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Supporting Information

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Supporting Information

for

Synthesis of Macrocyclic Heptaoxazole, A Potent G-Quadruplex Binder

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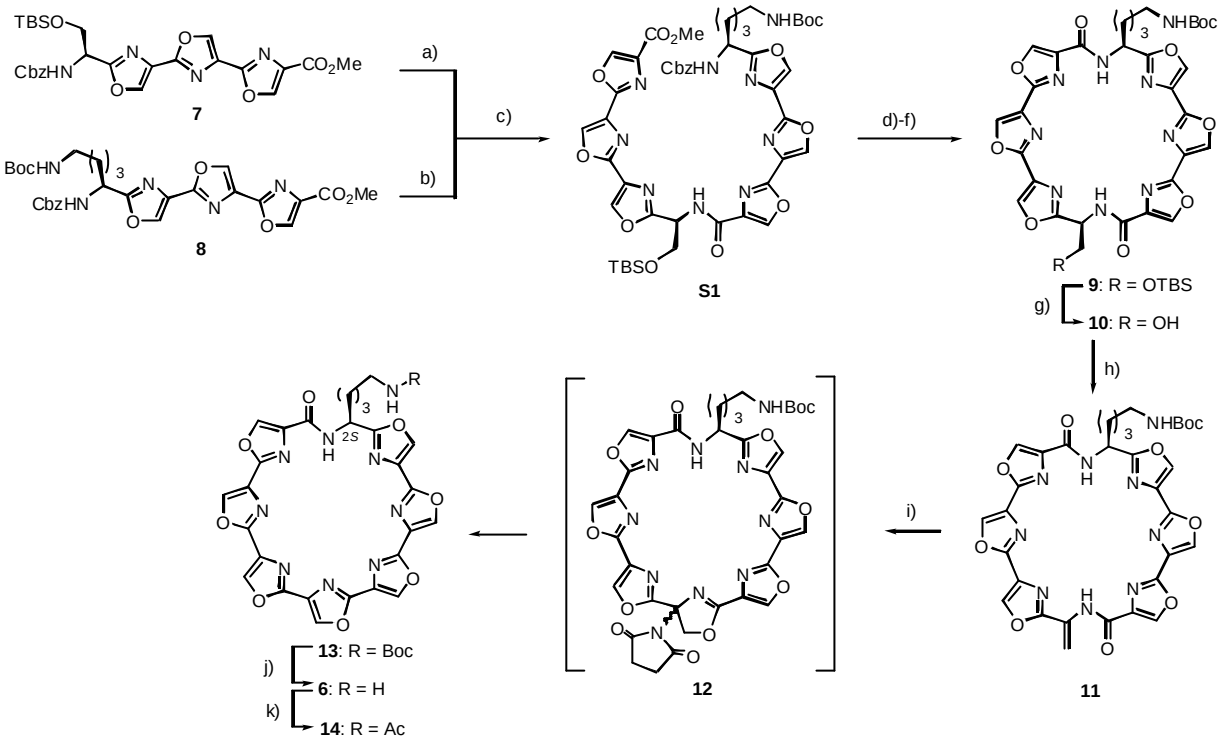
General

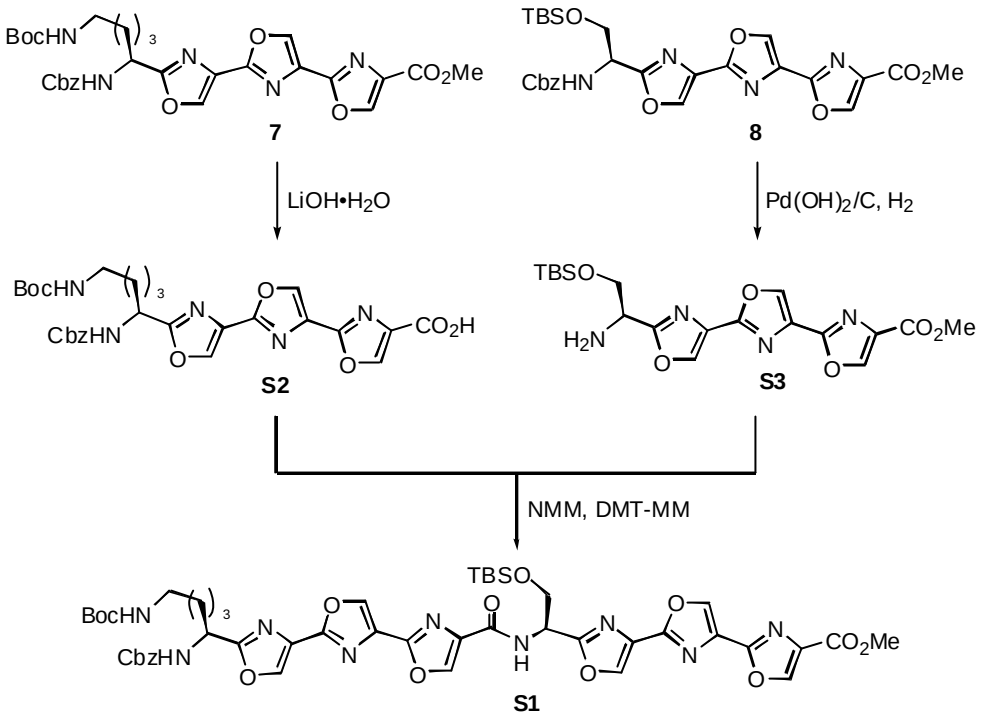
Flash chromatography was performed on Silica gel 60 (spherical, particle size 0.040 ~ 0.100 µm; Kanto). Optical rotations were measured on a JASCO DIP 1000 polarimeter, using the sodium D line. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECX 400. The spectra are referenced internally according to residual solvent signals of $CDCl_3$ (^{1}H NMR; d = 7.26 ppm, ^{13}C NMR; d = 77.0 ppm), CD_3OD (^{1}H NMR; d = 3.30 ppm, ^{13}C NMR; d = 49.0 ppm), $(CD_3)_2SO$ (^{1}H NMR; d = 2.50 ppm, ^{13}C NMR; d = 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 shift (δ, ppm). Mass spectra were recorded on JEOL JMS-T100X spectrometer with ESI-MS mode using methanol as solvent. CD spectra were recorded on a JASCO-810 spectropolarimeter (Jasco, Easton, MD) using a quartz cell of 1-mm optical path length and an instrument scanning speed of 100 nm/min with a response time of 1 s, and over a wavelength range of 200-320 nm. Fluorescence was scanned with a phosphorimager (Typhoon 8600, Molecular Dynamics). All oligonucleotides purified were obtained from Sigma Genosys and dissolved in double-distilled water to be used without further purification.

Synthesis of L1H1-7OTD (**6**) and L1A1-7OTD (**14**).



Scheme S1. Synthesis of L1H1-7OTD (**6**) and L1A1-7OTD (**14**). a) $Pd(OH)_2/C$, H_2, THF/MeOH; b) $LiOH•H_2O$, THF/H_2O; c) DMT-MM, NMM, THF/H_2O, 91% from **7** and **8**; d) $LiOH•H_2O$, THF/H_2O; e) $Pd(OH)_2/C$, H_2, THF/MeOH; f) Et^iPr_2N, DMAP, DPPA, DMF/CH_2Cl_2, 3 mM, 79% from **9**; g) HF•py, THF; h) MsCl, Et_3N, CH_2Cl_2 then DBU, 96% from **10**; i) NBS, Cs_2CO_3, MeCN, 65 ºC, 31%; j) TFA, $CHCl_3$, 96%; k) Ac_2O, CH_2Cl_2, 64%.

Bis-trioxazole **S1**



Synthesis of **S2**: To a solution of trioxazole **7** (1.07 g, 1.80 mmol) in THF-H_2O (3:1, 30 mL), was added LiOH (98.2 mg, 2.34 mmol) at 0 ºC. After stirring at room temperature for 45 min, Dowex® 50WX4 ion-exchange resign was added. The resulting mixture was filtered through a cotton with MeOH, to give carboxylic acid **S2** solution, which was used without further purification. TLC R_f = 0.1 (3:2:1 $CHCl_3$/EtOAc/MeOH)

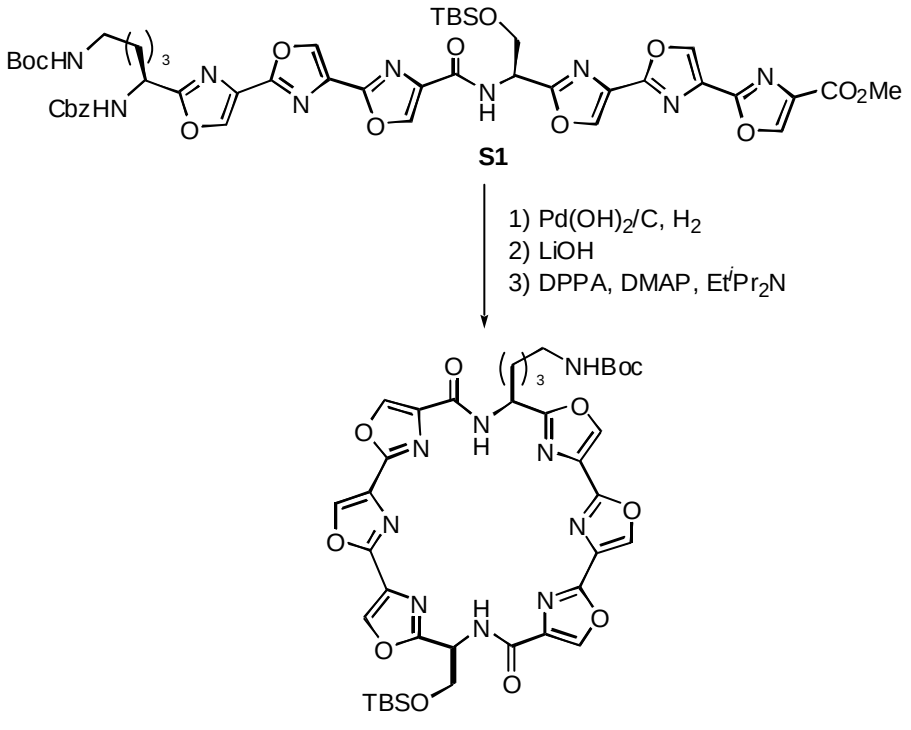
Synthesis of **S3**: to a solution of trioxazole **8** (1.02 g, 1.80 mmol) in MeOH-THF (1:1, 30 mL) was added 20% $Pd(OH)_2$/C (30 mg) and the reaction mixture was stirred at room temperature under an atmosphere of hydrogen gas (balloon). After 14 h, $CHCl_3$ (10 mL) was added to the reaction mixture and was filtered through a pad of celite and eluted with $CHCl_3$-MeOH (1:1). The solution was concentrated in vacuo to give amine **S3**, which was used without further purification. TLC R_f = 0.6 ($CHCl_3$/EtOAc/MeOH 3:2:1)

Synthesis of **S1**: to a solution of carboxylic acid **S2** in THF-H_2O-MeOH (3:1:1), was added the amine **S3**, NMM (400 µL, 3.60 mmol), and DMT-MM (986 mg, 3.60 mmol), and the mixture was stirred at room temperature. After stirring for 25 h, the reaction mixture was concentrated and the resulting mixture was extracted with $CHCl_3$. The organic layer was washed with 0.1 N HCl and H_2O, dried over $MgSO_4$, filtrated and concentrated in vacuo. The residue was purified on silica gel ($CHCl_3$-

AcOEt-MeOH = 3:2:1) to give bis-trioxazole **S1** (1.64 g, 91%, 3 steps). TLC R_f = 0.8 ($CHCl_3$/EtOAc/MeOH 3:2:1)

Spectral data for **S1**: $[\alpha]_D^{25}$ = 11.9 (*c* 1.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) *d* 8.43 (s, 1H), 8.32 (m, 5H), 7.85 (d, *J* = 8.7Hz, 1H), 7.35 (m, 5H), 5.56 (m, 2H), 5.12 (s, 2H), 5.03 (m, 1H), 4.56 (br, 1H), 4.23 (dd, *J* = 4.2, 10.2 Hz, 1H), 4.08 (dd, *J* = 4.8 10.2 Hz, 1H), 3.95 (s, 3H), 3.10 (br, 2H), 2.03 (br, 1H), 1.95 (m, 1H), 1.40 (m, 13H), 0.84 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) *d* 165.5, 163.4, 161.2, 159.9, 156.0, 155.8, 155.4, 154.4, 143.9, 141.6, 139.7, 139.6, 139.3, 139.1, 136.7, 136.0, 134.4, 130.9, 130.8, 128.5, 128.2, 128.15, 79.2, 67.2, 64.1, 52.3, 49.3, 49.26, 39.8, 35.5, 29.5, 28.4, 25.7, 22.3, 18.1, -5.6; HRMS (ESI, M+Na) calcd for $C_{47}H_{55}N_9O_{14}SiNa$ 1020.3535, found 1020.3498.

