Supporting Information:

Synthesis and Photophysical Properties of Sulfonamidophenyl Porphyrins as Models for Activatable Photosensitizers

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1. Comparison of NMR spectra of 2cSAM and 2tSAM.

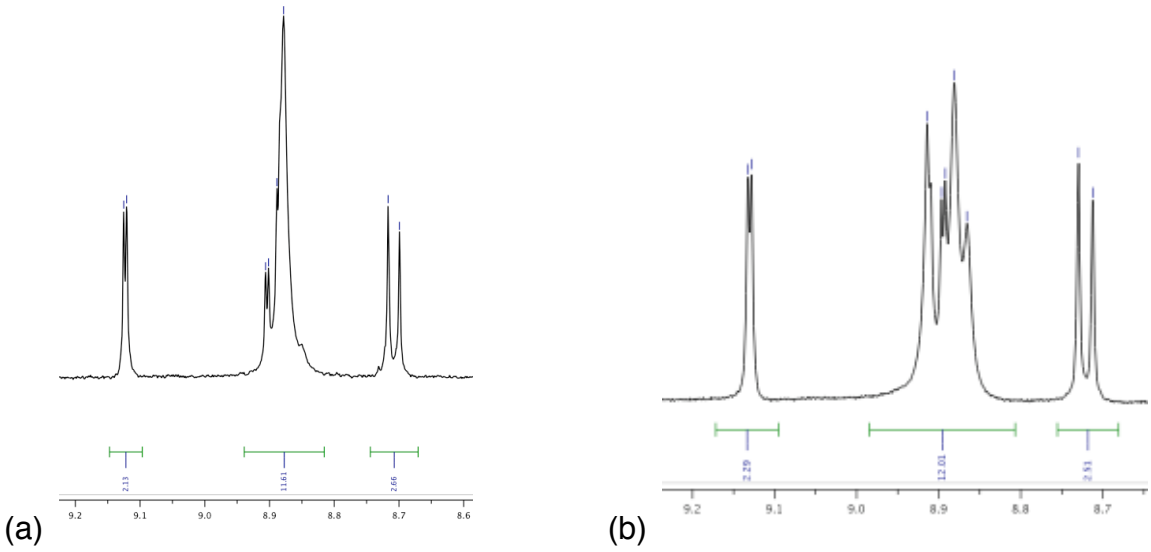


Figure S1. Expanded aromatic region showing pyrrolic β protons (a) **2cSAM**, (b) **2tSAM**.

2. Extinction coefficients of the Soret band of 1-4 in THF.

Table S1.

Compound	Soret (nm)	log ε (L mol^{-1} cm^{-1})
TPP	417	5.6
1	418	5.3
2c	424	5.8
2t	424	5.3
3	432	5.4
4	434	5.4

All spectra obtained in THF

3. Fluorescence activation of porphyrin 4SAM-mPEG with various thiols.

We have looked at the kinetics of some of the thiols [glutathione (GSH), thioglycolic acid (TGA), dithiothreitol (DTT) and L-cysteine (Cys)] in order to determine the rate of sulfonamide cleavage in an SPP (Figure S2). A solution of sulfonamidophenyl porphyrin **4SAM-mPEG** (1 μM) in DMF was treated with each of the thiol (1 mM, 1000 equiv) in HEPES buffer (DMF/HEPES 1:1, 2 mL,

pH = 7.4; resulting concentrations for porphyrin is 0.5 μM and the analyte is 0.5 mM). Each solution of porphyrin 4SAM-mPEG was then excited at 437 nm while monitoring maximum change in the fluorescence intensity at 686 nm over time (min). All the thio-mediated cleavage experiments were performed in triplicates. Among the thiols cysteine seemed to be the fastest, whereas glutathione seemed to be the slowest to cleave off the sulfonamide bond present in porphyrin **4SAM-mPEG**. Other two thiols (TGA and DTT) seemed to be moderate to sulfonamide cleavage. Hence, depending upon the thiol substrate the rate of sulfonamide cleavage in porphyrins can vary drastically.

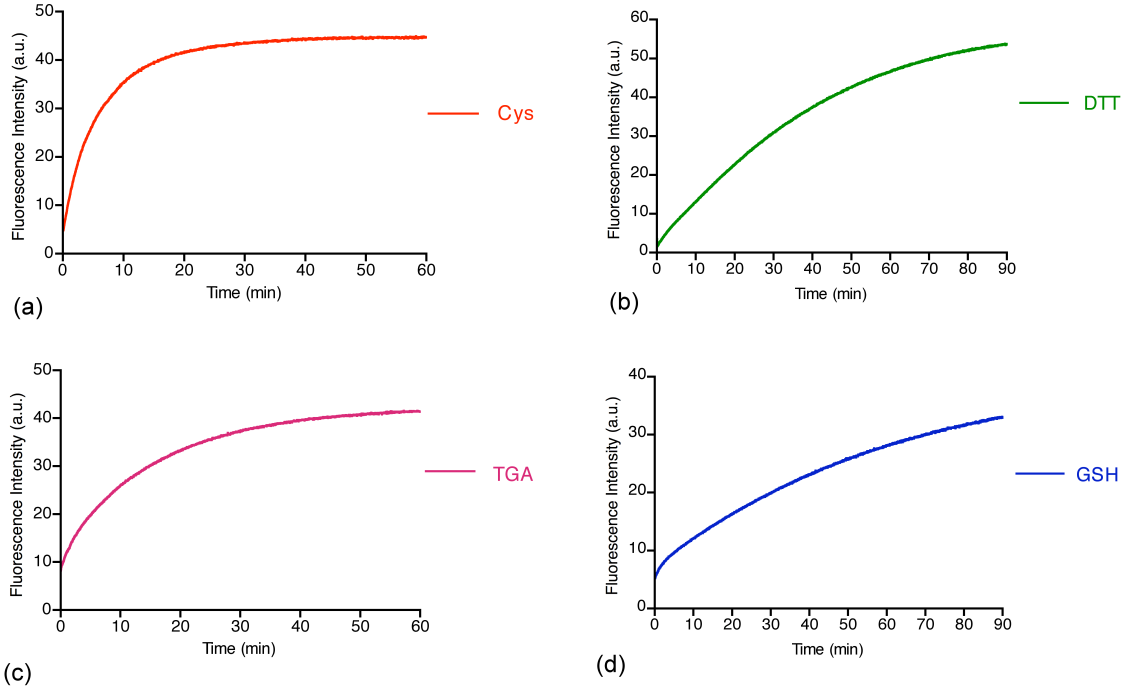


Figure S2. Change in fluorescence intensity upon treatment of porphyrin **4SAM-mPEG** (λ_{ex} = 437 nm, λ_{em} = 686 nm) with different thiols (a) Cysteine (Cys), (b) Dithiothreitol (DTT), (c) Thioglycolic acid (TGA) and (d) Glutathione reduced (GSH).

4. Experimental section

General. All chemicals and solvents were purchased from chemical companies were used as received without further purification. $CHCl_3$ was stabilized with 0.8% ethanol. Anhydrous acetone, CH_2Cl_2 and $CHCl_3$ (stabilized with 0.8% EtOH) were reagent grade and were used as received. Silica gel (40 μm average particle size) was used for column chromatography. Absorption and fluorescence spectra were collected in DMF at room temperature unless noted otherwise. LCMS data were collected on a HPLC equipped with a diode array detector, a ESI-MS module, and a RPC18 column at a flow rate of 0.3 mL/ min. High performance liquid chromatography (HPLC) data were collected from an instrument equipped with a diode array detector set to detect at 420 nm, and a fraction collector. Gradients were run with buffer A (H_2O/0.1% trifluoroacetic acid (TFA)) and buffer B (90% acetonitrile/10% H_2O/0.1% TFA). For analytical HPLC a C-18 reverse phase column was used with dimensions of 250 mm x 4.6 mm. For semi-preparative HPLC a C-18 reverse phase column was used with dimensions of 250 mm x 21.2 mm. Microwave-assisted syntheses were carried out on a CEM Discover microwave instrument. High-resolution eletrospray ionization (ESI) mass spectra were obtained from a Fourier transform ion cyclotron resonance spectrometer (FT-ICR-MS) in the Department of Chemistry Instrumentation Facility (DCIF) at the Massachusetts Institute of Technology. All ^1H NMR spectra (500 MHz) and ^{13}C NMR spectra (125 MHz) were collected at the Department of Chemistry, University of Connecticut, in DMF unless noted otherwise. Non-commercial compounds, PEG_3-bromoacetate,[1] porphyrins **1**, **2**, **3**,[2] **4**,[3] and TPP[4] were prepared according to literature procedures. Fluorescence quantum yields were calculated using TPP as standard as described previously.[5]

Singlet oxygen quantum yields.

Singlet oxygen quantum yields were calculated as previously described.[5] Stock solution of the respective porphyrins were made up in air-saturated DMF with optical densities equal to 0.3 at 650 nm.

Additionally a stock solution of 1,3-diphenylisobenzofuran (DPBF, 0.25 M in DMF) was mixed. All solutions were kept in the dark. To a fluorescence cuvette was added 2.0 mL of the porphyrin solution and 5 μL of the DPBF solution, which was allowed to mix. The solution was irradiated with a laser (BW Tec) at 650 nm (60 mW) while stirring. After 10 s irradiation, the laser was shut off, and the fluorescence of the probe molecule was measured (excitation 471 nm, emission 495 nm). Singlet oxygen quantum yields were then calculated from the initial

slope of the fluorescence intensity decrease per time, utilizing the following equation:

$$\Phi_{\Delta}(U) = \Phi_{\Delta}(St) \times S(U) / S(St)$$

where U and St denote unknown and standard, and S represents the slope. **TPP** was used as the standard.

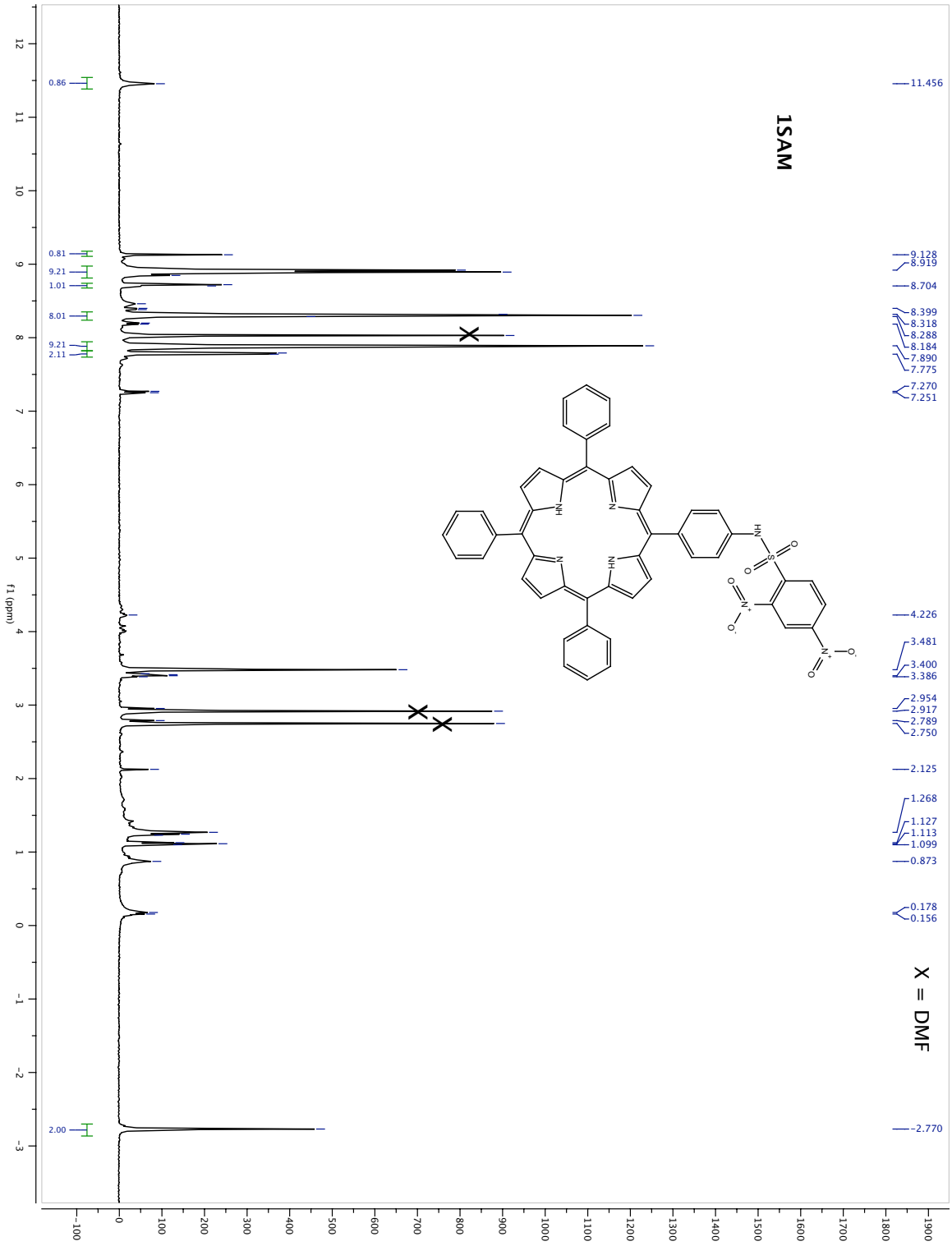
Kinetic experiments.

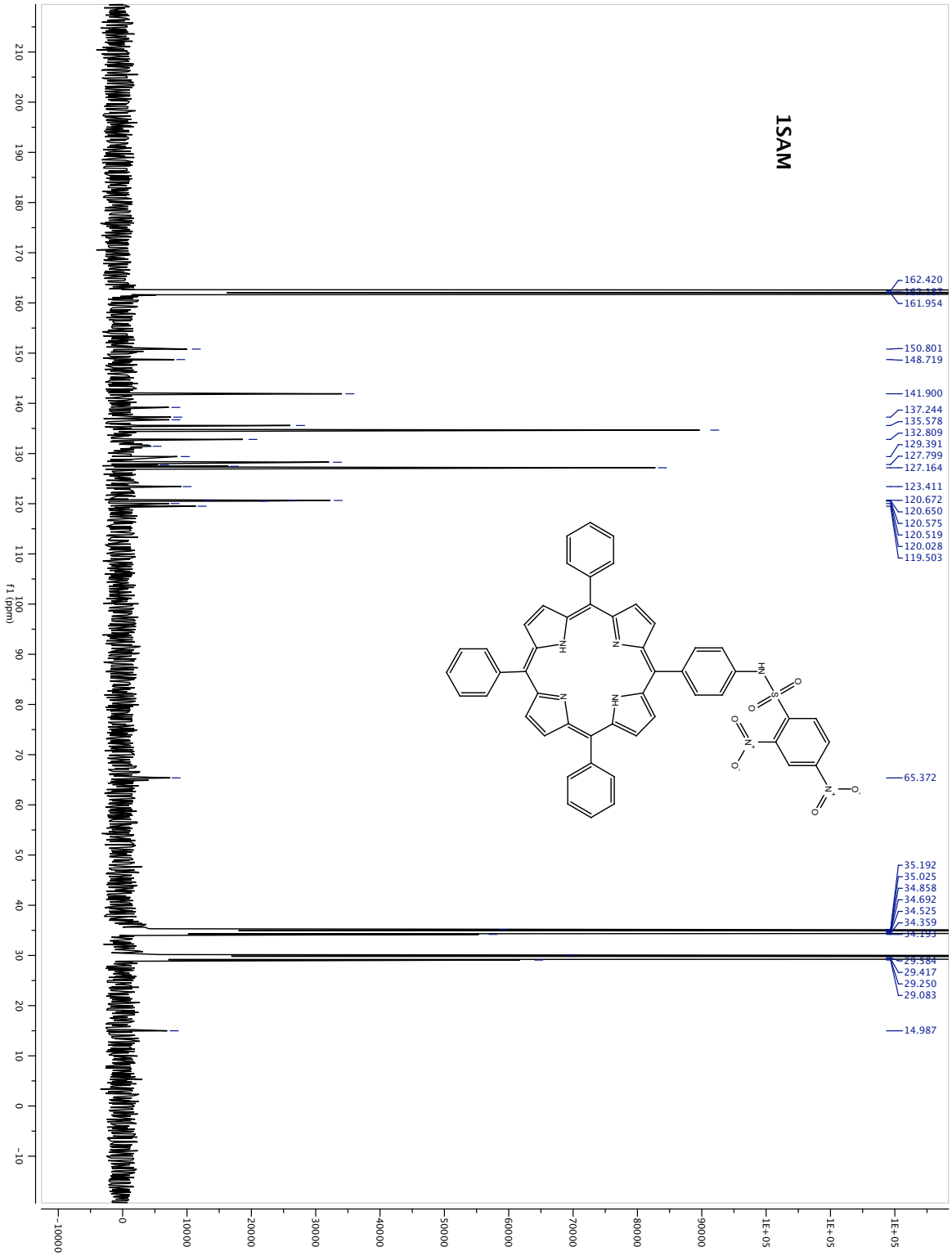
(i) A solution of each of the SPP (0.5 μM) in DMF was treated with a large excess of thioglycolic acid (2.5 mM, 500 equiv), and the kinetics was examined by monitoring the fluorescence intensity increase over time at the excitation and emission maxima of each resulting aminophenylporphyrin.

