

Supporting Information

Design, synthesis and biological evaluation of rhein-piperazine-furanone hybrids as potential anticancer agents

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¹ These authors contributed equally to this work.

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General remark

Reagents and solvents were purchased from Adamas, Aldrich, and Energy Chemical, and used without further purification unless otherwise stated. The progress of the organic chemical reaction was monitored by thin-layer chromatography (TLC) (Qingdao Haiyang Chemical, China). ¹H and ¹³C NMR spectra were recorded on a Bruker Avance III 400 MHz spectrometer. The FT-IR spectra recorded on a Shimadzu FTIR-8400S Fourier Transform Infrared Spectrophotometer (400–4000 cm⁻¹) with KBr pellets. High-resolution mass spectrums were recorded on a Thermo Fisher LTQ Orbitrap XL. The bioassays were carried out by Wuhan Biofavor Biotech Service Co., Ltd.

¹H NMR, ¹³C NMR and HRMS for hybrids 5a–5j

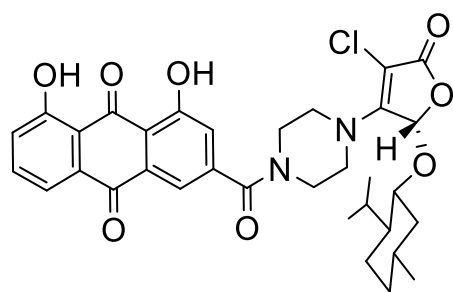
zss-326-H

11.950
11.789

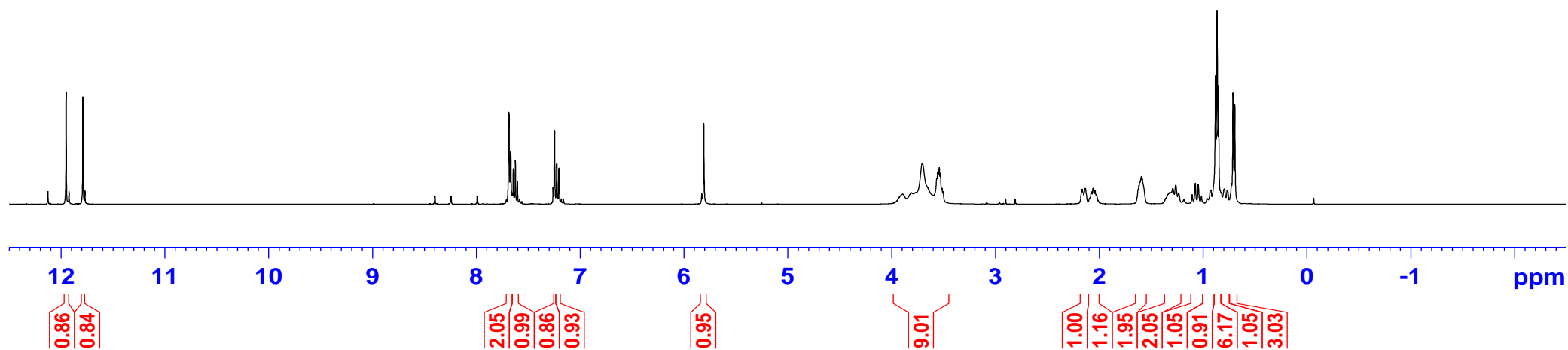
7.686
7.683
7.669
7.667
7.643
7.622
7.603
7.260
7.248
7.245
7.226
7.223
7.205
7.202

5.807

3.891
3.808
3.703
3.554
3.539
3.529
3.513
3.502
2.164
2.133
2.073
2.056
2.038
2.026
1.617
1.594
1.585
1.331
1.322
1.315
1.290
1.262
1.233
1.182
1.103
1.073
1.044
1.014
0.955
0.930
0.923
0.880
0.864
0.849
0.794
0.767
0.761
0.726
0.710
0.693



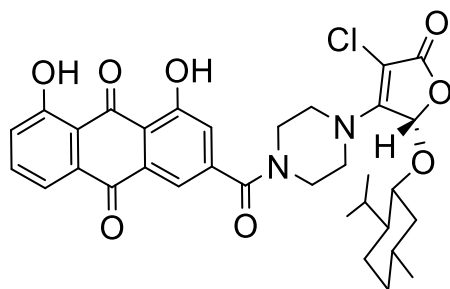
5a



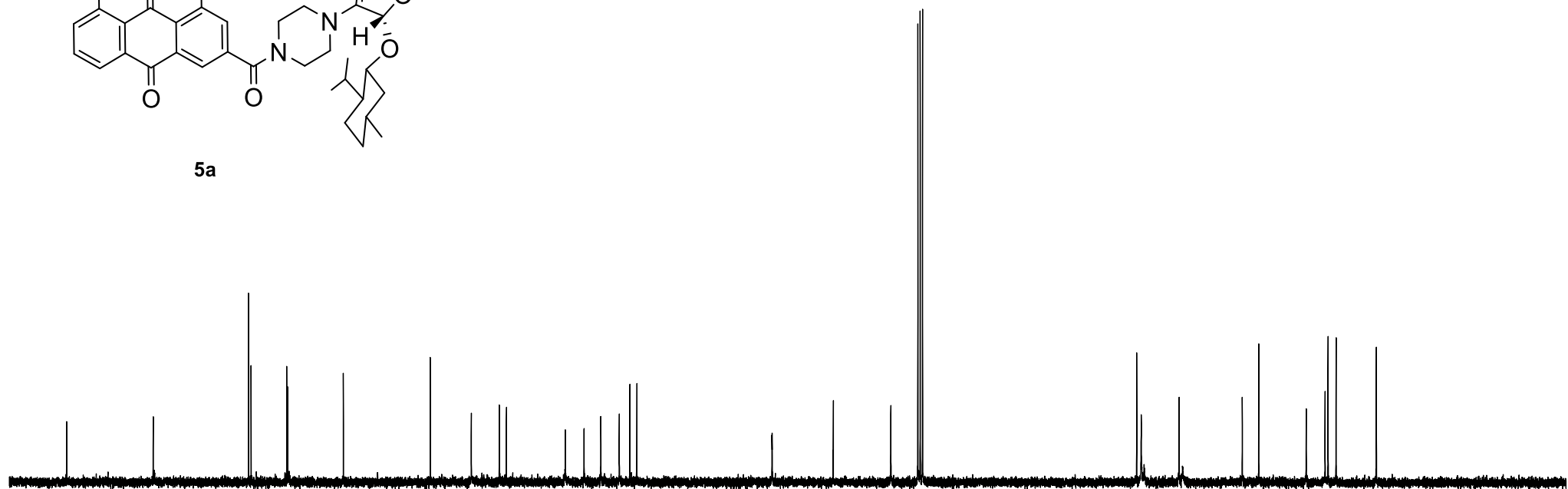
¹H NMR (400 MHz, CDCl₃) spectrum of **5a**

zss-326-C

192.15
180.53
167.66
167.33
162.52
162.39
154.90
143.21
137.67
133.89
132.94
124.99
122.47
120.22
117.72
116.31
115.35
97.12
88.87
81.11
77.47
77.16
76.84
47.96
47.35
42.26
41.79
33.73
31.51
25.11
22.57
22.17
21.09
15.66

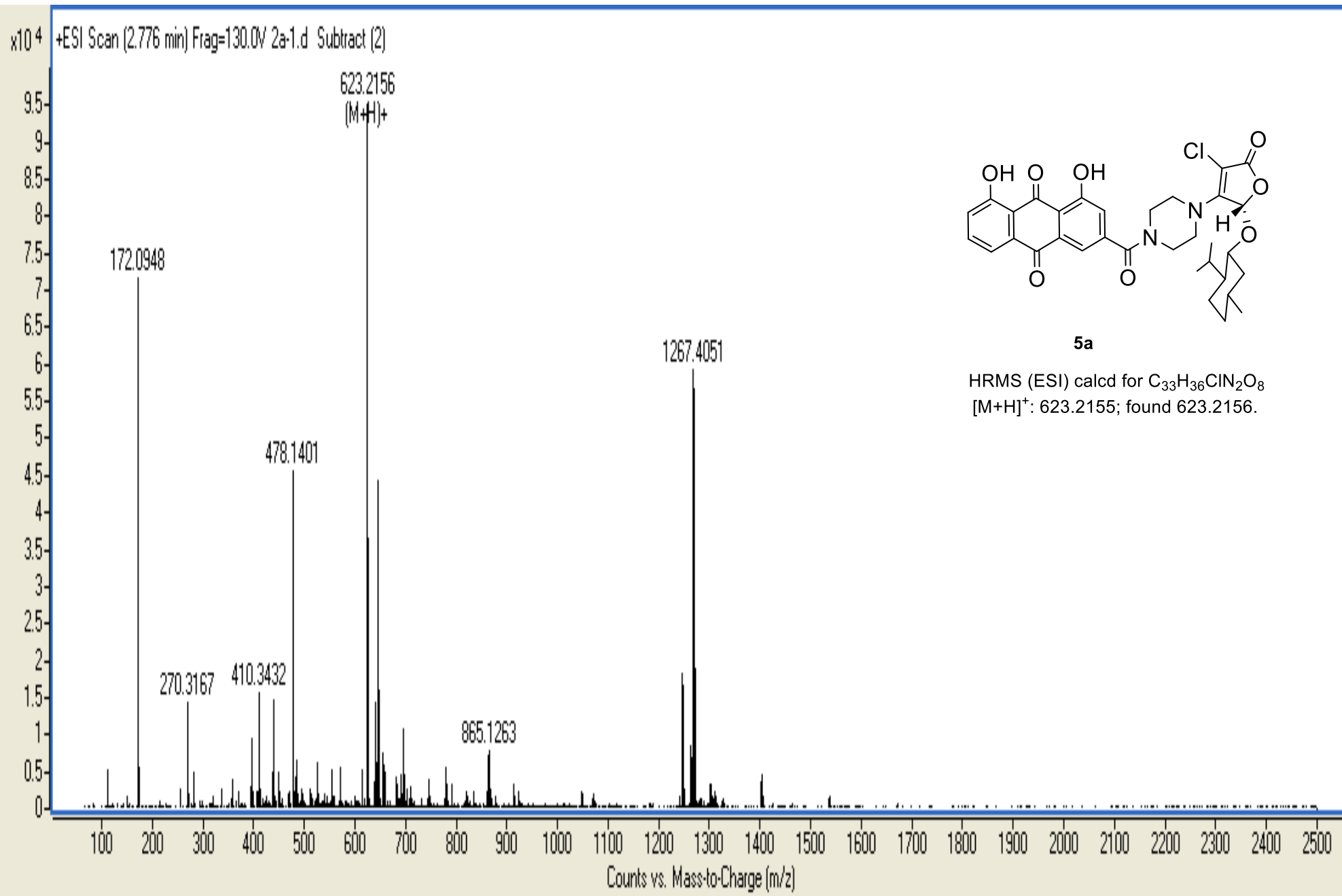


5a



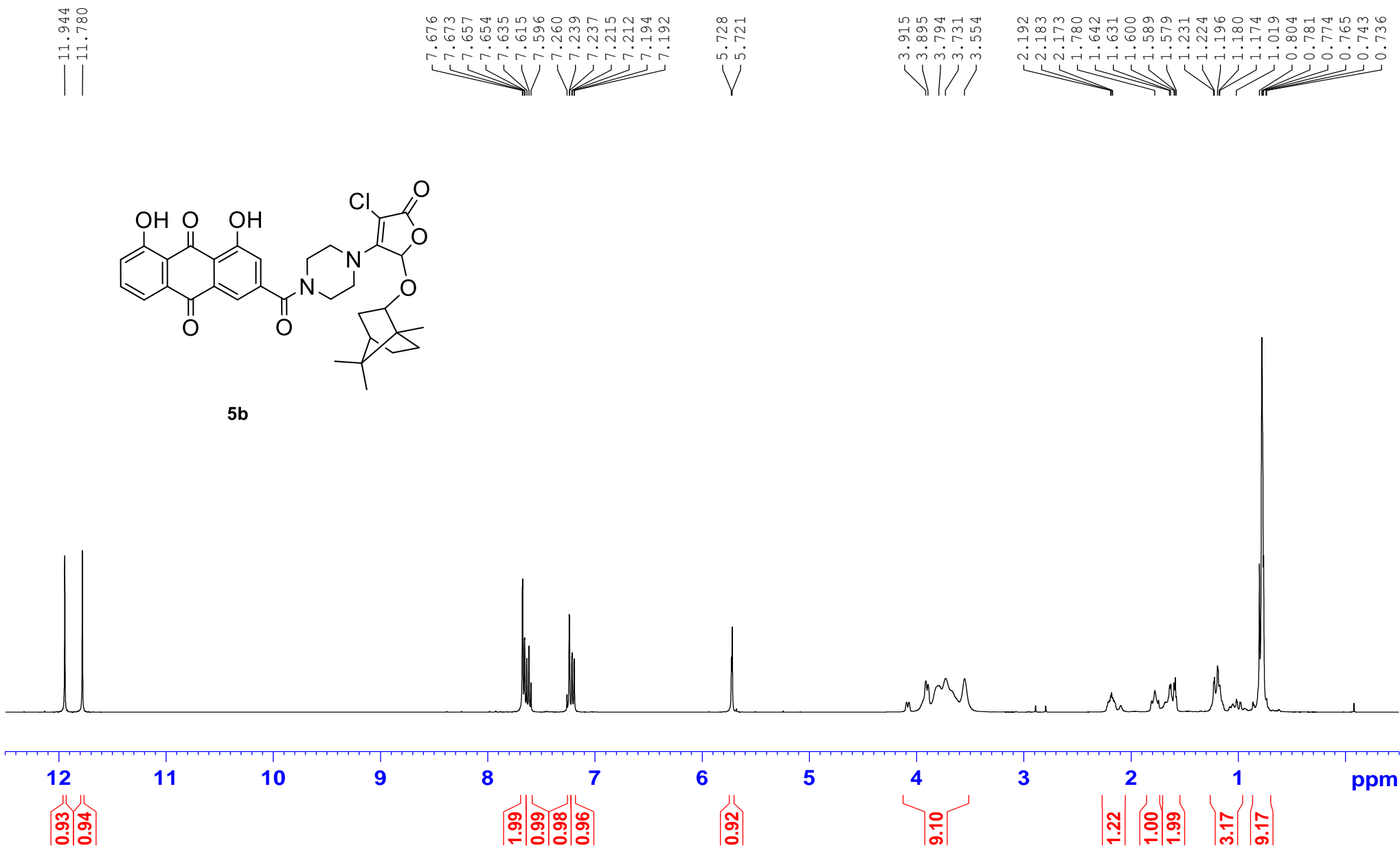
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

