

Isomerizable (*E/Z*)-Alkynyl-*O*-Methyl Oximes Employing TMSCl-NCS in Chlorinative Cyclization for the Direct Synthesis of 4-Chloroisoxazoles

Wilailak Kaewsri,^c Charnsak Thongsornkleeb,^{*,a,c} Jumreang Tummatorn,^{b,c} and Somsak Ruchirawat^{b,c}

^aLaboratory of Organic Synthesis, Chulabhorn Research Institute, 54 Kamphaeng Phet 6, Laksi, Bangkok 10210, Thailand.

^bLaboratory of Medicinal Chemistry, Chulabhorn Research Institute, 54 Kamphaeng Phet 6, Laksi, Bangkok 10210, Thailand.

^cProgram on Chemical Biology, Chulabhorn Graduate Institute, Center of Excellence on Environmental Health and Toxicology (EHT), Ministry of Education, 54 Kamphaeng Phet 6, Laksi, Bangkok 10210, Thailand.

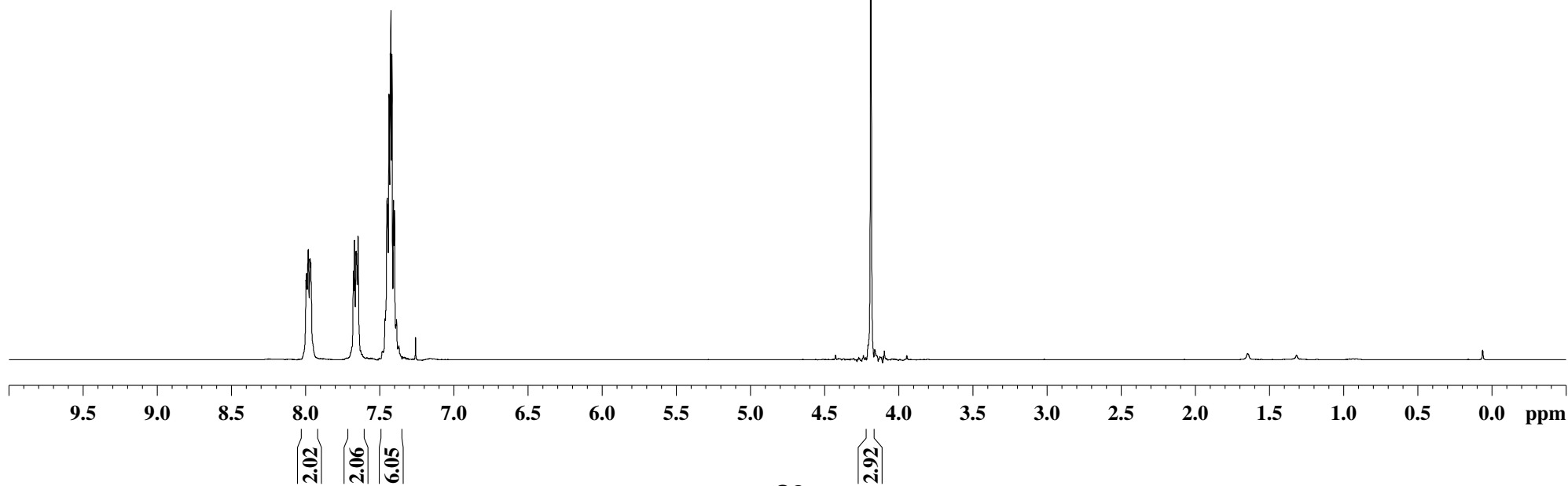
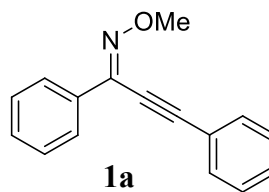
Supporting Information

Contents:	Pages
1. Copies of ¹ H and ¹³ C NMR Spectra of Compounds 1a-1u	S2–S49
2. Copies of ¹ H and ¹³ C NMR Spectra of Compounds 2a-2u	S50–S61, S64–S111
3. Copies of ¹ H and ¹³ C NMR Spectra of Compound 3d	S62–S63

WK-I-9-H

7.998
7.995
7.991
7.984
7.973
7.971
7.966
7.680
7.673
7.661
7.658
7.647
7.466
7.453
7.450
7.438
7.431
7.429
7.426
7.419
7.409
7.402
7.393
7.388

4.190



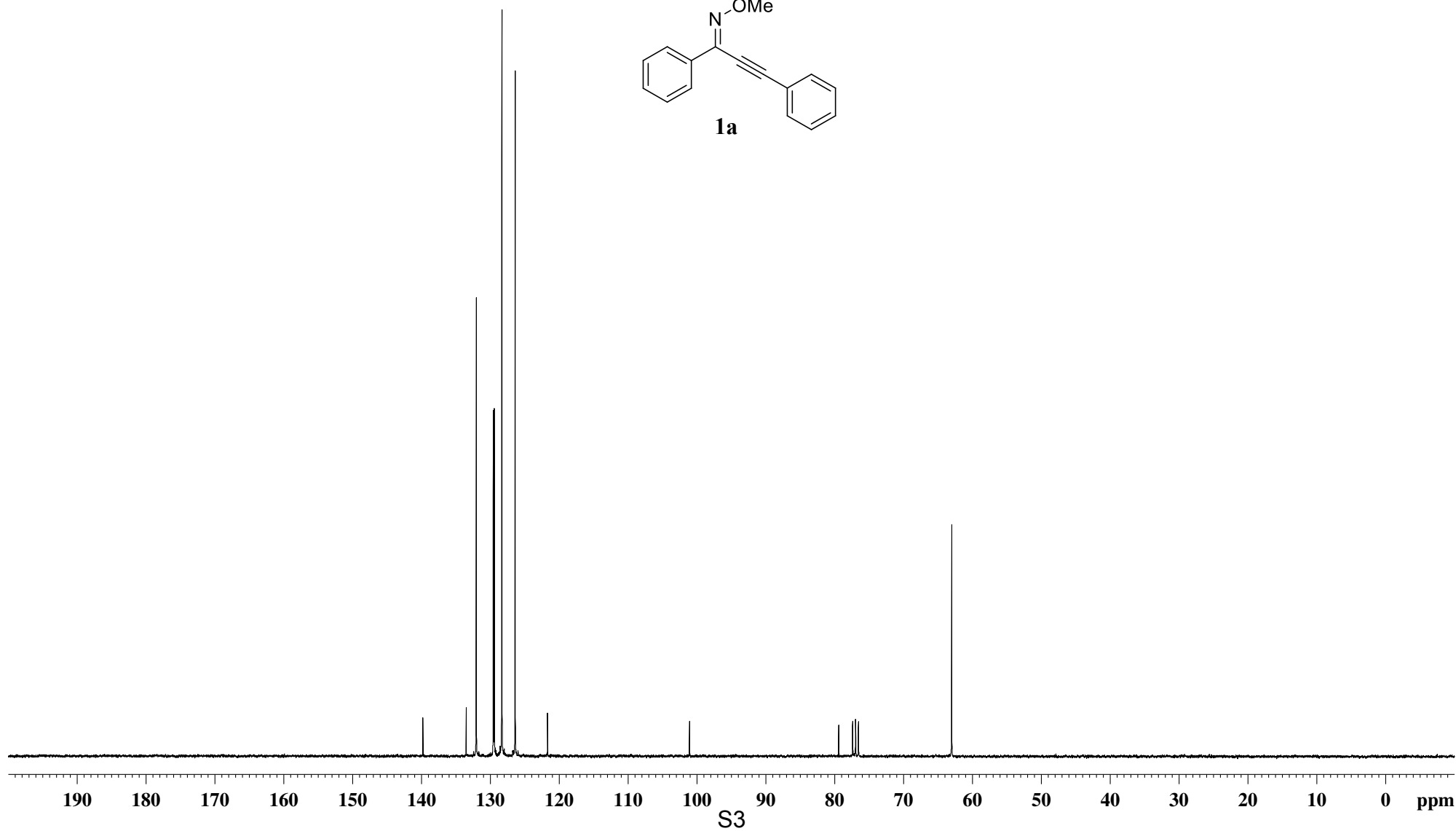
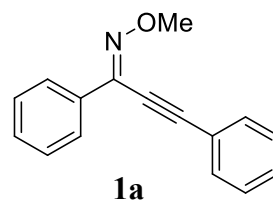
WK-I-9-C

139.84
133.54
132.08
129.60
129.45
128.38
128.36
126.43
121.74

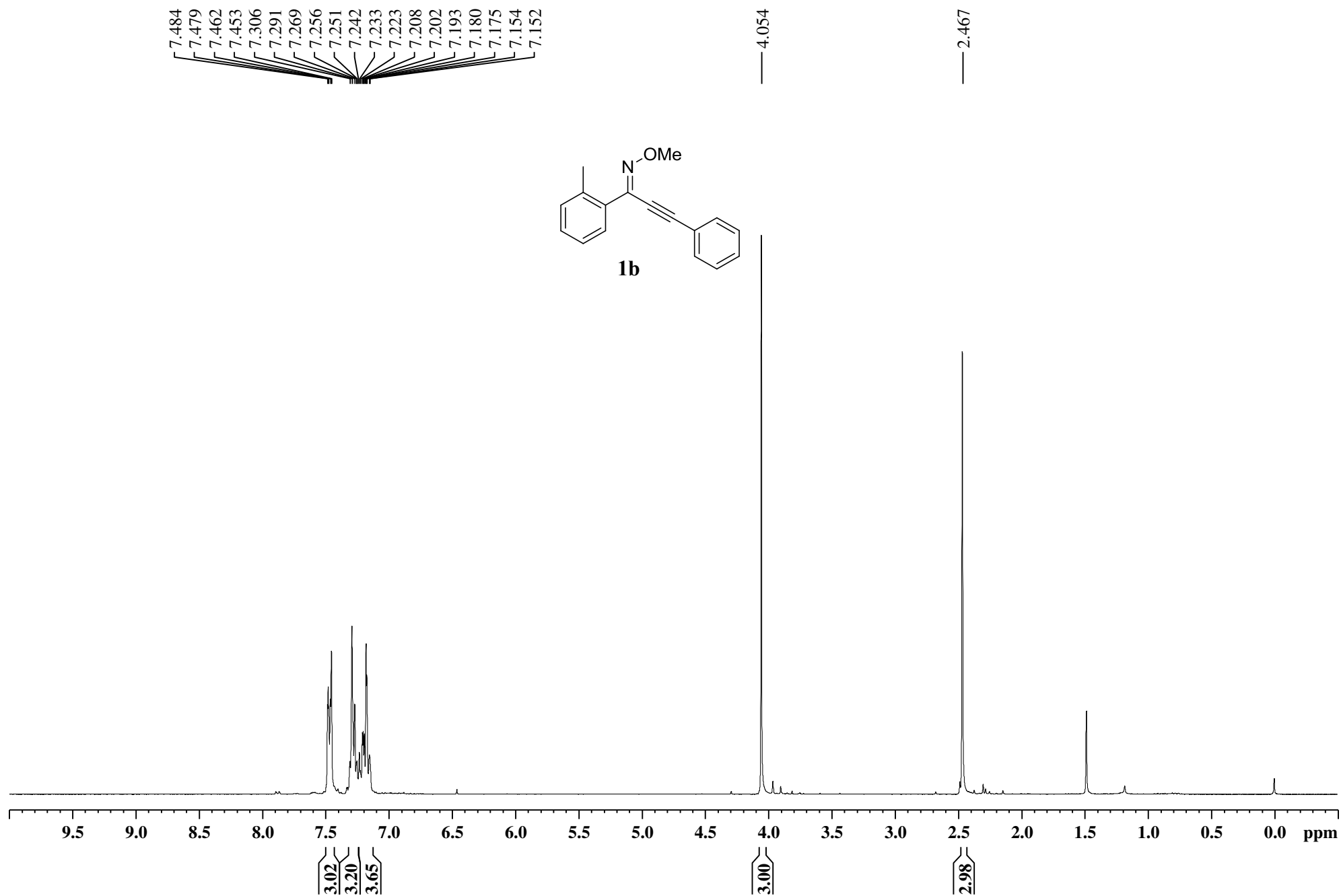
101.11

79.44

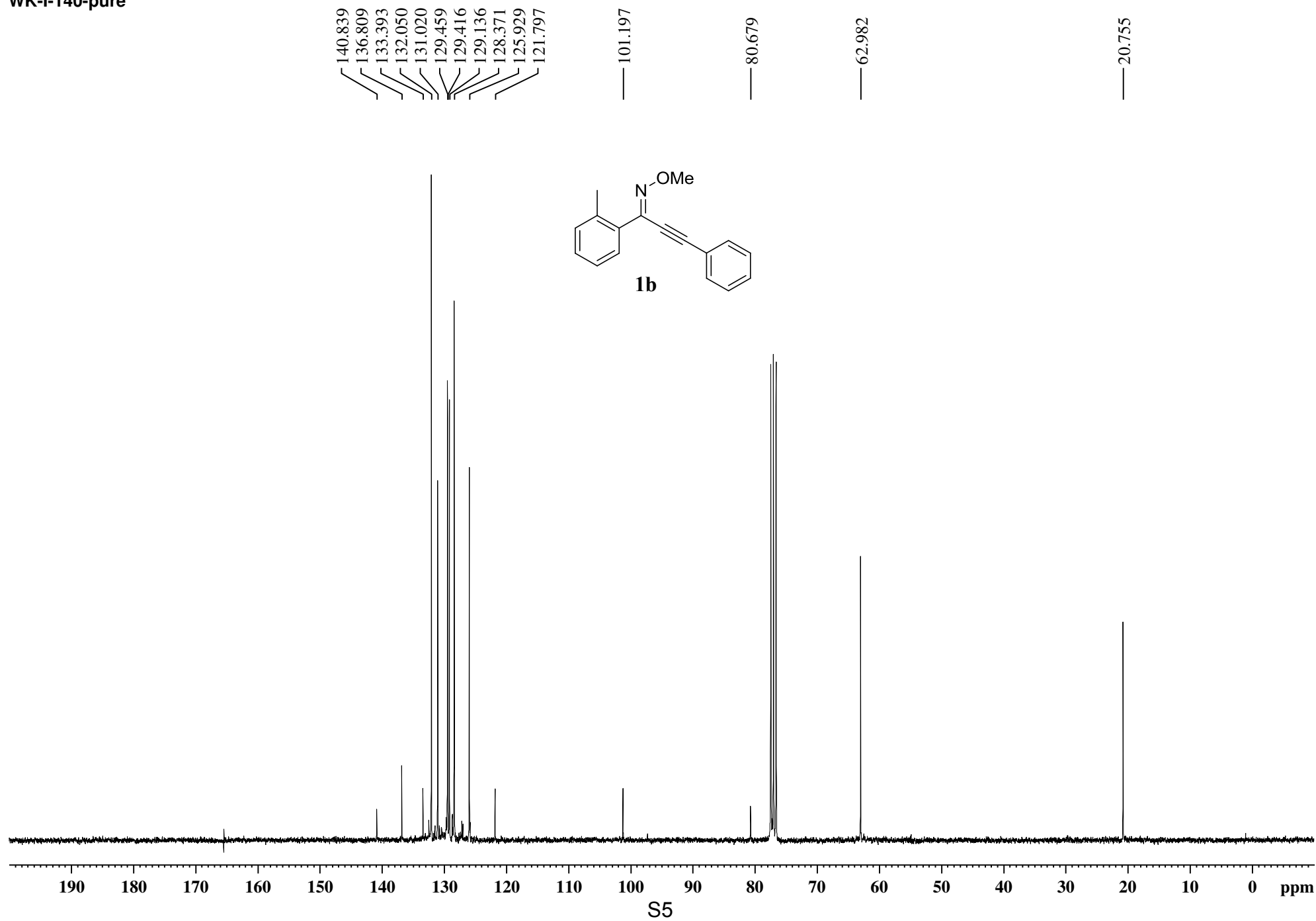
63.03



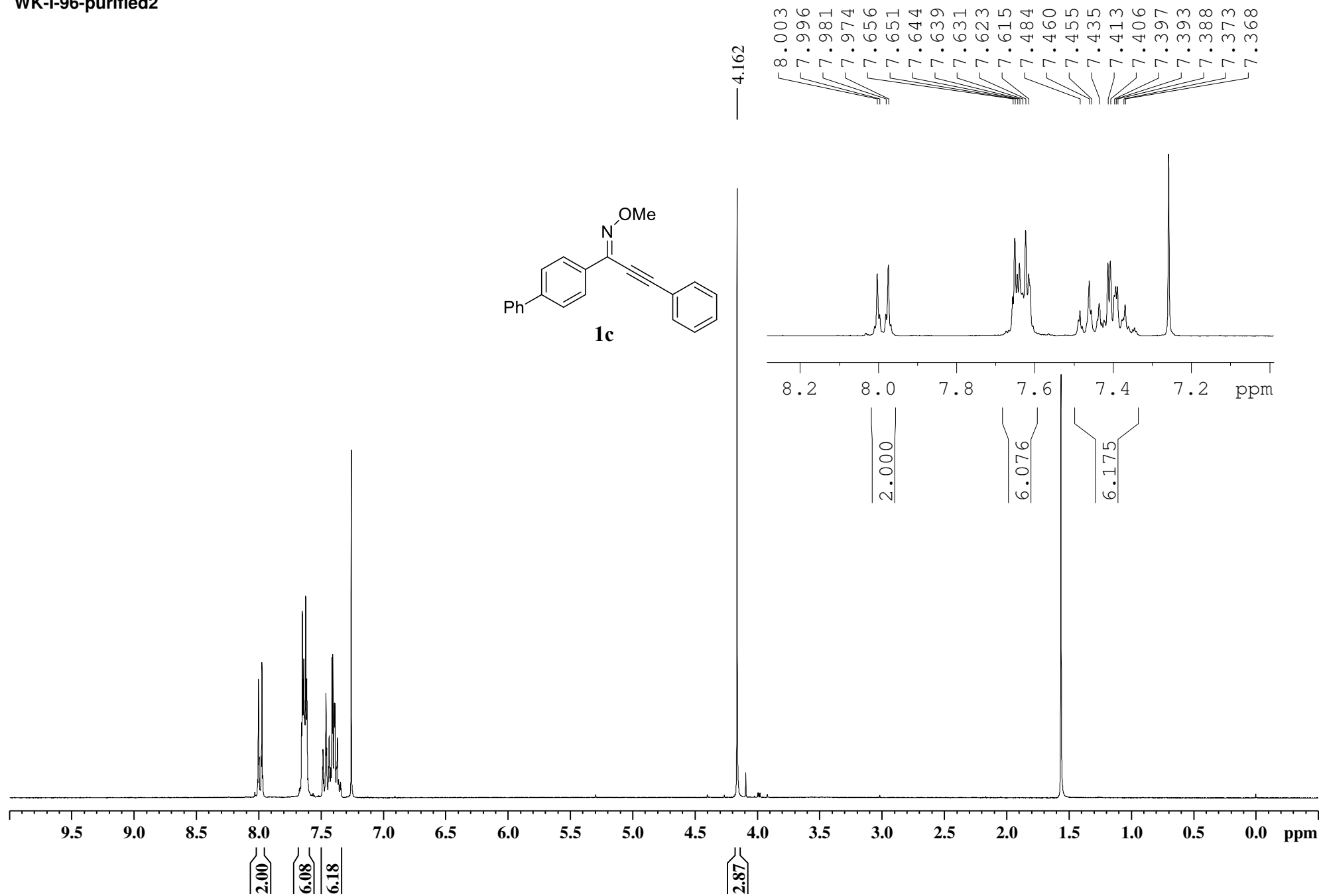
WK-I-140-pure



WK-I-140-pure



WK-I-96-purified2



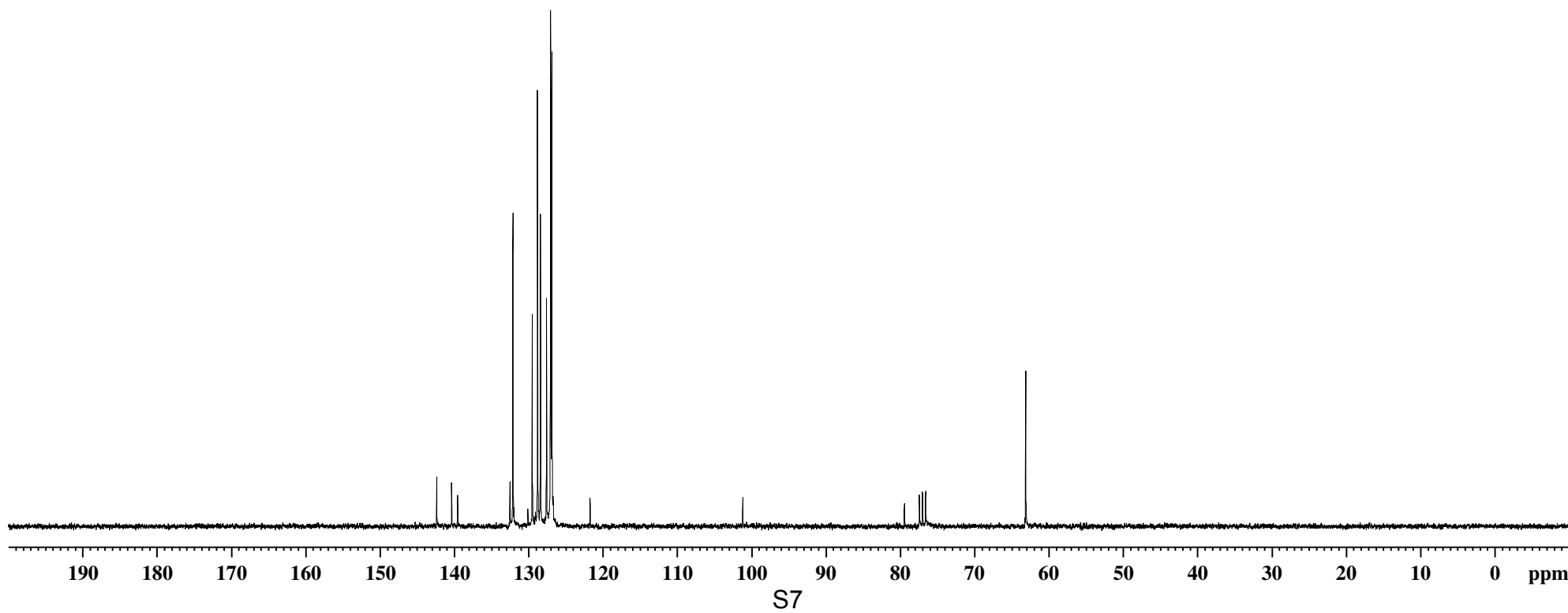
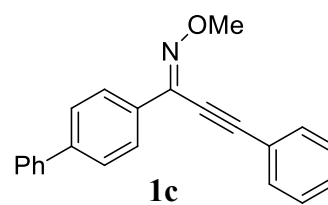
WK-I-96-purified2-Edited

142.35
140.35
139.56
132.50
132.11
129.50
128.79
128.41
127.59
127.05
127.01
126.87
121.71

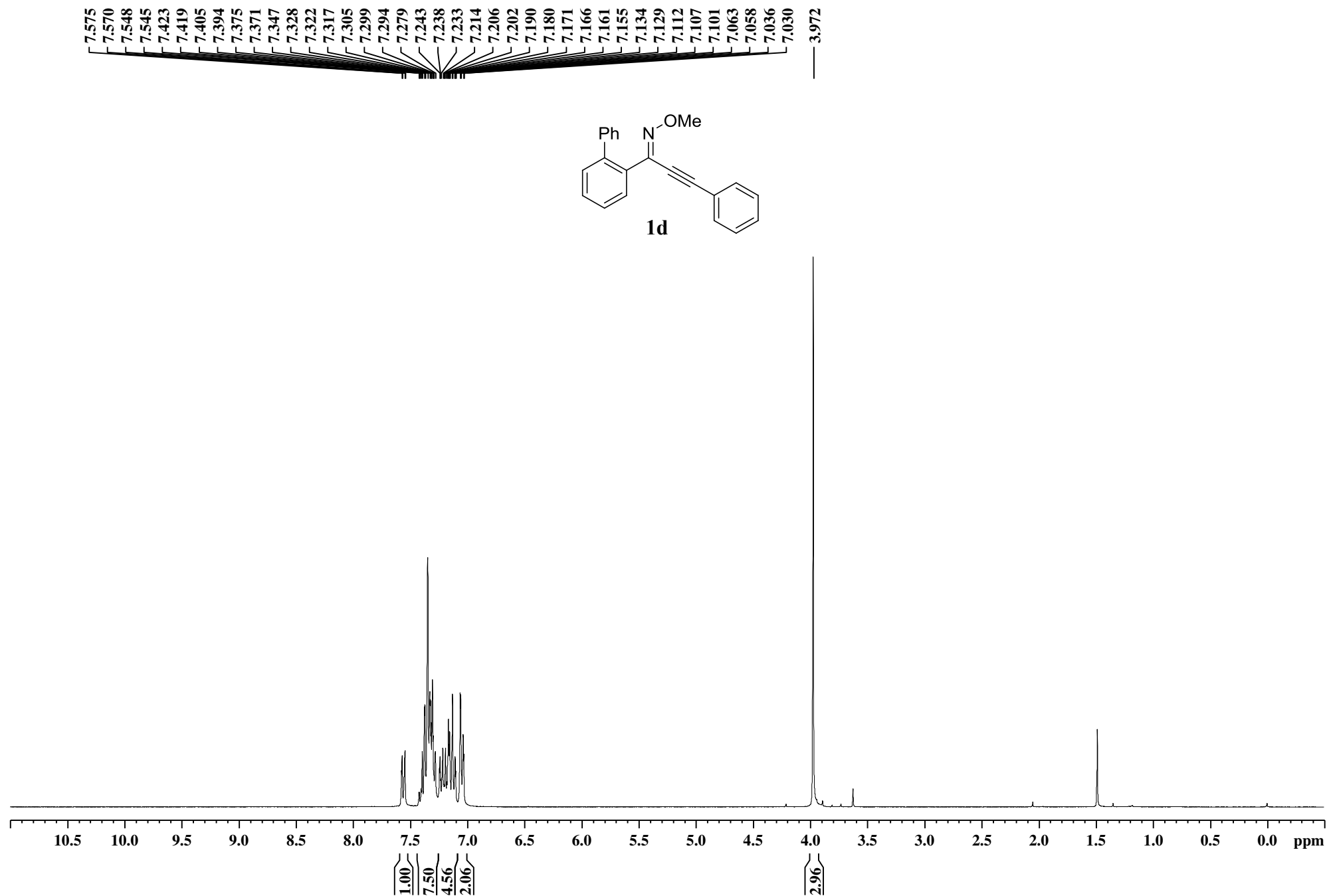
101.17

79.43

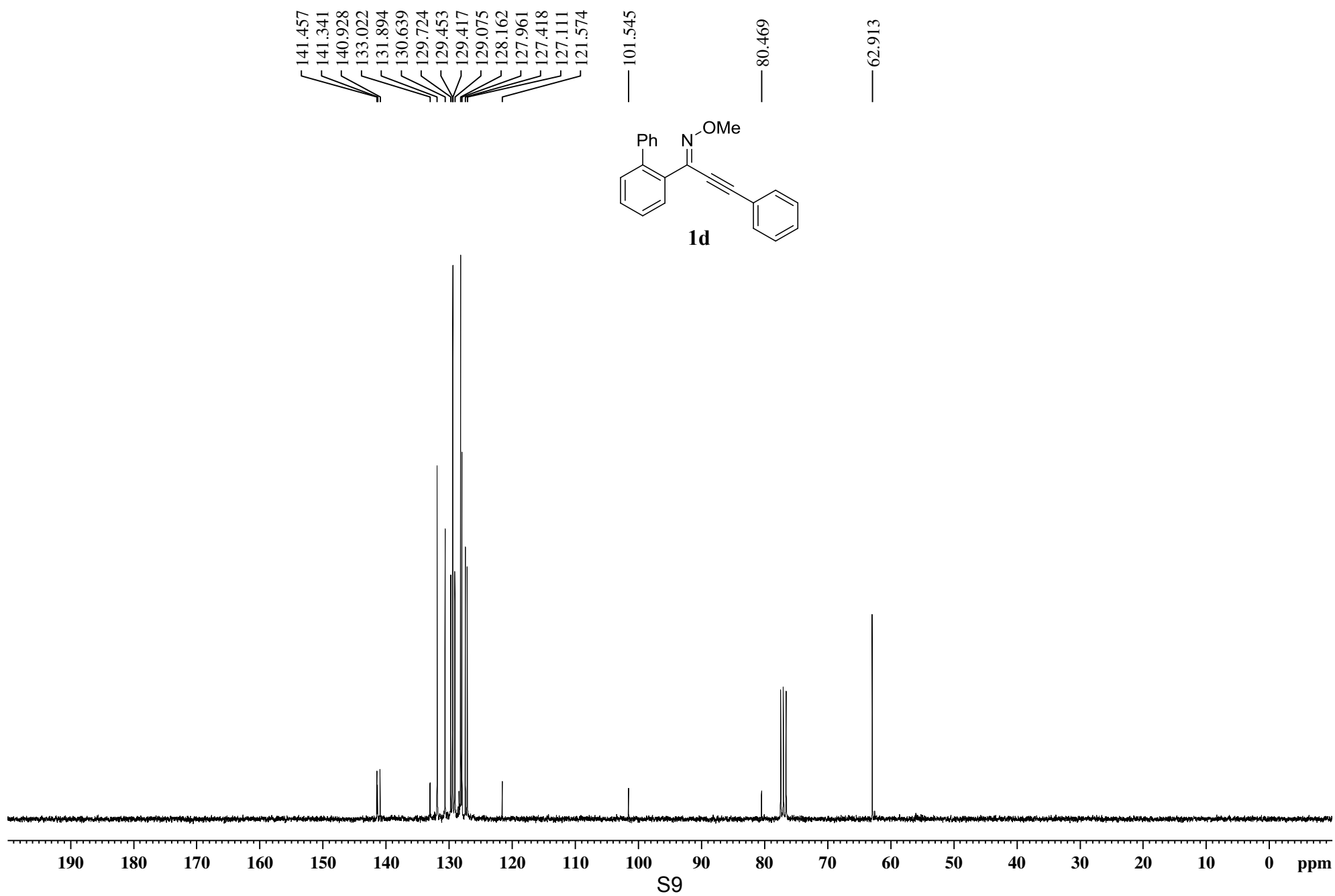
63.11



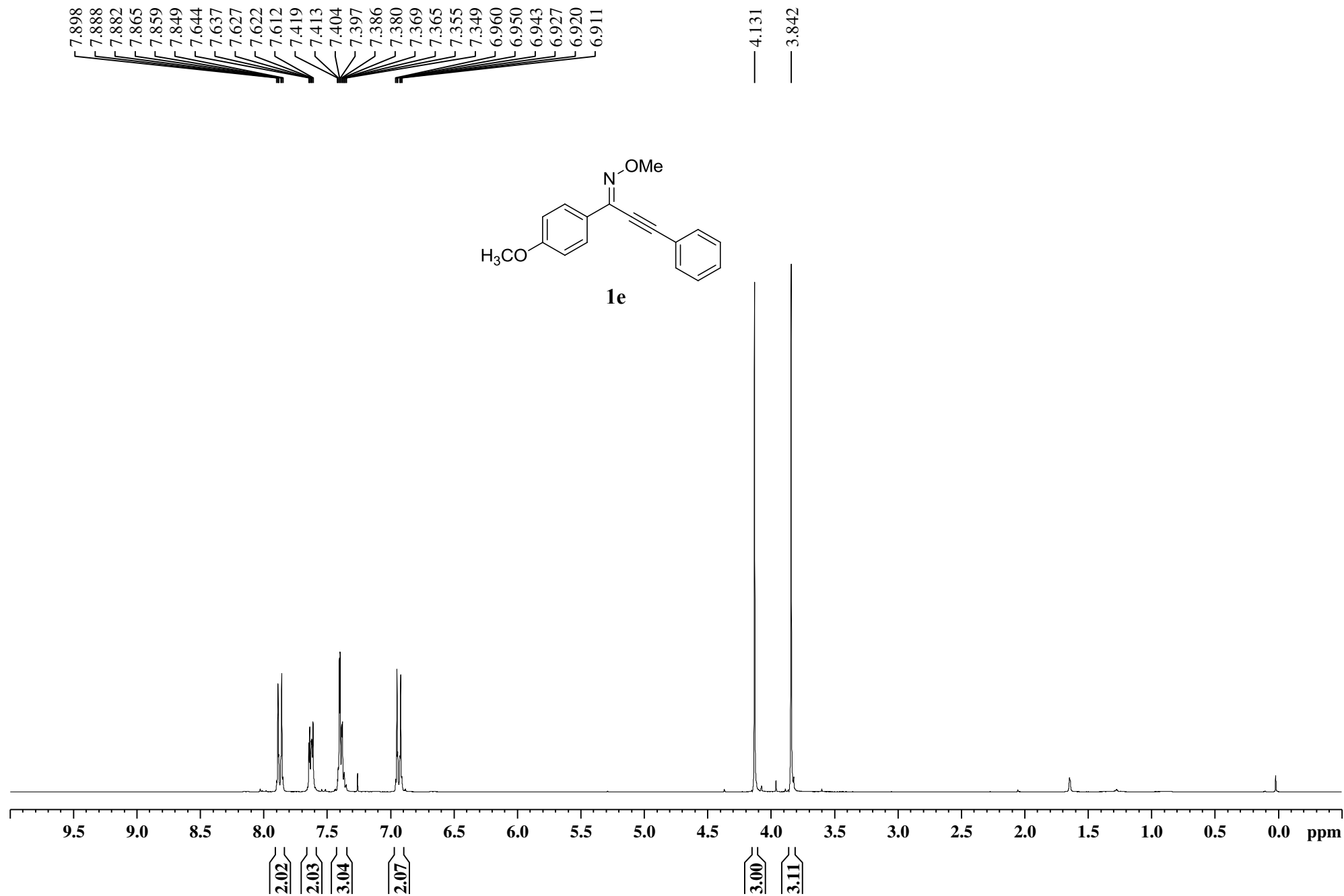
WK-I-179-TOP



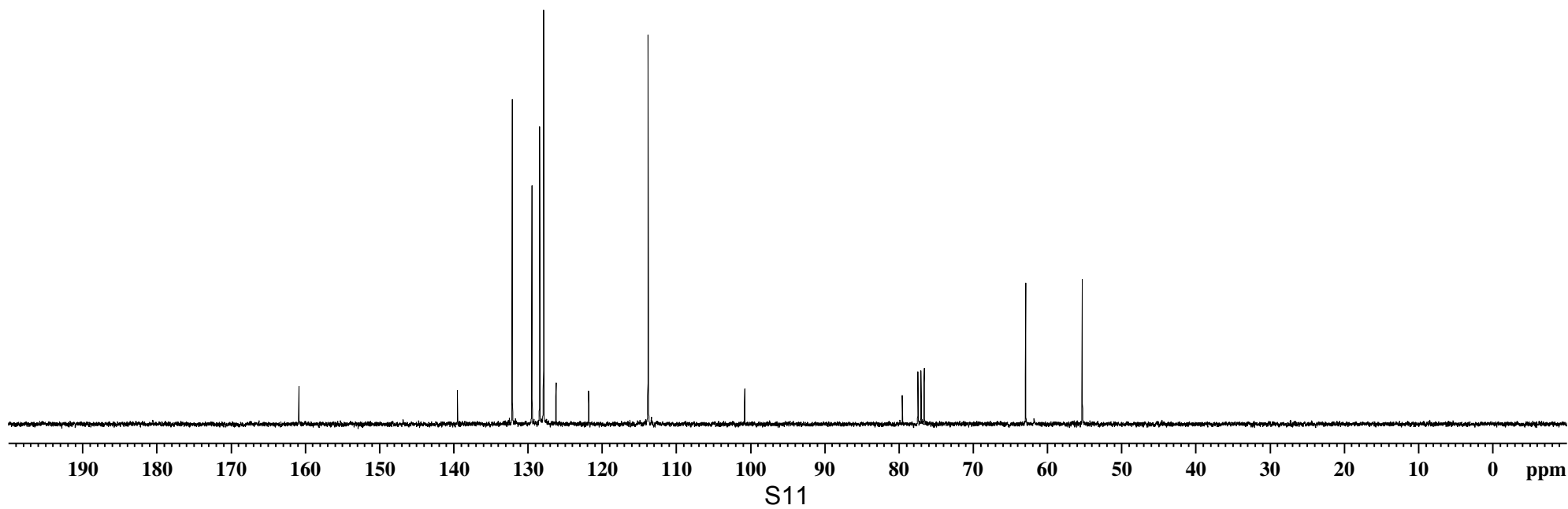
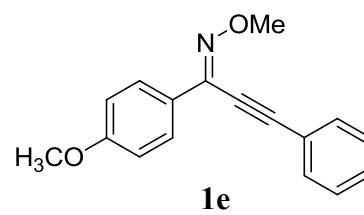
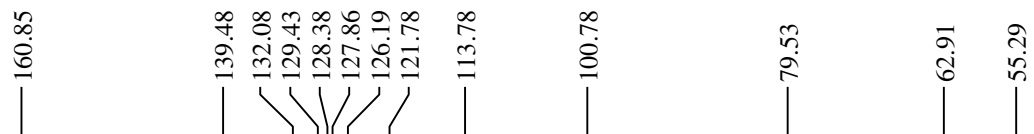
WK-I-179-TOP



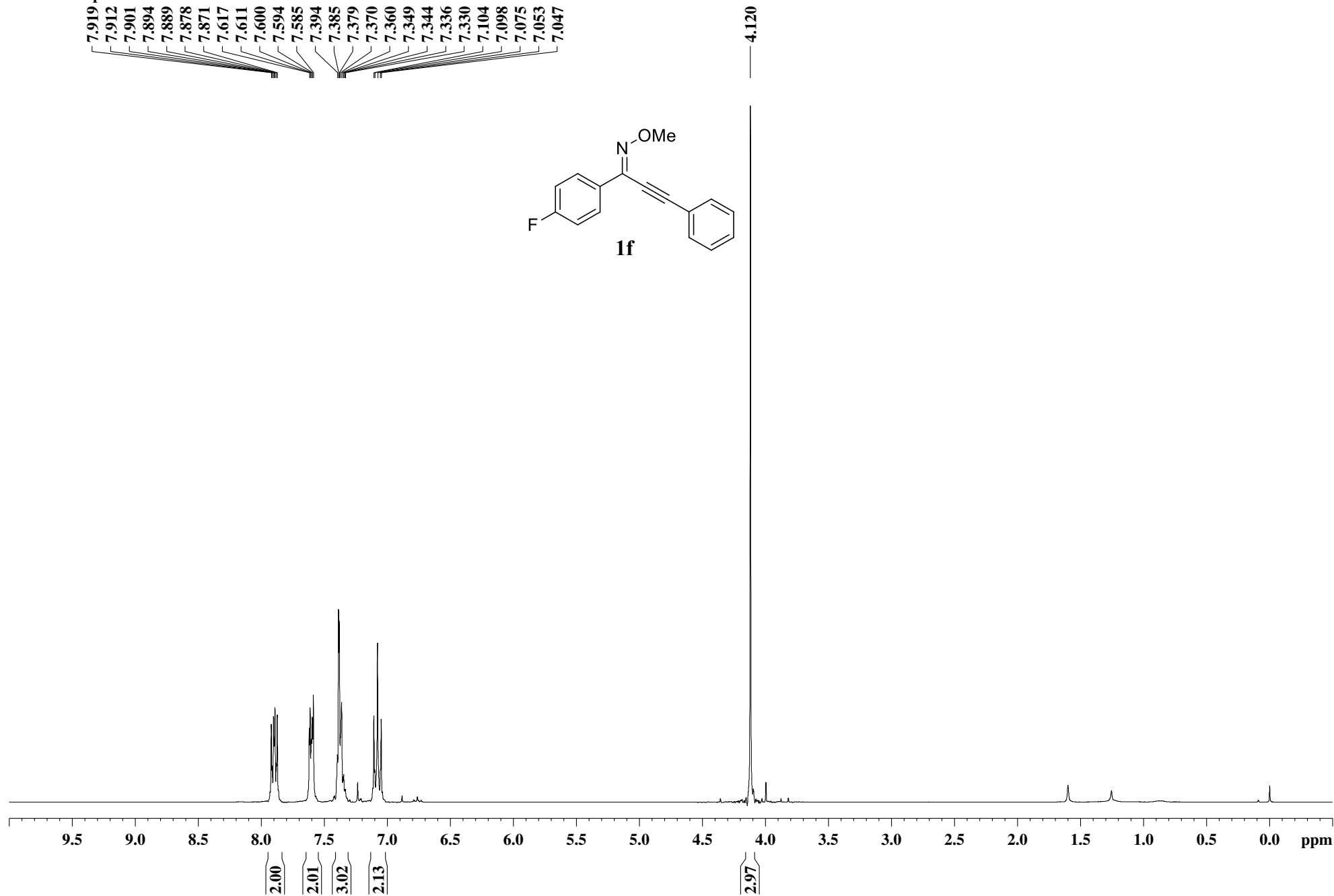
WK-I-61



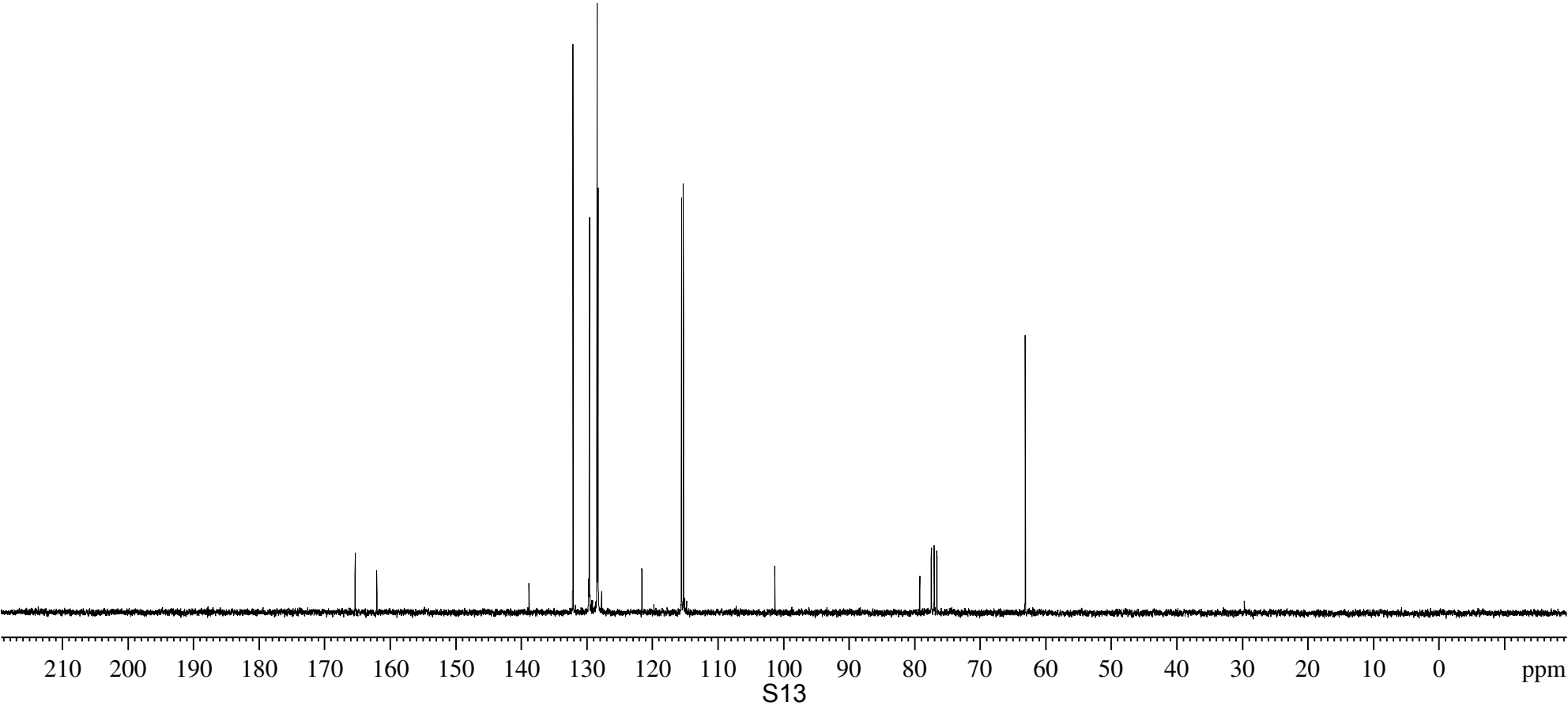
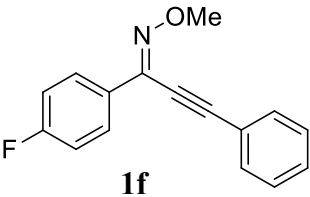
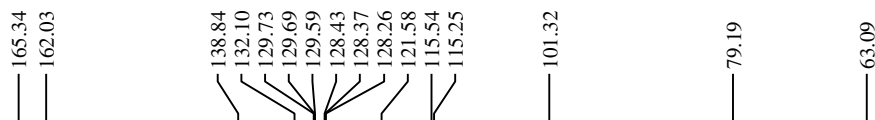
WK-I-61