(ii) A solution of sulfonamidophenyl porphyrin 4SAM-mPEG (1 μM) in DMF and each of the analyte (1 mM, 1000 equiv) in HEPES buffer (pH = 7.4) were incubated at 37 °C for 15 min in DMF/HEPES (1:1, 2 mL, pH = 7.4; resulting concentrations for porphyrin is 0.5 μM and the analyte is 0.5 mM). Each solution of porphyrin 4SAM-mPEG was then excited at 437 nm while monitoring the fluorescence intensity 686 nm.

5. Spectral data

Solvent gradients utilized for analyses noted below HPLC spectra.


1SAM
X = DMF
f1 (ppm)
11.456
9.128
8.919
8.704
8.399
8.318
8.288
8.184
7.890
7.775
7.270
7.251
4.226
3.481
3.400
3.386
2.954
2.917
2.789
2.750
2.125
1.268
1.127
1.113
1.099
0.873
0.178
0.156
-2.770
0.86
0.81
9.21
1.01
8.01
9.21
2.11
2.00


1SAM
f1 (ppm)
162.420
161.954
150.801
148.719
141.900
137.244
135.578
132.809
129.391
127.799
127.164
123.411
120.672
120.650
120.575
120.519
120.028
119.503
65.372
35.192
35.025
34.858
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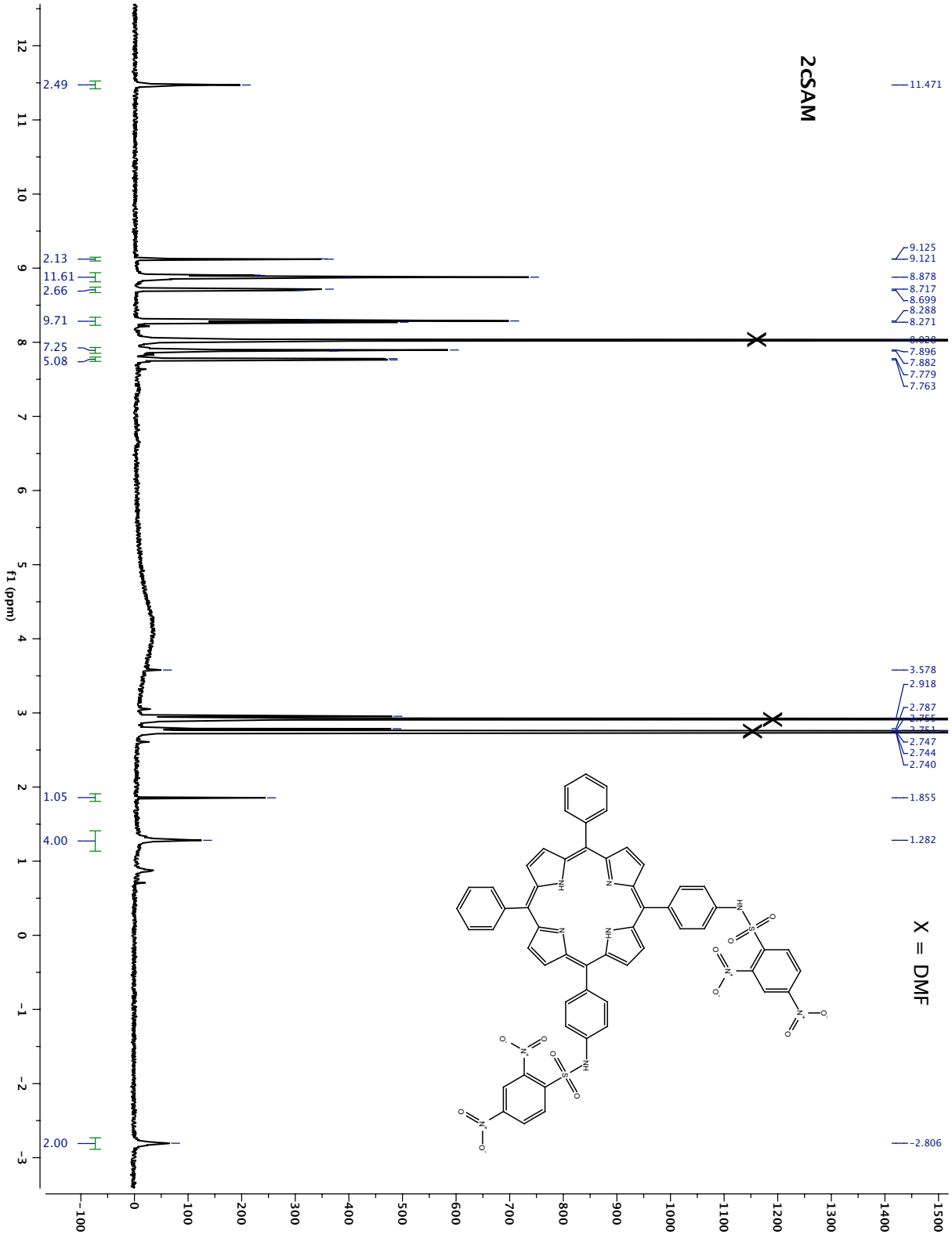
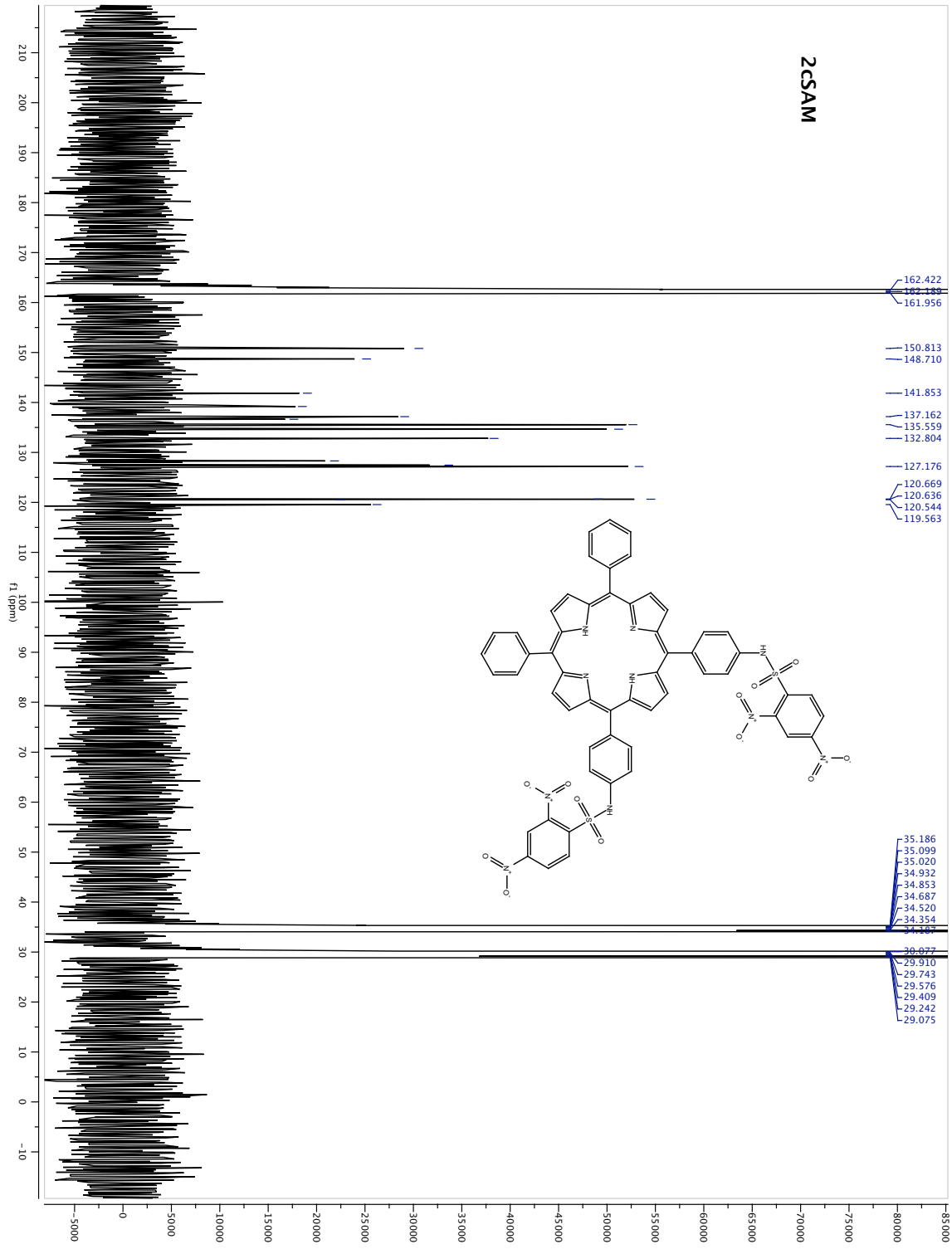
34.525
34.359
29.584
29.417
29.250
29.083
14.987


2cSAM
X = DMF
f1 (ppm)
2.49
2.13
11.61
2.66
9.71
7.25
5.08
1.05
4.00
2.00
11.471
9.125
9.121
8.878
8.717
8.699
8.288
8.271
7.896
7.882
7.779
7.763
3.578
2.918
2.787
2.747
2.744
2.740
1.855
1.282
-2.806