¹³C NMR (101 MHz, CDCl₃) spectrum of 5a

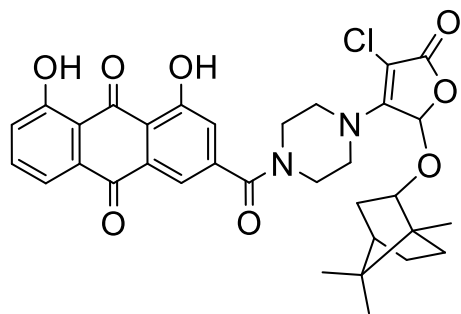


HRMS spectrum of **5a**

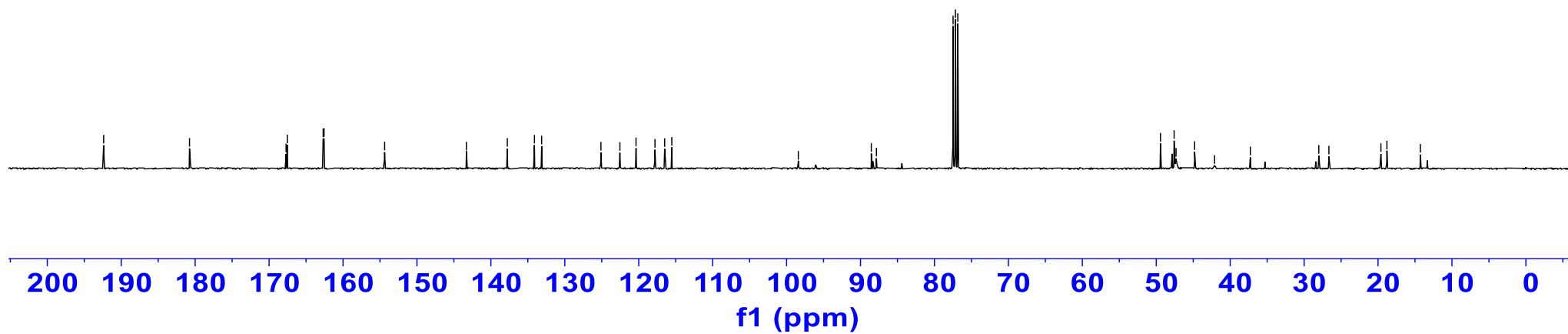
zss-324-H



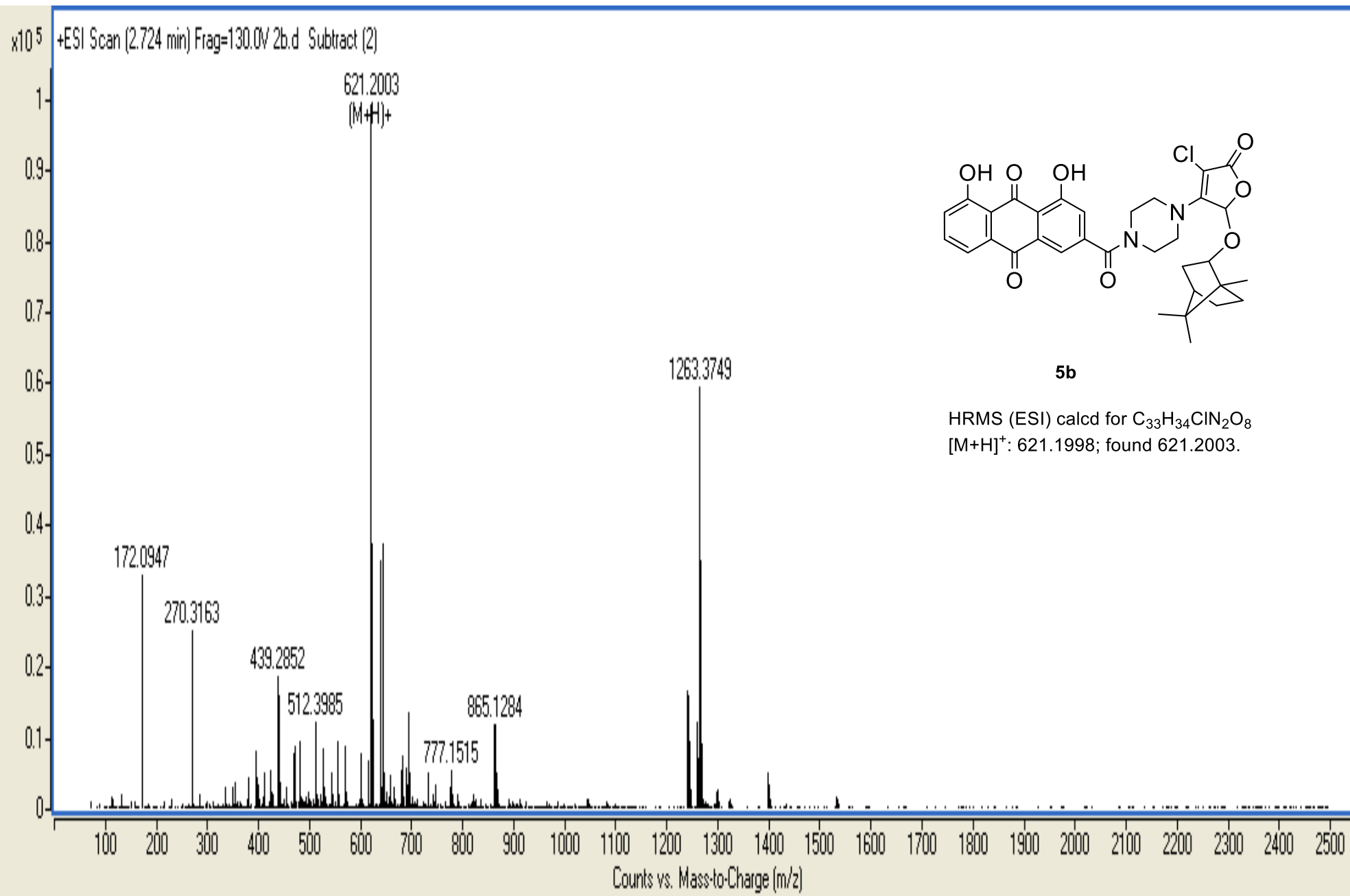
— 192.37
 — 180.76
 { 167.70
 { 167.54
 { 162.68
 { 162.57
 — 154.37
 — 143.31
 / 137.77
 / 134.11
 / 133.13
 / 125.11
 / 122.55
 / 120.37
 / 117.80
 / 116.49
 / 115.52
 — 98.41
 { 88.54
 { 87.85
 { 77.48
 { 77.16
 { 76.84
 / 49.42
 / 47.58
 / 47.32
 / 44.81
 / 42.11
 / 37.27
 / 28.01
 / 26.64
 / 19.61
 / 18.80
 / 14.27



5b



¹³C NMR (101 MHz, CDCl₃) spectrum of **5b**



HRMS spectrum of **5b**

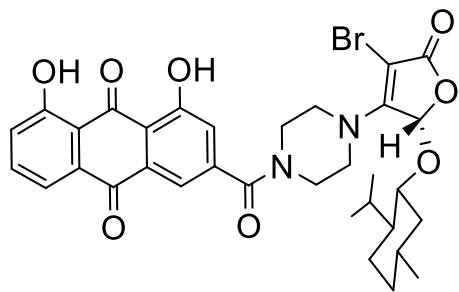
zss-325-H

12.035
11.873

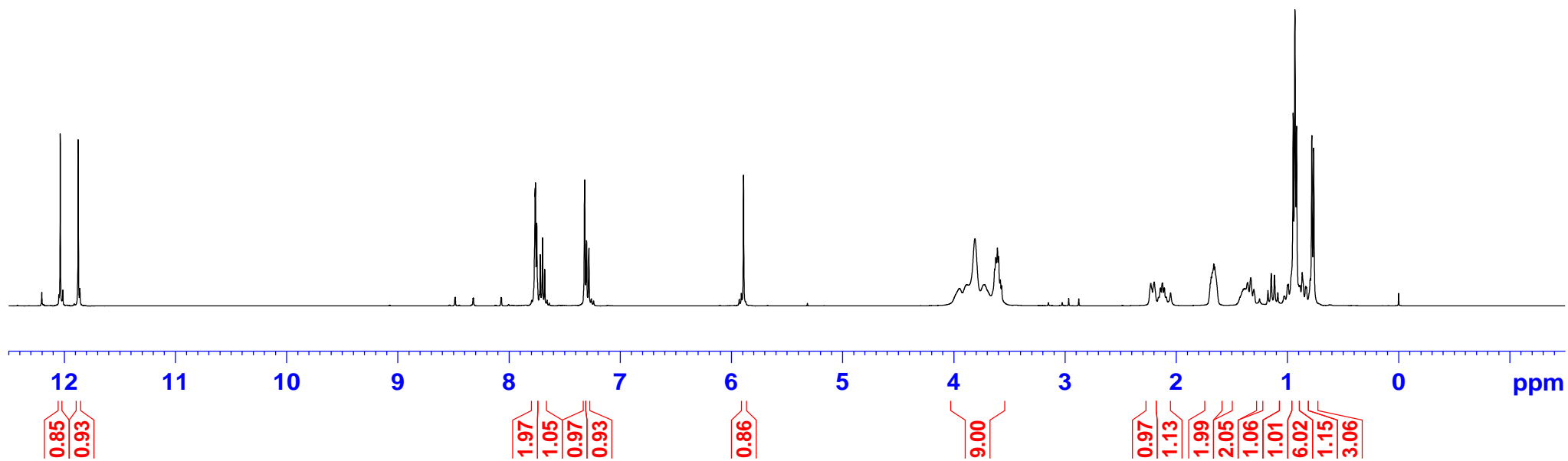
7.766
7.763
7.751
7.719
7.699
7.680
7.322
7.319
7.304
7.302
7.284
7.282

5.892

3.883
3.810
3.722
3.633
3.623
3.608
3.597
3.582
3.571
2.229
2.198
2.140
2.123
2.106
1.685
1.676
1.662
1.652
1.357
1.329
1.144
1.116
0.999
0.991
0.948
0.932
0.917
0.890
0.885
0.866
0.835
0.828
0.795
0.780
0.763



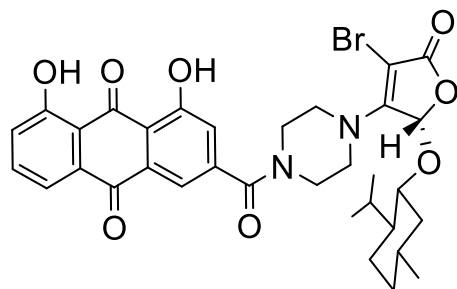
5c



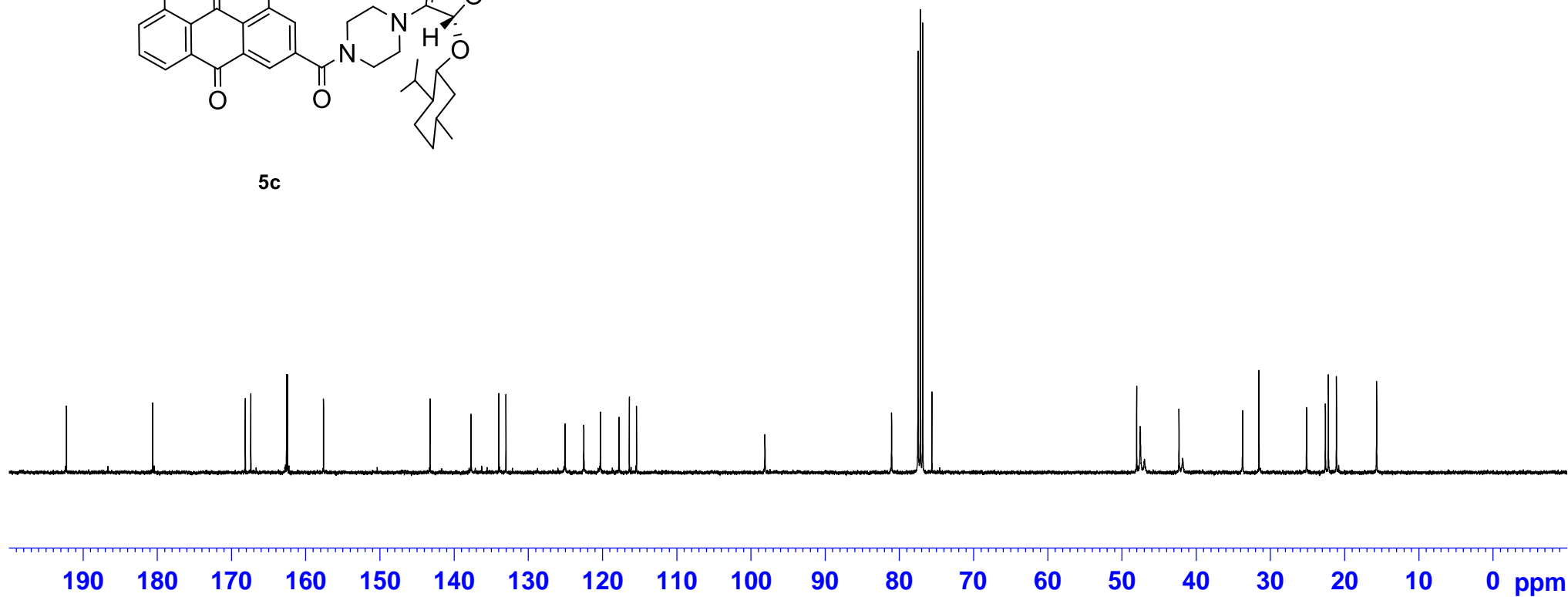
¹H NMR (400 MHz, CDCl₃) spectrum of 5c

zss-325-C

192.23
180.61
168.12
167.38
162.58
162.45
157.59
143.23
137.71
133.96
133.01
125.03
122.51
120.27
117.76
116.37
115.41
98.12
81.03
77.48
77.16
76.84
75.60
48.01
47.52
42.31
41.80
33.77
31.56
25.15
22.61
22.21
21.12
15.71

