Supporting Information for

Total Synthesis of the Fellutamides, Lipopeptide Proteasome Inhibitors. Sustainable Peptide Bond Formation

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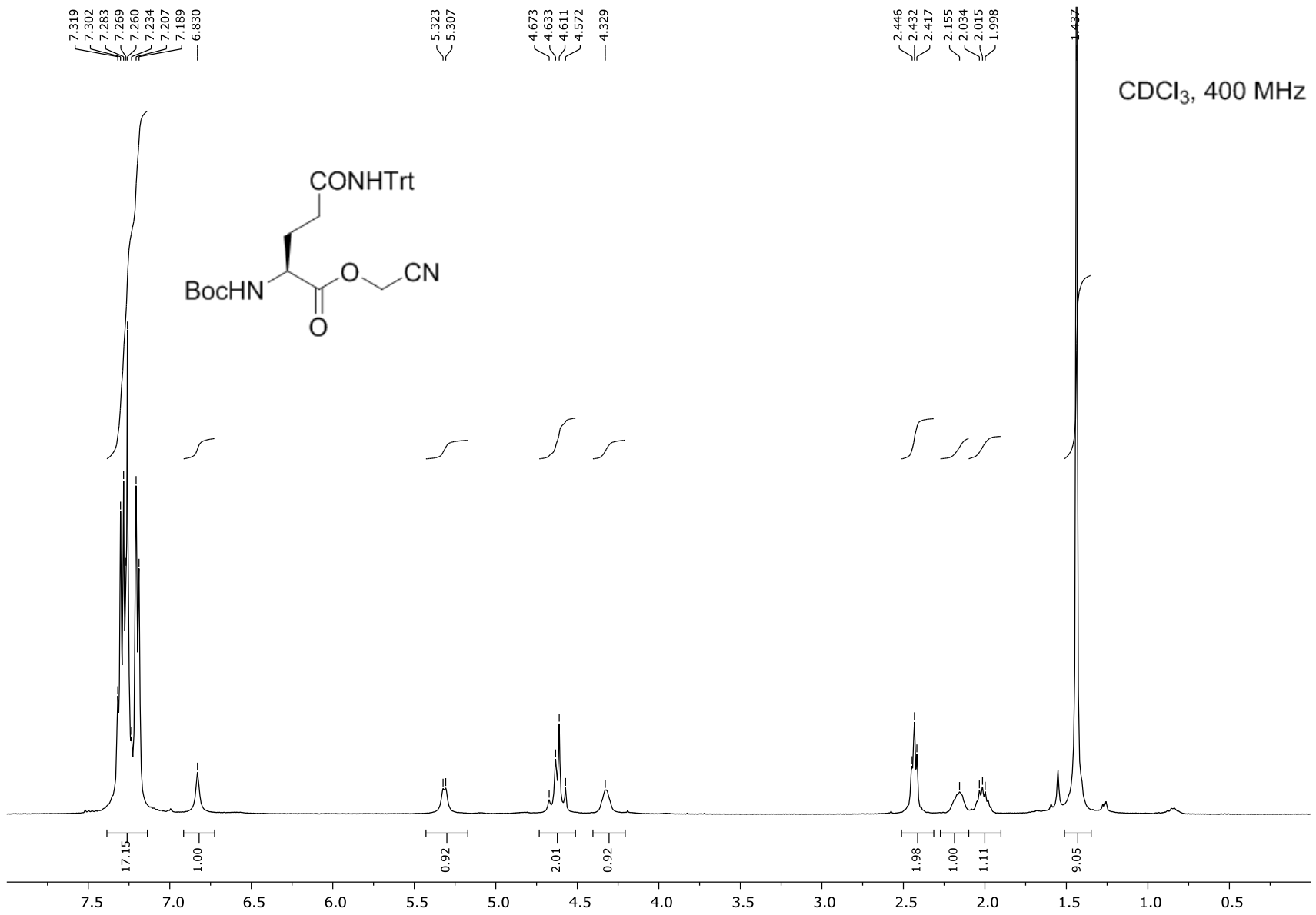
Contents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7.283
7.269
7.260
7.234
7.207
7.189
6.830
5.323
5.307
4.673
4.633
4.611
4.572
4.329
2.446
2.432
2.417
2.155
2.034
2.015
1.998
1.437
CDCl3, 400 MHz
CONHTrt
BocHN
O
CN
O
17.15
1.00
0.92
2.01
0.92
1.98
1.00
1.11
9.05
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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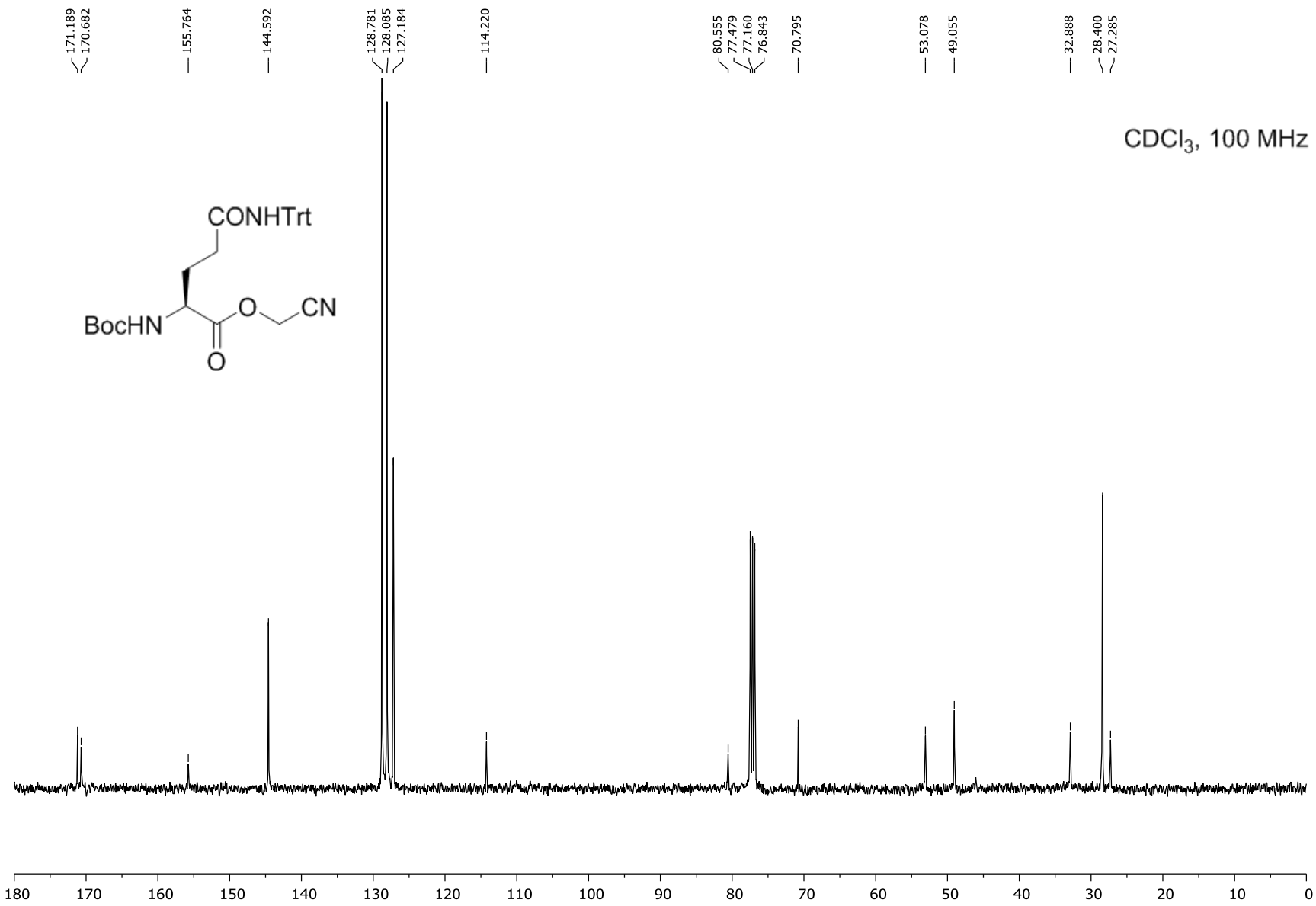
1.0
0.5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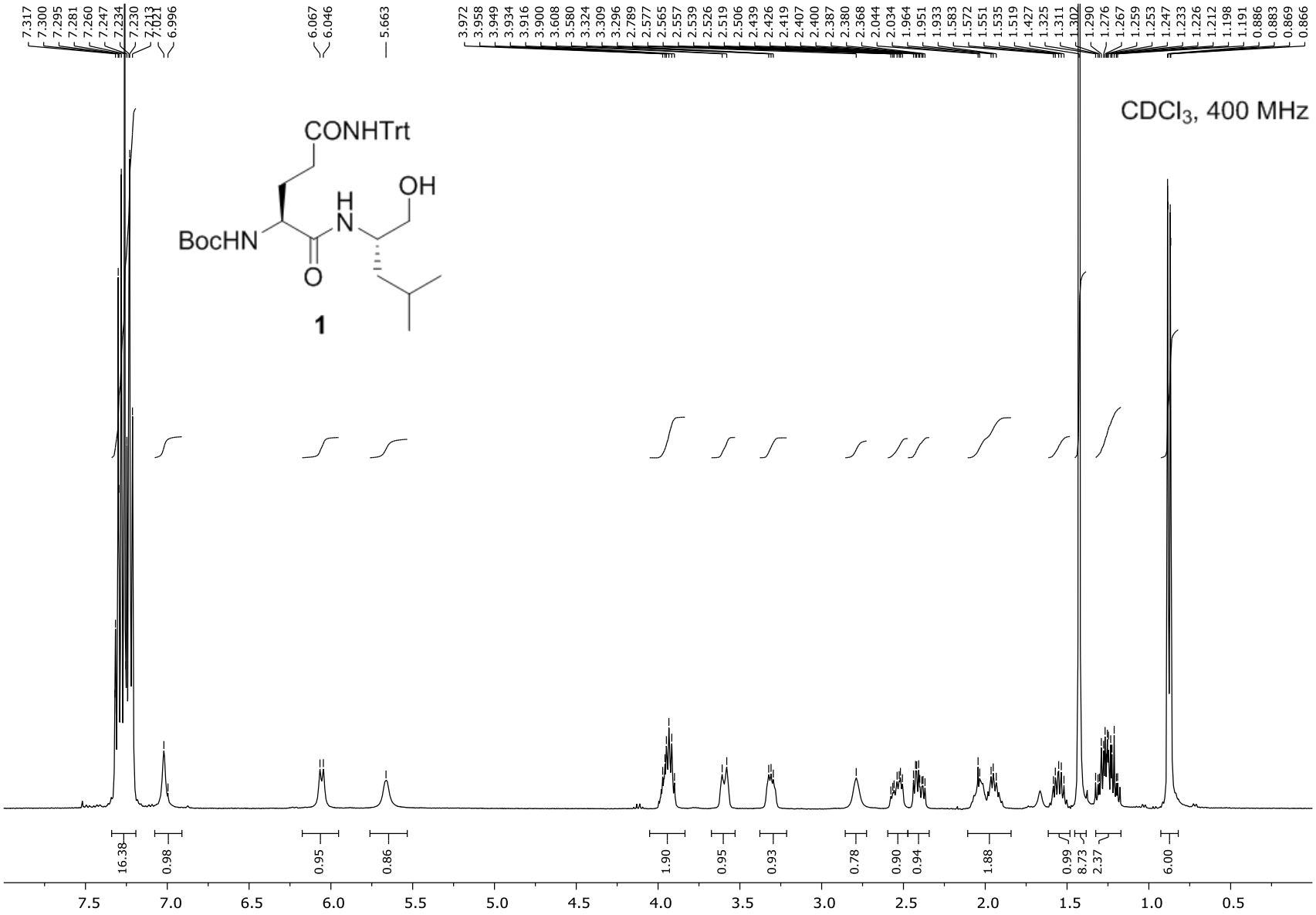
170.682
155.764
144.592
128.781
128.085
127.184
114.220
80.555
77.479
77.160
76.843
70.795
53.078
49.055
32.888
28.400
27.285
CDCl3, 100 MHz
CONHTrt
BocHN
O
O
CN
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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7.295
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7.260
7.247
7.234
7.230
7.213
7.211
7.021
6.996
6.067
6.046
5.663
3.972
3.958
3.949
3.934
3.916
3.900
3.608
3.580
3.324
3.309
3.296
2.789
2.577
2.565
2.557
2.539
2.526
2.519
2.506
2.439
2.426
2.419
2.407
2.400
2.387
2.380
2.368
2.044
2.034
1.964
1.951
1.933
1.583
1.572
1.551
1.535
1.519
1.427
1.325
1.311
1.302
1.290
1.276
1.267
1.259
1.253
1.247
1.233
1.226
1.212
1.198
1.191
0.886
0.883
0.869
0.866
CDCl3, 400 MHz
CONHTrt
BocHN
H
N
OH
O
1
16.38
0.98
0.95
0.86
1.90
0.95
0.93
0.78
0.90
0.94
1.88
0.99
8.73
2.37
6.00
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
2.5
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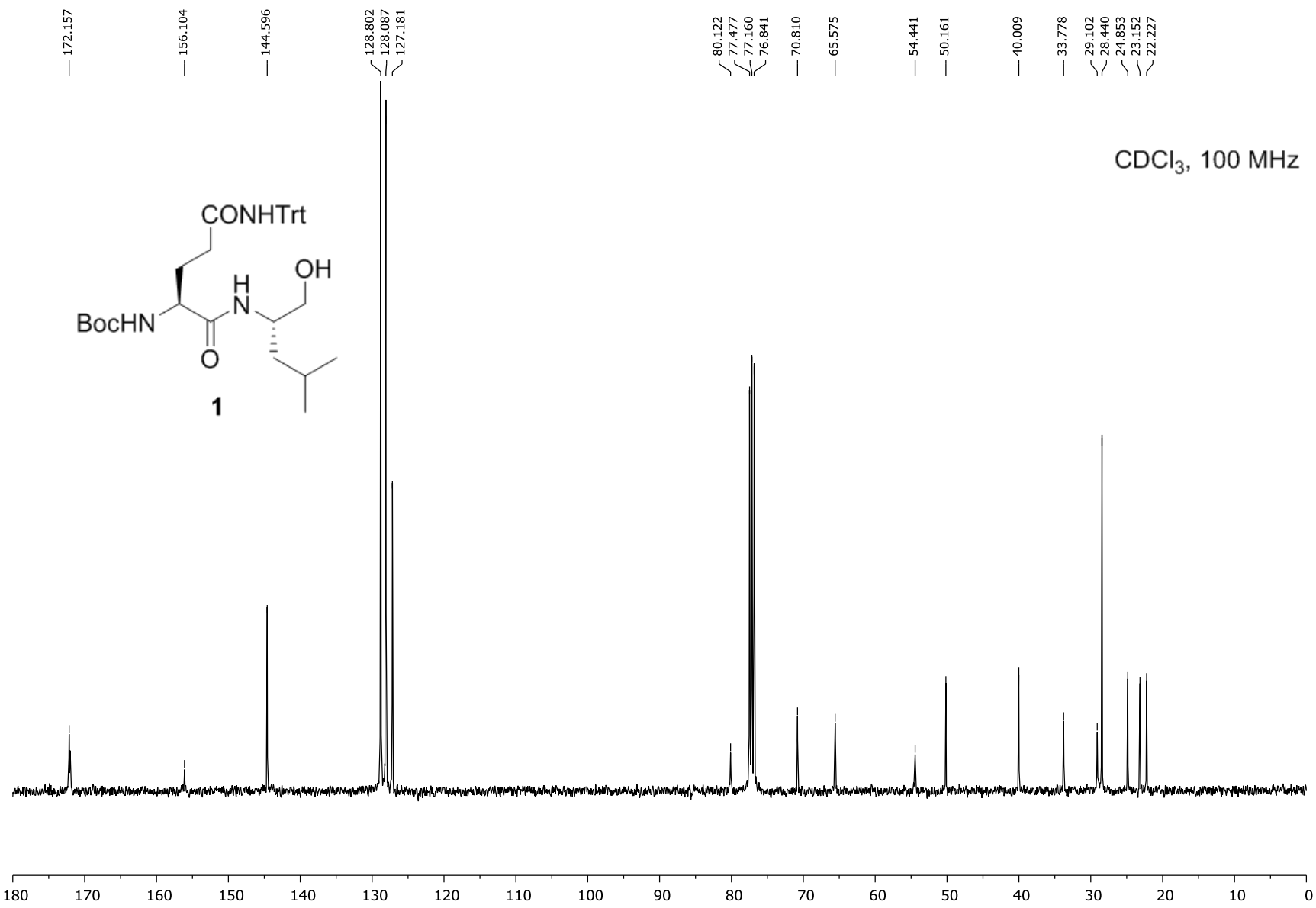
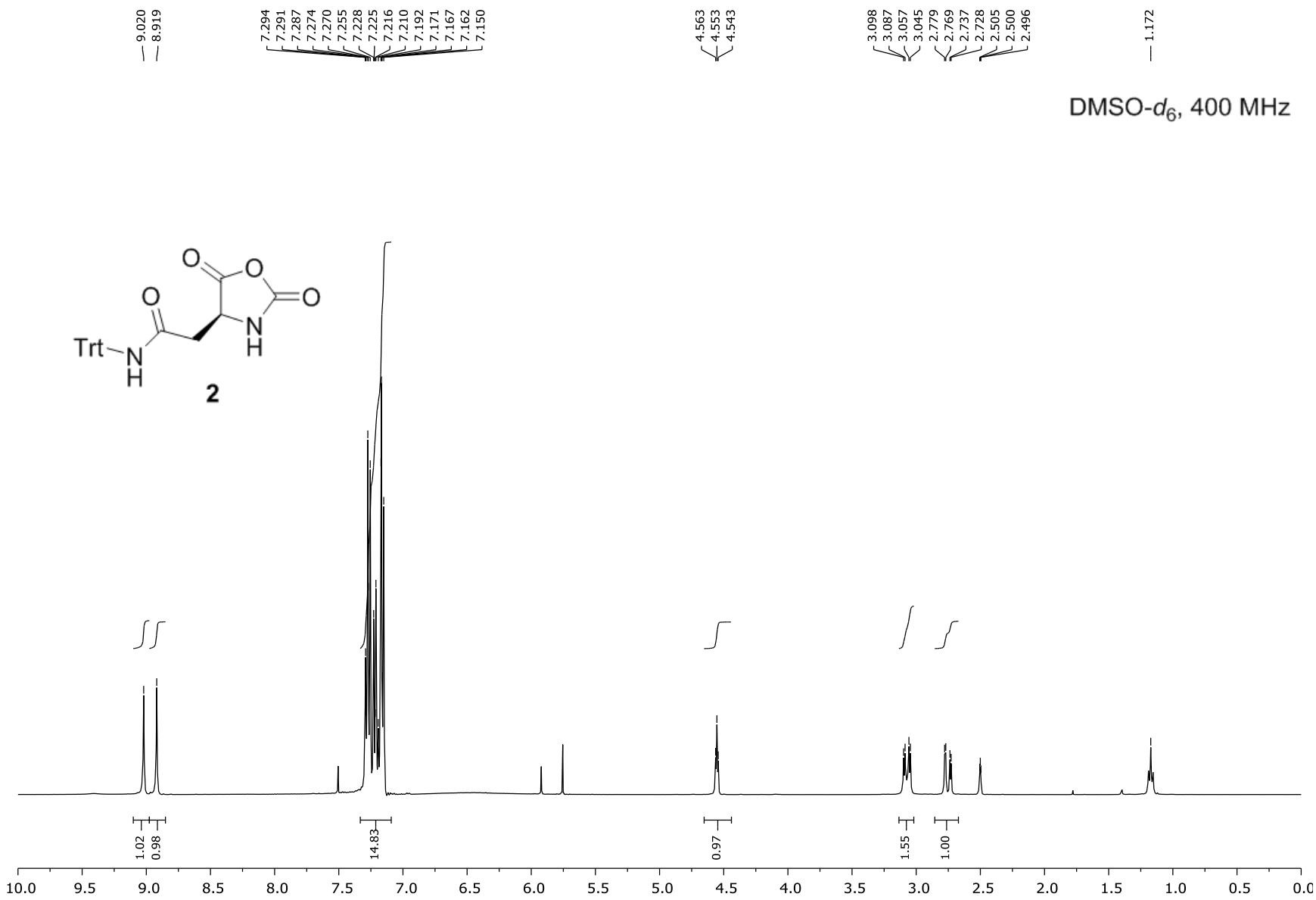
1.5
1.0
0.5