2cSAM
f1 (ppm)
162.422
162.189
161.956
150.813
148.710
141.853
137.162
135.559
132.804
127.176
120.669
120.636
120.544
119.563
35.186
35.099
35.020
34.932
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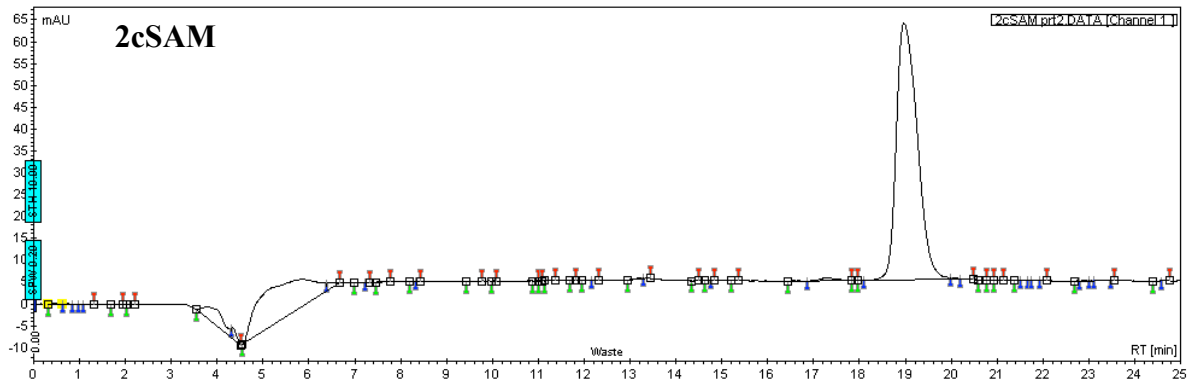
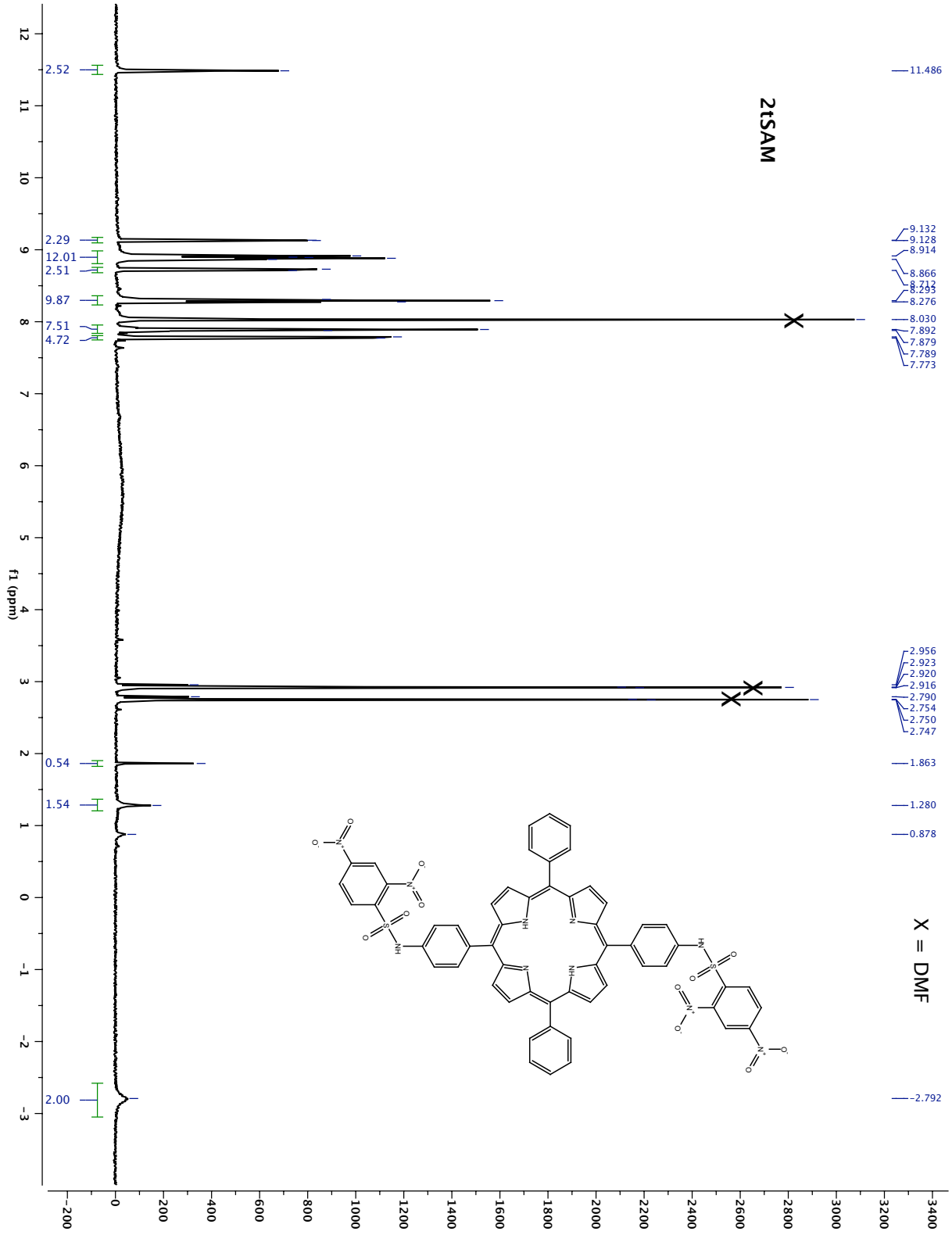
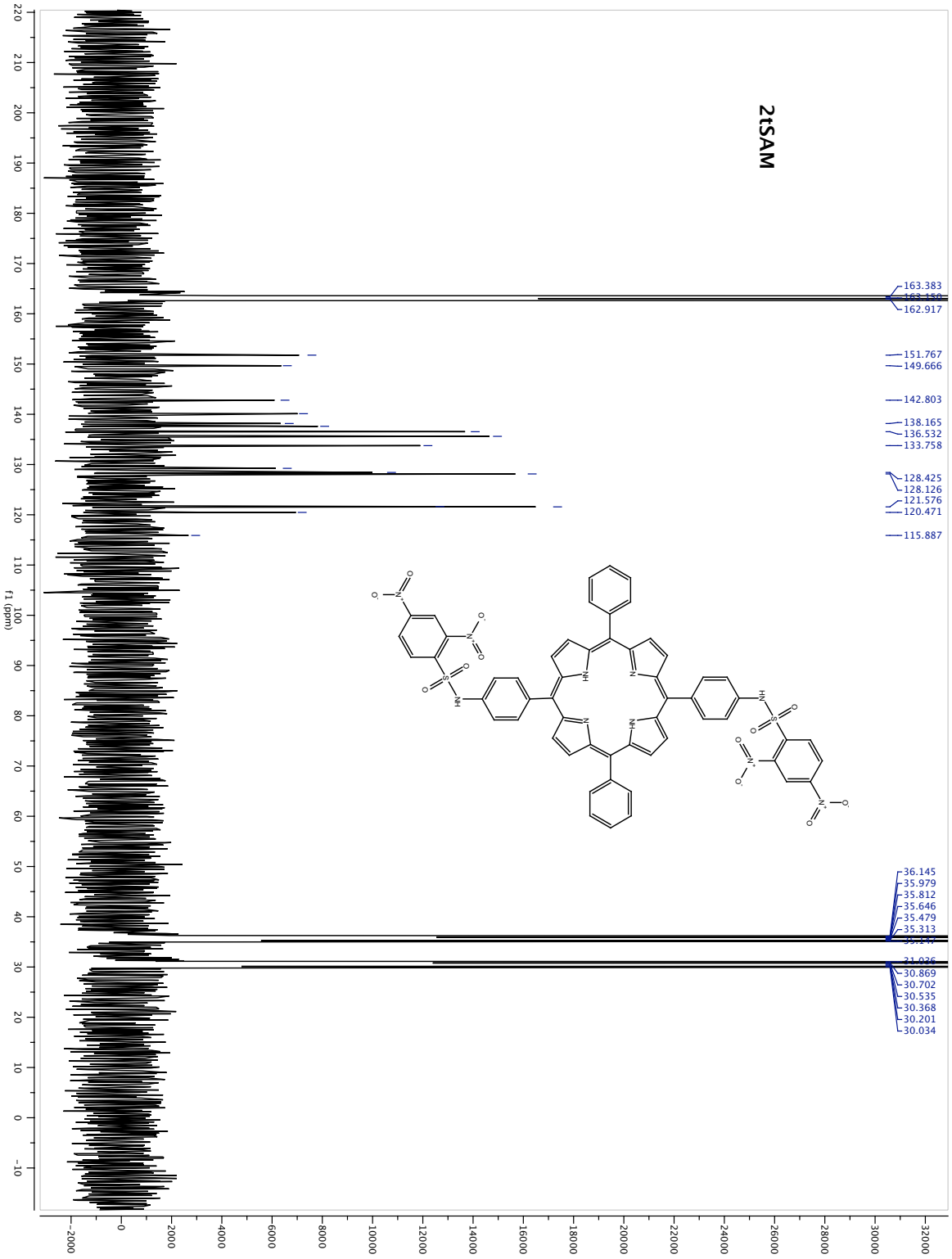
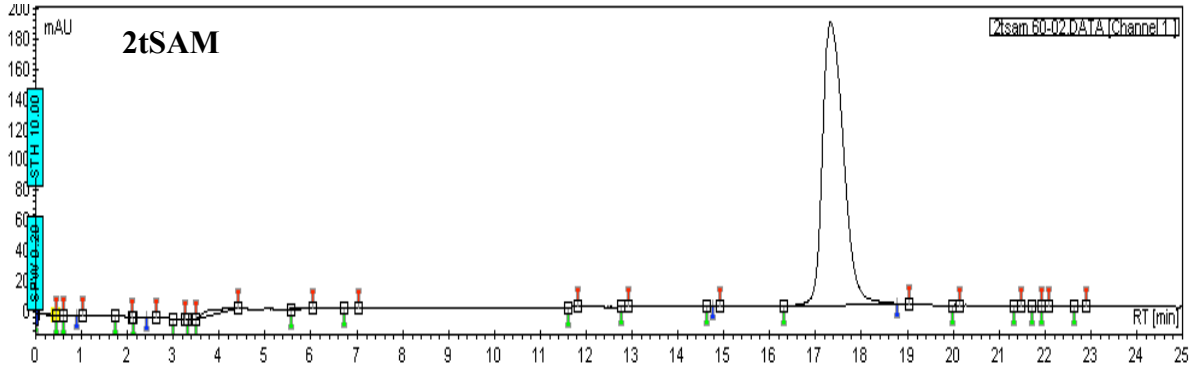
29.743
29.576
29.409
29.242
29.075



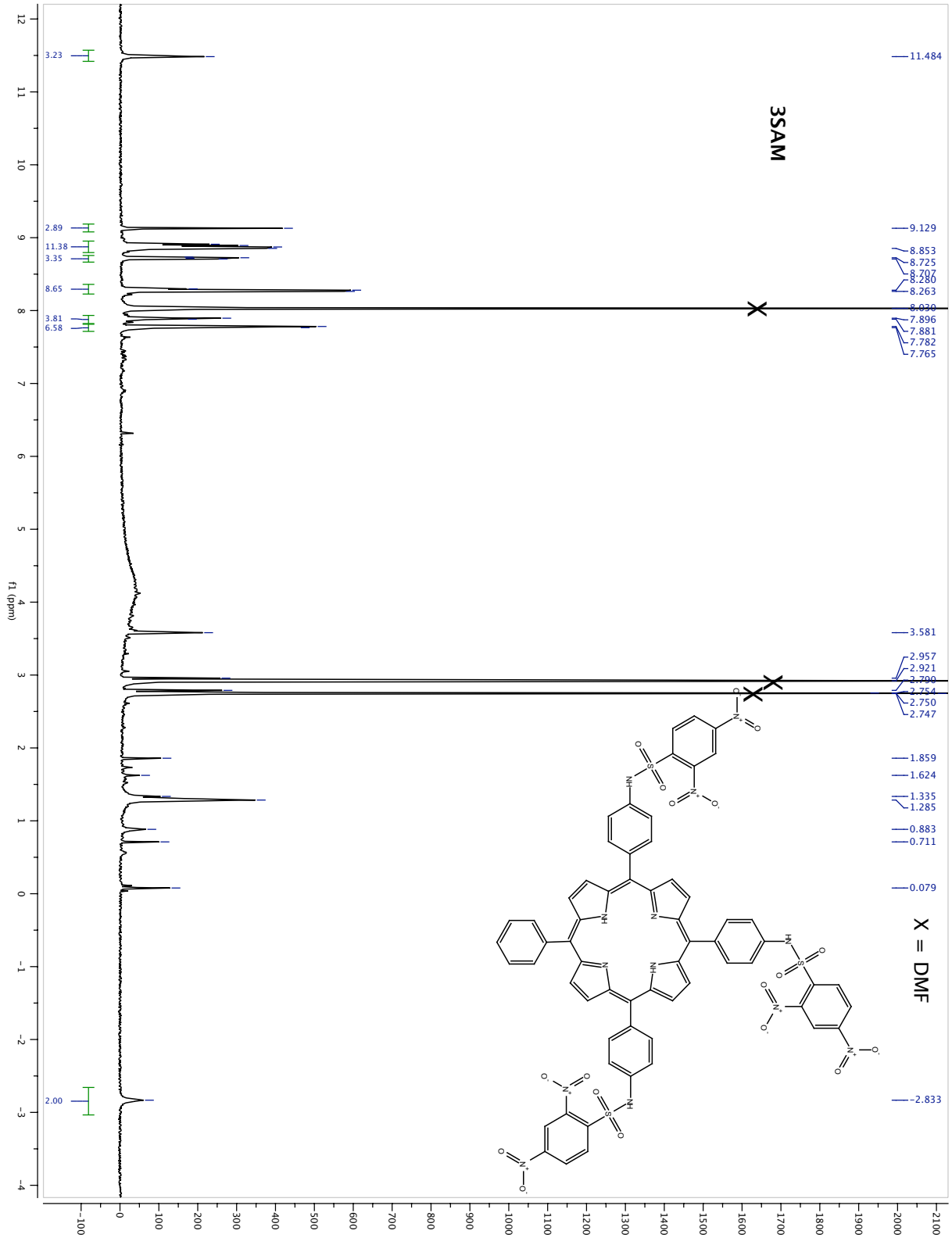
Gradient from 60% to 0% Buffer A

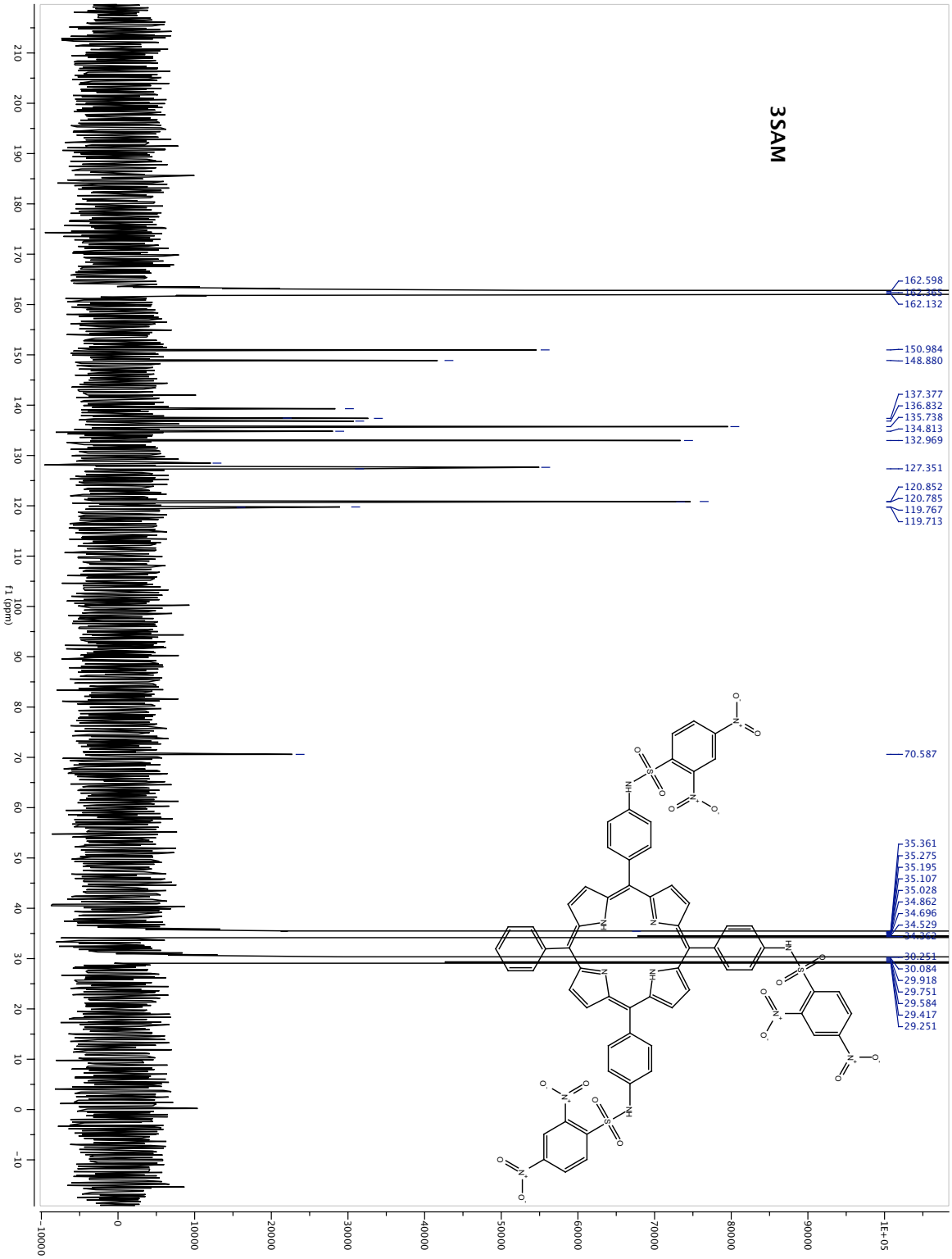

2tSAM
X = DMF
f1 (ppm)
2.52
2.29
12.01
2.51
9.87
7.51
4.72
0.54
1.54
2.00
11.486
9.132
9.128
8.914
8.866
8.712
8.293
8.276
8.030
7.892
7.879
7.789
7.773
2.956
2.923
2.920
2.916
2.790
2.754
2.750
2.747
1.863
1.280
0.878
-2.792


2tSAM
f1 (ppm)
163.383
162.917
151.767
149.666
142.803
138.165
136.532
133.758
128.425
128.126
121.576
120.471
115.887
36.145
35.979
35.812
35.646
35.479
35.313
30.869
30.702
30.535
30.368
30.201
30.034



Gradient from 60% to 0% Buffer A


3SAM
X = DMF
f1 (ppm)
11.484
9.129
8.853
8.725
8.707
8.280
8.263
8.030
7.896
7.881
7.782
7.765
3.581
2.957
2.921
2.790
2.754
2.750
2.747
1.859
1.624
1.335
1.285
0.883
0.711
0.079
-2.833
3.23
2.89
11.38
3.35
8.65
3.81
6.58
2.00


