Supporting information

Synthesis of macrocyclic hexaoxazoles with tri-substituted side chains and their stabilization ability of telomeric G-quadruplex

Yue Ma [1], Keisuke Iida [2], Shogo Sasaki [1], Takatsugu Hirokawa [3,4,5], Brahim Heddi [6], Anh-Tuân Phan [6], Kazuo Nagasawa [1,*]

1. Department of Biotechnology and Life Science, Tokyo University of Agriculture and Technology, 2-24-16 Naka-cho, Koganei, Tokyo 184-8588 (Japan)
2. Department of Chemistry, Chiba University, 1-33 Yayoi, Inage, Chiba 263-8522 (Japan)
3. Transborder Medical Research center, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, 305-8575 (Japan)
4. Division of Biomedical Science, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, 305-8575 (Japan)
5. Molecular Profiling Research Center for Drug Discovery, National Institute of Advanced Industrial Science and Technology, 2-4-7 Aomi, Koto-ward, Tokyo 135-0064 (Japan)
6. Division of Physics and Applied Physics, Nanyang Technological University, Singapore 637371 (Singapore)

*E-mail: knaga@cc.tuat.ac.jp

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1. Supplementary Tables

Table S1. Sequences of oligonucleotides used in this paper

Oligonucleotide	Sequence
Flu-telo21	5’-FAM-d[GGG TTA GGG TTA GGG TTA GGG]-TAMRA-3’
Flu-*c-kit*	5’-FAM-d[GGG AGG GCG CTG GGA GGA GGG]-TAMRA-3’
Flu-*K-ras*	5’-FAM-d[AGG GCG GTG TGG GAA GAG GGA AGA GGG GGA GG]-TAMRA-3’
Flu-dsDNA	5’-FAM-d[TAT AGC TAT ATT TTT TTA TAG CTA TA]-TAMRA-3’
telo24	5’-d[TTA GGG TTA GGG TTA GGG TTA GGG]- 3’

Table S2. Energy profiles of docking study of top 100 poses for compounds **3**, **4a**, **4b**, **5a**, and **5b** with parallel-type telomeric G4.

	3	4a	4b	5a	5b
1	-9.055	-10.328	-10.329	-10.434	-10.612
2	-8.48	-10.242	-10.287	-10.277	-10.594
3		-10.111	-10.27	-10.229	-10.544
4		-10.037	-10.253	-10.161	-10.492
5		-9.754	-10.242	-10.039	-10.441
6		-9.681	-10.221	-9.982	-10.396
7		-9.596	-10.205	-9.831	-10.378
8		-9.553	-10.184	-9.808	-10.356
9		-9.521	-10.128	-9.753	-10.344
10		-9.439	-10.089	-9.721	-10.202
11		-9.438	-9.994	-9.715	-10.188
12		-9.43	-9.978	-9.693	-10.038
13		-9.429	-9.939	-9.667	-10.035
14		-9.32	-9.938	-9.642	-10.032
15		-9.308	-9.874	-9.636	-10.03
16		-9.307	-9.872	-9.629	-10.002
17		-9.282	-9.822	-9.609	-9.97
18		-9.267	-9.806	-9.588	-9.97
19		-9.265	-9.789	-9.537	-9.967
20		-9.257	-9.78	-9.492	-9.963
21		-9.254	-9.759	-9.47	-9.956
22		-9.252	-9.754	-9.4	-9.953
23		-9.24	-9.693	-9.388	-9.941
24		-9.184	-9.684	-9.382	-9.927
25		-9.175	-9.635	-9.382	-9.914
26		-9.168	-9.63	-9.38	-9.908
27		-9.161	-9.619	-9.366	-9.875
28		-9.147	-9.615	-9.363	-9.87
29		-9.103	-9.609	-9.361	-9.869
30		-9.061	-9.603	-9.361	-9.858
31		-9.021	-9.595	-9.314	-9.856
32		-9.011	-9.554	-9.275	-9.853
33		-8.988	-9.554	-9.27	-9.847
34		-8.978	-9.543	-9.258	-9.833
35		-8.974	-9.531	-9.251	-9.822
36		-8.967	-9.52	-9.249	-9.815
37		-8.96	-9.492	-9.178	-9.804
38		-8.954	-9.49	-9.177	-9.803
39		-8.934	-9.458	-9.17	-9.789
40		-8.898	-9.454	-9.164	-9.778
41		-8.889	-9.454	-9.15	-9.775
42		-8.883	-9.446	-9.137	-9.765
43		-8.872	-9.439	-9.134	-9.762
44		-8.786	-9.417	-9.121	-9.752
45		-8.744	-9.389	-9.103	-9.704
46		-8.728	-9.387	-9.102	-9.68
47		-8.691	-9.366	-9.097	-9.671
48		-8.685	-9.358	-9.087	-9.668
49		-8.627	-9.329	-9.085	-9.647
50		-8.614	-9.319	-9.071	-9.62
51		-8.501	-9.293	-9.061	-9.587
52		-8.46	-9.28	-9.061	-9.577
53		-8.457	-9.25	-9.042	-9.563
54		-8.448	-9.249	-9.042	-9.562
55		-8.423	-9.249	-9.036	-9.556
56		-8.394	-9.242	-9.03	-9.551
57		-8.392	-9.236	-9.023	-9.551
58		-8.377	-9.229	-9.013	-9.55
59		-8.356	-9.203	-9.007	-9.513
60		-8.343	-9.196	-8.994	-9.51
61		-8.331	-9.188	-8.988	-9.503
62		-8.308	-9.183	-8.974	-9.47
63		-8.306	-9.171	-8.973	-9.451
64		-8.286	-9.169	-8.97	-9.447
65		-8.26	-9.148	-8.964	-9.437
66		-8.257	-9.098	-8.958	-9.412
67		-8.224	-9.091	-8.941	-9.412
68		-8.22	-9.075	-8.933	-9.397
69		-8.217	-9.037	-8.923	-9.392
70		-8.198	-9.004	-8.916	-9.389
71		-8.174	-9.003	-8.915	-9.388
72		-8.114	-9.002	-8.882	-9.34
73		-8.081	-8.981	-8.88	-9.339
74		-8.06	-8.976	-8.88	-9.313
75		-8.055	-8.966	-8.876	-9.299
76		-8.028	-8.963	-8.854	-9.255
77		-8.005	-8.957	-8.852	-9.238
78		-7.977	-8.954	-8.851	-9.23
79		-7.969	-8.942	-8.842	-9.201
80		-7.967	-8.925	-8.822	-9.173
81		-7.951	-8.915	-8.811	-9.169
82		-7.949	-8.911	-8.795	-9.169
83		-7.945	-8.892	-8.792	-9.157
84		-7.942	-8.871	-8.777	-9.147
85		-7.929	-8.854	-8.777	-9.132
86		-7.923	-8.837	-8.757	-9.124
87		-7.911	-8.813	-8.738	-9.12
88		-7.908	-8.781	-8.733	-9.087
89		-7.904	-8.741	-8.718	-9.084
90		-7.897	-8.731	-8.639	-9.083
91		-7.897	-8.714	-8.611	-9.083
92		-7.879	-8.702	-8.595	-9.067
93		-7.878	-8.668	-8.579	-9.056
94		-7.836	-8.654	-8.565	-9.047
95		-7.527	-8.646	-8.485	-9.039
96		-7.501	-8.006	-8.403	-9.015
97		-7.272	-7.916	-8.153	-8.965
98		-7.195	-7.712	-7.675	-8.931
99		-7.172	-7.457	-7.503	-8.916
100		-7.07	-7.43	-7.38	-8.827

2. Supplementary Figures

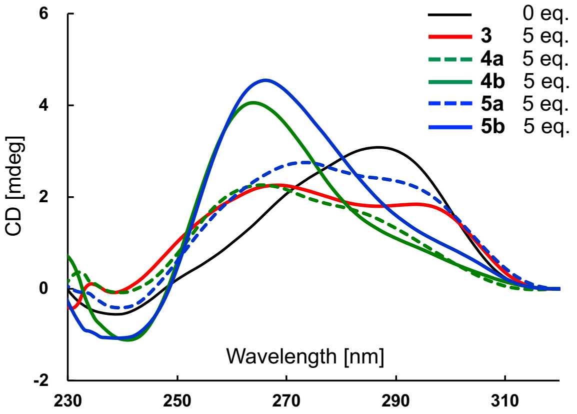


Figure S1. CD spectra of **3**, **4a**, **4b**, **5a**, and **5b** in the presence of telomeric G4 under potassium condition

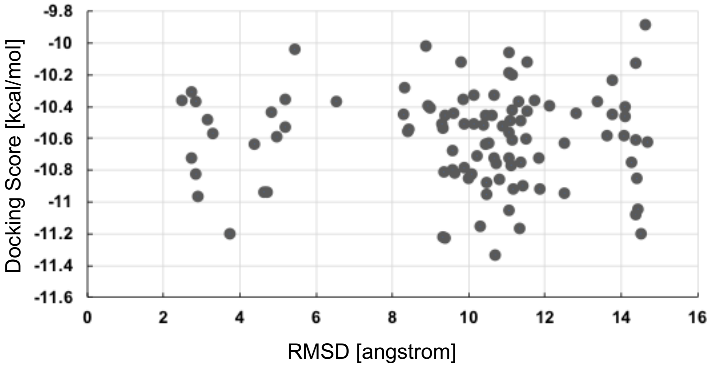
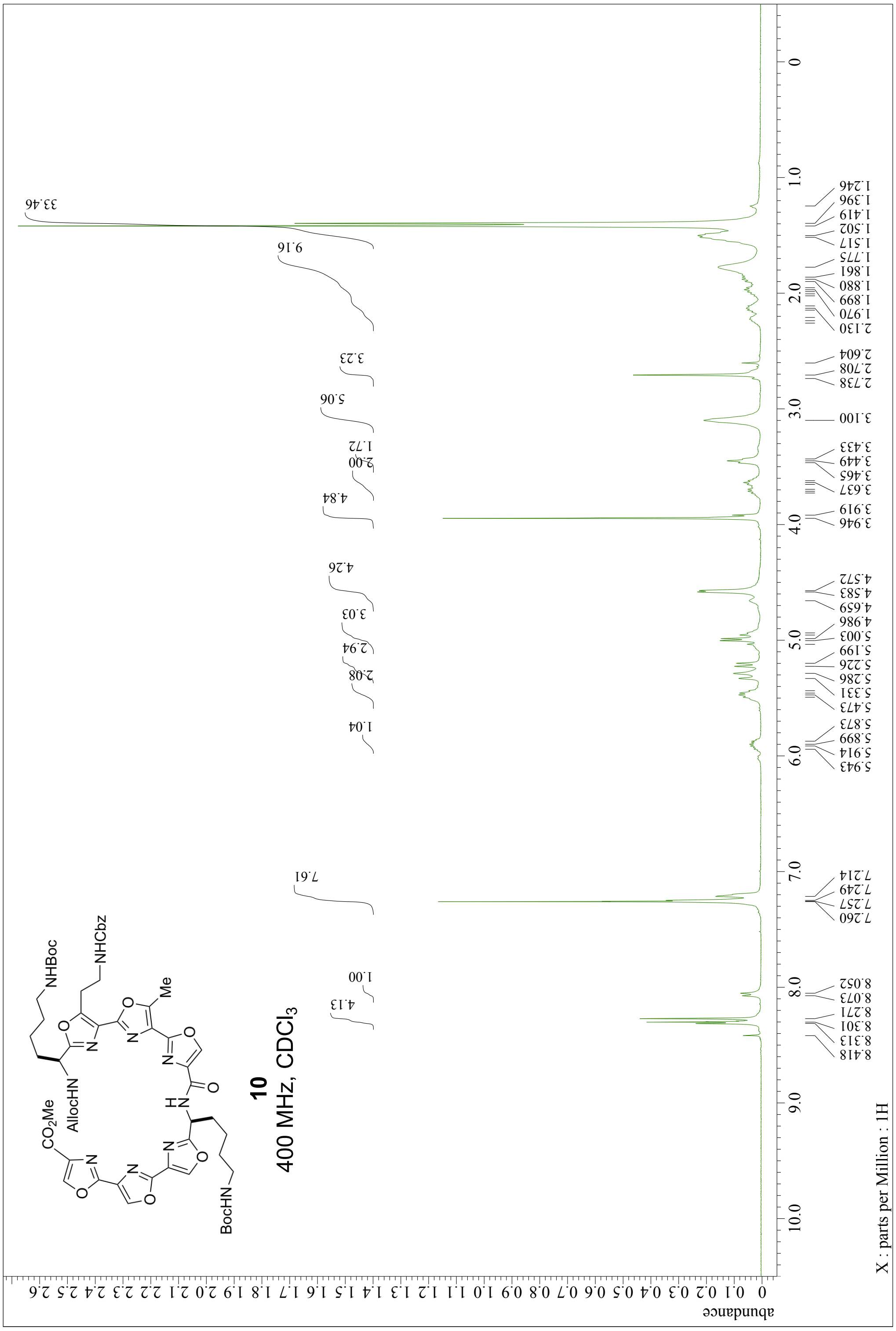


