# Supplementary Material

# Direct organocatalytic Wittig/Hetero-Diels-Alder reactions in one-pot: synthesis of highly-substituted tetrahydropyranones

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**Dedicated to Prof. Dr. J. S. Yadav in appreciation of his outstanding contributions to synthetic organic chemistry**

**Contents:**

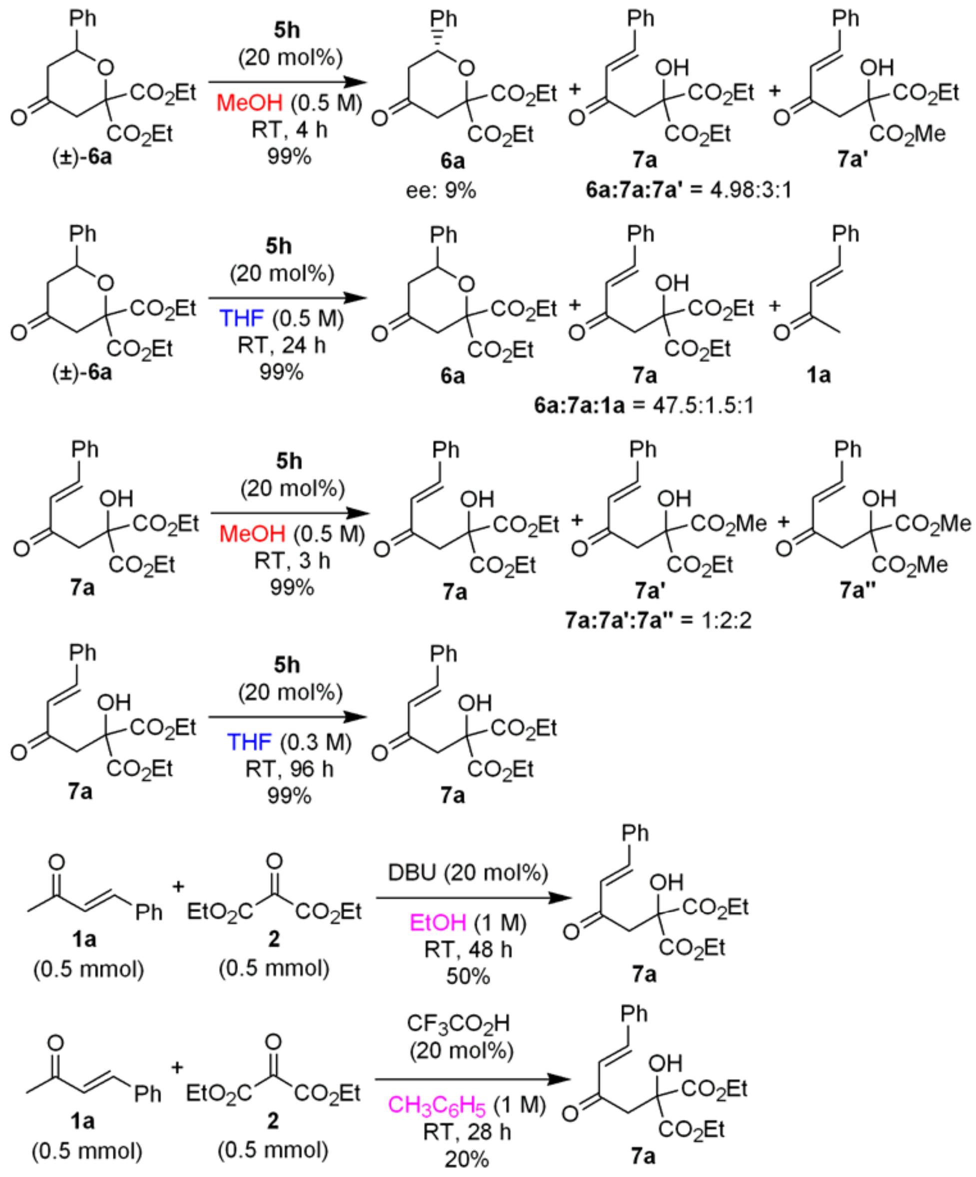
**General Methods:** The $^1$H NMR and $^{13}$C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta$ = 0) for $^1$H NMR and relative to the central $CDCl_3$ resonance ($\delta$ = 77.0) for $^{13}$C NMR. *In the $^{13}$C NMR spectra, the nature of the carbons (C, CH, $CH_2$ or $CH_3$) were determined by recording the DEPT-135 and DEPT-90 experiments, and is given in parentheses.* The coupling constants *J* are given in Hz. Column chromatography was performed using Acme's silica gel (particle size 0.063-0.200 mm). High-resolution mass spectra were recorded on micromass ESI-TOF MS. IR spectra were recorded on JASCO FT/IR-5300. The enantiomeric excess (*ee*) of the products were determined by HPLC using Daciel chiralcel OD-H or Daciel chiralpak AS or Daciel chiralpak AD columns with *i*-PrOH/hexane as eluent. HPLC was carried out using a Hitachi organizer consisting of a D-2500 Chromato-Integrator, a L-4000 UV-Detector, and a L-6200A Intelligent Pump. For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. $H_2SO_4$ (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating and/or by exposure to iodine vapour.

**Materials:** All solvents and commercially available chemicals were used as received.

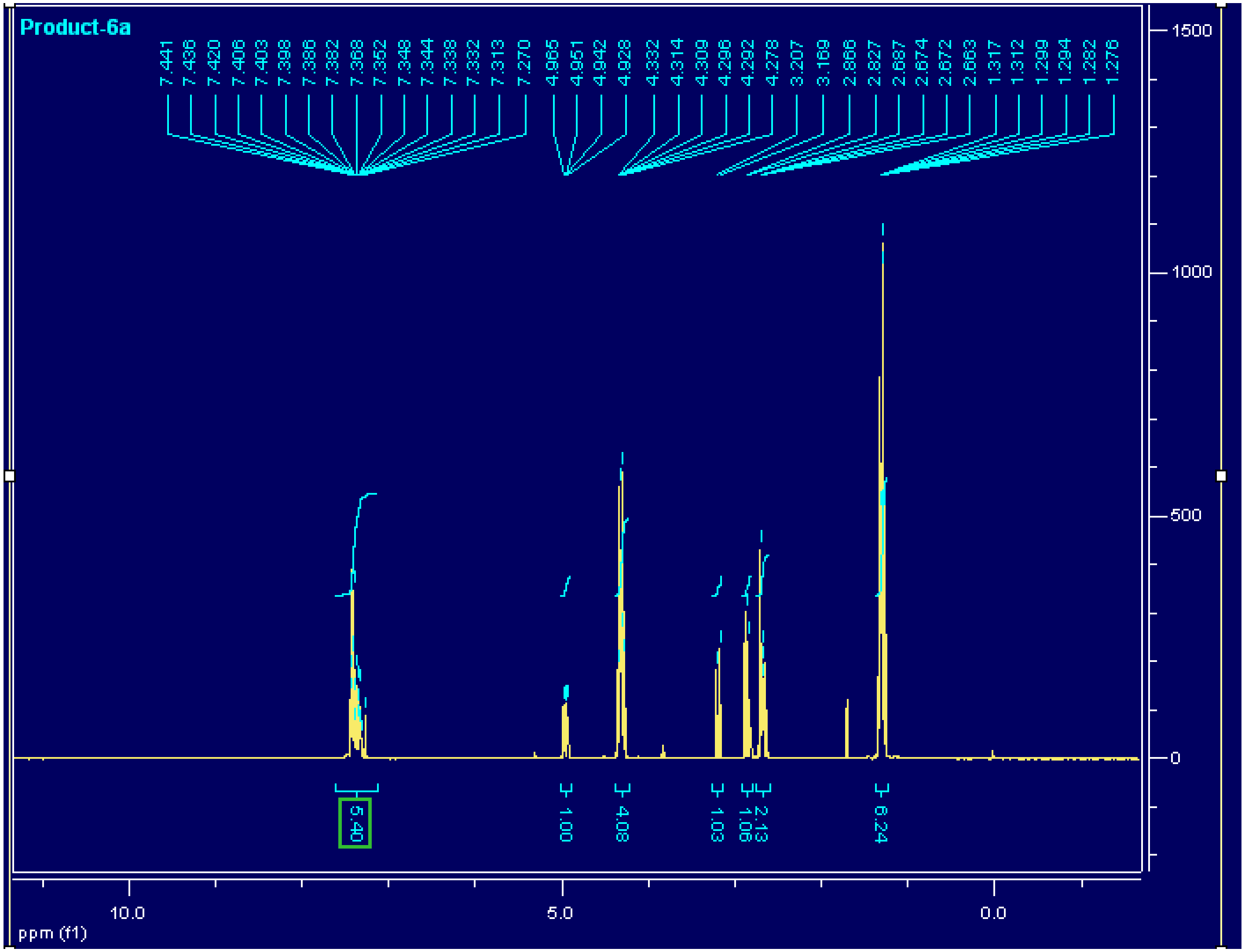
**General Experimental Procedures for the Asymmetric Hetero-Diels-Alder Reactions:**

**Chiral Amine or Amino Acid-Catalyzed Asymmetric Hetero-Diels-Alder Reactions:** In an ordinary glass vial equipped with a magnetic stirring bar, to 1.0 mmol of the enone **1** and 1mL of solvent, catalyst amine **5** (20 mol%) was added and the reaction mixture was stirred at ambient temperature for 5 minutes. To the reaction mixture 0.5 mmol of diethylketomalonate **2** was added and stirred at ambient temperature for the time indicated in Tables 1, 2, 3 and 4. The crude reaction mixture was directly loaded on silica gel column with or without aqueous work-up and pure hetero-Diels-Alder **6** and aldol **7** products were obtained by flash column chromatography (silica gel, mixture of hexane/ethyl acetate).

**(*S*)-1-(2-Pyrrolidinylmethyl)pyrrolidine 5h Catalyzed Wittig/Hetero-Diels-Alder Reactions in One-Pot:** In an ordinary glass vial equipped with a magnetic stirring bar, to 0.6 mmol of the phosphorane **3** and 1mL of EtOH, 0.6 mmol of the aldehyde **4** was added and the reaction mixture was stirred at 70° C for the time indicated in the Table 5. To the reaction mixture catalyst amine **5h** (20 mol%) was added and the reaction mixture was stirred at ambient temperature for 5 minutes. Then 0.3 mmol of diethylketomalonate **2** was added and stirred at ambient temperature for the time indicated in Table 5. The crude reaction mixture was directly loaded on silica gel column with or without aqueous work-up and pure tandem Wittig/hetero-Diels-Alder **6** and Wittig/aldol **7** products were obtained by flash column chromatography (silica gel, mixture of hexane/ethyl acetate).