3SAM
162.598
162.365
162.132
150.984
148.880
137.377
136.832
135.738
134.813
132.969
127.351
120.852
120.785
119.767
119.713
70.587
35.361
35.275
35.195
35.107
35.028
34.862
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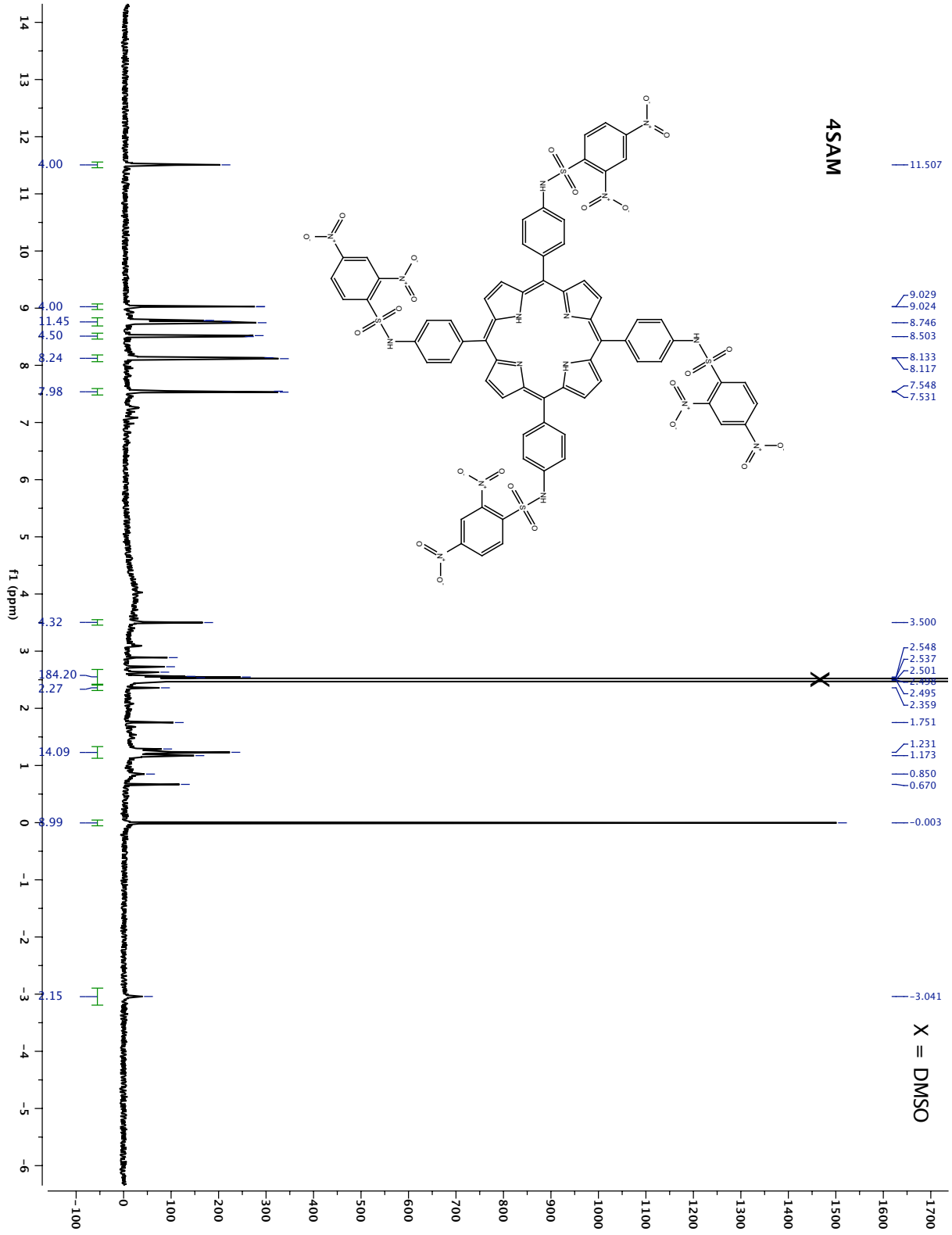
34.529
30.251
30.084
29.918
29.751
29.584
29.417
29.251
f1 (ppm)


4SAM
X = DMSO
f1 (ppm)
4.00
4.00
11.45
4.50
8.24
7.98
4.32
184.20
2.27
14.09
8.99
2.15
11.507
9.029
9.024
8.746
8.503
8.133
8.117
7.548
7.531
3.500
2.548
2.537
2.501
2.495
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1.751
1.231
1.173
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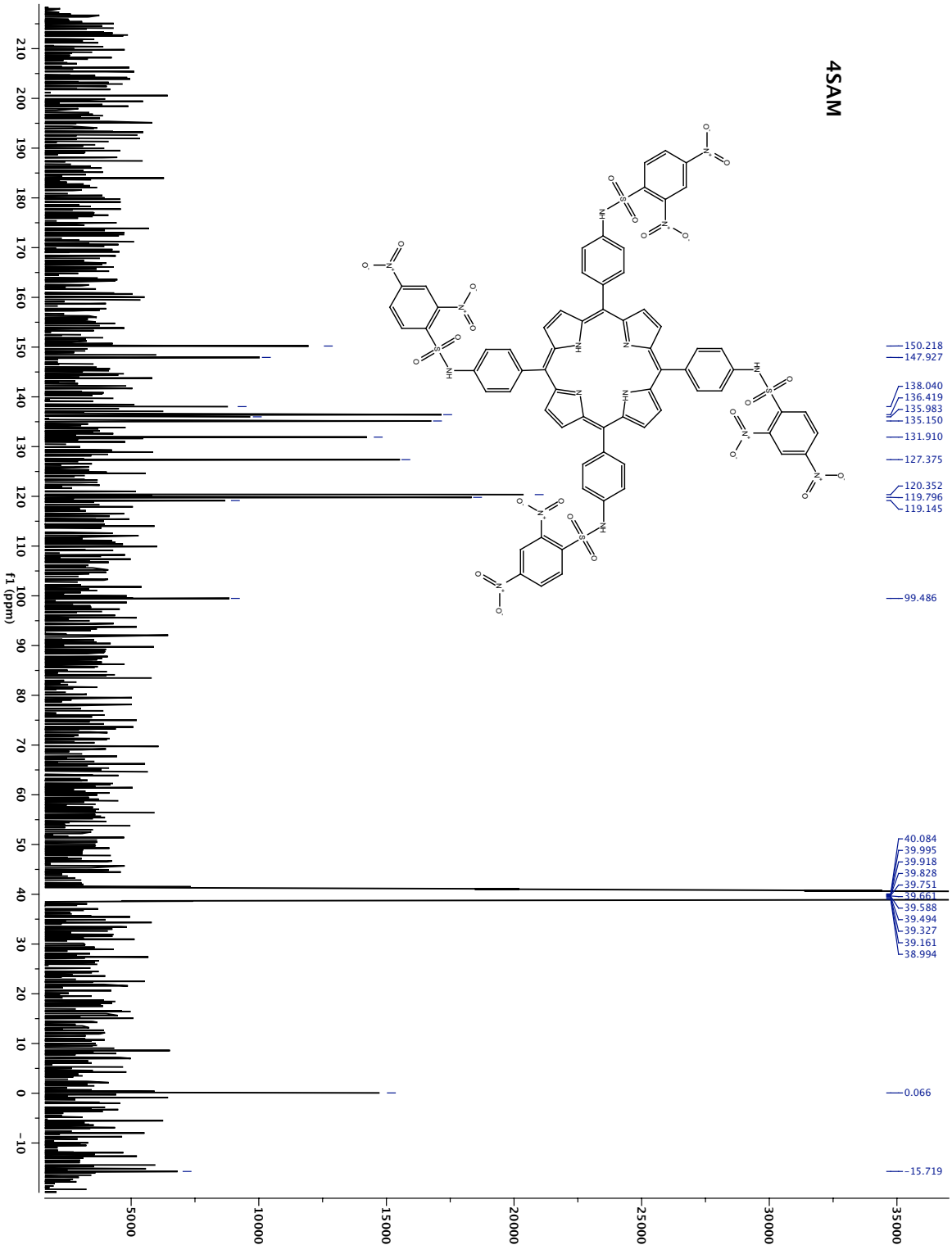
-0.003
-3.041


4SAM
f1 (ppm)
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147.927
138.040
136.419
135.983
135.150
131.910
127.375
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119.796
119.145
99.486
40.084
39.995
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39.751
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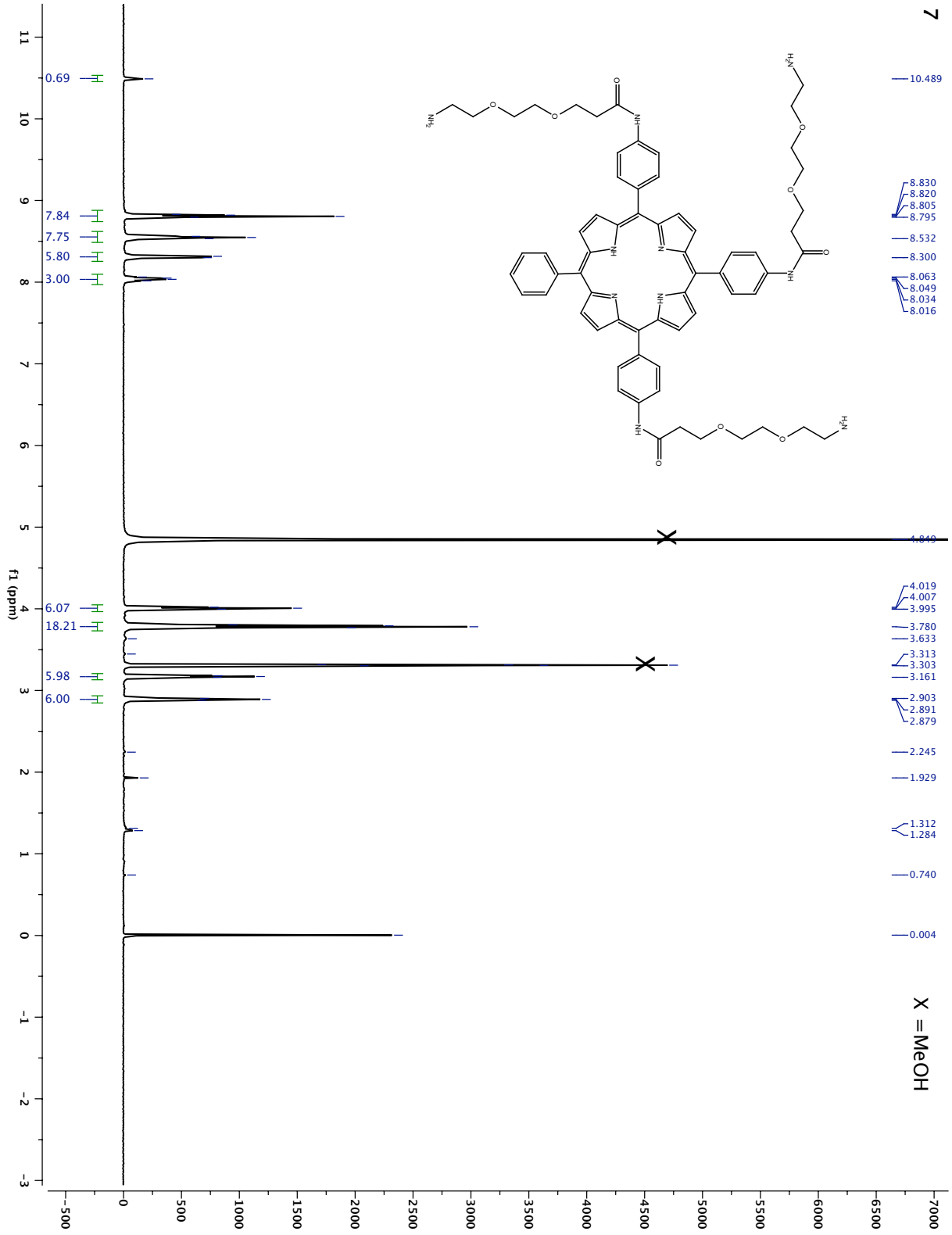
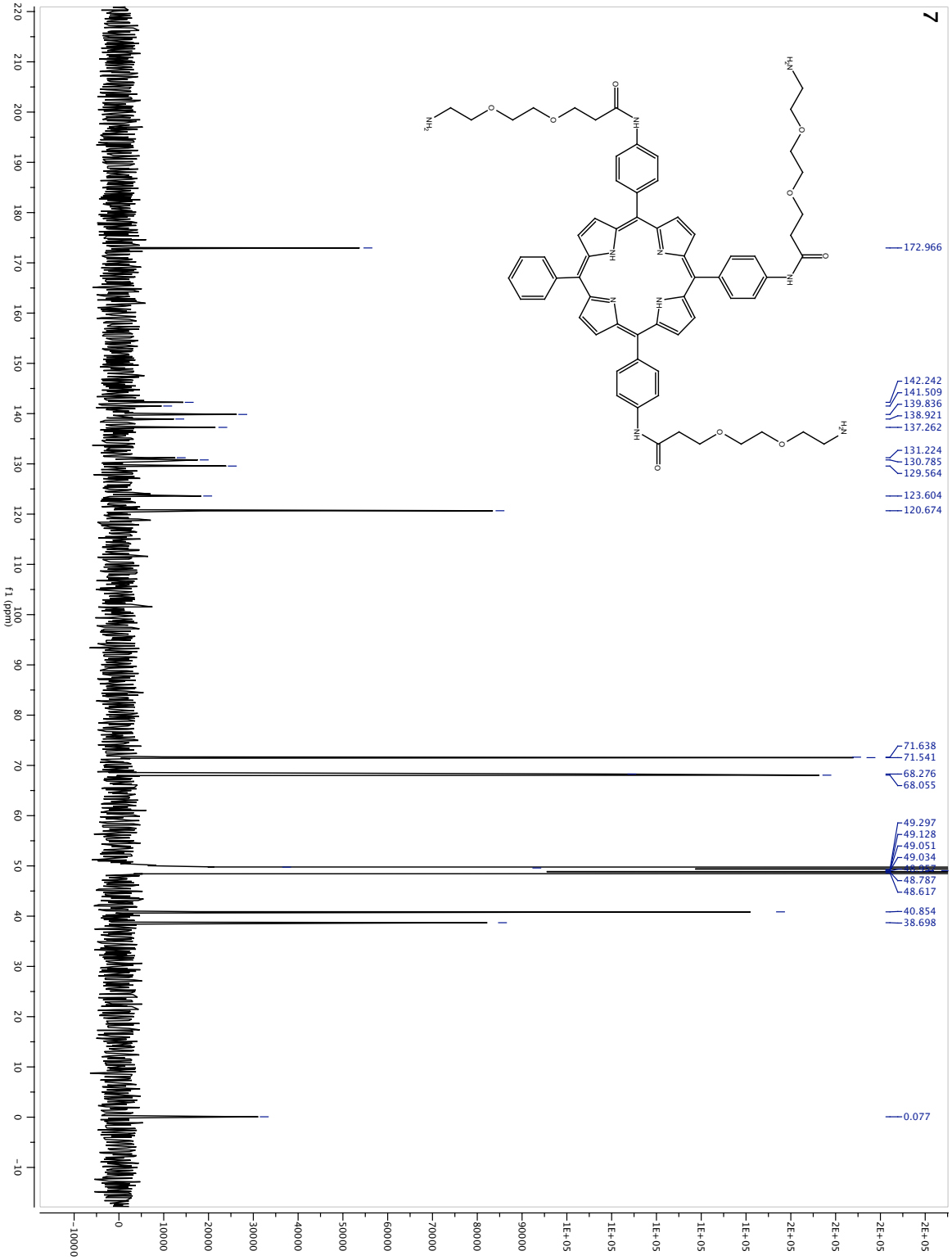
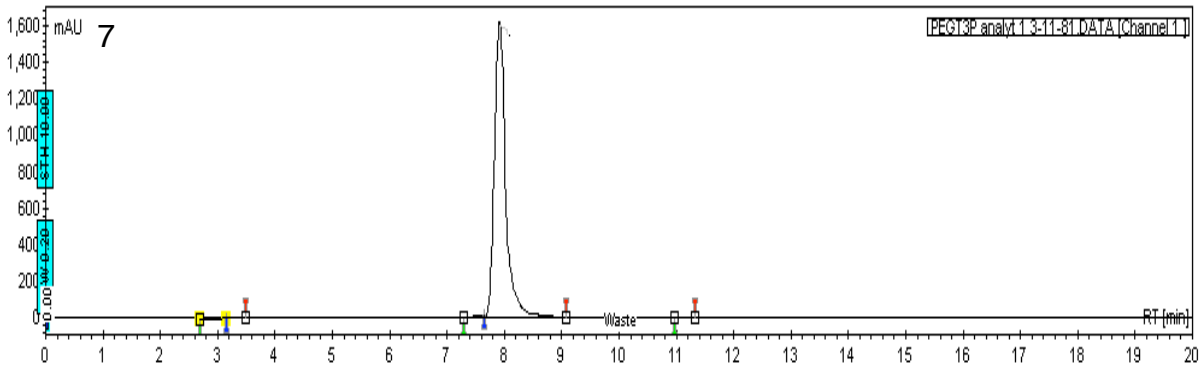
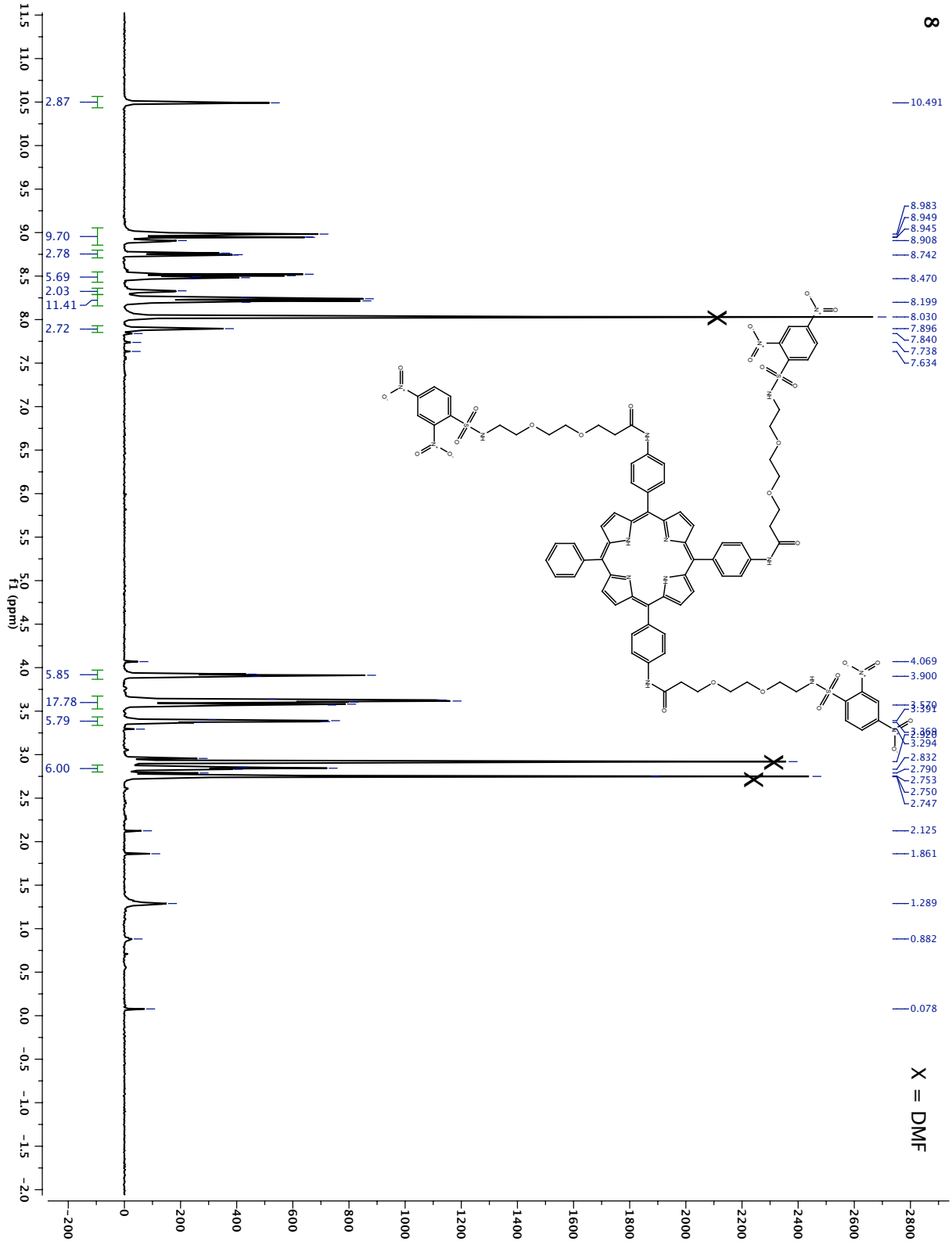

