Supporting information

Vinylnaphthalene embedded hexaoxazole as a fluorescence turn-on type G-quadruplex ligand

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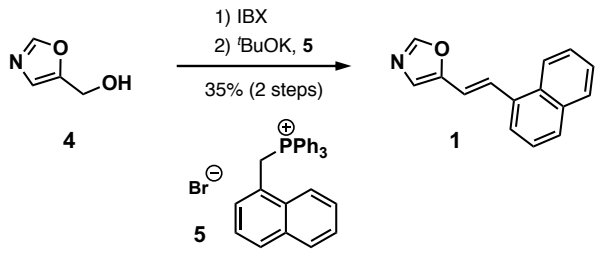
1. Synthesis

General

Flash chromatography was performed on silica gel 60 (spherical, particle size 0.040–0.100 mm; Kanto Co., Inc., Japan) and preparative-TLC (PLC) was performed using PLC silica gel 60 F_{254} (0.5 mm, Merck Ltd., Germany). Optical rotations were measured on a JASCO P-2200 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-AL300 (300 MHz), JNM-ECX 400 (400 MHz) and JNM-ECA 500 (500 MHz). The spectra are referenced internally according to the residual solvent signals of $CDCl_3$ (^{1}H NMR; δ = 7.26 ppm, ^{13}C NMR; δ = 77.0 ppm), DMSO-d_6 (^{1}H NMR; δ = 2.50 ppm, ^{13}C NMR; δ = 39.5 ppm). Data for ^{1}H NMR are recorded as follows; chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet; br, broad), integration, coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shifts (δ, ppm). Mass spectra were recorded on a JEOL JMS-T100LC spectrometer with ESI-MS mode using MeOH as a solvent.

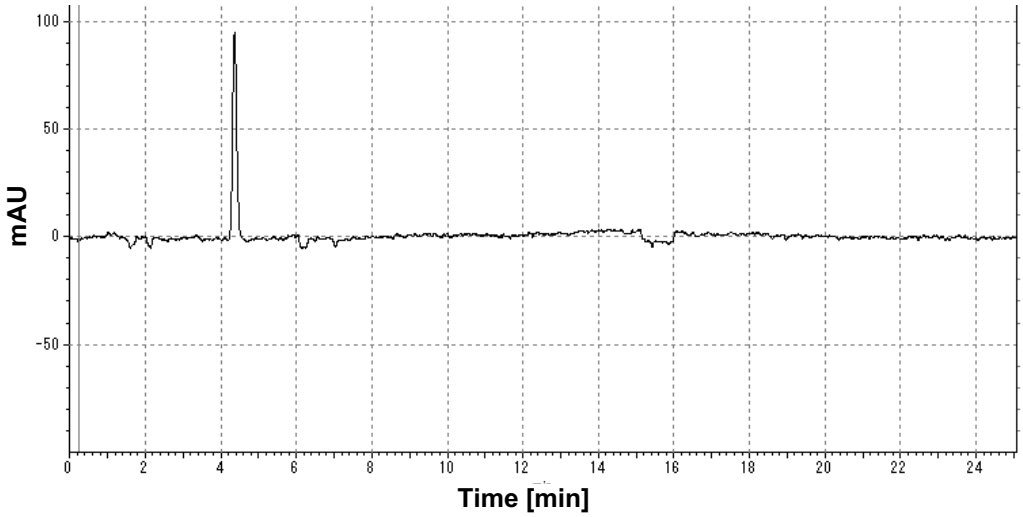
Compound 1



To a solution of **4**[1] (68.2 mg, 688 μmol) in EtOAc (1 mL) was added 2-iodoxybenzoic acid (296 mg, 1.03 mmol) at room temperature under argon atmosphere. The resulting mixture was refluxed for 1 h, and then filtered through a pad of Celite® and eluted with EtOAc. The filtrates were concentrated *in vacuo* to give an aldehyde, which was used without further purification. To a solution of **5** (231 mg, 479 mmol) in THF (1 mL) was added with potassium *tert*-butoxide (39.0 mg, 351 mmol) and the solution of aldehyde in THF (1 mL) at room temperature under argon atmosphere. After stirred for 1 h, the reaction mixture was filtrated through a pad of Celite® and eluted with EtOAc, and the filtrates were concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate 20:1) to give **1** (25.1 mg, 35%, 2

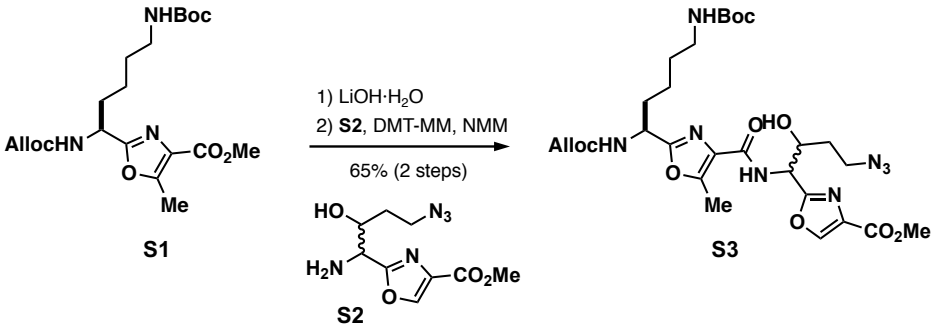
steps).

Spectral data for **1**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 8.3 Hz, 1H), 7.96-7.82 (m, 4H), 7.72 (d, J = 7.2 Hz, 1H), 7.59-7.47 (m, 3H), 7.14 (s, 1H), 6.99 (d, J = 15.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 150.5, 133.7, 133.6, 131.2 128.8, 128.7, 127.2, 126.4, 126.0, 125.6, 124.3, 124.2, 123.5, 115.4, 29.7; HRMS (ESI, M+H) calcd for $C_{15}H_{12}N_1O_1$ 222.09189, found 222.09187.



Purity analysis of **1** was conducted via reverse phase HPLC with using Hitachi L-2455 with C18 UG80 S5, 5.0 μm, 4.6 mm × 250 mm (Chemicals Evaluation and Research Institute, Japan) detected at 324 nm, and a mobile phase was constructed of CH_3CN-H_2O-TFA (60:40:0.1).

Compound S3

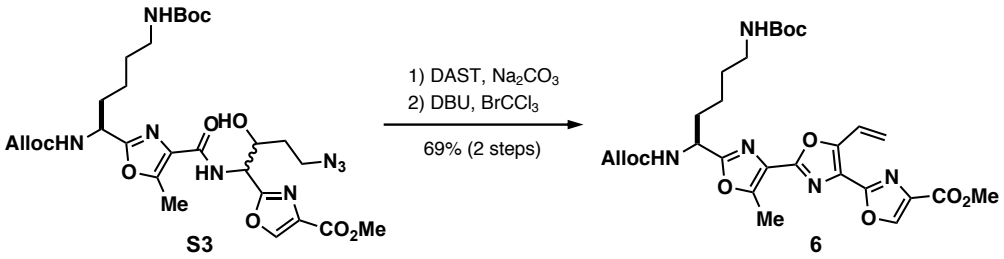


To a solution of **S1**[2] (7.96 g, 18.7 mmol) in THF-H_2O (3:1, 160 mL) was added $LiOH{\cdot}H_2O$ (1.57 g, 37.4 mmol) at room temperature. After stirred for 1 h, the reaction mixture was quenched with 3 N HCl to give carboxylic acid as a THF-H_2O solution,

which was used without further purification. Then, to a solution of the crude carboxylic acid was added NMM (6.90mL, 62.4 mmol), DMT-MM (9.20 g, 31.2 mmol) and amine **S2**[3] (6.15 g, 15.6 mmol) at room temperature. After stirred for 17 h, the reaction mixture was quenched with 1.2N HCl. The organic layer was extracted with $CHCl_3$, washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 150:1) to give amide **S3** (7.82 g, 65%, 2 steps).

Spectral data for **S3**: $[\alpha]_D^{25}$= -22.6 (*c* 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.74 (br, 1H), 5.93 (br, 1H), 5.41-5.29 (m, 3H), 5.22 (d, *J* = 11.0 Hz, 1H), 4.86 (br, 1H), 4.60-4.58 (m, 4H), 4.23 (br, 1H), 3.91 (s, 3H), 3.54-3.51 (m, 2H), 3.11-3.07 (m, 2H), 2.60 (s, 3H), 1.93-1.63 (m, 4H), 1.51-1.38 (m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 161.6, 161.2, 161.1, 156.2, 155.7, 154.2, 144.4, 133.1, 132.5, 128.2, 118.0, 79.2, 70.3, 66.0, 52.3, 51.5, 49.0, 48.0, 39.9, 33.4, 32.6, 29.7, 29.5, 28.4, 22.3, 11.7; HRMS (ESI, M+Na) calcd for $C_{28}H_{40}N_8O_{10}Na$ 671.2765, found 671.2749.

Compound 6

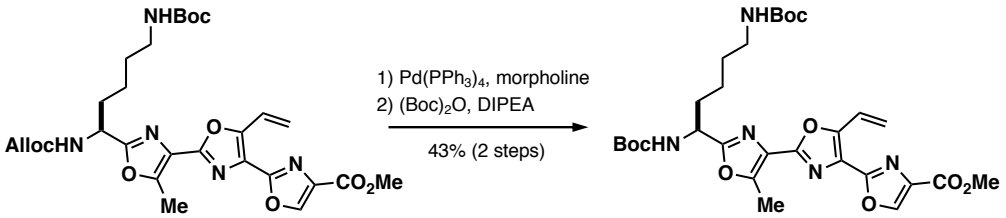


To a solution of amide **S3** (7.82 g, 12.1 mmol) in dry CH_2Cl_2 (120 ml) was cooled to 0 ˚C and was treated with Na_2CO_3 (3.85 g, 36.3 mmol) and DAST (2.34 ml, 14.5 mmol) under argon atmosphere. After stirring for 30 min, the mixture was quenched with saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over $MgSO_4$, filtered and then concentrated *in vacuo*. To a solution of the crude oxazoline in dry CH_2Cl_2 (60 ml) was cooled to 0 ˚C and was treated with DBU (9.05 ml, 60.5 mmol) and $BrCCl_3$ (6.00 ml, 60.5 mmol) under argon atmosphere. After stirring for 15 h, the reaction was quenched with 1.2 N HCl, and the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, filtered, and then

concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 200:1) to give trioxazole **6** (4.88 g, 69%, 2 steps).

Spectral data for **6**: $[\alpha]_D^{25}$= -21.4 (*c* 0.44, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ8.31 (s, 1H), 7.40 (dd, *J* = 17.4, 11.0 Hz, 1H), 6.11 (d, *J* = 17.4 Hz, 1H), 5.97-5.87 (m, 1H), 5.63 (d, *J* = 12.4 Hz, 1H), 5.51 (d, *J* = 8.7 Hz, 1H), 5.32 (d, *J* = 16.9 Hz, 1H), 5.22 (d, *J* = 10.5 Hz, 1H), 4.96 (dt, *J* = 8.2, 7.8 Hz, 1H), 4.59-4.58 (br, 3H), 3.95 (s, 3H), 3.10 (br, 2H), 2.73 (s, 3H), 2.05-1.83 (m, 2H), 1.58-1.36 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ162.9, 161.5, 156.2, 156.0, 155.7, 155.3, 151.6, 149.6, 143.7, 134.5, 132.5, 125.4, 124.5, 121.5, 119.4, 117.9, 77.2, 66.0, 52.3, 49.2, 40.0, 33.8, 29.5, 28.4, 22.3, 11.9; HRMS (ESI, M+Na) calcd for $C_{28}H_{35}N_5O_9Na$ 608.2333, found 608.2337.

Compound 7



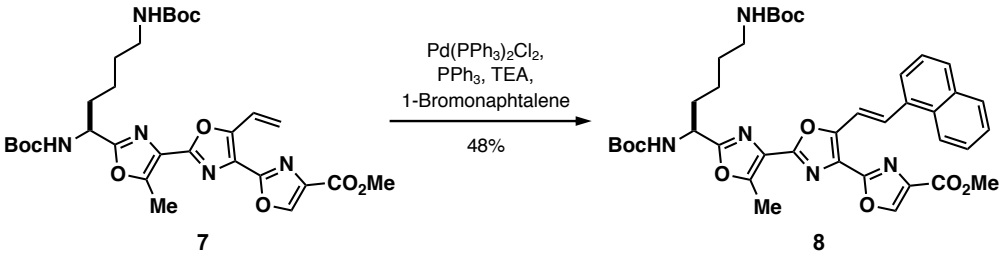
6 **7**

To a solution of trioxazole **6** (150 mg, 256 μmol) in THF (8.5 mL) was added morpholine (22.3 μL, 2.56 mmol) and $Pd(PPh_3)_4$ (59.0 mg, 51.0 μmol) at room temperature under argon atmosphere. After stirred for 10 min, the reaction mixture was concentrated *in vacuo* to give amine, which was used without further purification. To a solution of crude amine in CH_2Cl_2 (1 mL) was added with ^{i}Pr$_2$NEt (91.0 μL, 537 μmol) and $(Boc)_2O$ (78.1 mg, 358 μmol) at room temperature under argon atmosphere. After stirred for 6 h, the reaction mixture was quenched with 1.2 N HCl, and the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 200:1) to give Boc-trioxazole **7** (66.3 mg, 43%, 2 steps).

Spectral data for **7**: $[\alpha]_D^{25}$= -46.4 (*c* 0.50, $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6) δ9.02 (s, 1H), 7.65-7.54 (m, 1H), 7.27 (dd, *J* = 17.9, 11.7 Hz, 1H), 6.78 (t, *J* = 5.5 Hz, 1H), 6.05 (d, *J* = 17.5 Hz, 1H), 5.74 (d, *J* = 12.4 Hz, 1H), 4.64 (br, 1H), 3.86 (s, 3H), 2.91-2.87 (m, 2H), 2.69 (s, 3H), 1.81-1.74 (m, 2H), 1.47-1.29 (m, 22H); ^{13}C NMR (125 MHz, $CDCl_3$)

δ163.3, 161.4, 156.1, 156.0, 155.3, 155.2, 151.5, 149.5, 143.7, 134.4, 132.1, 132.0, 131.9, 129.4, 128.5, 128.4, 125.4, 124.4, 121.5, 119.4, 80.1, 79.0, 67.7, 52.2, 48.6, 40.0, 38.8, 34.0, 30.5, 29.5, 28.9, 28.4, 28.3, 23.9, 22.9, 22.4, 14.0, 11.9, 11.0; HRMS (ESI, M+Na) calcd for $C_{29}H_{39}N_5O_9Na$ 624.2646, found 624.2651.

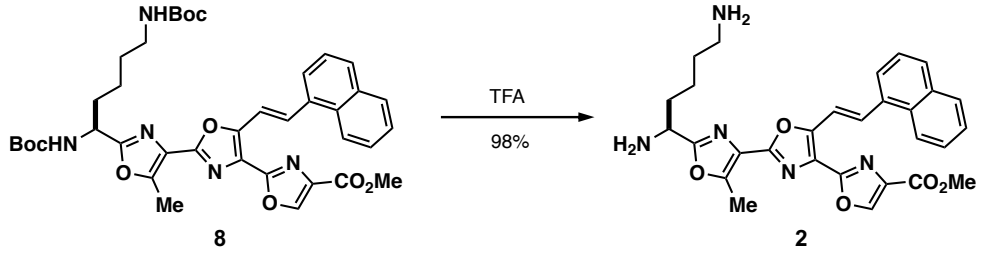
Compound 8



7 8

To a solution of **7** (5.2 mg, 8.60 μmol) in CH_3CN (210 μL) was added 1-Bromonapthalene (3.60 μl, 259 μmol), Et_3N (36.0 μl, 258 μmol), PPh_3 (1.30 mg, 5.16 μmol) and $Pd(PPh_3)_2Cl_2$ (78.1 mg, 358 μmol) at room temperature under argon atmosphere, and then the reaction mixture was heated at 90 °C. After stirred for 24 h, the resulting mixture was filtrated through a pad of Celite® and eluted with $CHCl_3$-MeOH (9:1). The filtrates were concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel (hexane/ethyl acetate 3:2) to give **8** (3.0 mg, 48 %). Spectral data for **8**: $[\alpha]_D^{25}$= -36.9 (*c* 0.84, $CHCl_3$); ^{1}H NMR (400 MHz, DMSO-d_6) δ9.06 (s, 1H), 8.45 (d, *J* = 16.0 Hz, 1H), 8.39 (d, *J* = 8.7 Hz, 1H), 8.02-8.00 (m, 2H), 7.97 (d, *J* = 6.9 Hz, 1H), 7.72 (d, *J* = 16.5 Hz, 1H), 7.70-7.55 (m, 4H), 6.80 (t, *J* = 5.5 Hz, 1H), 4.67 (dt, *J* = 8.7, 6.0 Hz, 1H), 3.88 (s, 3H), 2.92-2.91 (m, 2H), 2.76 (s, 3H), 1.91-1.74 (m, 2H), 1.41-1.23 (m, 22H); ^{13}C NMR (100 MHz, DMSO-d_6) δ163.7, 160.9, 155.6, 155.3, 154.9, 151.7, 149.2, 145.7, 133.5, 133.4, 132.6, 130.7, 130.0, 129.5, 128.7, 127.0, 126.3, 125.9, 125.3, 123.9, 123.5, 123.3, 114.6, 78.4, 77.3, 52.0, 48.6, 32.1, 29.0, 28.2, 22.7, 11.6; HRMS (ESI, M+Na) calcd for $C_{39}H_{45}N_5O_9Na$ 750.3115, found 750.3075.

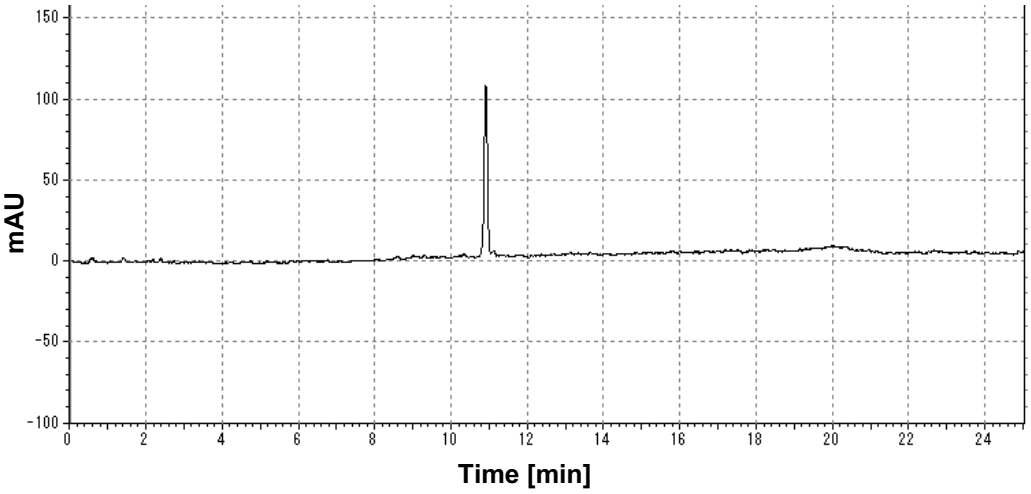
Compound 2



8 **2**

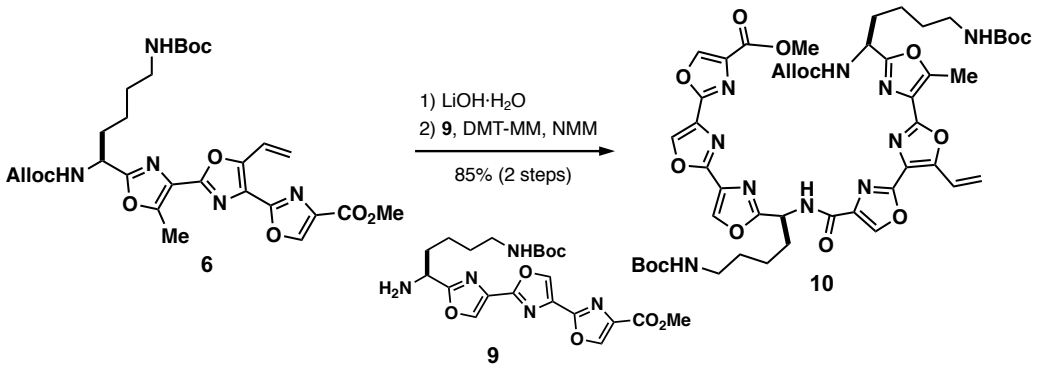
To a solution of **8** (3.00 mg, 4.12 μmol) in CH_2Cl_2 (1 mL) was added TFA (2 mL) at room temperature, and the mixture was stirred for 10 min. The reaction mixture was concentrated *in vacuo* to give **2** (2.50 mg, 98%).

Spectral data for **2**: $[\alpha]_D^{25}$= +7.0 (*c* 0.60, MeOH); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.06 (s, 1H), 8.86 (br, 2H), 8.46 (d, J = 16.6 Hz, 1H), 8.37 (d, J = 8.6 Hz, 1H), 8.02 (d, J = 8.0 Hz, 2H), 7.98 (d, J = 7.5 Hz, 1H), 7.77-7.61 (m, 6H), 4.68 (m, 1H), 3.88 (s, 3H), 2.84 (s, 3H), 2.80-2.78 (m, 2H), 2.04-1.97 (m, 2H), 1.59-1.56 (m, 2H), 1.41-1.39 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.0, 159.2, 155.6, 154.4, 153.1, 149.6, 145.9, 140.6, 133.6, 133.5, 132.5, 130.7, 130.5, 129.8, 128.9, 127.2, 126.5, 126.0, 125.5, 124.2, 124.1, 123.3, 114.6, 79.2, 69.8, 52.2, 47.6, 38.5, 31.0, 26.5, 21.5, 11.8; HRMS (ESI, M+H) calcd for $C_{29}H_{30}N_5O_5$ 528.2247, found 528.2202.



Purity analysis of **2** was conducted via reverse phase HPLC with using Hitachi L-2455 with C18 UG80 S5, 5.0 μm, 4.6 mm × 250 mm (Chemicals Evaluation and Research Institute, Japan) detected at 364 nm, and a mobile phase was constructed of CH_3CN-H_2O-TFA (20:80:0.1).

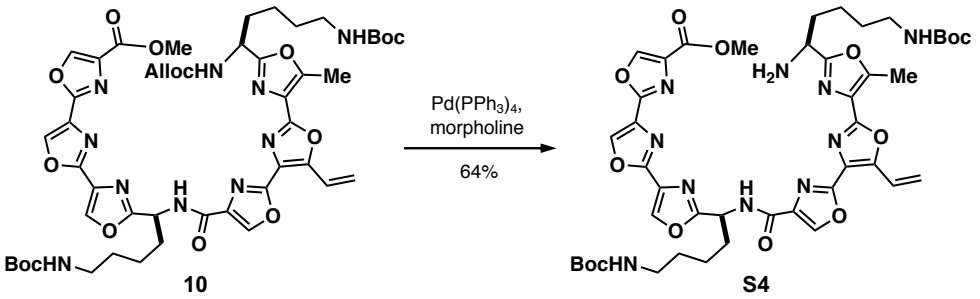
Compound 10



To a solution of trioxazole **6** (4.88 g, 8.33 mmol) in THF-H_2O (3:1, 80 mL) was added LiOH·H_2O (701 mg, 16.7 mmol) at room temperature, and stirred for 1 h. The reaction mixture was quenched with 3 N HCl to give carboxylic acid as a THF-H_2O solution, which was used without further purification. To a solution of carboxylic acid (THF-H_2O) was added NMM (3.68 mL, 33.3 mmol), DMT-MM (4.92 g, 16.7 mmol), and amine **9**, and the mixture was stirred at room temperature. After stirred for 17 h, the reaction mixture was quenched with 1.2N HCl, and the organic layer was extracted with $CHCl_3$, washed with saturated aqueous $NaHCO_3$, dried over MgSO4, and filtered. The filtrates were concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 150:1) to give bistrioxazole **10** (7.22 g, 85%, 2 steps).

Spectral data for **10**: $[\alpha]_D^{25}$= +3.0 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.33 (s, 1H), 8.32 (s, 1H), 8.31 (s, 1H), 7.48 (d, *J* = 9.2 Hz, 1H), 7.30 (dd, *J* = 17.4, 11.5 Hz, 1H), 6.13 (d, *J* = 17.4 Hz, 1H), 5.97-5.87 (m, 1H), 5.68 (d, *J* = 11.9 Hz, 1H), 5.54-5.48 (m, 3H), 5.32 (d, *J* = 16.9 Hz, 1H), 5.22 (d, *J* = 9.6 Hz, 1H), 4.97 (dt, *J* = 8.2, 7.8 Hz, 1H), 4.59-4.58 (m, 3H), 3.95 (s, 3H), 3.11 (br, 4H), 2.75 (s, 3H), 2.27-1.85 (m, 4H), 1.55-1.24 (m, 26H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 163.0, 161.2, 160.0, 156.0, 155.9, 155.7, 155.4, 155.3, 151.7, 149.4, 143.9, 141.6, 139.6, 139.3, 136.6, 134.3, 132.5, 130.8, 129.8, 125.4, 124.4, 121.3, 119.7, 117.9, 79.1, 77.2, 65.9, 52.3, 49.1, 46.7, 40.1, 39.9, 33.7, 33.4, 29.6, 29.5, 28.3, 22.8, 22.3, 12.0; HRMS (ESI, M+Na) calcd for $C_{48}H_{58}N_{10}O_{15}Na$ 1037.3981, found 1037.4027.

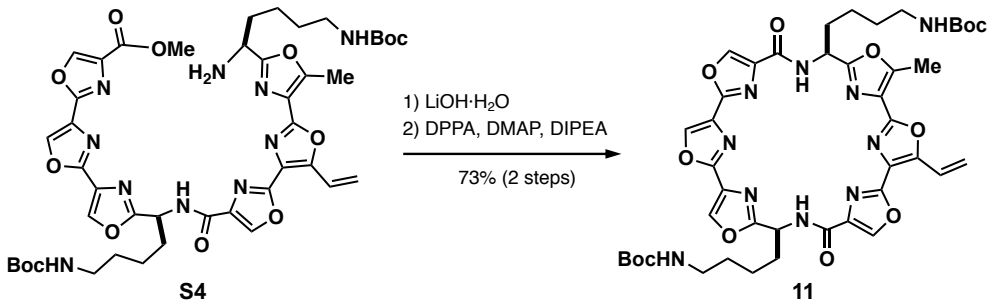
Compound S4



To a solution of bistrioxazole **10** (7.22 g, 7.11 mmol) in THF (250 mL) was added morpholine (6.19 mL, 2.64 mmol) and $Pd(PPh_3)_4$ (1.64 g, 1.42 mmol) at room temperature under argon atmosphere. After stirred for 3 h, the reaction mixture was concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 50:1) to give amine **S4** (4.24 g, 64%).

Spectral data for **S4**: $[\alpha]_D^{25}$= +31.4 (*c* 0.79, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.324 (s, 1H), 8.317 (s, 1H), 8.30 (s, 1H), 7.49 (d, *J* = 9.2 Hz, 1H), 7.30 (dd, *J* = 17.4, 11.5, 1H), 6.13 (d, *J* = 17.4 Hz, 1H), 5.67 (d, *J* = 11.9 Hz, 1H), 5.50 (dt, *J* = 8.2, 6.9 Hz, 1H), 4.58 (br, 2H), 4.07 (t, *J* = 6.9 Hz, 1H), 3.95 (s, 3H), 3.12-3.11 (m, 4H), 2.75 (s, 3H), 2.24-1.79 (m, 6H), 1.56-1.40 (m, 26H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 164.8, 161.2, 159.9, 155.9, 155.7, 155.4, 155.3, 151.5, 149.3, 143.8, 141.5, 139.6, 139.3, 136, 6, 134.3, 130.7, 129.8, 125.4, 124.1, 121.2, 119.6, 79.0, 77.2, 52.3, 49.9, 46.7, 40.2, 35.2, 33.4, 29.7, 29.4, 28.3, 22.9, 22.8, 11.9; HRMS (ESI, M+Na) calcd for $C_{44}H_{54}N_{10}O_{13}Na$ 953.3770, found 953.3742.

Compound 11

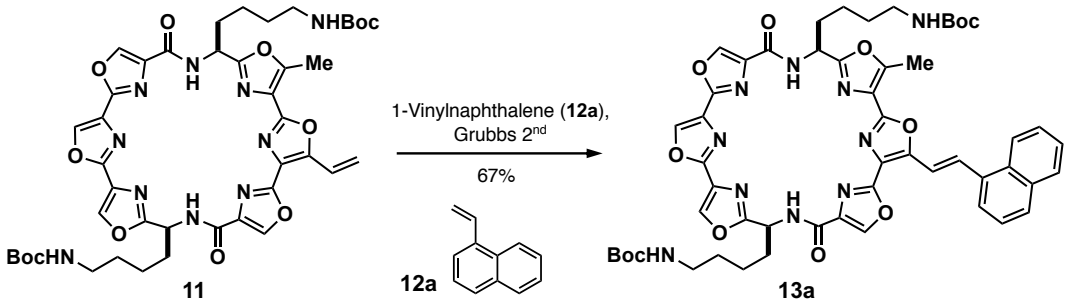


To a solution of the amine **S4** (1.22 g, 1.20 mmol) in THF-H_2O (3:1, 40 mL) was

added $LiOH \cdot H_2O$ (101 mg, 2.40 mmol) at room temperature. After stirred for 40 min, the reaction mixture was quenched with 3 N HCl, and concentrated *in vacuo* to give carboxylic acid, which was used without further purification. To a solution of the crude carboxylic acid in dry DMF (400 mL) were added diisopropylethylamine (816 μL, 4.80 mmol), DMAP (293 mg,2.40 mmol) and DPPA (2.60 mL, 12.0 mmol) at room temperature under argon atmosphere, and then the reaction mixture was heated at 70 °C. After stirred for 10 h, the reaction mixture was quenched with 1.2 N HCl. The resulting mixture was extracted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 100:1) to give amide **11** (782 mg, 73%, 2 steps).

Spectral data for **11**: $[\alpha]_D^{25}$= -3.0 (*c* 0.95, $CHCl_3$); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.12 (s, 1H), 9.09 (s, 1H), 8.92 (s, 1H), 8.91 (s, 1H), 8.36-8.29 (m, 2H), 7.20 (dd, J = 17.4, 11.5 Hz, 1H), 6.78 (d, J = 5.5 Hz, 1H), 6.77 (d, J = 5.5 Hz, 1H), 6.09 (d, J = 17.4 Hz, 1H), 5.78 (d, J = 11.9 Hz, 1H), 5.43 (dt, J = 6.9, 5.0 Hz, 1H), 5.35 (dt, J = 6.9, 5.0 Hz, 1H), 2.85-2.83 (br, 4H), 2.77 (s, 3H), 2.05-1.90 (m. 4H), 1.33-1.08 (m, 26H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.5, 162.2, 158.74, 158.70, 155.7, 155.5, 155.1, 155.0, 154.5, 152.6, 148.9, 142.5, 141.7, 141.0, 136.2, 136.1, 129.8, 128.5, 125.0, 123.5, 120.8, 120.5, 79.2, 77.2, 47.4, 47.2, 33.3, 29.1, 28.1, 21.1, 21.0, 11.8; HRMS (ESI, M+Na) calcd for $C_{43}H_{50}N_{10}O_{12}Na$ 921.3507, found 921.3487.