Macrocyclic bisamide **10**

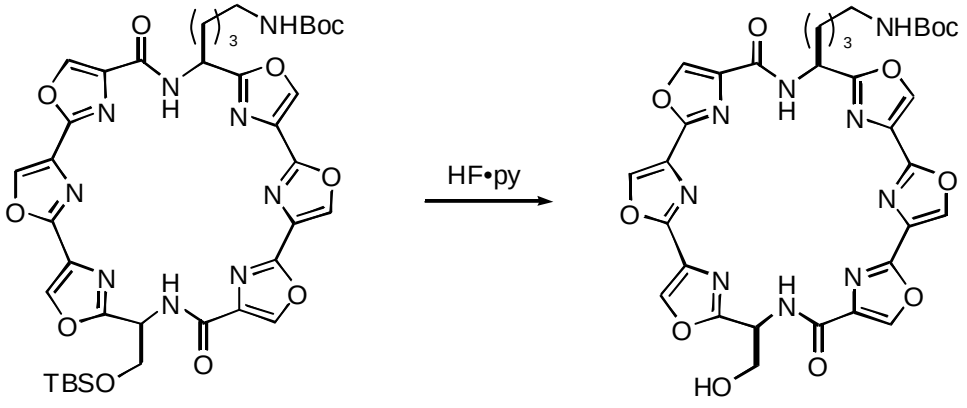


To a solution of bis-trioxazole **S1** (310 mg, 0.311 mmol) in MeOH/THF (1:1, 30 mL), and 20% $Pd(OH)_2$/C (15 mg) was added. The mixture was stirred at room temperature under hydrogen (balloon) for 3 h. The reaction mixture was filtered through a pad of Celite and the filtrates were concentrated in vacuo to give amine. The crude amine was dissolved in THF-H_2O (3:1, 10 mL) and lithium hydroxide (23.5 mg, 0.560 mmol) was added at 0 ºC and was stirred at room temperature for 0.5 h. To the re-

action mixture was added Dowex® 50WX4 ion-exchange resign. The resulting mixture was filtered through a cotton with MeOH, and the filtrates were concentrated in vacuo to give amino acid. To a solution of the crude amino acid in DMF-CH_2Cl_2 (1:2, 100 mL) was added DMAP (179 mg, 1.47 mmol), diisopropylethylamine (250 µL, 1.47 mmol), and DPPA (320 µL, 1.47 mmol). The resulting mixture was stirred for another 3 days at room temperature. To the reaction mixture was added H_2O and the organic layer was extracted with AcOEt. The extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel column (AcOEt-MeOH = 100:1) to give **9** as a pale yellow solid (179 mg, 69%, 3 steps). TLC R_f = 0.7 (3:2:1 $CHCl_3$/EtOAc/MeOH)

Spectral data for **9**: $[\alpha]^{25}_D$ = 22.1 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) *d* 8.54 (d, *J* = 7.3 Hz, 1H), 8.50 (d, *J* = 7.3 Hz, 1H), 8.23-8.19 (m, 6H), 5.42 (m, 2H), 4.17 (dd, *J* = 4.6, 9.6 Hz, 1H), 3.97 (dd, *J* = 6.4, 9.6 Hz 1H), 3.06 (br, 2H), 2.30 (m, 1H), 2.09 (m, 1H), 2.00 (m, 1H), 1.48 (m, 13H), 0.81 (s, 9H), 0.00 (s, 3H), -0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *d* 164.7, 163.8, 159.9, 159.8, 156.1, 156.0, 155.9, 154.6, 140.9, 139.2, 138.4, 138.3, 136.9, 136.8, 130.9, 129.8, 129.6, 79.0, 64.5, 50.2, 47.9, 40.3, 34.5, 29.7, 29.5, 28.4, 25.7, 21.9, 18.2, -5.56; HRMS (ESI, M+Na) calcd for $C_{38}H_{45}N_9O_{11}Na$ 854.2906, found854.2910.

Macrocyclic bisamide **10**

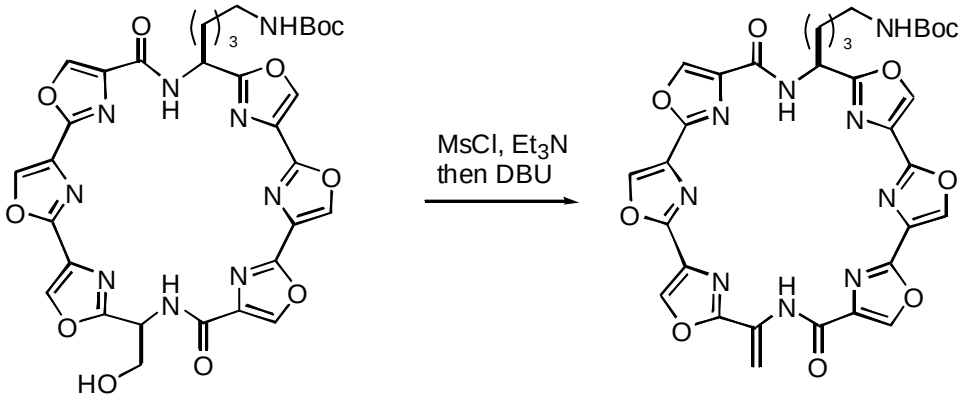


9 **10**

To a solution of **9** (228 mg, 0.275 mmol) in dry THF (40 mL), was added HF•py (1.6 mL) and the mixture was stirred for 2 h. To the reaction mixture was added $NaHCO_3$aq and the organic layer was extracted with AcOEt. The residue was purified by silica gel column (30:20:1 $CHCl_3$/AcOEt/MeOH) to give **10** as a white solid (198 mg, 99%). TLC R_f = 0.5 ($CHCl_3$/EtOAc/MeOH 3:2:1).

Spectral data for **10**: $[\alpha]^{25}_{D}$ –3.1 = (*c* 2.1, $CHCl_3$:MeOH = 3:1); ^{1}H NMR (400 MHz, $[D_6]$DMSO) *d* 9.13 (s, 1H), 9.12 (s, 1H), 9.11 (s, 1H), 9.10 (s, 1H), 8.94 (s, 1H), 8.92 (s, 1H), 8.37 (d, *J* = 7.3 Hz, 1H), 8.31 (d, *J* = 7.3 Hz, 1H), 6.79 (t, *J* = 5.5 Hz, 1H), 5.42 (dt, *J* = 5.5, 6.9 Hz, 1H), 5.36 (dt, *J* = 3.7, 6.9 Hz, 1H), 5.29 (t, *J* = 6.4 Hz, 1H), 3.91 (m, 2H), 2.83 (m, 2H), 2.07 (br, 1H), 1.90 (br, 1H), 1.32-1.28 (br, 12H), 1.05 (br, 1H); ^{13}C NMR (100 MHz, DMSO d-6) *d* 164.5, 163.3, 158.7, 155.8, 155.7, 154.5, 142.5, 141.9, 141.1, 129.8, 128.5, 128.4, 79.1, 77.2, 61.9, 50.5, 47.5, 33.2, 29.1, 28.1, 21.0; HRMS (ESI, M+H) calcd for $C_{32}H_{31}N_9O_{11}Na$ 740.2041, found 740.2027.

Enamide **11**



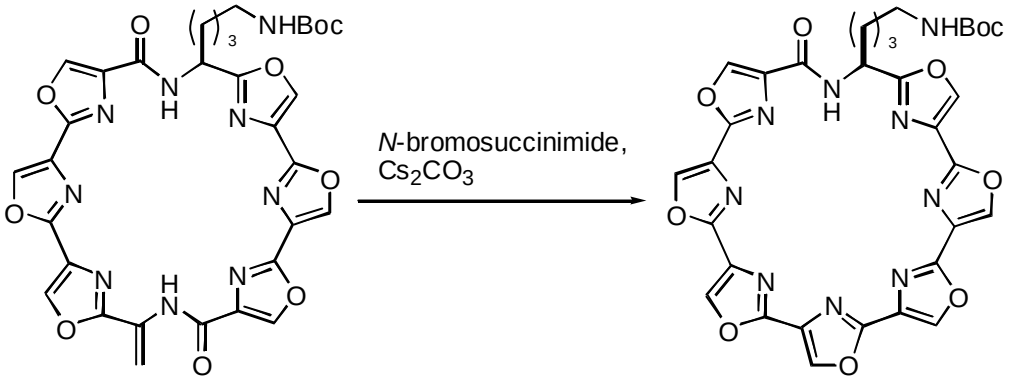
10 **11**

To a solution of **10** (198 mg, 0.275 mmol) in CH_2Cl_2 (60 mL), was added Et_3N (300 µL, 2.75 mmol), MsCl (110 µL, 1.38 mmol), and the mixture was stirred for 1 h at room temperature. To the reaction mixture, was added DBU (420 µL, 2.75 mmol), the mixture was stirred for another 1 h at room temperature. To the reaction mixture was added 0.05 N HCl and the organic layer was extracted with AcOEt, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel ($CHCl_3$/AcOEt/MeOH 3:2:1) to give Enamide **11** as a white solid (186 mg, 97%).). TLC R_f = 0.7 ($CHCl_3$/EtOAc/MeOH 3:2:1)

Spectral data for **11**: $[\alpha]^{25}_{D}$ = -5.3 (*c* 1.8, $CHCl_3$/MeOH 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) *d* 9.72 (s, 1H), 8.63 (d, 1H, *J* = 7.2 Hz), 8.28 (m, 6H), 6.81 (s, 1H), 5.89 (s, 1H), 5.40 (dt, 1H, *J* = 5.5, 7.2 Hz), 4.58 (br, 1H), 3.04 (br, 2H), 2.15 (br, 1H), 1.95 (br, 1H), 1.42 (m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$) *d* 165.7, 159.8, 159.4, 159.0, 156.1, 155.9, 155.8, 154.7, 154.6, 141.8, 140.8, 139.8, 139.5, 138.9, 138.5, 137.3, 136.9,

131.0, 130.9, 130.5, 129.6, 128.0, 104.7, 79.0, 48.0, 40.3, 34.1, 29.5, 28.3, 21.6; HRMS (ESI, M+Na) calcd for $C_{32}H_{29}N_9O_{10}Na$ 722.1935, found 722.1935.

Heptaoxazole **13**



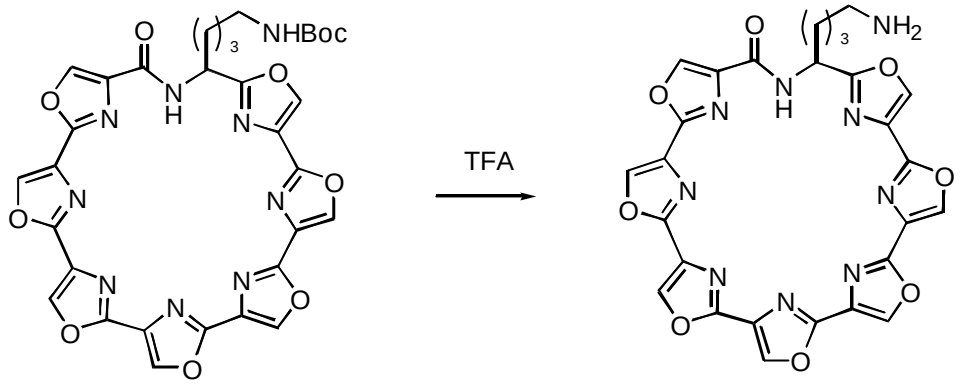
11 **13**

To a solution of **11** (25.3 mg, 36.0 μmol) in MeCN (10 mL), was added Cs_2CO_3 (58.6 mg, 0.18 mmol), *N*-bromosuccineimide (7.0 mg, 0.40 mmol) at room temperature and was heated to 65 ºC. After 14 h, the reaction mixture was filtered through a pad of celite and eluted with $CHCl_3$. The residue was purified by silica gel ($CHCl_3$/AcOEt/MeOH 3:2:1) to give heptaoxazole **13** as a pale yellow solid (9.0 mg, 36%). TLC R_f = 0.2 ($CHCl_3$/EtOAc/MeOH 3:2:2).

Spectral data for **12**: ^{1}H NMR (400 MHz, [D_6]DMSO) *d* 9.08 (s, 1H), 9.04 (s, 1H), 9.03 (s, 1H), 9.02 (s, 1H), 8.92 (s, 1H), 8.87 (s, 1H), 8.52 (br, 1H), 6.81 (t, *J* = 5.0 Hz, 1H), 5.40 (dt, *J* = 5.5, 6.9 Hz, 1H), 4.83 (d, *J* = 10 Hz, 1H), 4.72 (d, *J* = 10 Hz, 1H), 2.82 (m, 2H), 2.48 (m, 4H), 2.00 (br, 1H), 1.88 (br, 1H), 1.32-1.27 (br, 13H); HRMS (ESI, M+Na) calcd for $C_{86}H_{32}N_{10}O_{12}Na$ 819.2098, found 819.2092. TLC R_f = 0.6 ($CHCl_3$/EtOAc/MeOH 3:2:2).

Spectral data for **13**: $[\alpha]_D^{25}$ = 14.1 (*c* 0.3, MeOH); ^{1}H NMR (400 MHz, DMSO d-6) *d* 9.00 (s, 1H), 8.95 (s, 1H), 8.94 (s, 1H), 8.90 (s, 1H), 8.86 (s, 1H), 8.85 (s, 1H), 8.82 (s, 1H), 8.44 (br, 1H), 6.73 (dd, *J* = 5.0, 6.0 Hz, 1H), 5.45 (br, 1H), 2.76 (dt, *J* = 5.0, 5.9 Hz, 2H), 1.98 (br, 1H), 1.83 (br, 1H), 1.26 (br, 13H); ^{13}C NMR (100 MHz, CD_3OD) *d* 165.5, 161.6, 158.4, 157.9, 157.5, 157.3, 156.2, 144.5, 142.4, 142.3, 142.0, 141.2, 140.3, 139.8, 137.7, 131.4, 130.8, 130.6, 130.0, 79.7, 40.9, 35.0, 30.6, 28.7, 22.5; HRMS (ESI, M+Na) calcd for $C_{32}H_{27}N_9O_{10}Na$ 720.1779, found 720.1773.