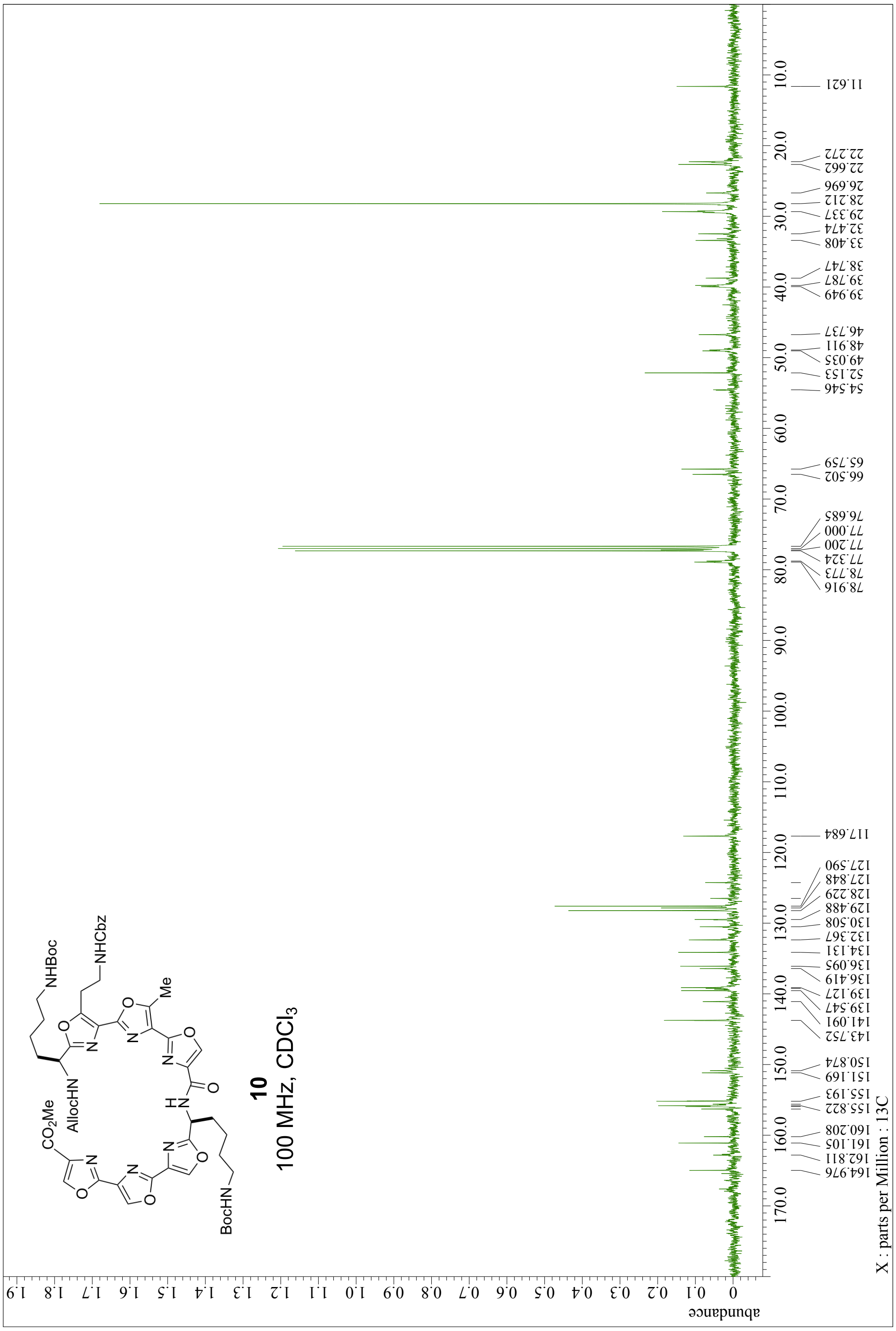
Figure S2. Correlation between the docking score and the RMSD of the top 100 poses for re-docking benchmark (PDB ID: 3UYH)

2. ^{1}H and ^{13}C NMR spectra for 10, 11, 13, 3, 16a, 4a, 16b, 4b, 19a, 5a, 19b, 5b.



