ar was added t-BuOK (753 mg, 6.7 mmol) in THF (18 ml). The resulting mixture was stirred at 0 °C for 75 min. A solution of compound **12** (1.00 g, 2.20 mmol) in THF (36 ml) was added dropwise via cannula, and the reaction mixture was stirred at 0 °C for 2 h. The reaction mixture was diluted with AcOEt (50 ml) and water (30 ml). The organic layer was separated and the aqueous layer was extracted with AcOEt (3 x 20 ml). The combined organic layers were dried over $MgSO_4$, filtered, and

concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 4:1) to afford methylene amide **13** (840 mg, 85%) as a colorless oil: $[a]_D^{25}$ –42 (c 0.054, $CHCl_3$); IR (neat) 2927, 2858, 1647, 1425, 1396, 1109, 1032, 822, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.04 (s, 9H), 1.30 (s, 3H), 2.39 (dd, *J* = 15.6 Hz, 1.8 Hz, 1H), 2.48 (dd, *J* = 14.7 Hz, 4.6 Hz, 1H), 2.68 (dd, *J* = 14.7, 7.3 Hz, 1H), 2.82 (d, *J* = 15.6 Hz, 1H), 2.94 (s, 3H), 3.02 (s, 3H), 3.41 (d, *J* = 10.1 Hz, 1H), 3.52 (d, *J* = 10.1 Hz, 1H), 4.85 (ddd, *J* = 7.3, 4.6, 1.8 Hz, 1H), 4.89 (dd, *J* = 4.1, 1.8 Hz, 1H), 4.96 (dd, *J* = 4.1, 1.8 Hz, 1H), 7.35-7.42 (m, 6H), 7.63-7.65 (4H, m) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.3, 24.3, 26.8, 35.5, 37.7, 40.7, 41.1, 68.7, 77.9, 82.6, 105.6, 127.6(x2), 129.6, 129.6, 133.5(x2), 135.6, 135.6, 151.5, 170.6.

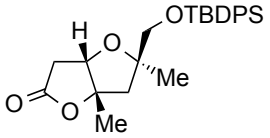
Iodolactone **14**



14

To a solution of compound **13** (896 mg, 1.98 mmol) in THF (14.6 ml) and water (7.3 ml) at 0 °C was added a solution of I_2 (1.80 g, 7.1 mmol) in THF (7.3 ml). The resulting mixture was stirred at 0 °C for 11 h. The reaction mixture was quenched by addition of a saturated aqueous solution of $Na_2S_2O_3$ (10 ml) and extracted with AcOEt (3 x 50 ml). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 19:1) to afford iodolactone **14** (909 mg, 83%) as a colorless oil: $[a]_D^{27}$ –19.0 (c 0.35, $CHCl_3$); IR (neat) 2934, 2858, 1786, 1425, 1152, 1109, 928, 822, 741, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.08 (s, 9H), 1.23 (s, 3H), 2.34 (d, *J* = 14.2 Hz, 1H), 2.57 (d, *J* = 14.2 Hz, 1H), 2.61 (d, *J* = 18.3 Hz, 1H), 2.95 (dd, *J* = 18.3, 5.5 Hz, 1H), 3.30 (d, *J* = 11.0 Hz, 1H), 3.44 (d, *J* = 10.5 Hz, 1H), 3.48 (d, *J* = 11.0 Hz, 1H), 3.61 (d, *J* = 10.5 Hz, 1H), 4.54 (d, *J* = 5.5 Hz, 1H), 7.39-7.47 (m, 6H), 7.63-7.68 (m, 4H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 8.1, 19.2, 24.6, 27.0, 38.6, 45.5, 70.2, 82.2, 85.1, 94.6, 127.9(x2), 129.9(x2), 132.8, 132.9, 135.6, 135.6, 174.6.

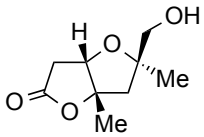
Furanolactone **6**



6

To a solution of compound **14** (781 mg, 1.42 mmol) in toluene (11 ml) under Ar was added Bu3SnH (827 mg, 2.84 mmol). The resulting mixture was heated at reflux for 20 min. After being cooled to room temperature, the mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 8:1) to afford lactone **6** (563 mg, 93%) as a white crystalline: $[a]_D^{30}$ –33.2 (c 0.40, $CHCl_3$); IR (KBr) 2967, 2931, 2862, 1786, 1425, 1185, 1146, 1105, 1090, 1073, 825, 814, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.07 (s, 9H), 1.20 (s, 3H), 1.45 (s, 3H), 2.24 (d, *J* = 14.2 Hz, 1H), 2.43 (d, *J* = 14.2 Hz, 1H), 2.69 (d, *J* = 2.4 Hz, 2H), 3.40 (d, *J* = 10.5 Hz, 1H), 3.60 (d, *J* = 10.5 Hz, 1H), 4.45 (dd, *J* = 2.4, 2.4 Hz, 1H), 7.37-7.44 (m, 6H), 7.64-7.68 (m, 4H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.2, 22.2, 24.5, 26.8, 37.3, 44.8, 70.3, 83.3, 85.2, 95.1, 127.8(x2), 129.8, 129.8, 133.0(x2), 135.6(x2), 175.2.

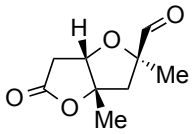
Hydroxy lactone **15**



15

To a solution of compound 6 (840 mg, 1.98 mmol) in THF (20 ml) at 0 °C under Ar was added AcOH (169 μl, 2.97 mmol) and Bu_4NF (1 M in THF, 2.97 ml, 2.97 mmol). The reaction mixture was stirred at 0 °C for 19 h. The mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate) to afford hydroxyl lactone **15** (357 mg, 97%) as a colorless oil: $[a]_D^{28}$ –46.9 (c 1.44, $CHCl_3$); IR (neat) 3465(br), 2979, 2934, 2876, 1774, 1265, 1142, 1069, 938 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 1.24 (s, 3H), 1.48 (s, 3H), 1.97 (dd, *J* = 7.3, 5.5 Hz, 1H), 2.24 (d, *J* = 14.2 Hz, 1H), 2.29 (d, *J* = 14.2 Hz, 1H), 2.67 (d, *J* = 18.3 Hz, 1H), 2.75 (dd, *J* = 18.3, 4.6 Hz, 1H), 3.39 (dd, *J* = 11.5, 7.3 Hz, 1H), 3.50 (dd, *J* = 11.5, 5.5 Hz, 1H), 4.42 (d, *J* = 4.6 Hz, 1H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 22.0, 23.9, 37.2, 44.4, 68.5, 83.0, 85.0, 95.1, 175.3.

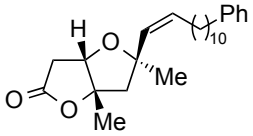
Aldehyde **16**



16

To a solution of oxalyl chloride (76 μl, 0.88 mmol) in CH_2Cl_2 (2 ml) at –78 °C under Ar was added DMSO (126 μl, 1.77 mmol) in CH_2Cl_2 (0.3 ml) and compound **15** in CH_2Cl_2 (2.2 ml). After the reaction mixture was stirred at –78 °C for 1 h, Et_3N (0.49 ml, 3.53 mmol) was added and allowed to warm to room temperature for 30 min. The reaction mixture was quenched by addition of water (5 ml) and extracted with CH_2Cl_2 (3 x 10 ml). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1:1) to afford aldehyde **16** (909 mg, 83%) as a pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.39 (s, 3H), 1.46 (s, 3H), 2.26 (d, J = 14.7 Hz, 1H), 2.52 (d, J = 14.7 Hz, 1H), 2.77 (d, J = 2.8 Hz, 2H), 4.25 (t, J = 2.8, 2.8 Hz, 1H), 9.51 (s, 1H,).

Unsaturated lactone **18**

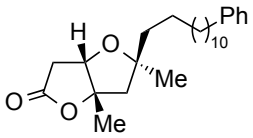


18

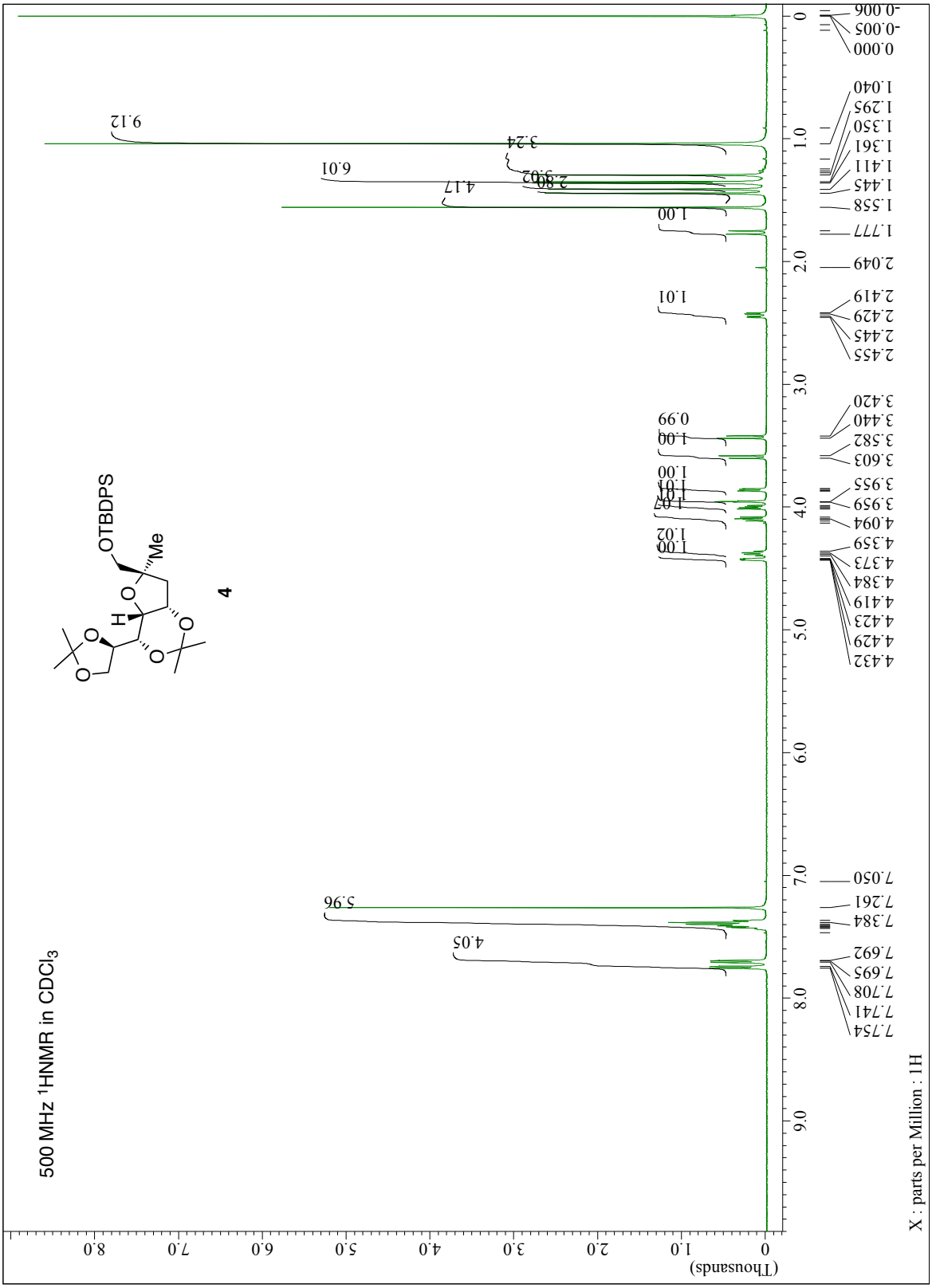
To a solution of **17** (410 mg, 0.715 mmol) in THF (1.5 ml) at –78 °C under Ar was BuLi (2.6 M in hexane, 0.16 ml, 0.4 mmol). The resulting mixture was stirred at –78 °C for 30 min and 0 °C for 1h. After the mixture was cooled at –78 °C, a solution of aldehyde **16** (46.2 mg, 0.237 mmol) in THF (0.7 ml) was added dropwise. The reaction mixture was stirred at –78 °C for 2.5 h and warmed to room temperature for 30 min. A saturated aqueous solution of NH_4Cl was added and extracted with Et_2O (3 x 5 ml). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 9:1) to afford (*Z*)-alkene **18** (29.7 mg, 31%) as a pale yellow oil: $[\alpha]_D^{30}$ –24.2 (c 0.55, $CHCl_3$); IR (neat) 2924, 2851, 1782, 1455, 1138, 1069, 960, 942, 745 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.41 (s, 3H), 1.46 (s, 3H), 1.60 (tt, J = 7.8, 7.8, 7.3, 7.3 Hz, 2H), 2.13 (q, J

= 7.3, 7.3, 7.3, 7.3 Hz, 1H), 2.19 (q, *J* = 7.3, 7.3, 7.3, 7.3 Hz, 1H), 2.22 (d, *J* = 13.8 Hz, 1H), 2.37 (d, *J* = 13.8 Hz, 1H), 2.59 (t, *J* = 7.8, 7.8 Hz, 2H), 2.68 (d, *J* = 18.3 Hz, 1H), 2.76 (dd, *J* = 18.3, 5.5 Hz, 1H), 4.24 (d, *J* = 5.5 Hz, 1H), 5.33 (dt, *J* = 11.9, 7.3, 7.3 Hz, 1H), 5.41 (d, *J* = 11.9 Hz, 1H), 7.15-7.18 (m, 3H), 7.25-7.28 (m, 2H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 23.4, 27.9, 29.3, 29.4–29.7(x 8), 31.5, 36.0, 52.1, 81.2, 84.4, 94.2, 125.5, 128.2, 128.4, 132.0, 134.7, 142.9, 175.2.

Plakortone L (**1**)