L1H1-7OTD (**6**)

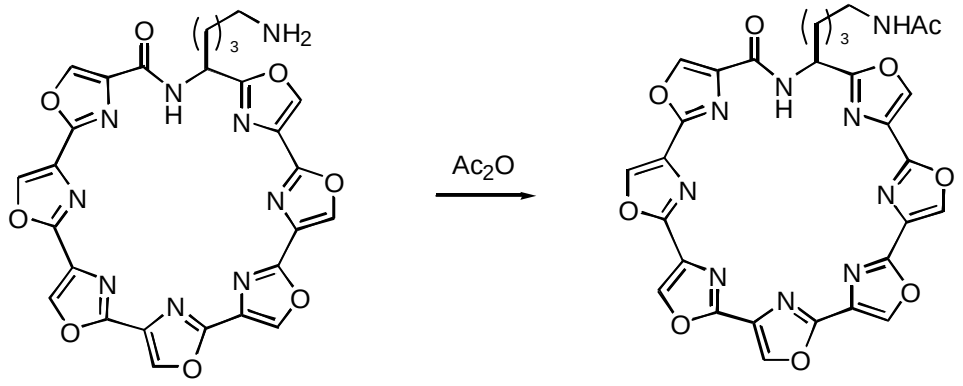


13 **6**

To a solution of **13** (31.0 mg, 44.4 μmol) in $CHCl_3$ (9.5 mL), was added TFA (0.5 mL) and the mixture was stirred for 24 h. The reaction mixture was concentrated in vacuo to give L1H1-7OTD (**6**) as a white solid (27.0 mg, 99%).

Spectral data for L1H1-7OTD (**6**): $[\alpha]_D^{25}$ = -77.2 (*c* 0.9, MeOH); ^{1}H NMR (400 MHz, $[D_6]$DMSO) *d* 8.97 (s, 1H), 8.93 (s, 1H), 8.86 (s, 1H), 8.83 (br, 2H), 8.71 (s, 1H), 8.66 (s, 1H), 8.06 (br, 2H), 7.62 (br, 1H), 5.33 (dt, *J* = 4.6, 5.5 Hz, 1H), 3.22 (br, 2H), 2.06 (m, 1H), 1.70 (br, 3H), 1.24 (br, 1H), 0.91 (br, 1H); ^{13}C NMR (100 MHz, DMSO d-6) *d* 163.1, 158.6, 155.7, 155.3, 155.2, 154.8, 154.2, 142.8, 142.6, 140.9, 140.8, 140.6, 140.4, 139.9, 139.7, 139.1, 139.0, 138.7, 138.5, 135.7, 129.4, 128.8, 128.7, 128.6, 127.9, 47.8, 47.6, 32.4, 26.5, 19.5; HRMS (ESI, M+H) calcd for $C_{27}H_{20}N_9O_8$ 598.1435, found 598.1467.

L1A1-7OTD (**14**)

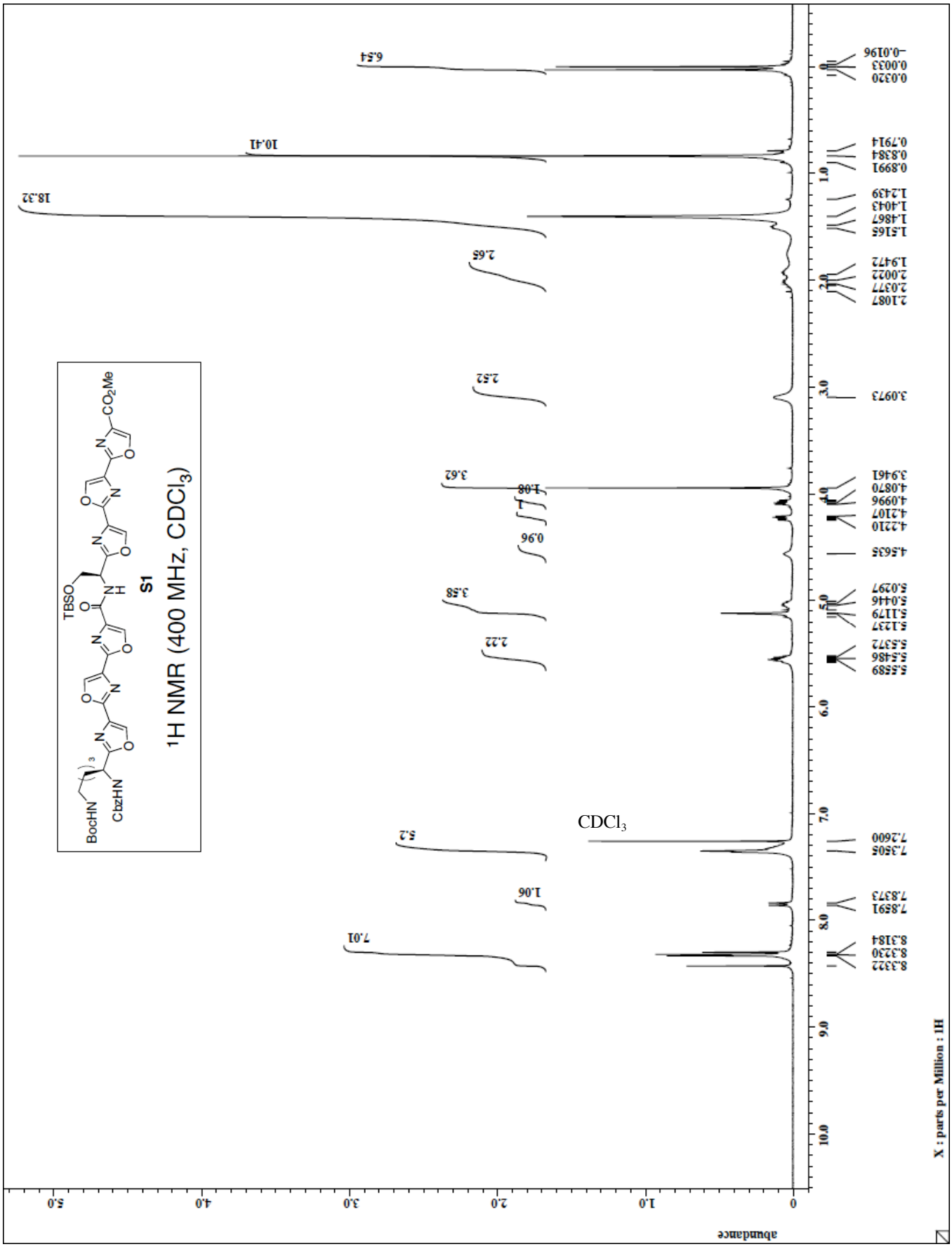


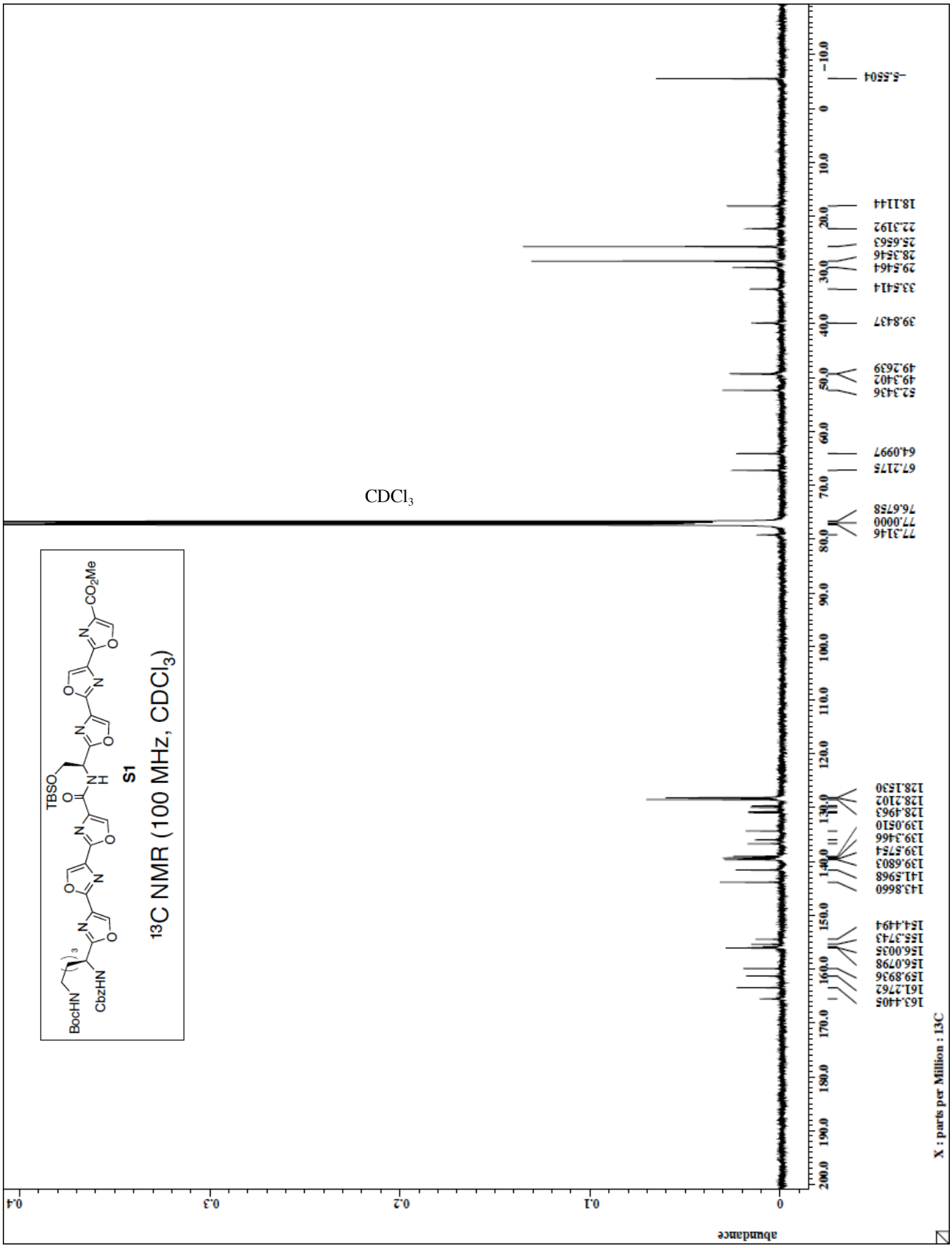
6 **14**

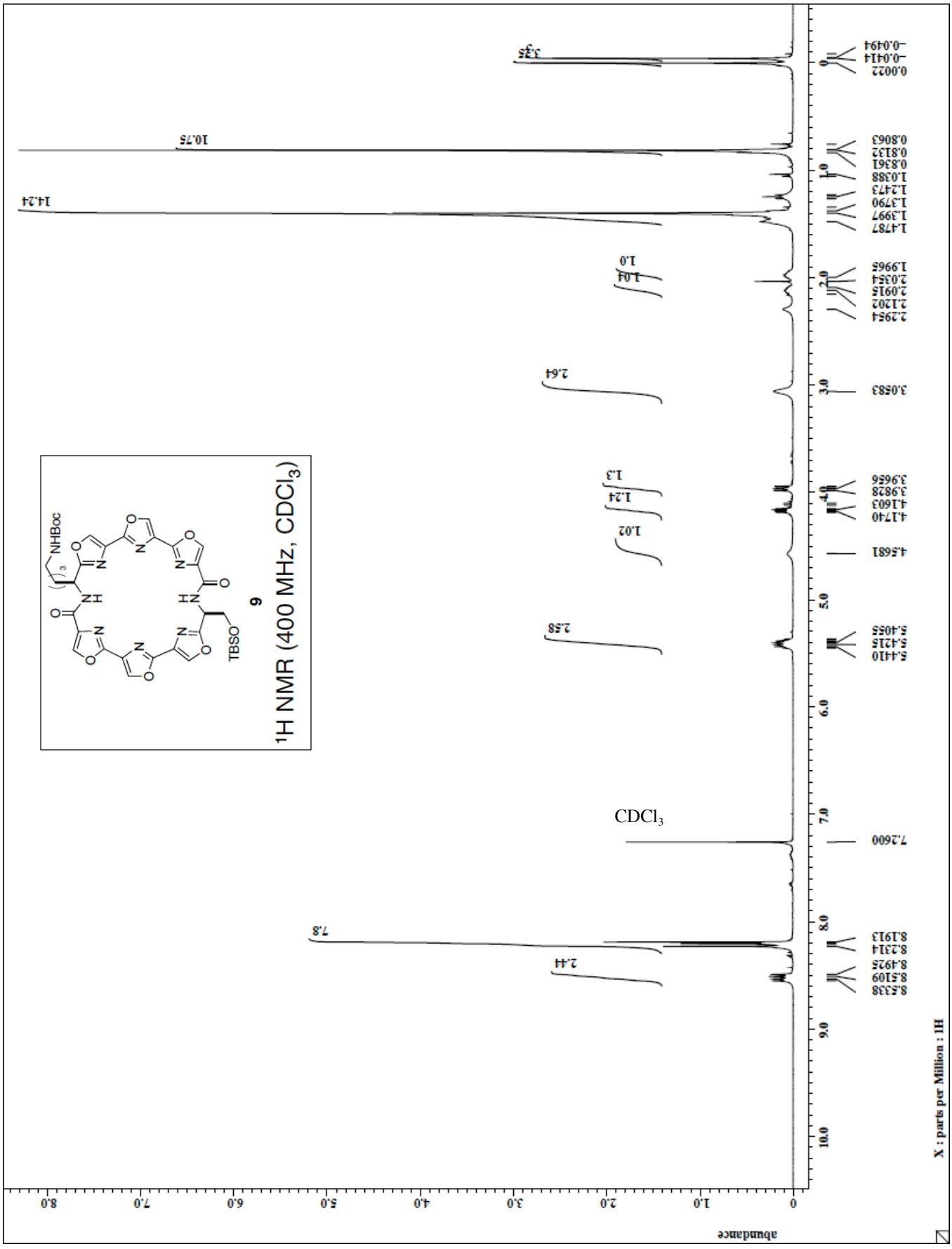
To a solution of **6** (18.0 mg, 30.1 μmol) in CH_2Cl_2 (2 mL) was added Ac_2O (1 mL) and the reaction mixture was stirred at 70 ºC. After 13 h, the reaction mixture was concentrated in vacuo and the residue was chromatographed on silica gel ($CHCl_3$/MeOH 3:2) to give L1A1-7OTD (**14**) as a brown powder (11.5 mg, 64%). TLC R_f = 0.1 ($CHCl_3$/EtOAc/MeOH 3:2:2). CD_3OD

