

Figliola, Marchal,
Groves and Thompson

Step-wise synthetic approach key to γ -conjugates of folate:
folate-conjugated prodigiosenes

Supplemental Information

Step-wise synthetic approach is necessary to access γ -conjugates of folate: folate-conjugated prodigiosenes

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[‡]Equal contributions

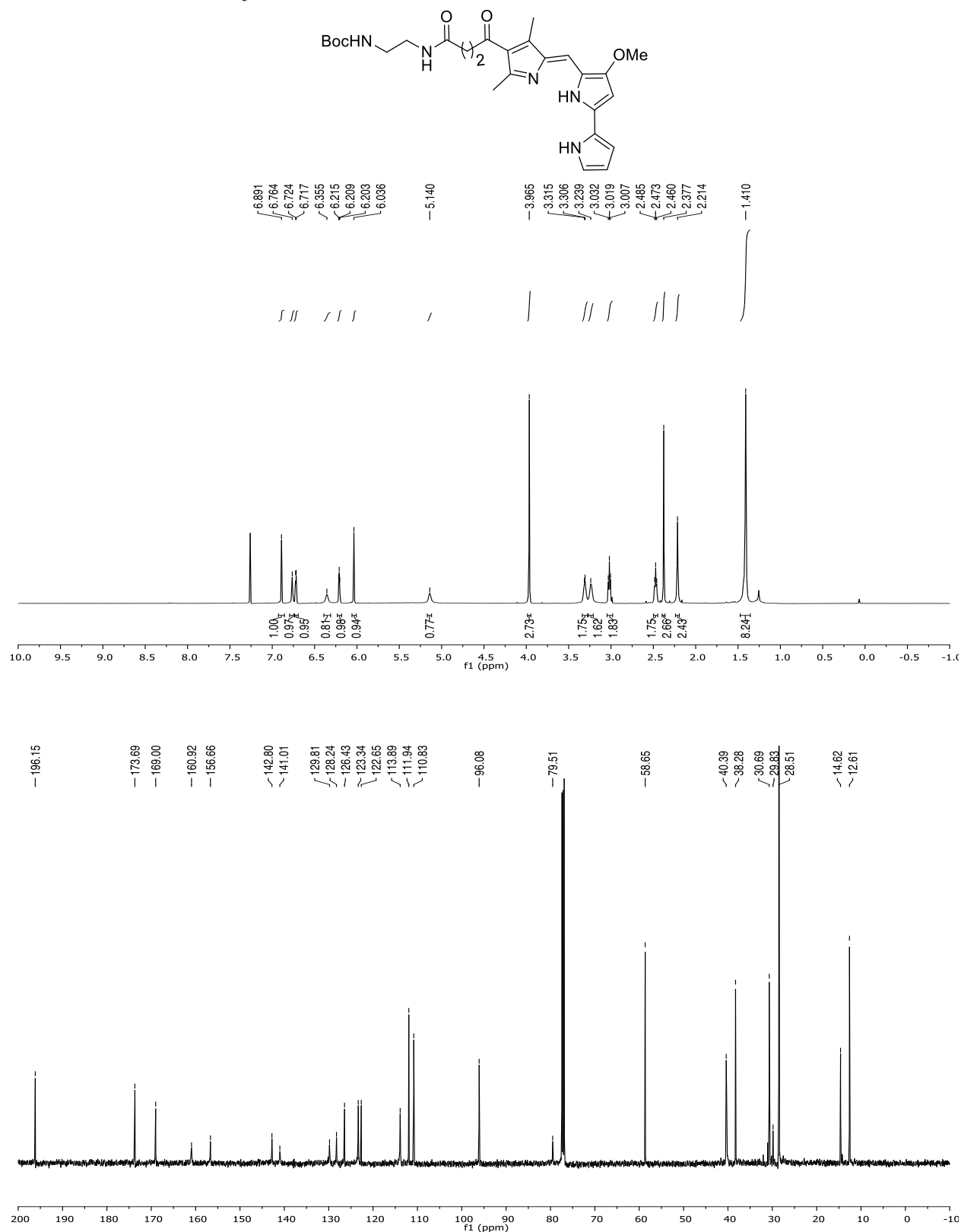
*alison.thompson@dal.ca; (T) 1-902-494-3305

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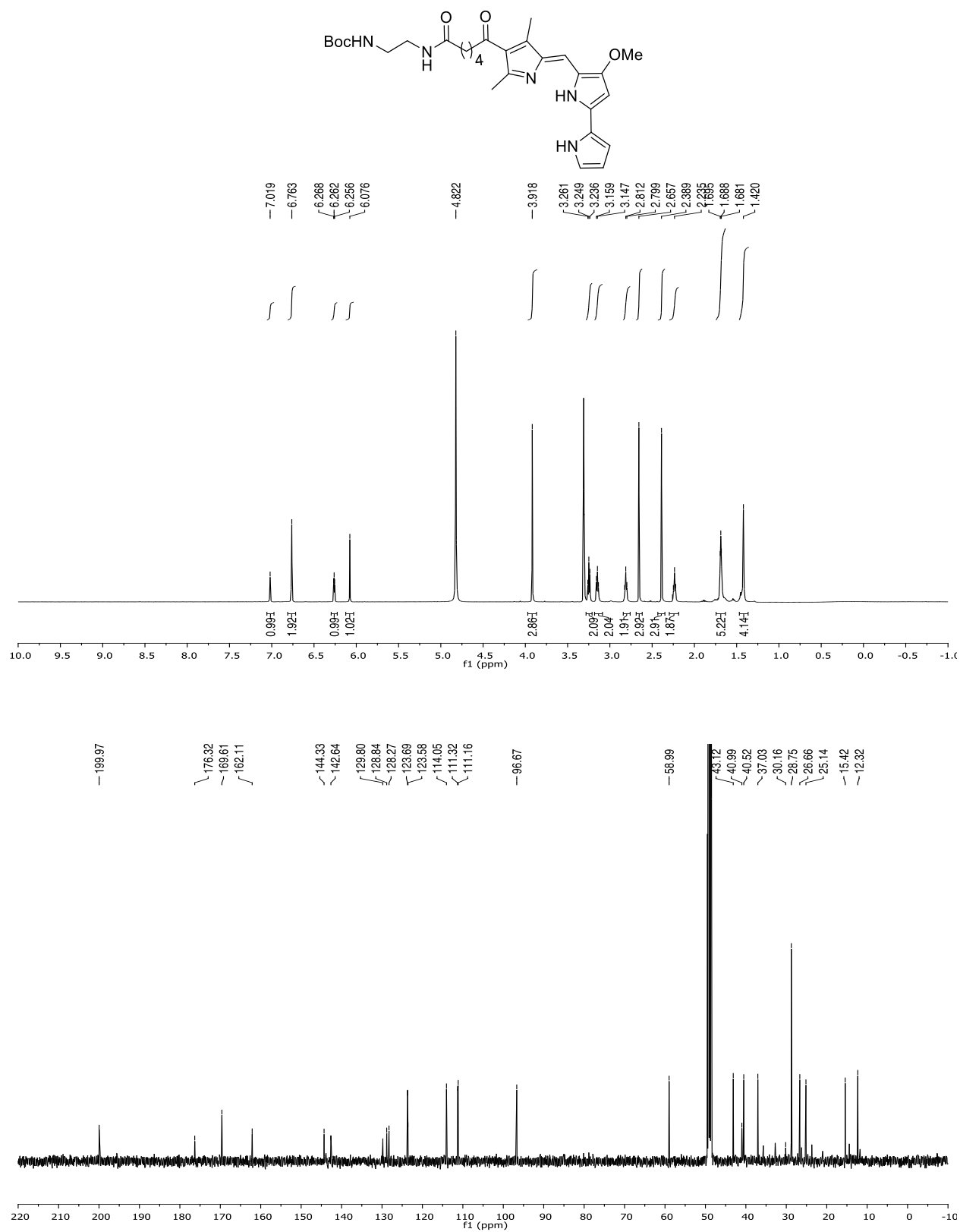
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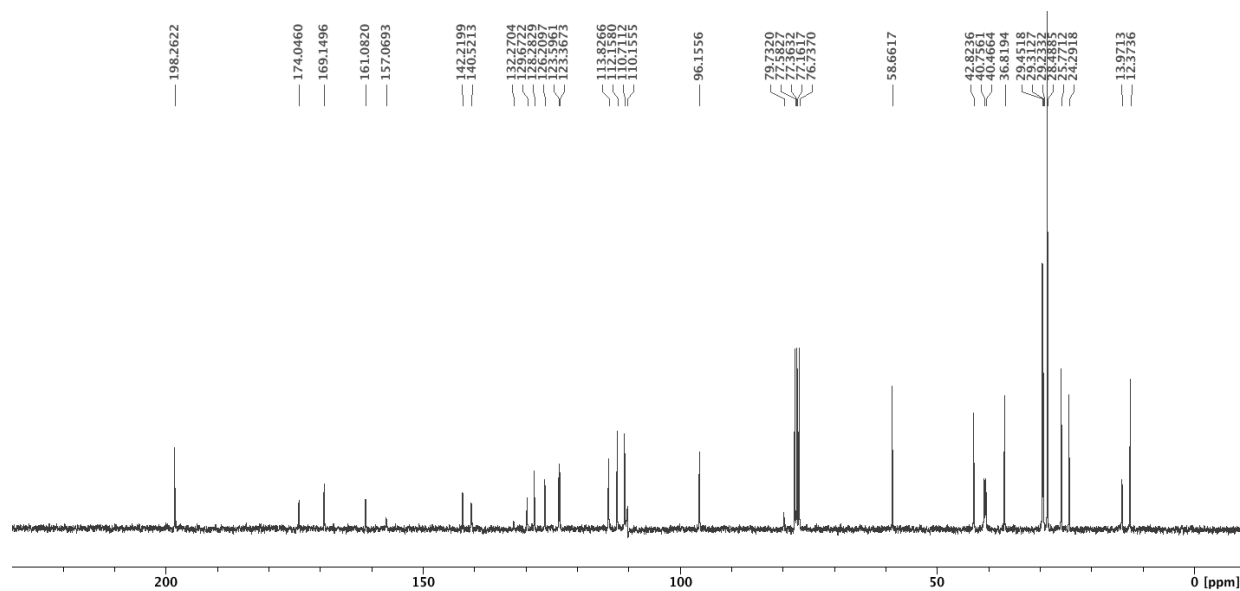
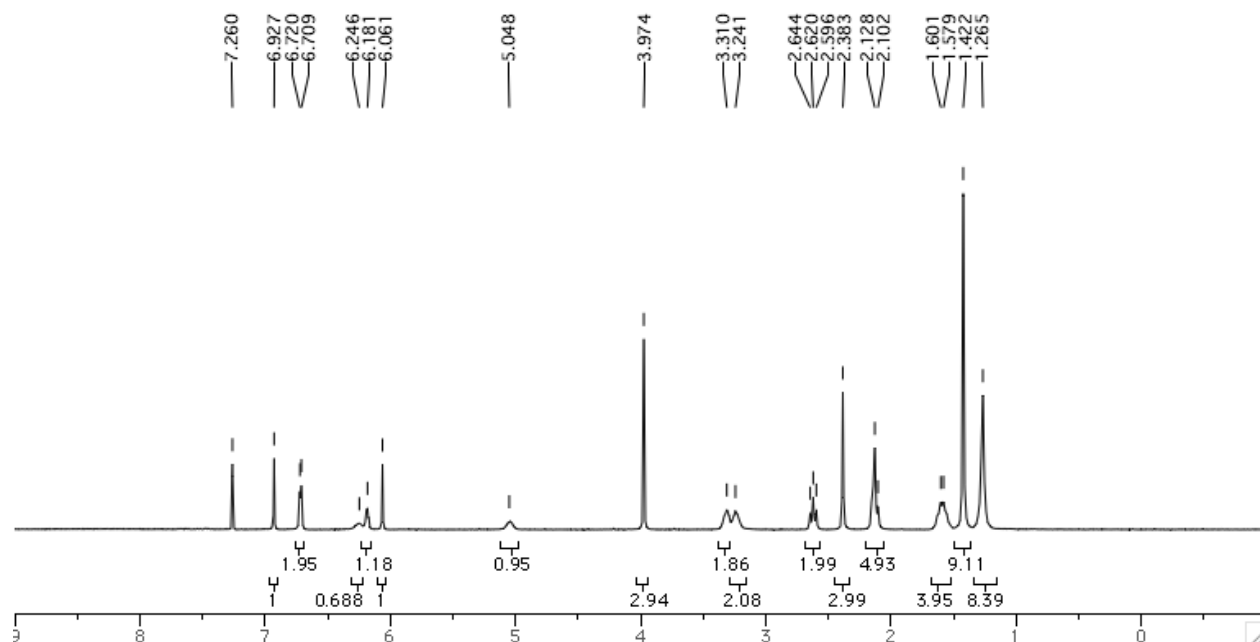
^1H and ^{13}C NMR Spectra