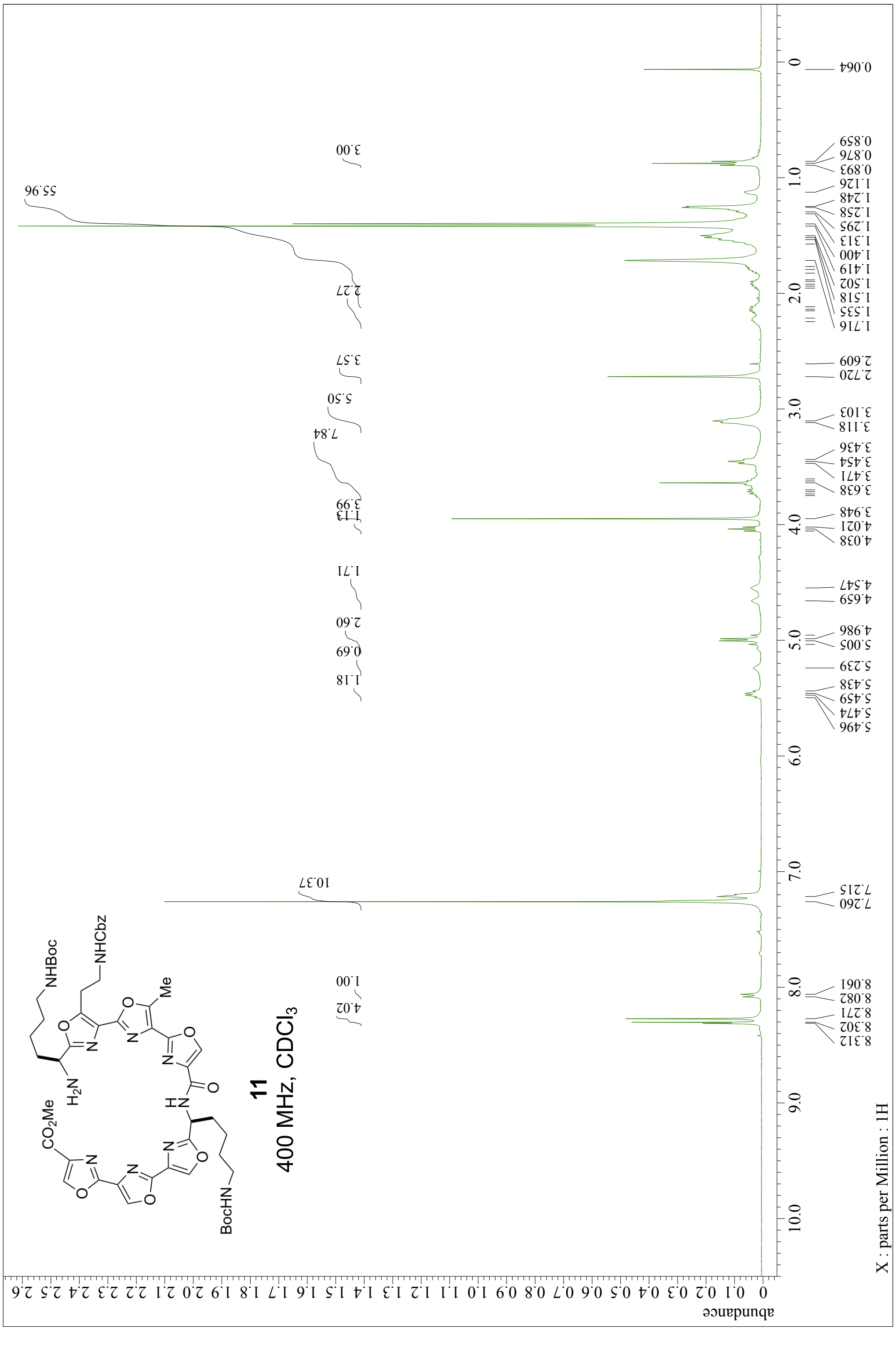
10

400 MHz, $CDCl_3$

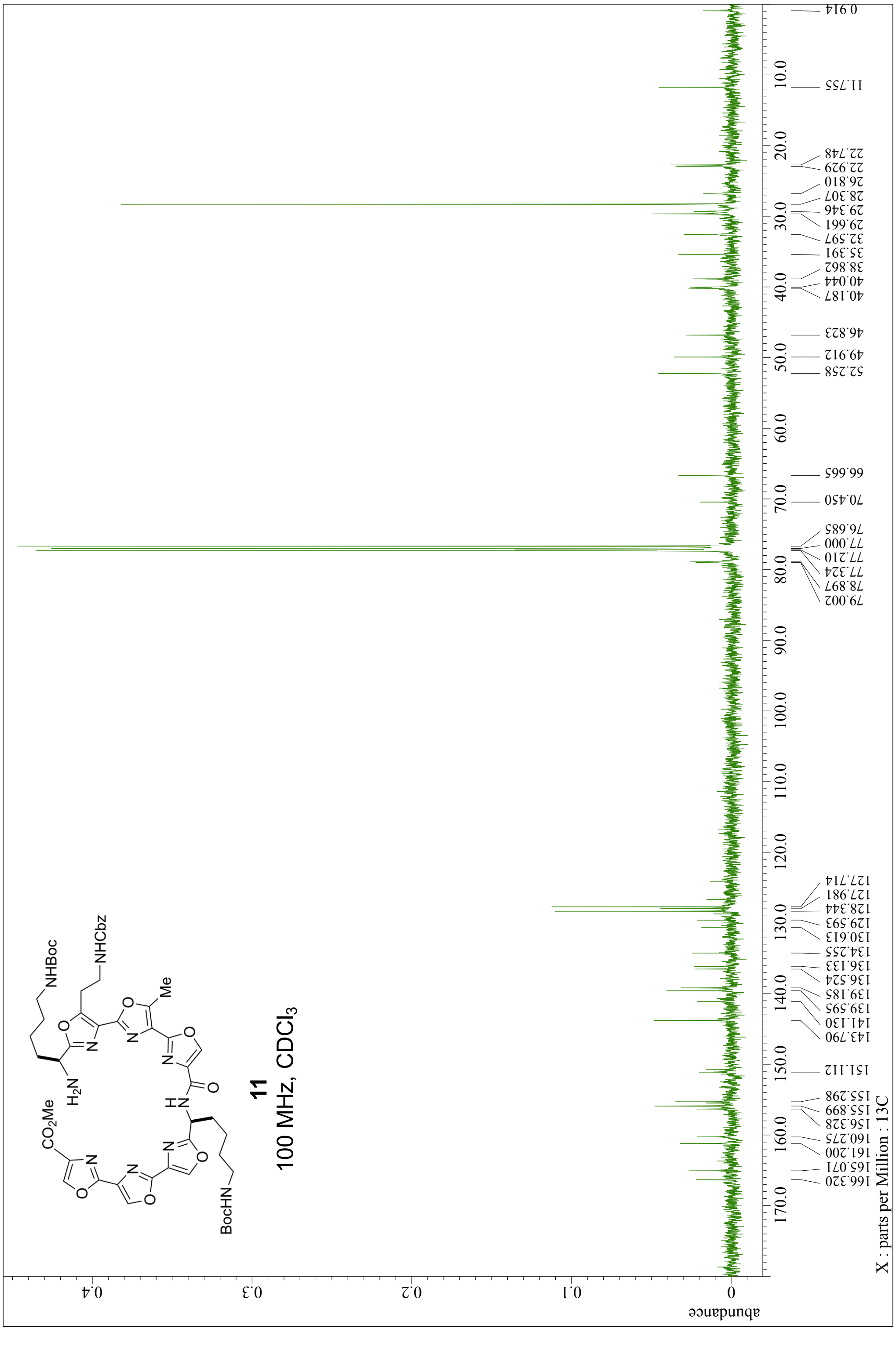


10

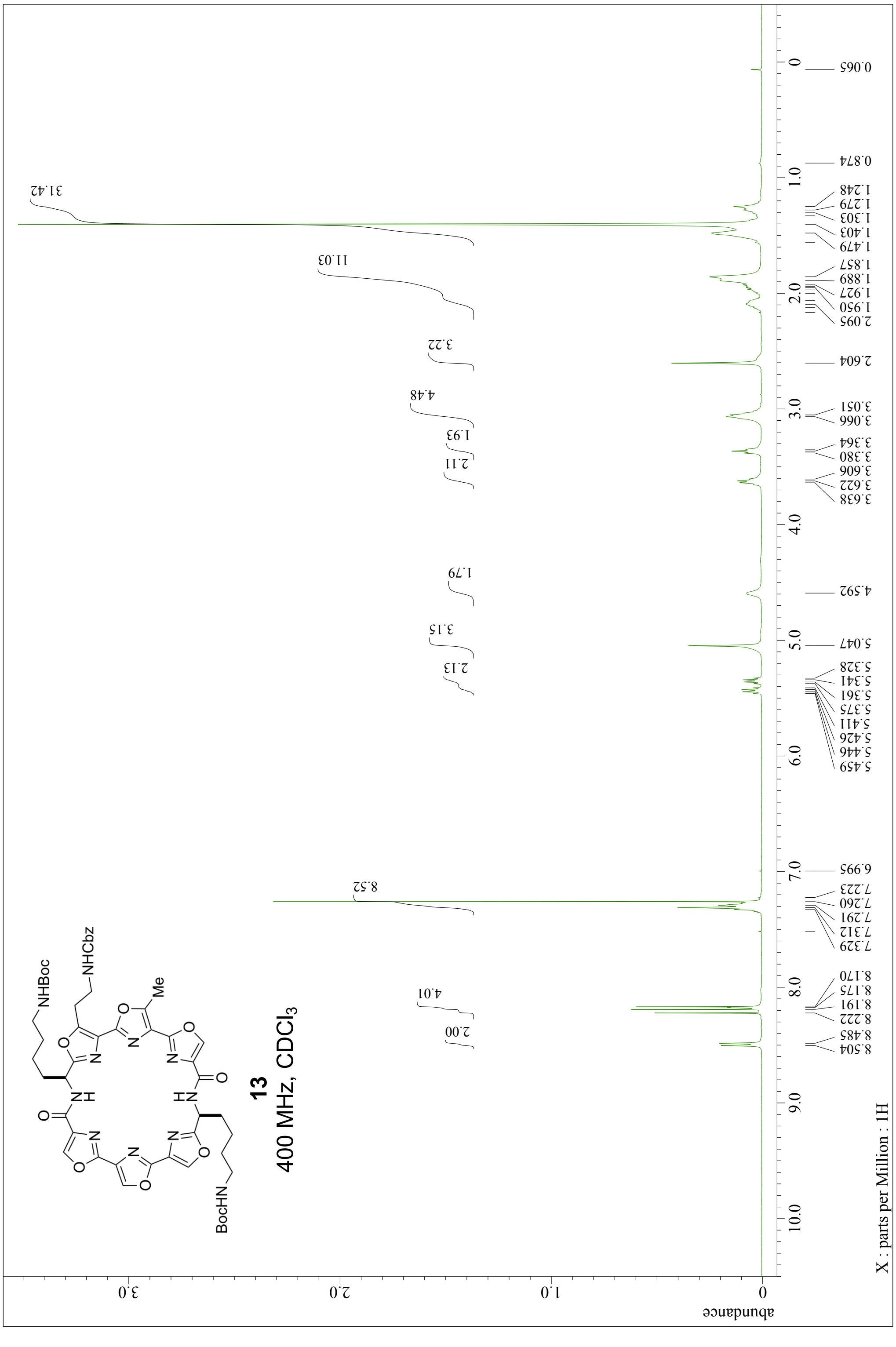
100 MHz, $CDCl_3$

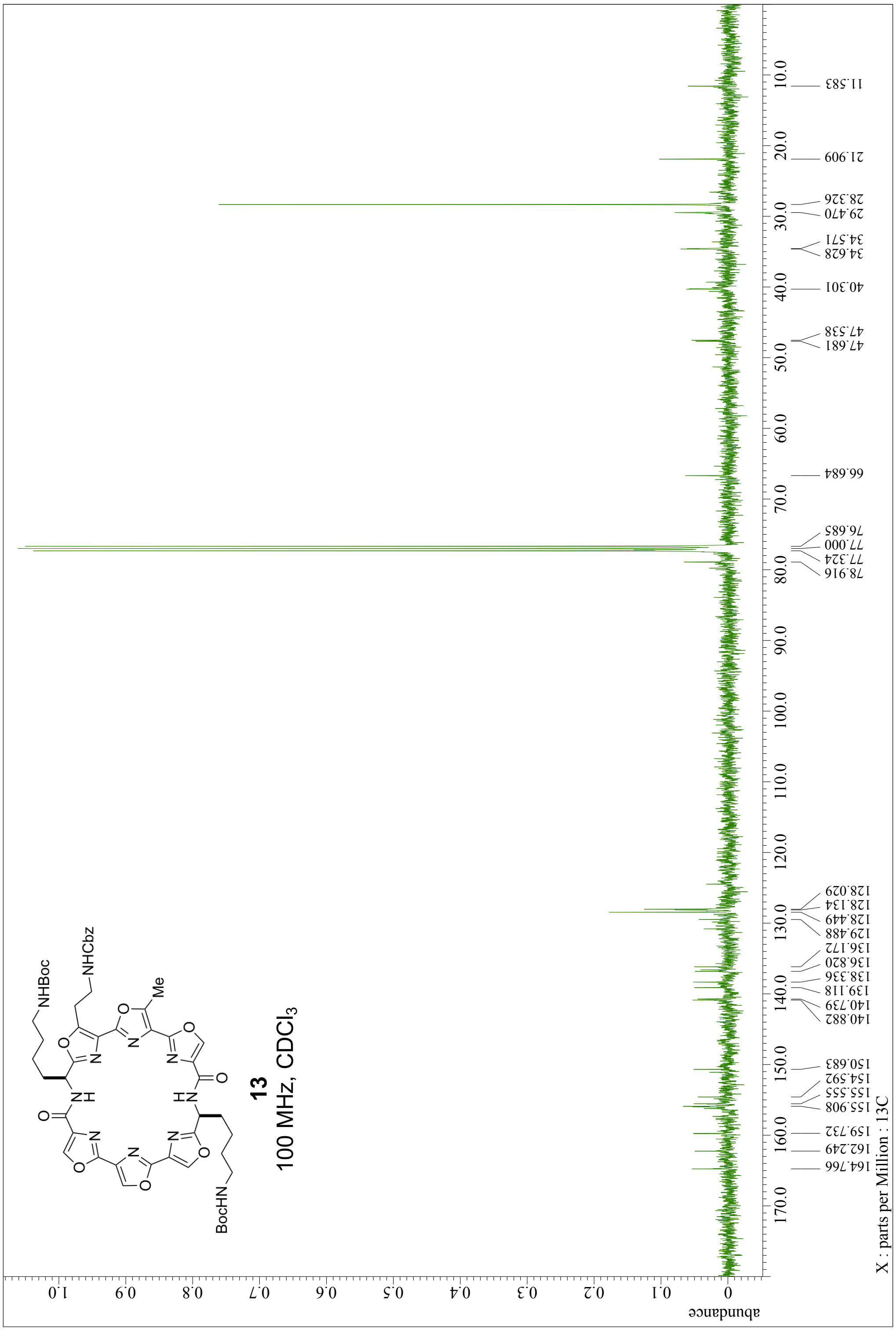

11

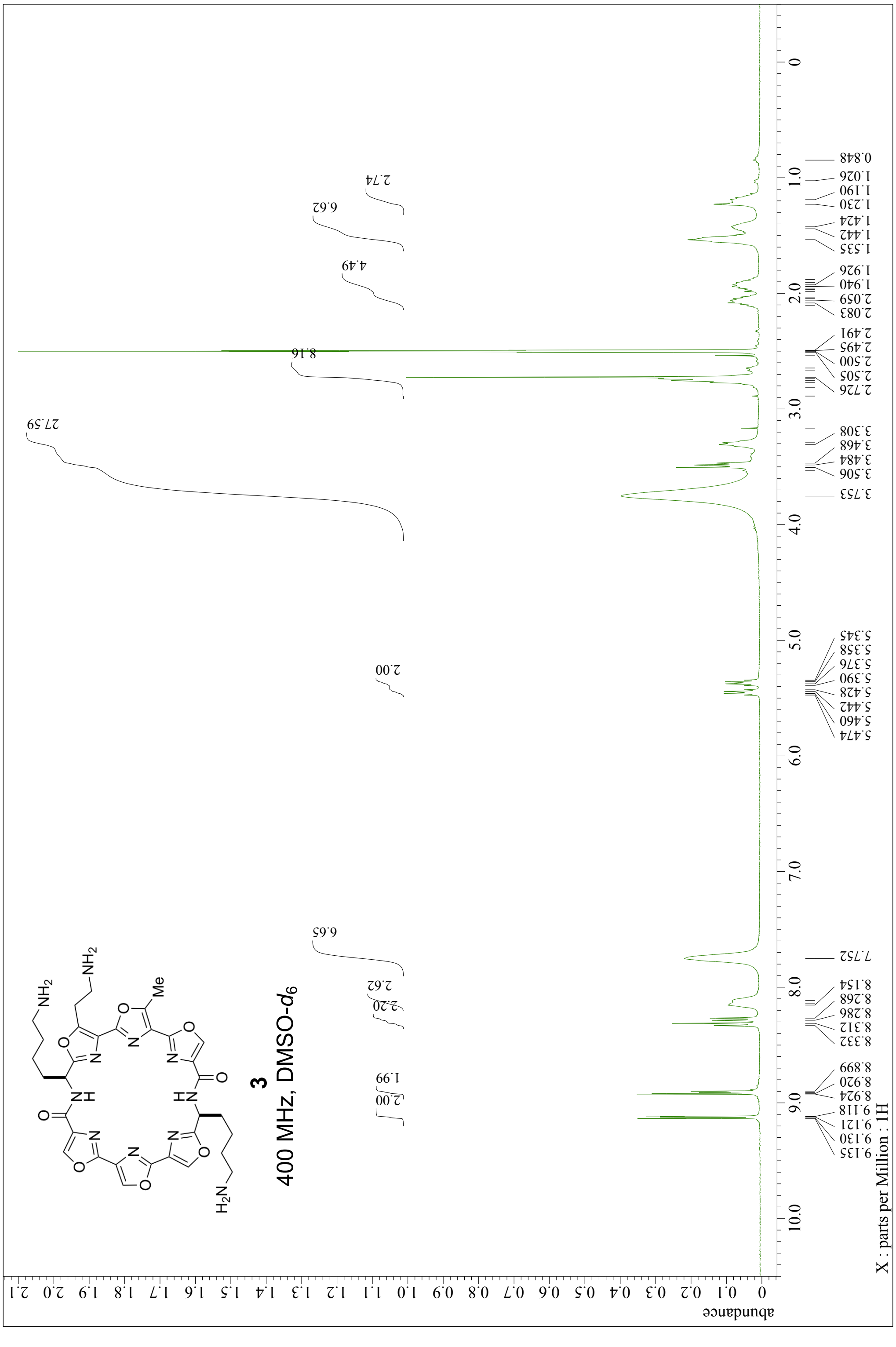
400 MHz, $CDCl_3$

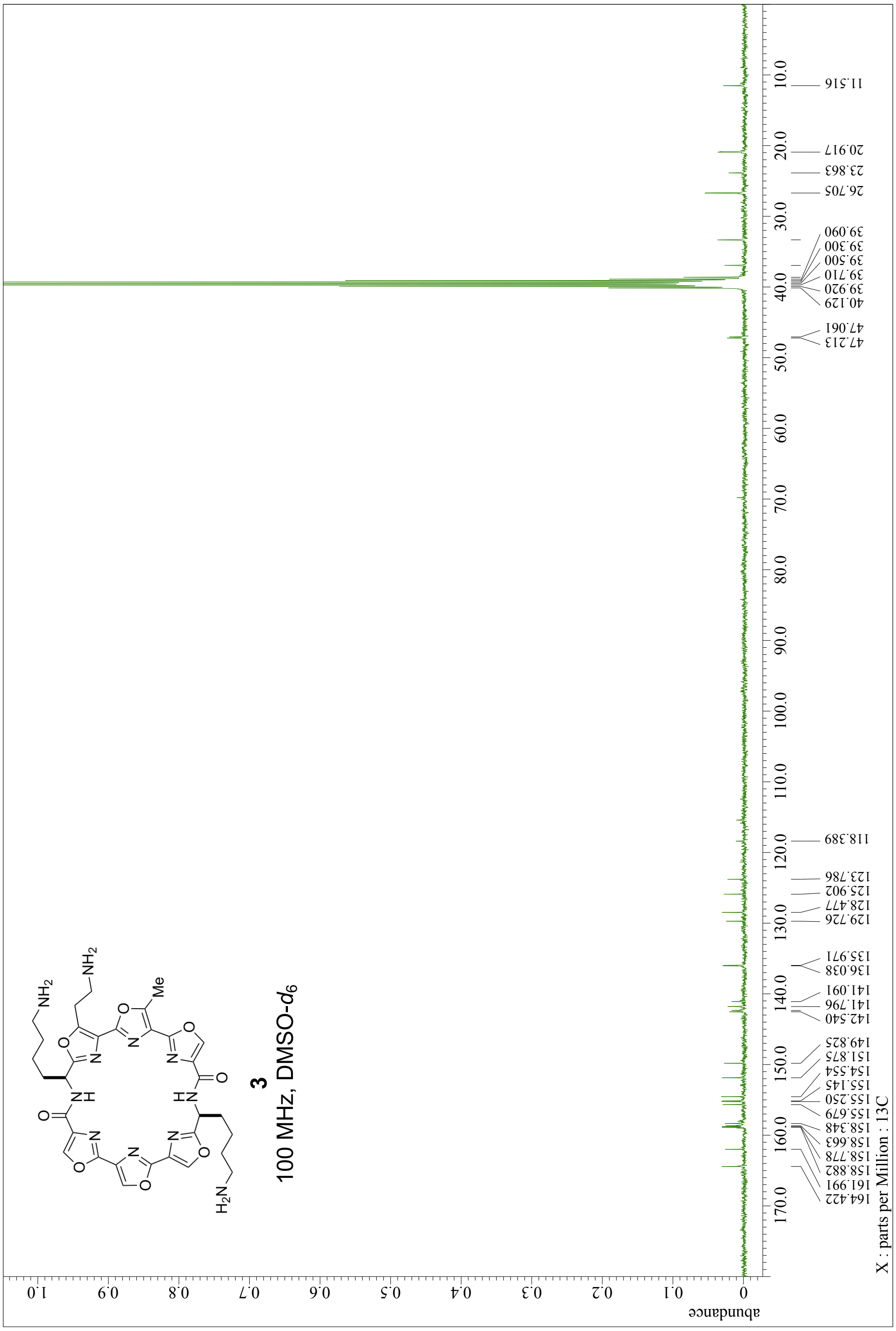


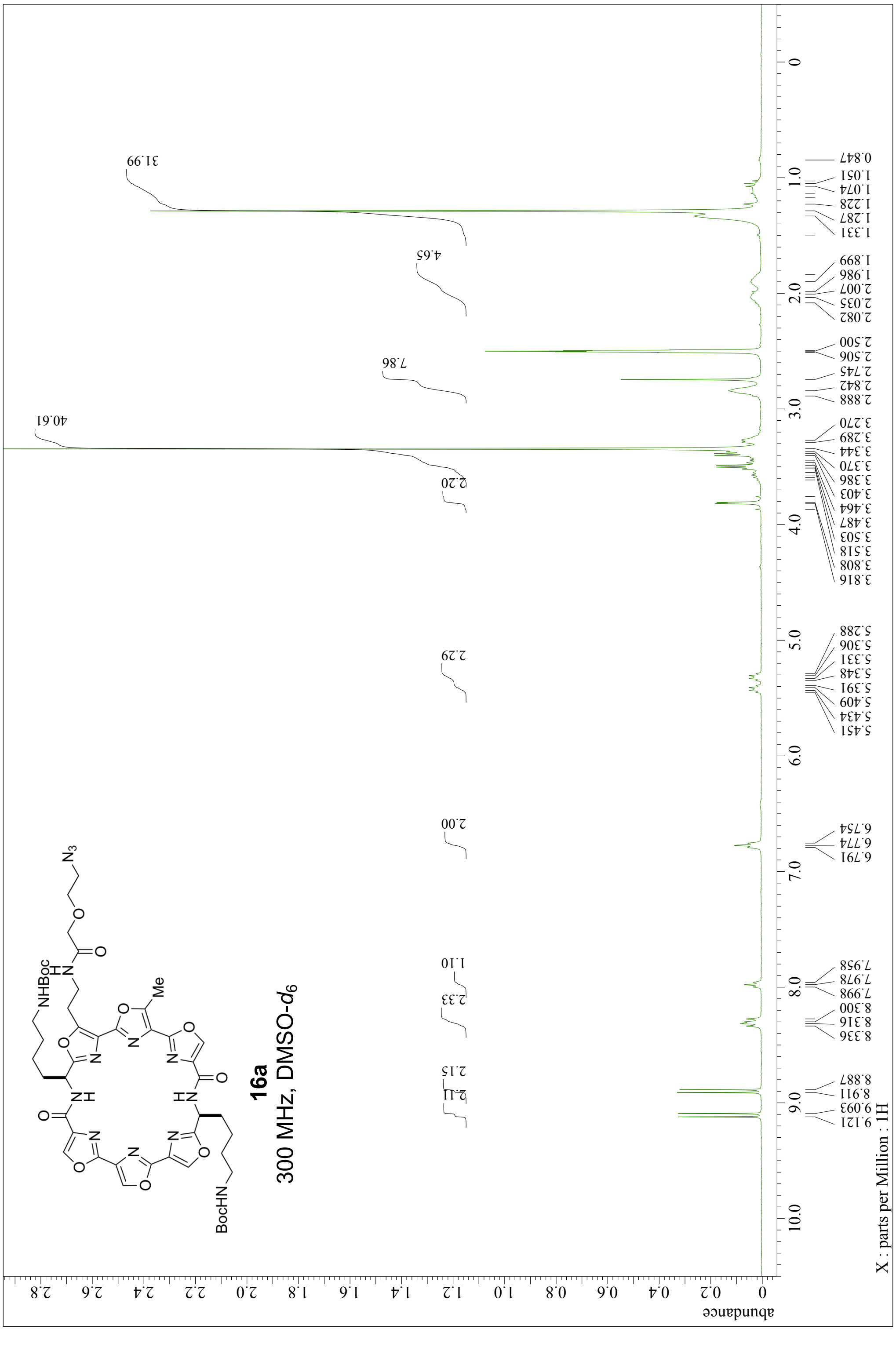
11
100 MHz, $CDCl_3$

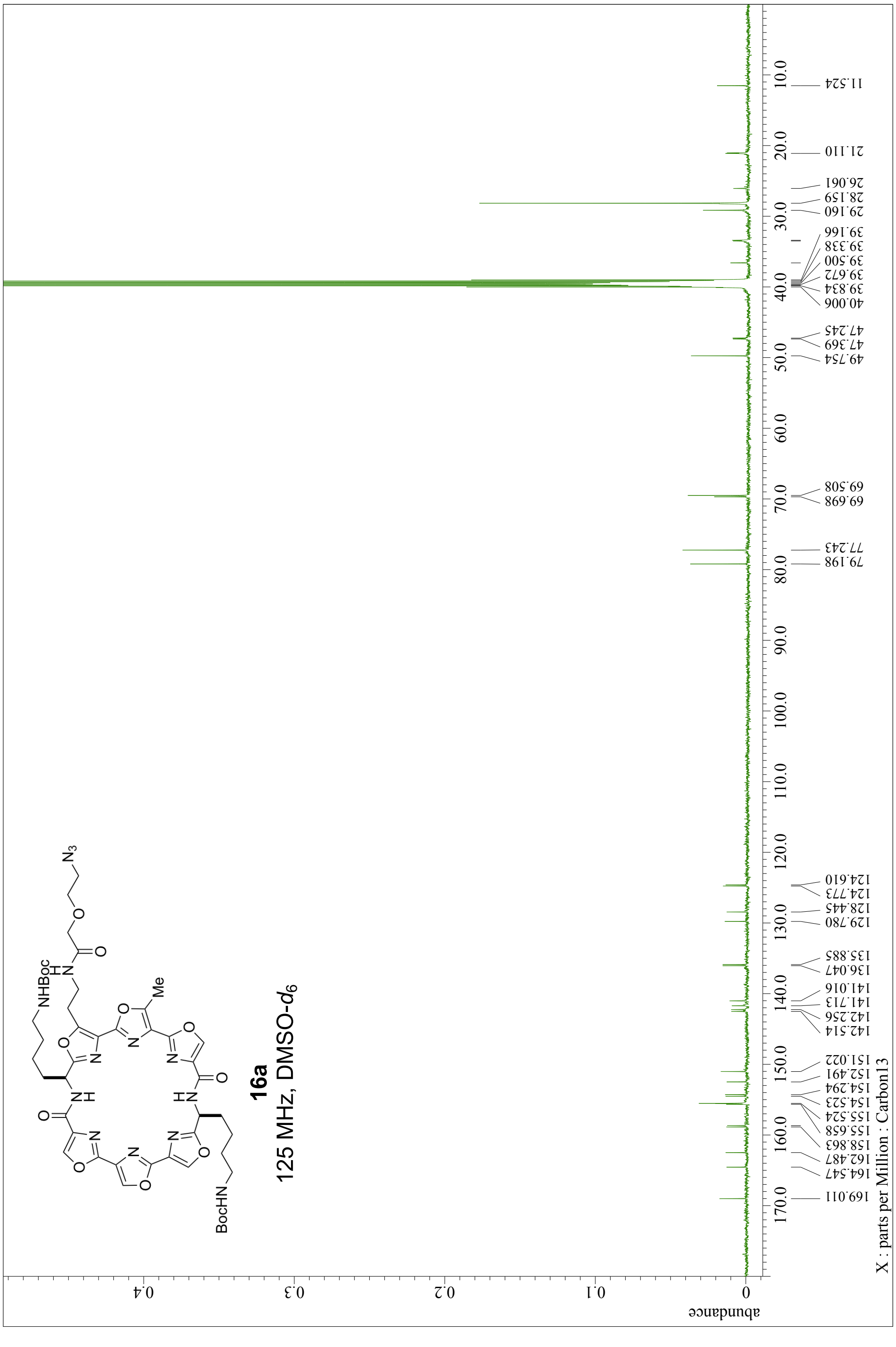

13
400 MHz, CDCl3
NHBoc
NHCbz
Me
BocHN
abundance
0
1.0
2.0
3.0
X : parts per Million : 1H
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.504
8.485
8.222
8.191
8.175
8.170
7.329
7.312
7.291
7.260
7.223
6.995
5.459
5.446
5.426
5.411
5.375
5.361
5.341
5.328
5.047
4.592
3.638
3.622