An ethanol solution (8 ml) of unsaturated lactone **18** (27.1 mg, 0.068 mmol) containing 10% Pd/C (10 mg) was stirred under H_2 for 27 h. After filtration, the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 9:1) to afford plakortone L (**1**) (22.4 mg, 82%) as a white solid: $[a]_D^{28}$ –20.4 (c 0.27, $CHCl_3$) {lit. $[a]_D$ –20.1 (c 0.0019, $CHCl_3$)}; IR (KBr) 2919, 2847, 1789, 1469, 1265, 1164, 1146, 1062, 942, 720 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.24–1.29 (m, 18H), 1.26 (s, 3H), 1.47 (s, 3H), 1.50 (m, 2H), 1.60 (tt, *J* = 7.8, 7.8, 7.3, 7.3 Hz, 2H), 1.98 (d, *J* = 14.2 Hz, 1H), 2.29 (d, *J* = 14.2 Hz, 1H), 2.59 (t, *J* = 7.8, 7.8 Hz, 2H), 2.67 (d, *J* = 18.3 Hz, 1H), 2.74 (dd, *J* = 18.3, 5.0 Hz, 1H), 4.31 (d, *J* = 5.0 Hz, 1H), 7.15-7.18 (m, 3H), 7.25-7.28 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 23.1, 24.4, 26.8, 29.4–30.0(x 8), 31.5, 36.0, 37.2, 41.8, 49.0, 81.9, 84.8, 94.5, 125.5, 128.2, 128.4, 142.9, 175.2.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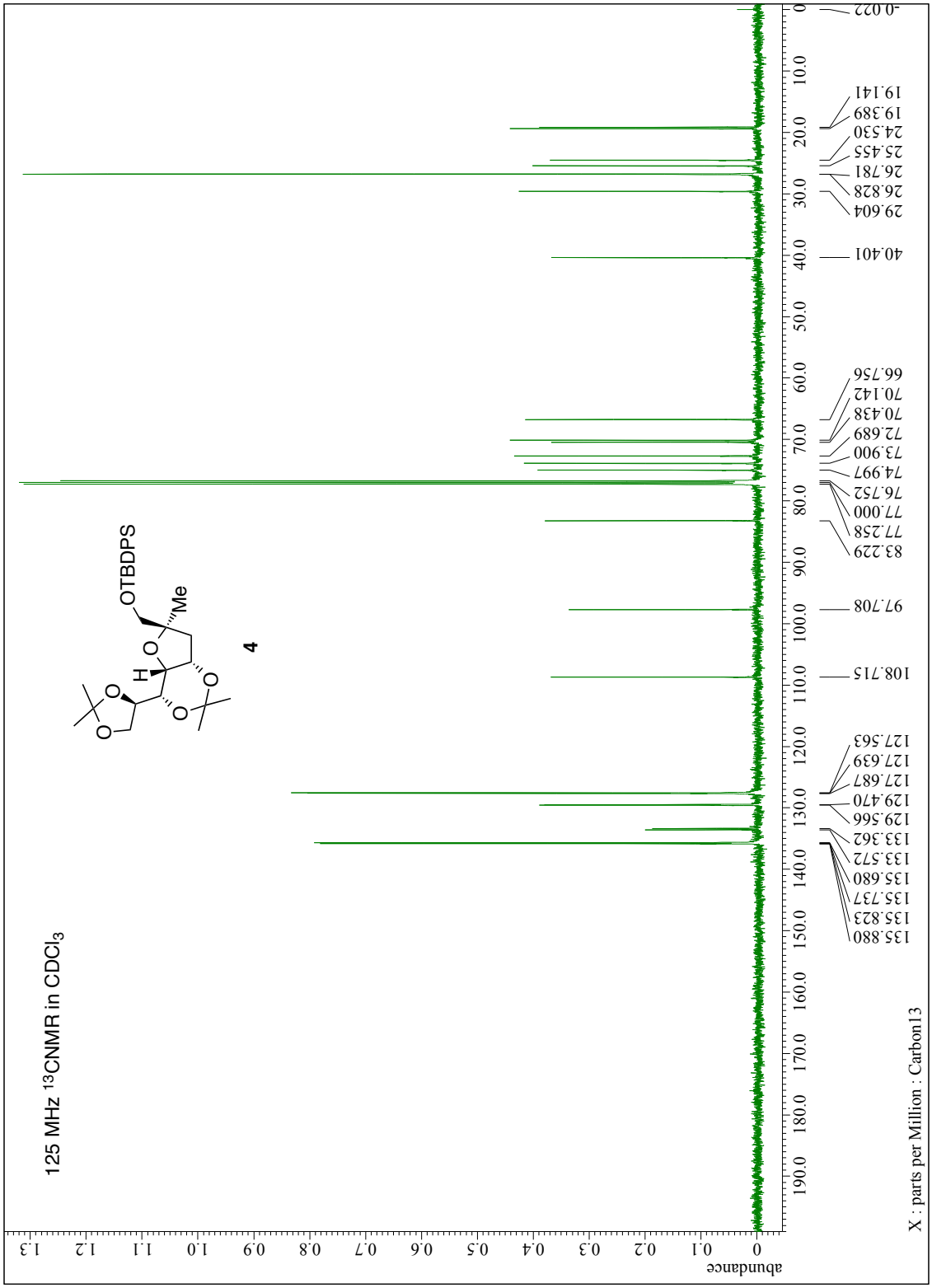
OTBDPS
Me
H
O
X : parts per Million : 1H
(Thousands)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OTBDPS
Me
H
O
4
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X : parts per Million : Carbon13
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135.680
133.572
133.362
129.566
129.470
127.687
127.639
127.563
108.715
97.708
83.229
77.258
77.000
76.752
74.997
73.900
72.689
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25.455
24.530
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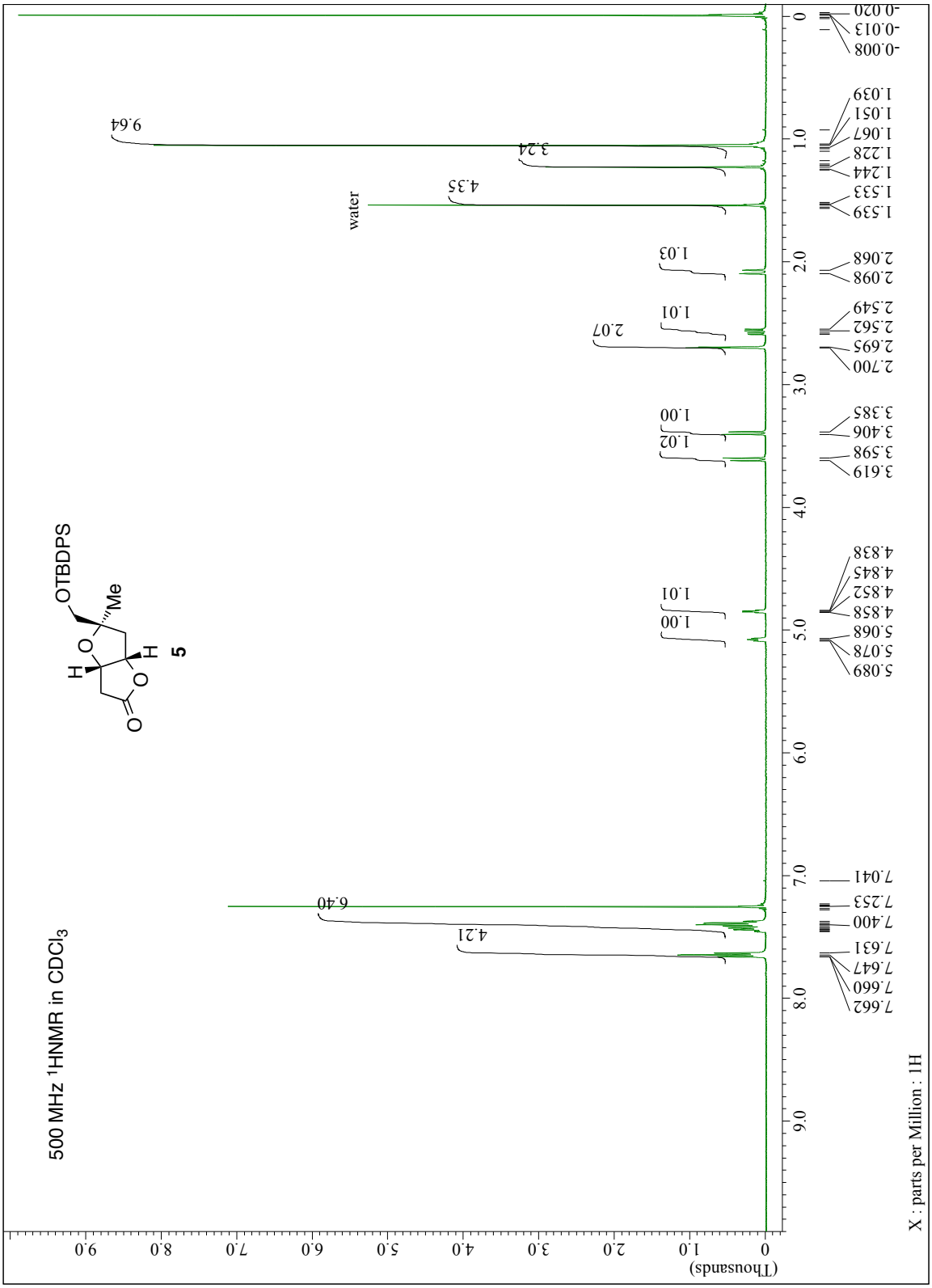
-0.022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O
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H