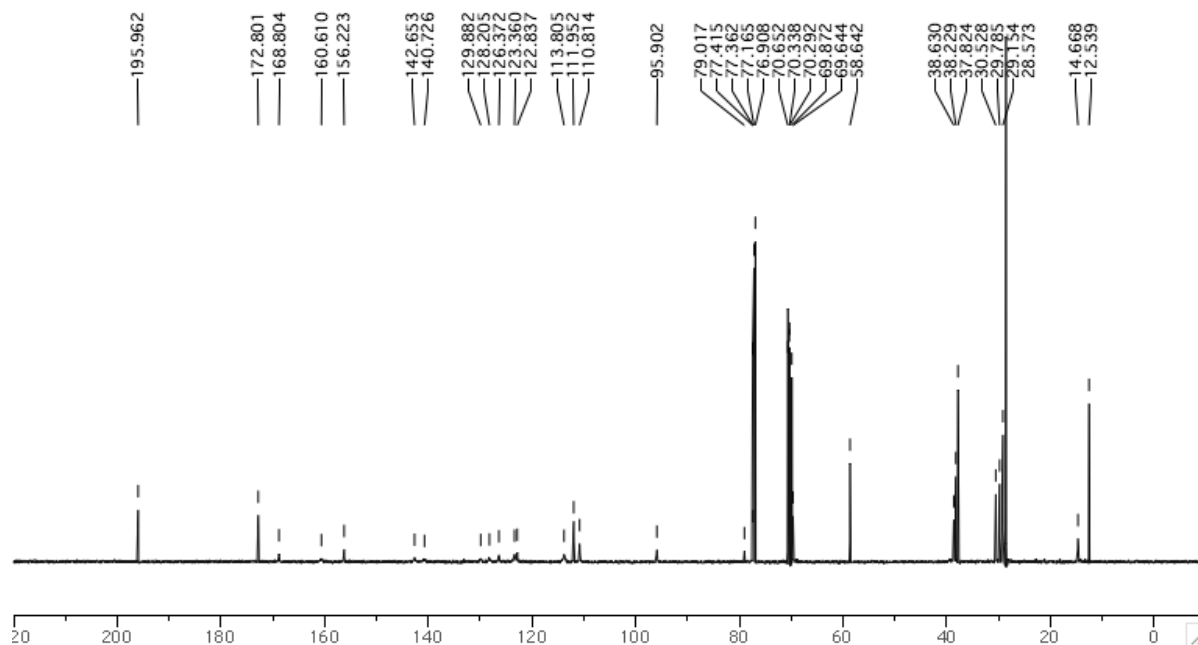
^1H and ^{13}C NMR in CDCl_3 of **8a**



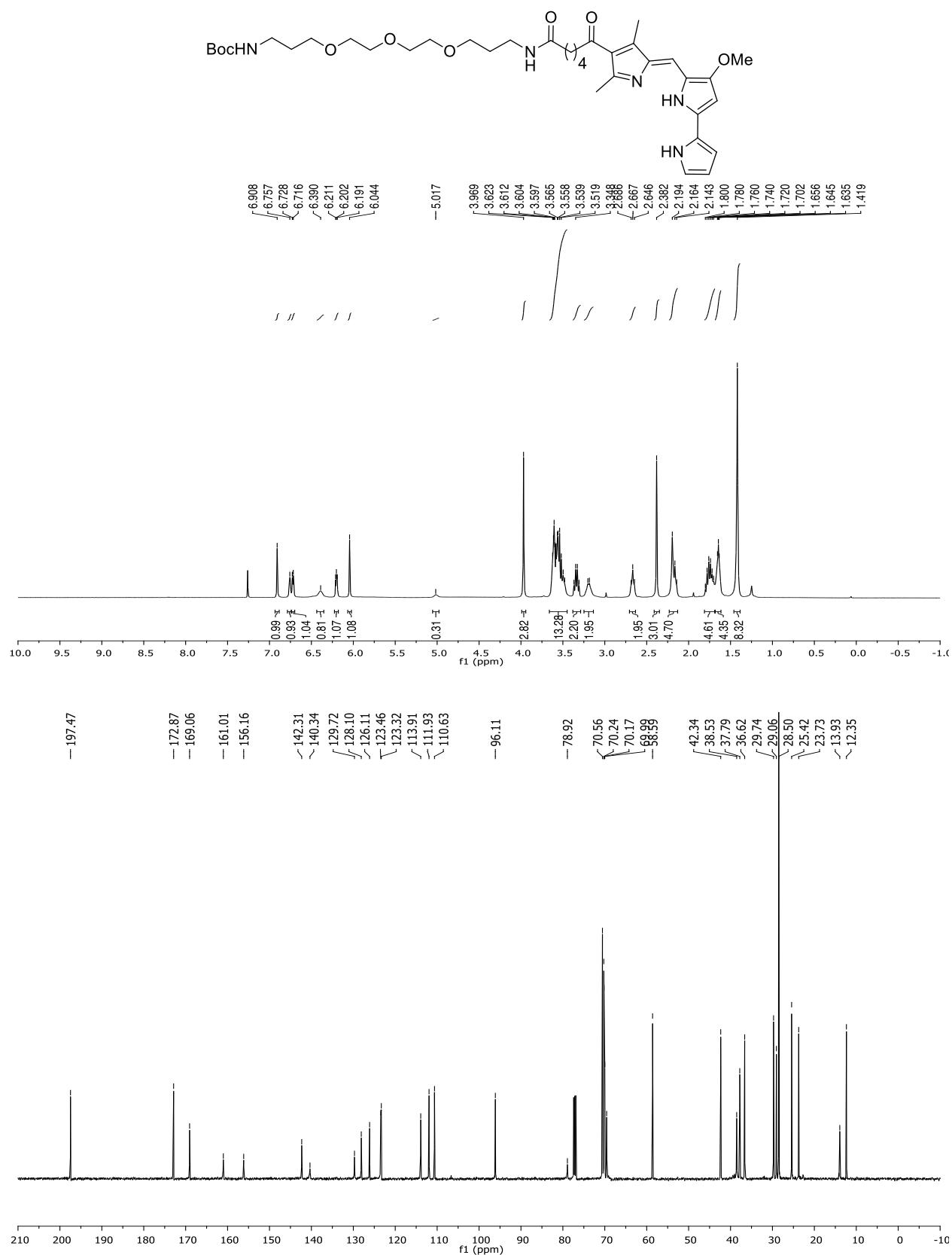
^1H and ^{13}C NMR in CD_3OD of **8b**



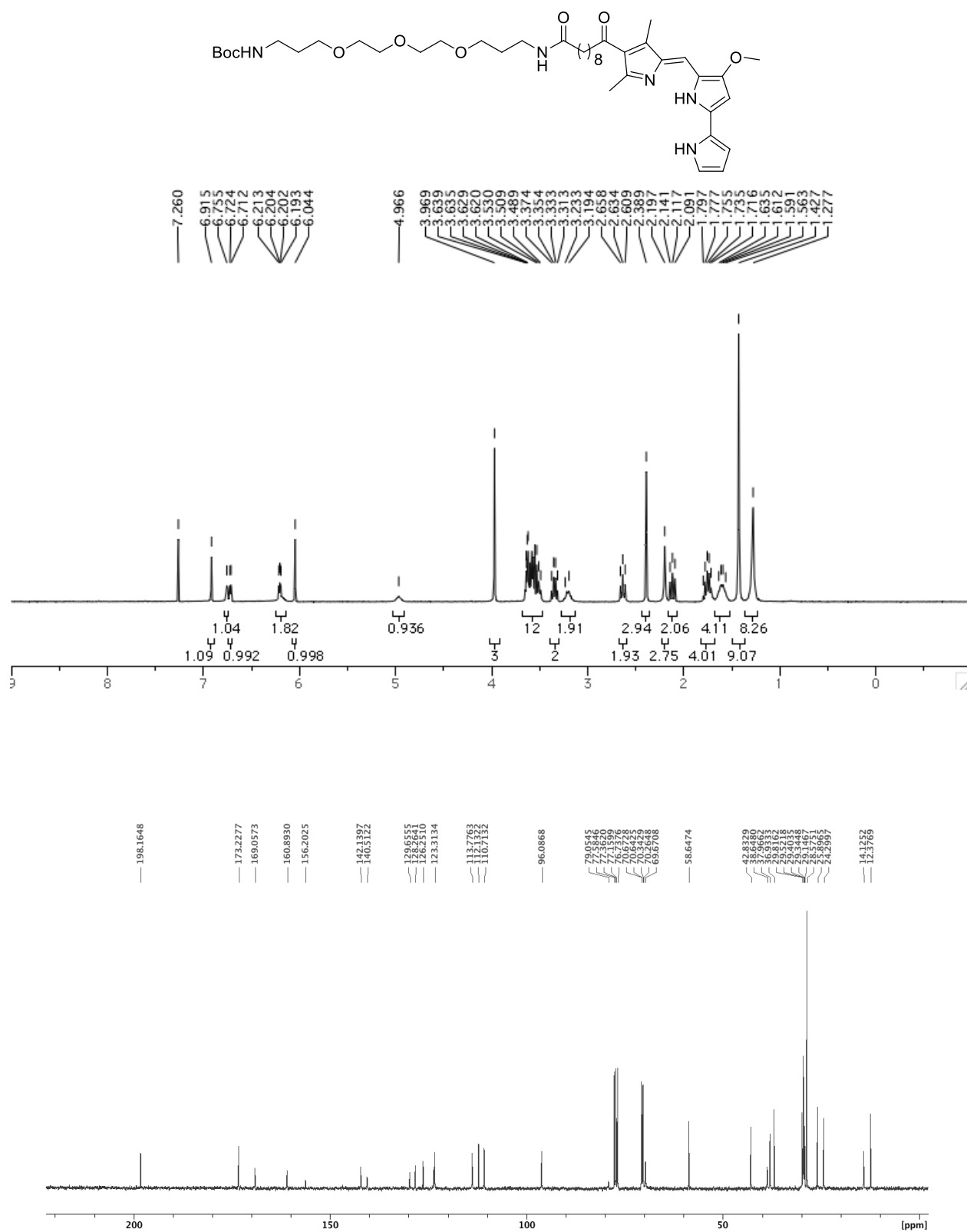
CC1=C(C)C(=C(C=C1)/C=C2/C(=C(C=C(C=C2)OC)N3C=CC(=C3)N4C=CC=CC4N)N)C(=O)C(=O)CC(=O)NCCNC(=O)C5=CC=CC=C5C(=O)OCC

COc1cc2c(cc1[nH]2)c3cc[nH]3C(=O)NCCOCCOCCOCCNC(=O)CC(=O)c4c(C)c(C)c(C)n4

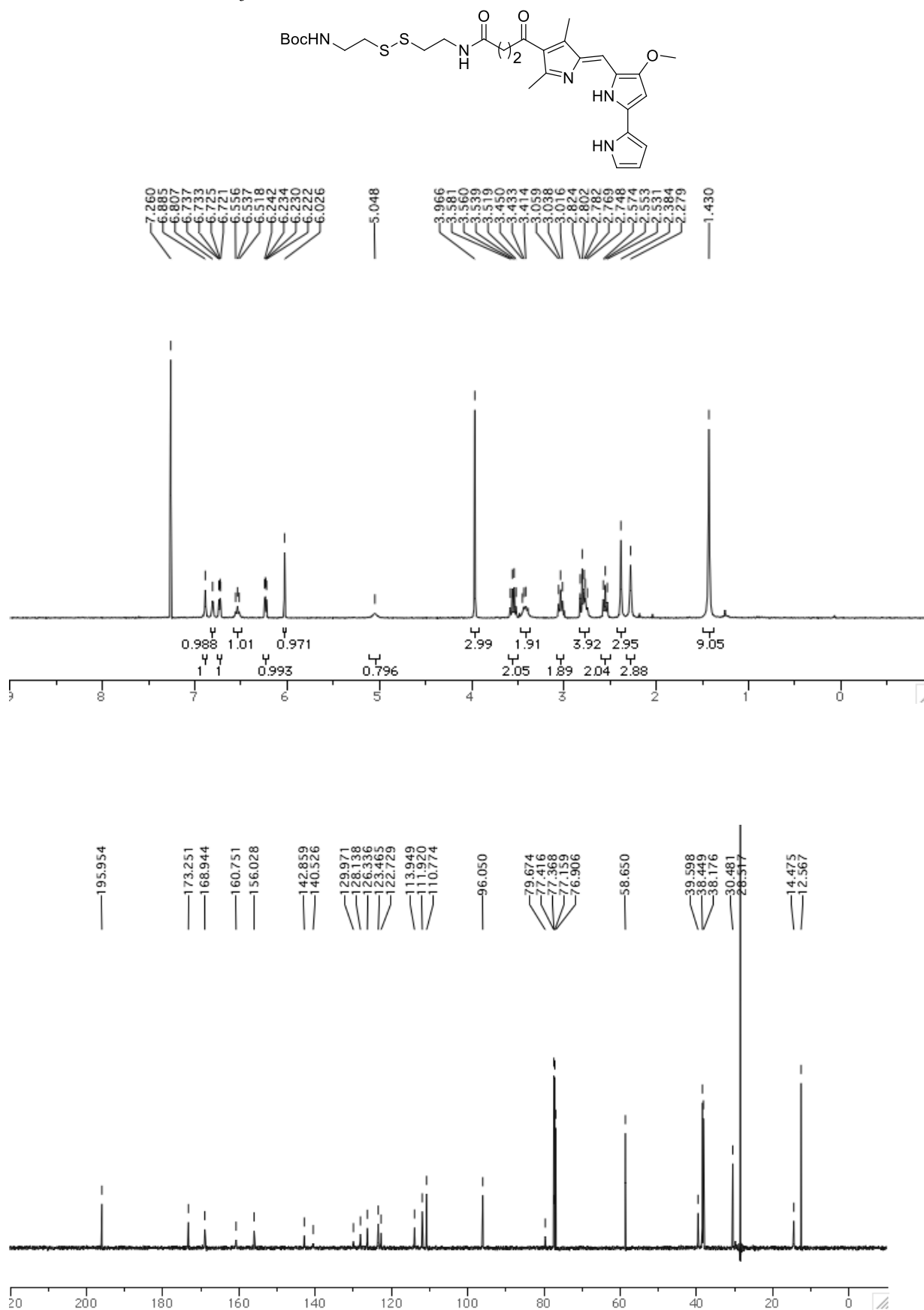
^1H and ^{13}C NMR in CDCl_3 of **9b**



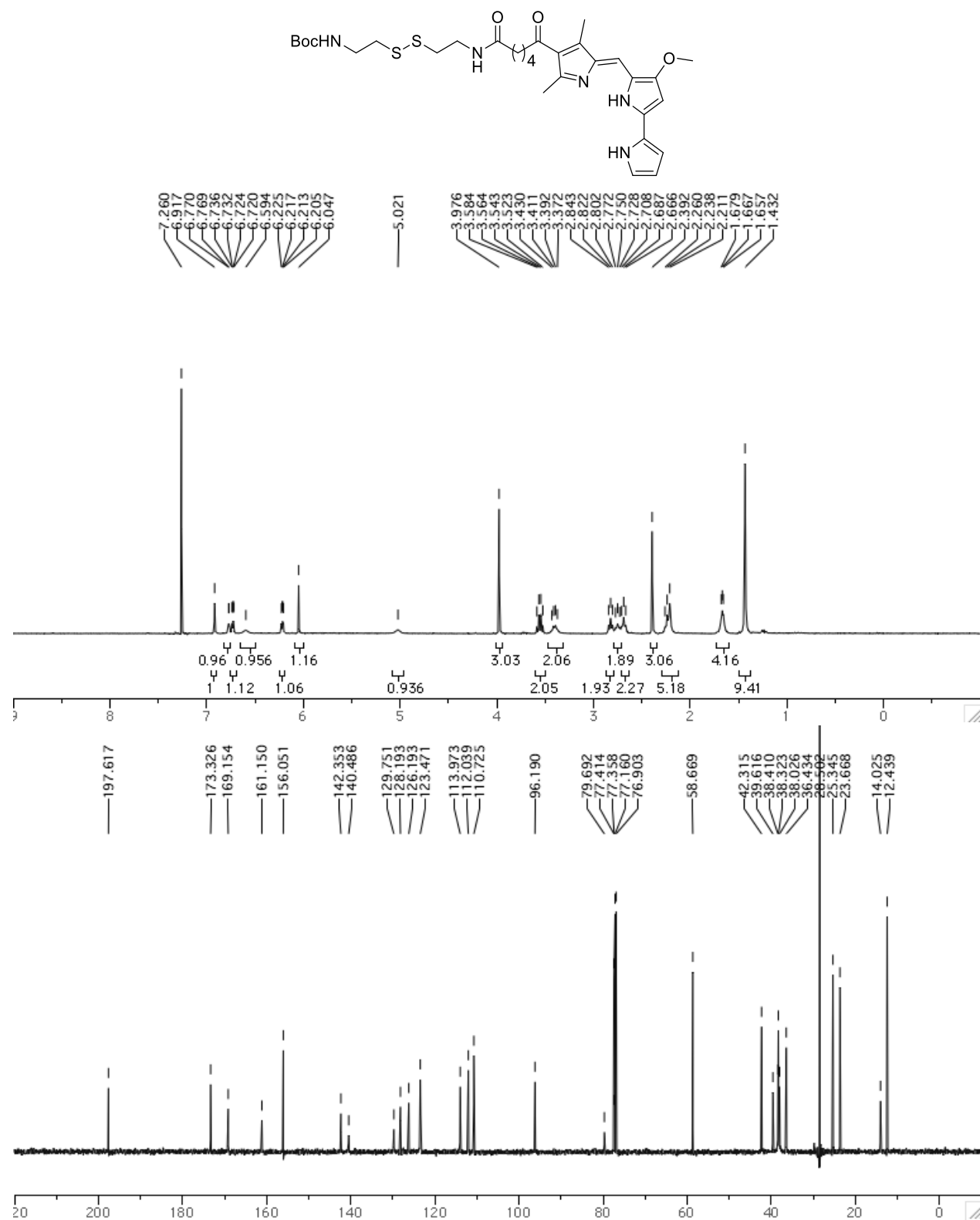
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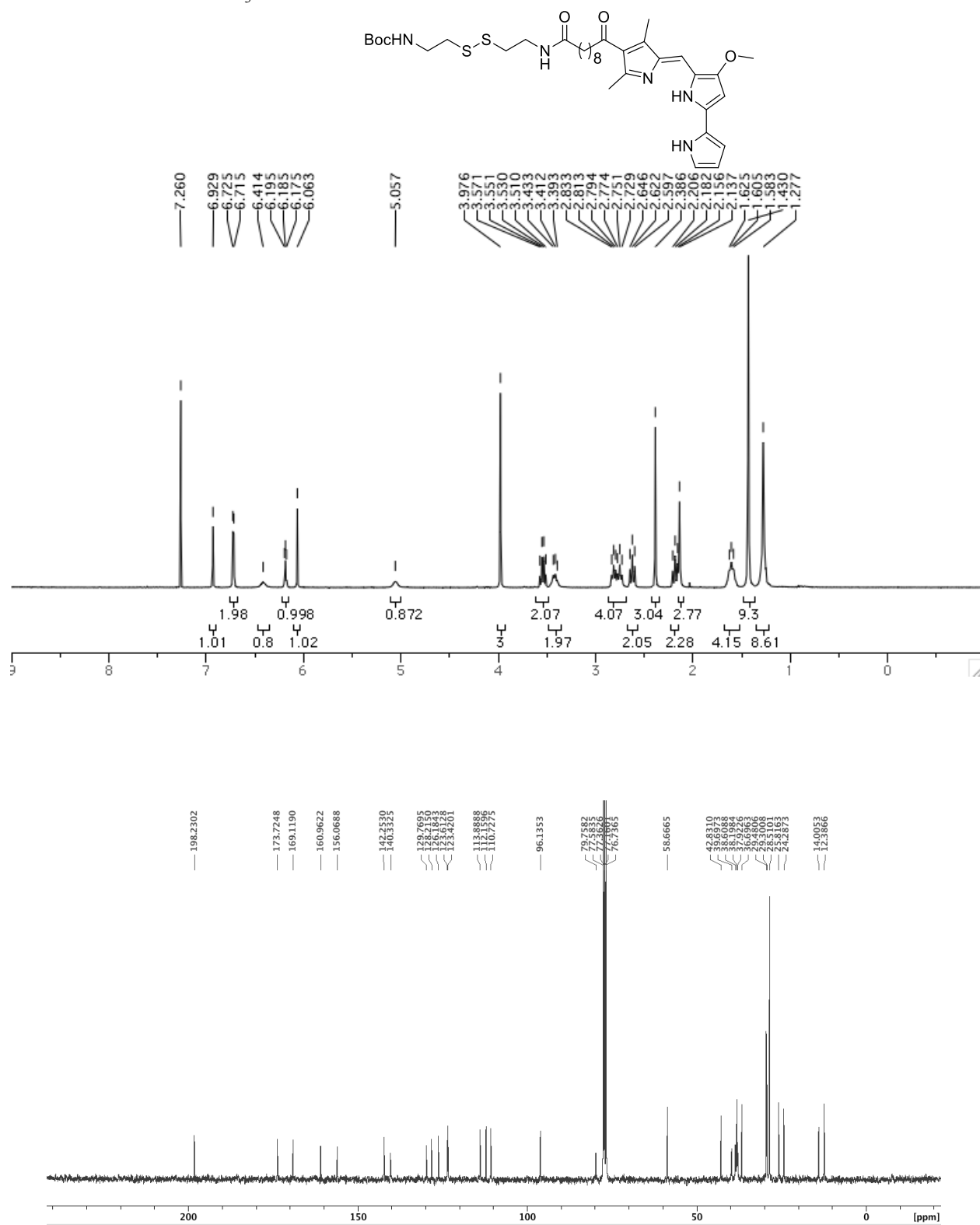
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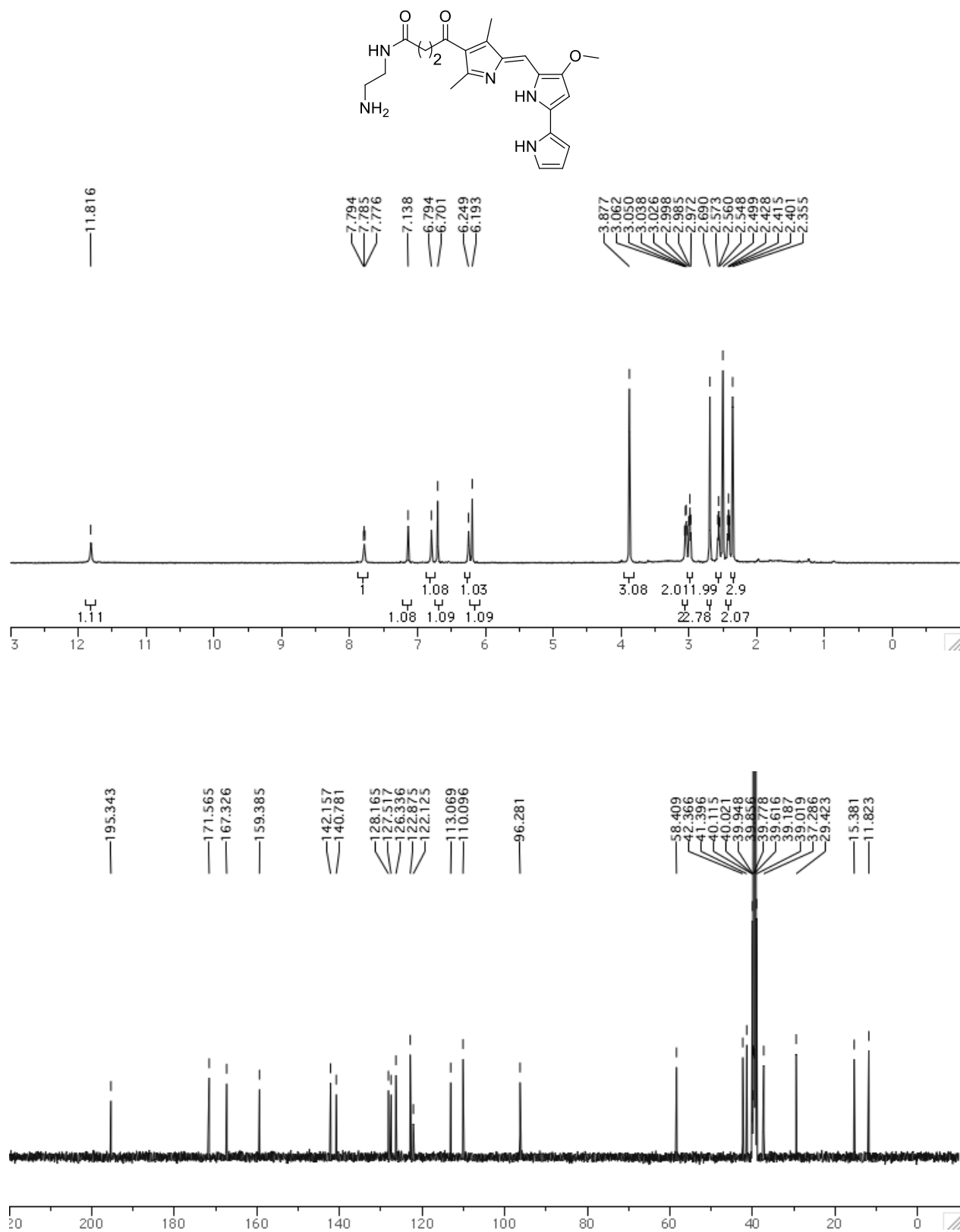
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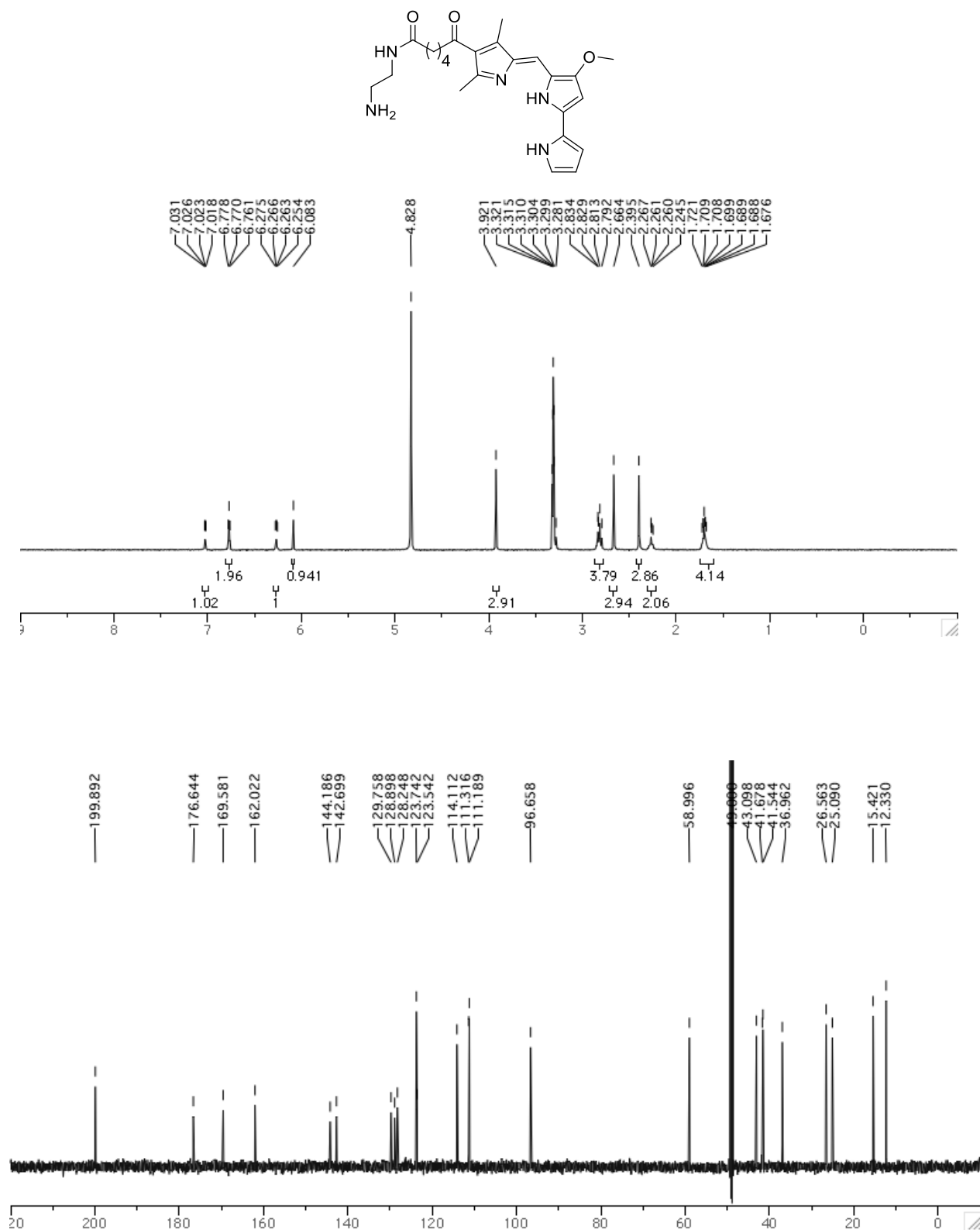
^1H and ^{13}C NMR in CDCl_3 of **10c**