Compound 13a

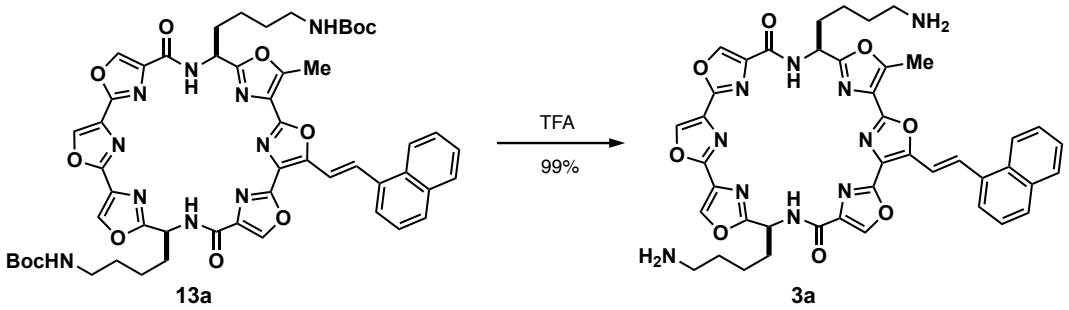


To a solution of **11** (40.0 mg, 44.5 μmol) in dry THF (1 mL) was added 1-vinylnaphthalene **12a** (68.6 mg, 445 μmol) and Grubbs 2nd (773 μg, 0.890 μmol) at room

temperature under argon atmosphere, and then the reaction mixture was heated at 90 ˚C. After stirred for 26 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 200:1) to give **13a** (31.5 mg, 67%).

Spectral data for **13a**: $[\alpha]_D^{25}$= -3.6 (*c* 0.95, $CHCl_3$); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.11 (s, 1H), 9.05 (s, 1H), 8.92 (s, 1H), 8.88 (s, 1H), 8.36-8.31 (m, 2H), 8.25 (d, *J* = 8.2 Hz, 1H), 8.11 (d, *J* = 15.6 Hz, 1H), 7.99-7.93 (m, 4H), 7.64-7.55 (m, 4H), 6.79-6.78 (m, 2H), 5.41-5.33 (m, 2H), 2.85-2.78 (m, 7H), 2.06 (br, 2H), 1.90 (br, 2H), 1.34-1.23 (m, 26H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4, 162.1, 158.81 158.3, 158.0, 155.7, 155.3, 155.1, 154.6, 152.8, 149.5, 143.0, 142.6, 141.8, 141.1 136.1, 136.0, 133.4, 132.4, 130.6, 130.1, 129.7, 128.8, 128.5, 127.0, 126.4, 125.8, 125.3, 124.1, 123.6, 123.1, 114.1, 47.2, 47.1, 33.5, 33.3, 26.7, 26.2, 25.8, 20.9, 12.0; HRMS (ESI, M+Na) calcd for $C_{53}H_{56}N_{10}O_{10}Na$ 1047.3977, found 1047.3939.

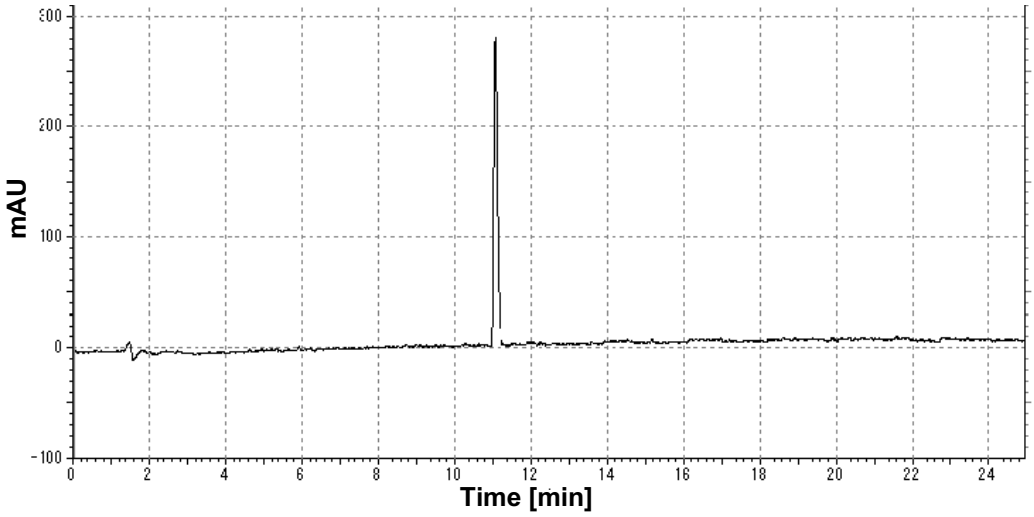
Compound 3a



To a solution of **13a** (31.5 mg, 29.9 μmol) in CH_2Cl_2 (1 mL) was added TFA (2 mL) at room temperature, and the mixture was stirred for 10 min. The reaction mixture was concentrated *in vacuo* to give **3a** (24.3 mg, 99%).

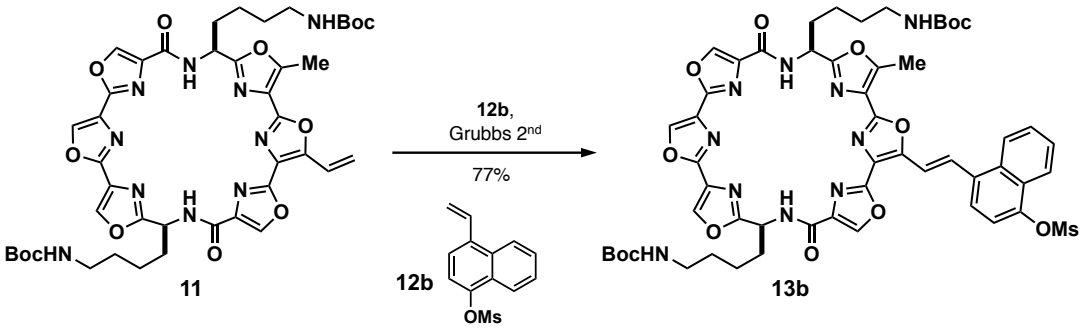
Spectral data for **3a**: $[\alpha]_D^{25}$= -34.5 (*c* 1.0, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.16 (s, 1H), 9.14 (s, 1H), 8.97 (s, 1H), 8.95 (s, 1H), 8.37-8.31 (m, 2H), 8.24 (d, *J* = 16.0 Hz, 1H), 8.04-8.00 (m, 3H), 7.69-7.63 (m, 9H), 5.47-5.39 (m, 2H), 2.92 (s, 3H), 2.76 (br, 4H), 2.08 (br, 2H), 1.95 (br, 2H), 1.55-1.23 (m, 8H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4, 162.1, 158.9, 158.8, 158.3, 158.0, 155.7, 155.3, 155.1, 154.6, 152.8, 149.5, 143.0, 142.6, 141.8, 141.1, 136.1, 136.0, 133.4, 132.4, 130.6, 130.1, 129.7, 128.8, 128.5, 127.0, 126.4, 125.8, 125.3, 124.1, 123.6, 123.1, 114.1, 47.2, 47.1, 33.5, 33.3, 26.7, 26.4,

26.2, 25.8, 20.9, 12.0; HRMS (ESI, M+Na) calcd for $C_{43}H_{40}N_{10}O_8Na$ 847.29283, found 847.29282.



Purity analysis of **3a** was conducted via reverse phase HPLC with using Hitachi L-2455 with C18 UG80 S5, 5.0 μm, 4.6 mm × 250 mm (Chemicals Evaluation and Research Institute, Japan) detected at 377 nm, and a mobile phase was constructed of CH_3CN-H_2O-TFA (20:80:0.1).

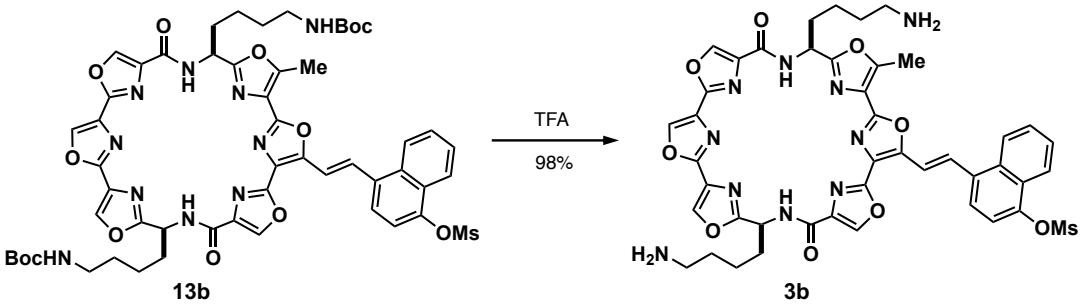
Compound 13b



To a solution of **11** (10.0 mg, 11.1 μmol) in dry THF (500 μL) was added **12b** (13.8 mg, 55.6 μmol) and Grubbs 2nd (717 μg, 0.560 μmol) at room temperature under argon atmosphere, and then the reaction mixture was heated at 90 ˚C. After stirred for 27 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 150:1) to give **13b** (9.60 mg, 77%).

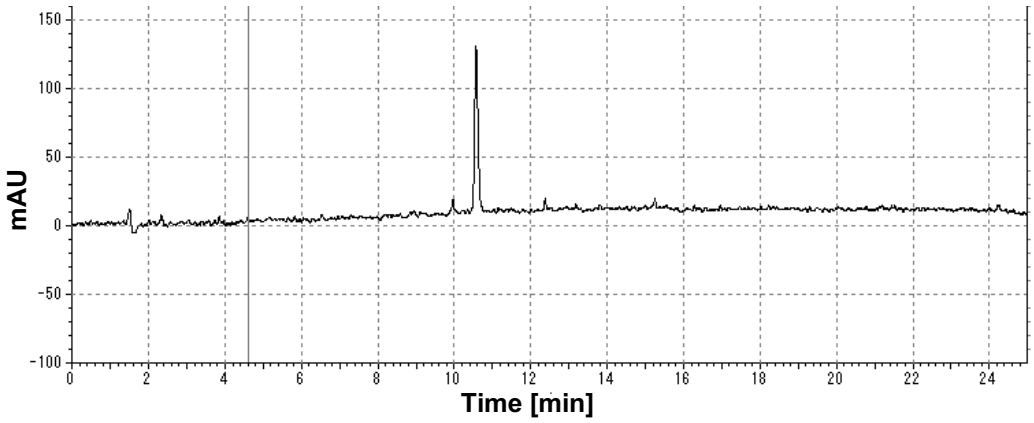
Spectral data for **13b**: $[\alpha]_D^{25}$= -5.8 (*c* 1.0, MeOH); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.12 (s, 1H), 9.08 (s, 1H), 8.93 (s, 1H), 8.92 (s, 1H), 8.38-8.31 (m, 3H), 8.21 (d, *J* = 8.6 Hz, 1H), 8.16 (d, *J* = 16.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.75-7.73 (m, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 16.0 Hz, 1H), 6.78-6.77 (m, 2H), 5.43-5.37 (m, 2H), 3.65 (s, 3H), 2.90 (s, 3H), 2.85-2.84 (m, 4H), 2.06 (br, 2H), 1.91 (br, 2H), 1.80-1.22 (m, 26H); ^{13}C NMR (125 MHz, DMSO-d_6) δ164.5, 162.2, 158.8, 158.7, 155.7, 155.5, 155.2, 154.5, 152.8, 149.2, 145.5, 142.9, 142.5, 141.6, 141.0, 136.2, 136.1, 132.2, 131.8, 129.8, 129.4, 128.5, 127.9, 127.5, 127.0, 125.7, 124.2, 123.8, 123.5, 122.3, 118.6, 115.3, 79.2, 77.2, 69.8, 47.4, 47.2, 38.3, 34.7, 34.2, 33.4, 29.1, 28.2, 26.3, 25.9, 25.8, 21.1, 12.0; HRMS (ESI, M+Na) calcd for $C_{54}H_{58}N_{10}O_{15}SNa$ 1141.3702, found 1141.3708.

Compound 3b



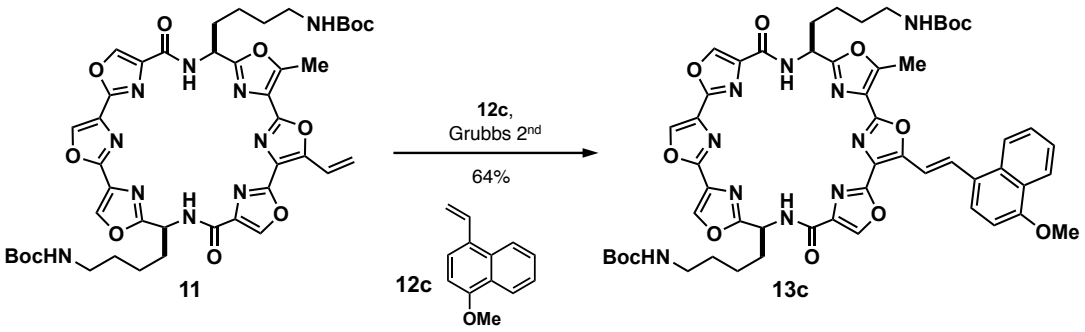
To a solution of **13b** (9.60 mg, 8.58 μmol) in CH_2Cl_2 (1 mL) was added TFA (2 mL) at room temperature, and the mixture was stirred for 10 min. The reaction mixture was concentrated *in vacuo* to give **3b** (7.72 mg, 98%).

Spectral data for **3b**: $[\alpha]_D^{25}$= -58.7 (*c* 0.45, MeOH); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.14 (s, 1H), 9.12 (s, 1H), 8.95 (s, 1H), 8.94 (s, 1H), 8.39 (d, *J* = 7.5 Hz, 1H), 8.36 (d, *J* = 6.9 Hz, 1H), 8.32 (d, *J* = 7.5 Hz, 1H), 8.24-8.22 (m, 1H), 8.18 (d, *J* = 15.5 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.78-7.61 (m, 8H), 5.45 (dt, *J* = 6.9, 5.7 Hz, 1H), 5.40 (dt, *J* = 6.9, 5.7 Hz, 1H), 3.64 (s, 3H), 2.92 (s, 3H), 2.78-2.69 (m, 4H), 2.08 (br, 2H), 1.95 (br, 2H), 1.80-1.16 (m, 8H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.4, 162.2, 158.9, 155.7, 155.2, 154.6, 153.0, 149.3, 145.5, 143.0, 142.6, 141.8, 141.1, 136.2, 136.0, 131.8, 129.7, 129.6, 128.5, 128.0, 127.6, 127.1, 125.7, 124.2, 123.9, 123.6, 122.4, 118.7, 115.3, 69.8, 47.2, 47.1, 38.6, 38.3, 34.7, 34.2, 33.5, 33.4, 26.7, 26.3, 25.8, 25.8, 21.0, 12.0; HRMS (ESI, M+Na) calcd for $C_{44}H_{42}N_{10}O_{11}SNa$ 941.2653, found 941.2629.



Purity analysis of **3b** was conducted via reverse phase HPLC with using Hitachi L-2455 with C18 UG80 S5, 5.0 μm, 4.6 mm × 250 mm (Chemicals Evaluation and Research Institute, Japan) detected at 373 nm, and a mobile phase was constructed of CH_3CN-H_2O-TFA (20:80:0.1).

Compound 13c

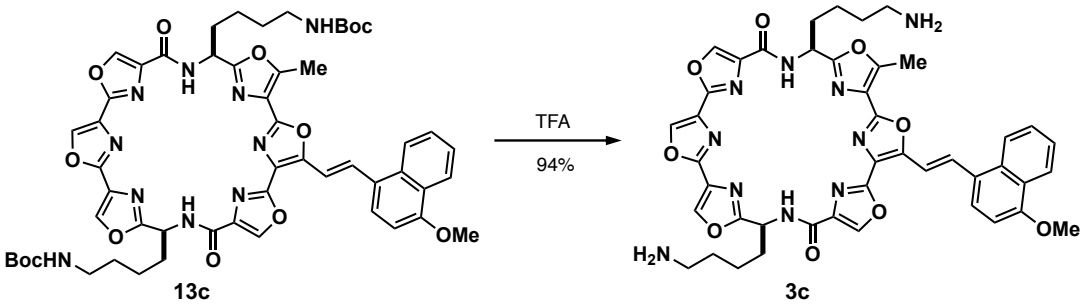


To a solution of **11** (40.0 mg, 44.5 μmol) in dry THF (1 mL) was added **12c** (82.0 mg, 445 μmol) and Grubbs 2nd (773 μg, 0.890 μmol) at room temperature under argon atmosphere, and then the reaction mixture was heated at 90 ˚C. After stirred for 32 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 100:1) to give **13c** (30.0 mg, 64%).

Spectral data for **13c**: $[\alpha]_D^{25}$= -12.5 (*c* 0.96, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.12 (s, 1H), 9.09 (s, 1H), 8.922 (s, 1H), 8.915 (s, 1H), 8.37 (d, *J* = 6.9 Hz, 1H), 8.33-8.32 (m, 1H), 8.27-8.23 (m, 2H), 8.09 (d, *J* = 16.0 Hz, 1H), 7.95 (d, *J* = 8.6 Hz, 1H), 7.68-7.65 (m, 1H), 7.60-7.57 (m, 1H), 7.51 (d, *J* = 15.5 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 6.80-6.77 (m, 2H), 5.42 (dt, *J* = 7.5, 5.2 Hz, 1H), 5.37 (dt, *J* = 7.5, 5.2 Hz, 1H), 4.04 (s, 3H),

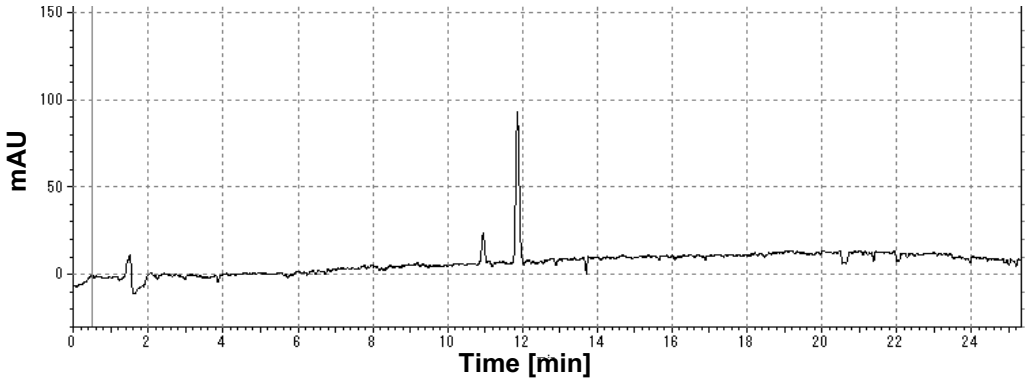
2.87-2.85 (m, 7H), 2.06 (br, 2H), 1.91 (br, 2H), 1.34-1.10 (m, 26H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 162.1, 158.8, 158.7, 156.1, 155.7, 155.5, 155.4, 154.6, 154.5, 152.5, 149.8, 142.7, 142.5, 141.6, 141.0, 136.14, 136.09, 131.5, 130.0, 129.8, 128.5, 127.5, 125.7, 125.1, 124.8, 124.7, 124.5, 123.6, 122.9, 122.2, 111.8, 104.7, 79.2, 77.2, 55.9, 47.4, 47.2, 33.4, 29.2, 28.2, 21.1, 21.0, 11.9; HRMS (ESI, M+Na) calcd for $C_{54}H_{58}N_{10}O_{13}Na$ 1077.4083, found 1077.4064.

Compound 3c



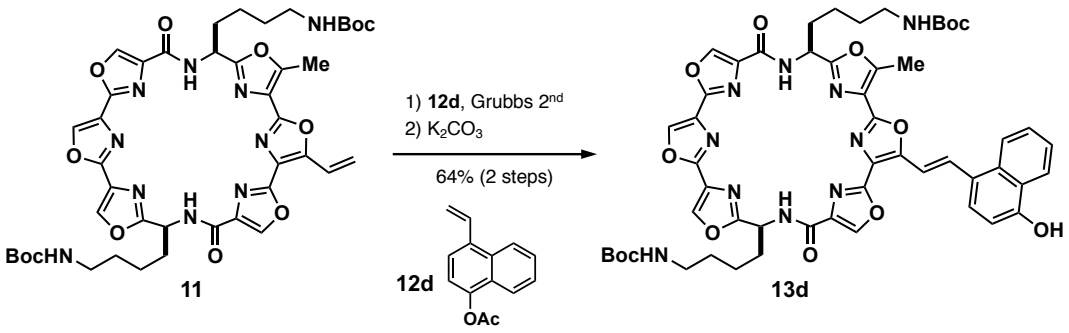
To a solution of **13c** (30.0 mg, 28.4 μmol) in CH_2Cl_2 (1 mL) was added TFA (2 mL) at room temperature, and the mixture was stirred for 10 min. The reaction mixture was concentrated *in vacuo* to give **3c** (23.0 mg, 94%).

Spectral data for **3c**: $[\alpha]_D^{25}$= -11.4 (*c* 0.70, MeOH); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.15 (s, 1H), 9.13 (s, 1H), 8.96 (s, 1H), 8.95 (s, 1H), 8.35 (d, *J* = 7.5 Hz, 1H), 8.32 (d, *J* = 7.5 Hz, 1H), 8.29-8.24 (m, 2H), 8.14 (d, *J* = 16.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.71-7.51 (m, 9H), 7.13 (d, *J* = 8.6 Hz, 1H), 5.46 (dt, *J* = 6.9, 5.7 Hz, 1H), 5.39 (dt, *J* = 6.9, 5.7 Hz, 1H), 4.05 (s, 3H), 2.90 (s, 3H), 2.79-2.74 (m, 4H), 2.08 (br, 2H), 1.94 (br, 2H), 1.58-1.22 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4, 162.0, 158.9, 158.8, 158.4, 158.1, 156.1, 155.7, 155.5, 154.7, 154.6, 152.6, 149.9, 142.6, 141.8, 141.1, 136.10, 136.06, 131.5, 130.2, 129.7, 128.5, 127.5, 125.7, 125.2, 124.8, 124.7, 124.4, 104.8, 104.7, 56.0, 55.8, 47.2, 47.0, 33.4, 26.7, 20.9, 11.9; HRMS (ESI, M+Na) calcd for $C_{44}H_{42}N_{10}O_9Na$ 877.3034, found 877.3014.



Purity analysis of **3c** was conducted via reverse phase HPLC with using Hitachi L-2455 with C18 UG80 S5, 5.0 μm, 4.6 mm × 250 mm (Chemicals Evaluation and Research Institute, Japan) detected at 399 nm, and a mobile phase was constructed of CH_3CN-H_2O-TFA (20:80:0.1).

Compound 13d

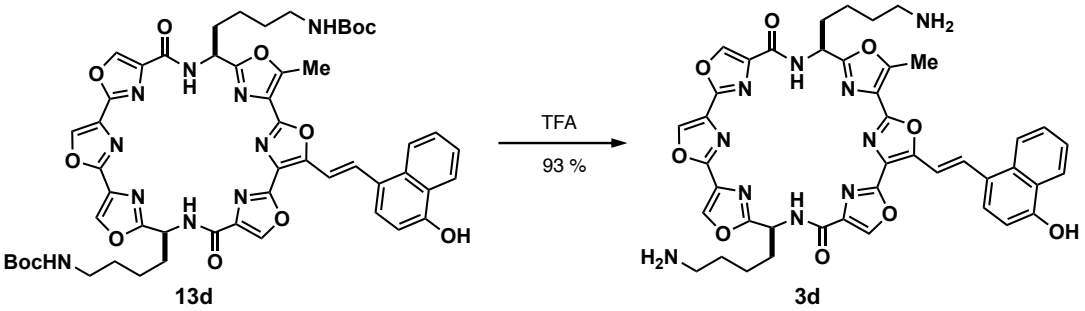


To a solution of **11** (40.0 mg, 44.5 μmol) in dry THF (1 mL) was added **12d** (94.5 mg, 445 μmol) and Grubbs 2nd (773 μg, 0.890 μmol) at room temperature under argon atmosphere, and then the reaction mixture was heated at 90 ˚C. After stirred for 28 h, the reaction mixture was concentrated *in vacuo* to give vinylnaphtylacetate-OTD, which was used without further purification. To a solution of crude compound in MeOH (50 μL) was added K_2CO_3 (1.98 mg, 445 μmol) at room temperature. After stirred for 1 h, the reaction mixture was quenched with 1.2 N HCl. The resulting mixture was extracted with $CHCl_3$, dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 50:1) to give **13d** (15.3 mg, 64%, 2 steps).

Spectral data for **13d**: $[\alpha]_D^{25}$= +9.9 (*c* 0.75, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6)

δ 9.13 (s, 1H), 9.08 (s, 1H), 8.92 (s, 1H), 8.90 (s, 1H), 8.36 (d, J = 7.5 Hz, 1H), 8.33-8.32 (m, 1H), 8.23-8.20 (m, 2H), 8.08 (d, J = 16.0 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.47 (d, J = 16.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 6.79-6.77 (m, 2H), 5.42 (dt, J = 7.5, 5.2 Hz, 1H), 5.37 (dt, J = 7.5, 5.2 Hz, 1H), 2.86-2.85 (m, 8H), 2.08 (br, 2H), 1.90 (br, 2H), 1.37-1.03 (m, 26H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.5, 162.1, 158.8, 158.7, 155.7, 155.5, 154.5, 152.4, 150.2, 142.5, 141.7, 141.0, 136.1, 132.1, 130.4, 129.8, 128.5, 127.3, 125.5, 124.9, 124.6, 124.0, 123.6, 122.8, 122.7, 110.4, 108.5, 79.2, 77.2, 69.8, 47.4, 47.3, 33.4, 29.2, 28.2, 21.1, 21.0, 11.9; HRMS (ESI, M+Na) calcd for $C_{53}H_{56}N_{10}O_{13}Na$ 1063.3926, found 1063.3897.

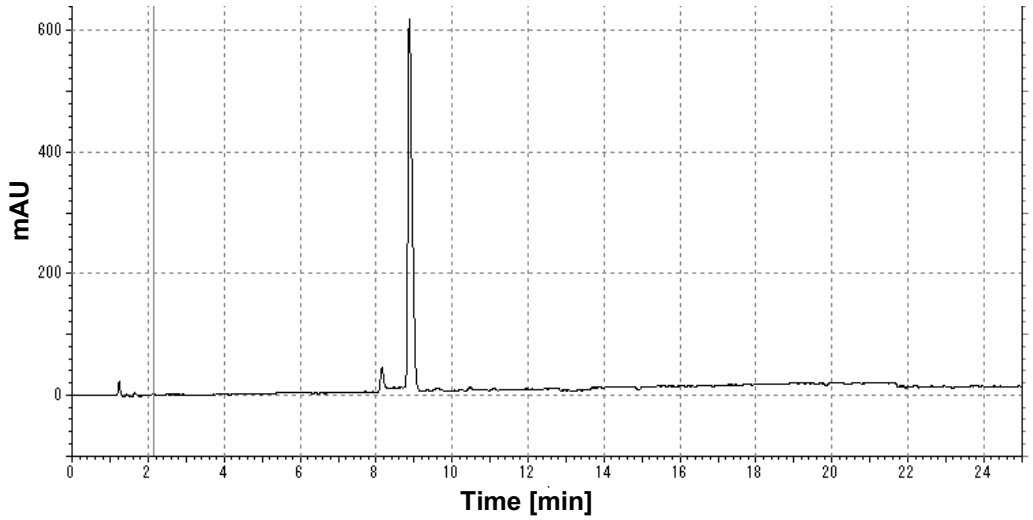
Compound 3d



13d 3d

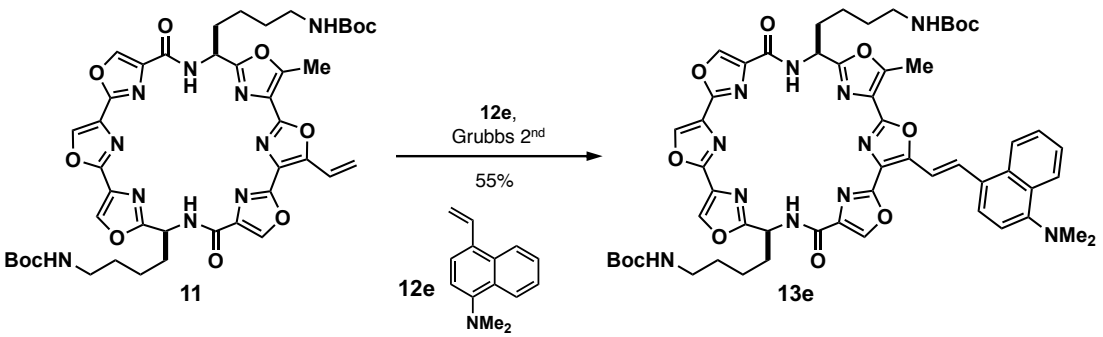
To a solution of **13d** (4.00 mg, 3.84 μmol) in CH_2Cl_2 (1 mL) was added TFA (2 mL) at room temperature, and the mixture was stirred for 20 min. The reaction mixture was concentrated *in vacuo* to give **3d** (3.00 mg, 93%).

Spectral data for **3d**: $[\alpha]_D^{25}$= -193 (*c* 0.86, MeOH); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.9 (br, 1H), 9.15 (s, 1H), 9.12 (s, 1H), 8.95 (s, 1H), 8.93 (s, 1H), 8.35-8.22 (m, 4H), 8.10 (d, J = 15.5 Hz, 1H), 7.89-7.47 (m, 8H), 7.01 (d, J = 7.5 Hz, 1H), 5.43-5.38 (m, 2H), 2.88 (s, 3H), 2.77 (br, 4H), 2.08 (br, 2H), 1.94 (br, 2H), 1.54-1.03 (m, 8H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.4, 162.0, 158.9, 158.8, 158.2, 158.0, 155.7, 155.6, 155.3, 154.6, 152.5, 150.2, 142.7, 142.6, 141.8, 141.1, 136.1, 136.0, 132.0, 130.5, 129.7, 128.5, 127.3, 125.5, 125.0, 124.5, 124.0, 123.7, 122.8, 122.7, 118.5, 116.1, 110.6, 108.5, 69.8, 47.2, 47.1, 33.4, 33.3, 26.7, 20.9, 11.9; HRMS (ESI, M+Na) calcd for $C_{43}H_{40}N_{10}O_9Na$ 863.2877, found 863.2830.