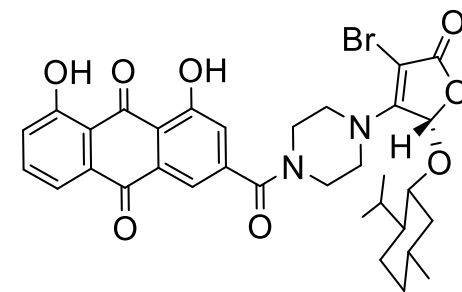
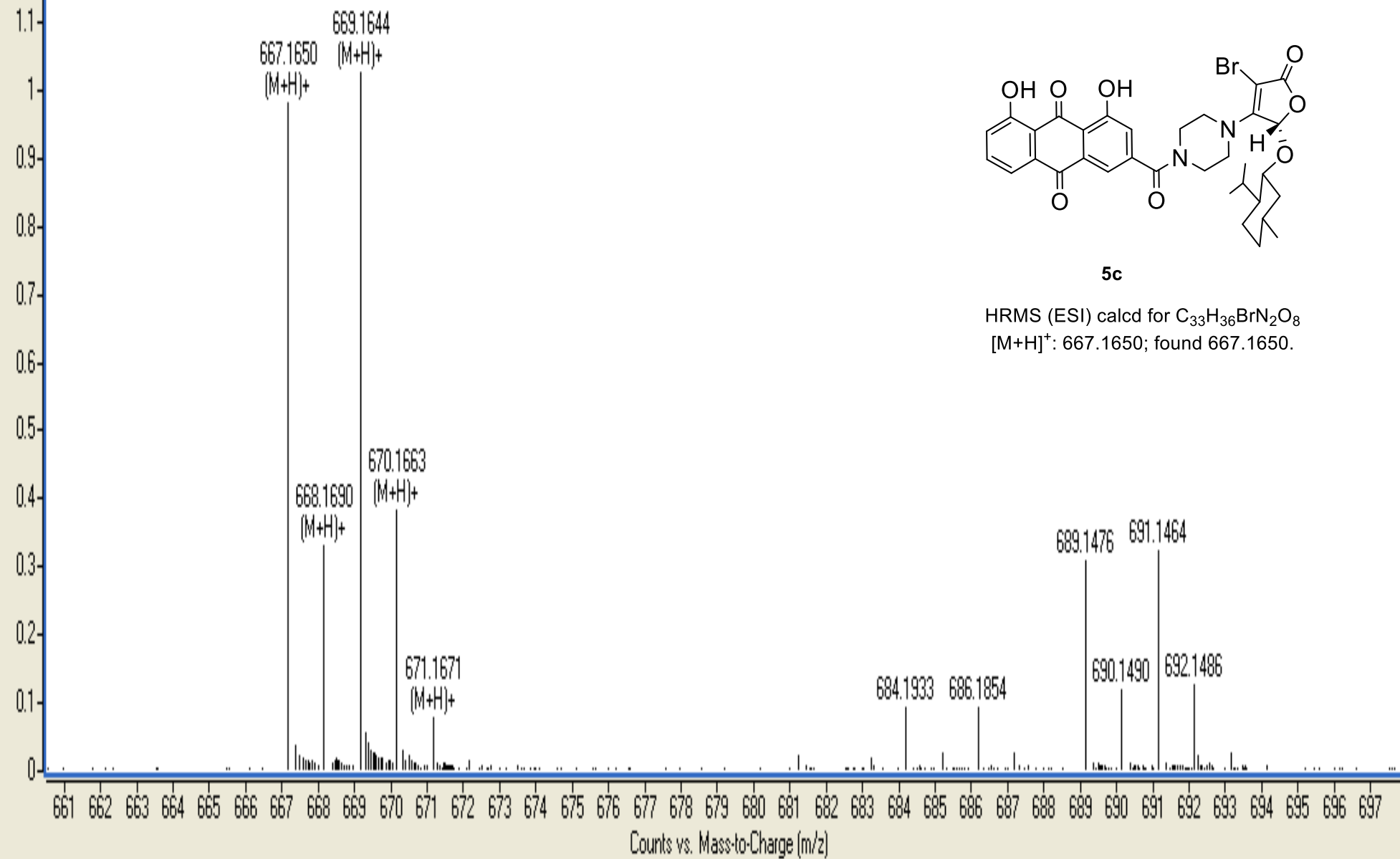


5c



^{13}C NMR (101 MHz, CDCl_3) spectrum of 5c

x10⁵ +ESI Scan (2.885 min) Frag=130.0V 2c.d Subtract (2)



5c

HRMS (ESI) calcd for C₃₃H₃₆BrN₂O₈
[M+H]⁺: 667.1650; found 667.1650.

HRMS spectrum of **5c**

zss-322-H

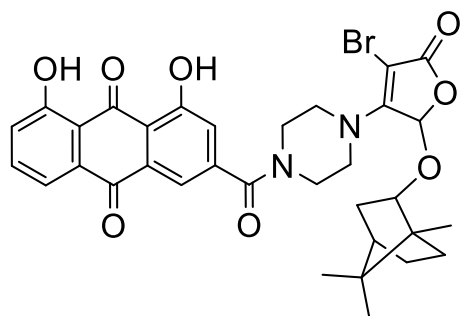
12.100
11.931

7.837
7.834
7.818
7.815
7.794
7.790
7.738
7.717
7.698
7.338
7.336
7.322
7.318
7.260

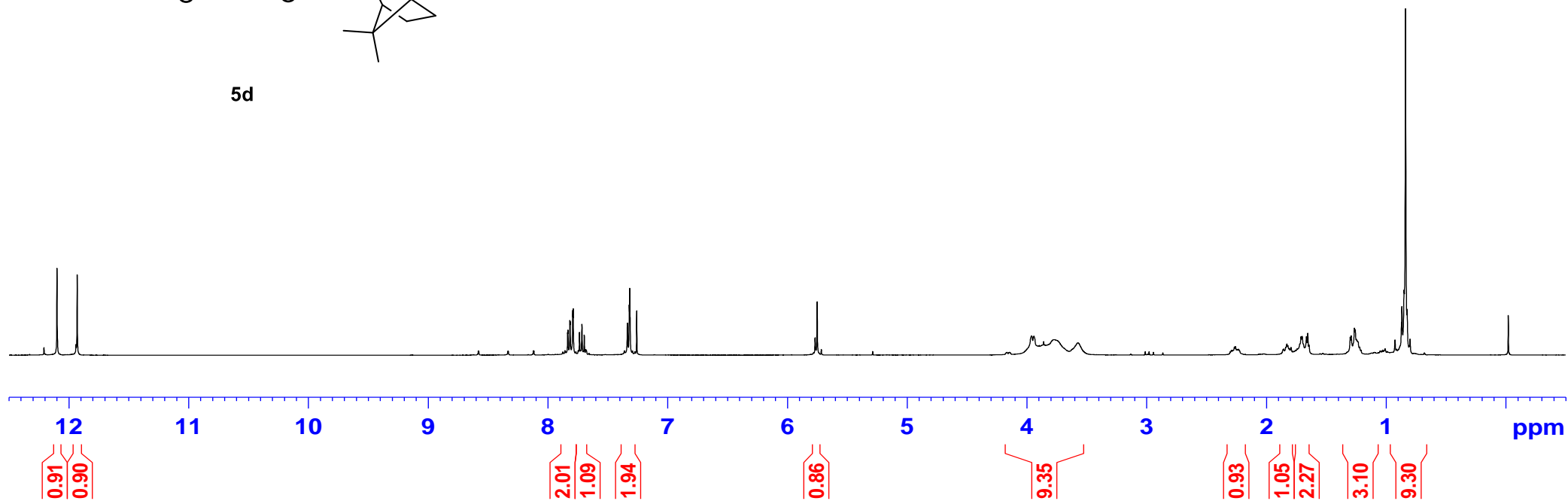
5.770
5.753

3.963
3.943
3.862
3.773
3.576

1.713
1.703
1.668
1.657
1.302
1.294
1.267
1.260
1.251
1.246
1.236
0.928
0.870
0.852
0.840
0.827
0.802

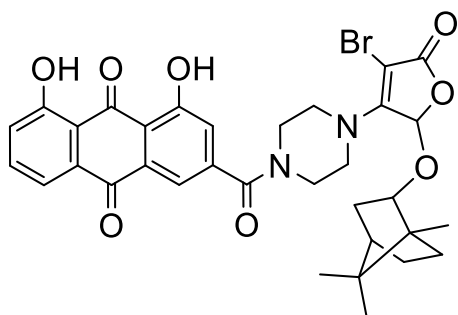


5d

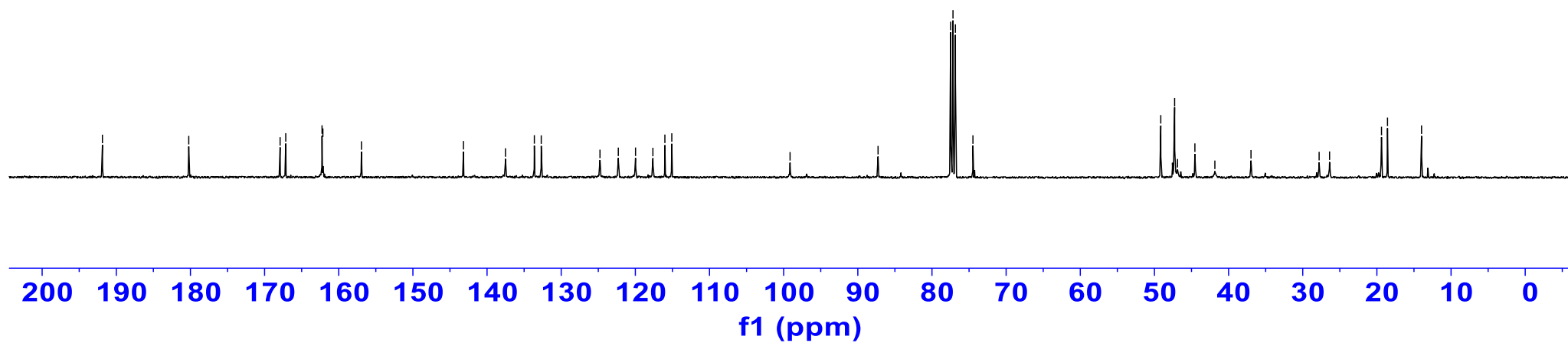


¹H NMR (400 MHz, CDCl₃) spectrum of 5d

— 191.87
 — 180.23
 { 167.91
 { 167.15
 { 162.25
 { 162.14
 { 156.94
 — 143.18
 { 137.52
 { 133.62
 — 132.69
 { 124.77
 { 122.30
 { 119.98
 { 117.63
 { 116.02
 { 115.09
 — 99.14
 — 87.27
 { 77.48
 { 77.16
 { 76.84
 { 74.48
 { 49.14
 { 47.28
 { 46.89
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 { 41.85
 { 36.98
 { 27.79
 { 26.38
 { 19.38
 { 18.57
 { 13.98

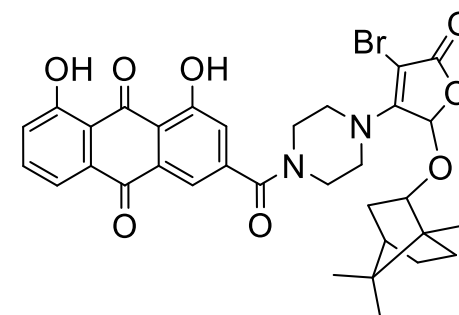
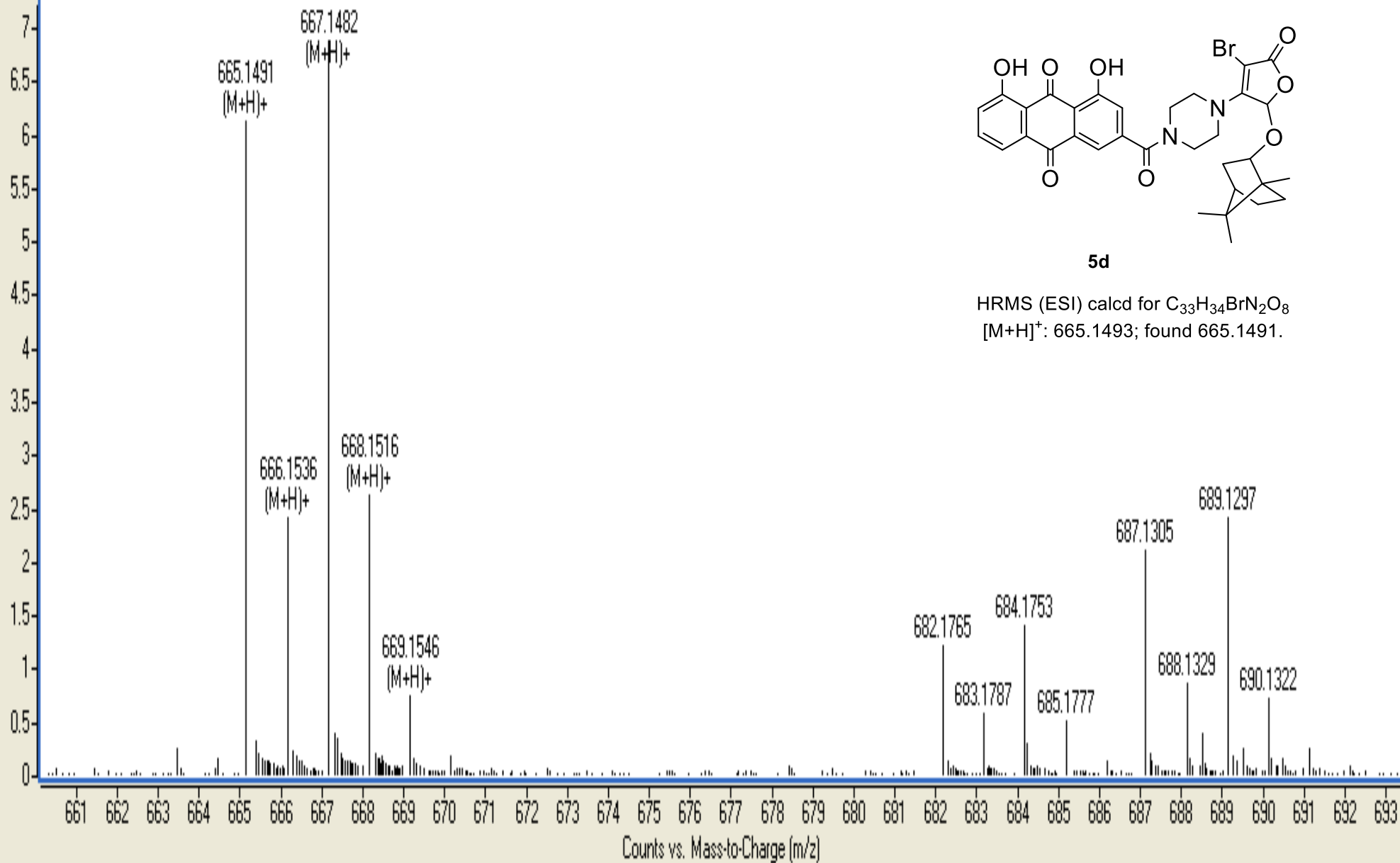