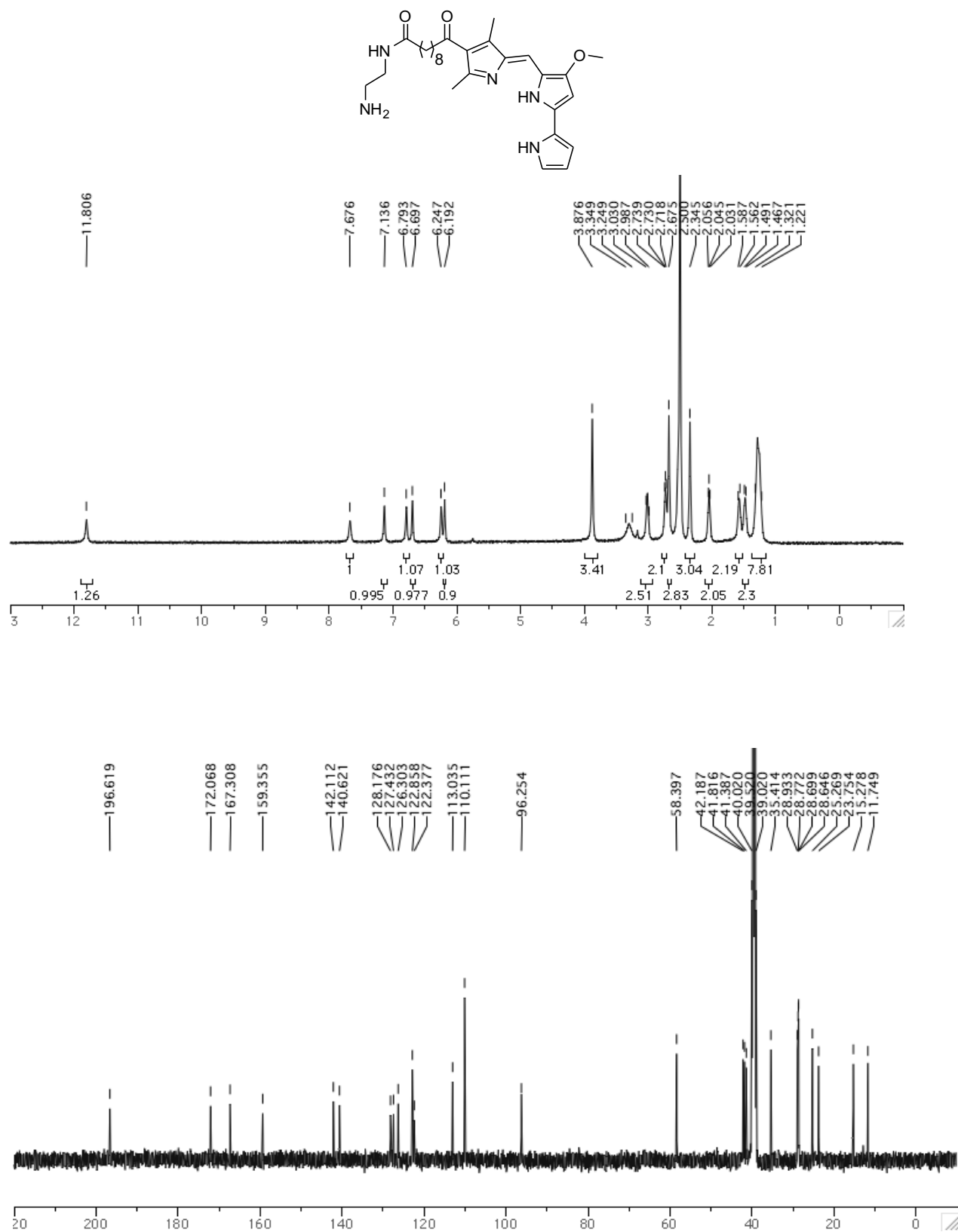
^1H and ^{13}C NMR in DMSO-d_6 of **2a**



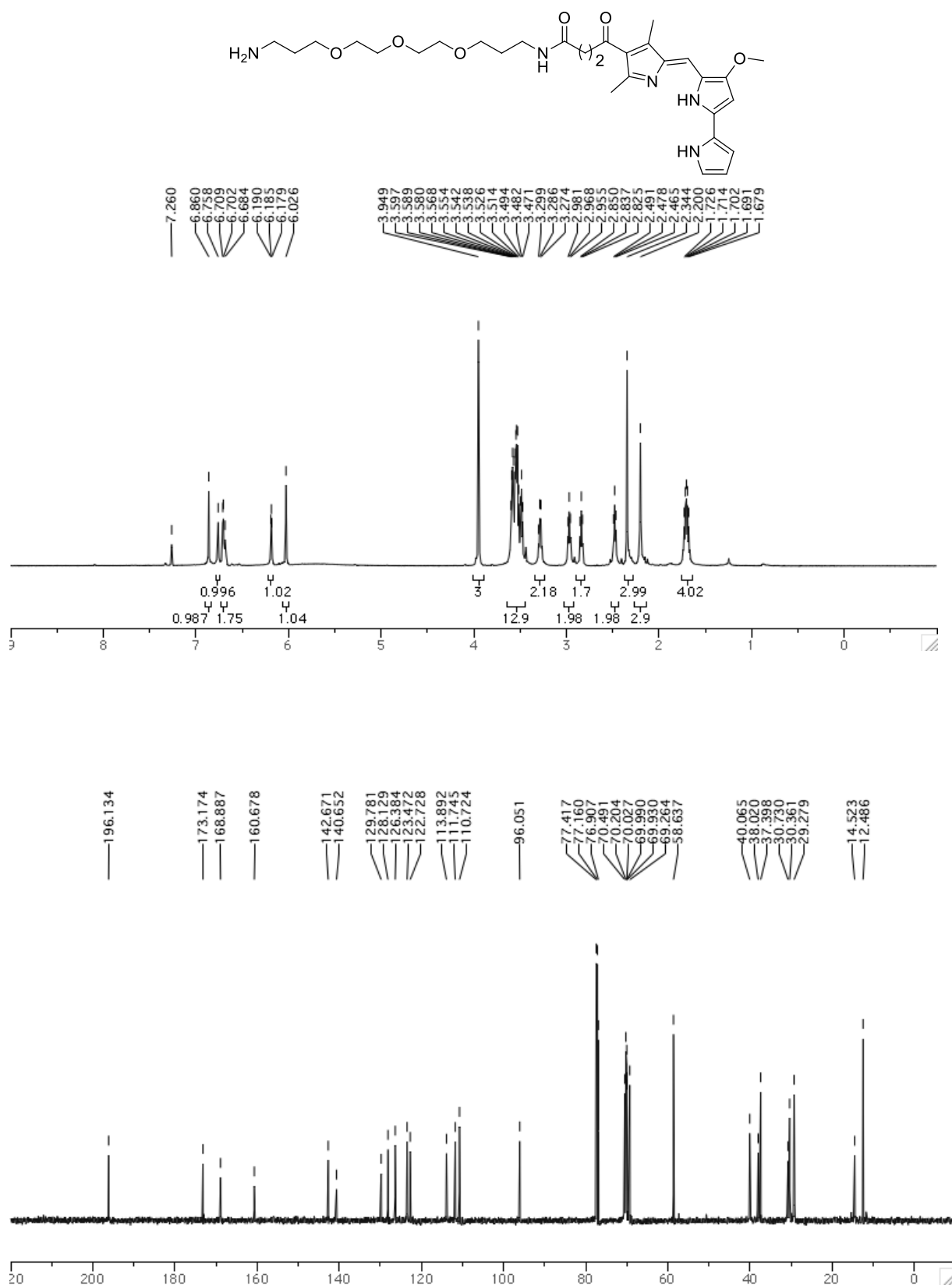
^1H and ^{13}C NMR in CD_3OD of **2b**



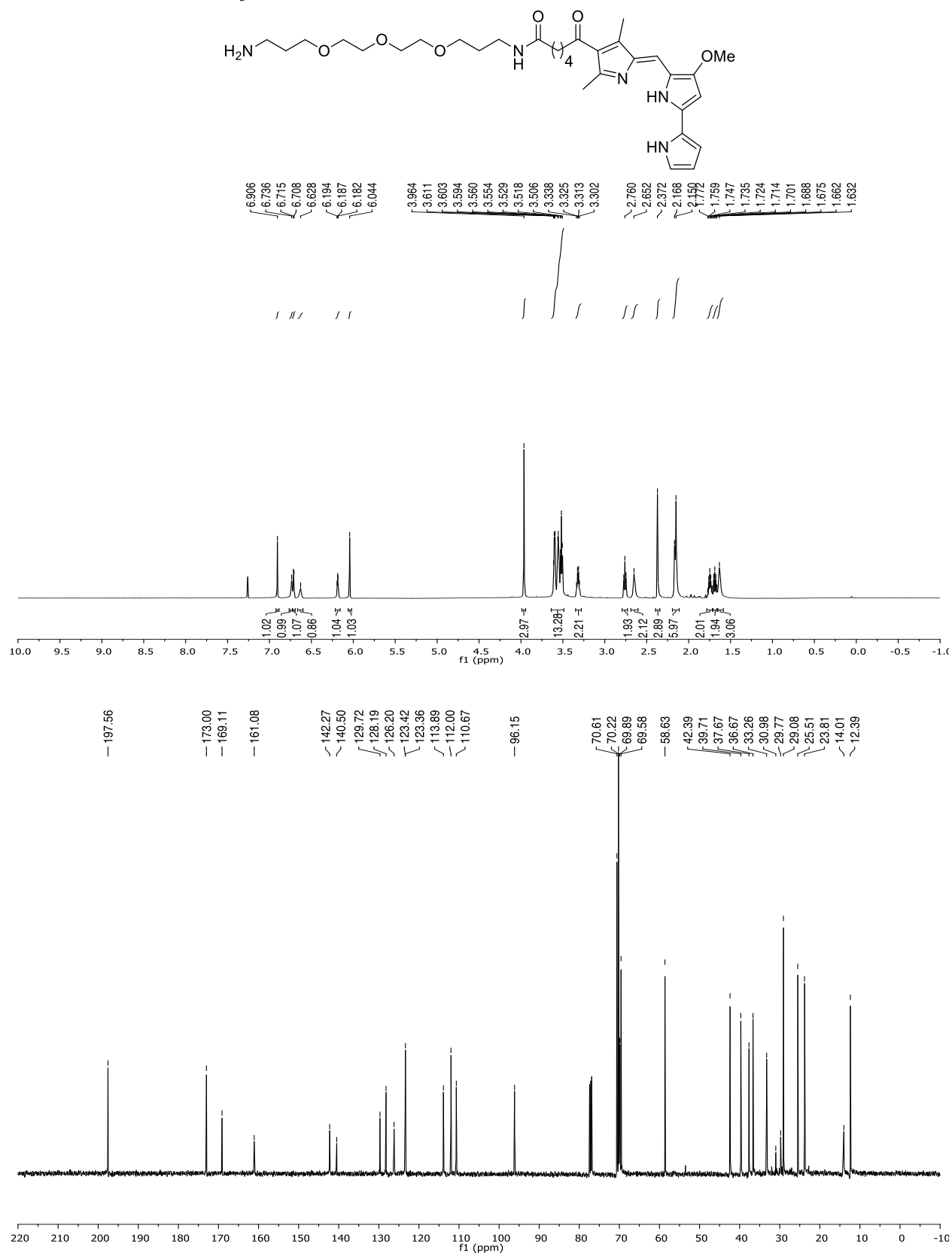
^1H and ^{13}C NMR in $\text{DMSO}-d_6$ of **2c**