172.157
156.104
144.596
128.802
128.087
127.181
80.122
77.477
77.160
76.841
70.810
65.575
54.441
50.161
40.009
33.778
29.102
28.440
24.853
23.152
22.227
CDCl3, 100 MHz
CONHTrt
OH
H
N
BocHN
O
1
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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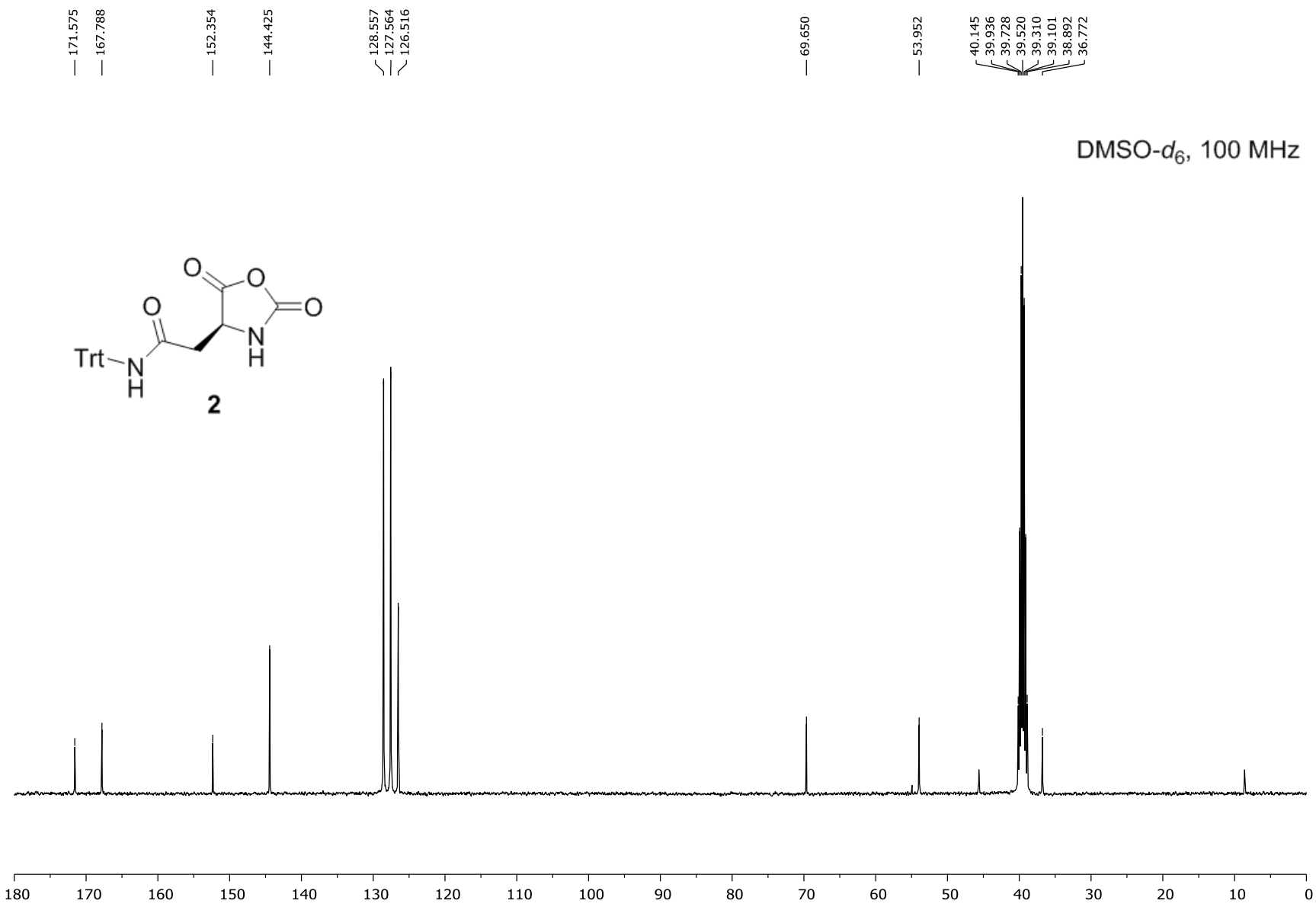
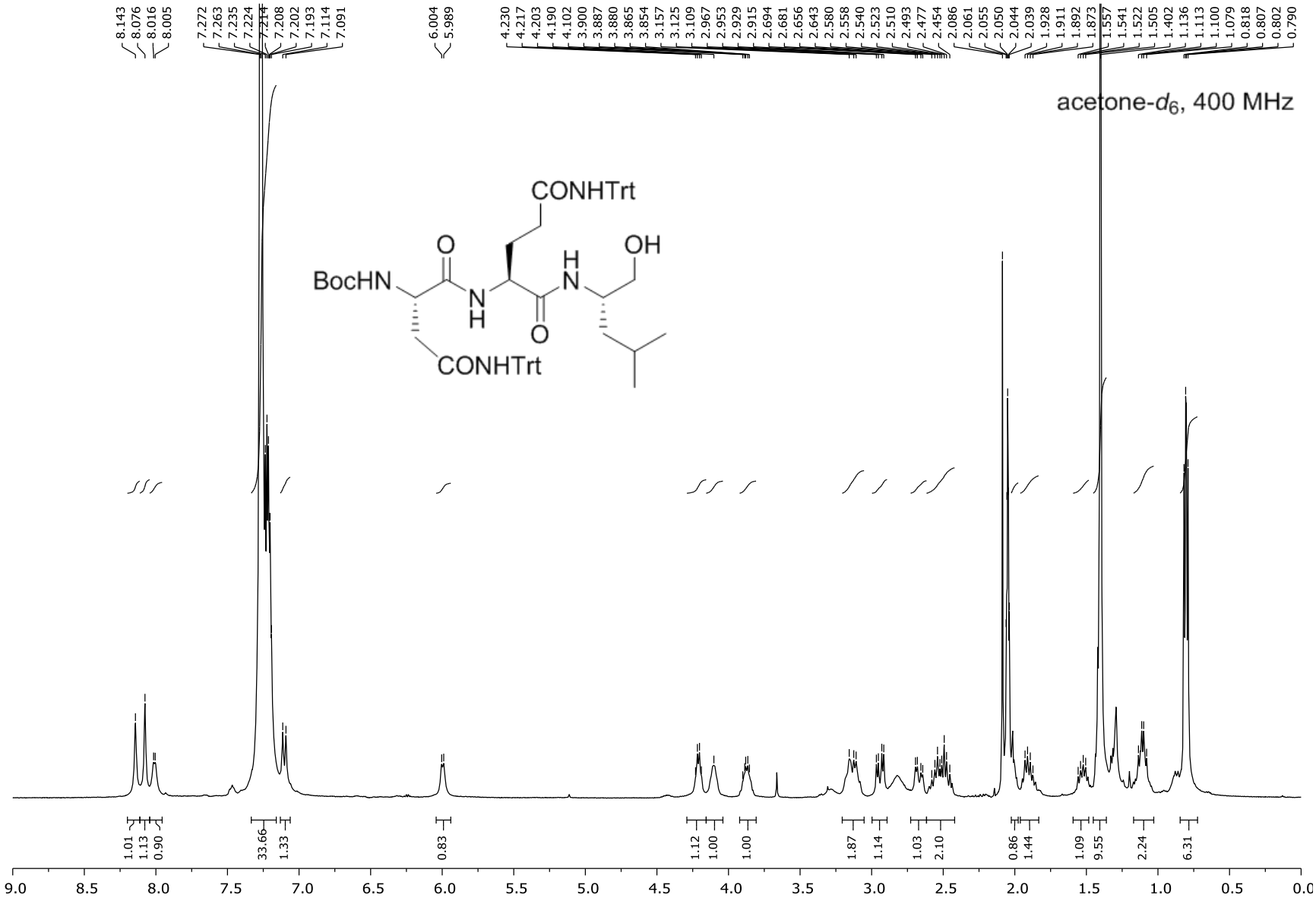
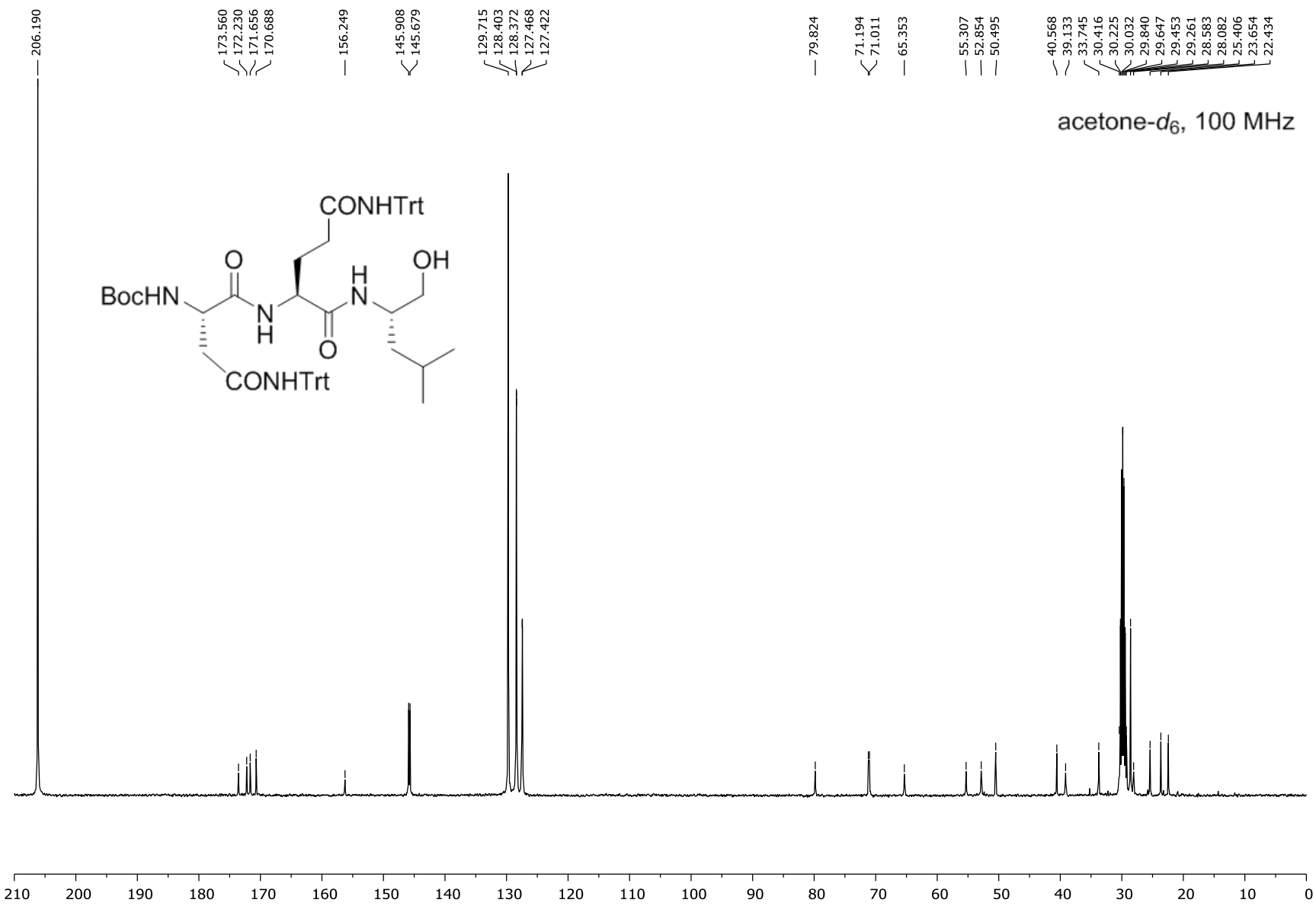
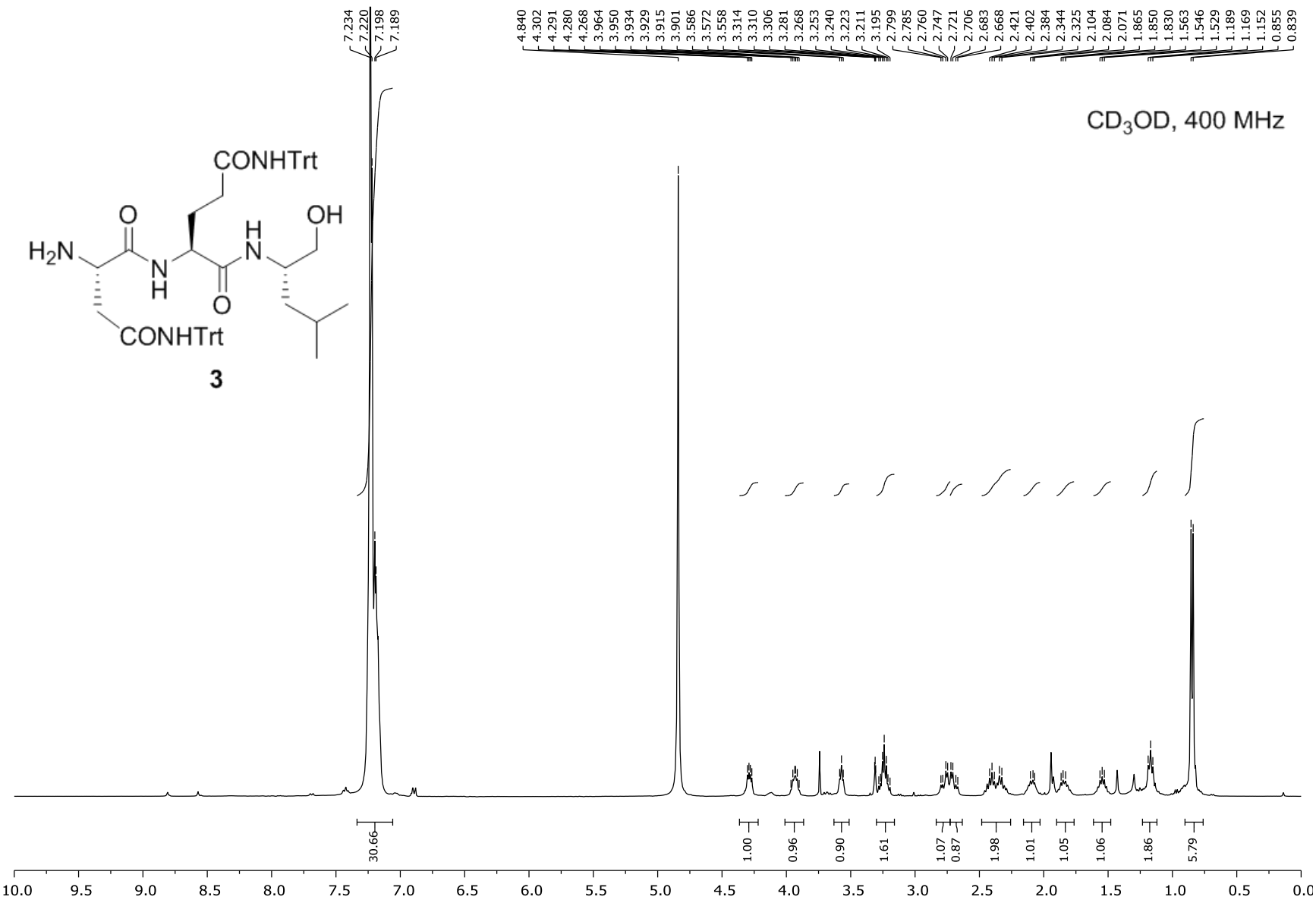
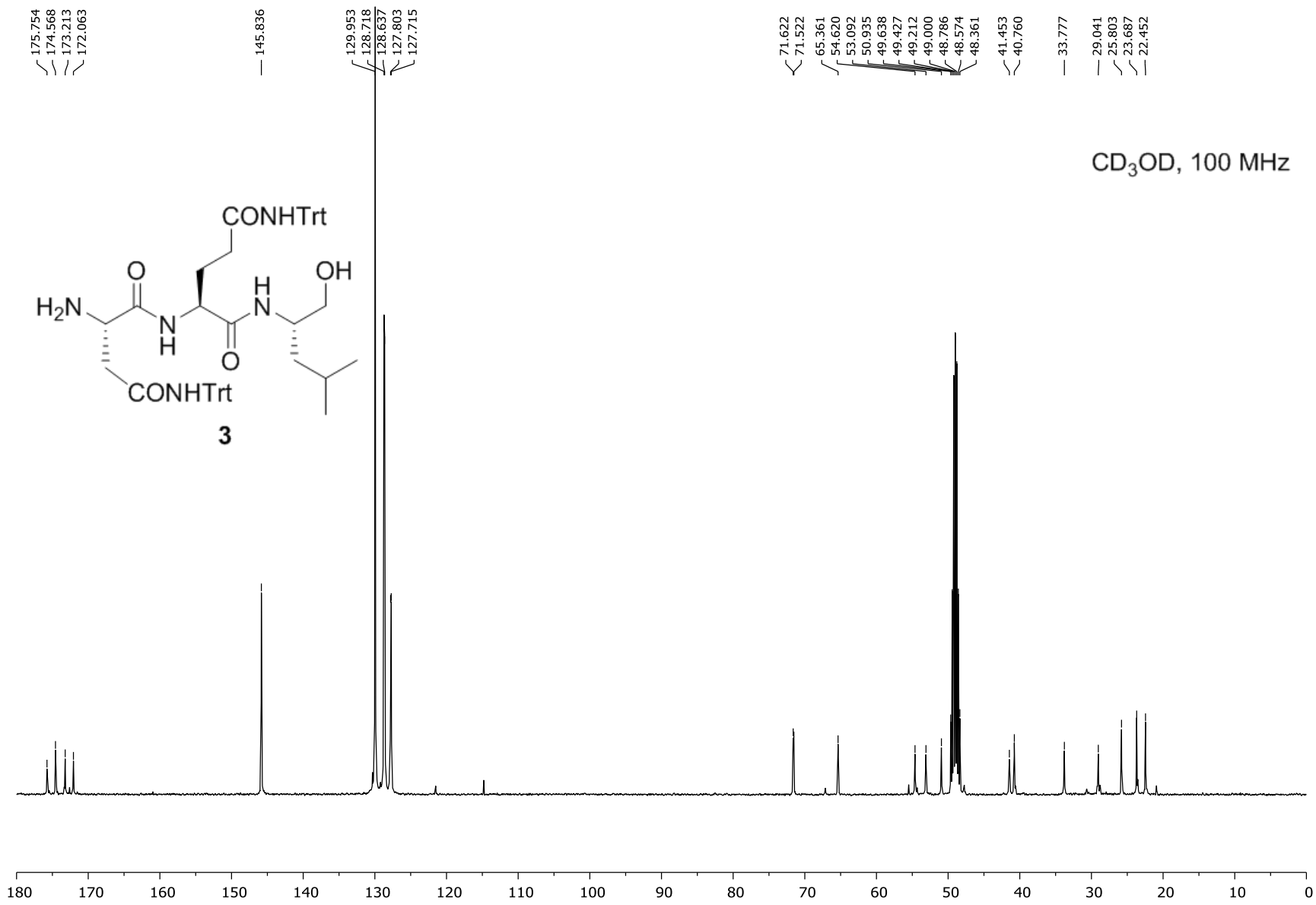
8.919
7.294
7.291
7.287
7.274
7.270
7.255
7.228
7.225
7.216
7.210
7.192
7.171
7.167
7.162
7.150
4.563
4.553
4.543
3.098
3.087
3.057
3.045
2.779
2.769
2.737
2.728
2.505
2.500
2.496
1.172
DMSO-d_6, 400 MHz
Trt
N
H
O
O
O
O
N
H
2
1.02
0.98
14.83
0.97
1.55
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