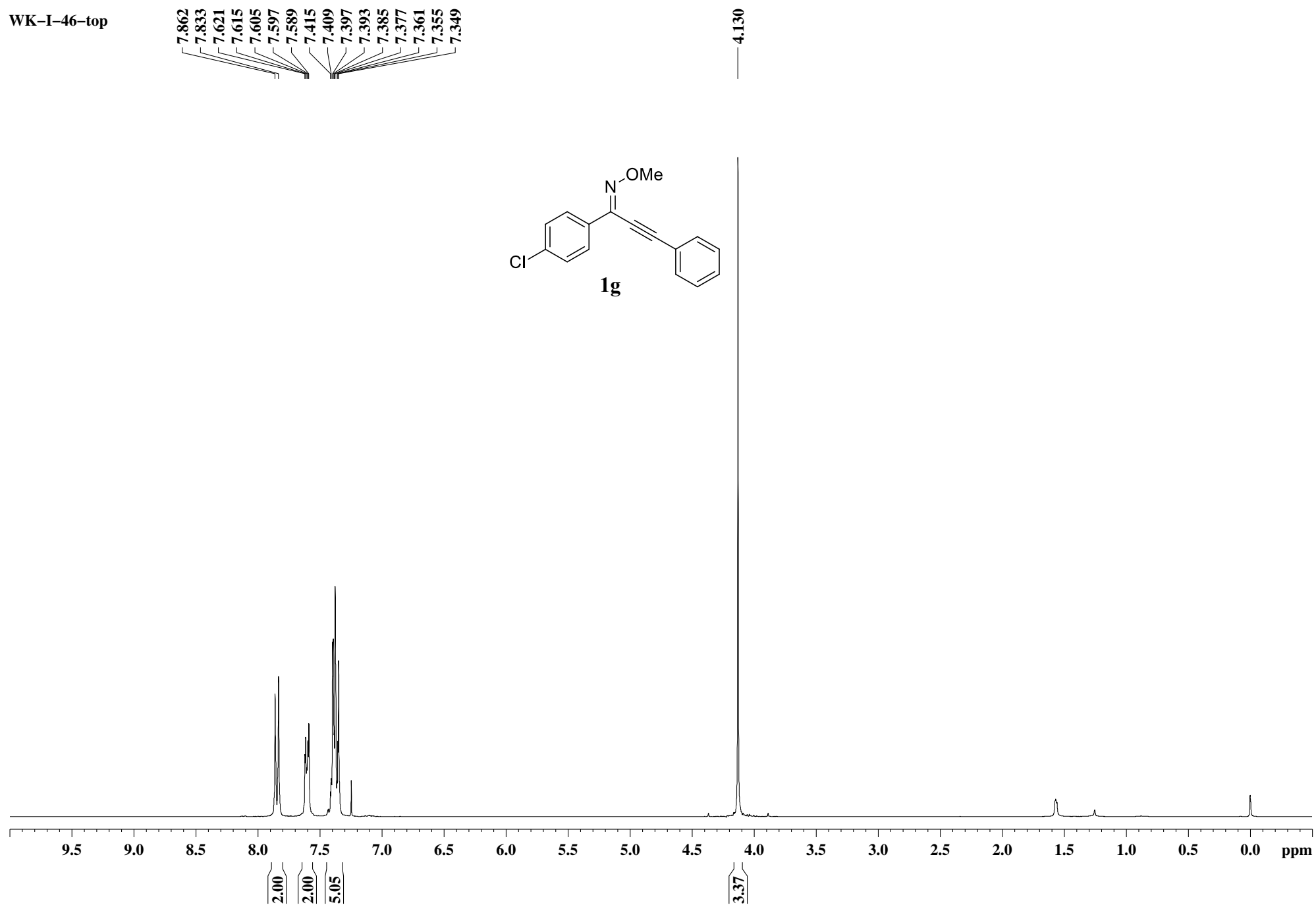
WK-I-51-pure



WK-I-51-pure



WK-I-46-top



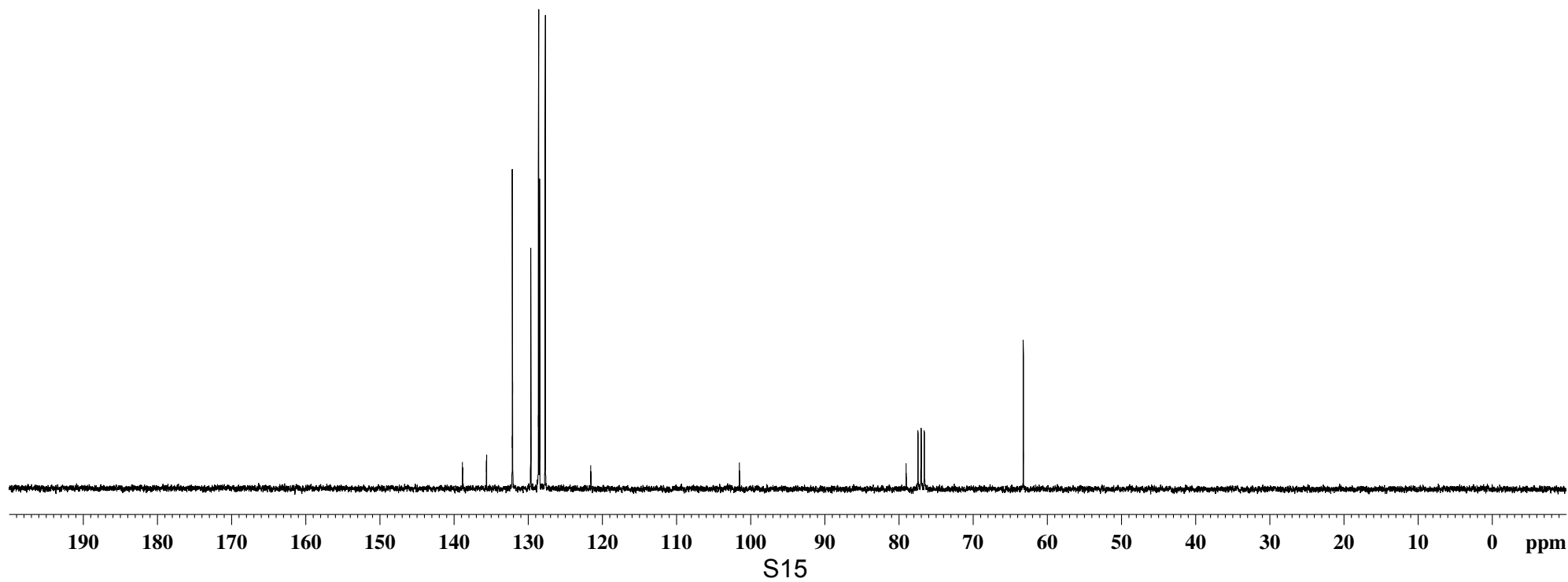
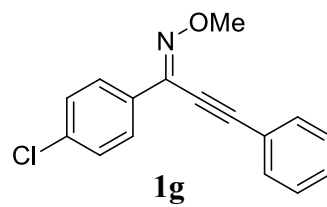
WK-I-46-top

138.881
135.651
132.166
132.109
129.682
128.638
128.493
127.734
121.579

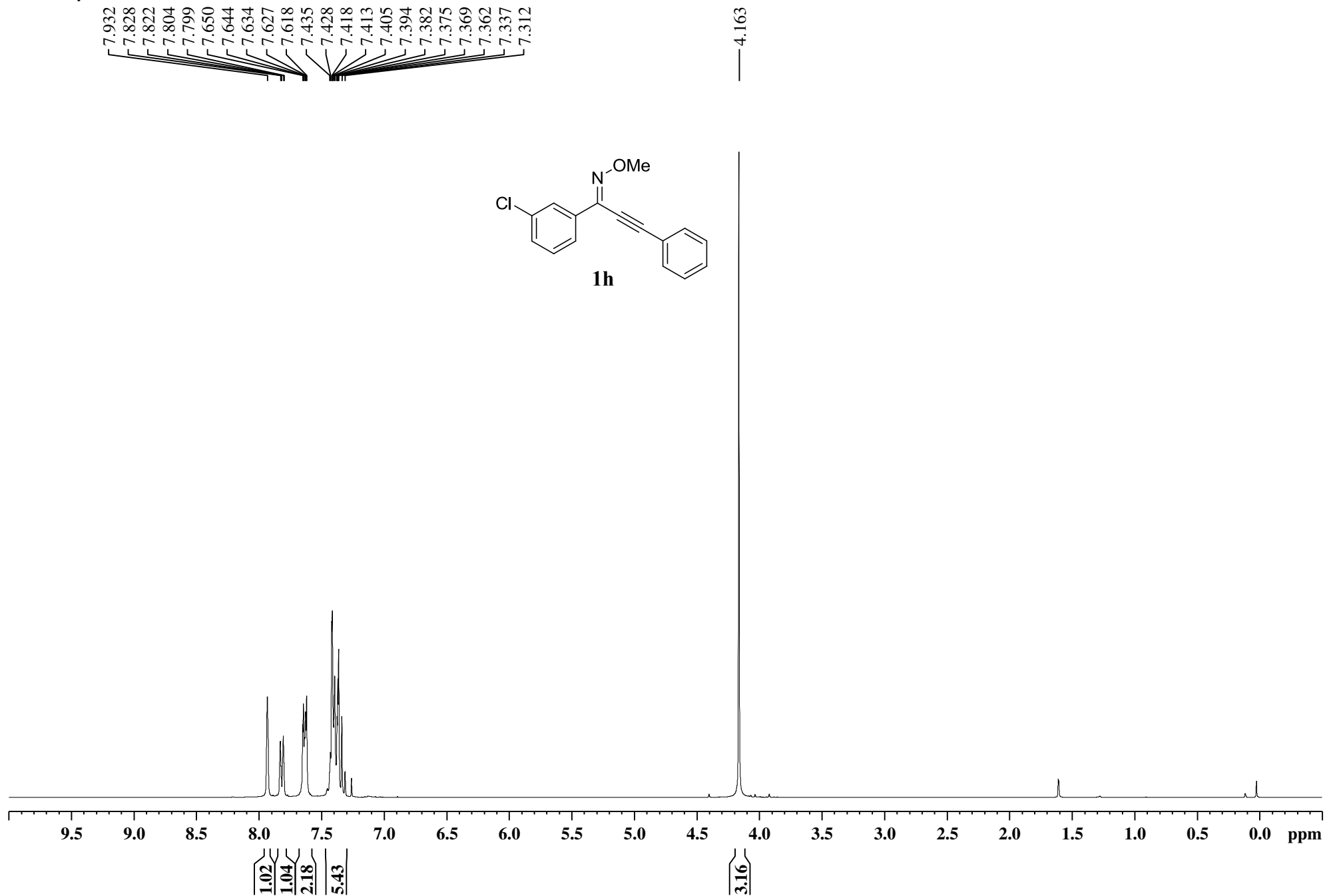
101.529

79.046

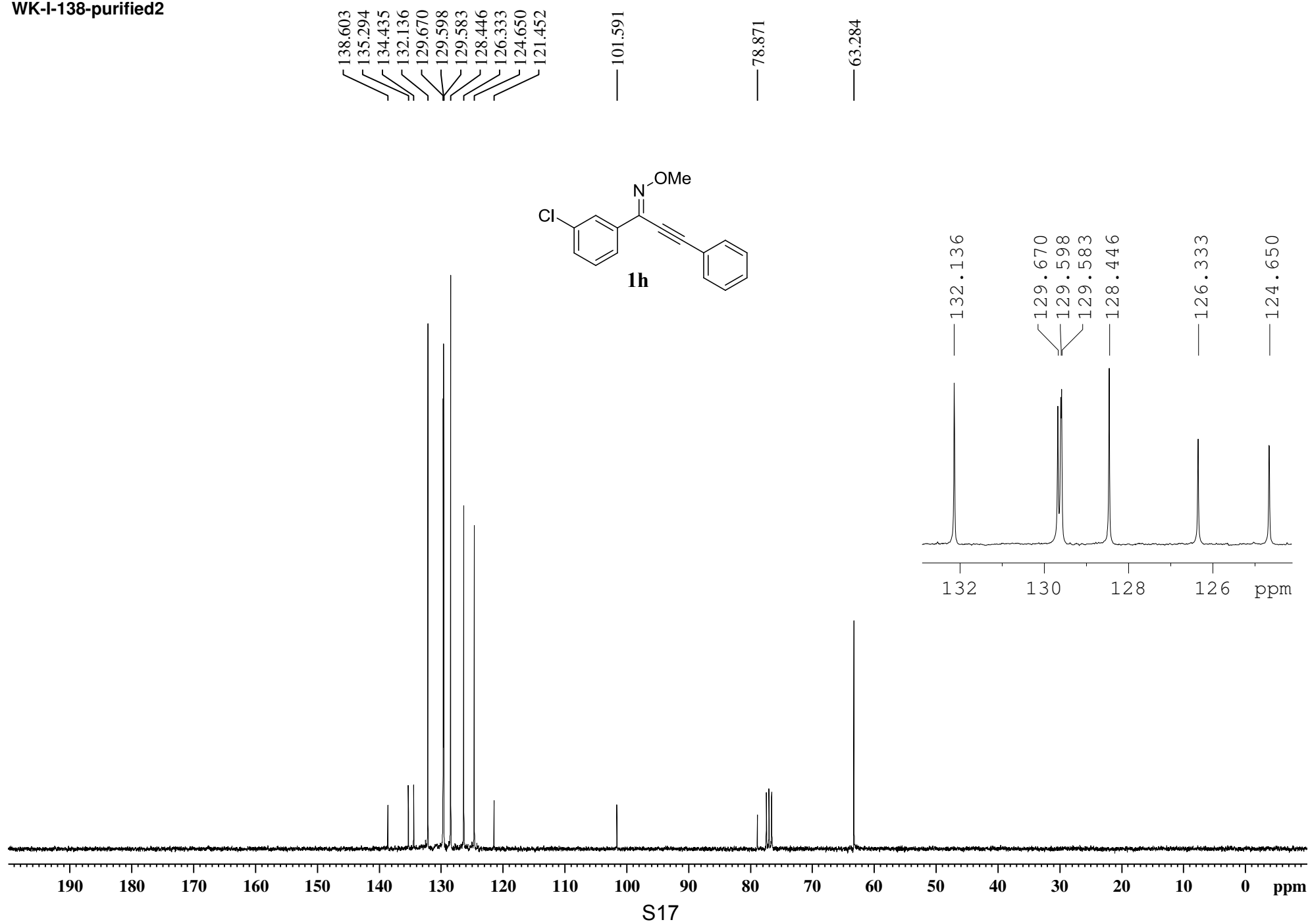
63.248



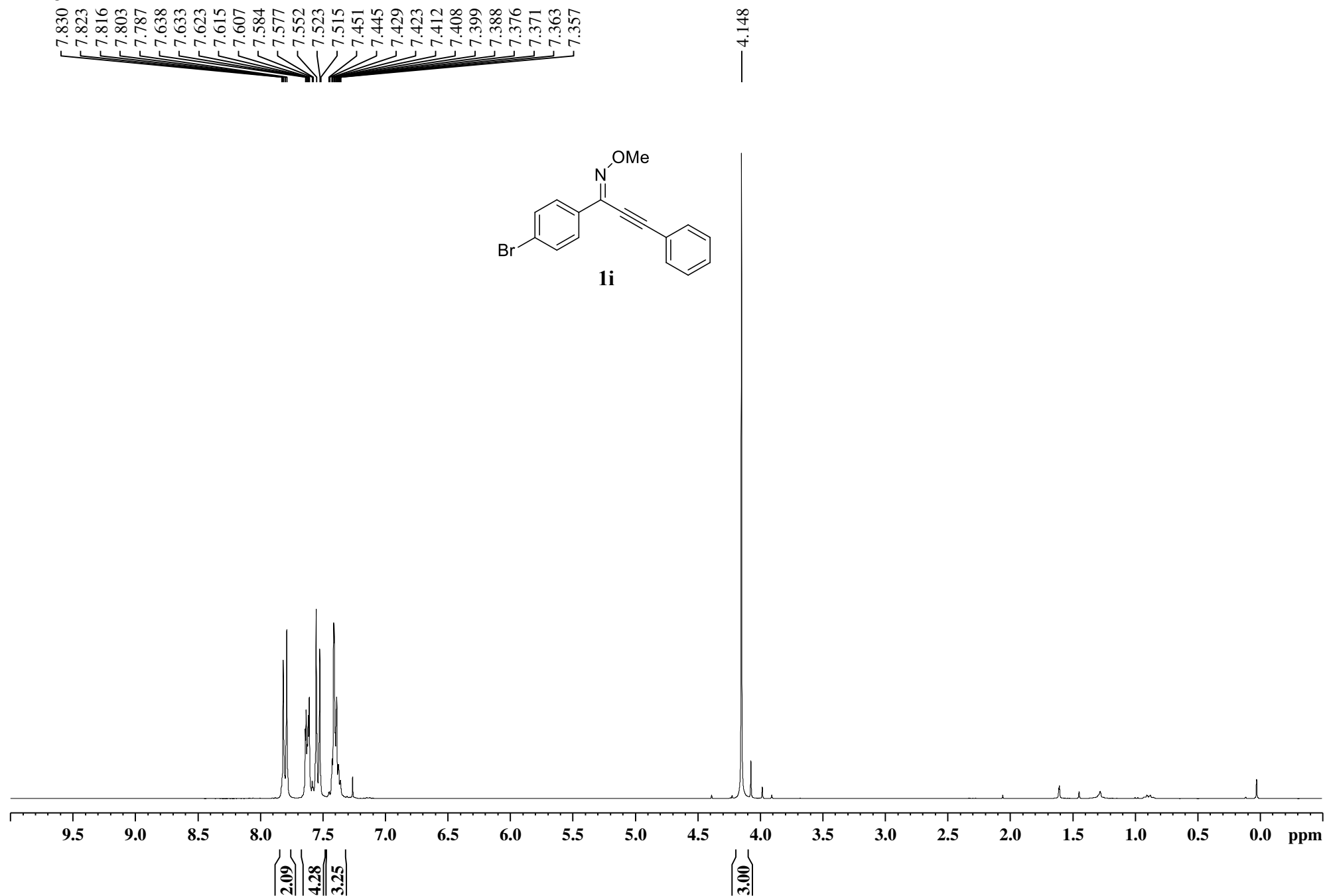
WK-I-138-purified2



WK-I-138-purified2



WK-I-73



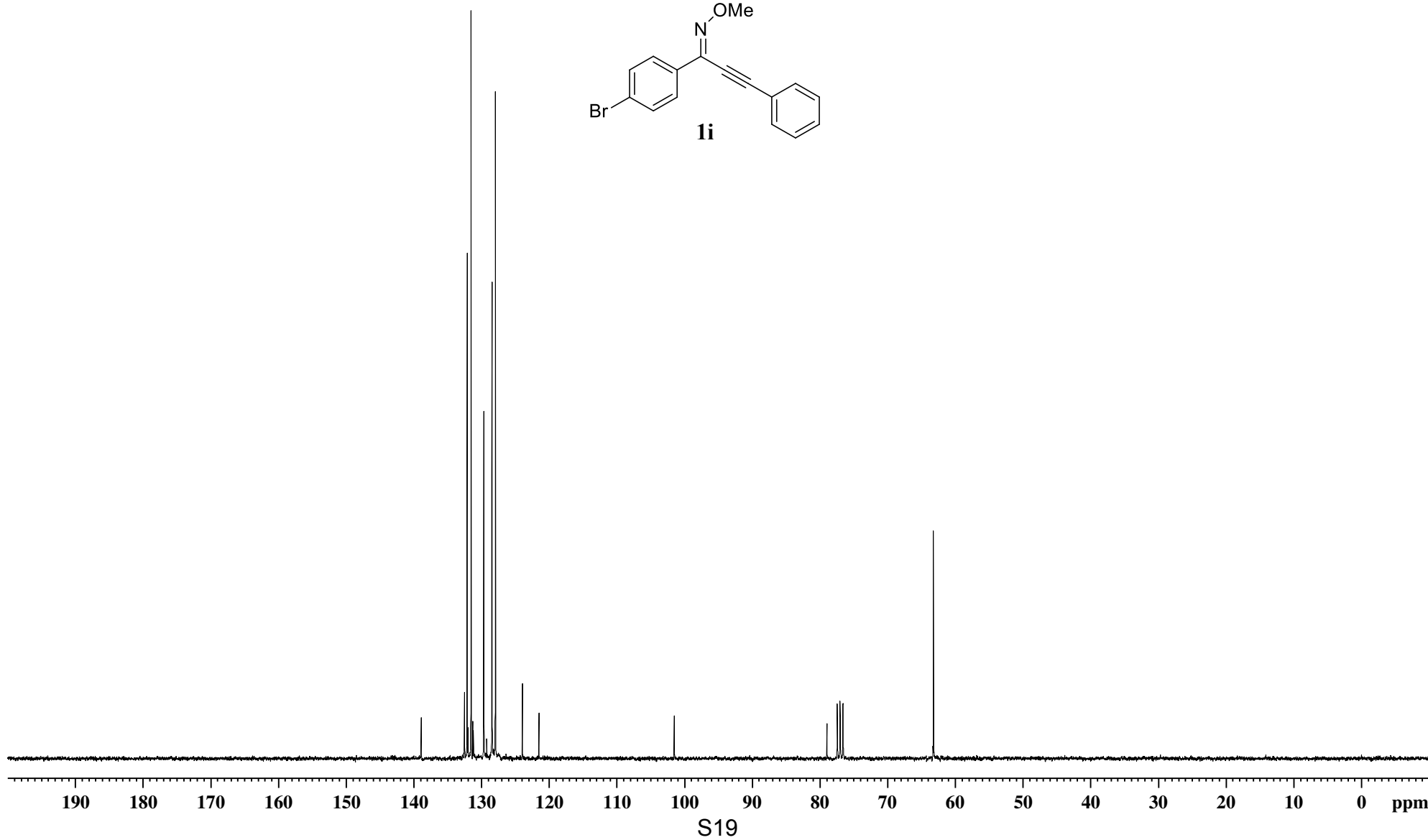
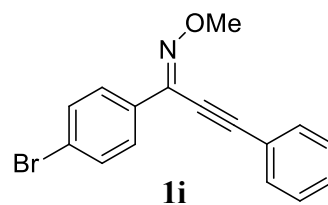
WK-I-73-purified

138.88
132.49
132.11
131.52
129.63
128.44
127.92
123.93
121.49

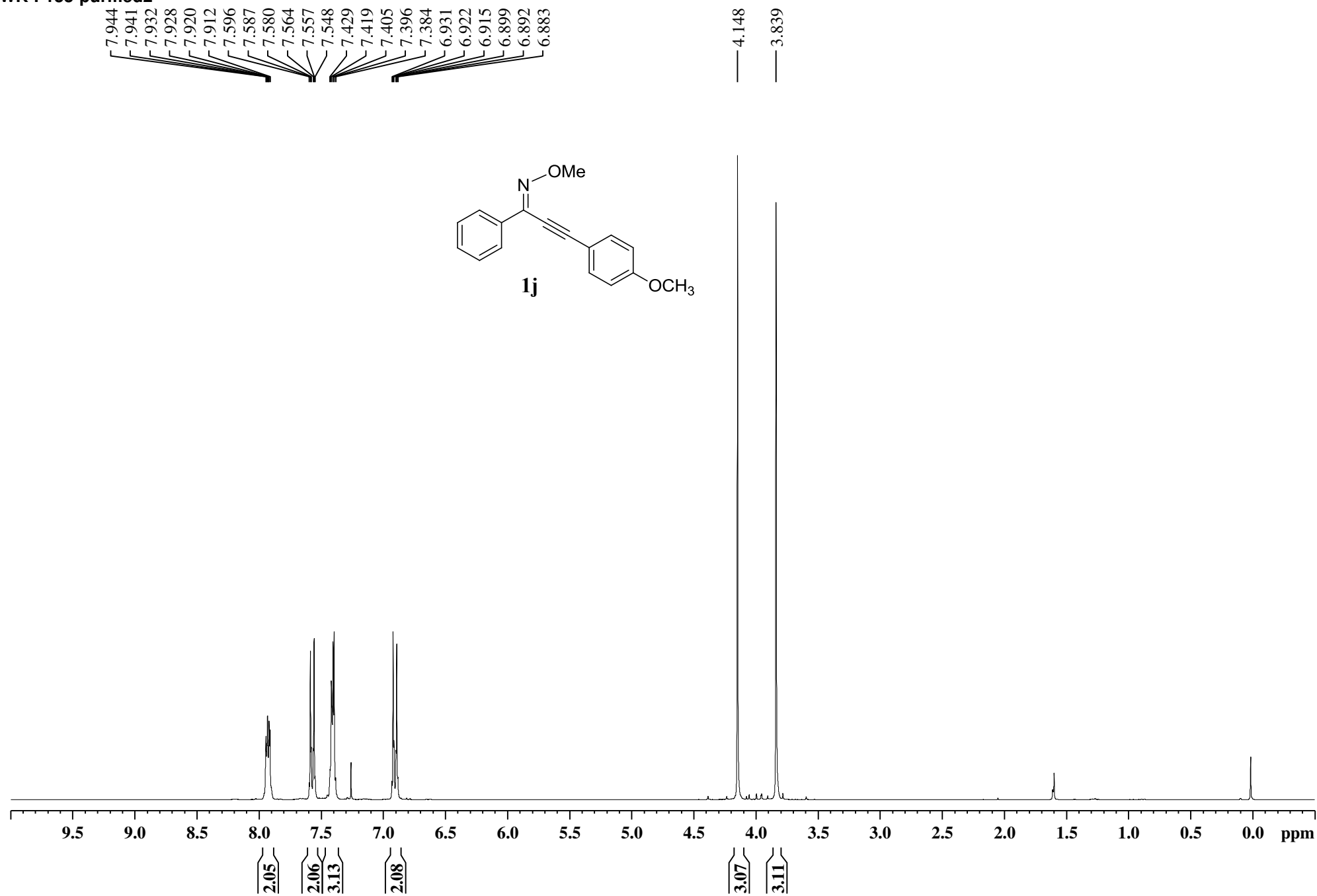
101.50

78.94

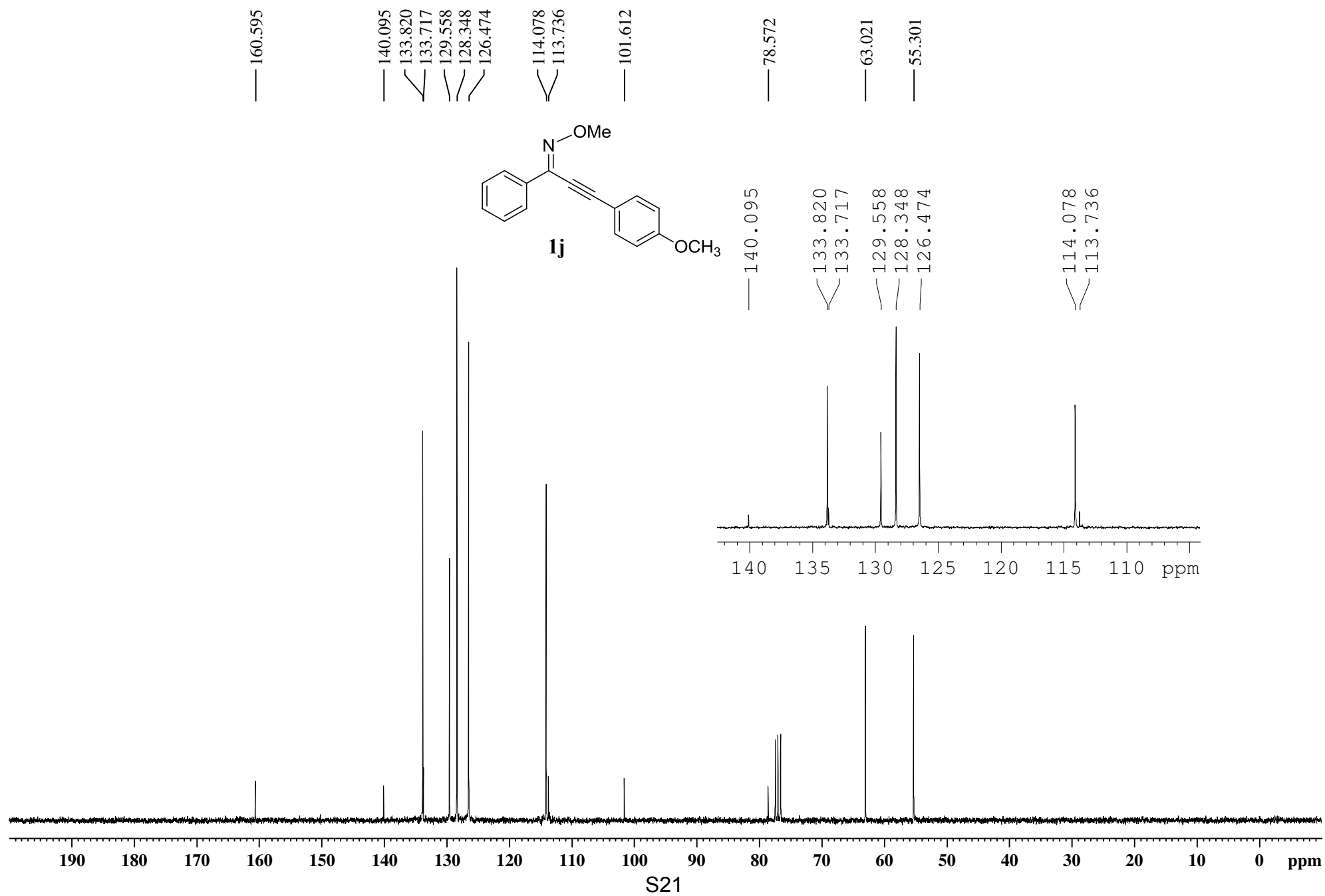
63.21



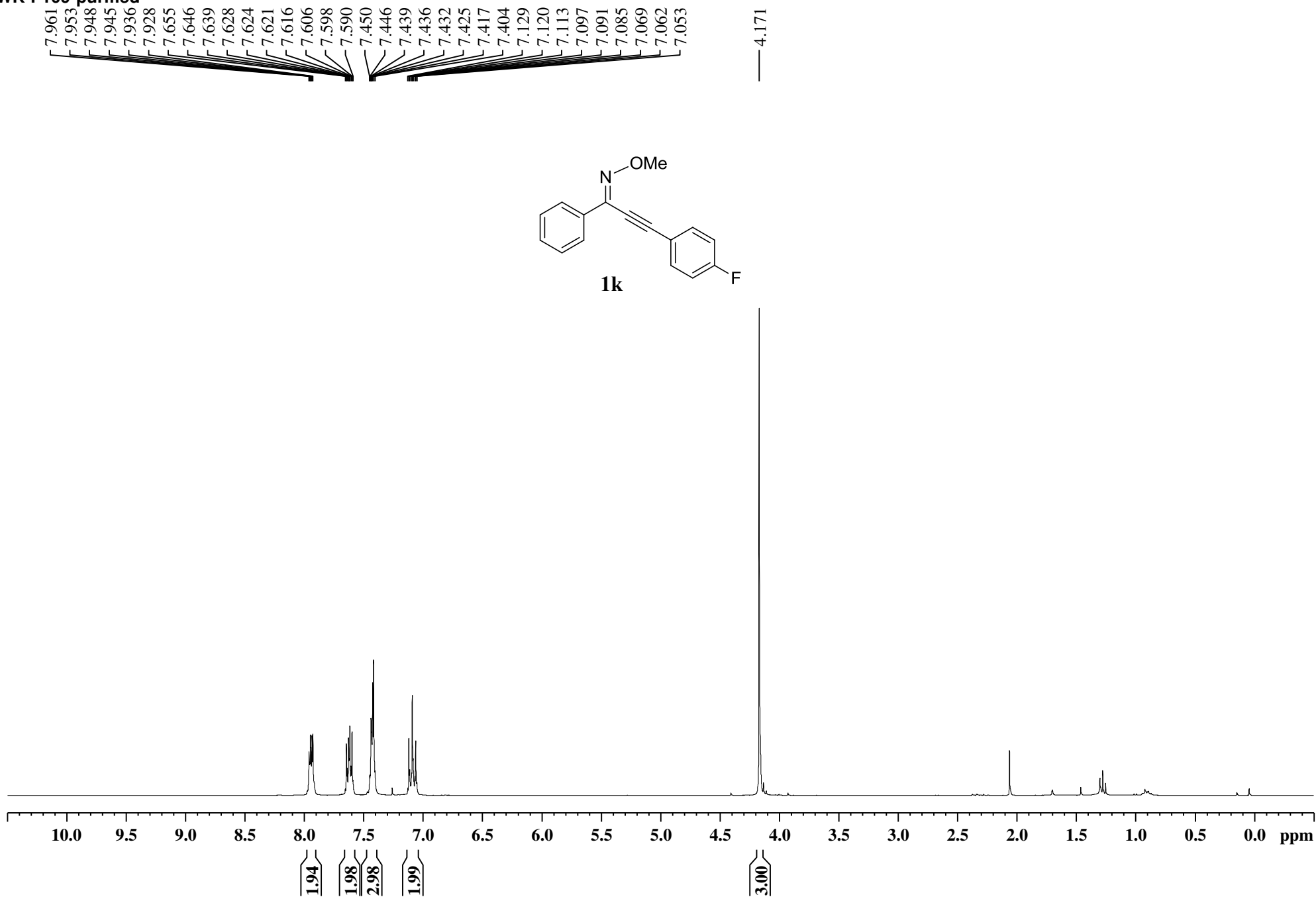
WK-I-133-purified2



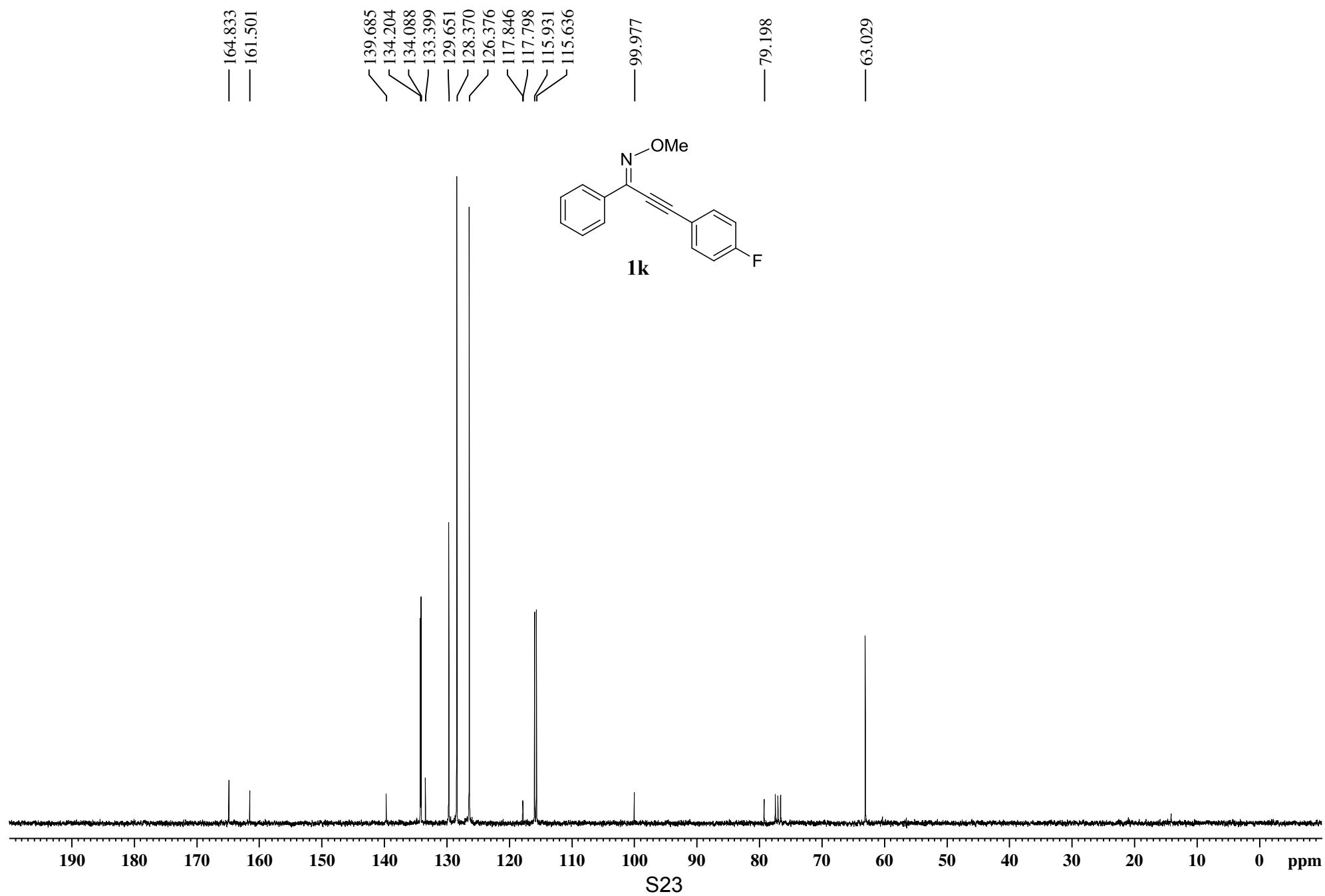
WK-I-133-purified2



WK-I-109-purified



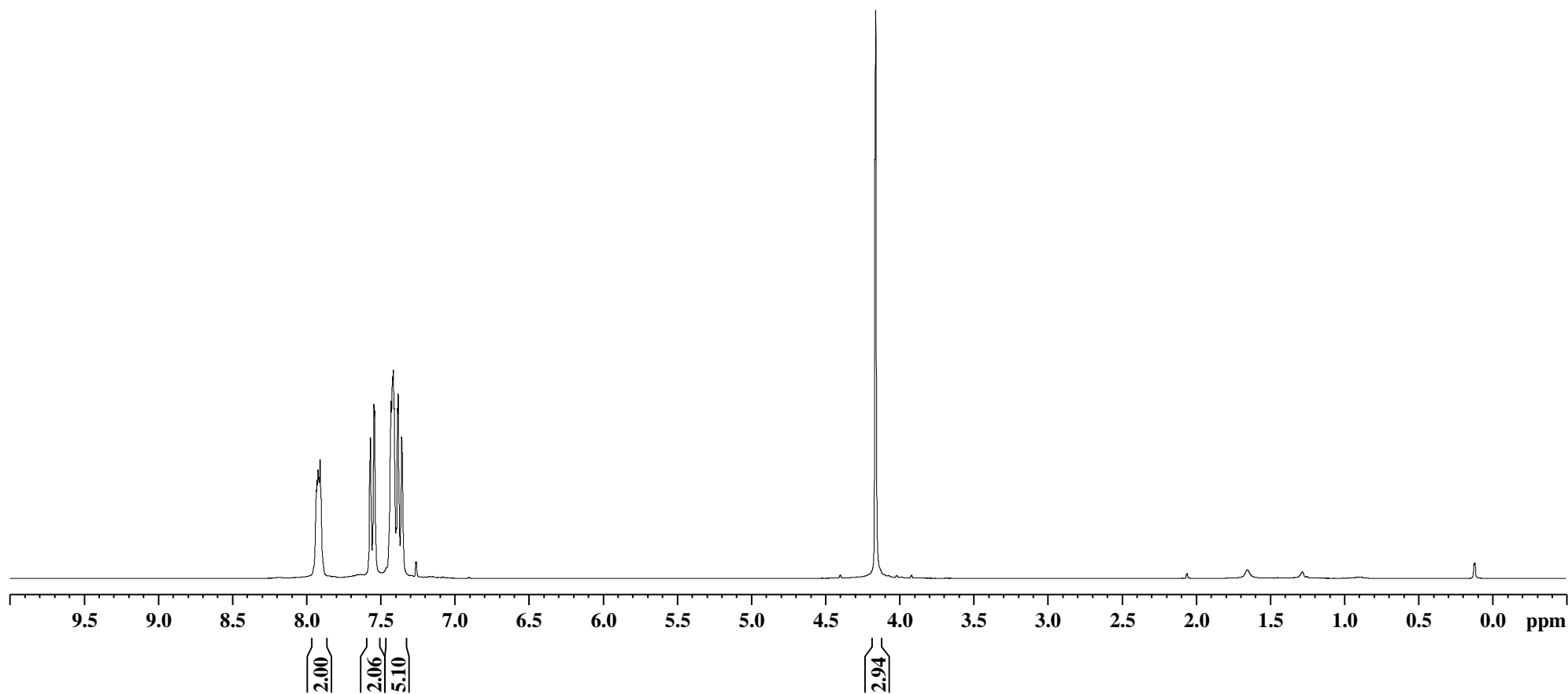
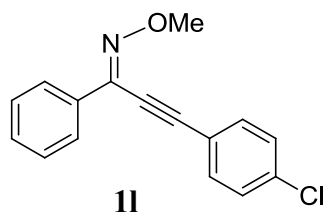
WK-I-109-purified



WK-I-117-purified2

7.930
7.926
7.921
7.915
7.906
7.571
7.567
7.544
7.539
7.427
7.416
7.412
7.406
7.393
7.384
7.380
7.356

4.157



S24

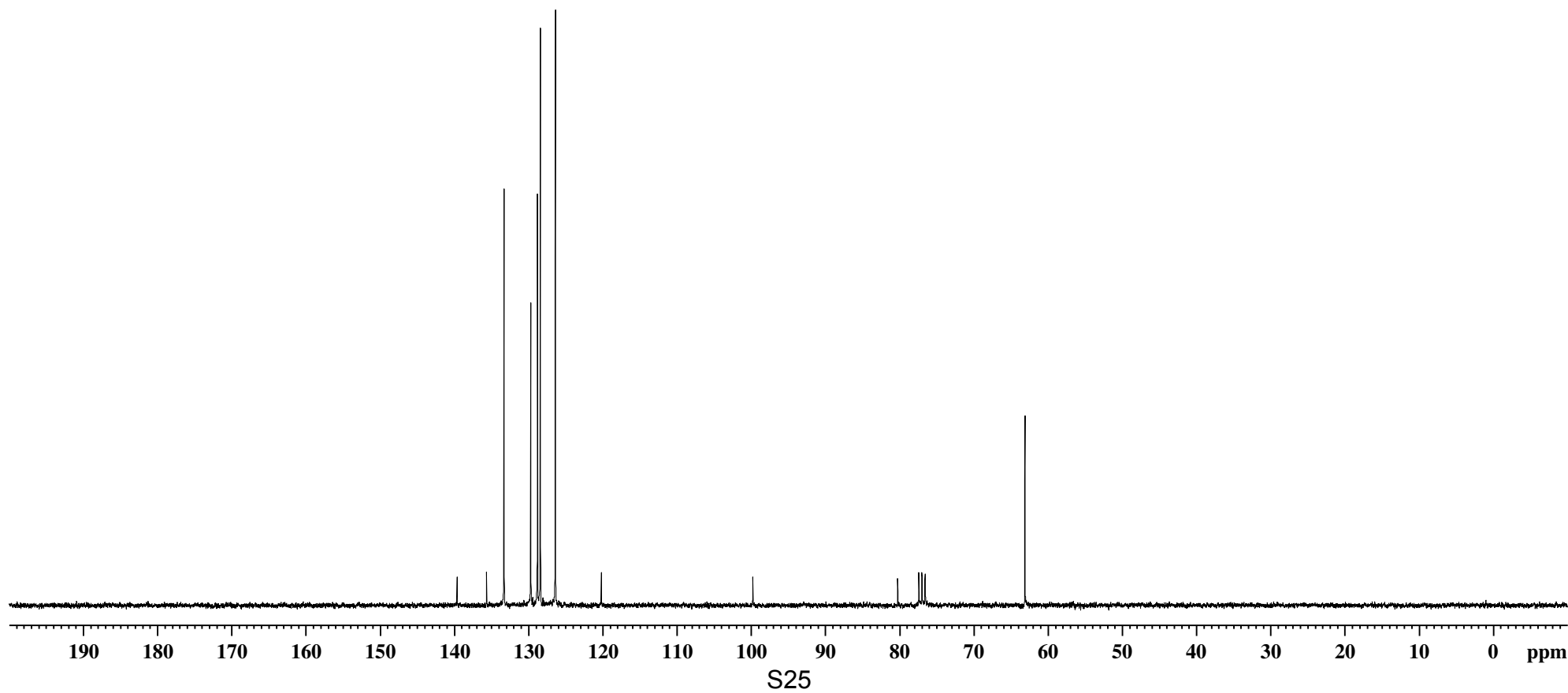
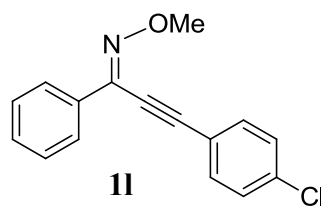
WK-I-117-purified2

139.63
135.67
133.31
129.71
128.80
128.41
126.39
120.19

99.79

80.26

63.12

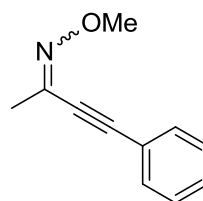


WK-I-234-purified

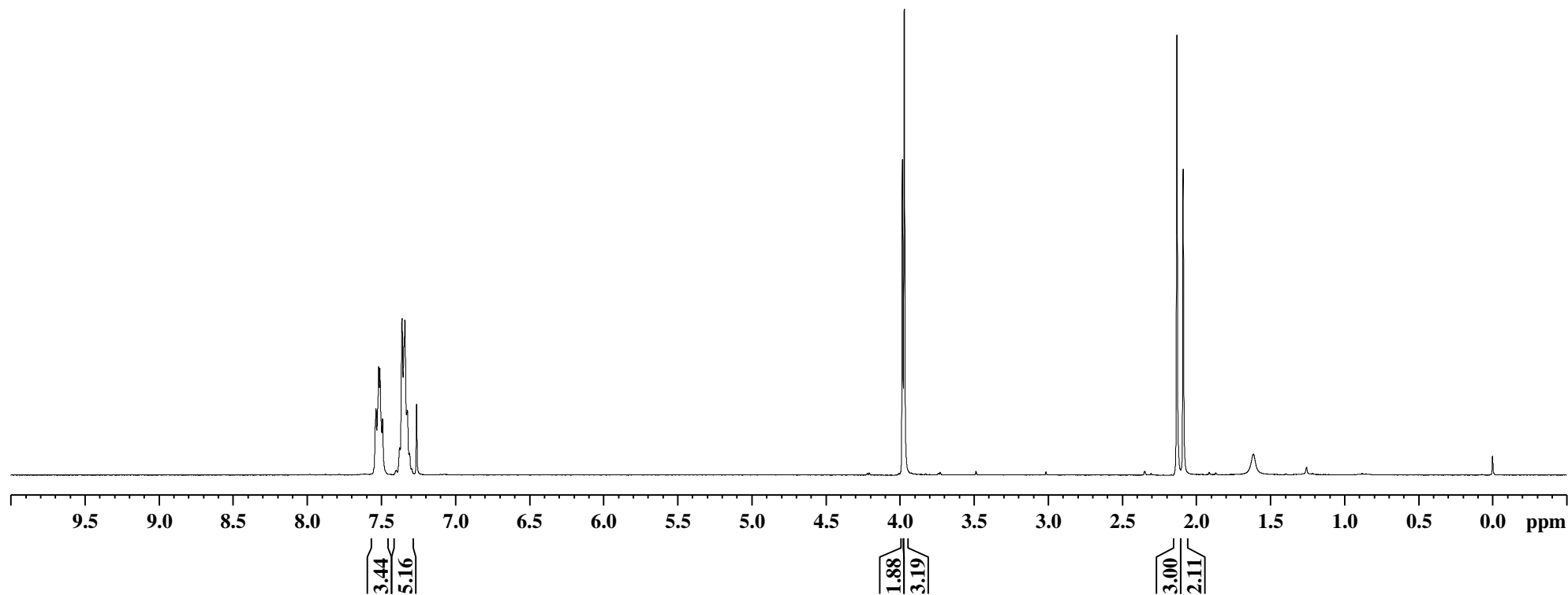
7.535
7.516
7.508
7.491
7.397
7.375
7.359
7.340
7.323
7.308
7.293