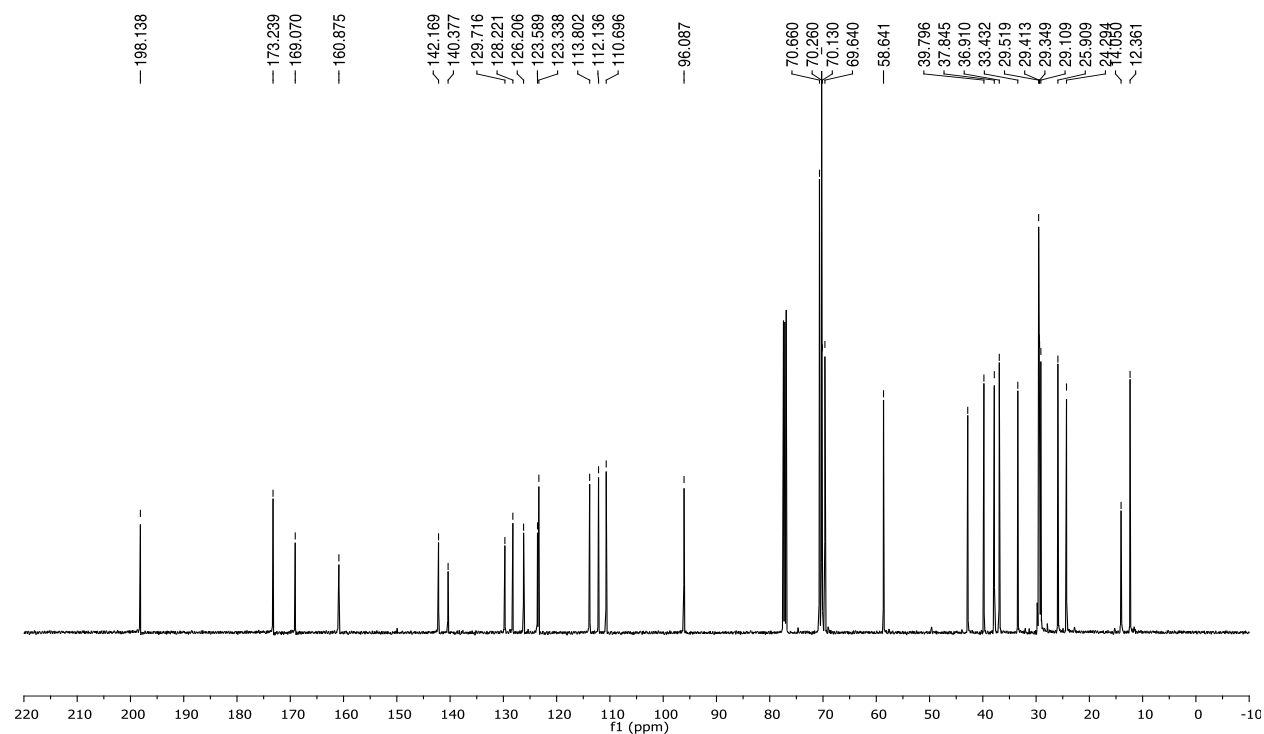


^1H and ^{13}C NMR in CDCl_3 of **3a**

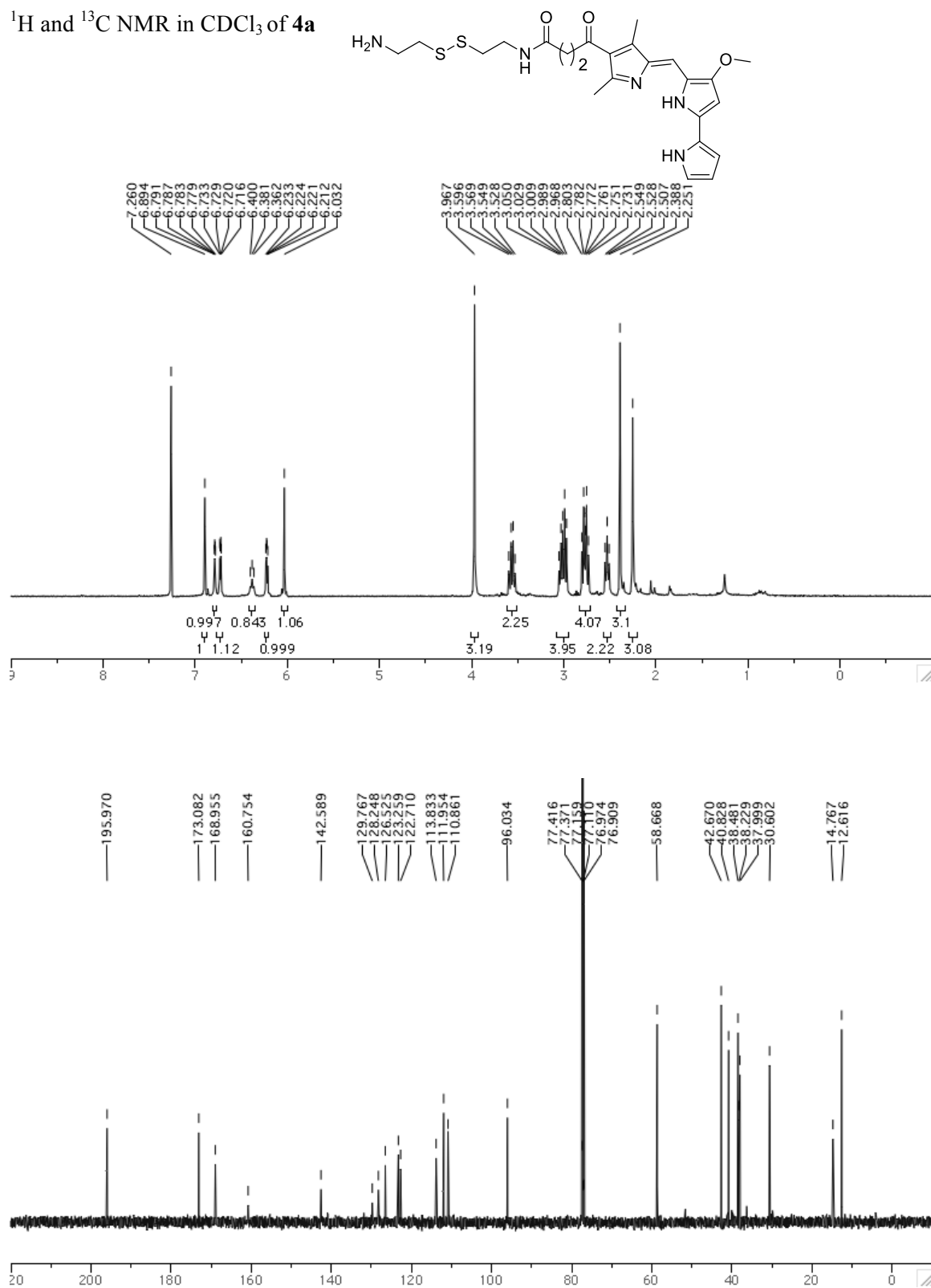


^1H and ^{13}C NMR in CDCl_3 of **3b**

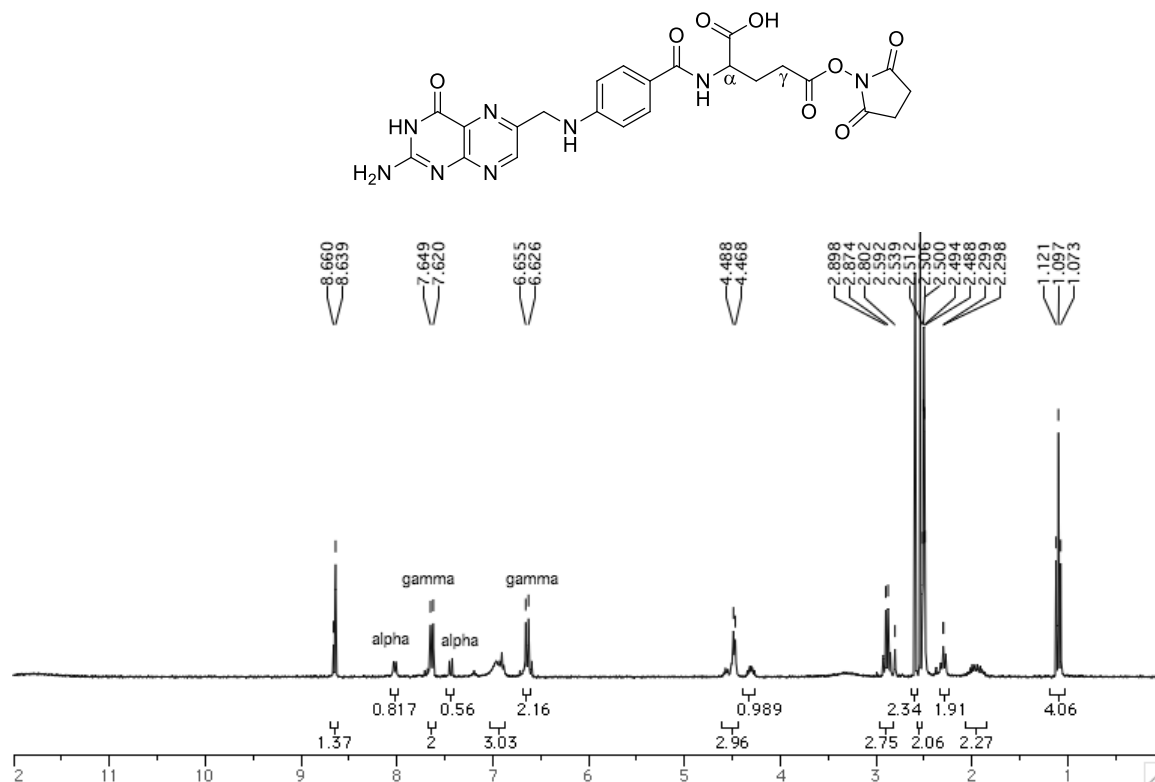


COC1=CC=C(C(=C1)/C=N/C2=CN(C)C(=O)N(CC2)C(=O)NCCCCOCCOCCOCCOCCN)C3=CC=NC=C3

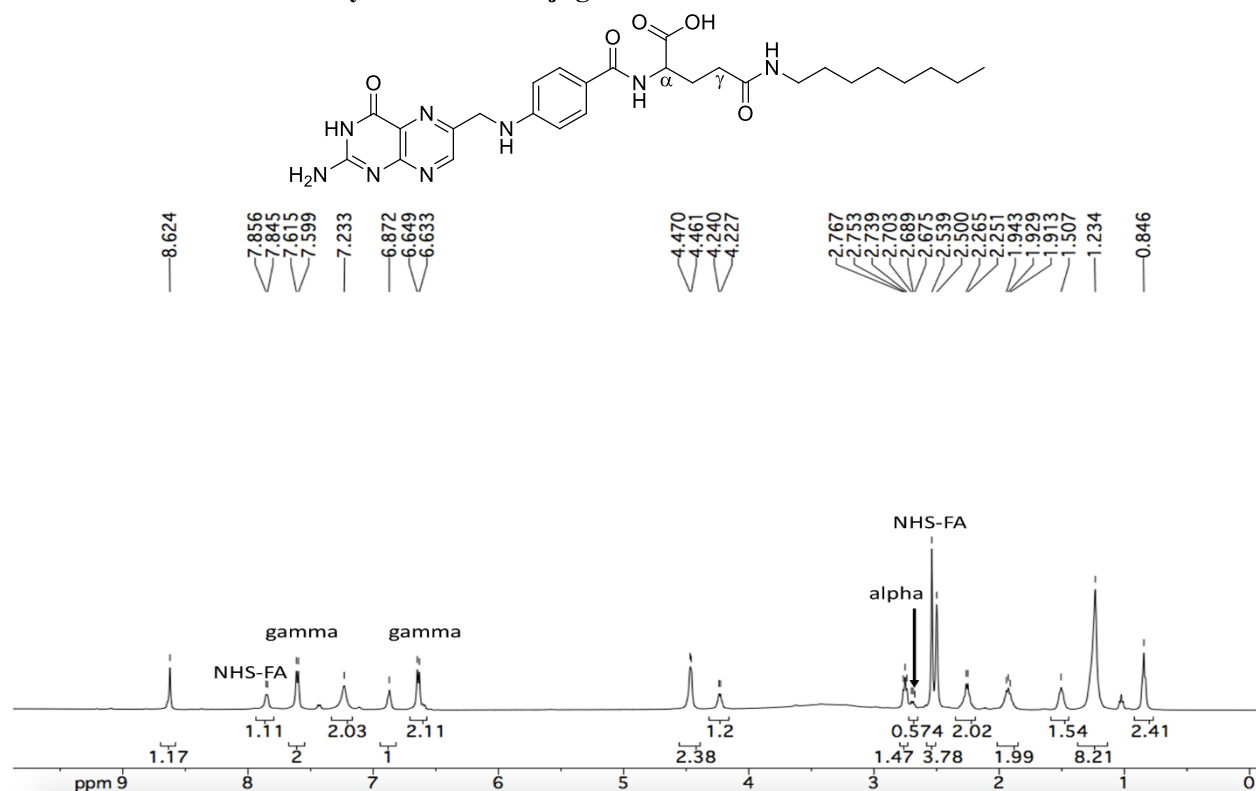
^1H and ^{13}C NMR in CDCl_3 of **4a**



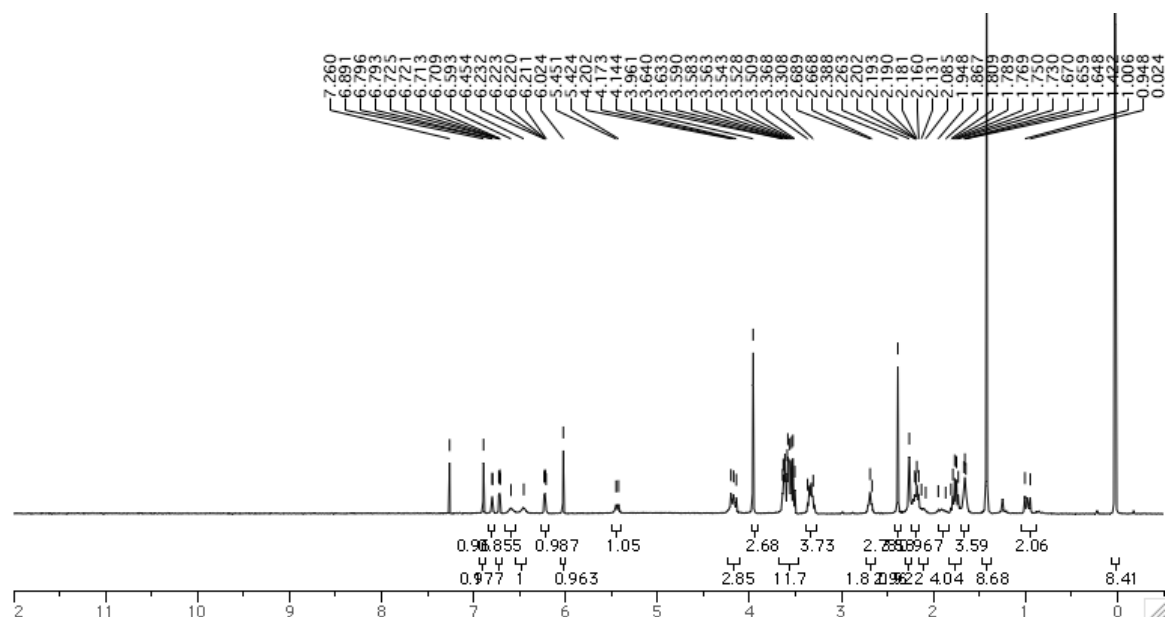
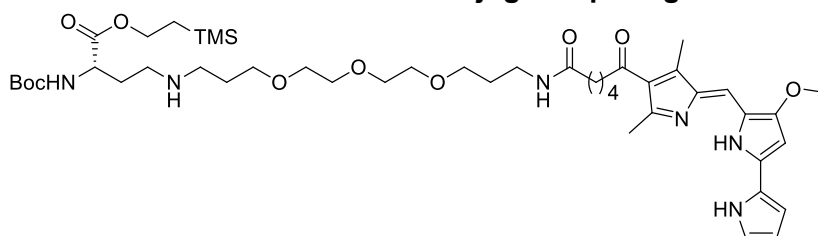
^1H NMR in DMSO- d_6 of **11**