**Scheme 3.** Effect of acid and amines on enone **1a**, HDA **6a** and aldol product **7a** at RT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7.368
7.352
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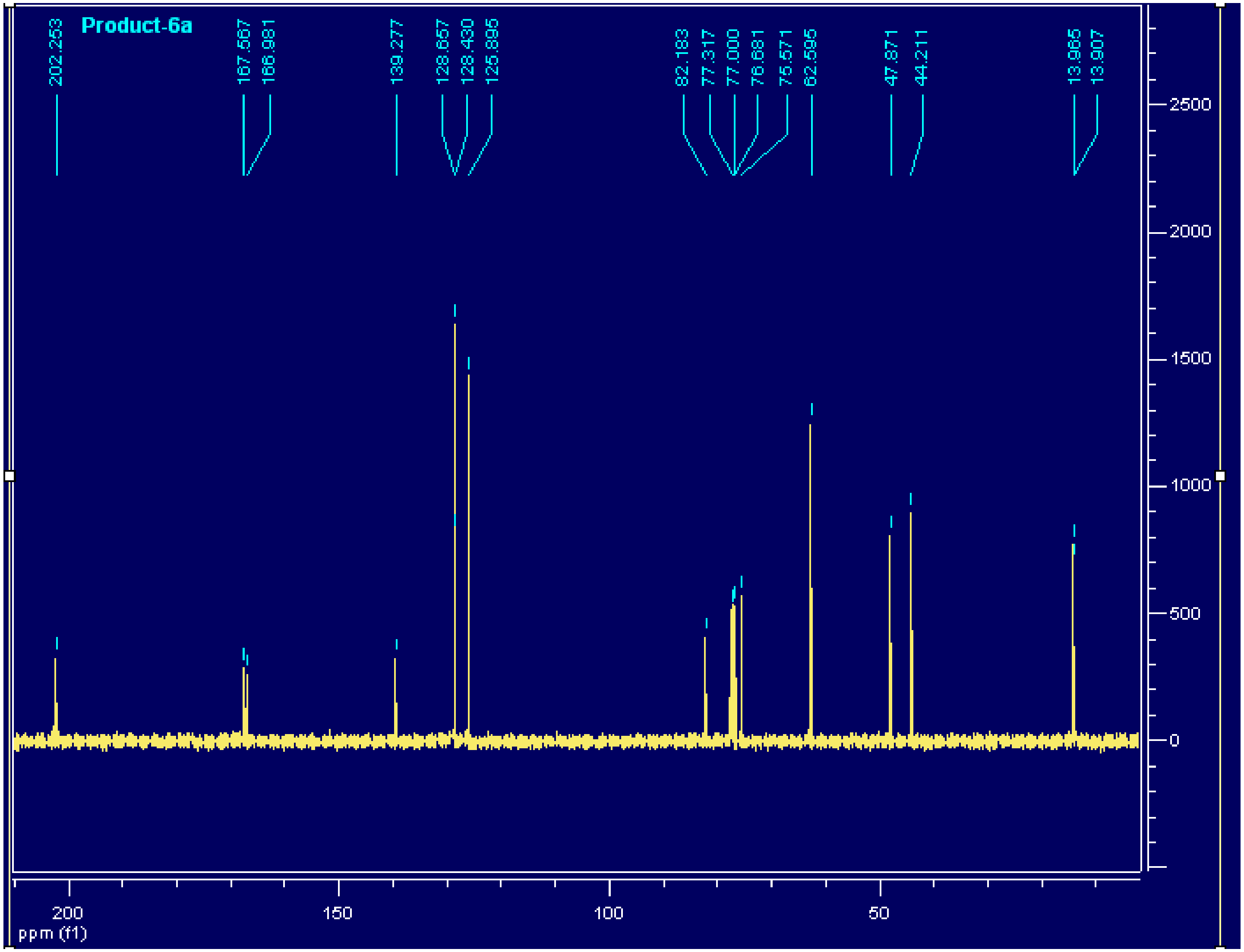
7.344
7.338
7.332
7.313
7.270
4.965
4.951
4.942
4.928
4.332
4.314
4.309
4.296
4.292
4.278
3.207
3.169
2.866
2.827
2.687
2.674
2.672
2.663
1.317
1.312
1.299
1.294
1.282
1.276
1500
1000
500
0
5.40
1.00
4.08
1.03
1.06
2.13
6.24
10.0
5.0
0.0
ppm (f1)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128.657
128.430
125.895
82.183
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77.000
76.681
75.571
62.595
47.871
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13.965
13.907
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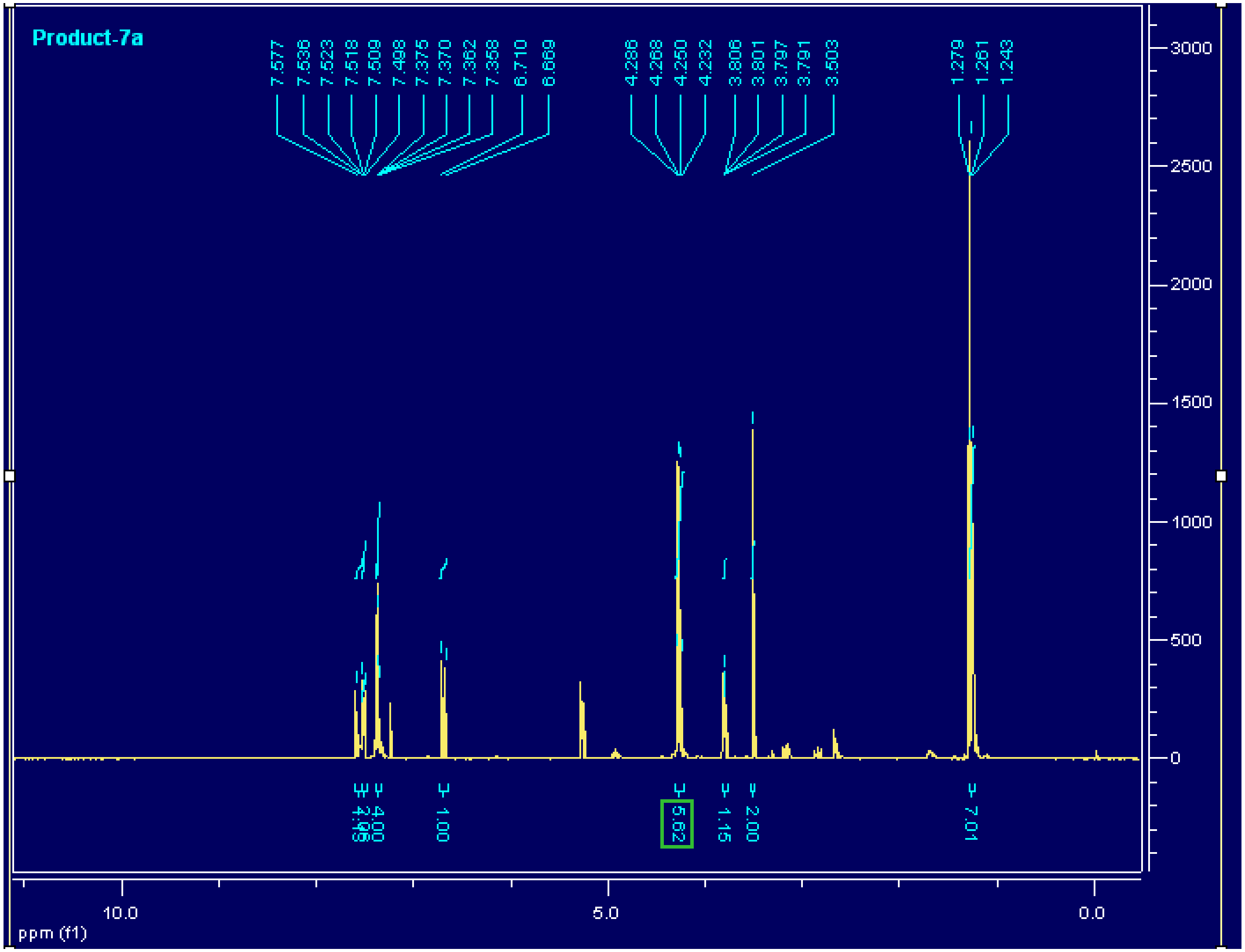
2000
1500
1000
500
0
200
150
100
50
ppm (f1)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7.509
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7.375
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7.362
7.358
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6.669
4.286
4.268
4.250
4.232
