Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
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Supporting Information

Total synthesis of the natural HDAC inhibitor Cyl-1

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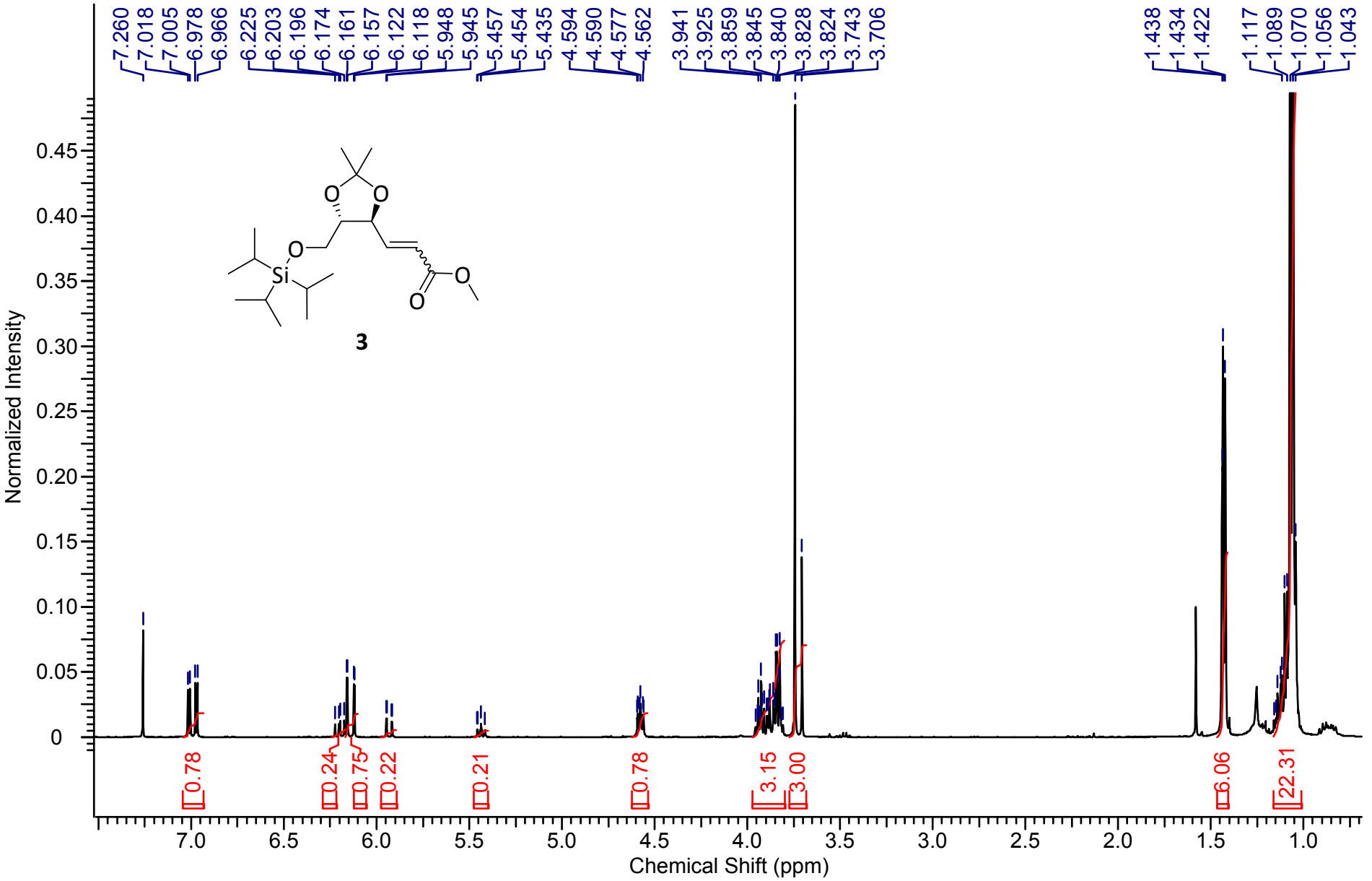
Institute for Organic Chemistry, Saarland University, 66123 Saarbrücken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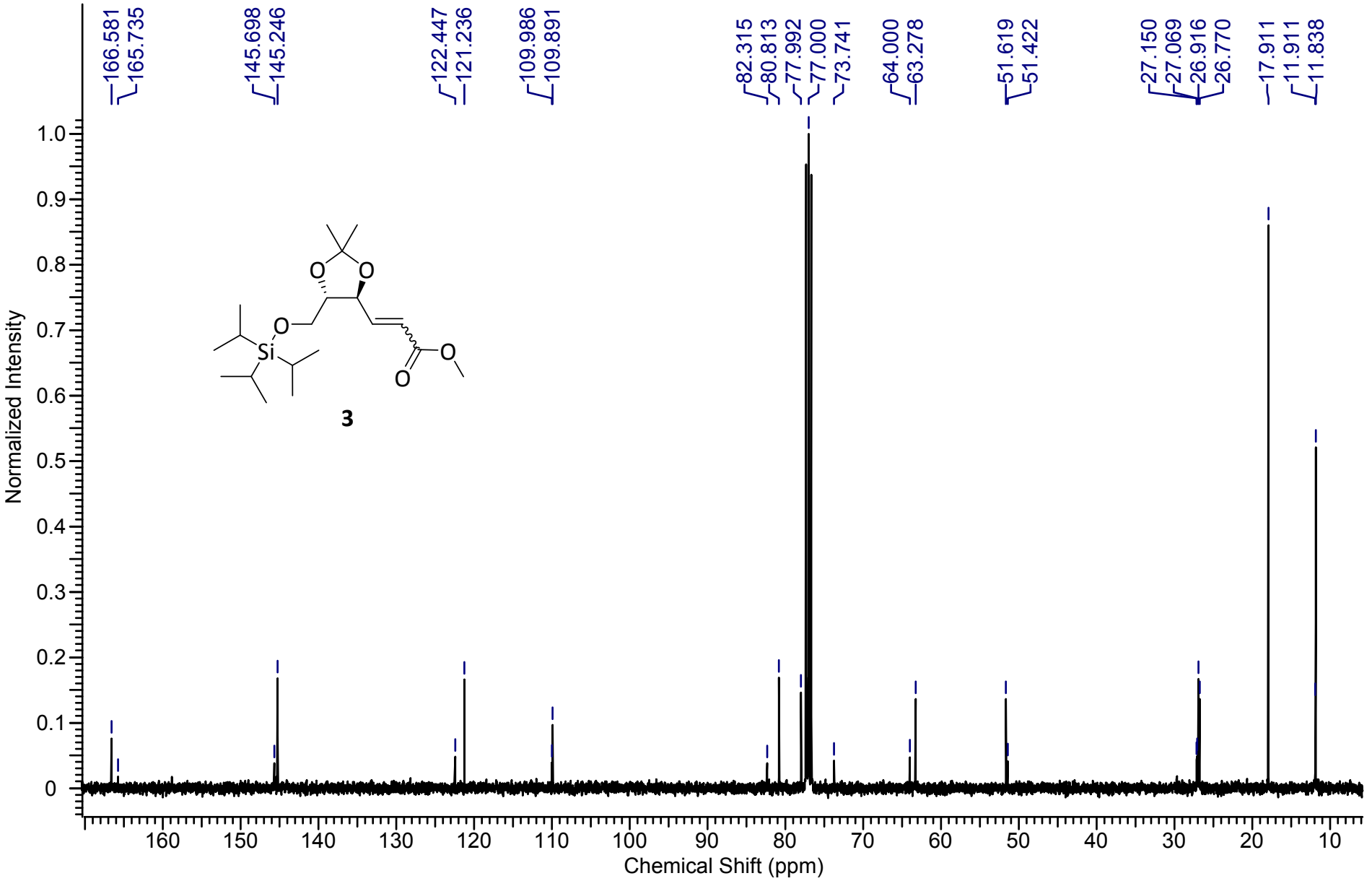
6.161
6.157
6.122
6.118
5.948
5.945
5.457
5.454
5.435
4.594
4.590
4.577
4.562
3.941
3.925
3.859
3.845
3.840
3.828
3.824
3.743
3.706
1.438
1.434
1.422
1.117
1.089
1.070
1.056
1.043
O
O
O
Si
O
O
3
Normalized Intensity
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.78
0.24
0.75
0.22
0.21
0.78
3.15
3.00
6.06
22.31
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
Chemical Shift (ppm)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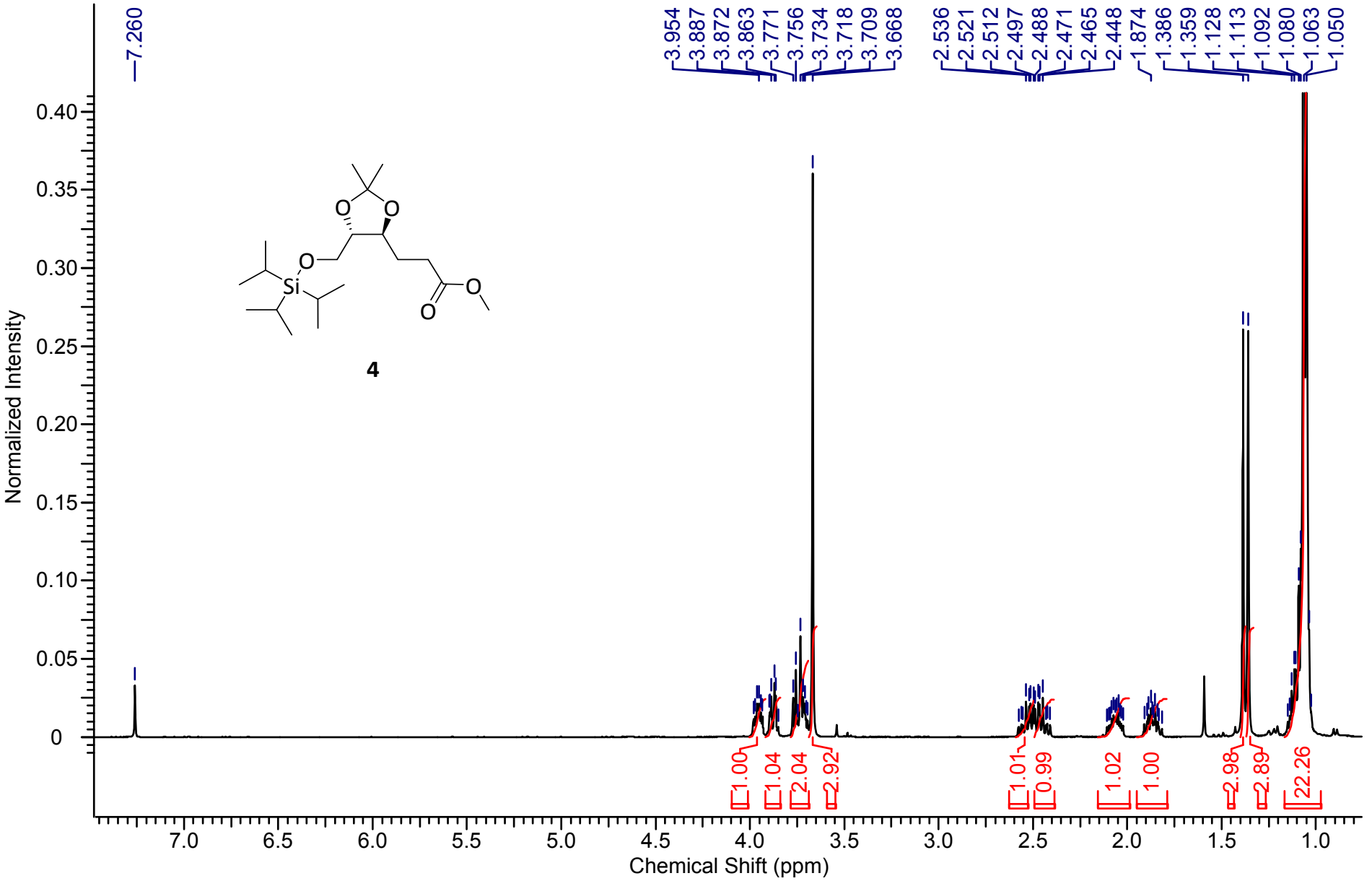
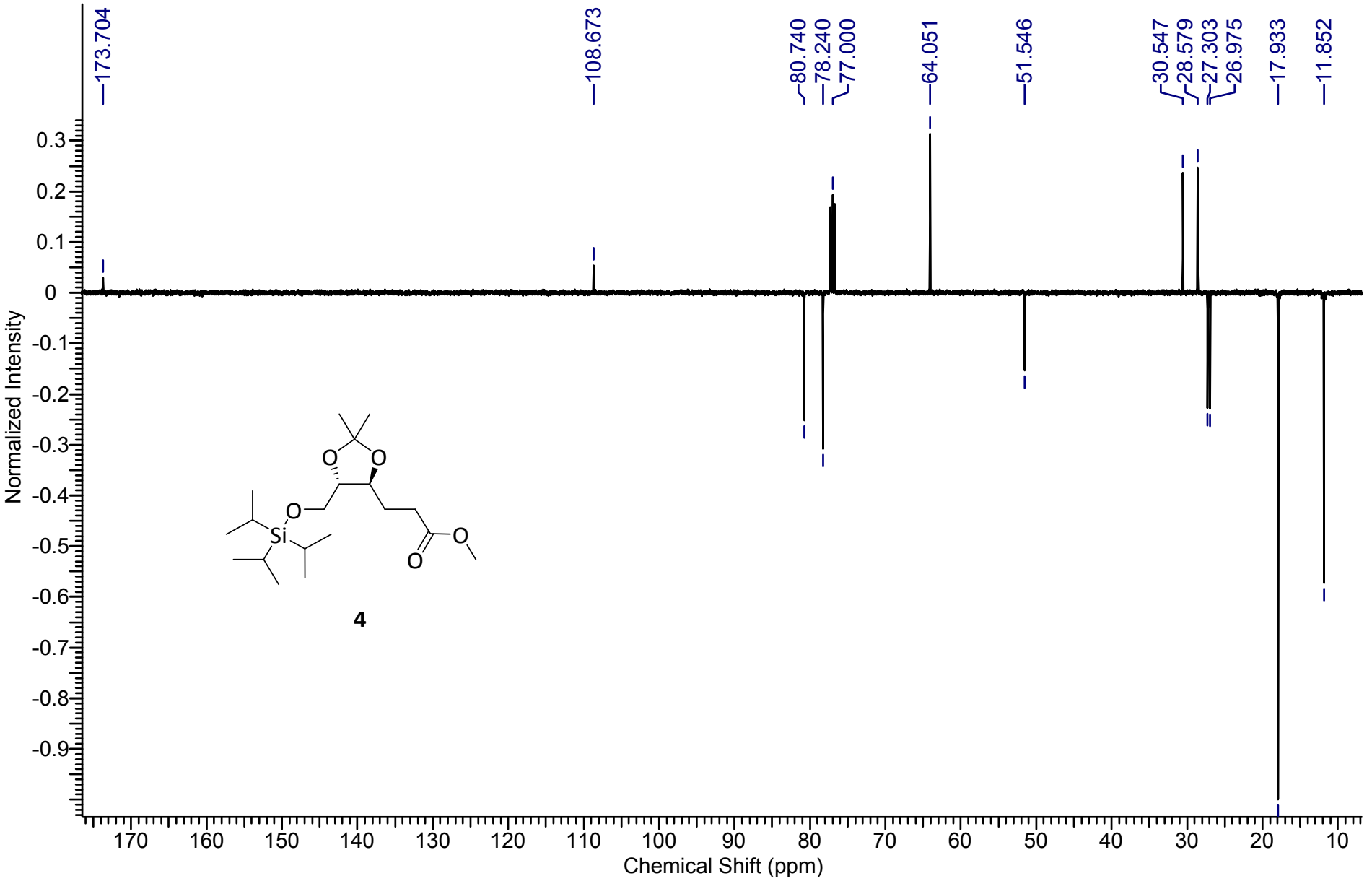
145.698
145.246
122.447
121.236
109.986
109.891
82.315
80.813
77.992
77.000
73.741
64.000
63.278
51.619
51.422
27.150
27.069
26.916
26.770
17.911
11.911
11.838
Normalized Intensity
Chemical Shift (ppm)
3


7.260
3.954
3.887
3.872
3.863
3.771
3.756
3.734
3.718
3.709
3.668
2.536
2.521
2.512
2.497
2.488
2.471
2.465
2.448
1.874
1.386
1.359
1.128
1.113
1.092
1.080
1.063
1.050
Normalized Intensity
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.00
1.04
2.04
2.92
1.01
0.99
1.02
1.00
2.98
2.89
22.26
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
Chemical Shift (ppm)
O
O
O
Si
O
O
O