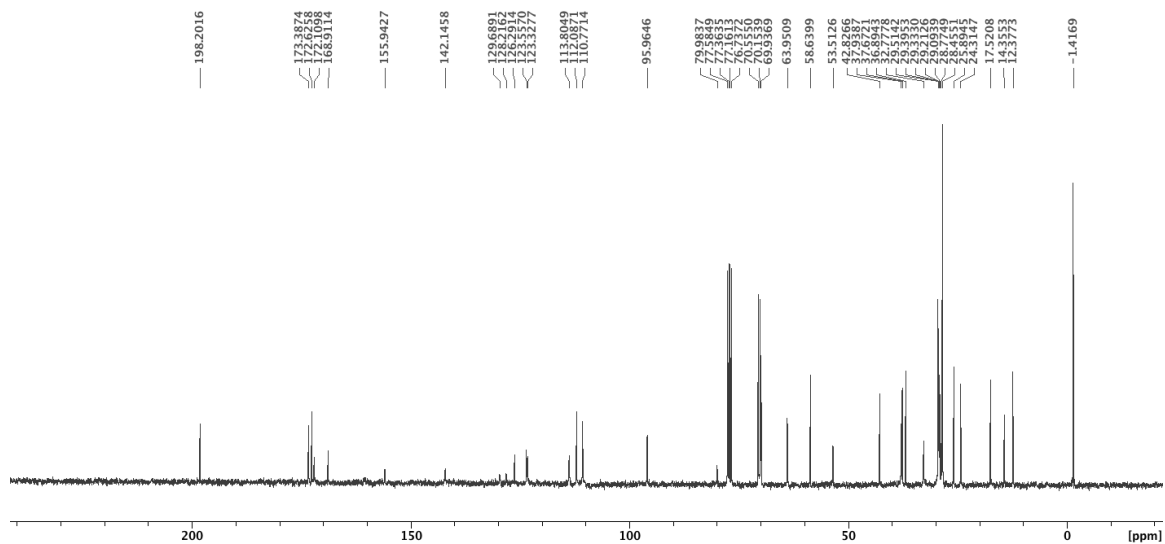
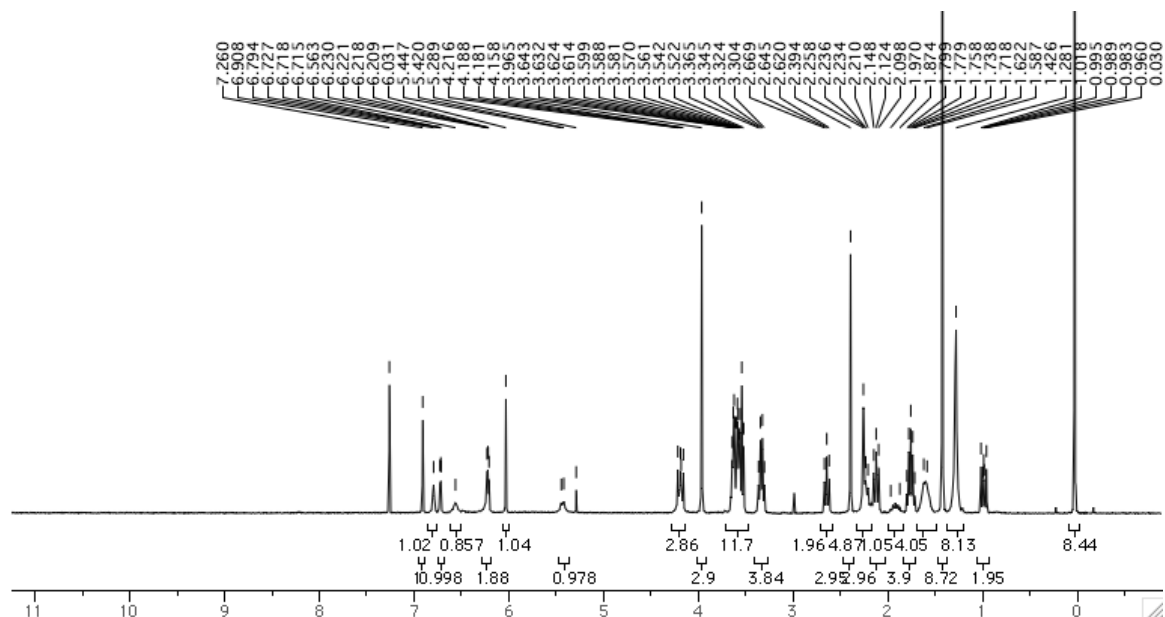


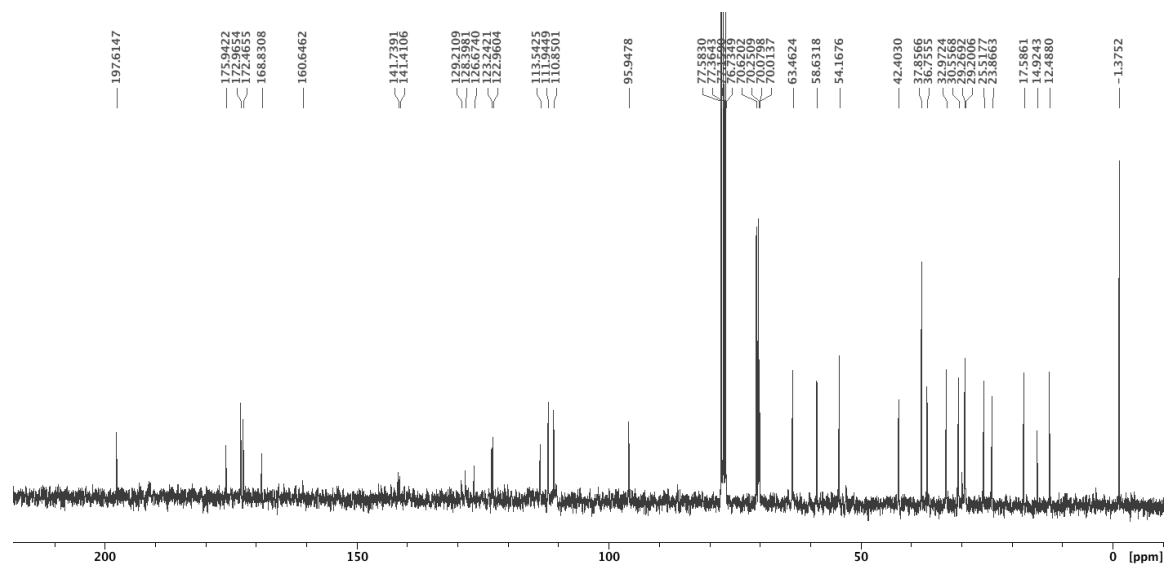
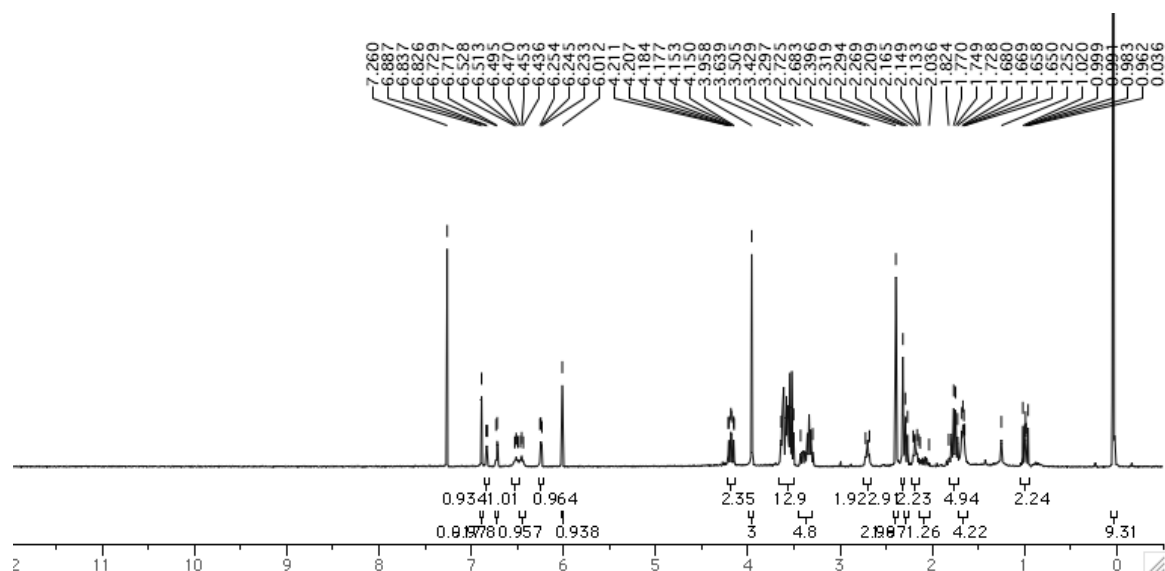
^1H NMR in DMSO- d_6 of octylamine-FA conjugate



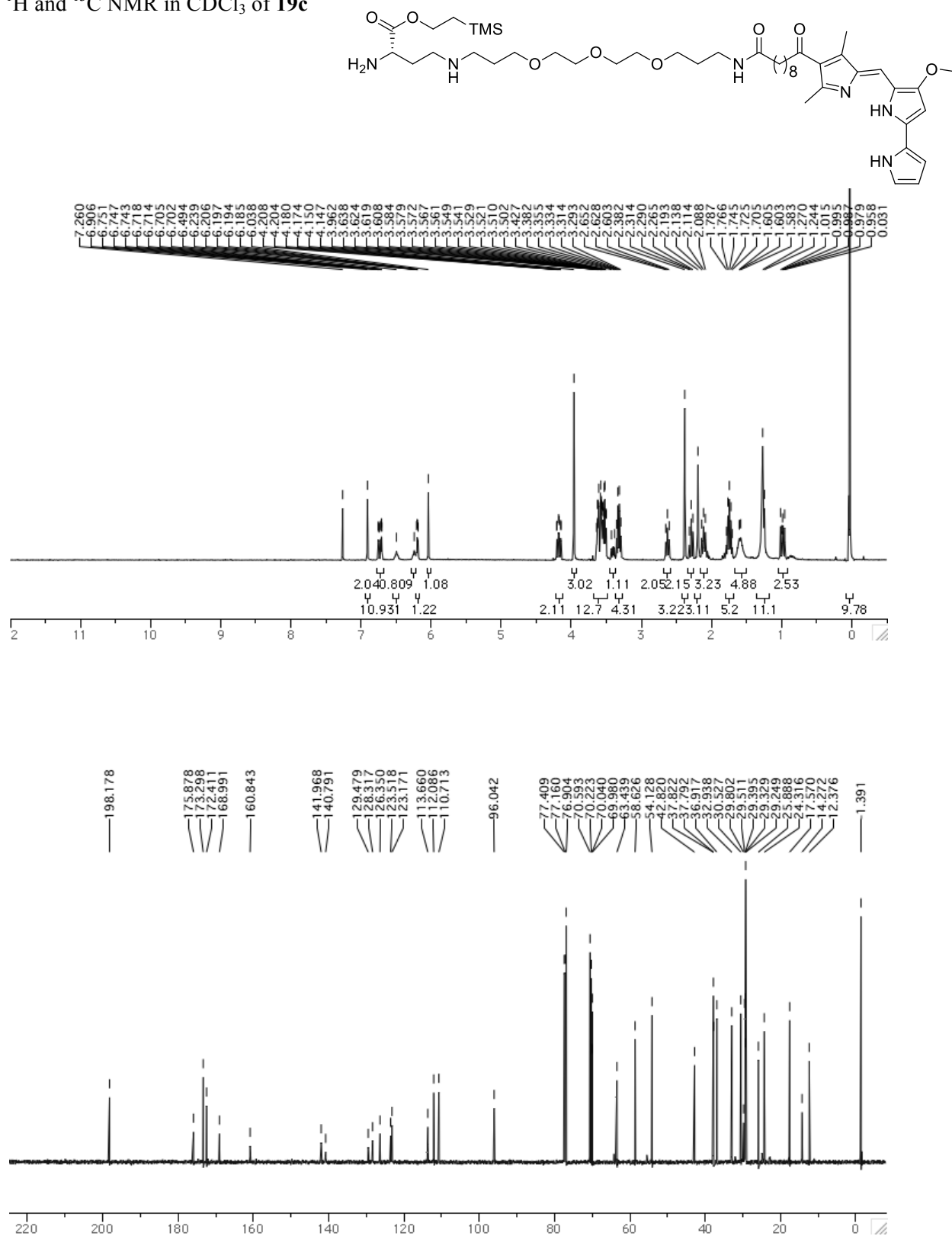
^1H and ^{13}C NMR in CDCl_3 of **18b**



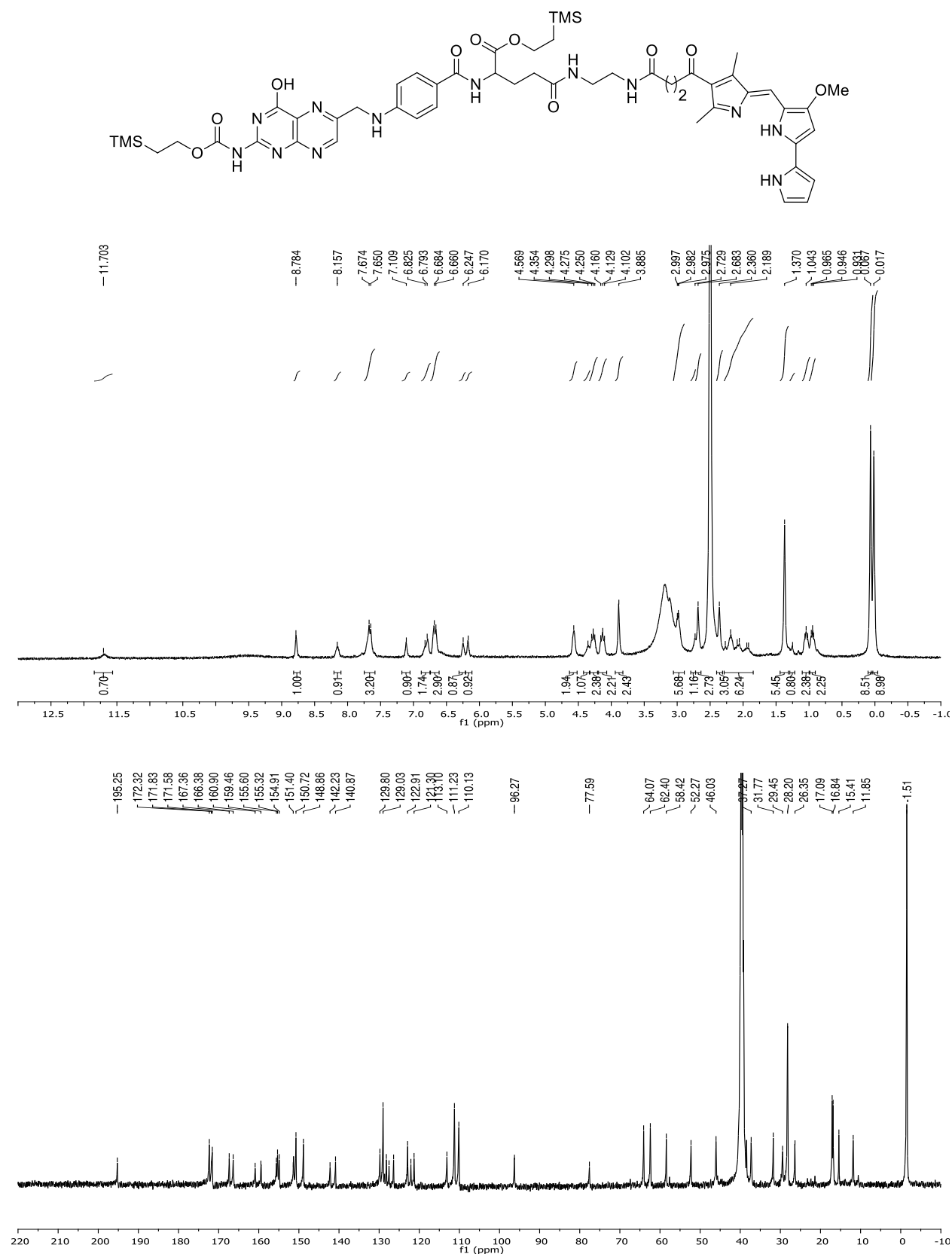
COc1cc2c(c[nH]1)/C=C3\C=C(C)N(C)C3=O.CC(C)(C)OC(=O)NCCOCCOCCOCCOCCOCCOCCOCC(=O)N[C@@H](CC(C)OC(=O)OCC(C)(C)C)C(=O)OCC(C)(C)C