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4.35
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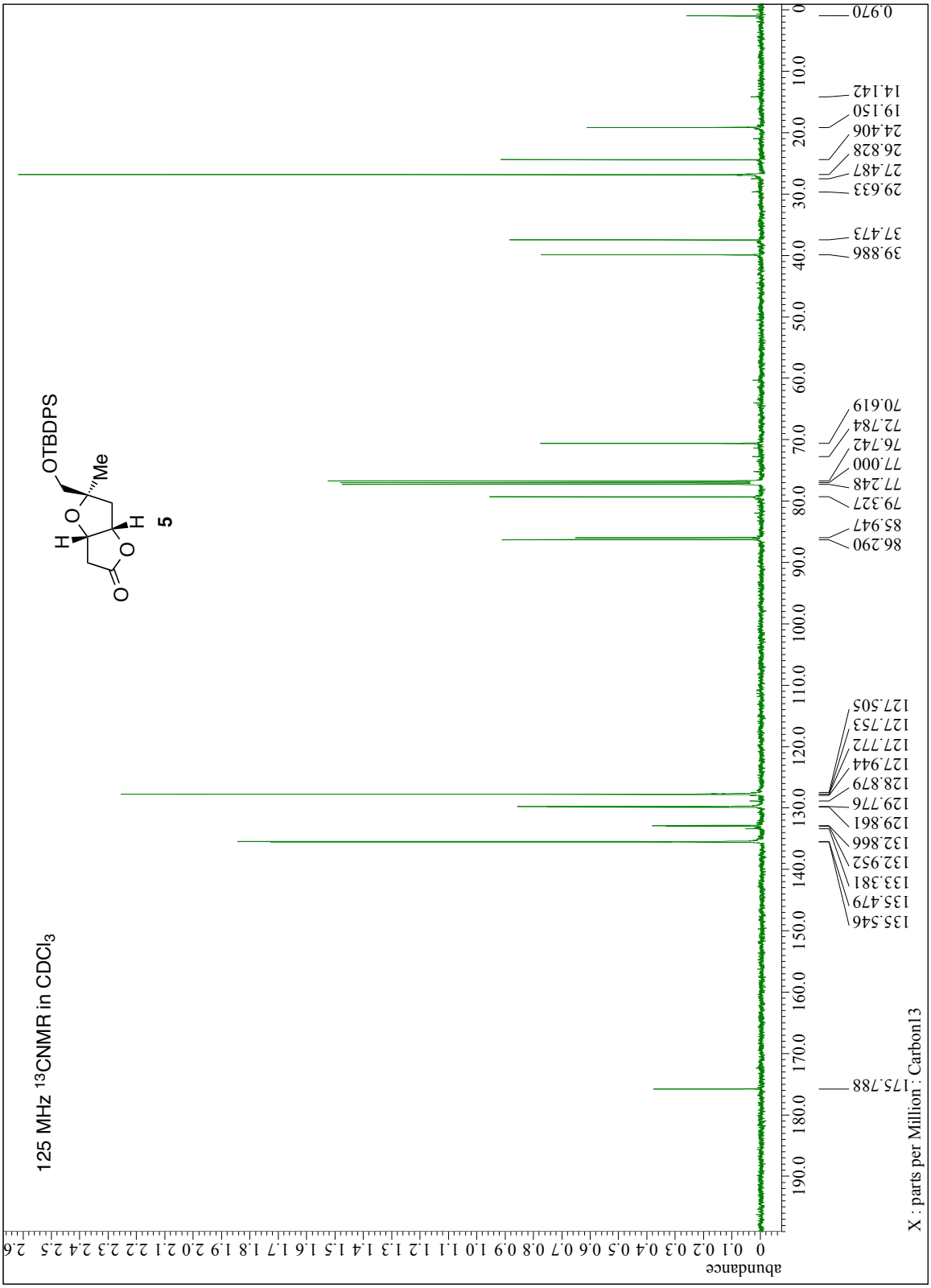
1.02
1.00
1.01
6.40
4.21
X : parts per Million : 1H
(Thousands)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OTBDPS
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H
O
O
H
O
5
X : parts per Million : Carbon13
abundance
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24.406
26.828
27.487
29.633
37.473
39.886
70.619
72.784
76.742
77.000
77.248
79.327
85.947
86.290
127.505
127.753
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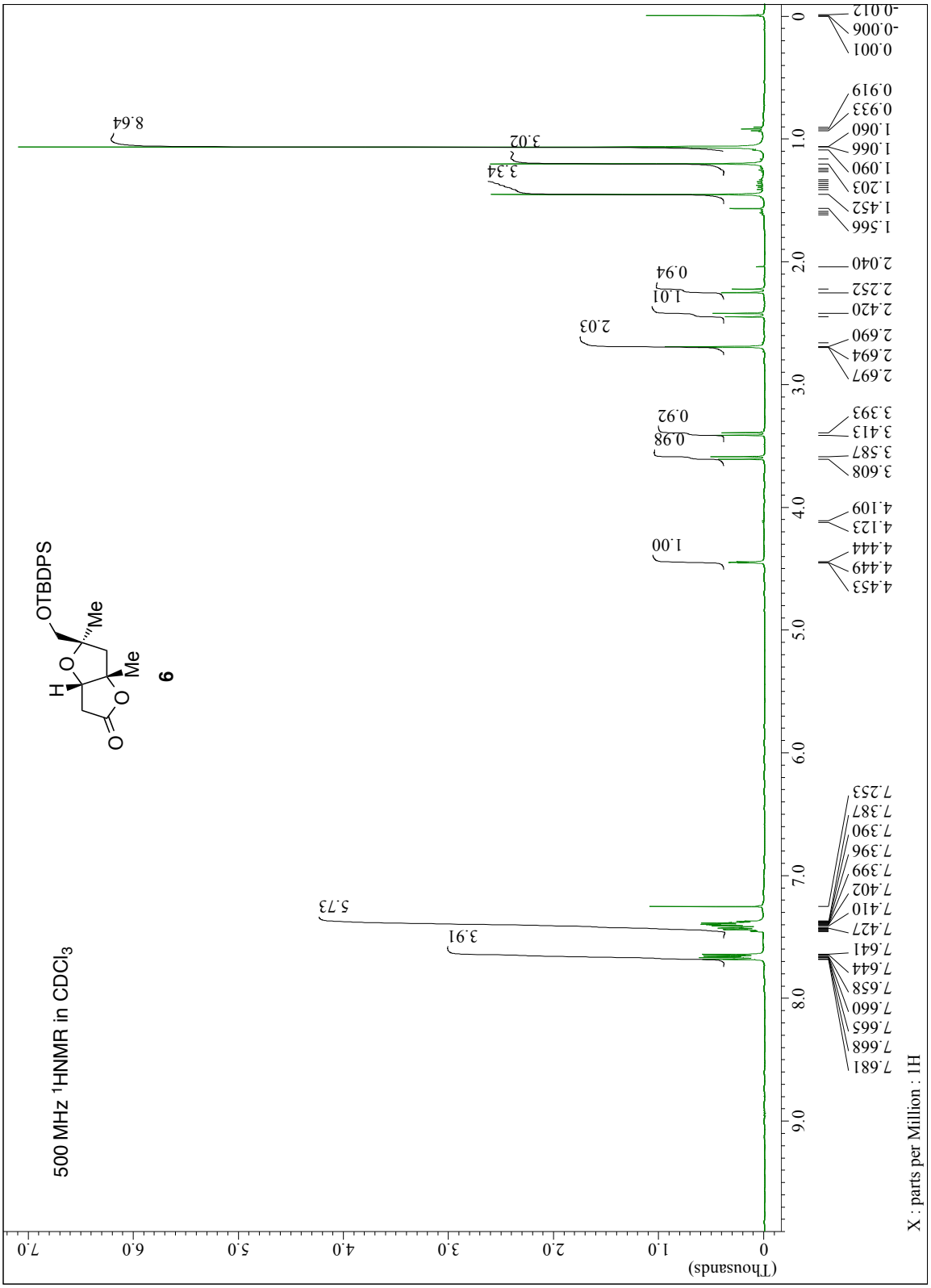
132.952
133.381
135.479
135.546
175.788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OTBDPS
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Me
H
O
O
O
O
9
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3.02
3.34
5.73
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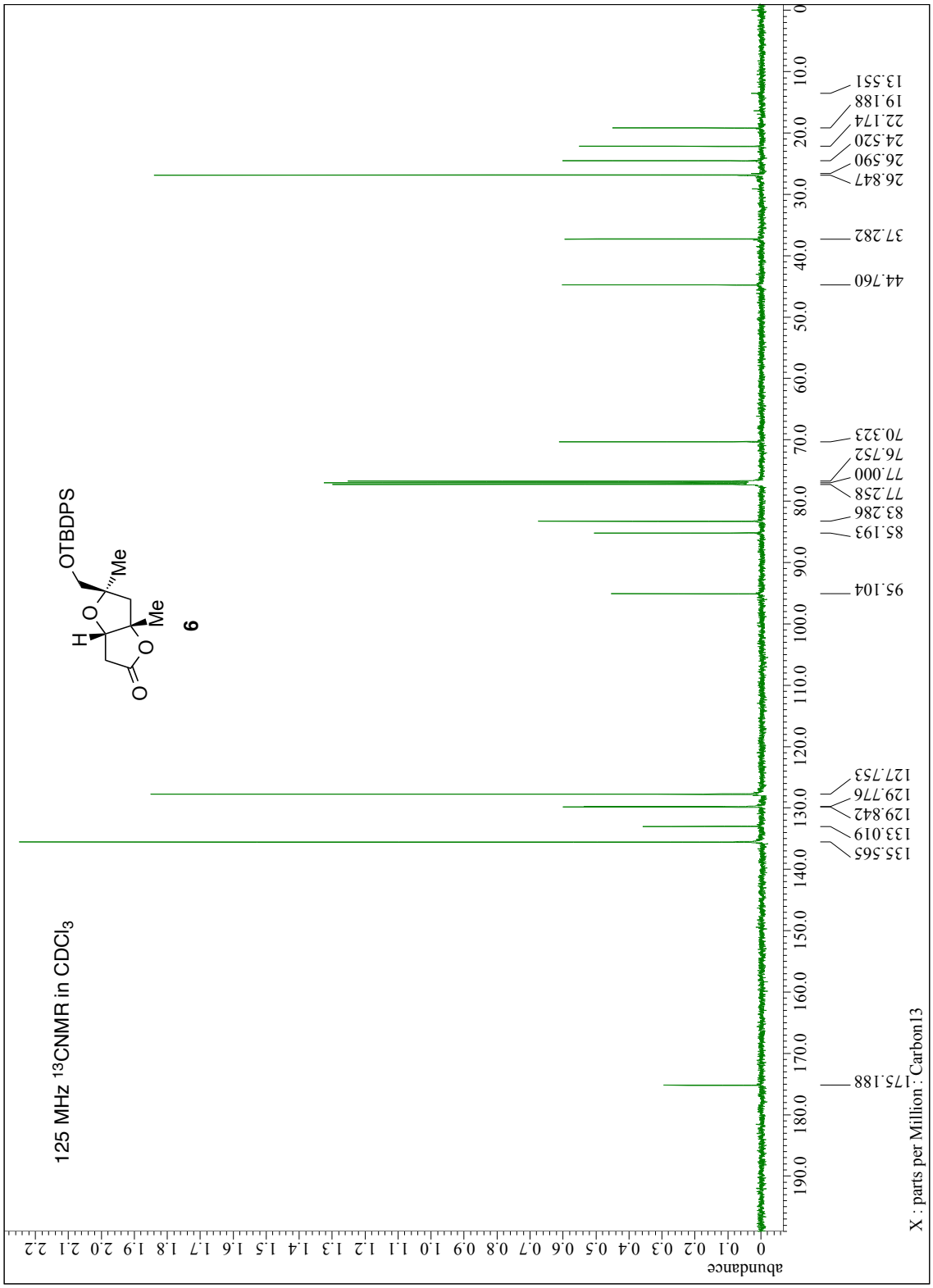
1.00
0.98
0.92
2.03
1.01
0.94
X : parts per Million : 1H
(Thousands)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OTBDPS
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Me
H
O
O
O
O
6
abundance
X : parts per Million : Carbon13
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133.019
129.842
129.776
127.753
95.104
85.193
83.286
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77.000
76.752
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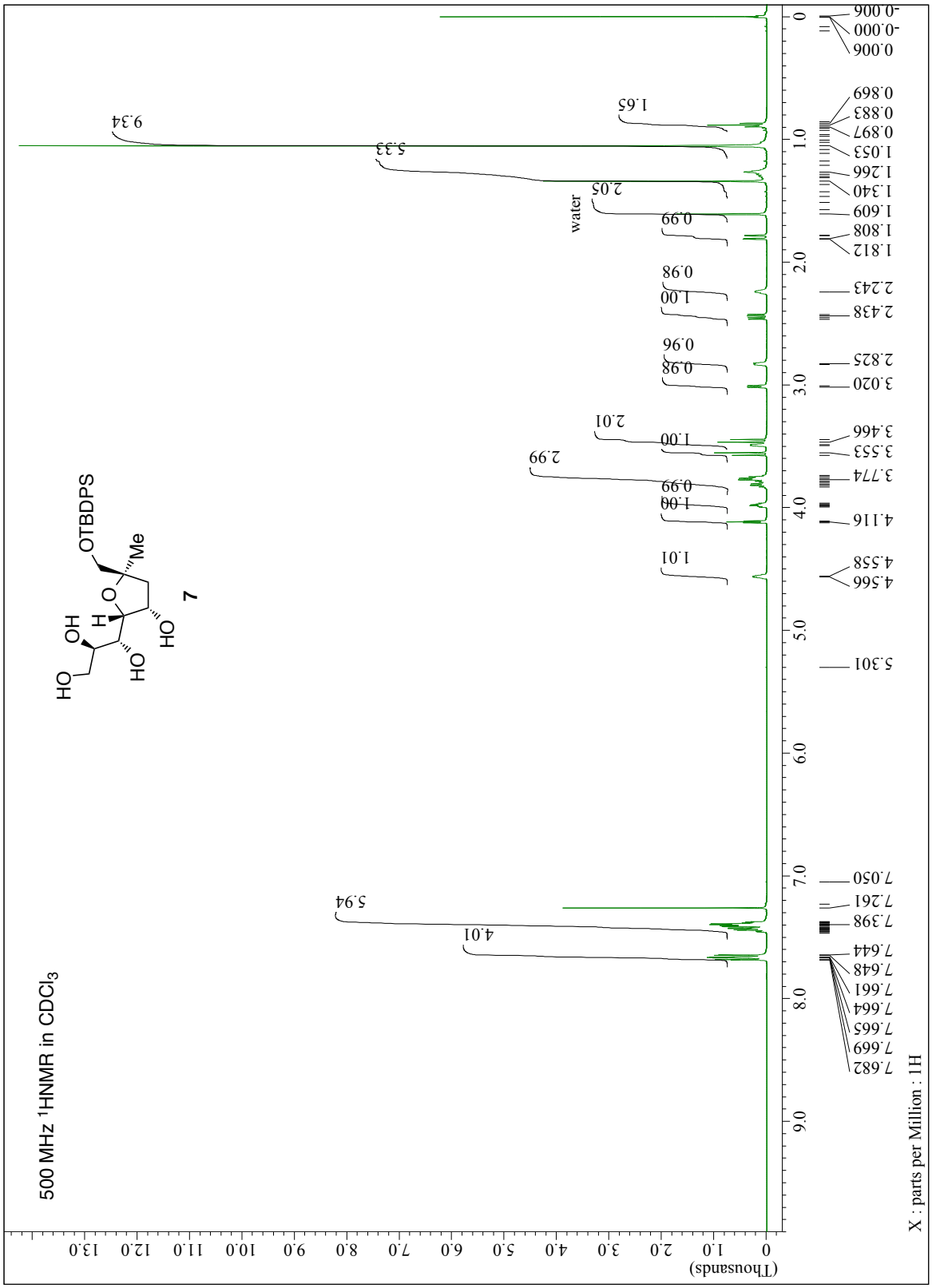
26.847
26.590
24.520
22.174
19.188
13.551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OTBDPS
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O
H
OH
HO
OH
HO
7
water
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4.01