3.806
3.801
3.797
3.791
3.503
1.279
1.261
1.243
3000
2500
2000
1500
1000
500
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10.0
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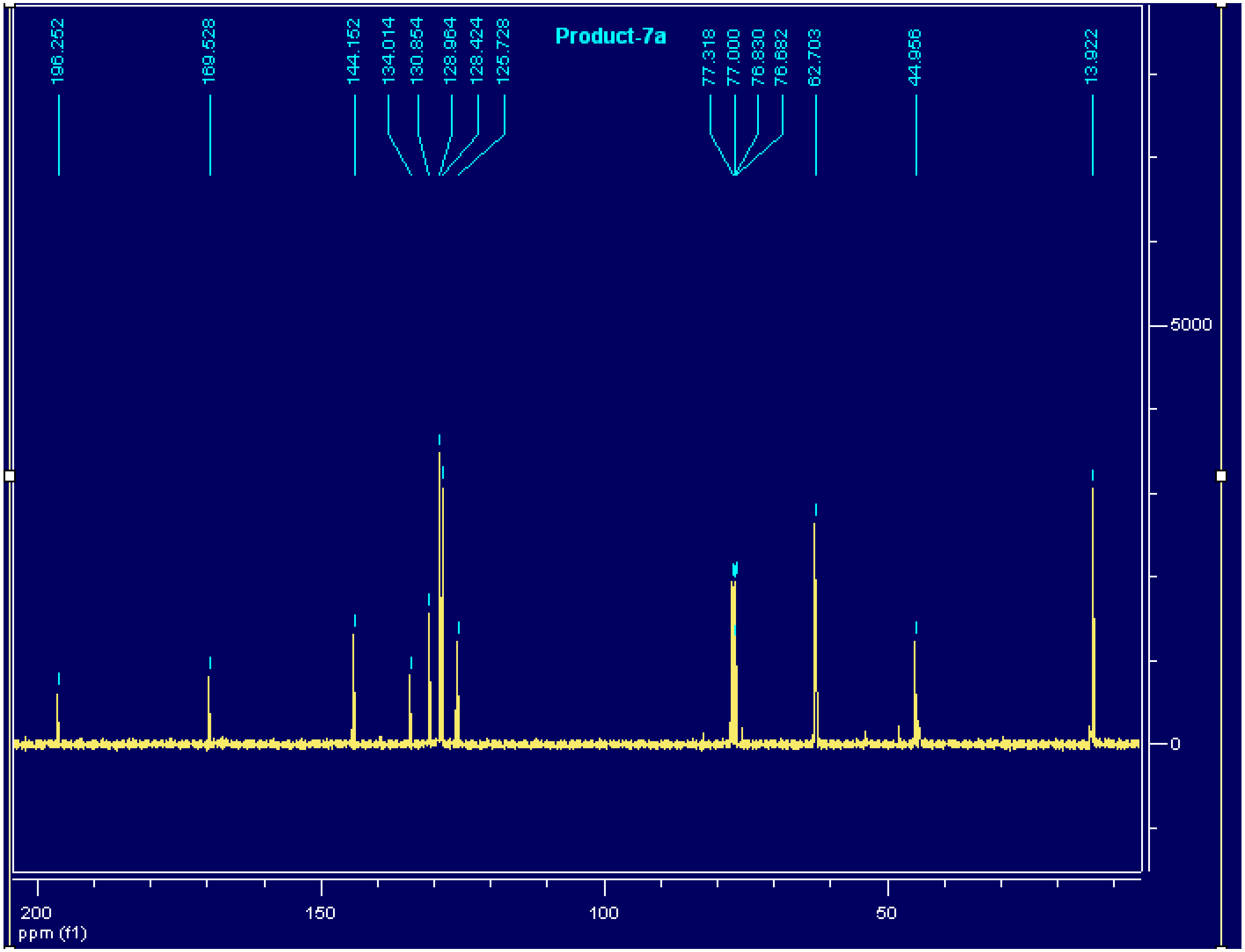
ppm (f1)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134.014
130.854
128.964
128.424
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76.682
62.703
44.956
13.922
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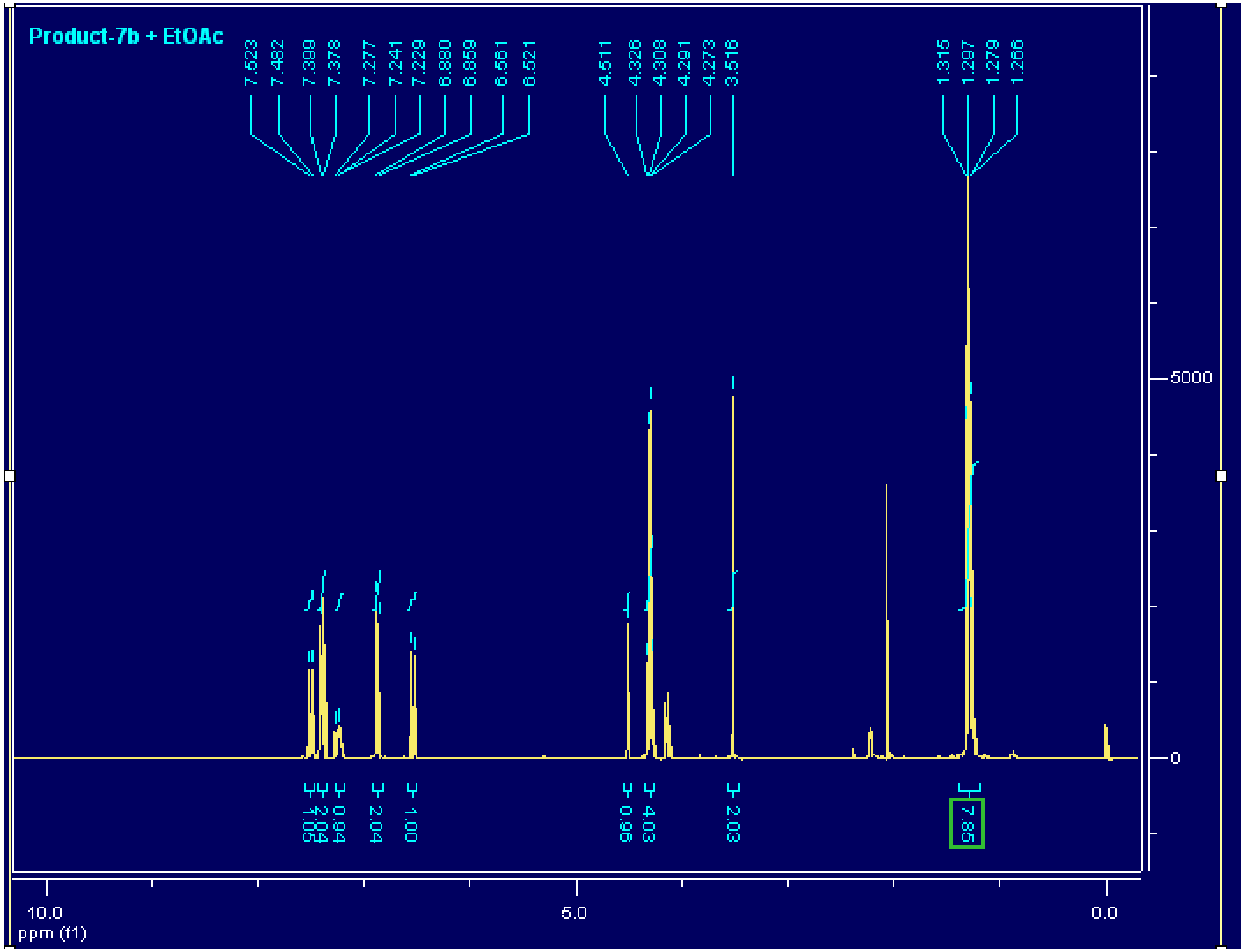
0
200
150
100
50
ppm (f1)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7.277
7.241
7.229
6.880
6.859
6.561
6.521
4.511
4.326
4.308
4.291
4.273
3.516
1.315
1.297
1.279
1.266
5000
0
1.05
2.04
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2.04
1.00
0.96
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2.03
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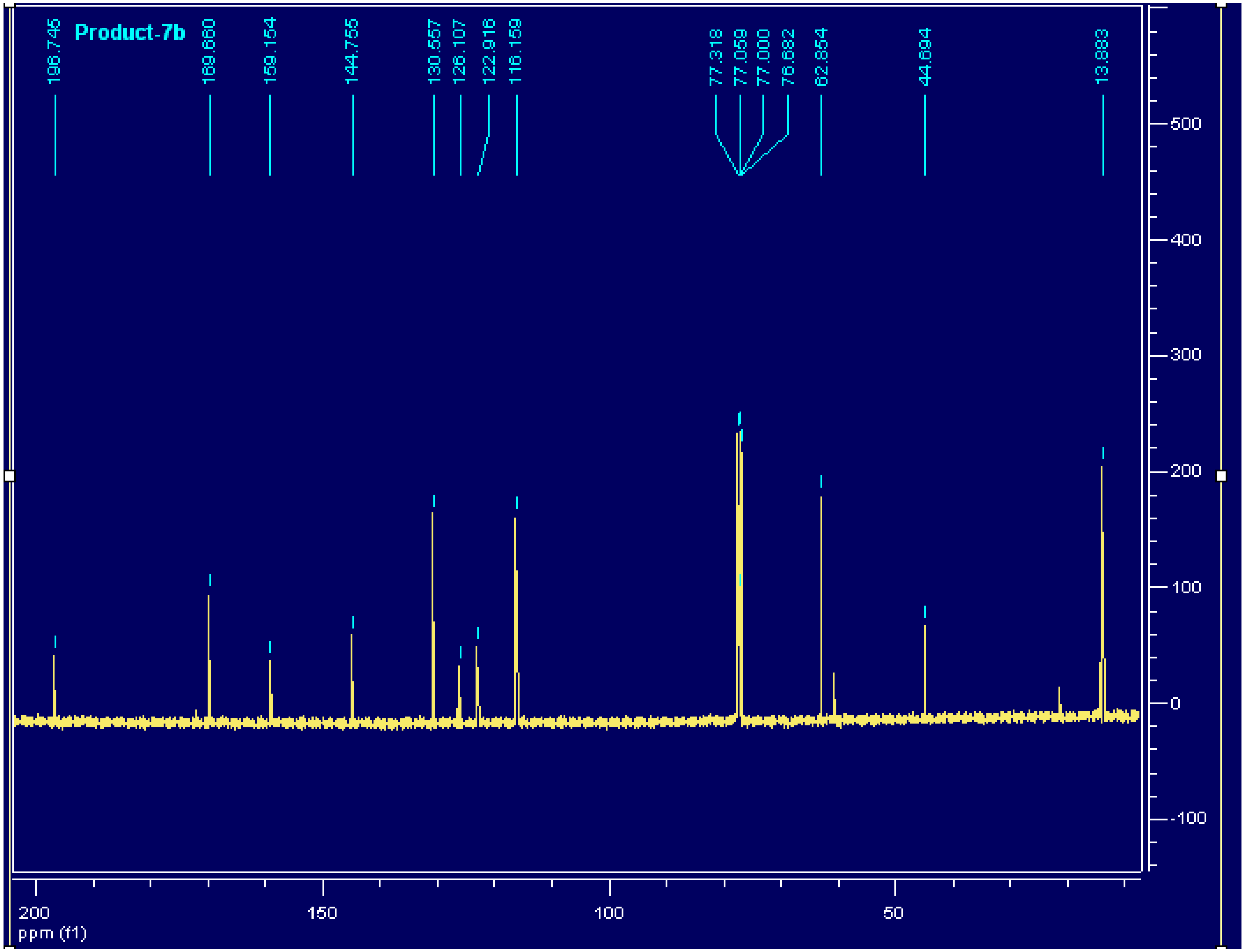
ppm (f1)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122.916
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77.318
77.059
77.000
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13.883