4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108.673
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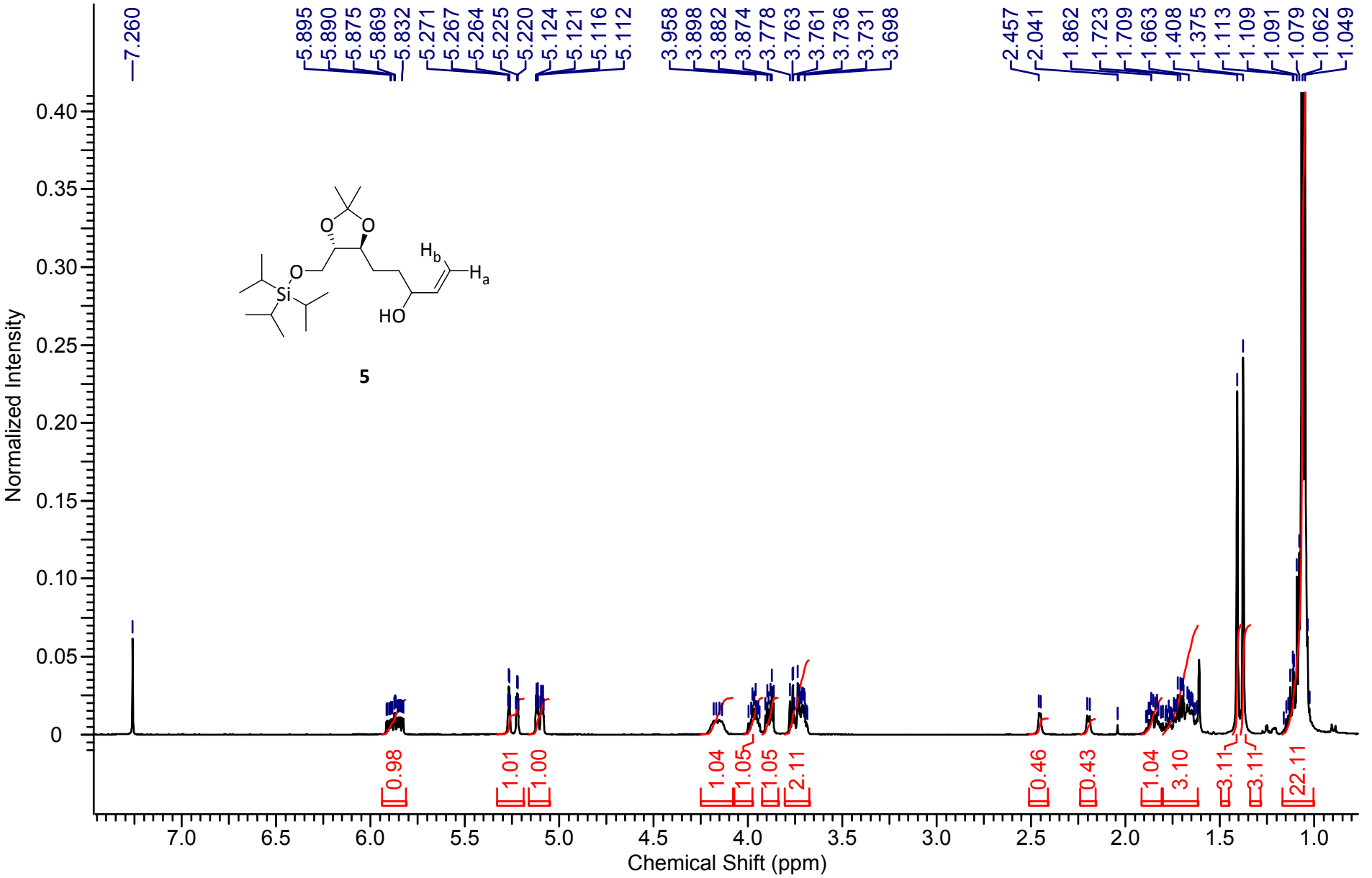
78.240
77.000
64.051
51.546
30.547
28.579
27.303
26.975
17.933
11.852
Normalized Intensity
Chemical Shift (ppm)
O
O
O
Si
O
O

4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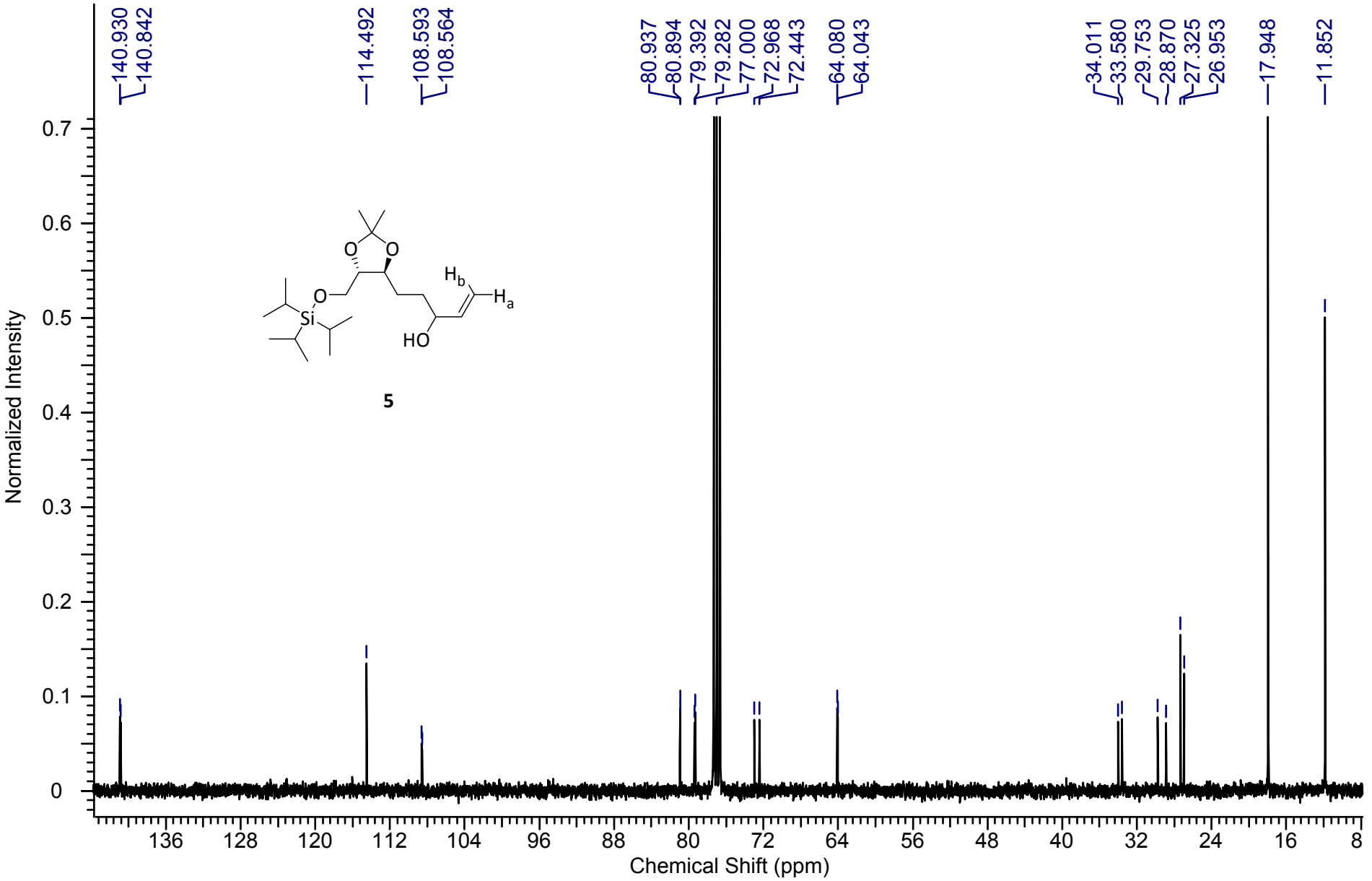
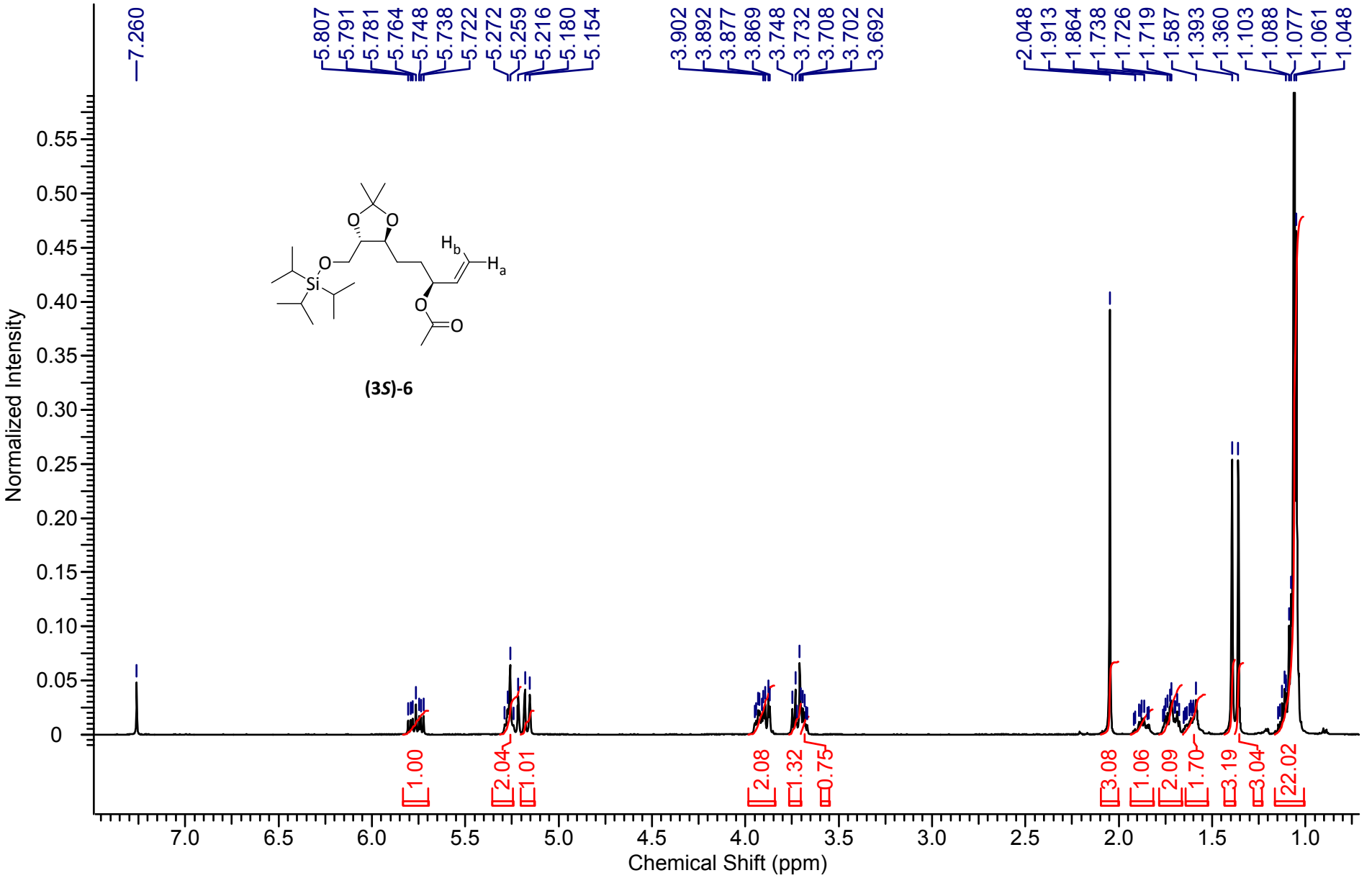
5.895
5.890
5.875
5.869
5.832
5.271
5.267
5.264
5.225
5.220
5.124
5.121
5.116
5.112
3.958
3.898
3.882
3.874
3.778
3.763
3.761
3.736
3.731
3.698
2.457
2.041
1.862
1.723
1.709
1.663
1.408
1.375
1.113
1.109
1.091
1.079
1.062
1.049
Normalized Intensity
Chemical Shift (ppm)
0.98
1.01
1.00
1.04
1.05
1.05
2.11
0.46
0.43
1.04
3.10
3.11
3.11
22.11
O
O
O
Si
HO
Hb
Ha

5


140.930
140.842
114.492
108.593
108.564
80.937
80.894
79.392
79.282
77.000
72.968
72.443
64.080
64.043
34.011
33.580
29.753
28.870
27.325
26.953
17.948
11.852
Normalized Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)
O
O
O
Si
HO
H_b
H_a
5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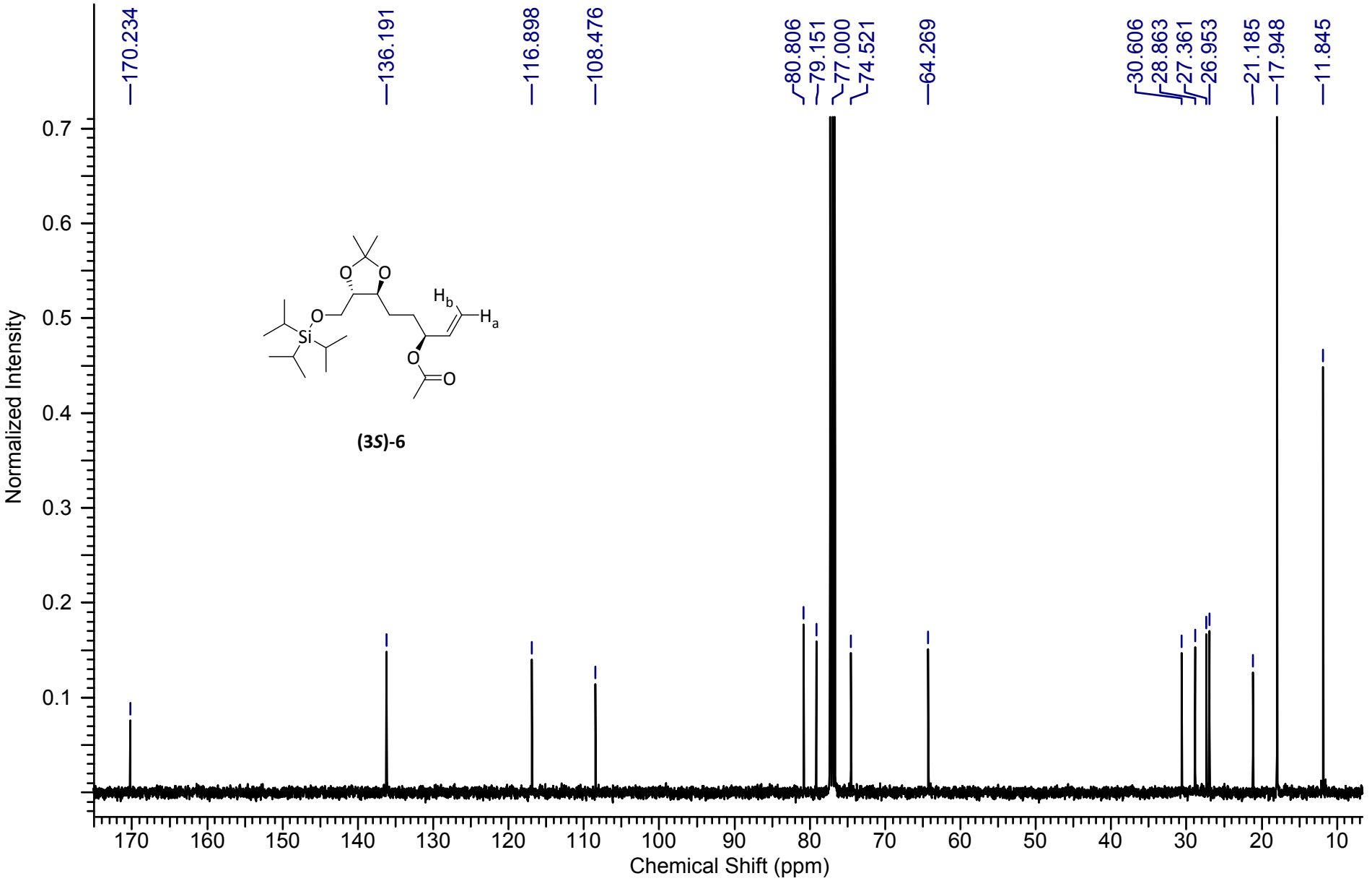
5.807
5.791
5.781
5.764
5.748
5.738
5.722
5.272
5.259
5.216
5.180
5.154
3.902
3.892
3.877
3.869
3.748
3.732
3.708
3.702
3.692
2.048
1.913
1.864
1.738
1.726
1.719
1.587
1.393
1.360
1.103
1.088
1.077
1.061
1.048
Normalized Intensity
Chemical Shift (ppm)
1.00
2.04
1.01
2.08
1.32
0.75
3.08
1.06
2.09
1.70
3.19
3.04
22.02
Si
O
O
O
O
H_b
H_a