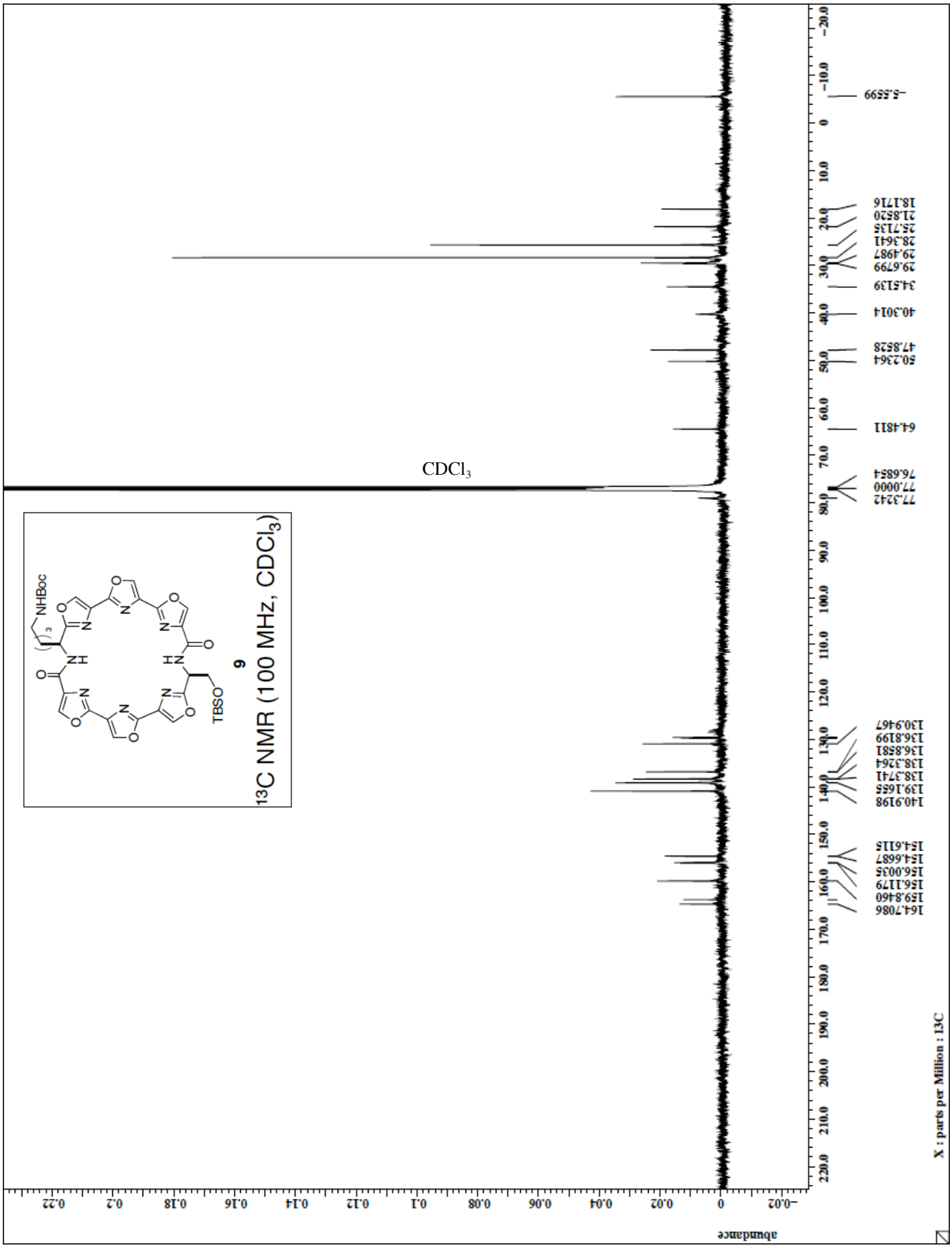
Spectral data for L1A1-7OTD (**14**): $[\alpha]_D^{25}$ = 1.3 (*c* 1.2, $CHCl_3$:MeOH = 5:1); ^{1}H NMR (400 MHz, [D_6]DMSO) *d* 8.97 (s, 1H), 8.94 (s, 1H), 8.90 (s, 1H), 8.88 (s, 1H), 8.82 (s, 1H), 8.81 (m, 2H), 8.47 (d, *J* = 7.0 Hz, 1H), 7.76 (t, *J* = 5.2 Hz, 1H), 5.43 (dt, *J* = 5.5, 7.0 Hz, 1H), 2.88 (dt, *J* = 5.2, 6.5 Hz, 2H), 1.96 (m, 1H), 1.84 (m, 1H), 1.67 (s, 3H), 1.28 (br, 3H), 1.00 (br, 1H); ^{13}C NMR (100 MHz, DMSO d-6) *d* 168.8, 163.8, 159.4, 155.7, 155.6, 155.4, 155.3, 155.2, 154.4, 143.2, 140.7, 139.7, 138.9, 138.5, 136.4, 129.8, 129.4, 129.3, 129.2, 128.5, 47.6, 38.2, 33.7, 28.6, 22.5, 21.3; HRMS (ESI, M+Na) calcd for $C_{29}H_{21}N_9O_9Na$ 662.1360, found 662.1343.

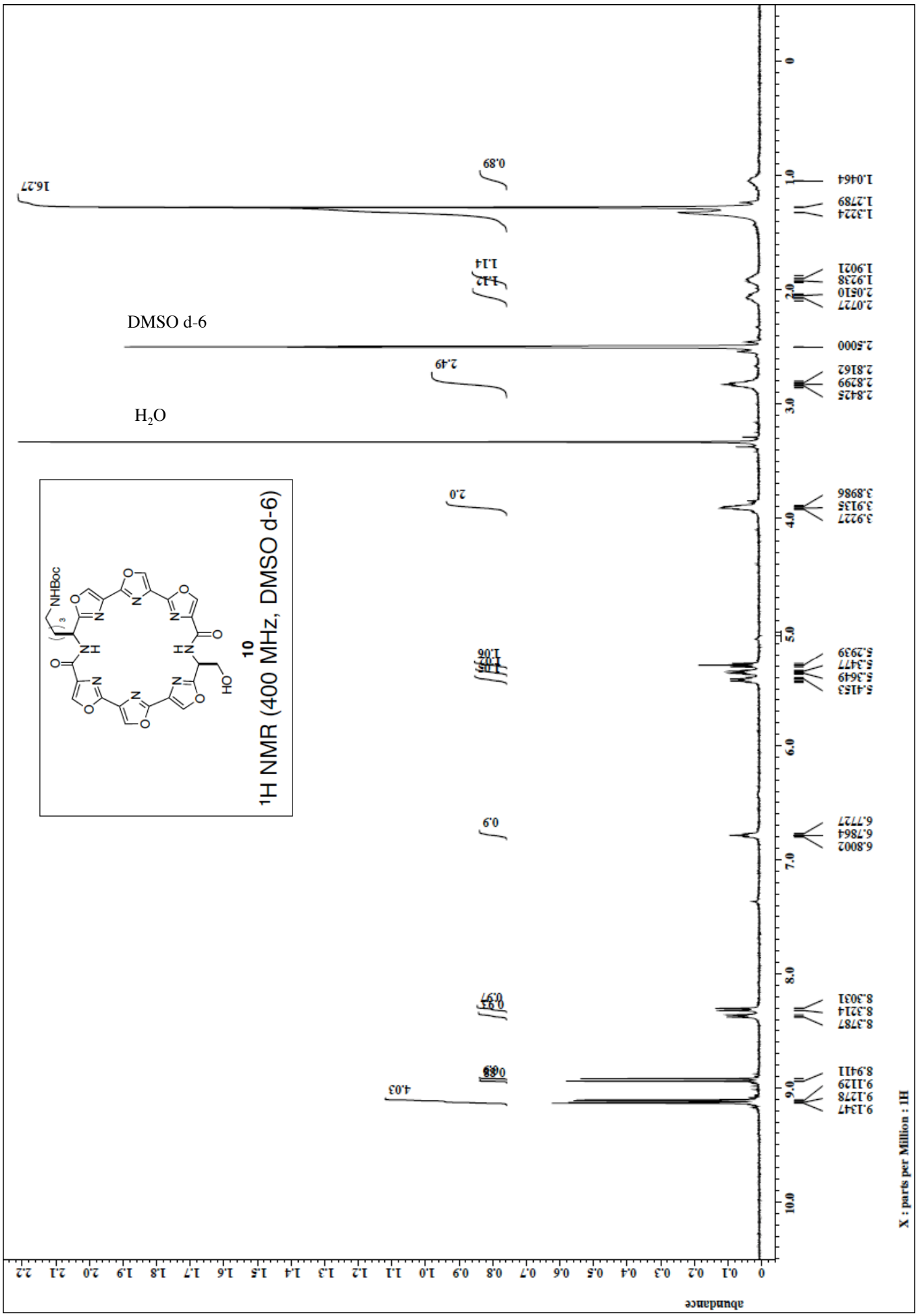
Copies of NMR spectra of compounds **6**-**14**.

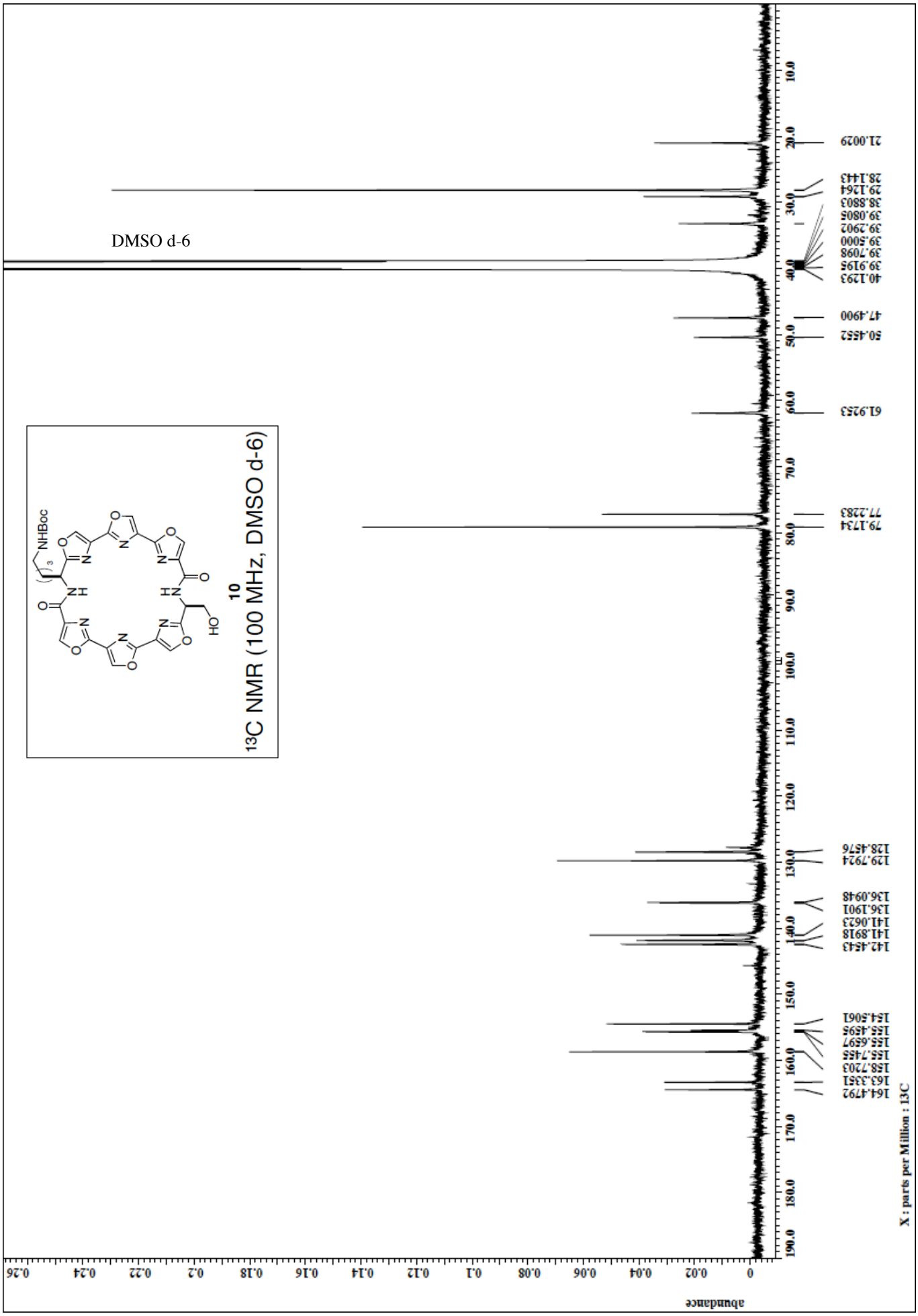



^{13}C NMR (100 MHz, $CDCl_3$)
S1
$CDCl_3$
X : parts per Million : 13C
abundance


^{1}H NMR (400 MHz, CDCl$_3$)
9
NHBoc
TBSO
CDCl$_3$
abundance
X : parts per Million : 1H