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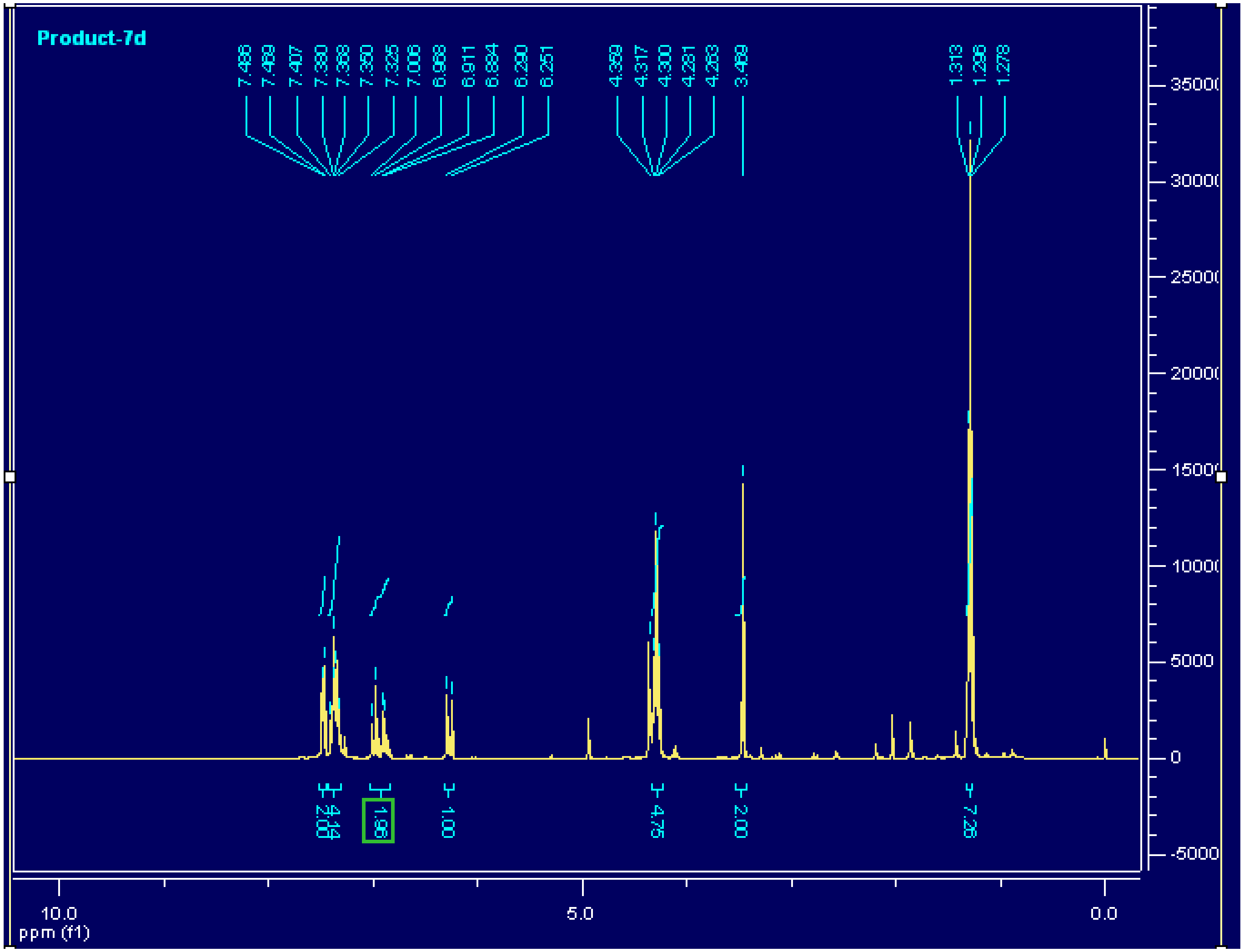
300
200
100
0
-100
200
150
100
50
ppm (f1)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7.350
7.325
7.006
6.988
6.911
6.894
6.280
6.251
4.359
4.317
4.300
4.281
4.263
3.469
1.313
1.296
1.278
2.06
4.14
1.96
1.00
4.75
2.00
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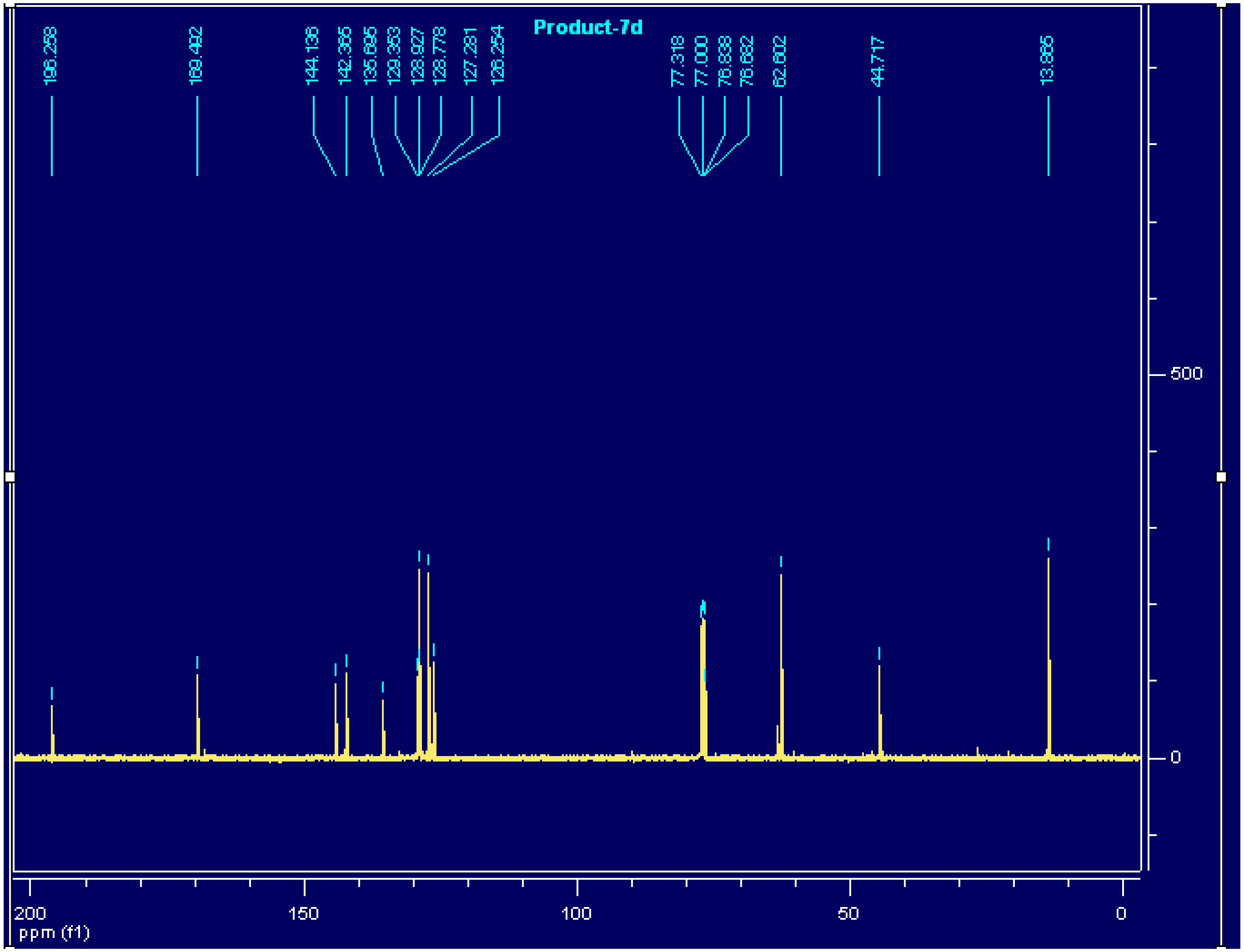
0.0
ppm (f1)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126.254
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76.682
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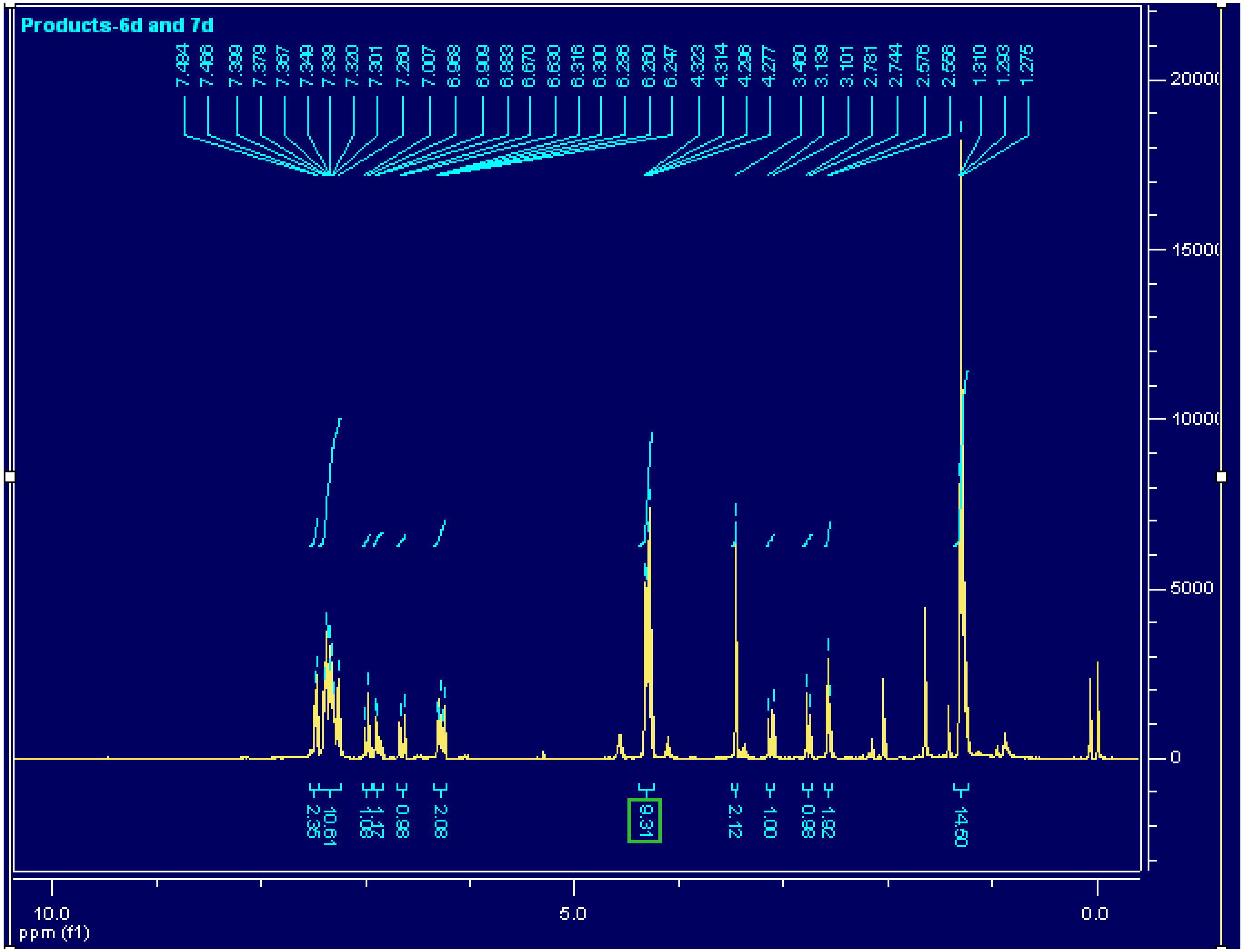
200
150
100
50
0
ppm (f1)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7.367
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7.339
7.320
7.301
7.280
7.007
6.988
6.909
6.883
6.670
6.630
6.316
6.300
6.286
6.260
6.247
4.323
4.314
4.296
4.277
3.480
3.139
3.101
2.781
2.744
2.576
2.566
1.310
1.293
1.275
20000
15000
10000
5000
0
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10.61
1.08
1.13
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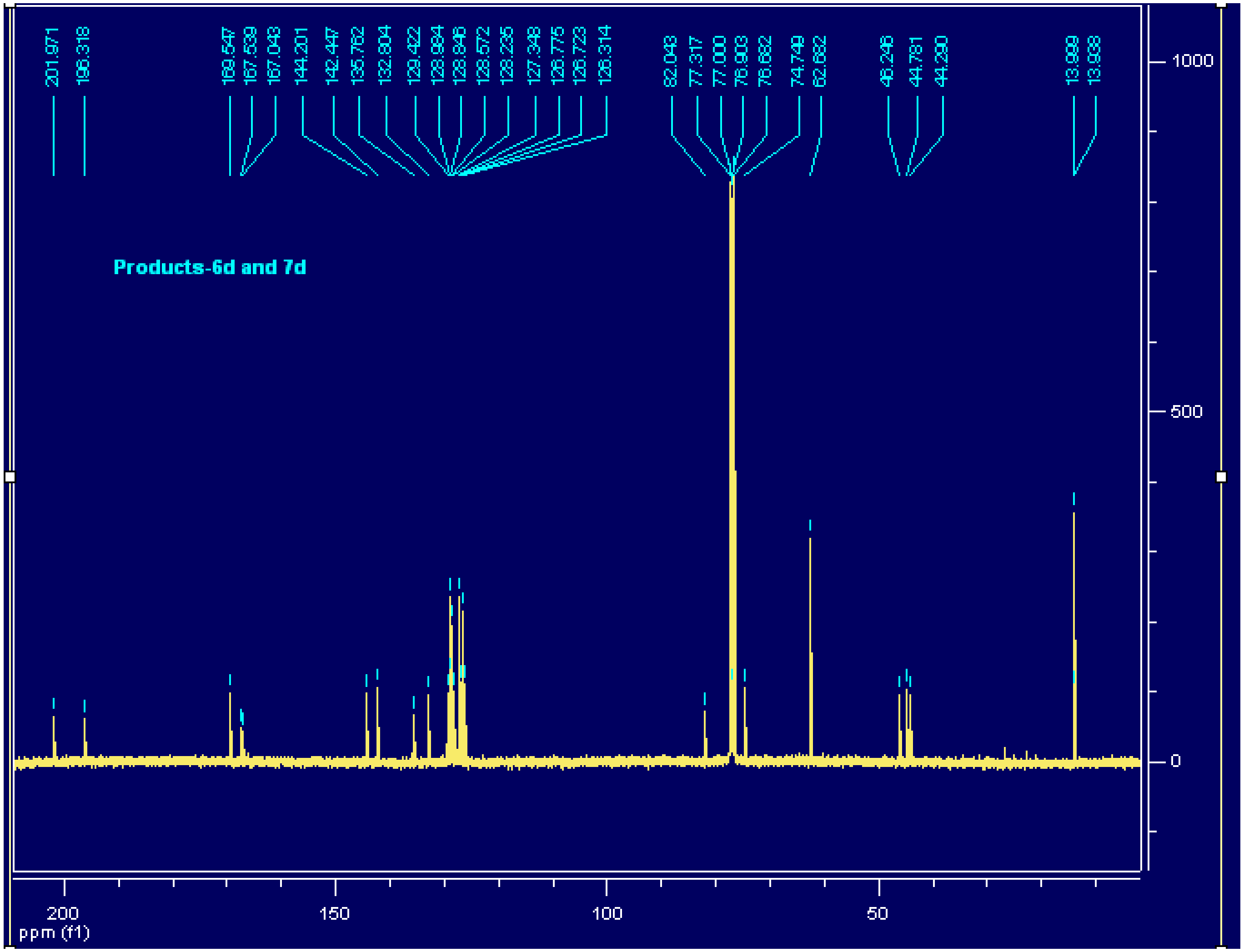
ppm (f1)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128.235