Purity analysis of **3d** was conducted via reverse phase HPLC with using Hitachi L-2455 with C18 UG80 S5, 5.0 μm, 4.6 mm × 250 mm (Chemicals Evaluation and Research Institute, Japan) detected at 400 nm, and a mobile phase was constructed of CH_3CN-H_2O-TFA (20:80:0.1).

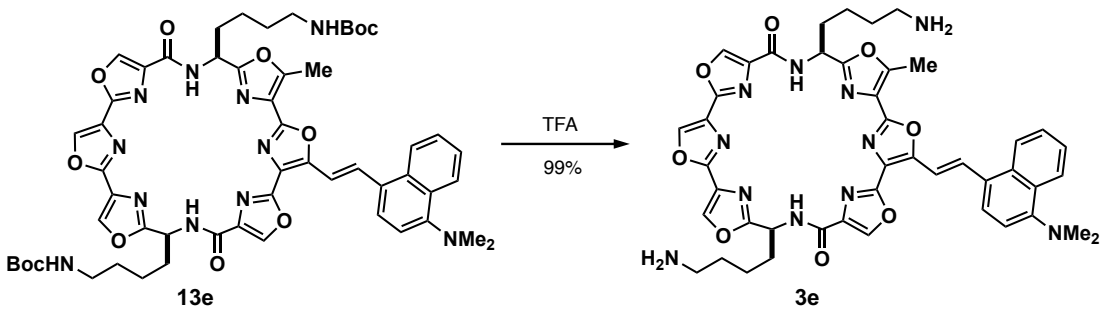
Compound 13e



To a solution of **11** (15.0 mg, 16.6 μmol) in dry THF (400 μL) was added **12e** (32.9 mg, 166 μmol) and Grubbs 2nd (1.50 mg, 1.70 μmol) at room temperature under argon atmosphere, and then the reaction mixture was heated at 90 ˚C. After stirred for 24 h, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH = 200:1) to give **13e** (10.0 mg, 55%).
Spectral data for **13e**: $[\alpha]_D^{25}$= -4.4 (*c* 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.12 (s, 1H), 9.09 (s, 1H), 8.93 (s, 1H), 8.92 (s, 1H), 8.37 (d, *J* = 7.3 Hz, 1H), 8.33-8.28 (m, 2H), 8.22 (d, *J* = 8.2 Hz, 1H), 8.14 (d, *J* = 15.6 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.66-7.59 (m, 2H), 7.55 (d, *J* = 15.6 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 6.78-6.77 (m, 2H),

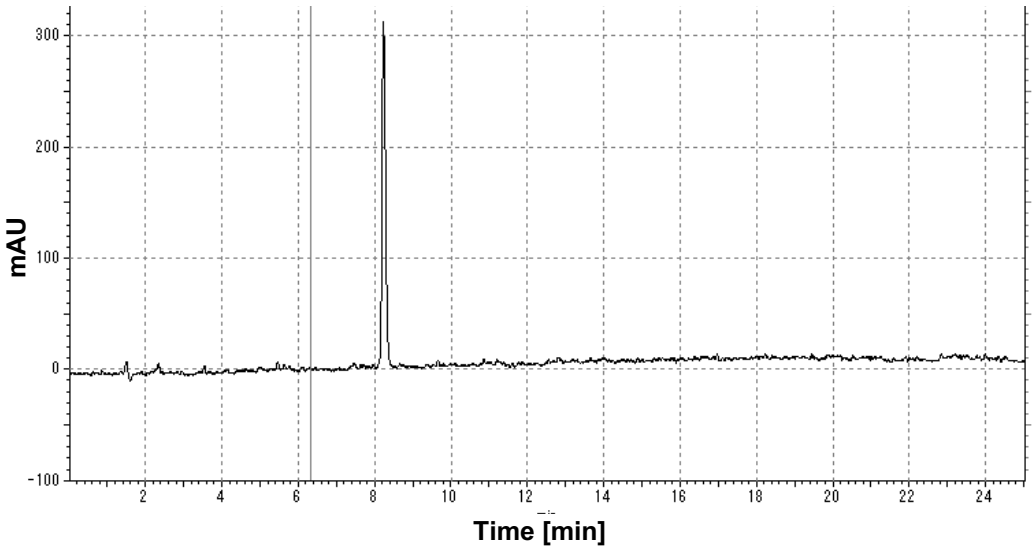
5.43 (dt, J = 7.3, 5.5 Hz, 1H), 5.38 (dt, J = 7.3, 5.5 Hz,1H), 2.90-2.85 (m, 13H), 2.07 (br, 2H), 1.90 (br, 2H), 1.35-1.23 (m, 26H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.5, 162.2, 158.8, 158.7, 155.7, 155.53, 155.46, 154.7, 154.5, 152.6, 152.1, 149.9, 142.7, 142.5, 141.7, 141.0, 136.2, 136.1, 132.0, 129.8, 128.5, 127.7, 126.8, 126.5, 125.4, 124.7, 124.6, 123.6, 113.8, 79.2, 77.2, 69.8, 47.4, 47.2, 44.7, 44.6, 33.4, 29.1, 28.2, 21.1,21.0, 12.0; HRMS (ESI, M+Na) calcd for $C_{55}H_{61}N_{11}O_{12}Na$ 1090.4399, found 1090.4355.

Compound 3e



To a solution of **13e** (10.0 mg, 9.37 μmol) in CH_2Cl_2 (1 mL) was added TFA (2 mL) at room temperature, and the mixture was stirred for 10 min. The reaction mixture was concentrated *in vacuo* to give **3e** (8.10 mg, 99%).

Spectral data for **3e**: $[\alpha]_D^{25}$= -107 (*c* 0.82, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.15 (s, 1H), 9.13 (s, 1H), 8.96 (s, 1H), 8.95 (s, 1H), 8.35 (d, J = 7.3 Hz, 1H), 8.33-8.29 (m, 2H), 8.22 (d, J = 8.2 Hz, 1H), 8.16 (d, J = 16.0 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.66-7.54 (m, 7H), 7.21 (d, J = 8.2 Hz, 1H), 5.46 (dt, J = 7.3, 5.5 Hz, 1H), 5.40 (dt, J = 7.3, 5.5 Hz, 1H), 2.92-2.90 (m, 9H), 2.81-2.73 (m, 4H), 2.08 (br, 2H), 1.96 (br, 2H), 1.56-1.02 (m, 8H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4, 162.1, 158.9, 158.8, 155.7, 155.5, 154.7, 154.6, 152.6, 152.2, 150.0, 142.8, 142.6, 141.8, 141.1, 136.1, 136.0, 132.0, 130.6, 129.7, 128.5, 127.8, 126.8, 126.4, 125.4, 124.8, 124.7, 124.5, 123.6, 113.8, 112.1, 69.8, 47.2, 47.0, 44.6, 33.5, 33.4, 26.7, 20.9, 12.0; HRMS (ESI, M+H) calcd for $C_{45}H_{46}N_{11}O_8$ 868.3531, found 868.3530.



Purity analysis of **3e** was conducted via reverse phase HPLC with using Hitachi L-2455 with C18 UG80 S5, 5.0 μm, 4.6 mm × 250 mm (Chemicals Evaluation and Research Institute, Japan) detected at 393 nm, and a mobile phase was constructed of CH_3CN-H_2O-TFA (20:80:0.1).

2. Materials

Table S1. Sequences of oligonucleotides used in this paper

Name	Sequence
telo24	5’ -d[TTA GGG TTA GGG TTA GGG TTA GGG]- 3’
telo22	5’ -d[GGG TTA GGG TTA GGG TTA GGG T]- 3’
c-myc	5’ -d[TGA GGG TGG GTA GGG TGG GTA A]- 3’
K-ras	5’ -d[AGG GCG GTG TGG GAA GAG GGA AGA GGG GGA GG]- 3’
c-kit1	5’ -d[AGG GAG GGC GCT GGG AGG AGG G]- 3’
bcl2	5’ -d[GGG CGC GGG AGG AAT TGG GCG GG]- 3’
dsDNA (hairpin)	5’ -d[TAT AGC TAT ATT TTT TTA TAG CTA TA]- 3’
mut telo24	5’ -d[TTA GAG TTA GAG TTA GAG TTA GAG]- 3’
C-telo24	5’-d[CCC TAA CCC TAA CCC TAA CCC TAA]- 3’

All oligonucleotides used in the experiment were purchased from Integrated DNA Technologies and Merck & Co. (USA) and were dissolved as stock solutions (1 mM) in MilliQ water to be used without further purification. All other reagents were obtained in the molecular biology grade from FUJIFILM Wako Pure Chemical Co. (Japan). Stock solutions of **1**, **2**, **3a**-**3e** (10 mM) were dissolved in DMSO and stored at -30 °C.

3. Fluorescence Studies

Fluorescence titration of compounds with addition of telo24 and dsDNA

Fluorescence titration were recorded on a Microplate Reader (Spark®, TECAN, Japan) using a 96 well plate (1/2 OptiPlate-96, Perkin Elmer, USA), and over the emission wavelength range of 350-750 nm. The oligonucleotides telo24 and dsDNA used in this protocol (Table S1) were diluted with 50 mM Tris-HCl buffer (with 100 mM KCl, pH 7.4) from 1.0 mM stock solutions to give a concentration of 50 μM. The solution was denatured at 99 ˚C for 5 min, and then slowly cooled to room temperature. Small aliquots of nucleotides were added into the solution containing compounds at fixed concentration (500 nM) in 50 mM Tris-HCl buffer (with 100 mM KCl, pH 7.4) diluted from 10 mM DMSO stock solution. The final concentration of nucleotides was varied from 0 to 2.5 μM, and incubated overnight. Finally, fluorescence spectra were representative of three averaged scans taken at corresponding excitation wavelength. K_d values were calculated by using the equation: Bound fraction = (([ligand]+[DNA]+ K_d)-(([ligand]+[DNA]+ K_d)^2-4×[ligand]×[DNA])$^{1/2}$)/(2×[ligand]).

Fluorescence intensity of 3e with addition of oligonucleotides

Fluorescence intensity were recorded on a Microplate Reader (Spark®, TECAN, Japan) using a 96 well plate (1/2 OptiPlate-96, Perkin Elmer, USA) at Em 602 nm. The oligonucleotides telo24, telo22, *c-myc*, *K-ras*, *c-kit1*, *bcl2*, dsDNA, mut telo24 and C-telo24 used in this protocol (Table S1) were diluted with 50 mM Tris-HCl buffer (with 100 mM KCl or 100 mM NaCl, pH 7.4) or 50 mM sodium cacodylate buffer (pH 5.8), respectively, from 1.0 mM stock solution to give a concentration of 5.0 μM. The solution was denatured at 99 ˚C for 5 min, and then slowly cooled to room temperature. Small aliquots of nucleotides were added into the solution containing compounds at fixed

concentration (500 nM) in 50 mM Tris-HCl buffer (with 100 mM KCl or 100 mM NaCl, pH 7.4) or 50 mM sodium cacodylate buffer (pH 5.8) diluted from 10 mM DMSO stock solution. The final concentration of nucleotides was varied from 0 to 2.5 μM, and incubated overnight. Finally, fluorescence intensity was representative of three averaged scans taken at Ex 399 nm. K_d values were calculated by using the equation: Bound fraction = (([ligand]+[DNA]+ K_d)-(([ligand]+[DNA]+ K_d)^2-4×[ligand]×[DNA])$^{1/2}$)/(2×[ligand]).

Viscosity analysis[4]

Viscosity analysis were recorded on a Fluorescence Photometer (FP-8600, JASCO, Japan) using a quartz cell of 10 mm with an optical path length, and over the emission wavelength range of 450-750 nm. **3e** were diluted with water-glycerol mixture (glycerol 0-80%) from 10 mM DMSO stock solutions to give a concentration of 10 μM. Finally, fluorescence spectra were representative of three averaged scans taken at 399 nm.

Fluorescence titration of the complex of 3e and telo24 by addition of C-telo24

Fluorescence titration were recorded on a Fluorescence Photometer (FP-8600, JASCO, Japan) using a quartz cell of 10 mm with an optical path length, and over the emission wavelength range of 450-750 nm. The oligonucleotides telo24 and C-telo24 used in this protocol (Table S1) were diluted with 50 mM Tris-HCl buffer (with 50 mM KCl, pH 7.4) from 1.0 mM stock solutions to give a concentration of 100 μM. The solution was denatured at 99 ˚C for 5 min, and then slowly cooled to room temperature, and then the solution of telo24 were added 100 μM compounds diluted from 10 mM DMSO stock solution, and incubated overnight. Then, small aliquots of C-telo24 were added into the multiple samples containing telo24 (1.5 μM) and **3e** (0.5 μM) in 50 mM Tris-HCl buffer (with 50 mM KCl, pH 7.4), and the final concentration of C-telo24 was varied from 0 to 7.5 μM, and incubated for 3 h. Finally, fluorescence spectra were representative of three averaged scans taken at Ex 399 nm.

Fluorescence image

Fluorescent image was performed with a UV Transilluminator (MLB-21, MaestroGen, China) using Tempered Hard-Glass Vials (S-06, NICHIDEN-RIKA GLASS Co., Ltd., Japan) at Ex 365 nm. The oligonucleotides telo24 and dsDNA used in this

protocol (Table S1) were diluted with 50 mM Tris-HCl buffer (with 100 mM KCl, pH 7.4) from 1.0 mM stock solutions to give a concentration of 30 μM. The solution was denatured at 99 ˚C for 5 min, and slowly cooled to room temperature, and then were added 20 μM compounds diluted from 10 mM DMSO stock solution.

Quantum yield[5]

The fluorescence quantum yield (Φ_F) of compounds were calculated relative to a standard solution of Quinine Sulfate in 0.5 M H_2SO_4 ($\Phi_F = 0.546$) and was determined using the following formula: $\Phi_x = \Phi_{ref} \times (A_{ref}/A_x) \times (F_x/F_{ref}) \times (\eta_x/\eta_{ref})^2$, where Φ is the fluorescence quantum yield, F is the measured integrated emission intensity, η is the refraction index of the solvents, and A is the optical density (absorbance). The x refers to the compounds of unknown quantum yield, and ref refers to the reference compound (Quinine Sulfate) of known quantum yield. UV/Vis absorption spectra were recorded on UV/Vis spectrometer (V-630, JASCO, Japan) using a quartz cell of 10 mm with an optical path length. Fluorescence spectra were recorded on a Microplate Reader (SH-9000Lab, CORONA ELECTRIC Co., Ltd., Japan) using a 96 well plate (1/2 OptiPlate-96, Perkin Elmer, USA).

4. Circular Dichroism (CD) Analysis

Circular Dichroism (CD) spectra

Circular Dichroism (CD) spectra were recorded on a J-720 spectropolarimeter (JASCO, Japan) using a quartz cell of 1 mm with an optical path length, and over a wavelength range of 220-320 nm. The oligonucleotide telo24 used in this protocol (Table S1) was diluted with 50 mM Tris-HCl buffer (with 100 mM KCl, pH 7.4) from 1.0 mM stock solutions to give a concentration of 10 μM. The solution was denatured at 99 °C for 5 min, and then slowly cooled to room temperature, and then were added 50 μM compounds diluted from 10 mM DMSO stock solutions, and incubated overnight. Finally, CD spectra were representative of five averaged scans taken at 25 °C.

Circular Dichroism (CD) melting analysis

A solution of telo24 (10 μM) containing compounds were prepared in 50 mM Tris-

HCl buffer (with 100 mM KCl, pH 7.4) as described above. Melting curves were obtained by monitoring the CD intensity at 290 nm on a J-720 spectropolarimeter (JASCO, Japan) by using a quartz cell of 1 mm with an optical path length, and the temperature was stepwise increase of 5 ˚C from 25 to 100 ˚C at 1.0 ˚C/min.

5. Computational analysis

Docking Study

For initial coordinates of **3e**, ionization and energy minimization were performed with the OPLS3e force field in the LigPrep script in the Maestro (Schrödinger, LLC, New York, NY, USA). These minimized structures were employed as input structures for docking simulations. The NMR structure of the telomeric G4 structure with L2H2-6M(2)OTD (PDB ID: 2MB3) was refined for docking simulations using constrained energy refinements in OPLS3e force field (Schrödinger LLC). The grid center for docking was defined by the reference position of L2H2-6M(2)OTD on the telomeric G4 structure. The proposed orientation of **3e** on the telomeric G4 structure was generated by a docking simulation using the Glide SP program[6] (Schrodinger LLC). This PDB entry (2MB3) was deposited as an ensemble of ten superimposed models. To incorporate the flexibility of telomeric G4, all models were refined and qualified for docking simulation. The best pose was selected according to the Glide XP docking score from each docking simulation.

The density functional theory (DFT) calculation[7]

The density functional theory (DFT) calculation was performed with the GAMESS program (version 11)[8, 9] using Becke's three-parameter function combined with Lee, Yang and Parr's correlation function (B3LYP).[10] The DFT calculation for geometry optimization was performed with the 6-31G basis set. The initial geometry of the model compound for the DFT calculation was obtained by a semi-empirical calculation with the PM7[11] method of MOPAC 2012.[12] Solvent's dielectric constant ($\varepsilon = 78.3$ for water) was taken into account for the calculation by applying the conductor-like screening (COSMO) model.[13] Analysis of the MOPAC and GAMESS log-files as well as molecular graphics were carried out using the Winmostar™ program[14]. All calculations were conducted on a PC carrying an Intel CoreTM i3 3220 processor (3.30 GHz) and 8-GB RAM.

6. Other Supporting Table and Figures

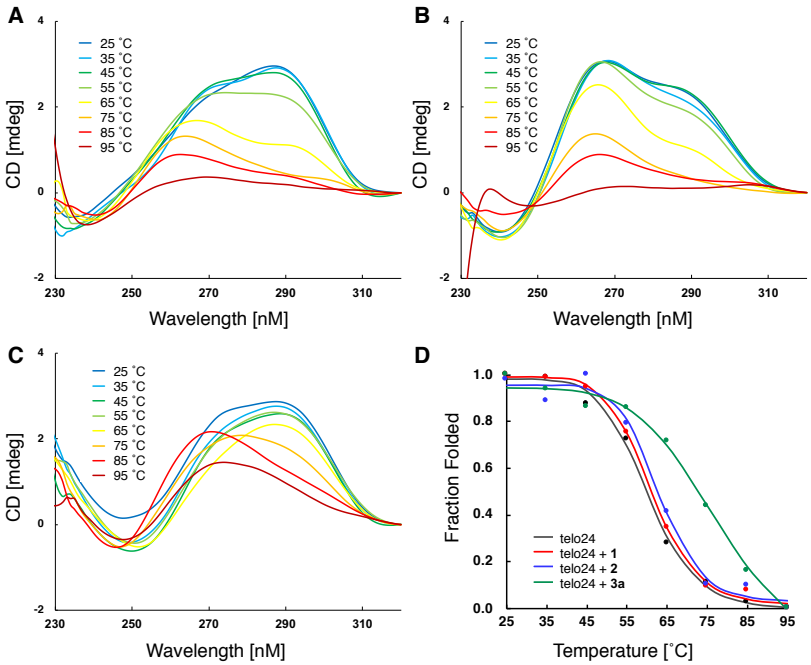


Figure S1. Circular Dichroism melting profiles for telo24 in 50 mM Tris-HCl buffer (with 100 mM KCl, pH 7.4) with compounds (10 μM); A) MO-VN (**1**); B) TO-VN (**2**); C) MO-VN (**3a**); D) the CD melting curves of telo24 with or without compounds **1**, **2**, **3a** were recorded at 290 nm.

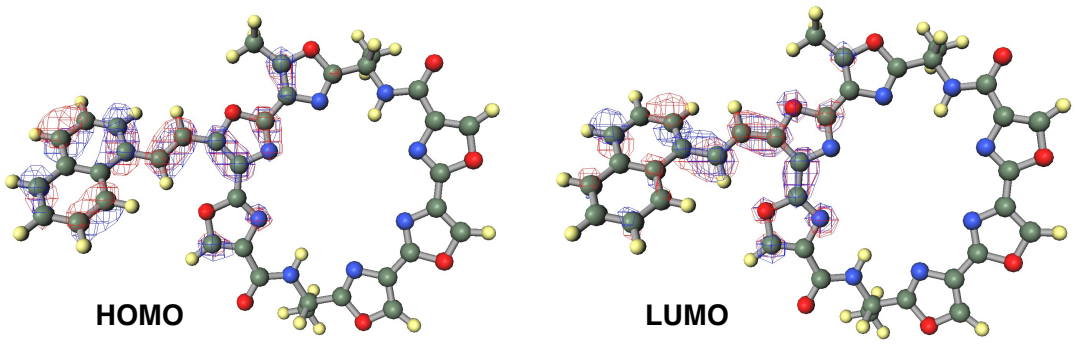


Figure S2. Frontier molecular orbitals HOMO and LUMO of compound **3a**.

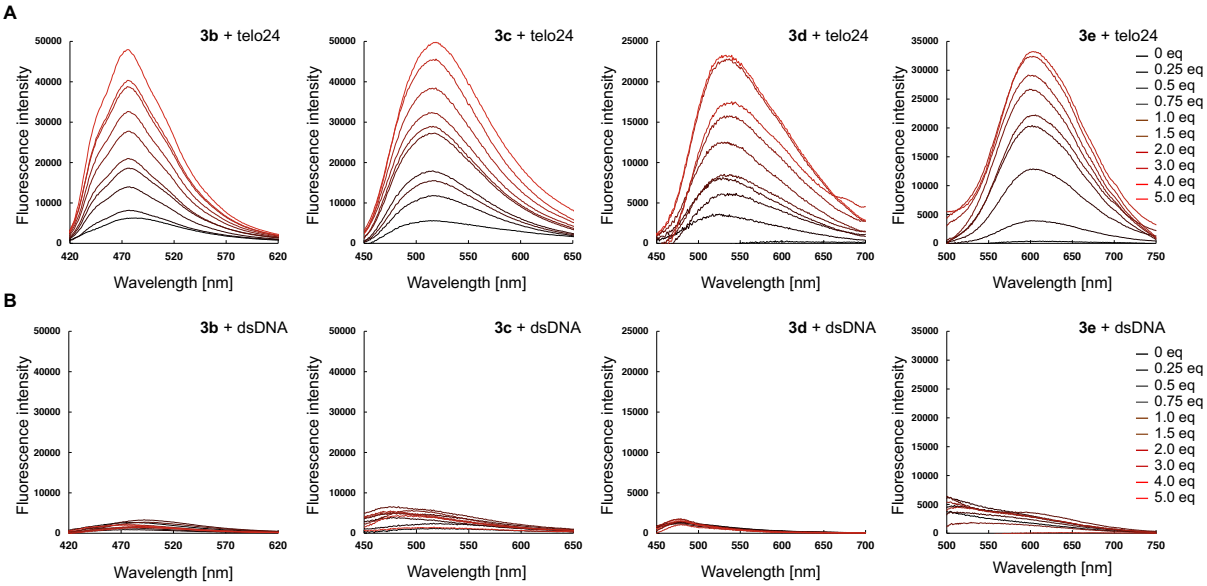


Figure S3. Fluorescence titration of **3b**-**3e** (0.5 μM) with stepwise addition of A) telo24 and B) dsDNA (0-5.0 mol equivalent) in 50 mM Tris-HCl buffer (with 100 mM KCl, pH 7.4).

Table S2. *K*d values [nM] of 3a-3d for telo24 and dsDNA

Ligands	telo24	dsDNA
3a	150	> 2500
3b	219	> 2500
3c	171	> 2500
3d	143	> 2500

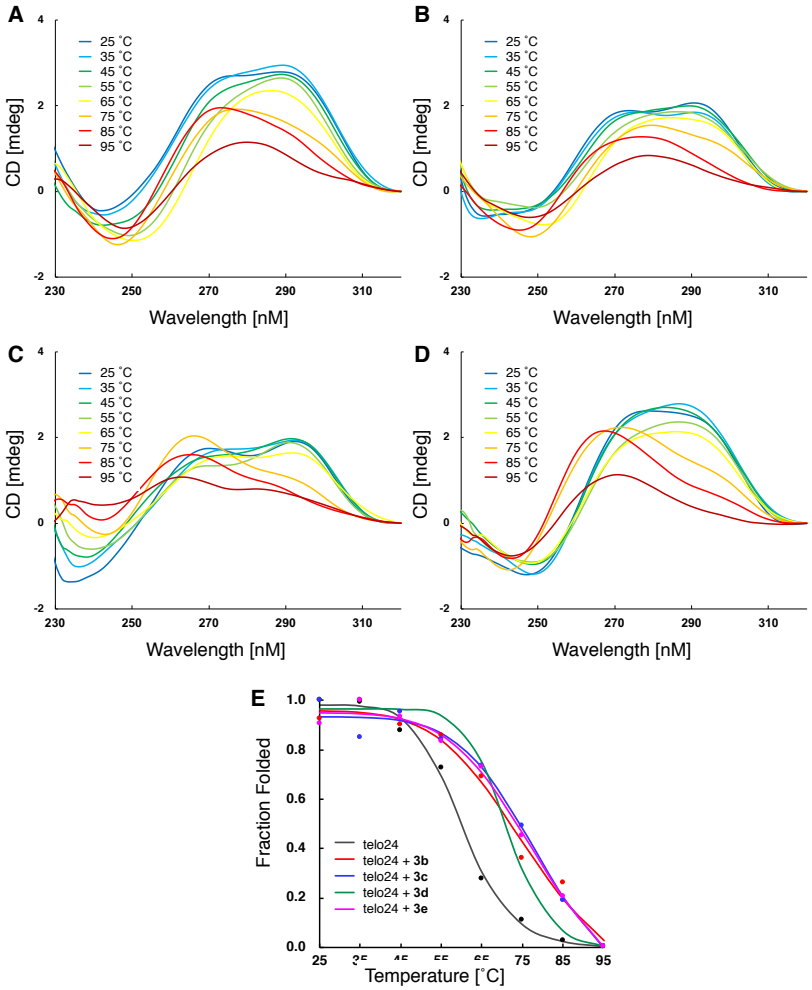


Figure S4. Circular Dichroism melting profiles for telo24 in 50 mM Tris-HCl buffer (with 100 mM KCl, pH 7.4) with compounds (10 μM); A) **3b**; B) **3c**; C) **3d**; D) **3e**; E) the CD melting curves of telo24 with or without compounds **3b**-**3e** were recorded at 290 nm.

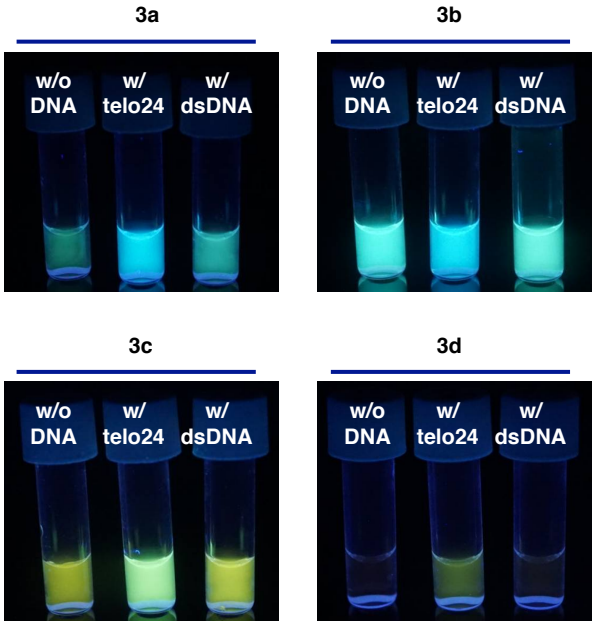


Figure S5. Fluorescence images of **3a**-**3d** without DNA (w/o) or with (w/) telo24 or dsDNA upon illumination with a UV lamp (365 nm).

Table S3. The quantum yield of **3e**, ThT, and TO in the absence of these compounds and in the presence of telo24 or dsDNA.

	Compounds		
	3e	**ThT**	**TO**
without DNA	0.00034	0.00022	0.0013
with telo24	0.010	0.050	0.059
with dsDNA	0.00035	0.0064	0.032
Φ_F ratio ($\Phi_{F\ telo24}/\Phi_{F\ dsDNA}$)	28.6	7.8	1.8

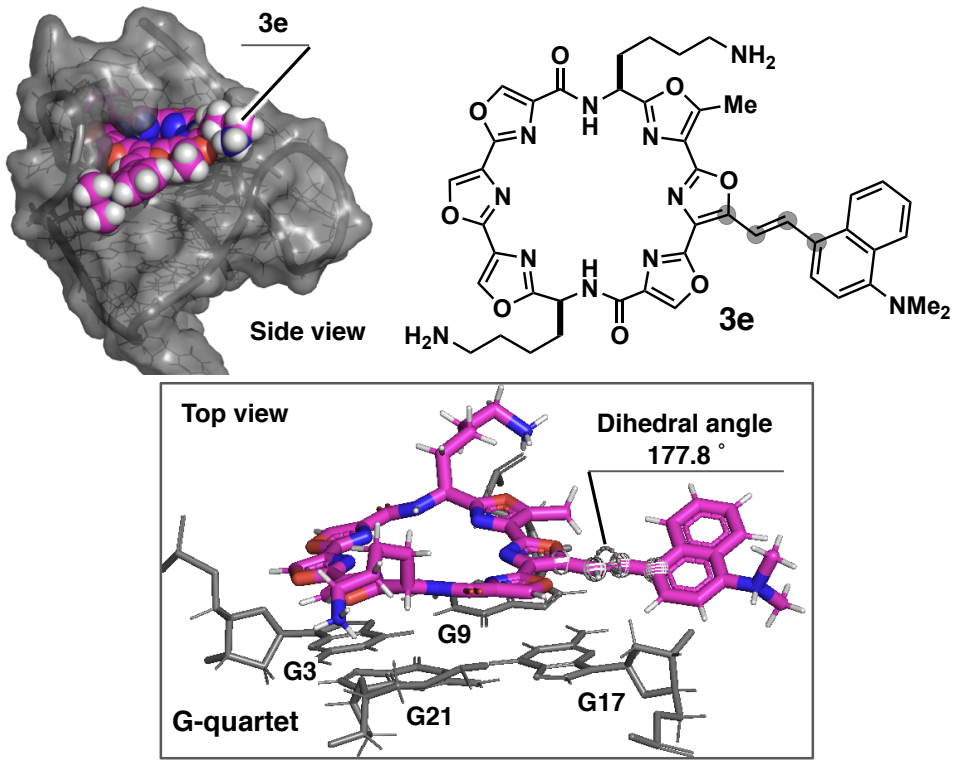


Figure S6. Docking model of hybrid type telomeric G4 with **3e**. The dihedral angle between C2-C27-C28-C33 in the side chain of OTD core is nearly 180 ° (177.8 °), and MO-VN moiety of **3d** is almost planar.