3.982
3.970

2.130
2.088



1m: E/Z = 41/59



WK-I-234-purified

142.106
137.230
131.877
131.708
129.207
128.839
128.185
121.775
121.530

98.863

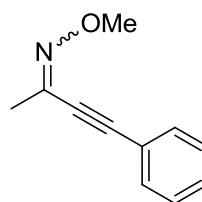
89.994

85.363

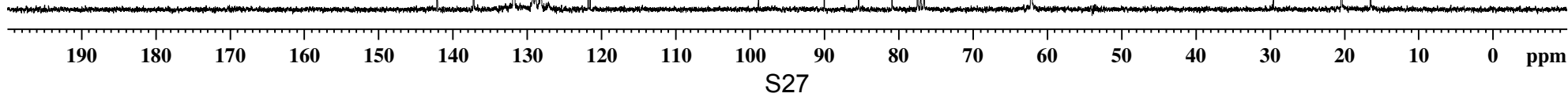
80.860

62.195
62.043

20.361
16.441

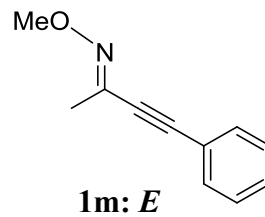


1m: E/Z = 41/59



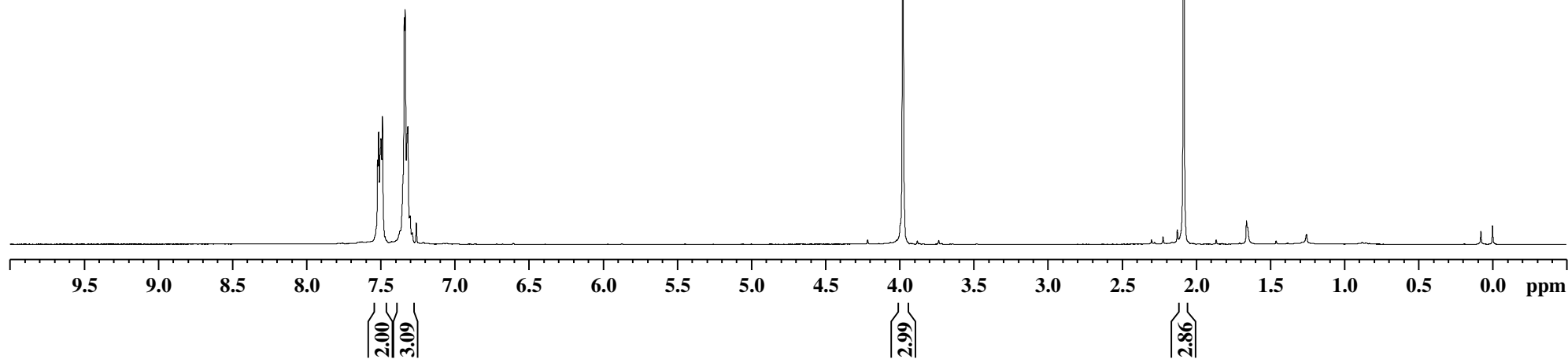
WK-II-53-Fr1-E isomer

7.519
7.513
7.497
7.487
7.339
7.333
7.316
7.304
7.300
7.291



3.977

2.083



WK-II-53-Fr1-E isomer

— 142.33

— 131.85

— 128.96

— 128.30

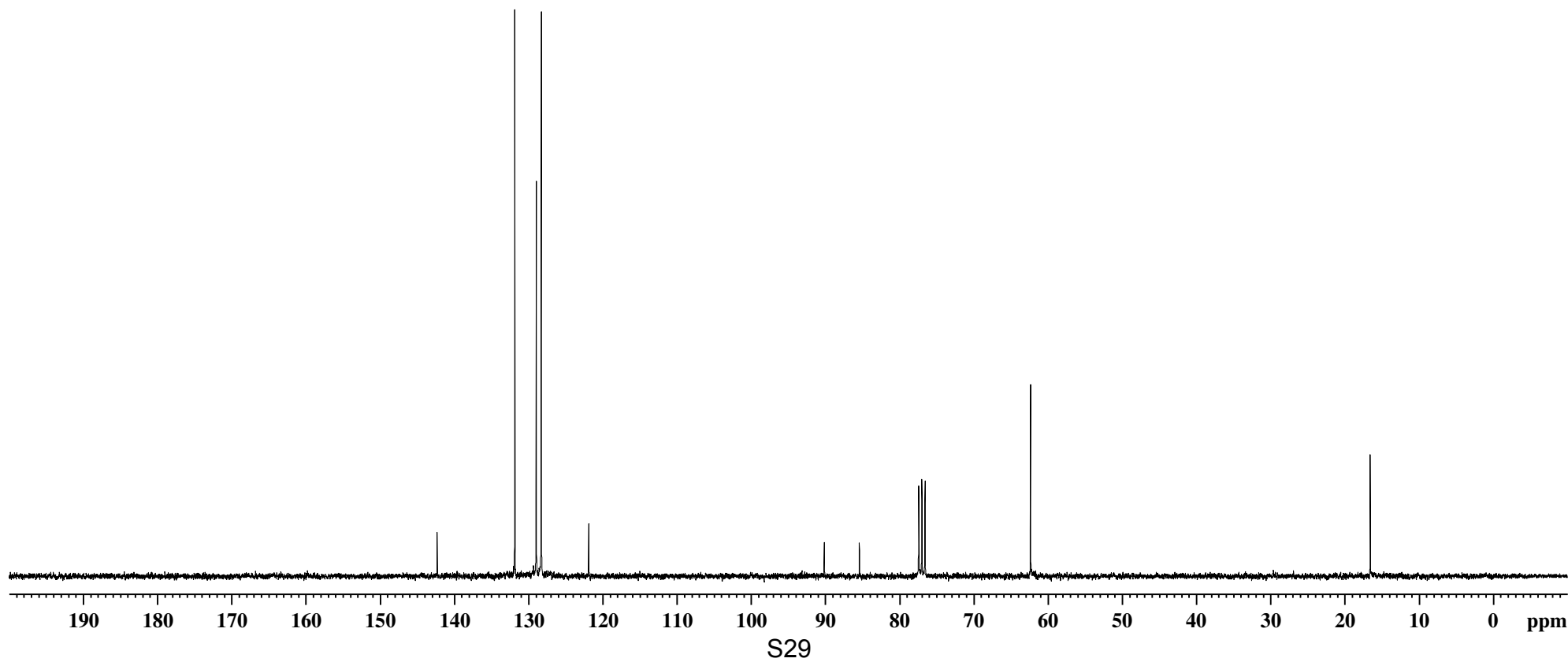
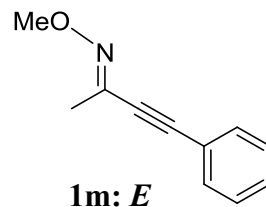
— 121.89

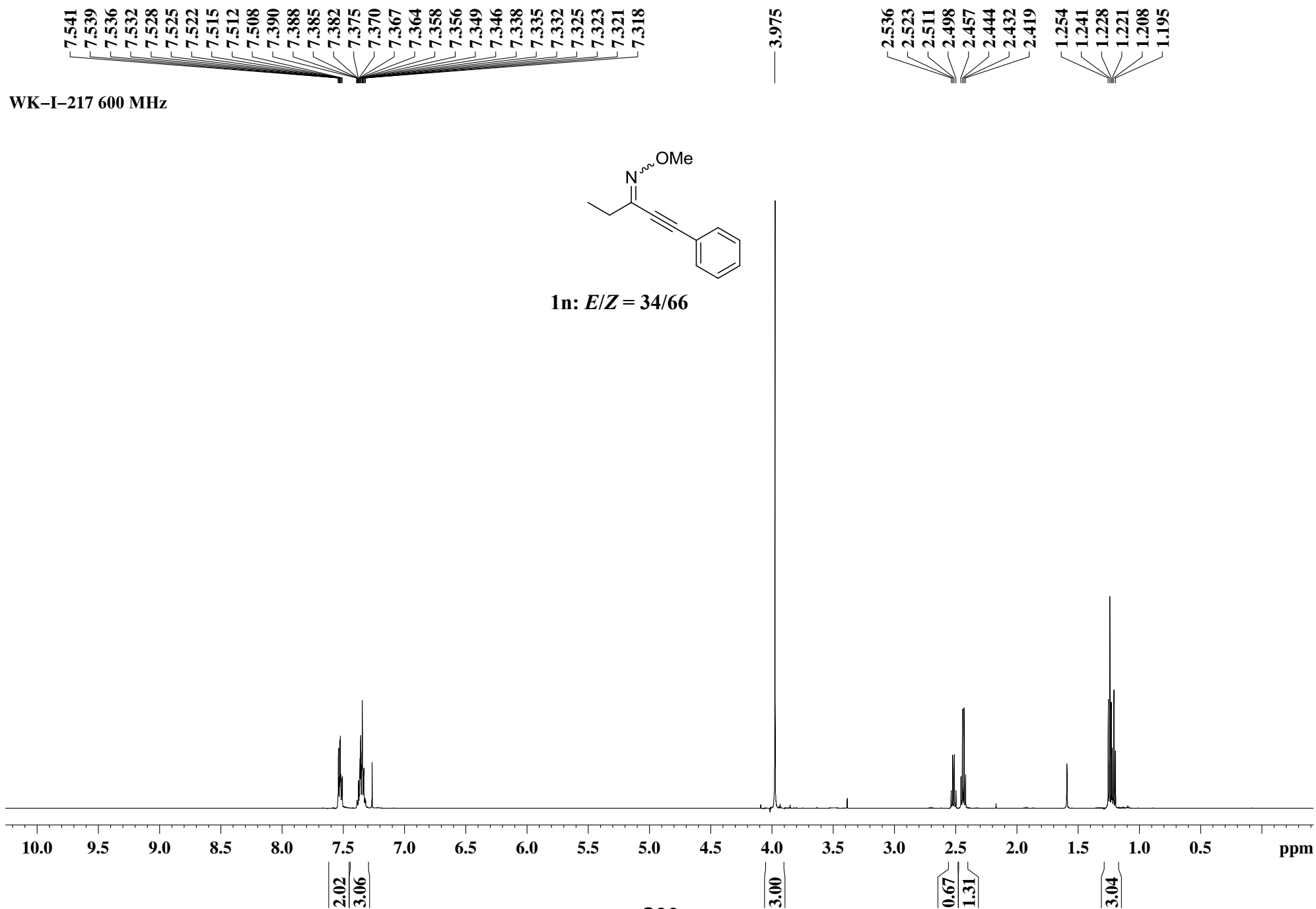
— 90.14

— 85.42

— 62.37

— 16.60





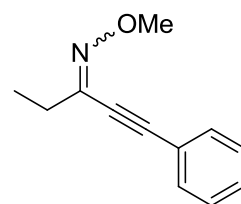
WK-I-217-300 MHz

7.569
7.563
7.551
7.545
7.537
7.519
7.425
7.420
7.398
7.385
7.382
7.371
7.364
7.347
7.332

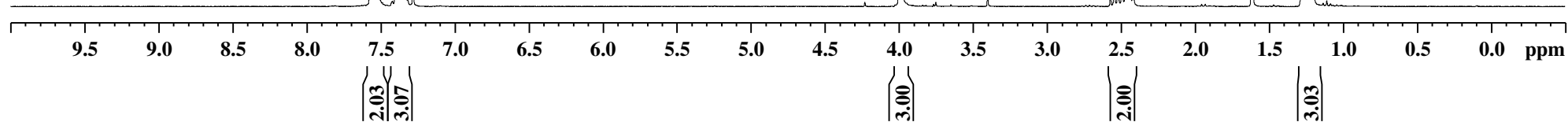
3.992

2.571
2.546
2.520
2.493
2.467
2.442
2.417

1.282
1.257
1.249
1.232
1.224
1.198



1n: *E/Z* = 34/66



WK-I-217-300 MHz

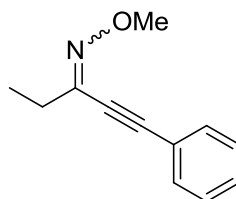
— 148.005
— 142.658
131.944
131.775
129.216
128.848
128.220
121.914
121.644

— 99.488
— 91.264
— 84.030
— 80.030

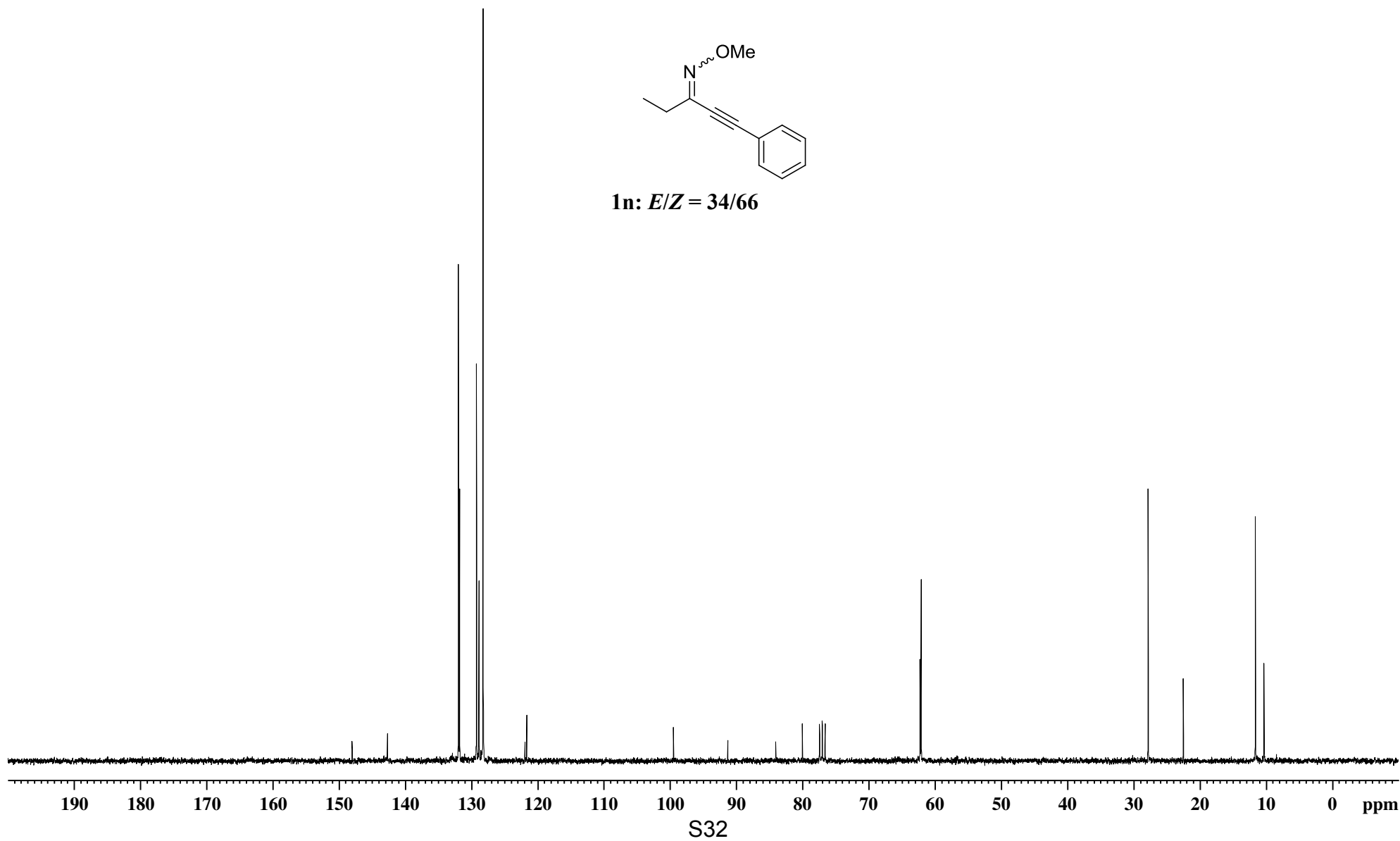
62.251
62.079

— 27.795
— 22.487

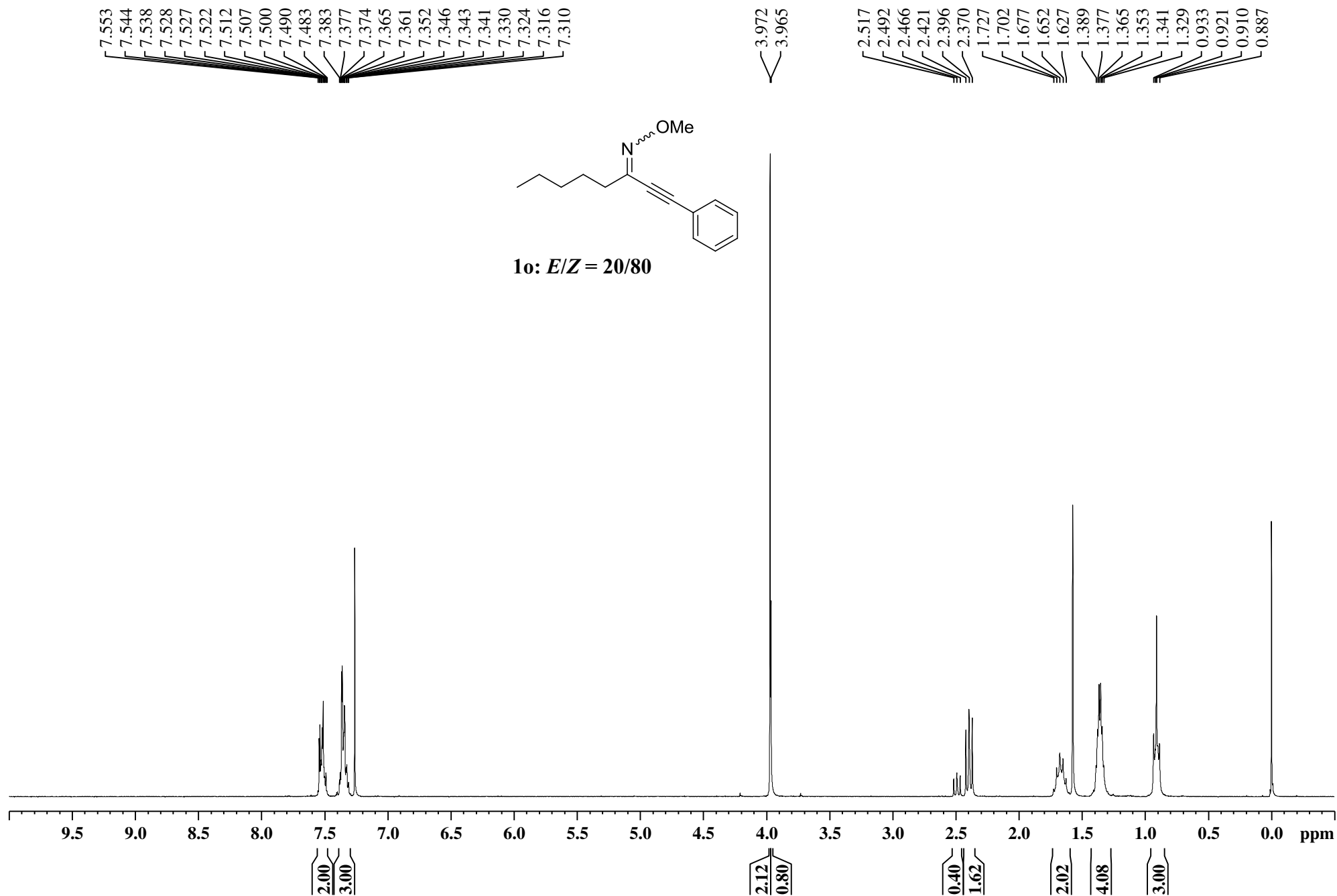
11.596
10.309



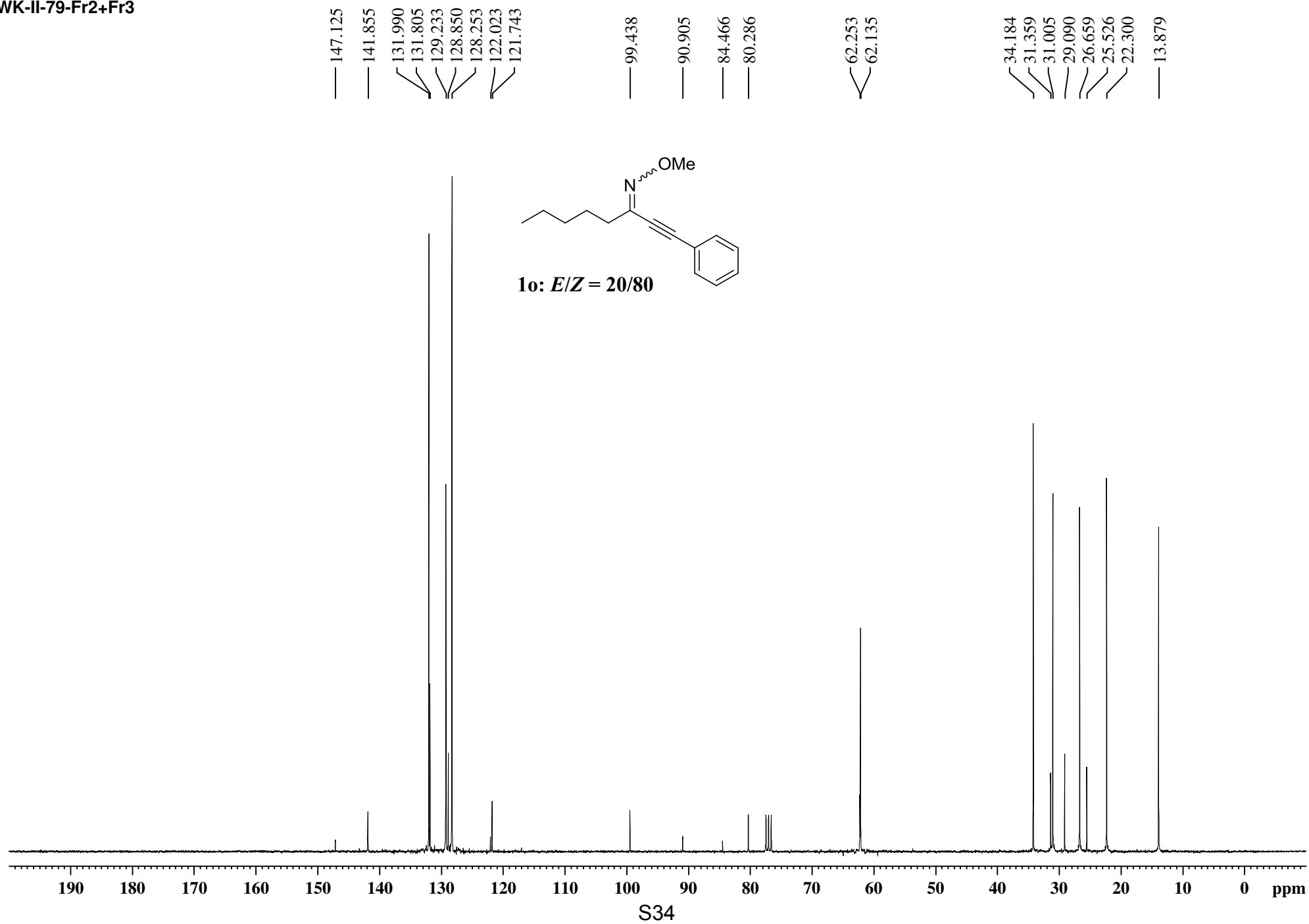
1n: *E/Z* = 34/66

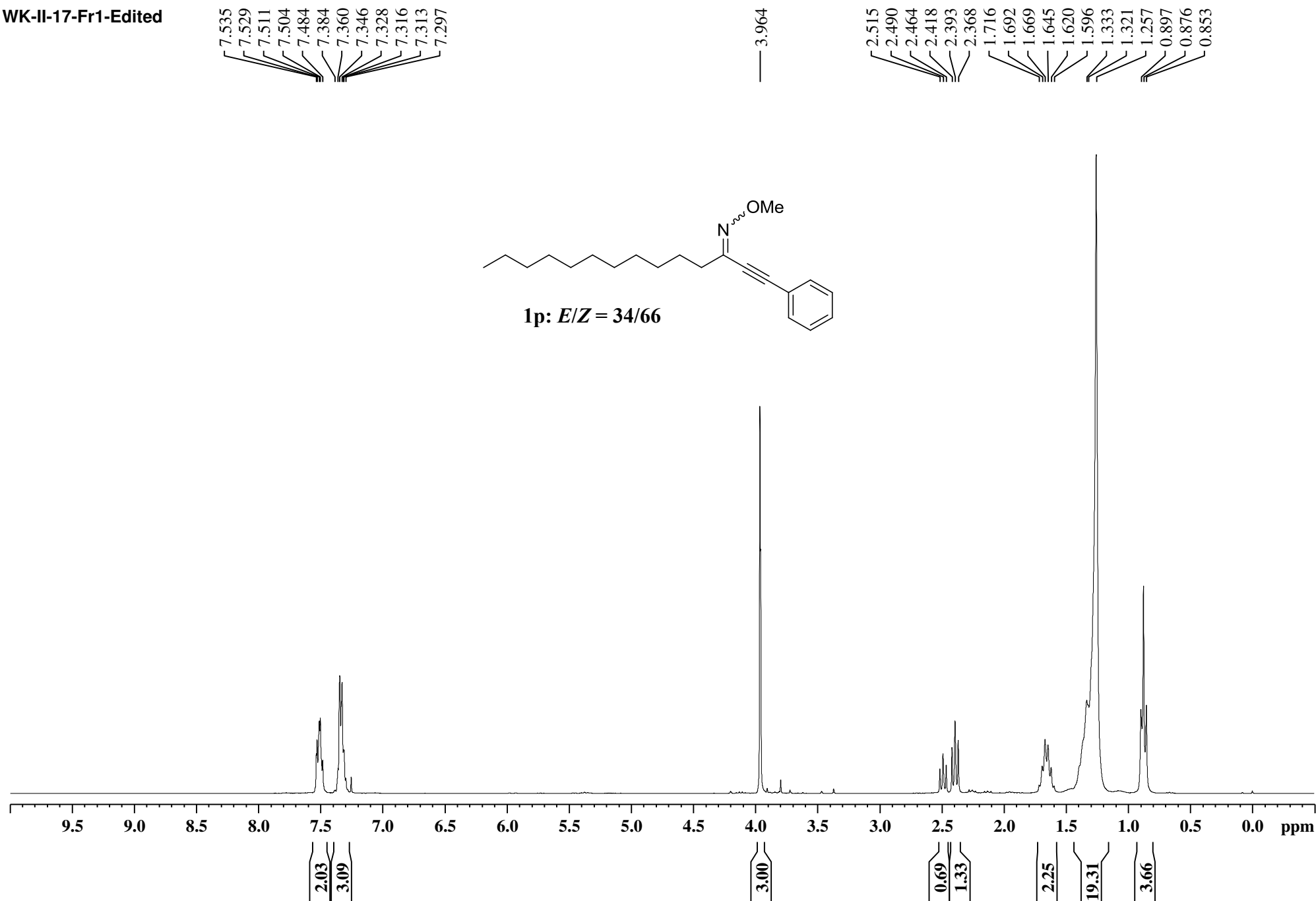


WK-II-79-Fr2+Fr3

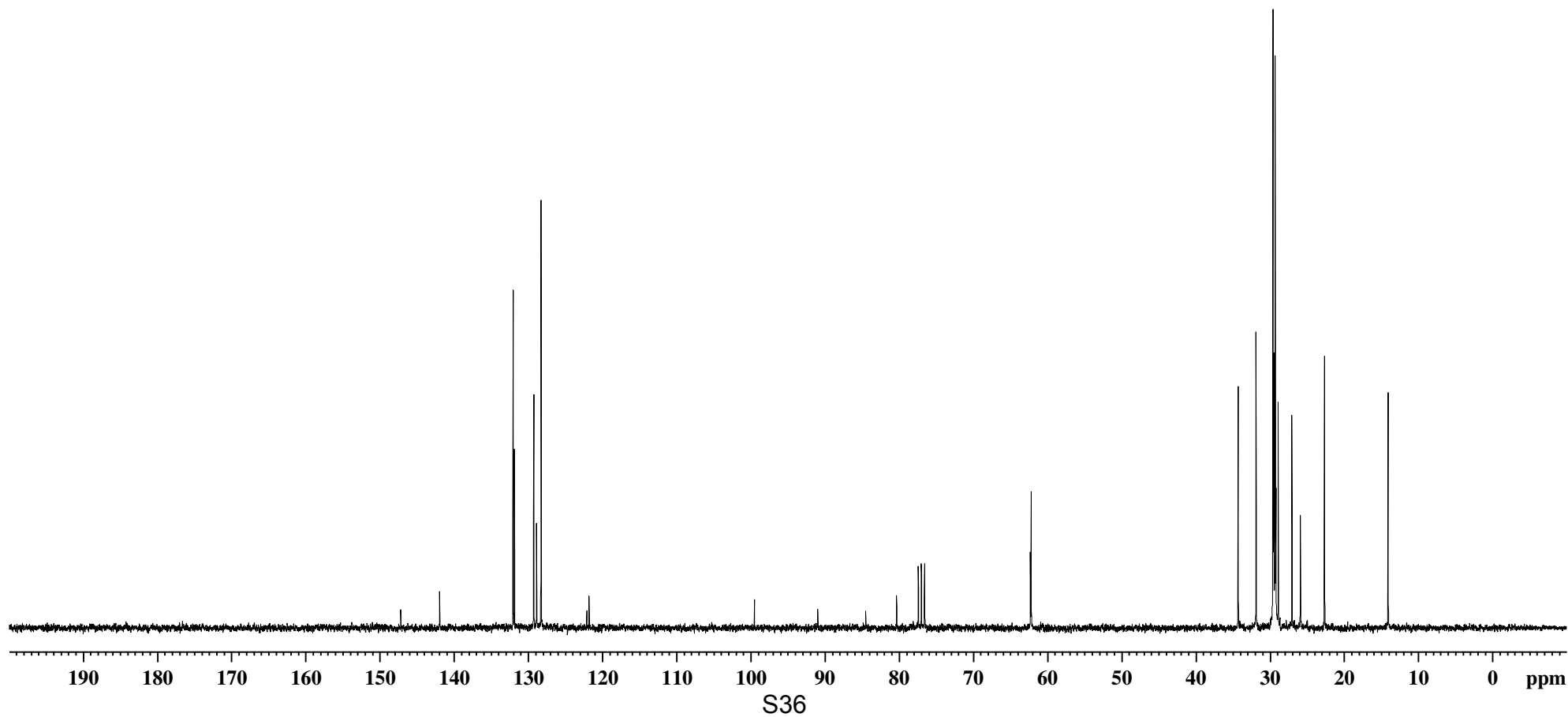
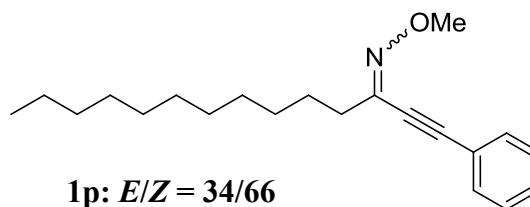


WK-II-79-Fr2+Fr3





WK-II-17-Fr1

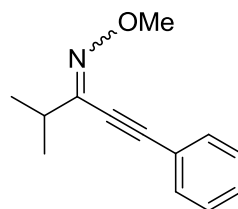


WK-II-8-pure

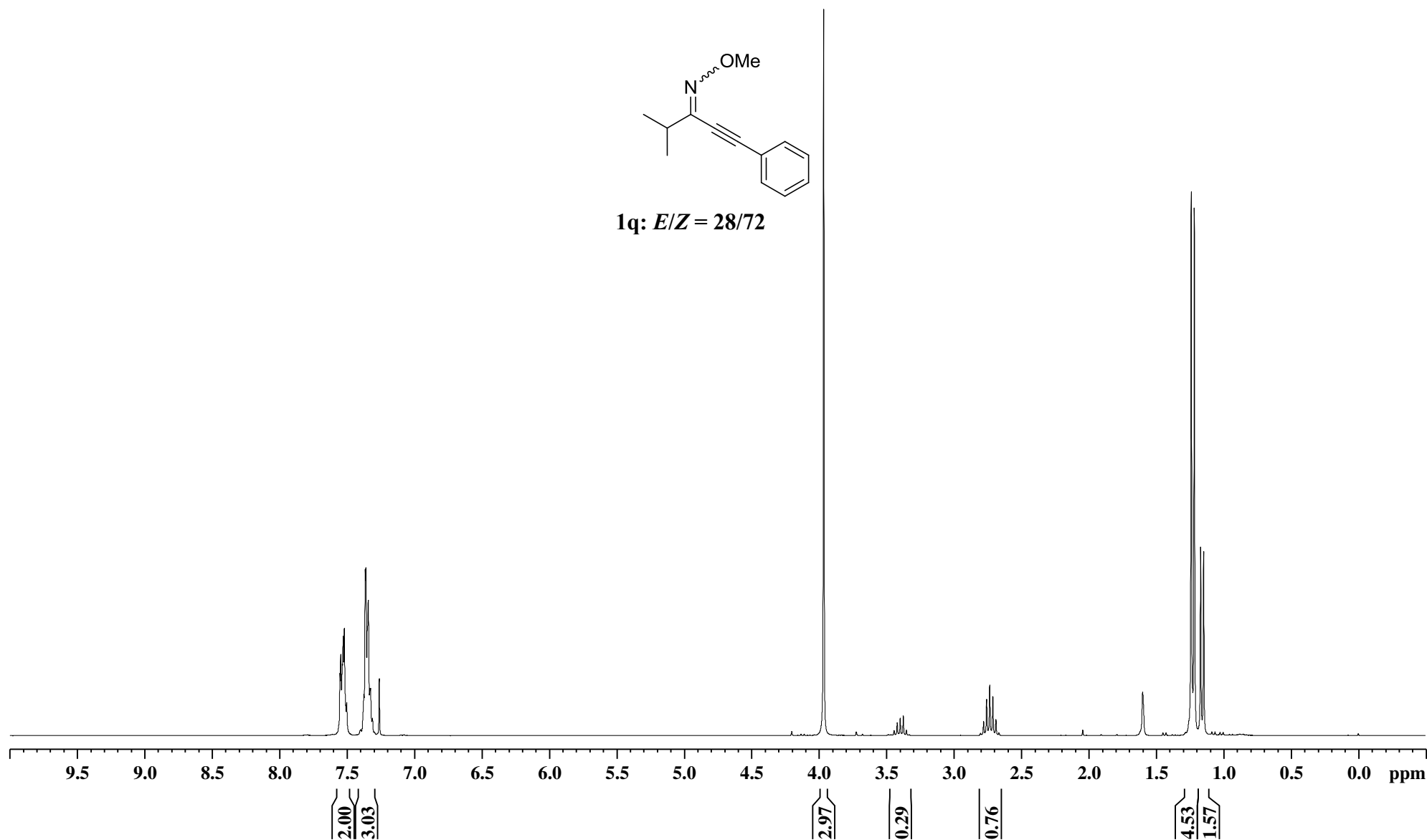
7.551
7.545
7.534
7.527
7.519
7.501
7.402
7.396
7.373
7.363
7.359
7.341
7.329
7.324
7.310
7.298

3.964
3.465
3.442
3.419
3.396
3.374
3.351
3.329
2.801
2.778
2.756
2.733
2.710
2.687
2.665

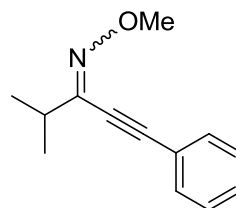
1.239
1.216
1.169
1.146



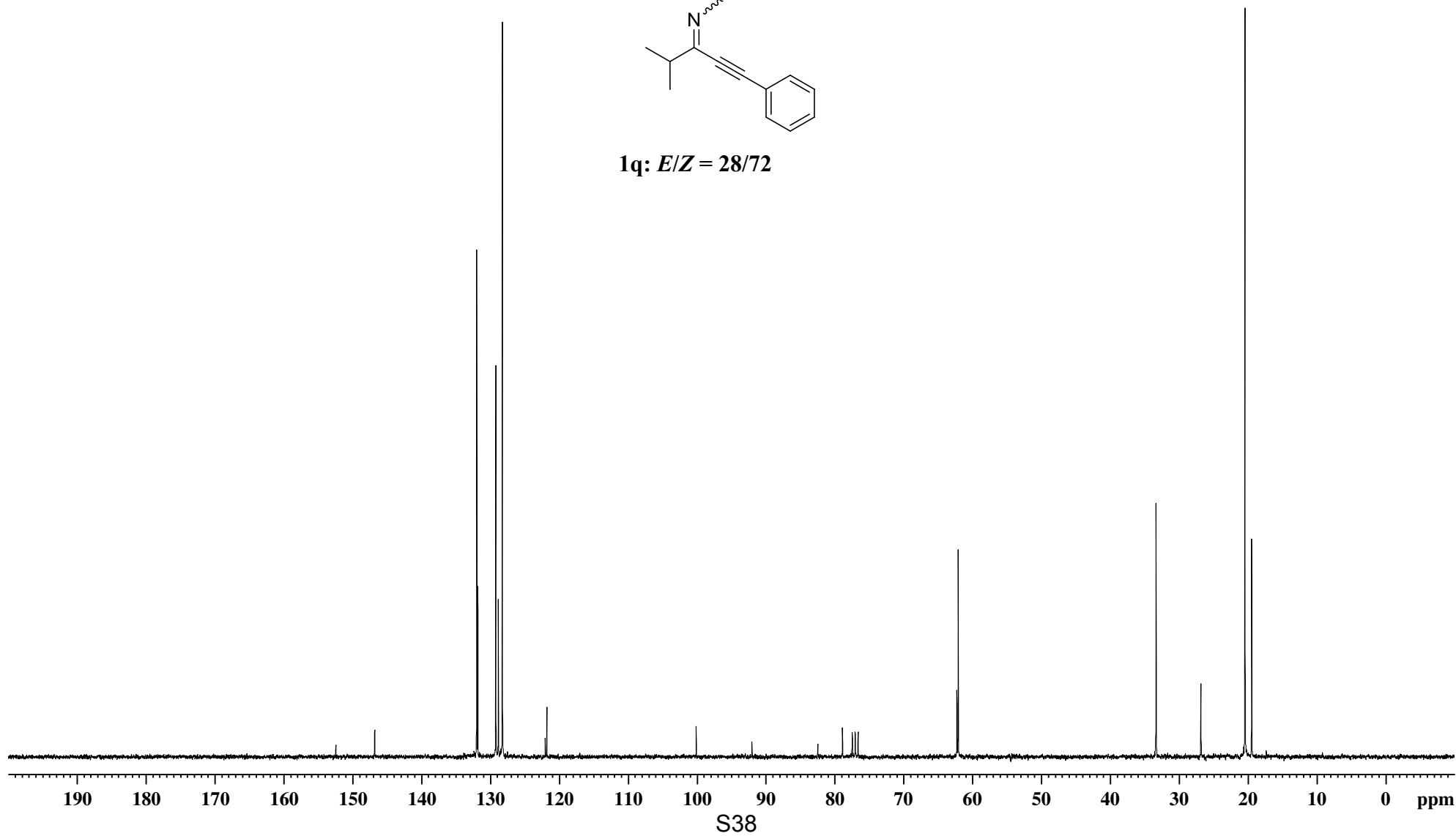
1q: *E/Z* = 28/72



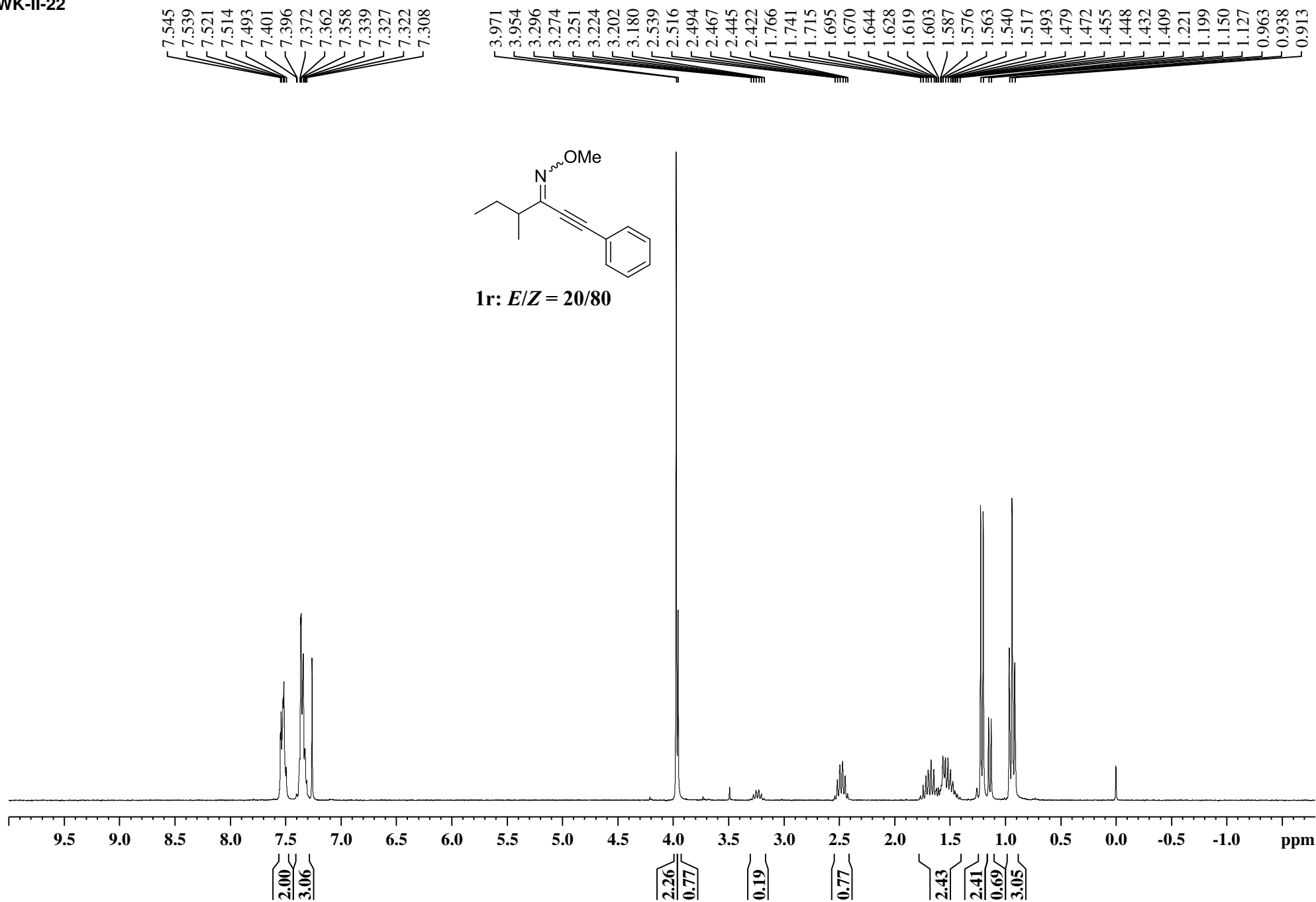
WK-II-8-impure



1q: *E/Z* = 28/72

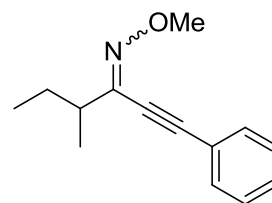
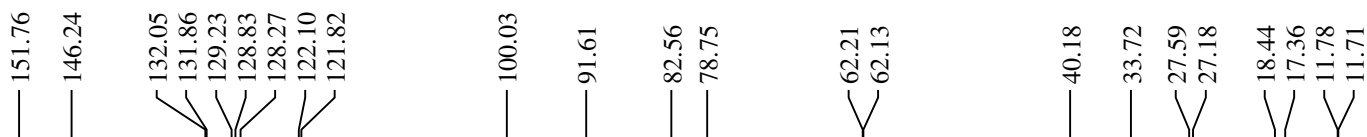