127.348
126.775
126.723
126.314
82.043
77.317
77.000
76.903
76.682
74.749
62.682
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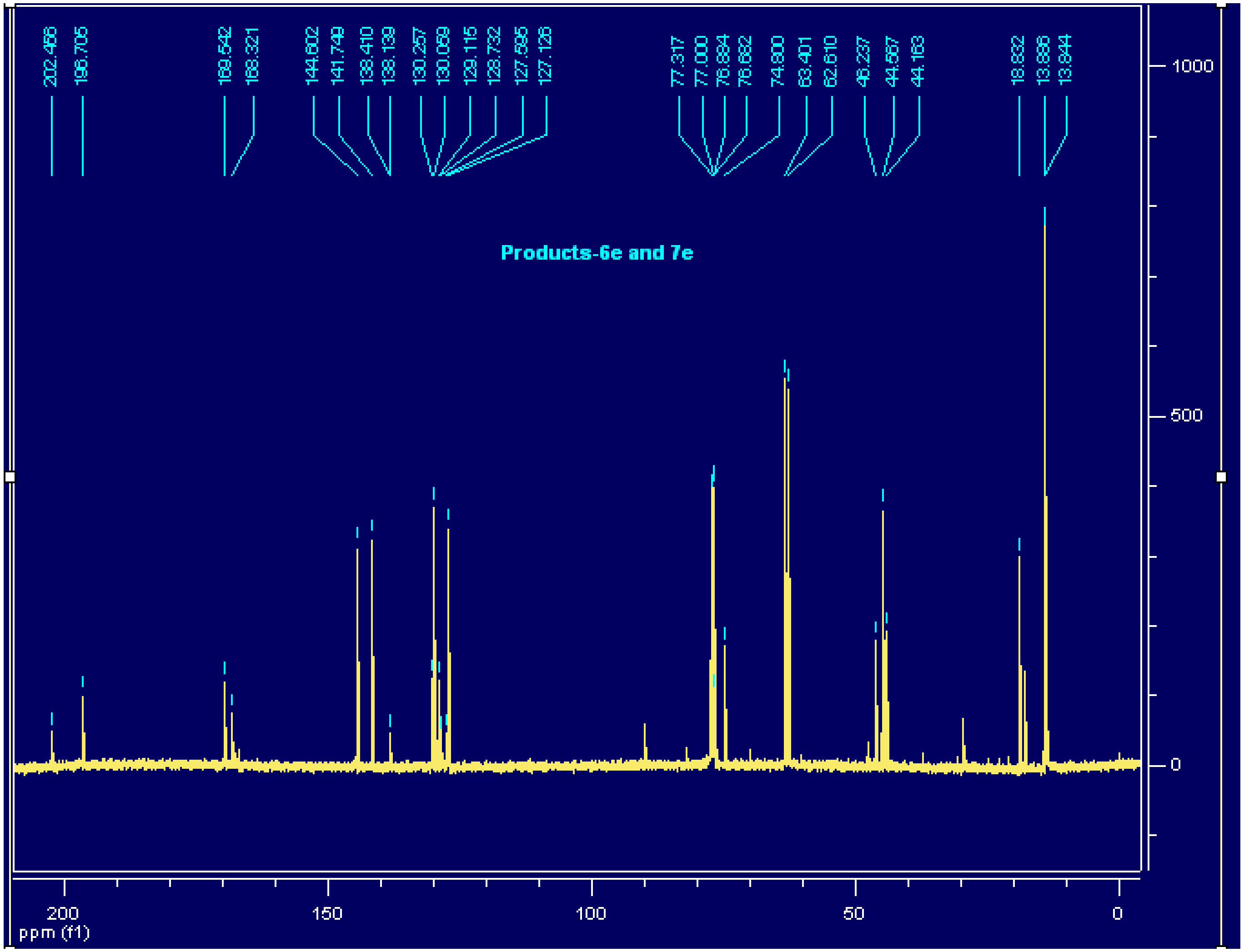
100
50
ppm (f1)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127.595
127.128
77.317
77.000
76.884
76.682
74.800
63.401
62.610
46.237
44.567
44.163
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13.844
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200
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100
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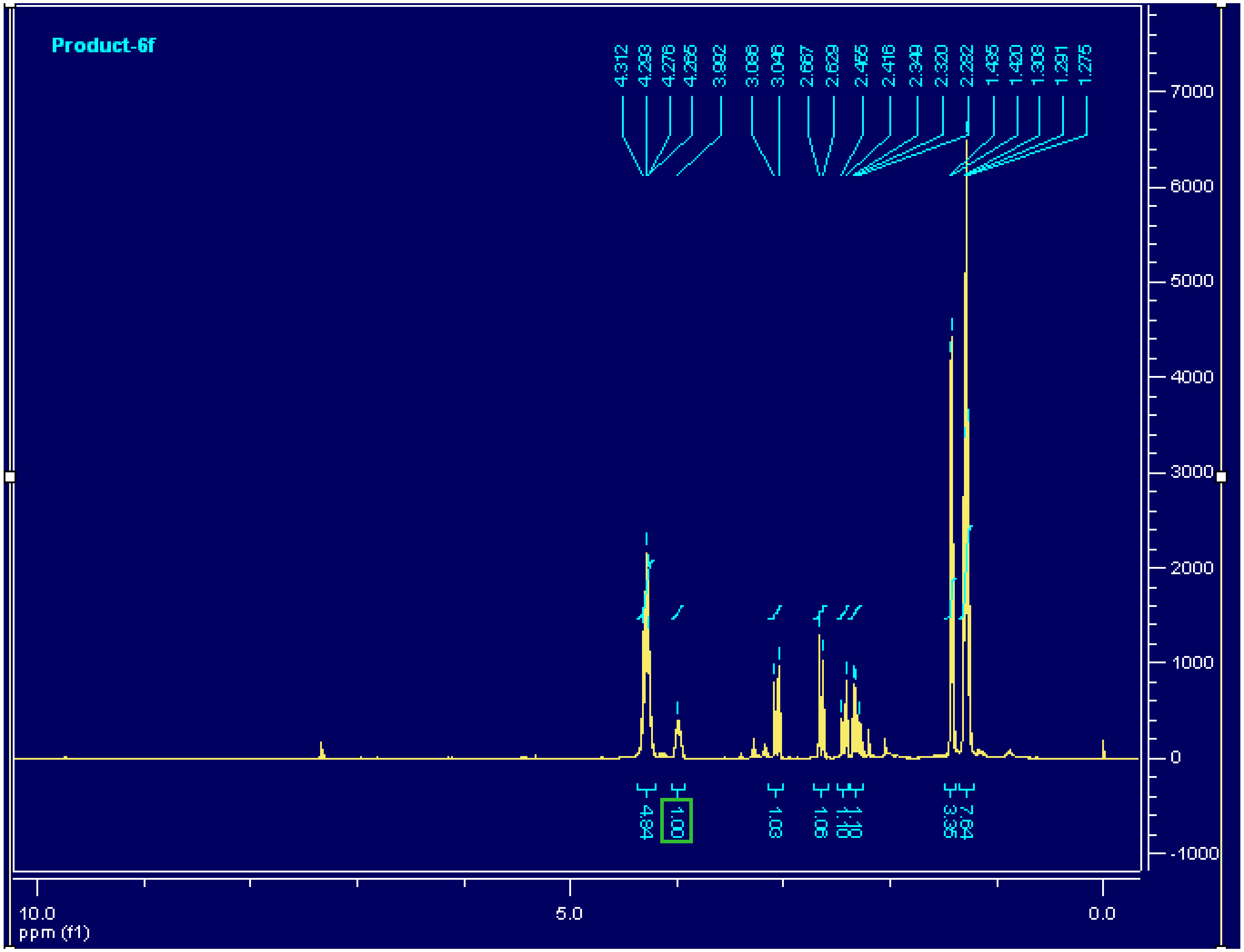
ppm (f1)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2.320
2.282
1.435
1.420
1.308
1.291
1.275
4.84
1.00
1.03
1.06
1.18
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ppm (f1)
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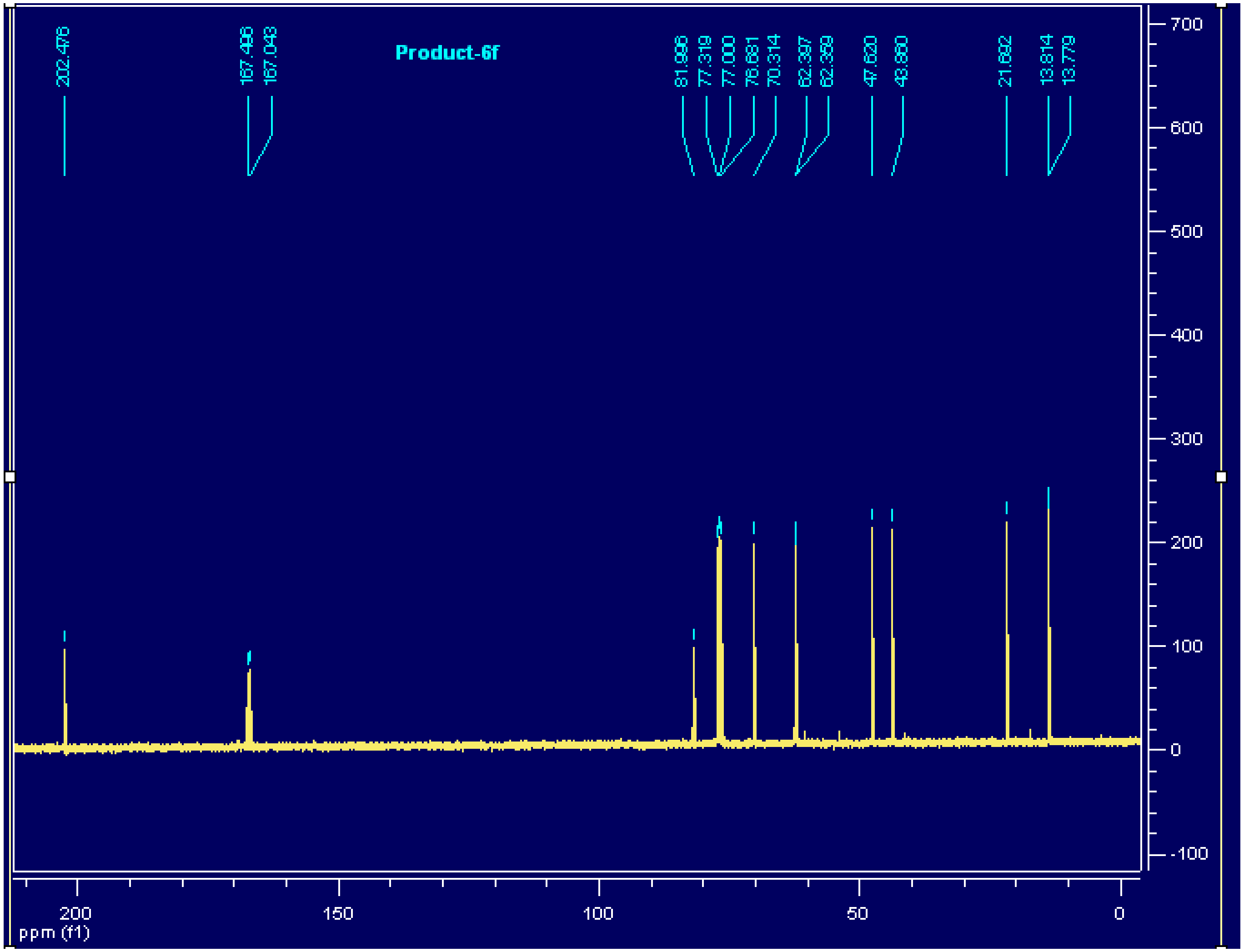
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21.692
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500
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300
200
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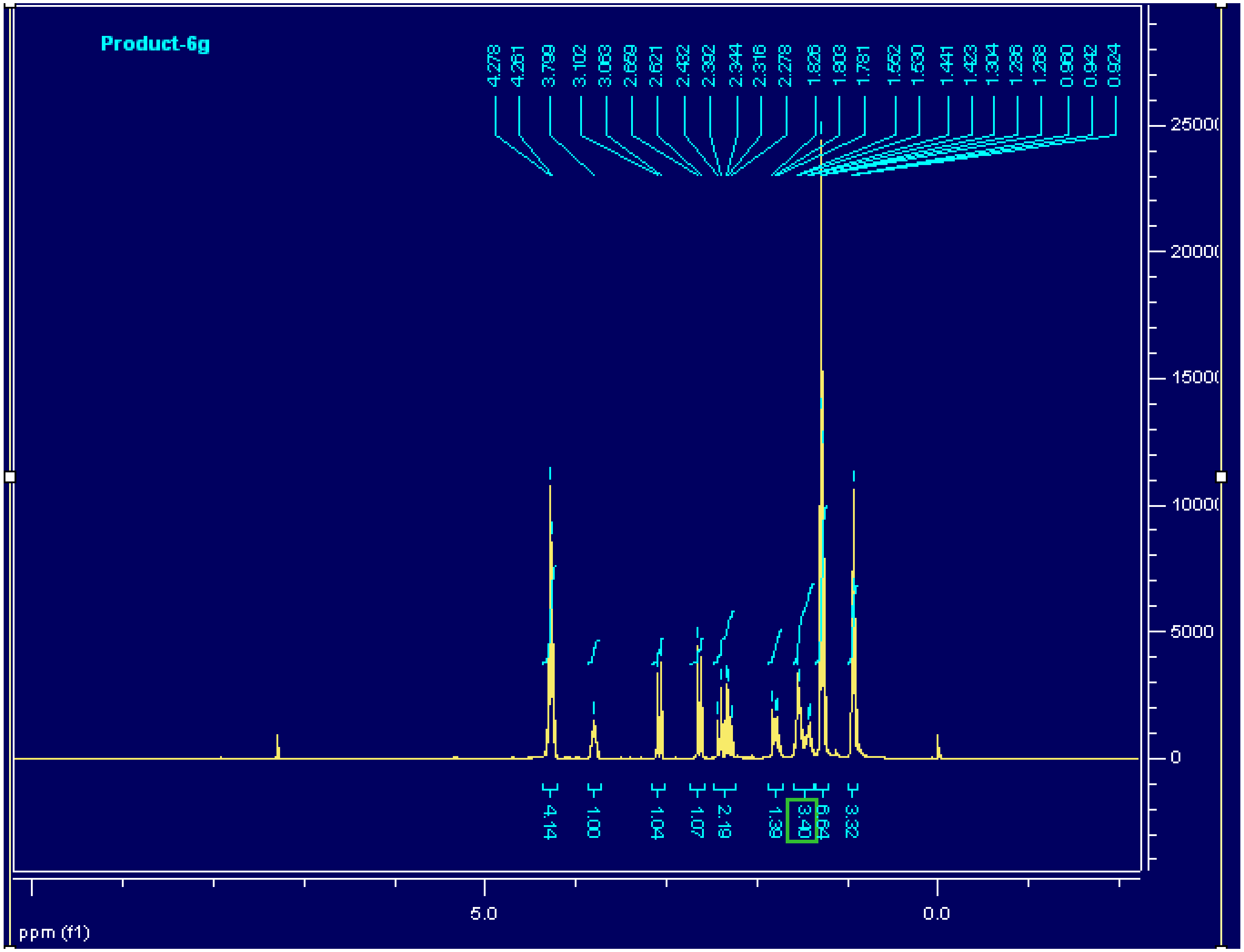