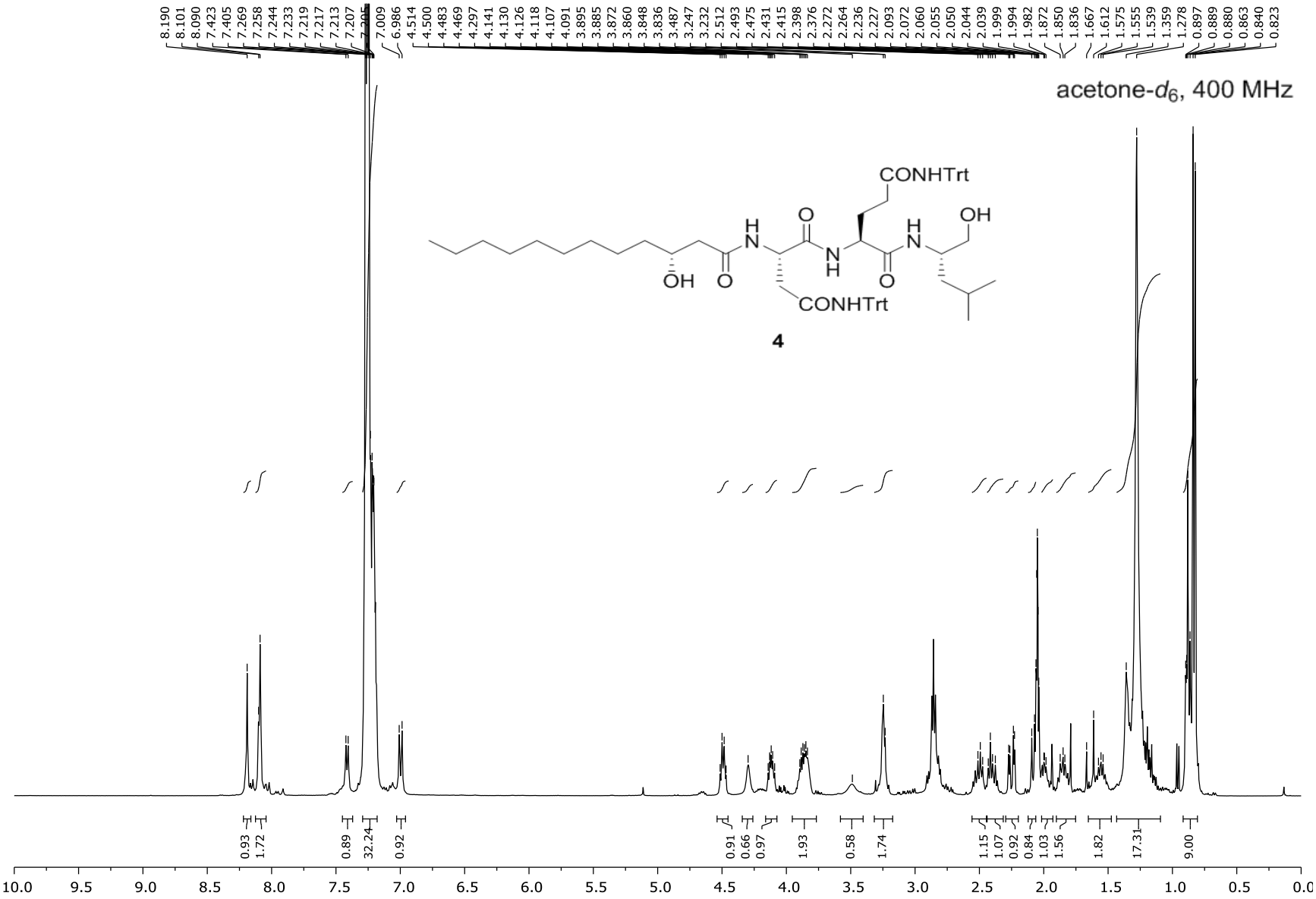

171.575
167.788
152.354
144.425
128.557
127.564
126.516
69.650
53.952
40.145
39.936
39.728
39.520
39.310
39.101
38.892
36.772
DMSO-d_6, 100 MHz
Trt
N
H
O
O
O
O
N
H
2
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

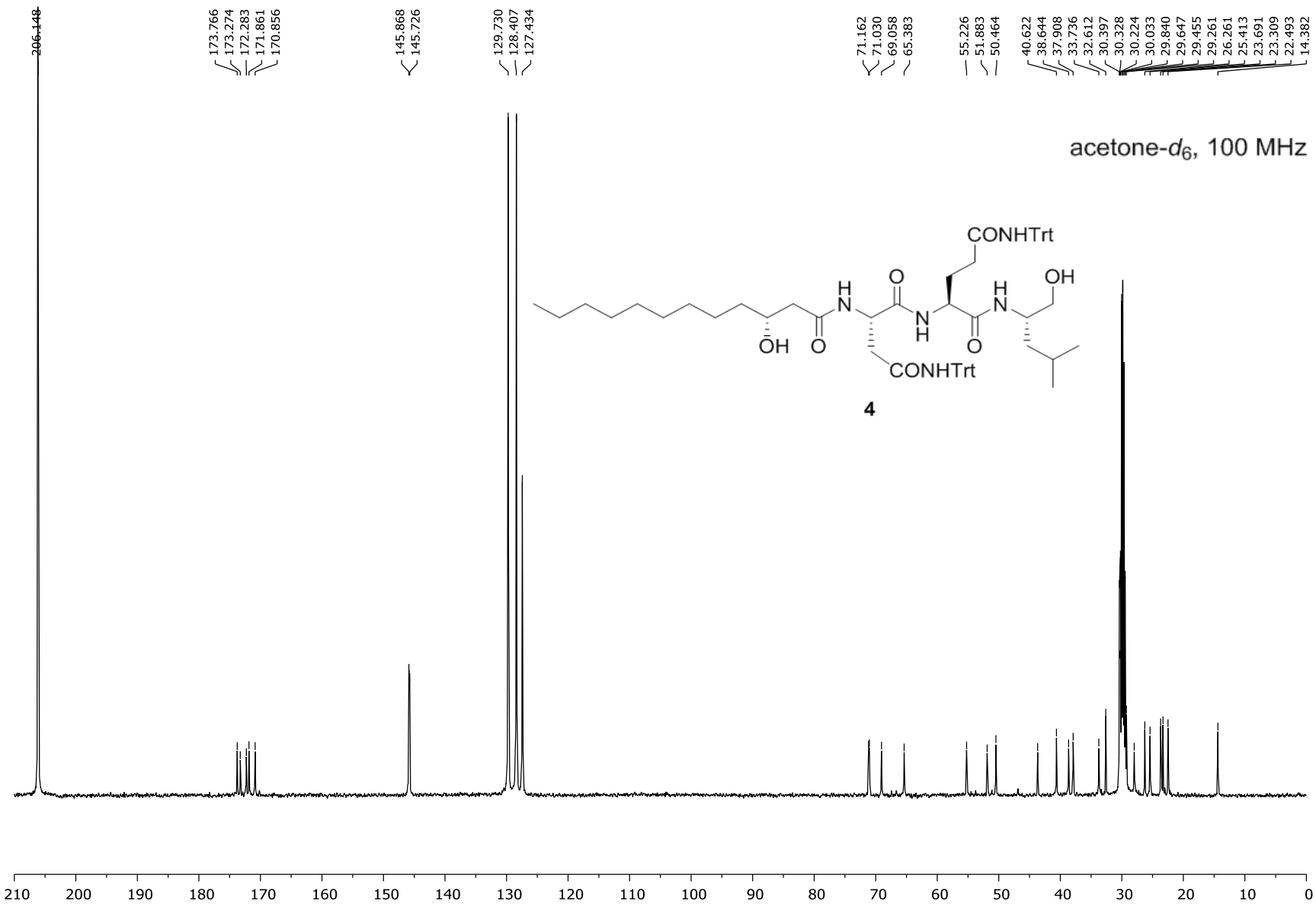

8.143
8.076
8.016
8.005
7.272
7.263
7.235
7.224
7.214
7.208
7.202
7.193
7.114
7.091
6.004
5.989
4.230
4.217
4.203
4.190
4.102
3.900
3.887
3.880
3.865
3.854
3.157
3.125
3.109
2.967
2.953
2.929
2.915
2.694
2.681
2.656
2.643
2.580
2.558
2.540
2.523
2.510
2.493
2.477
2.454
2.086
2.061
2.055
2.050
2.044
2.039
1.928
1.911
1.892
1.873
1.557
1.541
1.522
1.505
1.402
1.136
1.113
1.100
1.079
0.818
0.807
0.802
0.790
acetone-d_6, 400 MHz
CONHTrt
BocHN
O
N
H
O
H
N
OH
O
CONHTrt
1.01
1.13
0.90
33.66
1.33
0.83
1.12
1.00
1.00
1.87
1.14
1.03
2.10
0.86
1.44
1.09
9.55
2.24
6.31
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

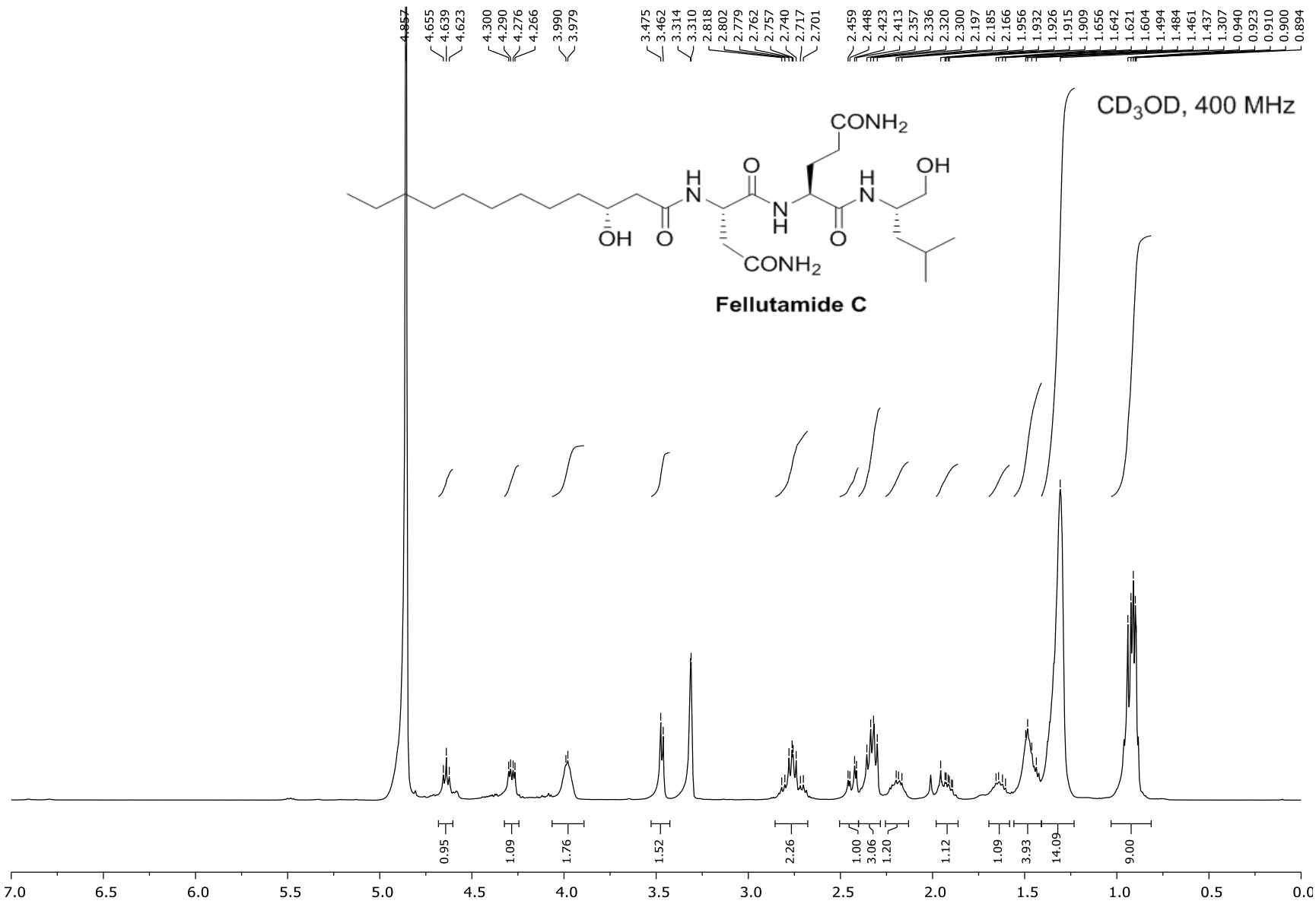

206.190
173.560
172.230
171.656
170.688
156.249
145.908
145.679
129.715
128.403
128.372
127.468
127.422
79.824
71.194
71.011
65.353
55.307
52.854
50.495
40.568
39.133
33.745
30.416
30.225
30.032
29.840
29.647
29.453
29.261
28.583
28.082
25.406
23.654
22.434
acetone-d_6, 100 MHz
CONHTrt
BocHN
O
N
H
H
N
OH
O
CONHTrt
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.234
7.220
7.198
7.189
4.840
4.302
4.291
4.280
4.268
3.964
3.950
3.934
3.929
3.915
3.901
3.586
3.572
3.558
3.314
3.310
3.306
3.281
3.268
3.253
3.240
3.223
3.211
3.195
2.799
2.785
2.760
2.747
2.721
2.706
2.683
2.668
2.421
2.402
2.384
2.344
2.325
2.104
2.084
2.071
1.865
1.850
1.830
1.563
1.546
1.529
1.189
1.169
1.152
0.855
0.839
CD3OD, 400 MHz
CONHTrt
O
H2N
N
H
O
H
N
OH
CONHTrt
3
30.66
1.00
0.96
0.90
1.61
1.07
0.87
1.98
1.01
1.05
1.06
1.86
5.79
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


175.754
174.568
173.213
172.063
145.836
129.953
128.718
128.637
127.803
127.715
71.622
71.522
65.361
54.620
53.092
50.935
49.638
49.427
49.212
49.000
48.786
48.574
48.361
41.453
40.760
33.777
29.041
25.803
23.687
22.452
CD3OD, 100 MHz
CONHTrt
H2N
O
N
H
H
N
OH
O
CONHTrt
3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