5d



¹³C NMR (101 MHz, CDCl₃) spectrum of **5d**

x10⁴ +ESI Scan (2.744 min) Frag=130.0V 2d.d Subtract (3)

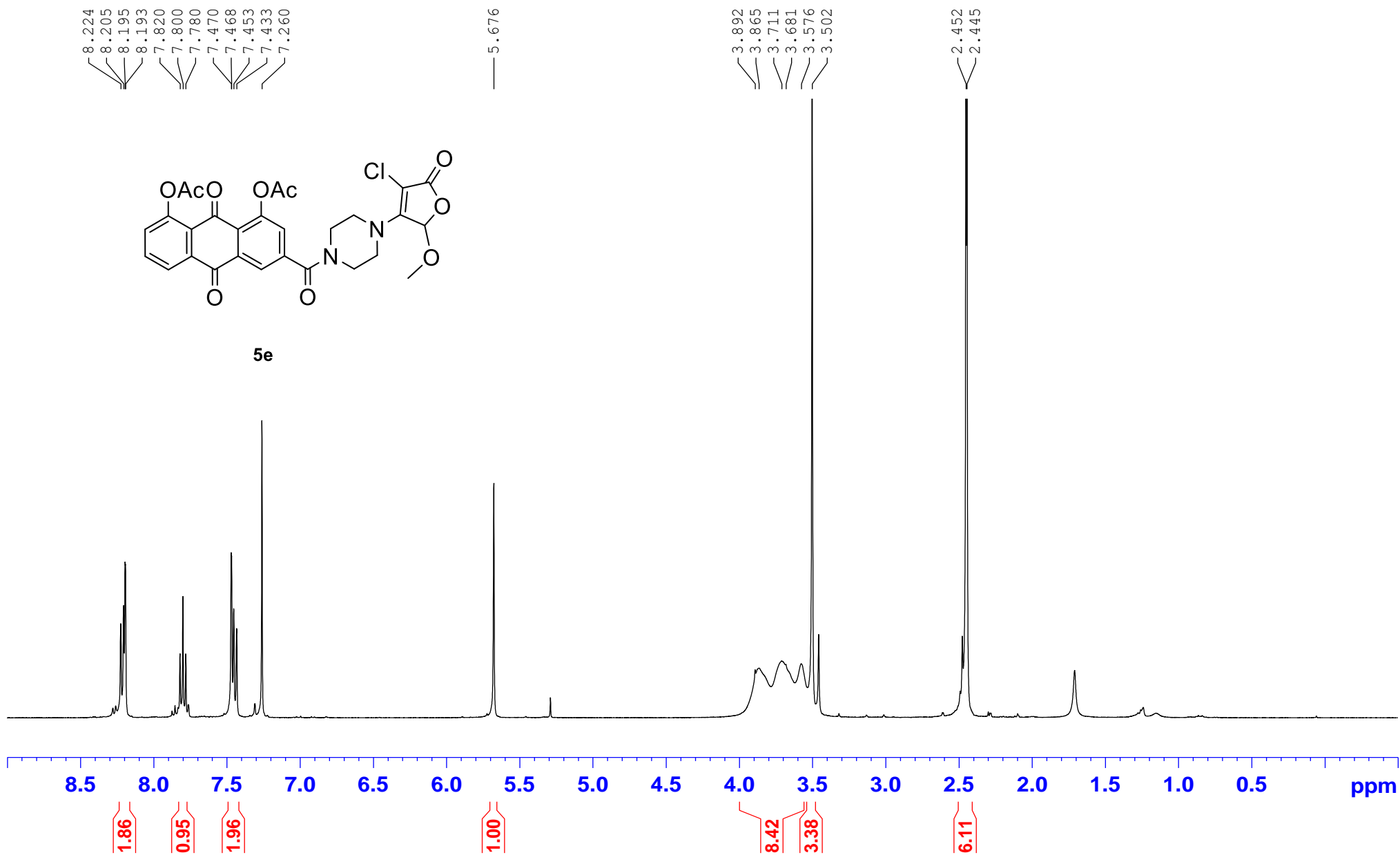


5d

HRMS (ESI) calcd for C₃₃H₃₄BrN₂O₈
[M+H]⁺: 665.1493; found 665.1491.

HRMS spectrum of **5d**

zss-318-H



¹H NMR (400 MHz, CDCl₃) spectrum of **5e**

zss-318-C

181.29
180.22

169.52
169.36
167.63
167.18

153.63
150.61
150.26

140.71
135.22
134.79
134.22
130.82
129.06
126.57
125.75
125.57
123.66

97.59

88.66

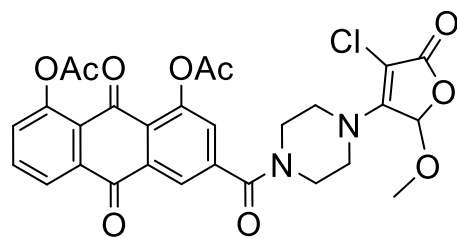
77.48
77.16
76.84

55.45

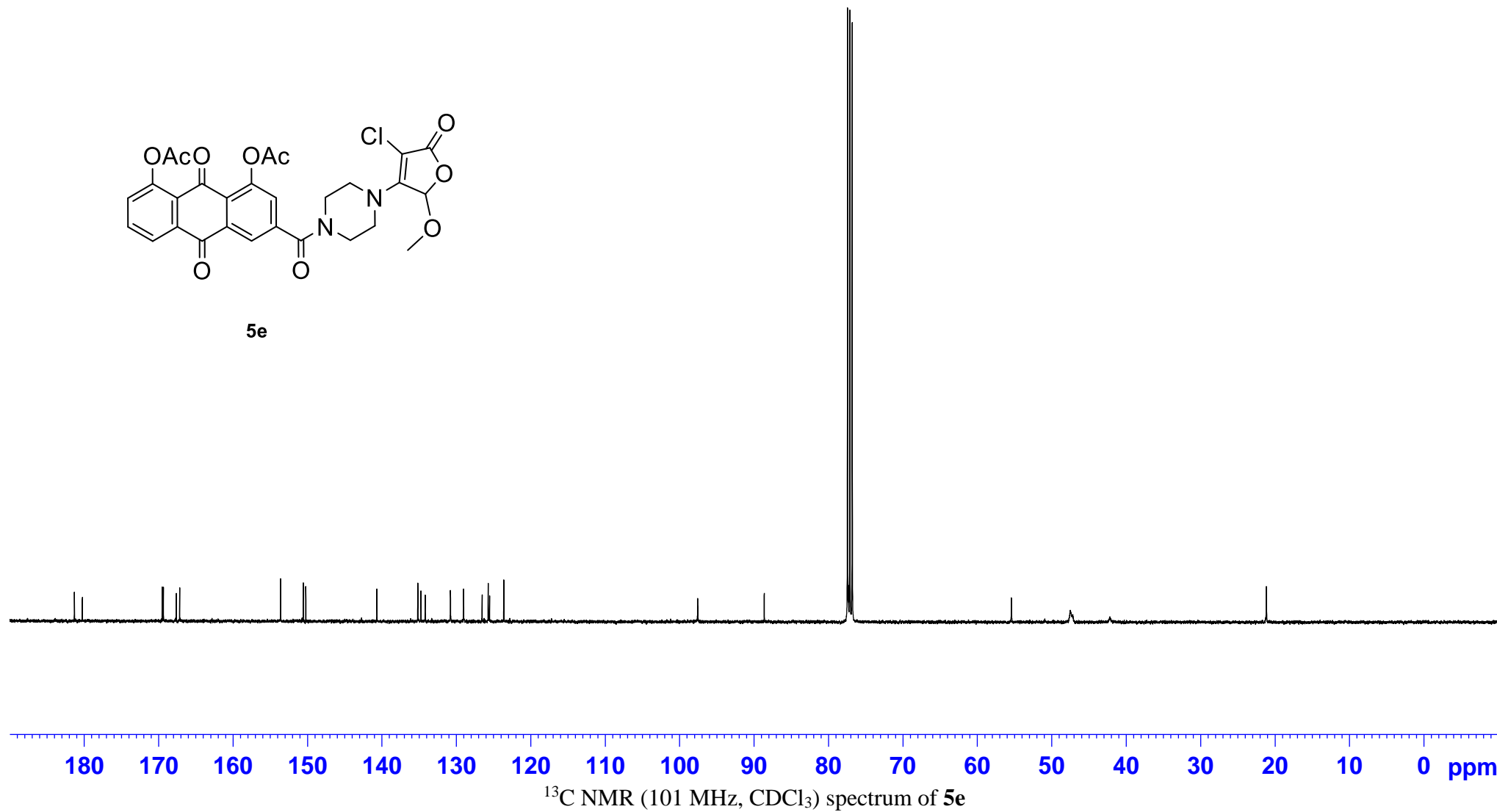
47.54

42.24

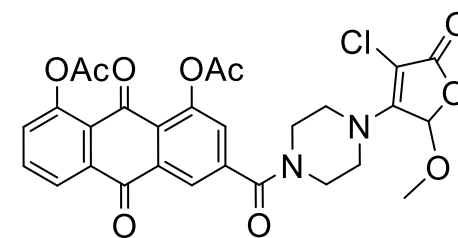
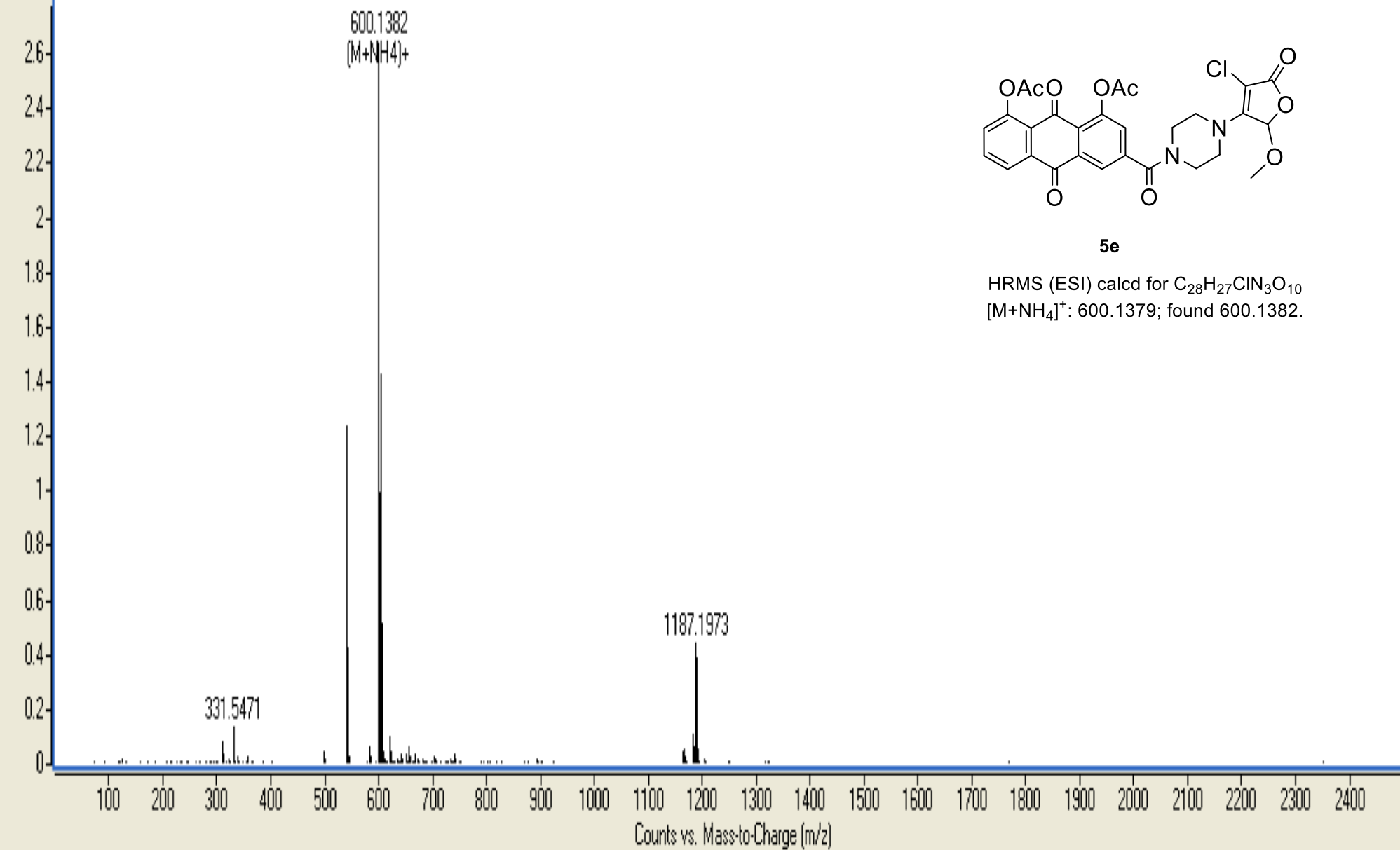
21.19



5e



x10⁵ +ESI Scan (0.765 min) Frag=130.0V 2e.d Subtract



5e

HRMS (ESI) calcd for C₂₈H₂₇ClN₃O₁₀
[M+NH₄]⁺: 600.1379; found 600.1382.