WK-II-22

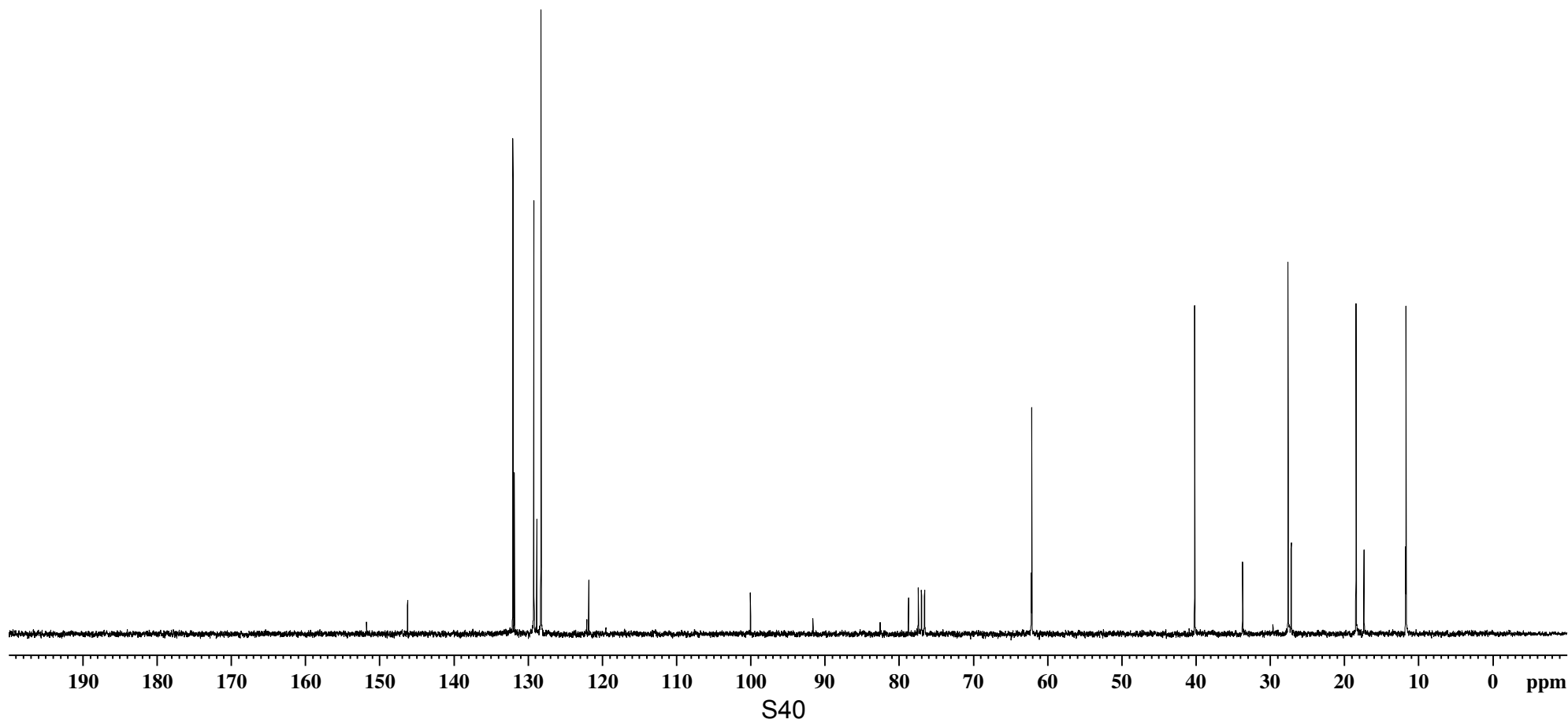


S39

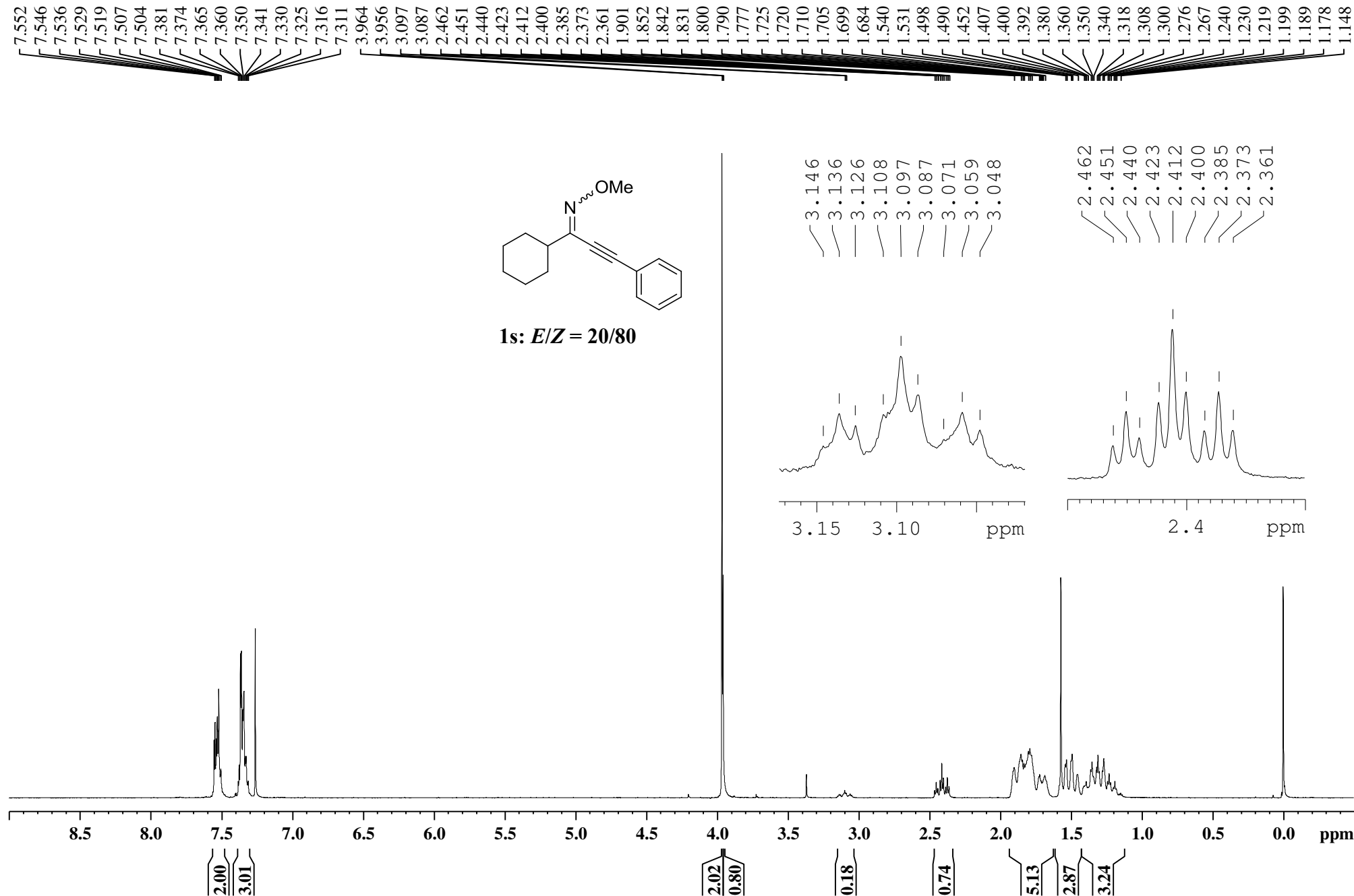
WK-II-21



1r: *E/Z* = 20/80



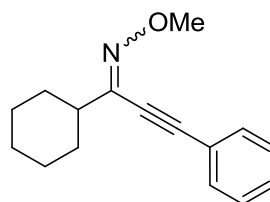
WK-II-96-H



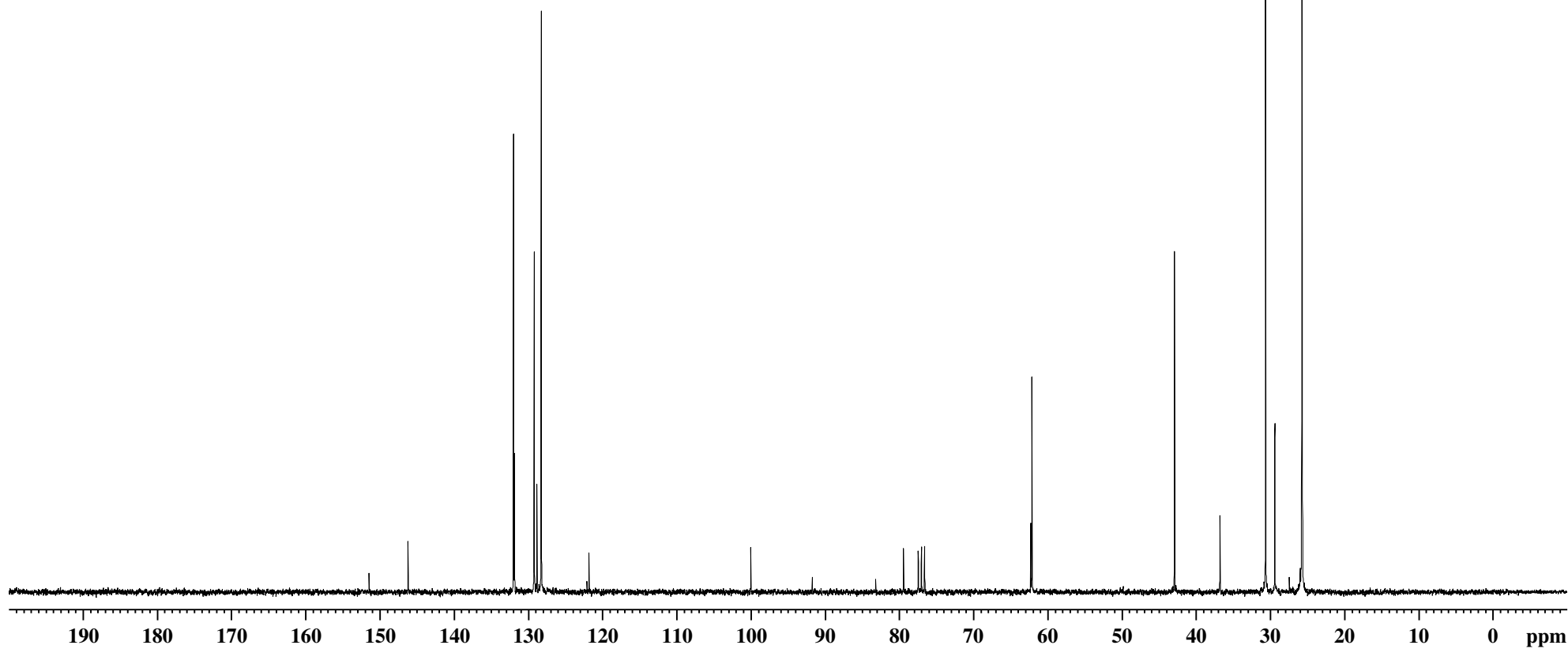
S41

WK-II-96-C

— 151.452
— 146.178
131.981
131.840
129.188
128.817
128.243
122.081
121.803
— 100.008
— 91.697
— 83.165
— 79.424
62.256
62.100
— 42.895
— 36.772
30.623
29.374
25.746
25.703
25.647

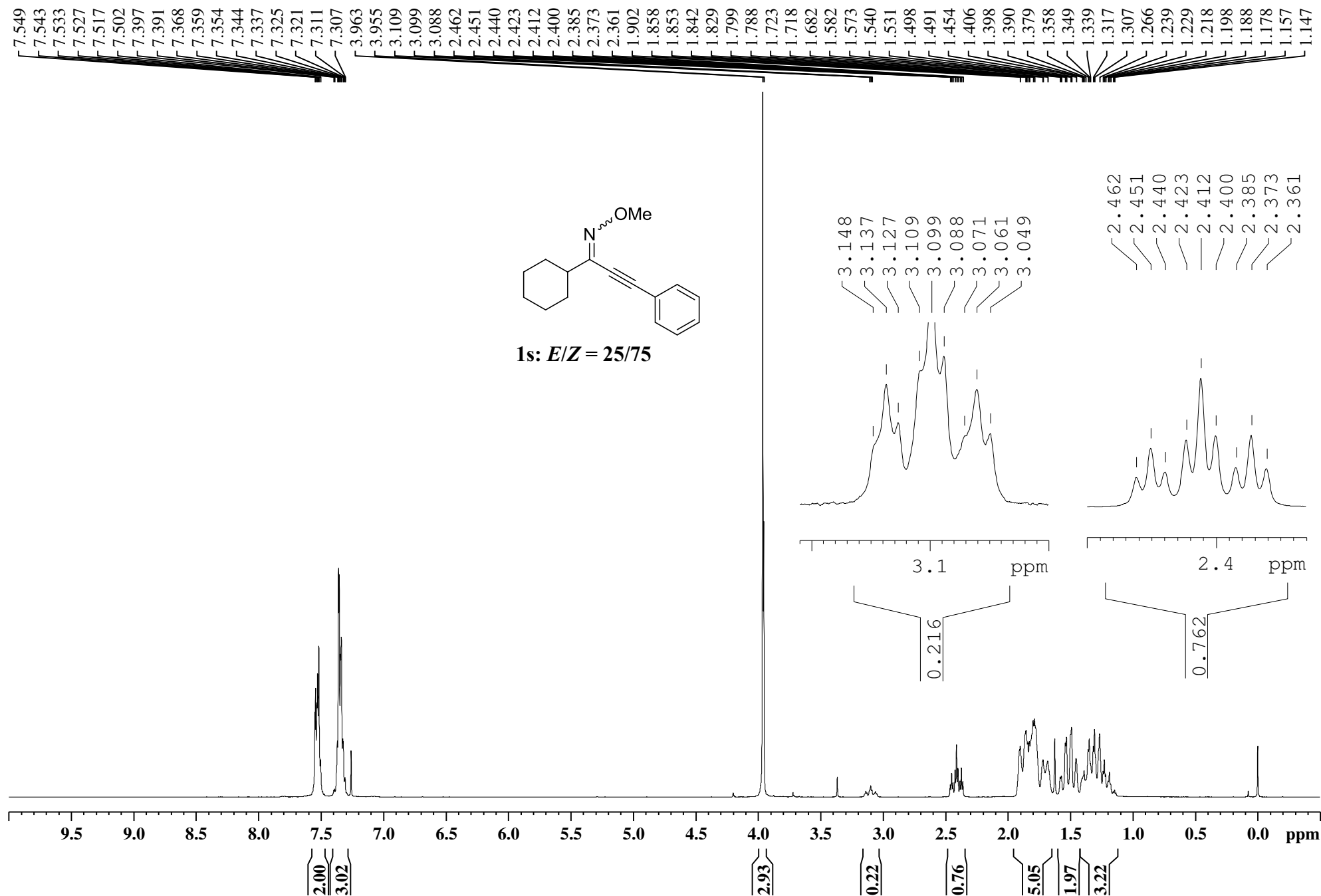


1s: *E/Z* = 20/80

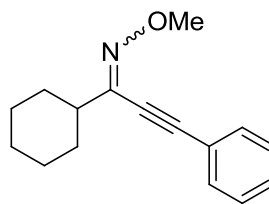
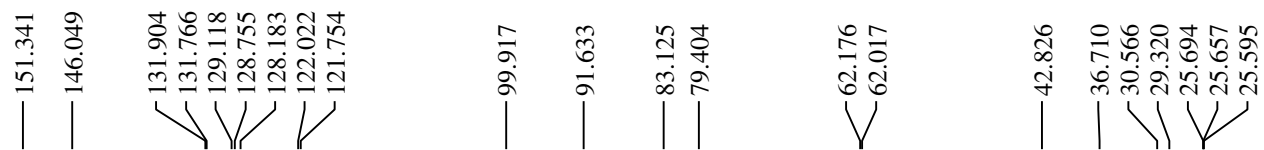


S42

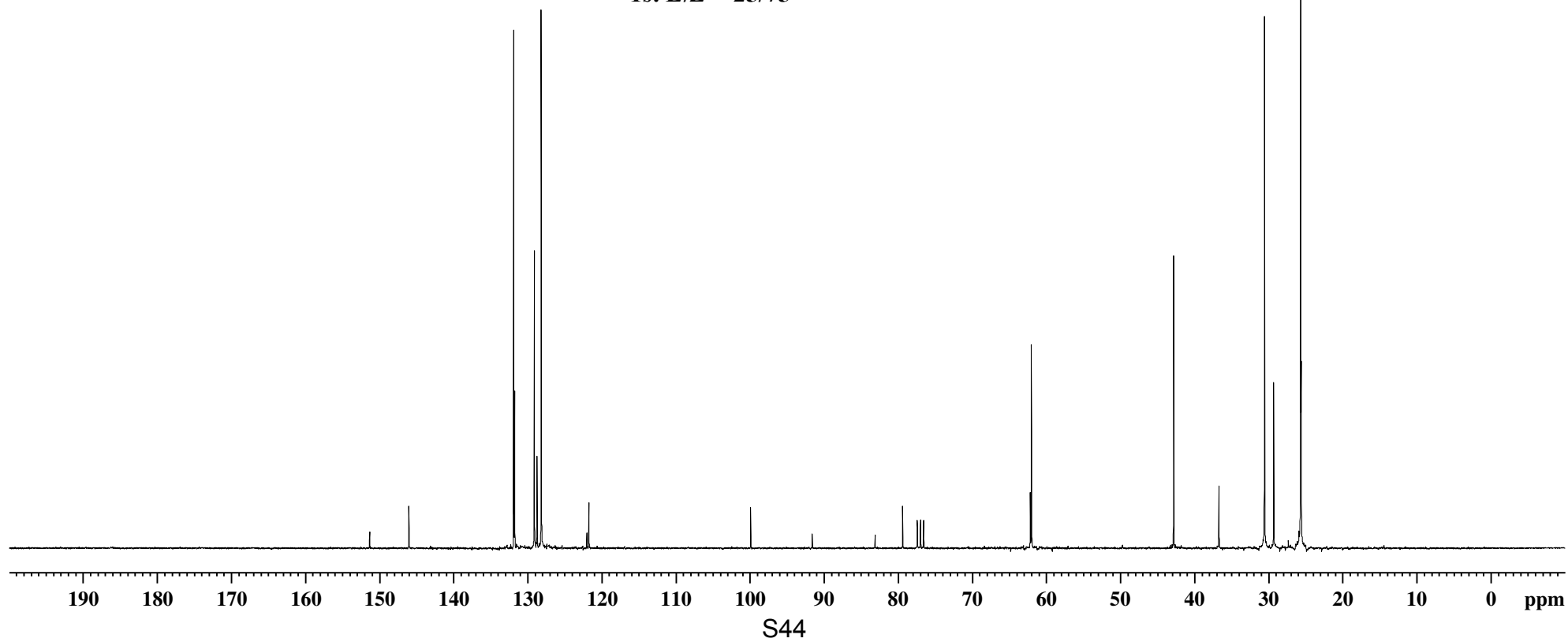
WK-II-96-H E/Z = 0.25/0.75



WK-II-96-H E/Z = 0.25/0.75



1s: E/Z = 25/75

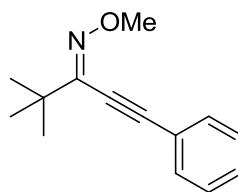


WK-I-239-purified

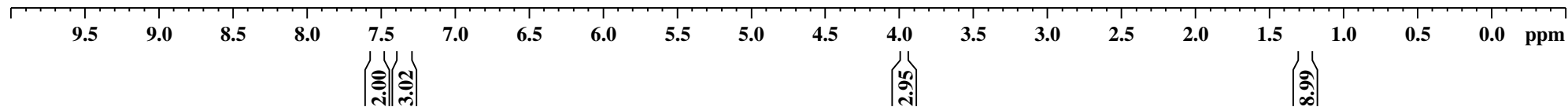
7.546
7.540
7.525
7.515
7.395
7.389
7.359
7.353
7.341
7.336
7.321
7.306

3.970

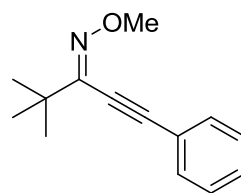
1.259



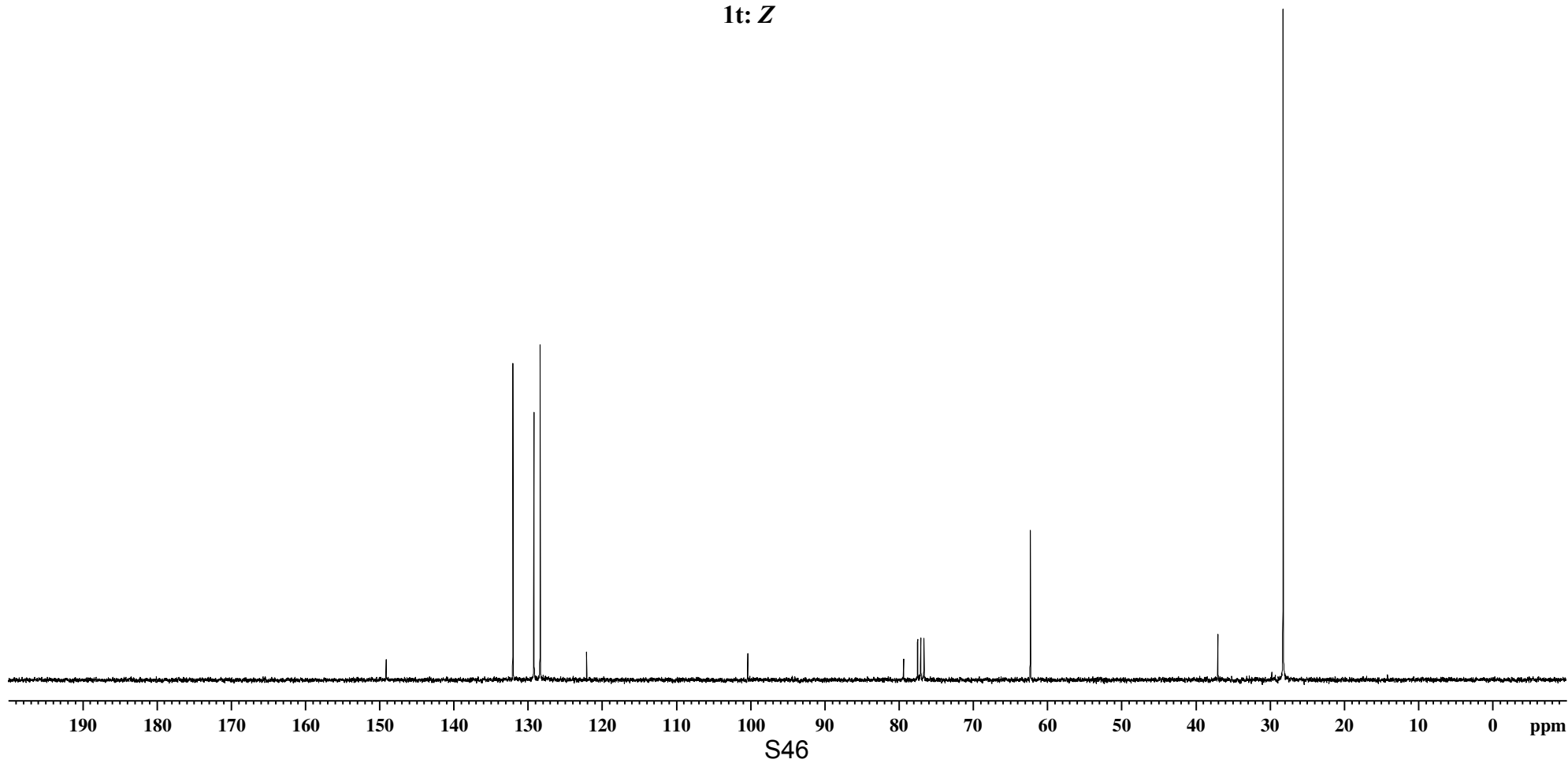
1t: Z



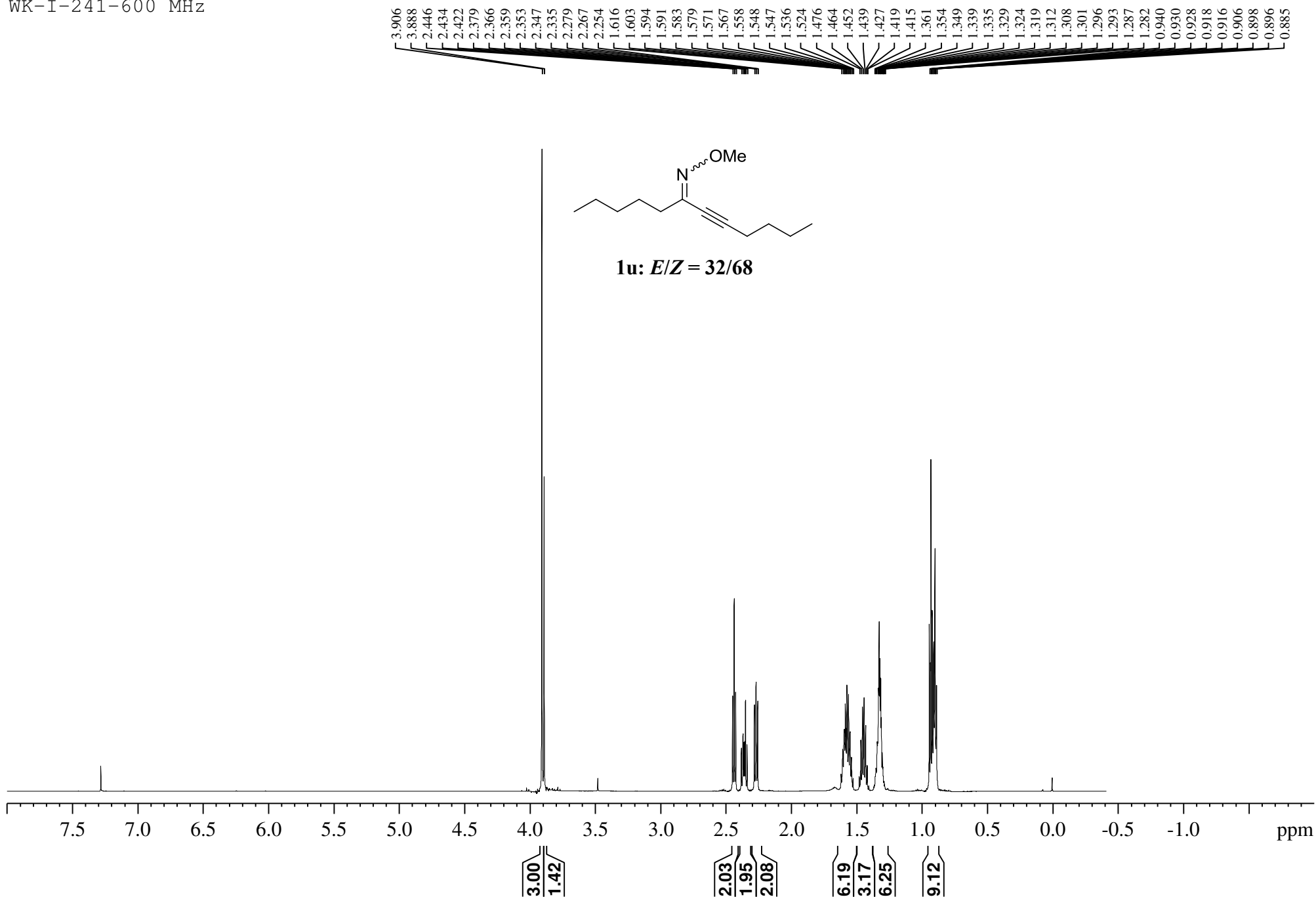
WK-I-239-purified



1t: *Z*

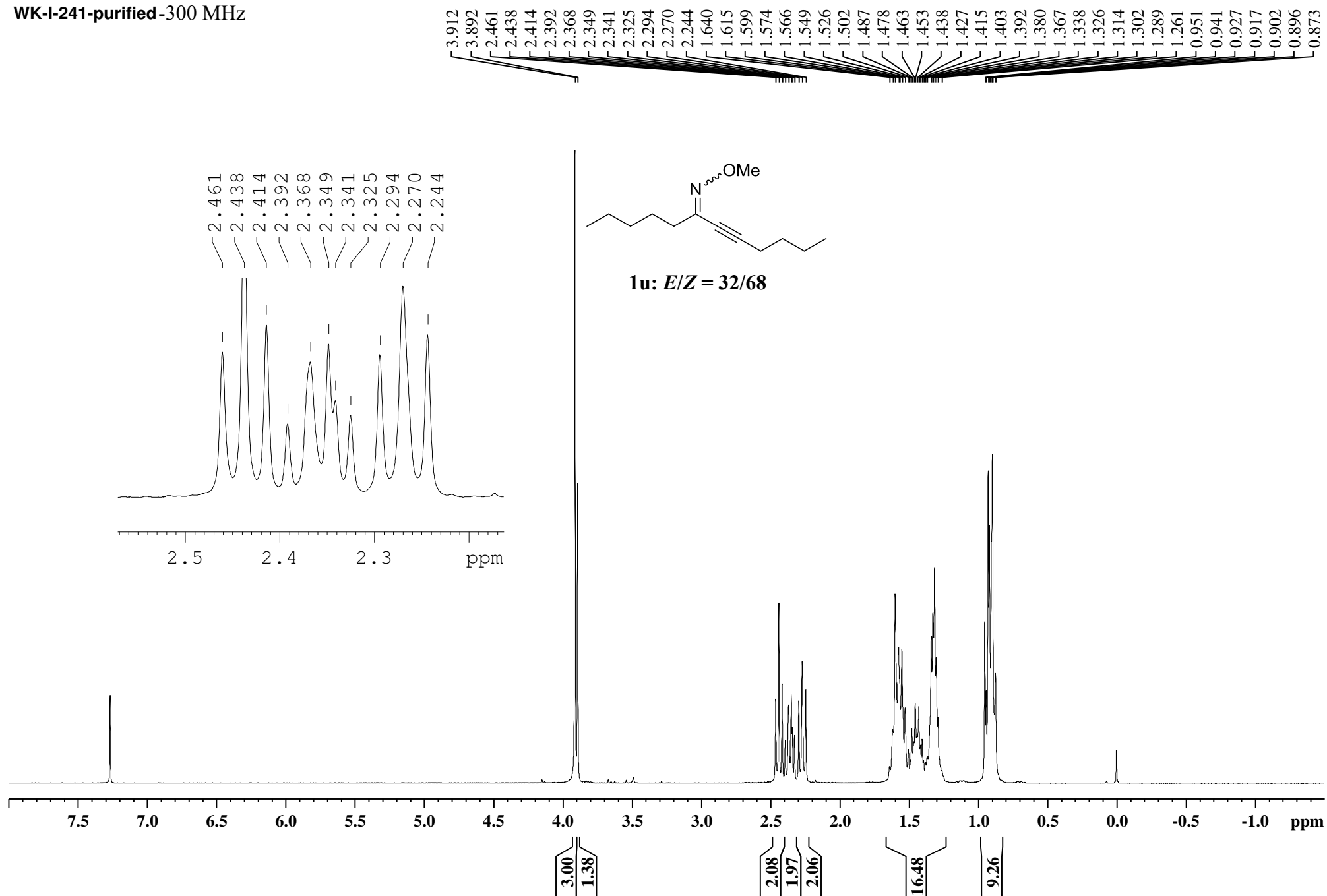


WK-I-241-600 MHz



S47

WK-I-241-purified-300 MHz



WK-I-241-purified

— 147.177

— 142.226

— 102.021

— 92.569

— 75.941

— 72.287

— 61.844

34.322

31.280

30.903

30.170

28.985

26.496

25.434

22.224

21.807

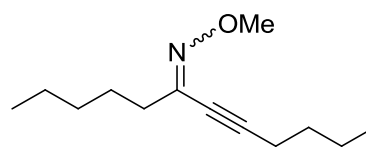
21.772

19.149

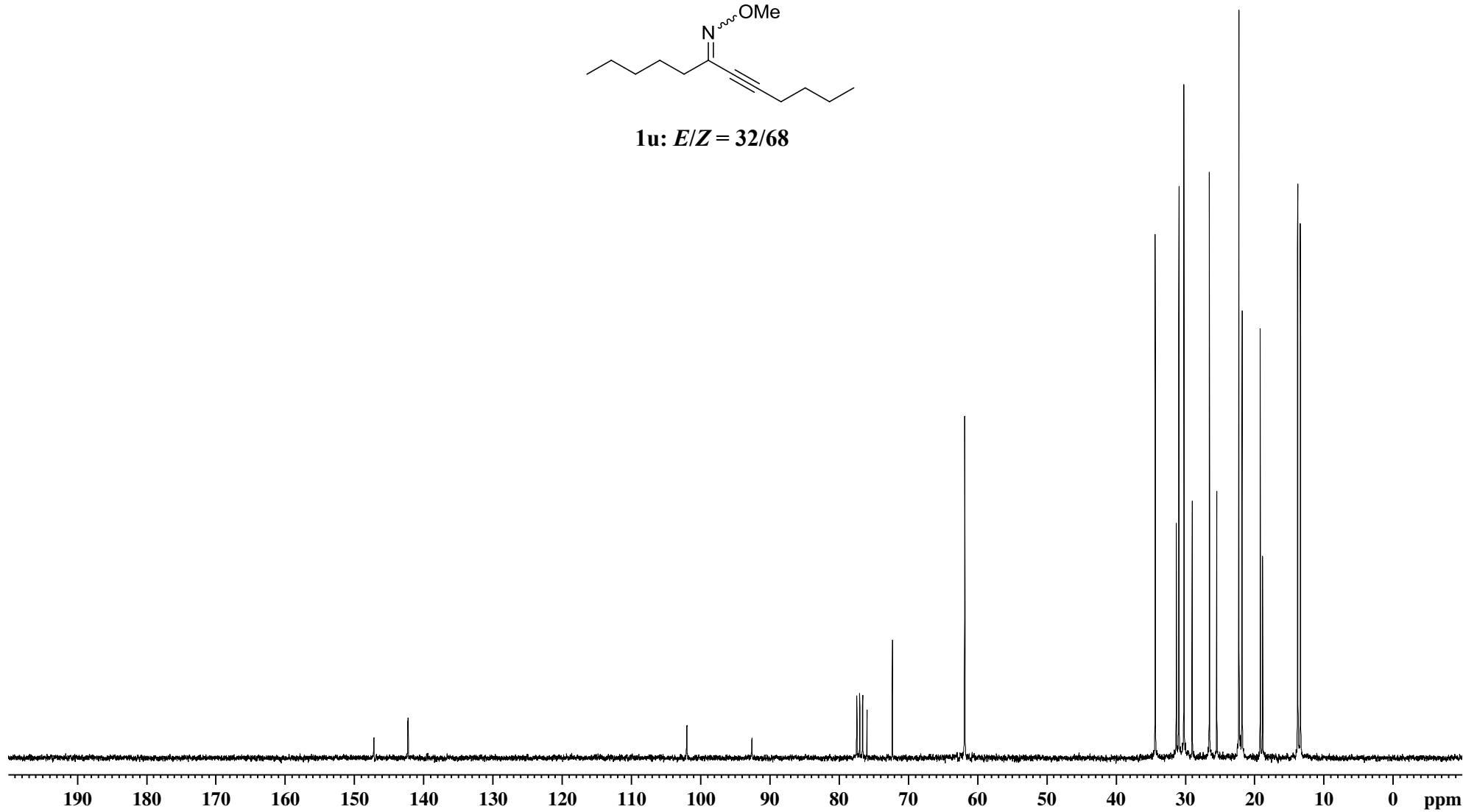
18.823

13.746

13.349



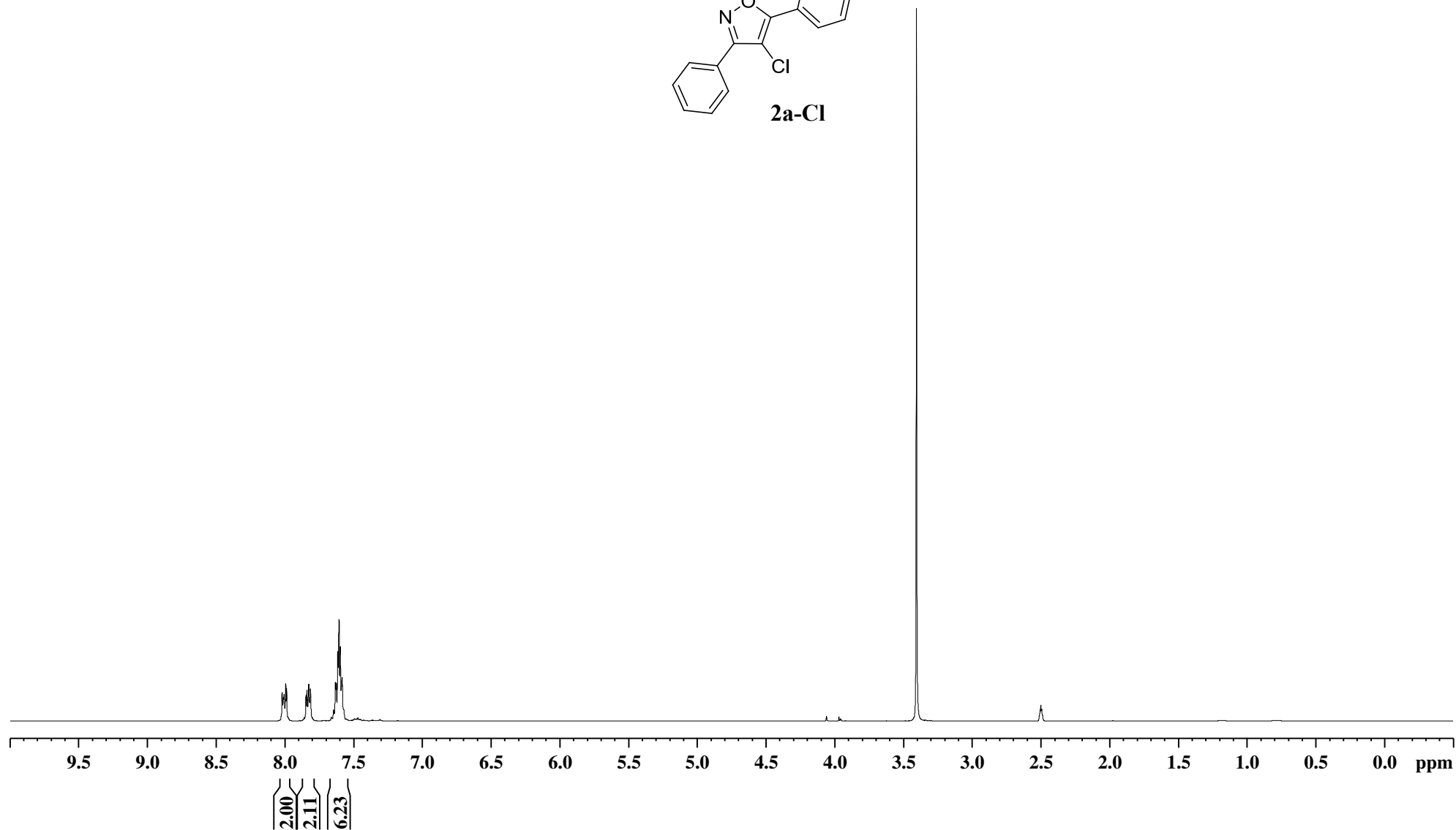
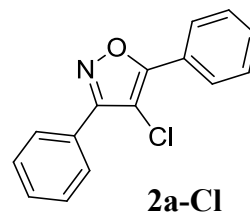
1u: *E/Z* = 32/68



S49

WK-I-29-column-DMSO

8.020
8.010
8.005
7.994
7.988
7.858
7.846
7.839
7.826
7.822
7.814
7.799
7.646
7.641
7.632
7.626
7.615
7.608
7.605
7.597
7.589
7.586
7.583
7.575
7.572

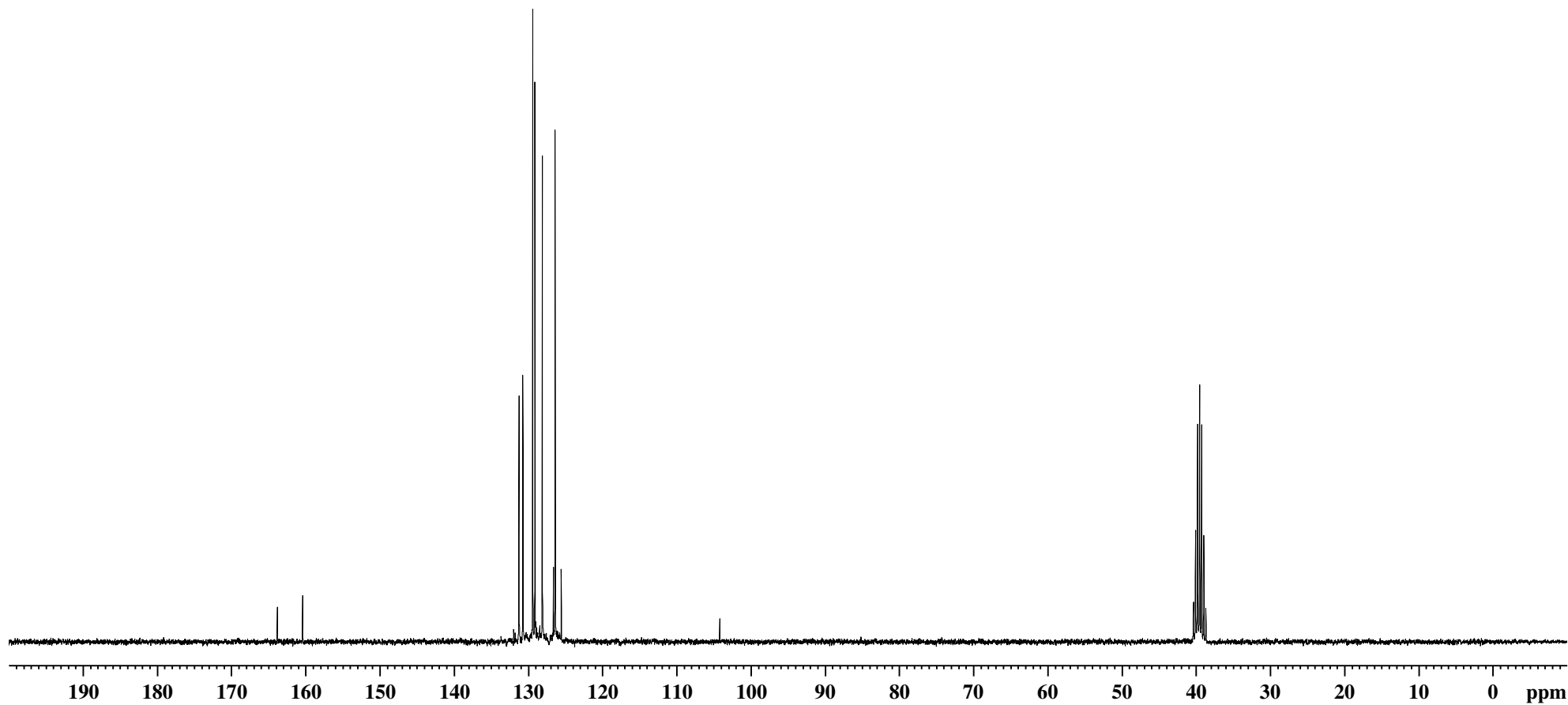
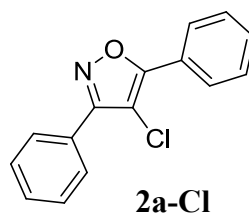


WK-I-29-column

— 163.804
— 160.400

131.238
130.711
129.389
129.096
128.082
126.594
126.360
125.530

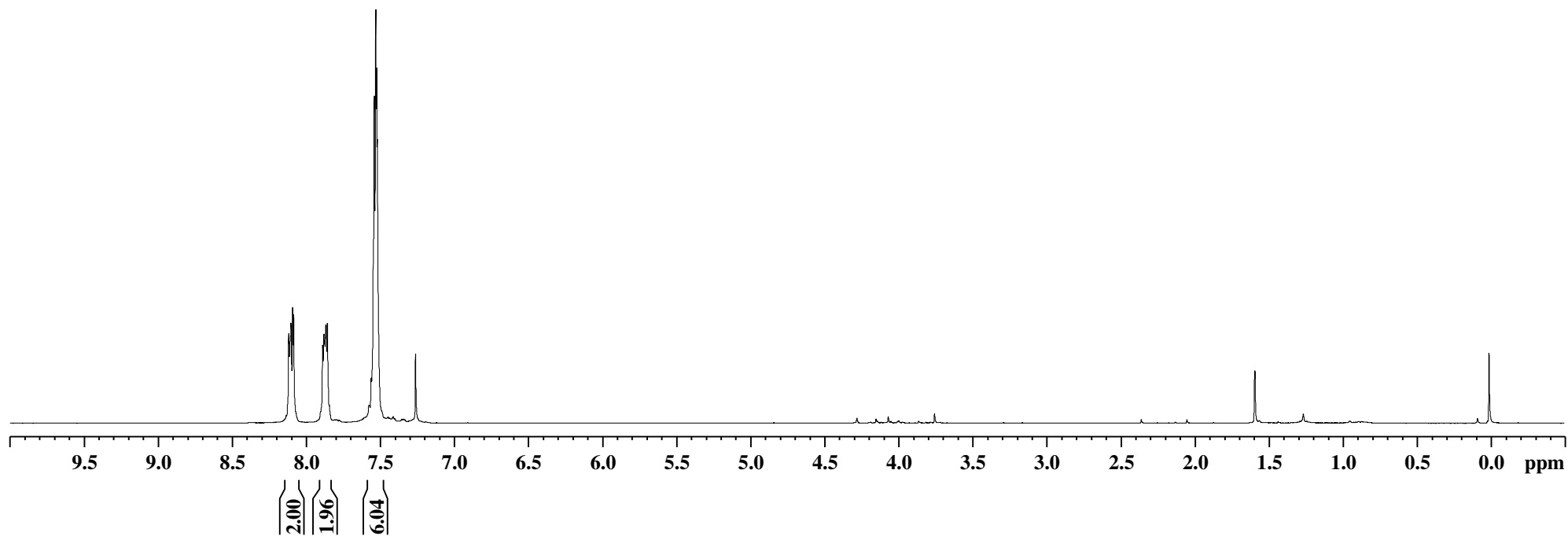
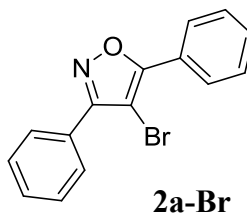
— 104.174



S51

WK-I-110-purified

8.116
8.106
8.101
8.090
8.084
7.887
7.878
7.874
7.865
7.855
7.538
7.528
7.522
7.518

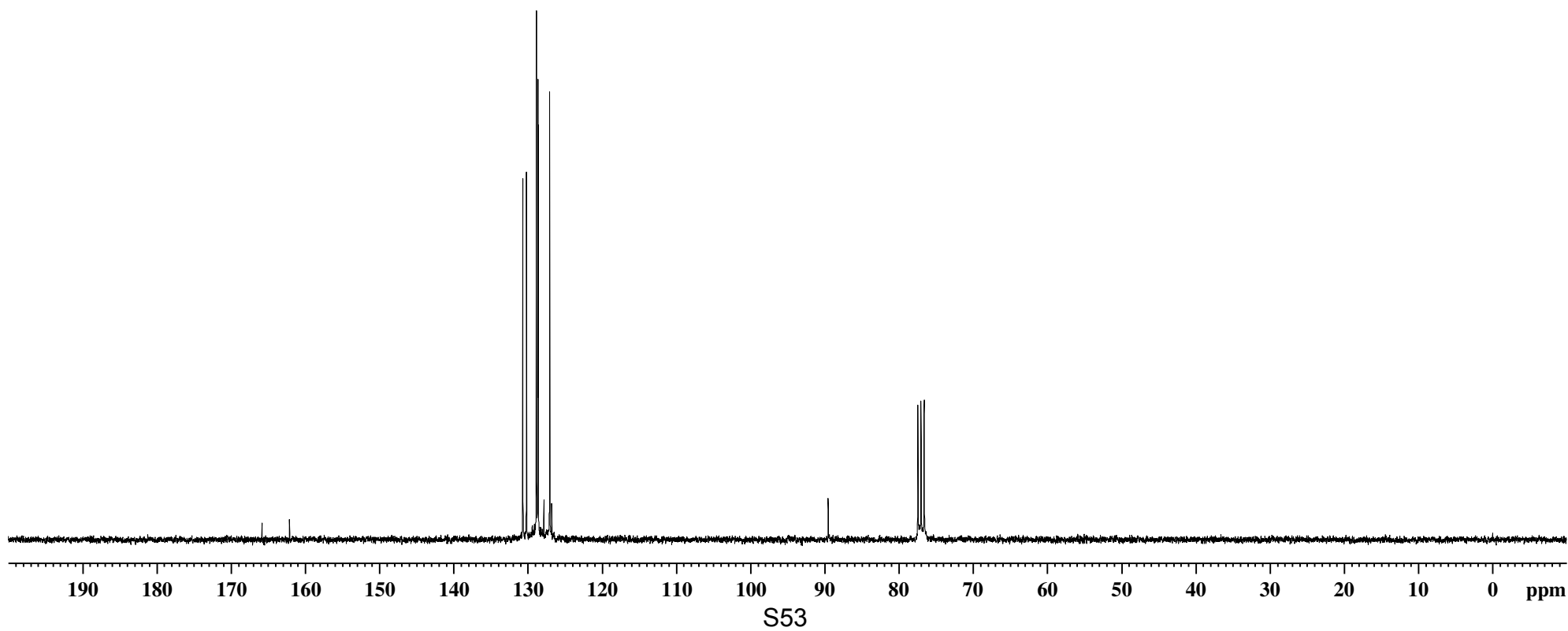
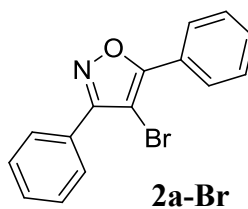