8.190
8.101
8.090
7.423
7.405
7.269
7.258
7.244
7.233
7.219
7.217
7.213
7.207
7.205
7.009
6.986
4.514
4.500
4.483
4.469
4.297
4.141
4.130
4.126
4.118
4.107
4.091
3.895
3.885
3.872
3.860
3.848
3.836
3.487
3.247
3.232
2.512
2.493
2.475
2.431
2.415
2.398
2.376
2.272
2.264
2.236
2.227
2.093
2.072
2.060
2.055
2.050
2.044
2.039
1.999
1.994
1.982
1.872
1.850
1.836
1.667
1.612
1.575
1.555
1.539
1.359
1.278
0.897
0.889
0.880
0.863
0.840
0.823
acetone-d_6, 400 MHz
CONHTrt
OH
H
N
O
N
H
O
H
N
OH
O
CONHTrt
4
0.93
1.72
0.89
32.24
0.92
0.91
0.66
0.97
1.93
0.58
1.74
1.15
1.07
0.92
0.84
1.03
1.56
1.82
17.31
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


206.148
173.766
173.274
172.283
171.861
170.856
145.868
145.726
129.730
128.407
127.434
71.162
71.030
69.058
65.383
55.226
51.883
50.464
40.622
38.644
37.908
33.736
32.612
30.397
30.328
30.224
30.033
29.840
29.647
29.455
29.261
26.261
25.413
23.691
23.309
22.493
14.382
acetone-d_6, 100 MHz
CONHTrt
OH
H
N
O
N
H
H
N
OH
OH
O
O
O
CONHTrt
4
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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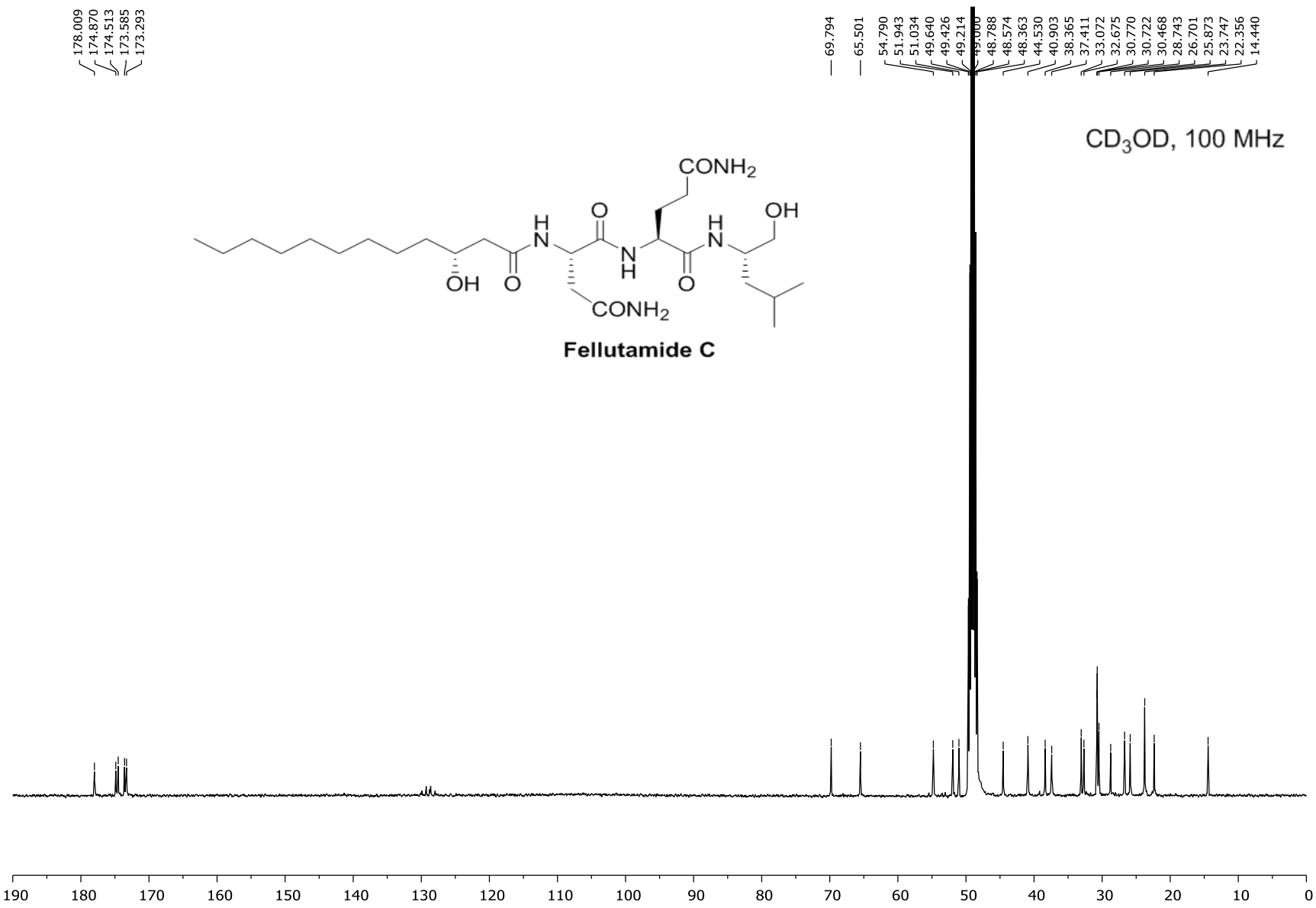
4.655
4.639
4.623
4.300
4.290
4.276
4.266
3.990
3.979
3.475
3.462
3.314
3.310
2.818
2.802
2.779
2.762
2.757
2.740
2.717
2.701
2.459
2.448
2.423
2.413
2.357
2.336
2.320
2.300
2.197
2.185
2.166
1.956
1.932
1.926
1.915
1.909
1.656
1.642
1.621
1.604
1.494
1.484
1.461
1.437
1.307
0.940
0.923
0.910
0.900
0.894
CD3OD, 400 MHz
CONH2
OH
H
N
O
N
H
O
H
N
OH
O
CONH2
Fellutamide C
0.95
1.09
1.76
1.52
2.26
1.00
3.06
1.20
1.12
1.09
3.93
14.09
9.00
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0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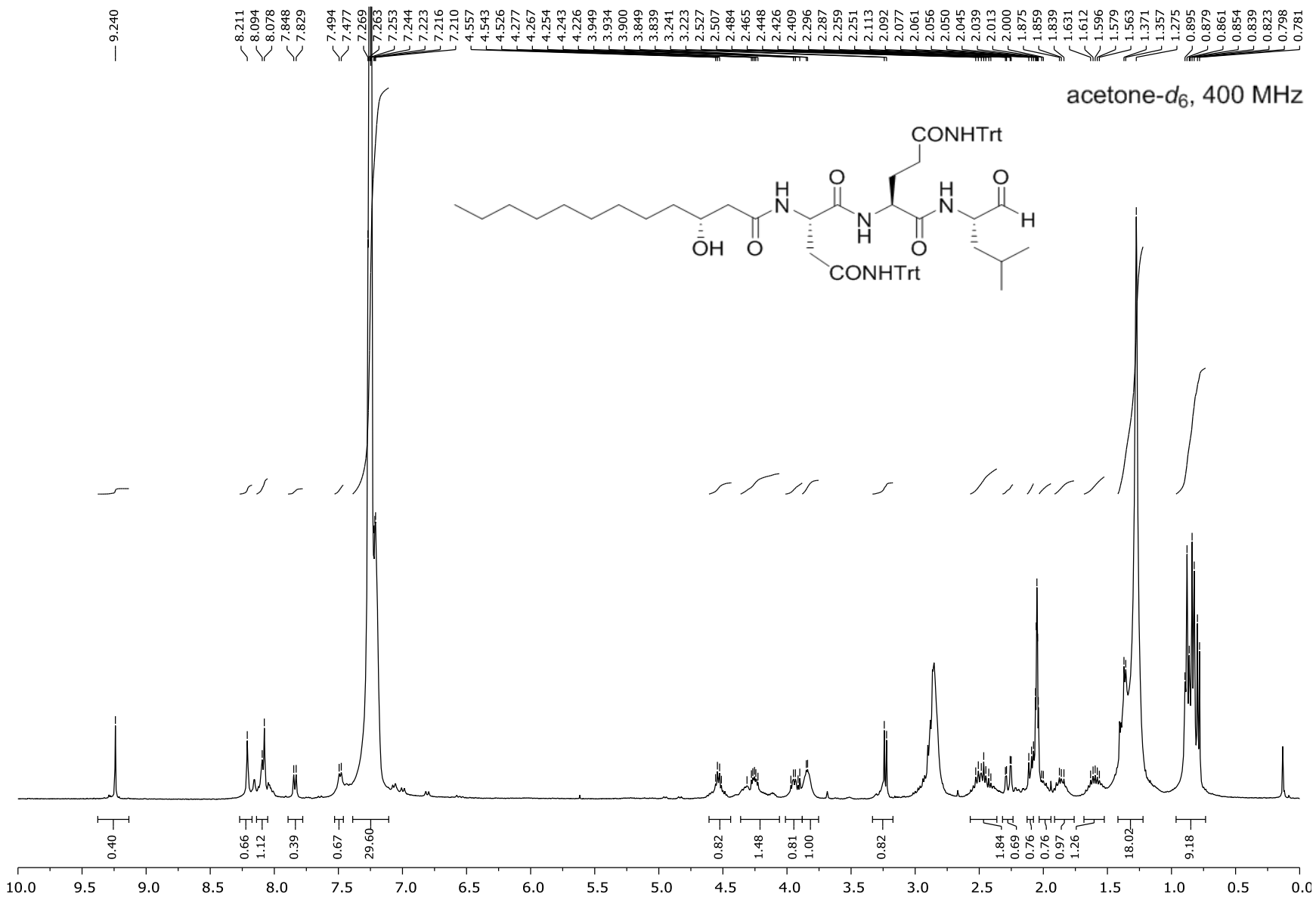
174.870
174.513
173.585
173.293
69.794
65.501
54.790
51.943
51.034
49.640
49.426
49.214
48.788
48.574
48.363
44.530
40.903
38.365
37.411
33.072
32.675
30.770
30.722
30.468
28.743
26.701
25.873
23.747
22.356
14.440
CD3OD, 100 MHz
CONH2
OH
H
N
O
N
H
O
H
N
OH
O
CONH2
Fellutamide C
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