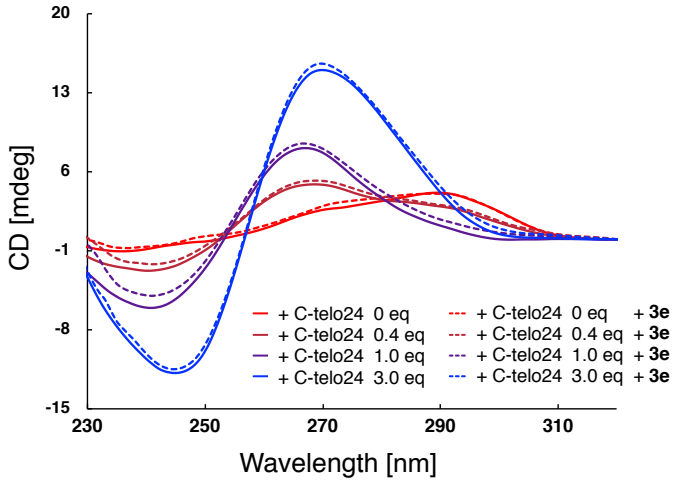


Figure S7. Circular Dichroism spectra of telo24 by stepwise addition of C-telo24 in the absence of **3e** (solid line) and presence of **3e** (dashed line).

7. Supplementary references

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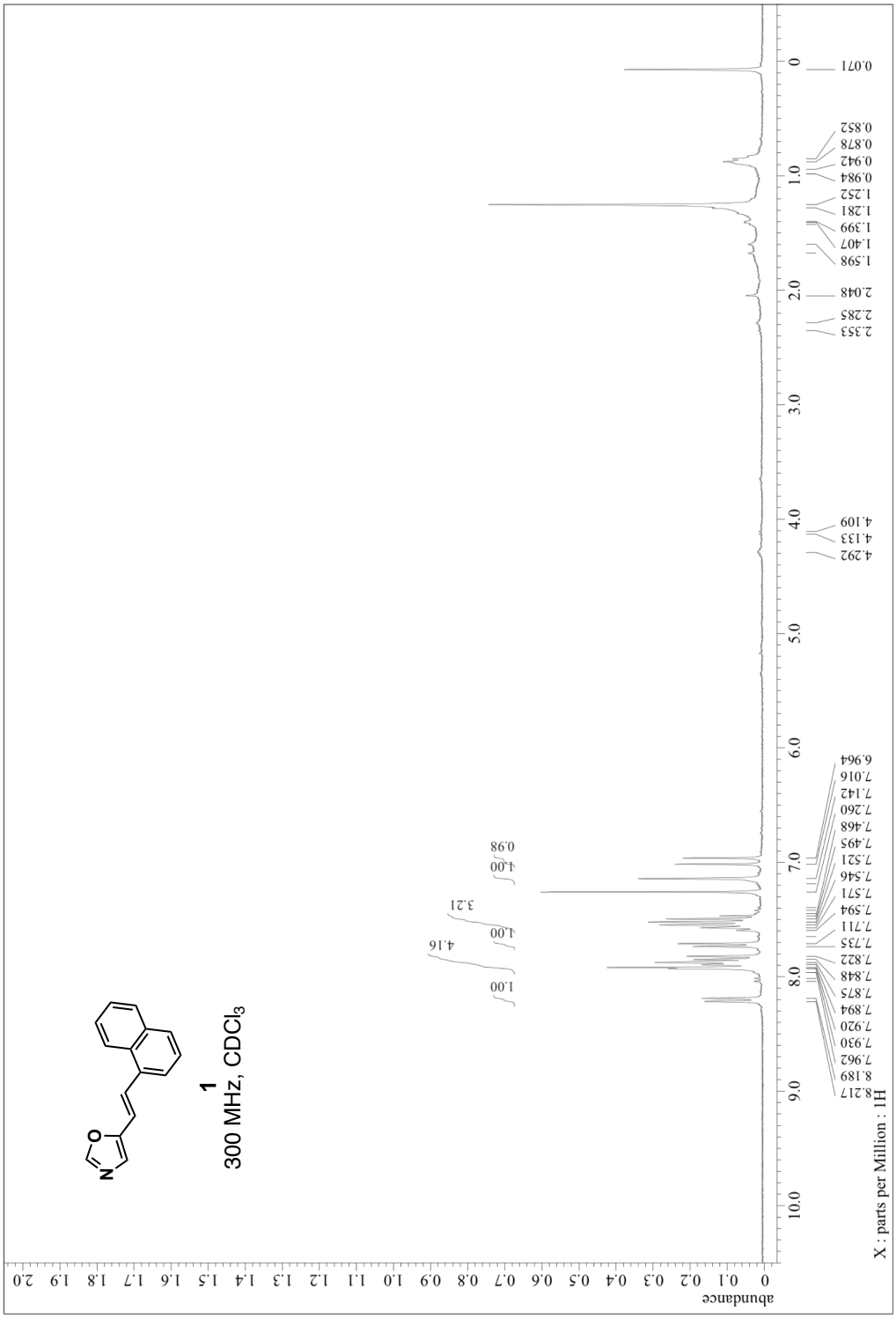
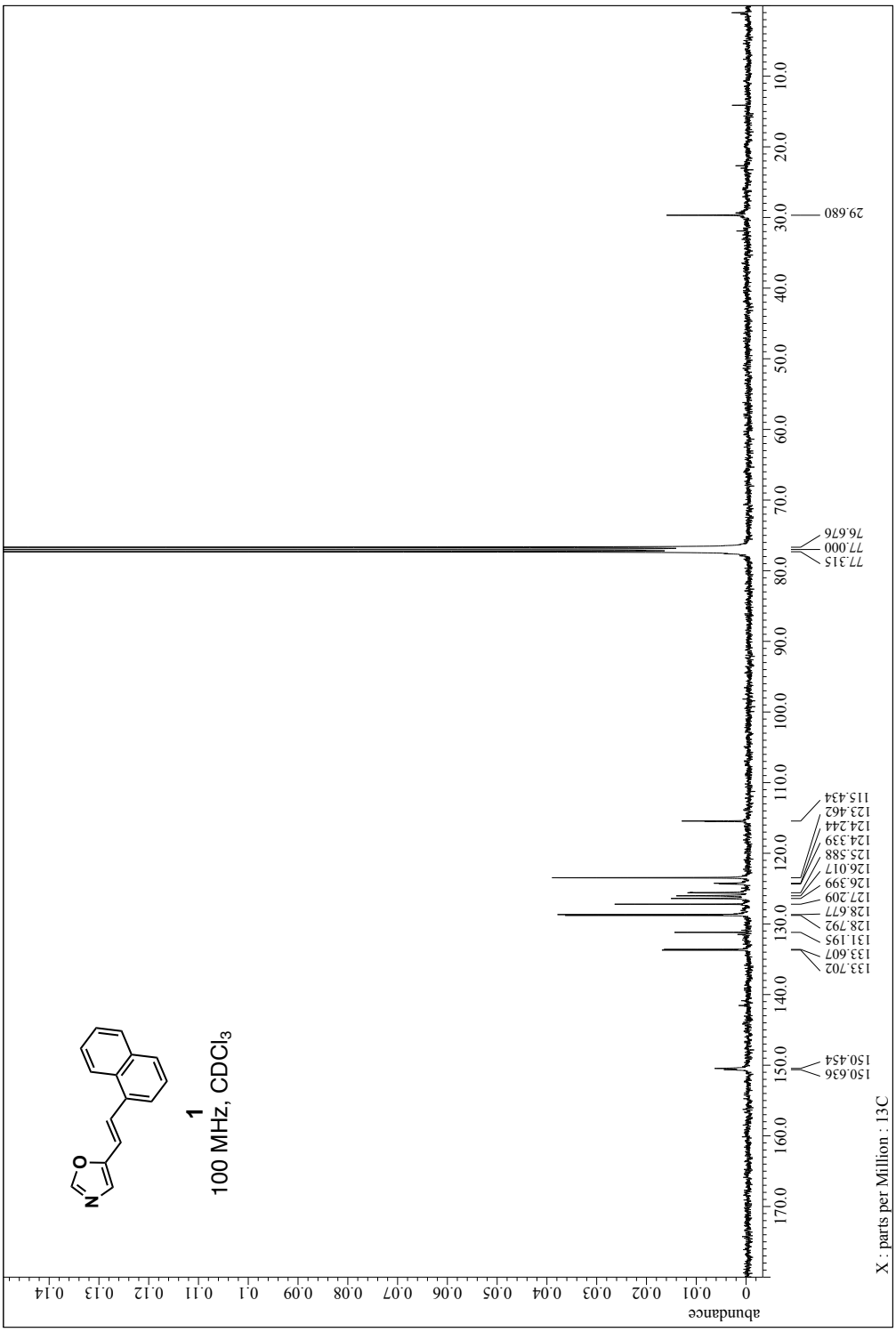
8. ^{1}H and ^{13}C NMR spectra for synthetic compounds

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100 MHz, CDCl3
abundance
X : parts per Million : 13C
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133.702
133.607
131.195
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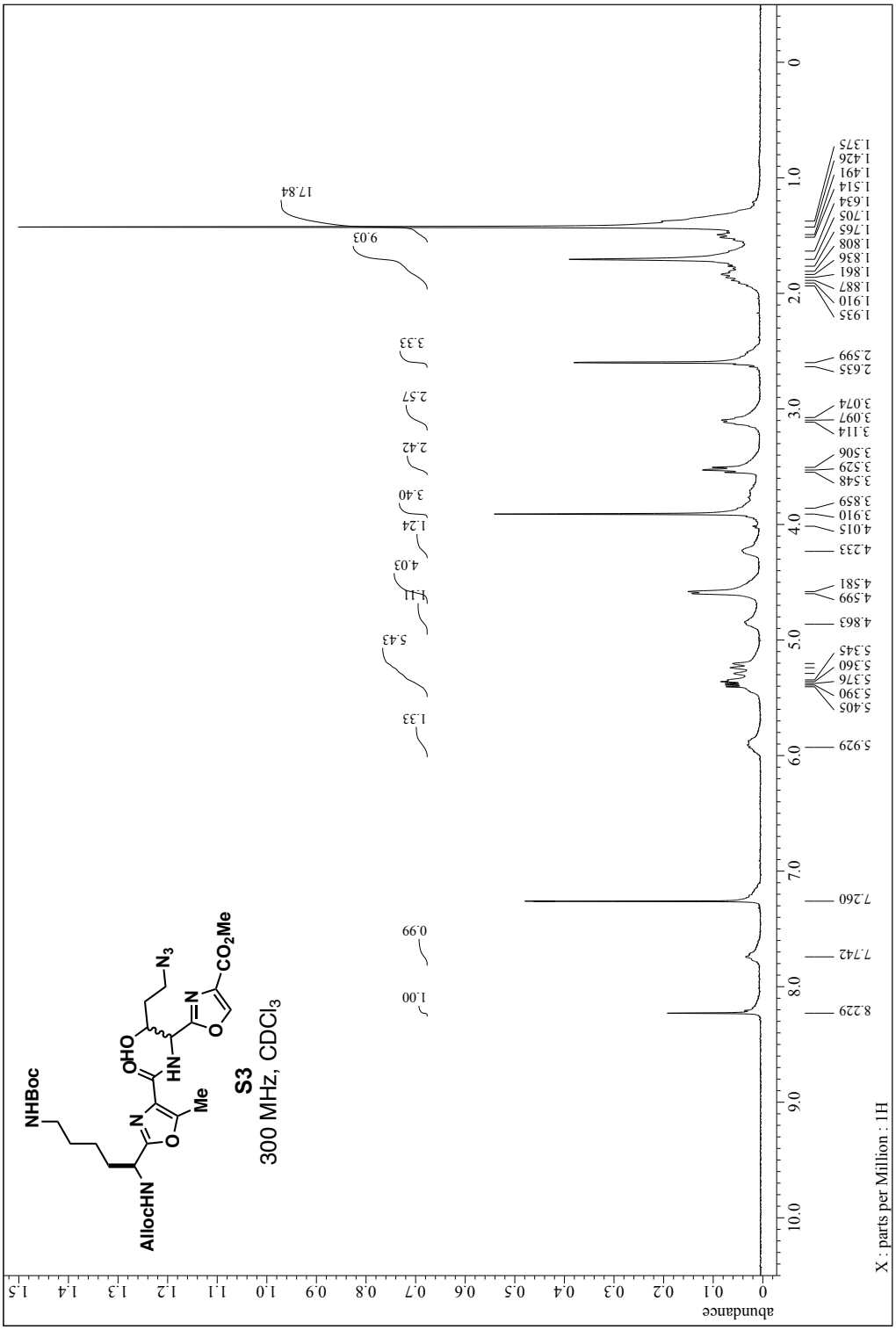
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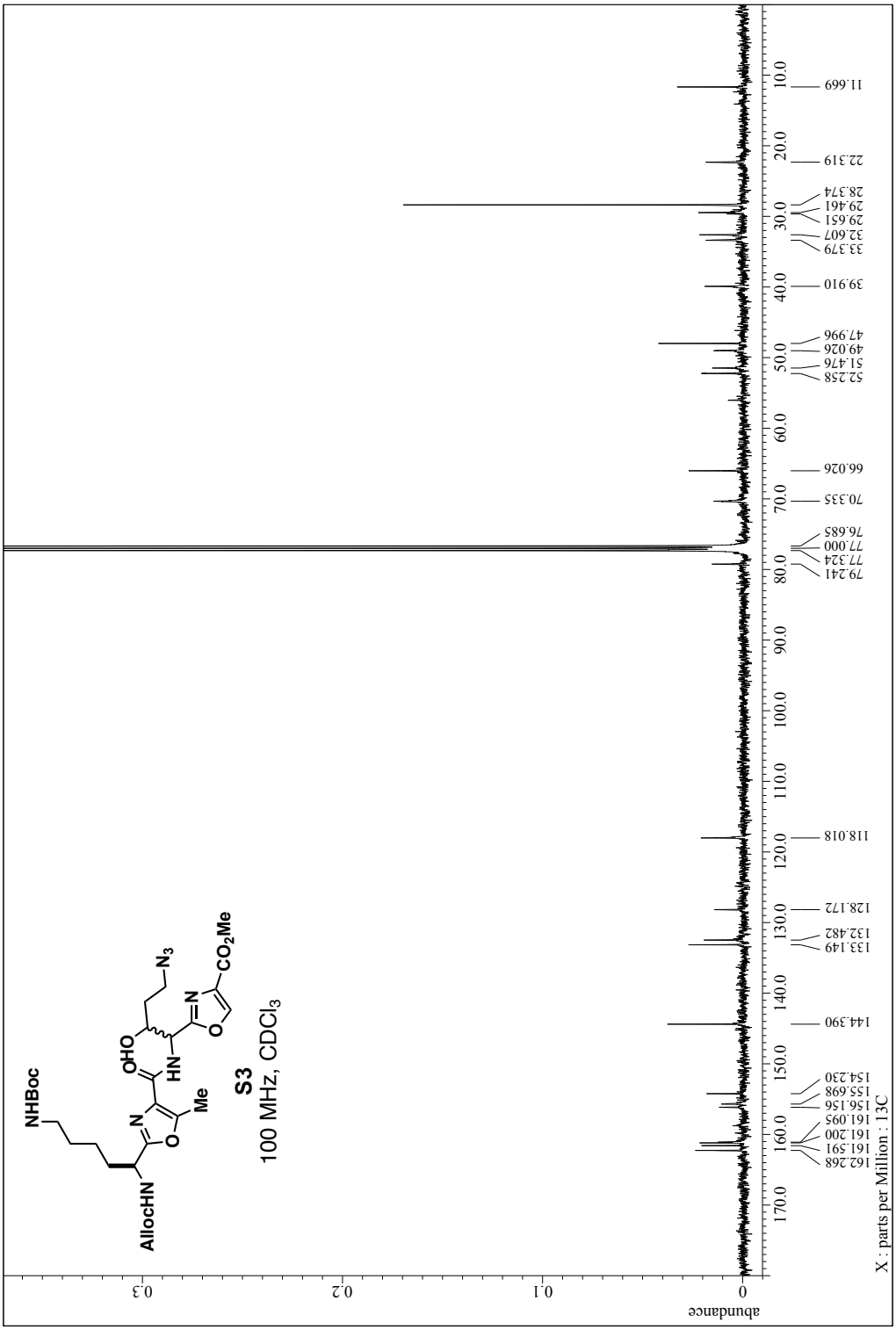
NHBoc
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100 MHz, CDCl3
abundance
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0.1
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X : parts per Million : 13C
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160.0
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140.0
130.0
120.0
110.0
100.0
90.0
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50.0
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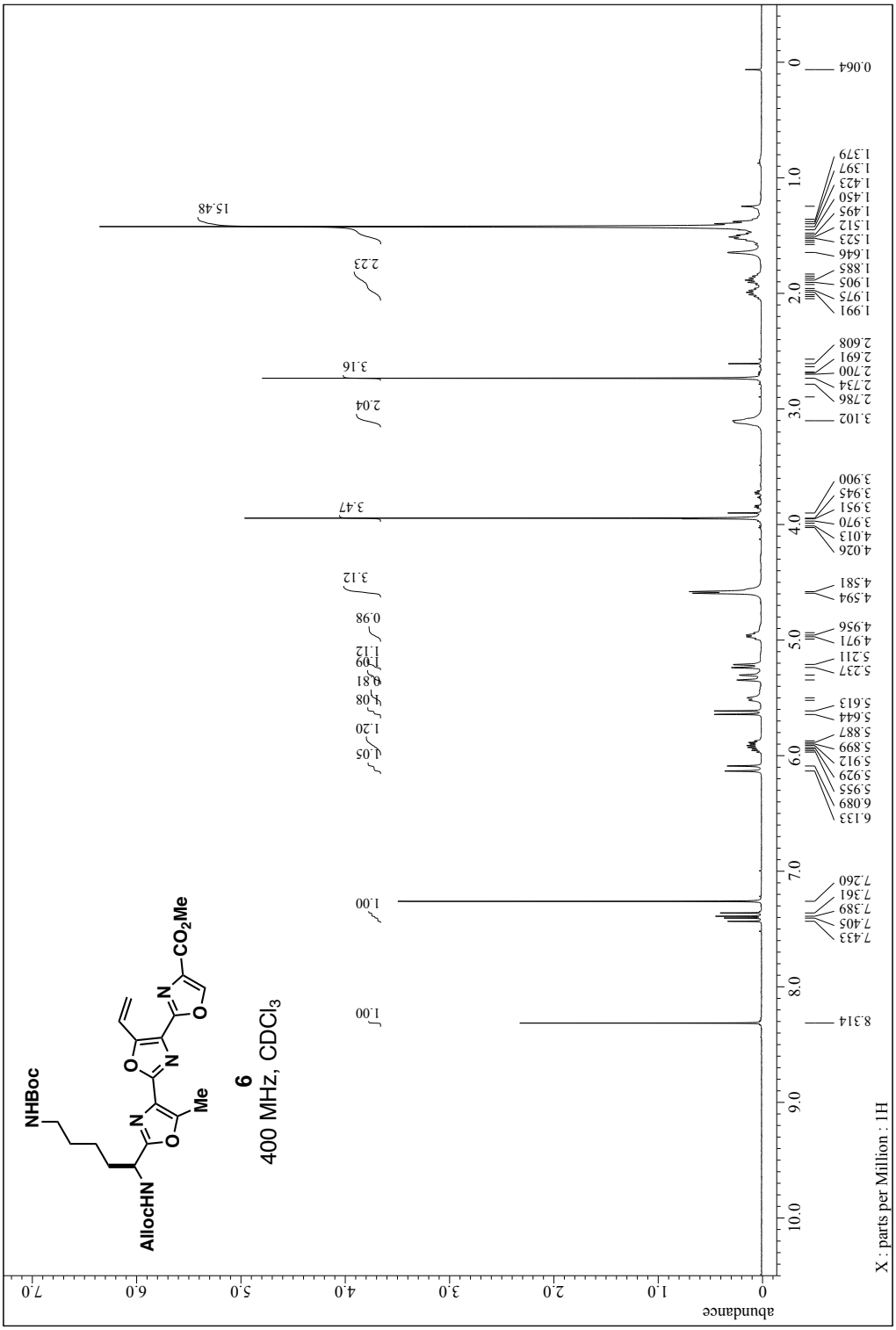
NHBoc
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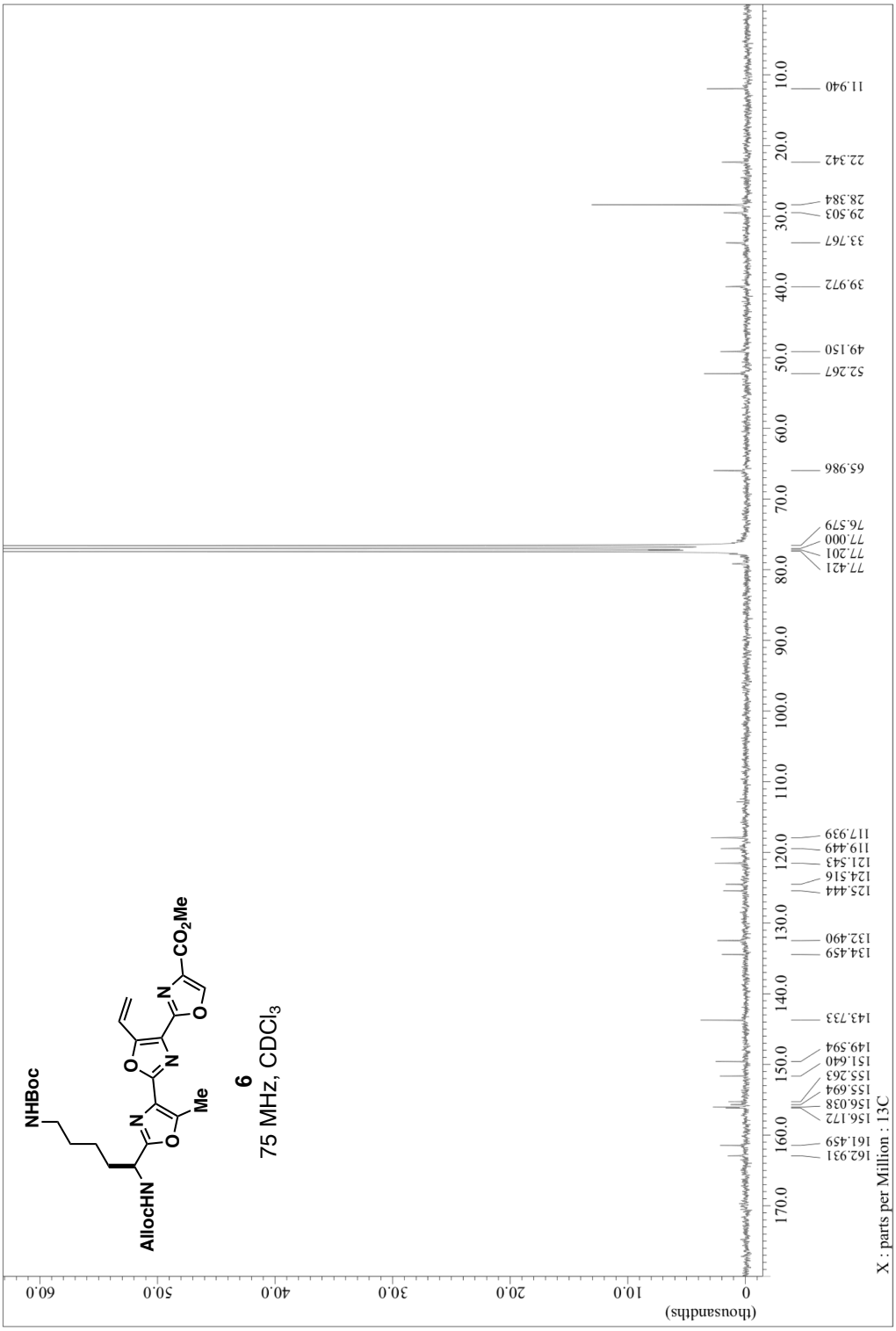
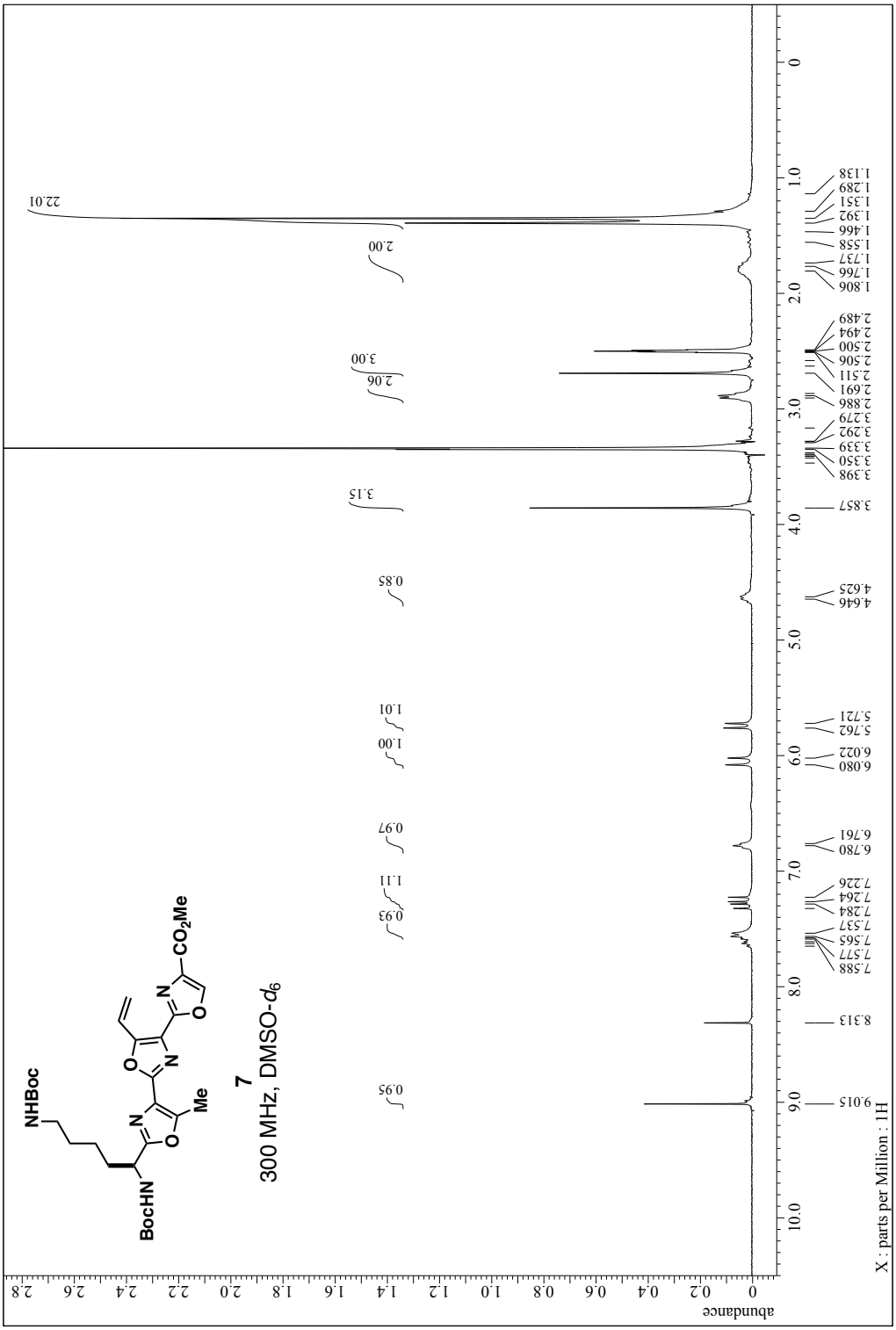
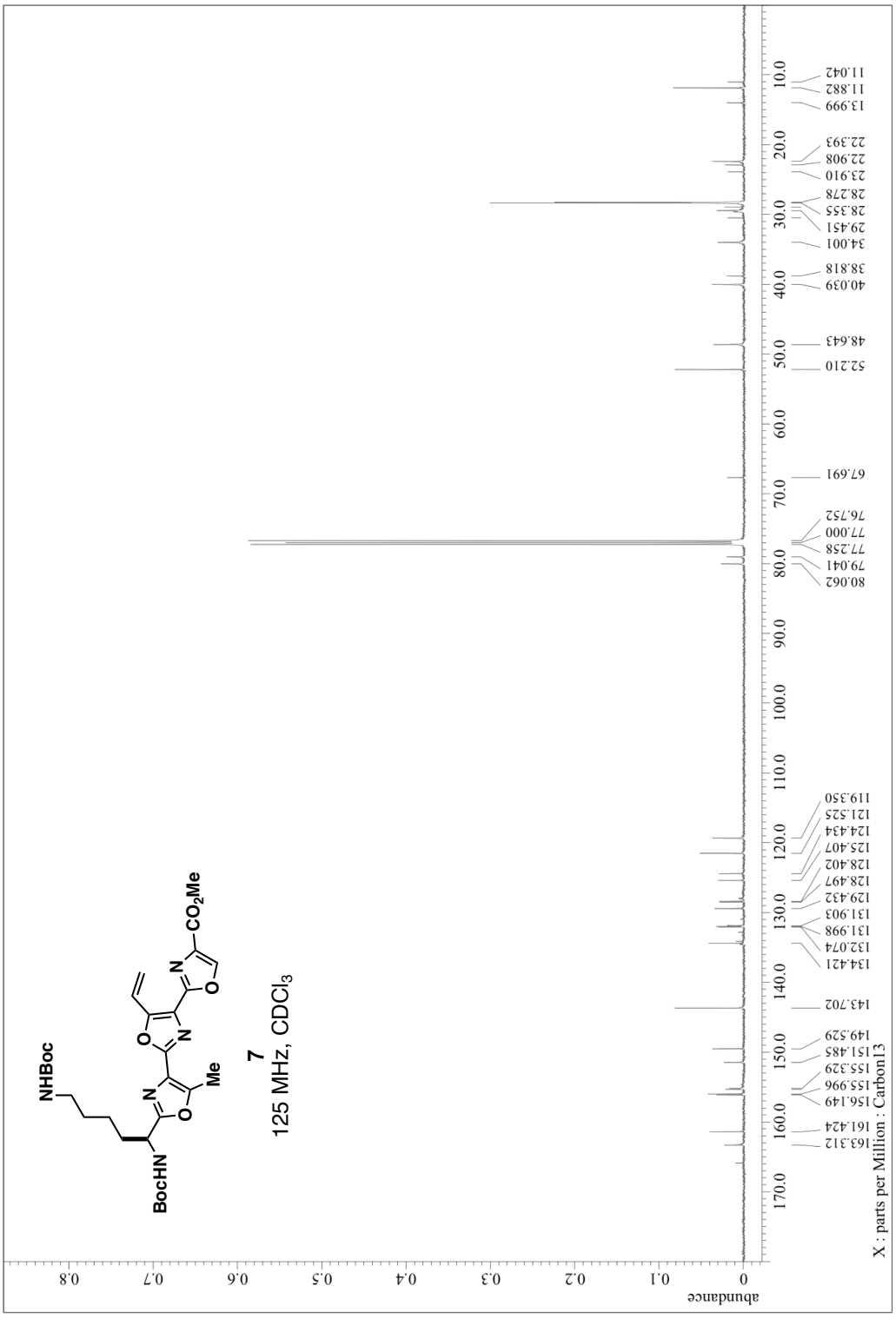
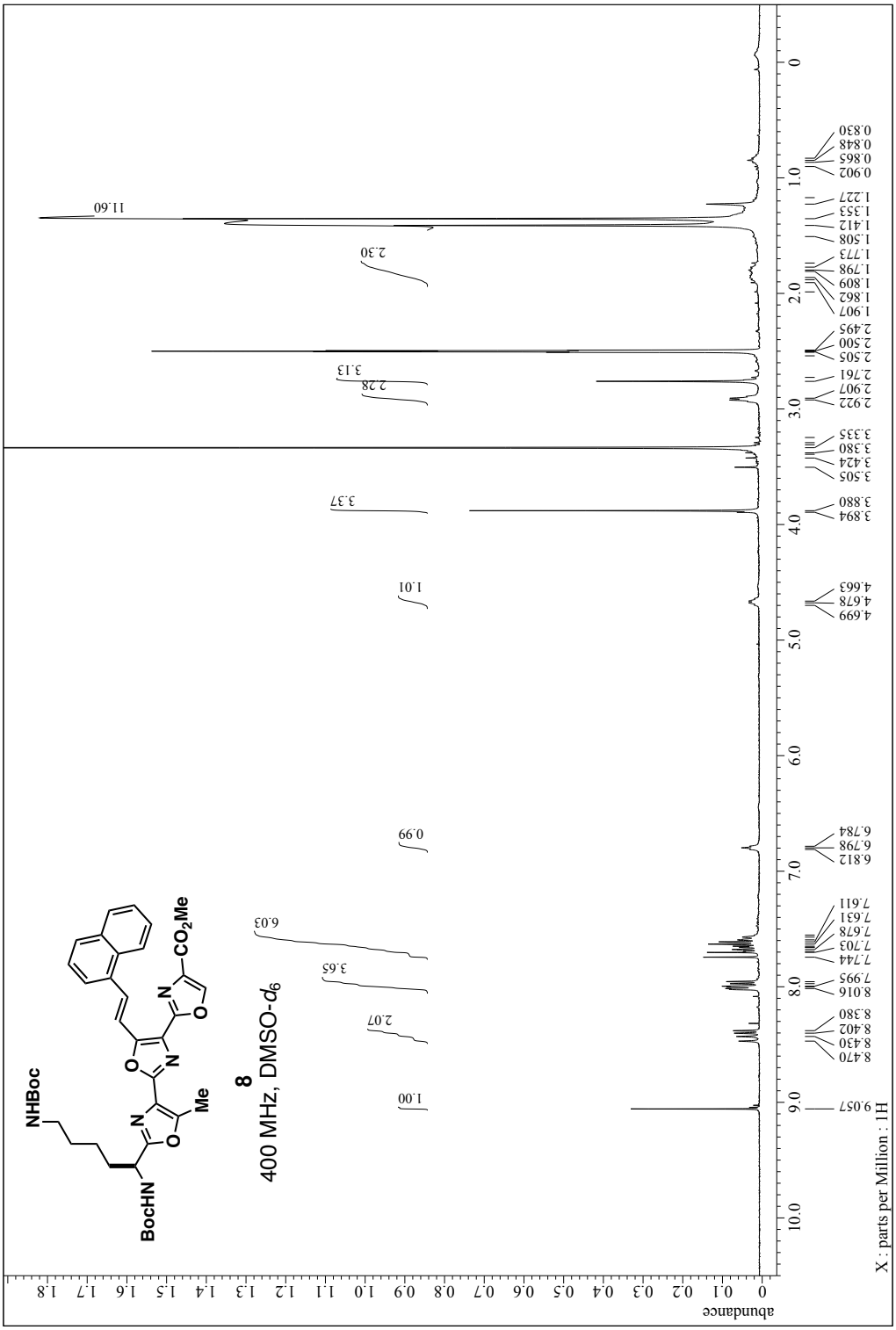
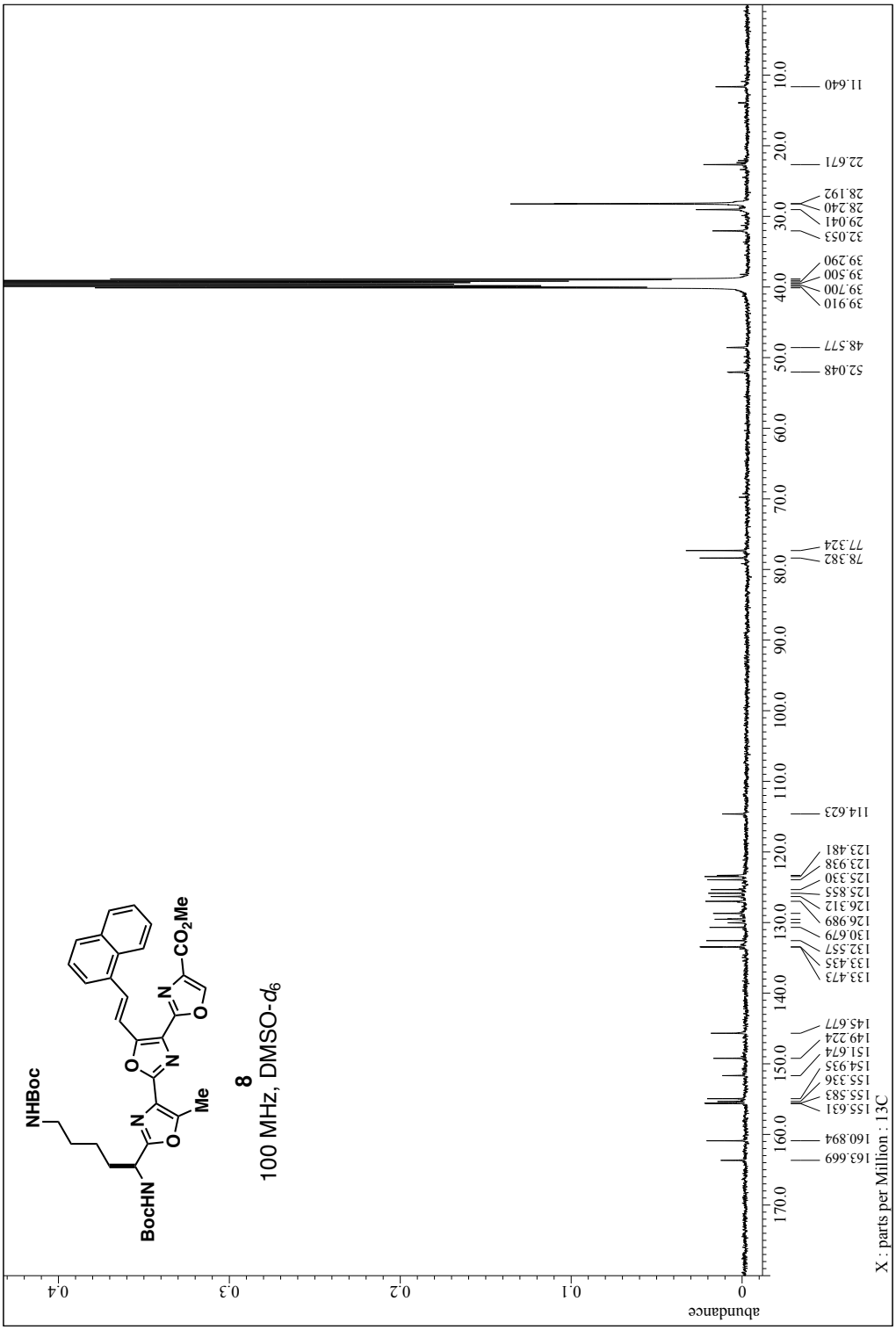
6
400 MHz, CDCl3
abundance
X : parts per Million : 1H