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1.65
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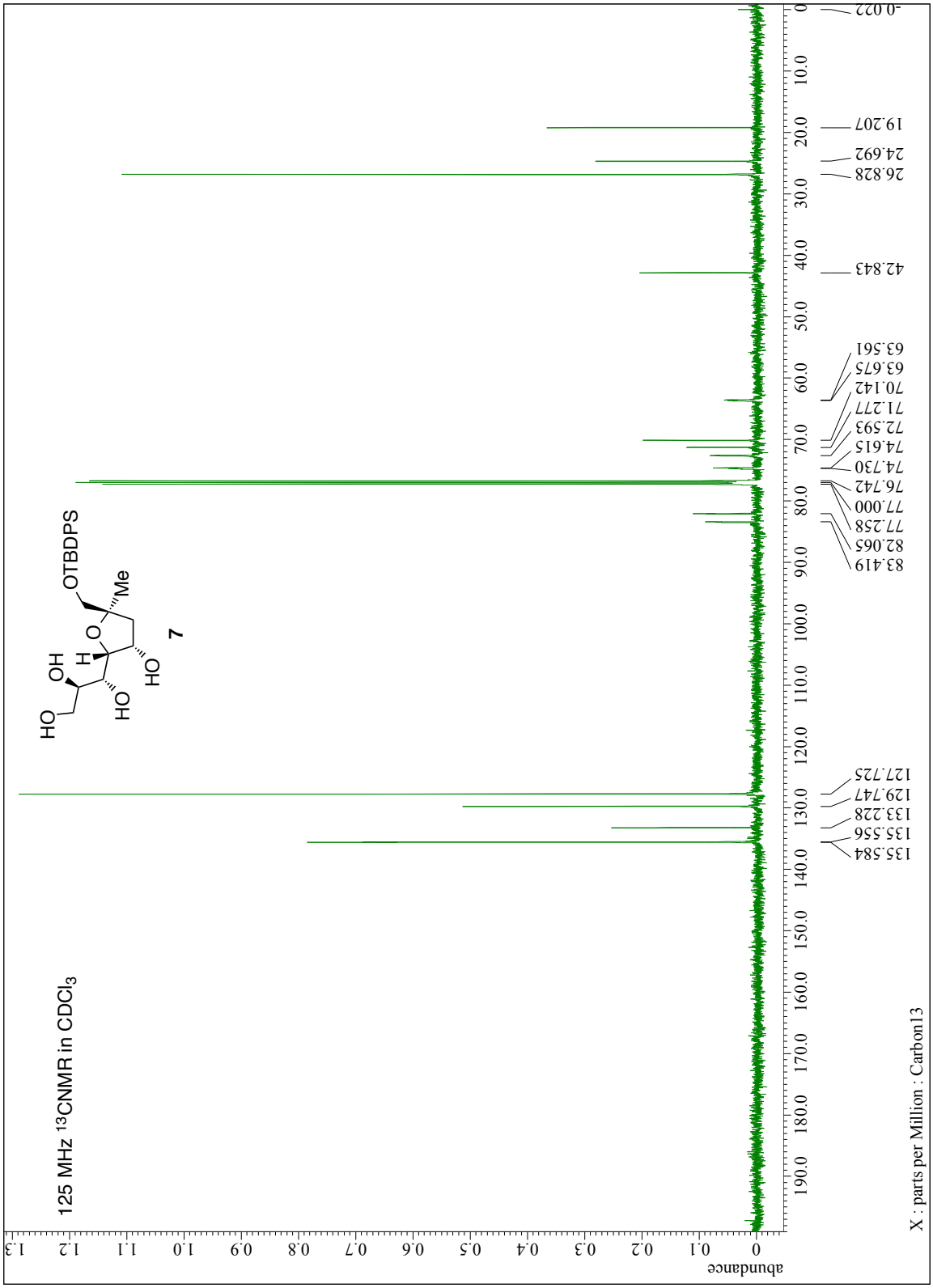
0.99
0.98
0.96
X : parts per Million : 1H
(Thousands)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OTBDPS
Me
O
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OH
HO
HO
HO
7
abundance
X : parts per Million : Carbon13
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129.747
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83.419
82.065
77.258
77.000
76.742
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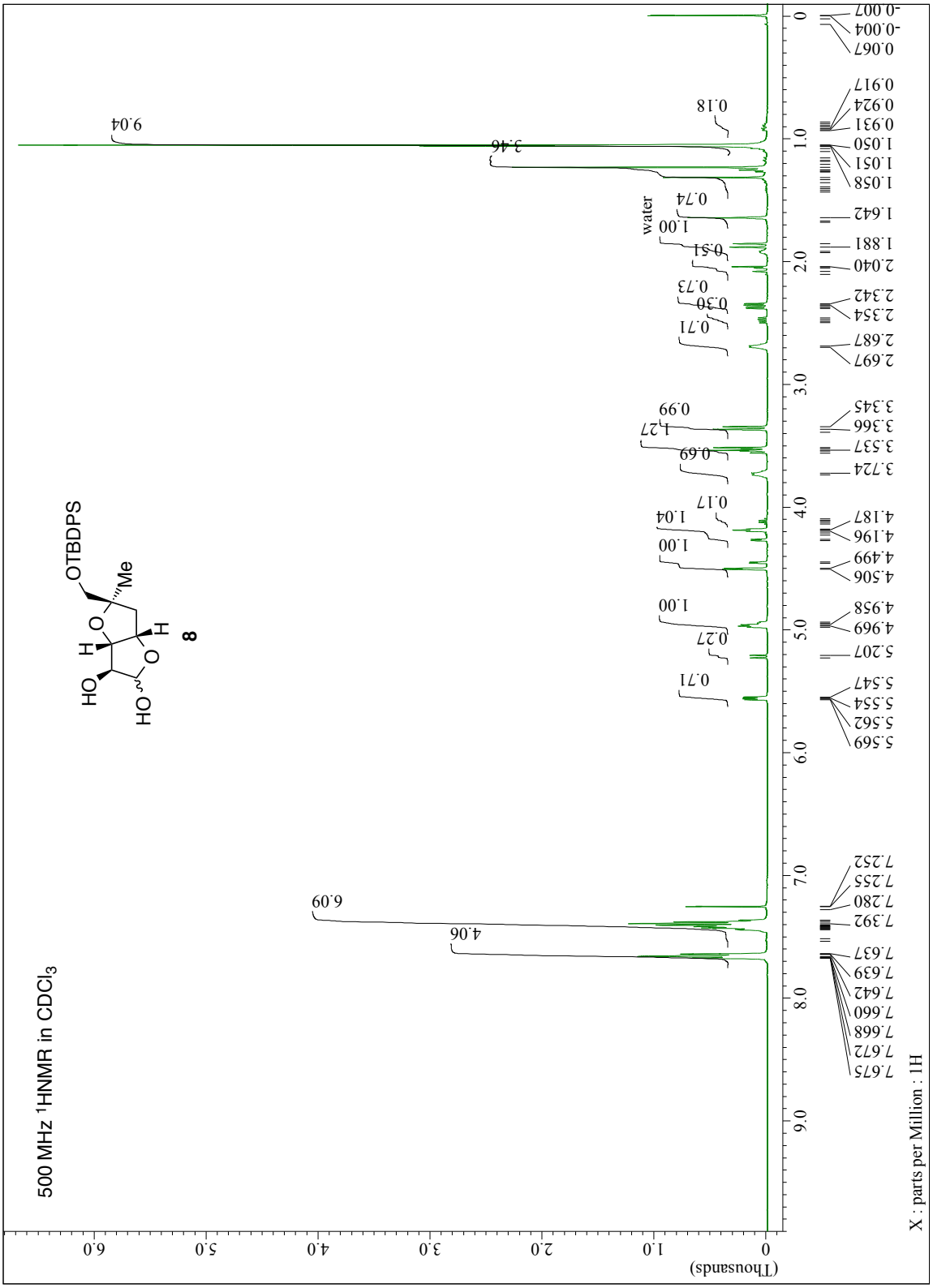
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OTBDPS
Me
HO
OH
H
O
H
O
(Thousands)
X : parts per Million : 1H
water
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3.46
1.27
1.04
1.00
0.99
0.91
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0.73
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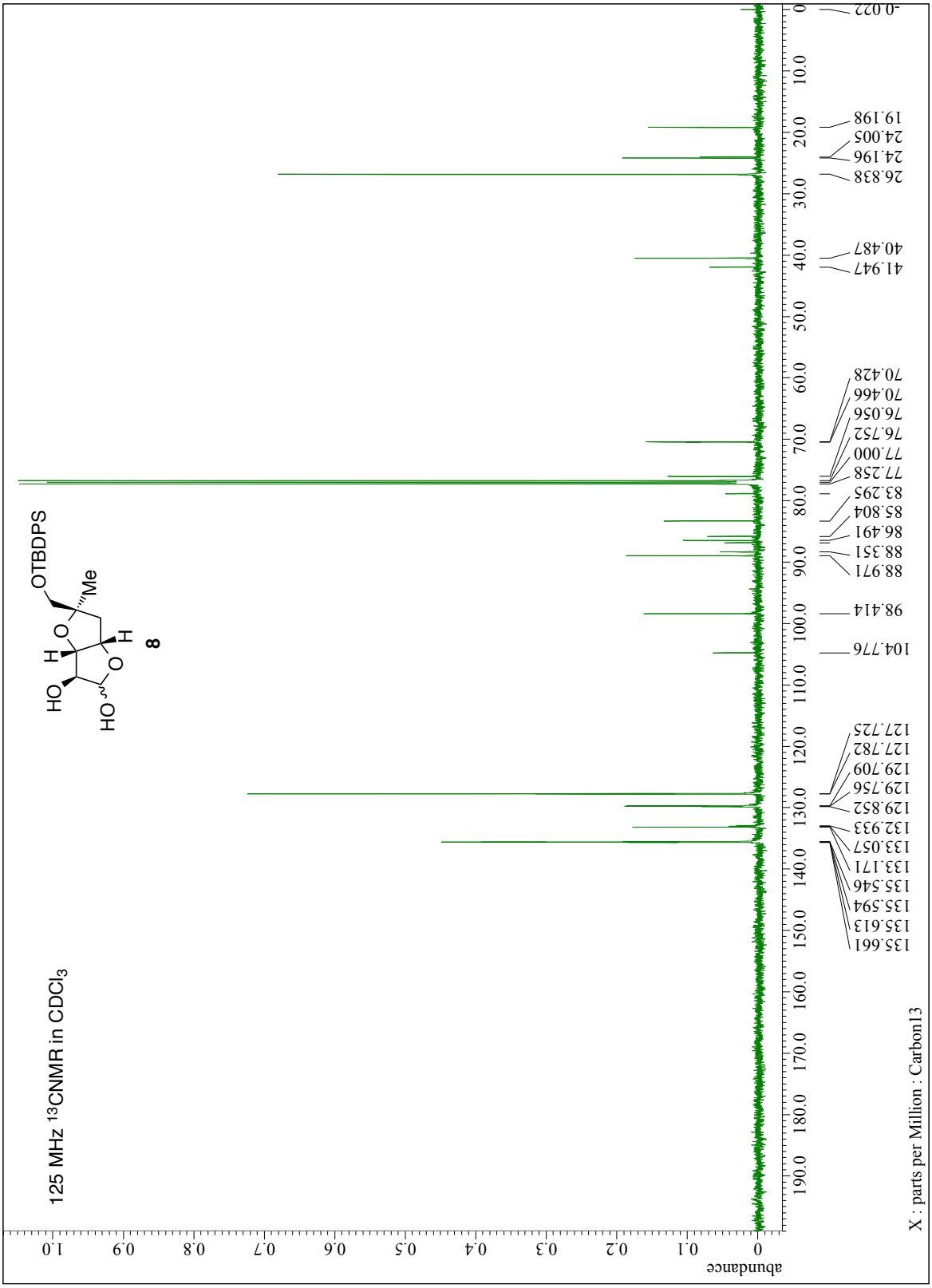
0.69
0.51
0.30
0.27
0.18
0.17
0.067
-0.004
-0.007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HO
OH
H
O
H
O
8
abundance
X : parts per Million : Carbon13
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24.196
26.838
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41.947
70.428
70.466
76.056
76.752
77.000
77.258
83.295
85.804
86.491
88.351
88.971
98.414
104.776
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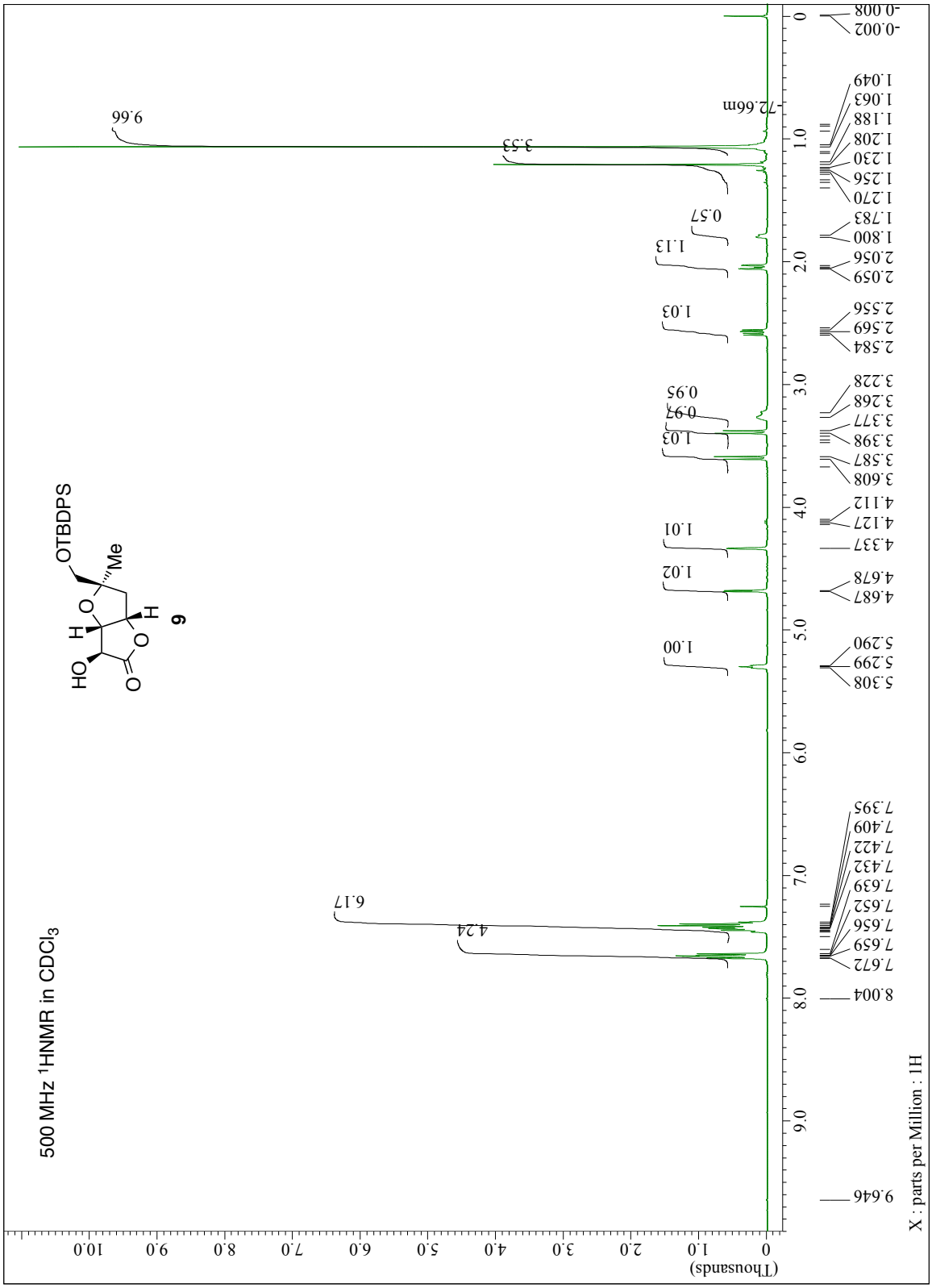
135.661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HO
H
O
O
O
H
6
X : parts per Million : 1H
(Thousands)
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3.268
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2.059
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1.230
1.208
1.188
1.063