(3*S*)-6


170.234
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116.898
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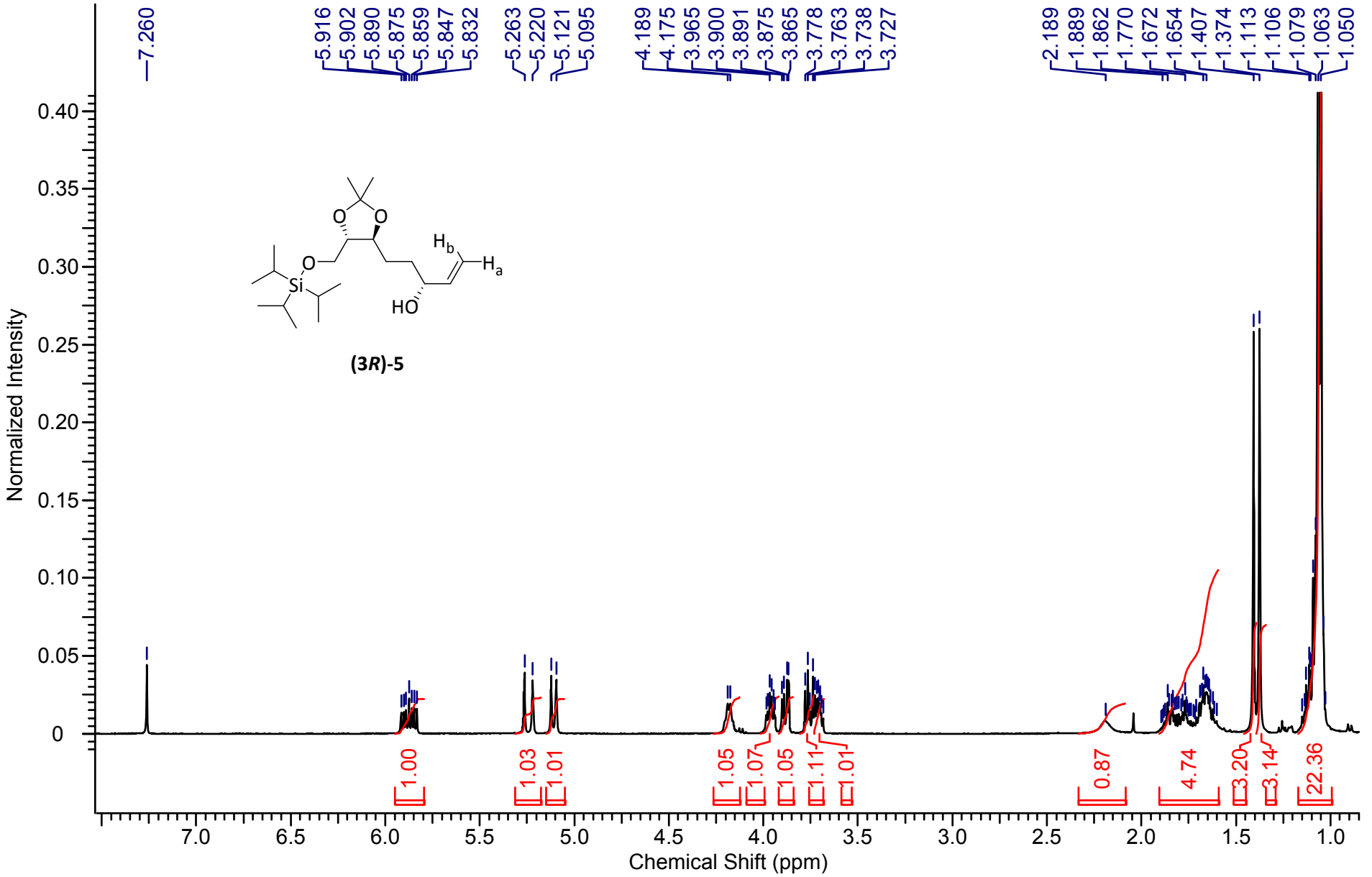
80.806
79.151
77.000
74.521
64.269
30.606
28.863
27.361
26.953
21.185
17.948
11.845
Normalized Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)
O
O
O
Si
H_b
H_a
O
O

(3*S*)-6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5.916
5.902
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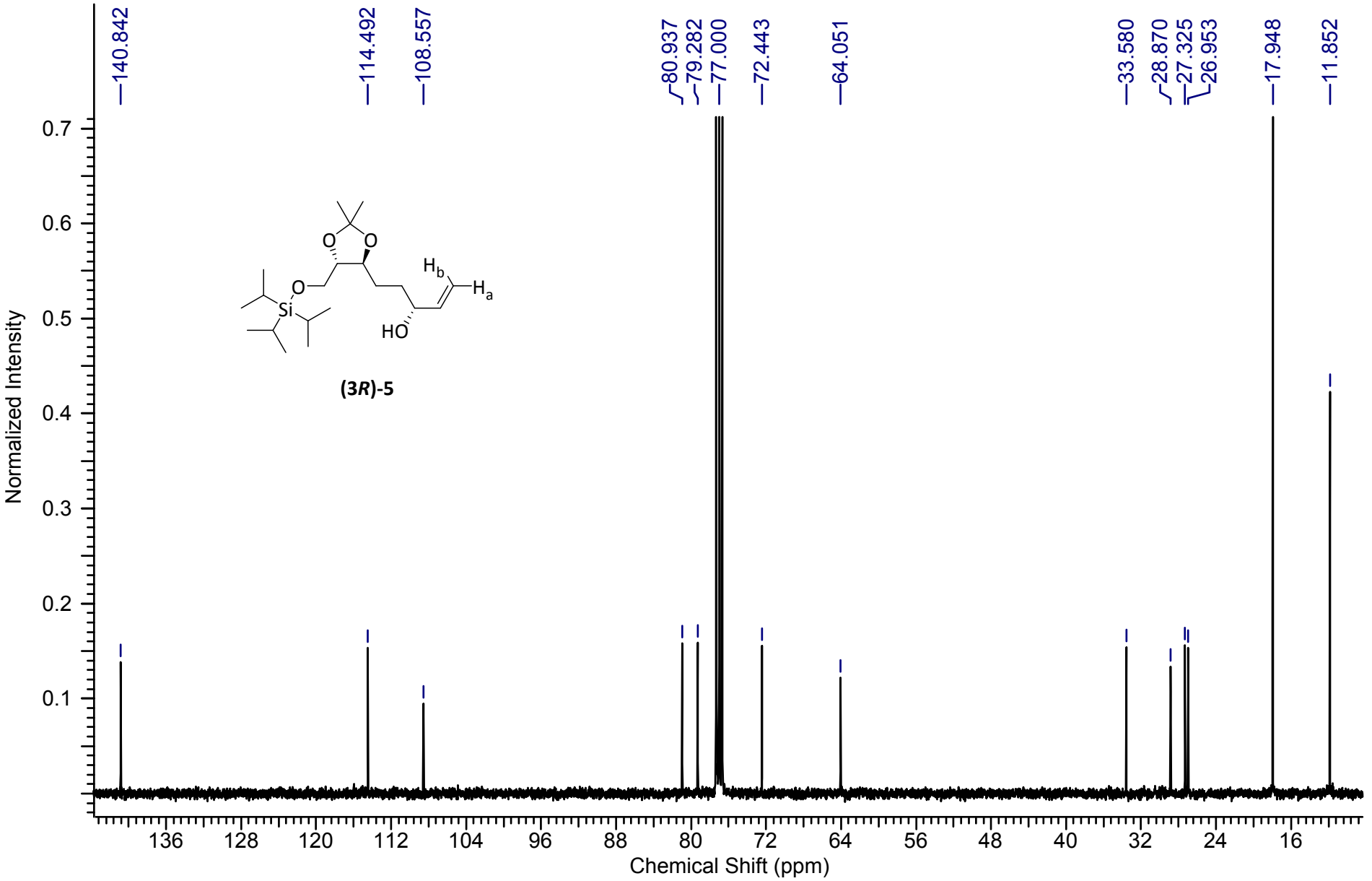
5.875
5.859
5.847
5.832
5.263
5.220
5.121
5.095
4.189
4.175
3.965
3.900
3.891
3.875
3.865
3.778
3.763
3.738
3.727
2.189
1.889
1.862
1.770
1.672
1.654
1.407
1.374
1.113
1.106
1.079
1.063
1.050
O
O
O
Si
HO
H_b
H_a
(3R)-5
Normalized Intensity
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.00
1.03
1.01
1.05
1.07
1.05
1.11
1.01
0.87
4.74
3.20
3.14
22.36
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
Chemical Shift (ppm)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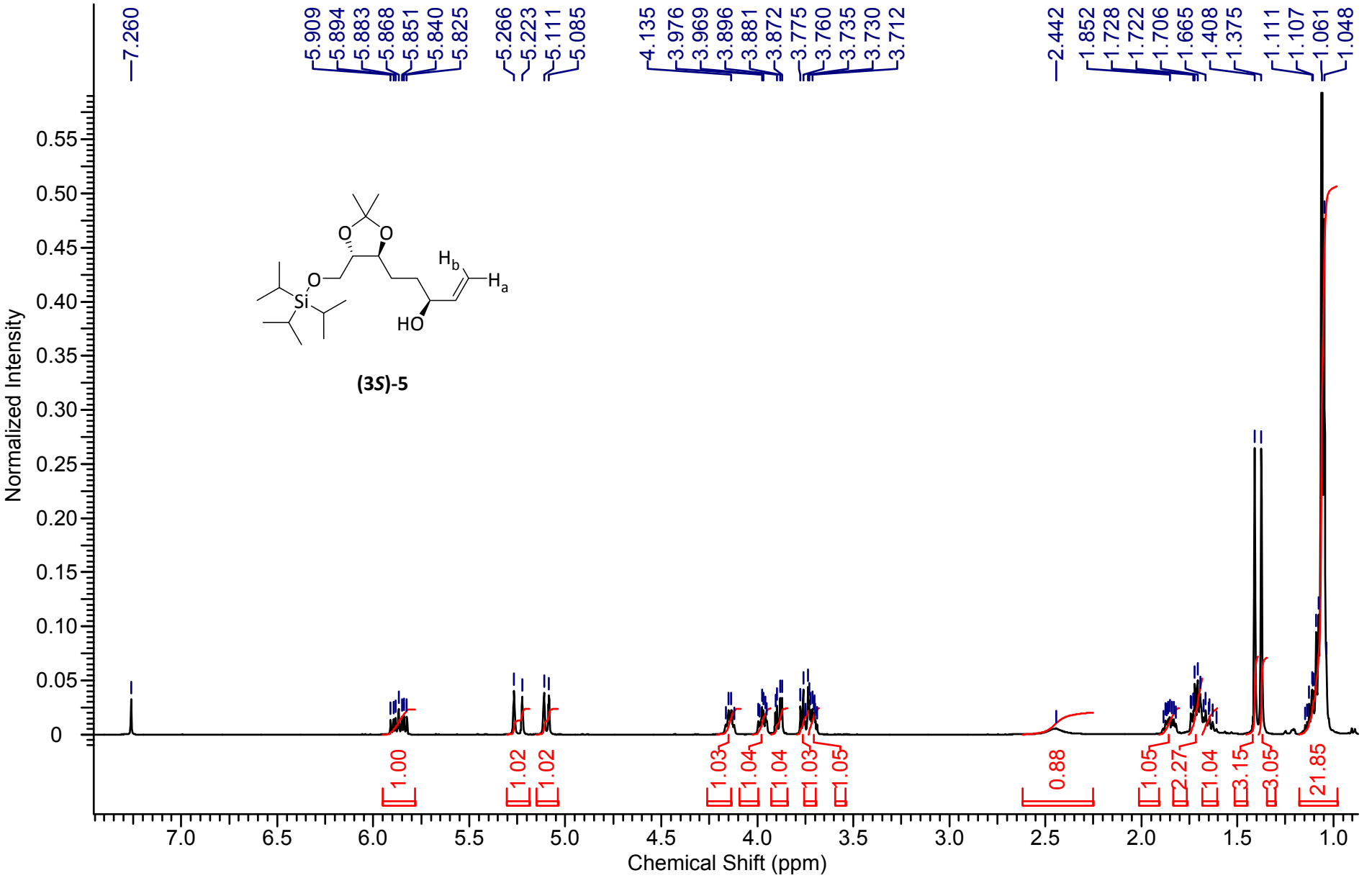
114.492
108.557
80.937
79.282
77.000
72.443
64.051
33.580
28.870
27.325
26.953
17.948
11.852
Normalized Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)
O
O
O
Si
HO
H_b
H_a

(3*R*)-5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5.851
5.840
5.825
5.266
5.223
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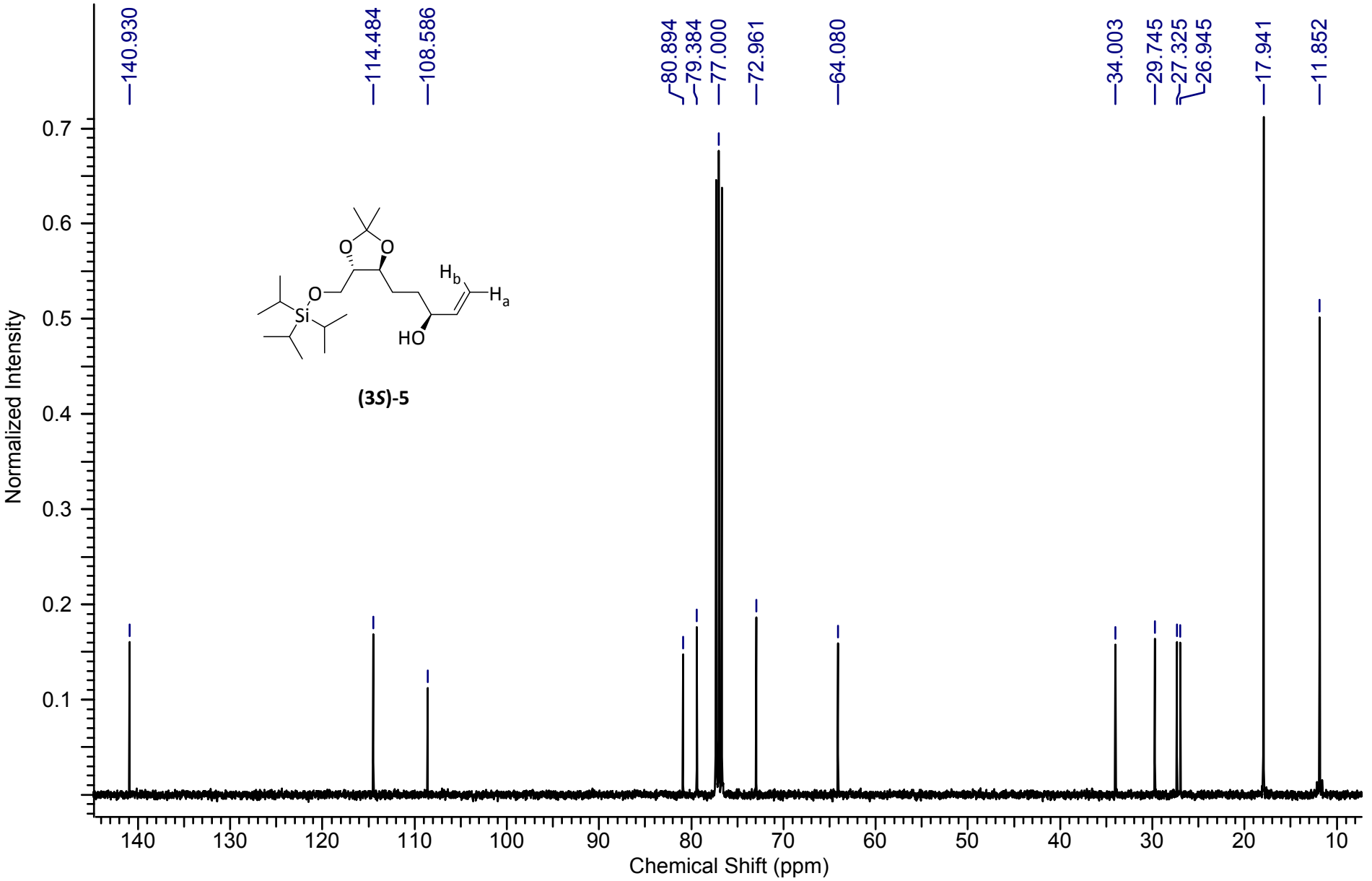
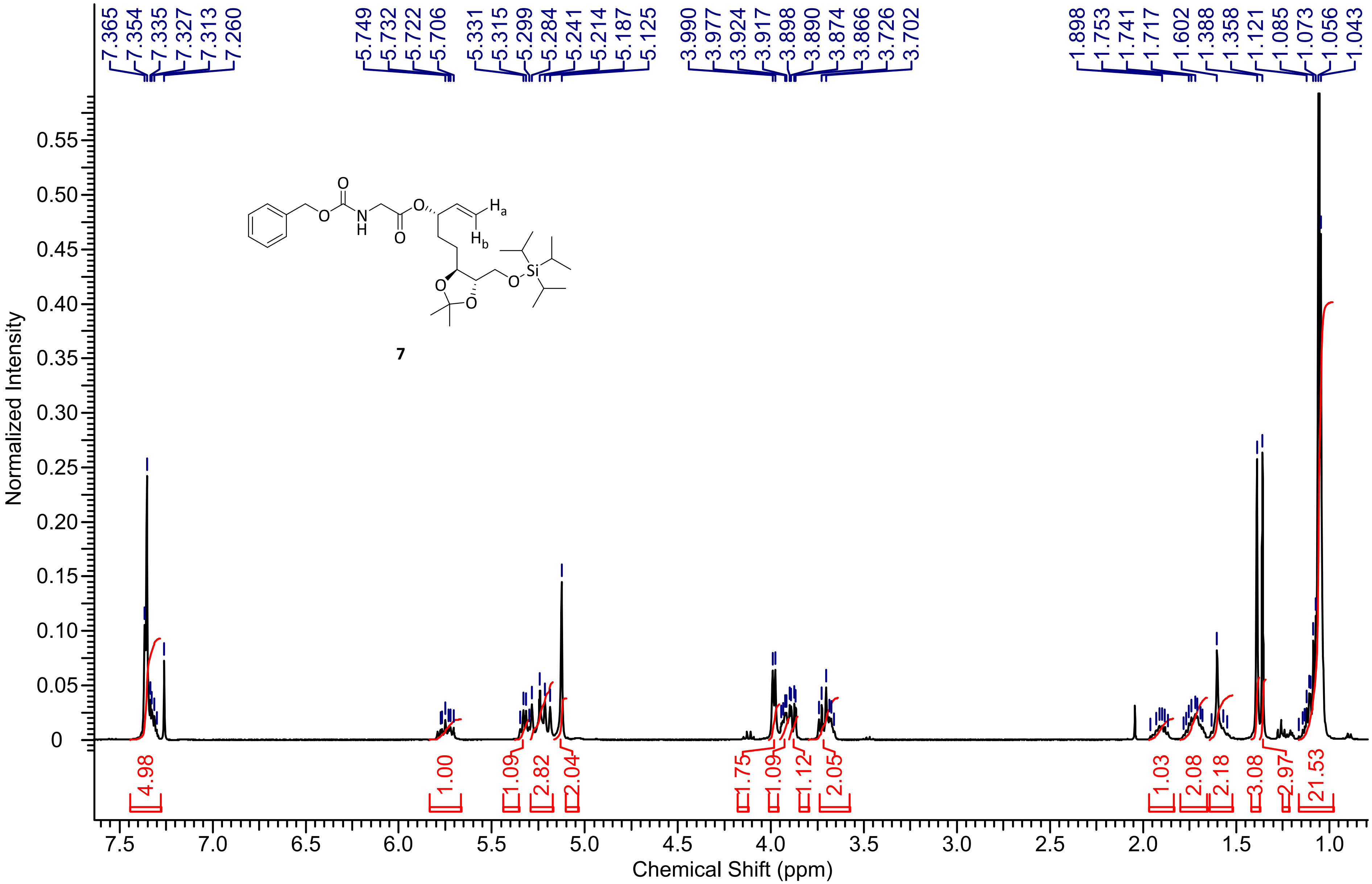
5.085
4.135
3.976
3.969
3.896
3.881
3.872
3.775
3.760
3.735
3.730
3.712
2.442
1.852
1.728
1.722
1.706
1.665
1.408
1.375
1.111
1.107
1.061
1.048
Normalized Intensity
Chemical Shift (ppm)
1.00
1.02
1.02
1.03
1.04
1.04
1.03
1.05
0.88
1.05
2.27
1.04
3.15
3.05
21.85
O
O
O
Si
HO
Hb
Ha