7
X = MeOH
f1 (ppm)
0.69
7.84
7.75
5.80
3.00
6.07
18.21
5.98
6.00
10.489
8.830
8.820
8.805
8.795
8.532
8.300
8.063
8.049
8.034
8.016
4.849
4.019
4.007
3.995
3.780
3.633
3.313
3.303
3.161
2.903
2.891
2.879
2.245
1.929
1.312
1.284
0.740
0.004


7
172.966
142.242
141.509
139.836
138.921
137.262
131.224
130.785
129.564
123.604
120.674
71.638
71.541
68.276
68.055
49.297
49.128
49.051
49.034
48.787
48.617
40.854
38.698
0.077
f1 (ppm)



Gradient from 80% to 20% Buffer A


8
X = DMF
f1 (ppm)
2.87
9.70
2.78
5.69
2.03
11.41
2.72
5.85
17.78
5.79
6.00
10.491
8.983
8.949
8.945
8.908
8.742
8.470
8.199
8.030
7.896
7.840
7.738
7.634
4.069
3.900
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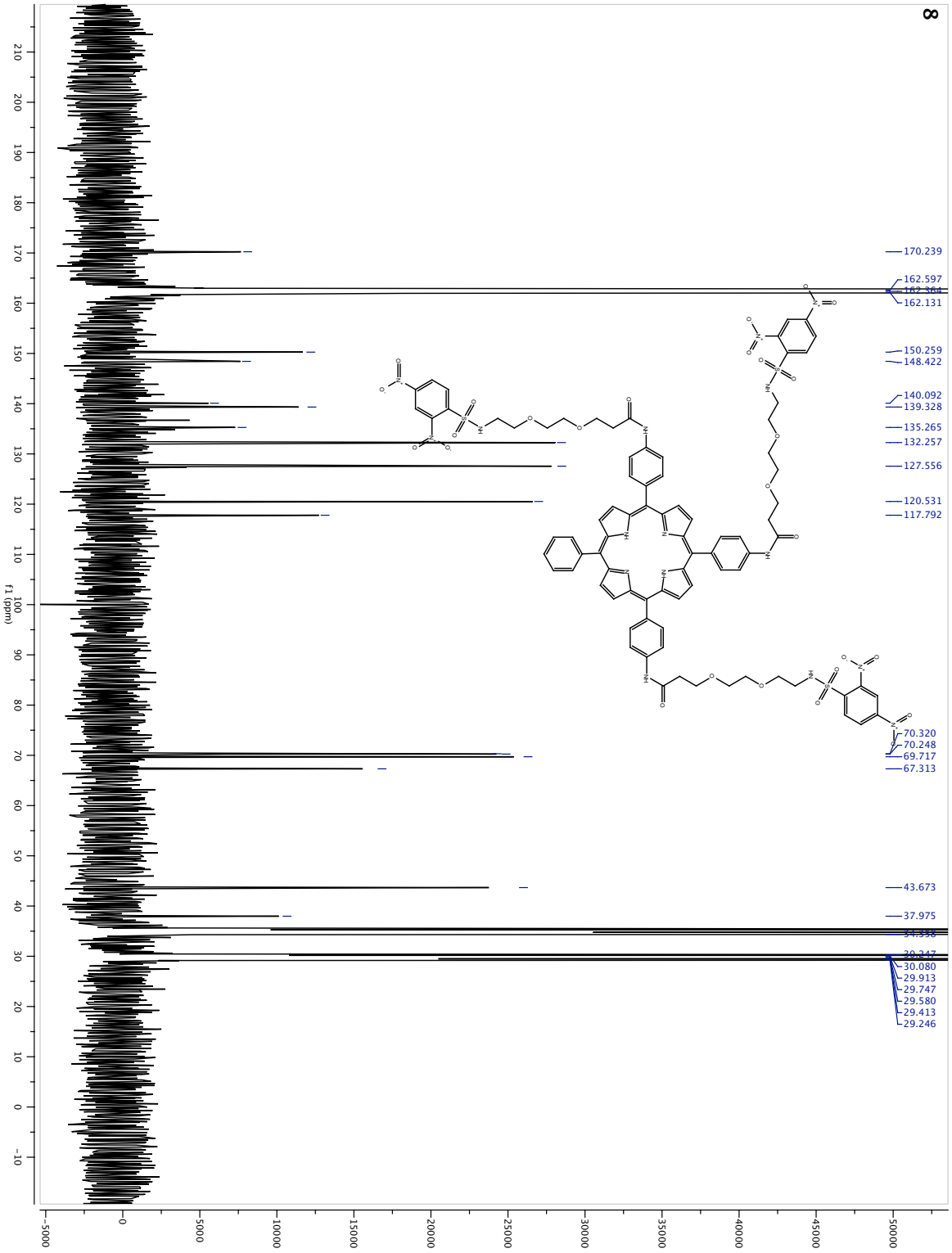
2.790
2.753
2.750
2.747
2.125
1.861
1.289
0.882
0.078


8
170.239
162.597
162.364
162.131
150.259
148.422
140.092
139.328
135.265
132.257
127.556
120.531
117.792
70.320
70.248
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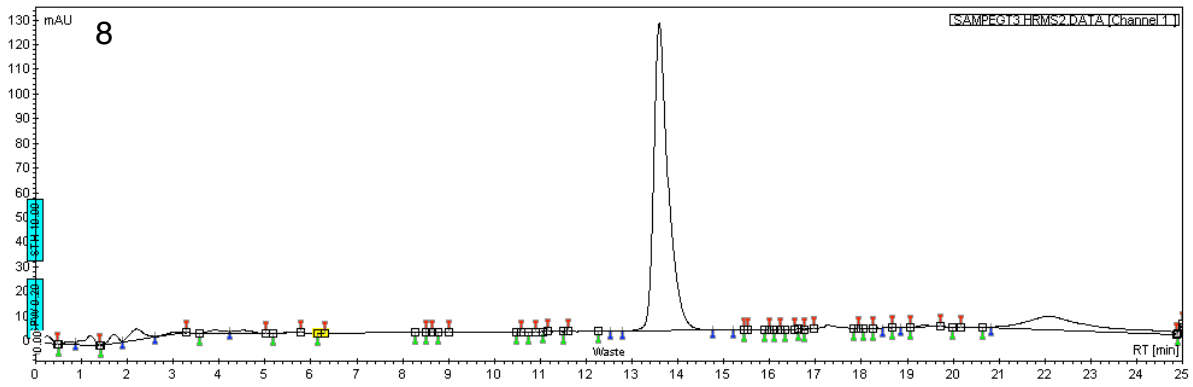
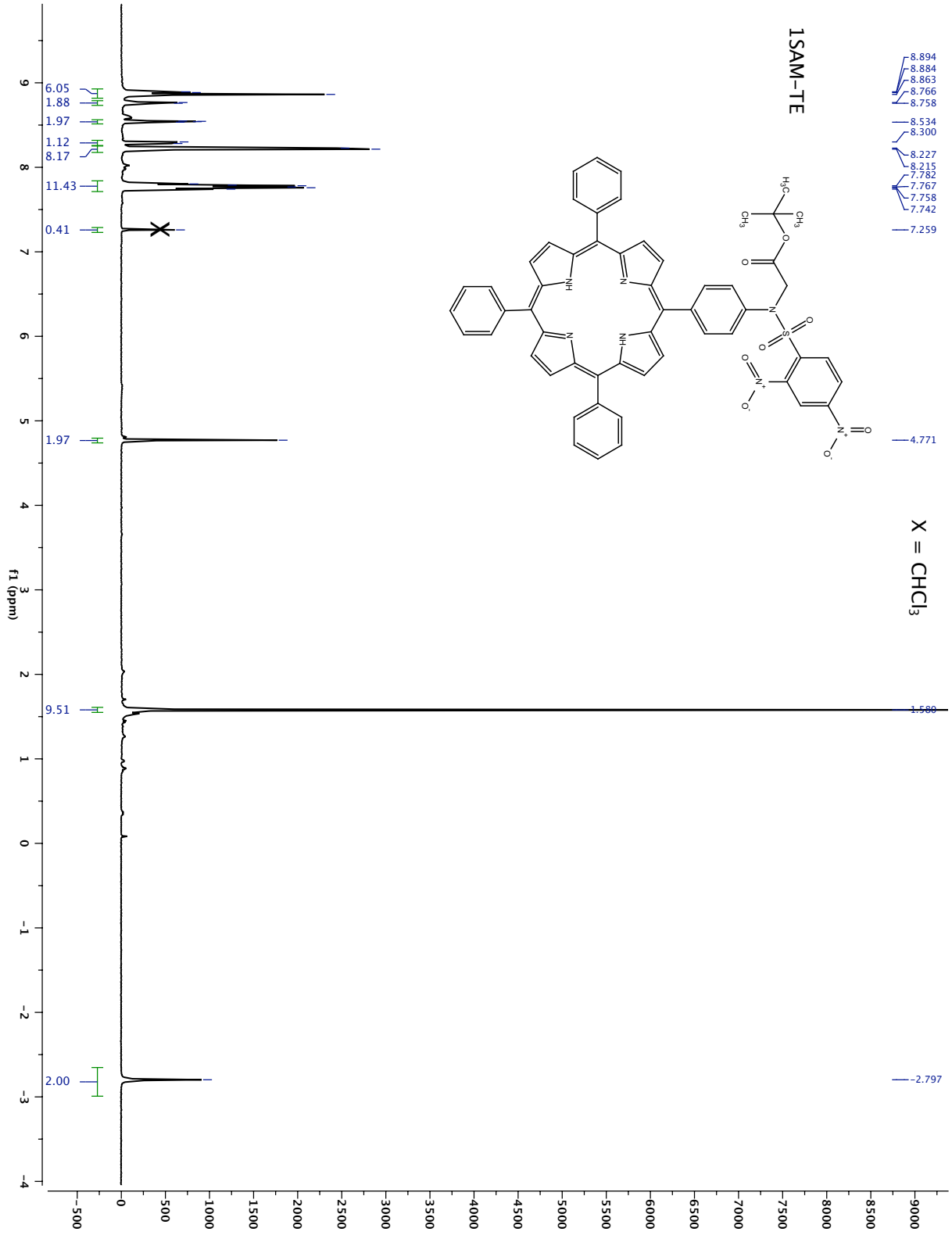
29.747
29.580
29.413
29.246
f1 (ppm)