-100
200
150
100
50
0
ppm (f1)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3.063
2.659
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2.316
2.278
1.826
1.803
1.781
1.562
1.530
1.441
1.423
1.304
1.286
1.268
0.960
0.942
0.924
25000
20000
15000
10000
5000
0
4.14
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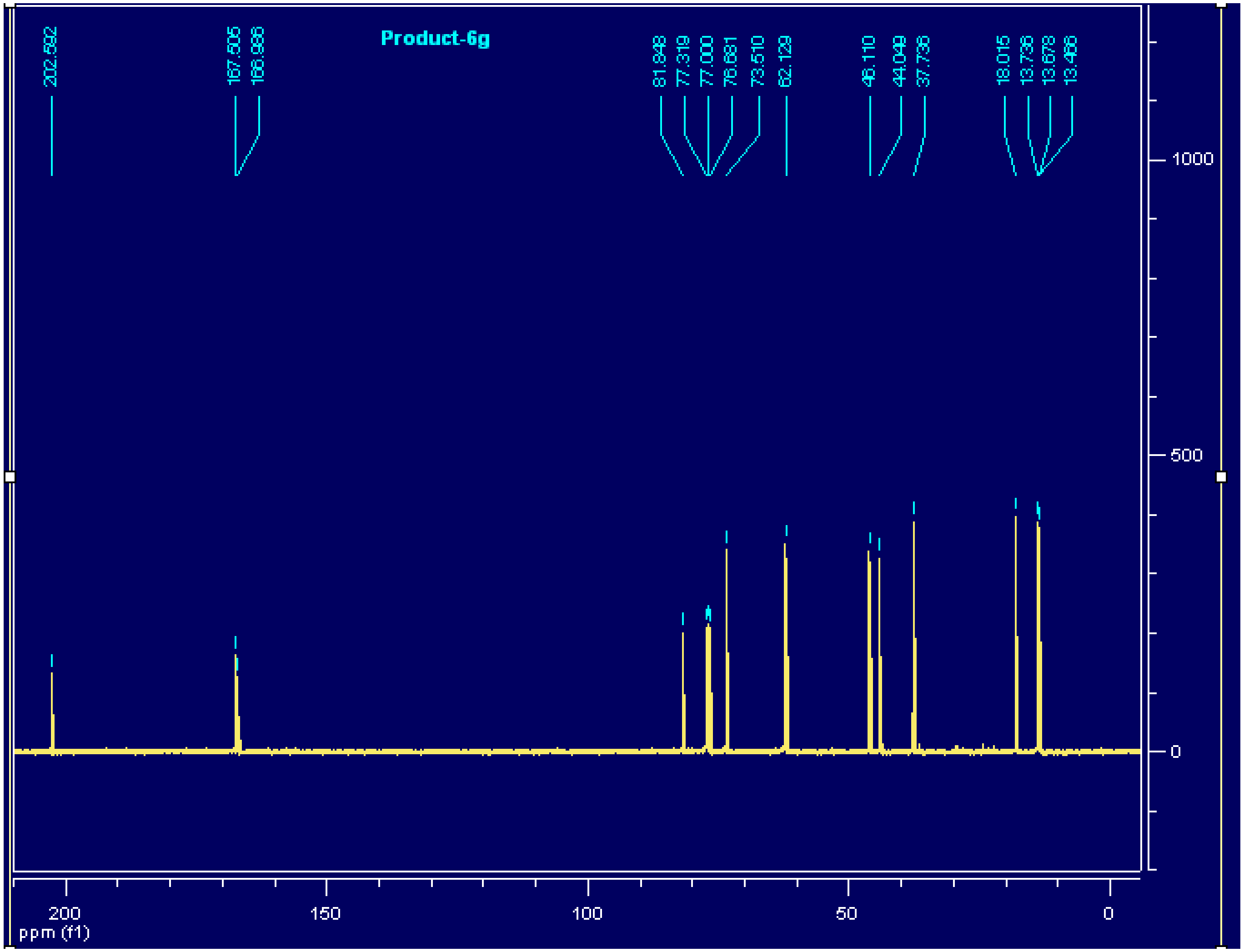
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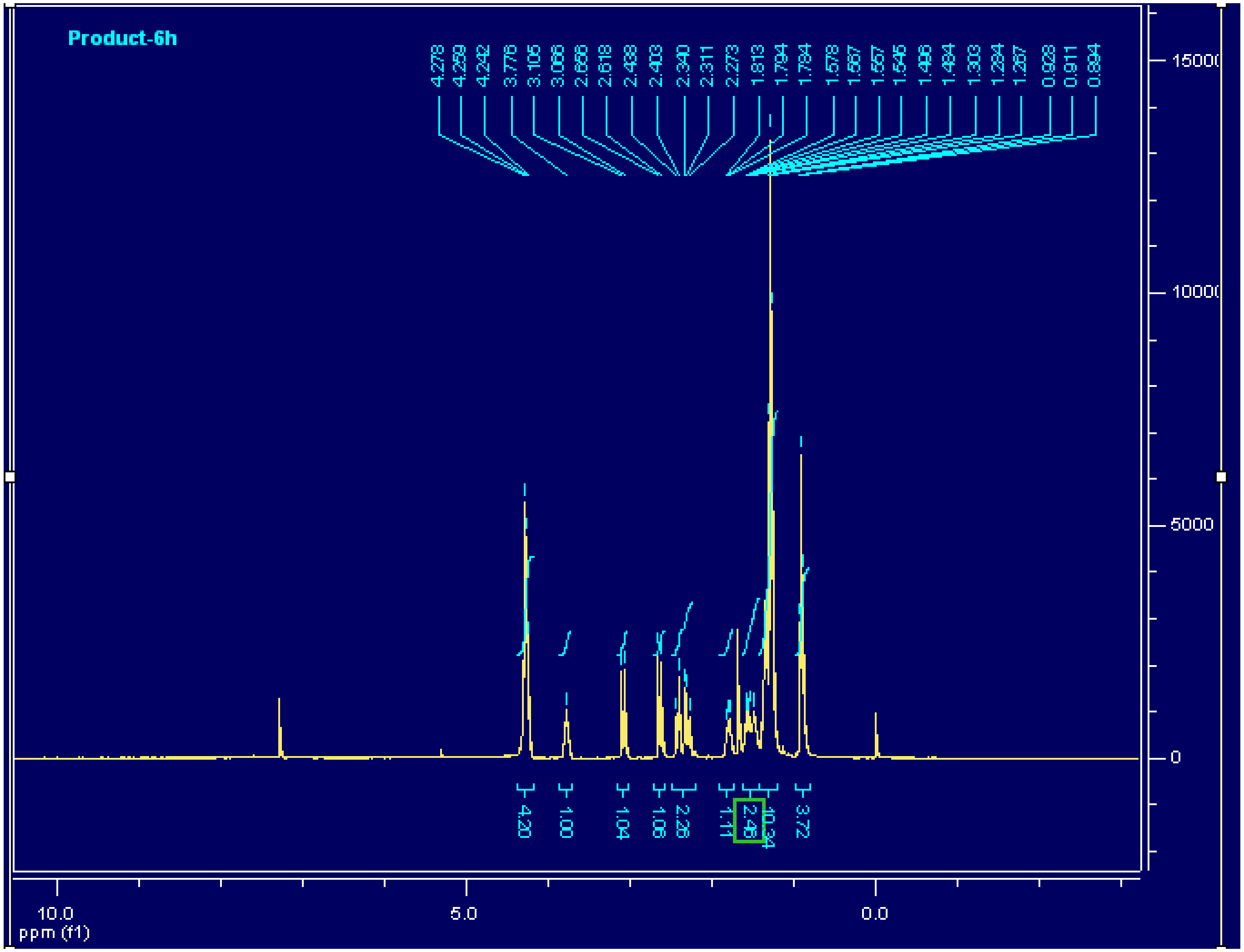
50
0
ppm (f1)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2.273
1.813
1.794
1.784
1.578
1.567
1.557
1.545
1.496
1.484
1.303
1.284
1.267
0.928
0.911
0.894
15000
10000
5000
0
4.20
1.00
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1.08
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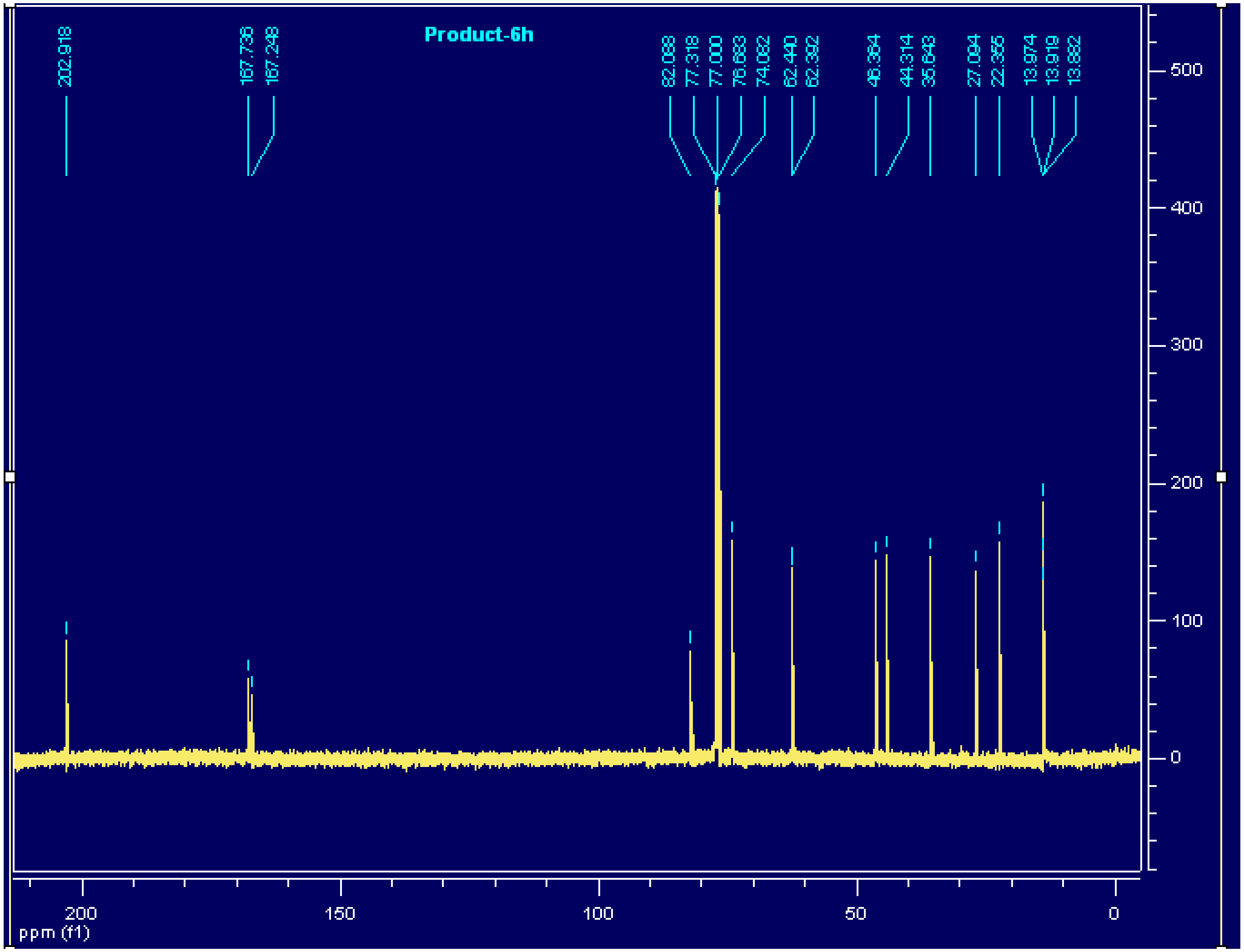
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74.082
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62.392
46.364
44.314
35.648
27.094
22.356
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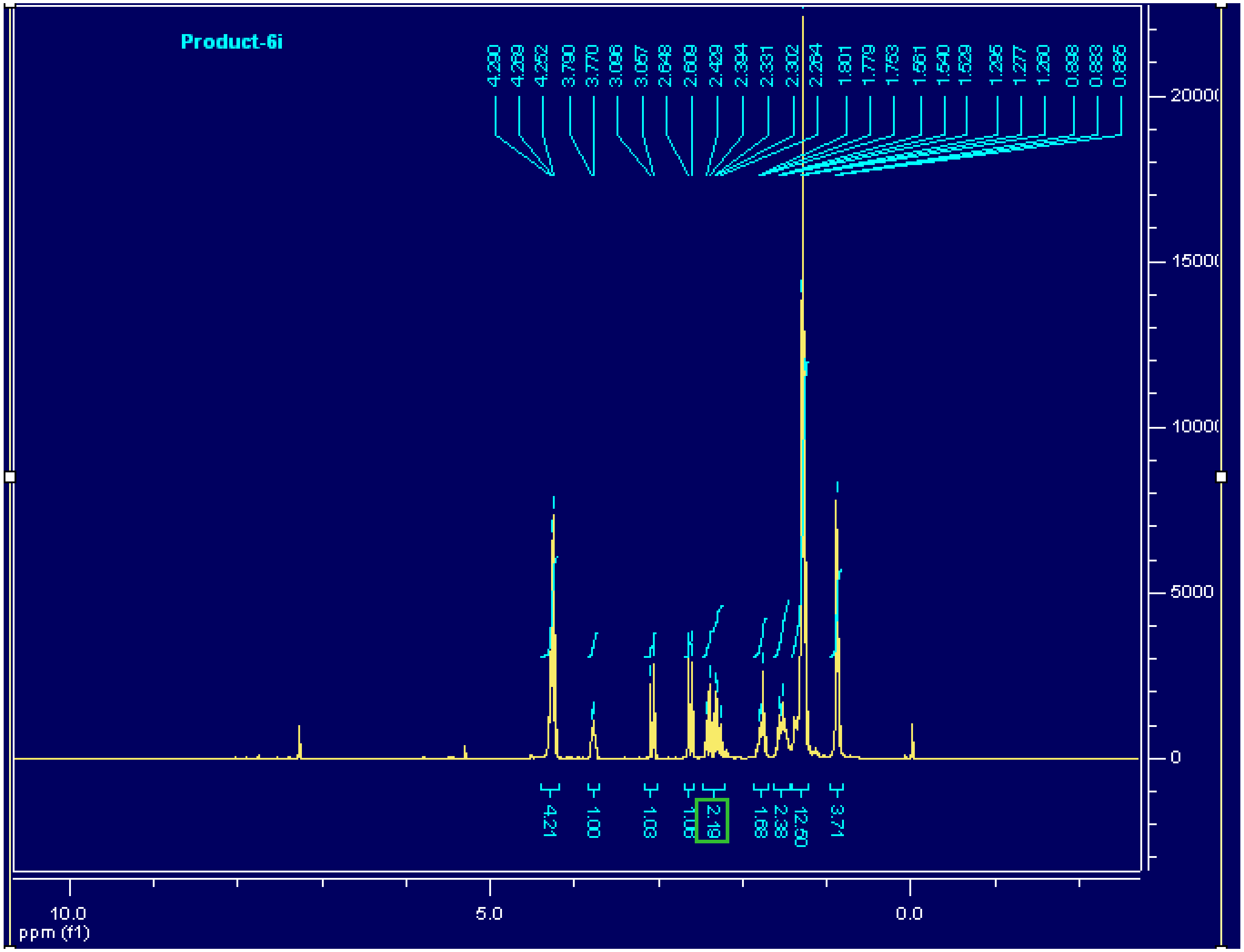
500
400
300
200
100
0
200
150
100
50
0