(3*S*)-5


140.930
114.484
108.586
80.894
79.384
77.000
72.961
64.080
34.003
29.745
27.325
26.945
17.941
11.852
Normalized Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)
O
O
O
Si
HO
Hb
Ha

(3*S*)-5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7.313
7.260
5.749
5.732
5.722
5.706
5.331
5.315
5.299
5.284
5.241
5.214
5.187
5.125
3.990
3.977
3.924
3.917
3.898
3.890
3.874
3.866
3.726
3.702
1.898
1.753
1.741
1.717
1.602
1.388
1.358
1.121
1.085
1.073
1.056
1.043
Normalized Intensity
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
7
4.98
1.00
1.09
2.82
2.04
1.75
1.09
1.12
2.05
1.03
2.08
2.18
3.08
2.97
21.53
7.5
7.0
6.5
6.0
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4.5
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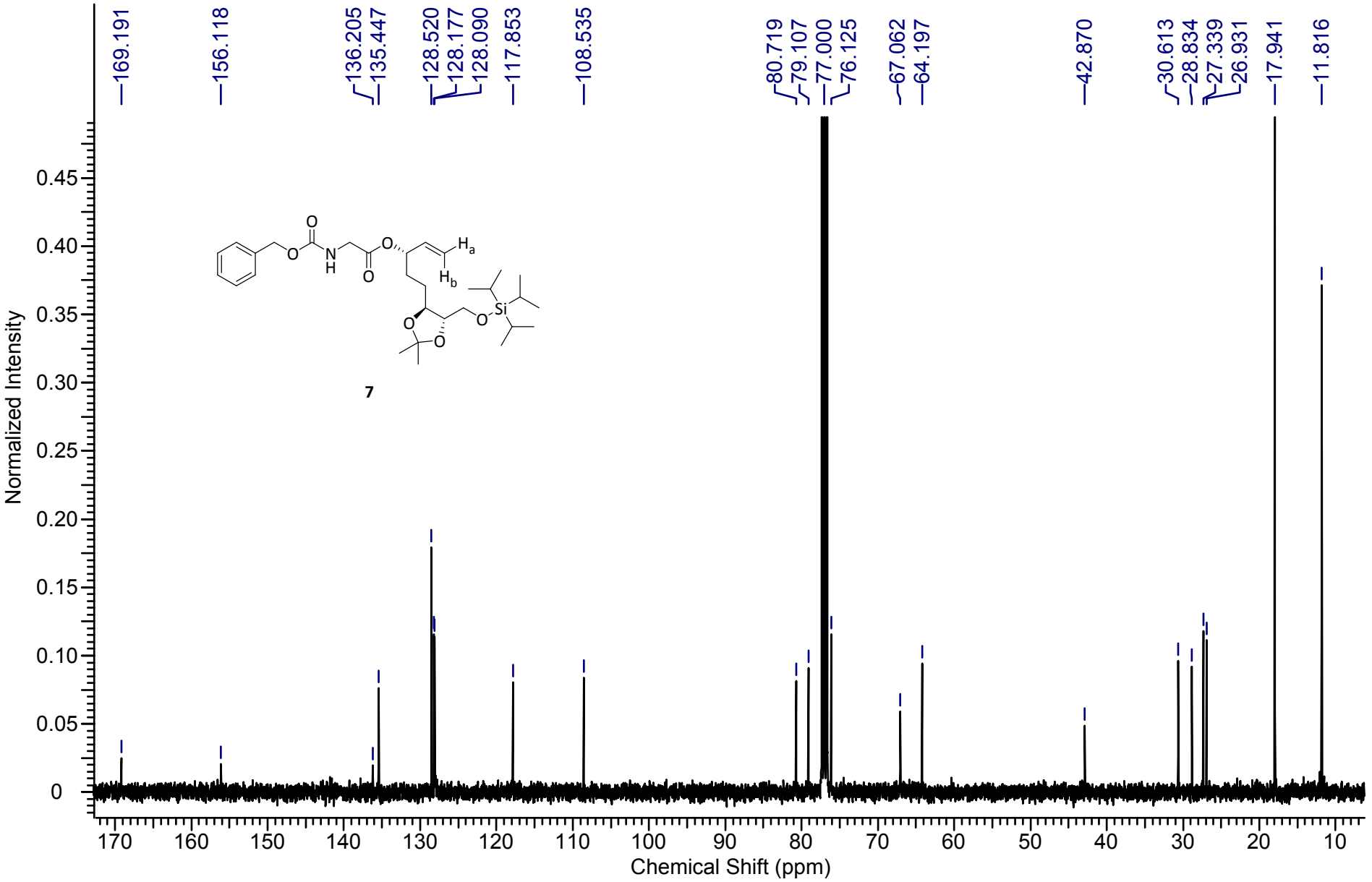
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)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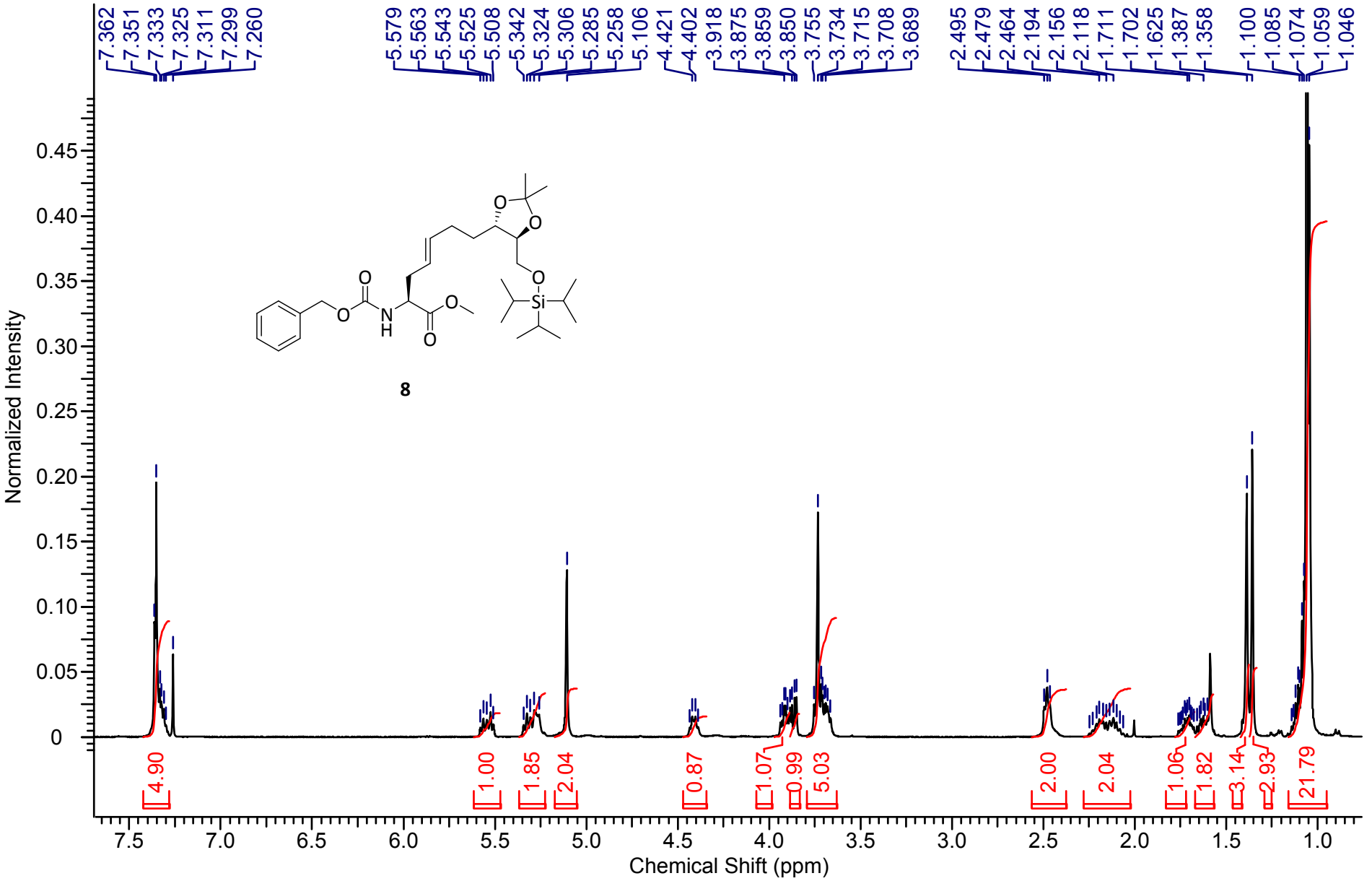
156.118
136.205
135.447
128.520
128.177
128.090
117.853
108.535
80.719
79.107
77.000
76.125
67.062
64.197
42.870
30.613
28.834
27.339
26.931
17.941
11.816
Normalized Intensity
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)
O
N
H
O
O
O
H_a
H_b
O
O
O
Si

7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5.579
5.563
5.543
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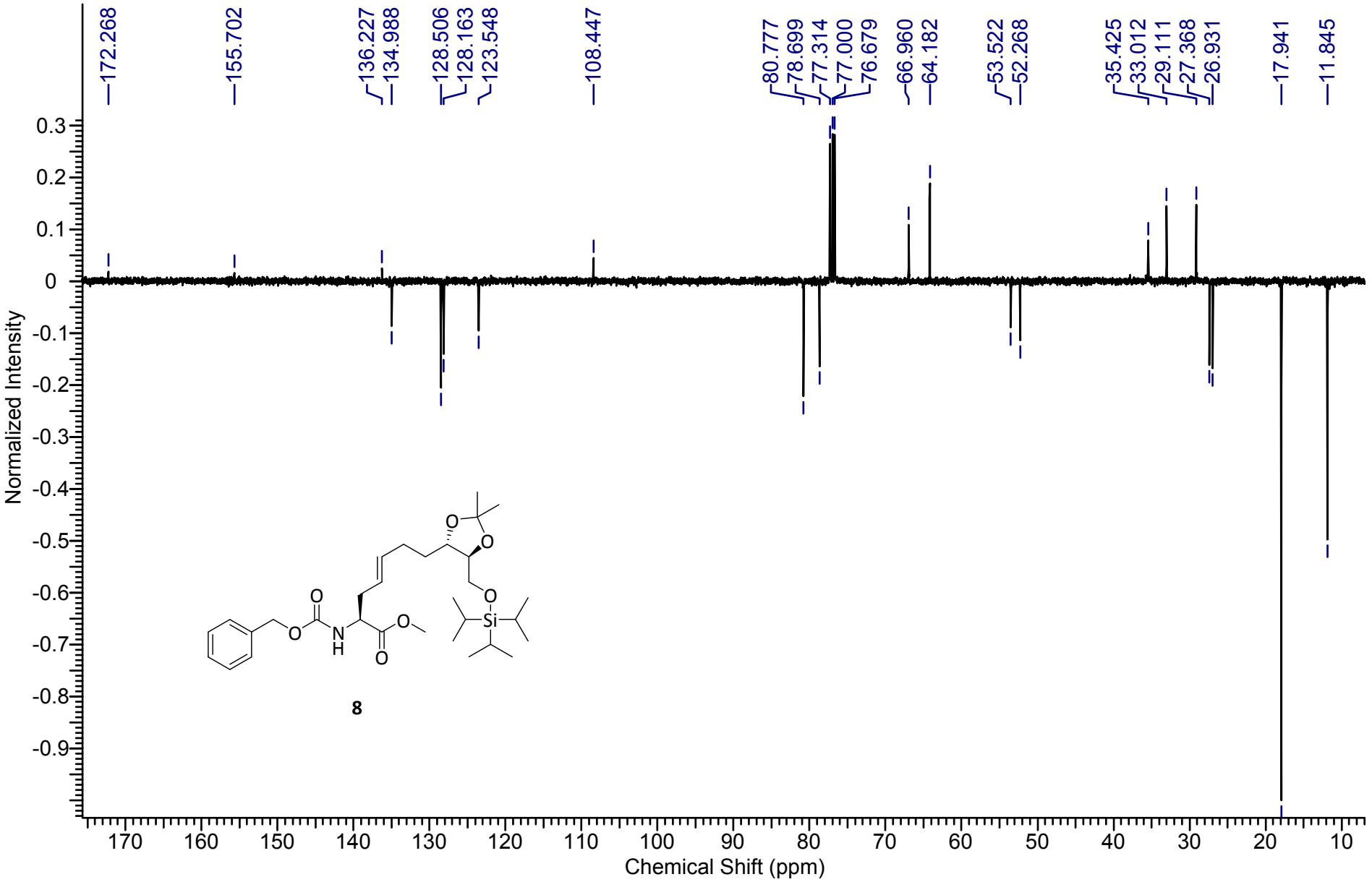
5.508
5.342
5.324
5.306
5.285
5.258
5.106
4.421
4.402
3.918
3.875
3.859
3.850
3.755
3.734
3.715
3.708
3.689
2.495
2.479
2.464
2.194
2.156
2.118
1.711
1.702
1.625
1.387
1.358
1.100
1.085
1.074
1.059
1.046
Normalized Intensity
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
4.90
1.00
1.85
2.04
0.87
1.07
0.99
5.03
2.00
2.04
1.06
1.82
3.14
2.93
21.79
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
Chemical Shift (ppm)
O
O
O
O
N
H
O
O
O
Si