Gradient from 60% to 0% Buffer A


1SAM-TE
X = CHCl3
f1 (ppm)
6.05
1.88
1.97
1.12
8.17
11.43
0.41
1.97
9.51
2.00
8.894
8.884
8.863
8.766
8.758
8.534
8.300
8.227
8.215
7.782
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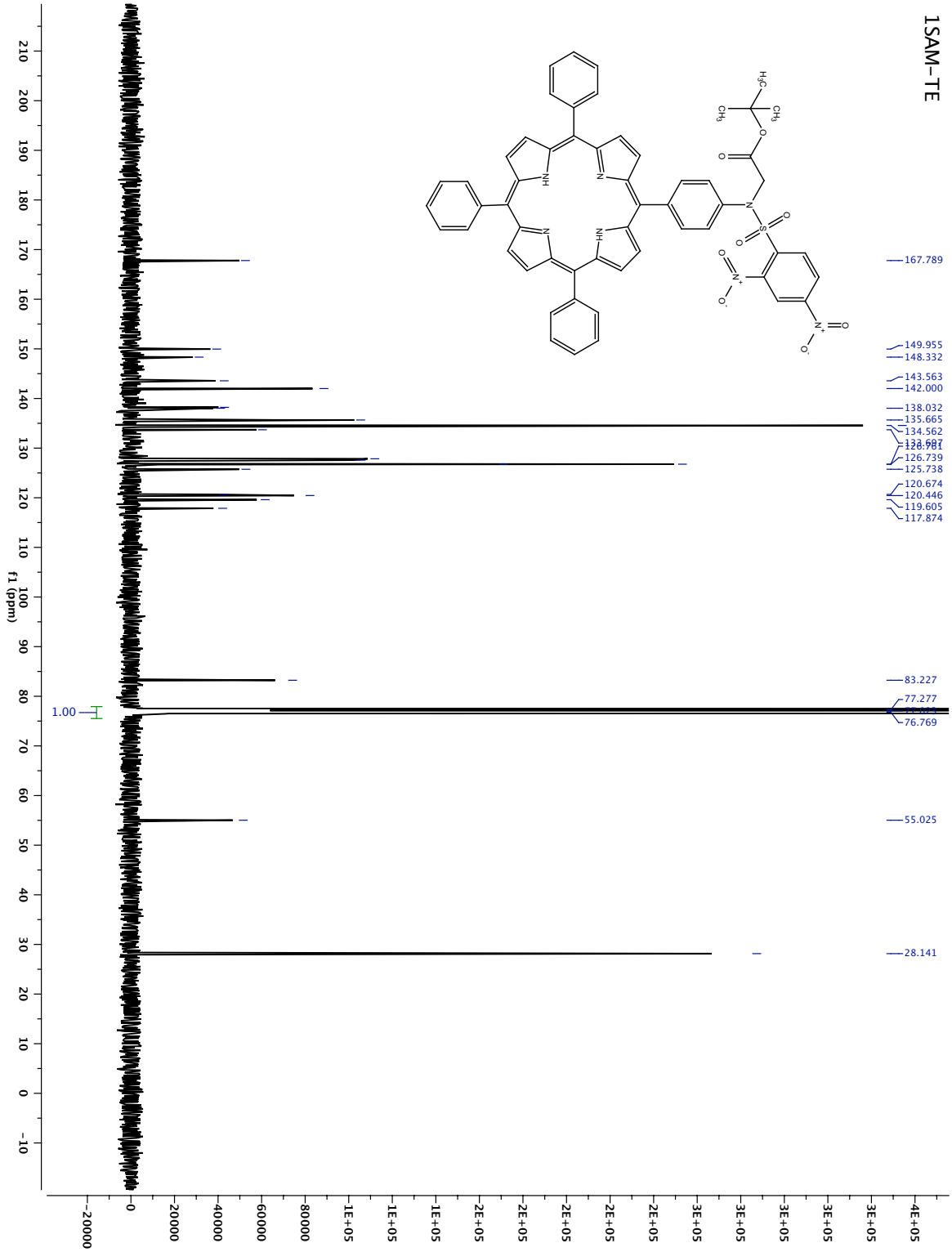
7.742
7.259
4.771
1.580
-2.797


1SAM-TE
f1 (ppm)
167.789
149.955
148.332
143.563
142.000
138.032
135.665
134.562
126.739
125.738
120.674
120.446
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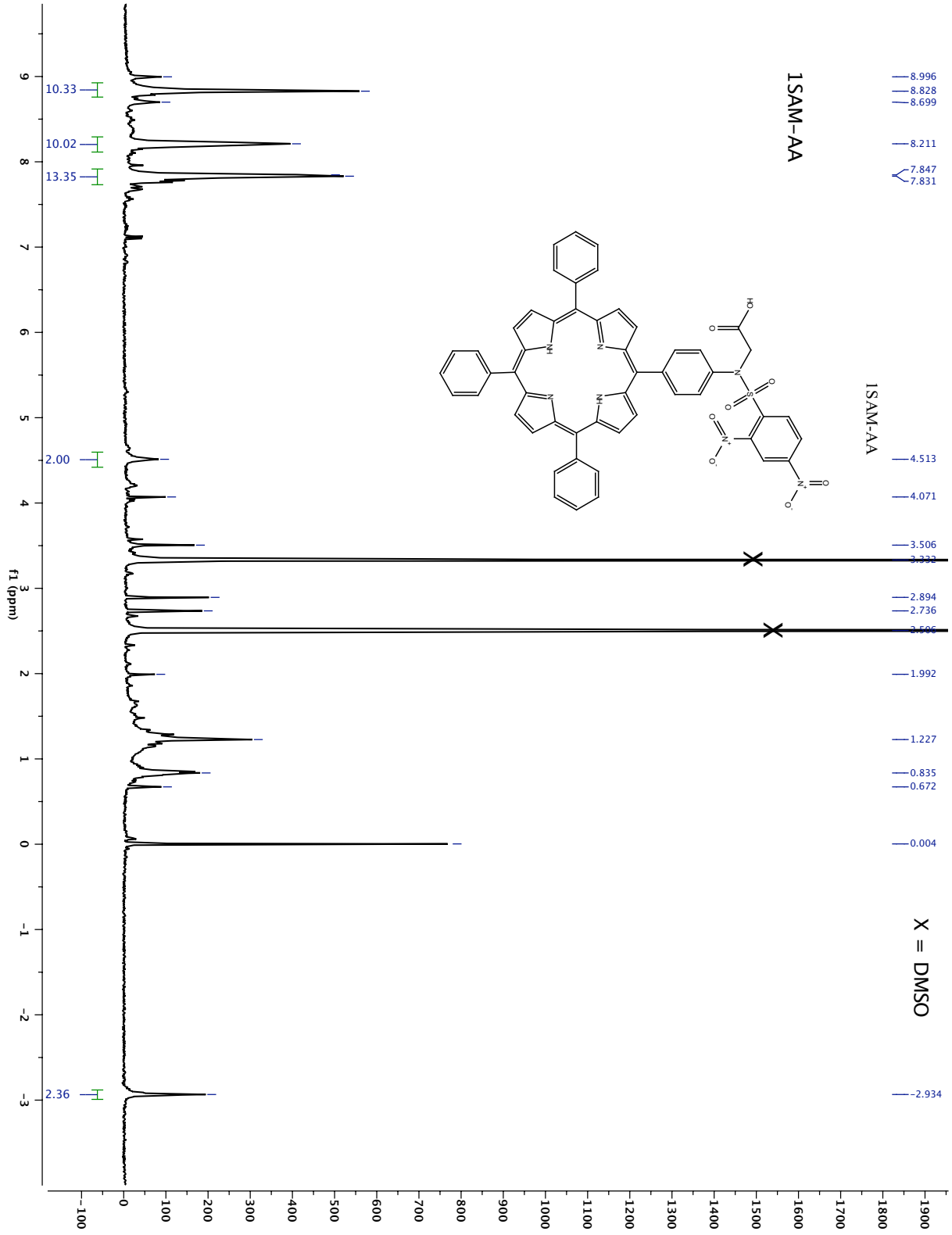
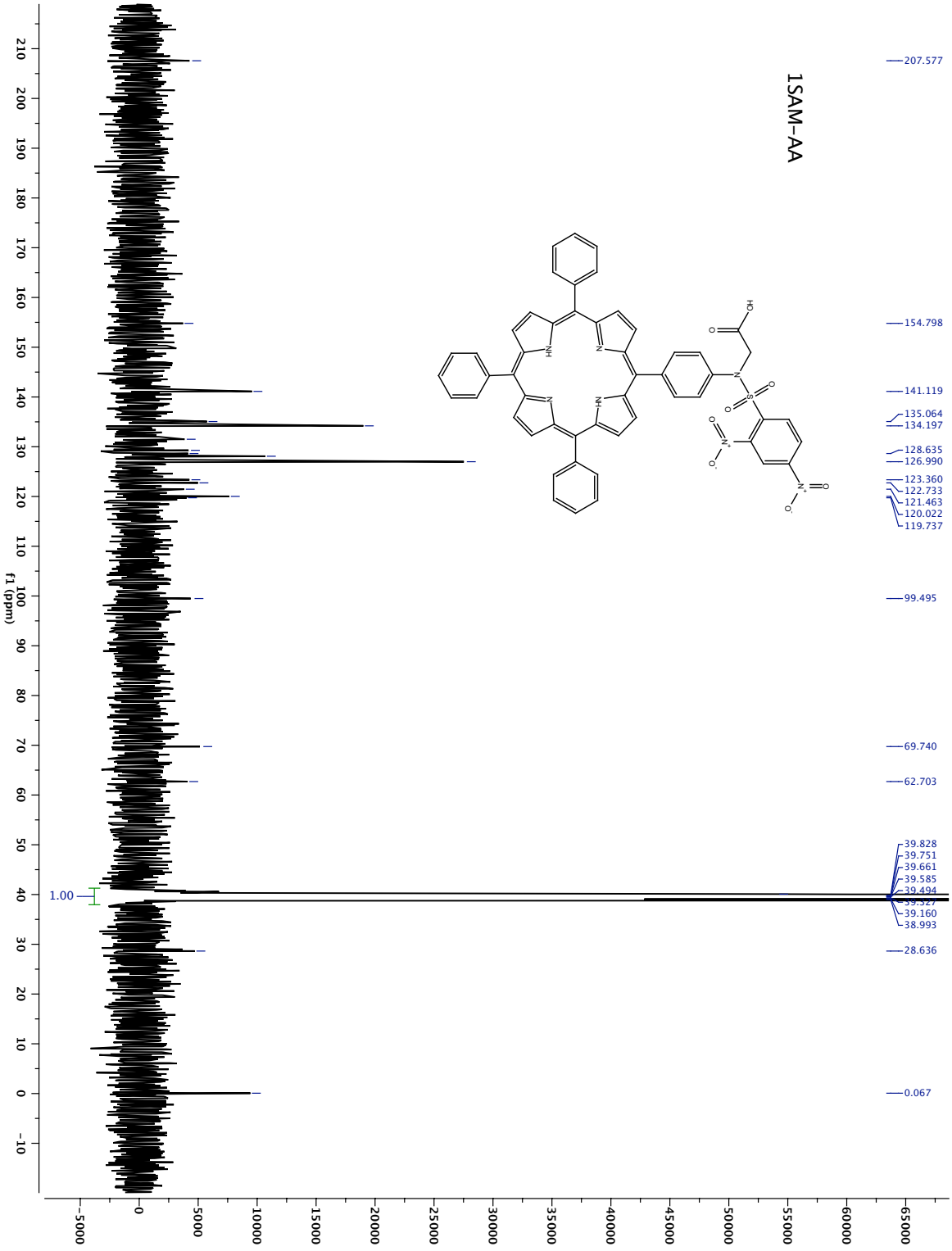
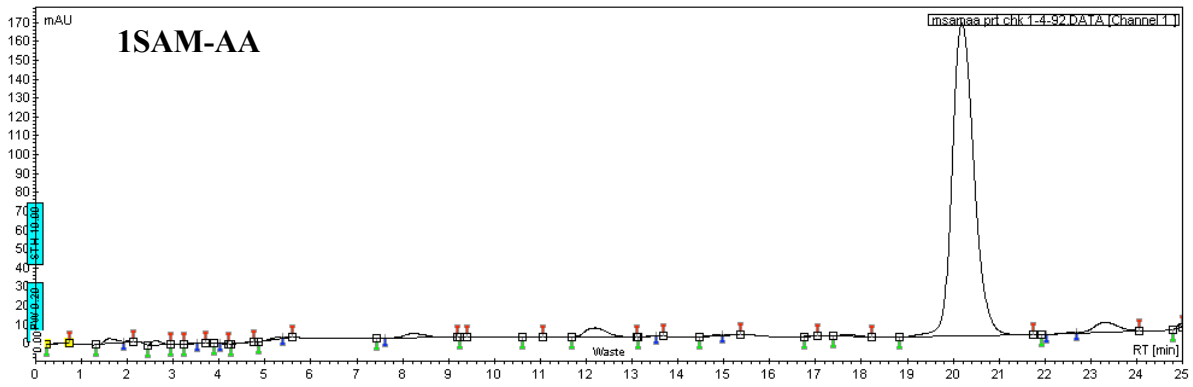
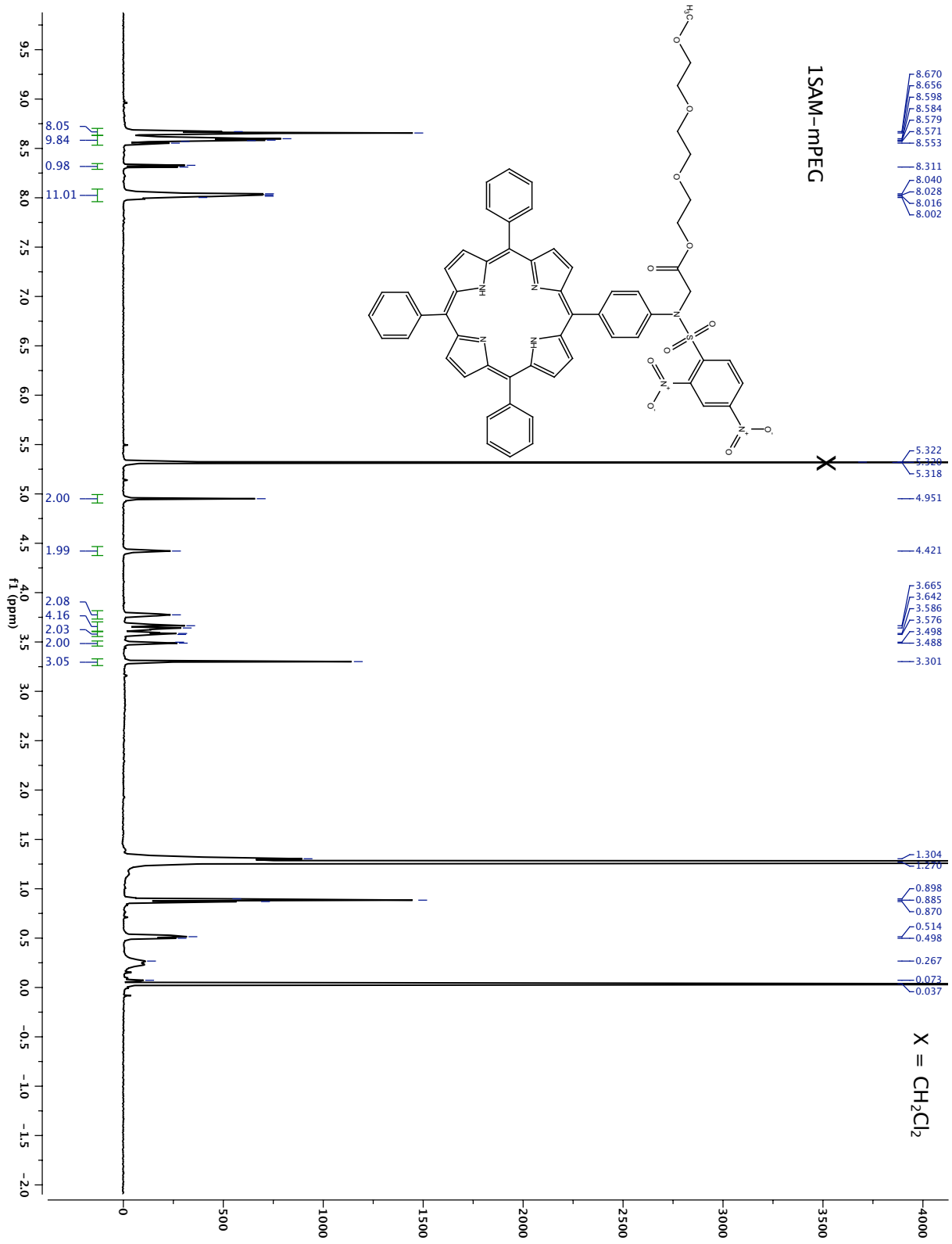
117.874
83.227
77.277
76.769
55.025
28.141
1.00