ppm (f1)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3.067
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2.302
2.264
1.801
1.779
1.753
1.561
1.540
1.523
1.295
1.277
1.260
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0.883
0.866
20000
15000
10000
5000
0
4.21
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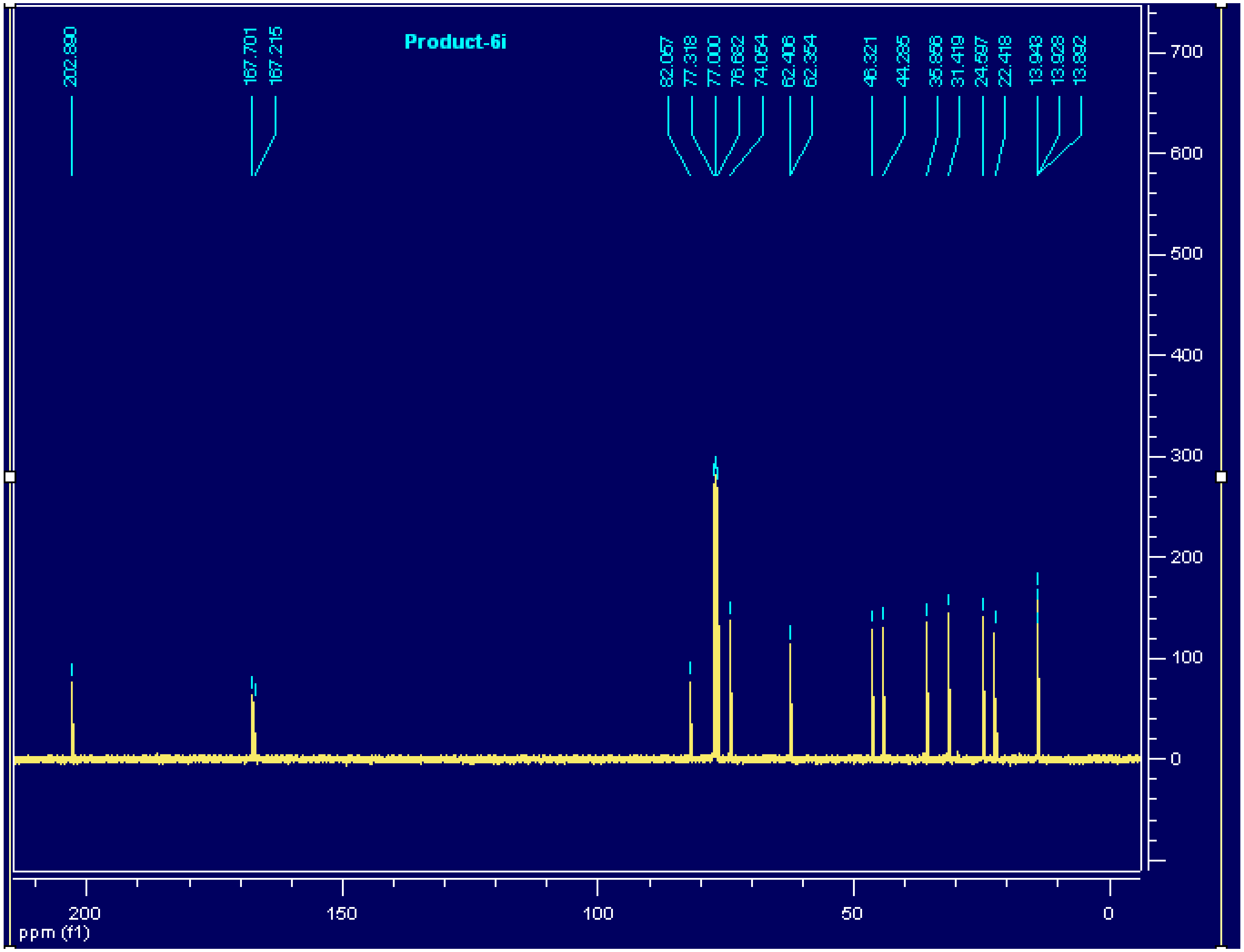
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35.856
31.419
24.597
22.418
13.943
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600
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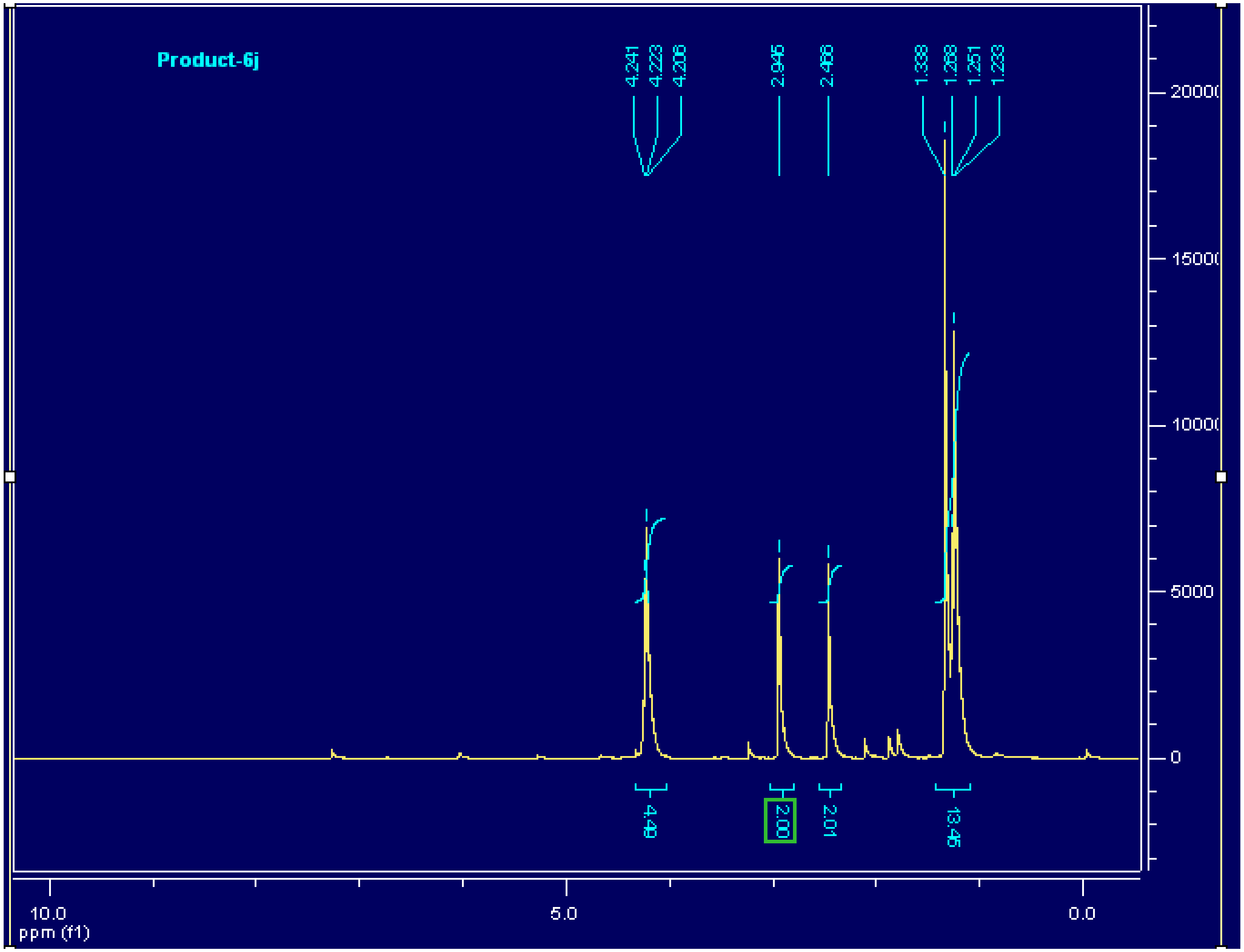
200
150
100
50
0
ppm (f1)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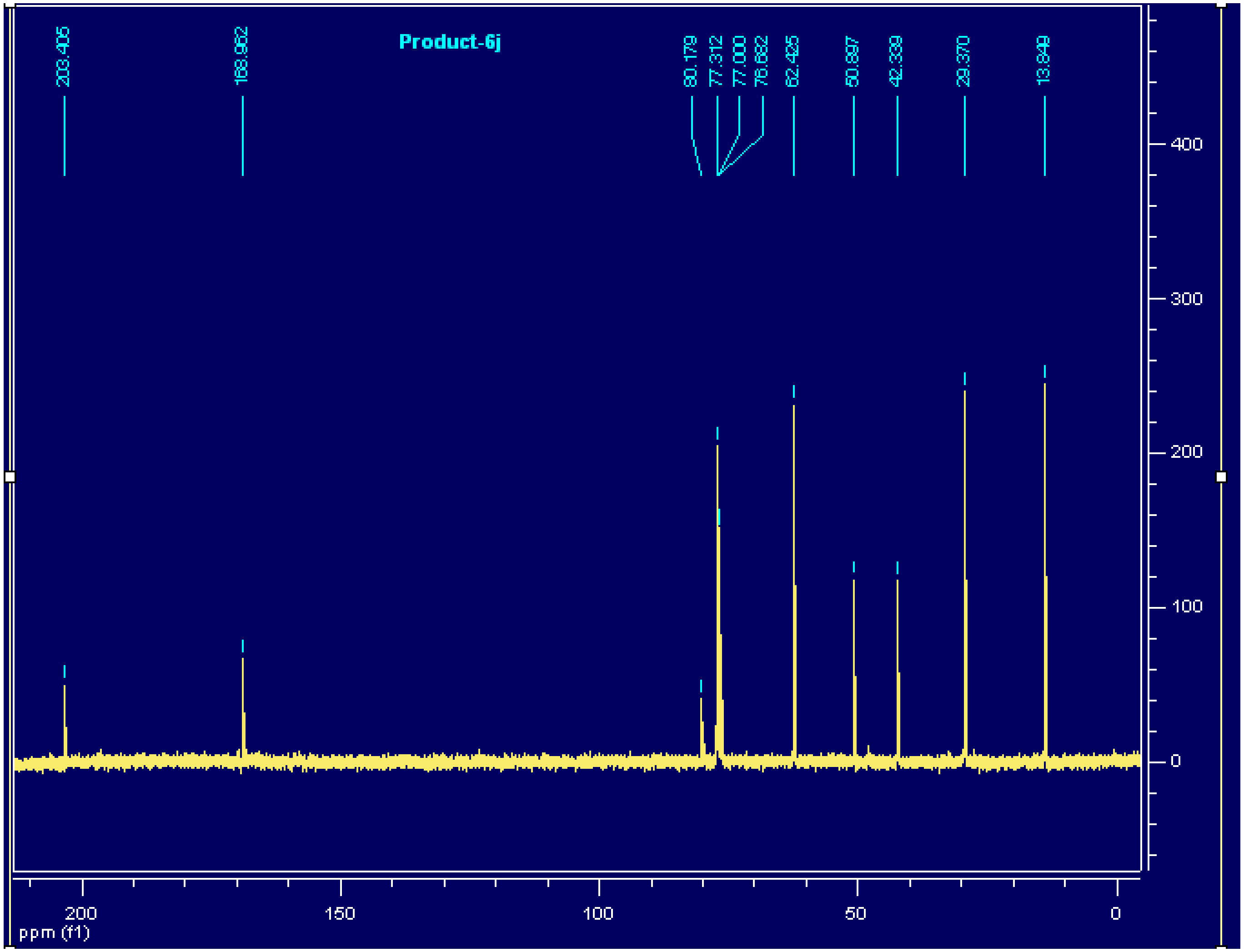
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80.179
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77.000
76.682
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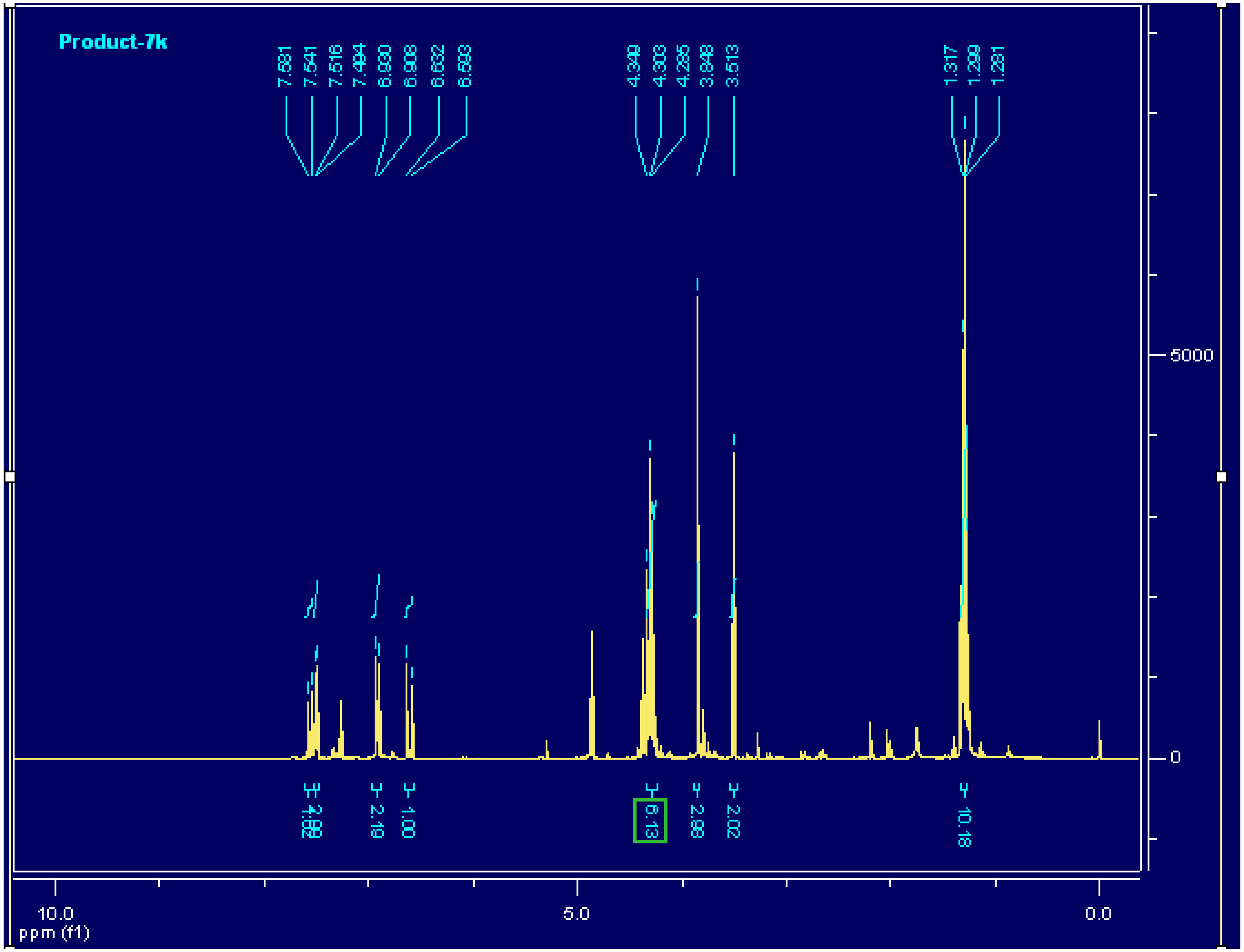
300
200
100
0
200
150
100
50
0
ppm (f1)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6.908
6.632
6.583
4.340
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4.285
3.848
3.513
1.317
1.299
1.281
4.02