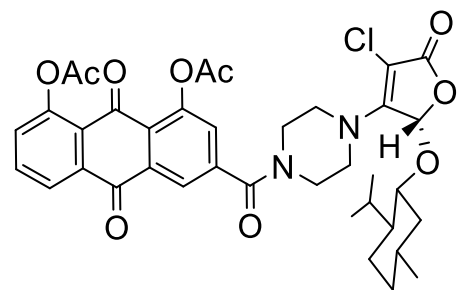
HRMS spectrum of **5e**

zss-313-H

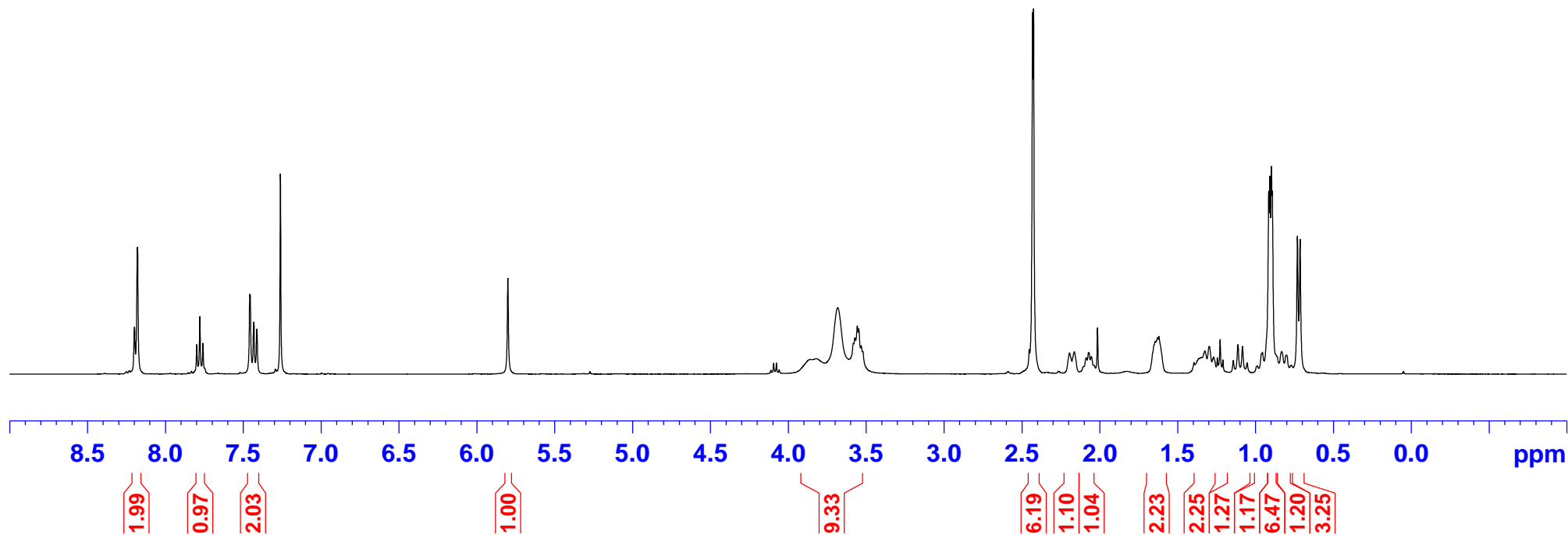
8.197
8.178
7.797
7.777
7.758
7.457
7.454
7.431
7.412
7.260

5.800

3.819
3.682
3.582
3.571
3.556
3.546
3.530
3.520
2.452
2.431
2.424
2.193
2.162
2.086
2.070
2.054
2.014
1.644
1.628
1.620
1.324
1.296
1.268
1.244
1.226
1.208
1.142
1.111
1.083
0.954
0.914
0.906
0.897
0.891
0.831
0.803
0.730
0.713



5f



¹H NMR (400 MHz, CDCl₃) spectrum of 5f

zss-313-C

181.17
180.16
169.41
169.20
167.74
167.01
154.87
150.52
150.19
140.61
135.14
134.72
134.17
130.73
129.01
126.51
125.66
125.50
123.64

97.16

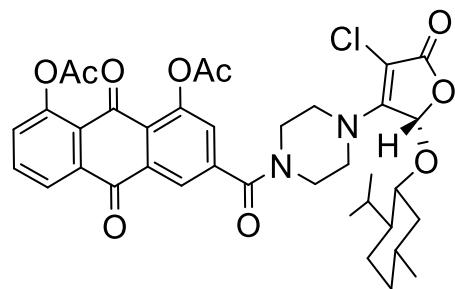
89.29

81.22
77.48
77.16
76.84

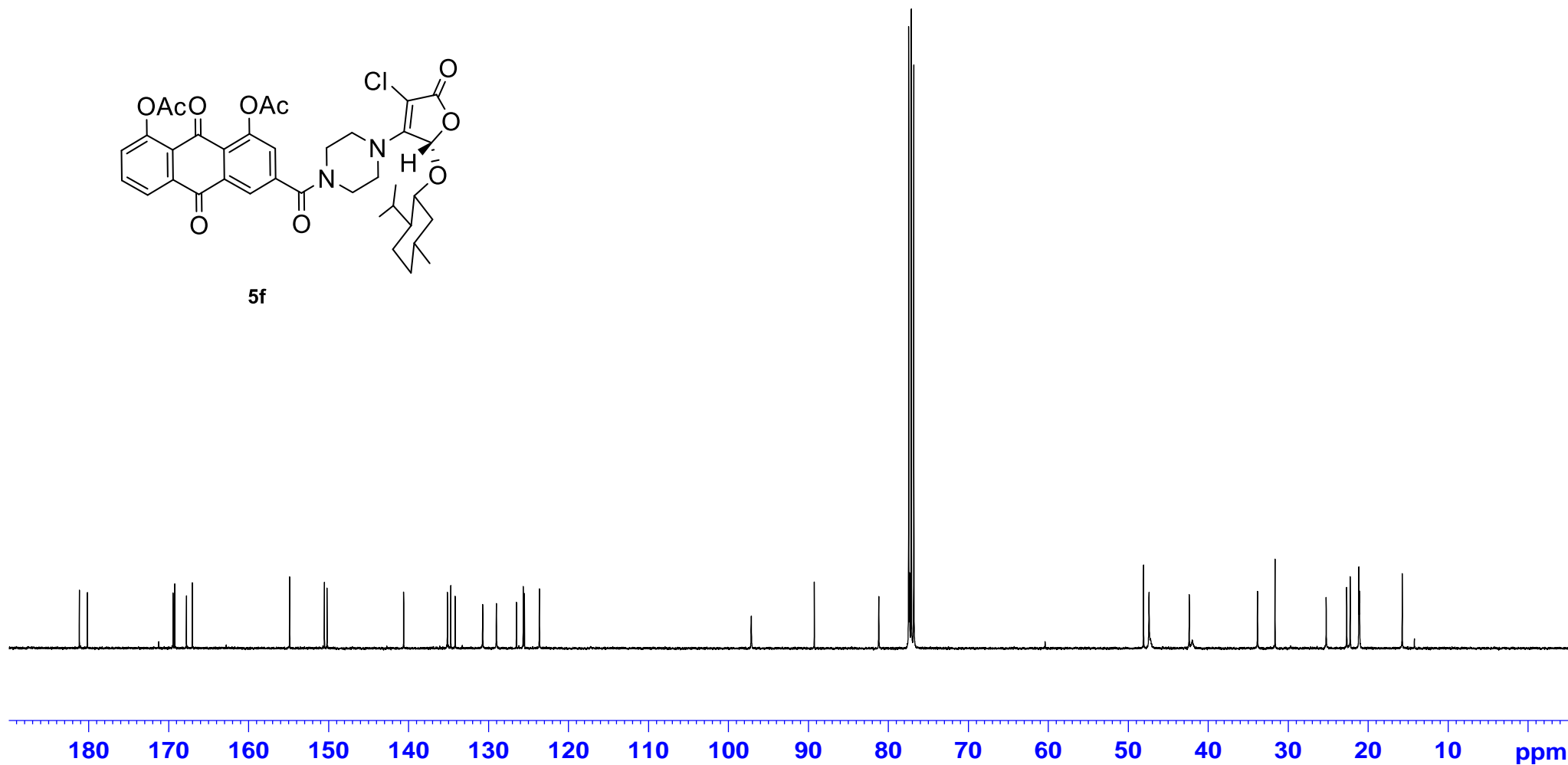
48.11
47.42
42.40
42.02

33.87
31.67

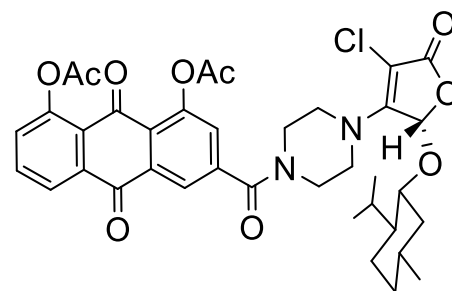
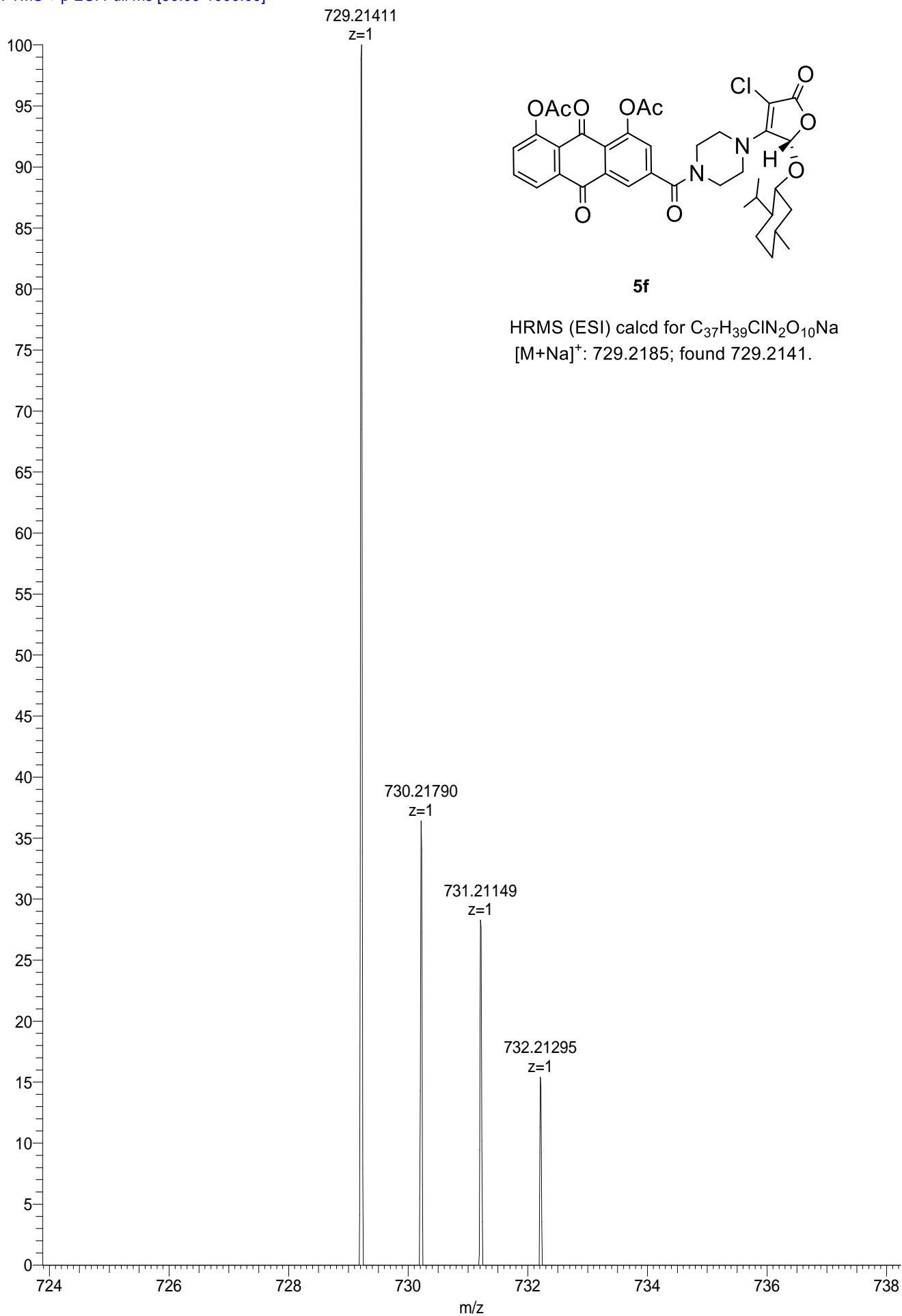
25.27
22.70
22.27
21.19
21.12
15.77



5f



¹³C NMR (101 MHz, CDCl₃) spectrum of 5f



5f

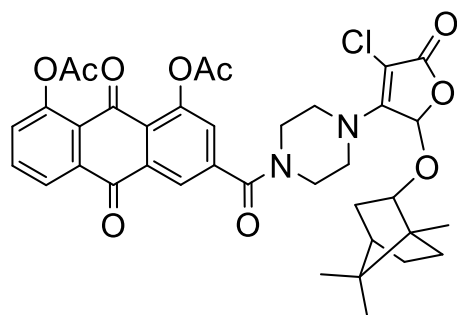
HRMS (ESI) calcd for C₃₇H₃₉ClN₂O₁₀Na
[M+Na]⁺: 729.2185; found 729.2141.