3.606
3.380
3.364
3.066
3.051
2.604
2.095
1.950
1.927
1.889
1.857
1.479
1.403
1.303
1.279
1.248
0.874
0.065
2.00
4.01
8.52
2.13
3.15
1.79
2.11
1.93
4.48
3.22
11.03
31.42


NHBoc
NHCbz
Me
O
N
H
BocHN
13
100 MHz, CDCl$_3$
11.583
21.909
28.326
29.470
34.571
34.628
40.301
47.538
47.681
66.684
76.685
77.000
77.324
78.916
128.029
128.134
128.449
129.488
136.172
136.820
138.336
139.118
140.739
140.882
150.683
154.592
155.555
155.908
159.732
162.249
164.766
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
X : parts per Million : 13C
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
abundance


3
400 MHz, DMSO-d_6
NH$_2$
NH$_2$
H$_2$N
Me
X : parts per Million : 1H
abundance
27.59
8.16
6.65
6.62
4.49
2.74
2.62
2.20
2.00
2.00
1.99
0.848
1.026
1.190
1.230
1.424
1.442
1.535
1.926
1.940
2.059
2.083
2.491
2.495
2.500
2.505
2.726
3.308
3.468
3.484
3.506
3.753
5.345
5.358
5.376
5.390
5.428
5.442
5.460
5.474
7.752
8.154
8.268
8.286
8.312
8.332
8.899
8.920
8.924
9.118
9.121
9.130
9.135
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
2.0
2.1

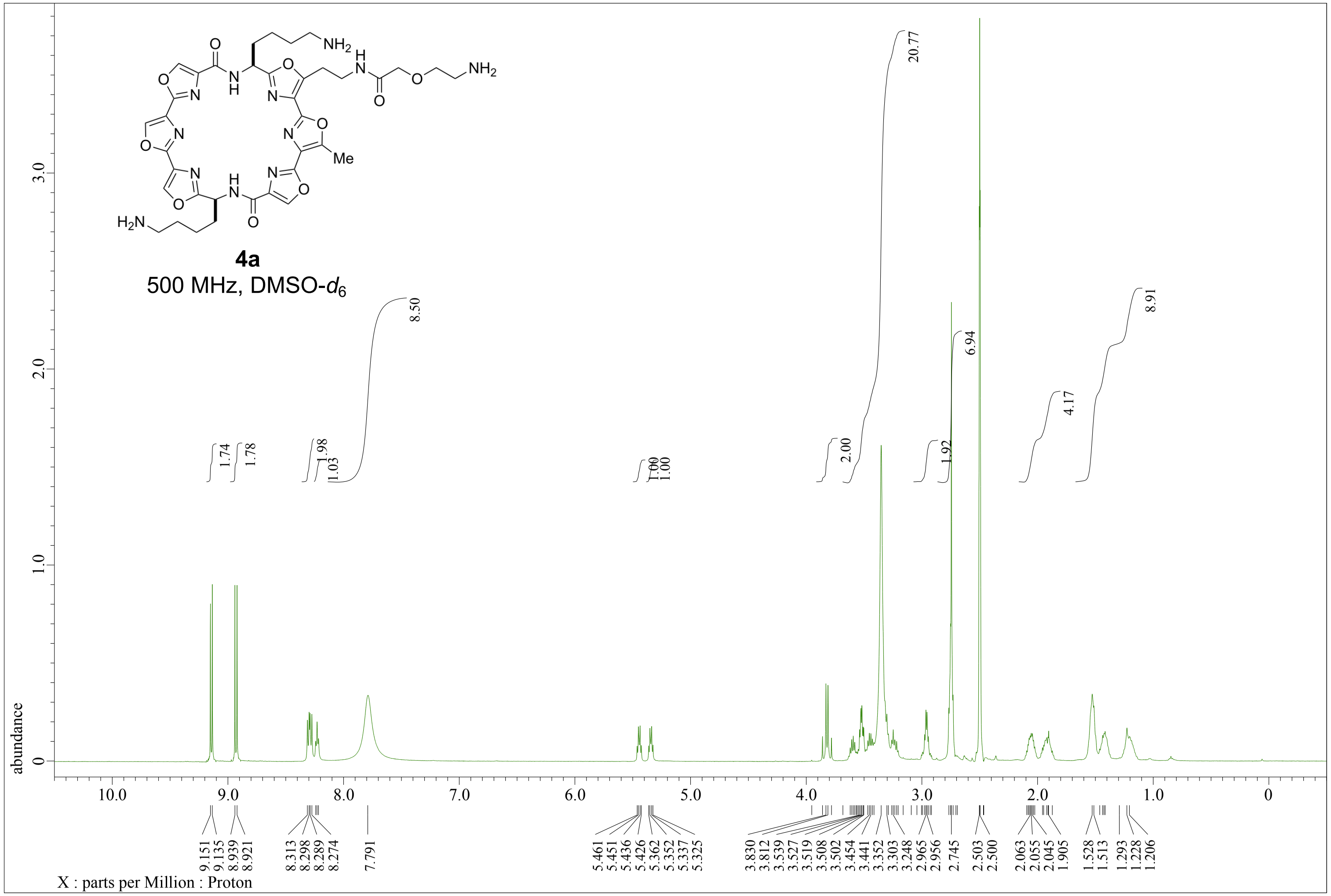

3
100 MHz, DMSO-d_6
NH2
NH2
Me
H2N
abundance
X : parts per Million : 13C
11.516
20.917
23.863
26.705
39.090
39.300
39.500
39.710
39.920
40.129
47.061
47.213
118.389
123.786
125.902
128.477
129.726
135.971
136.038
141.091
141.796
142.540
149.825
151.875
154.554
155.145
155.250
155.679
158.348
158.663
158.778
158.882
161.991
164.422