1.049
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-0.008
1.00
1.02
1.01
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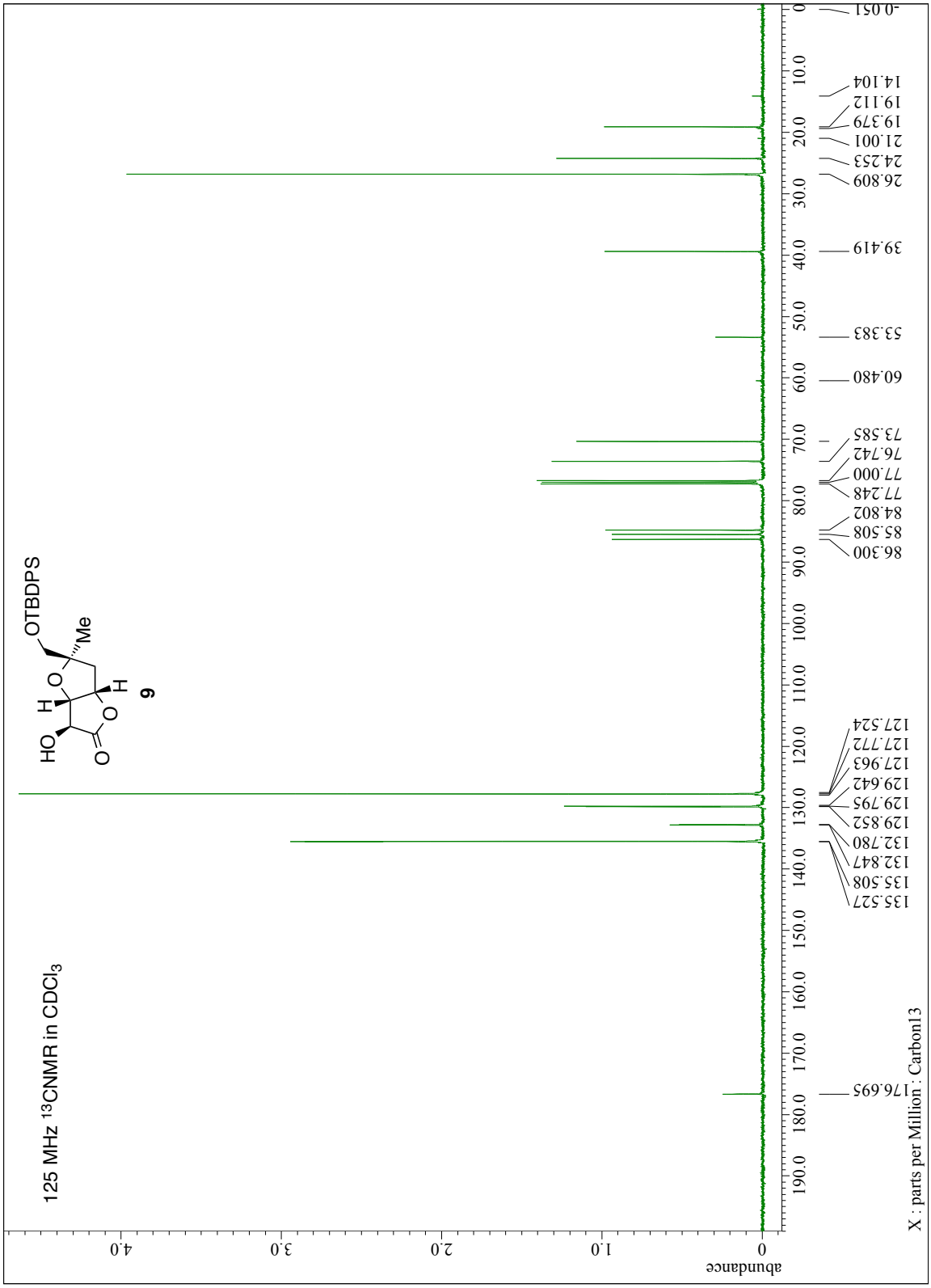
1.13
0.57
3.53
9.66
72.66m
6.17
4.24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OTBDPS
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HO
H
O
O
O
H
9
abundance
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2.0
1.0
0
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180.0
170.0
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
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127.524
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77.000
76.742
73.585
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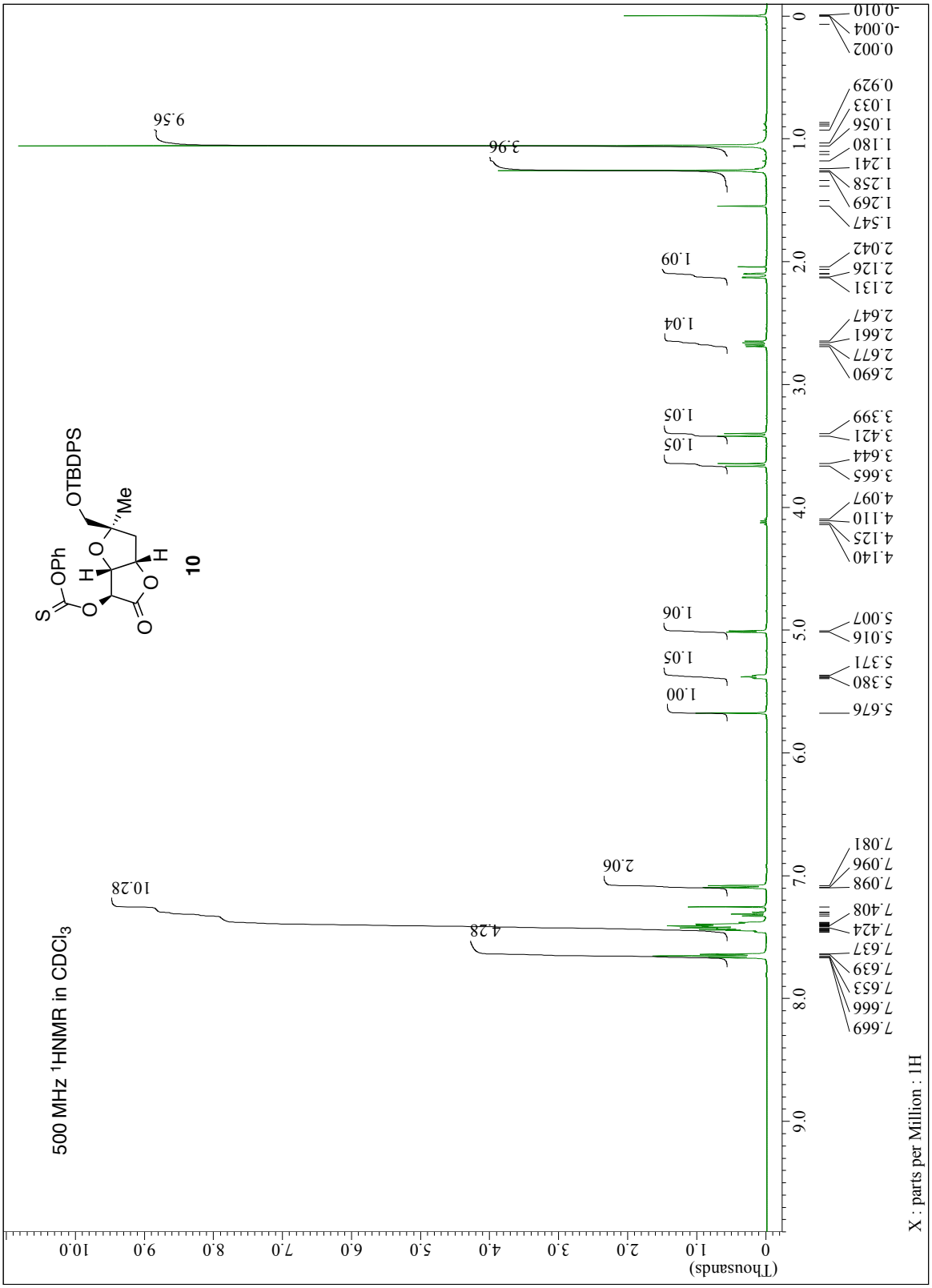
X : parts per Million : Carbon13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10
OTBDPS
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OPh
S
O
H
O
O
H
O
(Thousands)
X : parts per Million : 1H
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9.56
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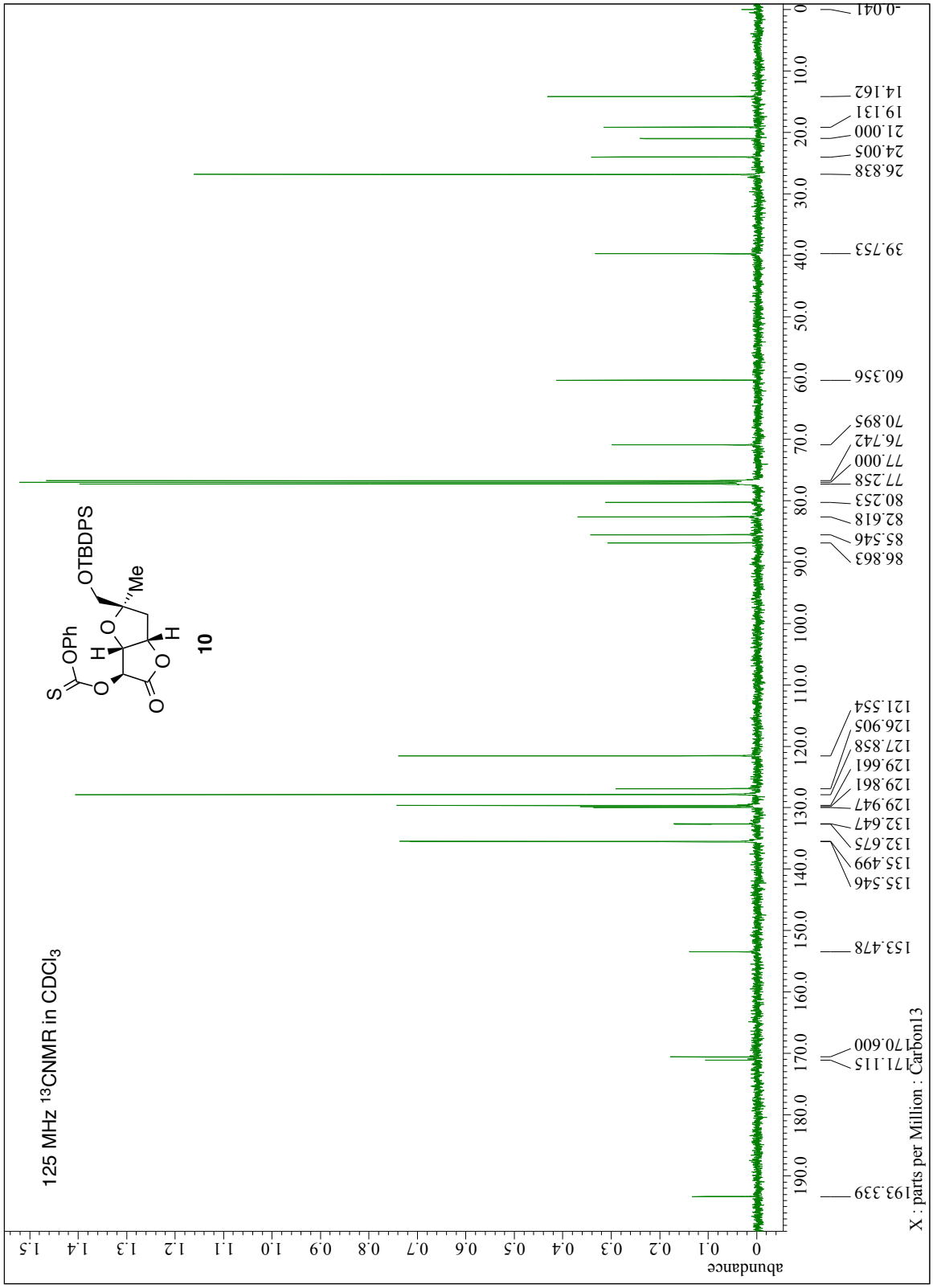
1.04
1.05
1.05
1.06
1.05
1.00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OTBDPS
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OPh
S
O
H
O
O
H
O
10
abundance
X : parts per Million : Carbon13
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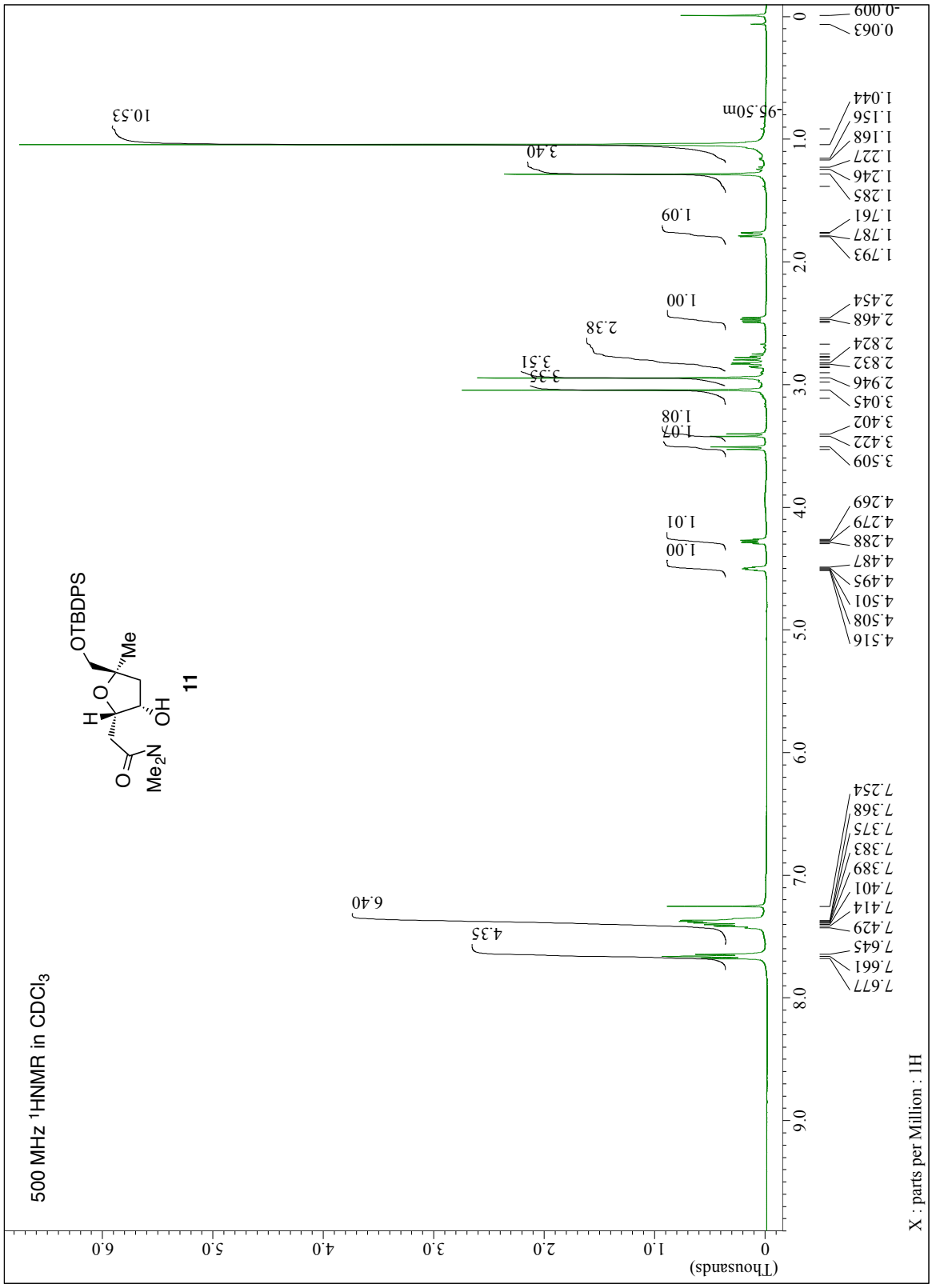
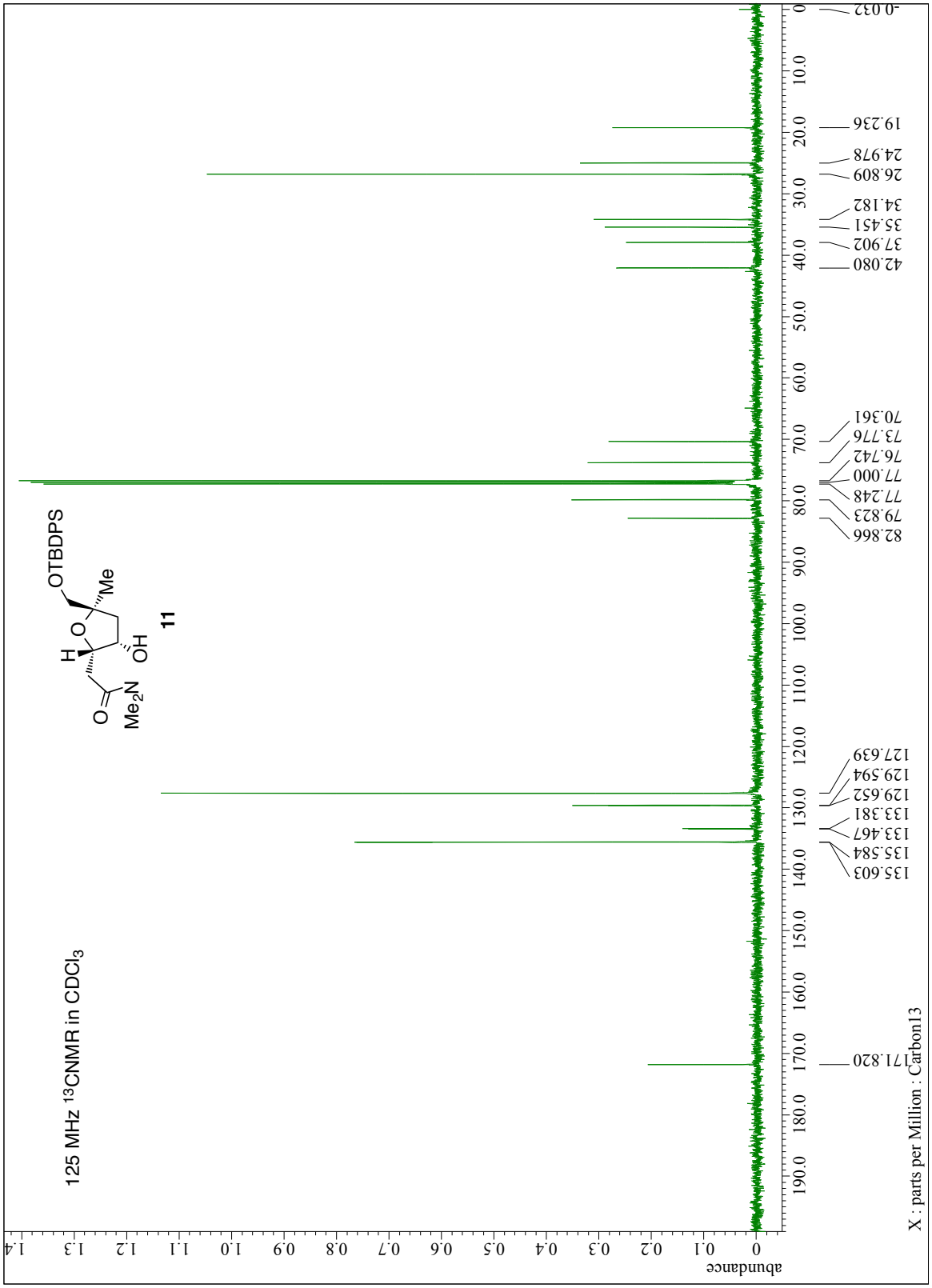
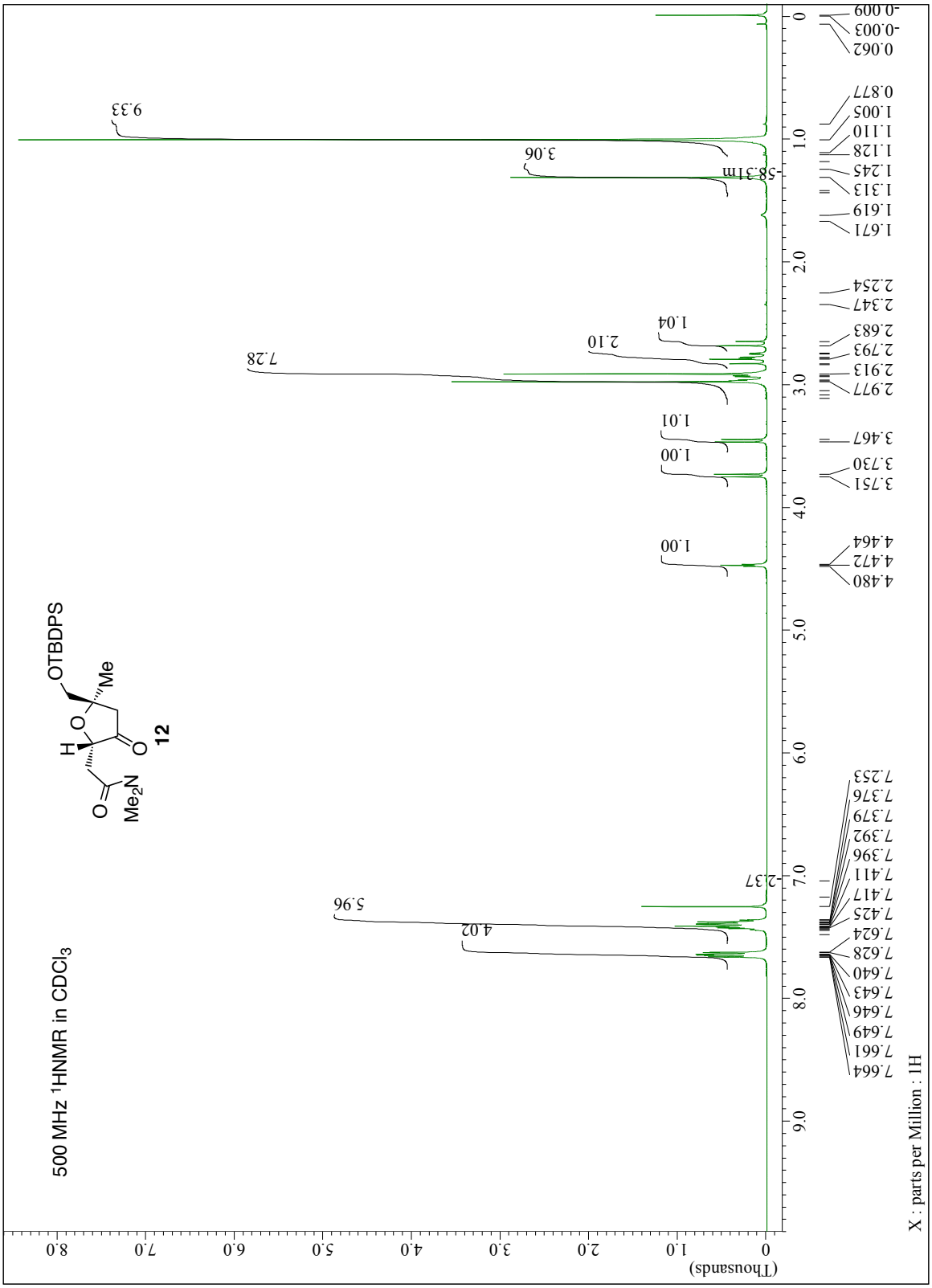
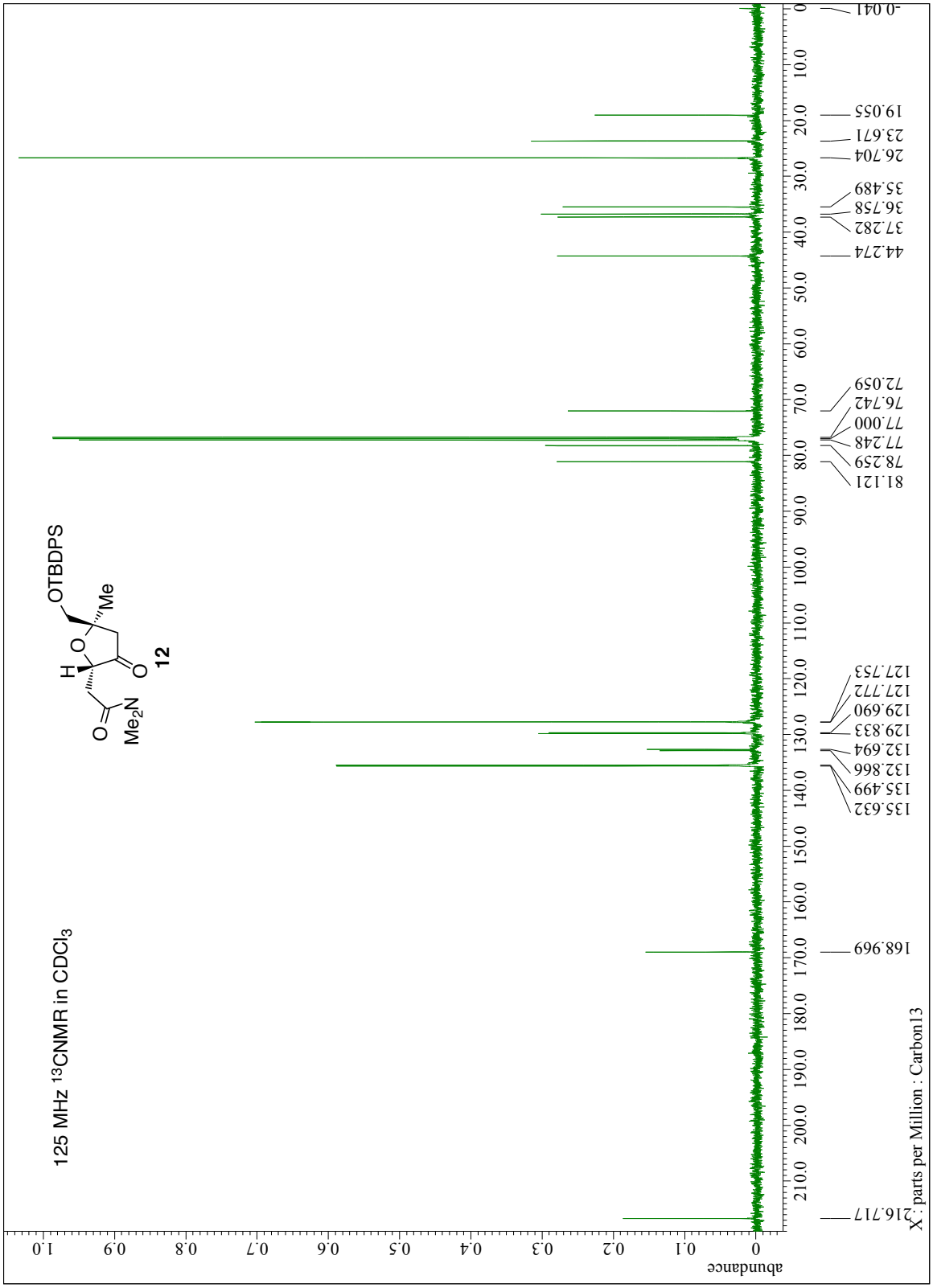
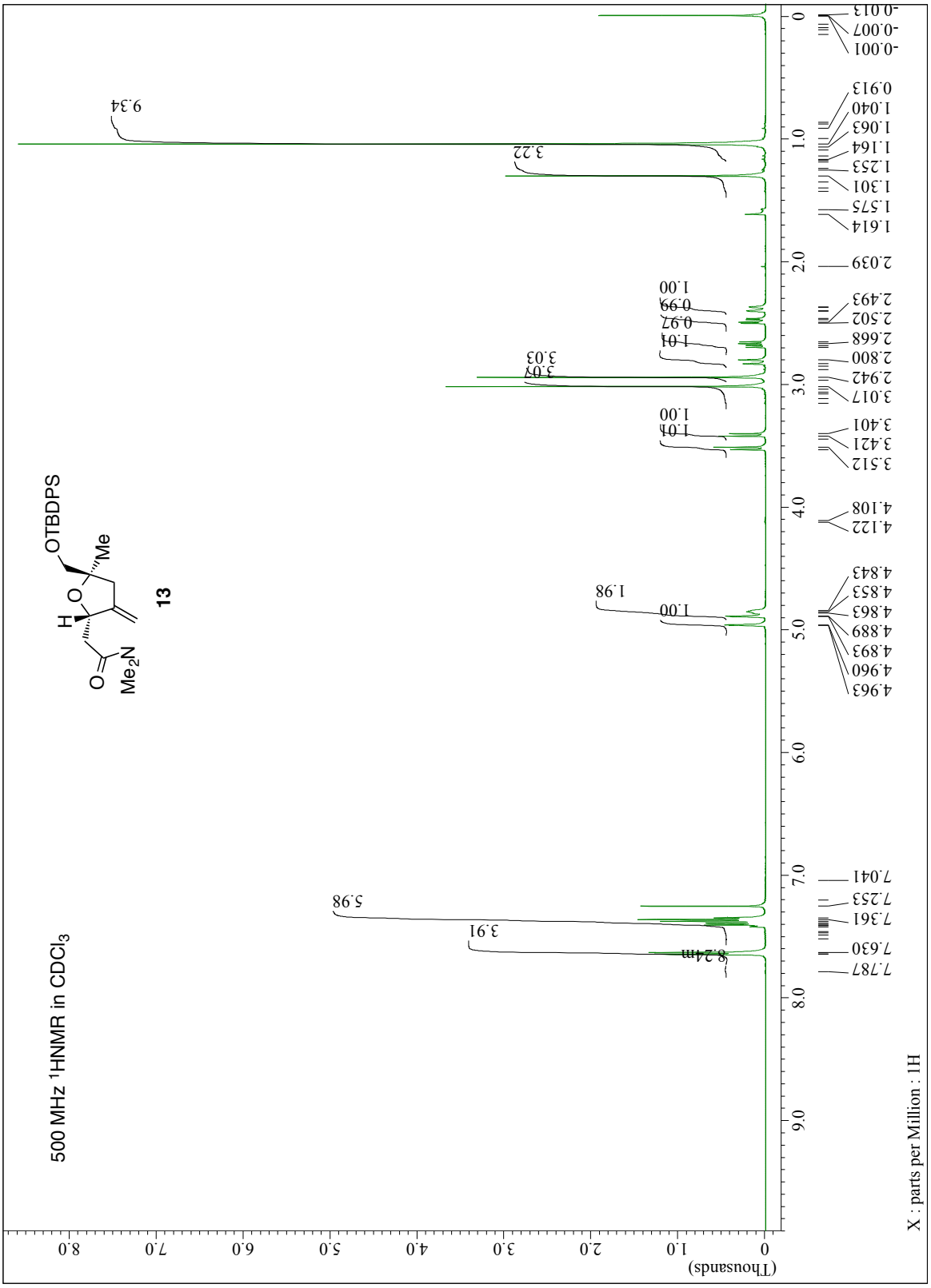
77.000
77.258
80.253
82.618
85.546
86.863
121.554
126.905
127.858
129.661
129.861
129.947
132.647
132.675
135.499
135.546
153.478
170.600
171.115
193.339