9.240
8.211
8.094
8.078
7.848
7.829
7.494
7.477
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7.263
7.253
7.244
7.223
7.216
7.210
4.557
4.543
4.526
4.277
4.267
4.254
4.243
4.226
3.949
3.934
3.900
3.849
3.839
3.241
3.223
2.527
2.507
2.484
2.465
2.448
2.426
2.409
2.296
2.287
2.259
2.251
2.113
2.092
2.077
2.061
2.056
2.050
2.045
2.039
2.013
2.000
1.875
1.859
1.839
1.631
1.612
1.596
1.579
1.563
1.371
1.357
1.275
0.895
0.879
0.861
0.854
0.839
0.823
0.798
0.781
acetone-d_6, 400 MHz
CONHTrt
OH
CONHTrt
0.40
0.66
1.12
0.39
0.67
29.60
0.82
1.48
0.81
1.00
0.82
1.84
0.69
0.76
0.97
1.26
18.02
9.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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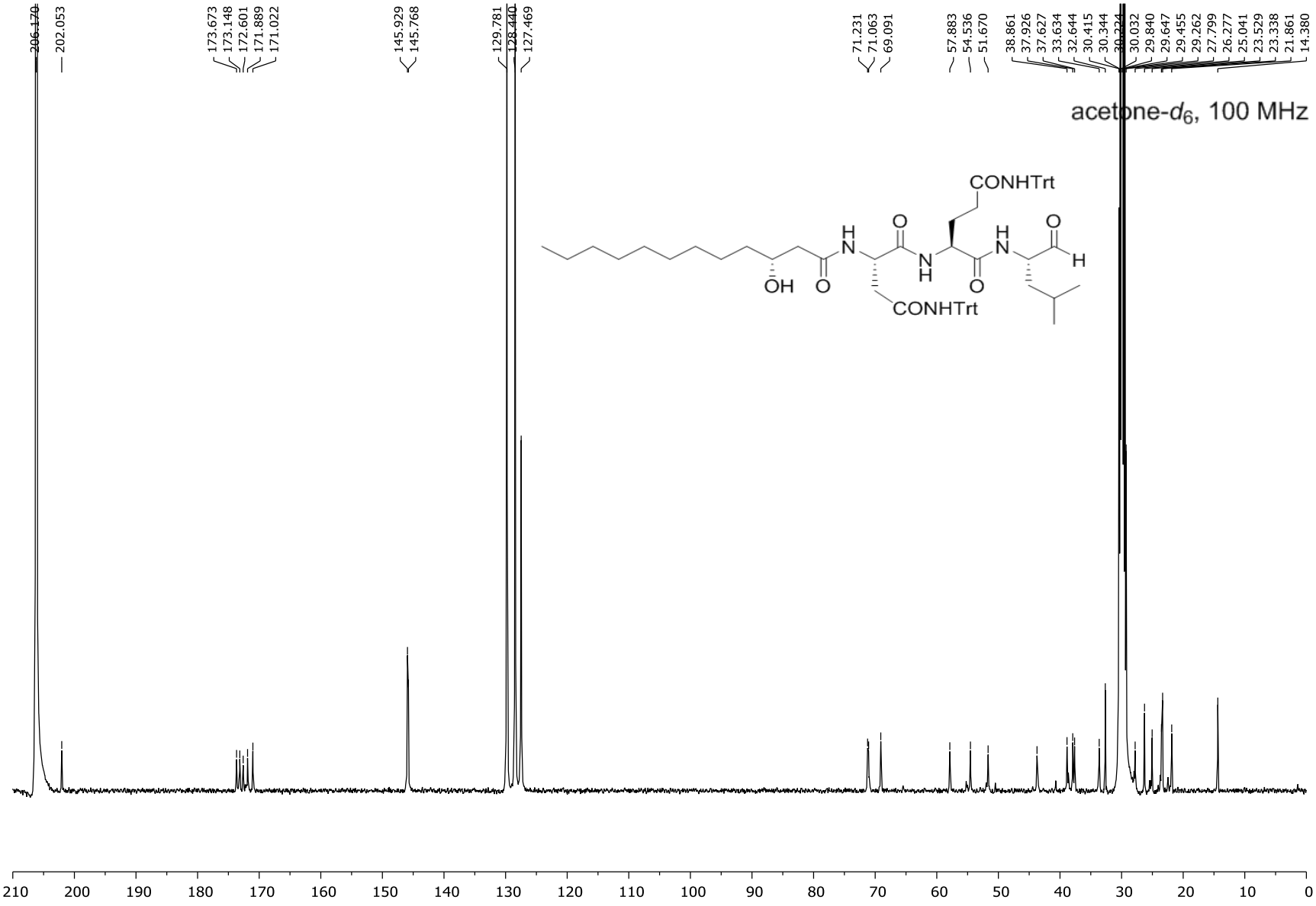
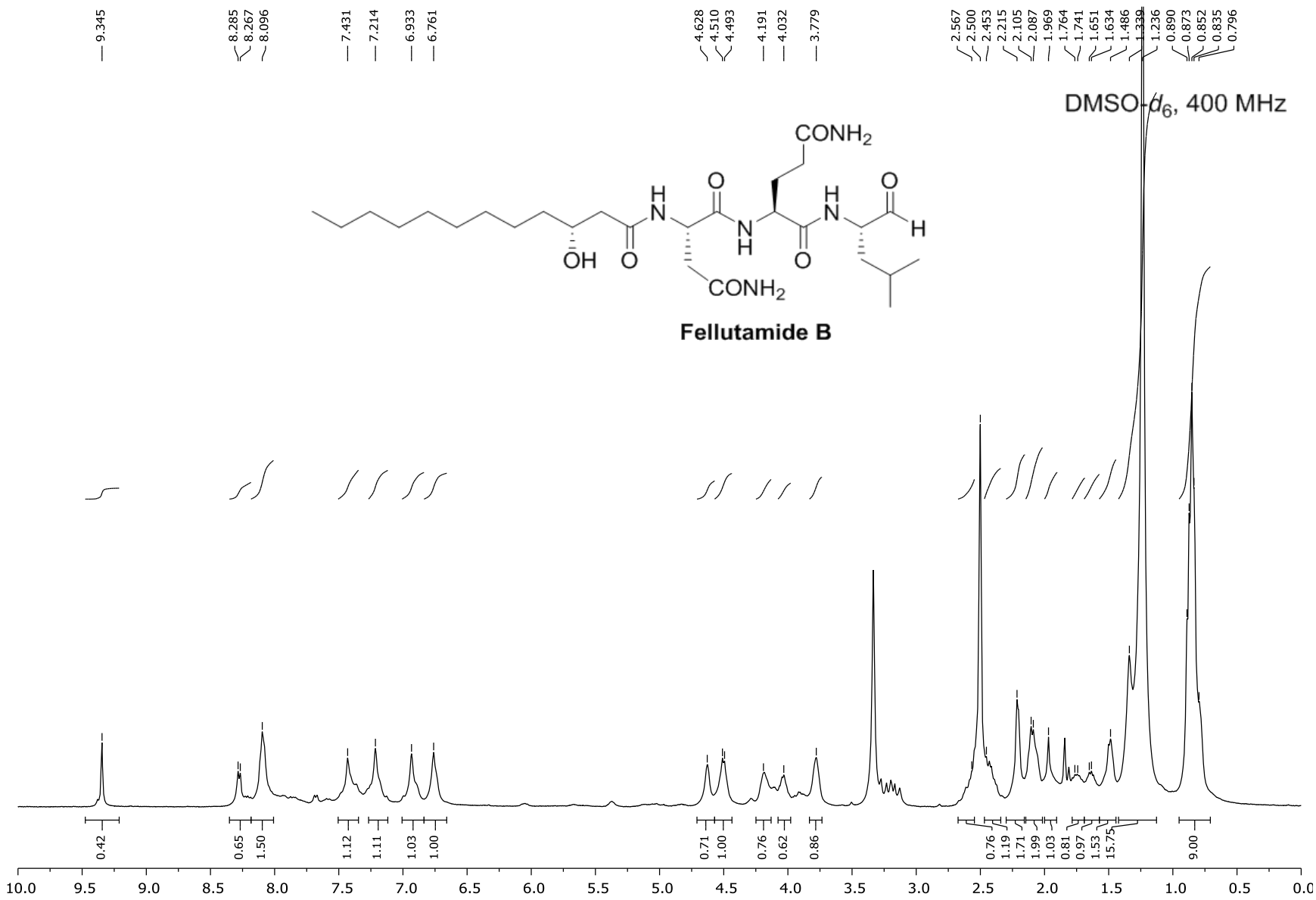
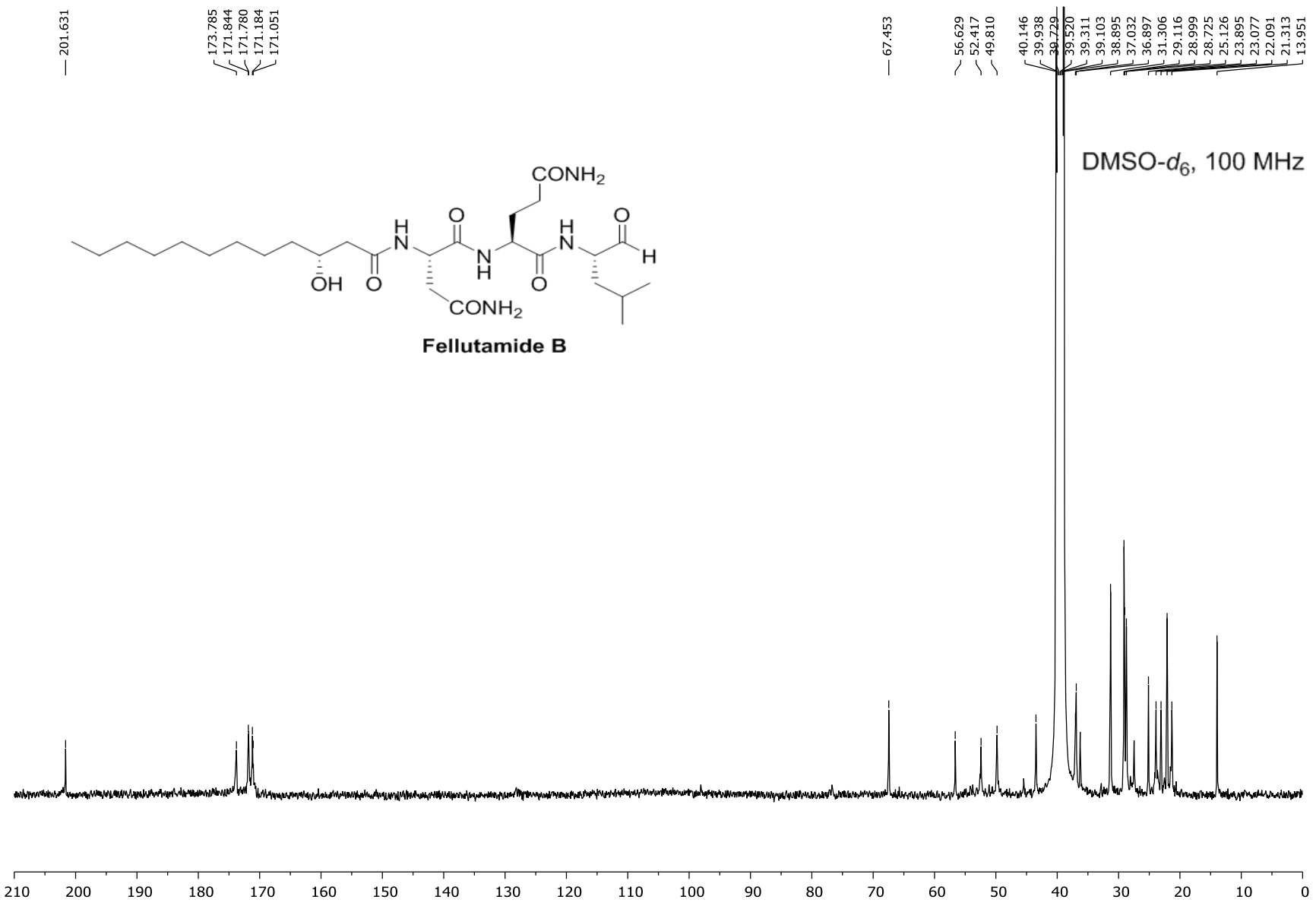
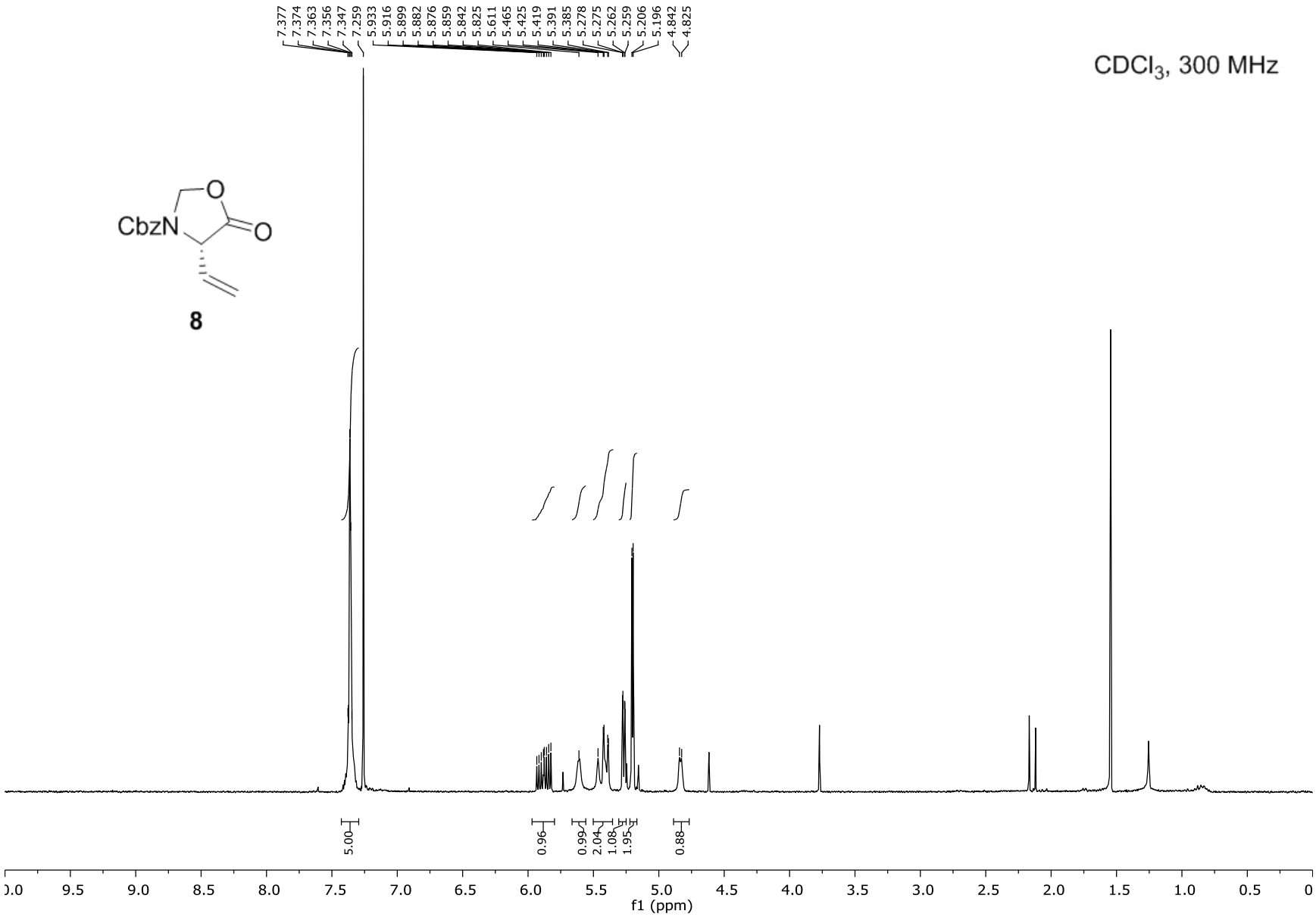
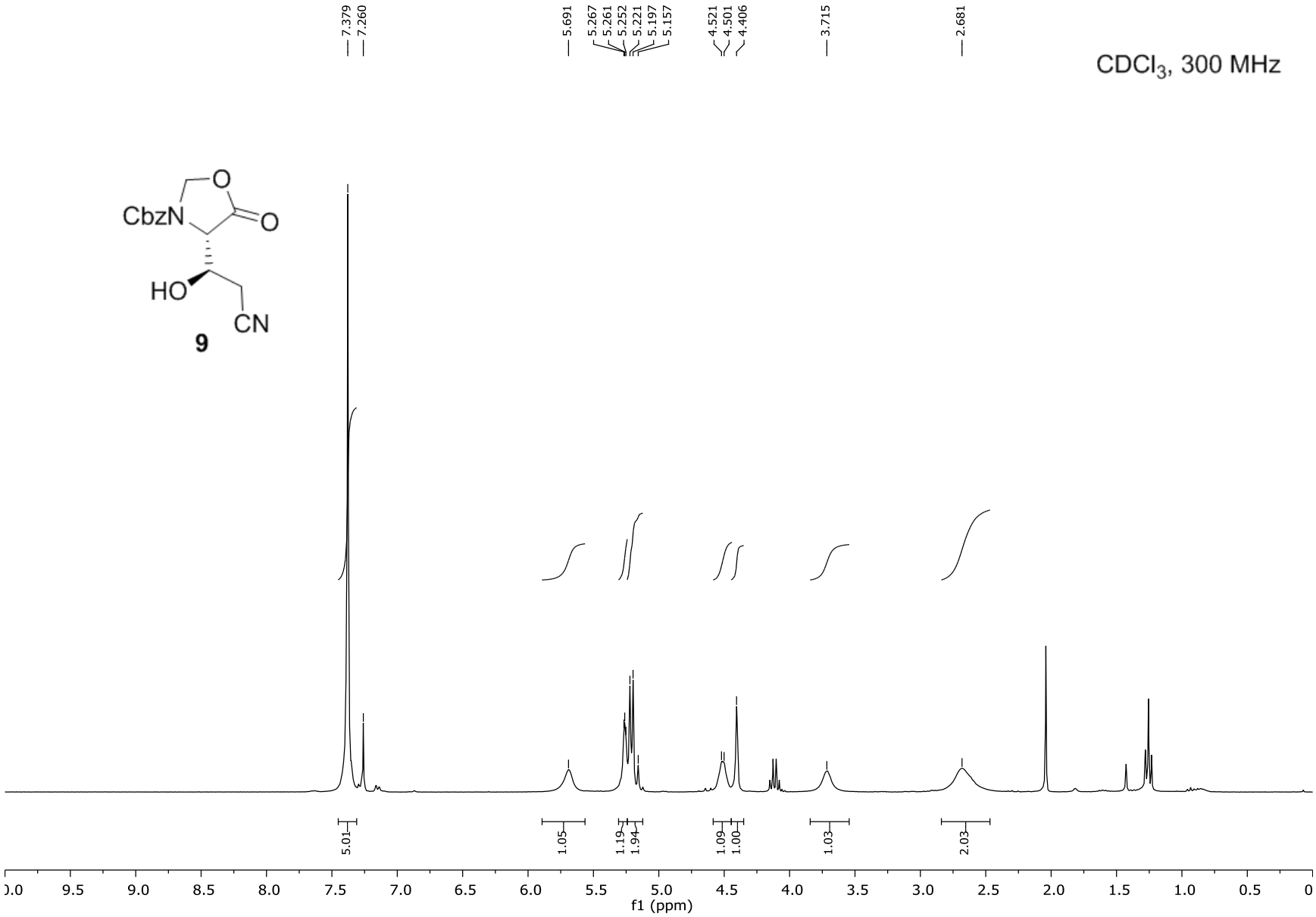
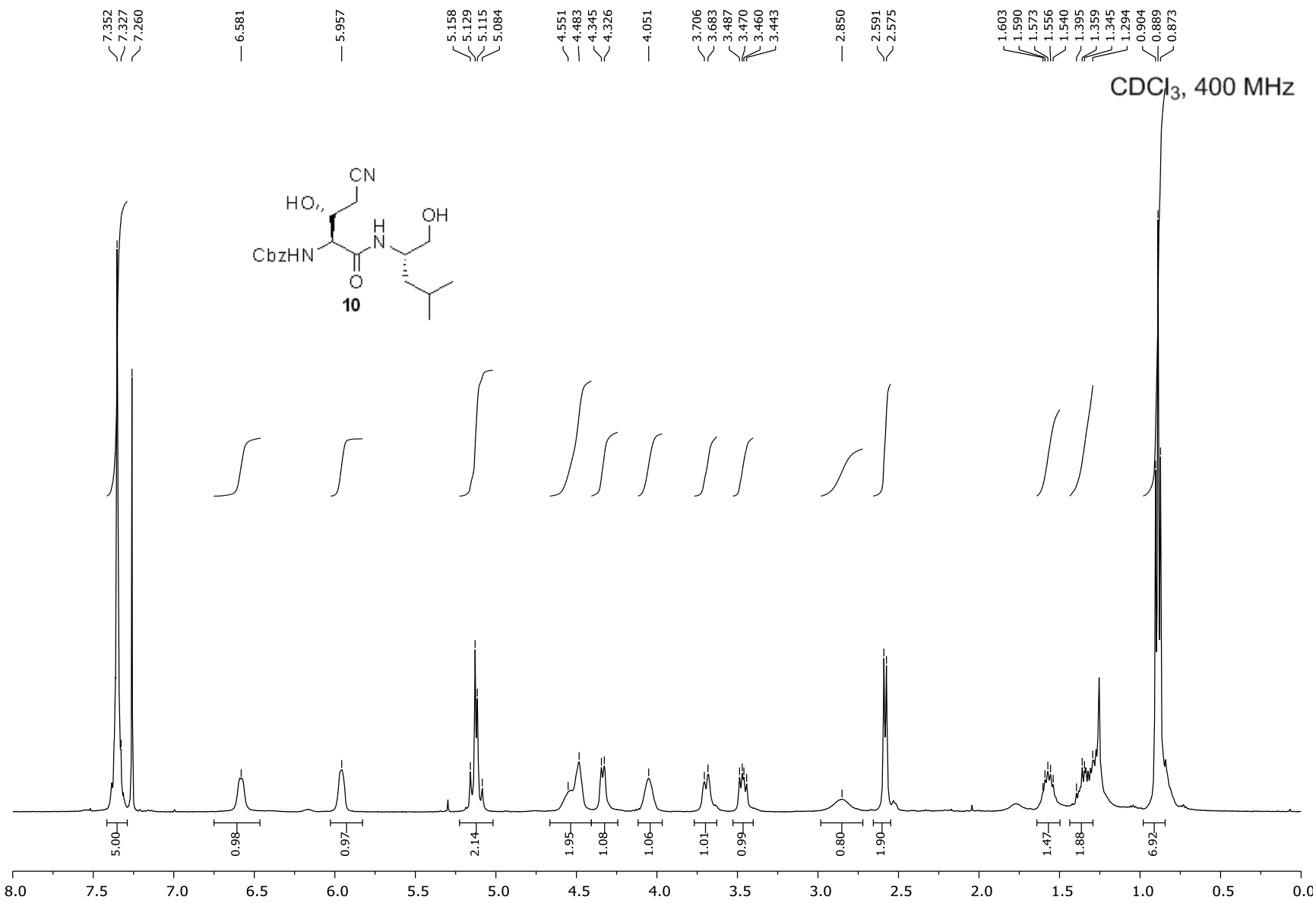

206.170
202.053
173.673
173.148
172.601
171.889
171.022
145.929
145.768
129.781
128.440
127.469
71.231
71.063
69.091
57.883
54.536
51.670
38.861
37.926
37.627
33.634
32.644
30.415
30.344
30.324
30.032
29.840
29.647
29.455
29.262
27.799
26.277
25.041
23.529
23.338
21.861
14.380
acetone-d_6, 100 MHz
CONHTrt
CONHTrt
OH
O
H
N
O
N
H
O
H
N
O
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