WK-I-110-purified2000

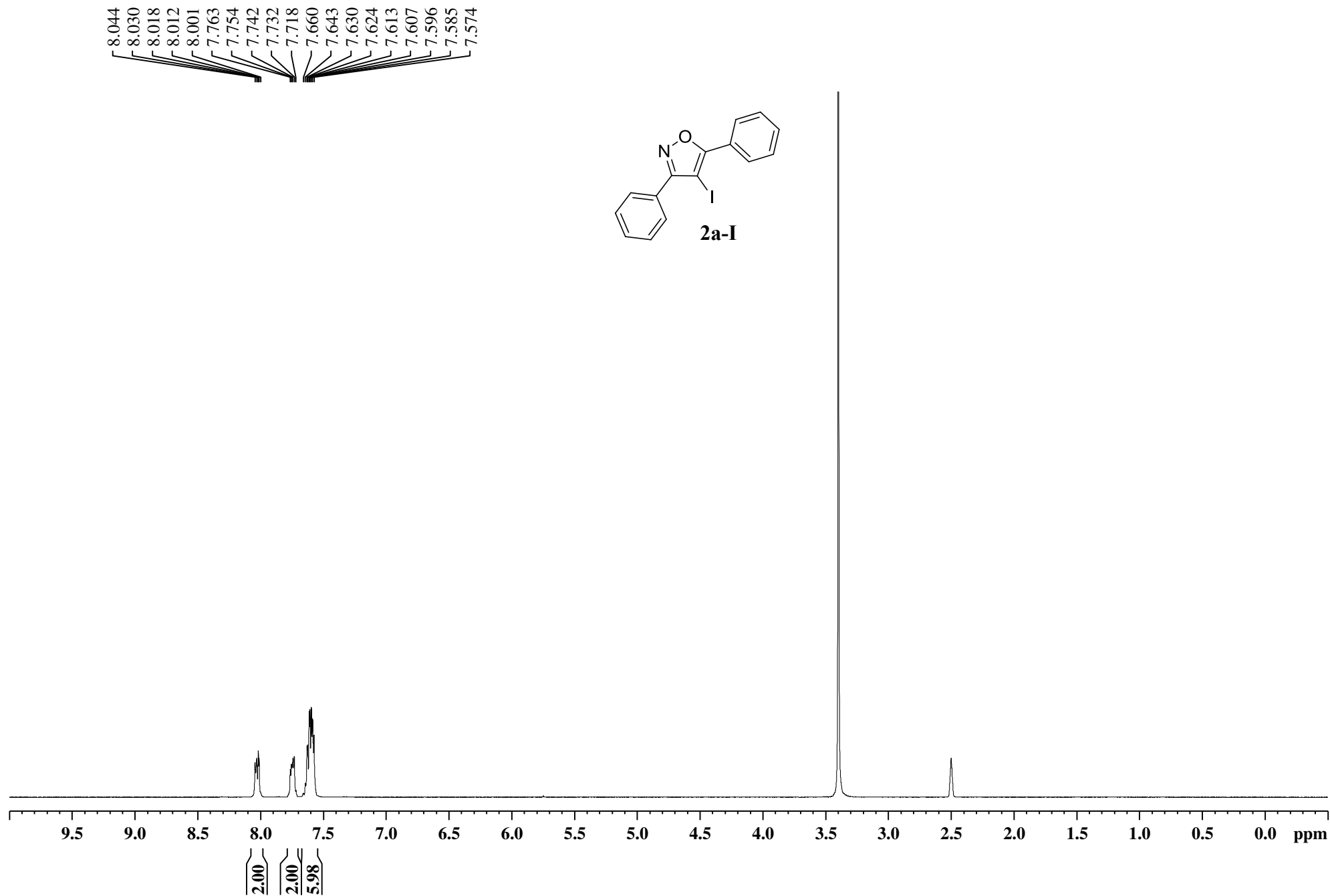
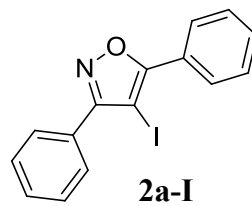
— 165.79
— 162.09

130.65
130.16
128.81
128.63
128.58
127.82
127.02
126.76

— 89.50



WK-I-113-purified

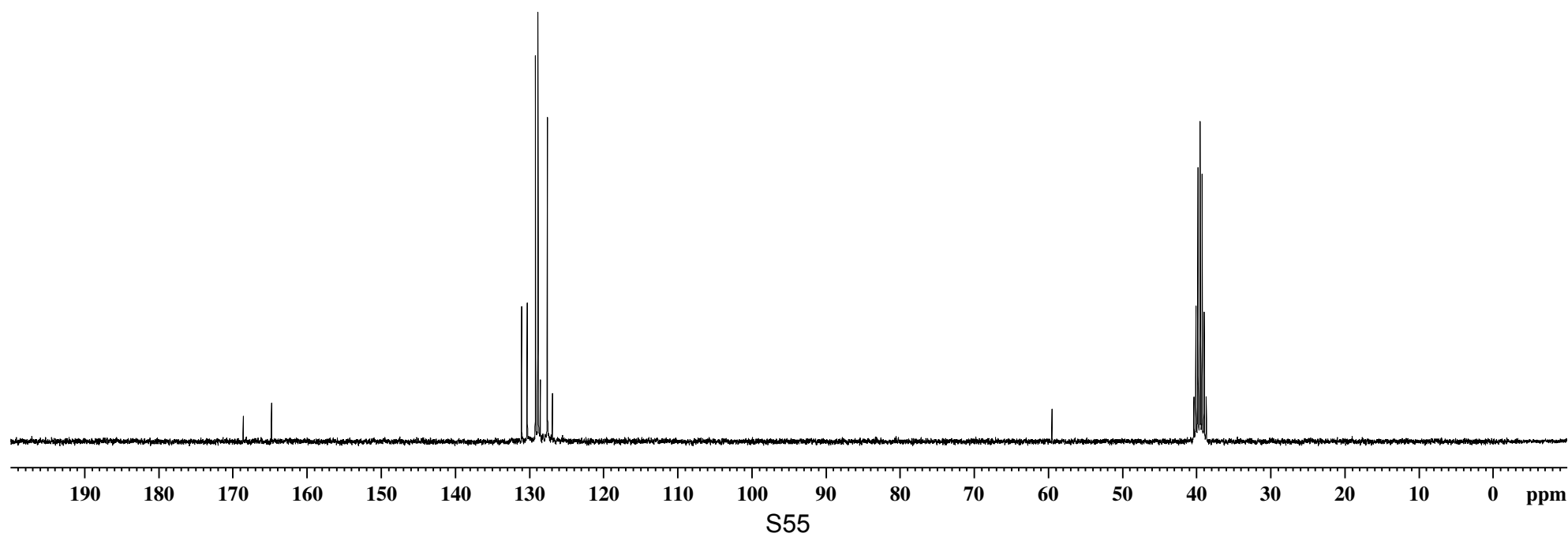
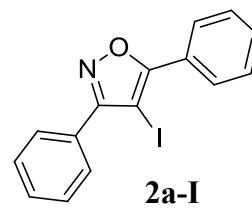


WK-I-113-purified

— 168.583
— 164.775

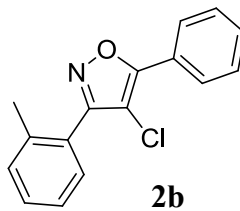
131.036
130.275
129.164
128.838
128.801
128.502
127.557
126.861

— 59.465

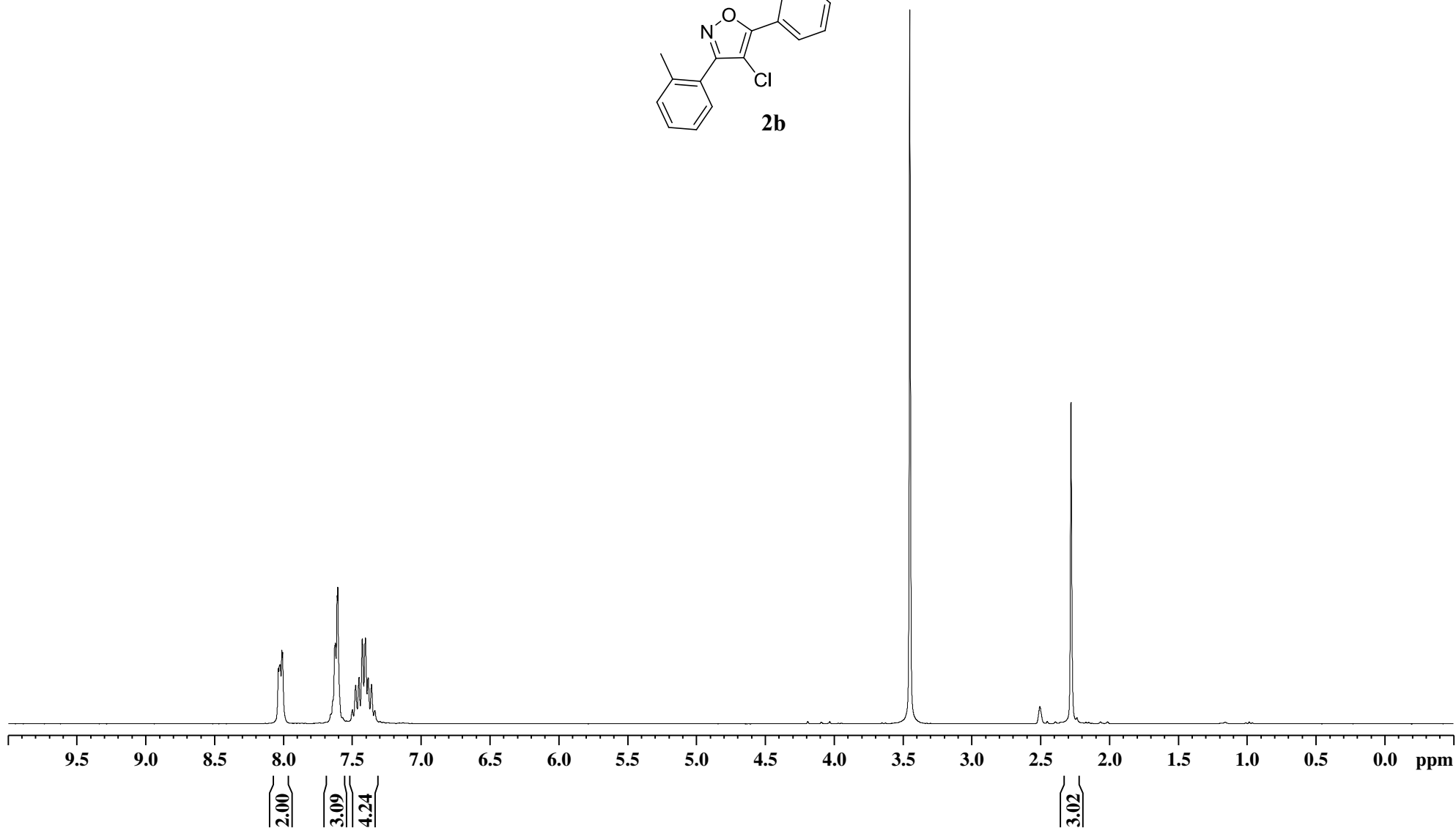


WK-I-154-check2

8.038
8.029
8.024
8.012
8.006
7.654
7.628
7.623
7.610
7.605
7.569
7.499
7.476
7.451
7.427
7.405
7.385
7.361
7.336



— 2.280



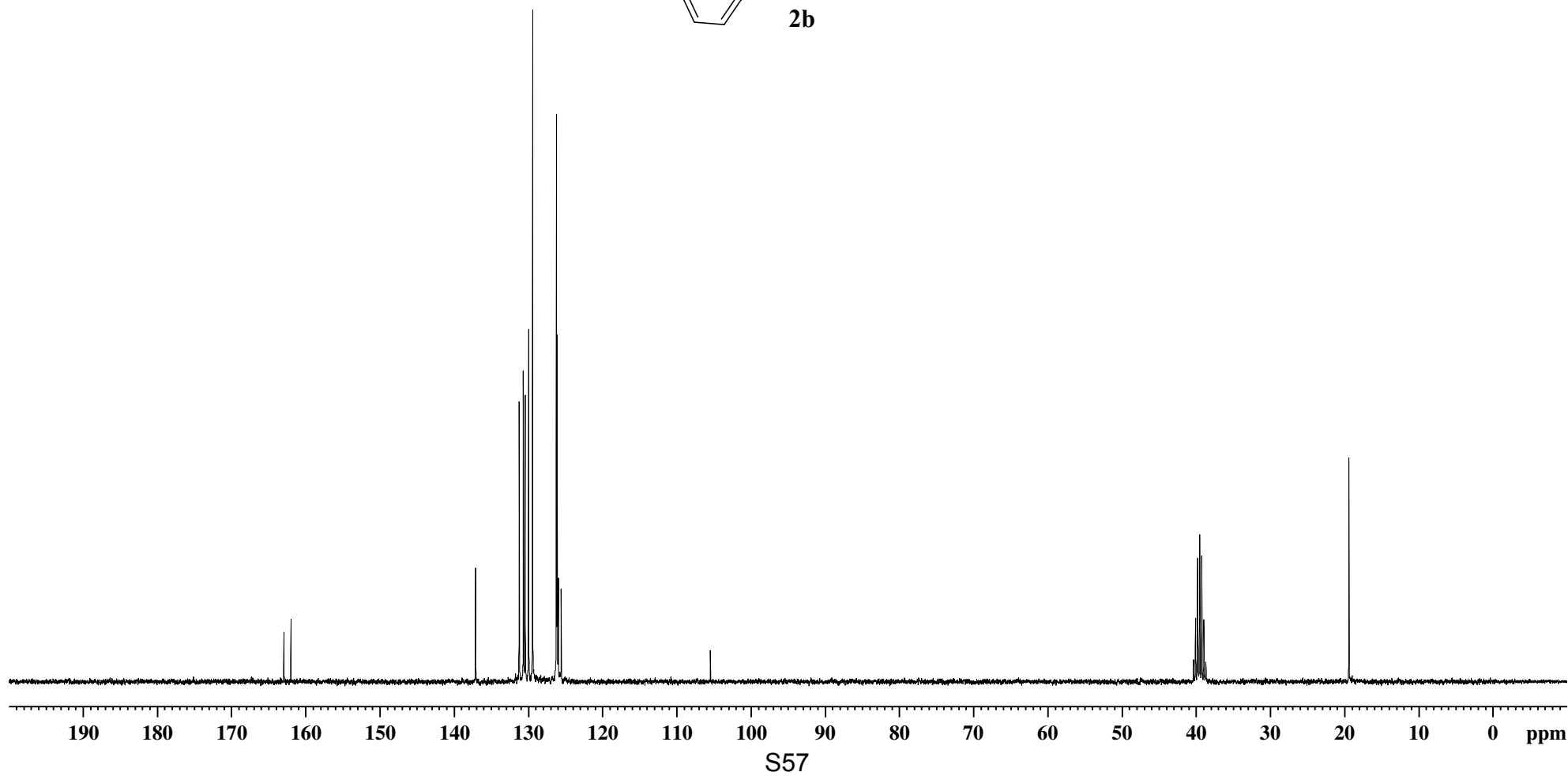
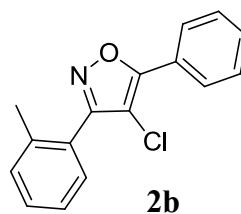
WK-I-154-check2

162.918
161.976

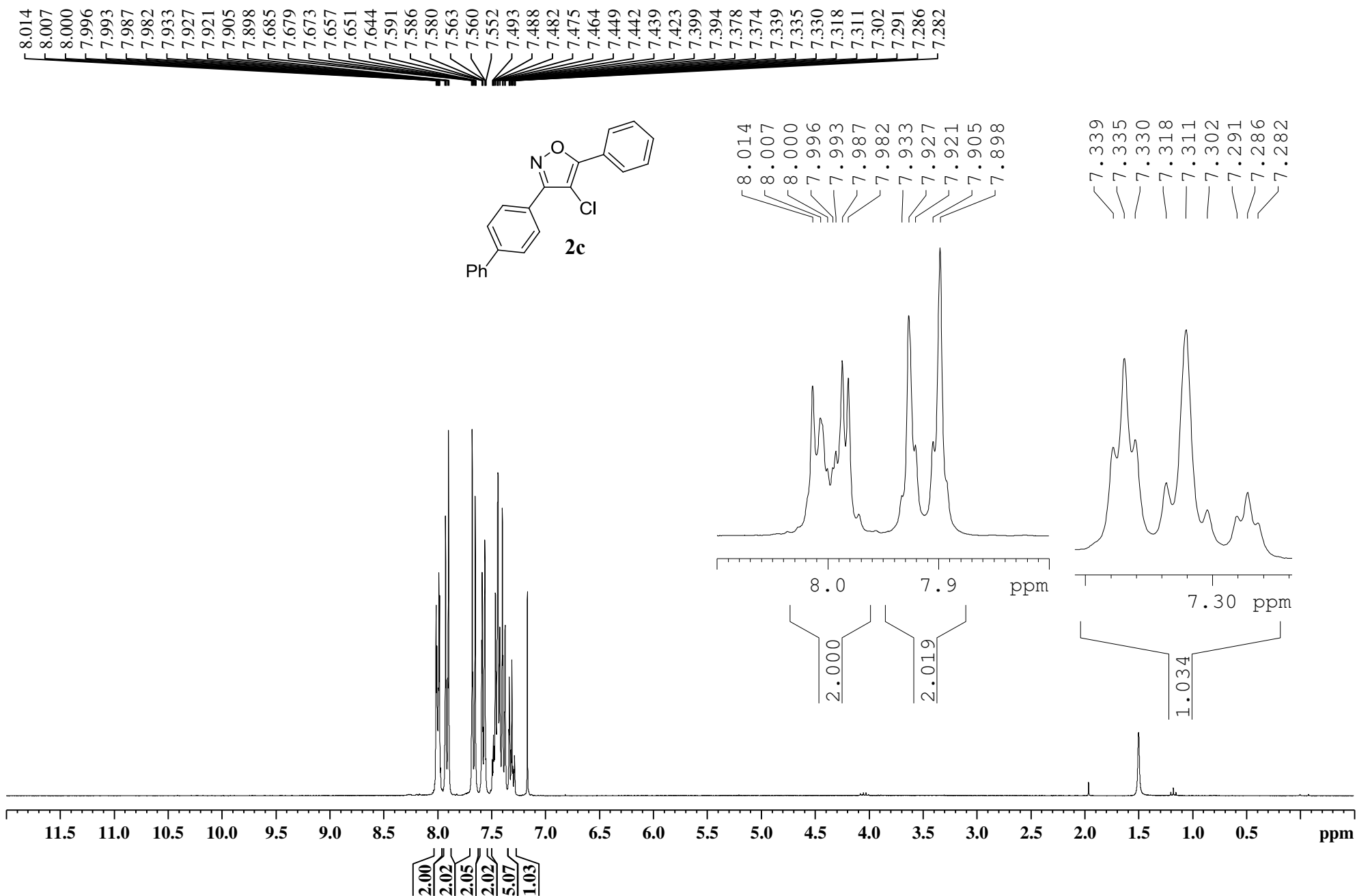
137.078
131.209
130.647
130.399
129.941
129.406
126.195
126.090
125.934
125.556

105.446

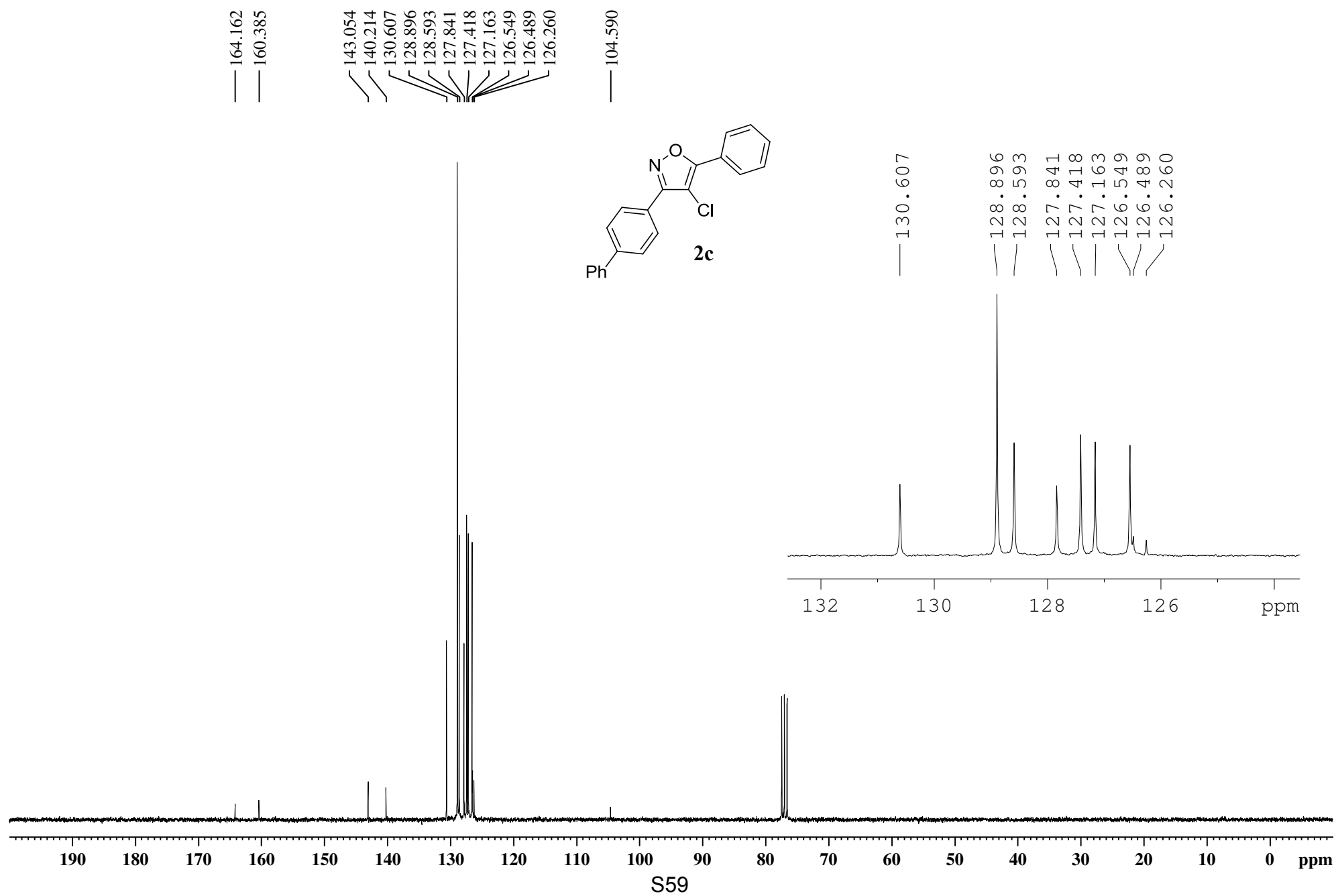
19.392



WK-I-120-purified2

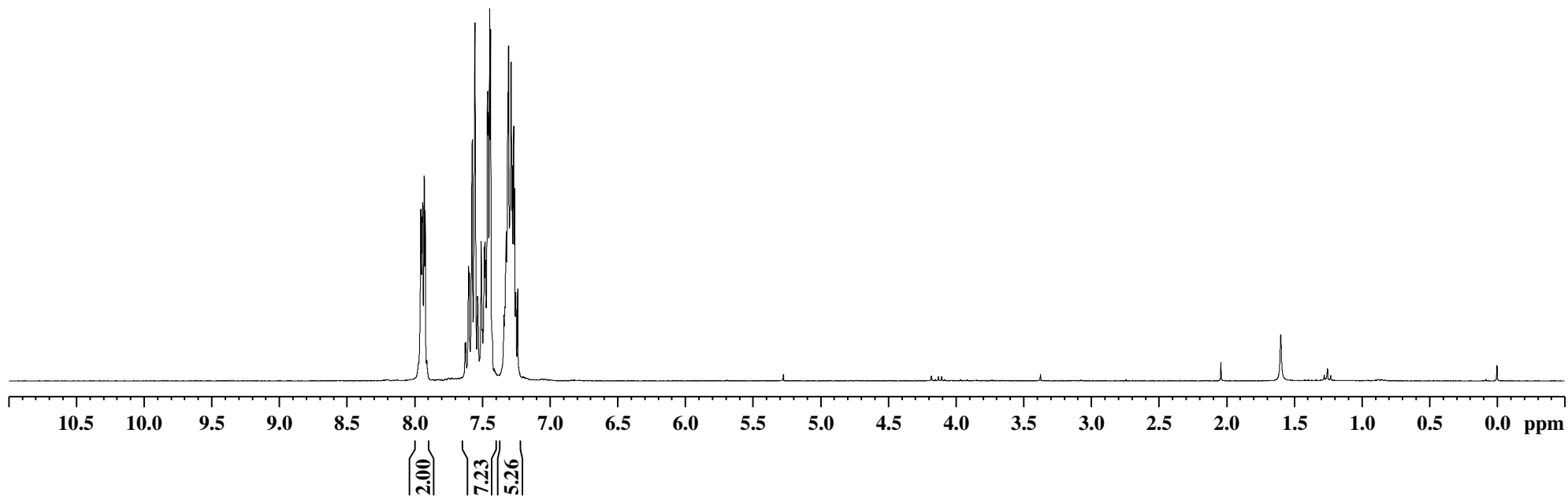
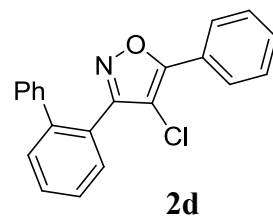


WK-I-120-purified2



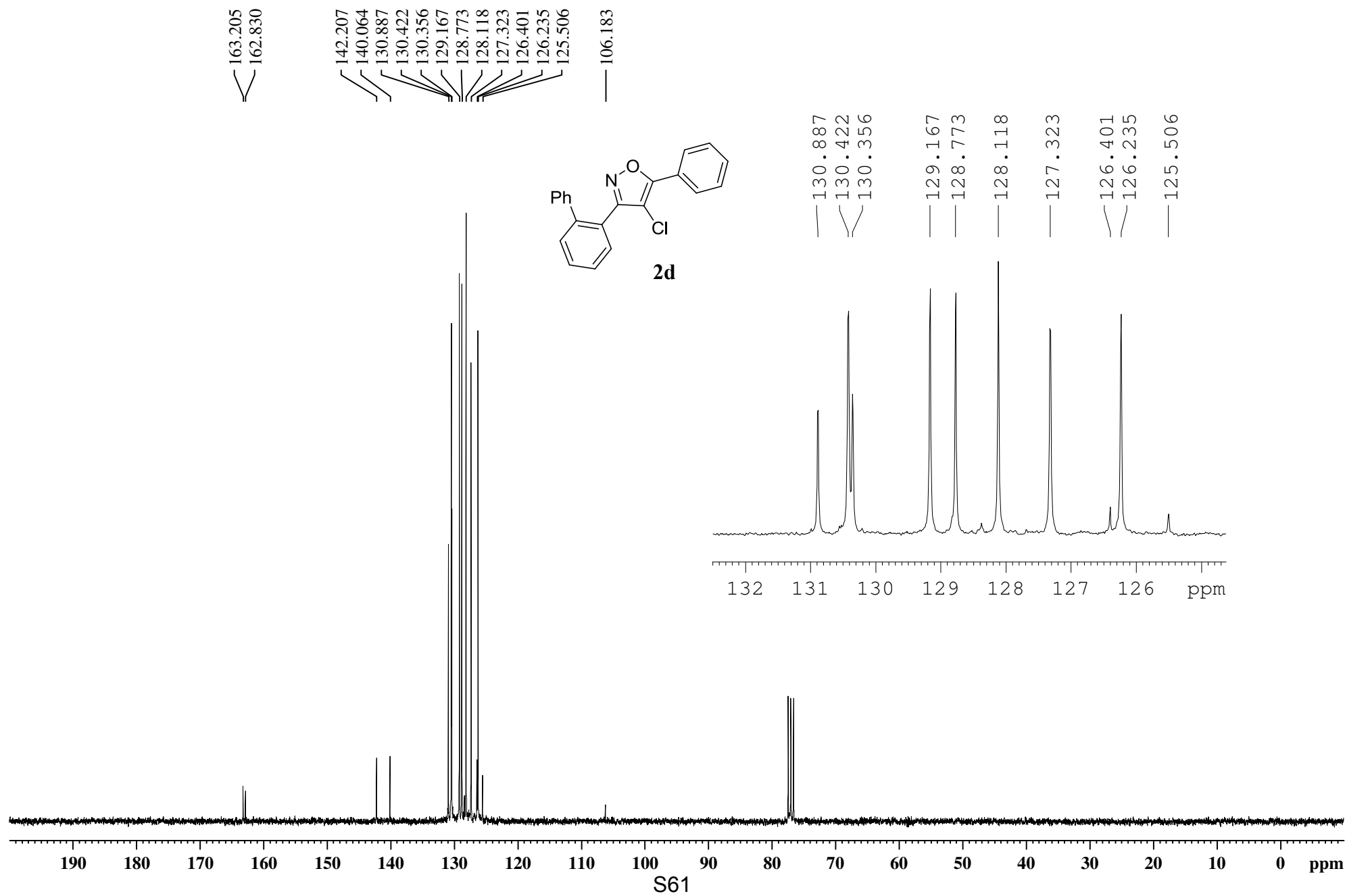
WK-I-192-Top

7.954
7.943
7.940
7.929
7.922
7.627
7.622
7.601
7.596
7.577
7.574
7.554
7.535
7.508
7.500
7.486
7.480
7.477
7.461
7.456
7.445
7.438
7.430
7.426
7.340
7.333
7.327
7.323
7.312
7.306
7.287
7.278
7.268
7.261
7.253
7.238



S60

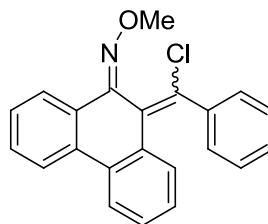
WK-I-192-Top



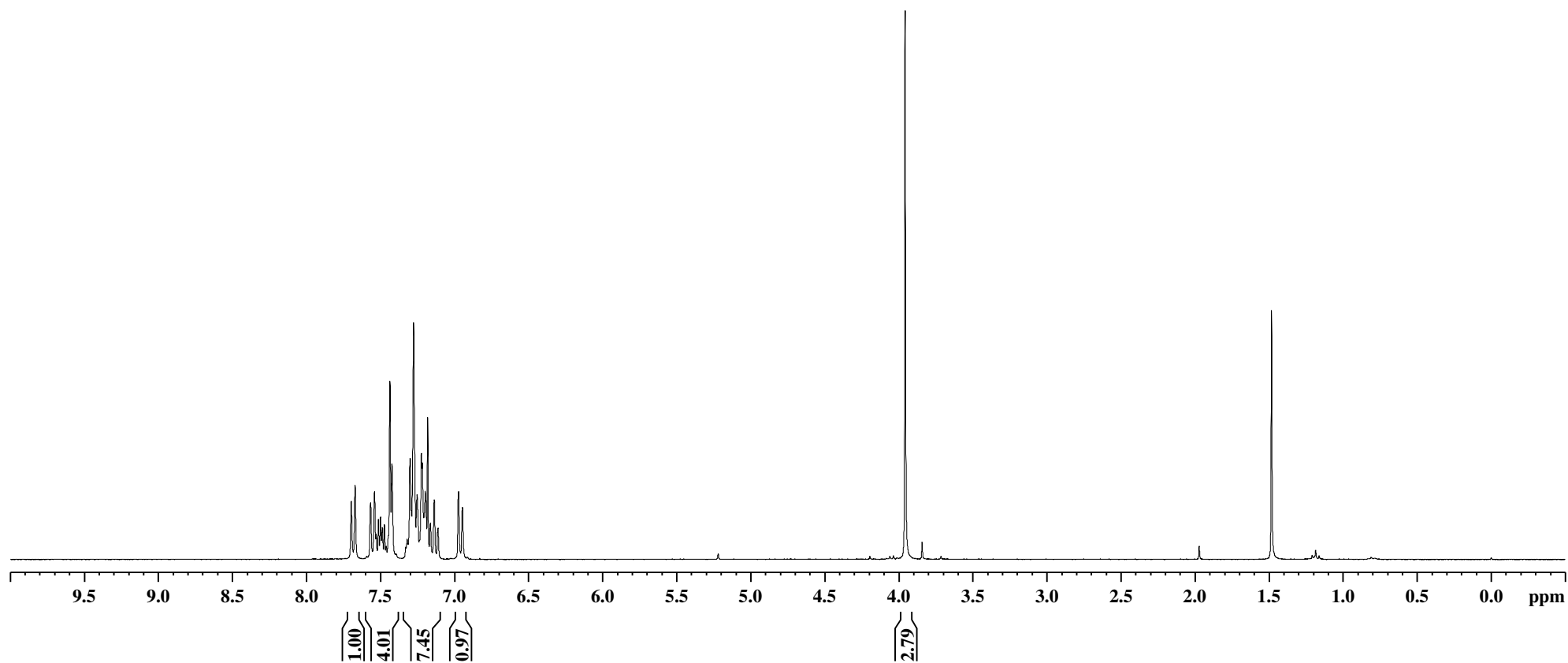
WK-I-192(b)-wash crystal

7.697
7.672
7.591
7.566
7.540
7.529
7.514
7.500
7.487
7.474
7.461
7.436
7.422
7.396
7.330
7.321
7.300
7.277
7.253
7.224
7.218
7.198
7.182
7.162
7.136
7.111
6.973
6.946

3.957



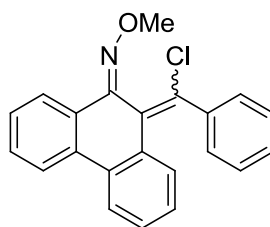
3d



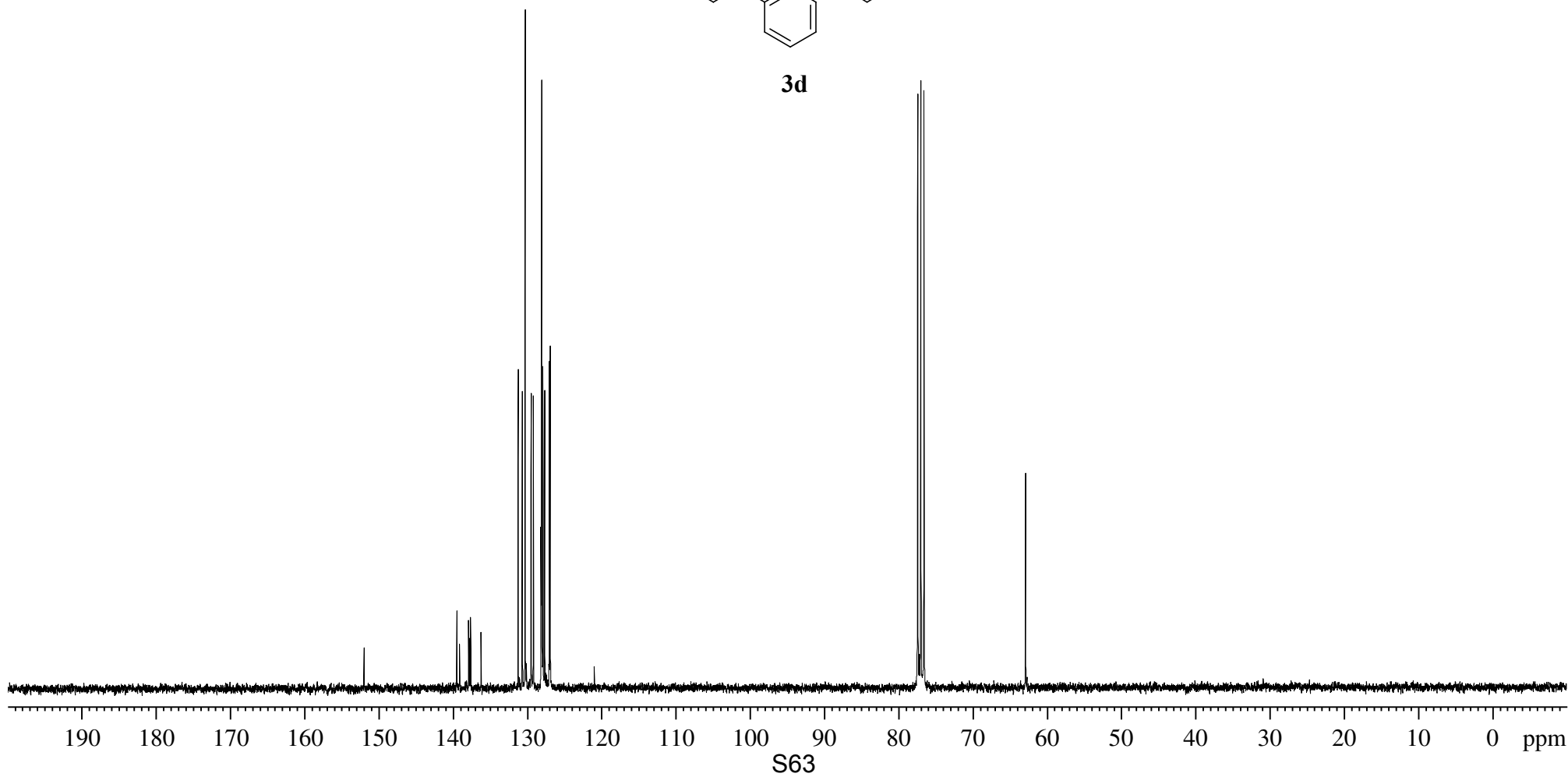
WK-I-192 (b)

152.01
139.51
139.13
137.92
137.80
137.64
136.26
131.25
130.69
130.31
130.13
129.51
129.19
128.15
128.09
127.90
127.66
127.04
126.92
120.99

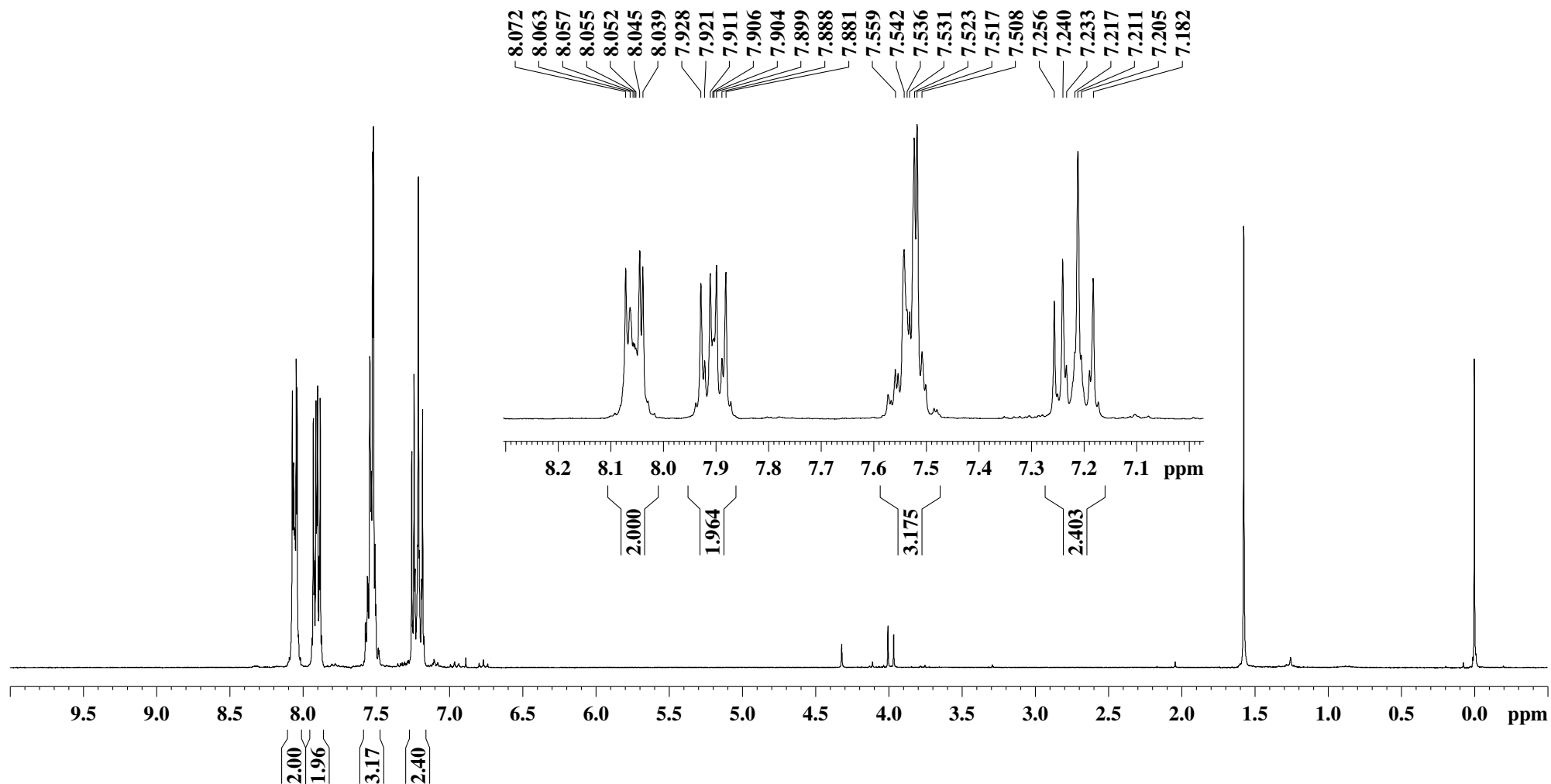
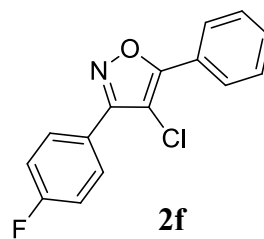
62.88



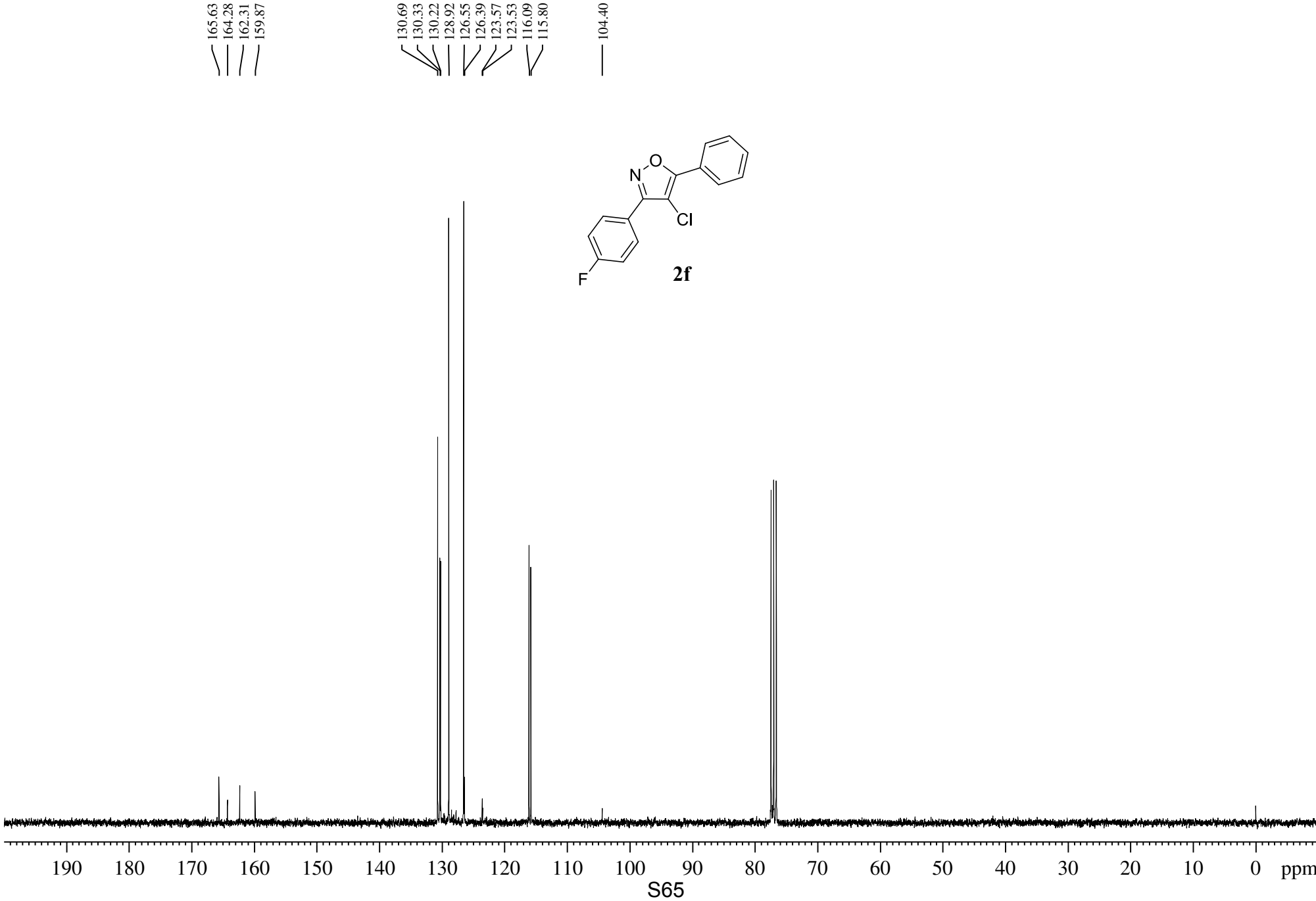
3d



WK-I-52-pure

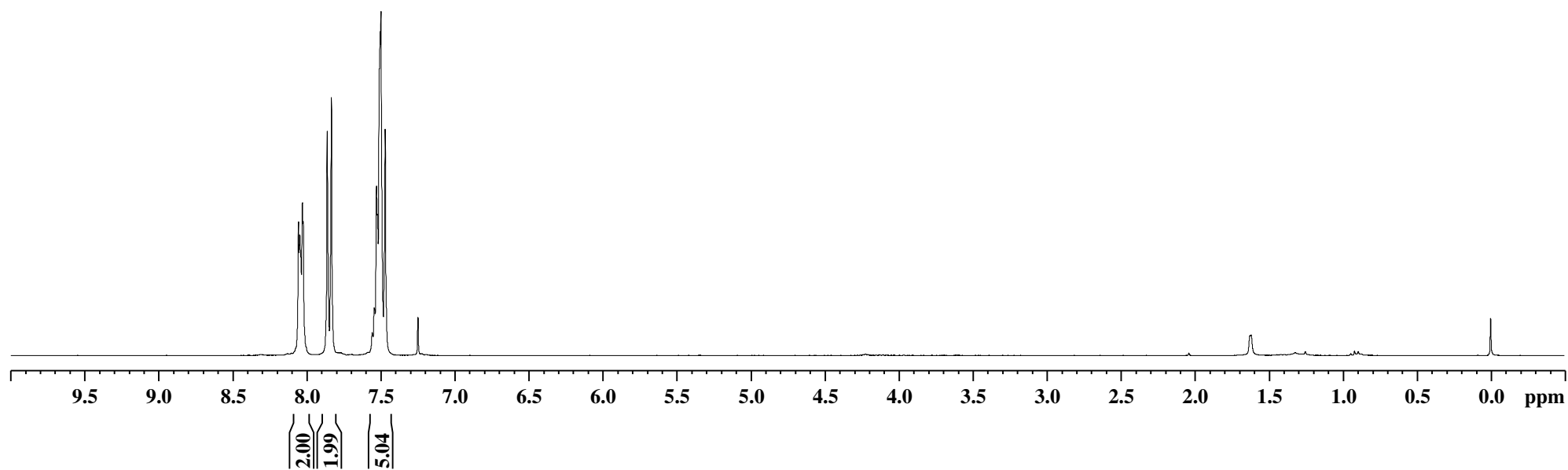
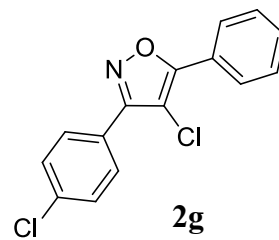


WK-I-52-pure



WK-I-47

8.055
8.046
8.028
8.024
8.023
7.860
7.832
7.558
7.543
7.527
7.521
7.508
7.503
7.497
7.469