HRMS spectrum of **5f**

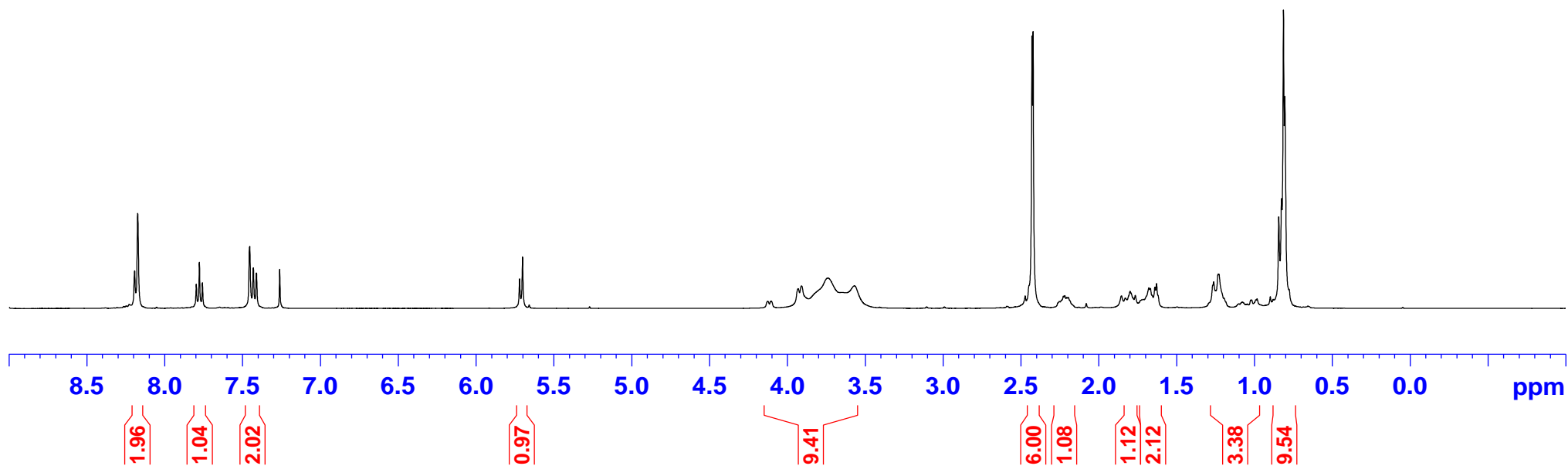
8.192
8.173
7.796
7.776
7.756
7.453
7.430
7.410
7.260

5.720
5.701

4.126
4.104
3.930
3.909
3.739
3.568
2.472
2.428
2.421
2.251
2.226
2.218
2.204
2.195
1.854
1.829
1.799
1.765
1.714
1.678
1.668
1.639
1.628
1.261
1.234
1.227
1.077
1.024
1.017
0.991
0.983
0.898
0.879
0.843
0.825
0.813
0.804
0.777



5g



¹H NMR (400 MHz, CDCl₃) spectrum of 5g

181.15
180.15
169.41
169.21
167.77
167.03
154.36
150.47
150.14
140.66
135.12
134.68
134.12
130.70
128.97
126.43
125.62
125.45
123.60

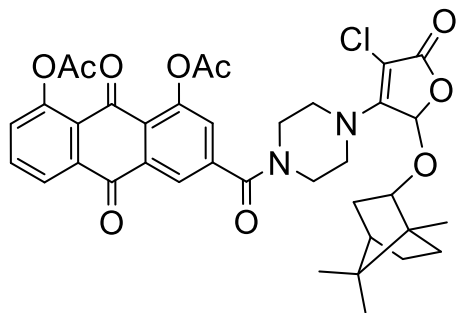
98.39

88.44
87.83

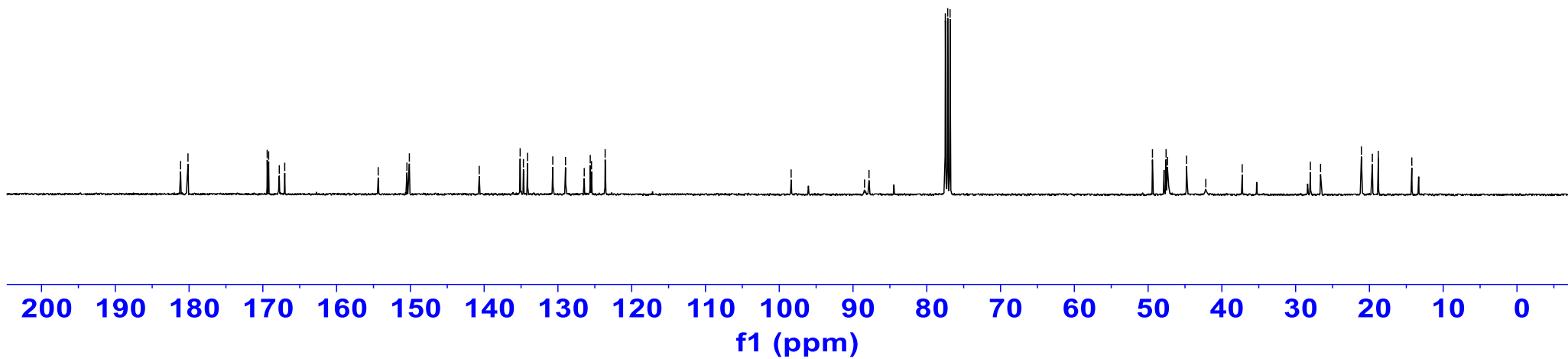
77.49
77.16
76.84

49.41
47.56
47.36
44.80
42.18
37.24

28.00
26.62
21.09
19.60
18.79
14.26

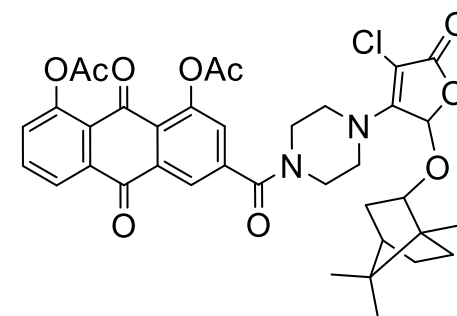


5g



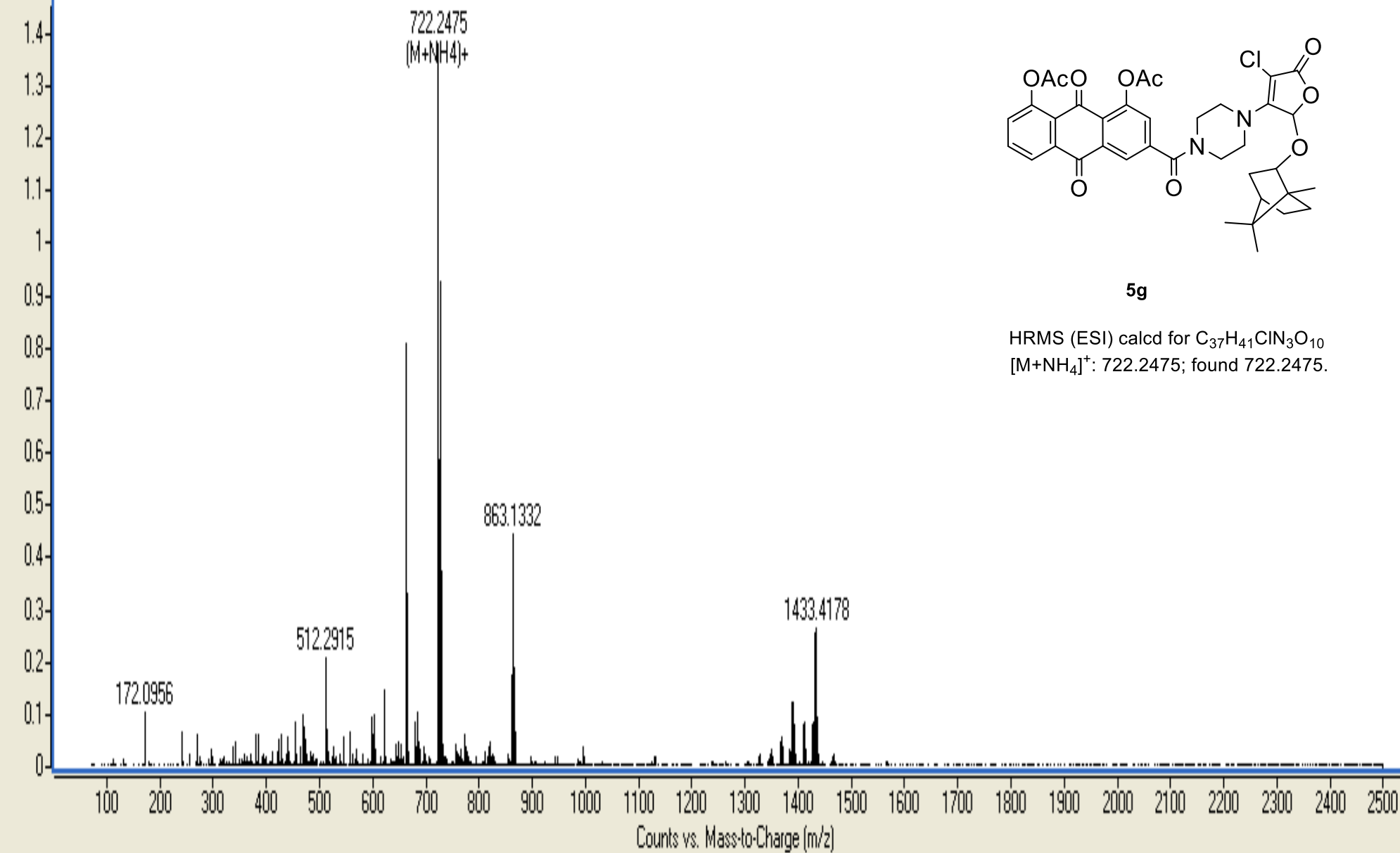
¹³C NMR (101 MHz, CDCl₃) spectrum of 5g

x10⁵ +ESI Scan (2.678 min) Frag=130.0V 2g.d Subtract (2)



5g

HRMS (ESI) calcd for C₃₇H₄₁ClN₃O₁₀
[M+NH₄]⁺: 722.2475; found 722.2475.



HRMS spectrum of **5g**

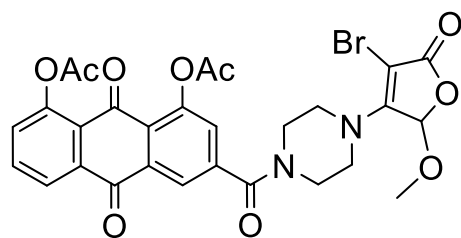
zss-319-H

8.188
8.163
7.798
7.778
7.758
7.446
7.429
7.410
7.260

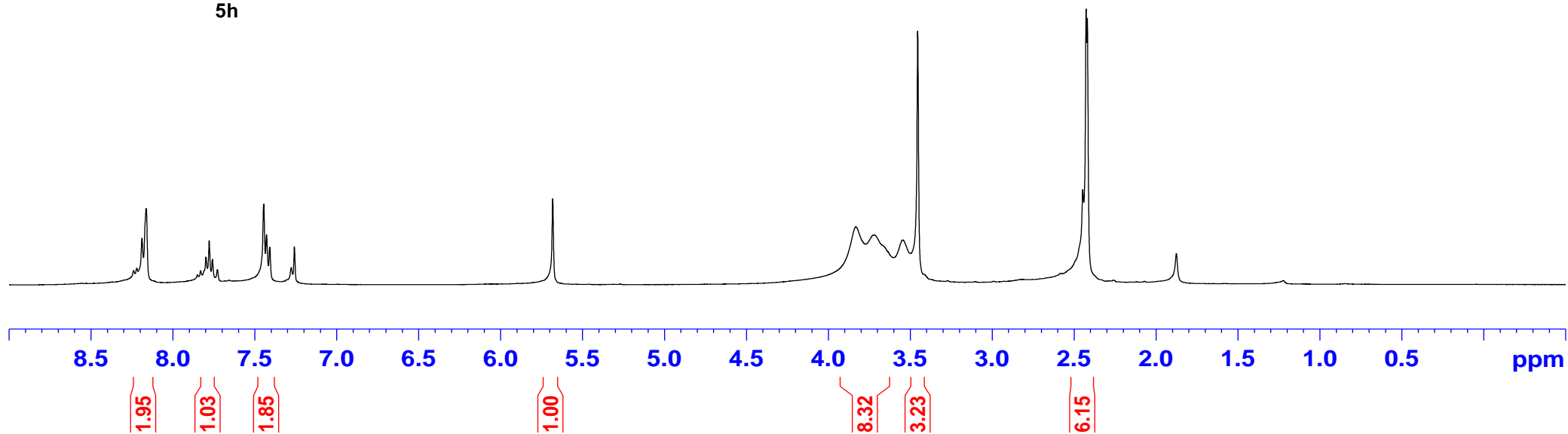
5.683

3.833
3.722
3.546
3.456

2.449
2.428
2.420



5h



¹H NMR (400 MHz, CDCl₃) spectrum of **5h**

zss-319-C

181.18
180.15
169.45
169.28
168.06
167.04
156.34
150.46
150.14
140.73
135.15
134.67
134.12
130.73
128.95
126.41
125.63
125.44
123.61