9
^{13}C NMR (100 MHz, $CDCl_3$)
$CDCl_3$
X : parts per Million : 13C
abundance


10
^{1}H NMR (400 MHz, DMSO d-6)
NHBoc
OH
H_2O
DMSO d-6
16.27
4.03
2.49
2.0
0.9
0.89
1.14
1.12
1.06
1.05
0.97
0.93
0.89
9.1347
9.1278
9.1129
8.9411
8.3787
8.3214
8.3031
6.8002
6.7864
6.7727
5.4153
5.3649
5.3477
5.2939
3.9227
3.9135
3.8986
2.8425
2.8299
2.8162
2.5000
2.0727
2.0510
1.9238
1.9021
1.3224
1.2789
1.0464
abundance
X : parts per Million : 1H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10
13C NMR (100 MHz, DMSO d-6)
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29.1264
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39.0805
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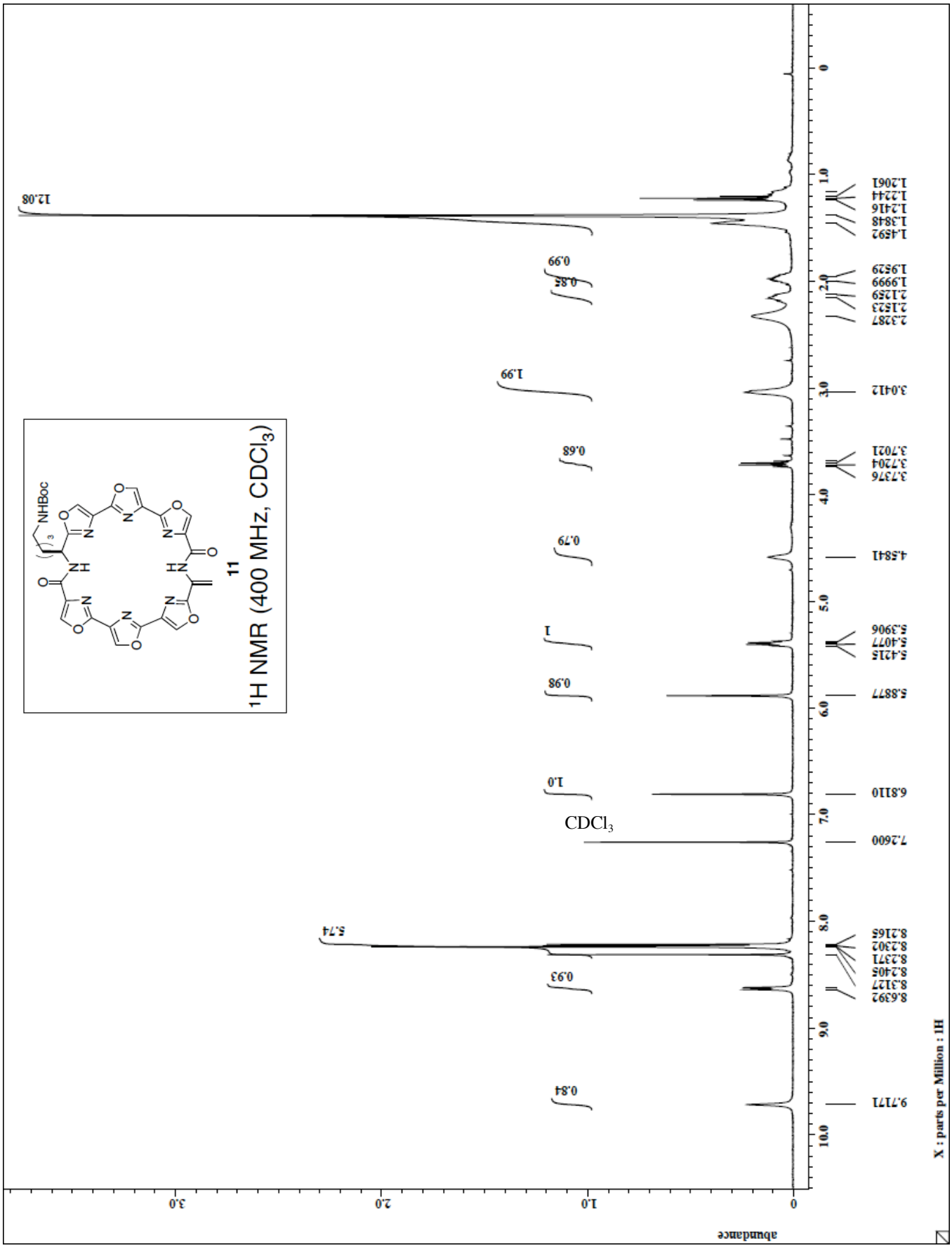
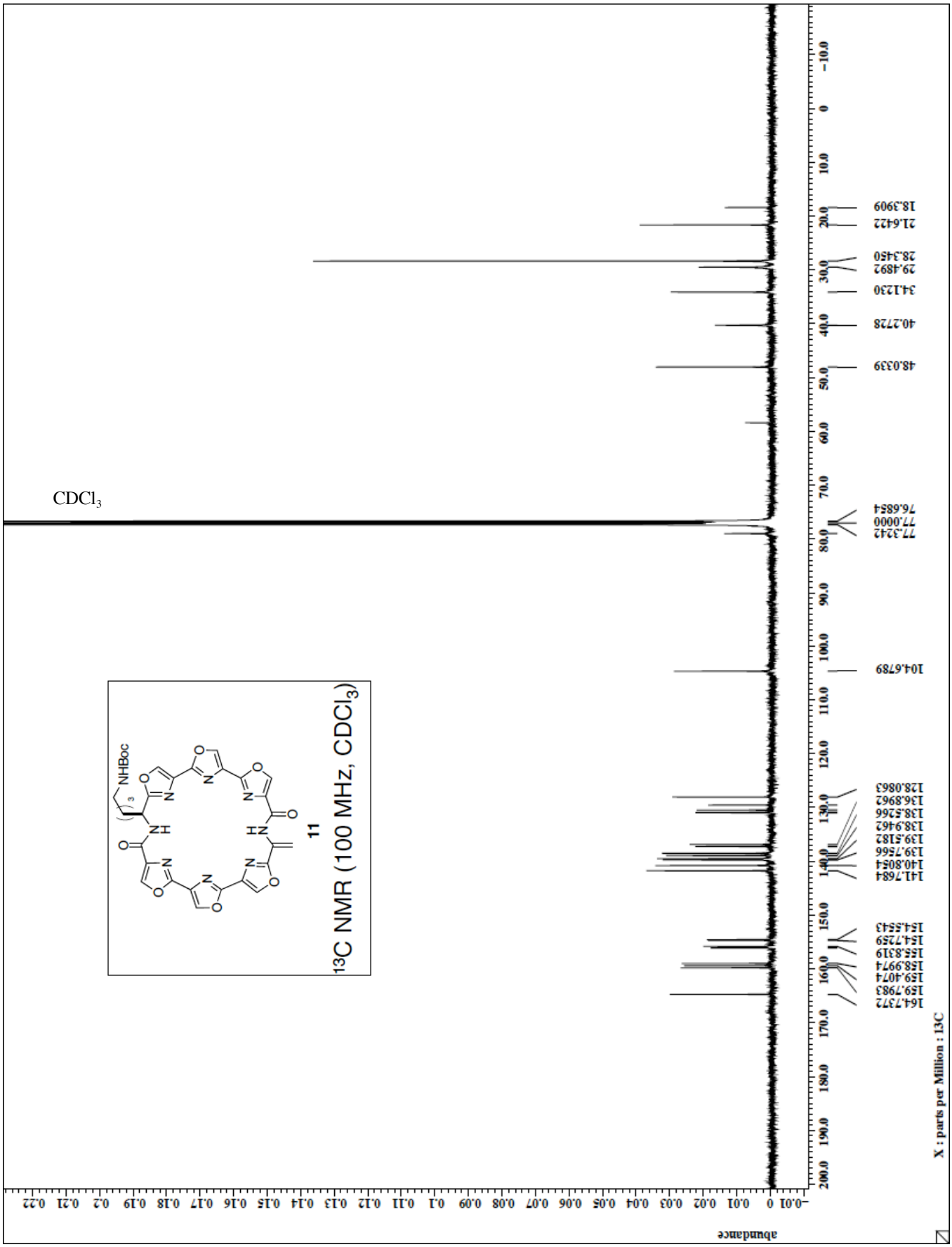
39.5000
39.7098
39.9195
40.1293
47.4900
50.4552
61.9253
77.2283
79.1734
128.4576
129.7924
136.0948
136.1901
141.0623
141.8918
142.4543
154.5061
155.4596
155.6597
155.7455
158.7203
163.3351
164.4792
X : parts per Million : 13C
abundance


11
^{1}H NMR (400 MHz, $CDCl_3$)
NHBoc
$CDCl_3$
X : parts per Million : 1H
abundance