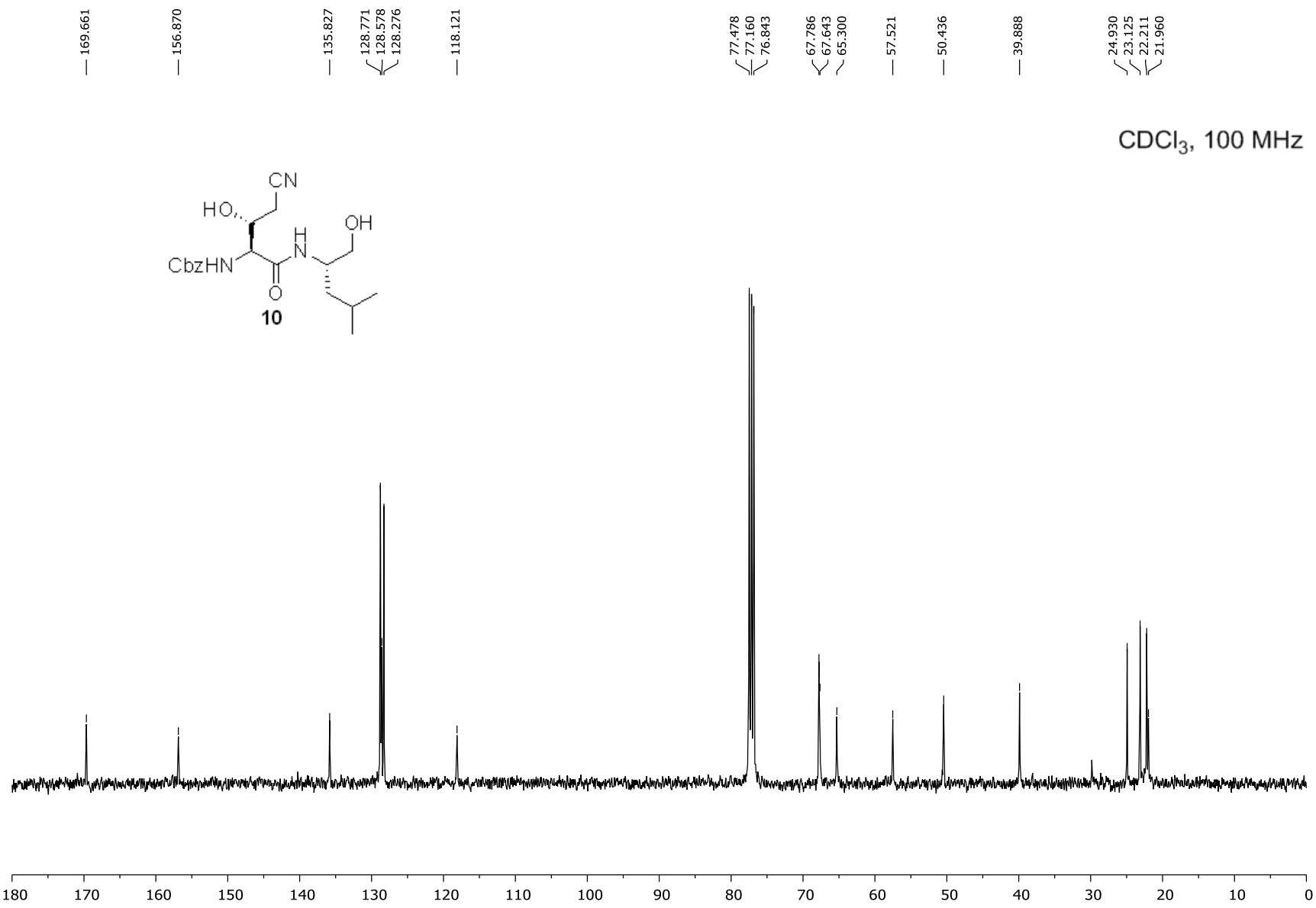

9.345
8.285
8.267
8.096
7.431
7.214
6.933
6.761
4.628
4.510
4.493
4.191
4.032
3.779
2.567
2.500
2.453
2.215
2.105
2.087
1.969
1.764
1.741
1.651
1.634
1.486
1.339
1.236
0.890
0.873
0.852
0.835
0.796
DMSO-d_6, 400 MHz
CONH2
OH
CONH2
Fellutamide B
0.42
0.65
1.50
1.12
1.11
1.03
1.00
0.71
1.00
0.76
0.62
0.86
0.76
1.19
1.71
1.99
1.03
0.81
0.97
1.53
15.75
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

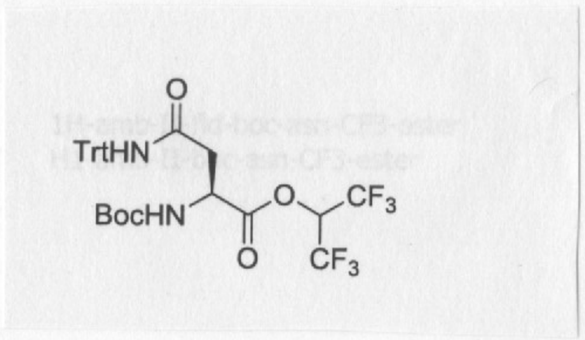

201.631
173.785
171.844
171.780
171.184
171.051
67.453
56.629
52.417
49.810
40.146
39.938
39.729
39.520
39.311
39.103
38.895
37.032
36.897
31.306
29.116
28.999
28.725
25.126
23.895
23.077
22.091
21.313
13.951
DMSO-d_6, 100 MHz
CONH2
OH
CONH2
Fellutamide B
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.377
7.374
7.363
7.356
7.347
7.259
5.933
5.916
5.899
5.882
5.876
5.859
5.842
5.825
5.611
5.465
5.425
5.419
5.391
5.385
5.278
5.275
5.262
5.259
5.206
5.196
4.842
4.825
CDCl3, 300 MHz
CbzN
O
O
8
5.00
0.96
0.99
2.04
1.08
1.95
0.88
f1 (ppm)

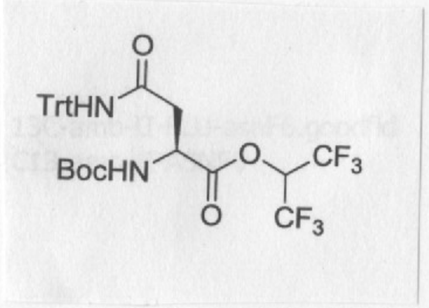

7.379
7.260
5.691
5.267
5.261
5.252
5.221
5.197
5.157
4.521
4.501
4.406
3.715
2.681
CDCl3, 300 MHz
CbzN
O
O
HO
CN
9
5.01
1.05
1.19
1.94
1.09
1.00
1.03
2.03
f1 (ppm)

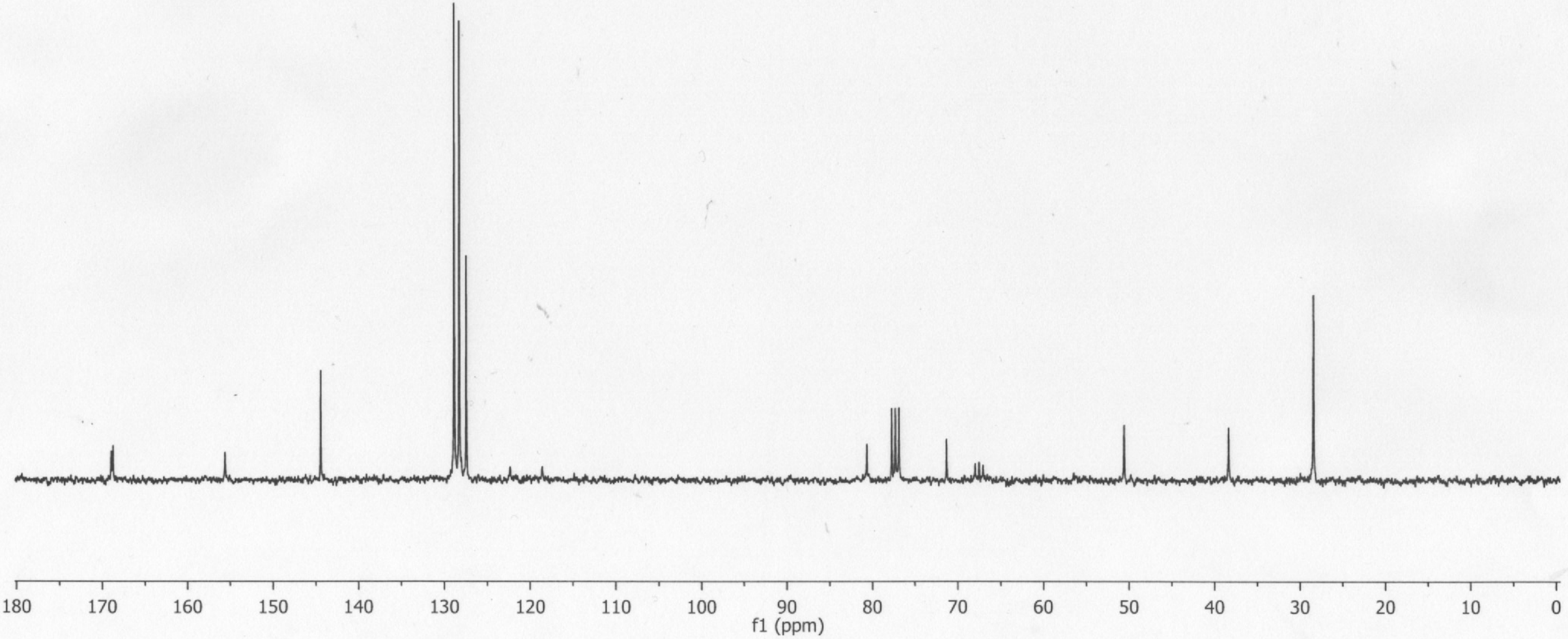

7.352
7.327
7.260
6.581
5.957
5.158
5.129
5.115
5.084
4.551
4.483
4.345
4.326
4.051
3.706
3.683
3.487
3.470
3.460
3.443
2.850
2.591
2.575
1.603
1.590
1.573
1.556
1.540
1.395
1.359
1.345
1.294
0.904
0.889
0.873
CDCl3, 400 MHz
CN
HO
H
N
OH
CbzHN
O
10
5.00
0.98
0.97
2.14
1.95
1.08
1.06
1.01
0.99
0.80
1.90
1.47
1.88
6.92
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


169.661
156.870
135.827
128.771
128.578
128.276
118.121
77.478
77.160
76.843
67.786
67.643
65.300
57.521
50.436
39.888
24.930
23.125
22.211
21.960
CDCl3, 100 MHz
CN
HO
OH
H
N
CbzHN
O
10
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

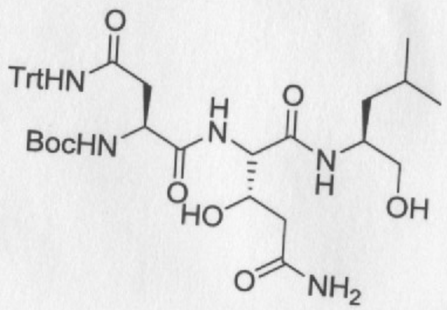

O
TrtHN
BocHN
O
O
CF3
CF3

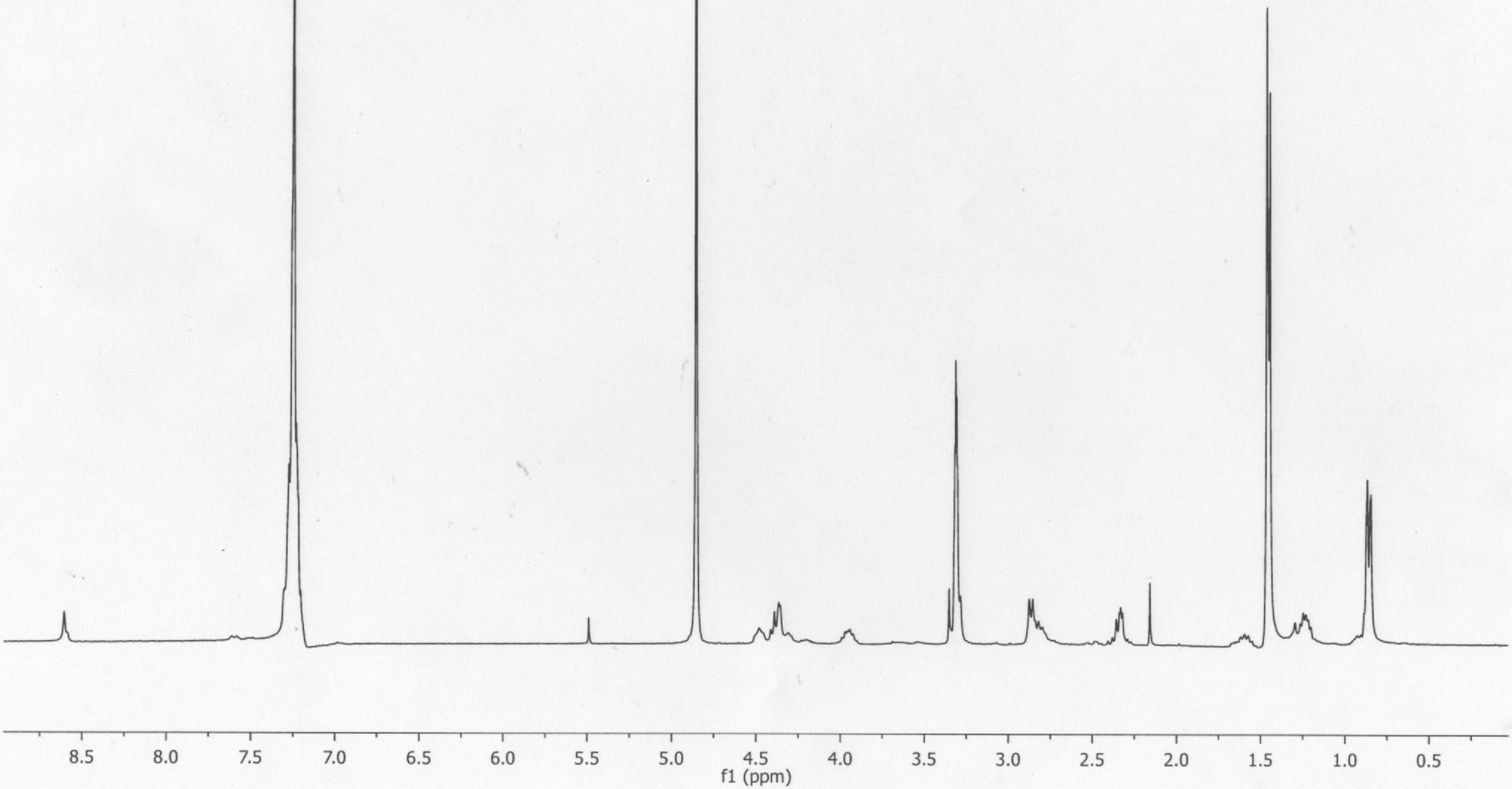
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

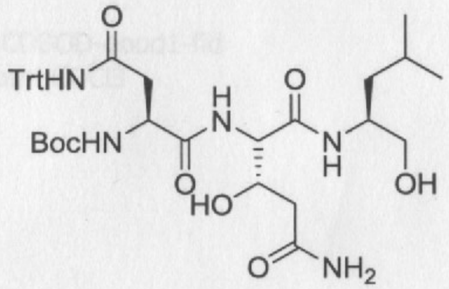

O
TrtHN
BocHN
O
O
CF3
CF3

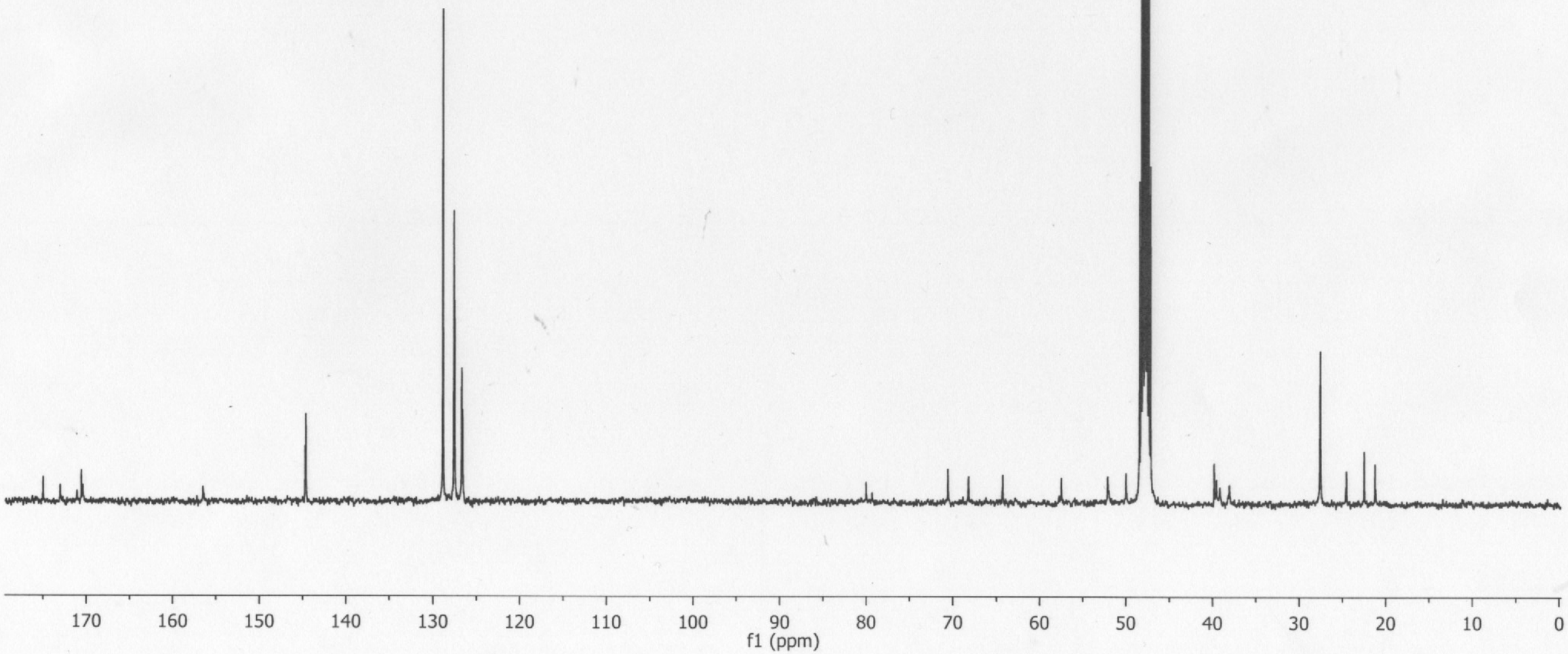

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

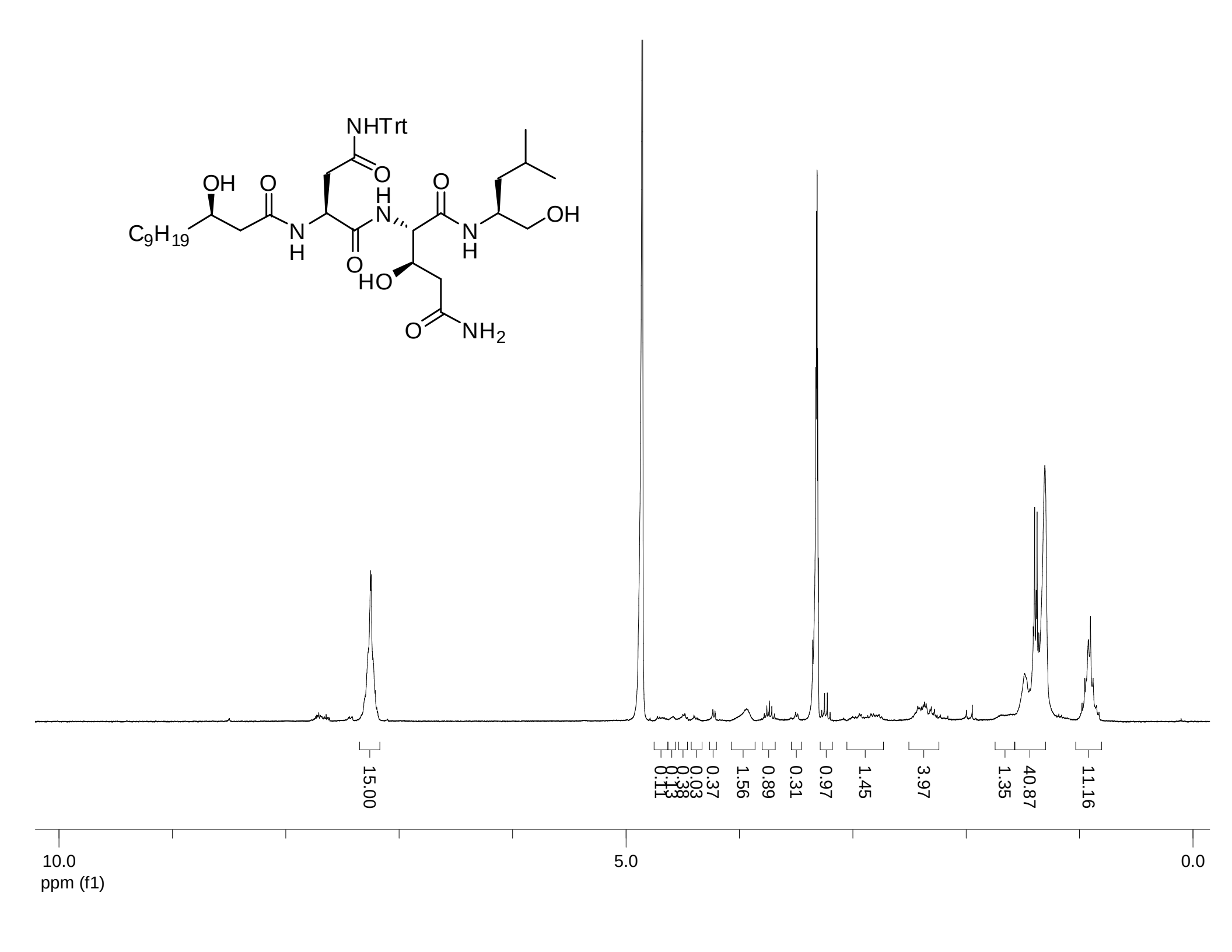
1H-amb-III-FlD-asn-coupling-good
H1-amb-III-FLD-asn-coupling-good