8


172.268
155.702
136.227
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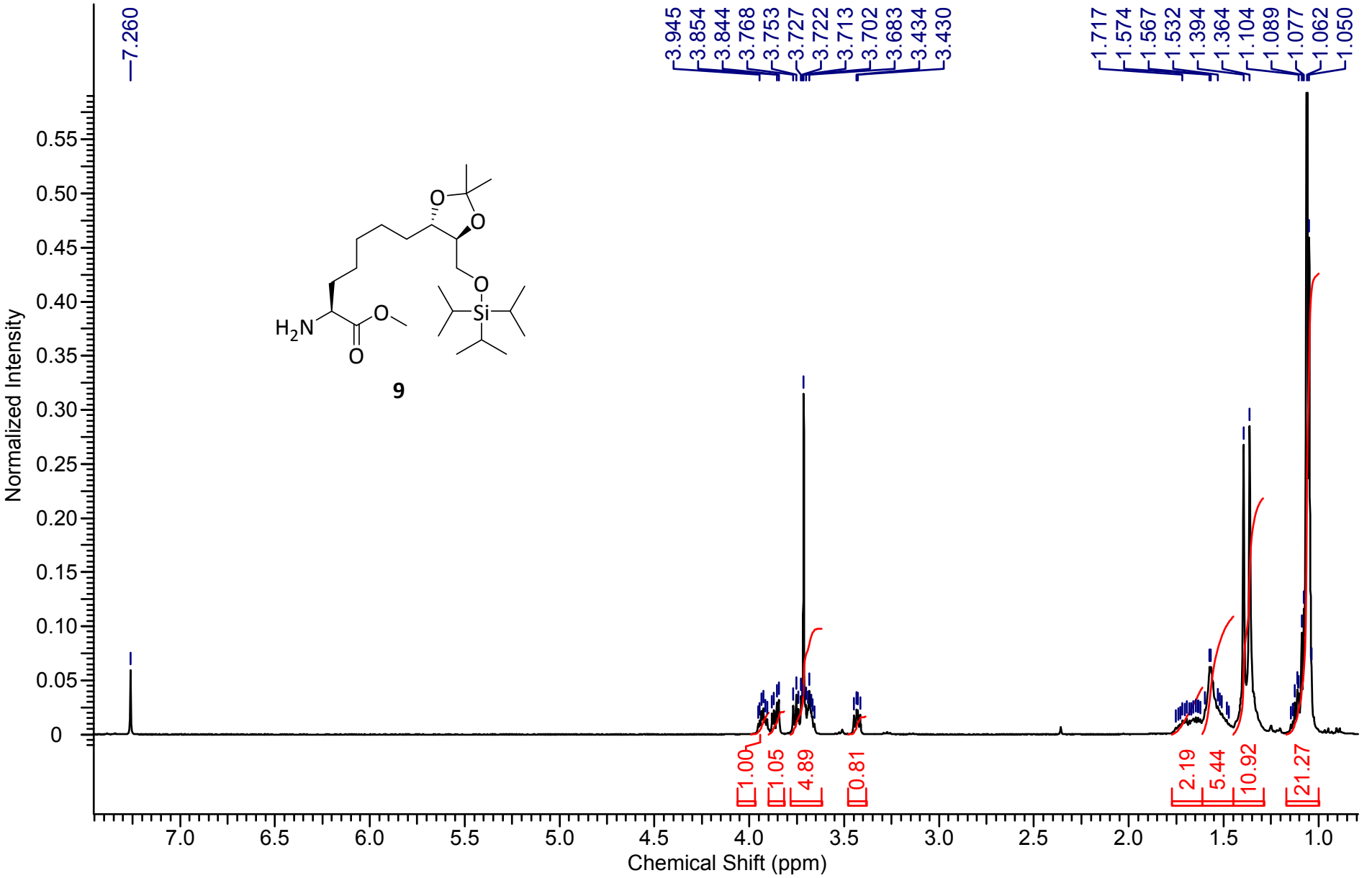
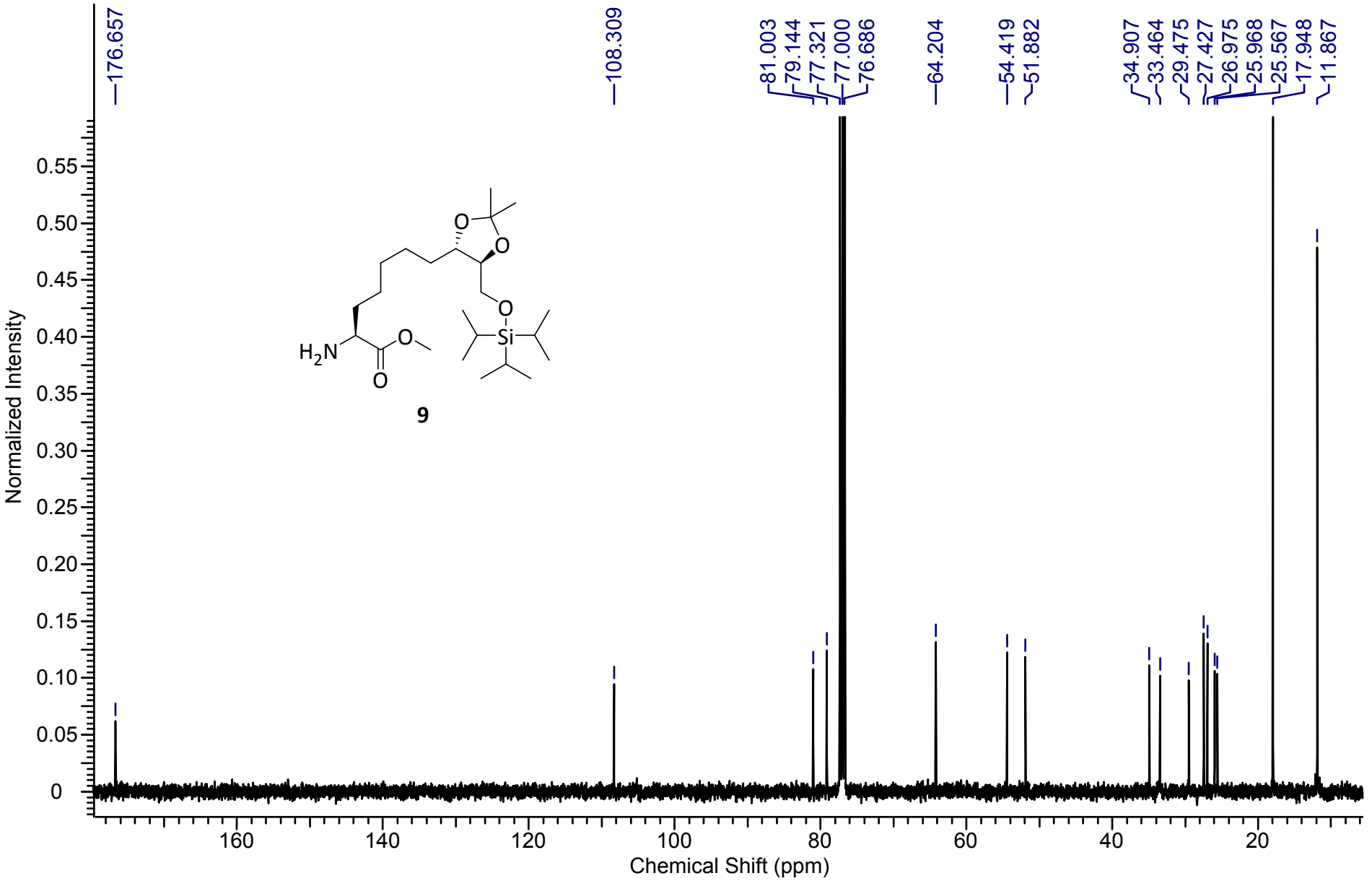
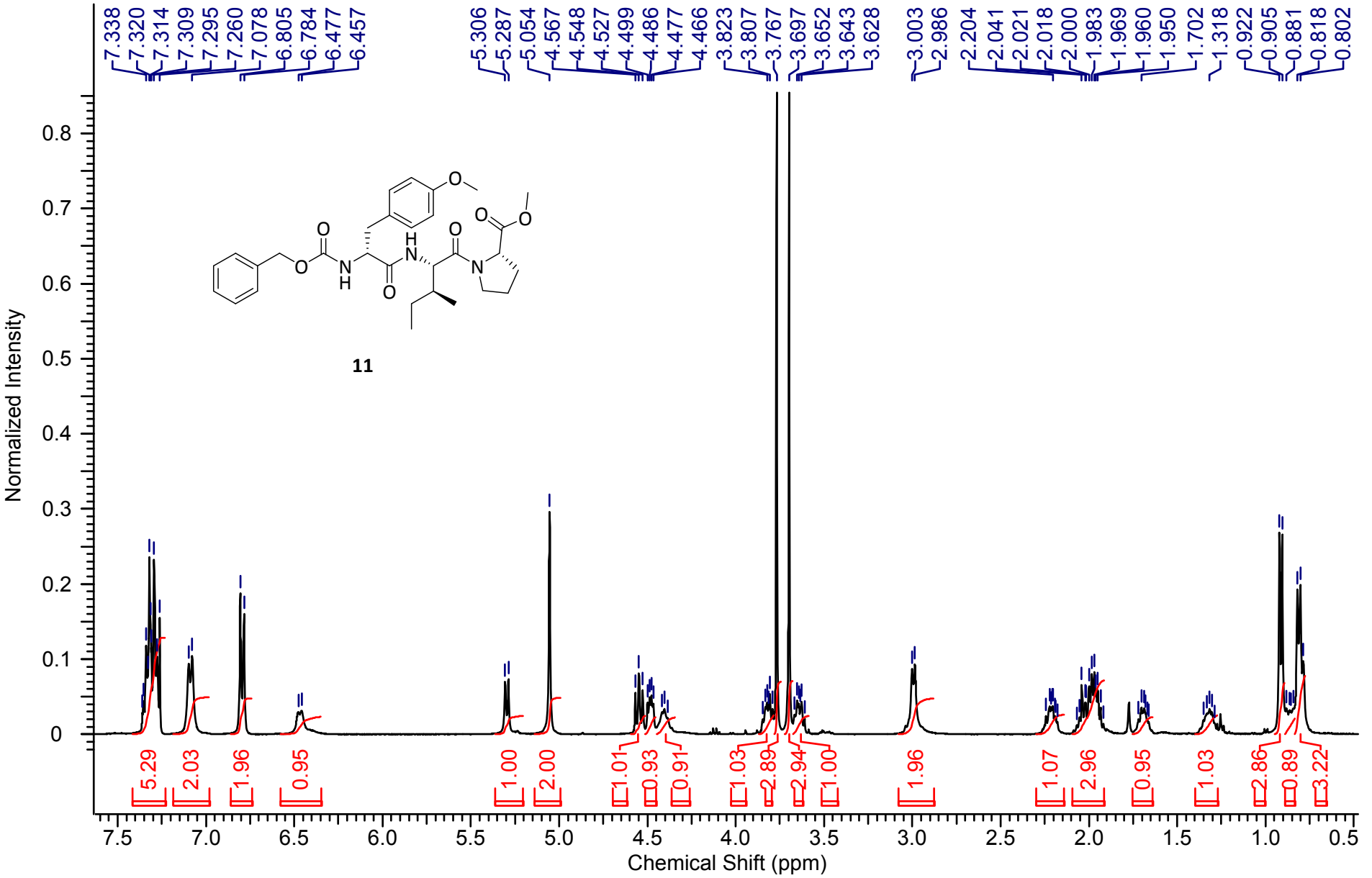
128.506
128.163
123.548
108.447
80.777
78.699
77.314
77.000
76.679
66.960
64.182
53.522
52.268
35.425
33.012
29.111
27.368
26.931
17.941
11.845
Normalized Intensity
Chemical Shift (ppm)
8


7.260
3.945
3.854
3.844
3.768
3.753
3.727
3.722
3.713
3.702
3.683
3.434
3.430
1.717
1.574
1.567
1.532
1.394
1.364
1.104
1.089
1.077
1.062
1.050
Normalized Intensity
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.00
1.05
4.89
0.81
2.19
5.44
10.92
21.27
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
Chemical Shift (ppm)

9


176.657
108.309
81.003
79.144
77.321
77.000
76.686
64.204
54.419
51.882
34.907
33.464
29.475
27.427
26.975
25.968
25.567
17.948
11.867
Normalized Intensity
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
160
140
120
100
80
60
40
20
Chemical Shift (ppm)
H2N
O
O
O
O
O
Si