98.49

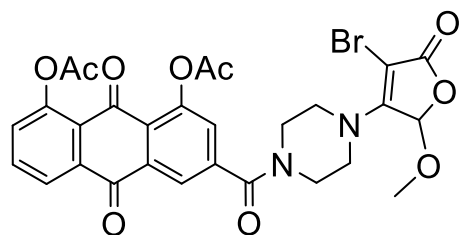
77.48
77.16
76.84
74.65

55.20

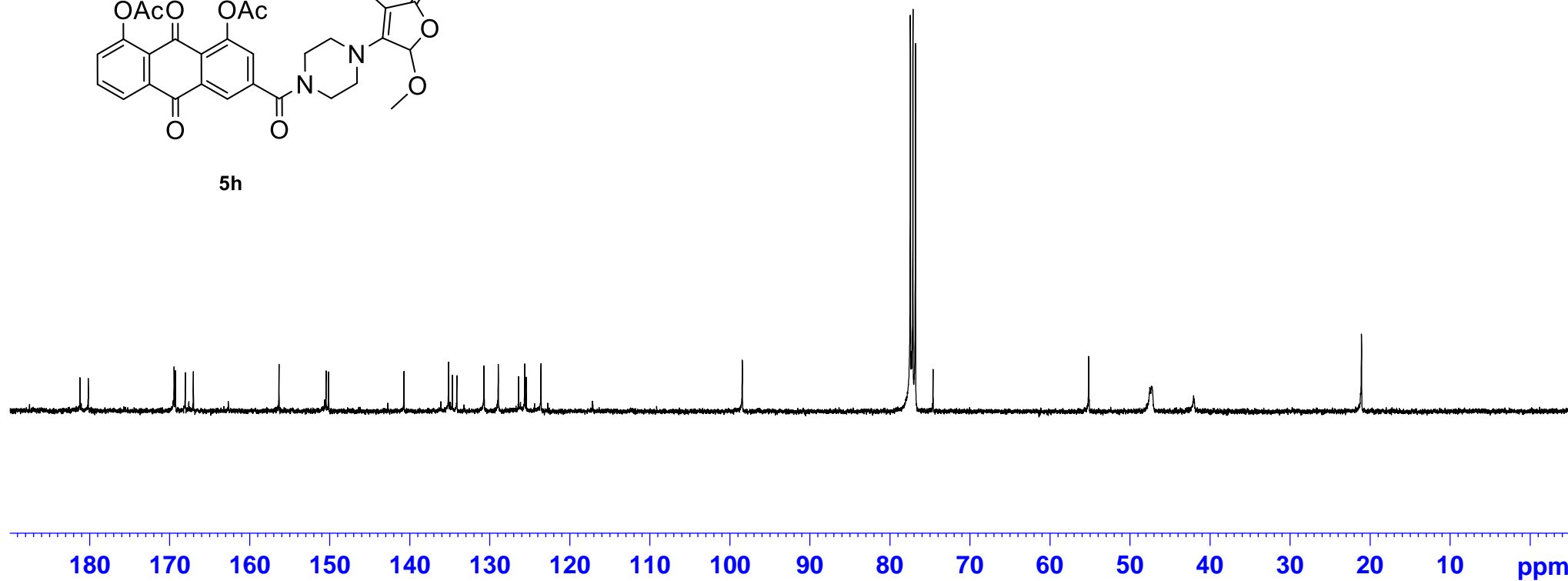
47.56

42.09

21.11

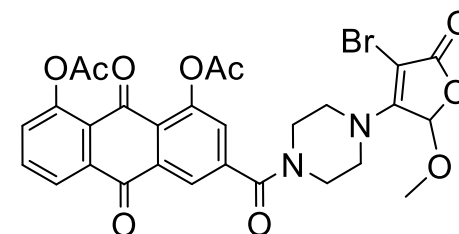
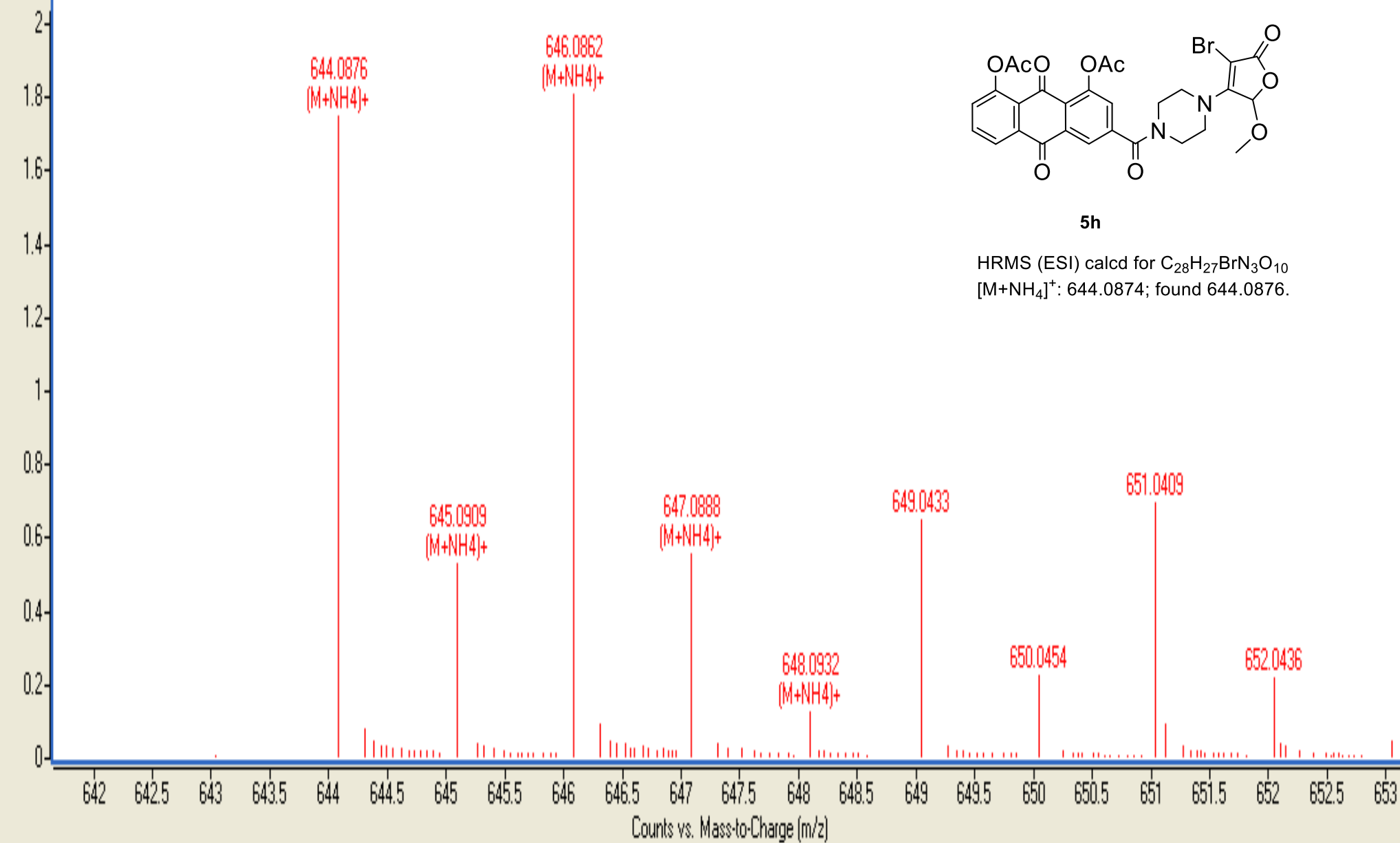


5h



¹³C NMR (101 MHz, CDCl₃) spectrum of 5h

x10⁵ +ESI Scan (2.138 min) Frag=130.0V 2h.d Subtract



5h

HRMS (ESI) calcd for C₂₈H₂₇BrN₃O₁₀
[M+NH₄]⁺: 644.0874; found 644.0876.

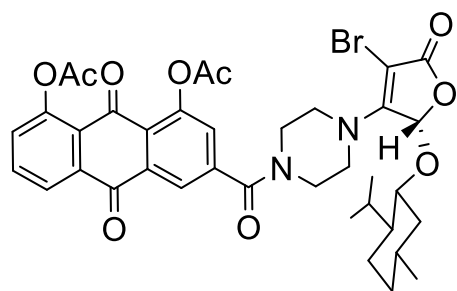
HRMS spectrum of **5h**

zss-315-H

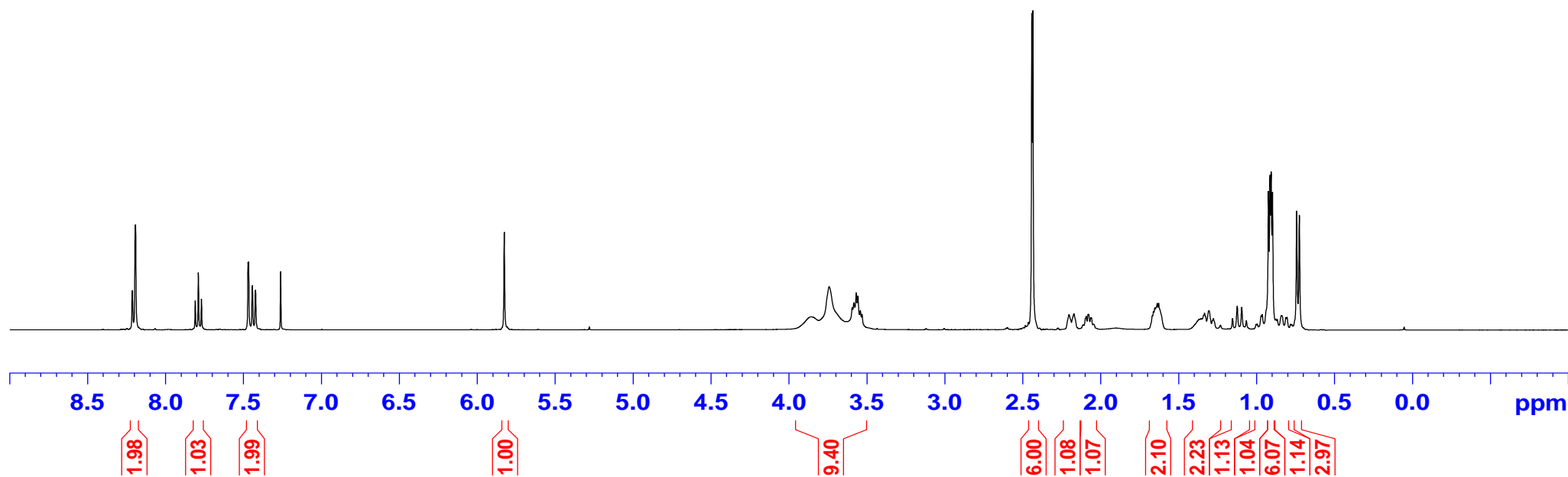
8.211
8.193
8.191
7.808
7.788
7.769
7.469
7.466
7.441
7.421
7.260

5.826

3.856
3.741
3.594
3.583
3.567
3.557
3.541
3.531
2.441
2.434
2.202
2.171
2.092
2.080
2.076
2.062
1.669
1.661
1.652
1.637
1.628
1.363
1.355
1.333
1.306
1.277
1.154
1.123
1.095
0.970
0.963
0.923
0.913
0.906
0.897
0.875
0.838
0.811
0.804
0.742
0.725



5i



¹H NMR (400 MHz, CDCl₃) spectrum of 5i

zss-315-C

181.21
180.19
169.46
169.26
168.22
167.07
157.58
150.56
150.22
140.62
135.17
134.75
134.19
130.76
129.05
126.56
125.71
125.53
123.66