CDCl3
11
13C NMR (100 MHz, CDCl3)
NHBoc
3
X : parts per Million : 13C
abundance
164.7372
159.7983
159.4074
158.9974
155.8319
154.7259
154.5543
141.7684
140.8054
139.7566
139.5182
138.9462
138.5266
136.8962
128.0863
104.6789
77.3242
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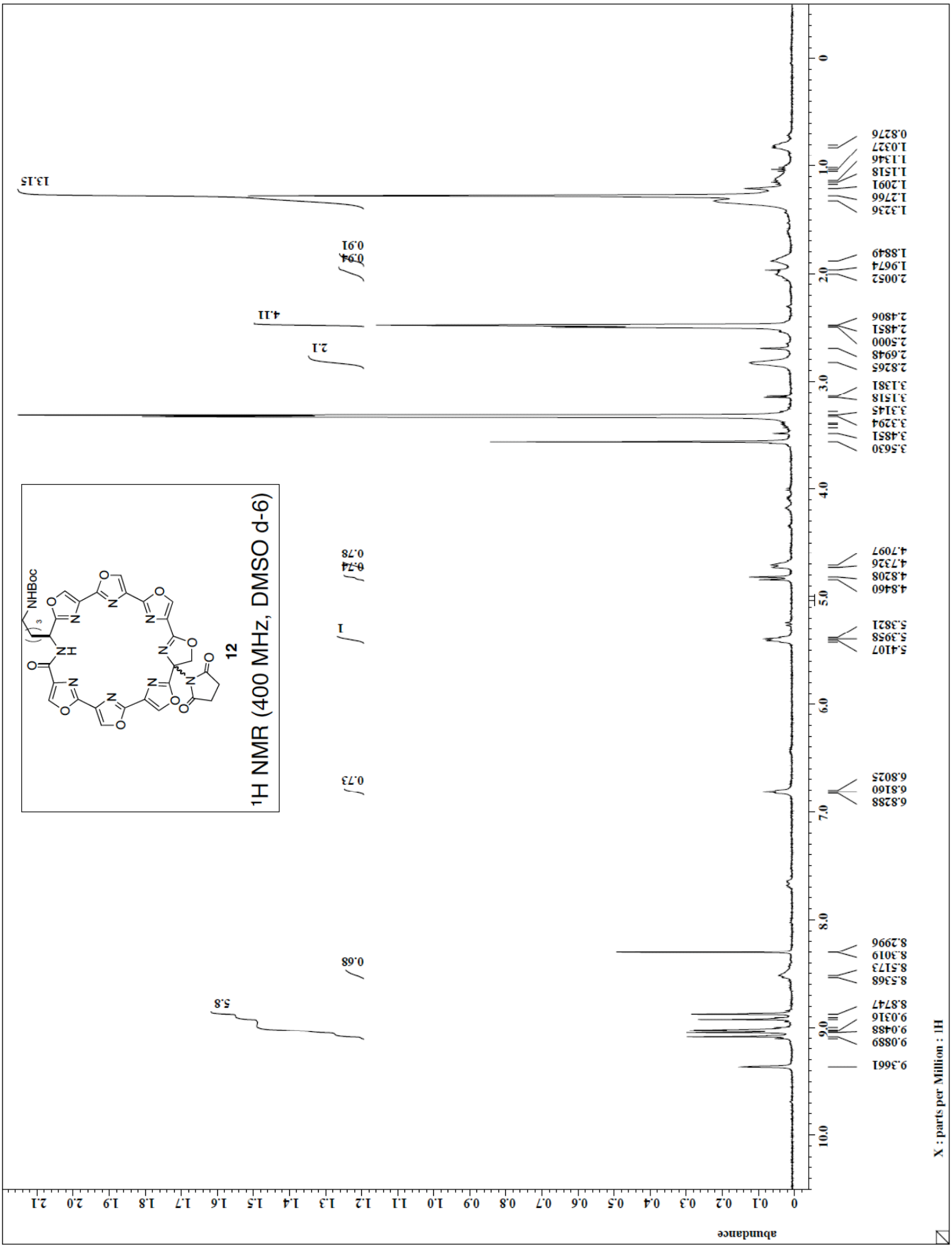
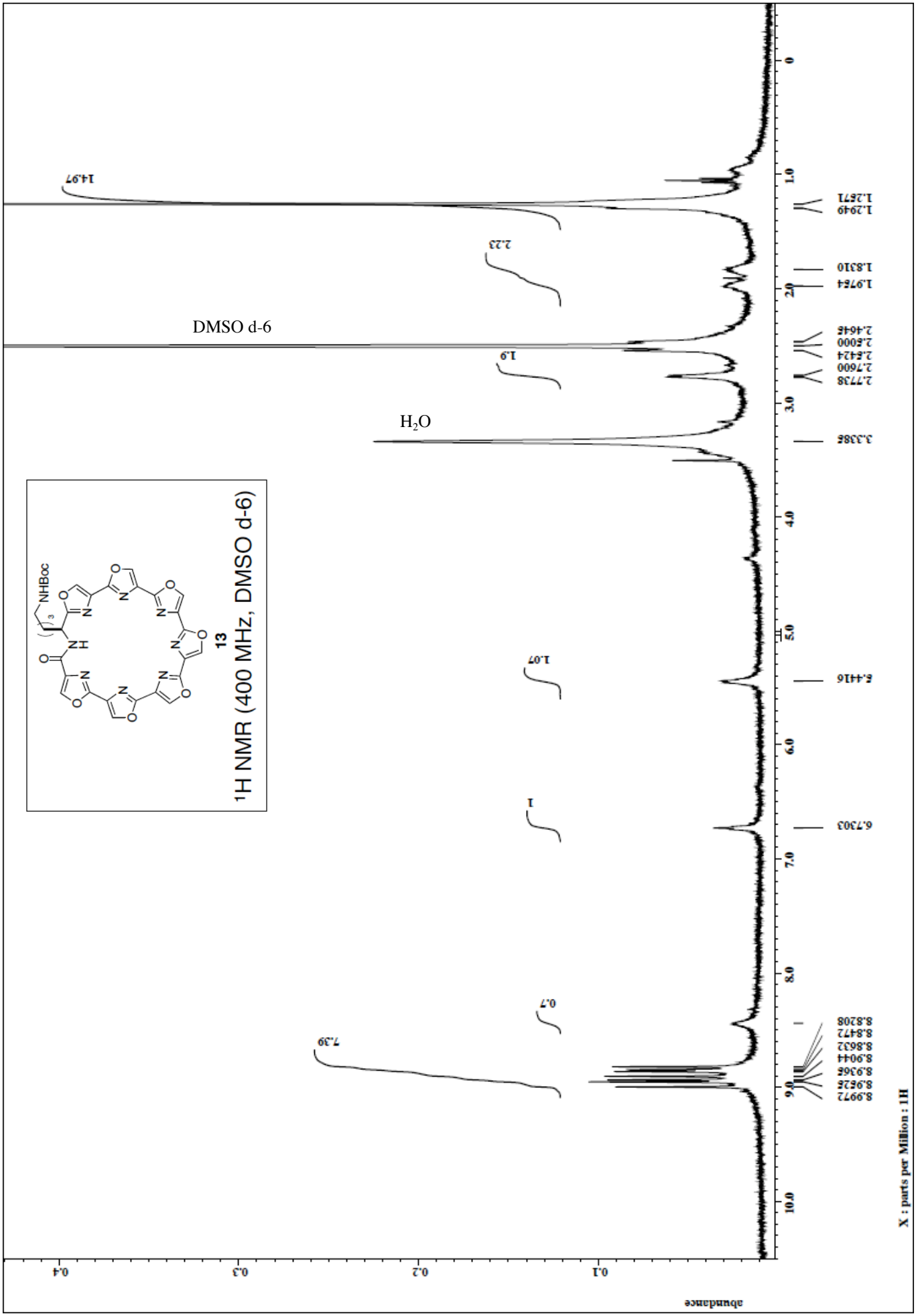
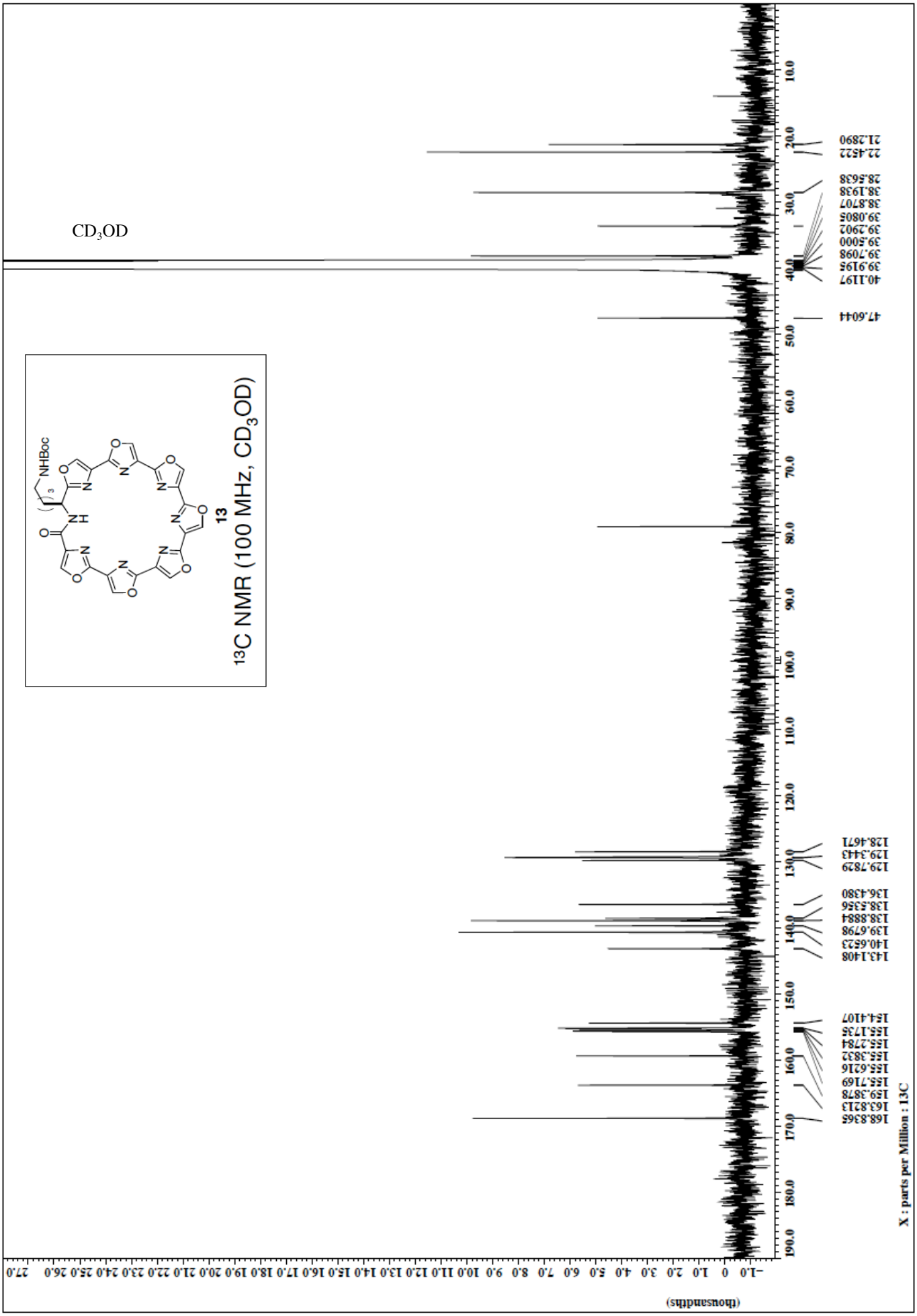
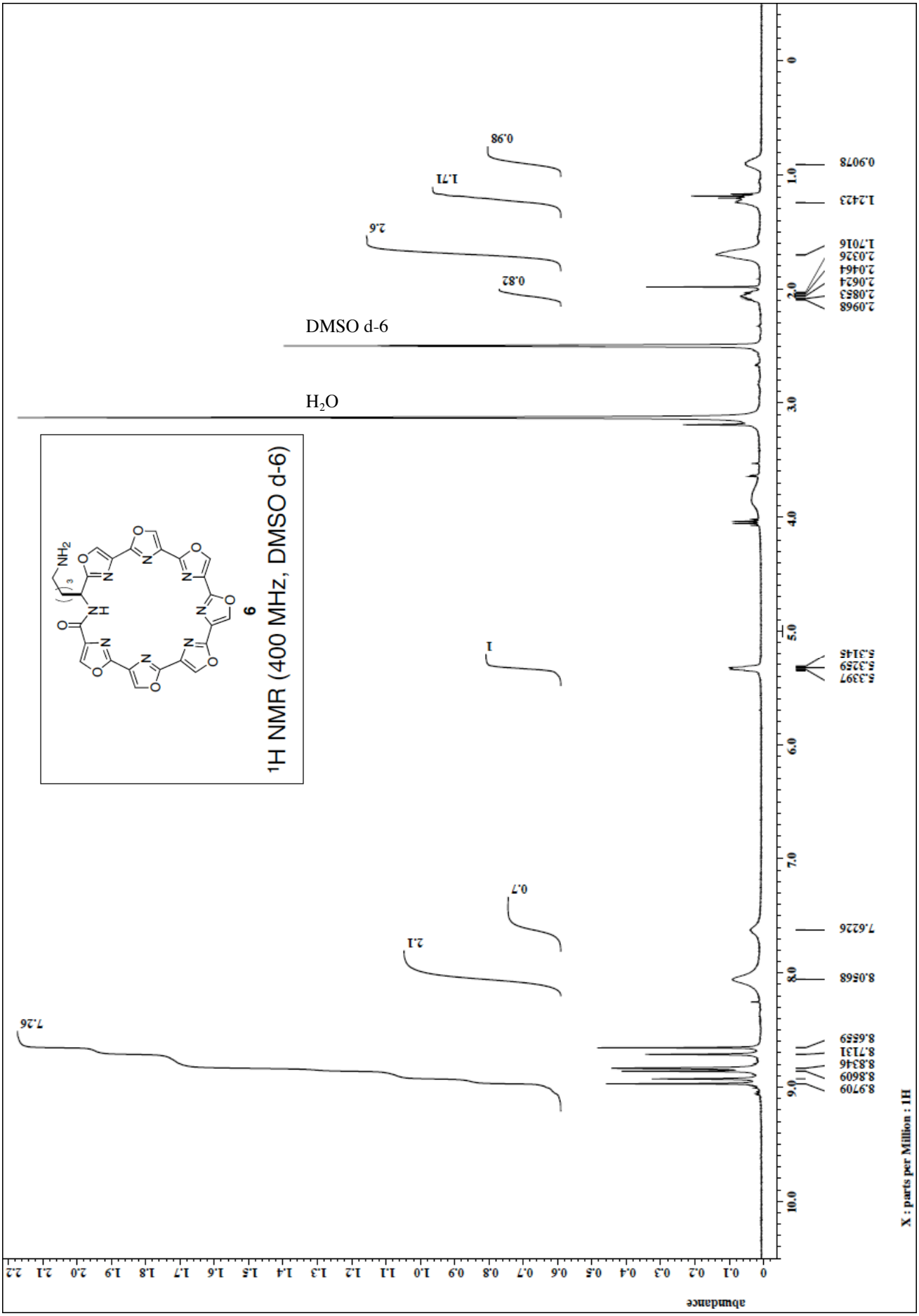
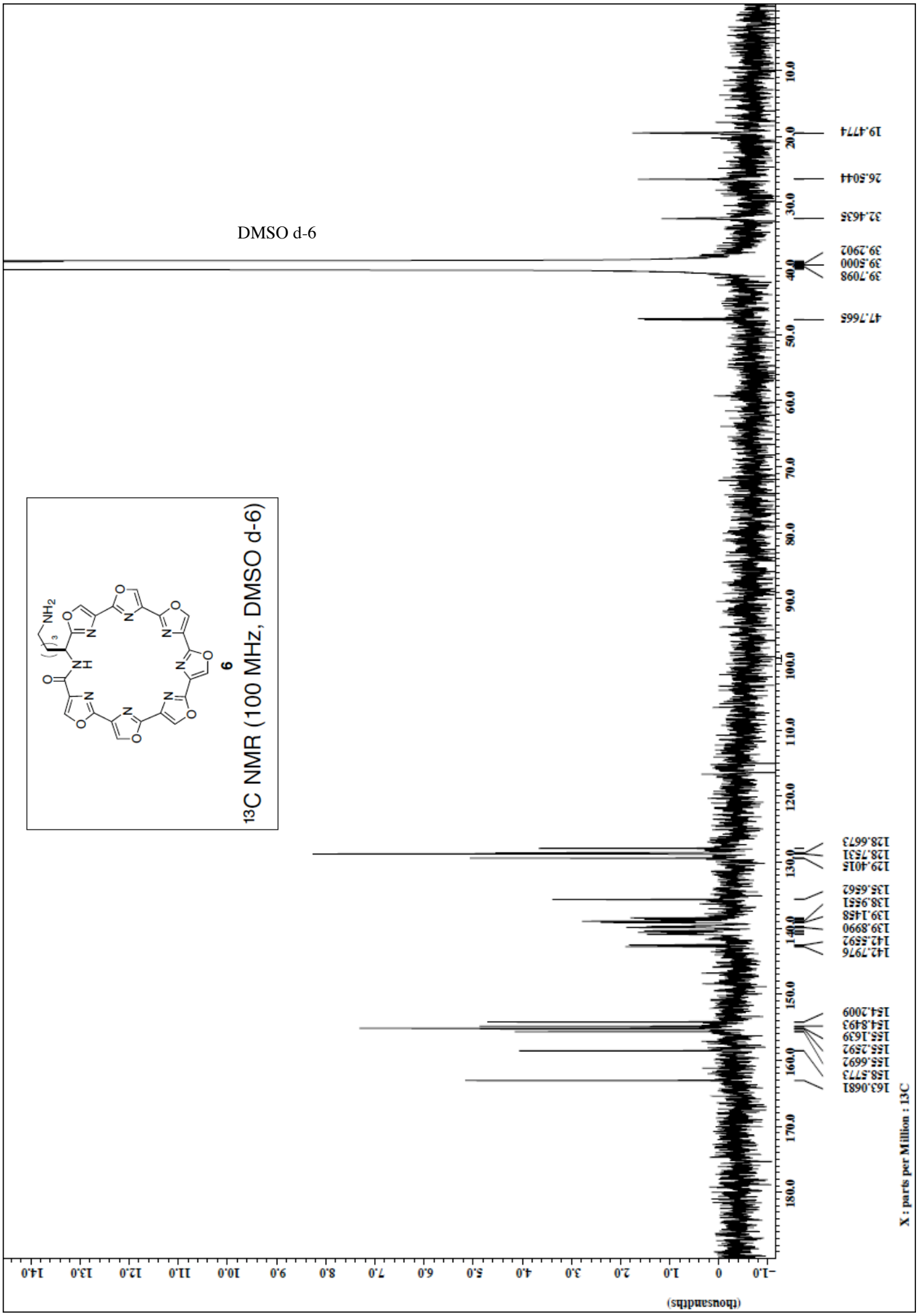
34.1230
29.4892
28.3450
21.6422
18.3909