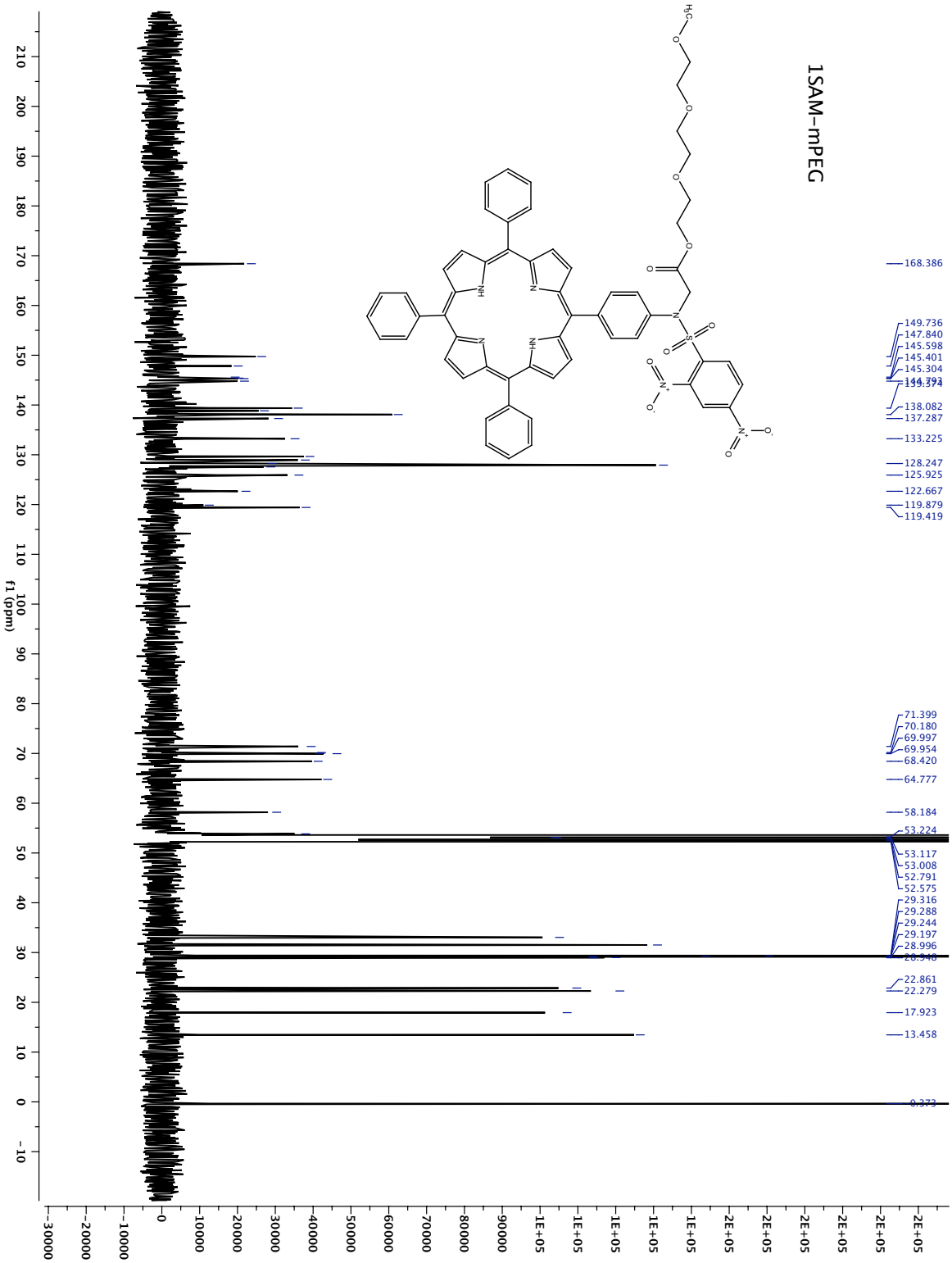

1SAM-AA
1SAM-AA
X = DMSO
f1 (ppm)
10.33
10.02
13.35
2.00
2.36
8.996
8.828
8.699
8.211
7.847
7.831
4.513
4.071
3.506
2.894
2.736
1.992
1.227
0.835
0.672
0.004
-2.934

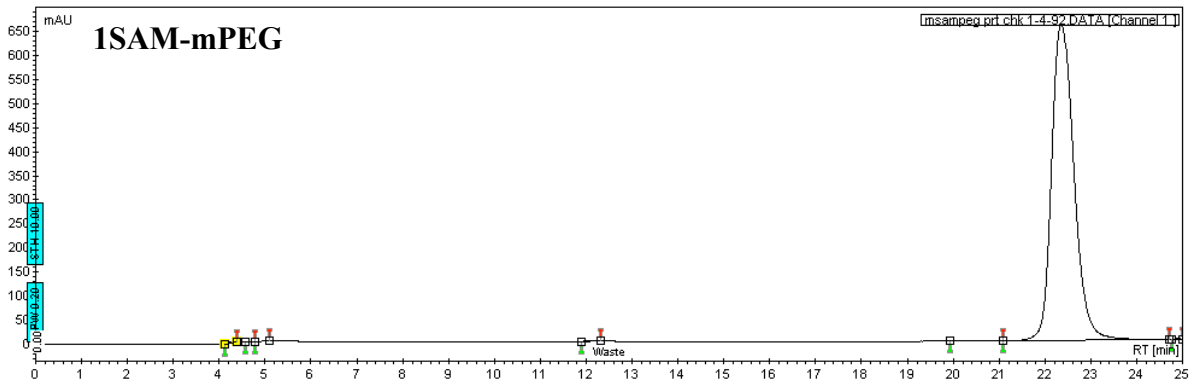

1SAM-AA
207.577
154.798
141.119
135.064
134.197
128.635
126.990
123.360
122.733
121.463
120.022
119.737
99.495
69.740
62.703
39.828
39.751
39.661
39.585
39.494
39.160
38.993
28.636
0.067
1.00
f1 (ppm)



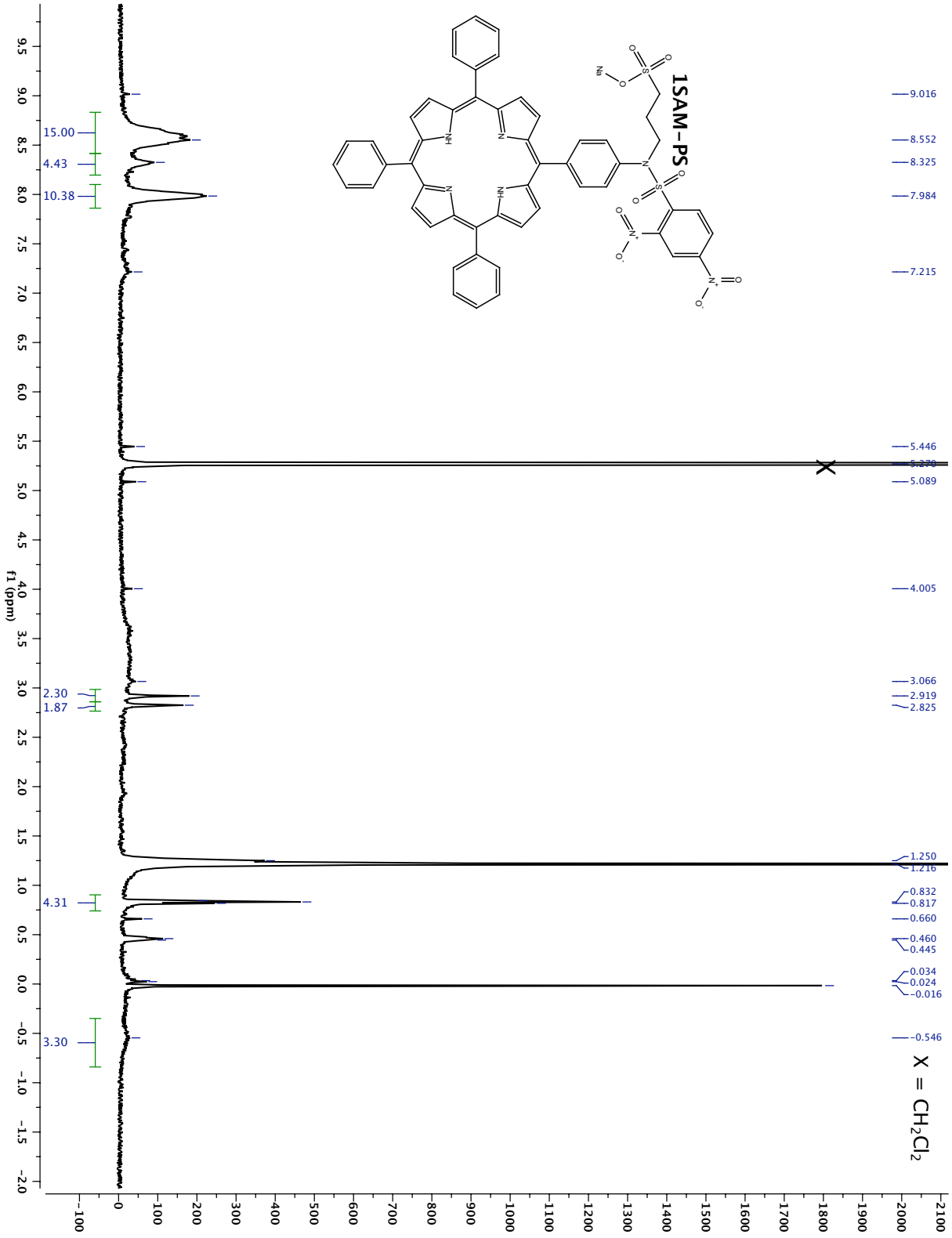
Gradient from 60% to 0% Buffer A

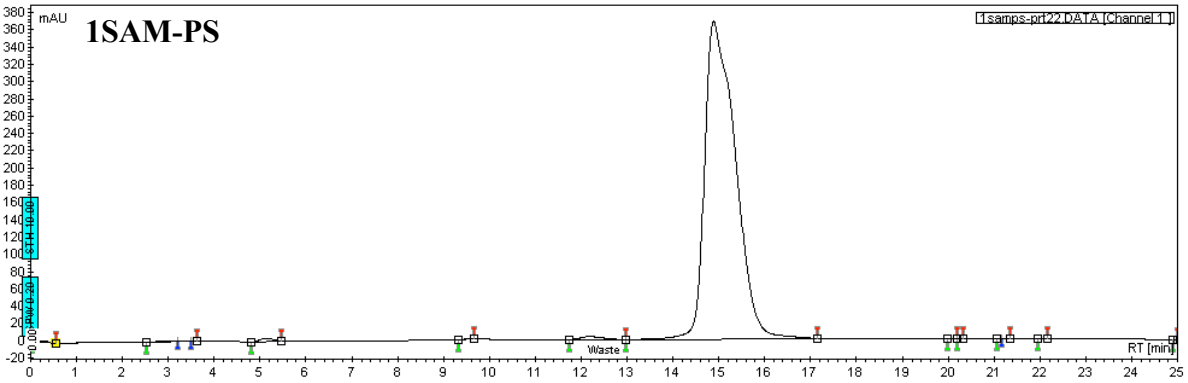

1SAM-mPEG
X = CH2Cl2
f1 (ppm)
8.05
9.84
0.98
11.01
2.00
1.99
2.08
4.16
2.03
2.00
3.05
8.670
8.656
8.598
8.584
8.579
8.571
8.553
8.311
8.040
8.028
8.016
8.002
5.322
5.320
5.318
4.951
4.421
3.665
3.642
3.586
3.576
3.498
3.488
3.301
1.304
1.270
0.898
0.885
0.870
0.514
0.498
0.267
0.073
0.037


1SAM-mPEG
f1 (ppm)
168.386
149.736
147.840
145.598
145.401
145.304
138.082
137.287
133.225
128.247
125.925
122.667
119.879
119.419
71.399
70.180
69.997
69.954
68.420
64.777
58.184
53.224
53.117
53.008
52.791
52.575
29.316
29.288
29.244
29.197
28.996
22.861
22.279
17.923
13.458
0.373