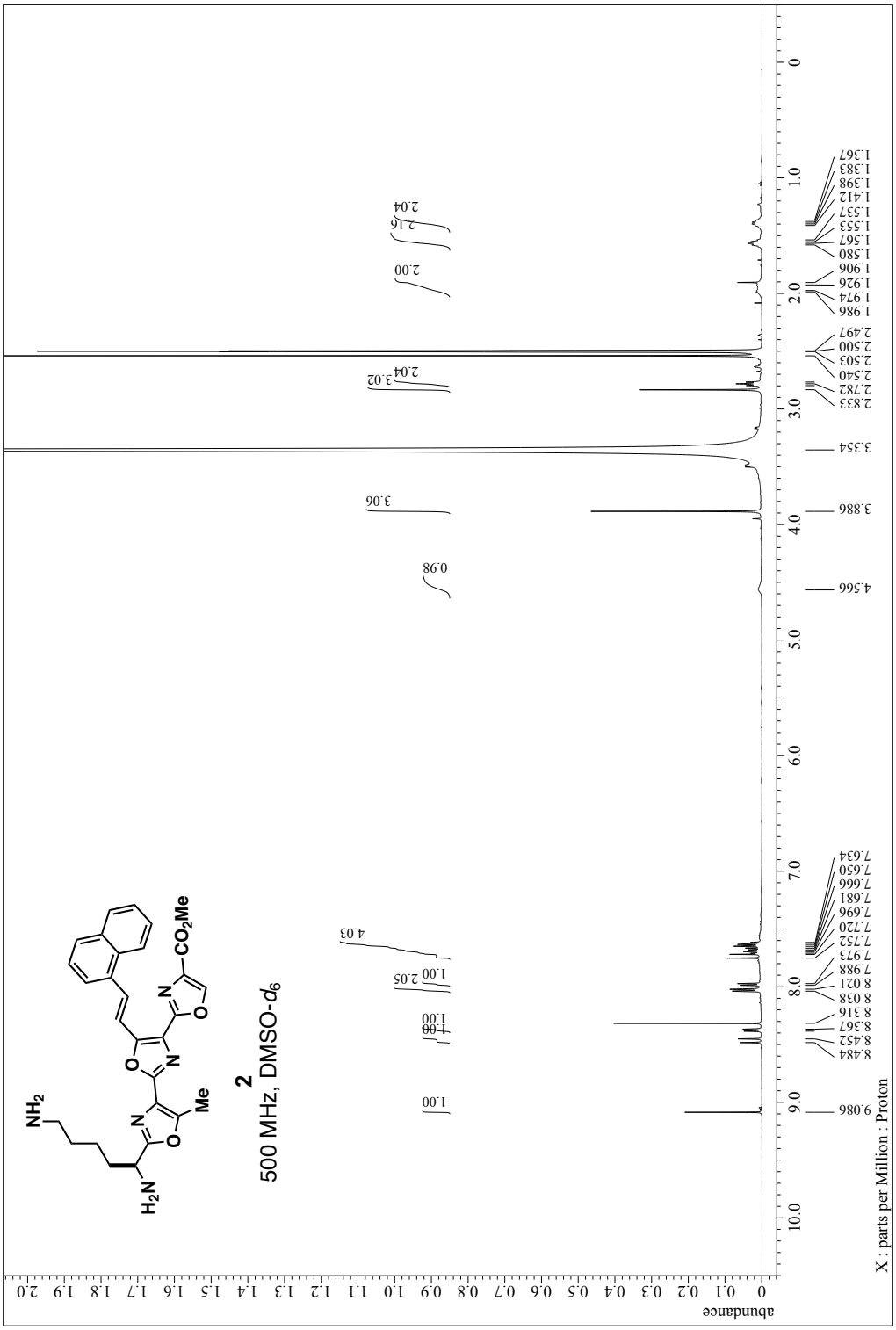

NHBoc
AllocHN
Me
CO2Me
6
75 MHz, CDCl3
(thousandths)
X : parts per Million : 13C
162.931
161.459
156.172
156.038
155.694
155.263
151.640
149.594
143.733
134.459
132.490
125.444
124.516
121.543
119.449
117.939
77.421
77.201
77.000
76.579
65.986
52.267
49.150
39.972
33.767
29.503
28.384
22.342
11.940

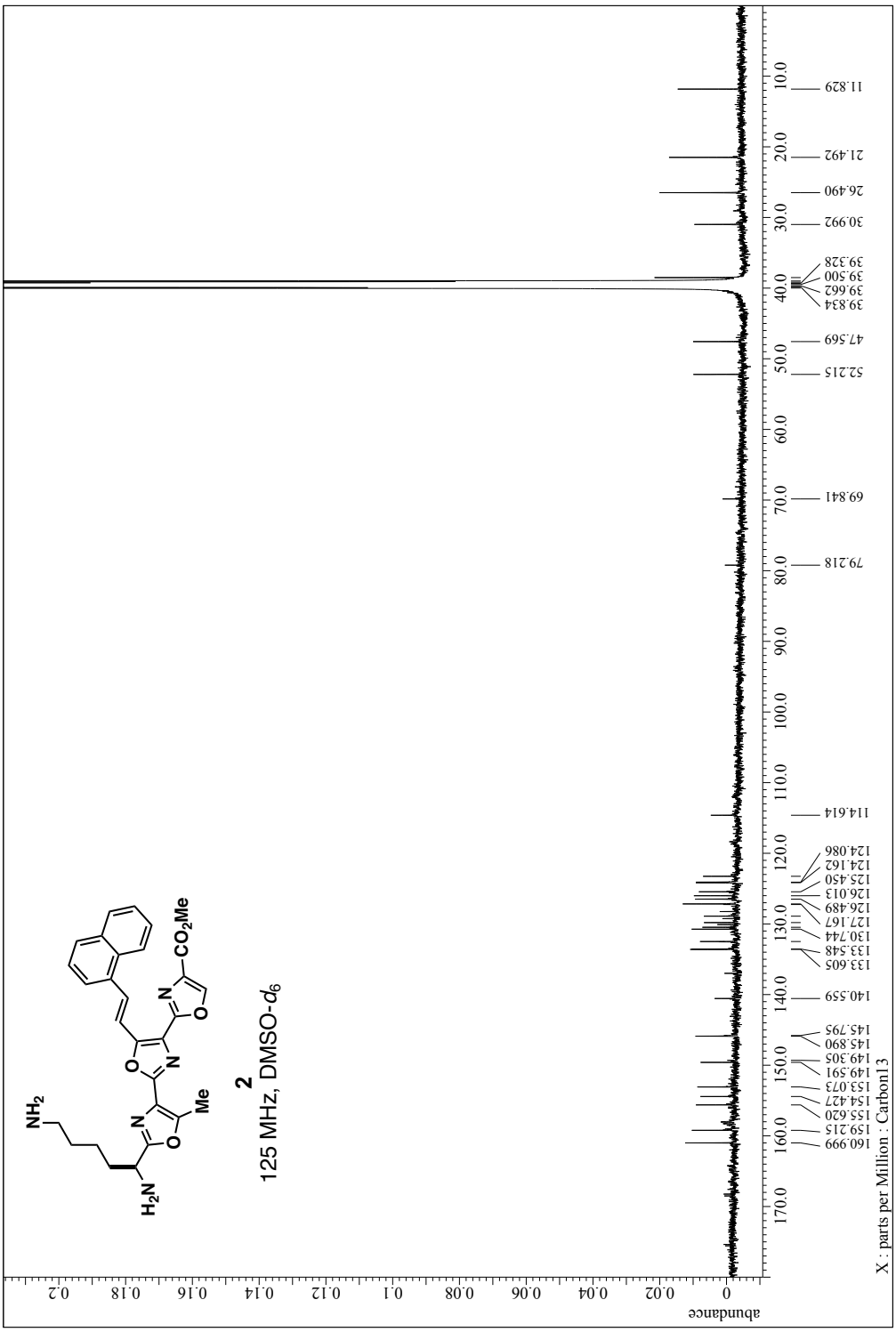

7
300 MHz, DMSO-d_6
NHBoc
BocHN
Me
CO_2Me
abundance
X : parts per Million : 1H

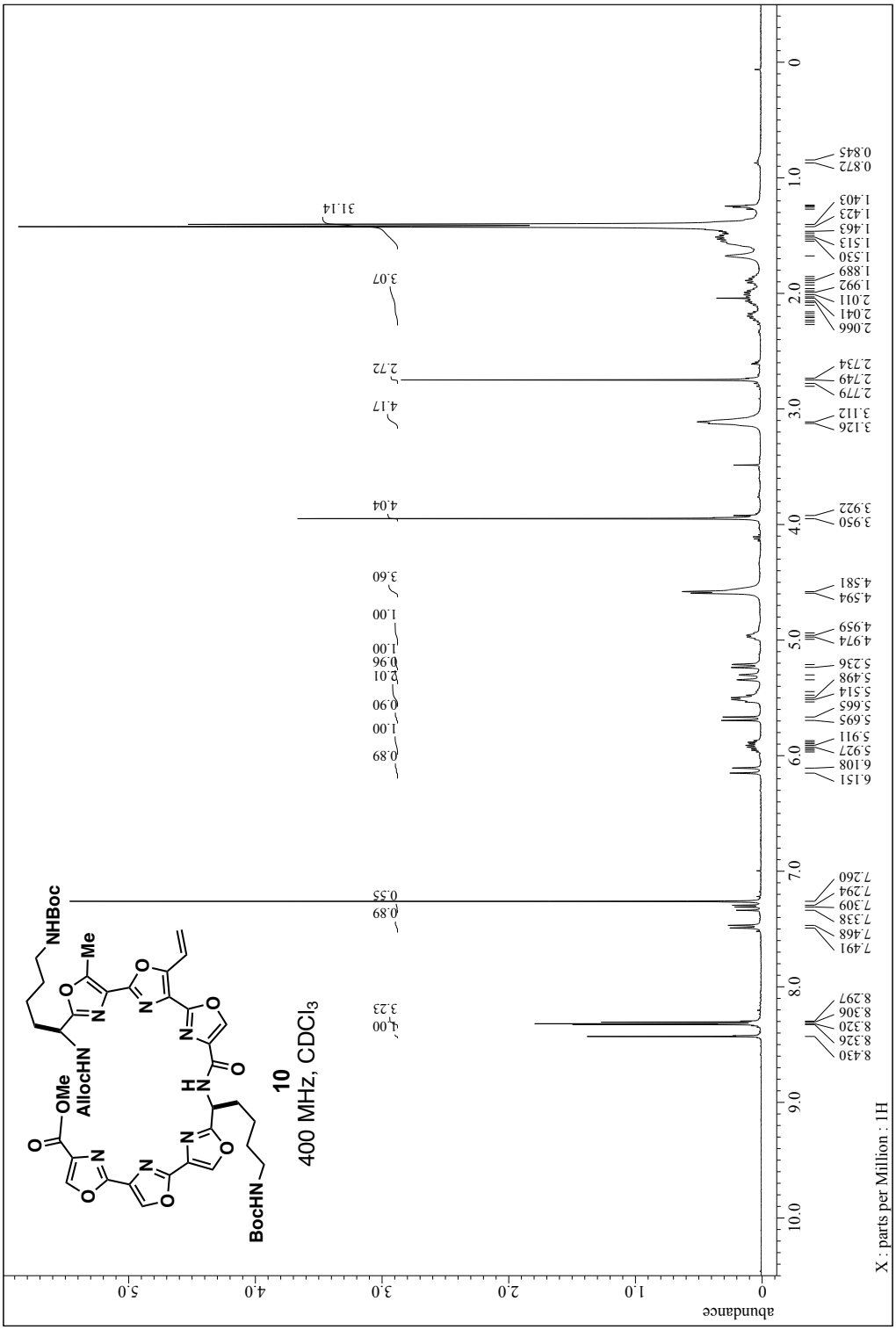

7
125 MHz, CDCl3
NHBoc
BocHN
Me
CO2Me
abundance
X : parts per Million : Carbon13
163.312
161.424
156.149
155.996
155.329
151.485
149.529
143.702
134.421
132.074
131.998
131.903
129.432
128.497
128.402
125.407
124.434
121.525
119.350
80.062
79.041
77.258
77.000
76.752
67.691
52.210
48.643
40.039
38.818
34.001
29.451
28.355
28.278
23.910
22.908
22.393
13.999
11.882
11.042

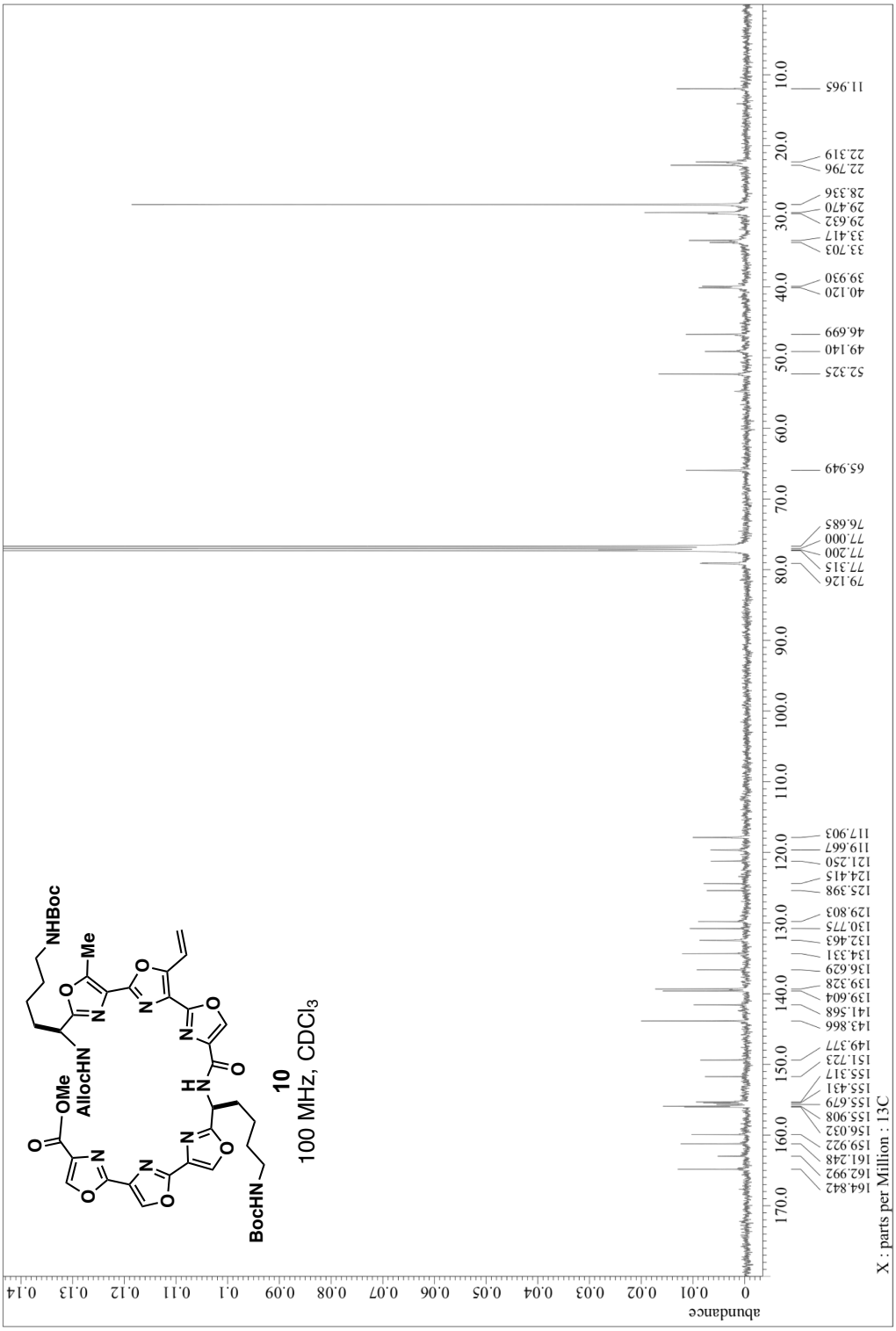

8
400 MHz, DMSO-d_6
NHBoc
BocHN
Me
CO_2Me
N
O
abundance
X : parts per Million : 1H
1.00
2.07
3.65
6.03
0.99
1.01
3.37
2.28
3.13
2.30
11.60

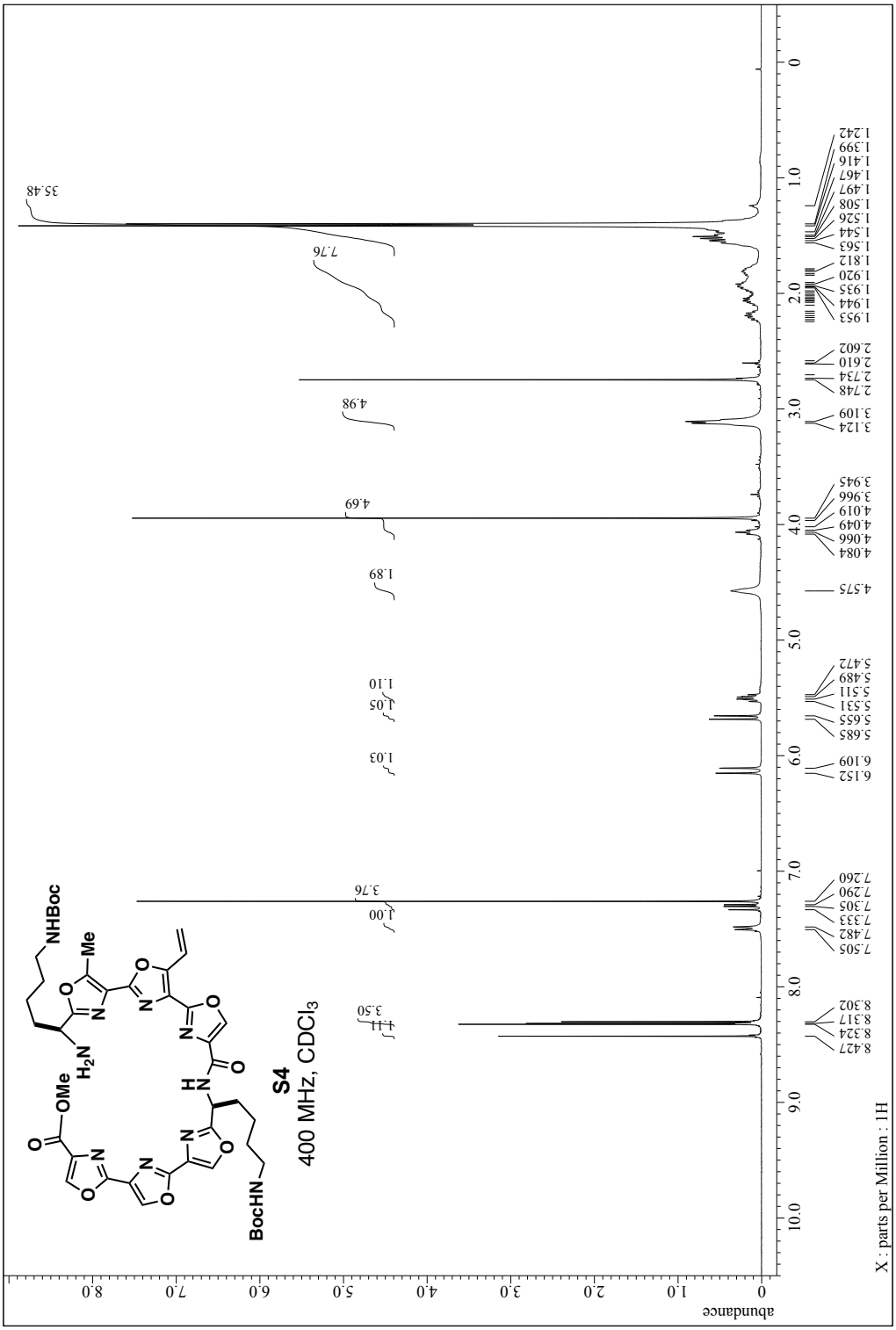

NHBoc
BocHN
Me
CO2Me
8
100 MHz, DMSO-d6
abundance
X : parts per Million : 13C
11.640
22.671
28.192
28.240
29.041
32.053
39.290
39.500
39.700
39.910
48.577
52.048
77.324
78.382
114.623
123.481
123.938
125.330
125.855
126.312
126.989
130.679
132.557
133.435
133.473
145.677
149.224
151.674
154.935
155.336
155.583
155.631
160.894
163.669