CC(C)C1=CC=C(C=C1)c2c(C1)nc(C(=O)NCCOCCOCCOCCOCCOCC(=O)NCC[C@H](C)C(=O)OCC[Si](C)(C)C)cc2C

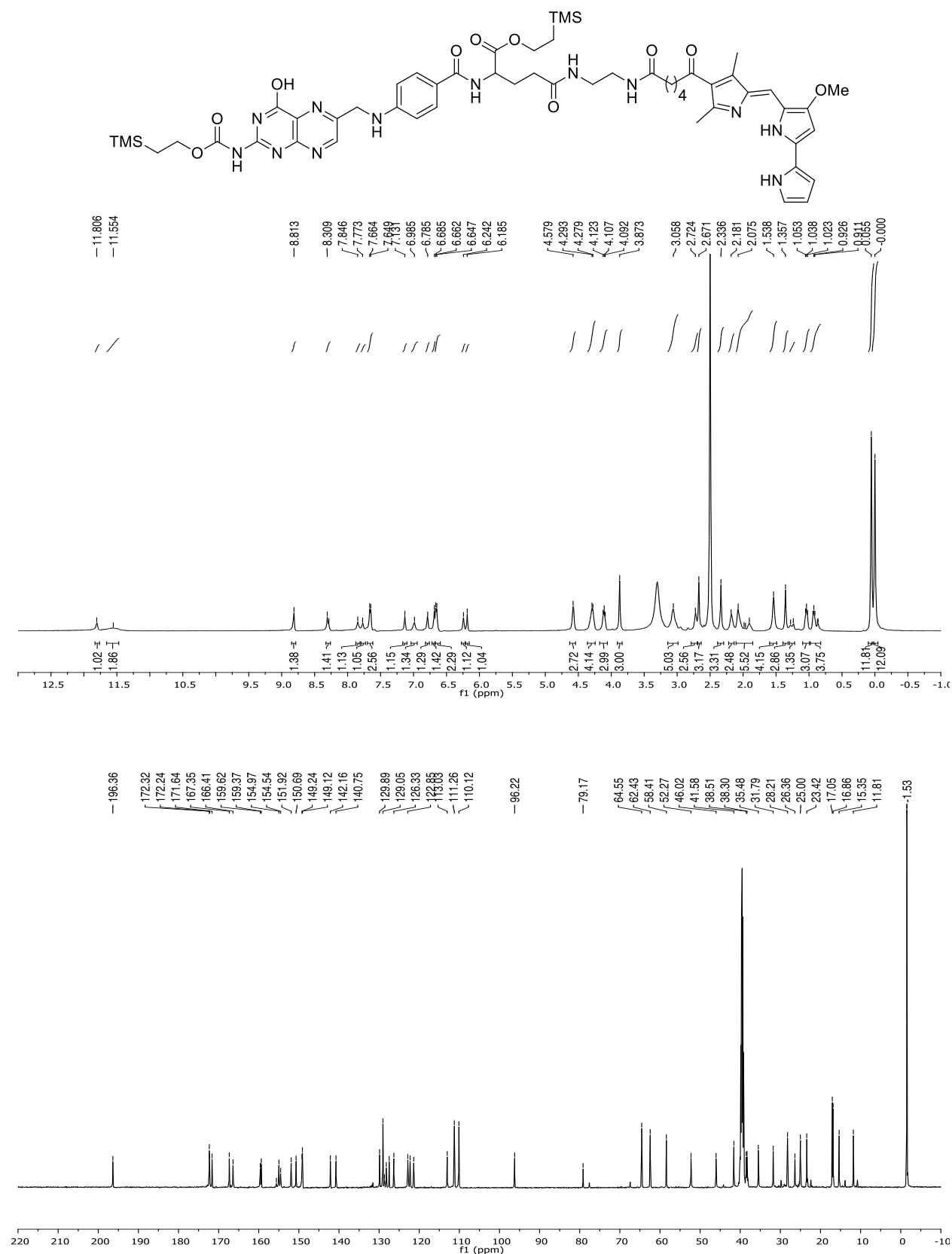
^1H and ^{13}C NMR in CDCl_3 of **19c**



^1H and ^{13}C NMR in DMSO-d_6 of **24a**



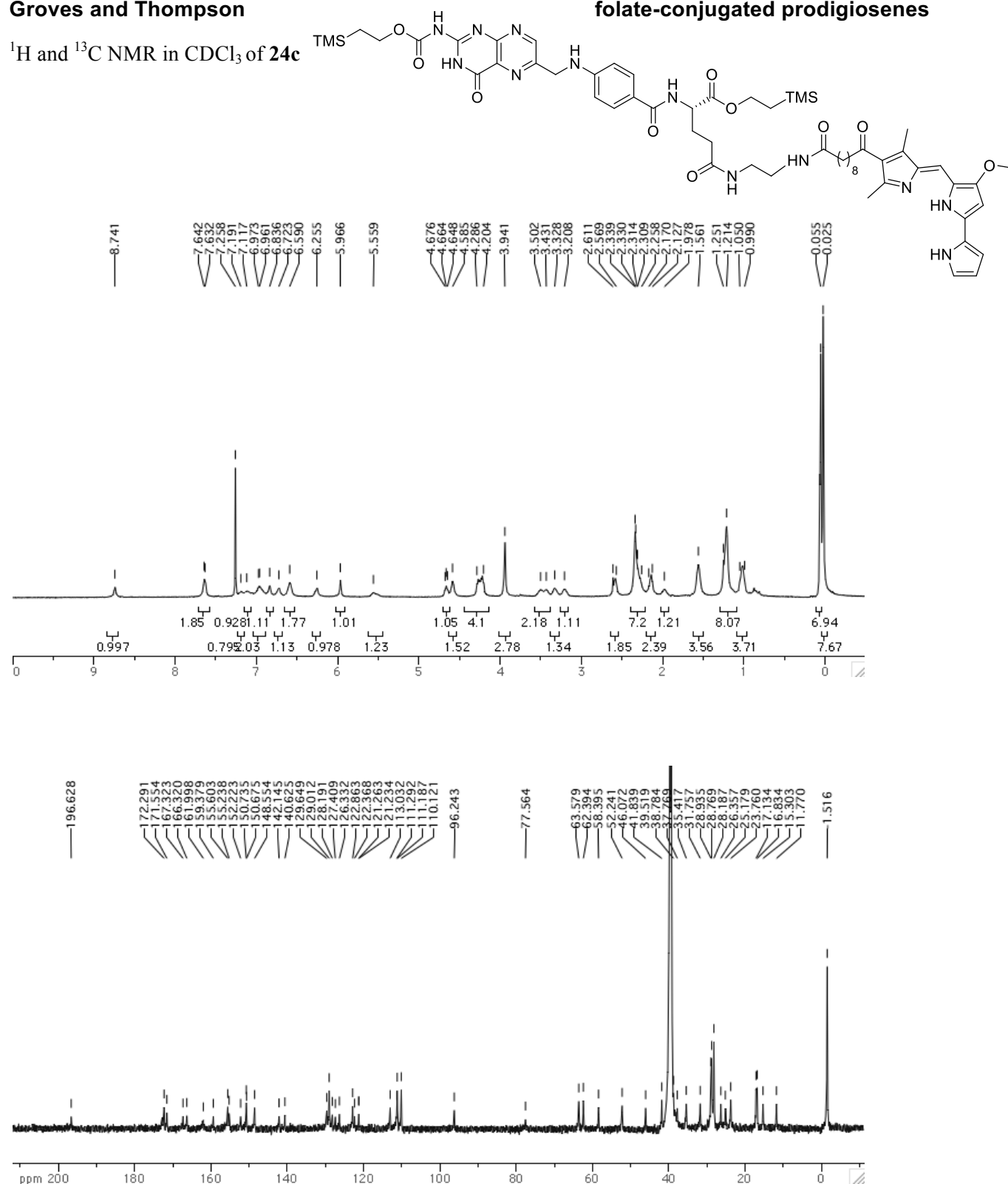
^1H and ^{13}C NMR in DMSO-d_6 of **24b**



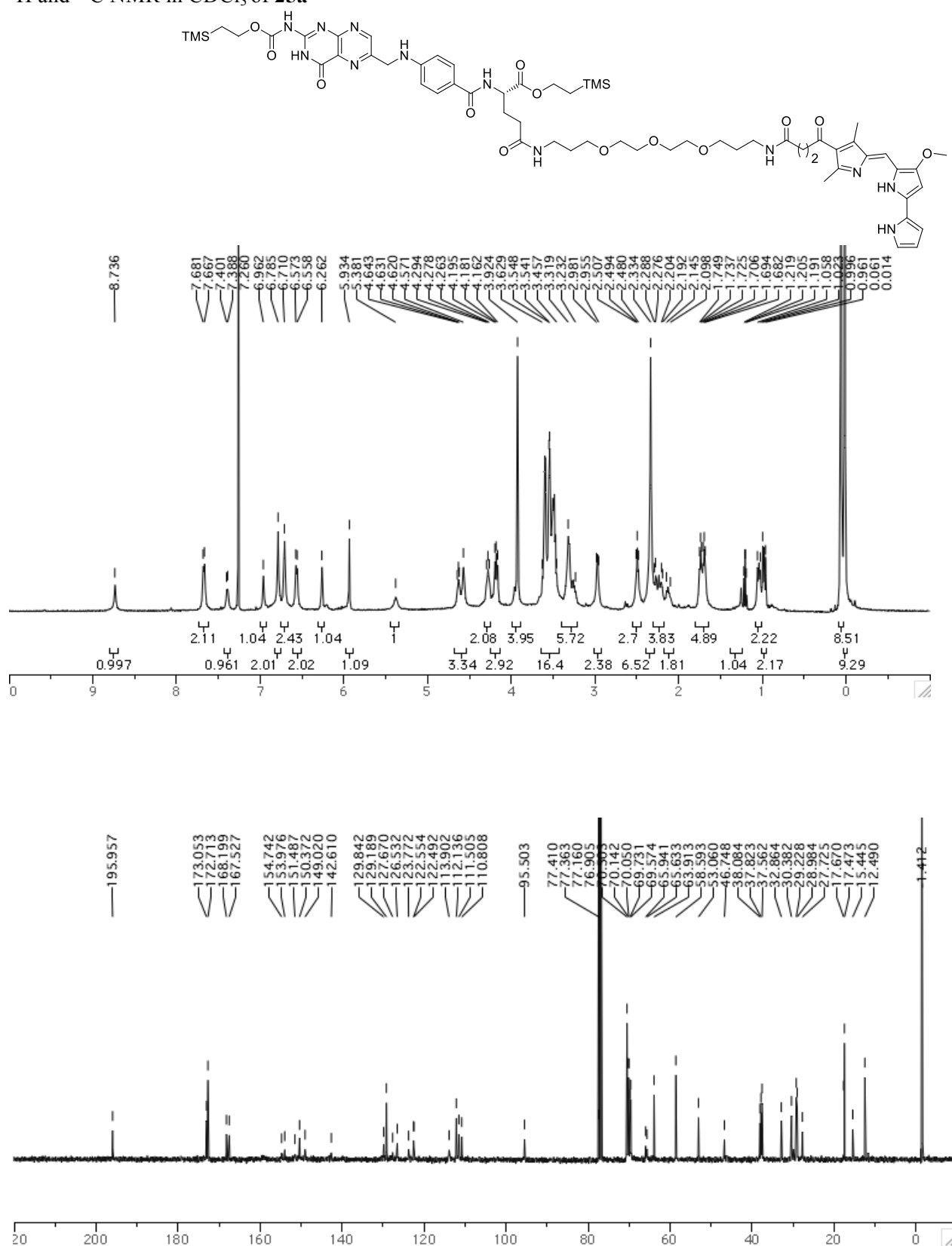
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Step-wise synthetic approach key to γ -conjugates of folate:
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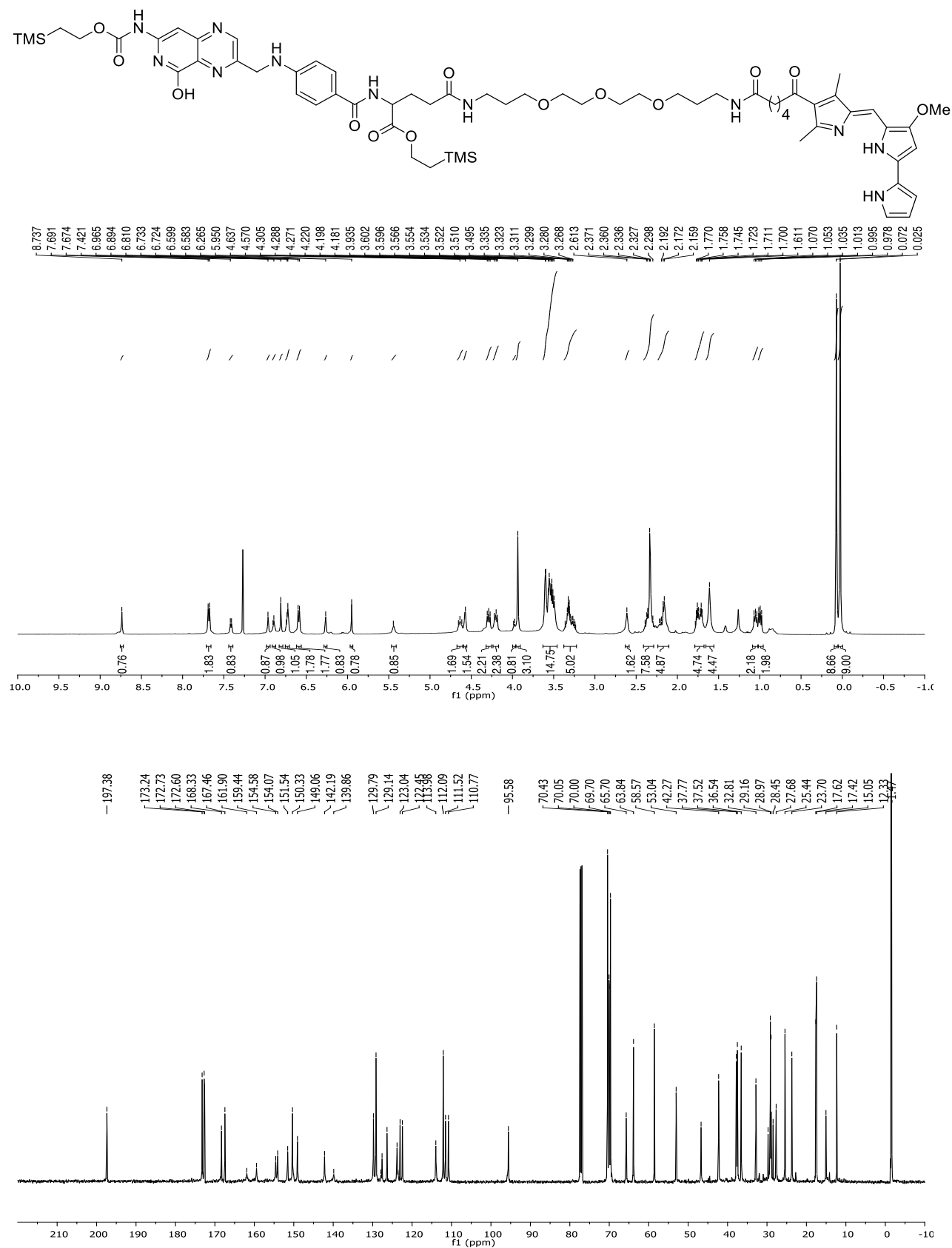
^1H and ^{13}C NMR in CDCl_3 of **24c**