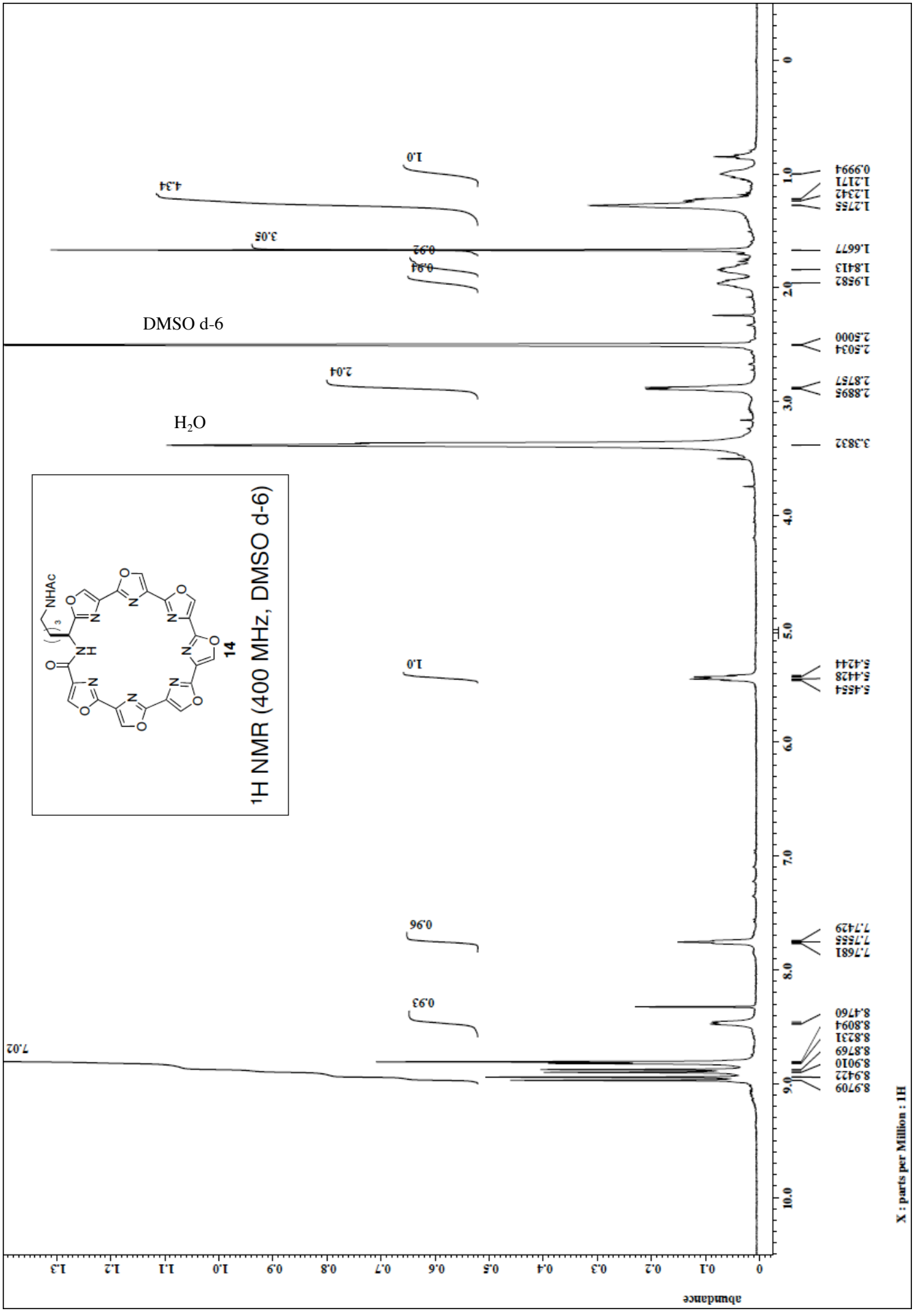

1H NMR (400 MHz, DMSO d-6)
12
NHBoc
X : parts per Million : 1H
abundance

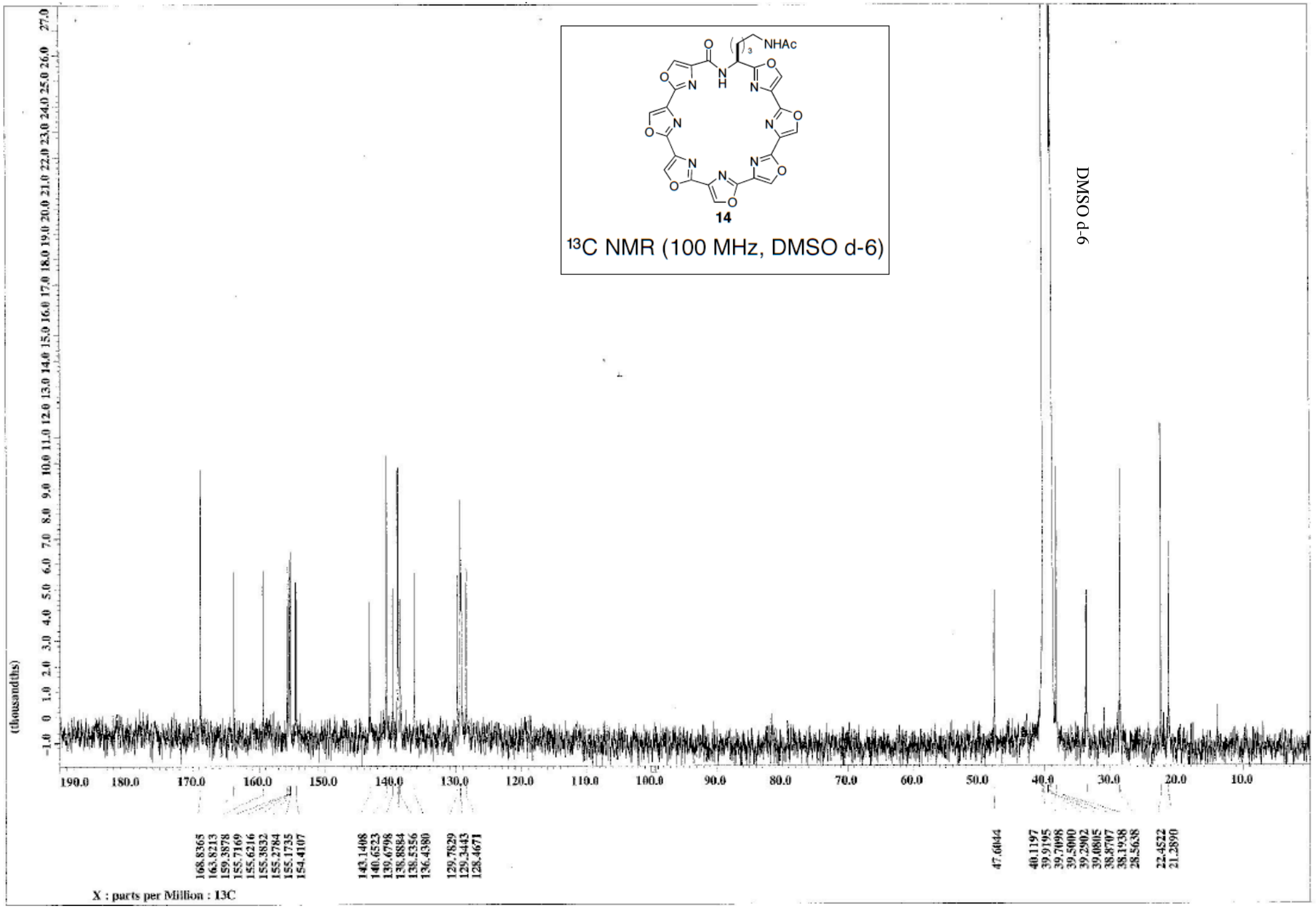

13
^{1}H NMR (400 MHz, DMSO d-6)
DMSO d-6
H_2O
X : parts per Million : 1H
abundance


13
^{13}C NMR (100 MHz, CD_3OD)
CD_3OD
NHBoc
168.8365
163.8213
159.3878
155.7169
155.6216
155.3832
155.2784
155.1735
154.4107
143.1408
140.6523
139.6798
138.8884
138.5356
136.4380
129.7829
129.3443
128.4671
47.6044
40.1197
39.9195
39.7098
39.5000
39.2902
39.0805
38.8707
38.1938
28.5638
22.4522
21.2890
X : parts per Million : 13C
(thousandths)


^{1}H NMR (400 MHz, DMSO d-6)
6
H_2O
DMSO d-6
X : parts per Million : 1H
abundance
8.9709
8.8609
8.8346
8.7131
8.6559
8.0568
7.6226
5.3397
5.3259
5.3145
2.0968
2.0853
2.0624
2.0464
2.0326
1.7016
1.2423
0.9078
7.26
2.1
0.7
1
0.82
2.6
1.71
0.98


DMSO d-6
^{13}C NMR (100 MHz, DMSO d-6)
6
19.4774
26.5044
32.4635
39.2902
39.5000
39.7098
47.7665
128.6673
128.7531
129.4015
135.6562
138.9551
139.1458
139.8990
142.5592
142.7976
154.2009
154.8493
155.1639
155.3592
155.6692
158.5773
163.0681
X : parts per Million : 13C
(thousandths)


^{1}H NMR (400 MHz, DMSO d-6)
14
NHAc
DMSO d-6
H_2O
X : parts per Million : 1H
abundance


NHAc
14
13C NMR (100 MHz, DMSO d-6)
DMSO d-6
(thousandths)
X : parts per Million : 13C
168.8365
163.8213
159.3878
155.7169
155.6216
155.3832
155.2784
155.1735
154.4107
143.1408
140.6523
139.6798
138.8884
138.5356
136.4380
129.7829
129.3443
128.4671
47.6044
40.1197
39.9195
39.7098
39.5000
39.2902
39.0805
38.8707
38.1938
28.5638
22.4522
21.3890

CD experiment

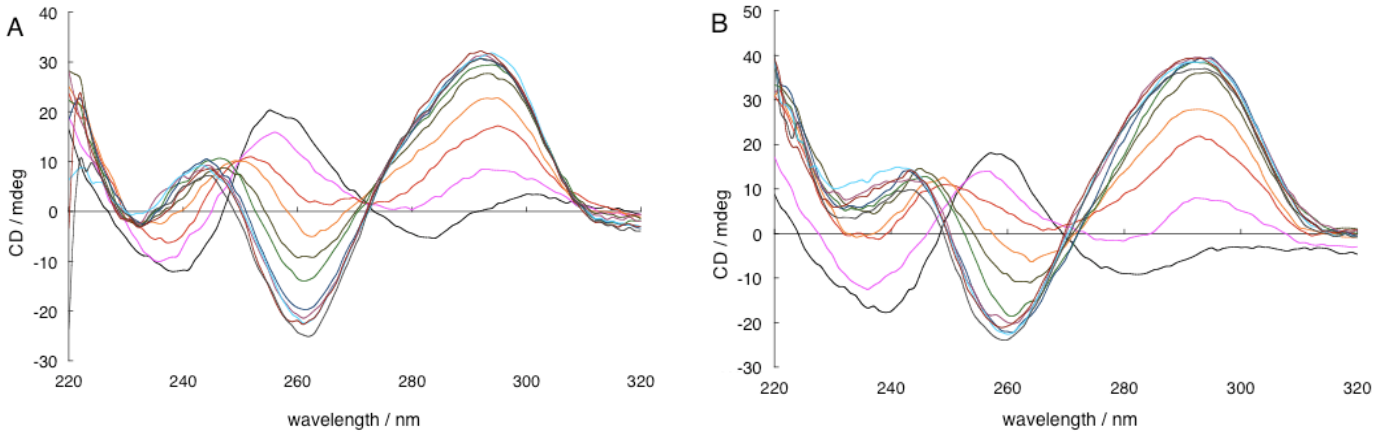


Figure S1. CD spectra of 10 μM ss-telo24 in Tris-HCl buffer (50 mM, pH 7.6, no salt added) in the presence of (A) 5-50 μM of L1H1-7OTD (**6**) and (B) 10-100 μM of L1A1-7OTD (**14**). All CD spectra were a representation of three averaged scans taken at 25 ºC. The signal baselines were corrected for signal contributions due to the buffer and DMSO for the samples containing **6** and **14**.