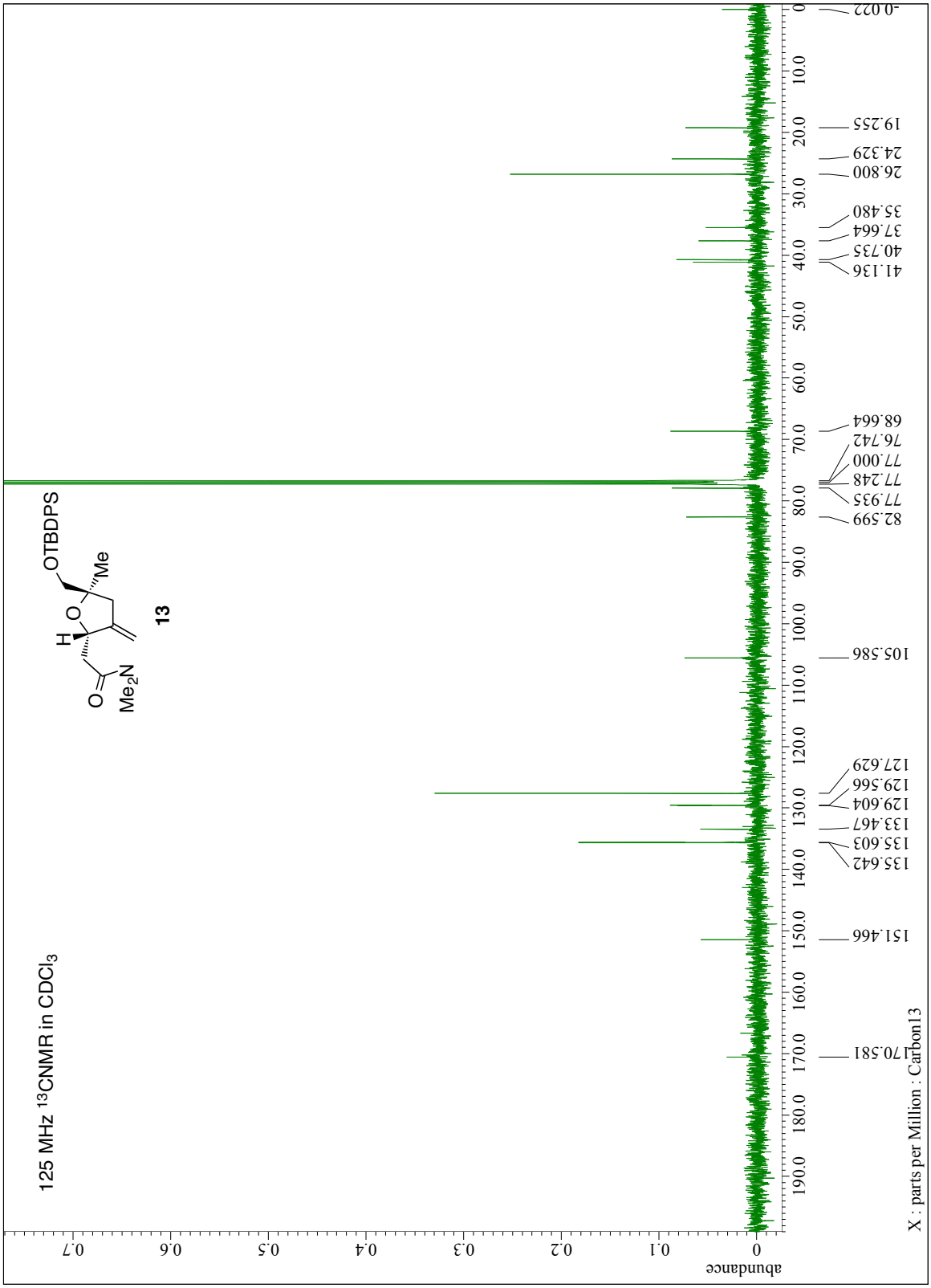

500 MHz ¹HNMR in CDCl₃
OTBDPS
Me
O
H
OH
O
Me₂N
11
(Thousands)
X : parts per Million : 1H

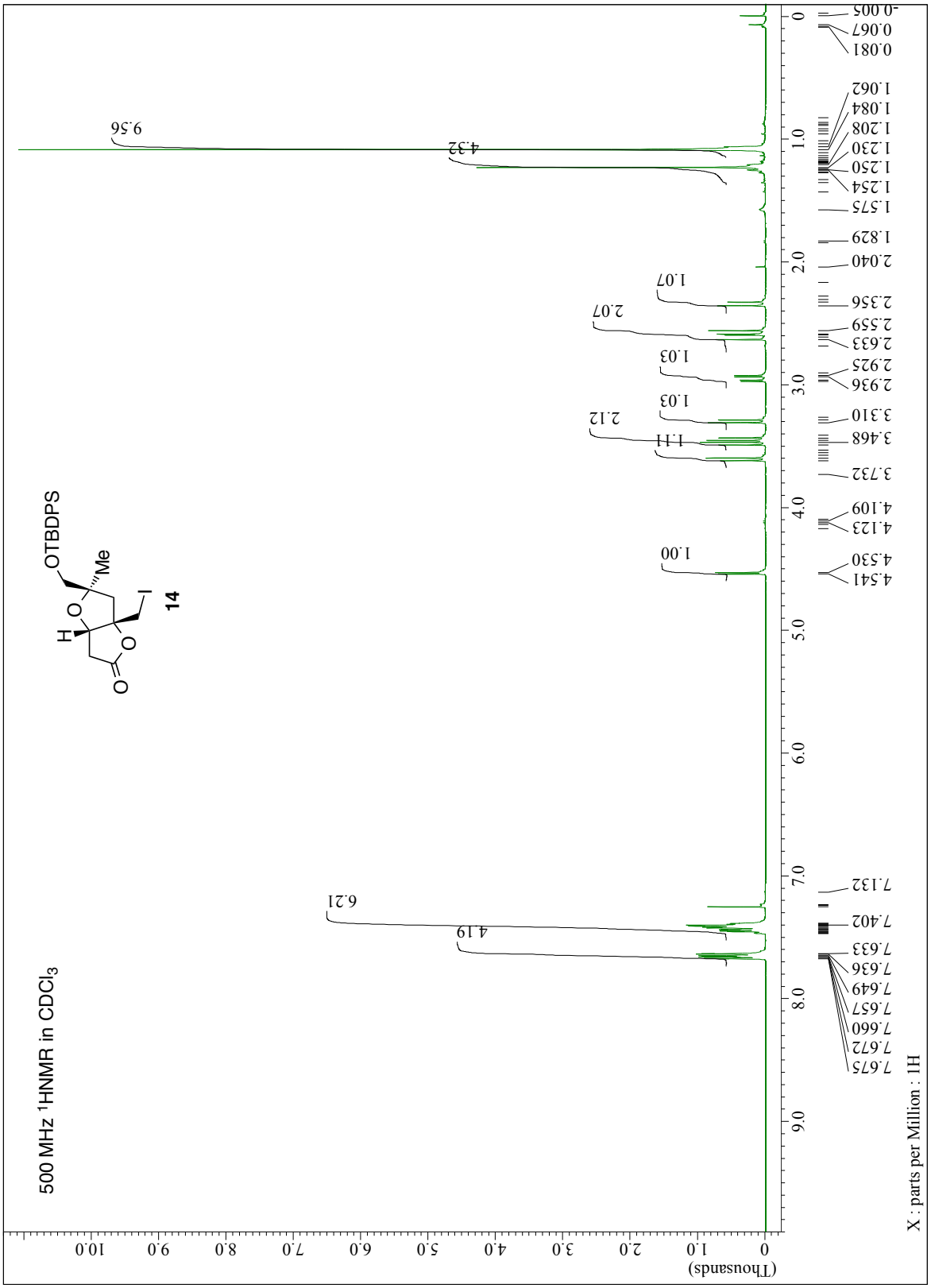

125 MHz 13CNMR in CDCl3
OTBDPS
Me
O
H
OH
O
Me2N
11
abundance
X : parts per Million : Carbon13
-0.032
19.236
24.978
26.809
34.182
35.451
37.902
42.080
70.361
73.776
76.742
77.000
77.248
79.823
82.866
127.639
129.594
129.652
133.381
133.467
135.584
135.603
171.820

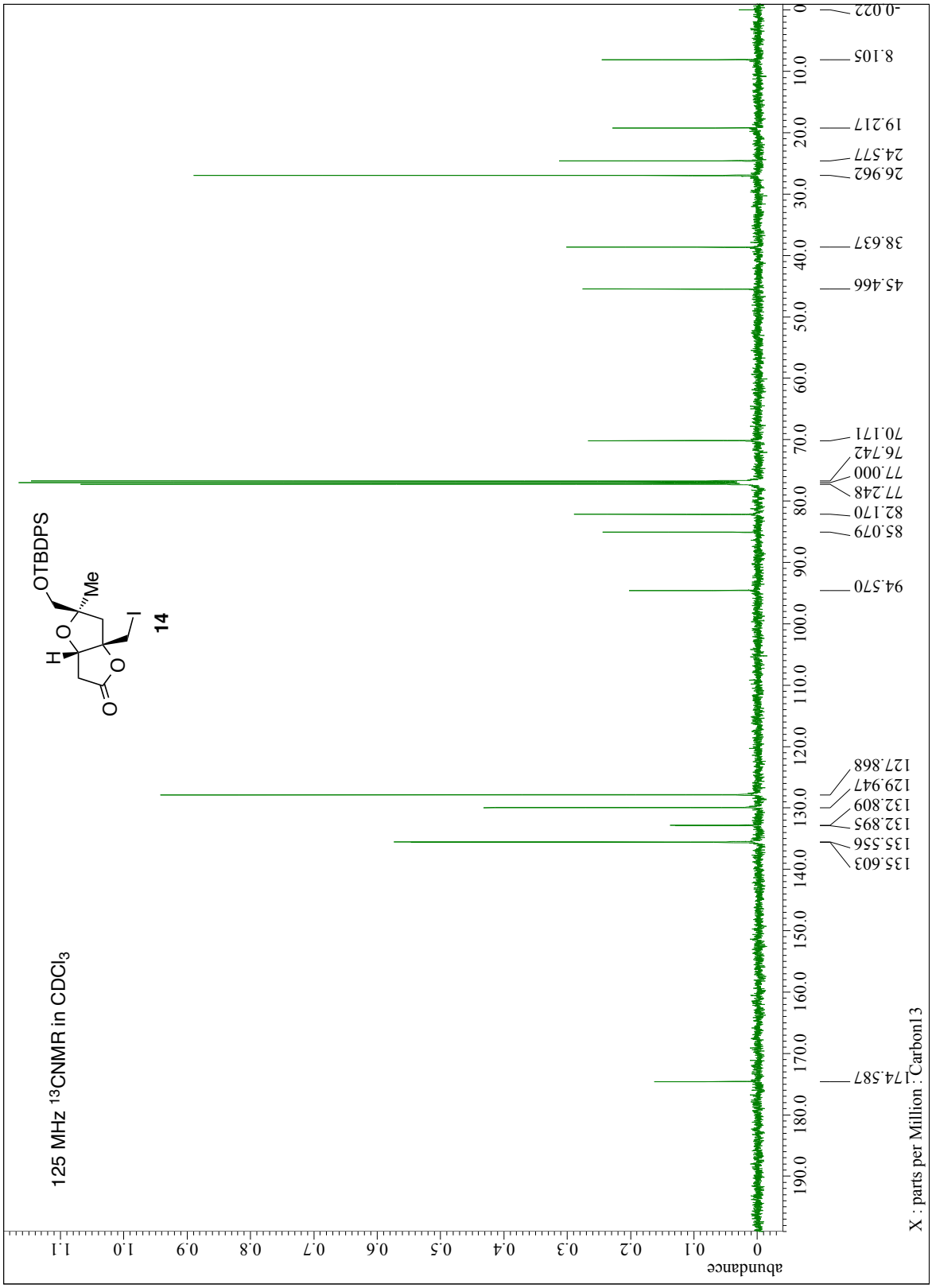

500 MHz 1HNMR in CDCl3
OTBDPS
Me
H
O
O
Me2N
O
12
9.33
7.28
5.96
4.02
3.06
2.37
2.10
1.04
1.00
1.00
1.01
1.00
-58.31m
X : parts per Million : 1H
(Thousands)