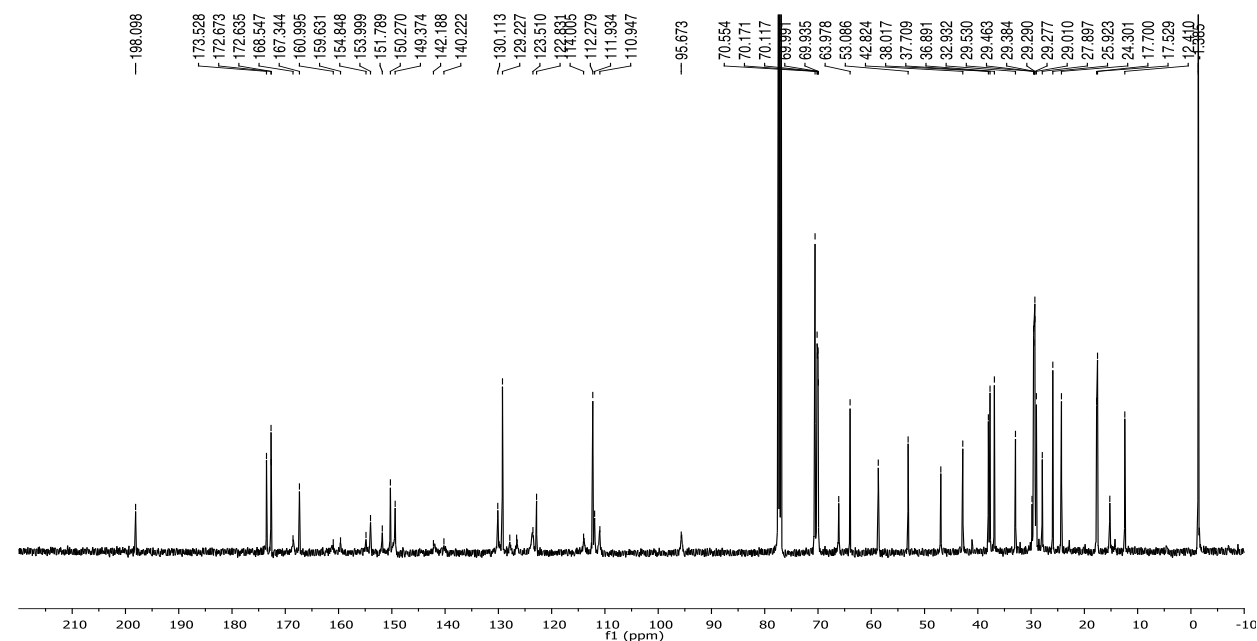


^1H and ^{13}C NMR in CDCl_3 of **25a**

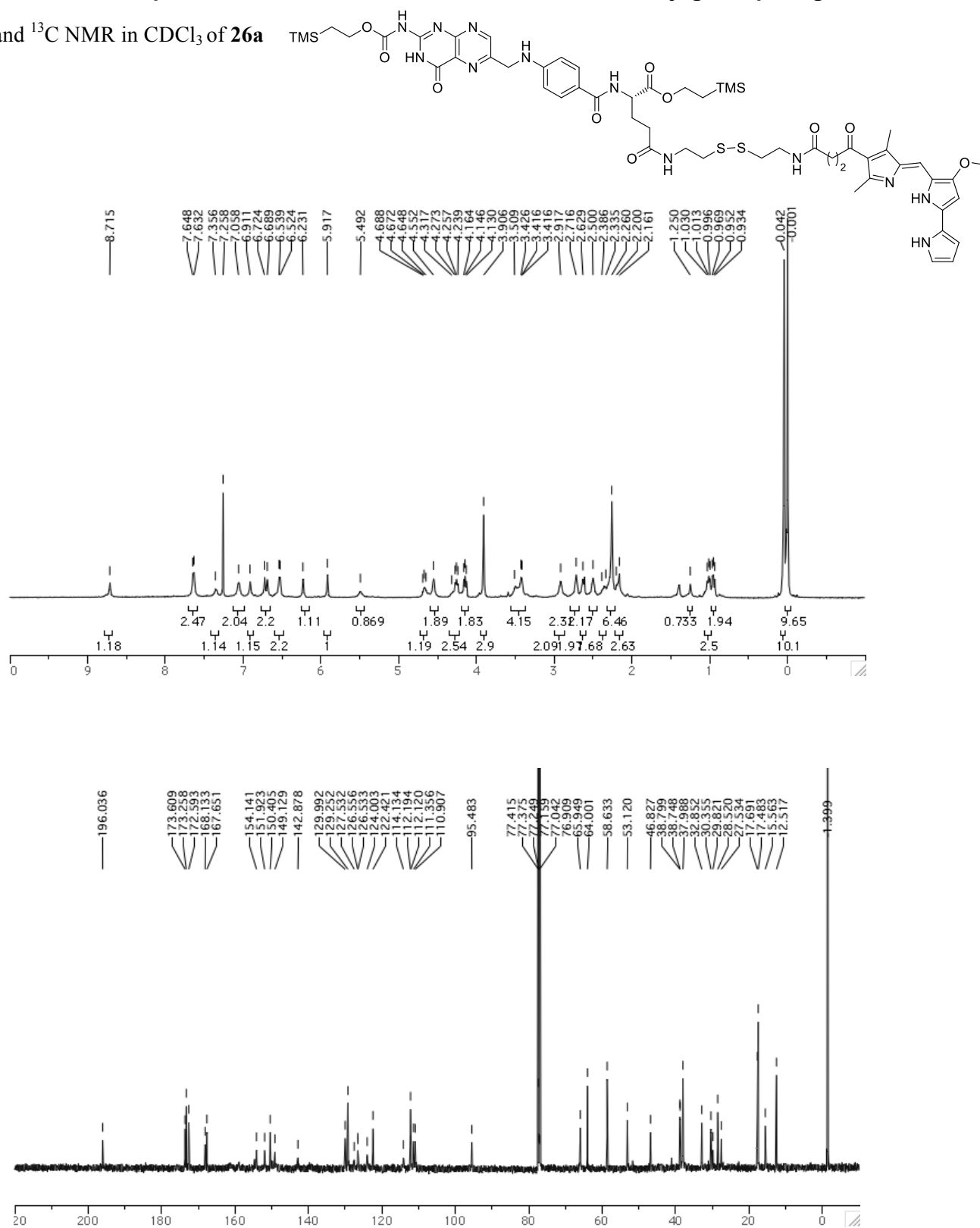


^1H and ^{13}C NMR in CDCl_3 of **25b**

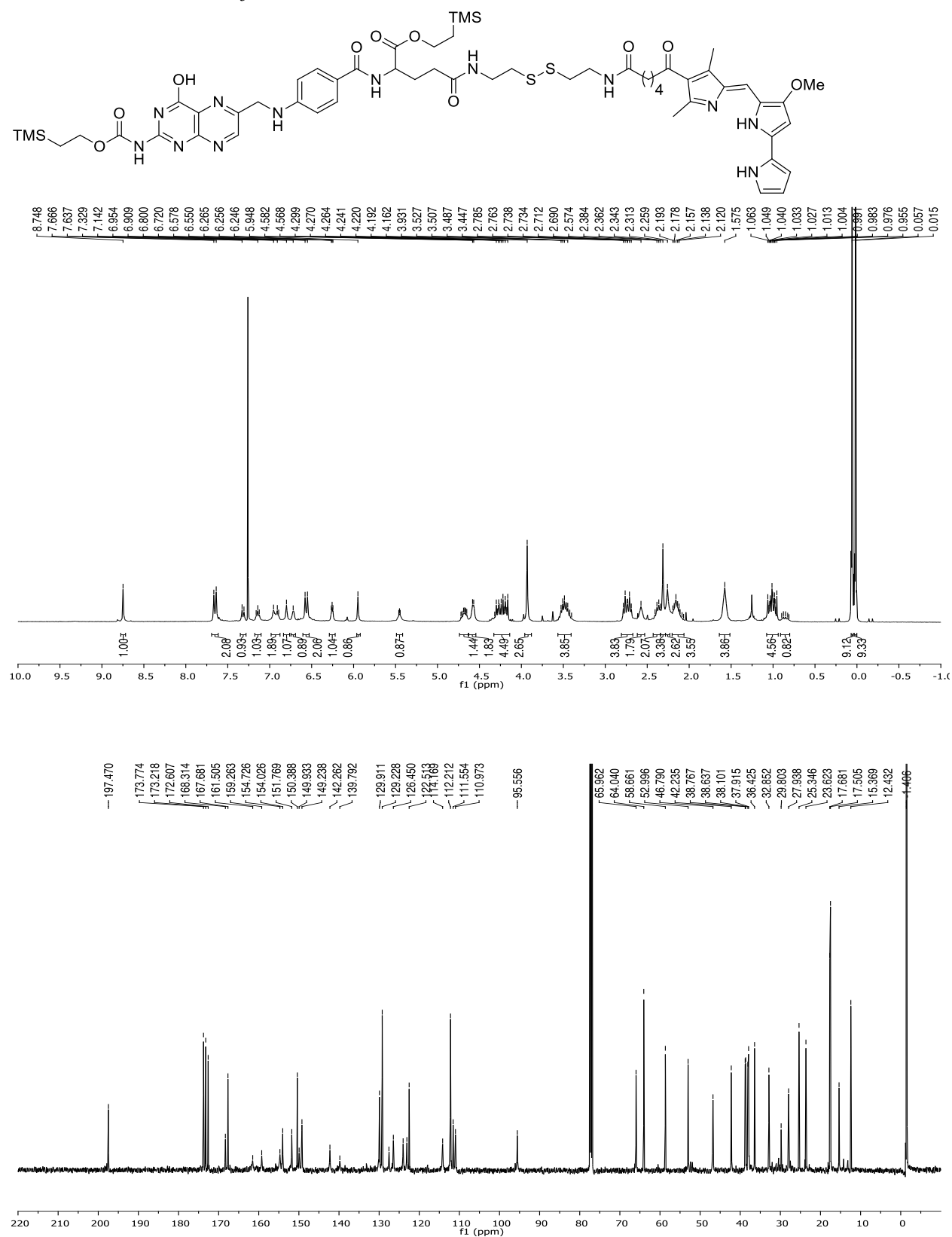


C[Si](C)(C)CCOC(=O)Nc1nc(O)c2nc(CNc3ccc(cc3)C(=O)NC(=O)[C@H](COCC[Si](C)(C)C)CCC(=O)NCCCOCCOCCOCCOCCOCC(=O)NCCCC(=O)c4c(C)n(C)c(/C=C/c5c(OC)cc6[nH]cnc56)[nH]7c8ccccc8[nH]7)/c4

^1H and ^{13}C NMR in CDCl_3 of **26a**



^1H and ^{13}C NMR in CDCl_3 of **26b**



Chemical structure of compound 10 is shown at the top right. The structure is a complex molecule featuring a pyrimidine ring system, a benzene ring, a thiazole ring, and a thiophene ring, all connected by various functional groups including amides, ethers, and a disulfide bridge.

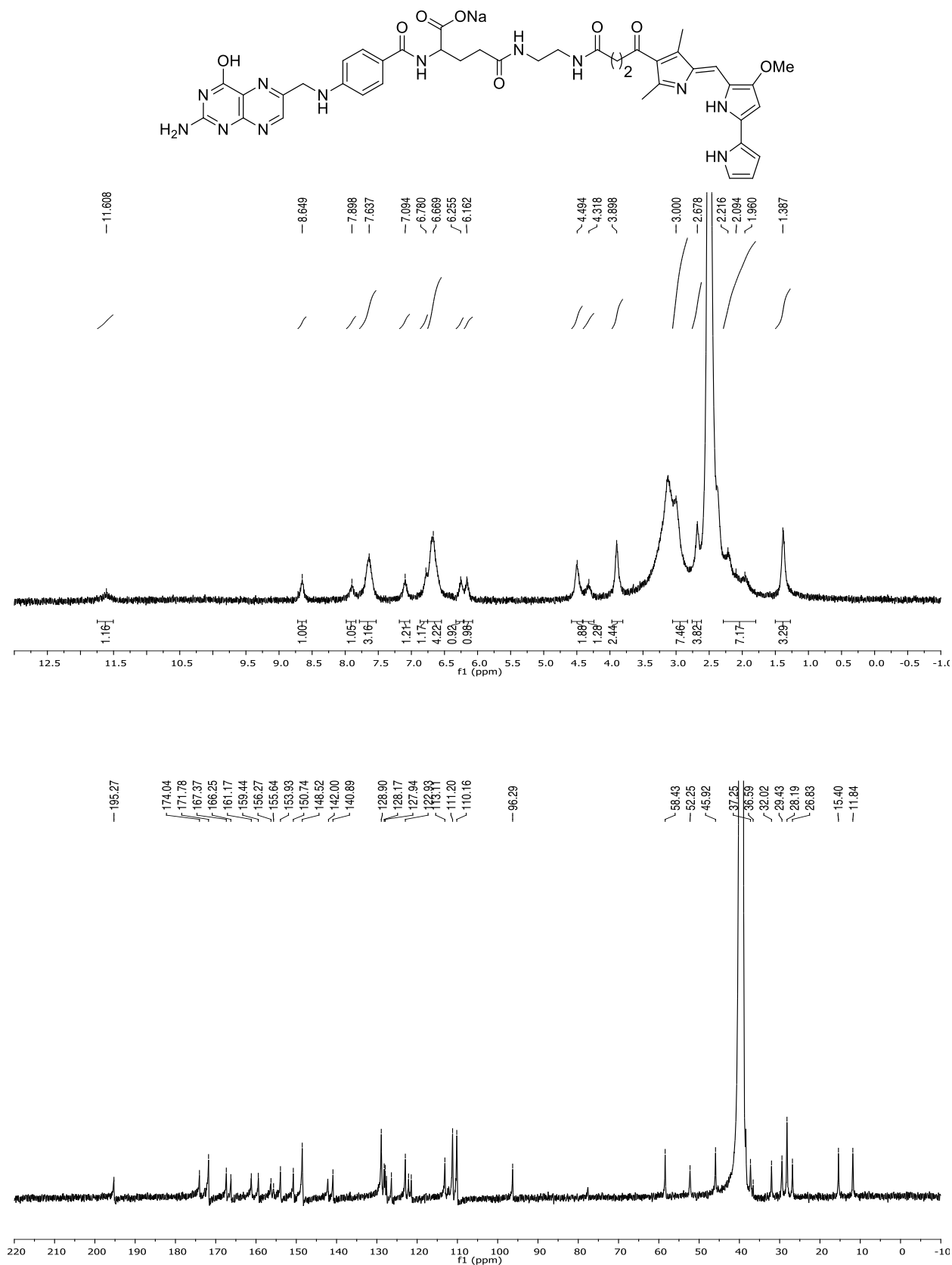
¹H NMR spectrum (top): The spectrum shows peaks from 0 to 10 ppm. The x-axis is labeled with chemical shifts in ppm. The y-axis represents intensity. The following table lists the chemical shifts and integrations for the peaks:

Chemical Shift (ppm)	Integration
8.737	1.24
7.631	2.22
7.616	1.13
7.354	1.72
7.342	1.13
7.260	1.72
7.247	1.13
6.837	2.08
6.703	2.08
6.702	2.08
6.568	1.09
6.553	1.09
6.206	0.937
5.971	0.937
5.590	1.32
4.678	1.87
4.668	2.32
4.598	3.33
4.583	3.33
4.261	4.51
4.245	4.51
4.203	4.51
4.189	4.51
4.186	4.51
4.171	4.51
3.925	2.06
3.516	5.56
3.489	5.56
3.403	3.44
2.747	2.33
2.734	2.33
2.682	2.07
2.667	2.07
2.577	2.07
2.356	4.21
2.336	4.21
2.216	4.21
2.135	4.21
2.120	4.21
2.105	4.21
1.554	4.8
1.542	4.8
1.530	4.8
1.243	9.82
1.207	9.82
1.059	4.53
1.004	4.53
0.984	4.53
0.976	4.53
0.972	4.53
0.038	9.58
0.004	10.7

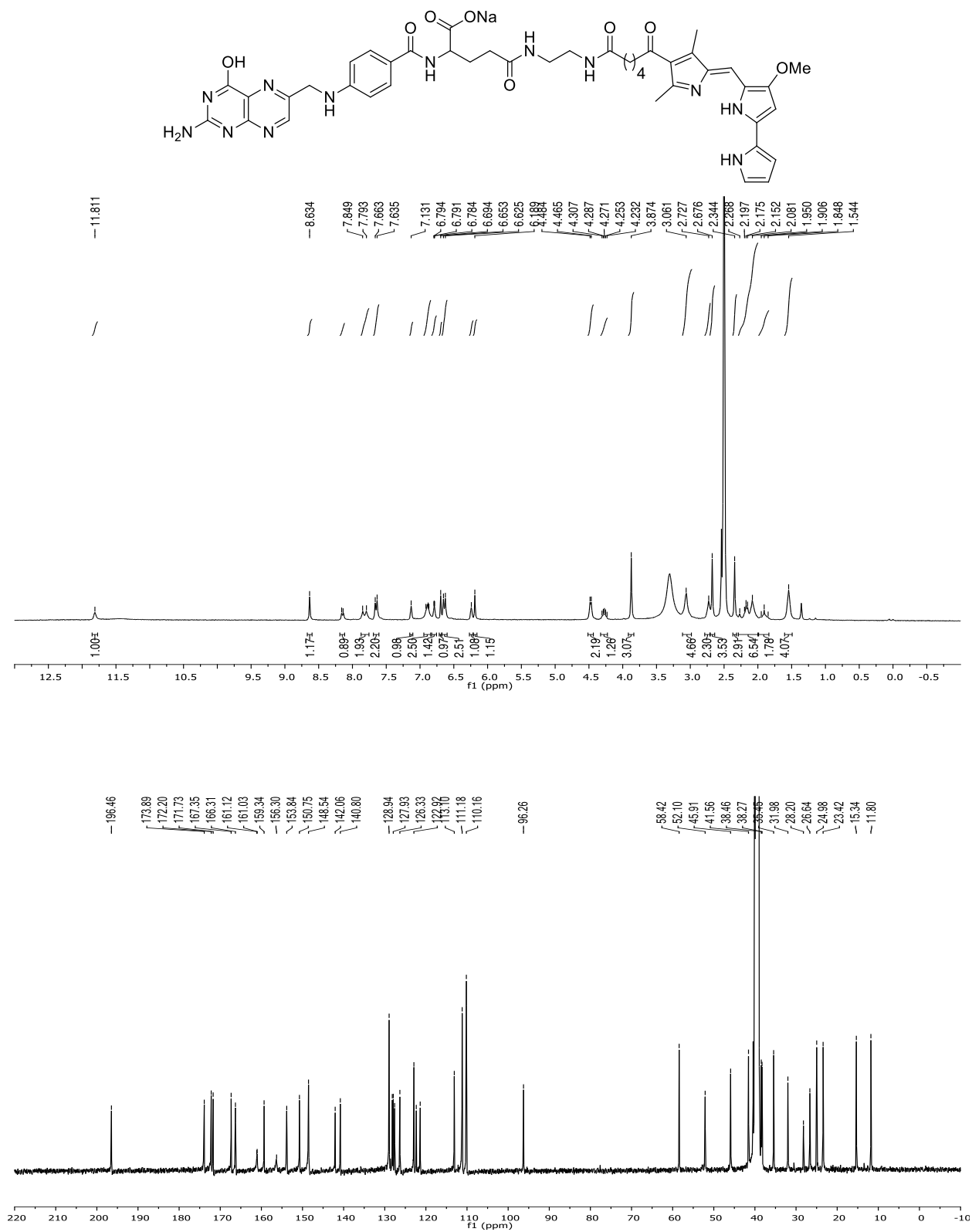
¹³C NMR spectrum (bottom): The spectrum shows peaks from 0 to 200 ppm. The x-axis is labeled with chemical shifts in ppm. The y-axis represents intensity. The following table lists the chemical shifts for the peaks:

Chemical Shift (ppm)
198.155
174.053
173.193
172.562
168.564
168.543
167.570
161.321
159.801
154.769
154.075
151.852
150.405
149.806
149.302
142.106
139.871
139.178
137.752
136.360
133.766
133.407
132.535
114.050
112.229
111.858
110.927
95.707
77.160
65.988
64.061
58.669
52.900
46.905
42.770
38.650
38.005
37.896
36.590
32.807
29.438
29.376
29.223
29.151
26.097
24.265
24.265
17.682
17.525
14.926
12.379
1.394

^1H and ^{13}C NMR in DMSO-d_6 of **27a**



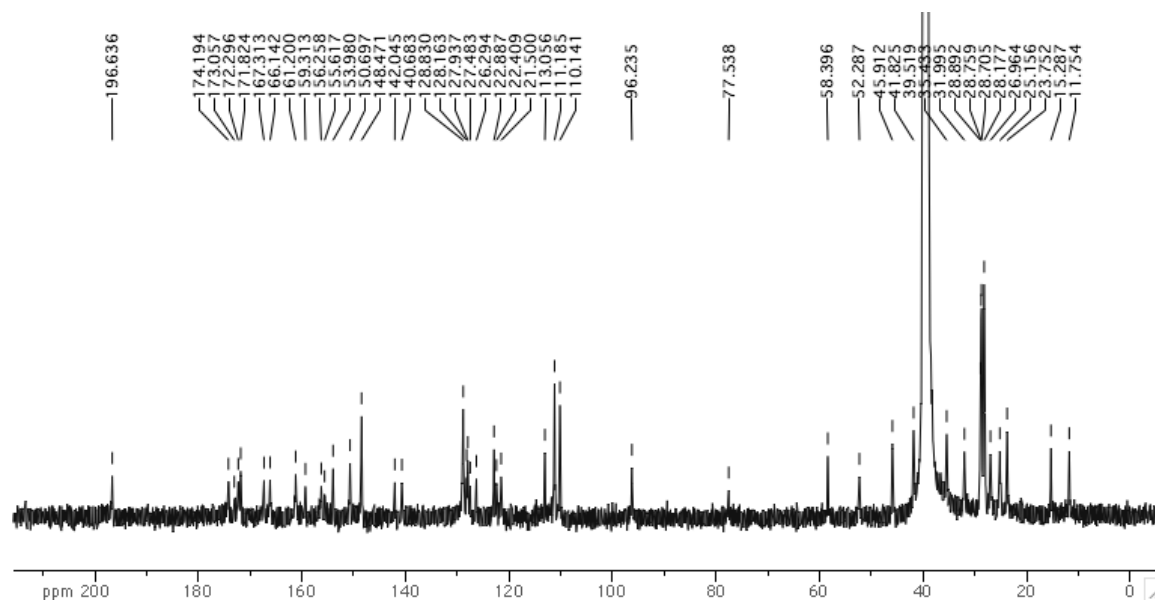
^1H and ^{13}C NMR in DMSO-d_6 of **27b**