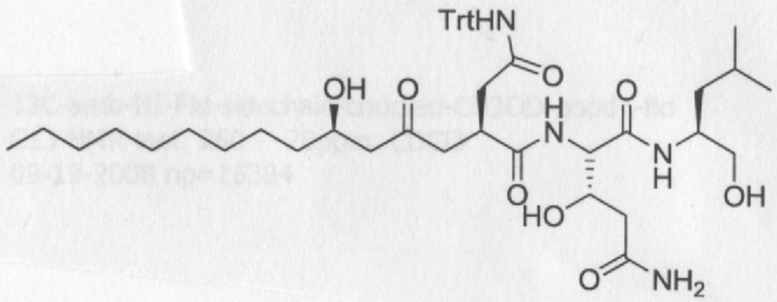




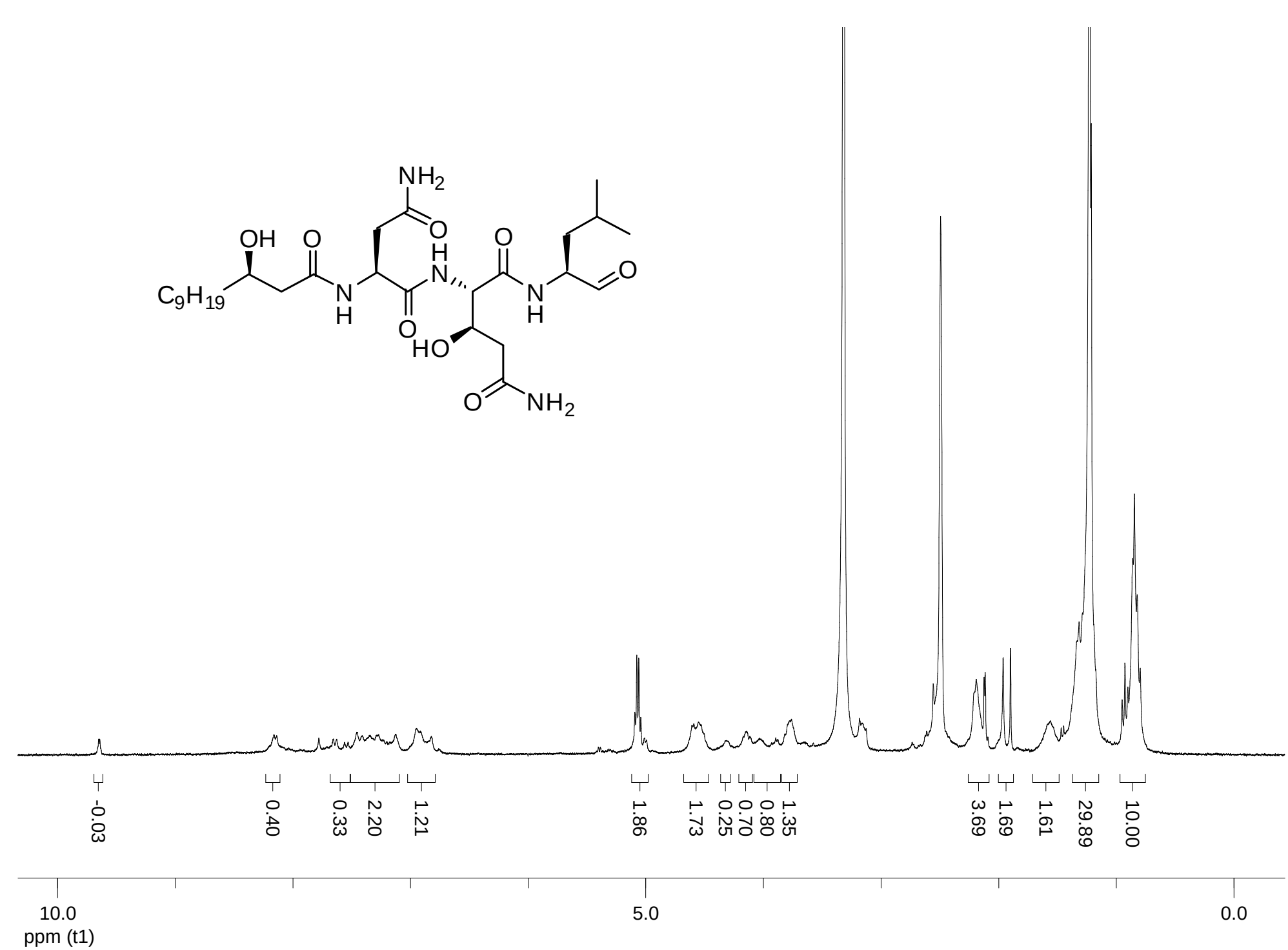

TrtHN
BocHN
O
H
N
O
N
H
OH
O
HO
O
NH2

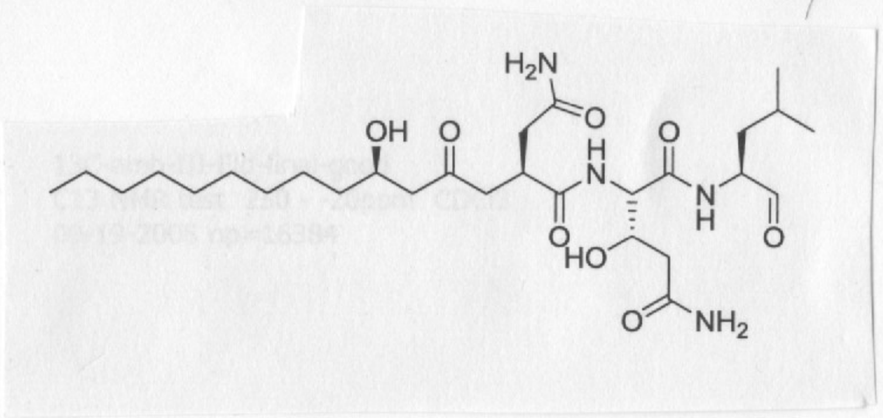

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


NHTrt
OH
O
O
H
N
O
N
OH
C9H19
N
H
O
HO
O
NH2
15.00
0.11
0.13
0.38
0.03
0.37
1.56
0.89
0.31
0.97
1.45
3.97
1.35
40.87
11.16
10.0
5.0
0.0
ppm (f1)


TrtHN
OH
O
O
H
N
O
N
H
OH
O
HO
O
NH2

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


NH2
OH
O
O
H
N
O
O
N
H
O
C9H19
N
H
O
HO
O
NH2
-0.03
0.40
0.33
2.20
1.21
1.86
1.73
0.25
0.70
0.80
1.35
3.69
1.69
1.61
29.89
10.00
10.0
ppm (t1)
5.0
0.0

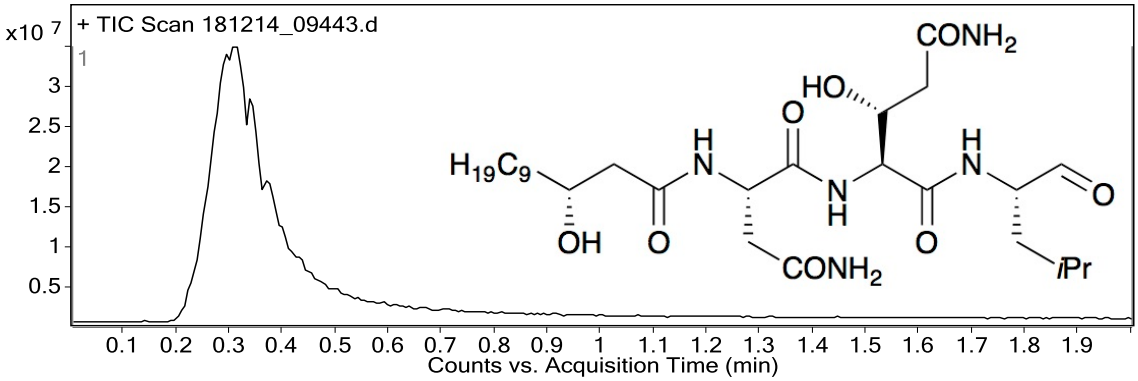

H2N
O
OH
O
H
N
O
N
H
O
O
HO
O
NH2

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

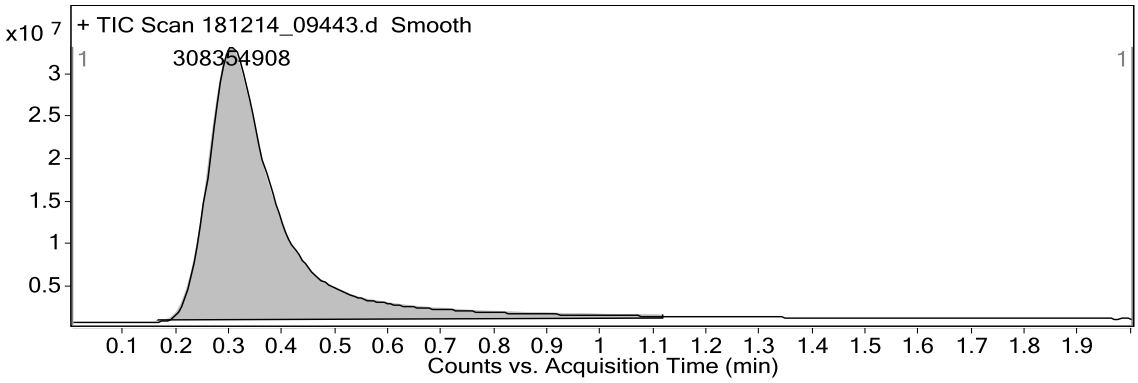
Qualitative Analysis Report

Data Filename	181214_09443.d	**Sample Name**	fid-final
Sample Type	Unknown	**Position**	P1-E-04
Instrument Name	UCR Chem TOF	**User Name**	Pirrings Account for NIH
Acq Method	MM_MIXED_FI_POS.M	**IRM Calibration Status**	Success
DA Method	DA_QUAL_ALL PURPOSE.M	**Comment**	FN|Easy-Access Method: 'FI MM Mixed positive ion'|C27H49N5O8

Fragmentor Voltage 115 **Ionization Mode** Mixed



Fragmentor Voltage 115 **Ionization Mode** Mixed

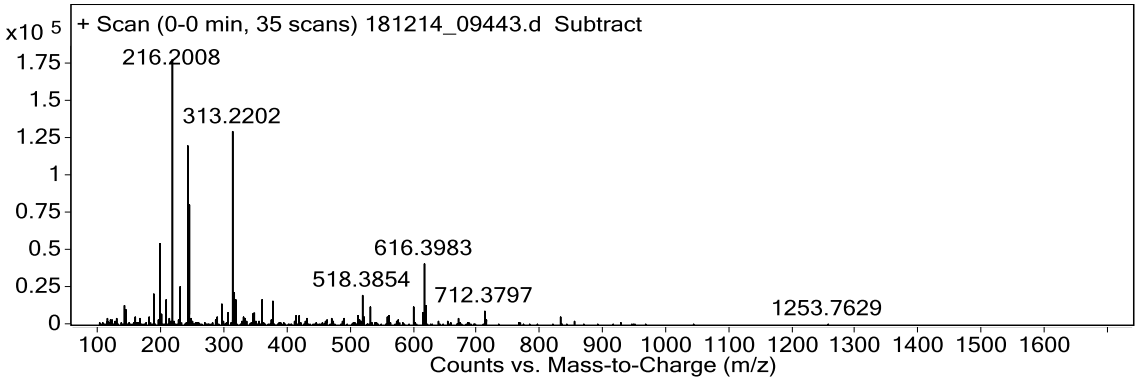


User Spectra

Spectrum Source Peak (1) in "+ TIC Scan Smo"

Fragmentor Voltage 115

Ionization Mode Mixed

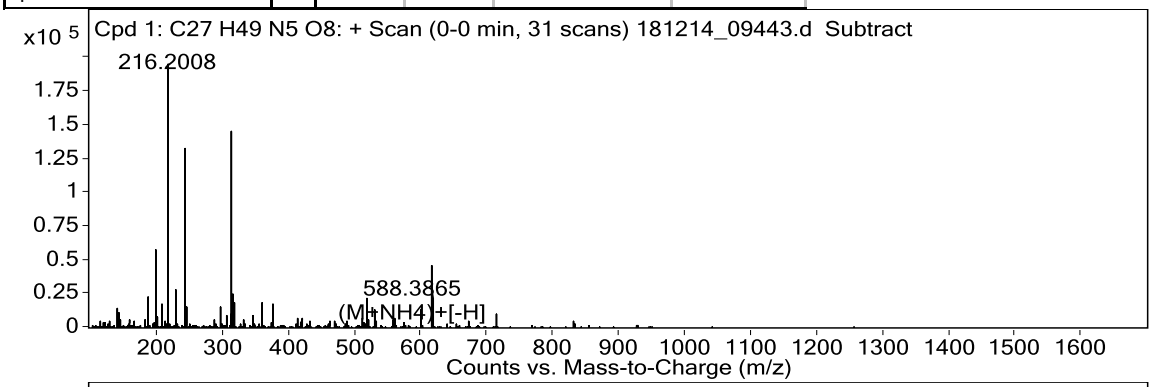


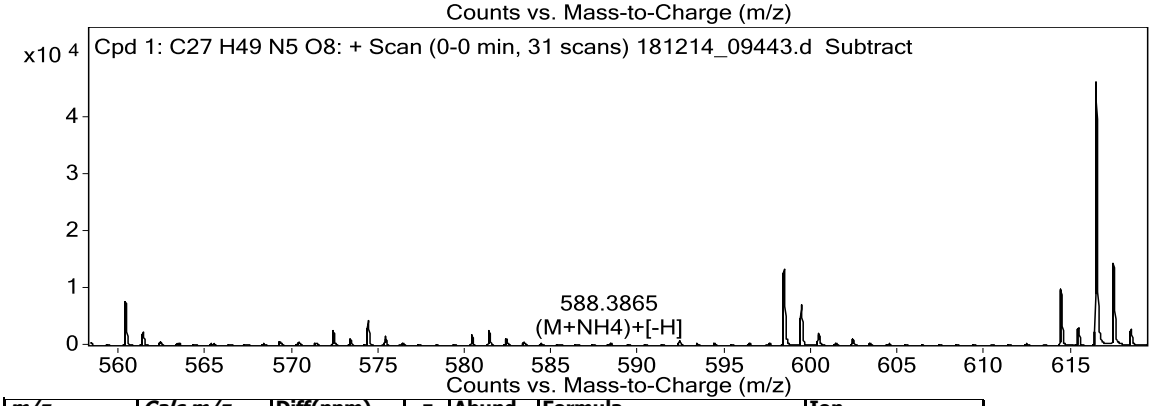
--- End Of Report ---

Formula Confirmation Report

Sample Name	fid-final	**Position**	P1-E-04	**Instrument Name**	UCR Chem TOF
User Name	Pirrings Account for	**Inj Vol**	0.5	**IRM Calibration Status**	Success
Data Filename	181214_09443.d	**ACQ Method**	MM_MIXED_FI_POS.M	**Comment**	FN|Easy-Access Method: 'FI MM Mixed posi
Acquired Time	12/18/2014 1:20:43 PM				

Compound Label	RT	Mass	Abund	Formula	Tgt Mass
Cpd 1: C27 H49 N5 O8	0	571.36	386	C27 H49 N5 O8	571.36