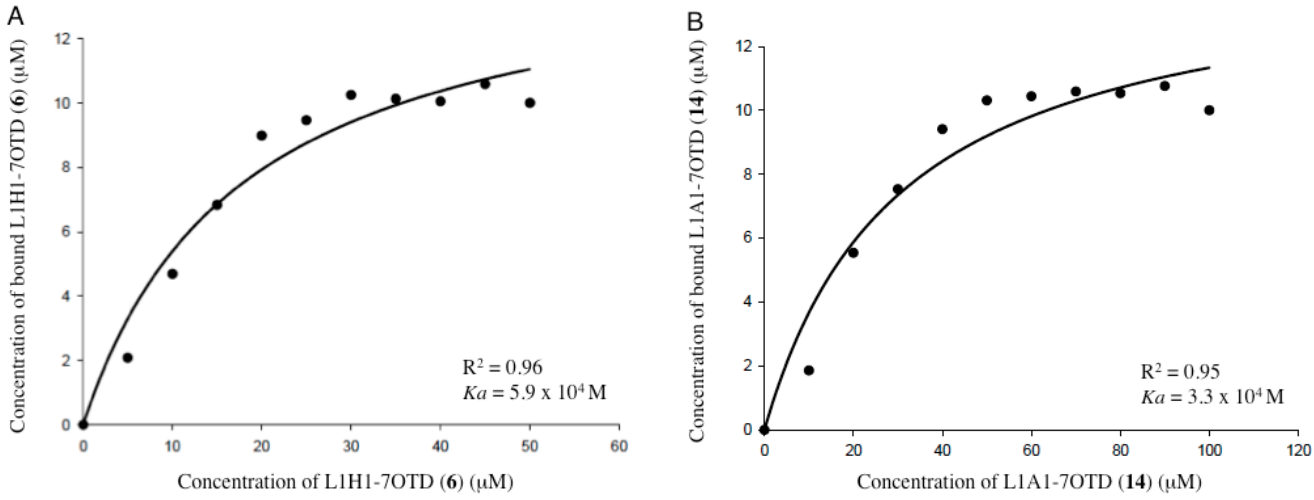


Figure S2. *Ka* values of L1H1-7OTD (**6**) and L1A1-7OTD (**14**) against ss-telo24 were calculated by one site saturation model of SigmaPlot^{R} ver.11 on the basis of CD/mdeg values at 292 nm in figure S1. (A) The binding constant *Ka* of L1H1-7OTD (**6**) was obtained with 5.9 x 10^4 M. (B) In the case of L1A1-7OTD (**14**), *Ka* was obtained with 3.3 x 10^4 M.

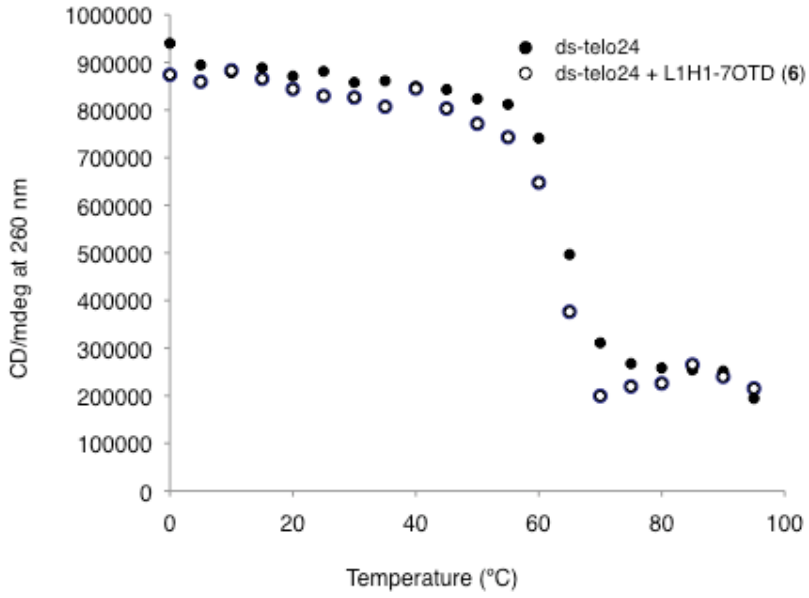


Figure S3. The CD melting curves of ds-telo24 (10 μM) at 260 nm in the absence or presence of L1H1-7OTD (**6**) (50 μM).

EMSA

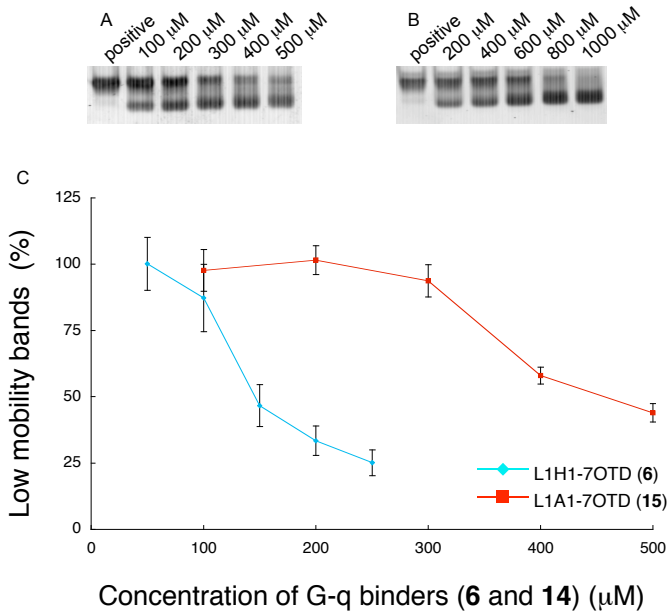


Figure S4. Effects of L1H1-7OTD (**6**) and L1A1-7OTD (**14**) on the formation of intramolecular G-quadruplex with ss-telo24 oligonucleotide. (A) ss-telo24 (50 μM) was incubated for 60 min with various concentrations of L1H1-6OTD (**6**) in 50 mM Tris-HCl buffer (pH 7.6). After incubation, samples were mixed with ficol 400 and run a 12% native PAGE with 1 x TBE at 4 ºC. All oligonucleotides were stained by Stains-all. (B) L1A1-6OTD (**14**) was used as G-quadruplex ligand. (C) The quantification of the fluorescent intensity by using phosphorimager. The oligonucleotides were quantified using ImageQuant 5.1 from Molecular Dynamics. Results represent means ± SEM of four independent experiments. EC_{50} values were calculated by the following equation. (intensity of the low mobility band in the presence of **6** or **14**) / (intensity of positive control band).

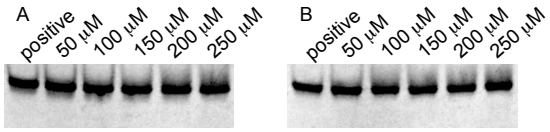


Figure S5. Evaluation of the interaction with ds-telo24 and L1H1-7OTD (**6**). EMSA of ds-telo24 (25 μM) in the presence of 7OTDs by native PAGE was performed. The ds-telo24 was incubated in the presence of various concentrations of (A) L1H1-7OTD (**6**) and (B) L1A1-7OTD (**14**) for 60 min in 50 mM Tris-HCl buffer. After incubation, samples were mixed with ficol 400 and run a 12% native PAGE with 1 x TBE at 4 ºC. All oligonucleotides were stained by ethidium bromide.

PCR stop assay

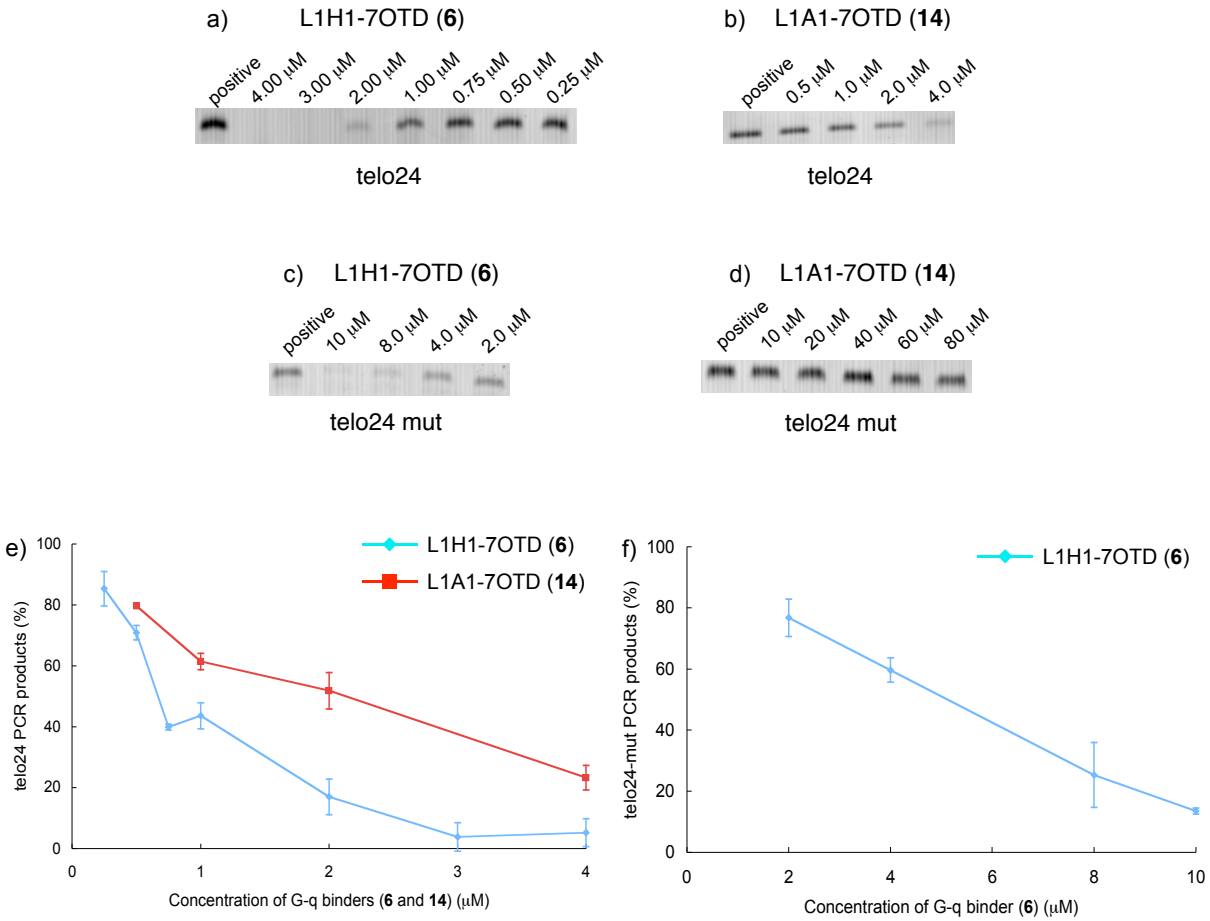


Figure S6. PCR stop assay of L1H1-7OTD (**6**) and L1A1-7OTD (**14**). Top panel presented the PCR product; a) **6**-telo24, b) **14**-telo24, c) **6**-telo24 mut, d) **14**-telo24 mut. Lower panel presented the quantification of the fluorescent intensity by using phosphorimager; e) (**6** and **14**)-telo24, f) **6**-telo24 mut. Results represent means +/-SD of three independent experiments. PCR inhibitory activities were calculated by the following equation. (intensity of the band in the presence of **6** or **14**) / (intensity of positive control band).

MTT assay

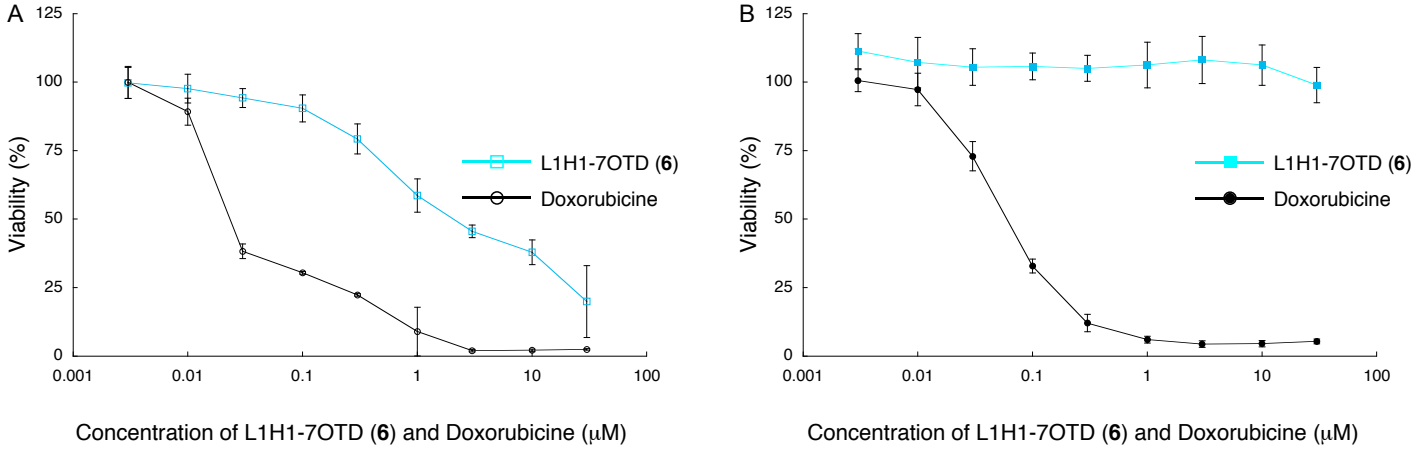


Figure S7. Dose-response curve of 6 days incubation of (A) HeLa cells and (B) Saos-2 cells in the presence of L1H1-7OTD (**6**) (open and blue squares) or Doxorubicin (open and black circles). Results represent means ± SD of five independent experiments.