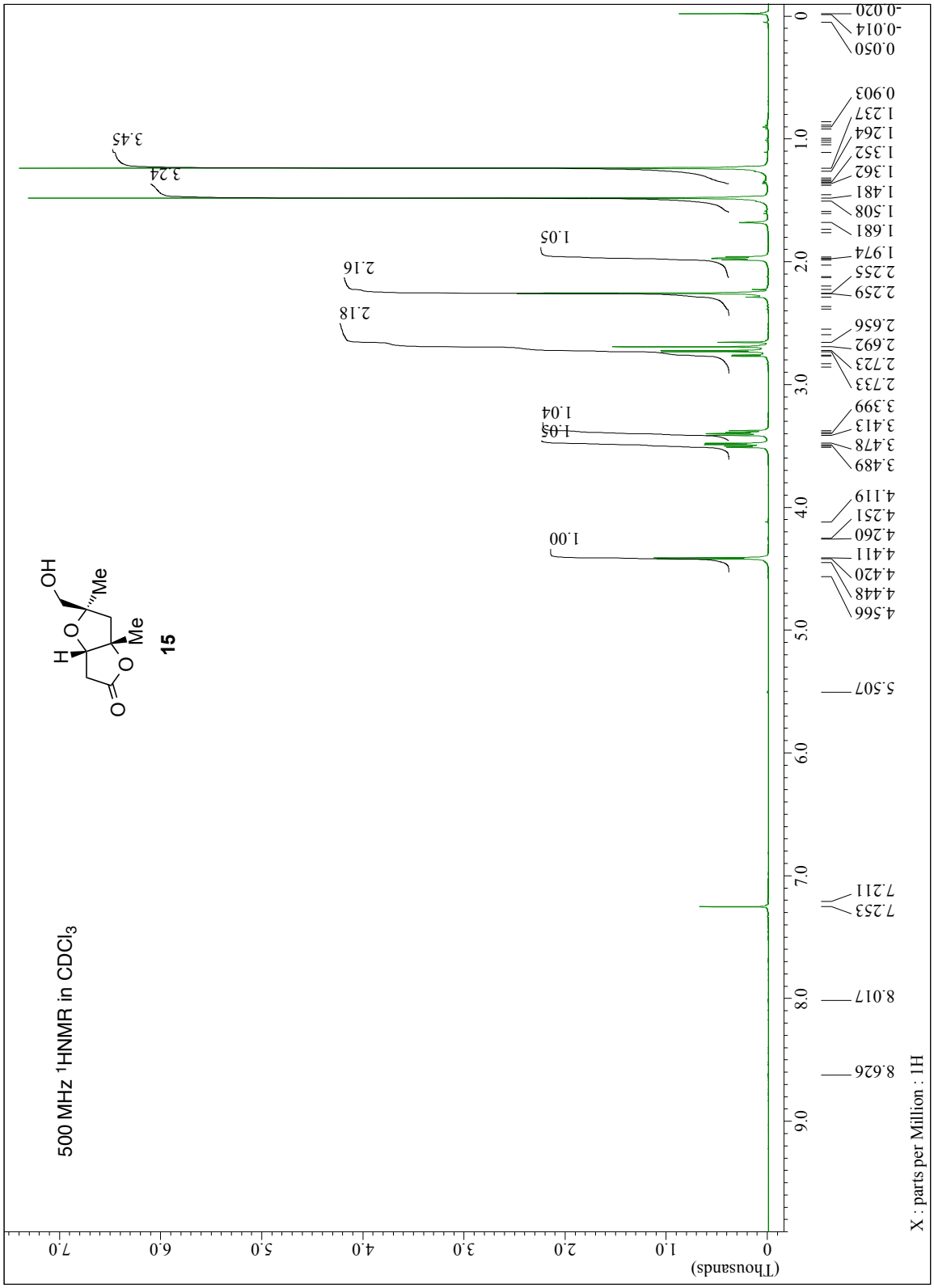

125 MHz 13CNMR in CDCl3
OTBDPS
Me
H
O
O
O
Me2N
12
abundance
X : parts per Million : Carbon13
216.717
168.969
135.632
135.499
132.866
132.694
129.833
129.690
127.772
127.753
81.121
78.259
77.248
77.000
76.742
72.059
44.274
37.282
36.758
35.489
26.704
23.671
19.055
-0.041

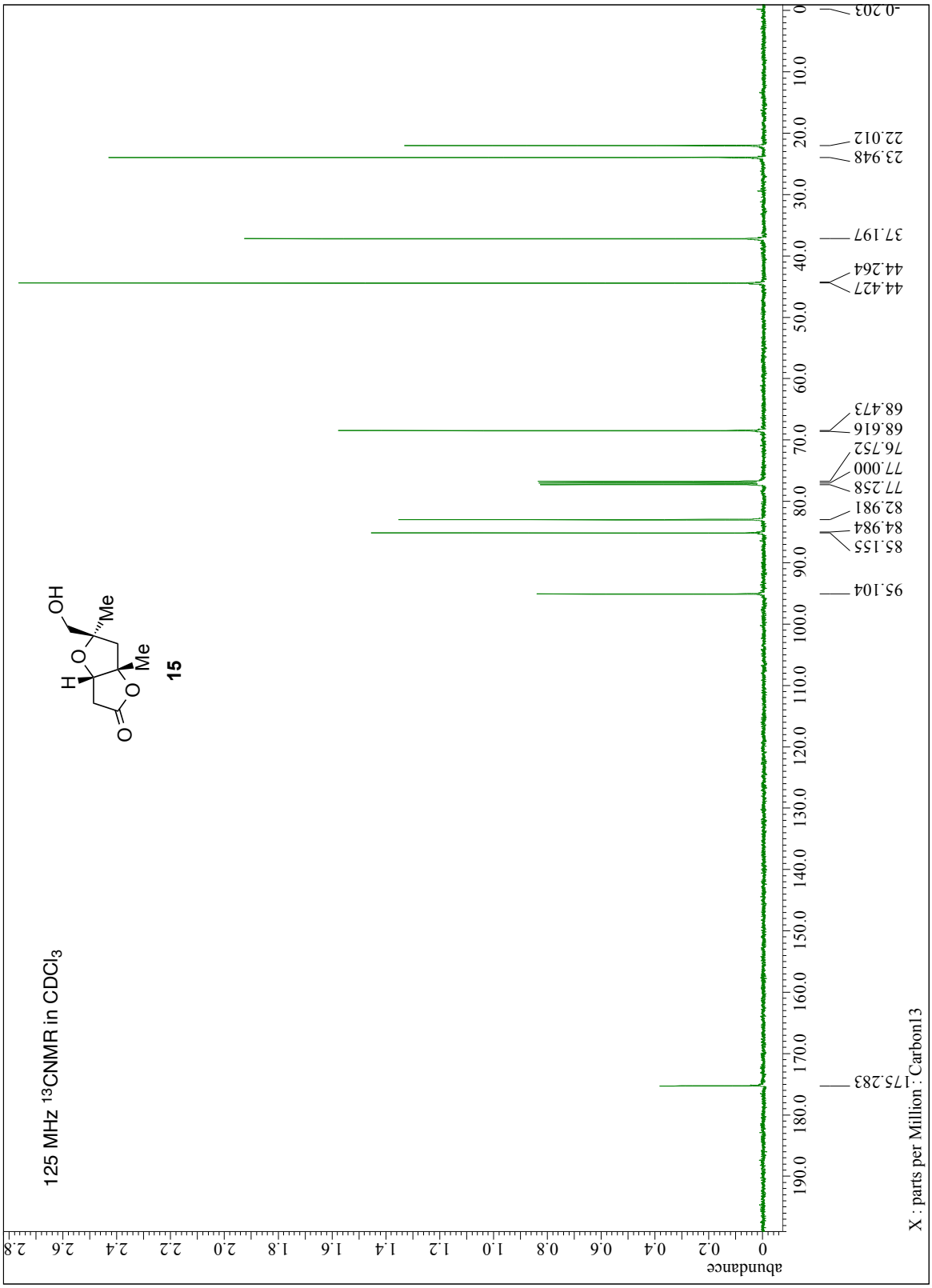

500 MHz ¹HNMR in CDCl3
13
OTBDPS
Me
H
O
O
Me2N
X : parts per Million : 1H
(Thousands)

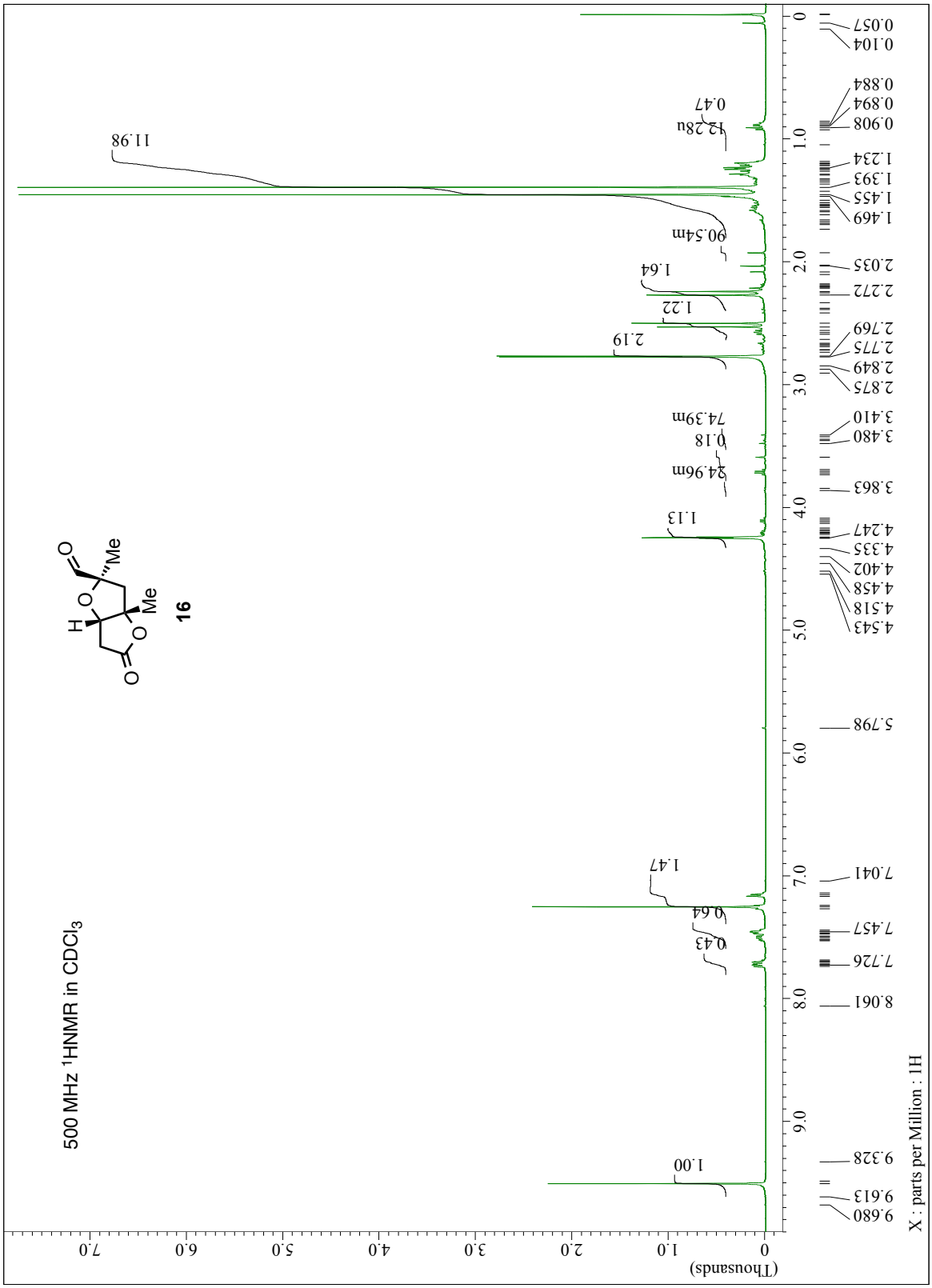

125 MHz 13CNMR in CDCl3
OTBDPS
Me
H
O
O
Me2N
13
170.581
151.466
135.642
135.603
133.467
129.604
129.566
127.629
105.586
82.599
77.935
77.248
77.000
76.742
68.664
41.136
40.735
37.664
35.480
26.800
24.329
19.255
-0.022
abundance
X : parts per Million : Carbon13

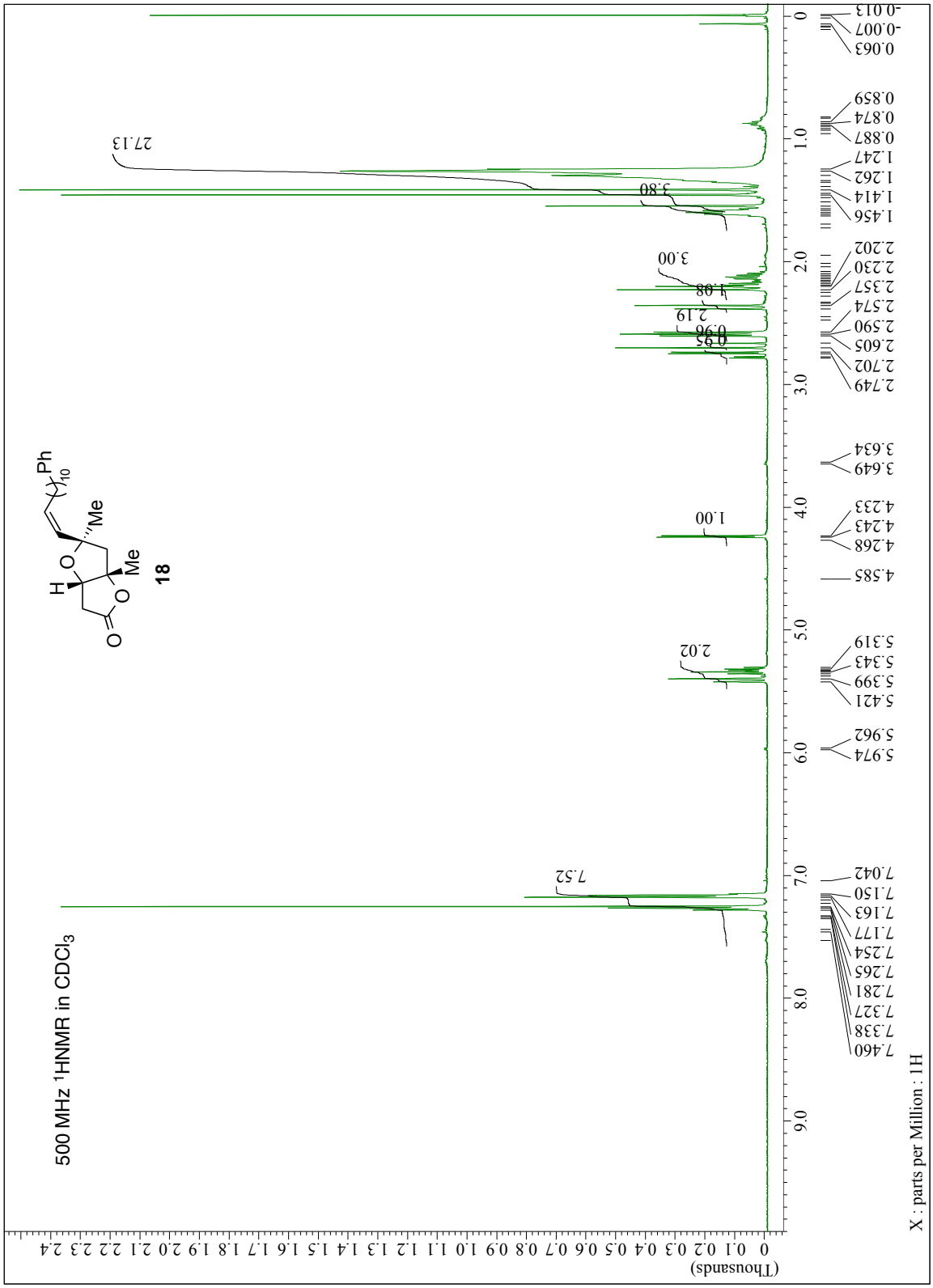

500 MHz ¹HNMR in CDCl₃
14
OTBDPS
Me
I
H
O
O
O
O
(Thousands)
X : parts per Million : 1H
9.56
4.32
6.21
4.19
1.00
1.11
2.12
1.03
1.03
2.07
1.07
7.132
7.402
7.633
7.636
7.649
7.657
7.660
7.672
7.675
4.541
4.530
4.123
4.109
3.732
3.468
3.310
2.936
2.925
2.633
2.559
2.356
2.040
1.829
1.575
1.254
1.250
1.230
1.208
1.084
1.062
0.081
0.067
-0.005