16a
300 MHz, DMSO-d_6



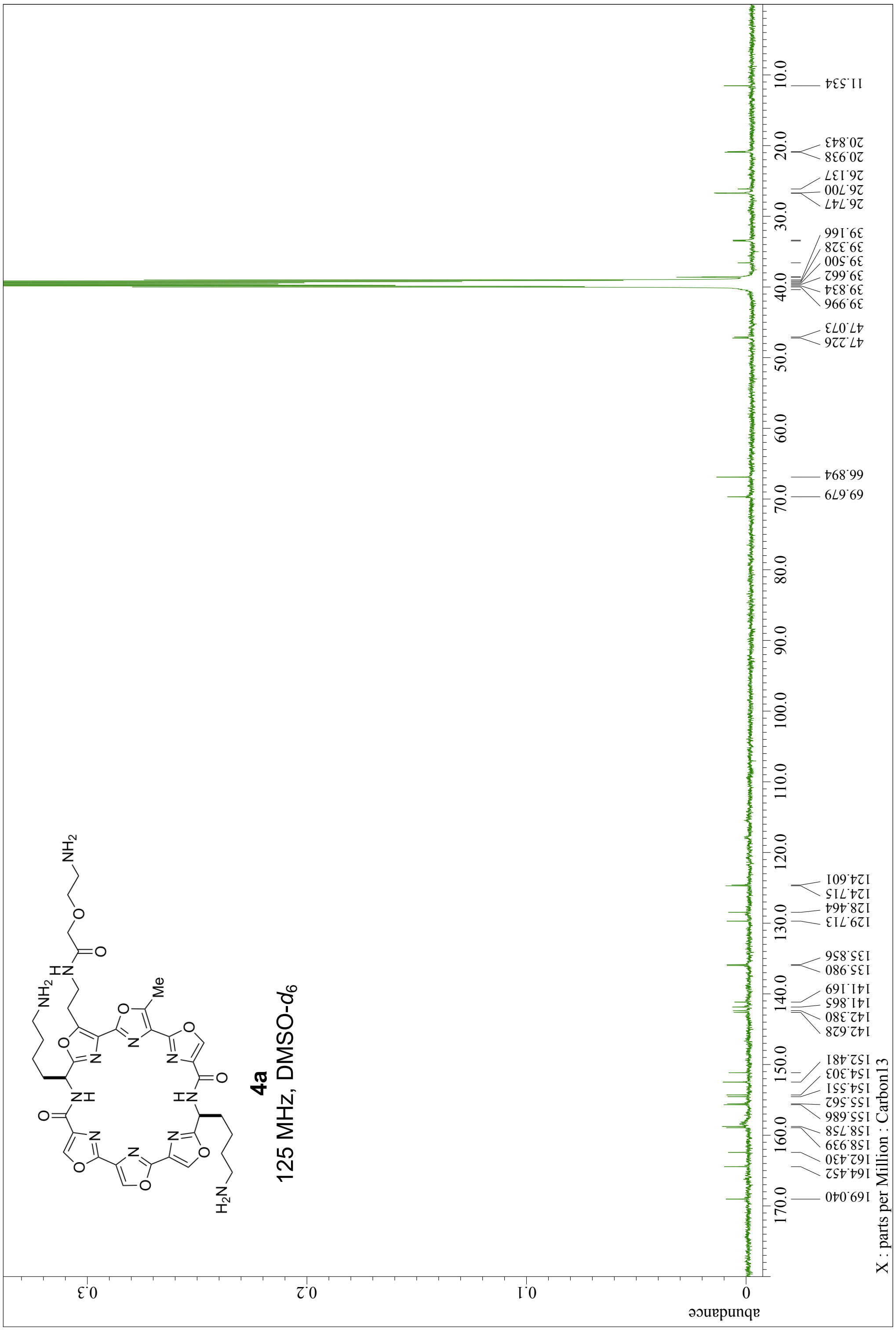
16a

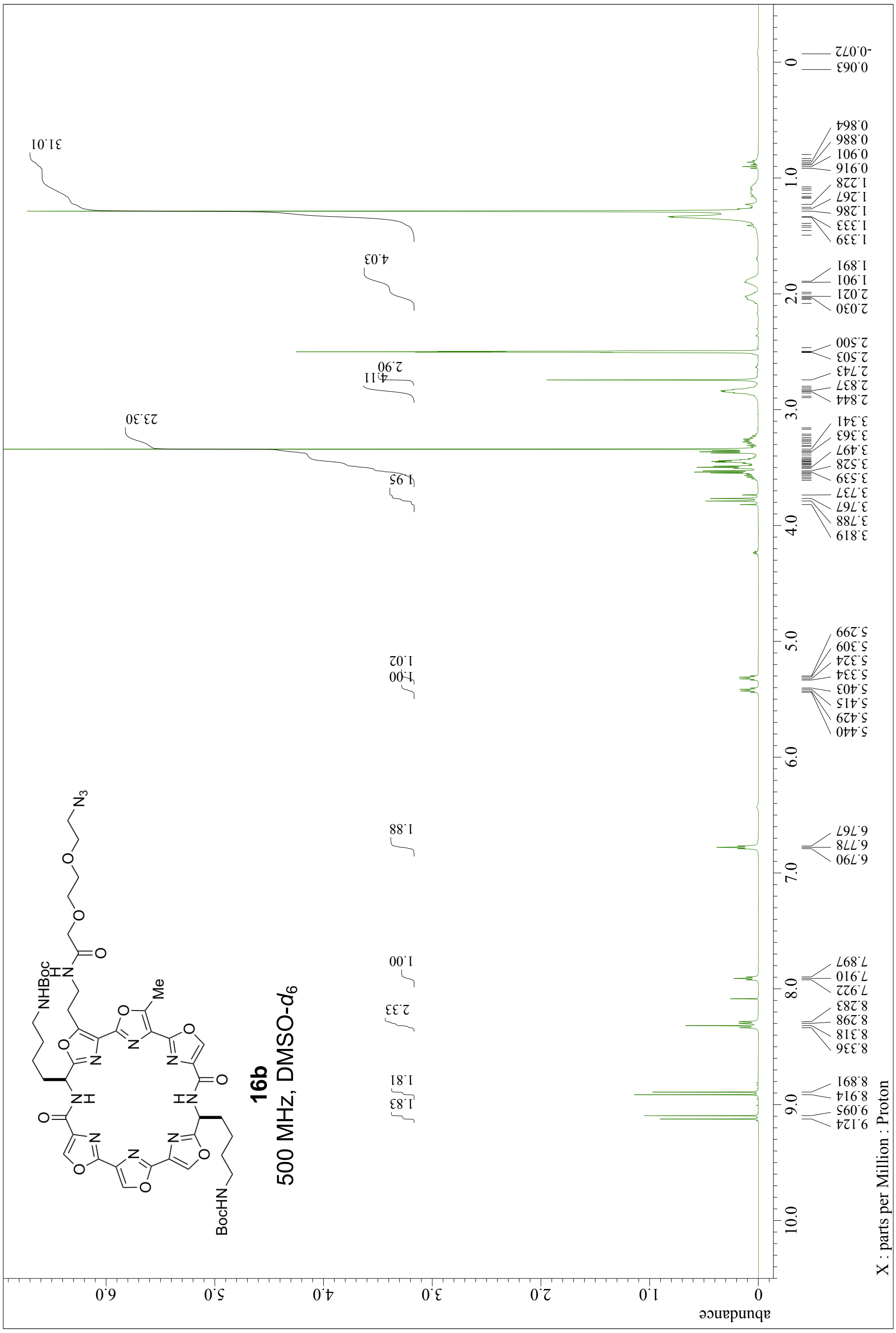
125 MHz, DMSO-d_6



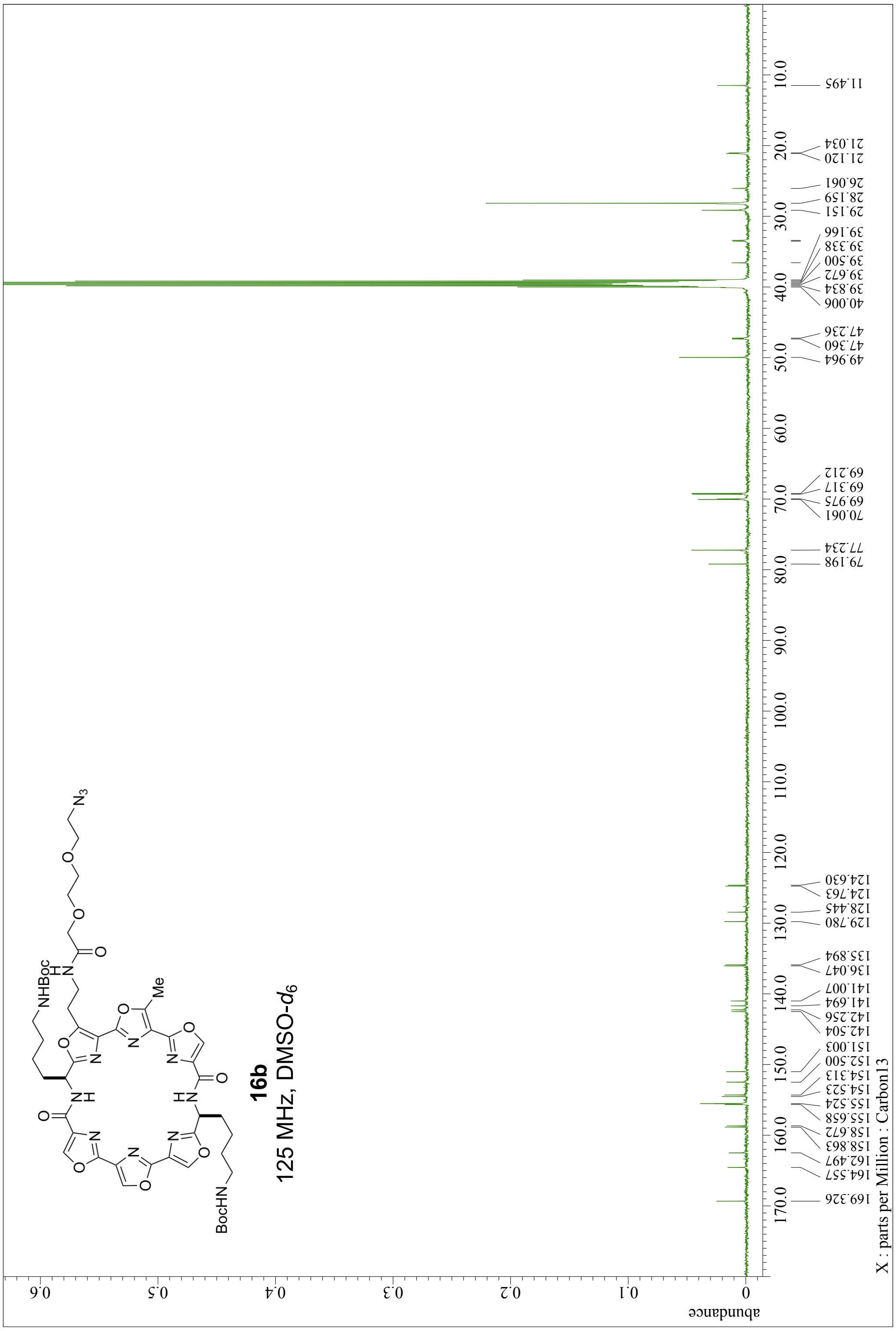
4a

500 MHz, DMSO-d_6


4a
125 MHz, DMSO-d_6
Me
X : parts per Million : Carbon13
abundance
0
0.1
0.2
0.3
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
11.534
20.843
20.938
26.137
26.700
26.747
39.166
39.328
39.500
39.662
39.834
39.996
47.073
47.226
66.894
69.679
124.601
124.715
128.464
129.713
135.856
135.980
141.169
141.865
142.380
142.628
152.481
154.303
154.551
155.562
155.686
158.758
158.939
162.430
164.452
169.040