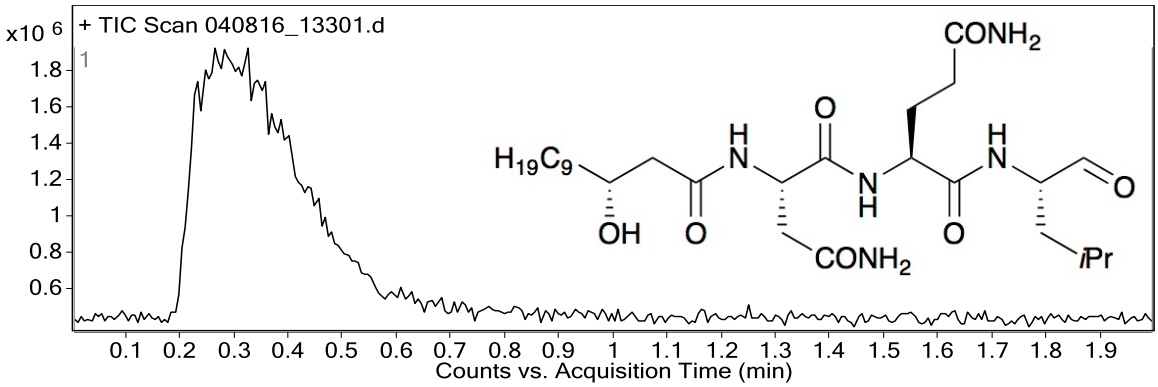


m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
212.0714				5332		
216.2008				195587		
216.3638				6768		
217.2018				24670		
588.3865	588.3841	4.14	1	390	C27 H52 N6 O8	(M+NH4)+[-H]
589.3945	589.3919	4.31	1	302	C27 H53 N6 O8	(M+NH4)+

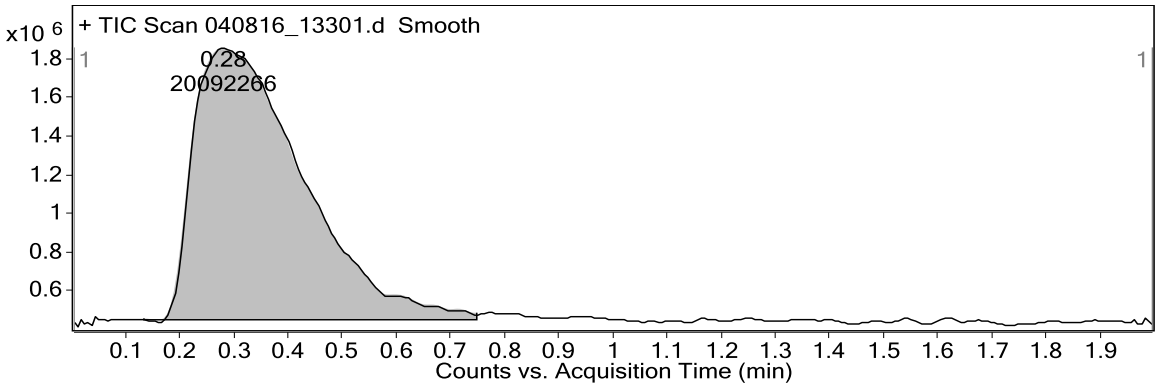
Qualitative Analysis Report

Data Filename	040816_13301.d	**Sample Name**	FZ-2-173
Sample Type	Unknown	**Position**	P1-A-07
Instrument Name	UCR Chem TOF	**User Name**	Pirrungs NSF Account
Acq Method	MM_MIXED_FI_POS.M	**IRM Calibration Status**	Success
DA Method	DA_QUAL_ALL PURPOSE.M	**Comment**	FELLUTAMIDE B|Easy-Access Method: 'FI MM Mixed positive ion'|C27H49N5O7

Fragmentor Voltage 115 **Ionization Mode** Mixed

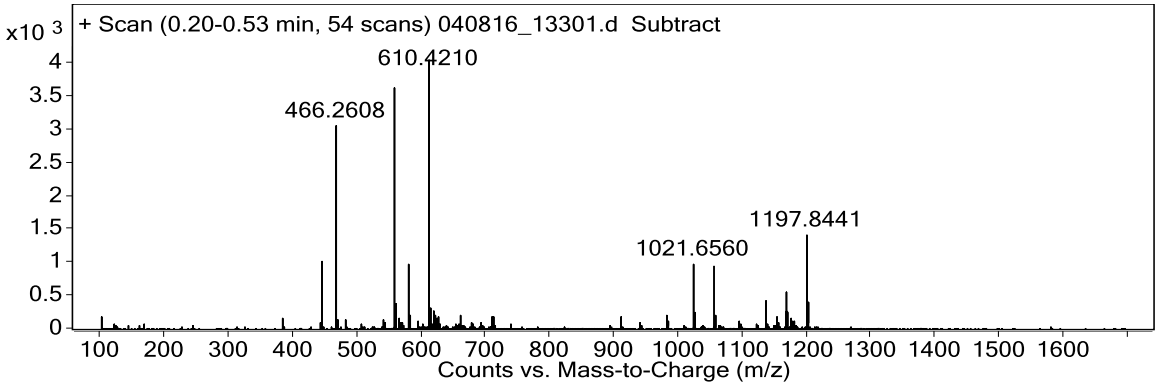


Fragmentor Voltage 115 **Ionization Mode** Mixed



User Spectra

Spectrum Source	**Fragmentor Voltage**	**Ionization Mode**
Peak (1) in "+ TIC Scan Smo"	115	Mixed



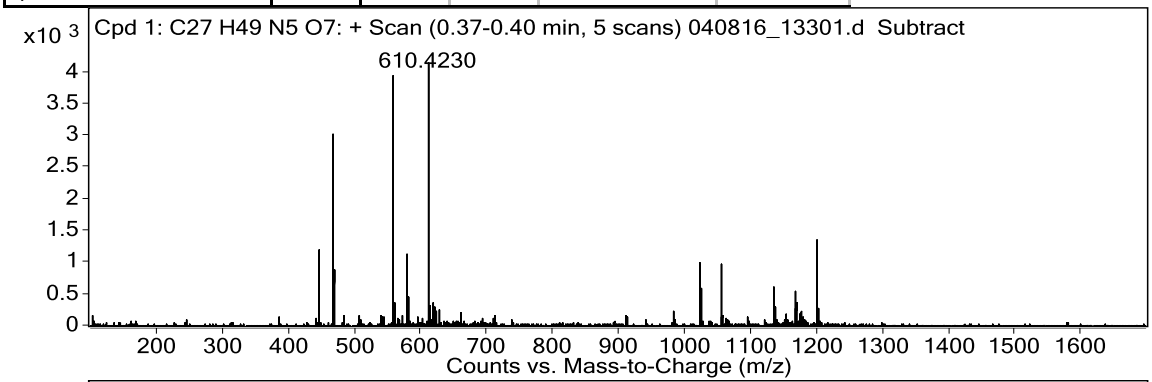
--- End Of Report ---

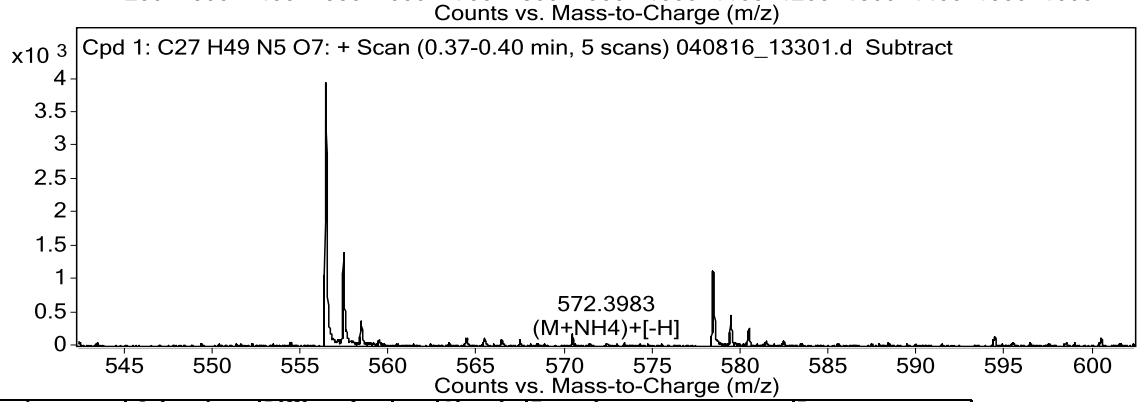
Formula Confirmation Report

Sample Name	FZ-2-173	**Position**	P1-A-07	**Instrument Name**	UCR Chem TOF
User Name	Pirrungs NSF Account	**Inj Vol**	0.5	**IRM Calibration Status**	Success
Data Filename	040816_13301.d	**ACQ Method**	MM_MIXED_FI_POS.M	**Comment**	FELLUTAMIDE B|Easy-Access Method: 'FI MM

Acquired Time 8/4/2016 2:47:03 PM

Compound Label	RT	Mass	Abund	Formula	Tgt Mass
Cpd 1: C27 H49 N5 O7	0.38	555.37	50	C27 H49 N5 O7	555.36



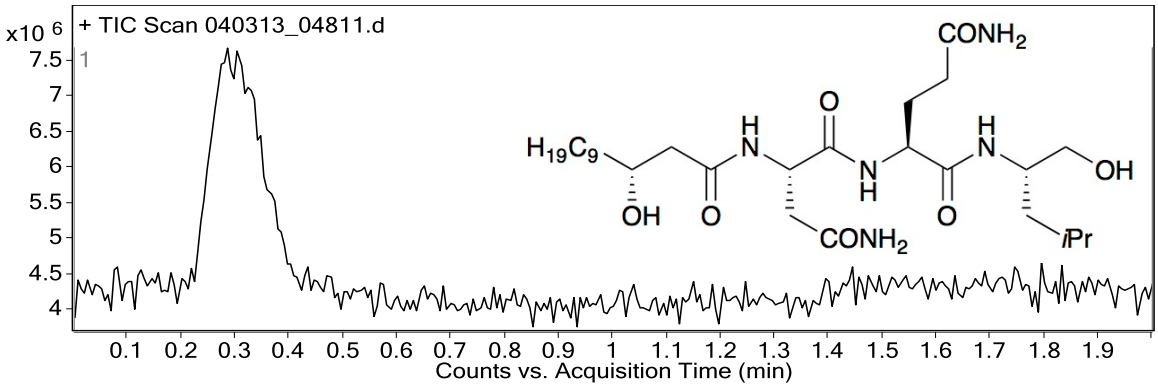


m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
572.3983	572.3892	15.93	1	52	C27 H52 N6 O7	(M+NH4)+[-H]
610.423				4142		
610.8688				183		
610.9545				198		
611.4226				1338		
612.4376				346		

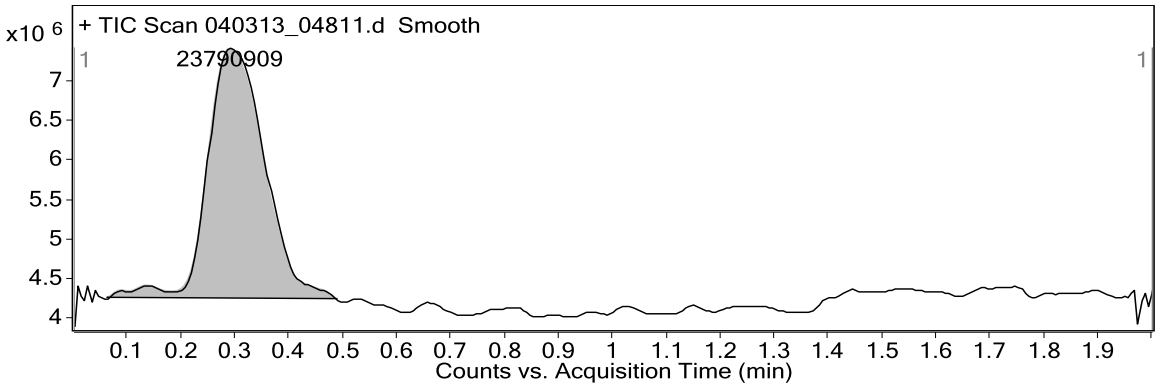
Qualitative Analysis Report

Data Filename	040313_04811.d	**Sample Name**	FZ-2-175
Sample Type	Unknown	**Position**	P1-A-01
Instrument Name	UCR Chem TOF	**User Name**	Pirrungs DOD Acct.
Acq Method	MM_MIXED_FI_POS.M	**IRM Calibration Status**	Success
DA Method	DA_QUAL_ALL PURPOSE.M	**Comment**	Fellutamide C|Easy-Access Method: 'FI MM Mixed positive ion'|C27H51N5O7

Fragmentor Voltage 115 **Ionization Mode** Mixed



Fragmentor Voltage 115 **Ionization Mode** Mixed

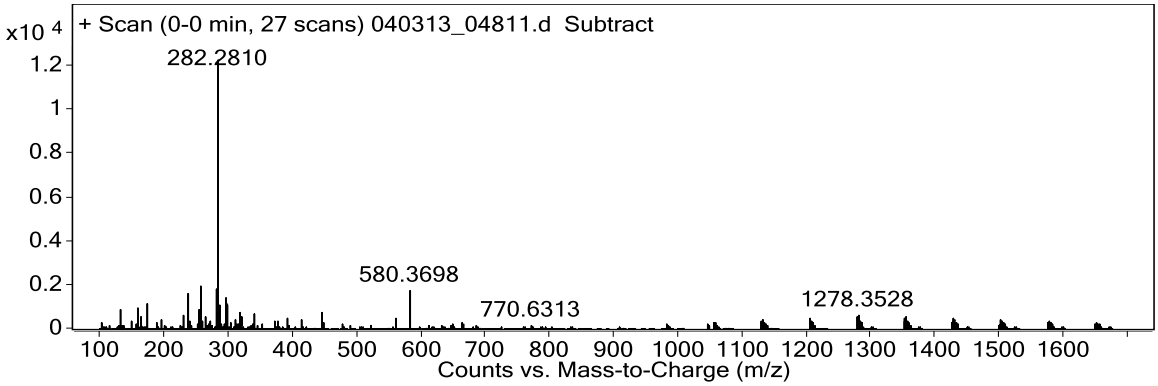


User Spectra

Spectrum Source Peak (1) in "+ TIC Scan Smo"

Fragmentor Voltage 115

Ionization Mode Mixed

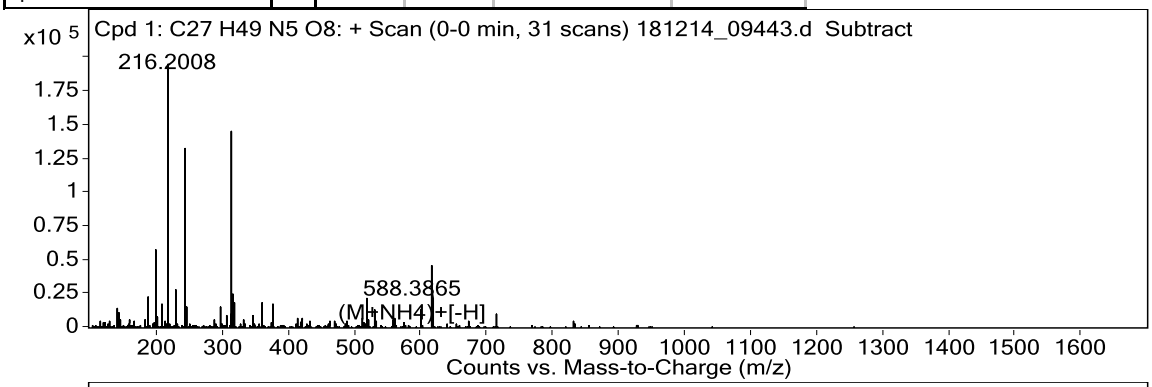


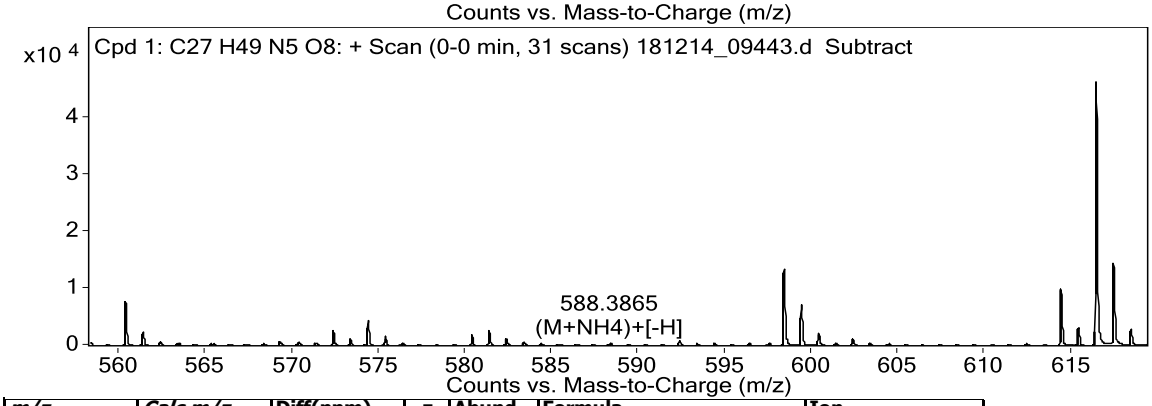
--- End Of Report ---

Formula Confirmation Report

Sample Name	fid-final	**Position**	P1-E-04	**Instrument Name**	UCR Chem TOF
User Name	Pirrings Account for	**Inj Vol**	0.5	**IRM Calibration Status**	Success
Data Filename	181214_09443.d	**ACQ Method**	MM_MIXED_FI_POS.M	**Comment**	FN|Easy-Access Method: 'FI MM Mixed posi
Acquired Time	12/18/2014 1:20:43 PM				

Compound Label	RT	Mass	Abund	Formula	Tgt Mass
Cpd 1: C27 H49 N5 O8	0	571.36	386	C27 H49 N5 O8	571.36





m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
212.0714				5332		
216.2008				195587		
216.3638				6768		
217.2018				24670		
588.3865	588.3841	4.14	1	390	C27 H52 N6 O8	(M+NH4)+[-H]
589.3945	589.3919	4.31	1	302	C27 H53 N6 O8	(M+NH4)+