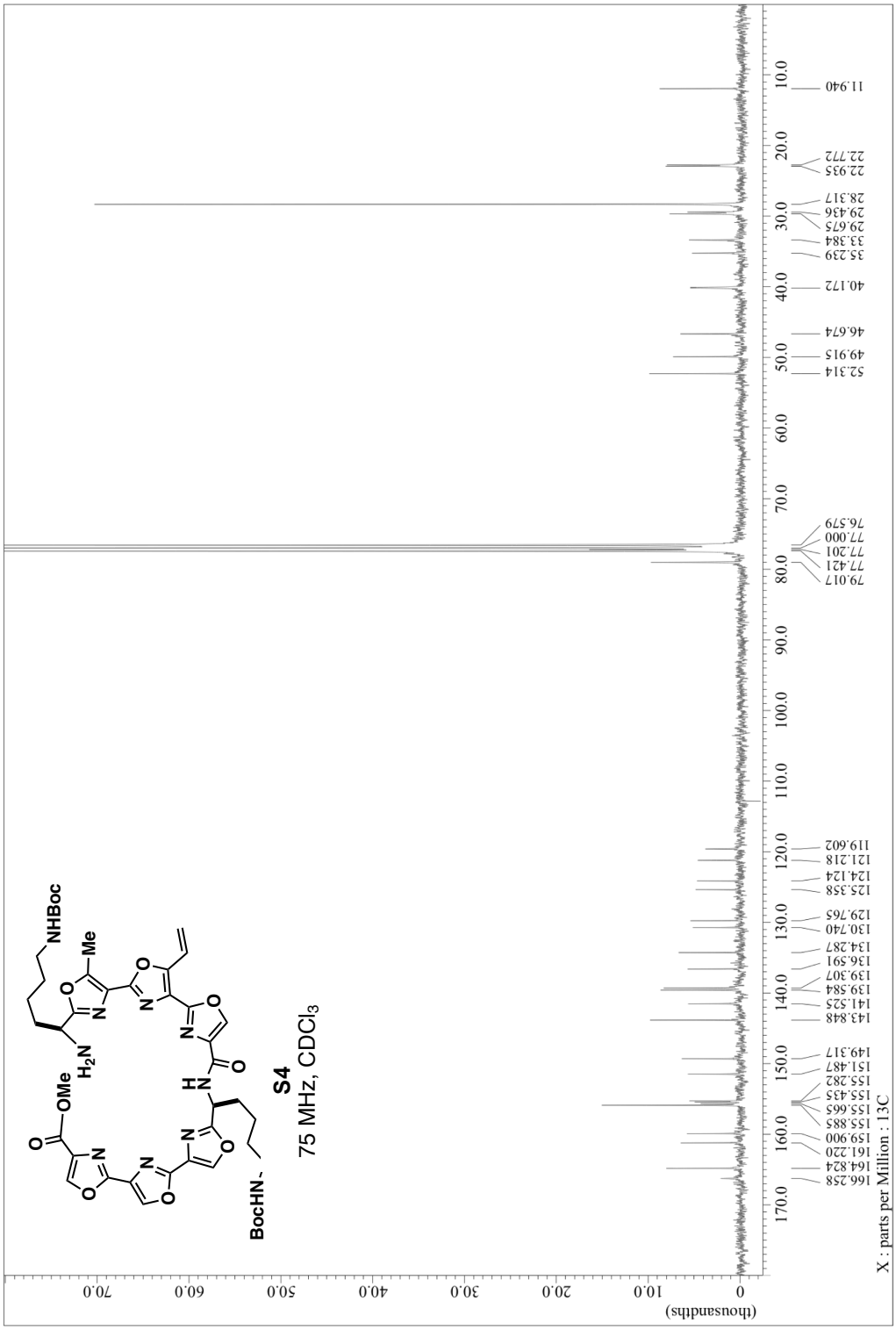

2
500 MHz, DMSO-d_6
X : parts per Million : Proton
abundance

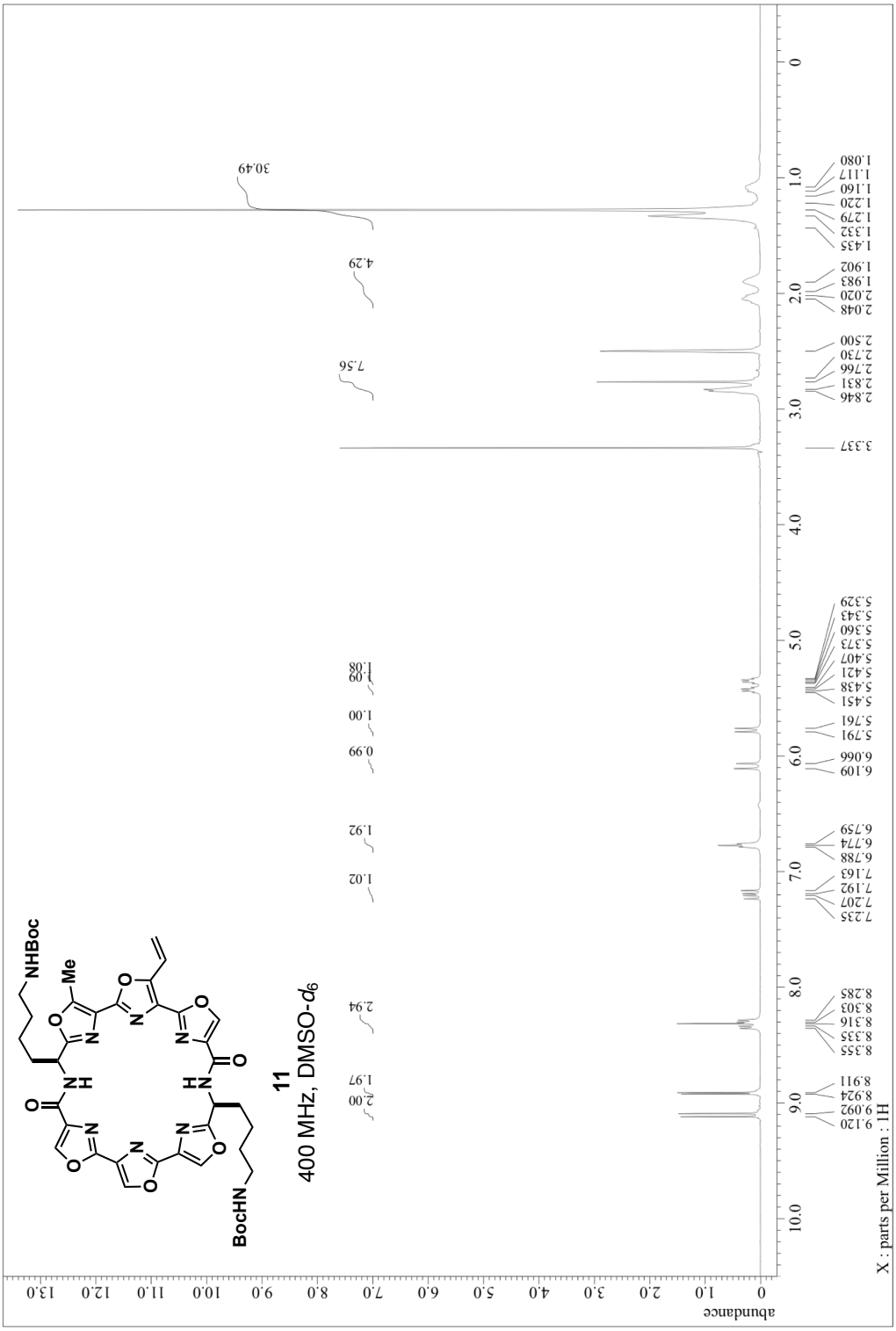

2
125 MHz, DMSO-d_6
abundance
X : parts per Million : Carbon13
160.999
159.215
155.620
154.427
153.073
149.591
149.305
145.890
145.795
140.559
133.605
133.548
130.744
127.167
126.489
126.013
125.450
124.162
124.086
114.614
79.218
69.841
52.215
47.569
39.834
39.662
39.500
39.328
30.992
26.490
21.492
11.829

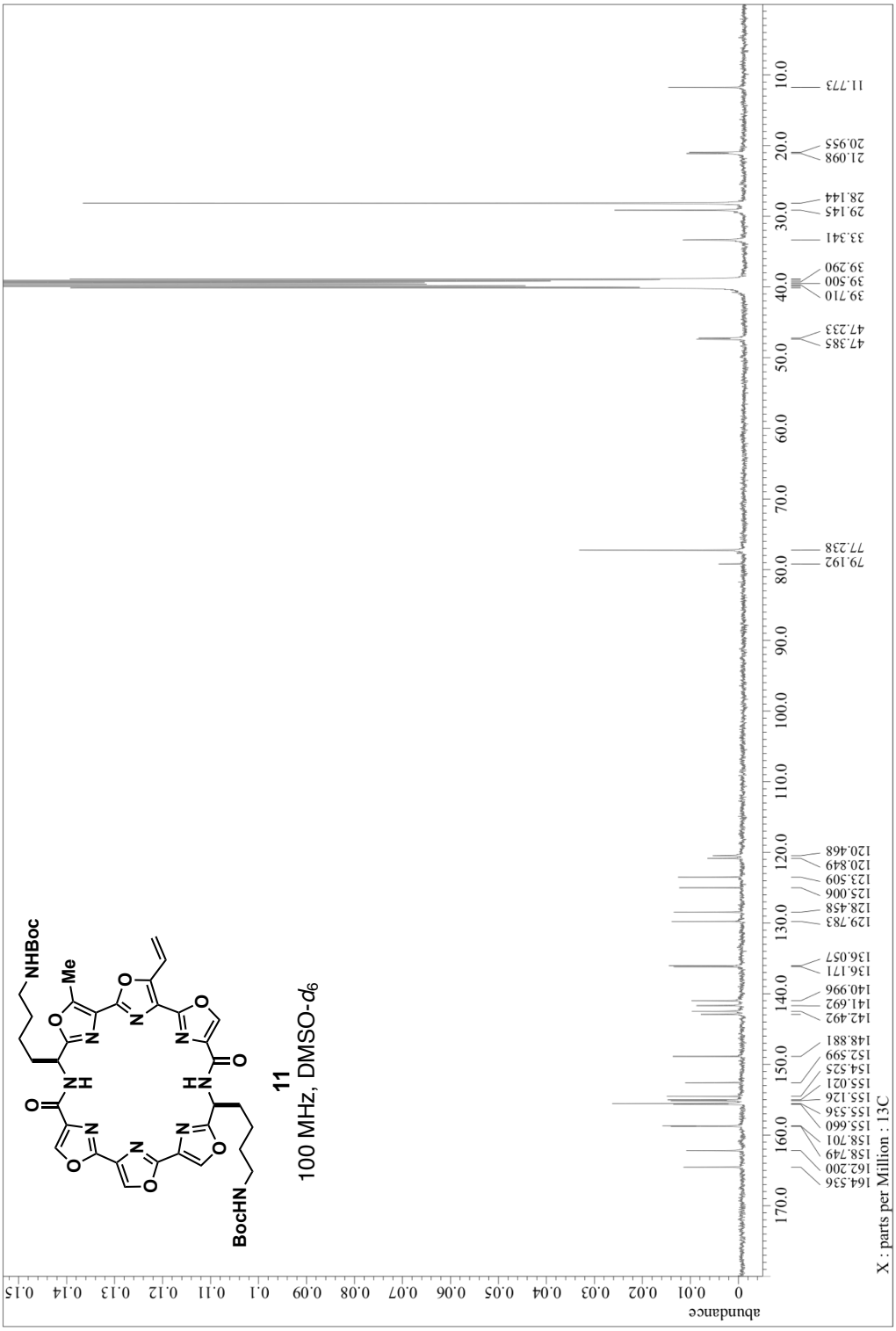

10
400 MHz, CDCl3
X : parts per Million : 1H
abundance

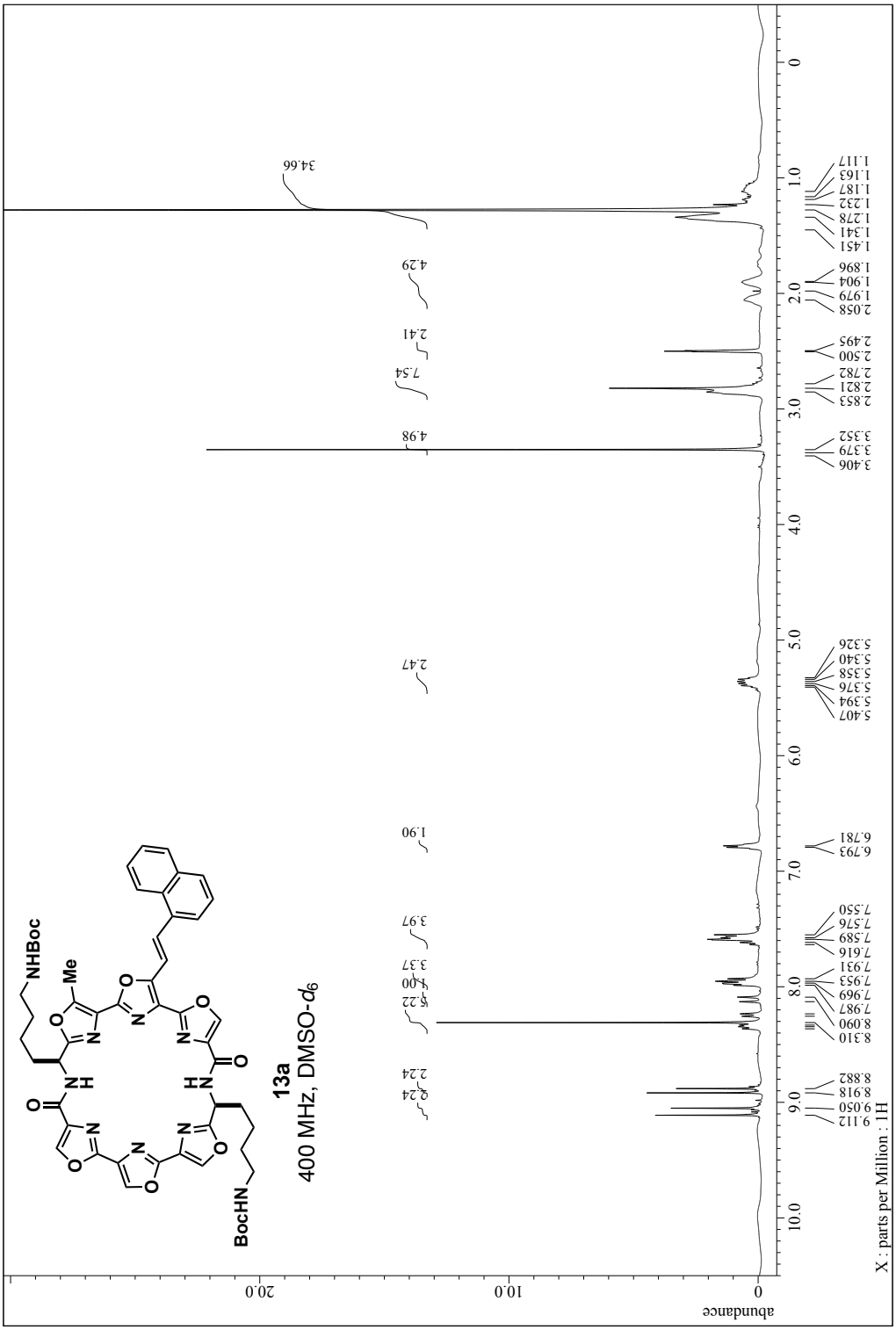

NHBoc
Me
OMe
AllocHN
BocHN
10
100 MHz, CDCl3
abundance
X : parts per Million : 13C
164.842
162.992
161.248
159.922
156.032
155.908
155.679
155.431
155.317
151.723
149.377
143.866
141.568
139.604
139.328
136.629
134.331
132.463
130.775
129.803
125.398
124.415
121.250
119.667
117.903
79.126
77.315
77.200
77.000
76.685
65.949
52.325
49.140
46.699
40.120
39.930
33.703
33.417
29.632
29.470
28.336
22.796
22.319
11.965

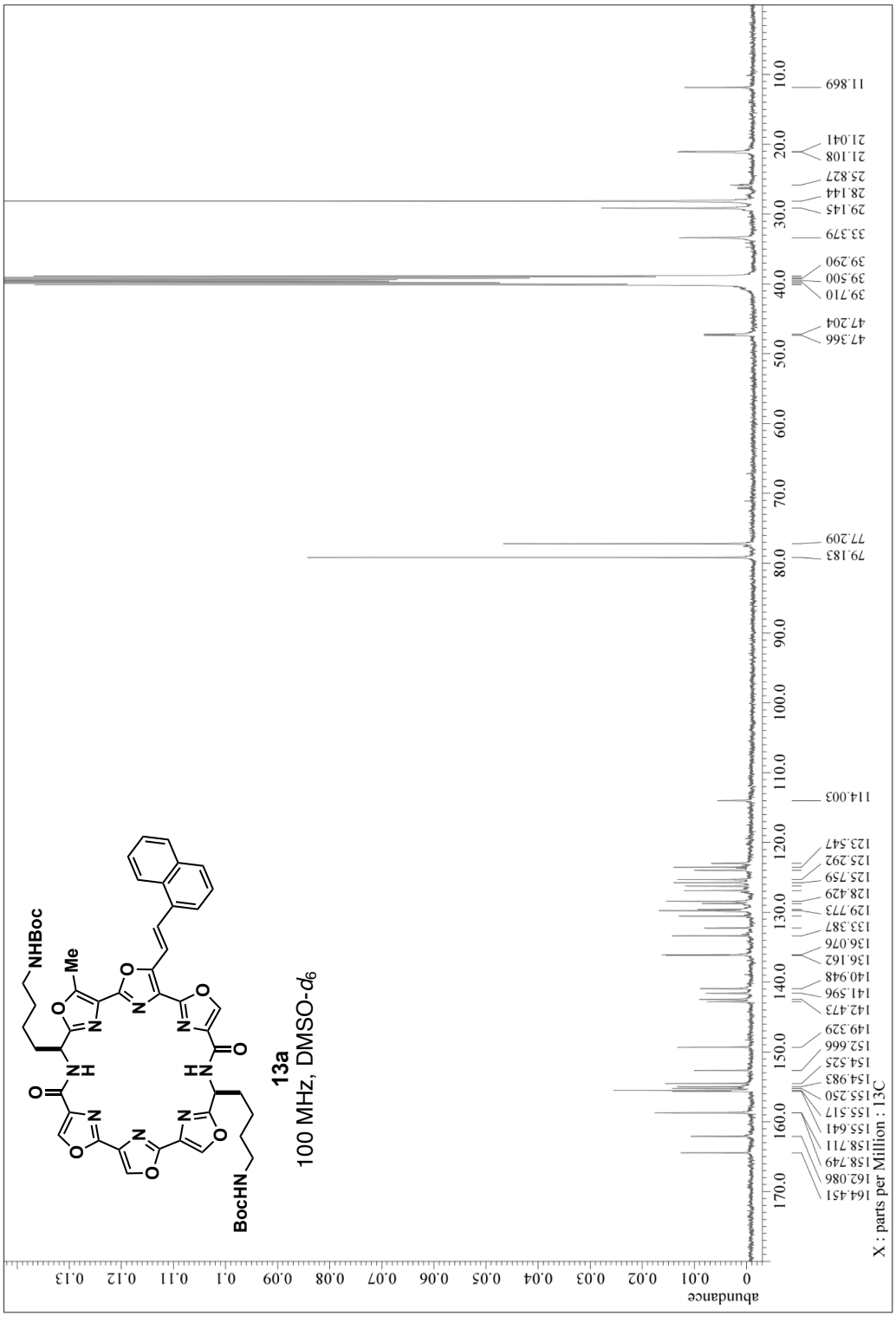

S4
400 MHz, CDCl3
X : parts per Million : 1H
abundance
NHBoc
Me
OMe
H2N
BocHN
8.427
8.324
8.317
8.302
7.505
7.482
7.333
7.305
7.290
7.260
6.152
6.109
5.685
5.655
5.531
5.511
5.489
5.472
4.575
4.084
4.066
4.049
4.019
3.966
3.945
3.124
3.109
2.748
2.734
2.610
2.602
1.953
1.944
1.935
1.920
1.812
1.563
1.544
1.526
1.508
1.497
1.467
1.416
1.399
1.242
35.48
7.76
4.98
4.69
1.89
1.05
1.10
1.03
3.76
1.00
3.50
4.11

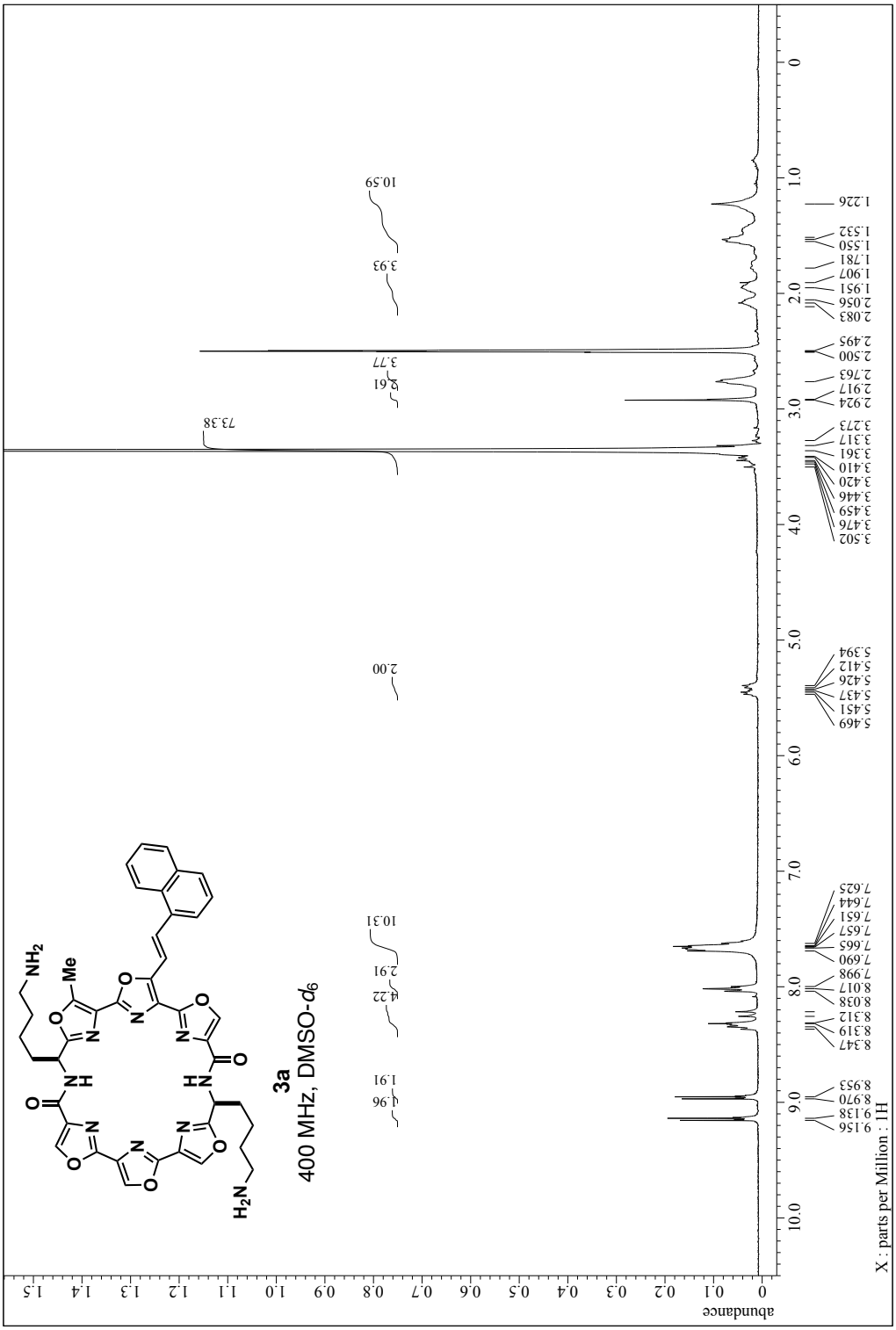

S4
75 MHz, CDCl3
X : parts per Million : 13C
(thousandths)
166.258
164.824
161.220
159.900
155.885
155.665
155.435
155.282
151.487
149.317
143.848
141.525
139.584
139.307
136.591
134.287
130.740
129.765
125.358
124.124
121.218
119.602
79.017
77.421
77.201
77.000
76.579
52.314
49.915
46.674
40.172
35.239
33.384
29.675
29.436
28.317
22.935
22.772
11.940

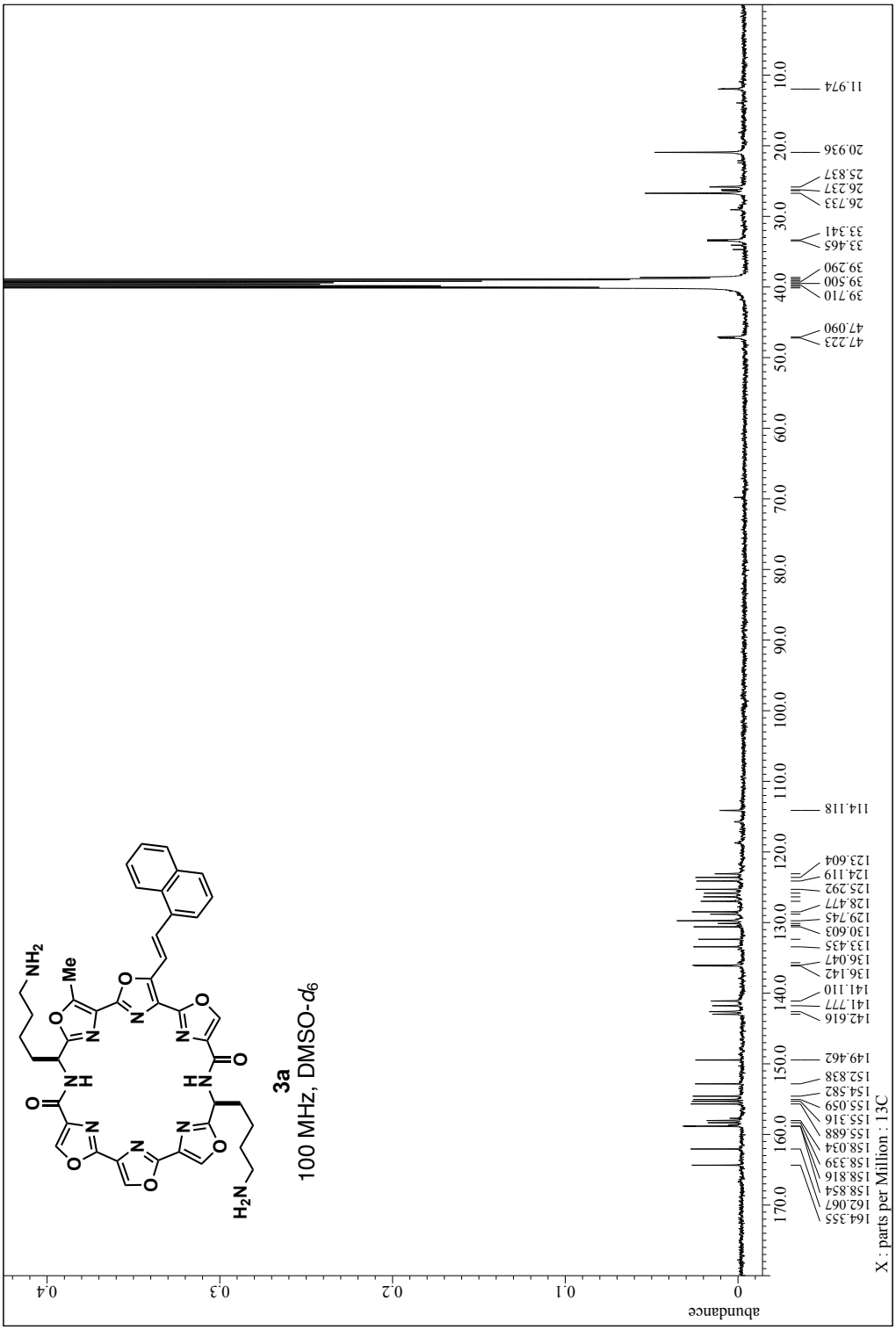

NHBoc
Me
BocHN
11
400 MHz, DMSO-d_6
abundance
X : parts per Million : 1H

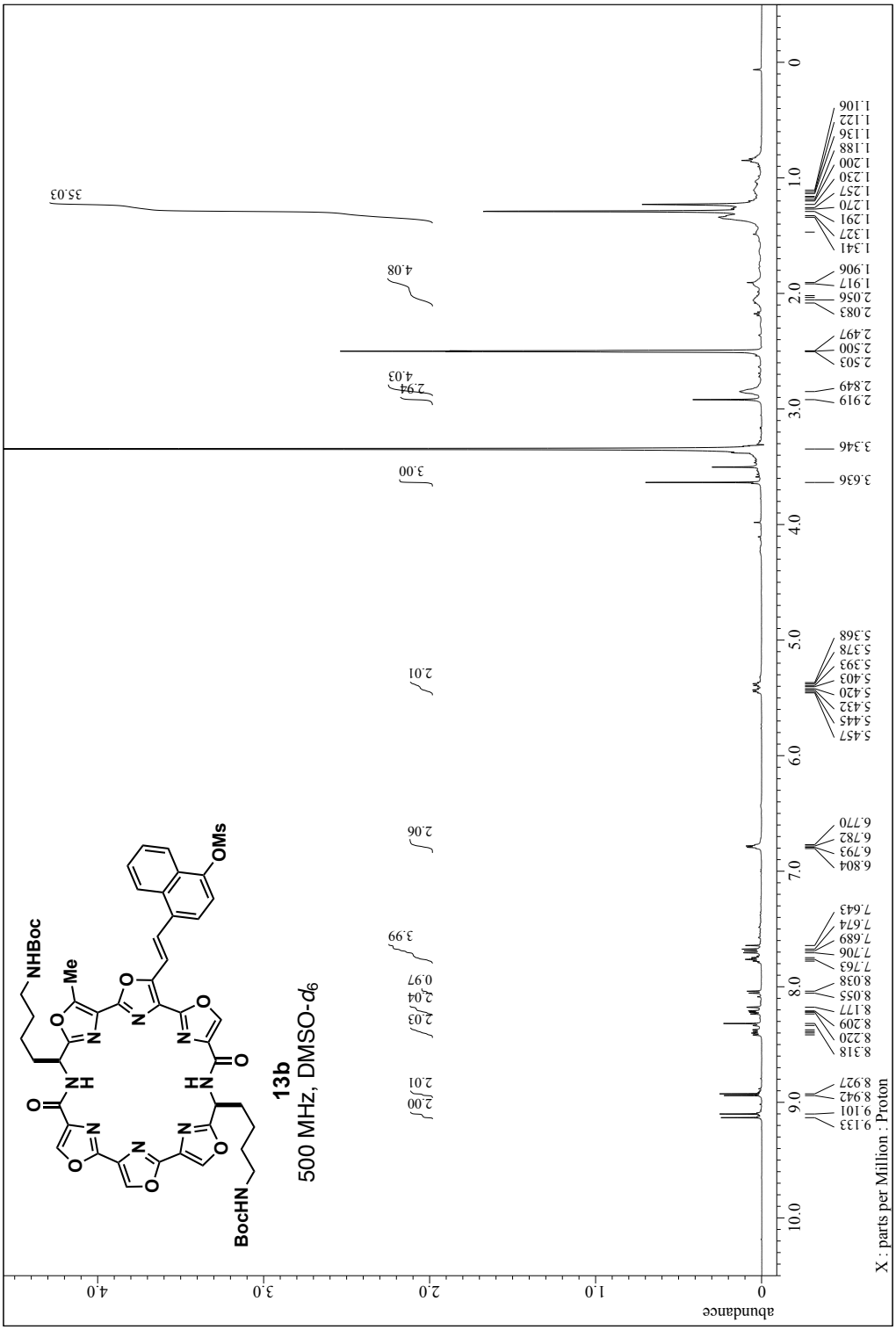

NHBoc
Me
BocHN
11
100 MHz, DMSO-d_6
abundance
X : parts per Million : 13C
164.536
162.200
158.749
158.701
155.660
155.536
155.126
155.021
154.525
152.599
148.881
142.492
141.692
140.996
136.171
136.057
129.783
128.458
125.006
123.509
120.849
120.468
79.192
77.238
47.385
47.233
39.710
39.500
39.290
33.341
29.145
28.144
21.098
20.955
11.773