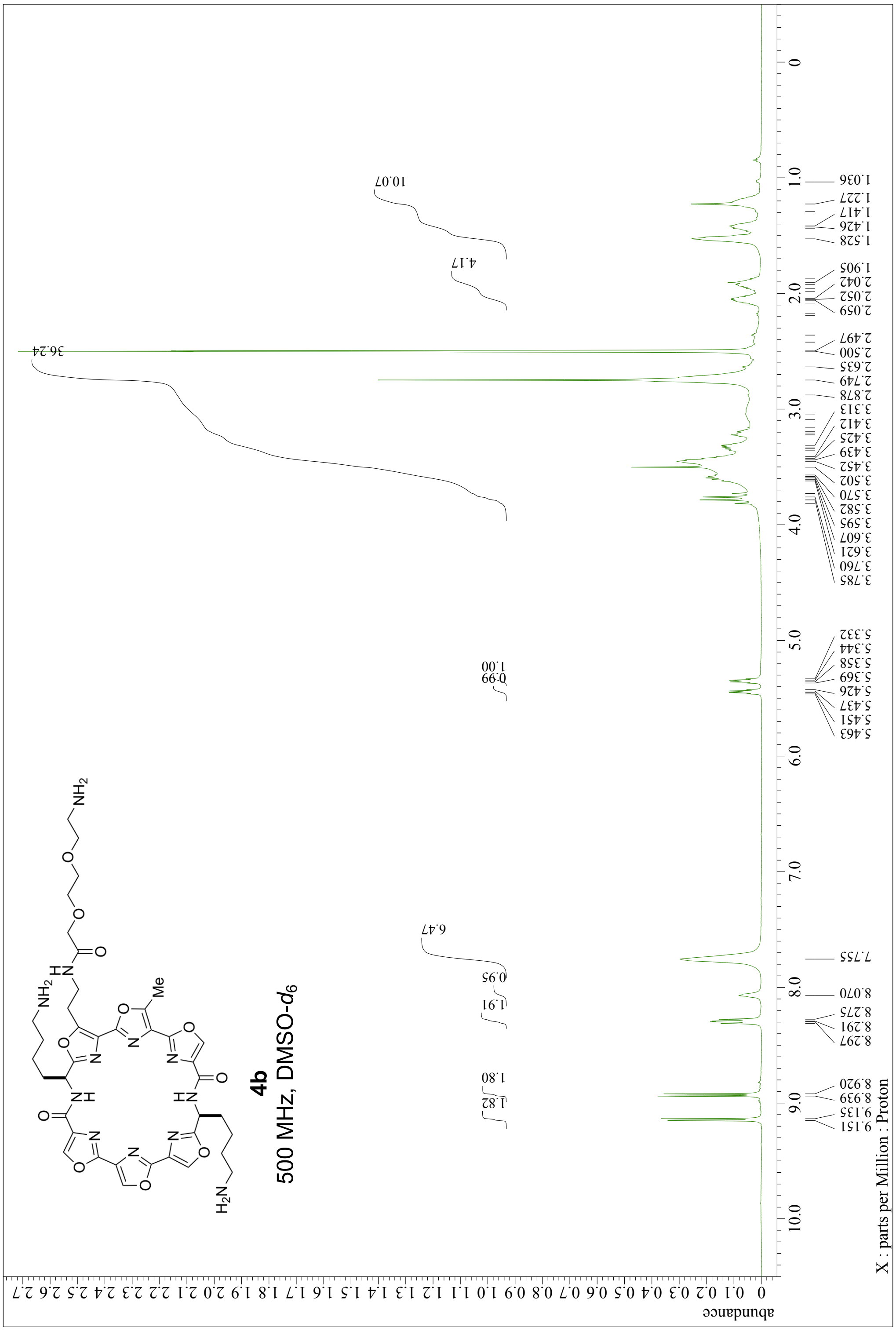

16b

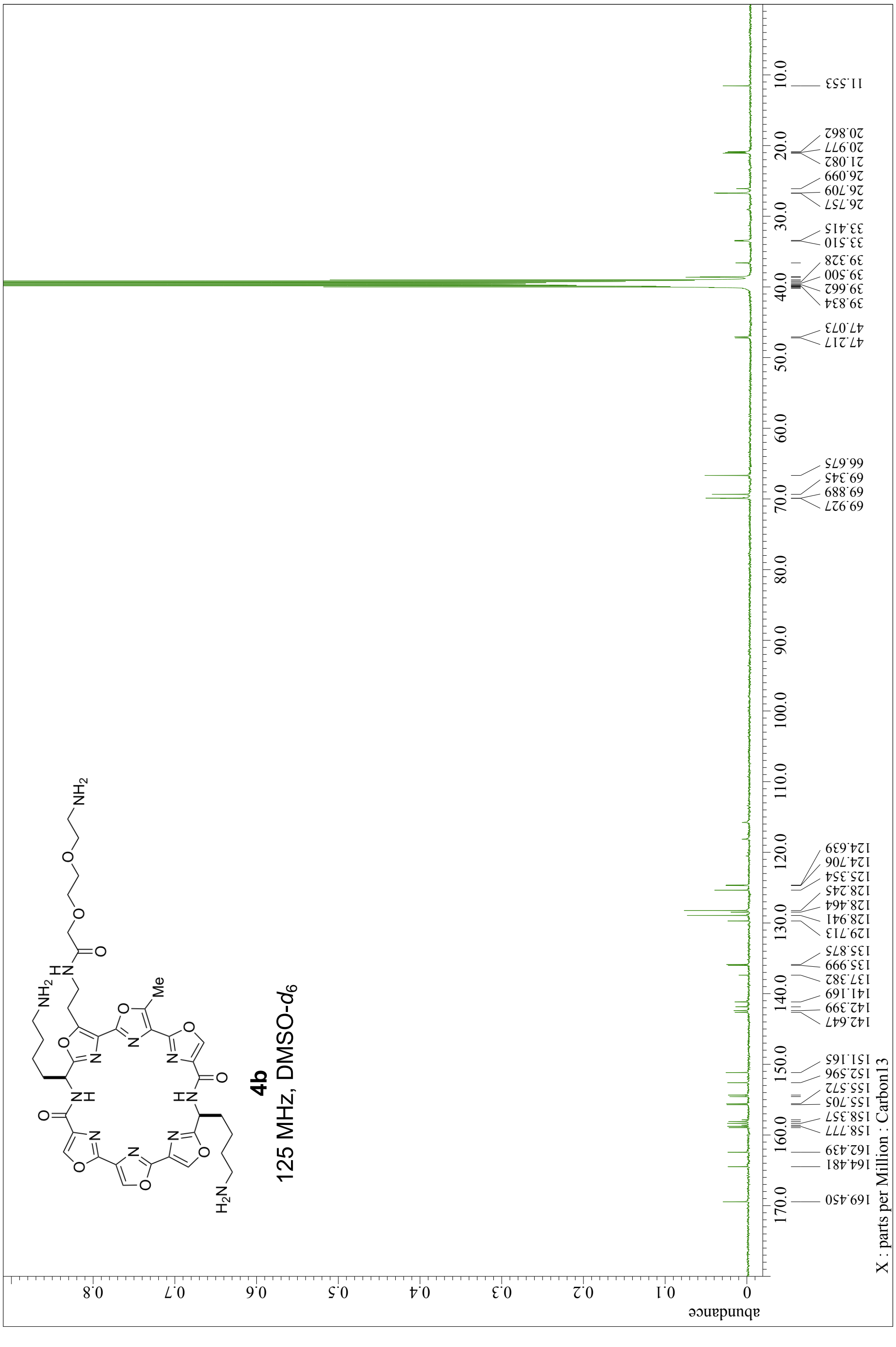
500 MHz, DMSO-d_6

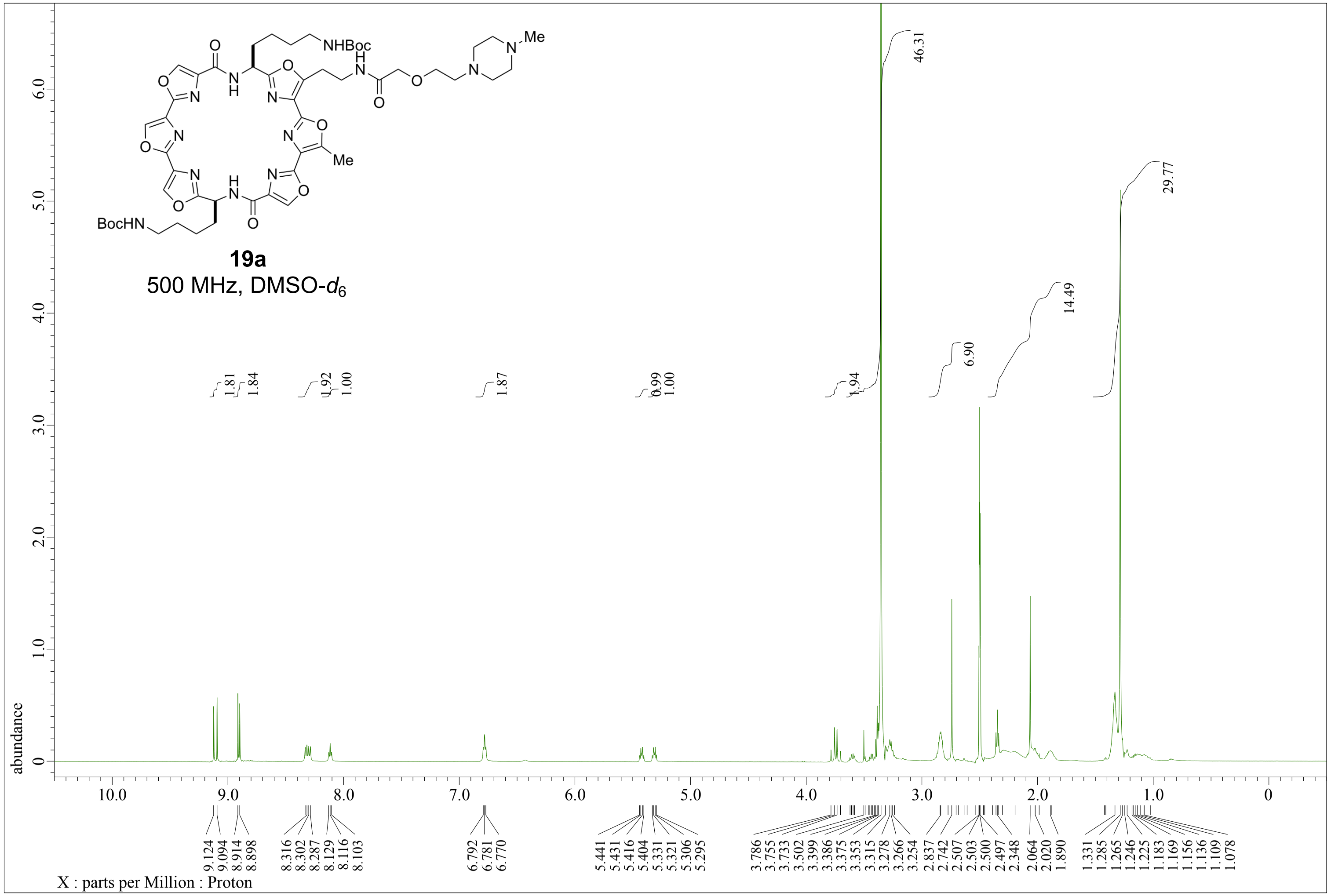


16b

125 MHz, DMSO-d_6

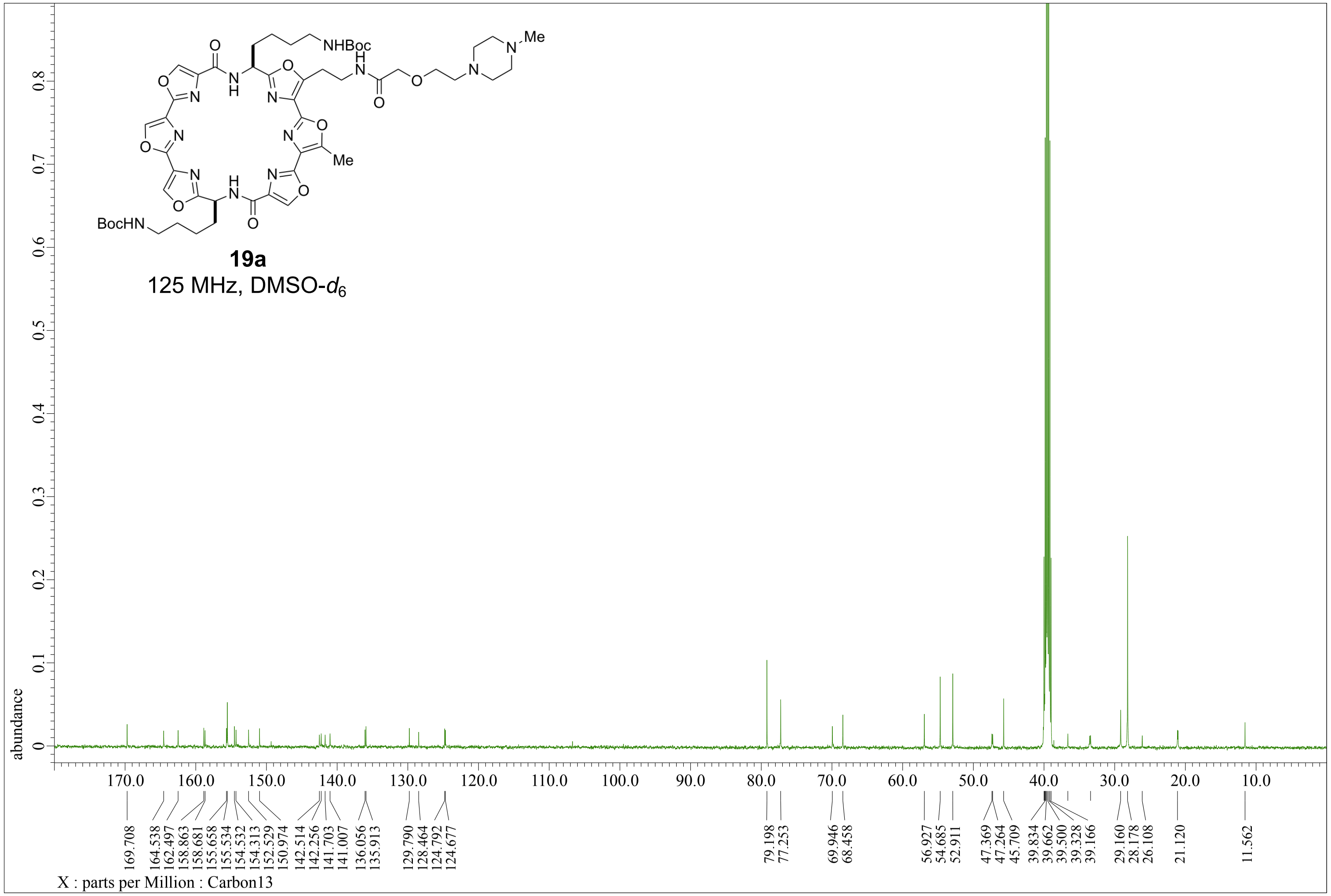

4b
500 MHz, DMSO-d_6
X : parts per Million : Proton
abundance
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8 1.9 2.0 2.1 2.2 2.3 2.4 2.5 2.6 2.7
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
9.151 9.135 8.939 8.920 8.297 8.291 8.275 8.070 7.755
5.463 5.451 5.437 5.426 5.369 5.358 5.344 5.332
3.785 3.760 3.621 3.607 3.595 3.582 3.570 3.502 3.452 3.439 3.425 3.412 3.313
2.878 2.749 2.635 2.500 2.497
2.059 2.052 2.042 1.905
1.528 1.426 1.417 1.227 1.036
1.82 1.80 1.91 0.95 6.47 0.99 1.00 36.24 4.17 10.07
NH2 H N O O O NH2 O Me N O N O N O H N O N O N O N O N H N H O H2N


4b
125 MHz, DMSO-d_6
NH$_2$
H$_2$N
Me
abundance
X : parts per Million : Carbon13
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
11.553
20.862
20.977
21.082
26.099
26.709
26.757
33.415
33.510
39.328
39.500
39.662
39.834
47.073
47.217
66.675
69.345
69.889
69.927
124.639
124.706
125.354
128.245
128.464
128.941
129.713
135.875
135.999
137.382
141.169
142.399
142.647
151.165
152.596
155.572
155.705
158.357
158.777
162.439
164.481
169.450