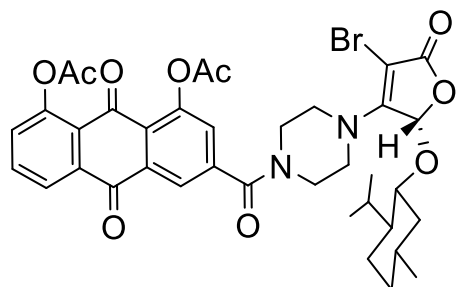
98.16

81.16
77.48
77.16
76.84
75.99

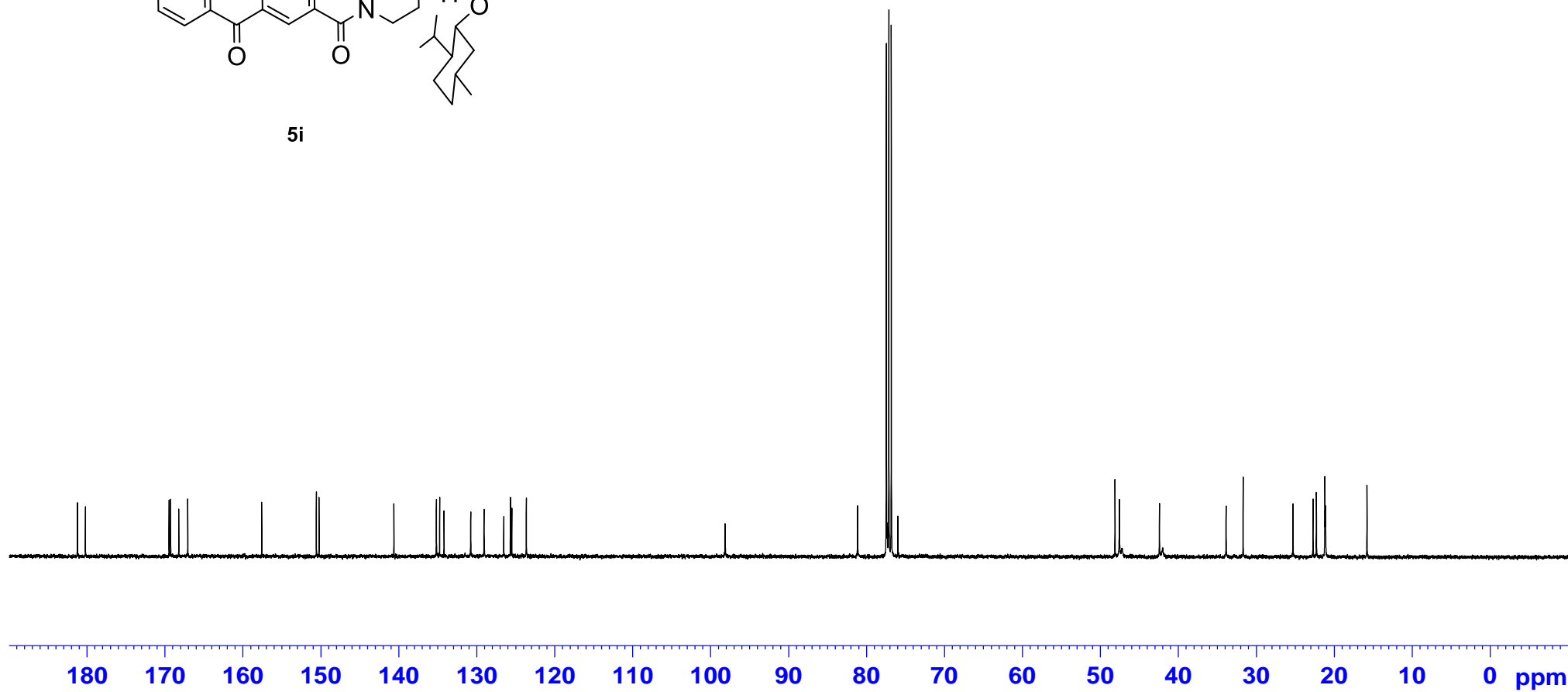
48.15
47.59
42.44
42.03

33.89
31.71

25.31
22.74
22.30
21.22
21.14
15.82

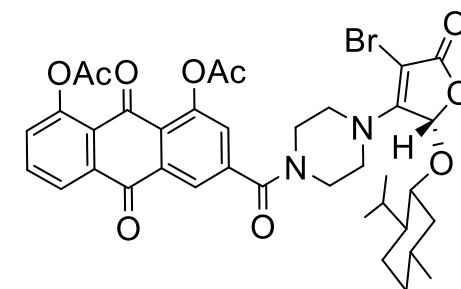


5i



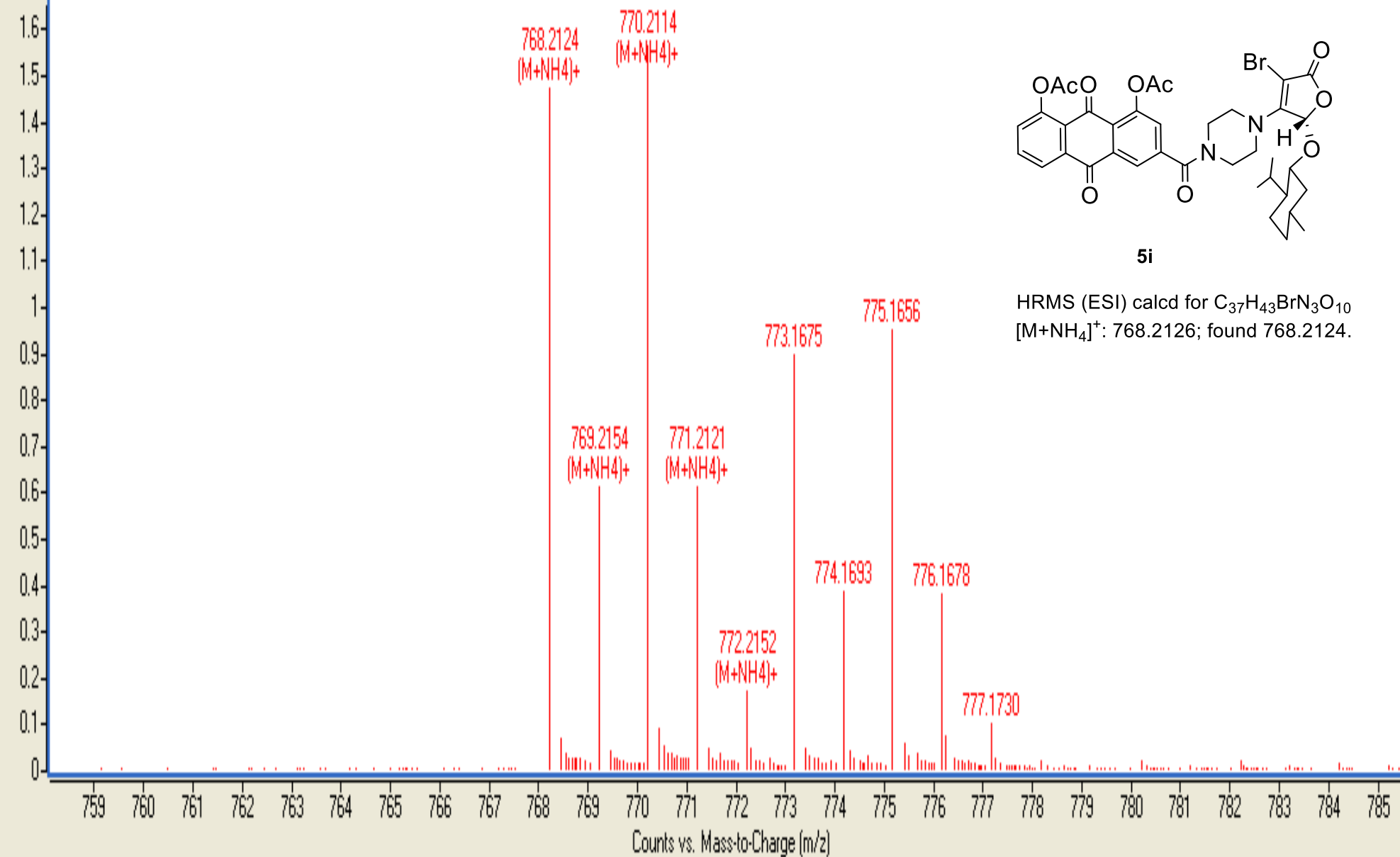
^{13}C NMR (101 MHz, CDCl_3) spectrum of **5i**

x10⁵ +ESI Scan (2.556 min) Frag=130.0V 21.d Subtract



5i

HRMS (ESI) calcd for C₃₇H₄₃BrN₃O₁₀
[M+NH₄]⁺: 768.2126; found 768.2124.

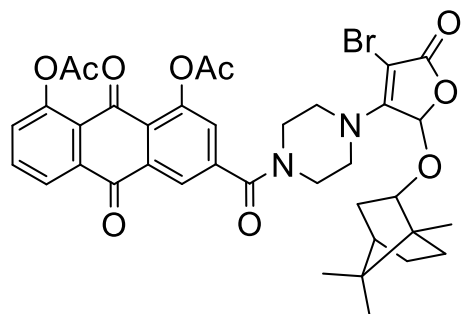


HRMS spectrum of **5i**

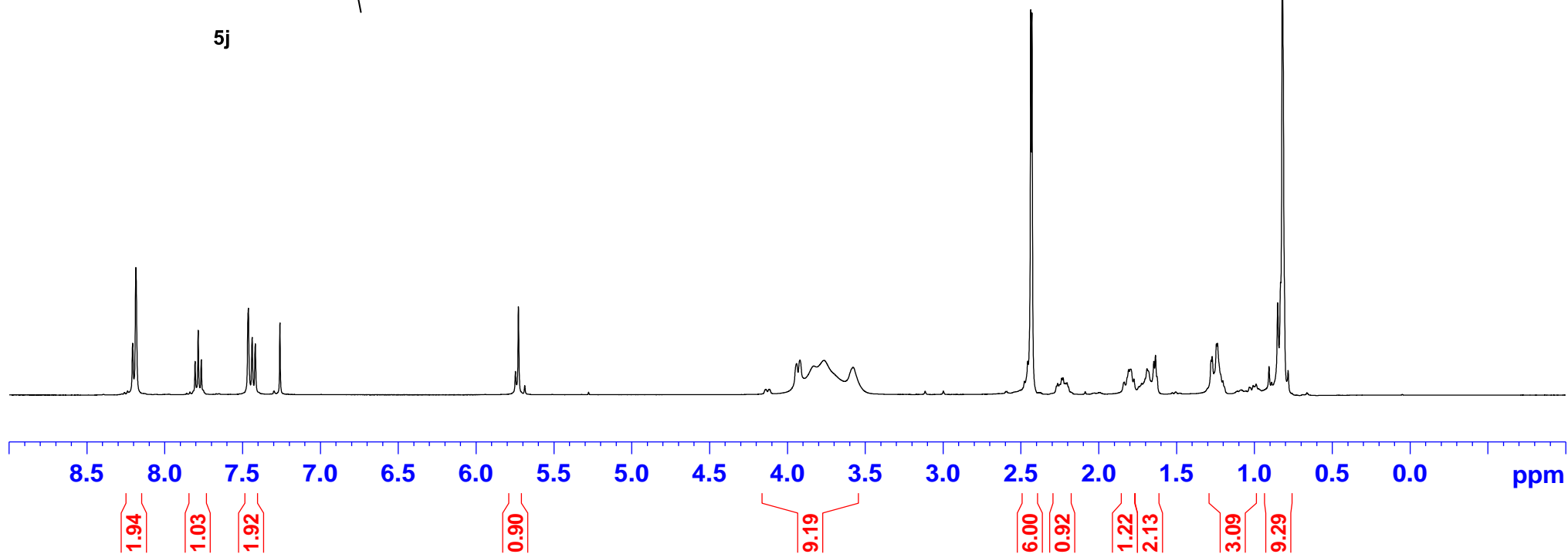
8.206
8.185
7.805
7.785
7.765
7.463
7.438
7.418
7.260

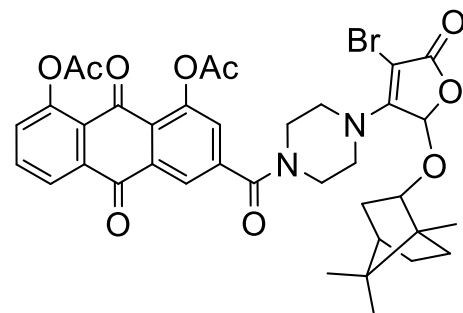
5.747
5.728

3.941
3.919
3.831
3.764
3.579
2.478
2.458
2.438
2.430
2.265
2.239
2.230
2.216
2.205
1.837
1.809
1.799
1.775
1.725
1.691
1.647
1.637
1.279
1.272
1.245
1.238
1.204
0.990
0.907
0.891
0.852
0.833
0.822
0.784



5j

 ^1H NMR (400 MHz, CDCl_3) spectrum of **5j**



5j

181.20
180.18
169.43
169.24
168.20
167.08
157.01
150.53
150.18
140.67
135.15
134.73
134.16
130.74
129.02
126.50
125.67
125.50
123.63

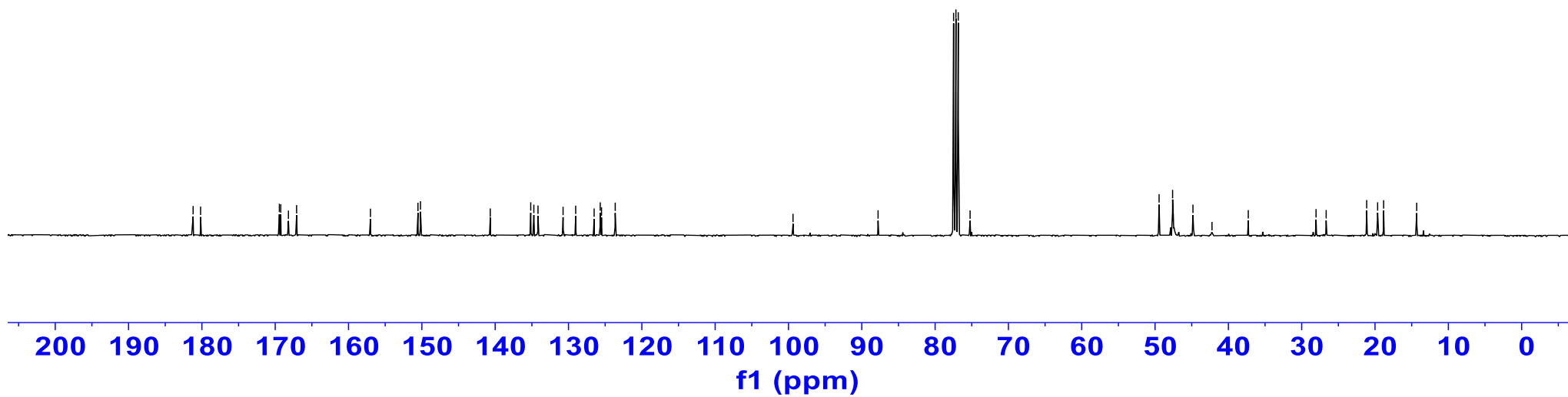
99.38

87.78

77.48
77.16
76.84
75.23

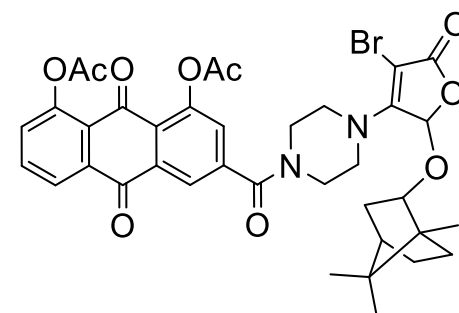
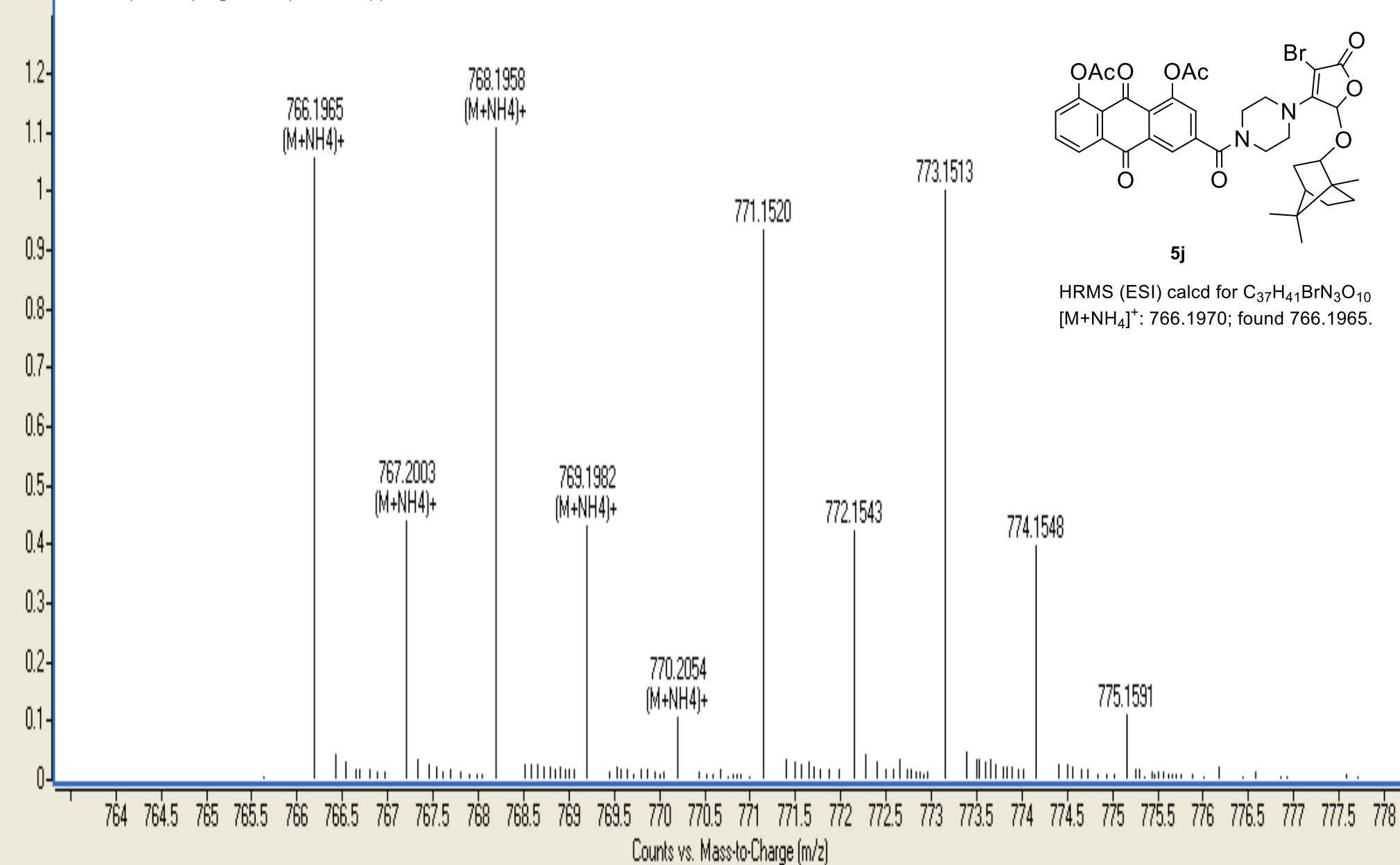
49.45
47.61
47.52
44.83
42.23
37.29

28.04
26.67
21.14
19.64
18.83
14.32



^{13}C NMR (101 MHz, CDCl_3) spectrum of 5j

x10⁵ +ESI Scan (2.765 min) Frag=130.0V 2;.d Subtract (3)



5j

HRMS (ESI) calcd for C₃₇H₄₁BrN₃O₁₀
[M+NH₄]⁺: 766.1970; found 766.1965.

HRMS spectrum of **5j**