9


7.338
7.320
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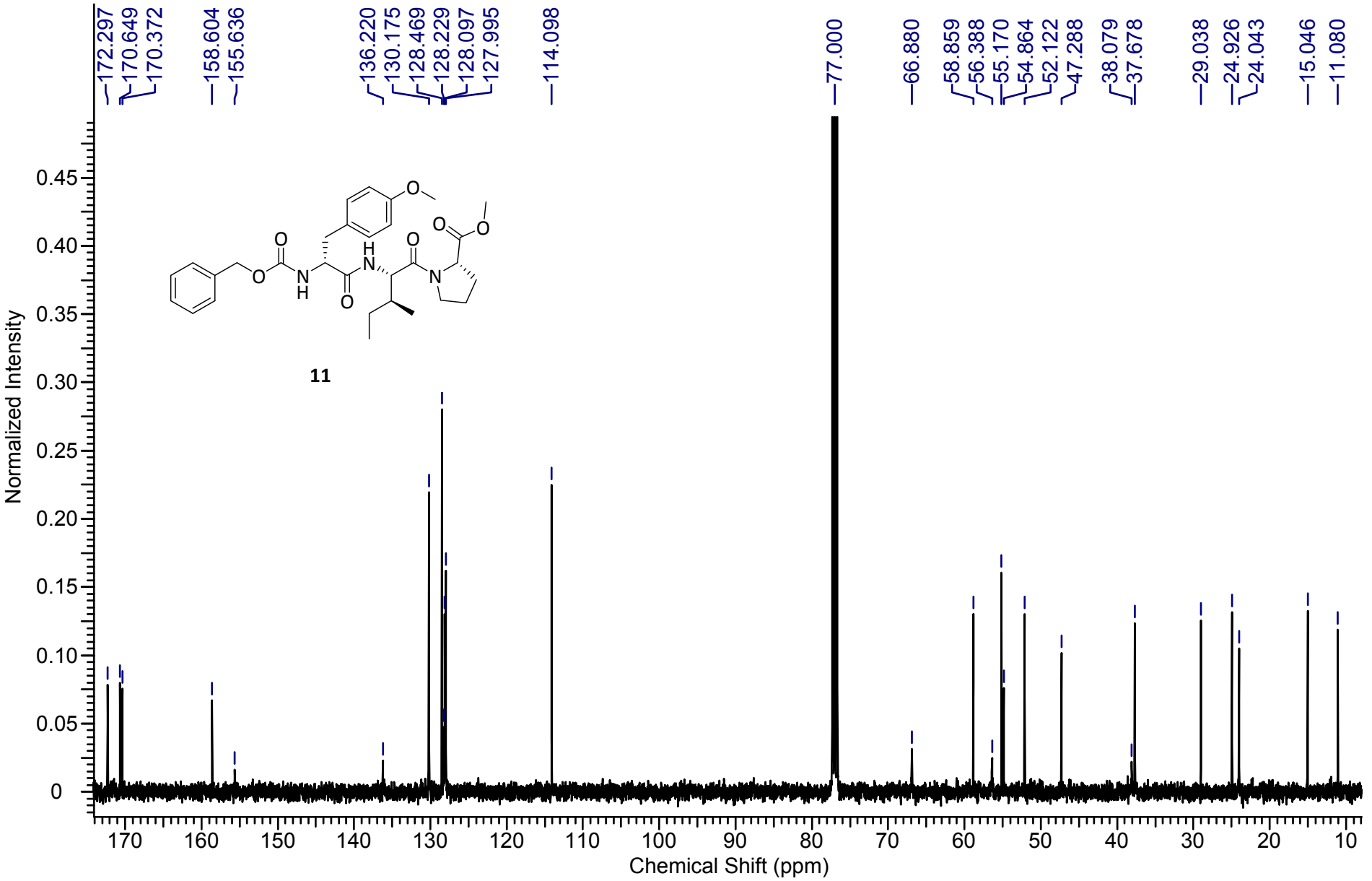
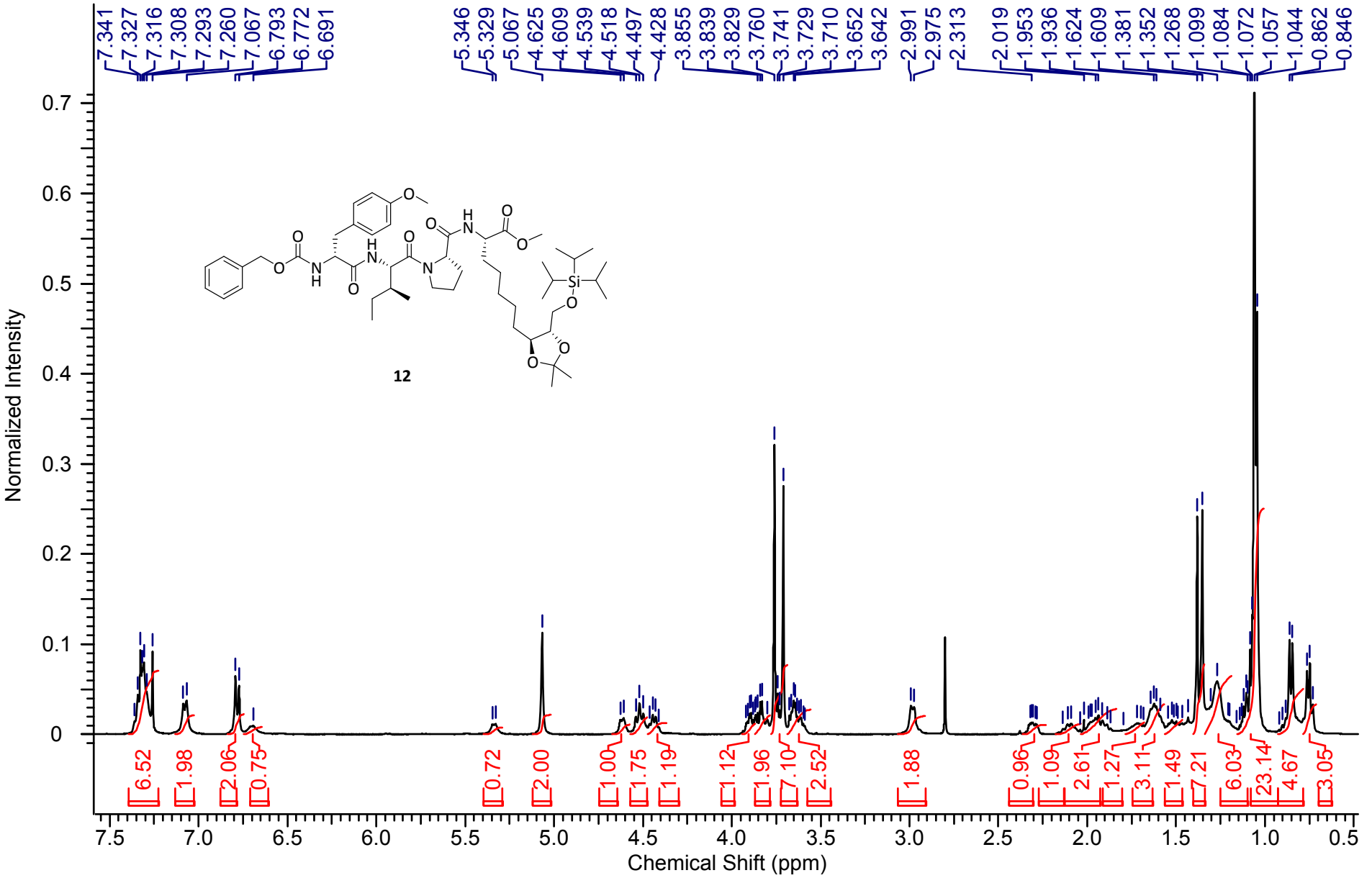
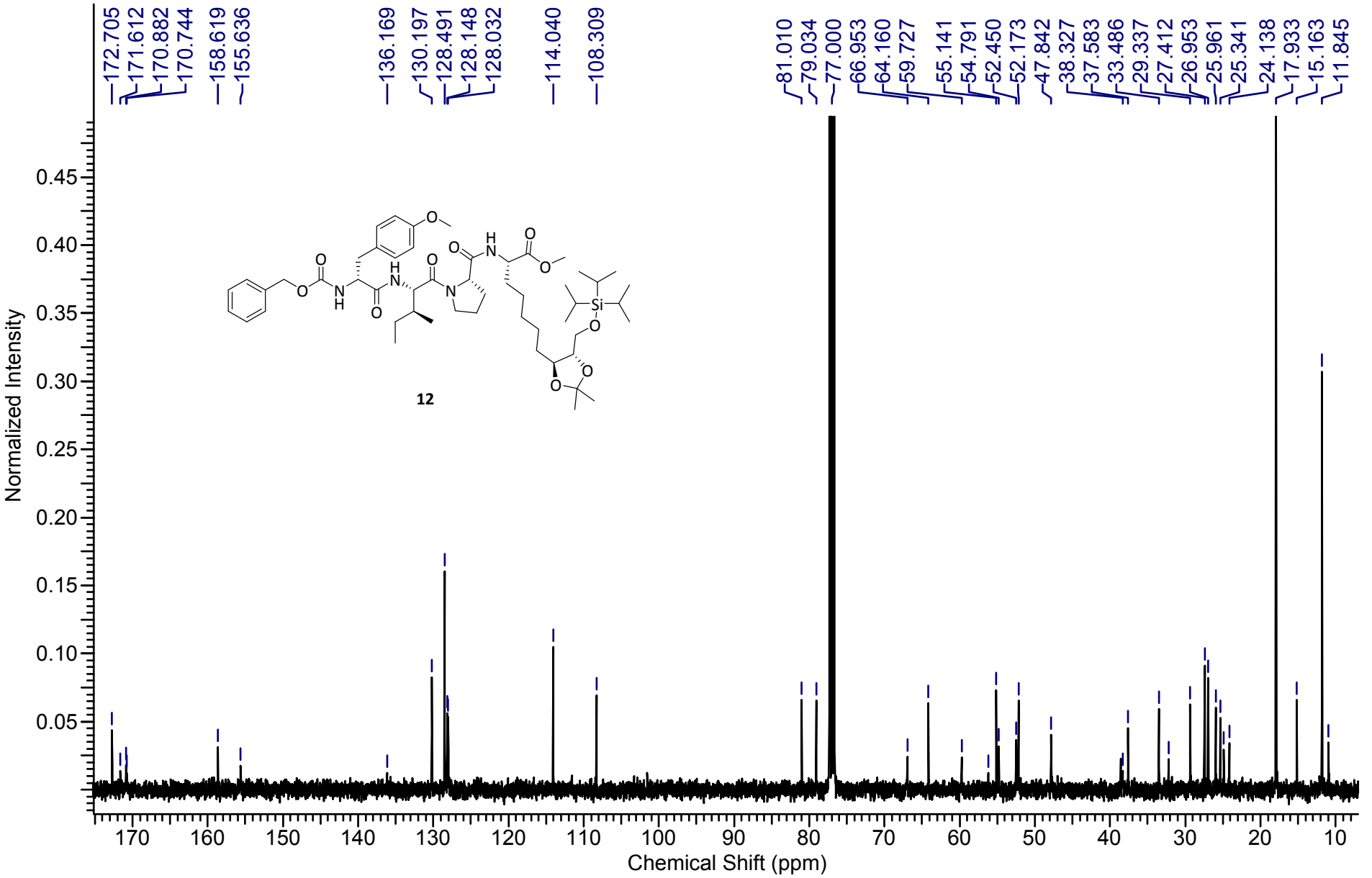
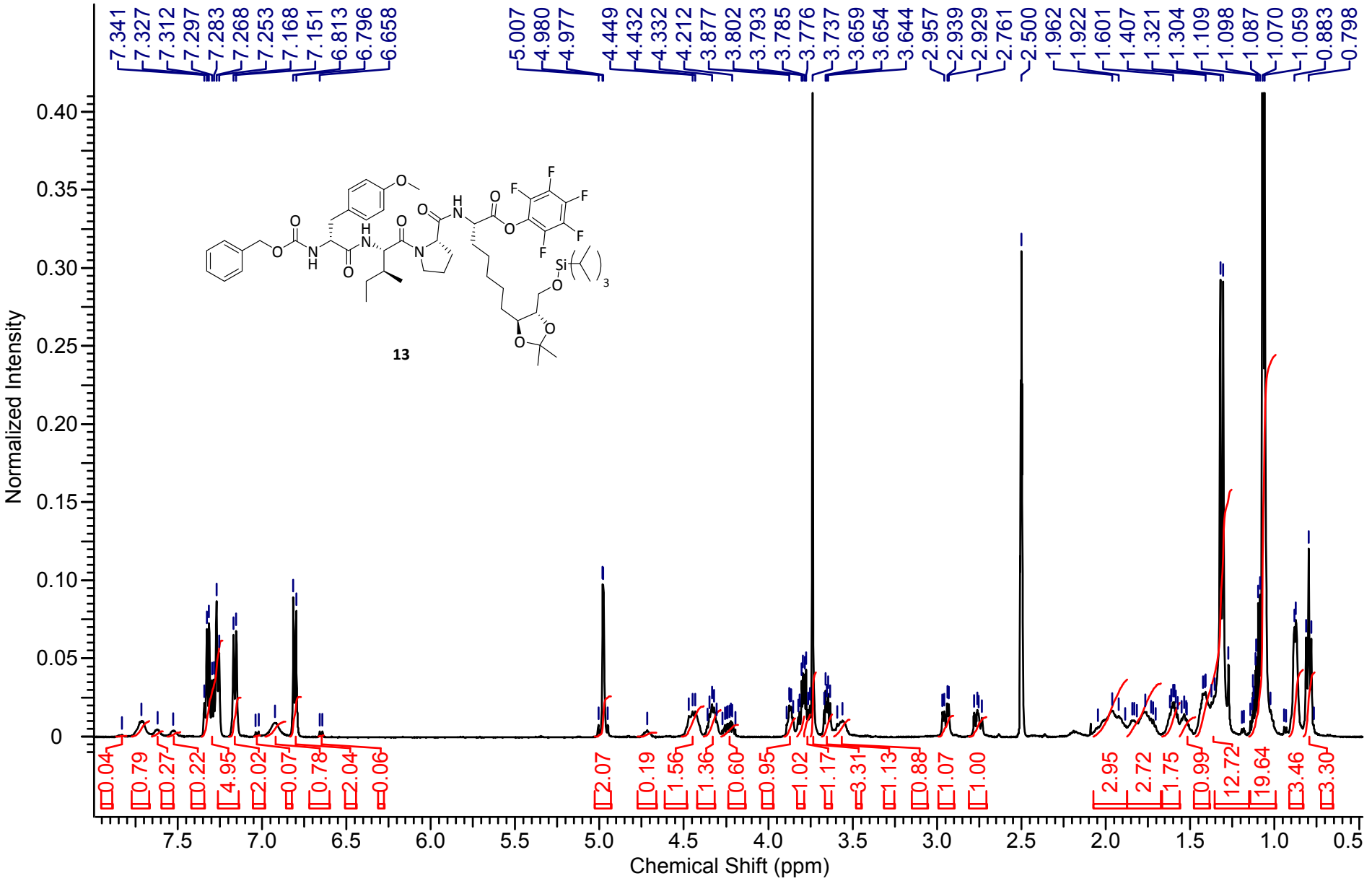
7.309
7.295
7.260
7.078
6.805
6.784
6.477
6.457
5.306
5.287
5.054
4.567
4.548
4.527
4.499
4.486
4.477
4.466
3.823
3.807
3.767
3.697
3.652
3.643
3.628
3.003
2.986
2.204
2.041
2.021
2.018
2.000
1.983
1.969
1.960
1.950
1.702
1.318
0.922
0.905
0.881
0.818
0.802
11
Normalized Intensity
Chemical Shift (ppm)
5.29
2.03
1.96
0.95
1.00
2.00
1.01
0.93
0.91
1.03
2.89
2.94
1.00
1.96
1.07
2.96
0.95
1.03
2.86
0.89
3.22

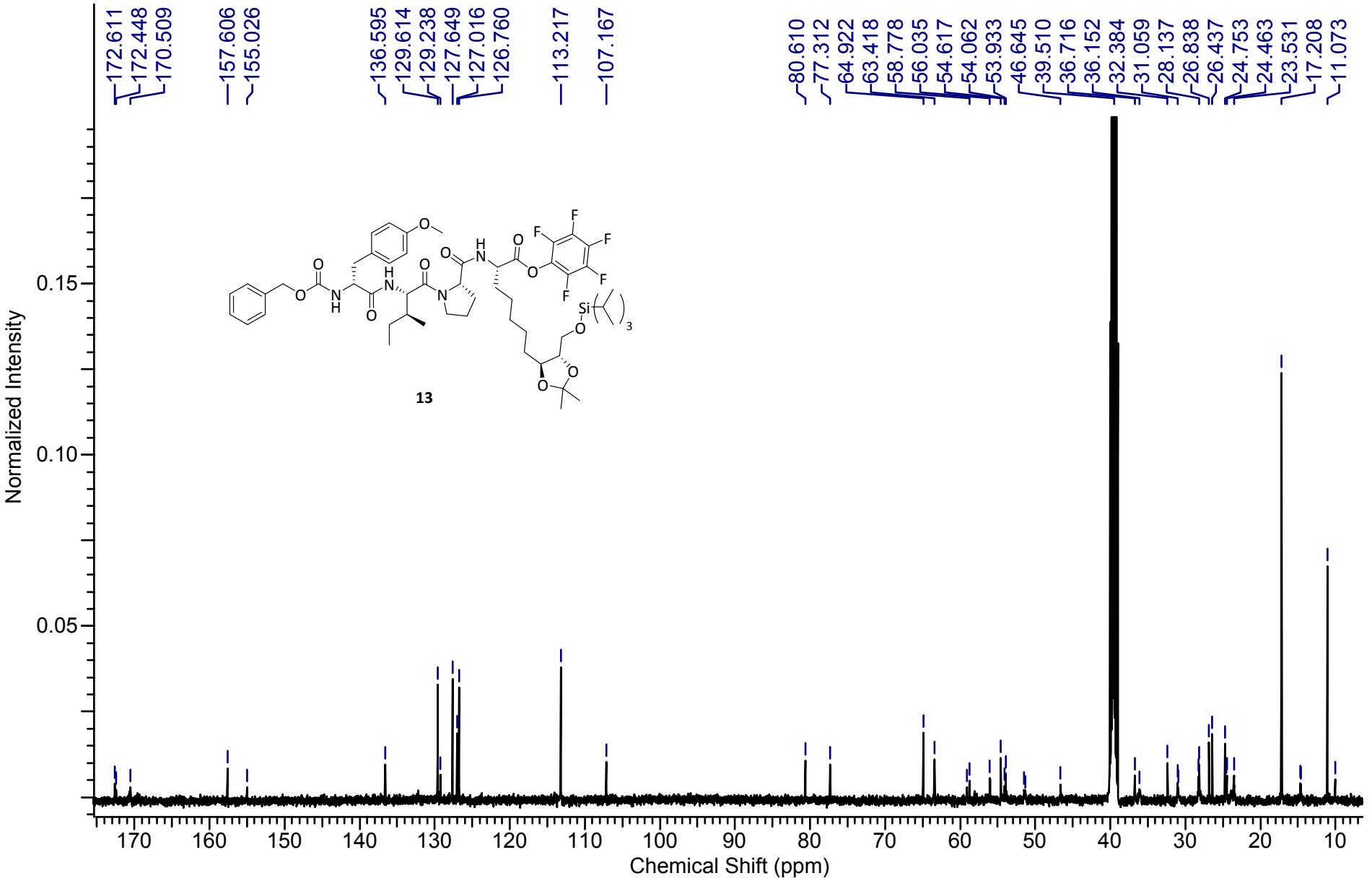

172.297
170.649
170.372
158.604
155.636
136.220
130.175
128.469
128.229
128.097
127.995
114.098
77.000
66.880
58.859
56.388
55.170
54.864
52.122
47.288
38.079
37.678
29.038
24.926
24.043
15.046
11.080
Normalized Intensity
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)
11


7.341
7.327
7.316
7.308
7.293
7.260
7.067
6.793
6.772
6.691
5.346
5.329
5.067
4.625
4.609
4.539
4.518
4.497
4.428
3.855
3.839
3.829
3.760
3.741
3.729
3.710
3.652
3.642
2.991
2.975
2.313
2.019
1.953
1.936
1.624
1.609
1.381
1.352
1.268
1.099
1.084
1.072
1.057
1.044
0.862
0.846
12
Normalized Intensity
Chemical Shift (ppm)
6.52
1.98
2.06
0.75
0.72
2.00
1.00
1.75
1.19
1.12
1.96
7.10
2.52
1.88
0.96
1.09
2.61
1.27
3.11
1.49
7.21
6.03
23.14
4.67
3.05

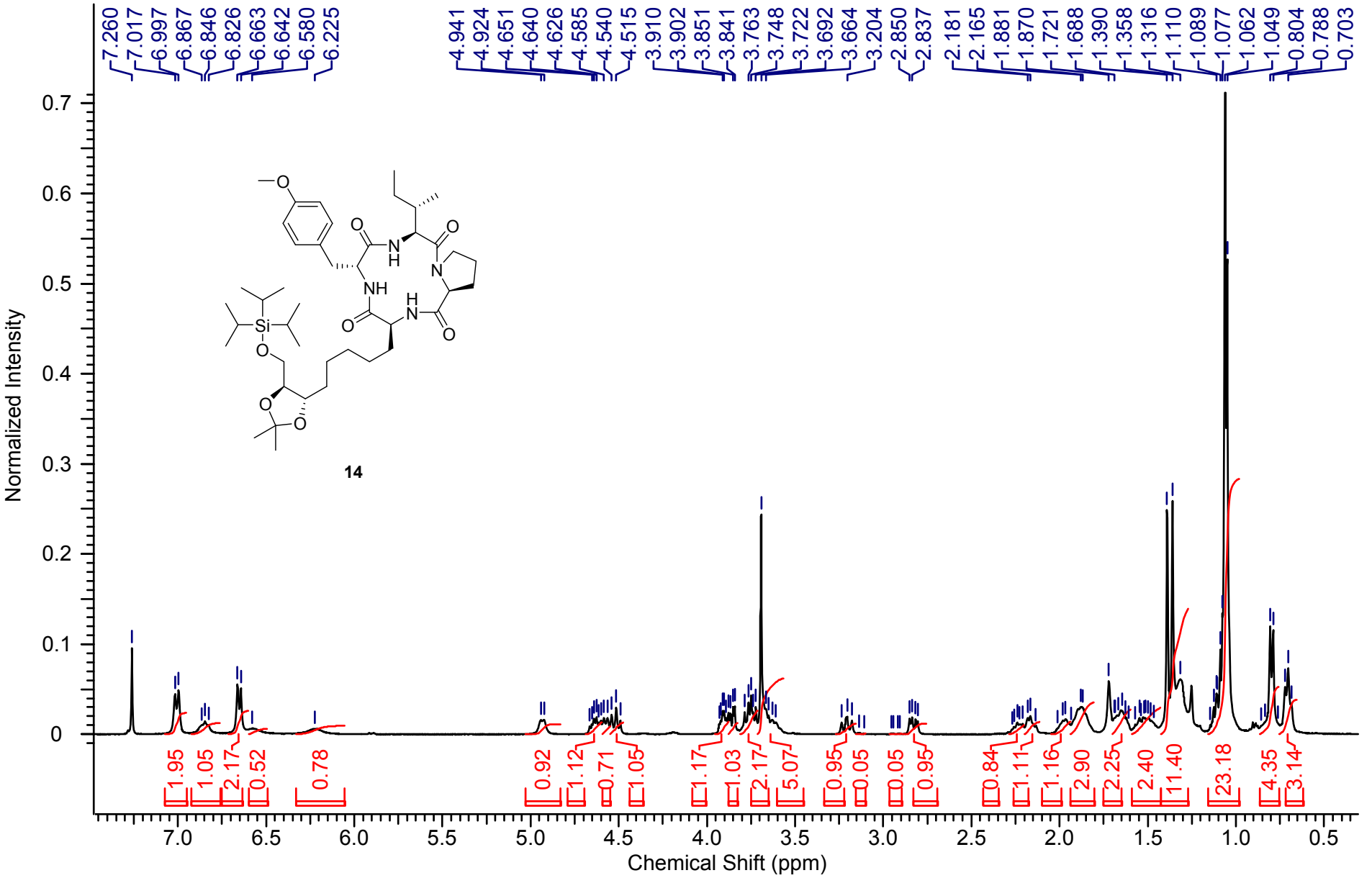

172.705
171.612
170.882
170.744
158.619
155.636
136.169
130.197
128.491
128.148
128.032
114.040
108.309
81.010
79.034
77.000
66.953
64.160
59.727
55.141
54.791
52.450
52.173
47.842
38.327
37.583
33.486
29.337
27.412
26.953
25.961
25.341
24.138
17.933
15.163
11.845
Normalized Intensity
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