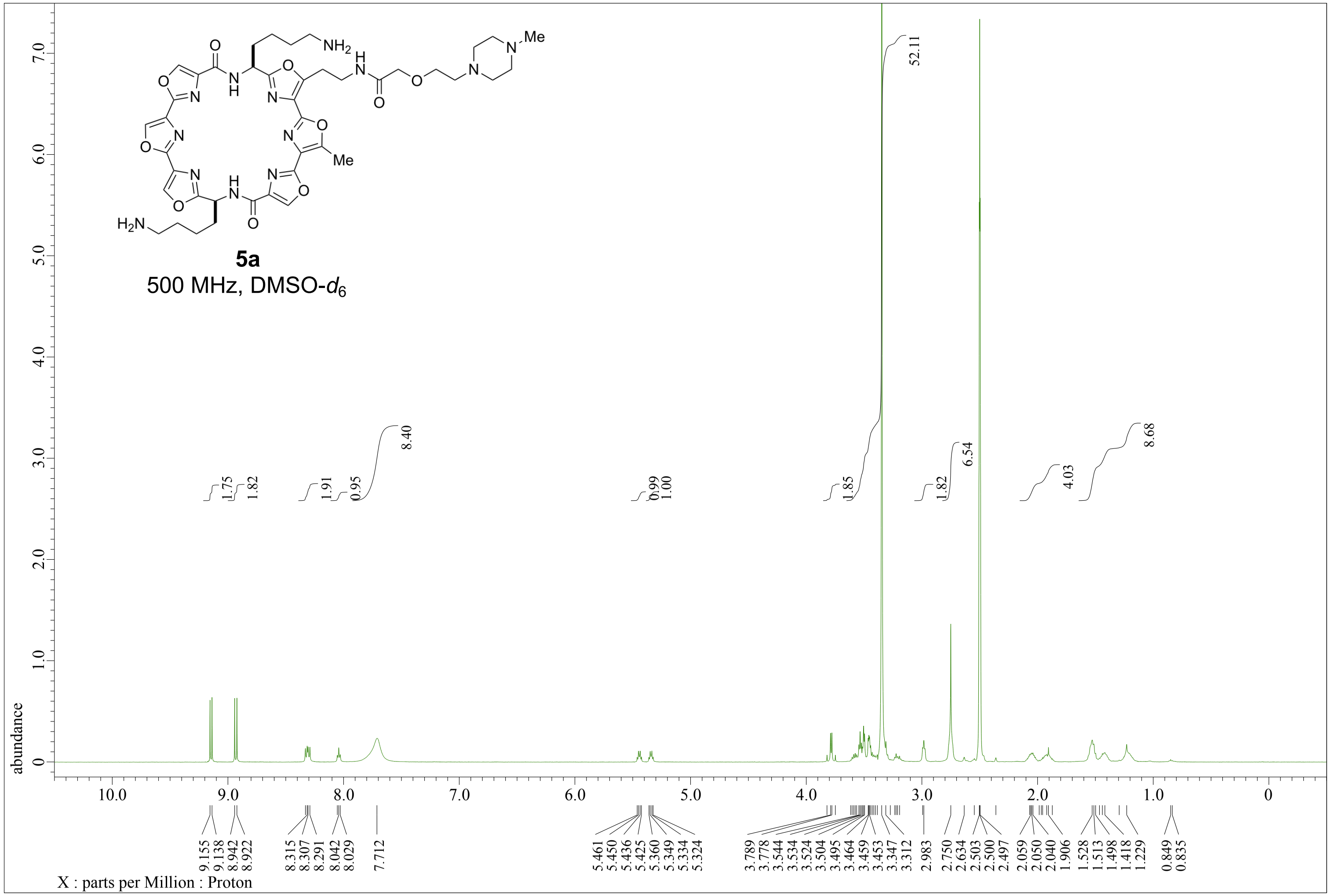
19a

500 MHz, DMSO-d_6

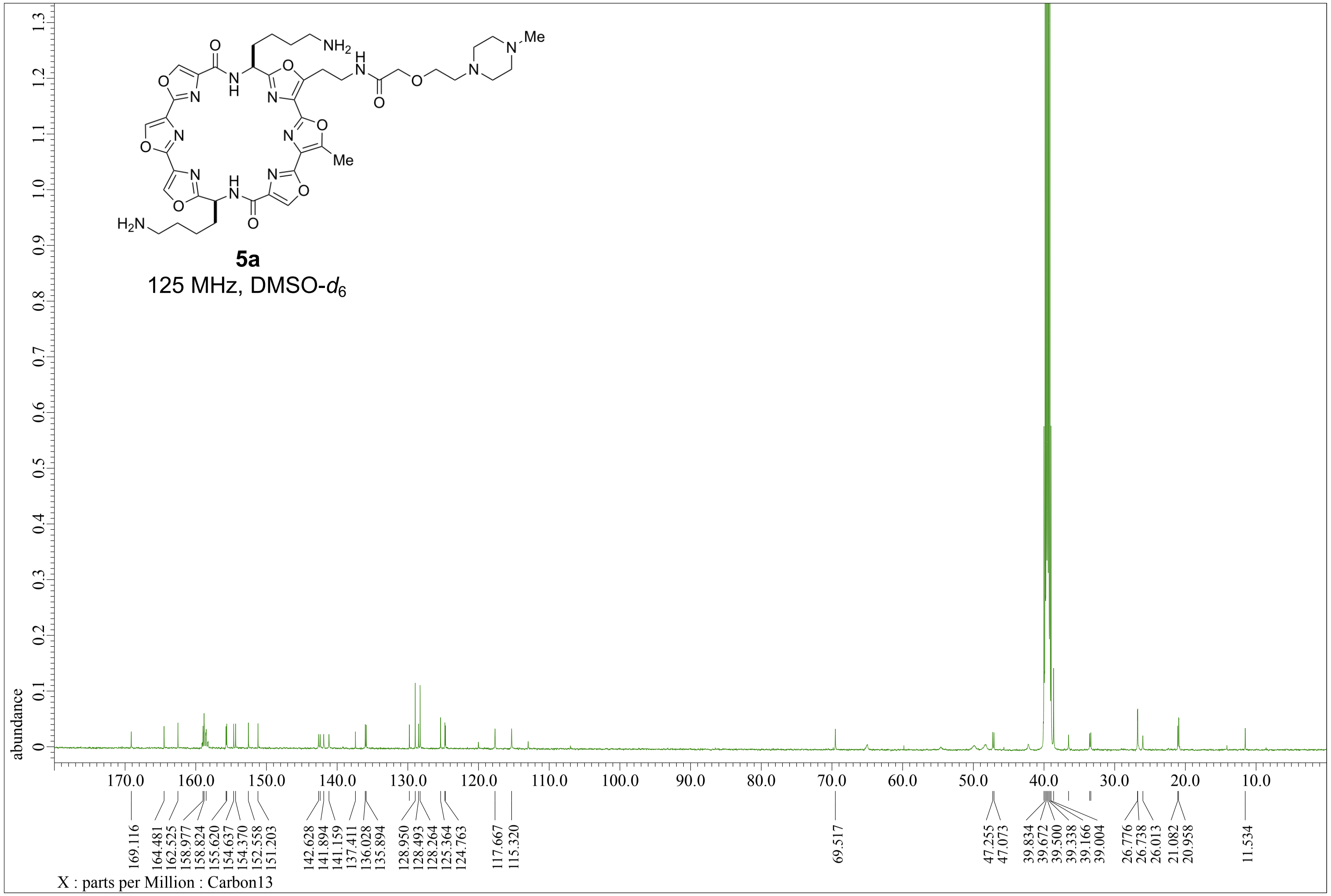


19a

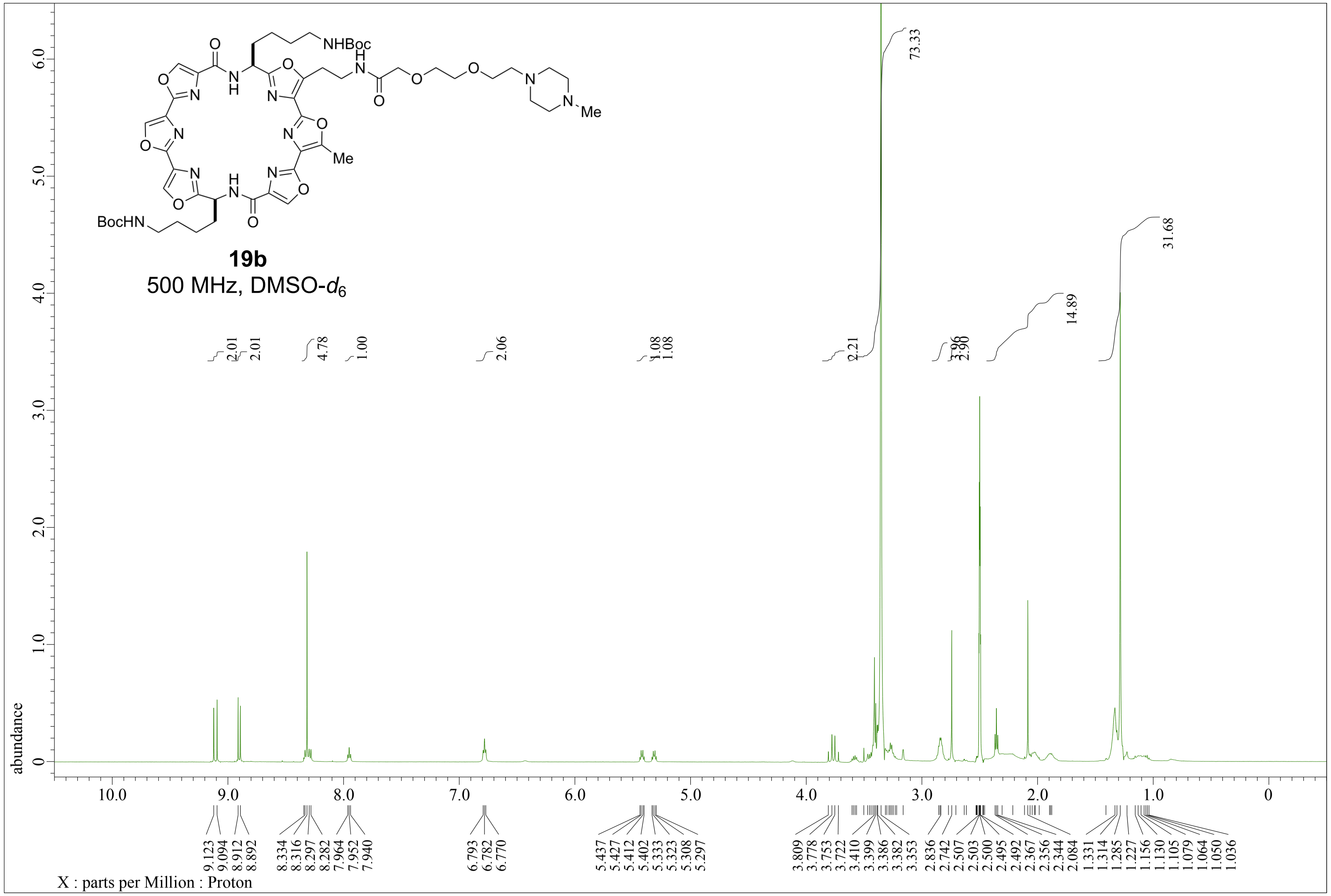
125 MHz, DMSO-d_6


5a

500 MHz, DMSO-d_6

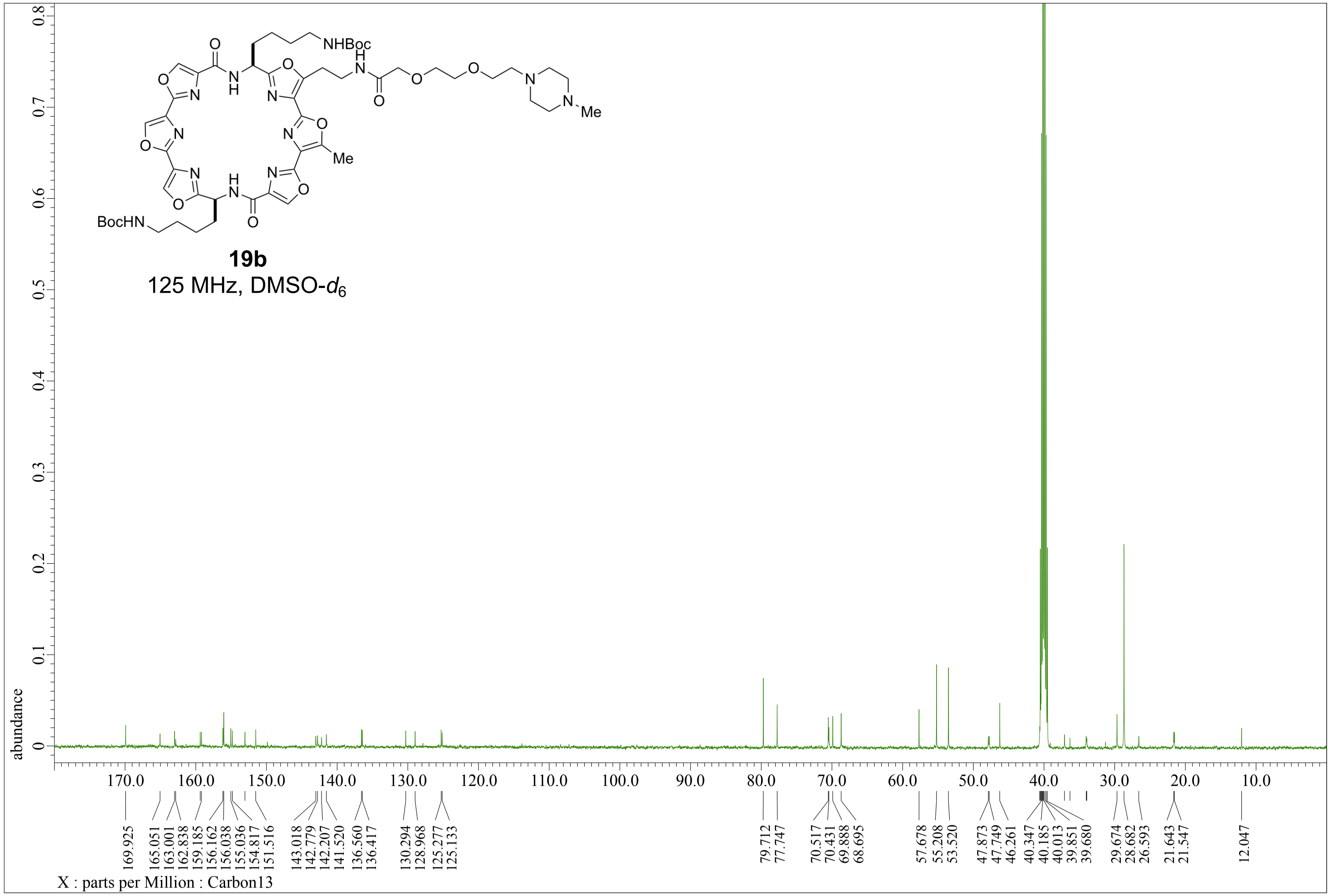

5a

125 MHz, DMSO-d_6



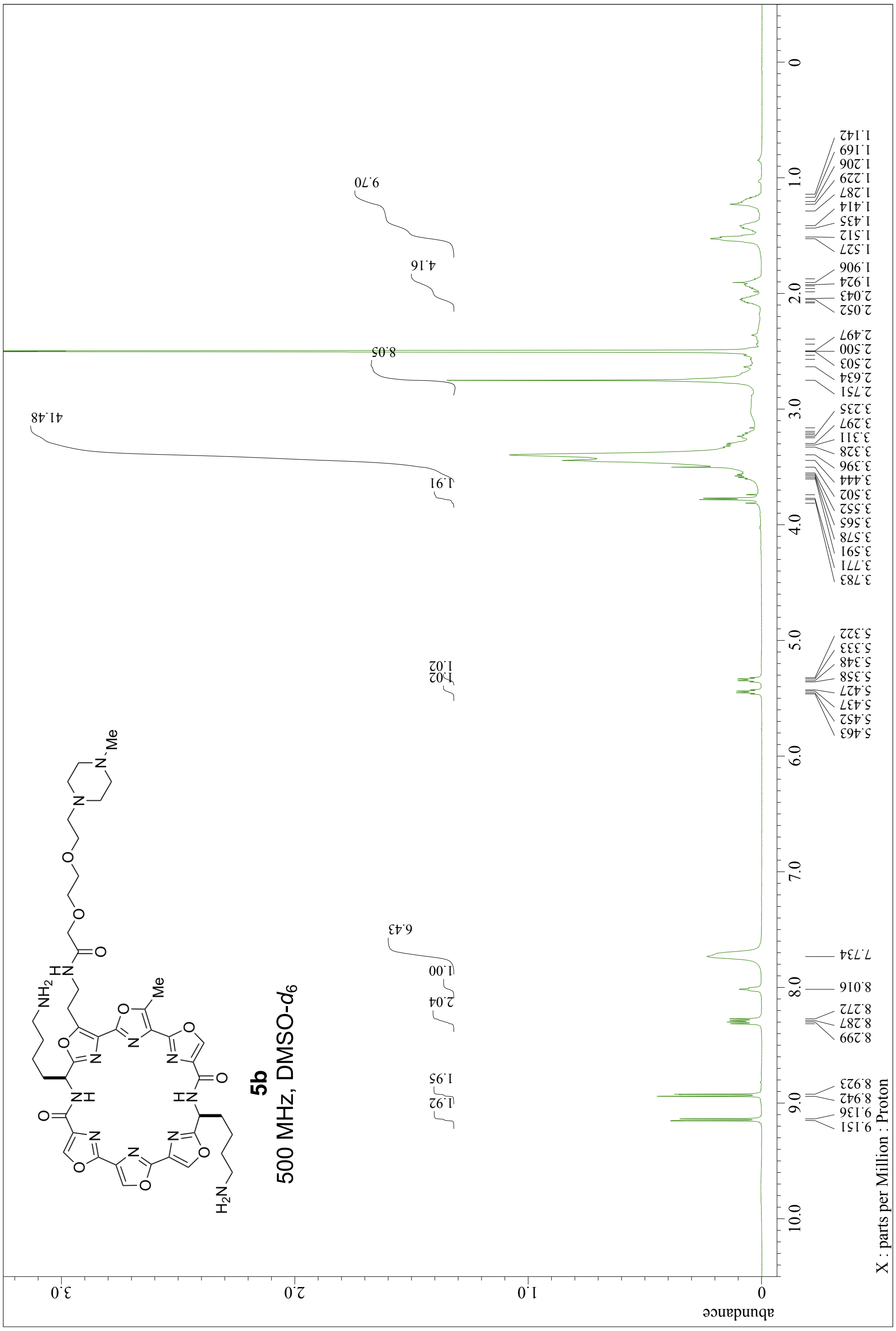
19b

500 MHz, DMSO-d_6



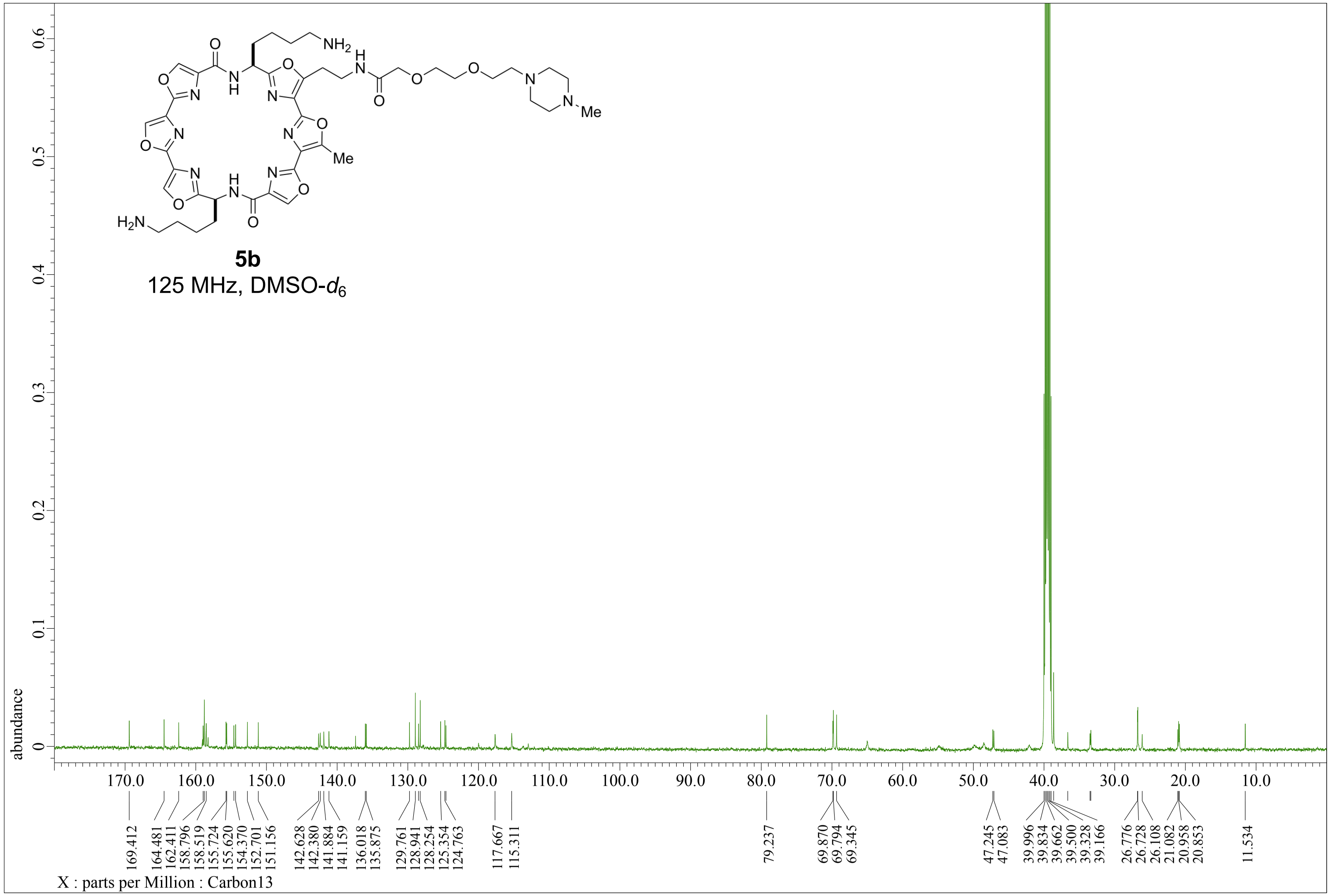
19b

125 MHz, DMSO-d_6



5b

500 MHz, DMSO-d_6


5b
125 MHz, DMSO-d_6
Me
NH$_2$
H$_2$N
N
O
H
abundance
0.6
0.5
0.4
0.3
0.2
0.1
0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
169.412
164.481
162.411
158.796
158.519
155.724
155.620
154.370
152.701
151.156
142.628
142.380
141.884
141.159
136.018
135.875
129.761
128.941
128.254
125.354
124.763
117.667
115.311
79.237
69.870
69.794
69.345
47.245
47.083
39.996
39.834
39.662
39.500
39.328
39.166
26.776
26.728
26.108
21.082
20.958
20.853
11.534
X : parts per Million : Carbon13