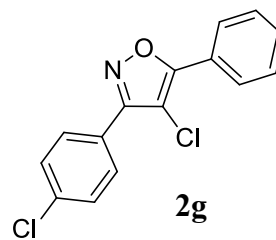


WK-I-47-purified

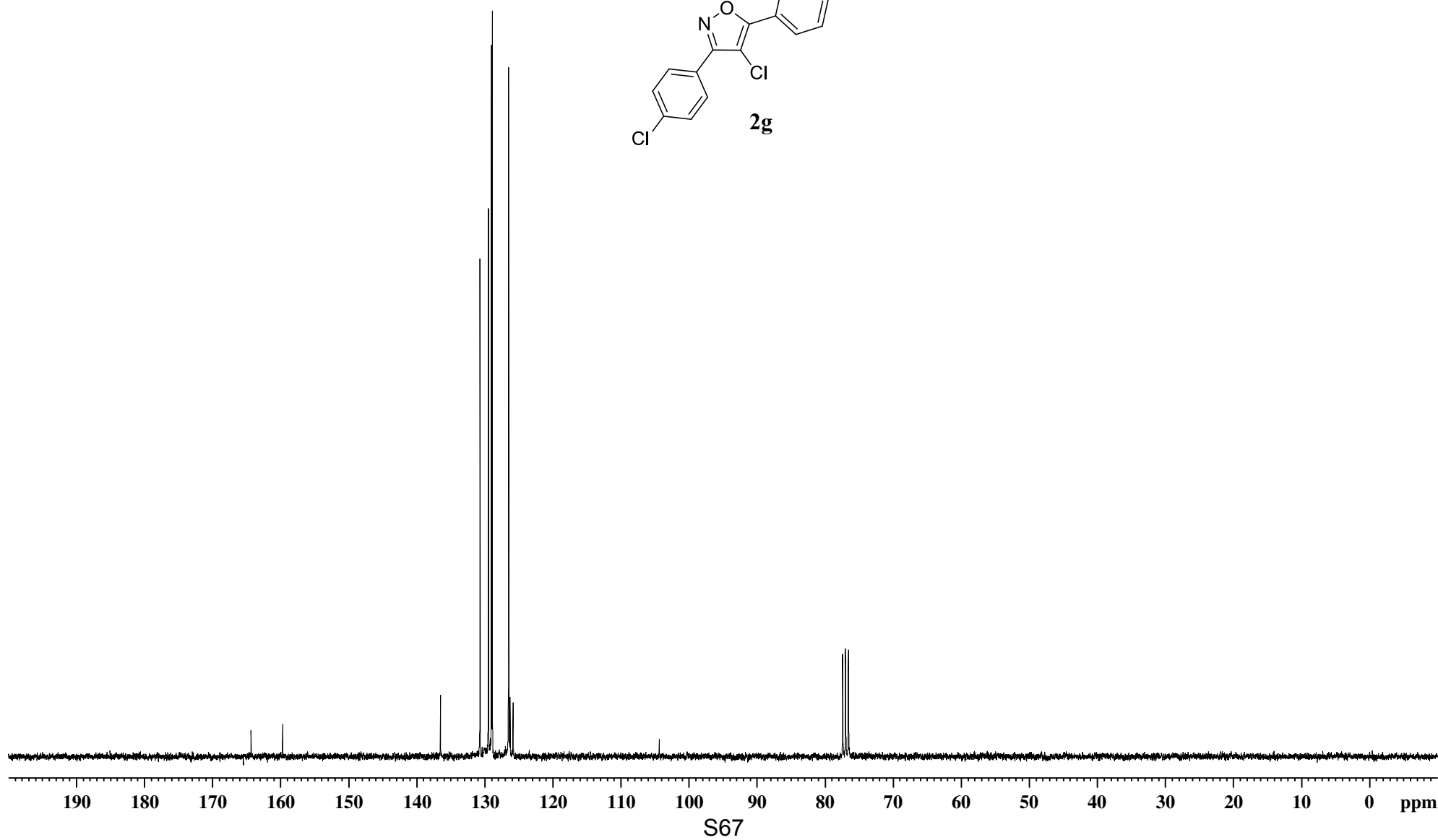
— 164.35
— 159.69

136.50
130.69
129.45
129.04
128.89
126.50
126.27
125.84

— 104.35

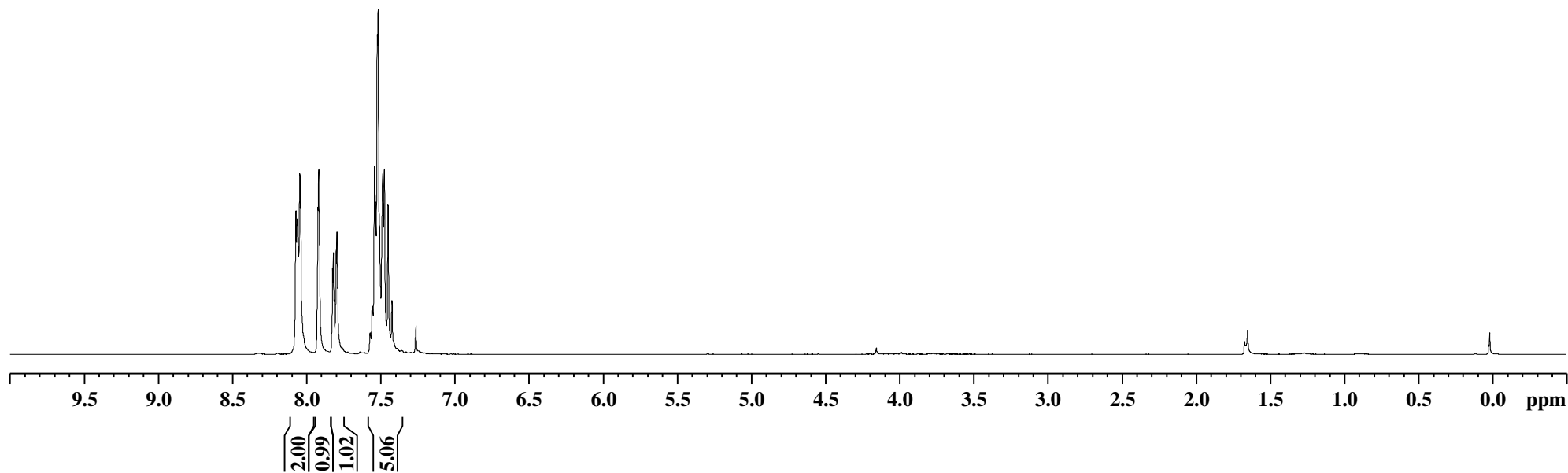
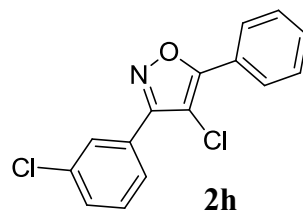


2g



WK-I-141-purified2

8.070
8.062
8.043
8.038
8.038
7.921
7.916
7.911
7.822
7.817
7.812
7.798
7.793
7.788
7.570
7.555
7.540
7.533
7.521
7.516
7.484
7.474
7.449
7.422

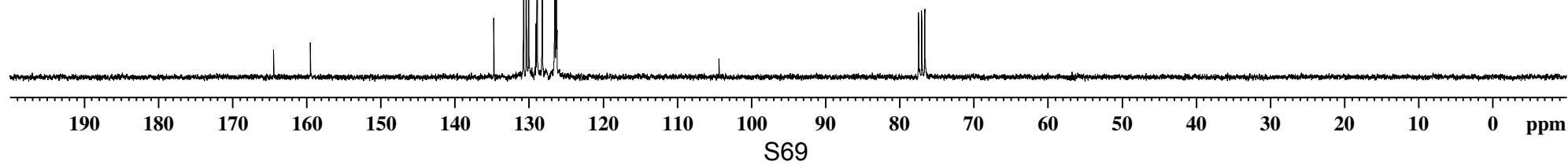
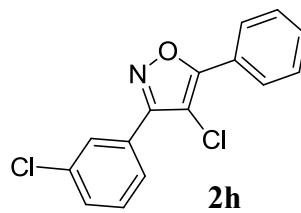


WK-I-141-purified2

— 164.42
— 159.46

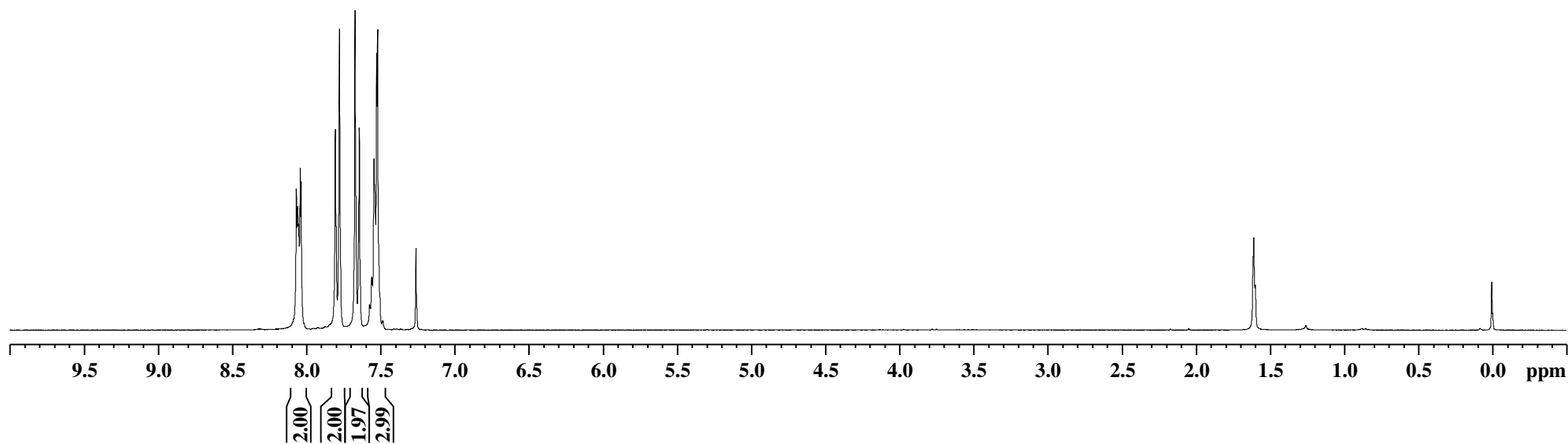
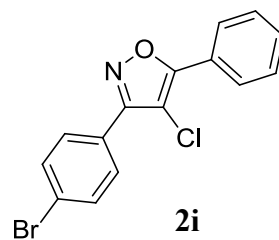
134.70
130.71
130.32
129.99
129.04
128.88
128.18
126.48
126.28
126.20

— 104.35



WK-I-132-purified

8.067
8.059
8.052
8.041
8.035
7.805
7.799
7.776
7.671
7.643
7.574
7.568
7.559
7.554
7.543
7.538
7.534
7.525
7.519
7.504

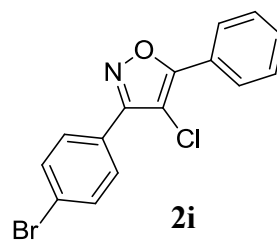


WK-I-132-purified

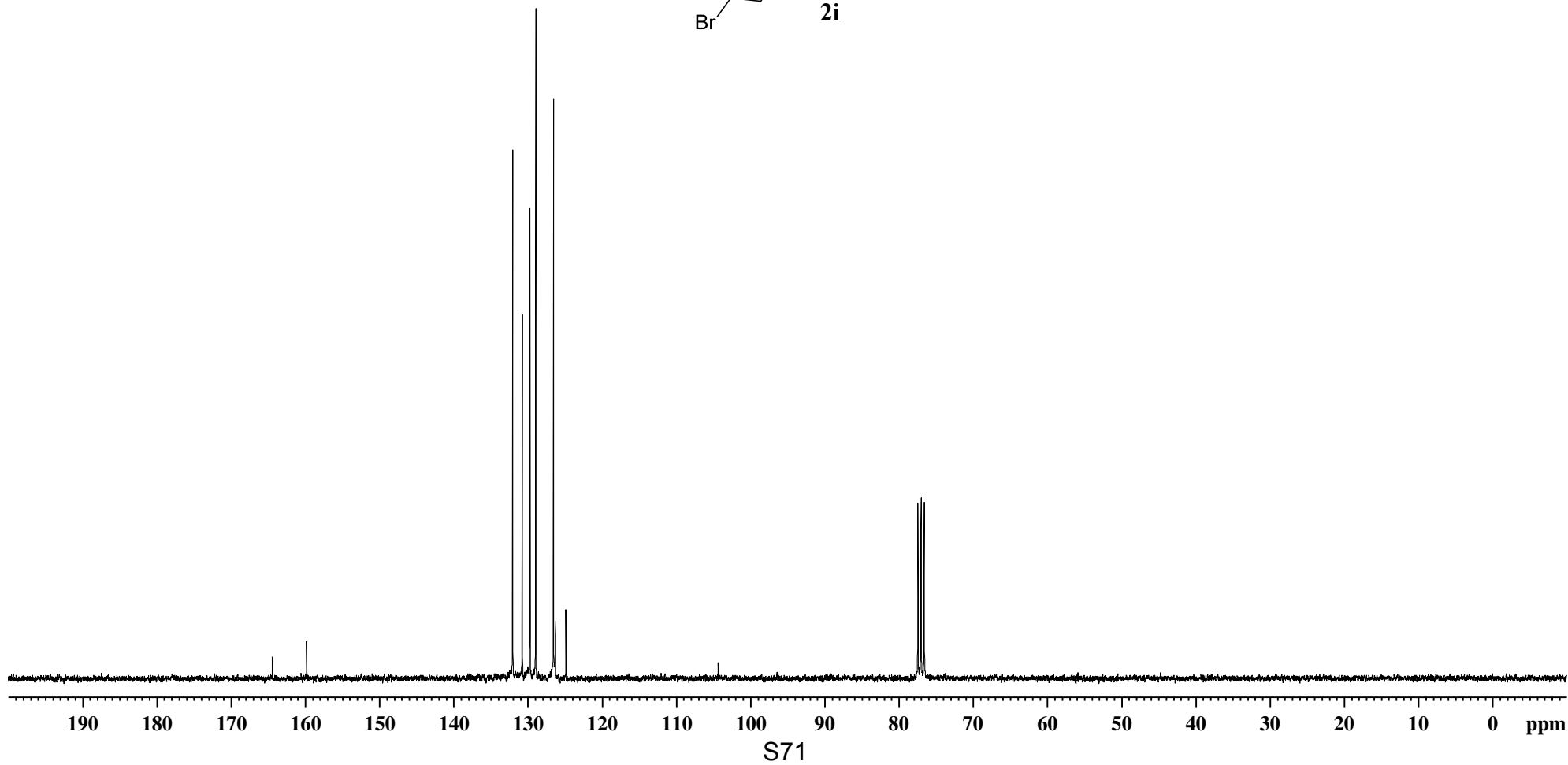
— 164.41
— 159.79

132.02
130.72
129.68
128.91
126.52
126.30
126.27
124.86

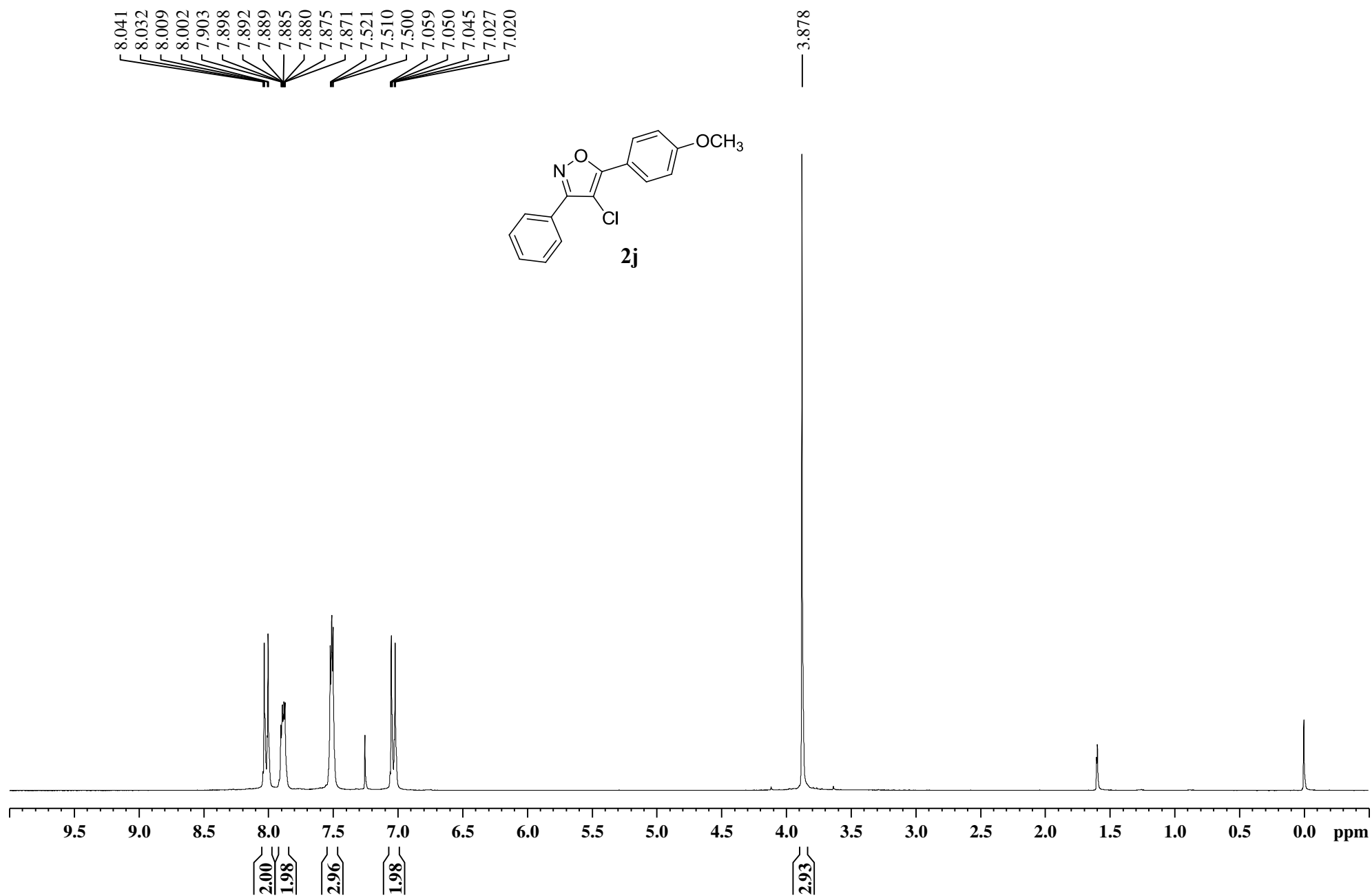
— 104.34



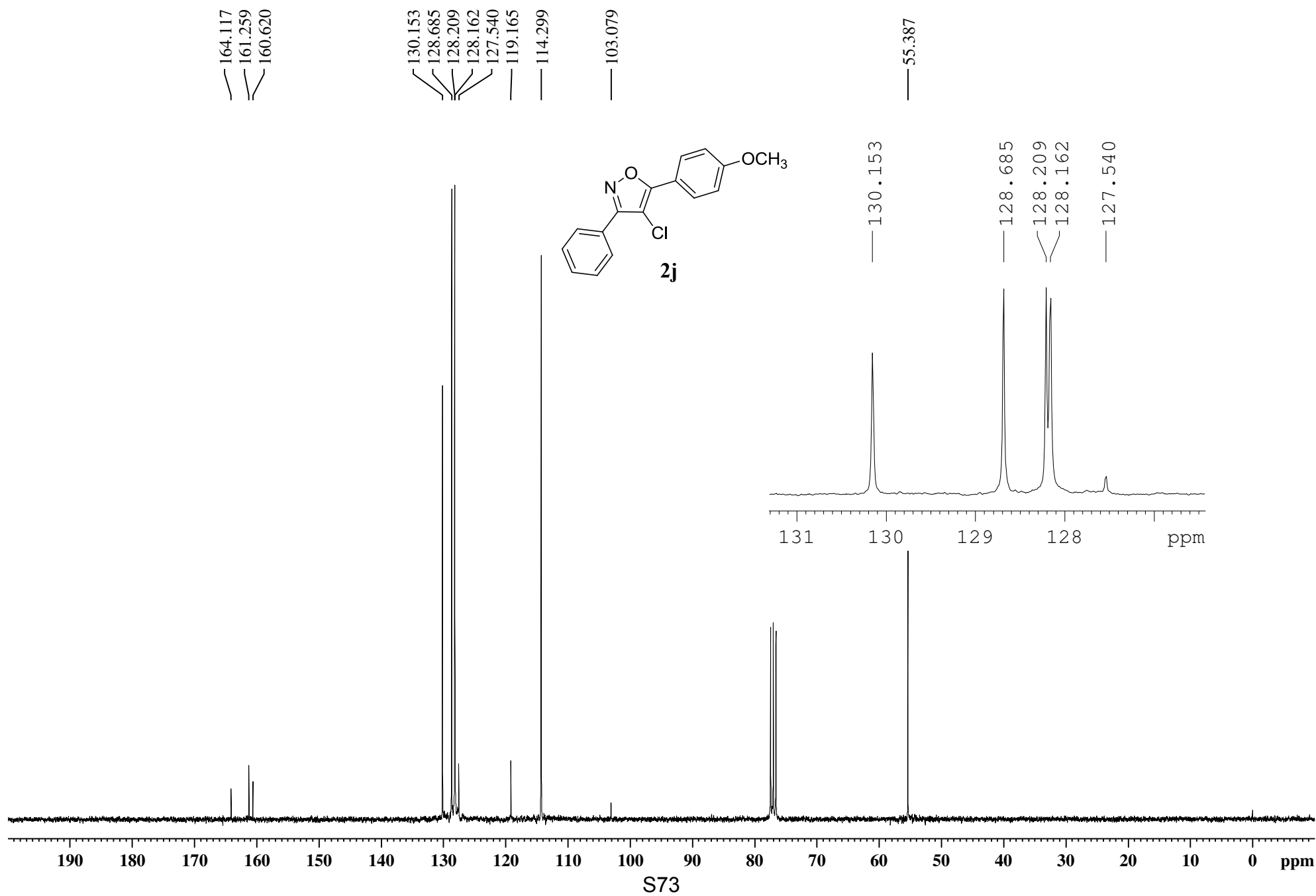
2i



WK-I-134-purified2

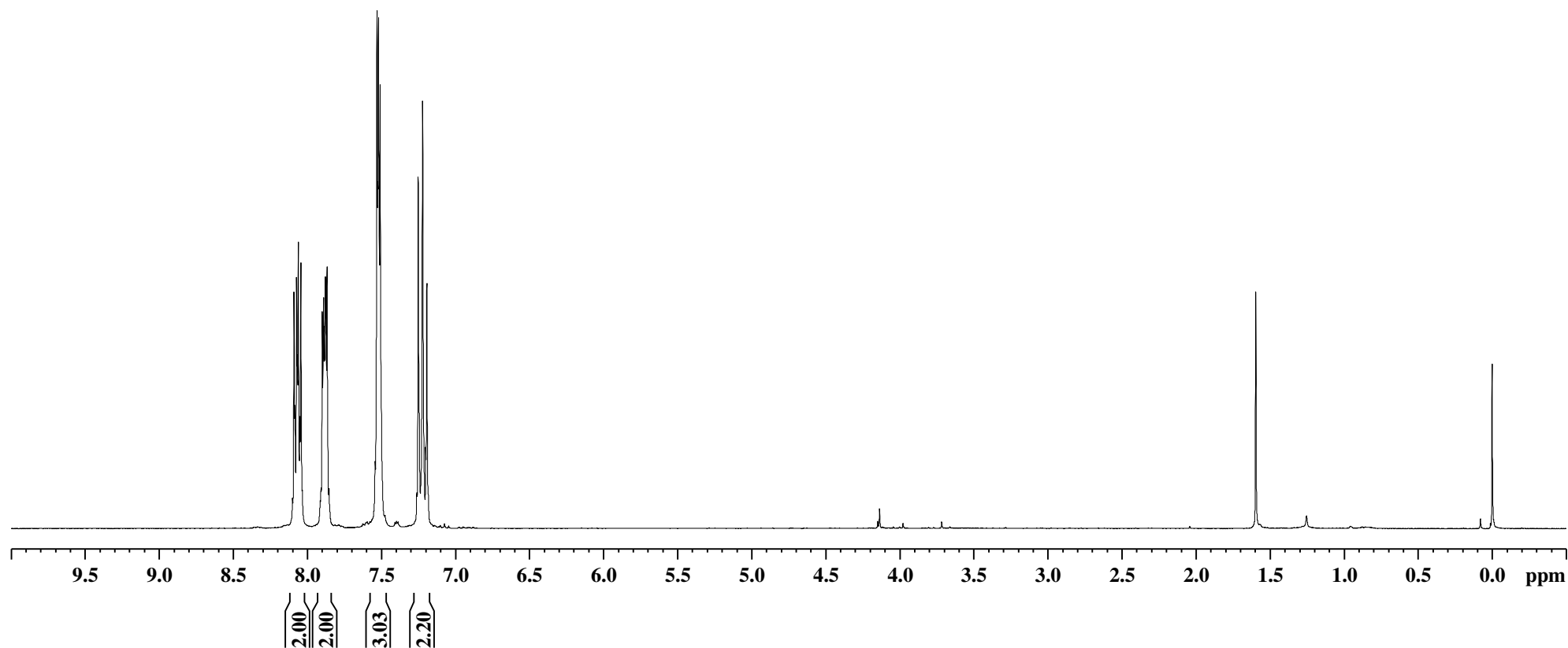
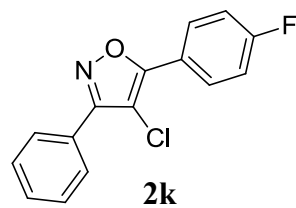


WK-I-134-purified2

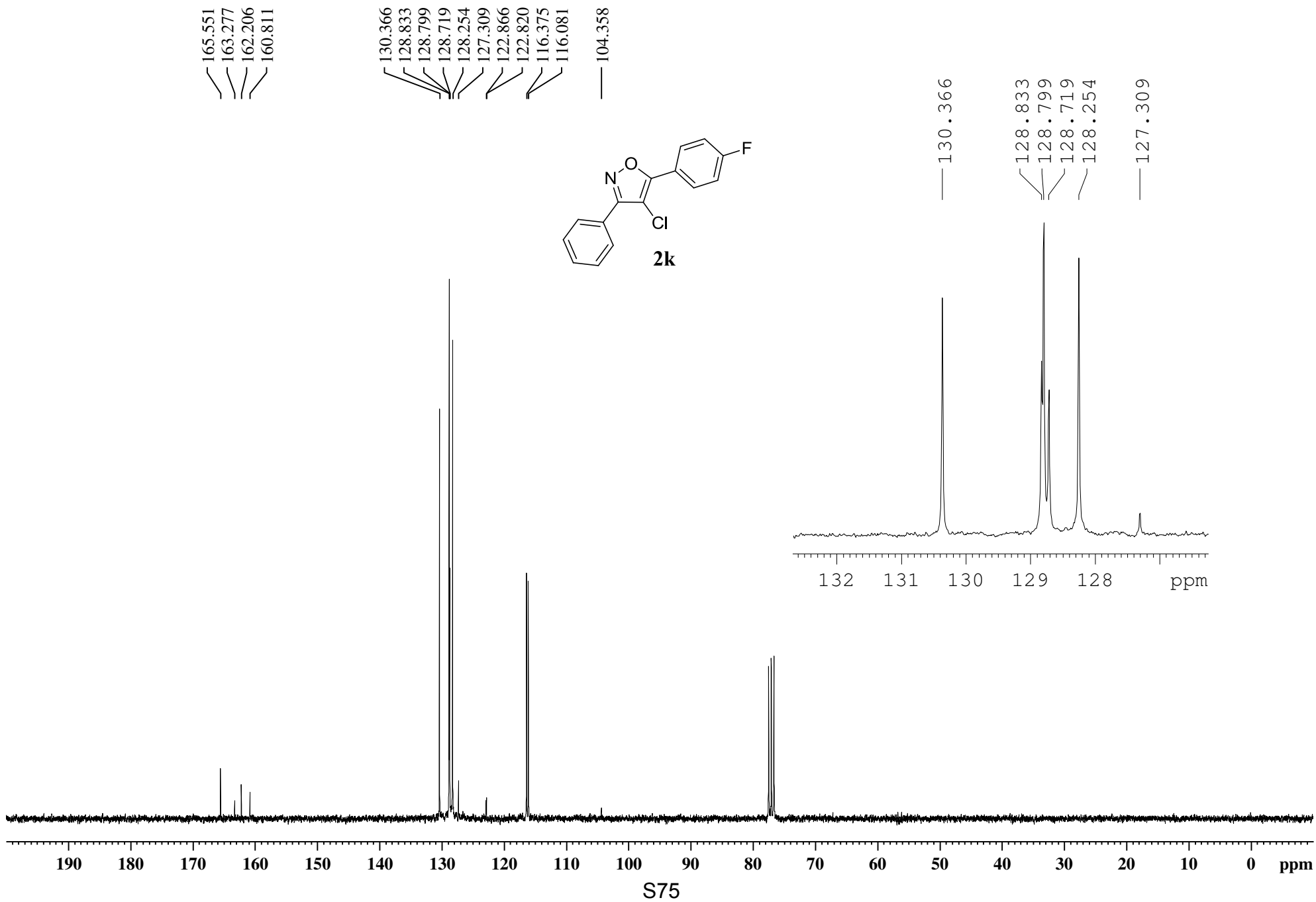


WK-I-111-purified

8.091
8.084
8.074
8.068
8.061
8.051
8.044
7.900
7.891
7.885
7.881
7.878
7.872
7.868
7.531
7.526
7.520
7.509
7.261
7.252
7.222
7.201
7.194
7.184

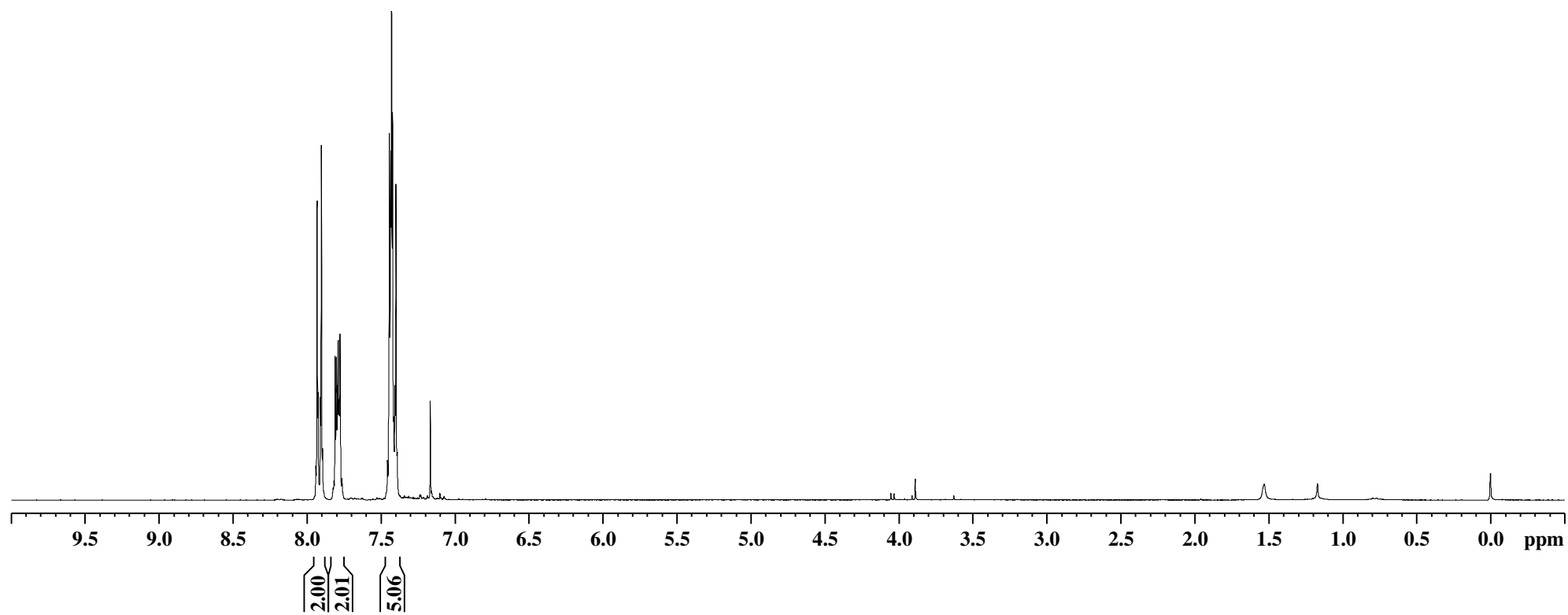
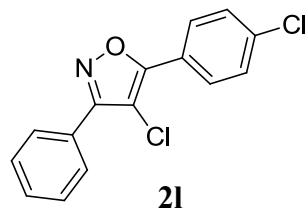


WK-I-111-purified



WK-I-119-purified

7.941
7.933
7.926
7.910
7.903
7.895
7.823
7.819
7.810
7.801
7.795
7.790
7.786
7.782
7.778
7.765
7.457
7.444
7.434
7.429
7.422
7.413
7.406
7.399
7.391

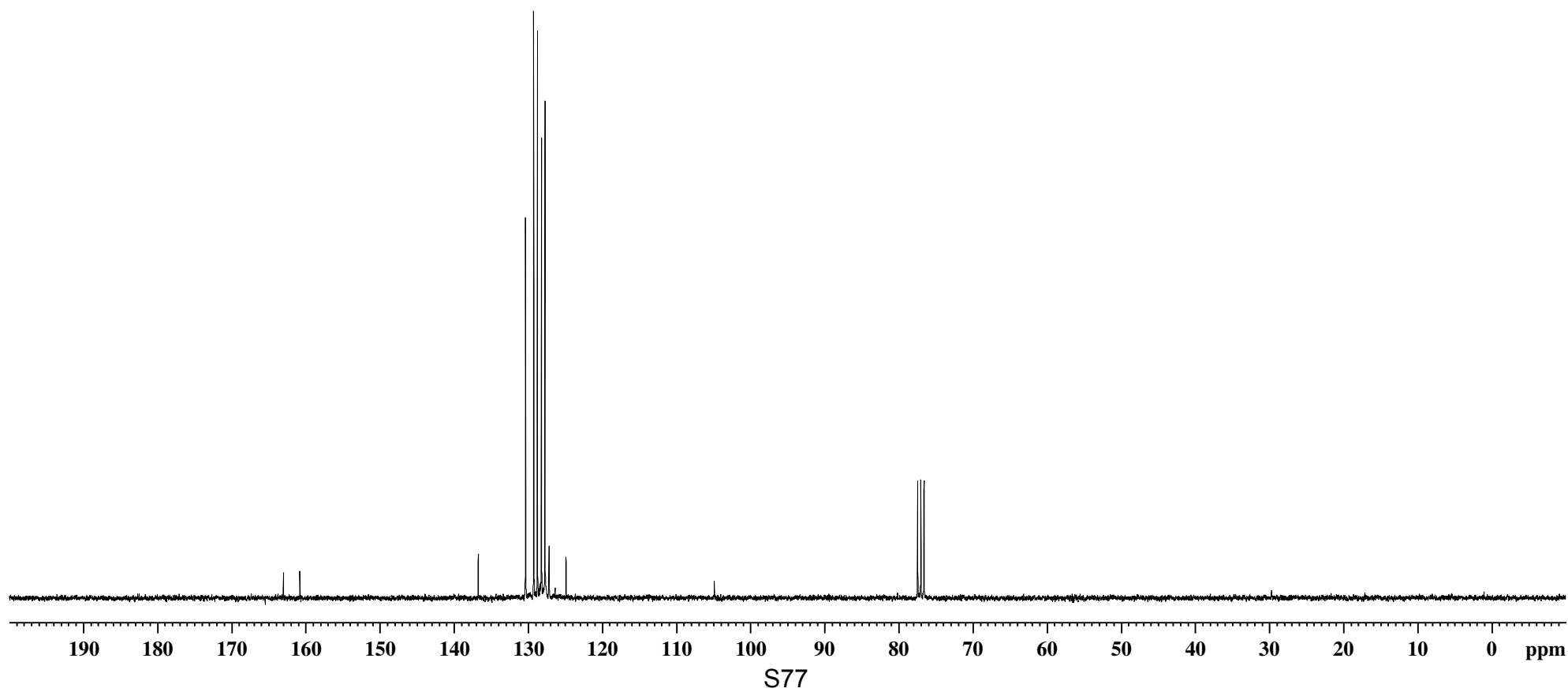
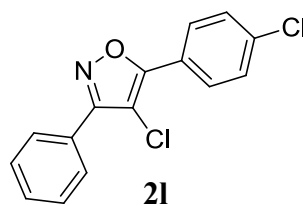


WK-I-119-purified

163.001
160.795

136.721
130.341
129.235
128.751
128.197
127.716
127.159
124.877

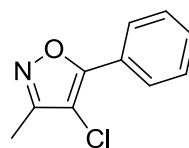
104.876



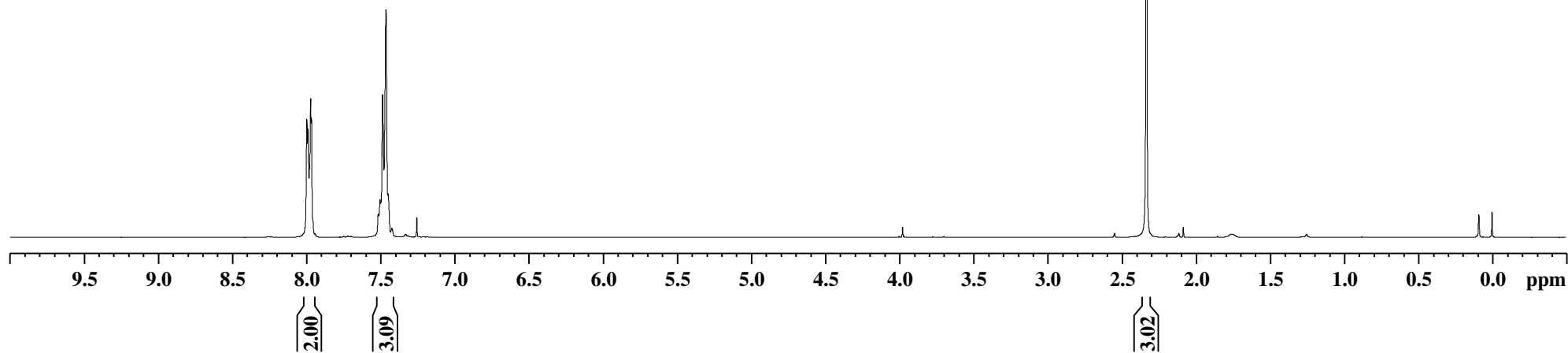
WK-II-55-Fr1

7.996
7.989
7.969
7.964
7.514
7.503
7.496
7.485
7.462
7.447

2.331



2m-Cl



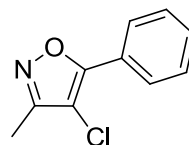
WK-II-55-Fr1

— 162.38
— 159.40

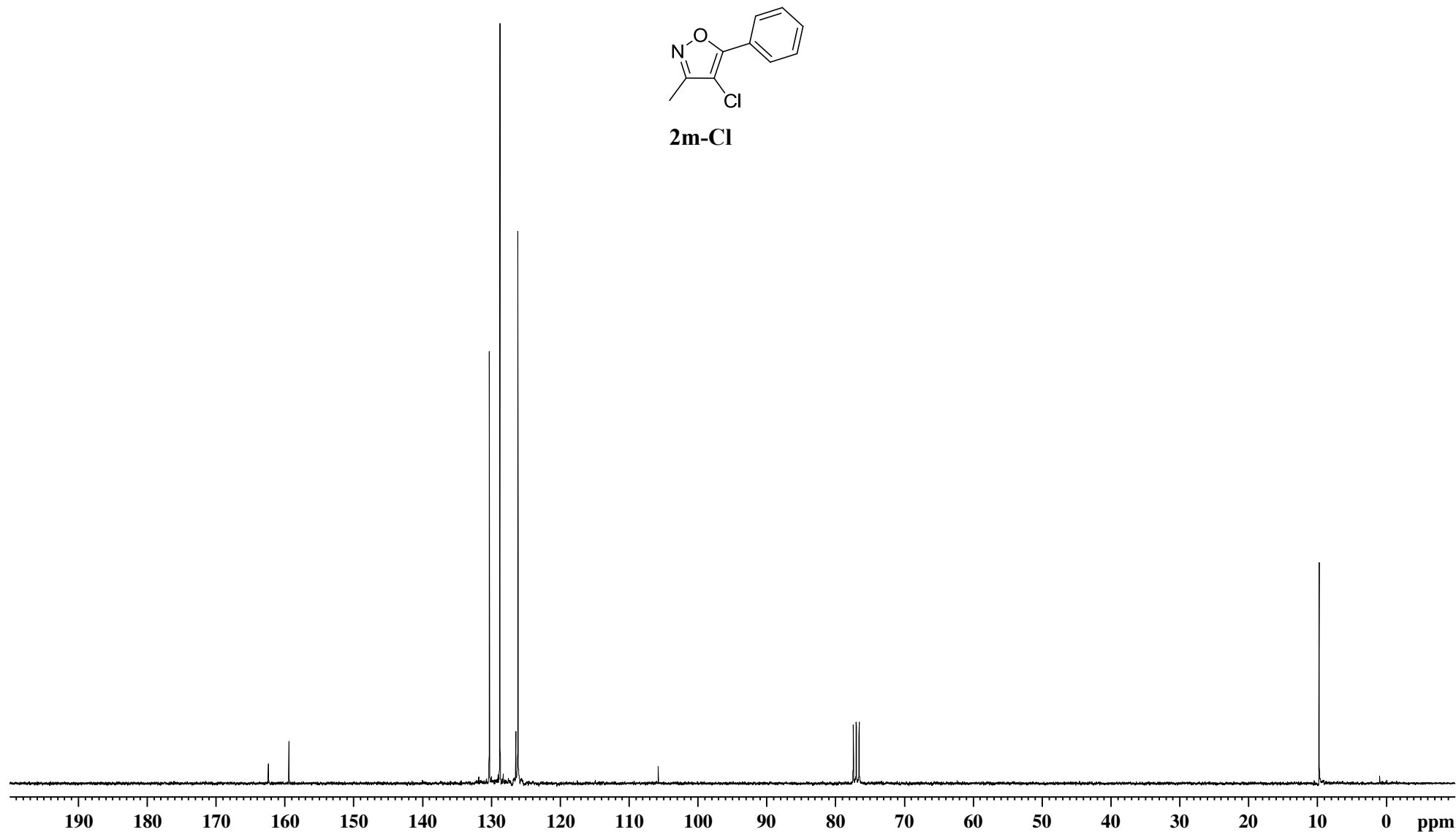
— 130.30
— 128.76
— 126.45
— 126.14

— 105.77

— 9.76



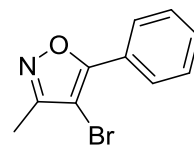
2m-Cl



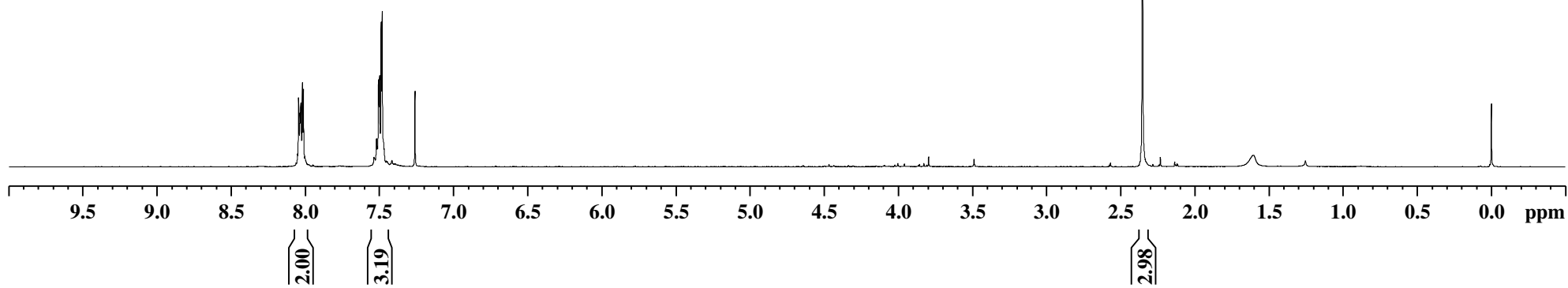
WK-III-37

8.045
8.035
8.030
8.025
8.019
8.013
7.520
7.515
7.506
7.499
7.488
7.482
7.473
7.468