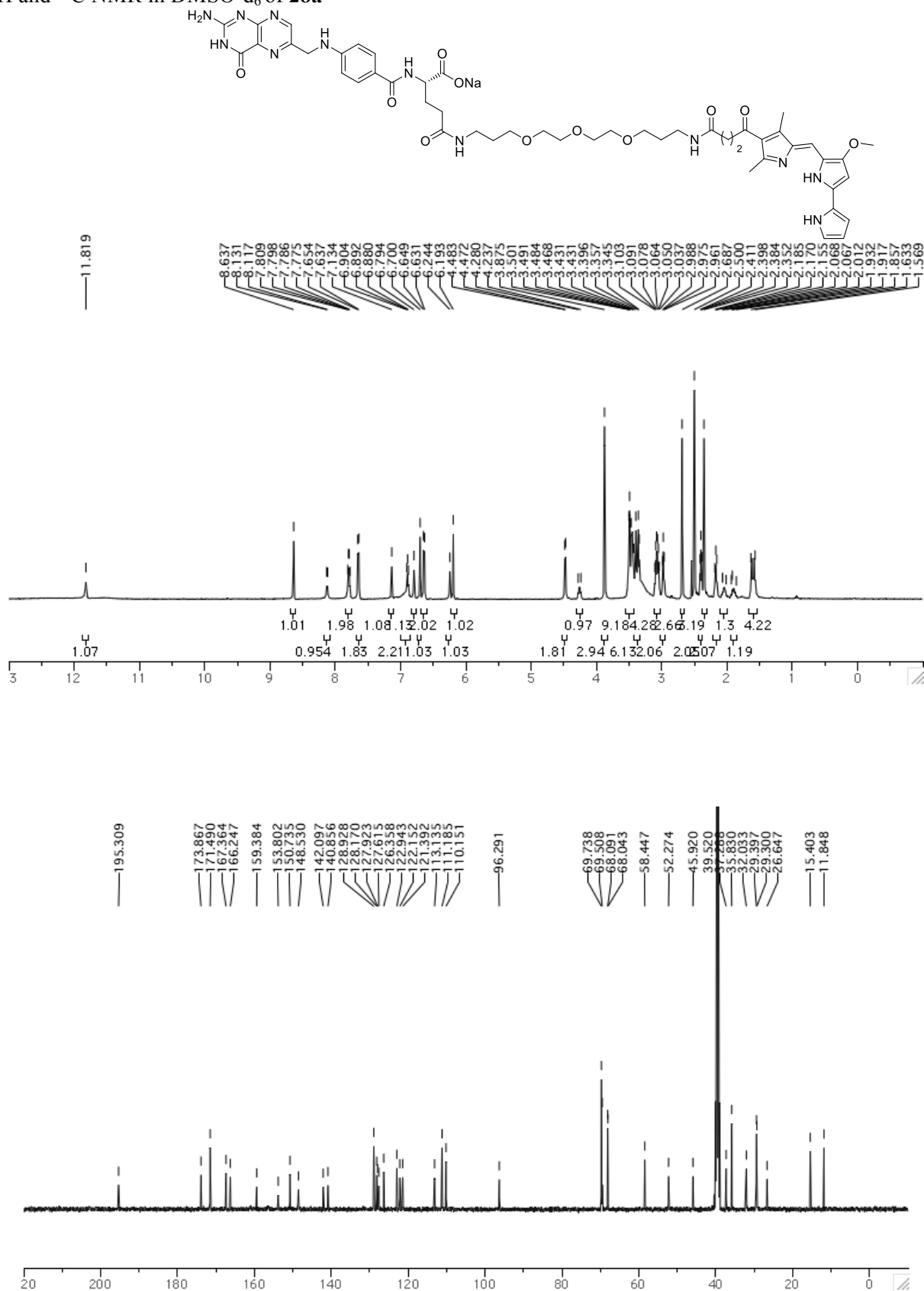
**Step-wise synthetic approach key to γ -conjugates of folate:
folate-conjugated prodigiosenes**

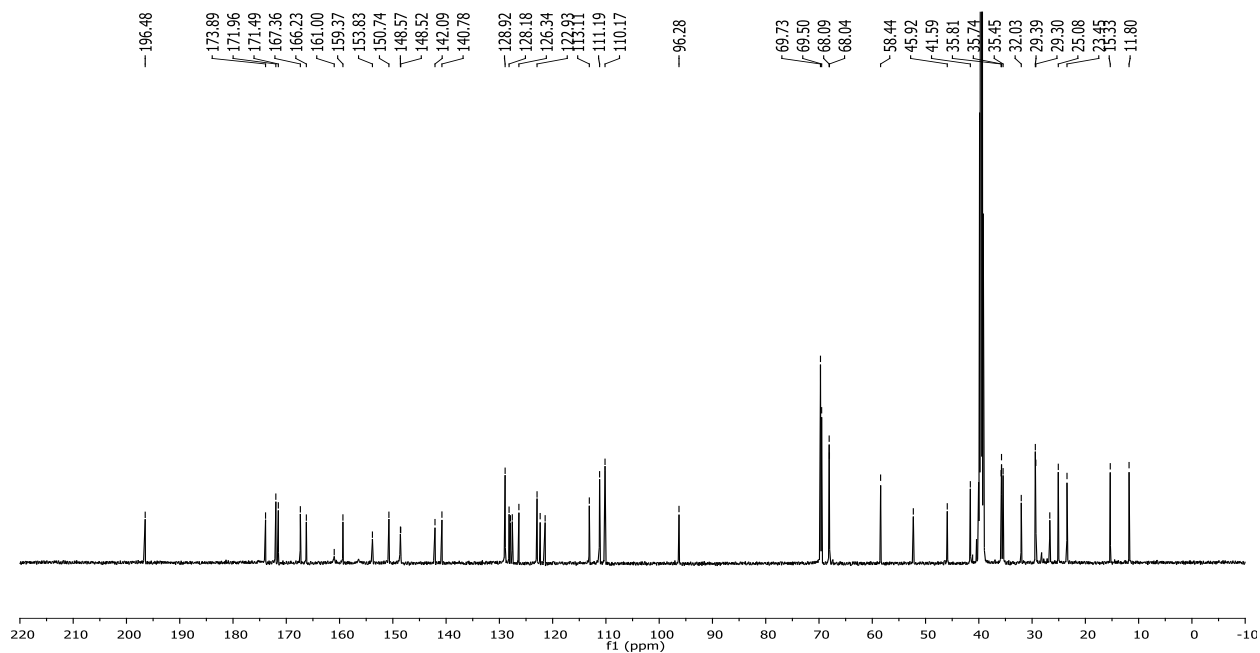
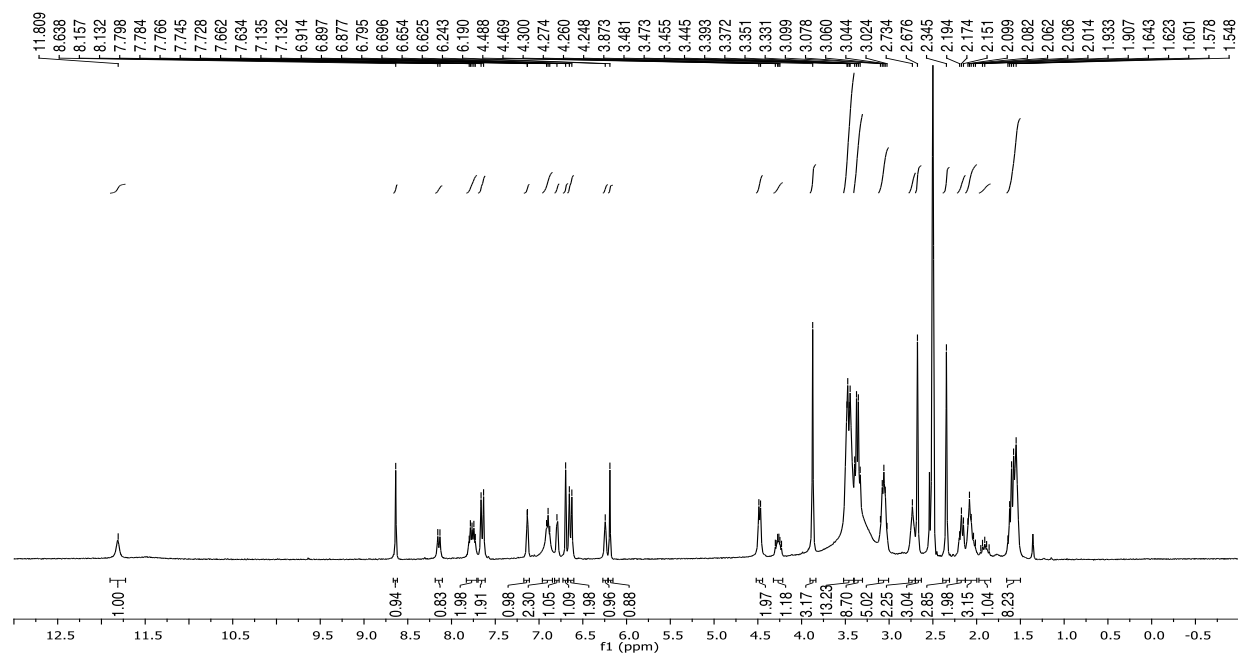
folate-conjugated prodigiosenes

Chemical structure of a folate-conjugated prodigiosene. The structure features a folate moiety (pteridine ring, p-aminobenzoyl group, and L-glutamate derivative) linked via an amide bond to a prodigiosene moiety (a triene system with a methoxy group and a phenyl ring).

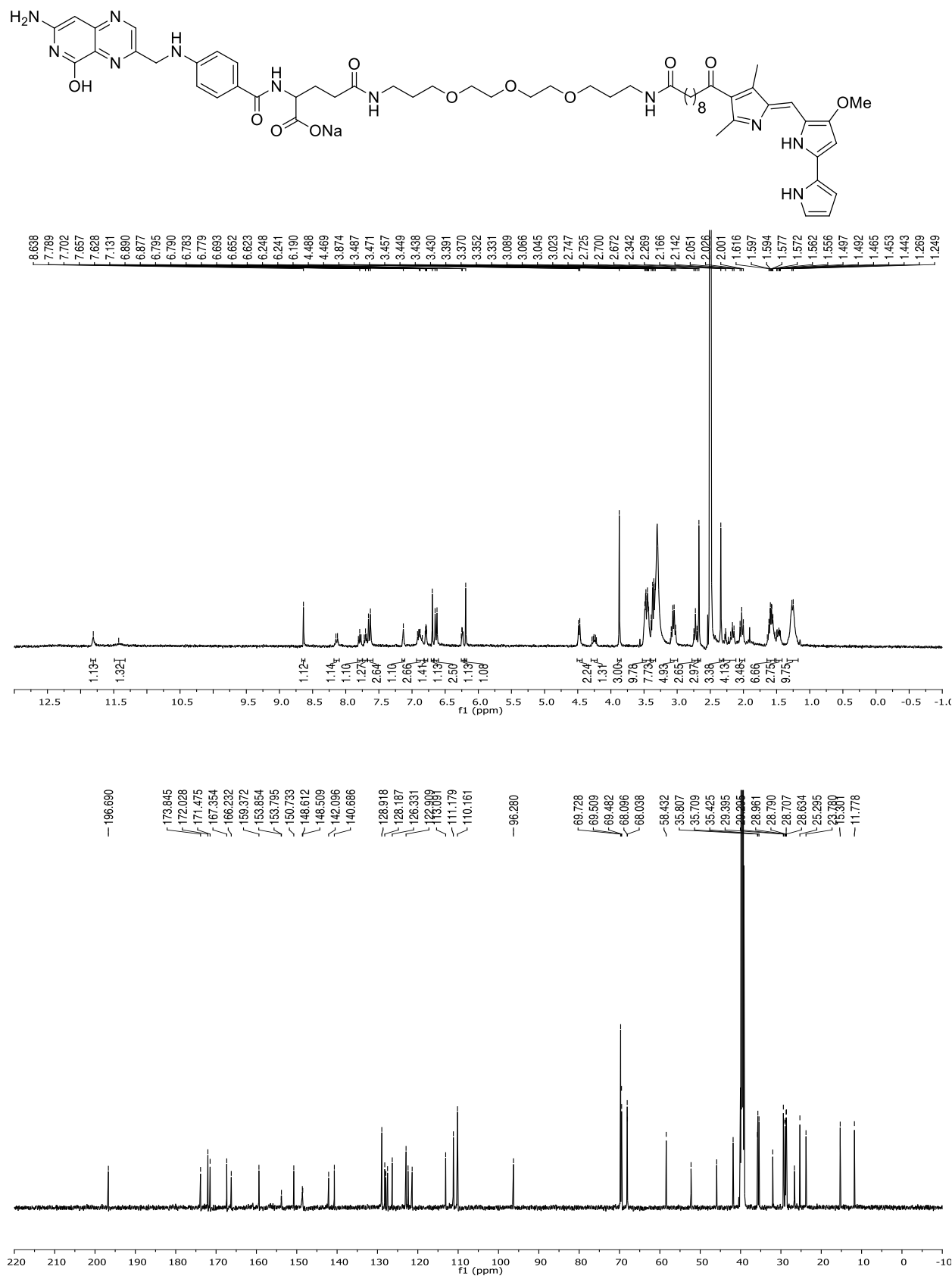


^1H and ^{13}C NMR in DMSO-d_6 of **28a**

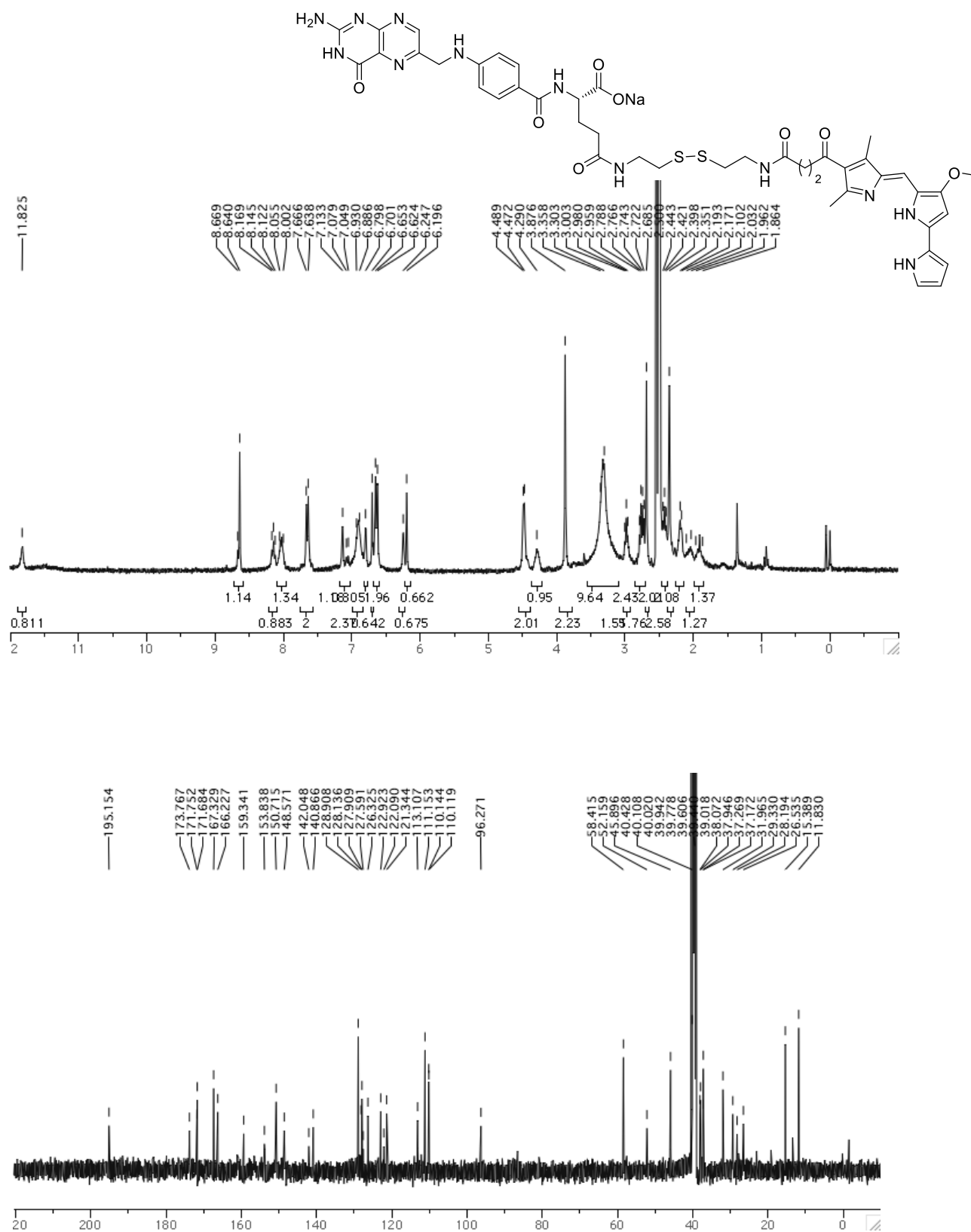


NC1=NC2=C(N1)N=CN=C2CNC3=CC=C(C=C3)C(=O)NC(=O)CC(=O)NCCOCCOCCOCCOCCNC(=O)CCCC(=O)c4c(C)c(C)n(c4)/C=C5C(=C6C(=CC=C5)N6)C(=C7C=CC(=C7)N8C=CC=CC=C8)OC

^1H and ^{13}C NMR in DMSO-d_6 of **28c**



^1H and ^{13}C NMR in DMSO-d_6 of **29a**



^1H and ^{13}C NMR in DMSO-d_6 of **29b**