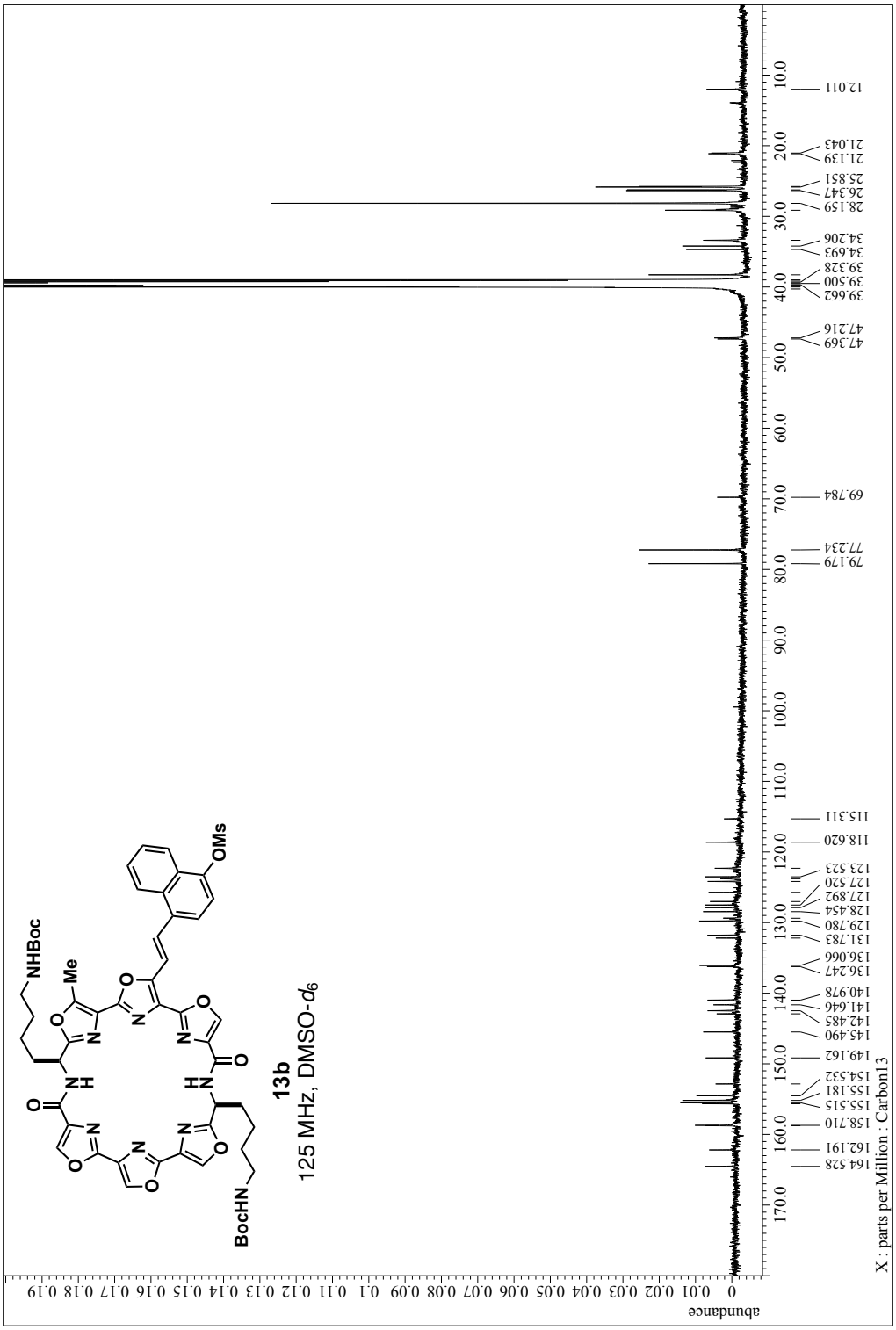

13a
400 MHz, DMSO-d_6
NHBoc
Me
BocHN
abundance
X : parts per Million : 1H

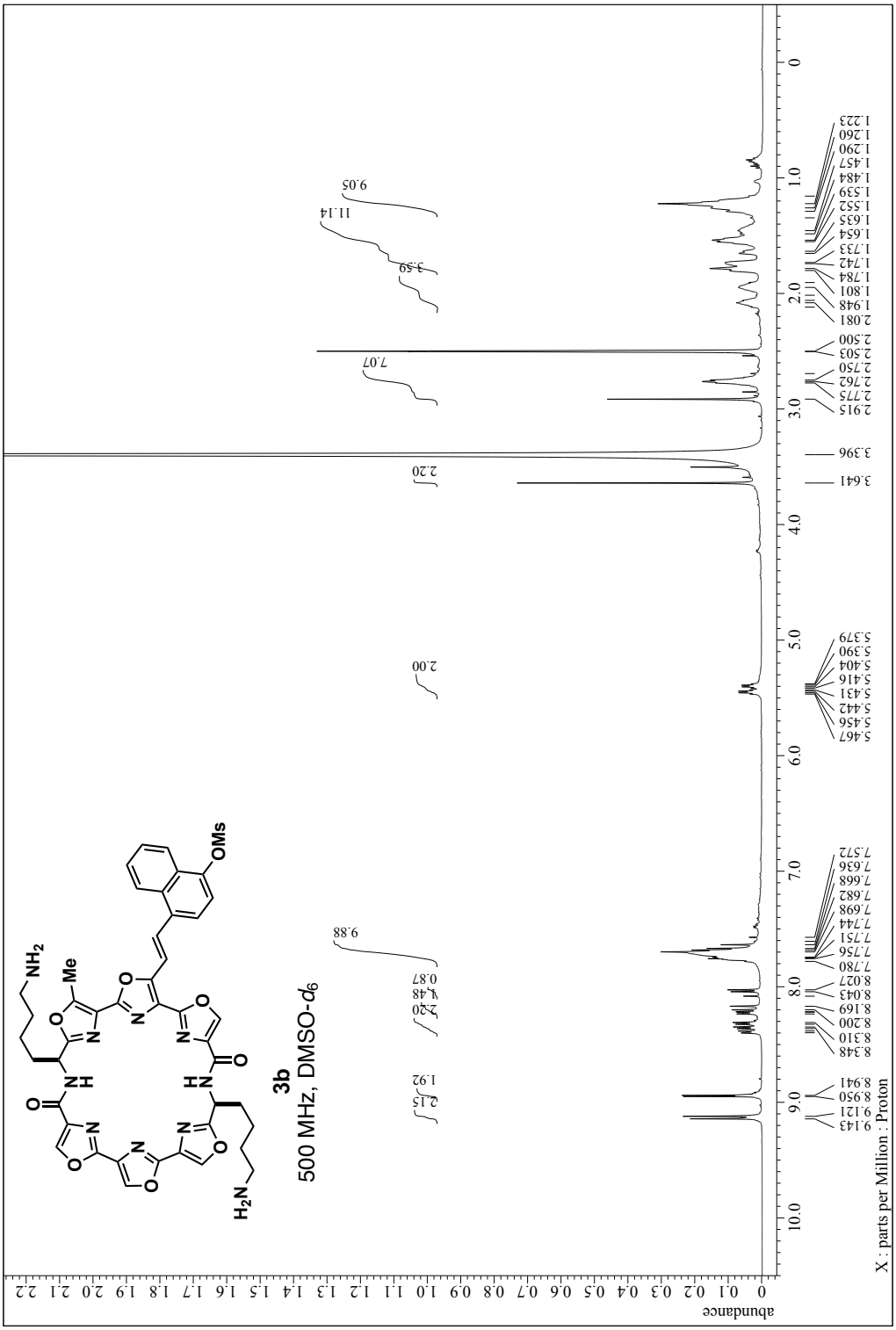

NHBoc
Me
BocHN
13a
100 MHz, DMSO-d_6
X : parts per Million : 13C
abundance
11.869
21.041
21.108
25.827
28.144
29.145
33.379
39.290
39.500
39.710
47.204
47.366
77.209
79.183
114.003
123.547
125.292
125.759
128.429
129.773
133.387
136.076
136.162
140.948
141.596
142.473
149.329
152.666
154.525
154.983
155.250
155.517
155.641
158.711
158.749
162.086
164.451

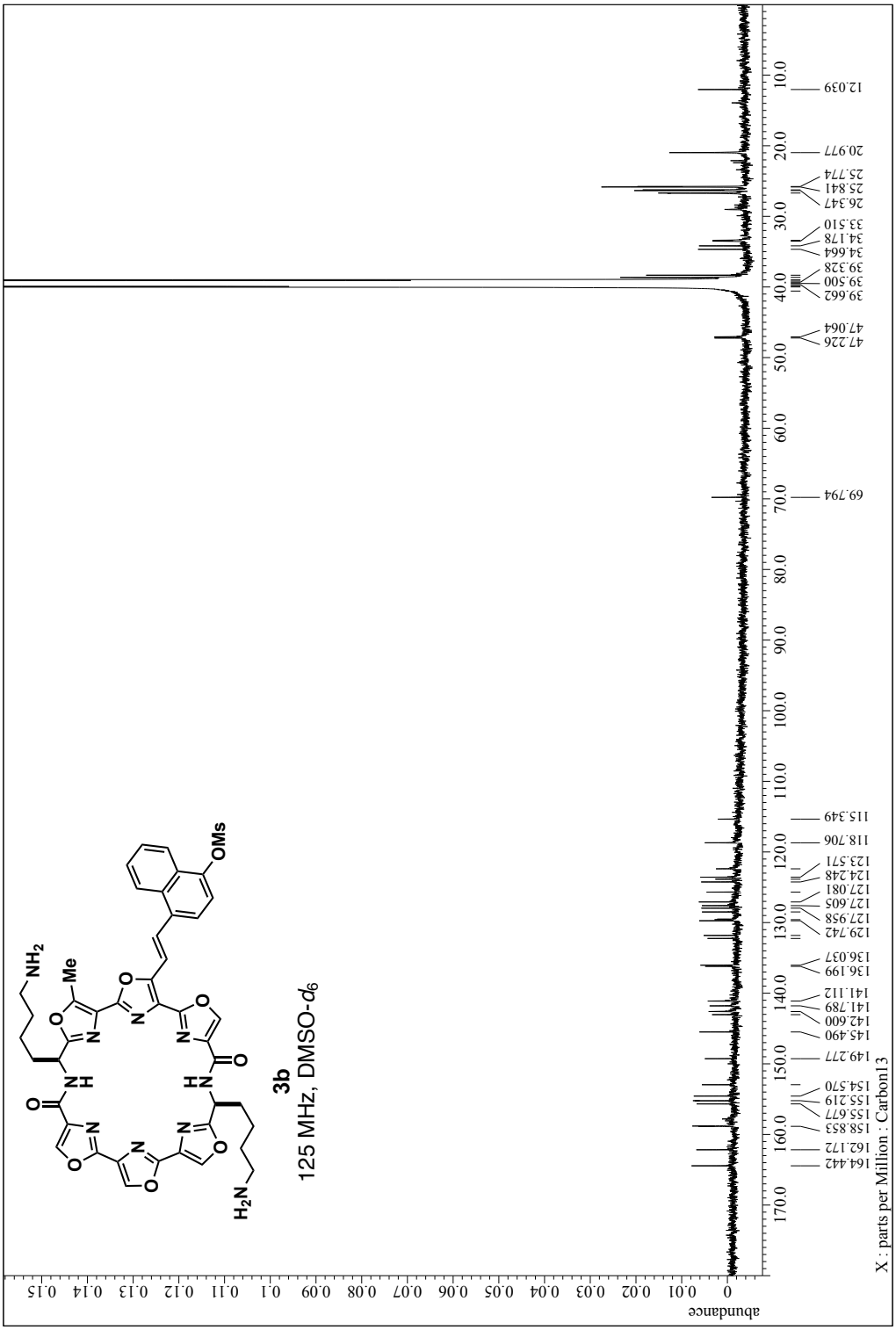

3a
400 MHz, DMSO-d_6
X : parts per Million : 1H
abundance
Me
NH_2
H_2N
9.156
9.138
8.970
8.953
8.347
8.319
8.312
8.038
8.017
7.998
7.690
7.665
7.657
7.651
7.644
7.625
5.469
5.451
5.437
5.426
5.412
5.394
3.502
3.476
3.459
3.446
3.420
3.410
3.361
3.317
3.273
2.924
2.917
2.763
2.500
2.495
2.083
2.056
1.951
1.907
1.781
1.550
1.532
1.226
10.59
3.93
3.77
3.61
73.38
2.00
10.31
2.91
4.22
1.91
2.96

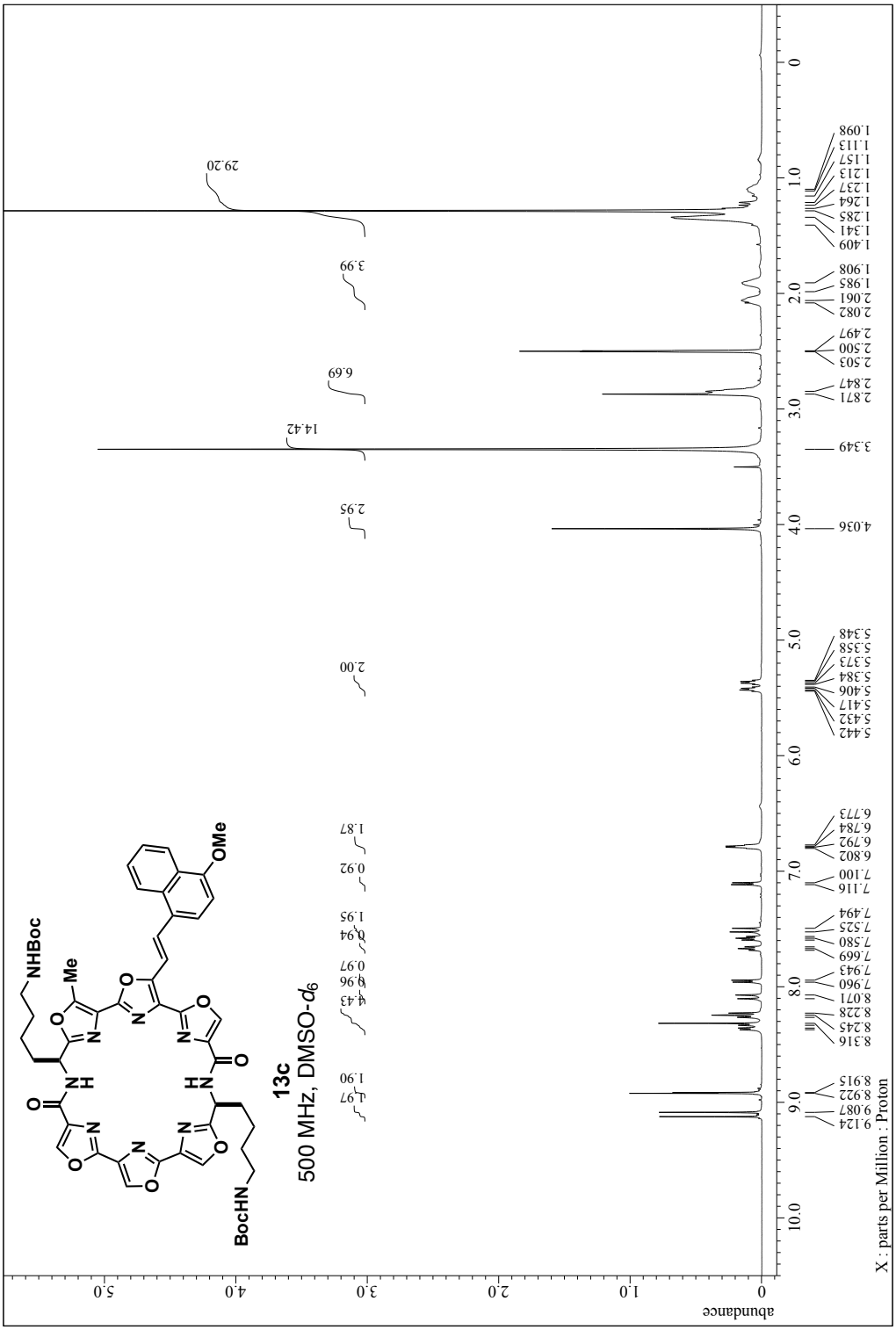

3a
100 MHz, DMSO-d_6
Me
NH_2
H_2N
abundance
X : parts per Million : 13C
164.355
162.067
158.854
158.816
158.339
158.034
155.688
155.316
155.059
154.582
152.838
149.462
142.616
141.777
141.110
136.142
136.047
133.435
130.603
129.745
128.477
125.292
124.119
123.604
114.118
47.223
47.090
39.710
39.500
39.290
33.465
33.341
26.733
26.237
25.837
20.936
11.974

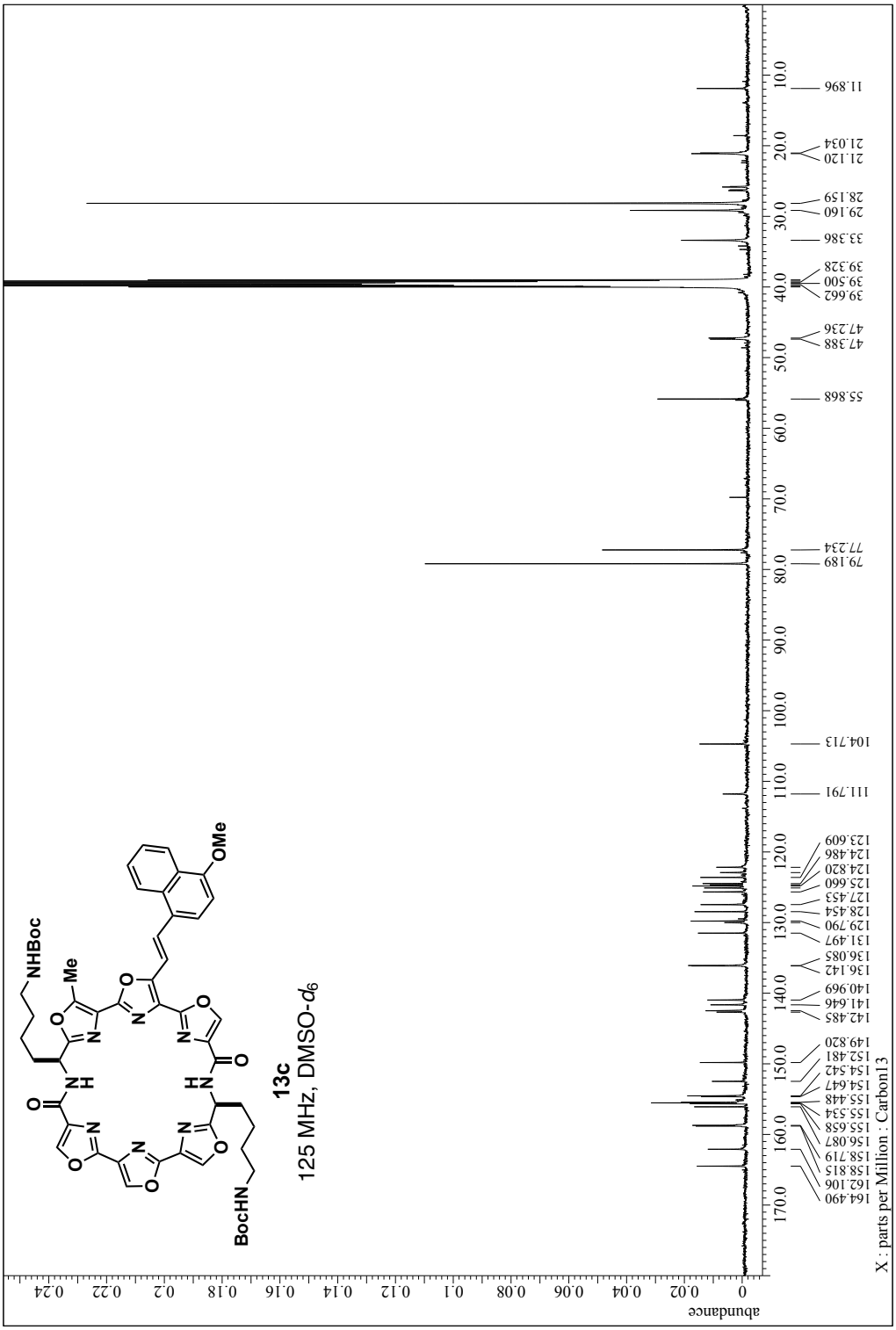

13b
500 MHz, DMSO-d_6
NHBoc
Me
OMs
BocHN
X : parts per Million : Proton
abundance

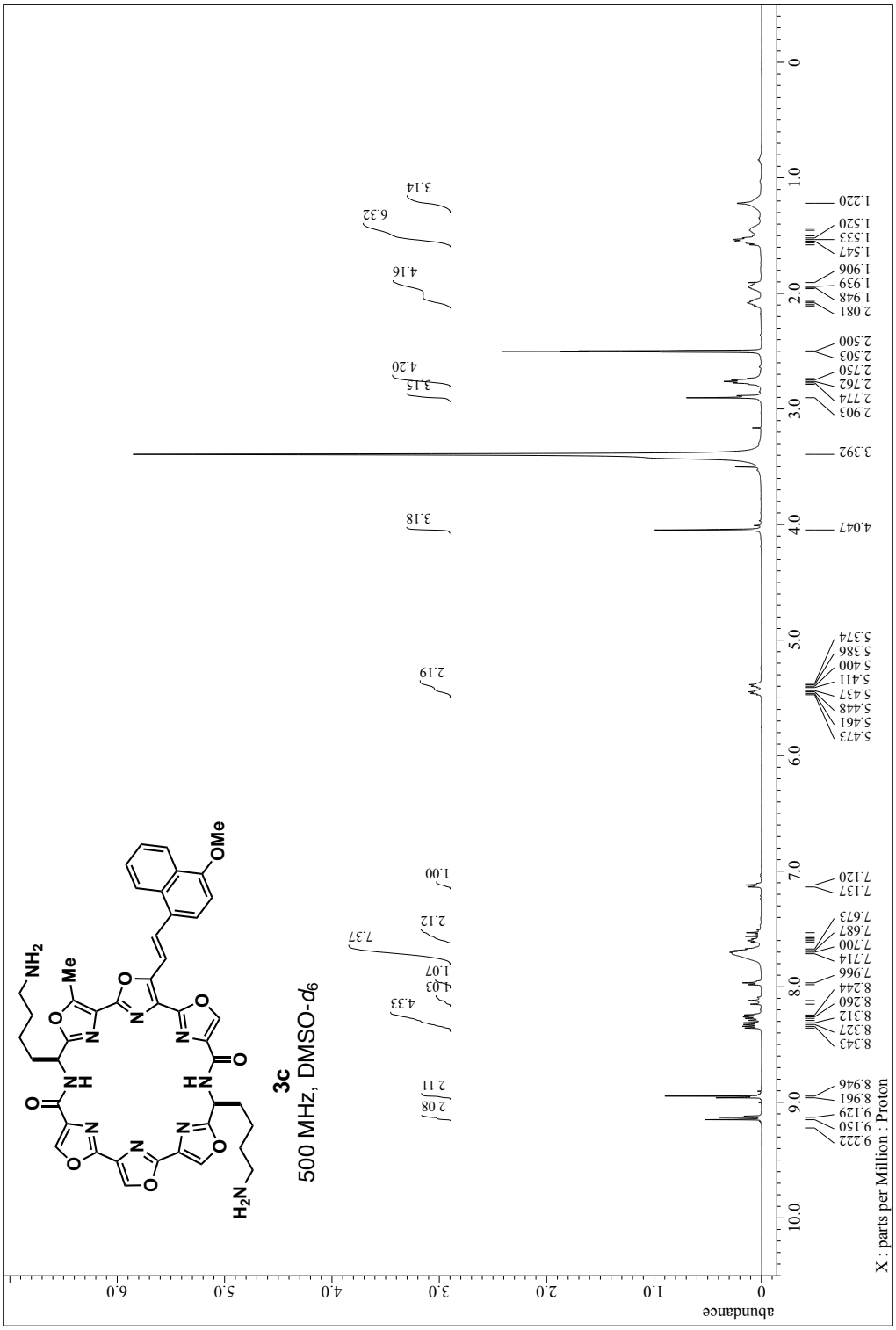

NHBoc
Me
OMs
BocHN
13b
125 MHz, DMSO-d_6
abundance
X : parts per Million : Carbon13

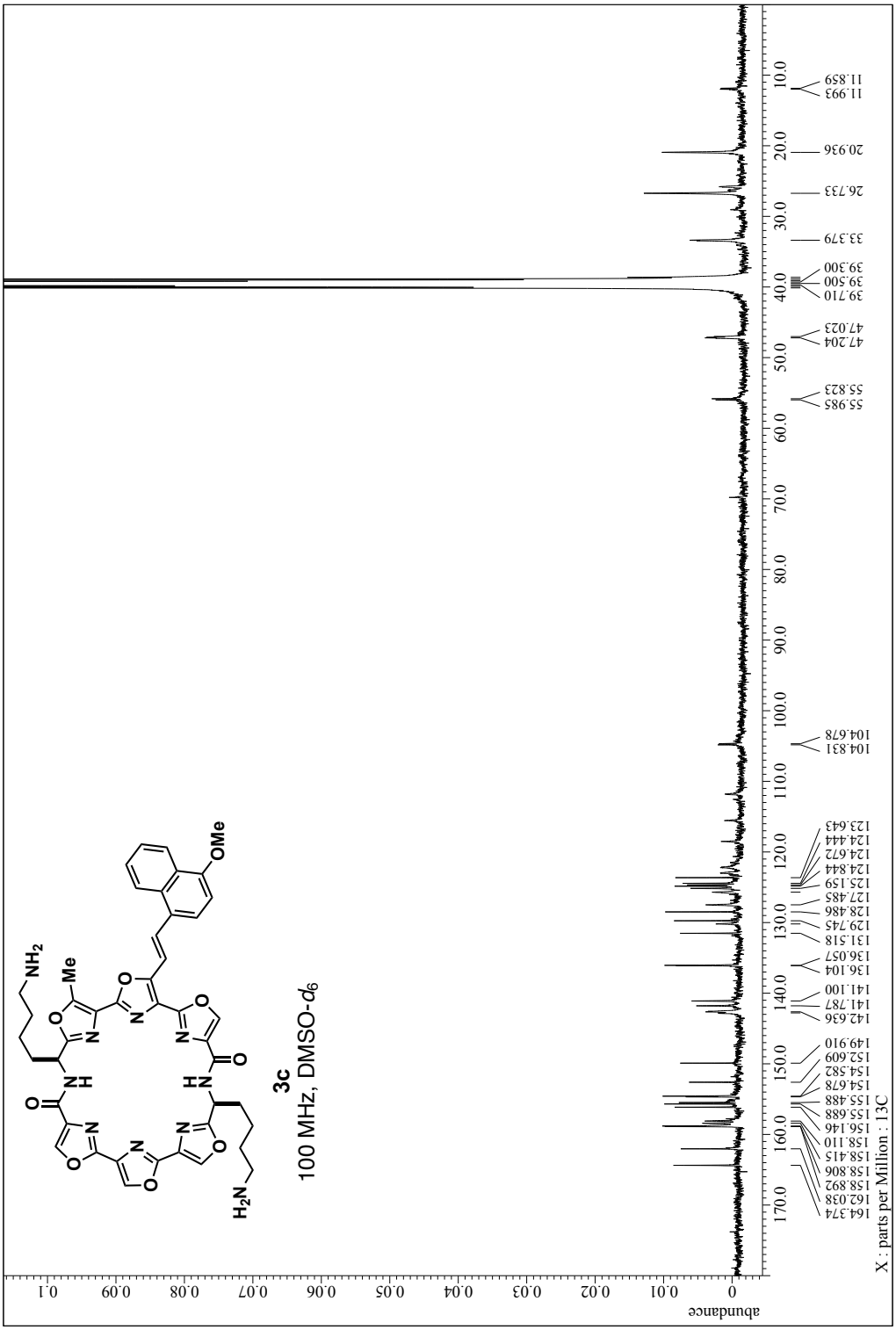

3b
500 MHz, DMSO-d6
X : parts per Million : Proton
abundance
Me
OMs
NH2
H2N

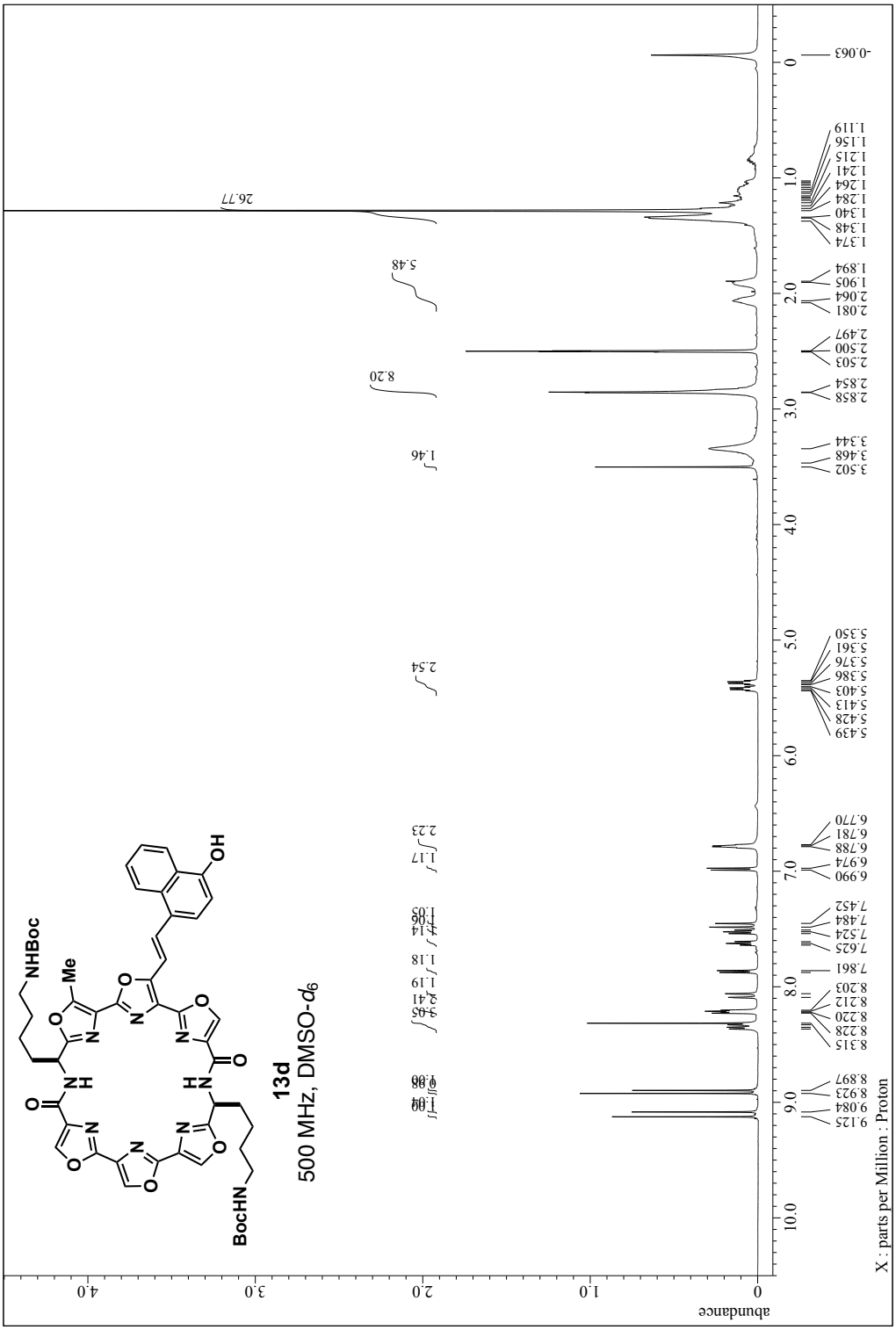

3b
125 MHz, DMSO-d_6
Me
OMs
NH_2
H_2N
abundance
X : parts per Million : Carbon13
164.442
162.172
158.853
155.677
155.219
154.570
149.277
145.490
142.600
141.789
141.112
136.199
136.037
129.742
127.958
127.605
127.081
124.248
123.571
118.706
115.349
69.794
47.226
47.064
39.662
39.500
39.328
34.664
34.178
33.510
26.347
25.841
25.774
20.977
12.039