— 2.354



2m-Br



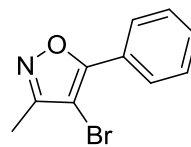
WK-III-37

— 164.213
— 160.646

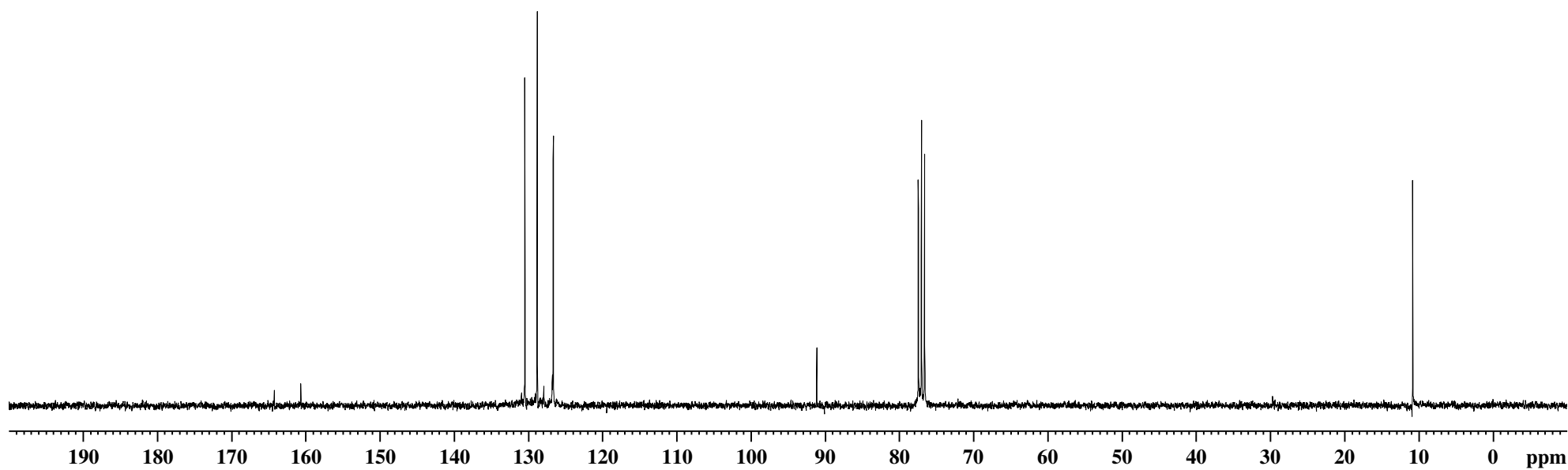
130.447
128.787
127.900
126.759
126.626

— 91.118

— 10.814



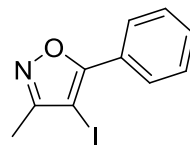
2m-Br



S81

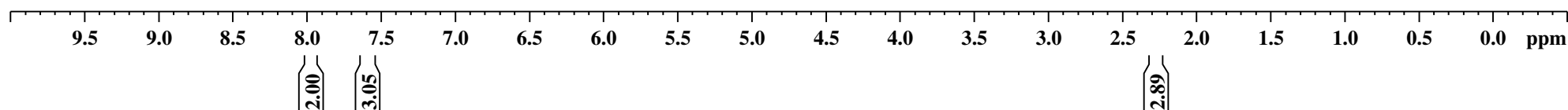
WK-III-30

7.988
7.979
7.973
7.962
7.956
7.610
7.605
7.595
7.588
7.577
7.571
7.562
7.556



2m-I

2.283



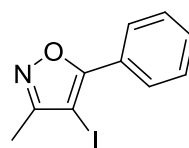
WK-III-30

— 166.733
— 163.180

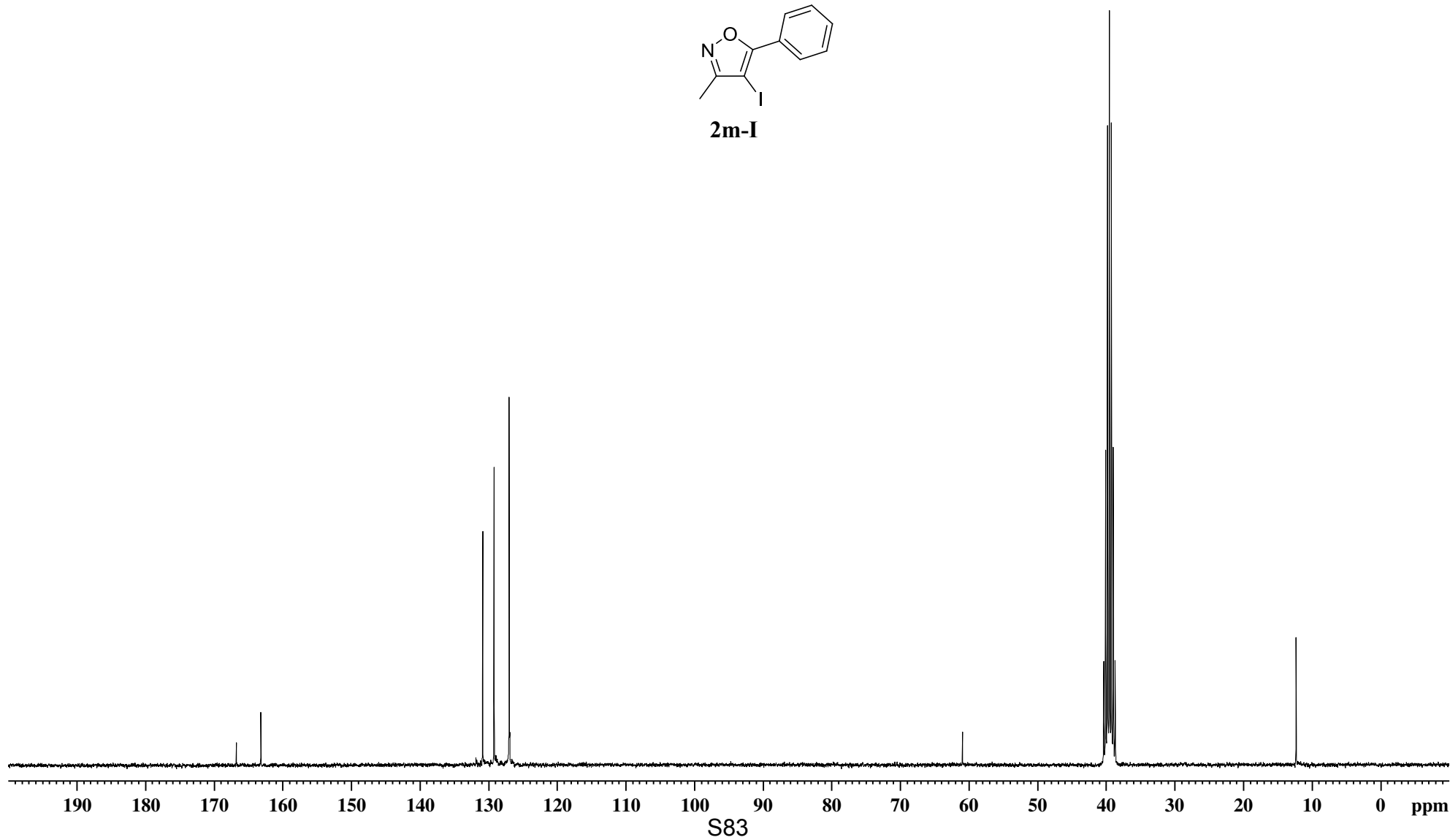
— 130.839
— 129.185
— 126.987
— 126.897

— 60.922

— 12.294



2m-I

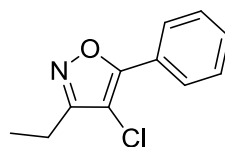


WK-I-221-sephadex2-Fr4-6

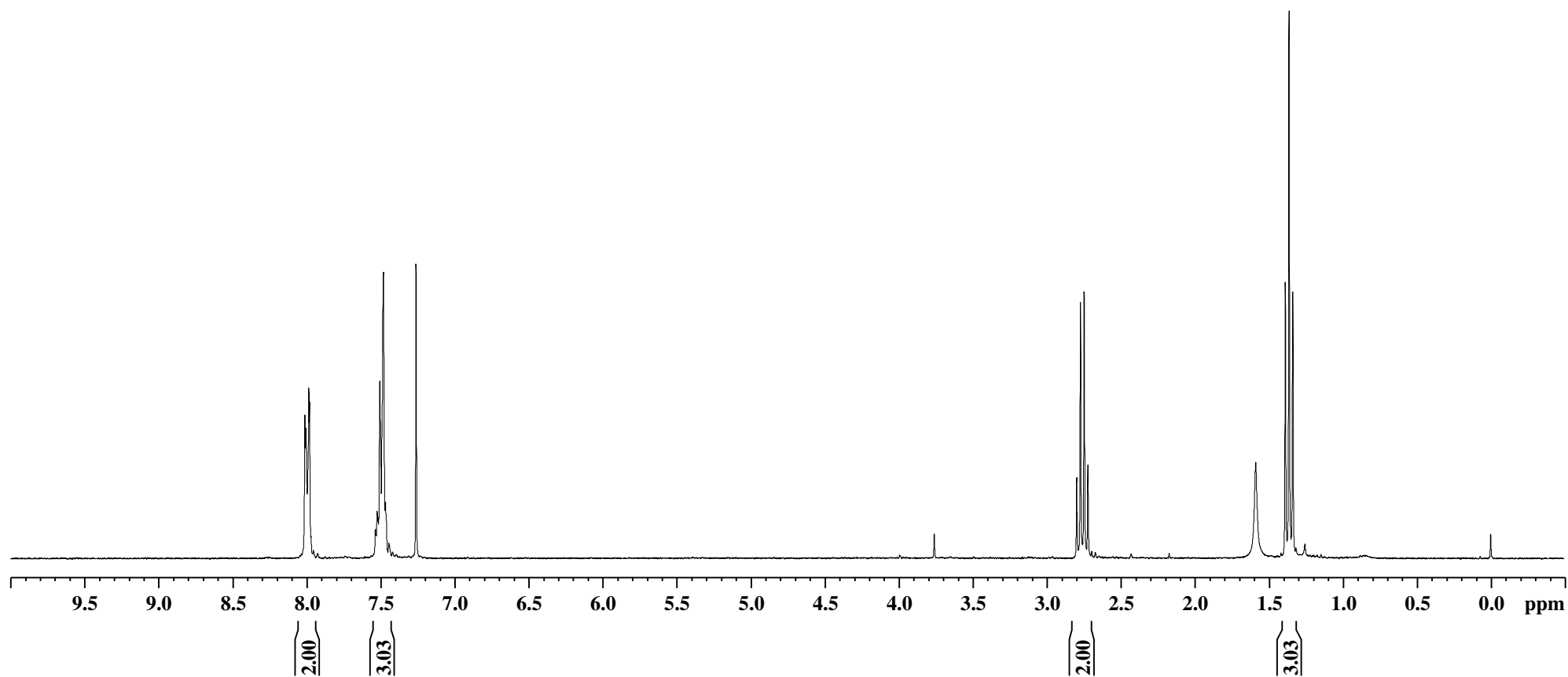
8.012
8.004
7.985
7.980
7.535
7.523
7.517
7.505
7.483
7.481
7.467

2.797
2.771
2.746
2.721

1.387
1.362
1.337



2n-Cl



WK-I-221-sephadex2-Fr4-6

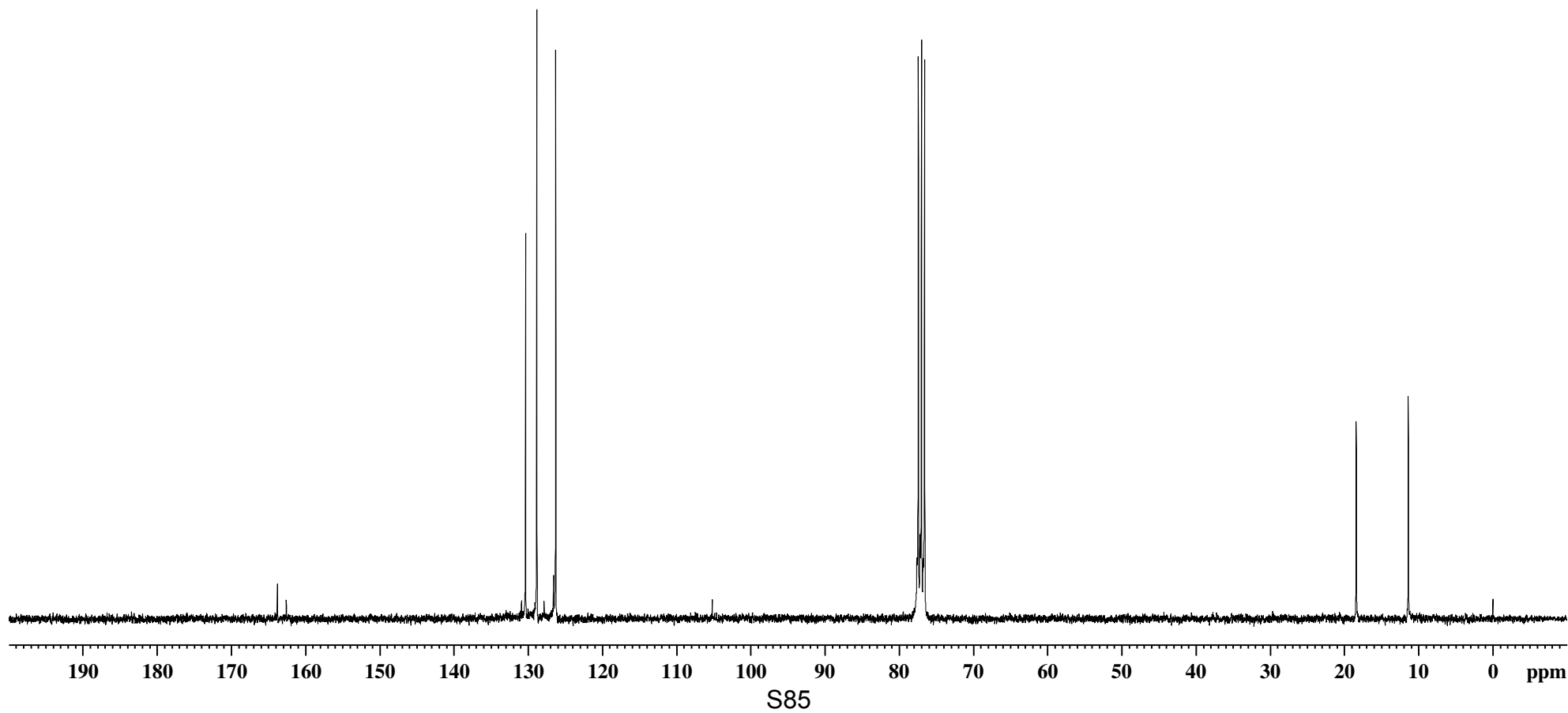
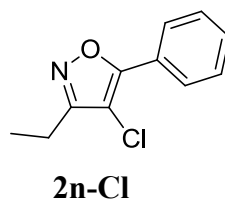
163.780
162.603

130.339
128.823
126.599
126.285

105.187

18.415

11.397

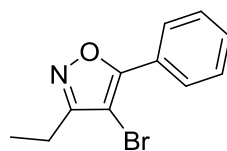


WK-II-137-sephadex

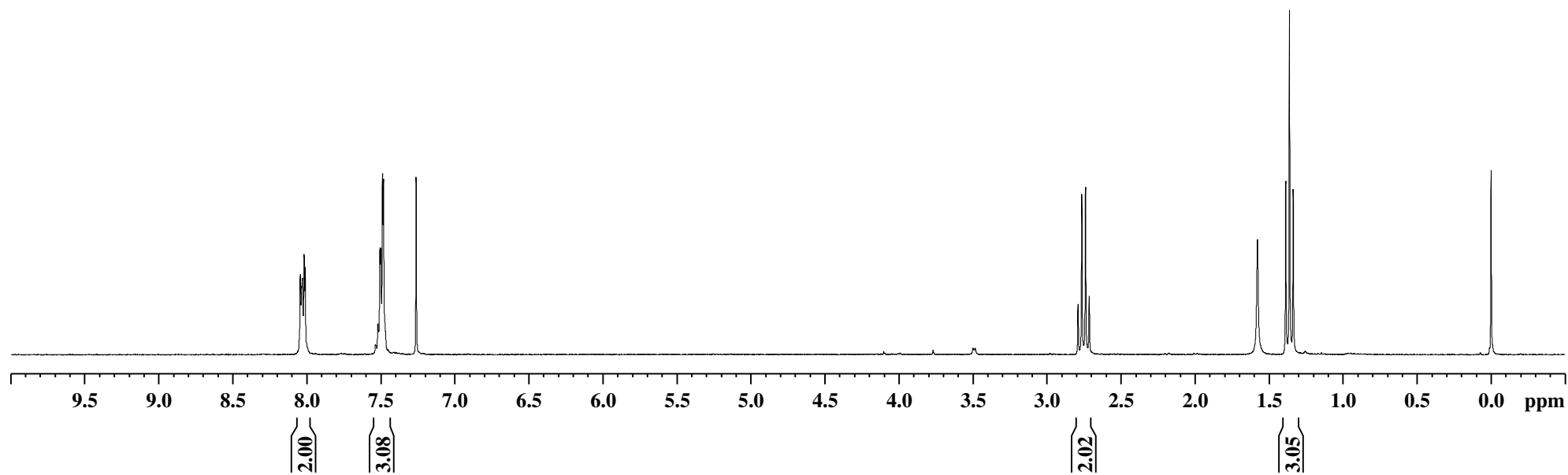
8.044
8.034
8.029
8.018
8.012
7.536
7.520
7.506
7.499
7.488
7.482

2.790
2.765
2.740
2.715

1.387
1.362
1.337



2n-Br



WK-II-137
C13
10/12/15

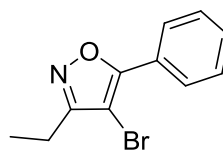
164.786
164.303

130.406
128.768
126.847
126.710

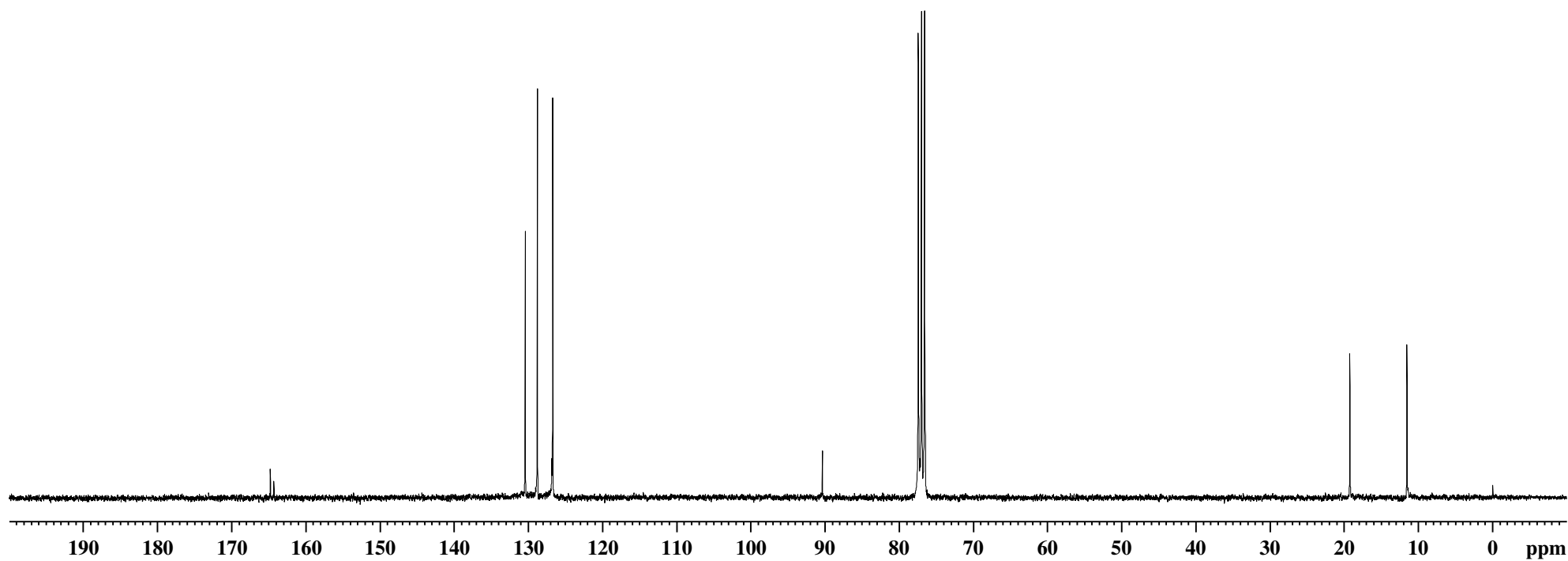
90.358

19.236

11.537



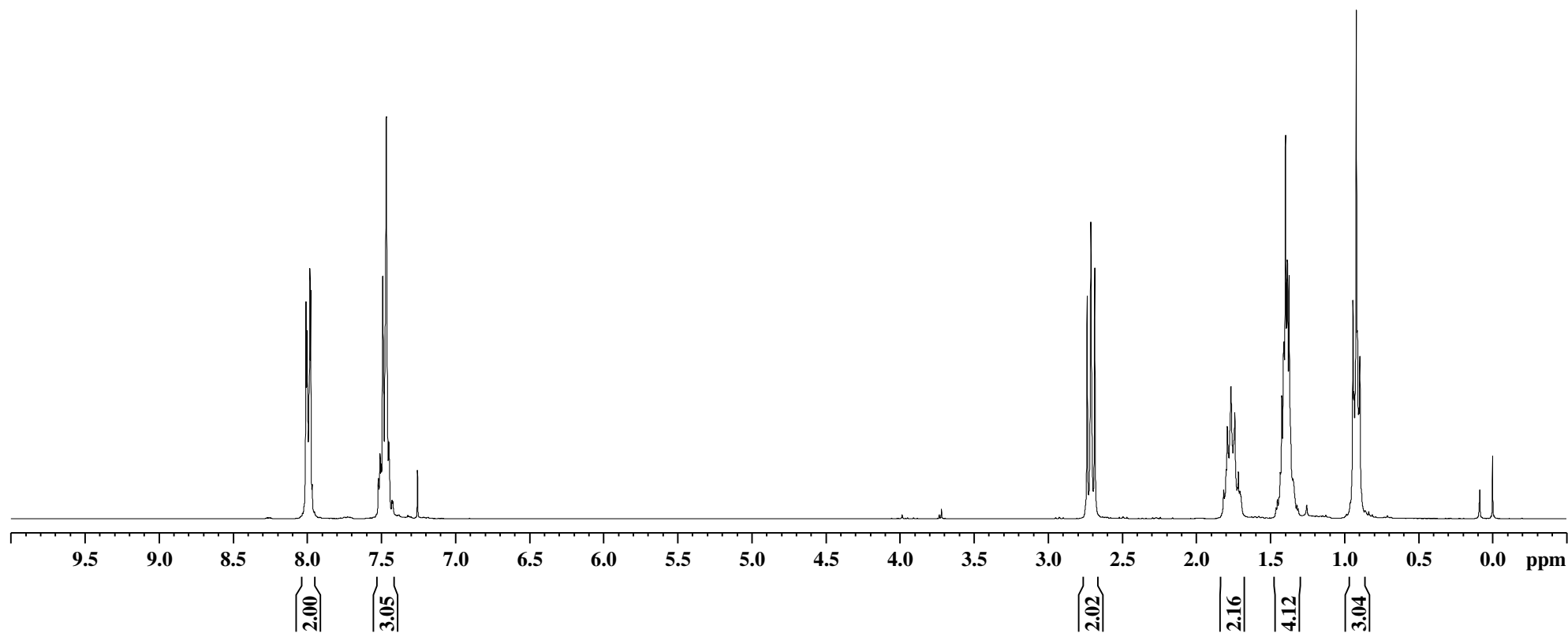
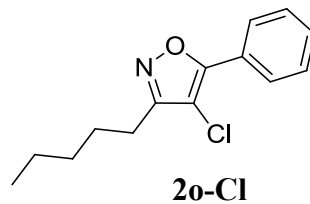
2n-Br



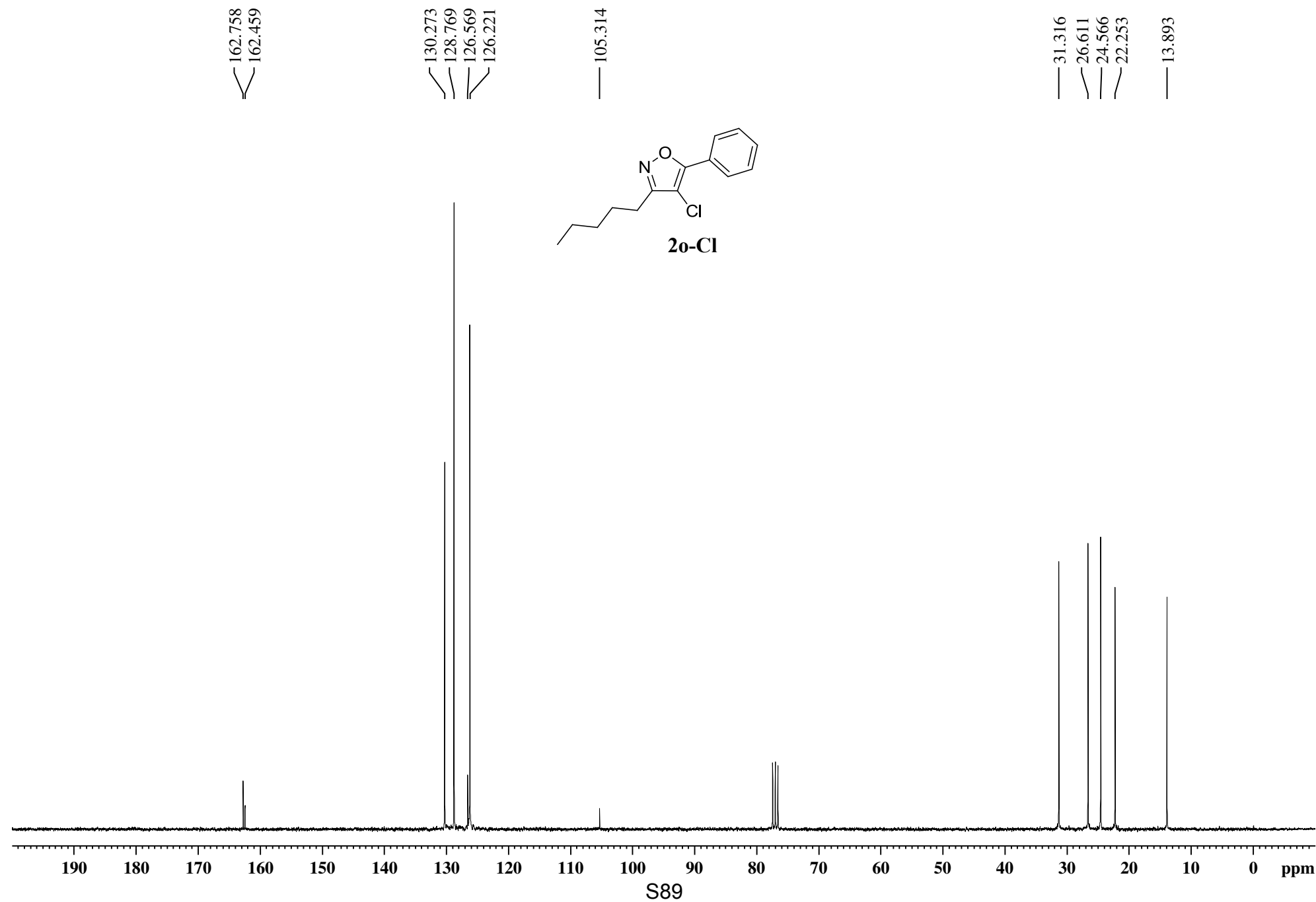
WK-II-71-Z-isomer cyclize-TOP

8.007
8.000
7.986
7.980
7.975
7.965
7.518
7.508
7.501
7.489
7.465
7.449
7.427
7.422

2.736
2.711
2.684
1.815
1.798
1.790
1.782
1.765
1.740
1.722
1.715
1.706
1.460
1.451
1.433
1.422
1.407
1.397
1.385
1.373
1.346
1.320
1.312
0.942
0.935
0.919
0.912



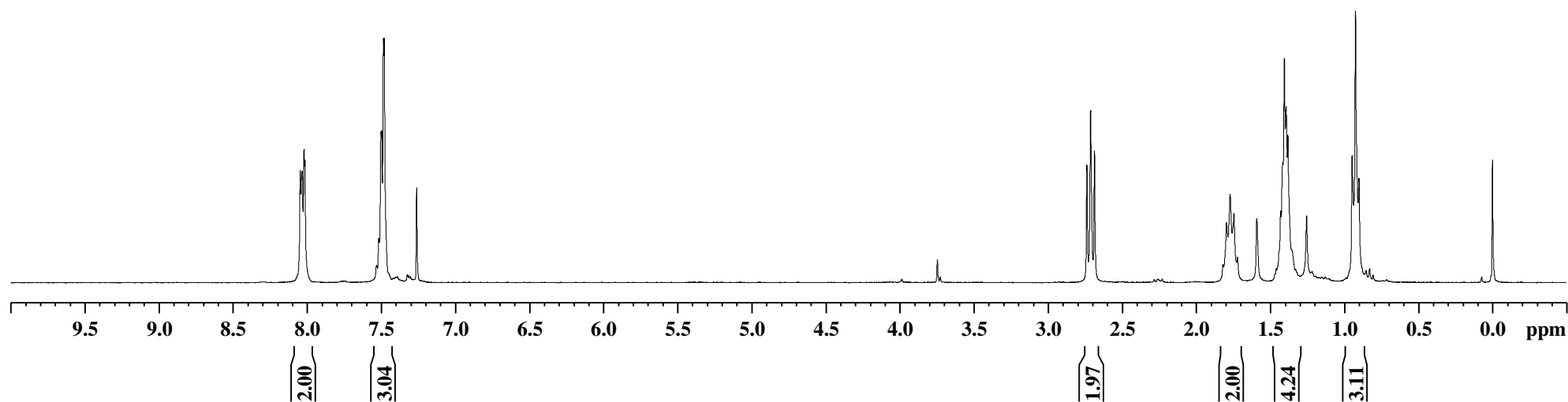
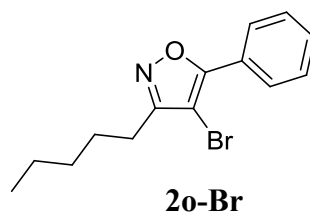
WK-II-71-Z-isomer cyclize-TOP



WK-II-133

8.046
8.033
8.020
8.014
7.530
7.516
7.501
7.496
7.484
7.478

2.737
2.712
2.686
1.820
1.795
1.770
1.745
1.721
1.459
1.430
1.416
1.405
1.393
1.381
1.329
0.947
0.924
0.901



S90

WK-II-133

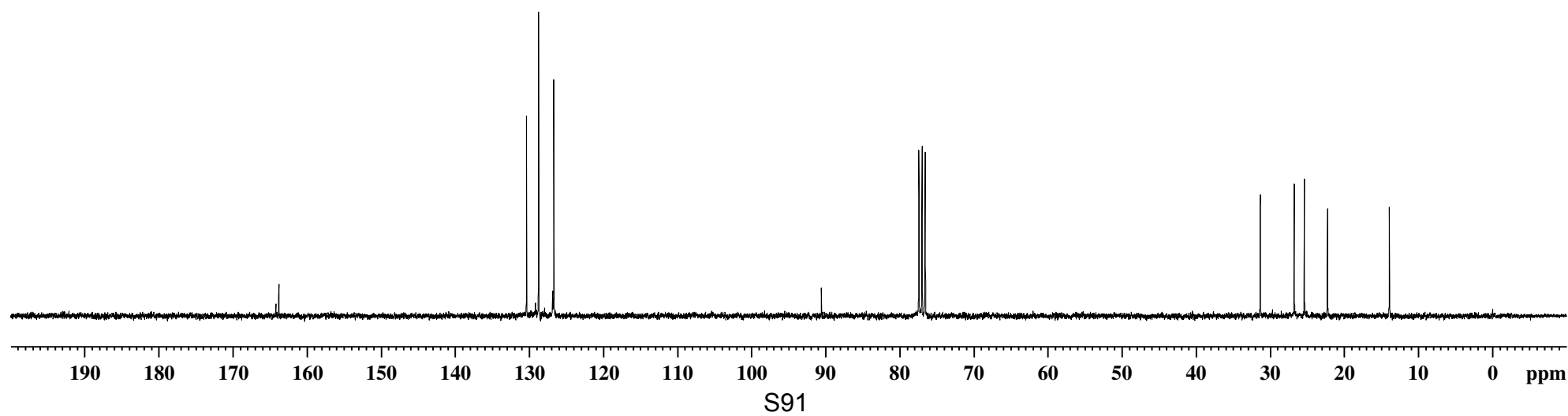
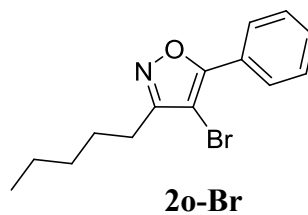
164.214
163.817

130.389
128.758
126.860
126.703

90.594

31.360
26.774
25.405
22.288

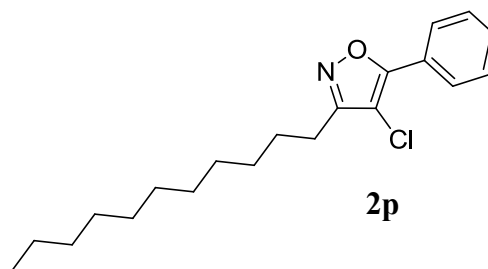
13.933



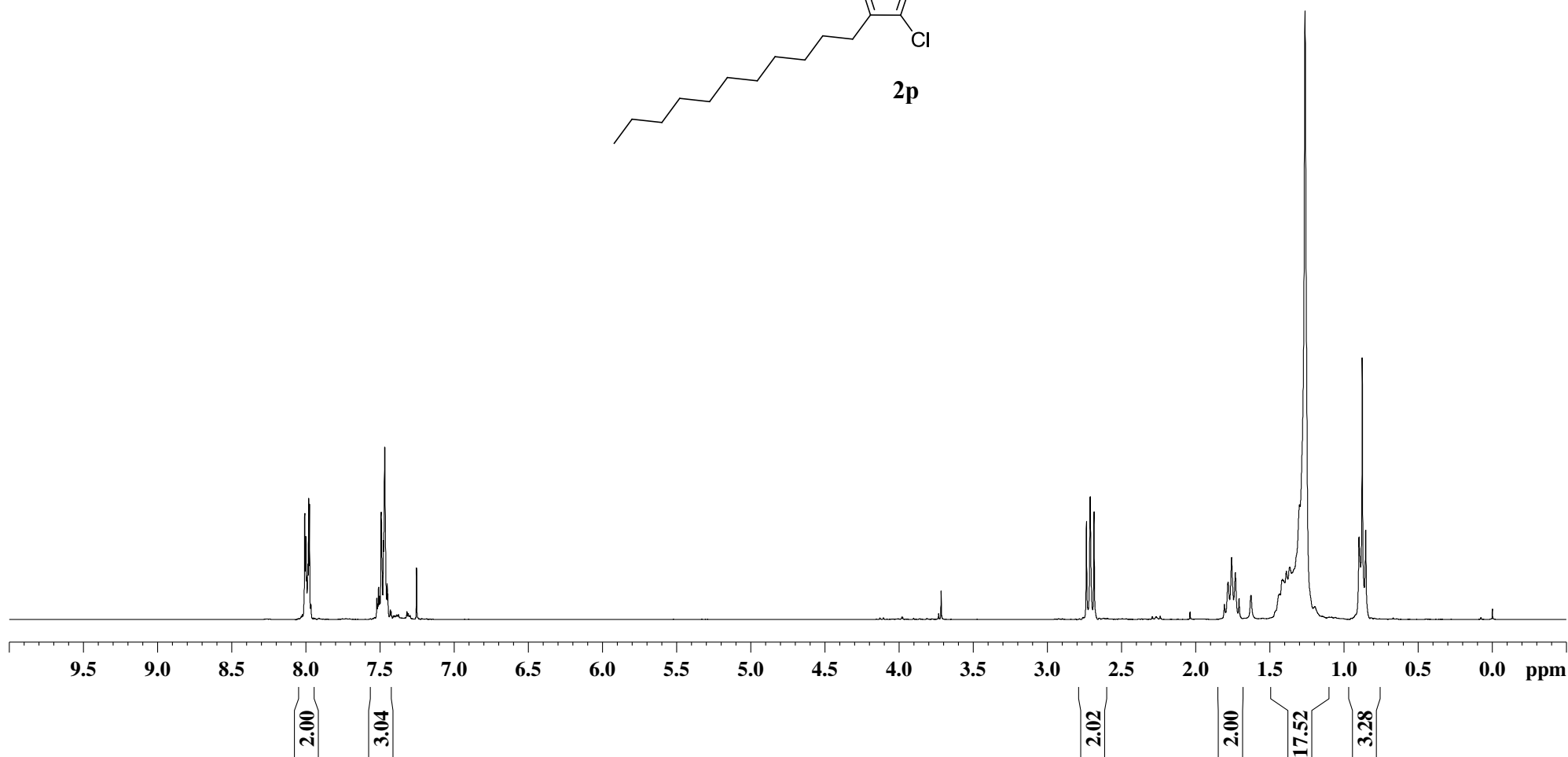
WK-II-15 pure

8.009
8.002
7.996
7.990
7.988
7.982
7.977
7.967
7.523
7.517
7.511
7.505
7.493
7.487
7.478
7.470
7.468
7.453
7.448

2.737
2.712
2.686
1.808
1.781
1.759
1.733
1.708
1.435
1.415
1.390
1.366
1.301
1.263
0.899
0.878
0.855



2p



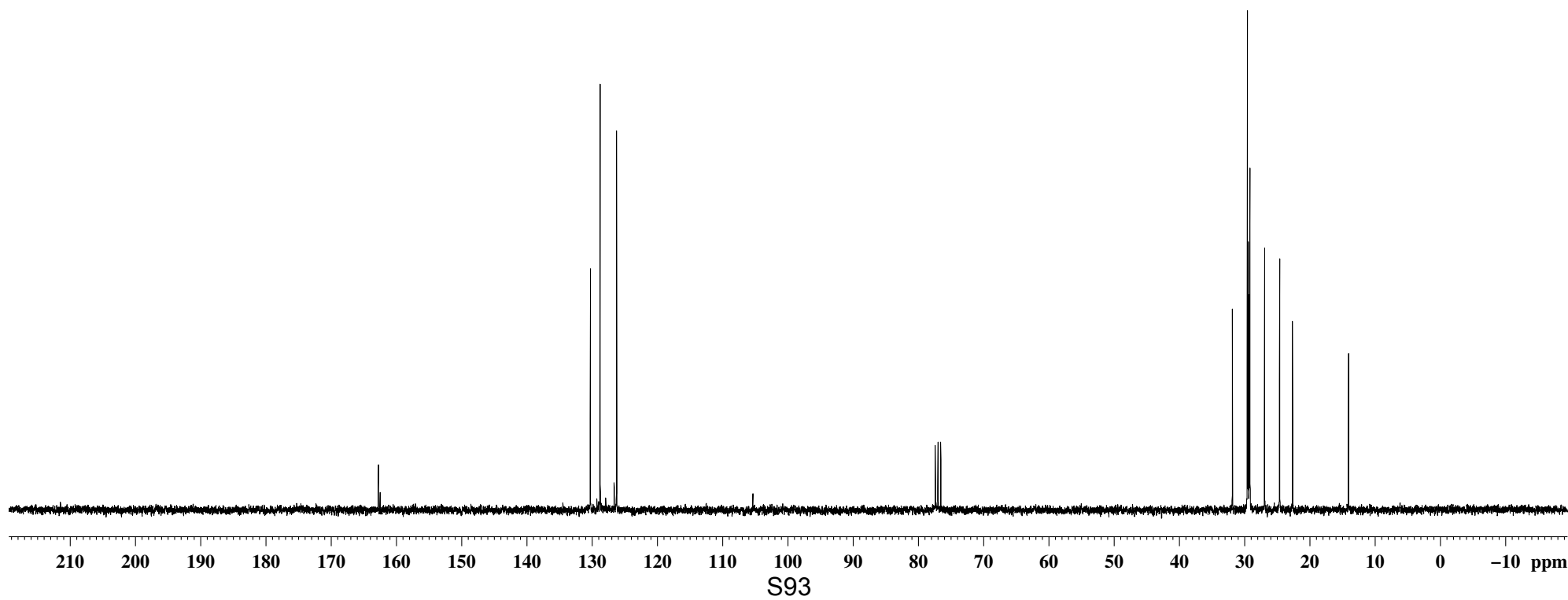
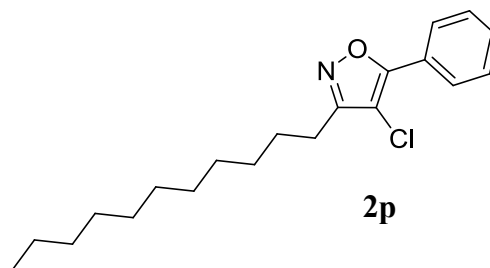
WK-II-15 pure

162.786
162.503

130.288
128.791
126.632
126.265

105.347

31.885
29.590
29.458
29.309
29.210
29.199
26.951
24.639
22.658
14.079

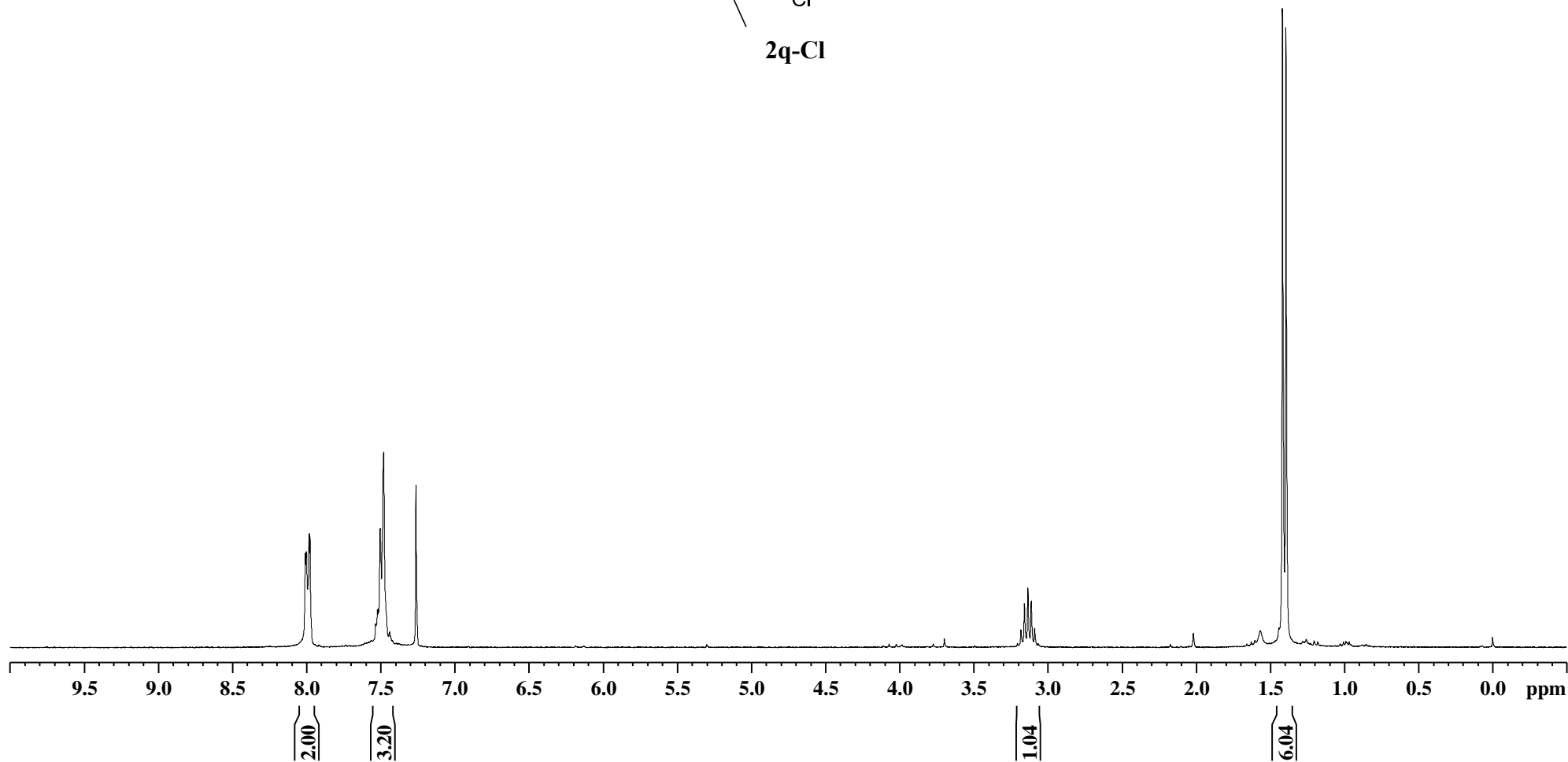
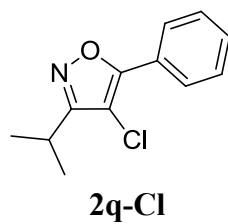


WK-II-11-sephadex-Fr22

8.007
8.000
7.981
7.975
7.532
7.521
7.515
7.502
7.481
7.478
7.438

3.204
3.180
3.157
3.134
3.111
3.088
3.065

1.416
1.393



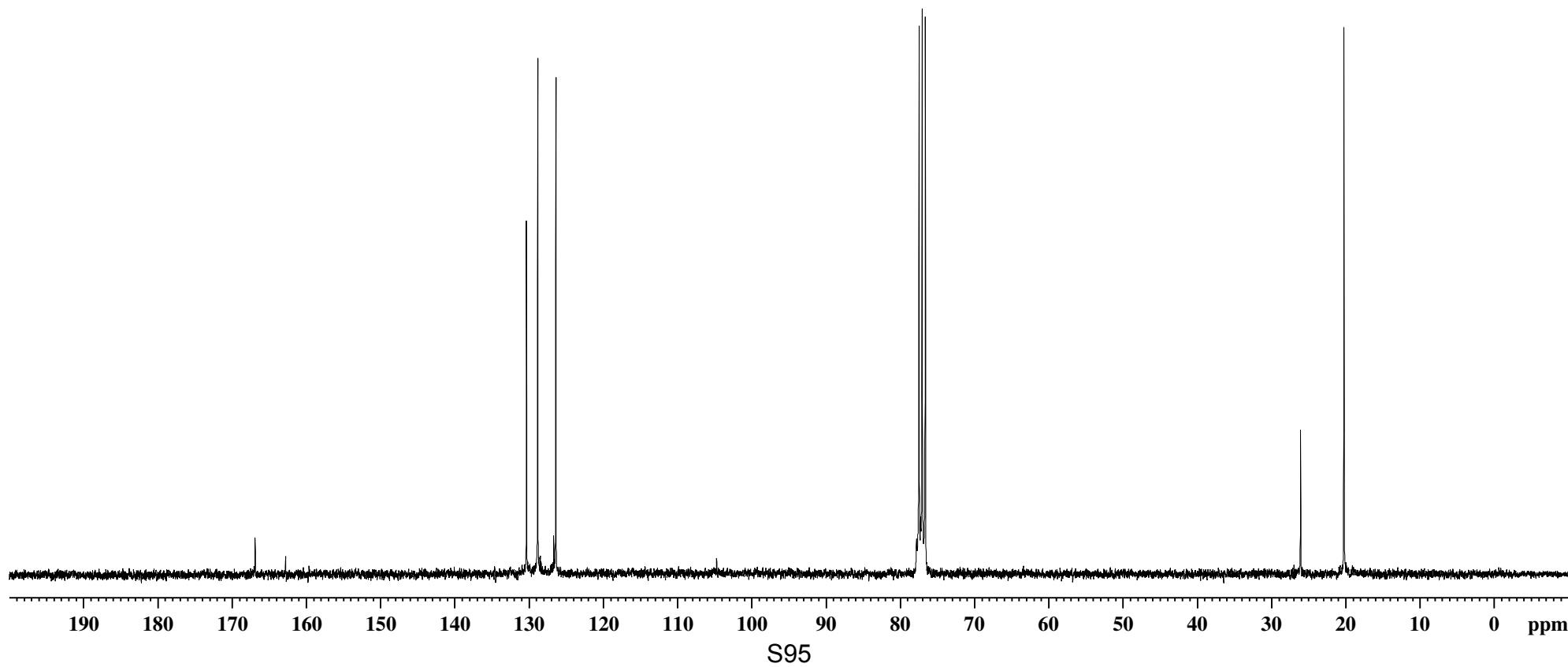
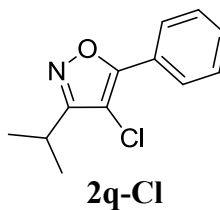
WK-II-11-sephadex-Fr22

— 166.860
— 162.765

130.304
128.800
126.640
126.353

— 104.691

— 26.021
— 20.192

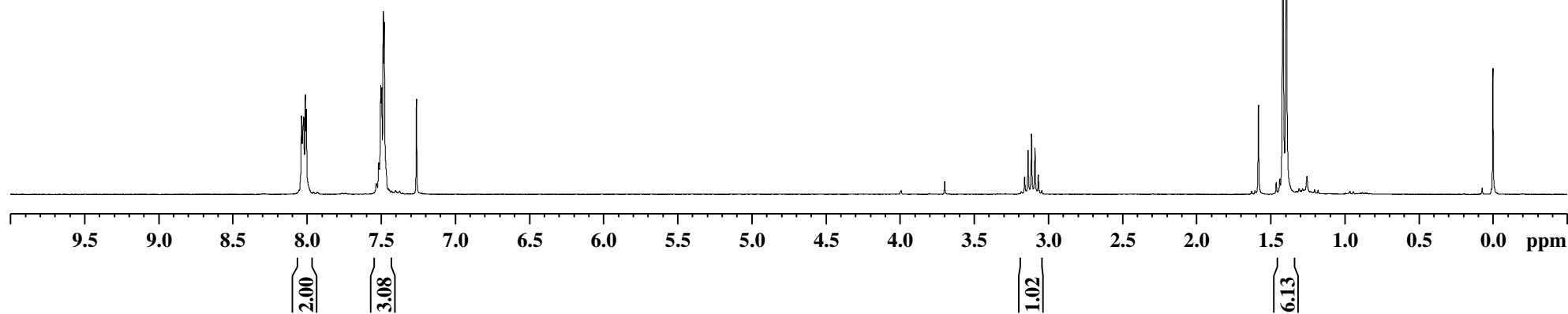
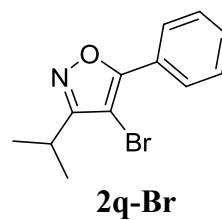