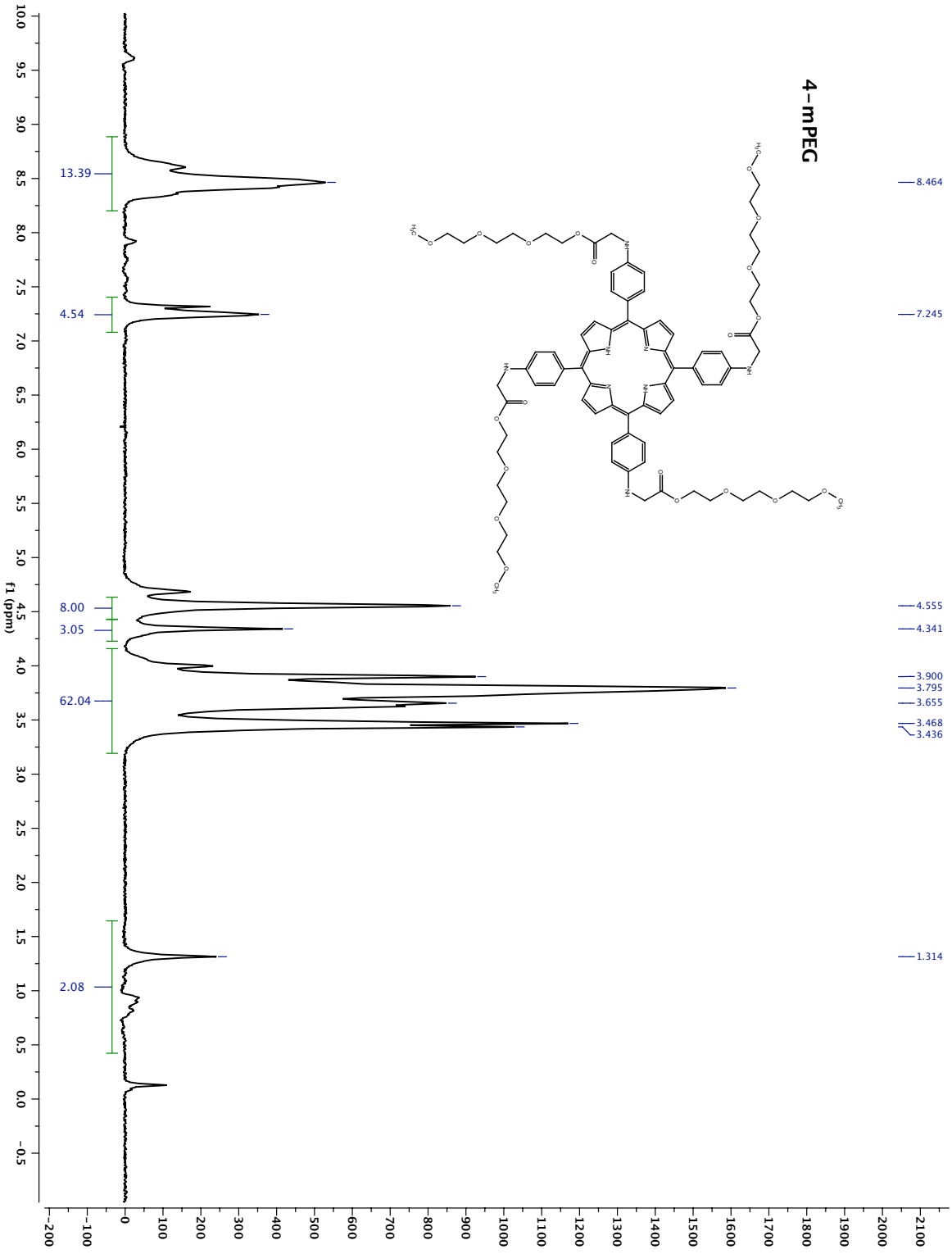


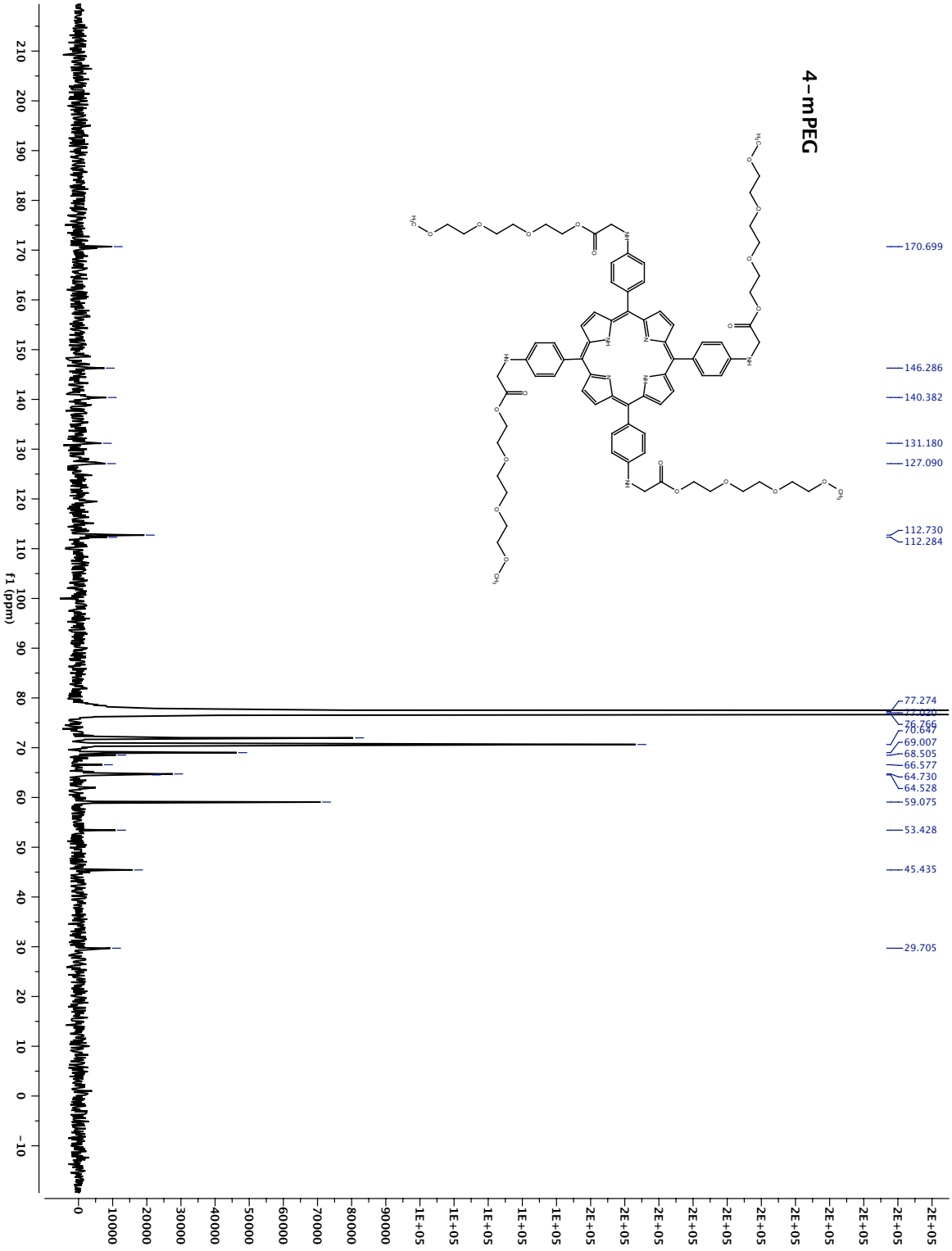
Gradient from 60% to 0% Buffer A

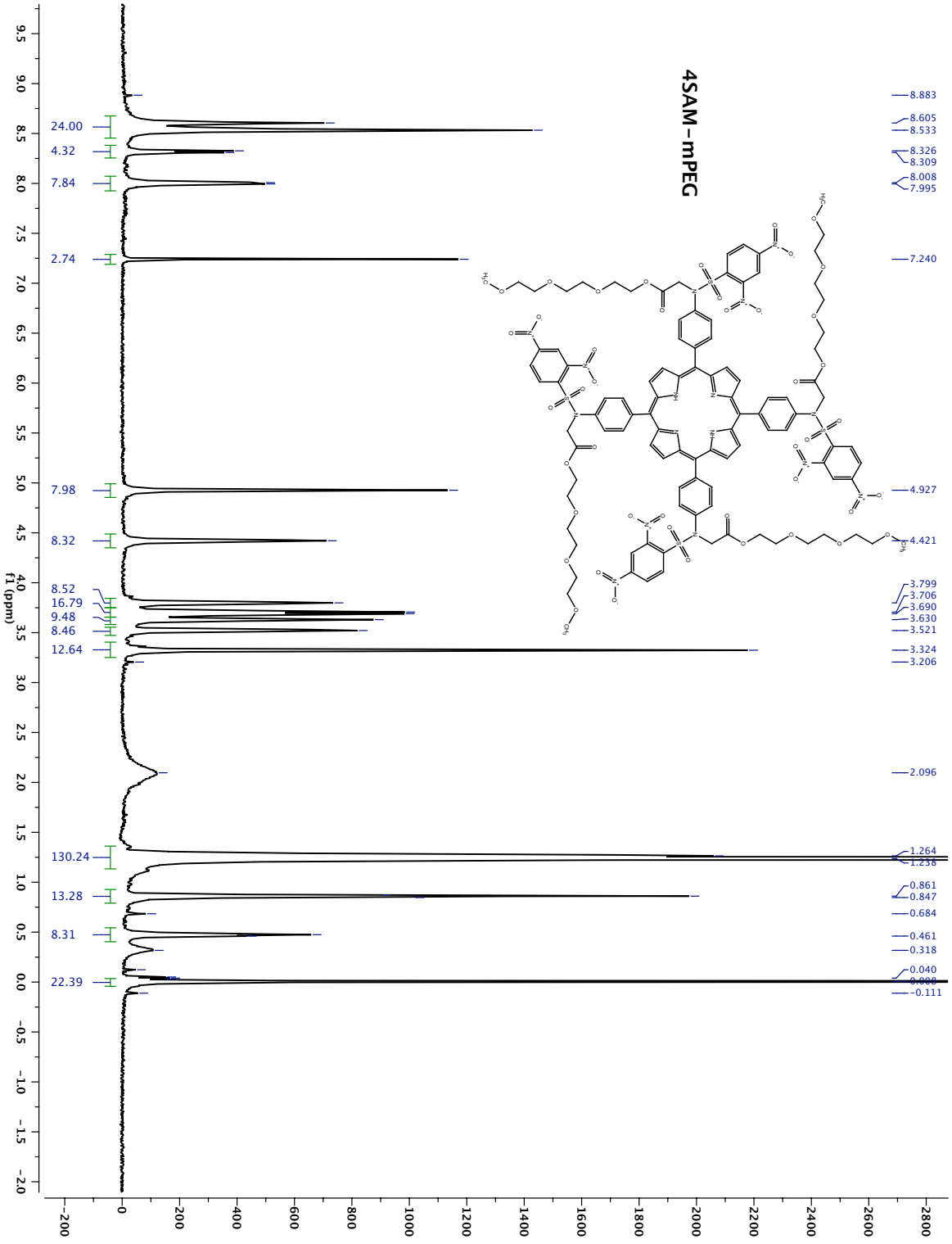

1SAM-PS
X = CH2Cl2
f1 (ppm)
15.00
4.43
10.38
2.30
1.87
4.31
3.30
9.016
8.552
8.325
7.984
7.215
5.446
5.089
4.005
3.066
2.919
2.825
1.250
1.216
0.832
0.817
0.660
0.460
0.445
0.034
0.024
-0.016
-0.546

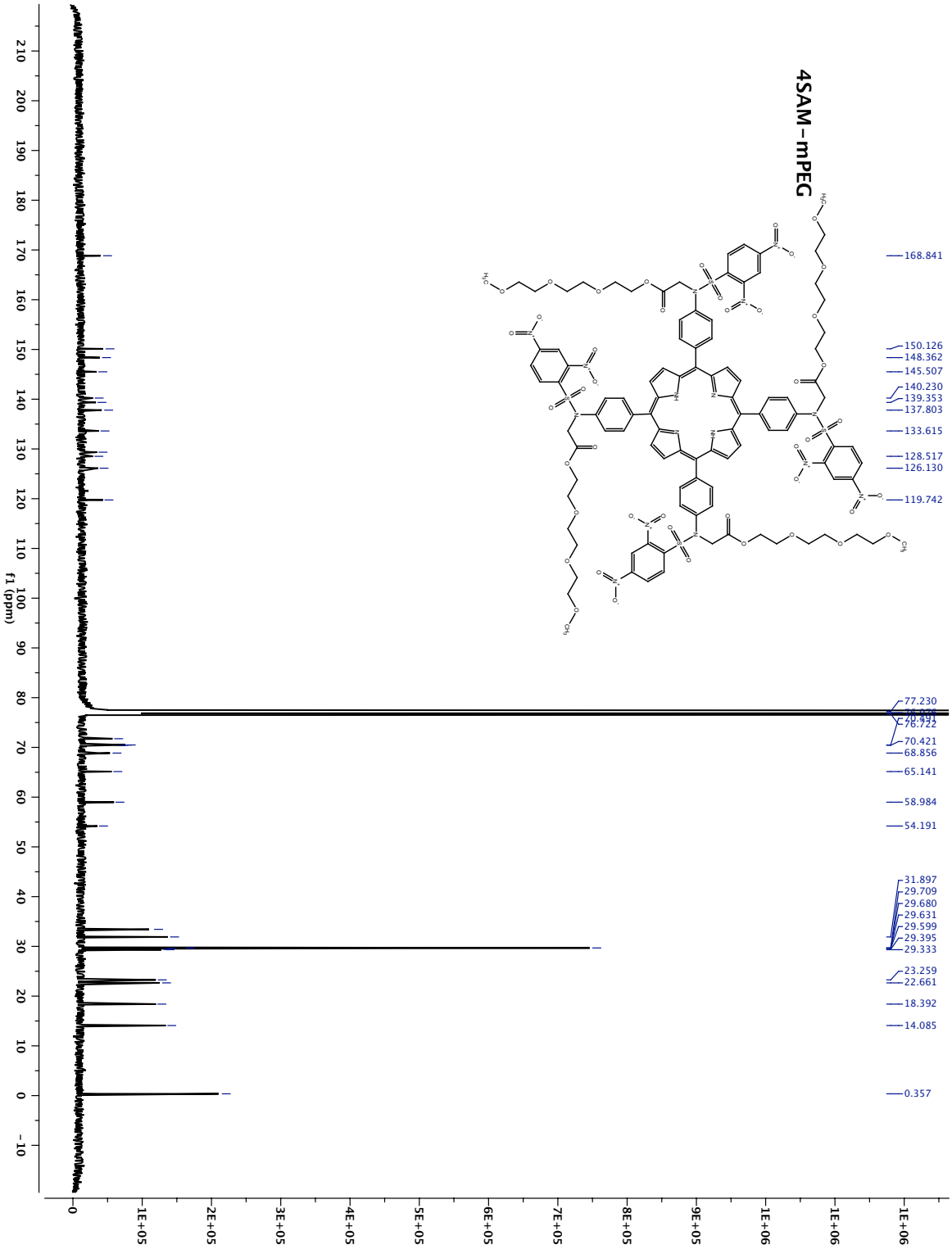


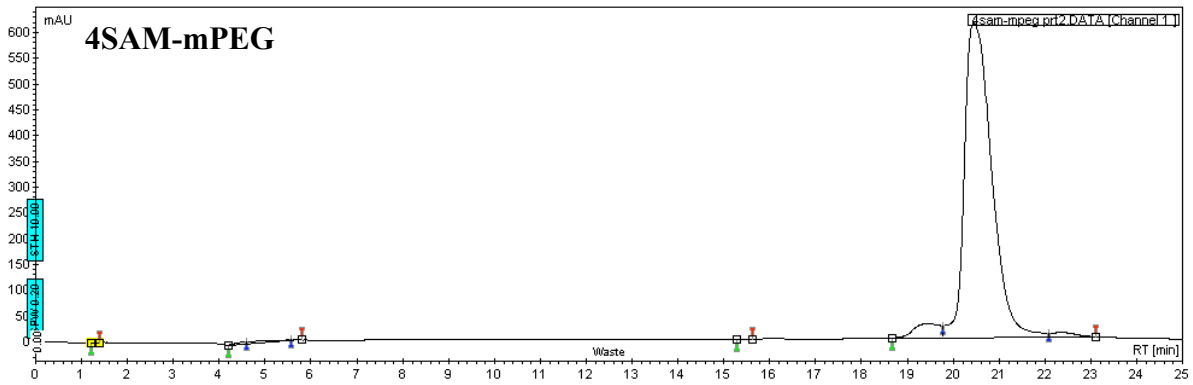
Gradient from 60% to 0% Buffer A


4-mPEG
13.39
4.54
8.00
3.05
62.04
2.08
8.464
7.245
4.555
4.341
3.900
3.795
3.655
3.468
3.436
1.314
f1 (ppm)


4-mPEG
170.699
146.286
140.382
131.180
127.090
112.730
112.284
77.274
77.020
76.766
70.647
69.007
68.505
66.577
64.730
64.528
59.075
53.428
45.435
29.705
f1 (ppm)


4SAM-mPEG
24.00
4.32
7.84
2.74
7.98
8.32
8.52
16.79
9.48
8.46
12.64
130.24
13.28
8.31
22.39
8.883
8.605
8.533
8.326
8.309
8.008
7.995
7.240
4.927
4.421
3.799
3.706
3.690
3.630
3.521
3.324
3.206
2.096
1.264
1.238
0.861
0.847
0.684
0.461
0.318
0.040
0.000
-0.111
f1 (ppm)


4SAM-mPEG
f1 (ppm)
168.841
150.126
148.362
145.507
140.230
139.353
137.803
133.615
128.517
126.130
119.742
77.230
76.722
70.421
68.856
65.141
58.984
54.191
31.897
29.709
29.680
29.631
29.599
29.395
29.333
23.259
22.661
18.392
14.085
0.357



Gradient from 60% to 0% Buffer A

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