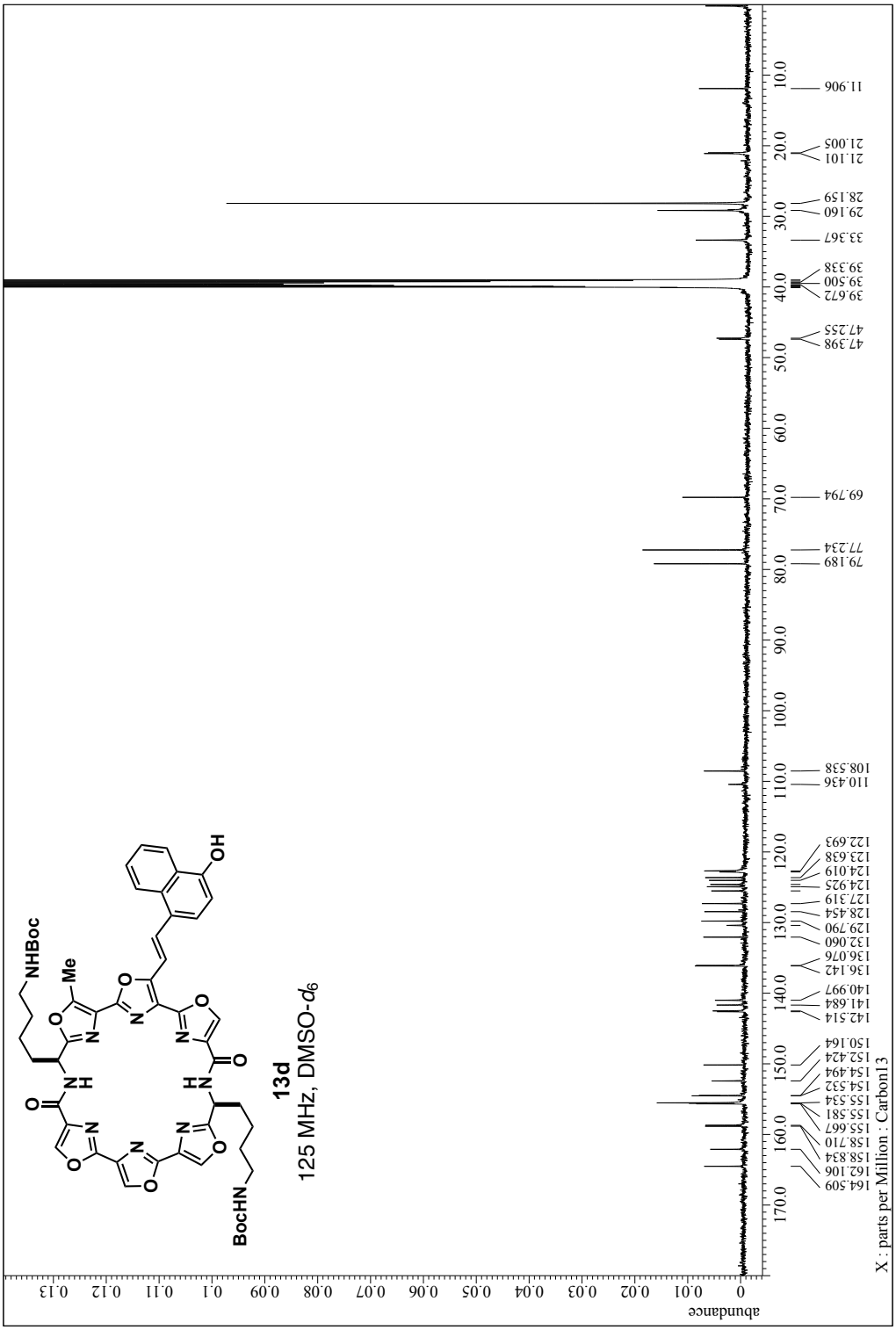

13c
500 MHz, DMSO-d_6
NHBoc
Me
OMe
BocHN
abundance
X : parts per Million : Proton

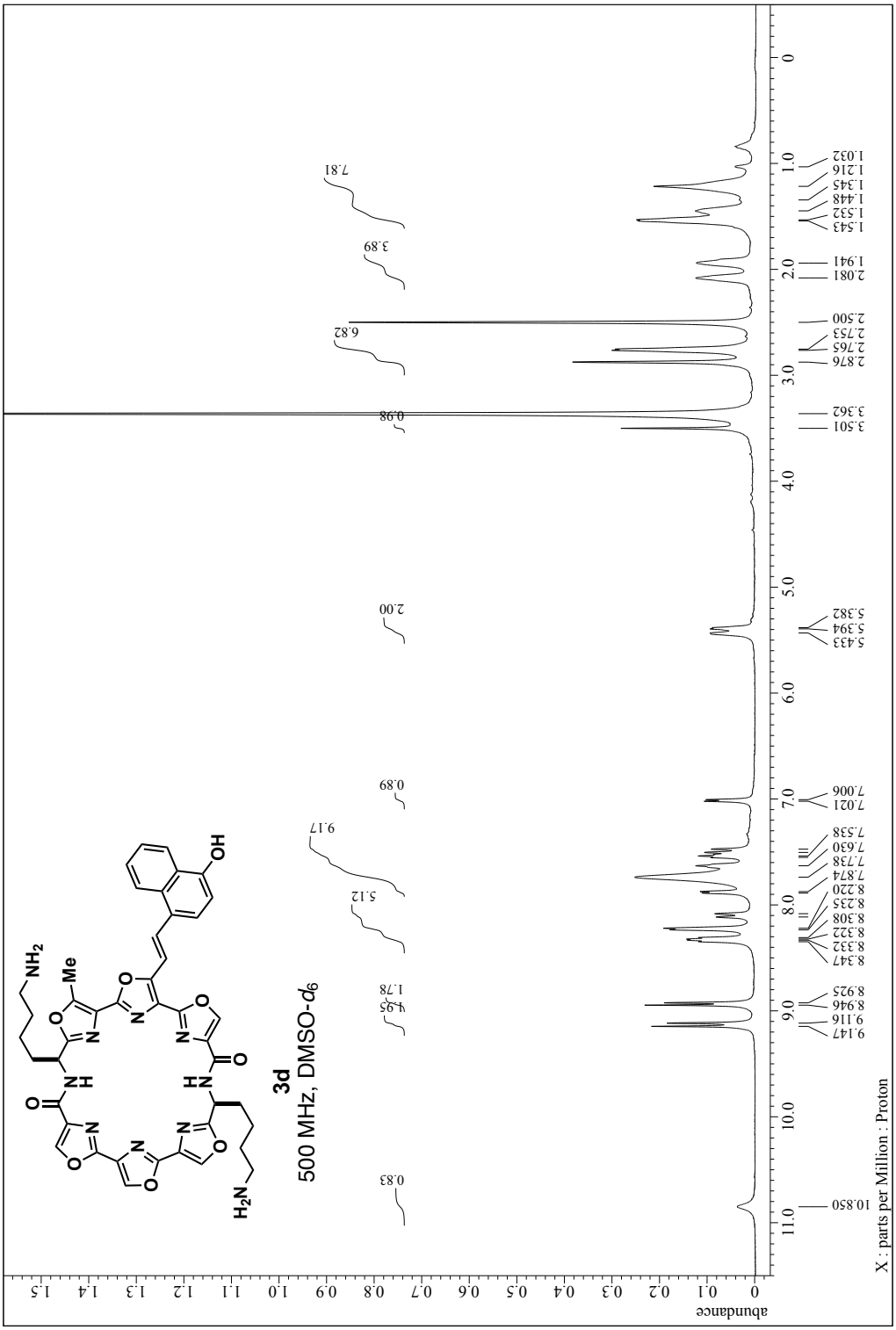

13c
125 MHz, DMSO-d_6
NHBoc
Me
OMe
BocHN
abundance
X : parts per Million : Carbon13
11.896
21.120
21.034
28.159
29.160
33.386
39.662
39.500
39.328
47.388
47.236
55.868
79.189
77.234
104.713
111.791
123.609
124.486
124.820
125.660
127.453
128.454
129.790
131.497
136.085
136.142
140.969
141.646
142.485
149.820
152.481
154.542
154.647
155.448
155.534
155.658
156.087
158.719
158.815
162.106
164.490

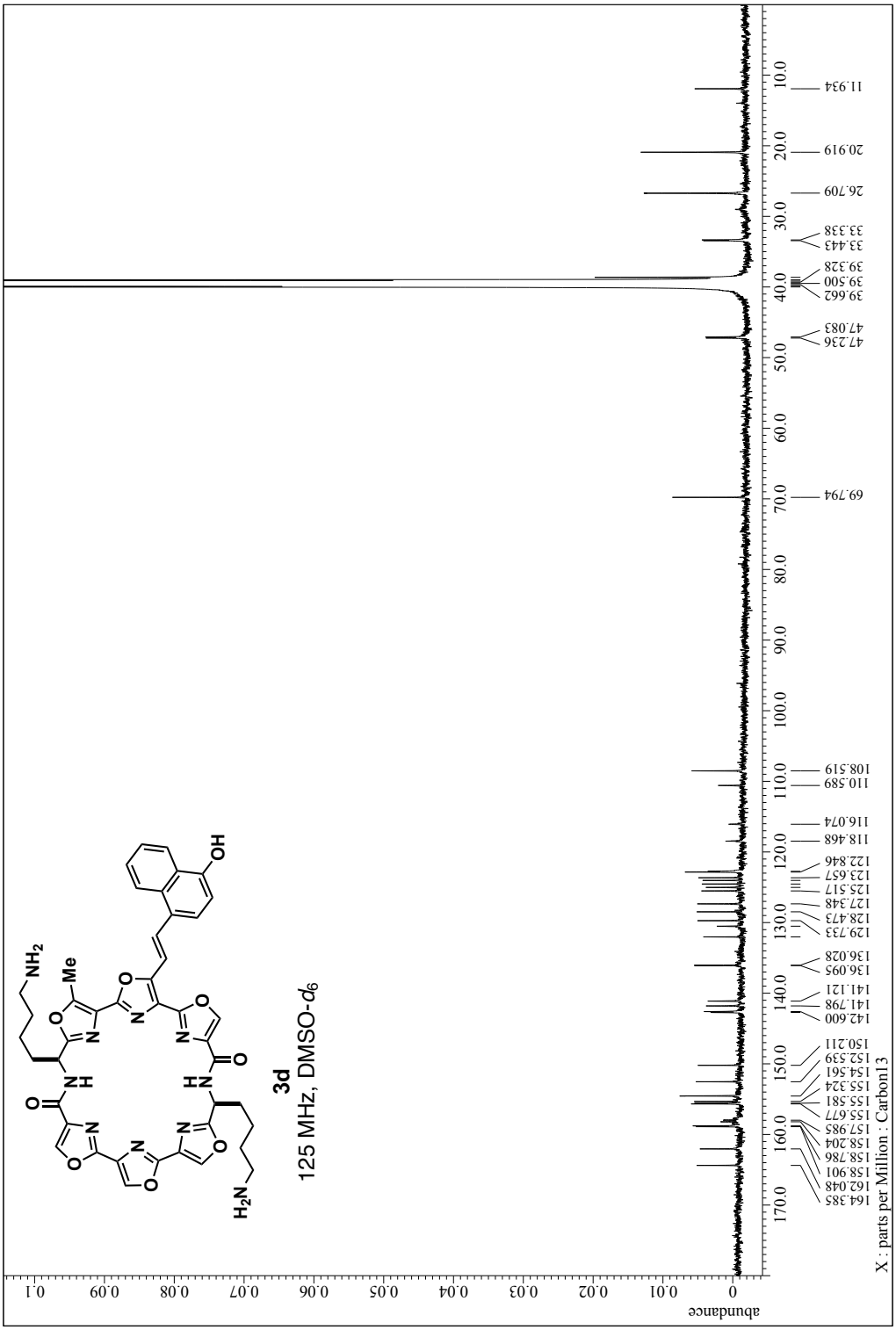

3c
500 MHz, DMSO-d_6
X : parts per Million : Proton
abundance
Me
OMe
NH_2
H_2N

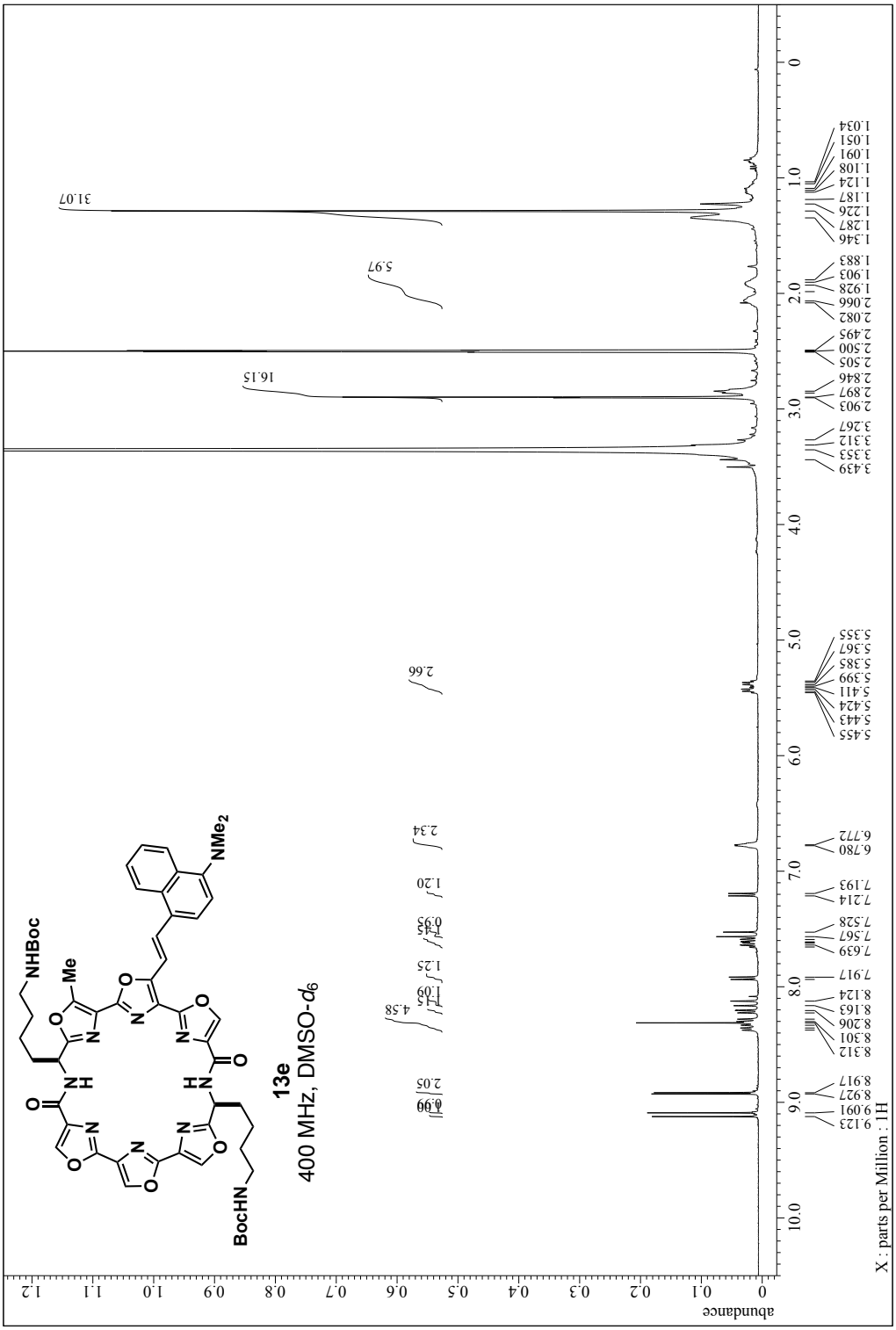

3c
100 MHz, DMSO-d_6
X : parts per Million : 13C
abundance

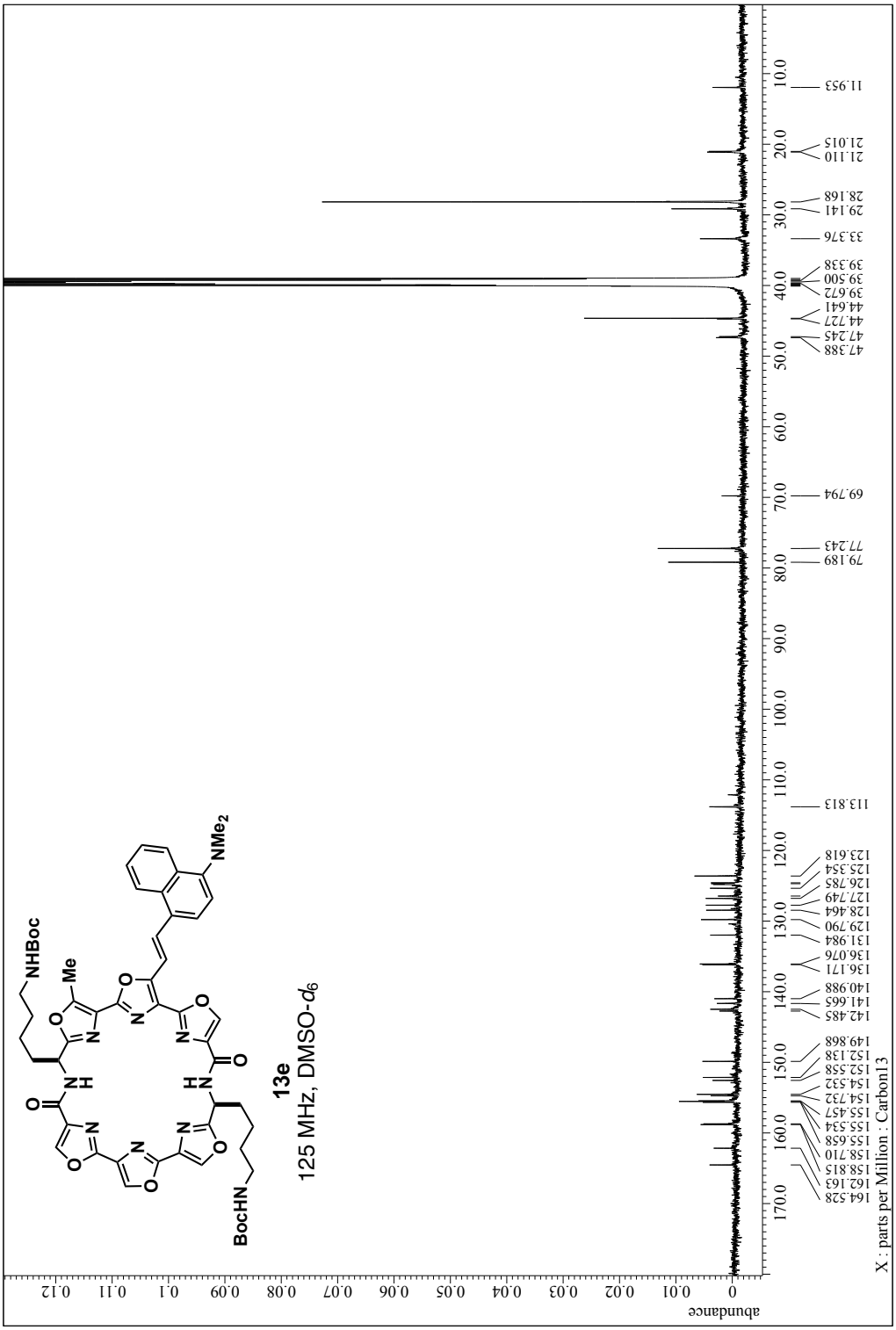

13d
500 MHz, DMSO-d_6
NHBoc
Me
BocHN
OH
abundance
X : parts per Million : Proton

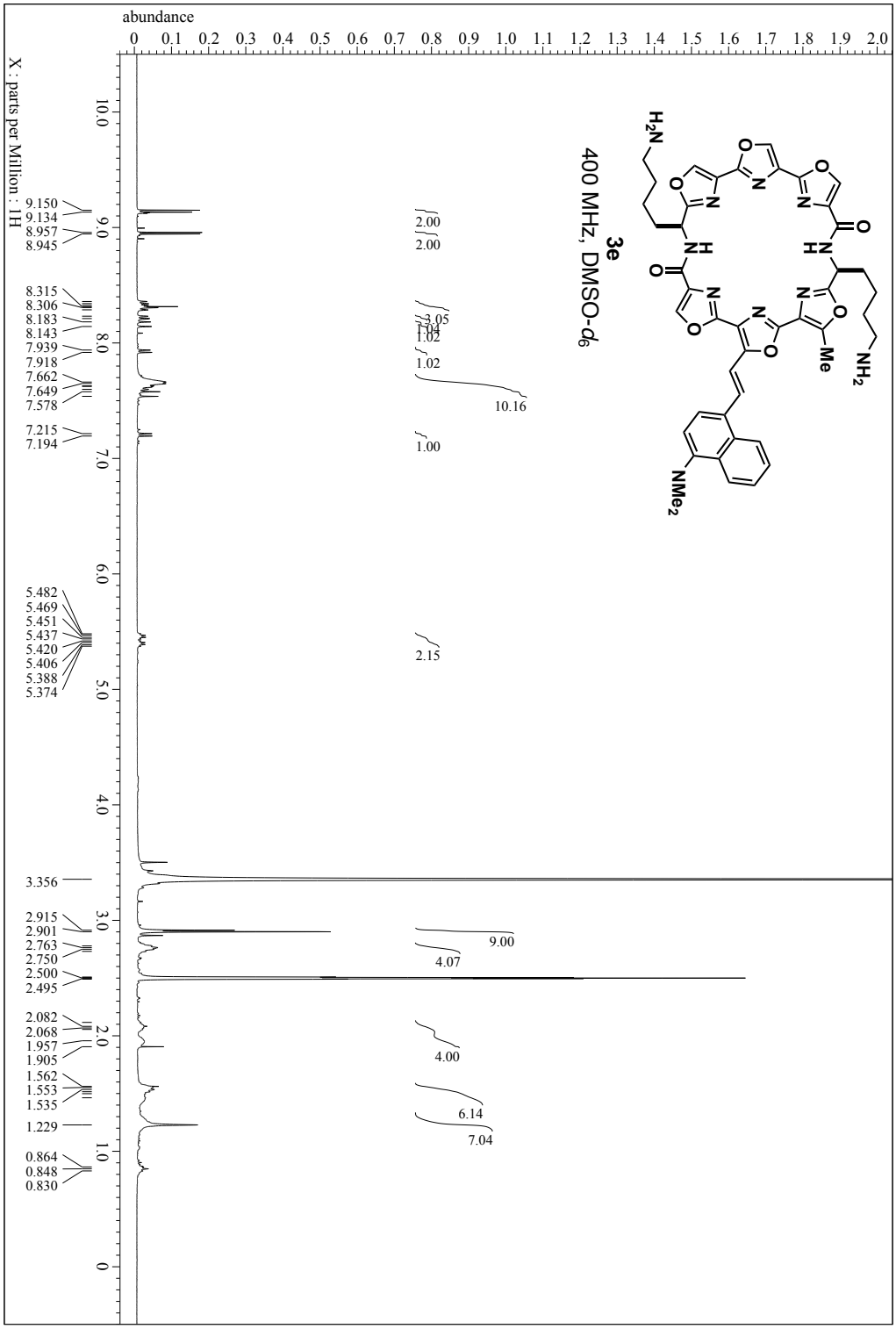

13d
125 MHz, DMSO-d_6
NHBoc
Me
OH
BocHN
abundance
X : parts per Million : Carbon13
11.906
21.101
21.005
28.159
29.160
33.367
39.338
39.500
39.672
47.255
47.398
69.794
77.234
79.189
108.538
110.436
122.693
123.638
124.019
124.925
127.319
128.454
129.790
132.060
136.076
136.142
140.997
141.684
142.514
150.164
152.424
154.494
154.532
155.534
155.581
155.667
158.710
158.834
162.106
164.509

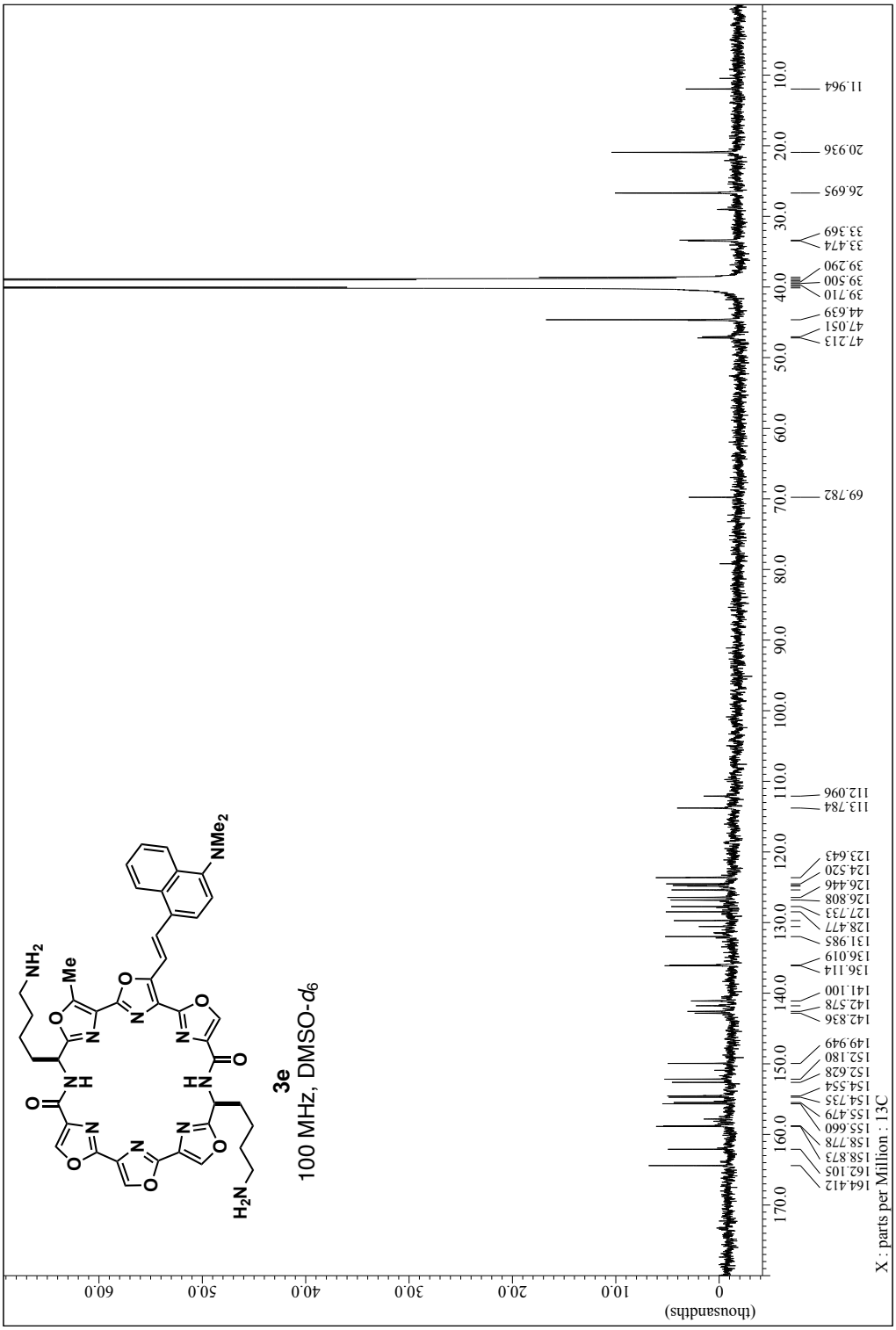

3d
500 MHz, DMSO-d6
X : parts per Million : Proton
abundance
Me
NH2
H2N
OH


3d
125 MHz, DMSO-d_6
Me
NH_2
H_2N
OH
abundance
X : parts per Million : Carbon13
11.934
20.919
26.709
33.338
33.443
39.328
39.500
39.662
47.083
47.236
69.794
108.519
110.589
116.074
118.468
122.846
123.657
125.517
127.348
128.473
129.733
136.028
136.095
141.121
141.798
142.600
150.211
152.539
154.561
155.324
155.581
155.677
157.985
158.204
158.786
158.901
162.048
164.385


13e
400 MHz, DMSO-d_6
NHBoc
Me
NMe2
BocHN
abundance
X : parts per Million : 1H
16.15
31.07
5.97
4.58
2.66
2.34
1.25
1.20
1.09
0.99
2.05
0.95


NHBoc
Me
NMe2
BocHN
13e
125 MHz, DMSO-d6
abundance
X : parts per Million : Carbon13
11.953
21.110
21.015
28.168
29.141
33.376
39.338
39.500
39.672
44.641
44.727
47.245
47.388
69.794
77.243
79.189
113.813
123.618
125.354
126.785
127.749
128.464
129.790
131.984
136.076
136.171
140.988
141.665
142.485
149.868
152.138
152.558
154.532
154.732
155.457
155.534
155.658
158.710
158.815
162.163
164.528


abundance
X : parts per Million : 1H
3e
400 MHz, DMSO-d_6
H_2N
NH_2
Me
NMe_2
9.150
9.134
8.957
8.945
8.315
8.306
8.183
8.143
7.939
7.918
7.662
7.649
7.578
7.215
7.194
5.482
5.469
5.451
5.437
5.420
5.406
5.388
5.374
3.356
2.915
2.901
2.763
2.750
2.500
2.495
2.082
2.068
1.957
1.905
1.562
1.553
1.535
1.229
0.864
0.848
0.830
2.00
2.00
3.05
1.04
1.02
1.02
10.16
1.00
2.15
9.00
4.07
4.00
6.14
7.04


3e
100 MHz, DMSO-d_6
NMe_2
Me
NH_2
H_2N
(thousandths)
X : parts per Million : 13C
11.964
20.936
26.695
33.369
33.474
39.290
39.500
39.710
44.639
47.051
47.213
69.782
112.096
113.784
123.643
124.520
126.446
126.808
127.733
128.477
131.985
136.019
136.114
141.100
142.578
142.836
149.949
152.180
152.628
154.554
154.735
155.479
155.660
158.778
158.873
162.105
164.412