12

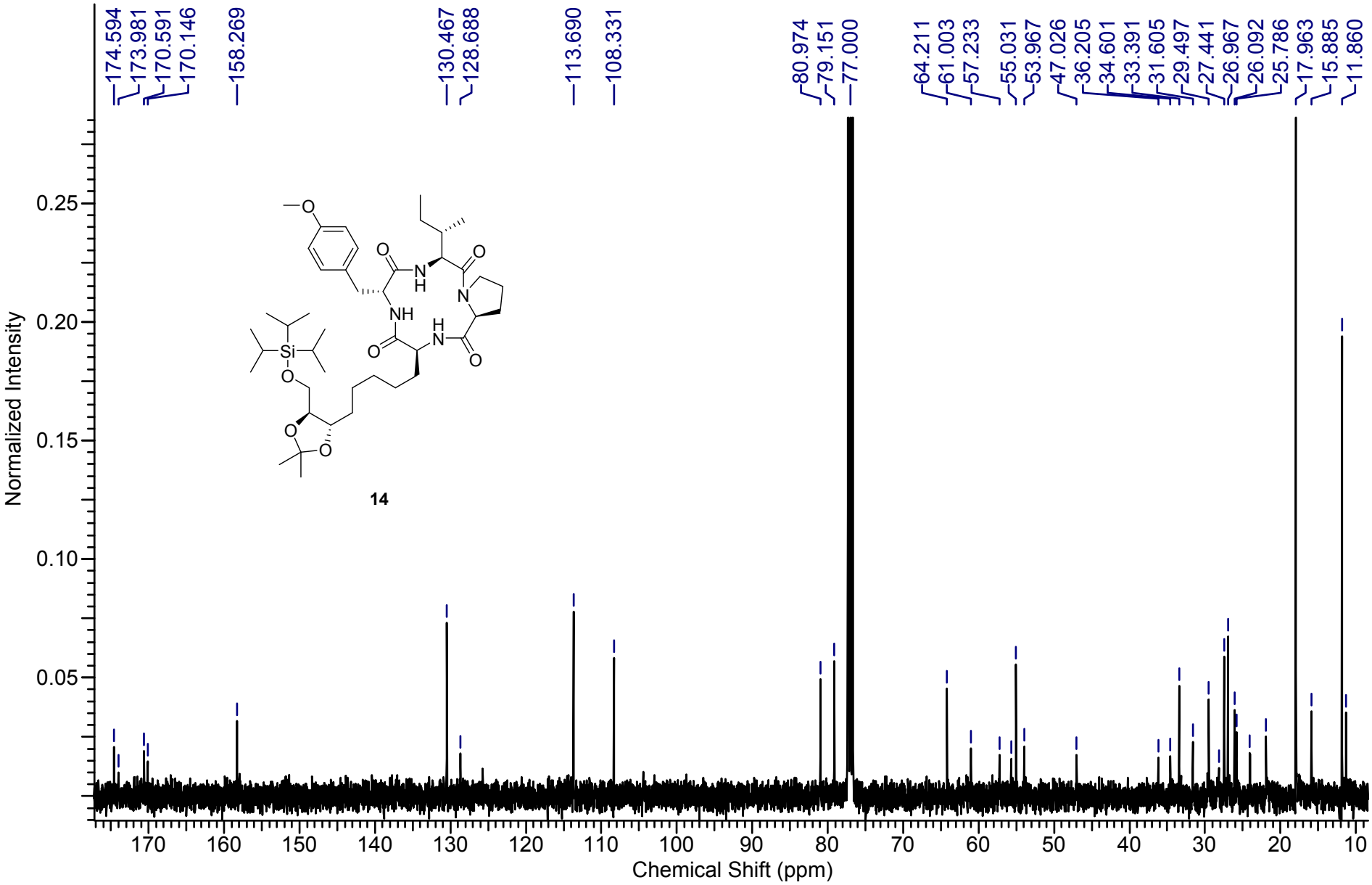

7.341
7.327
7.312
7.297
7.283
7.268
7.253
7.168
7.151
6.813
6.796
6.658
5.007
4.980
4.977
4.449
4.432
4.332
4.212
3.877
3.802
3.793
3.785
3.776
3.737
3.659
3.654
3.644
2.957
2.939
2.929
2.761
2.500
1.962
1.922
1.601
1.407
1.321
1.304
1.109
1.098
1.087
1.070
1.059
0.883
0.798
13
Normalized Intensity
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
0.04
0.79
0.27
0.22
4.95
2.02
0.07
0.78
2.04
0.06
2.07
0.19
1.56
1.36
0.60
0.95
1.02
1.17
3.31
1.13
0.88
1.07
1.00
2.95
2.72
1.75
0.99
12.72
19.64
3.46
3.30
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
Chemical Shift (ppm)

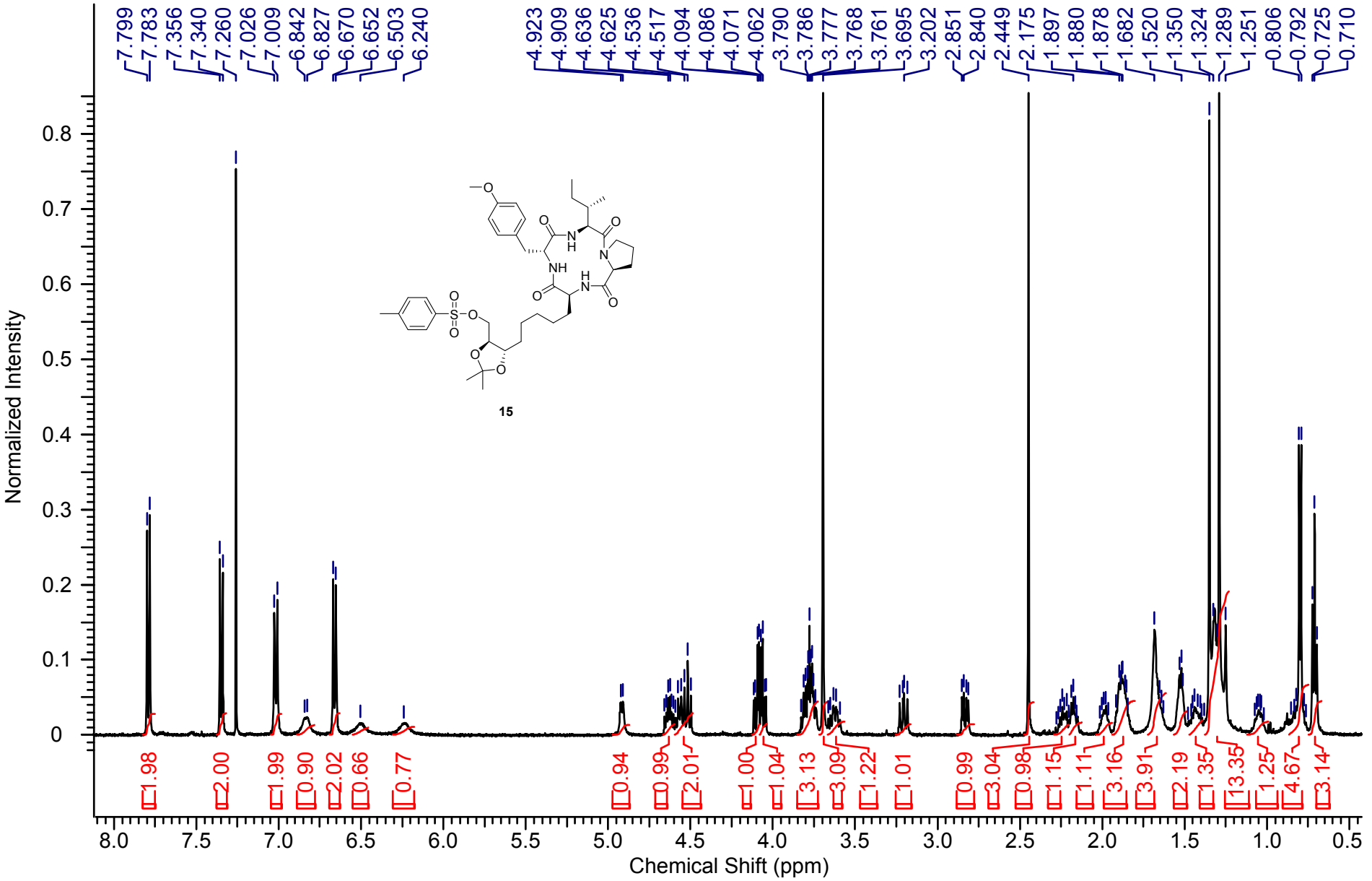

172.611
172.448
170.509
157.606
155.026
136.595
129.614
129.238
127.649
127.016
126.760
113.217
107.167
80.610
77.312
64.922
63.418
58.778
56.035
54.617
54.062
53.933
46.645
39.510
36.716
36.152
32.384
31.059
28.137
26.838
26.437
24.753
24.463
23.531
17.208
11.073
Normalized Intensity
0.15
0.10
0.05
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

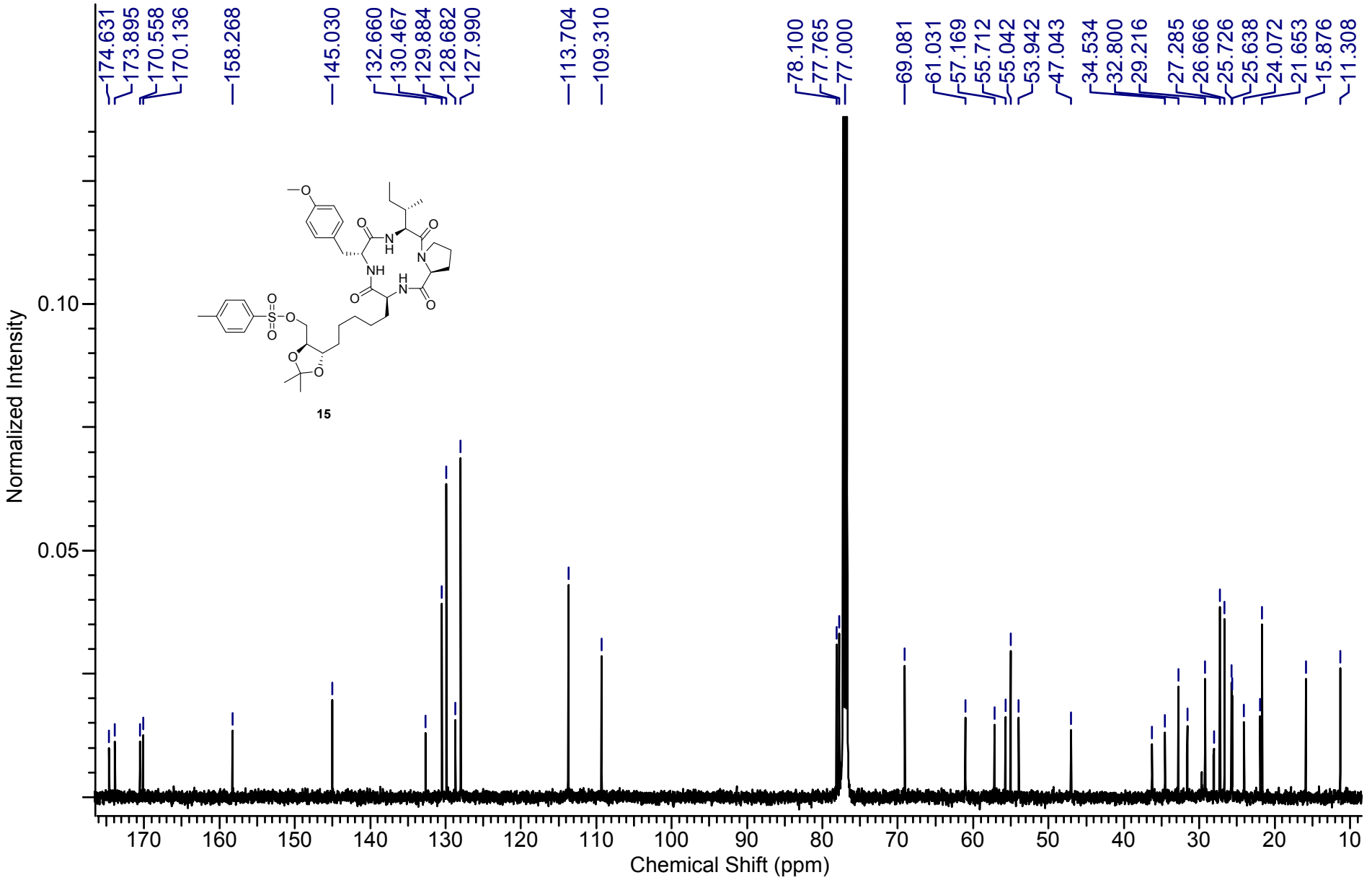
13

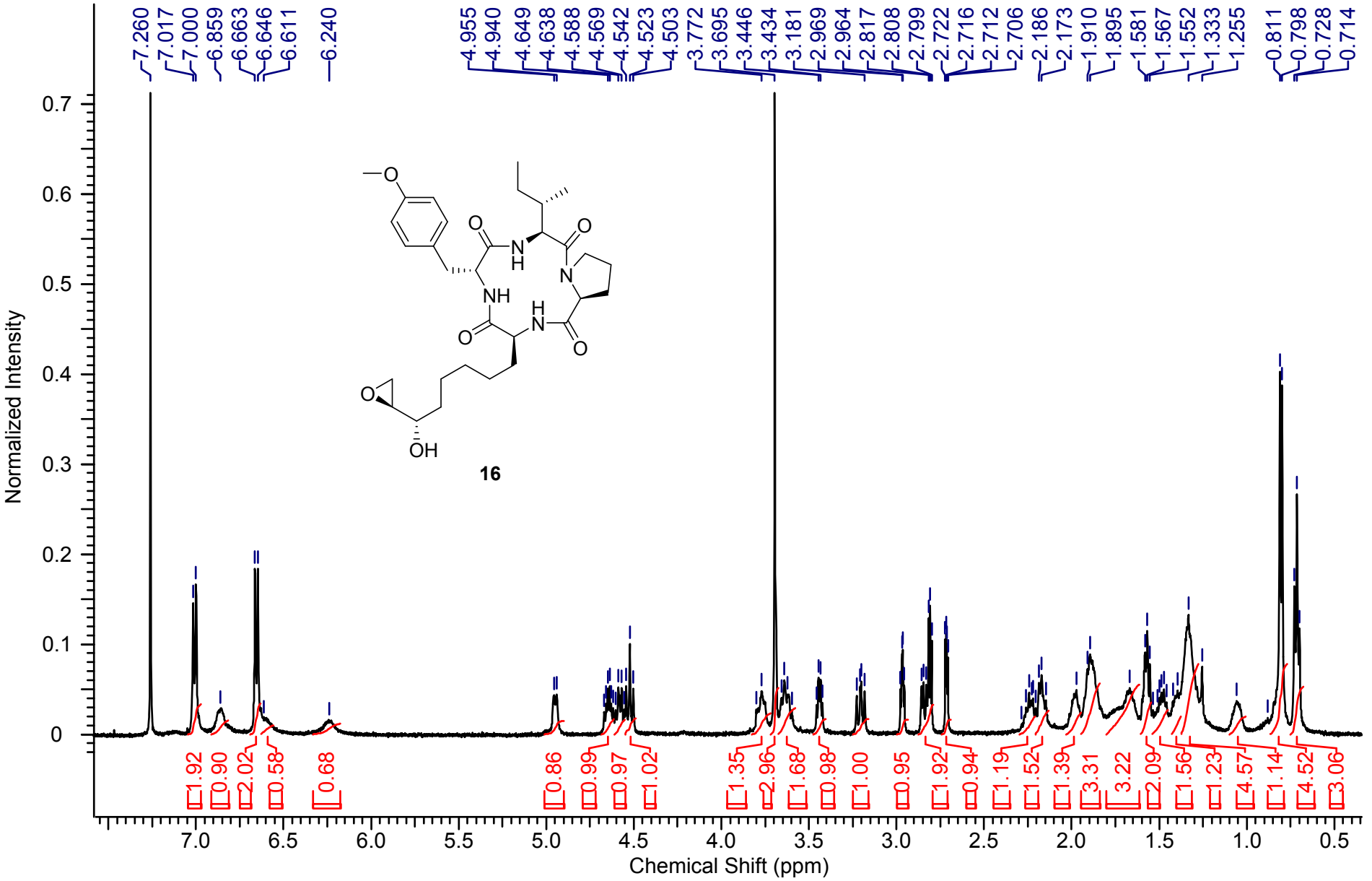

7.260
7.017
6.997
6.867
6.846
6.826
6.663
6.642
6.580
6.225
4.941
4.924
4.651
4.640
4.626
4.585
4.540
4.515
3.910
3.902
3.851
3.841
3.763
3.748
3.722
3.692
3.664
3.204
2.850
2.837
2.181
2.165
1.881
1.870
1.721
1.688
1.390
1.358
1.316
1.110
1.089
1.077
1.062
1.049
0.804
0.788
0.703
Normalized Intensity
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1.95
1.05
2.17
0.52
0.78
0.92
1.12
0.71
1.05
1.17
1.03
2.17
5.07
0.95
0.05
0.05
0.95
0.84
1.11
1.16
2.90
2.25
2.40
11.40
23.18
4.35
3.14
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
Chemical Shift (ppm)