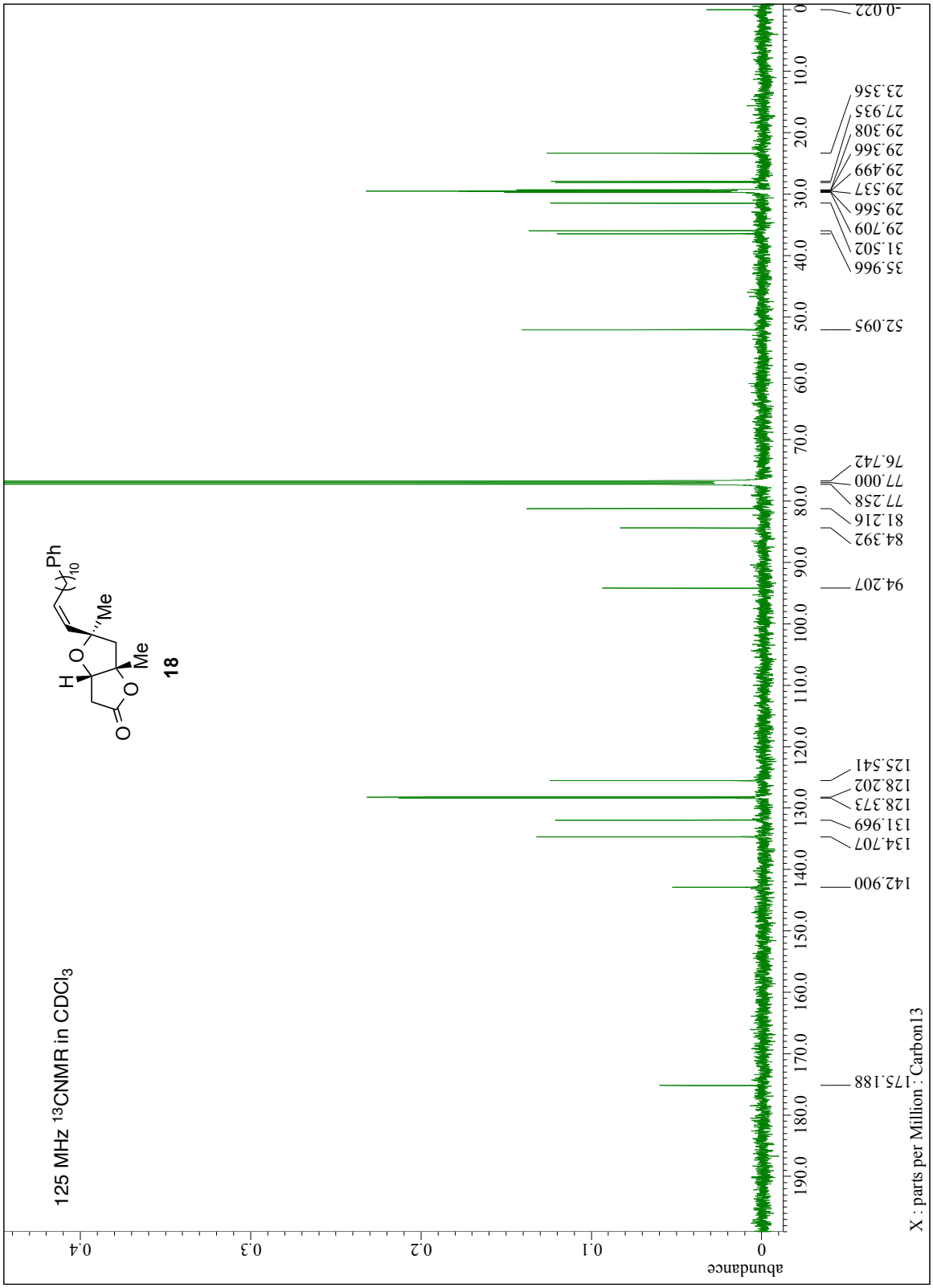

125 MHz 13CNMR in CDCl3
OTBDPS
Me
H
O
O
O
I
14
174.587
135.603
135.556
132.895
132.809
129.947
127.868
94.570
85.079
82.170
77.248
77.000
76.742
70.171
45.466
38.637
26.962
24.577
19.217
8.105
-0.022
X : parts per Million : Carbon13
abundance

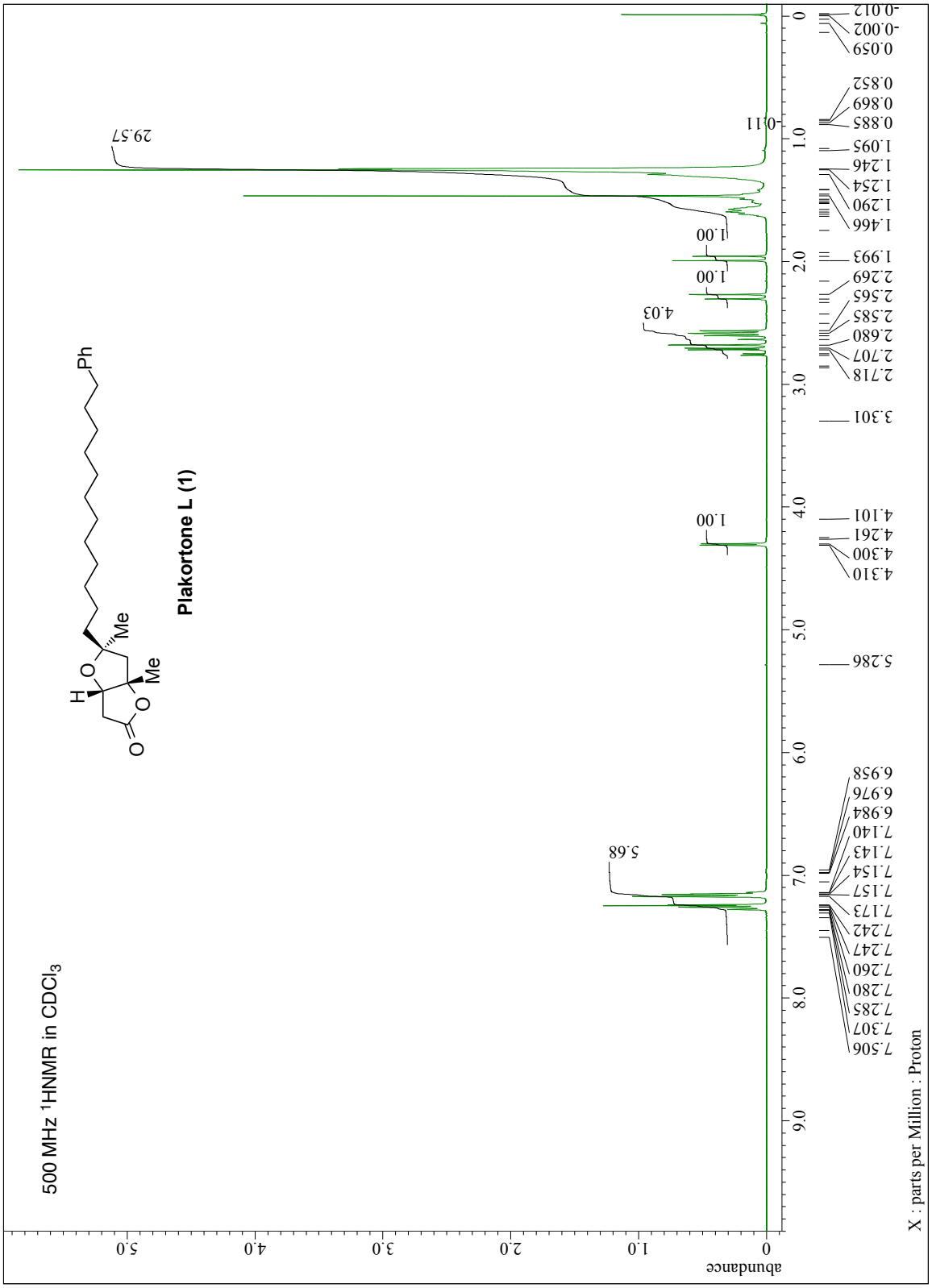

500 MHz 1HNMR in CDCl3
15
X : parts per Million : 1H
(Thousands)
8.626
8.017
7.253
7.211
5.507
4.566
4.448
4.420
4.411
4.260
4.251
4.119
3.489
3.478
3.413
3.399
2.733
2.723
2.692
2.656
2.259
2.255
1.974
1.681
1.508
1.481
1.362
1.352
1.264
1.237
0.903
0.050
-0.014
-0.020
1.00
1.05
1.05
1.04
2.18
2.16
1.05
3.24
3.45

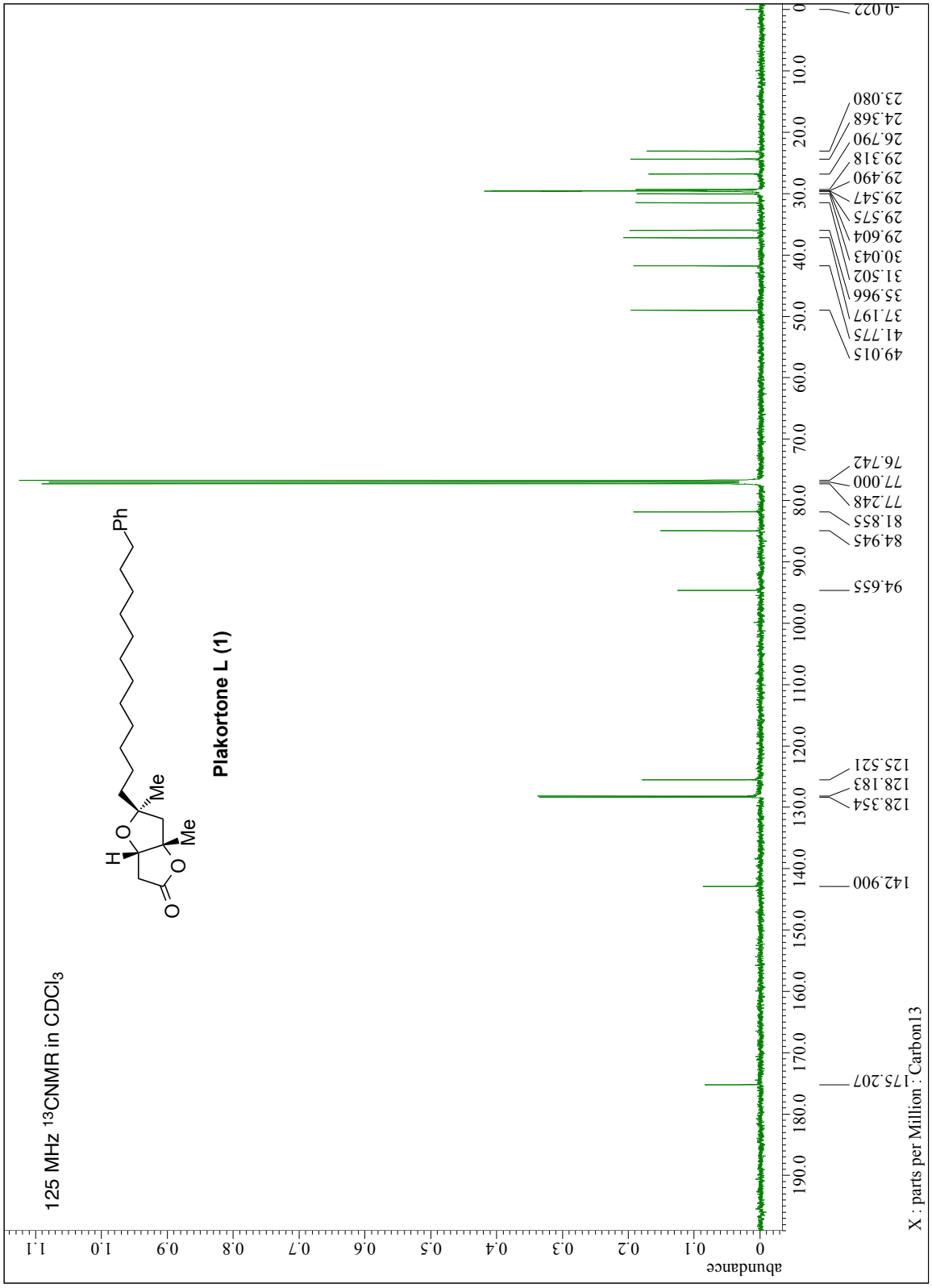

125 MHz 13CNMR in CDCl3
15
175.283
95.104
85.155
84.984
82.981
77.258
77.000
76.752
68.616
68.473
44.427
44.264
37.197
23.948
22.012
-0.203
X : parts per Million : Carbon13
abundance

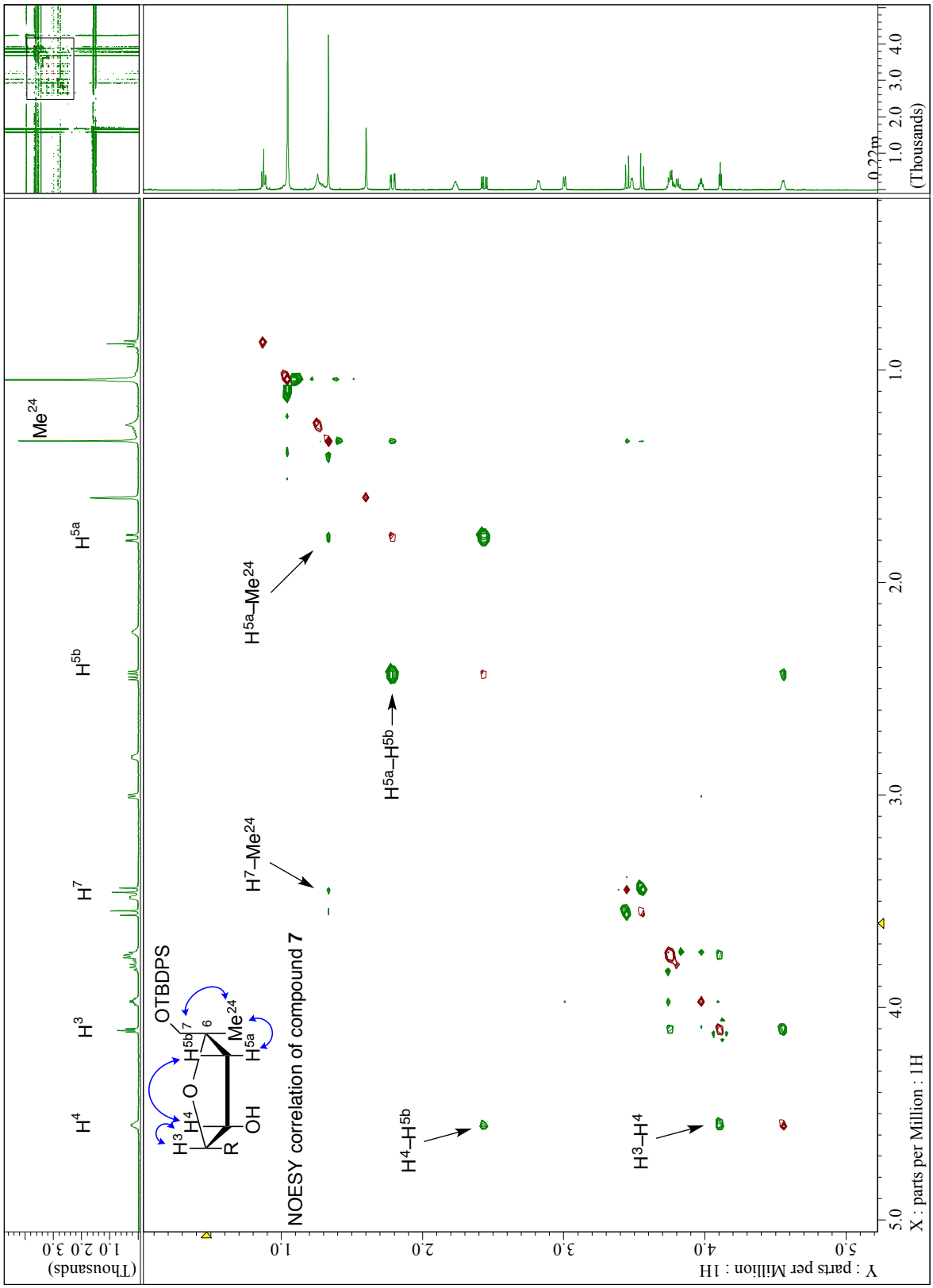

500 MHz ¹HNMR in CDCl3
16
Me
Me
H
O
O
O
O
(Thousands)
X : parts per Million : 1H
9.680
9.613
9.328
8.061
7.726
7.457
7.041
5.798
4.543
4.518
4.458
4.402
4.335
4.247
3.863
3.480
3.410
2.875
2.849
2.775
2.769
2.272
2.035
1.469
1.455
1.393
1.234
0.908
0.894
0.884
0.104
0.057
1.00
0.43
0.64
1.47
1.13
24.96m
0.18
74.39m
2.19
1.22
1.64
90.54m
11.98
12.28u
0.47


500 MHz 1HNMR in CDCl3
18
Ph
Me
Me
H
O
O
O
7.52
2.02
1.00
3.00
1.08
2.19
0.96
0.95
3.80
27.13
X : parts per Million : 1H
(Thousands)


125 MHz 13CNMR in CDCl3
18
X : parts per Million : Carbon13
abundance
175.188
142.900
134.707
131.969
128.373
128.202
125.541
94.207
84.392
81.216
77.258
77.000
76.742
52.095
35.966
31.502
29.709
29.566
29.537
29.499
29.366
29.308
27.935
23.356
-0.022


500 MHz 1HNMR in CDCl3
Plakortone L (1)
Ph
Me
Me
H
O
O
O
abundance
X : parts per Million : Proton
7.506
7.307
7.285
7.280
7.260
7.247
7.242
7.173
7.157
7.154
7.143
7.140
6.984
6.976
6.958
5.286
4.310
4.300
4.261
4.101
3.301
2.718
2.707
2.680
2.585
2.565
2.269
1.993
1.466
1.290
1.254
1.246
1.095
0.885
0.869
0.852
0.059
-0.002
-0.012
5.68
1.00
4.03
1.00
1.00
1.00
29.57
0.11


125 MHz 13CNMR in CDCl3
Plakortone L (1)
Ph
Me
Me
H
O
O
O
abundance
X : parts per Million : Carbon13
175.207
142.900
128.354
128.183
125.521
94.655
84.945
81.855
77.248
77.000
76.742
49.015
41.775
37.197
35.966
31.502
30.043
29.604
29.575
29.547
29.490
29.318
26.790
24.368
23.080
-0.022


NOESY correlation of compound 7
OTBDPS
H4–H5b
H3–H4
H7–Me24
H5a–H5b
H5a–Me24
X : parts per Million : 1H
Y : parts per Million : 1H
(Thousands)