WK-II-131-Ptlc

8.035
8.021
8.010
8.003
7.515
7.501
7.495
7.484
7.478

3.181
3.158
3.135
3.112
3.089
3.066
3.042

1.417
1.394



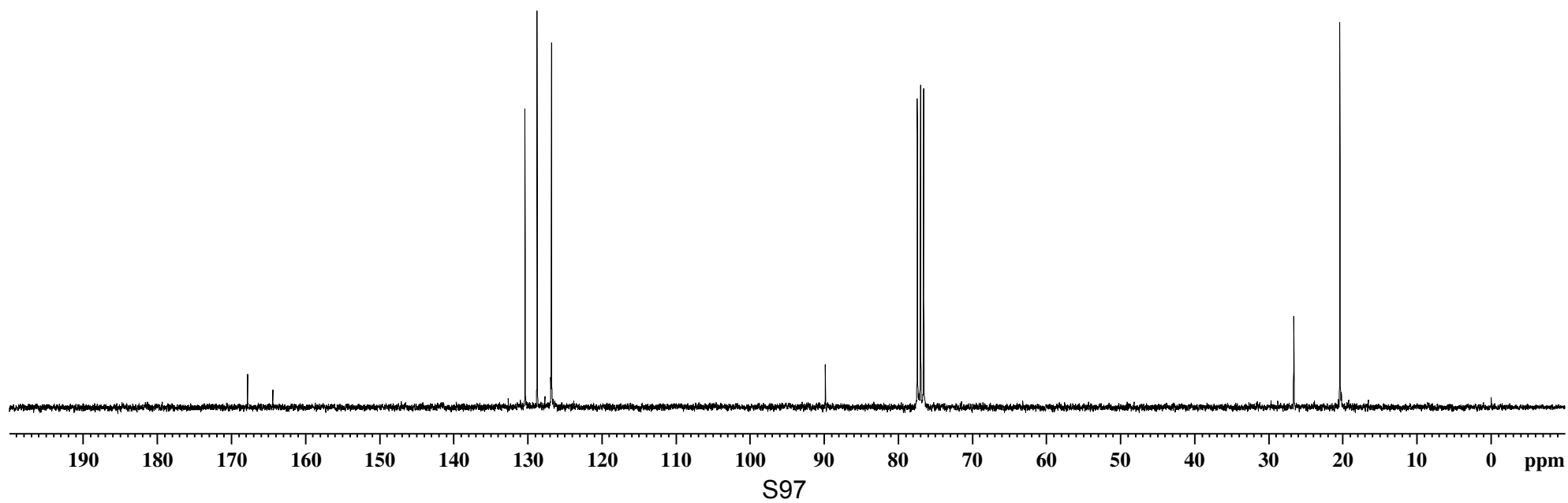
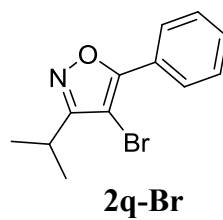
WK-II-131-PtIc

— 167.807
— 164.401

— 130.371
— 128.740
— 126.886
— 126.806

— 89.861

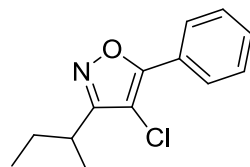
— 26.614
— 20.391



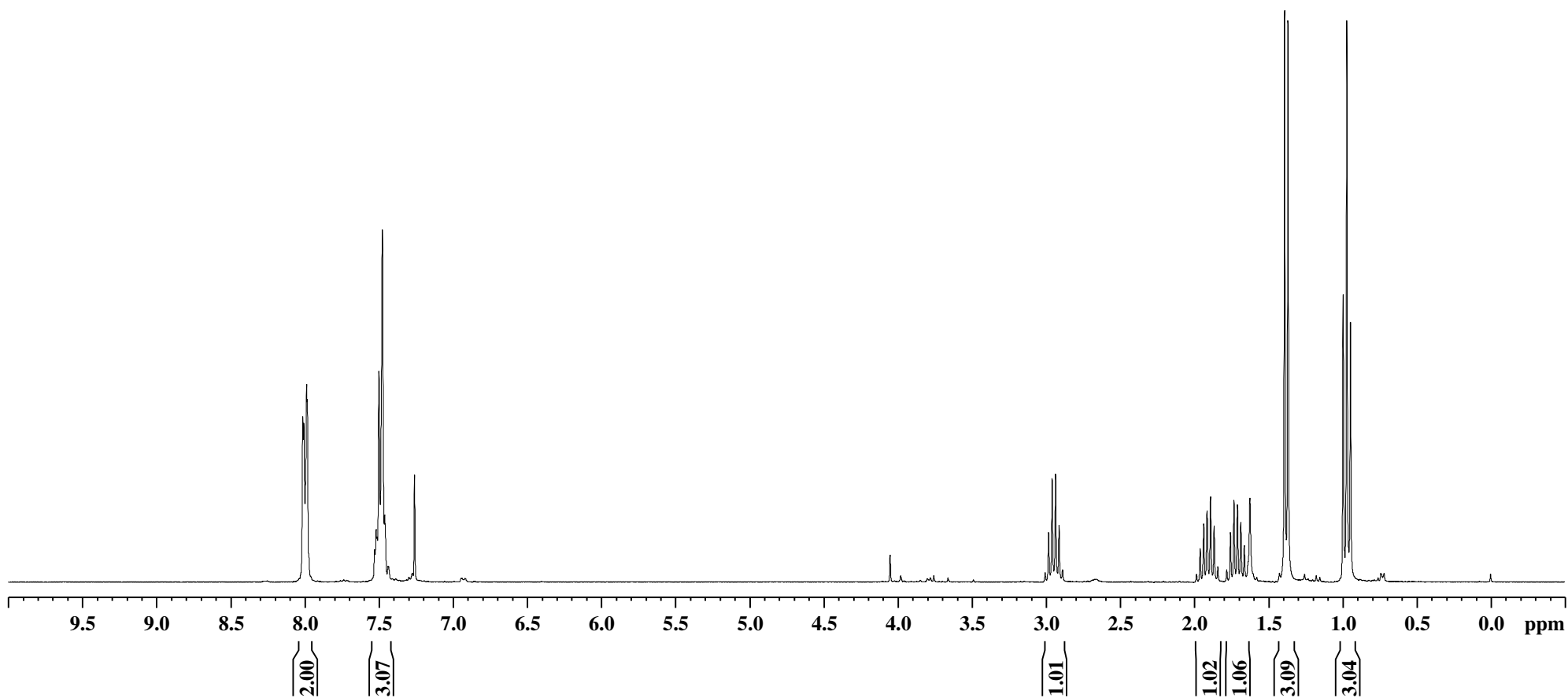
WK-II-24-Sephadex-Fr14-17-2

8.013
8.006
7.987
7.983
7.529
7.518
7.512
7.499
7.476
7.460
7.438

3.005
2.981
2.958
2.934
2.911
2.887
1.984
1.959
1.935
1.912
1.889
1.864
1.840
1.779
1.755
1.731
1.707
1.685
1.661
1.635
1.390
1.366
0.994
0.969
0.945



2r



WK-II-24-Sephadex-Fr14-17-2

— 165.991
— 162.685

— 130.283
— 128.784
— 126.650
— 126.345

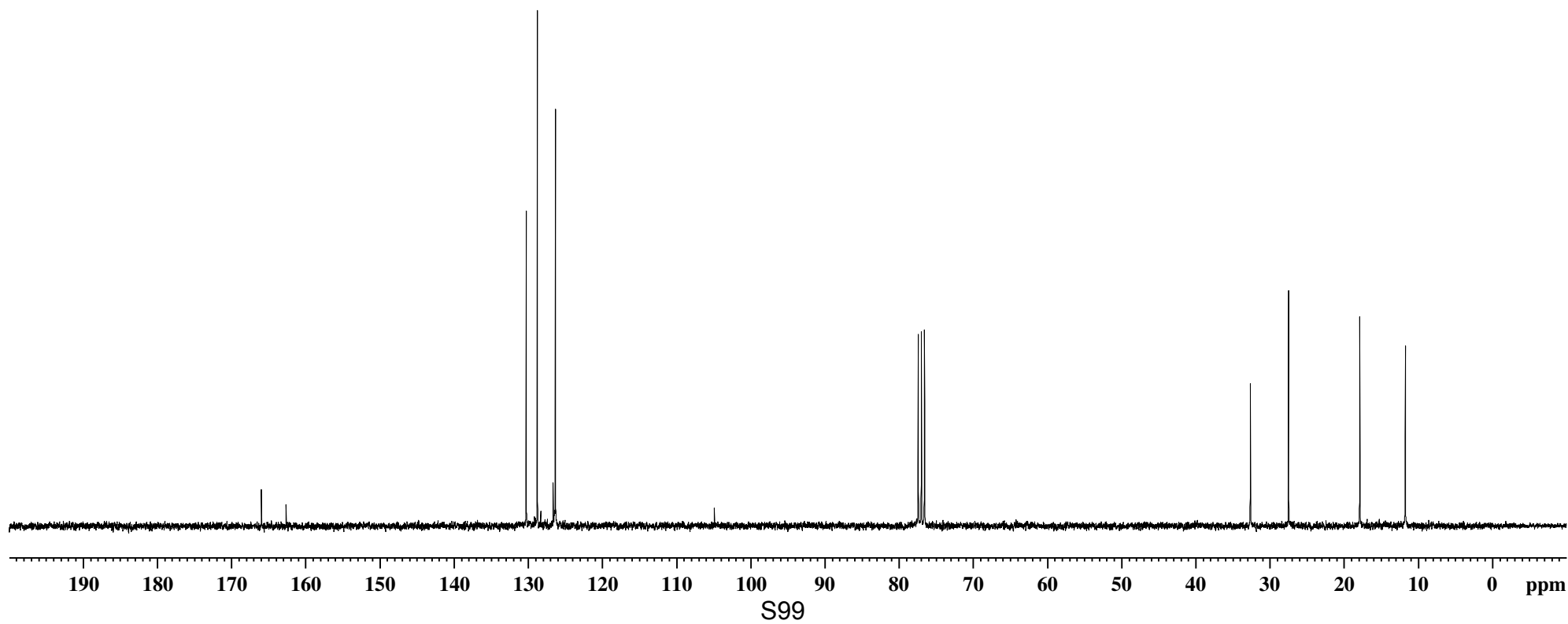
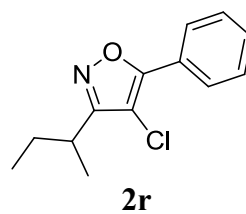
— 104.907

— 32.631

— 27.479

— 17.874

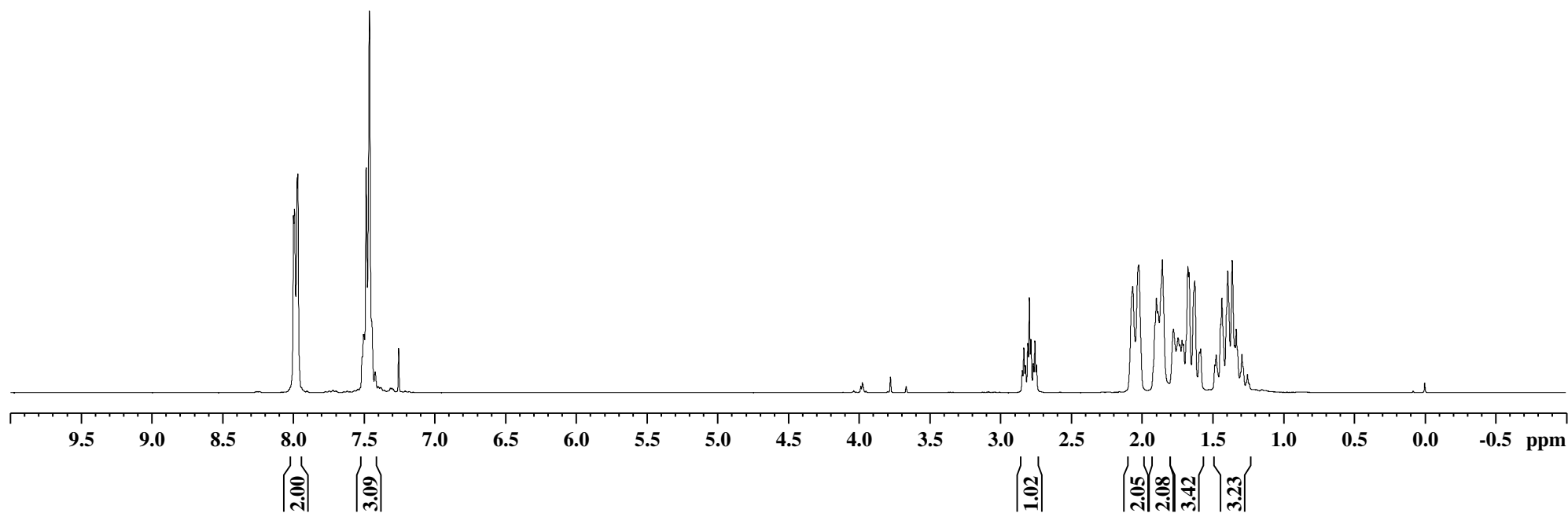
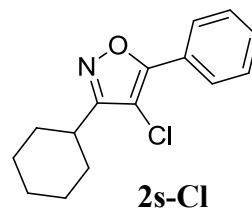
— 11.731



WK-II-23pure

7.997
7.991
7.971
7.966
7.514
7.509
7.503
7.498
7.484
7.461
7.446
7.420

2.845
2.834
2.822
2.806
2.795
2.783
2.767
2.756
2.744
2.064
2.021
1.896
1.885
1.854
1.777
1.743
1.729
1.715
1.705
1.674
1.666
1.625
1.592
1.584
1.484
1.474
1.443
1.433
1.392
1.360
1.343
1.332
1.292
1.252



S100

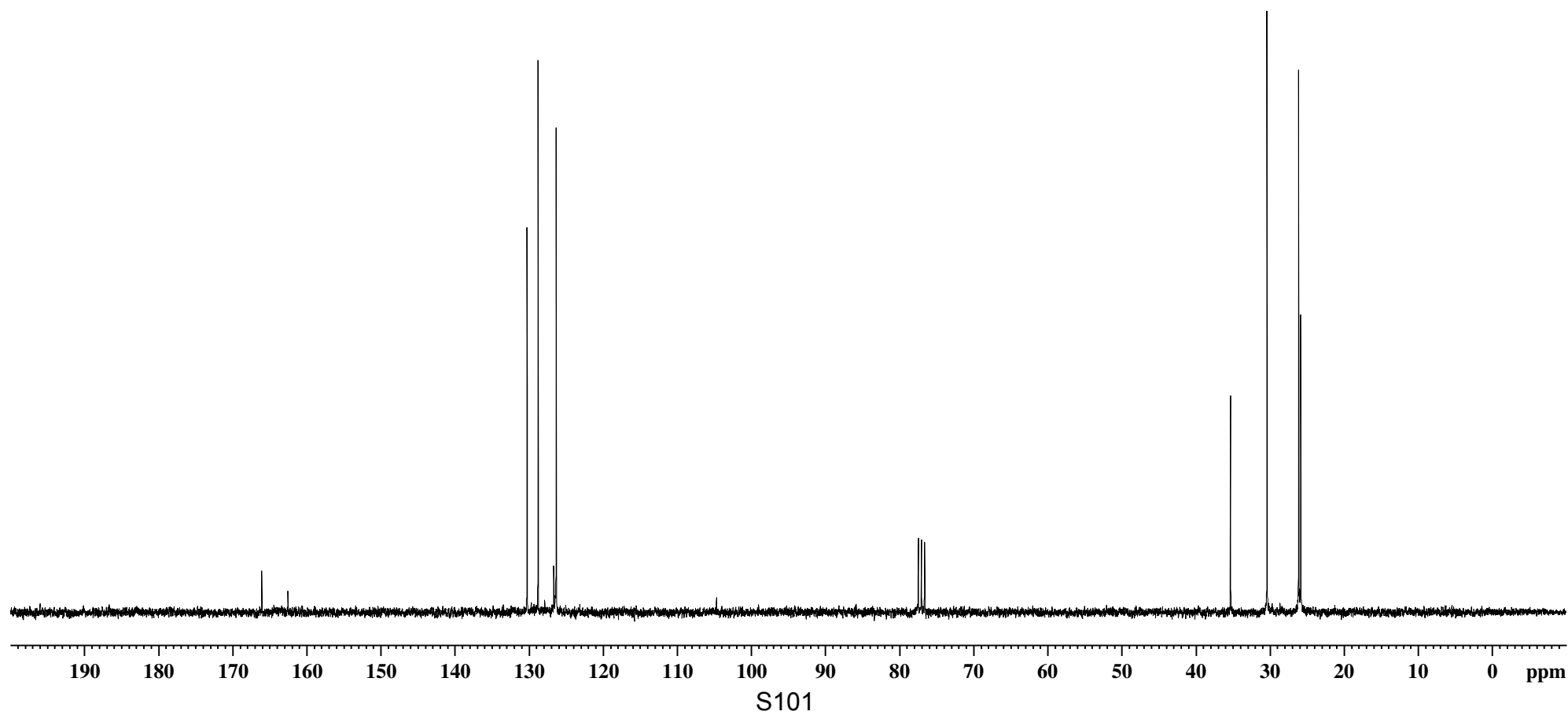
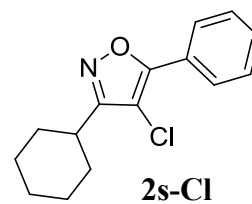
WK-II-23pure

— 166.049
— 162.522

— 130.232
— 128.749
— 126.638
— 126.311

— 104.683

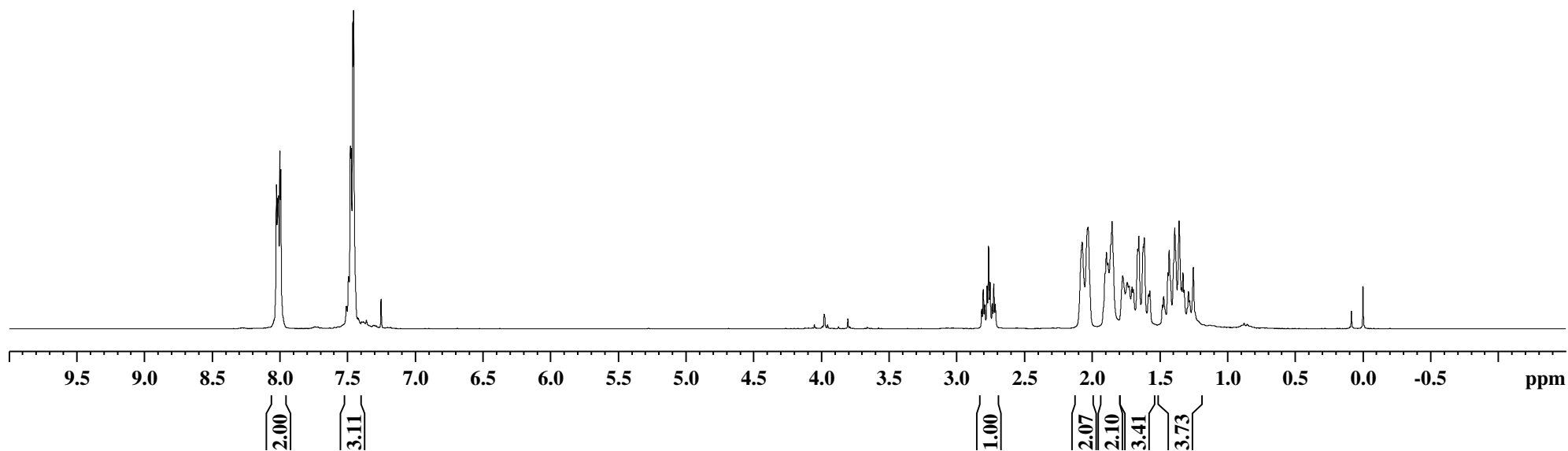
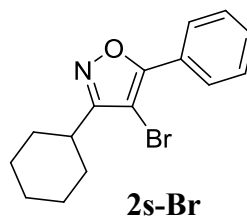
— 35.287
— 30.363
— 26.090
— 25.815



WK-II-134

8.026
8.017
8.012
8.000
7.994
7.509
7.494
7.490
7.479
7.473
7.462
7.456

2.816
2.804
2.793
2.777
2.765
2.754
2.738
2.726
2.715
2.074
2.030
1.895
1.884
1.863
1.853
1.775
1.741
1.729
1.706
1.696
1.664
1.656
1.623
1.615
1.583
1.574
1.482
1.472
1.441
1.431
1.390
1.358
1.340
1.330
1.320
1.289
1.280
1.253



S102

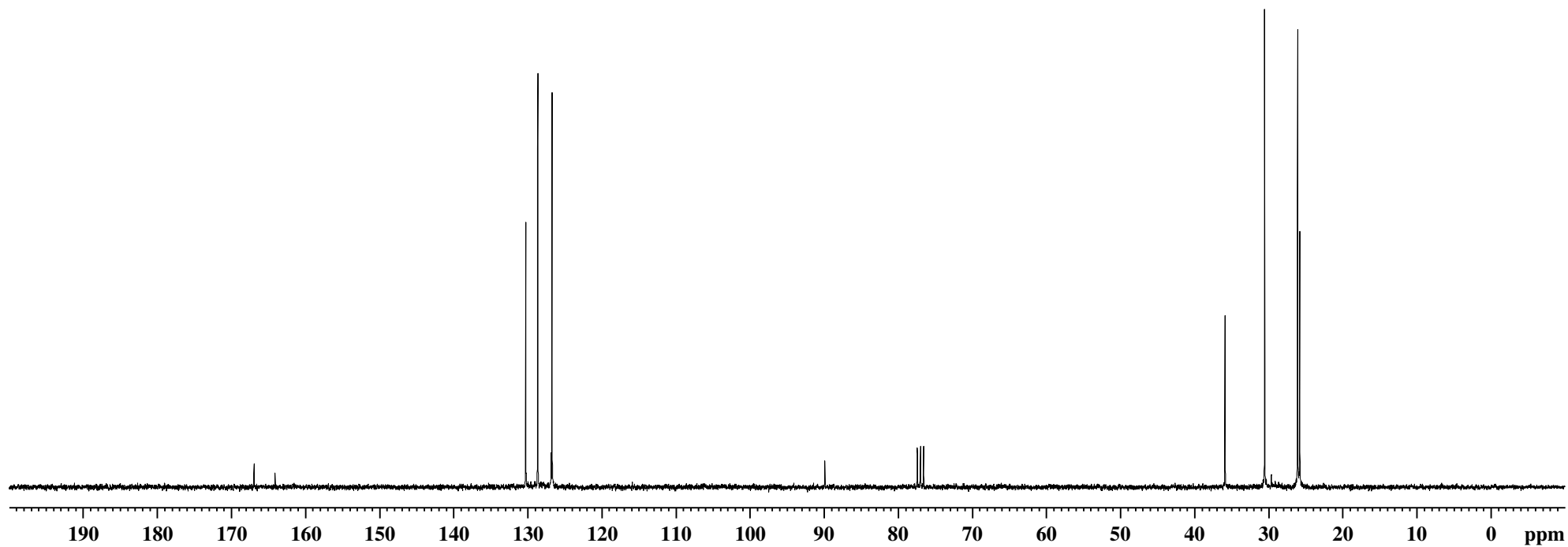
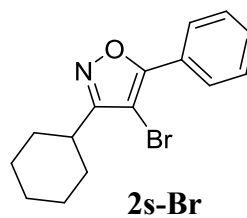
WK-II-134

166.956
164.107

130.280
128.666
126.849
126.729

89.914

35.902
30.559
26.108
25.812

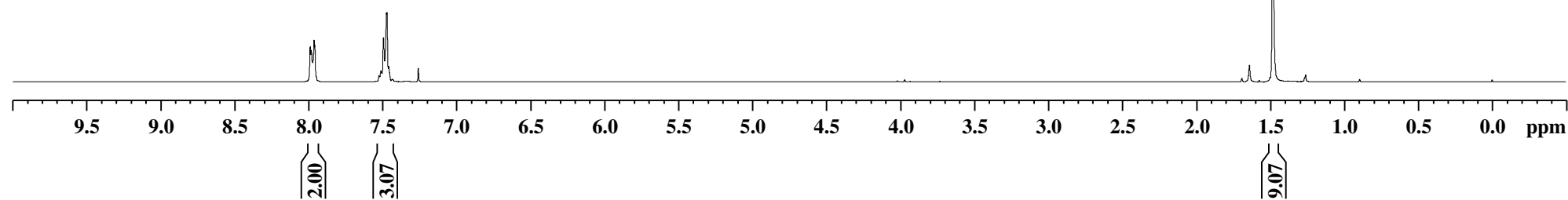
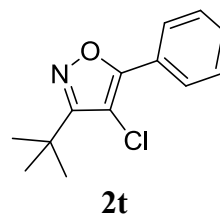


S103

WK-I-250-Fr17-19

7.989
7.981
7.962
7.957
7.524
7.511
7.506
7.494
7.473
7.470
7.458
7.435
7.431

1.481



S104

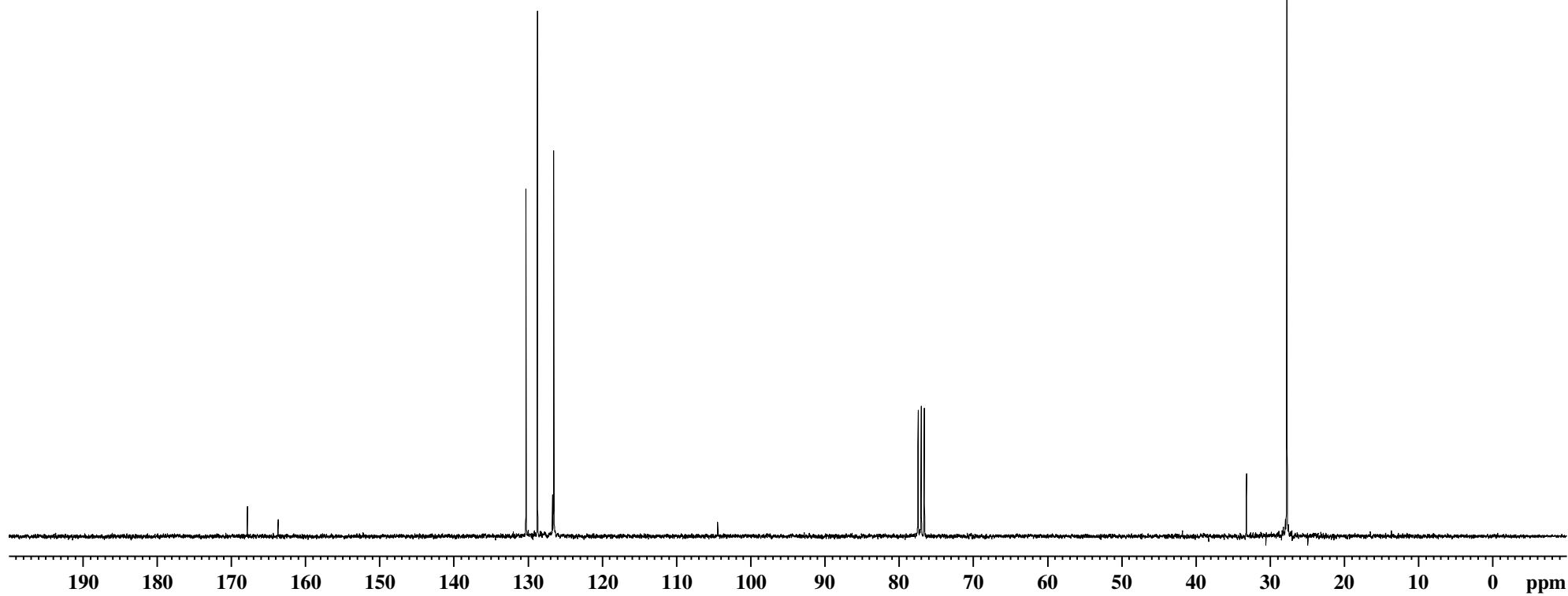
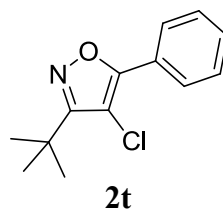
WK-I-250-Fr17-19

— 167.84
— 163.70

— 130.27
— 128.73
— 126.70
— 126.53

— 104.43

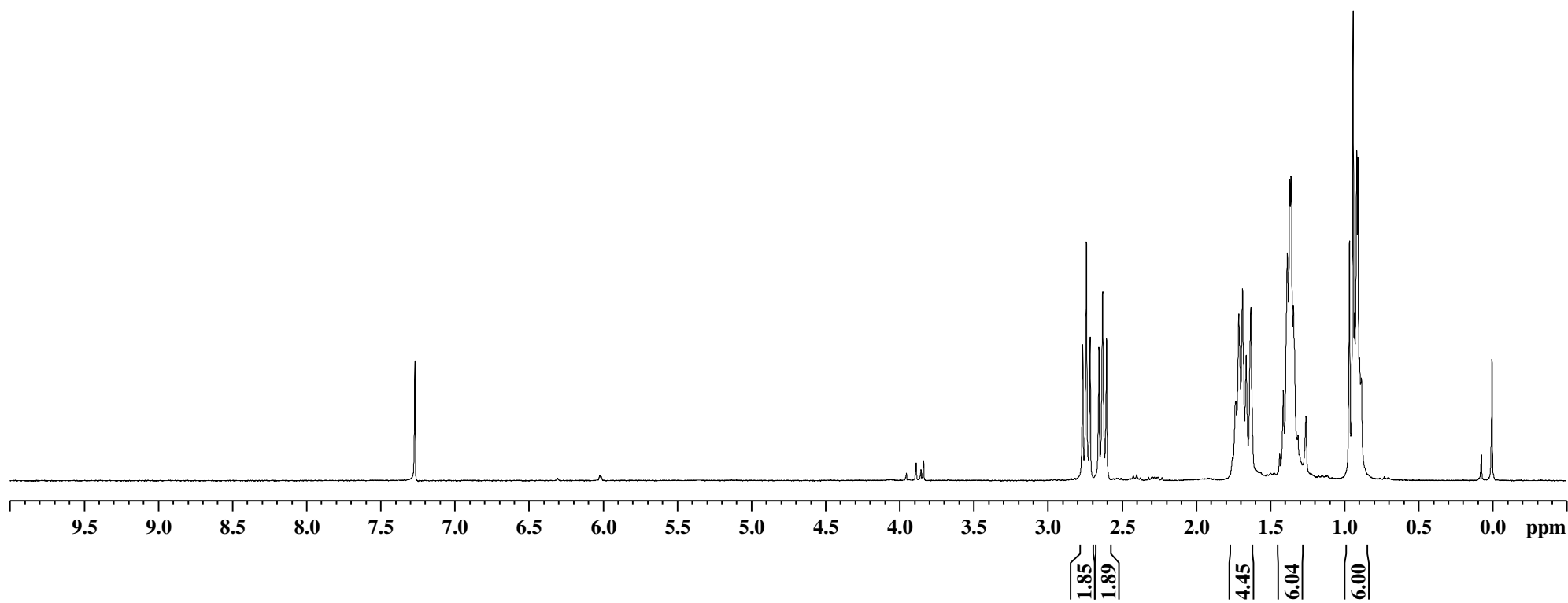
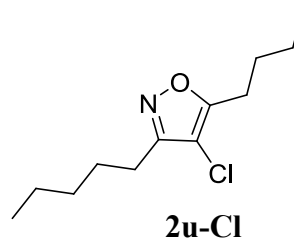
— 33.17
— 27.71



S105

WK-II-104-Top

2.761
2.736
2.711
2.652
2.627
2.600
1.732
1.728
1.708
1.683
1.658
1.432
1.408
1.381
1.364
1.356
1.340
1.309
1.299
0.961
0.937
0.927
0.912
0.904
0.894
0.881



S106

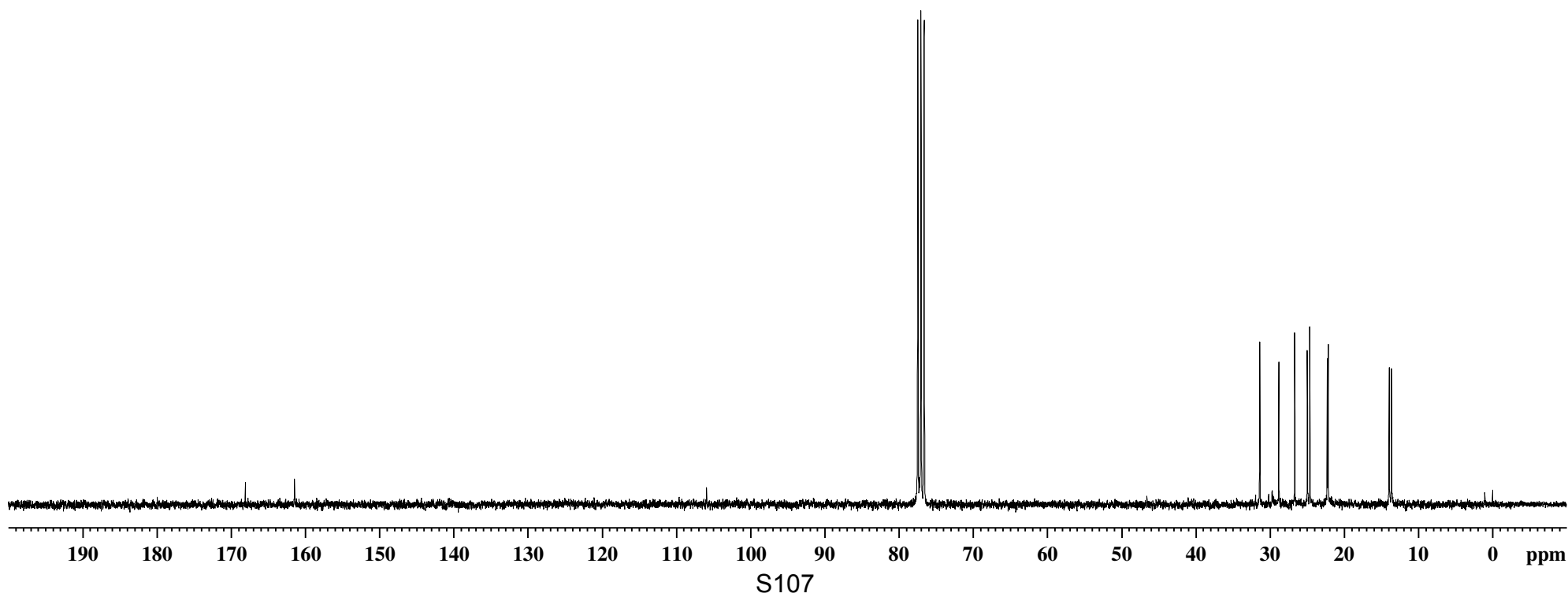
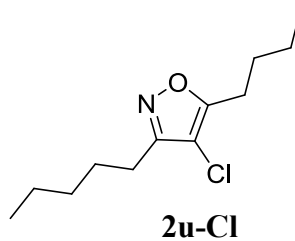
WK-II-104

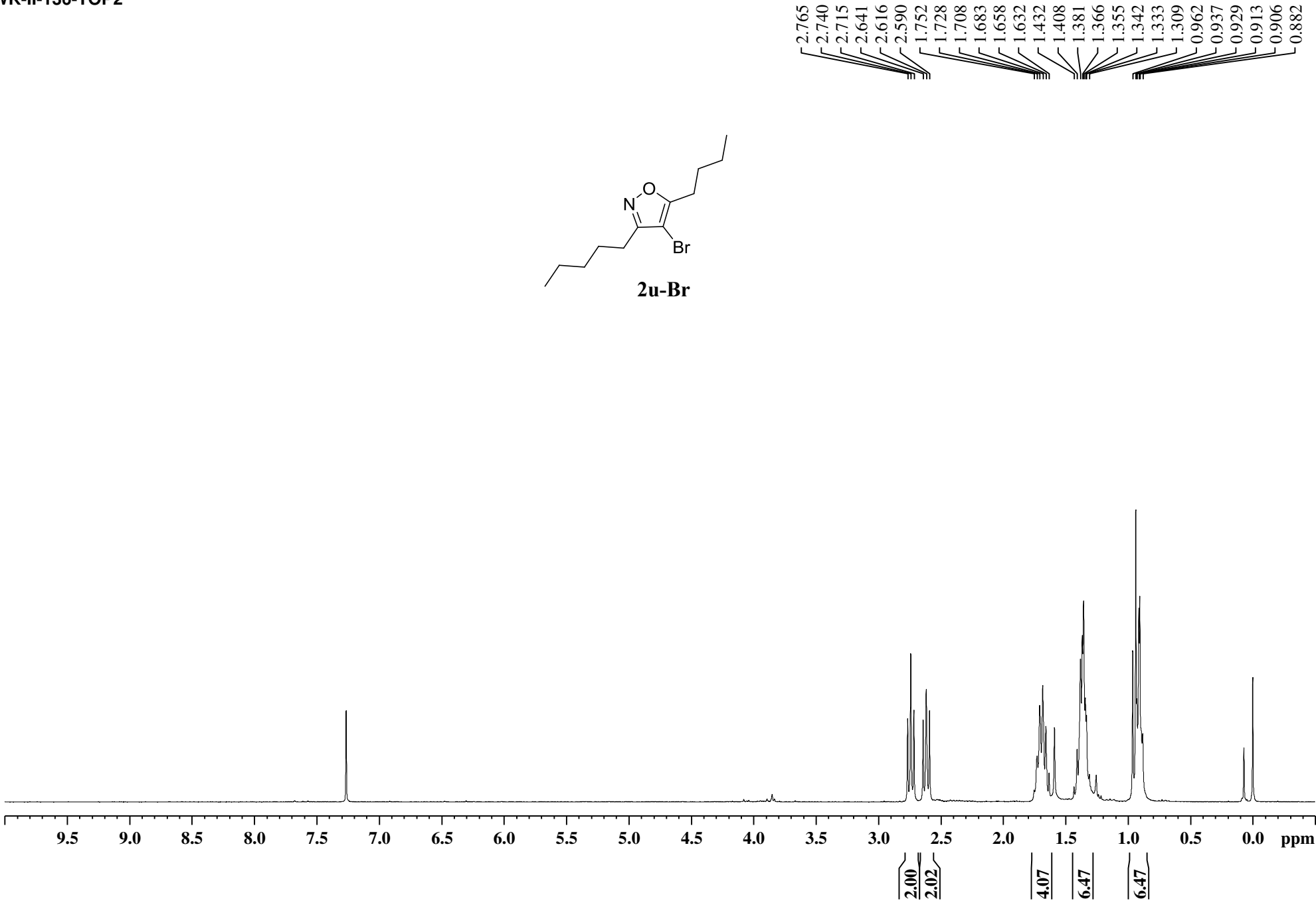
— 168.03

— 161.43

— 105.90

31.35
28.79
26.64
24.93
24.60
22.26
22.13
13.91
13.59





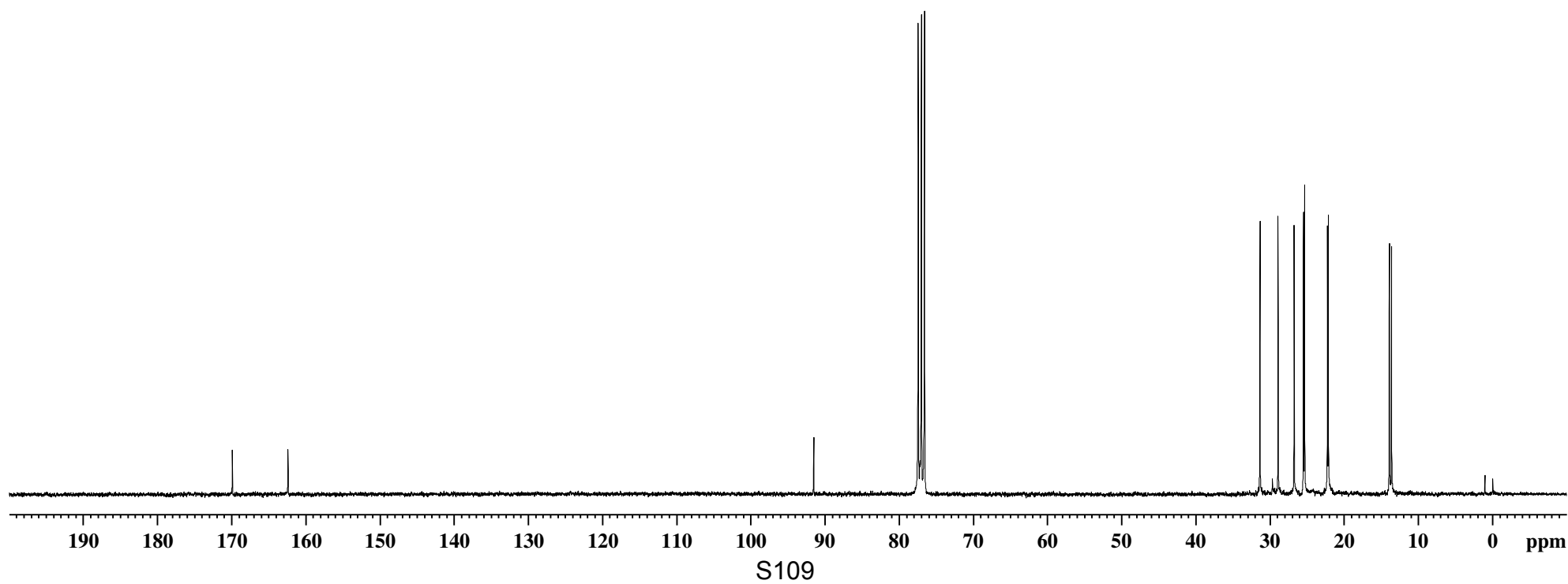
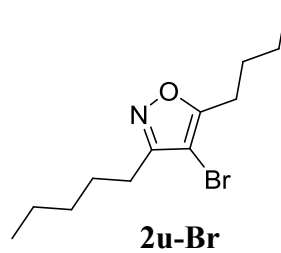
WK-II-136-TOP2

— 169.894

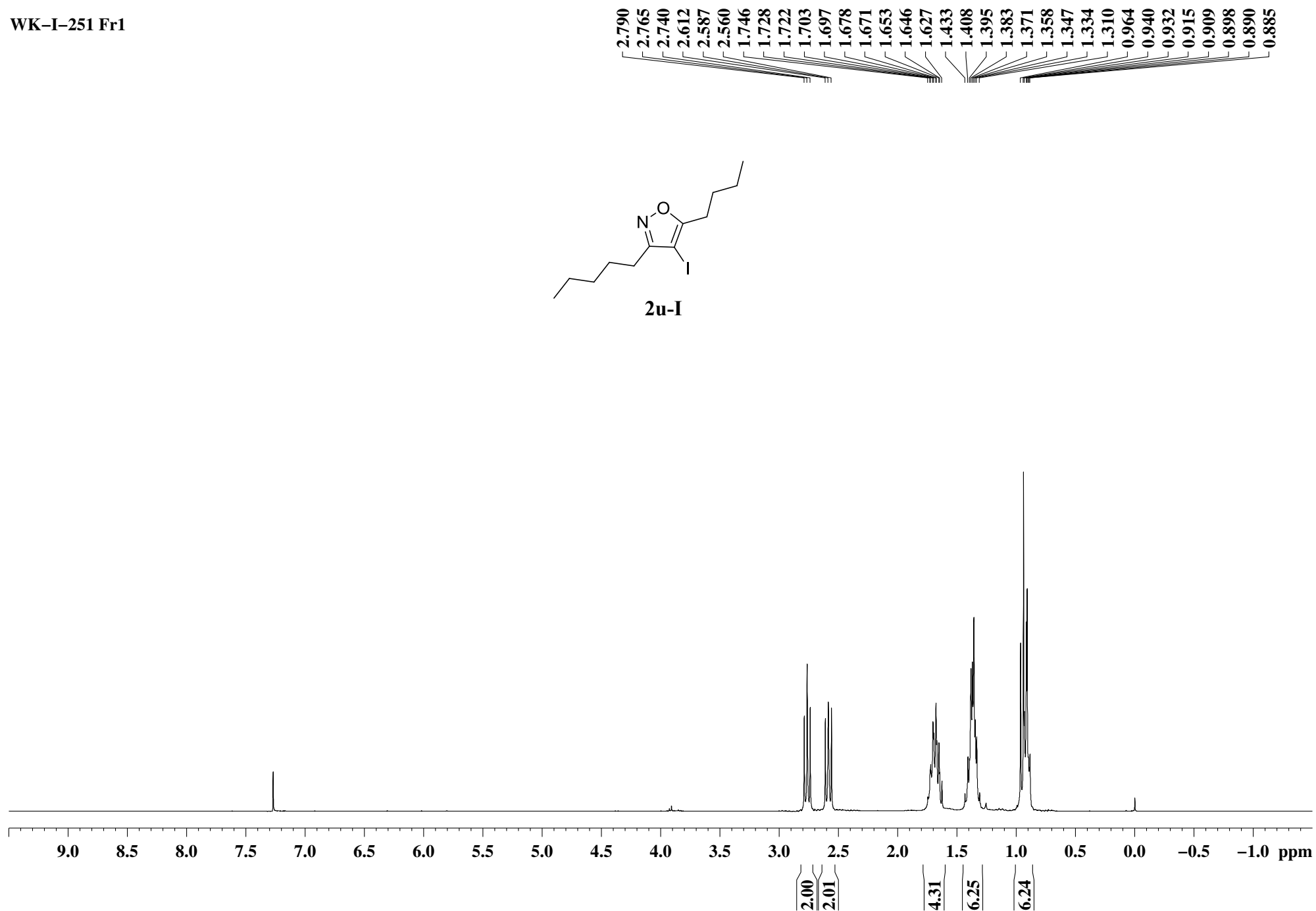
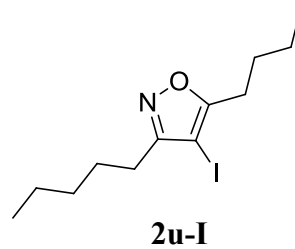
— 162.394

— 91.508

31.350
28.906
26.747
25.490
25.323
22.259
22.123
13.909
13.604



WK-I-251 Fr1



S110

WK-I-251 Fr1

— 173.277

— 164.340

— 58.874

31.346

29.223

26.980

26.609

26.477

22.255

22.122

13.901

13.617