14

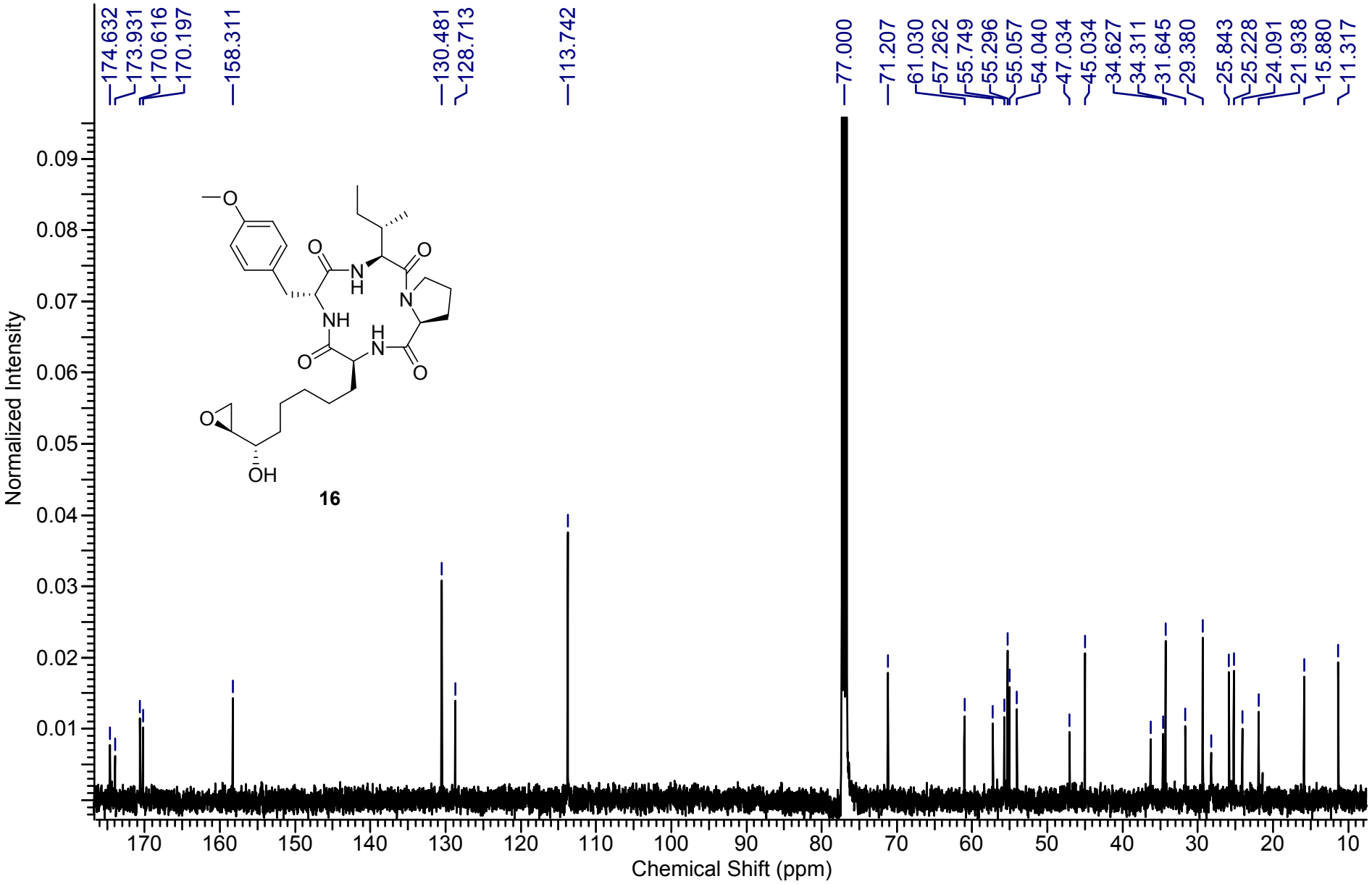

174.594
173.981
170.591
170.146
158.269
130.467
128.688
113.690
108.331
80.974
79.151
77.000
64.211
61.003
57.233
55.031
53.967
47.026
36.205
34.601
33.391
31.605
29.497
27.441
26.967
26.092
25.786
17.963
15.885
11.860
Normalized Intensity
0.25
0.20
0.15
0.10
0.05
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)
14


7.799
7.783
7.356
7.340
7.260
7.026
7.009
6.842
6.827
6.670
6.652
6.503
6.240
4.923
4.909
4.636
4.625
4.536
4.517
4.094
4.086
4.071
4.062
3.790
3.786
3.777
3.768
3.761
3.695
3.202
2.851
2.840
2.449
2.175
1.897
1.880
1.878
1.682
1.520
1.350
1.324
1.289
1.251
0.806
0.792
0.725
0.710
15
Normalized Intensity
Chemical Shift (ppm)
1.98
2.00
1.99
0.90
2.02
0.66
0.77
0.94
0.99
2.01
1.00
1.04
3.13
3.09
1.22
1.01
0.99
3.04
0.98
1.15
1.11
3.16
3.91
2.19
1.35
13.35
1.25
4.67
3.14

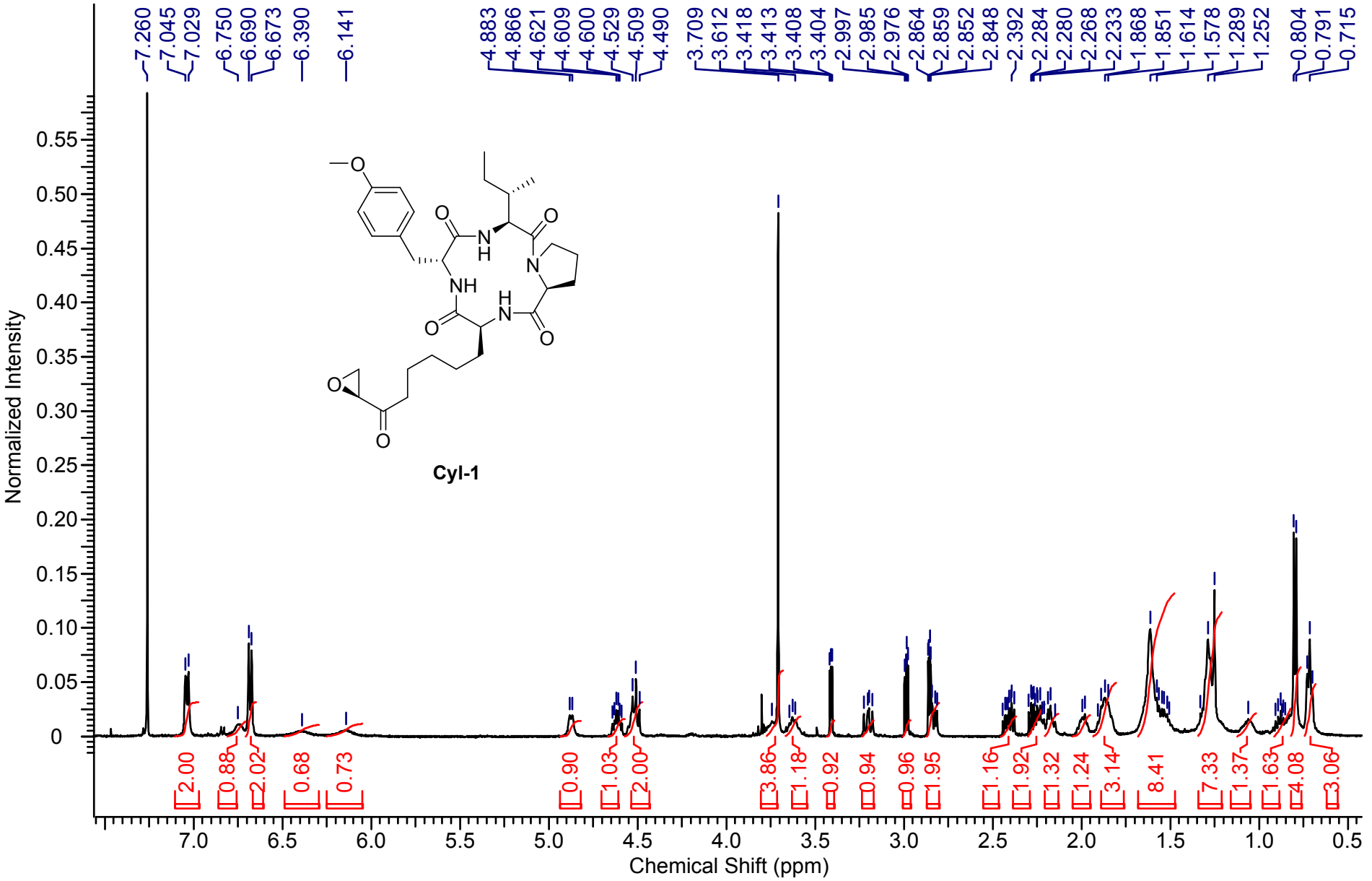

174.631
173.895
170.558
170.136
158.268
145.030
132.660
130.467
129.884
128.682
127.990
113.704
109.310
78.100
77.765
77.000
69.081
61.031
57.169
55.712
55.042
53.942
47.043
34.534
32.800
29.216
27.285
26.666
25.726
25.638
24.072
21.653
15.876
11.308
Normalized Intensity
0.10
0.05
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)
15


7.260
7.017
7.000
6.859
6.663
6.646
6.611
6.240
4.955
4.940
4.649
4.638
4.588
4.569
4.542
4.523
4.503
3.772
3.695
3.446
3.434
3.181
2.969
2.964
2.817
2.808
2.799
2.722
2.716
2.712
2.706
2.186
2.173
1.910
1.895
1.581
1.567
1.552
1.333
1.255
0.811
0.798
0.728
0.714
Normalized Intensity
Chemical Shift (ppm)
1.92
0.90
2.02
0.58
0.68
0.86
0.99
0.97
1.02
1.35
2.96
1.68
0.98
1.00
0.95
1.92
0.94
1.19
1.52
1.39
3.31
3.22
2.09
1.56
1.23
4.57
1.14
4.52
3.06

16


174.632
173.931
170.616
170.197
158.311
130.481
128.713
113.742
77.000
71.207
61.030
57.262
55.749
55.296
55.057
54.040
47.034
45.034
34.627
34.311
31.645
29.380
25.843
25.228
24.091
21.938
15.880
11.317
Normalized Intensity
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)
O
N
H
NH
OH

16


7.260
7.045
7.029
6.750
6.690
6.673
6.390
6.141
4.883
4.866
4.621
4.609
4.600
4.529
4.509
4.490
3.709
3.612
3.418
3.413
3.408
3.404
2.997
2.985
2.976
2.864
2.859
2.852
2.848
2.392
2.284
2.280
2.268
2.233
1.868
1.851
1.614
1.578
1.289
1.252
0.804
0.791
0.715
Normalized Intensity
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
2.00
0.88
2.02
0.68
0.73
0.90
1.03
2.00
3.86
1.18
0.92
0.94
0.96
1.95
1.16
1.92
1.32
1.24
3.14
8.41
7.33
1.37
1.63
4.08
3.06
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
Chemical Shift (ppm)
Cyl-1

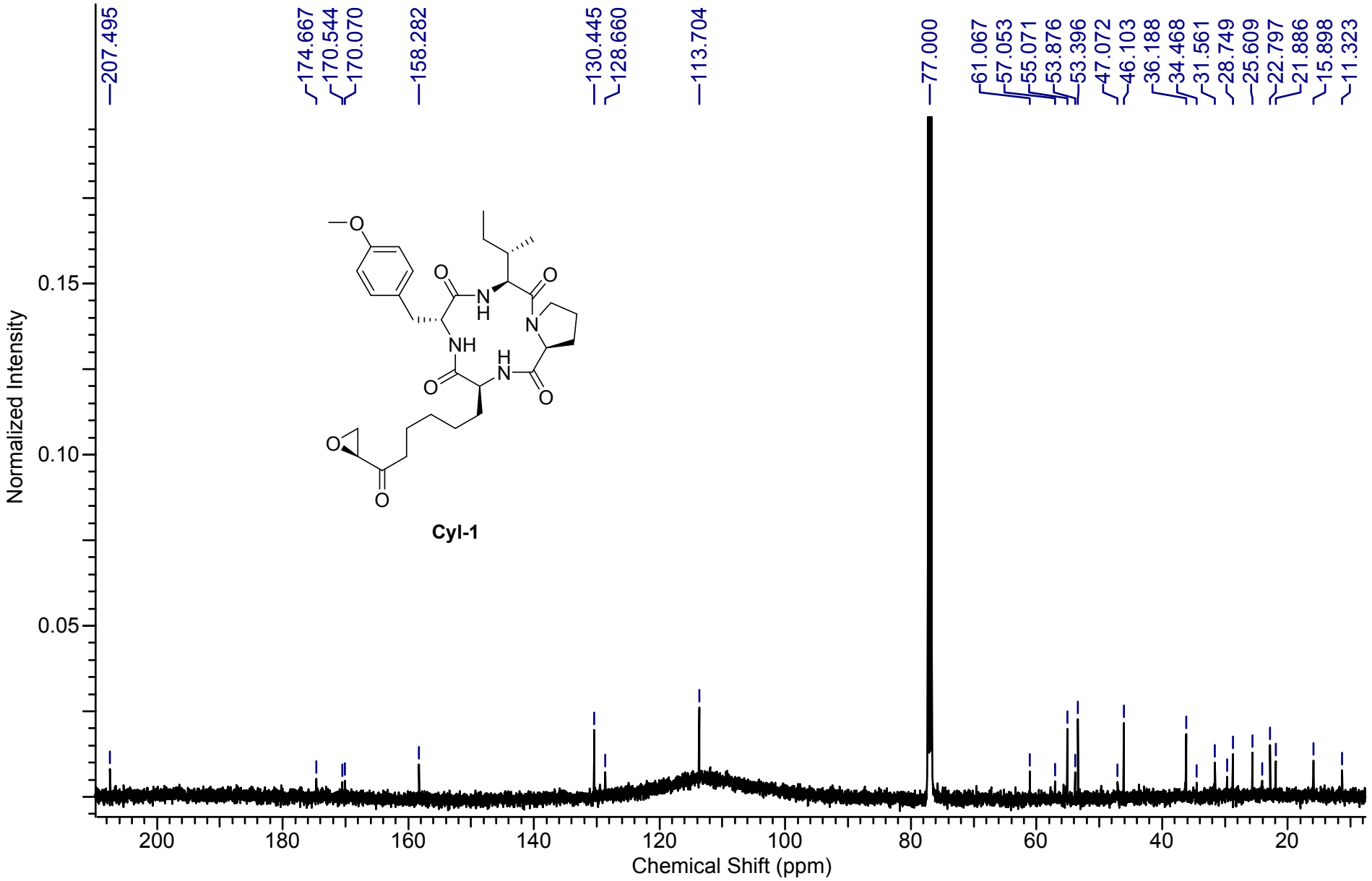

207.495
174.667
170.544
170.070
158.282
130.445
128.660
113.704
77.000
61.067
57.053
55.071
53.876
53.396
47.072
46.103
36.188
34.468
31.561
28.749
25.609
22.797
21.886
15.898
11.323
Normalized Intensity
0.15
0.10
0.05
200
180
160
140
120
100
80
60
40
20
Chemical Shift (ppm)
Cyl-1

Table 1: Comparison of the observed signals for Cyl-1 with literature data form S. Takayama *et al.*, Agric. Biol. Chem. **1984**, *48*, 839-842.

^{1}H-NMR

observed		literature data	
δ [ppm]	*J* [Hz]	δ [ppm]	*J* [Hz]
2.86	2.5, 5.8	2.86	2.5, 6.0
2.99	4.8, 5.8	2.99	4.5, 6.0
3.41	2.5, 4.5	3.41	2.5, 4.5

^{13}C-NMR

observed, δ [ppm]	literature data, δ [ppm]
46.1	46.2
53.4	53.5
207.5	207.4