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2.02
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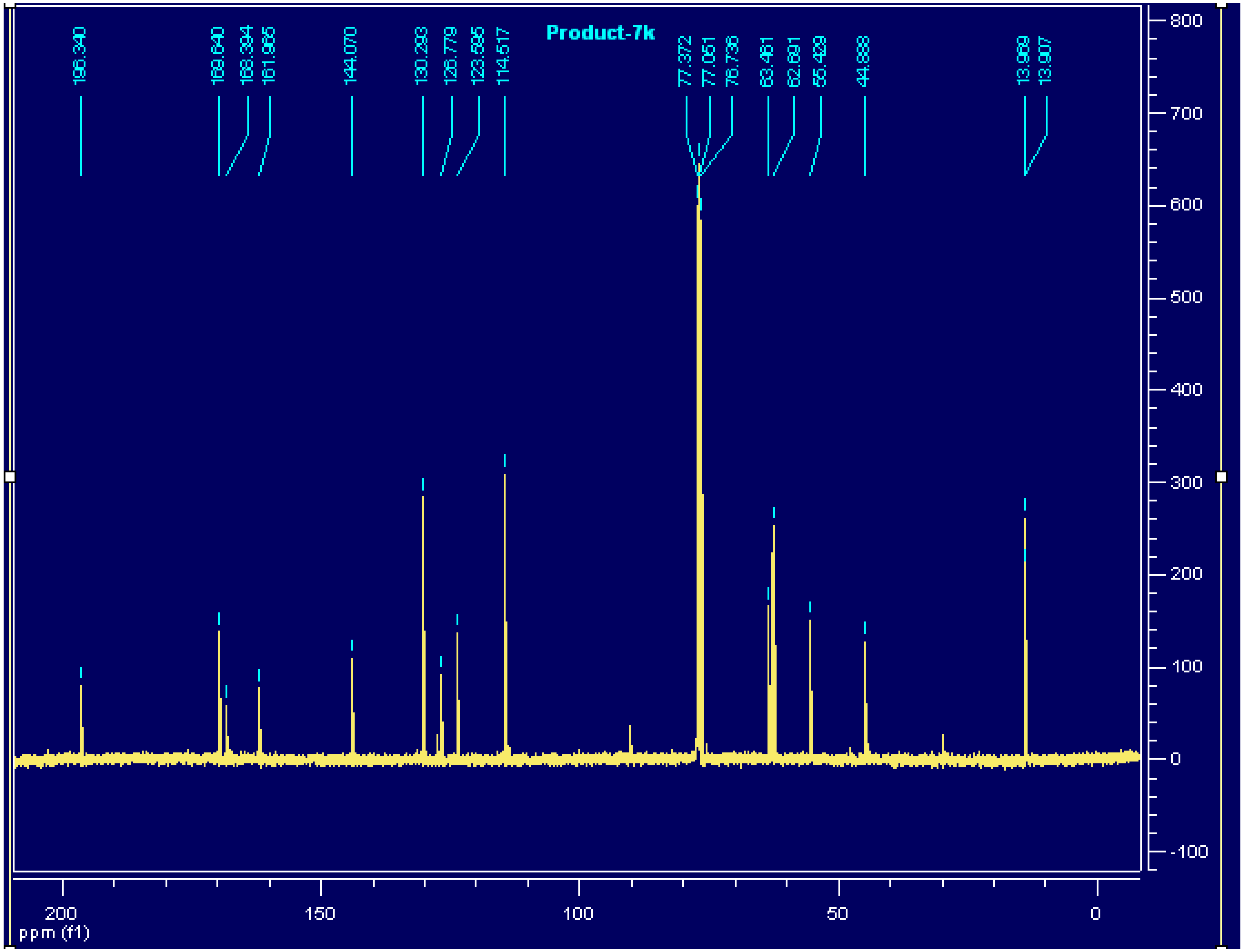
10.0
5.0
0.0
ppm (f1)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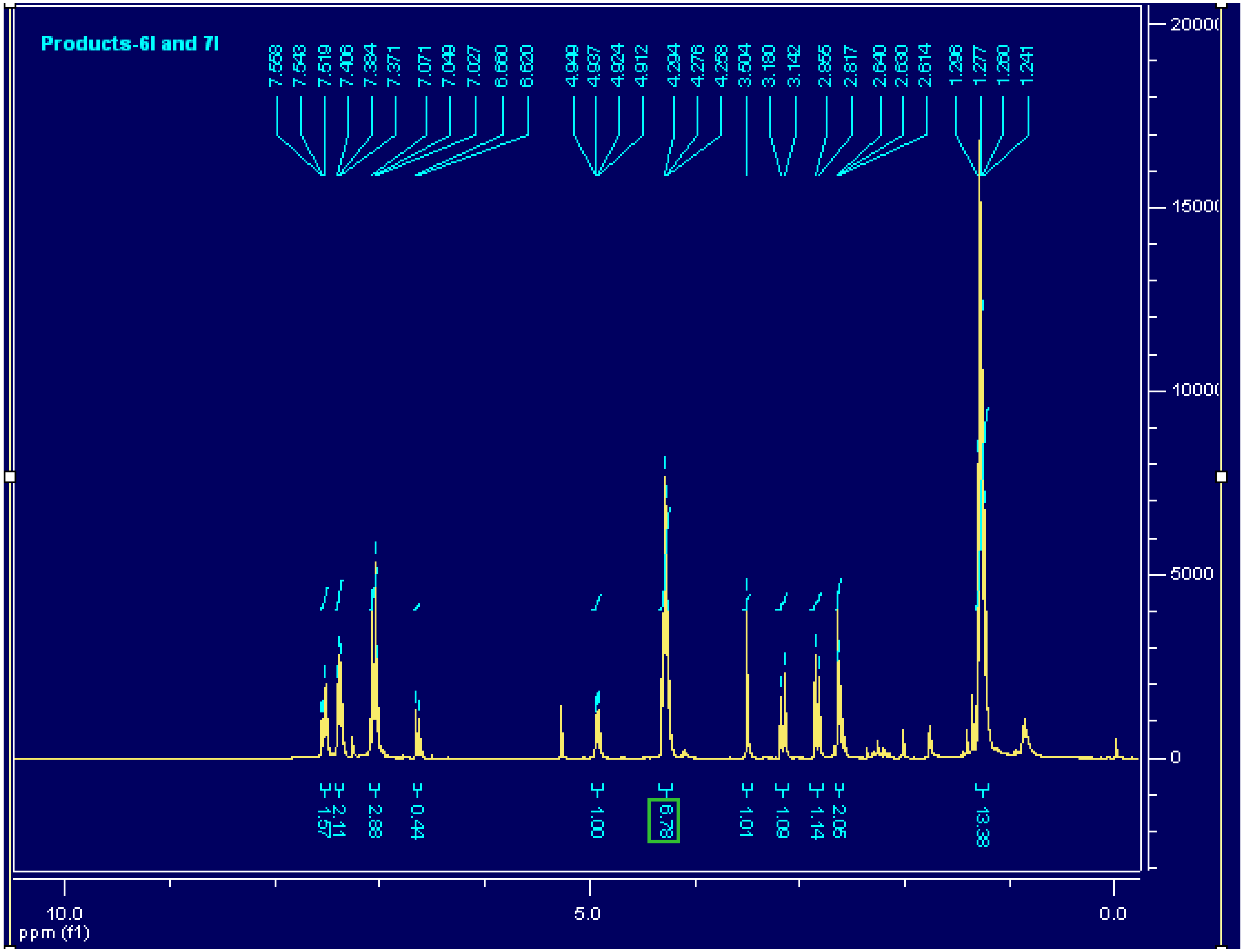
169.640
168.394
161.986
144.070
130.283
126.779
123.586
114.517
77.372
77.051
76.736
63.461
62.691
55.429
44.888
13.969
13.907
800
700
600
500
400
300
200
100
0
-100
200
150
100
50
0
ppm (f1)


Products-6l and 7l
7.558
7.543
7.519
7.406
7.394
7.371
7.071
7.049
7.027
6.680
6.620
4.949
4.937
4.924
4.912
4.294
4.276
4.258
3.604
3.180
3.142
2.855
2.817
2.640
2.630
2.614
1.296
1.277
1.260
1.241
20000
15000
10000
5000
0
1.57
2.11
2.88
0.44
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1.01
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1.14
2.06
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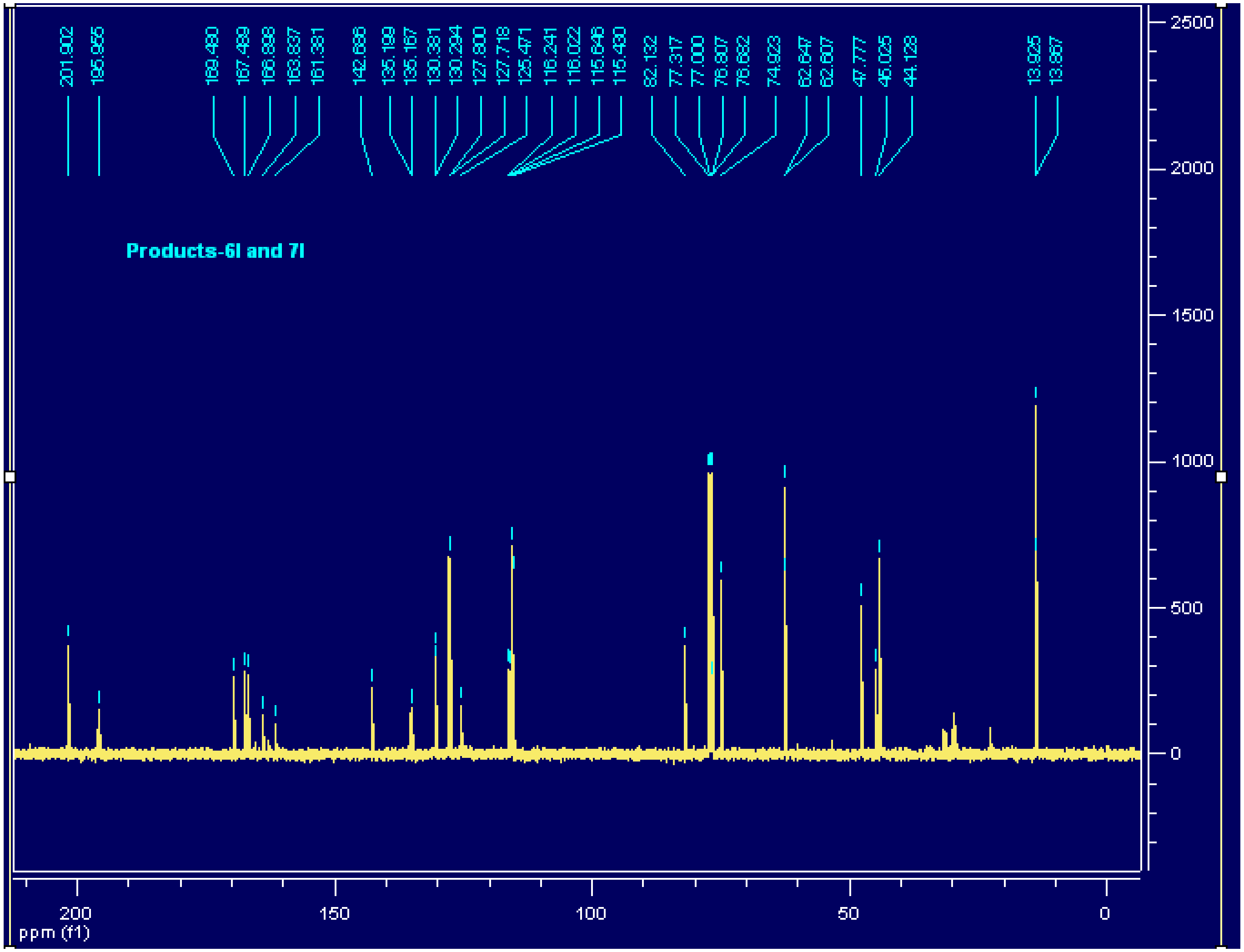
ppm (f1)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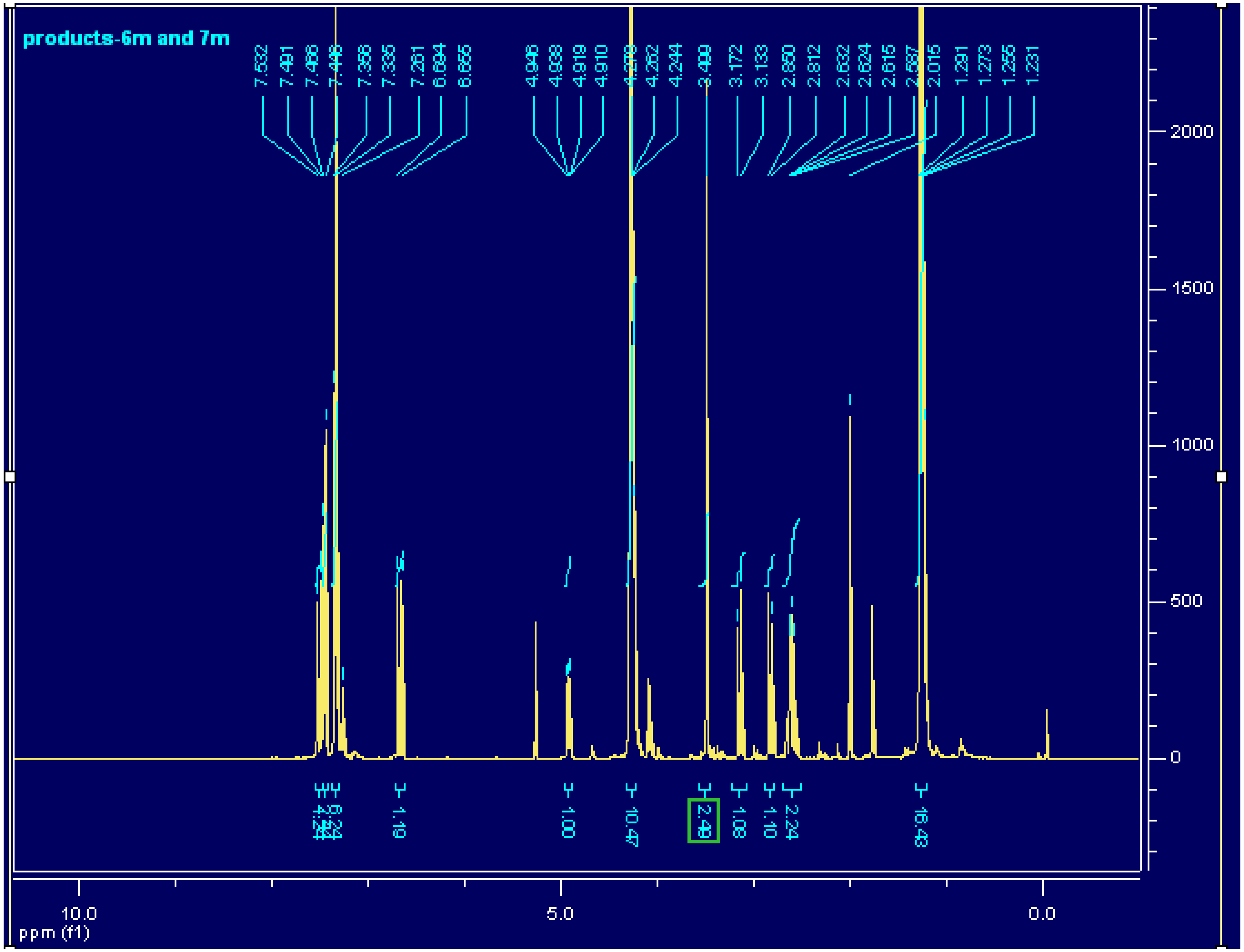
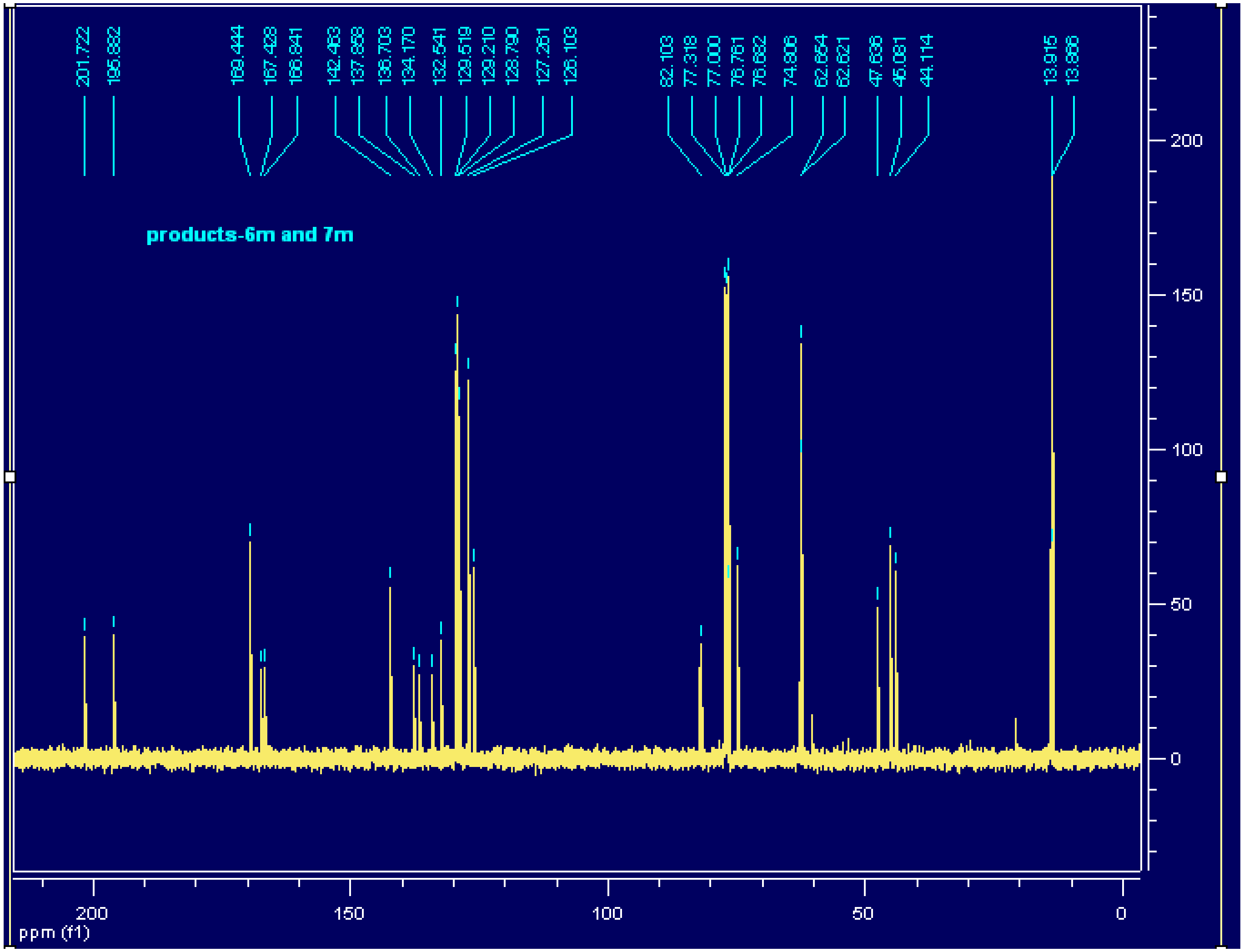
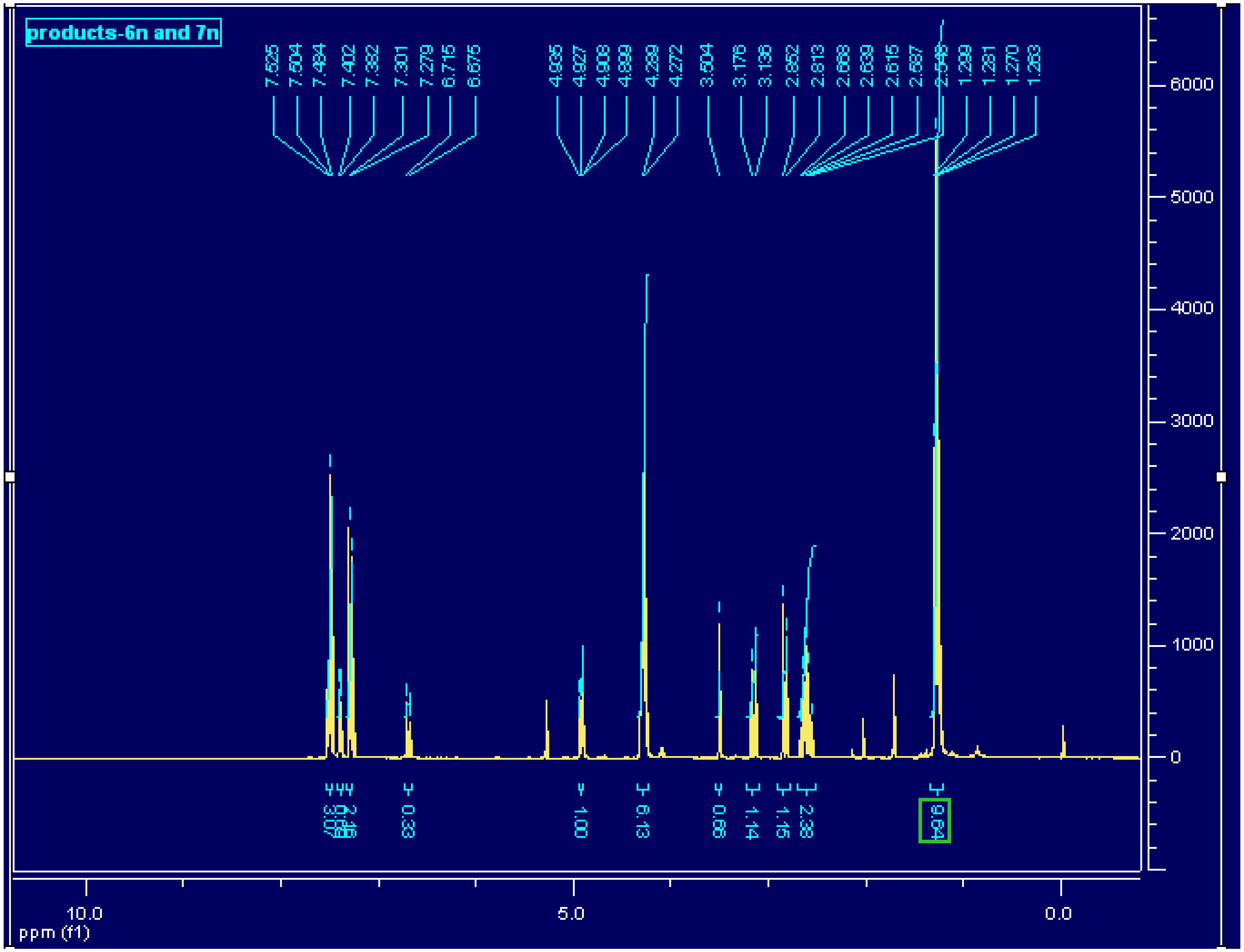
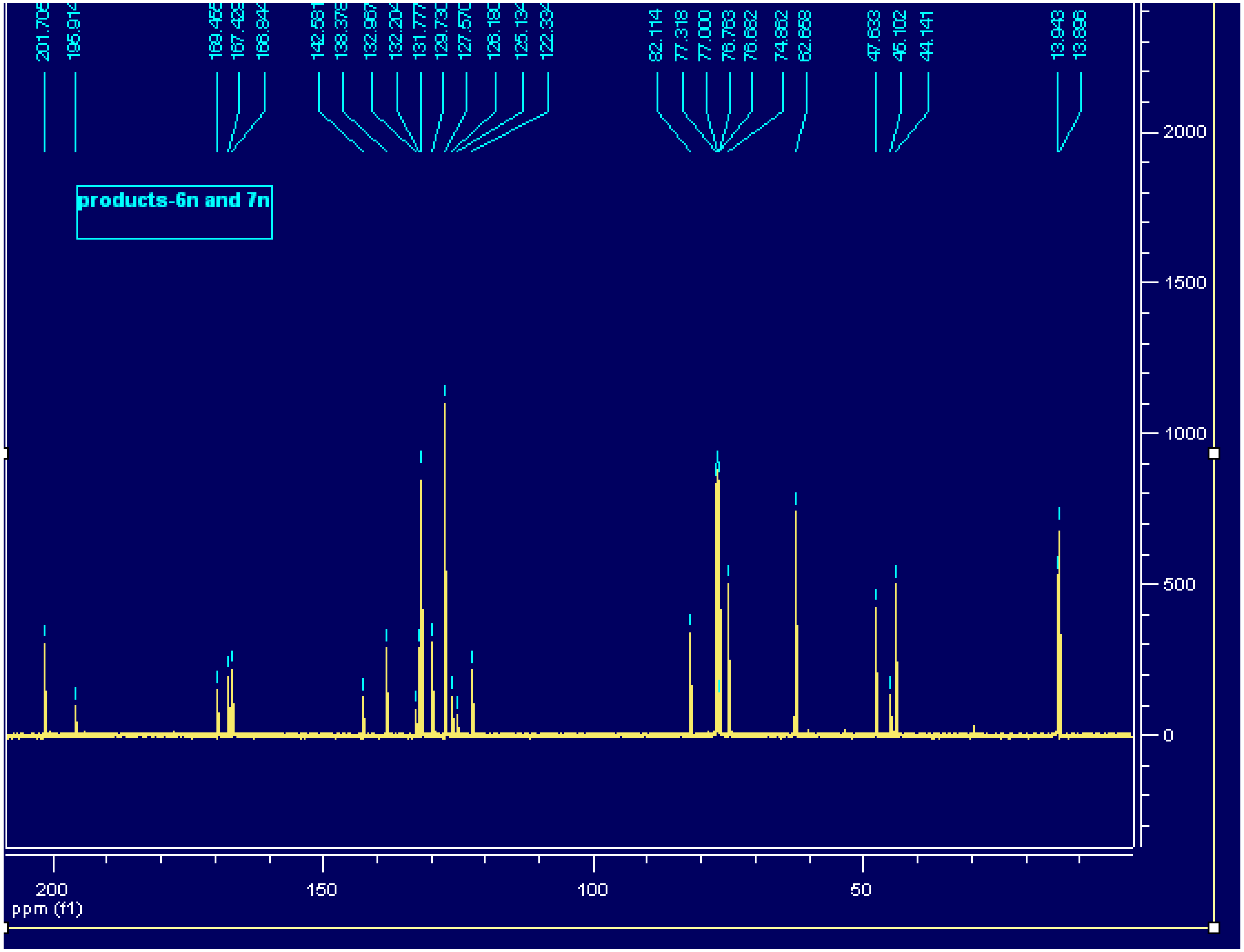
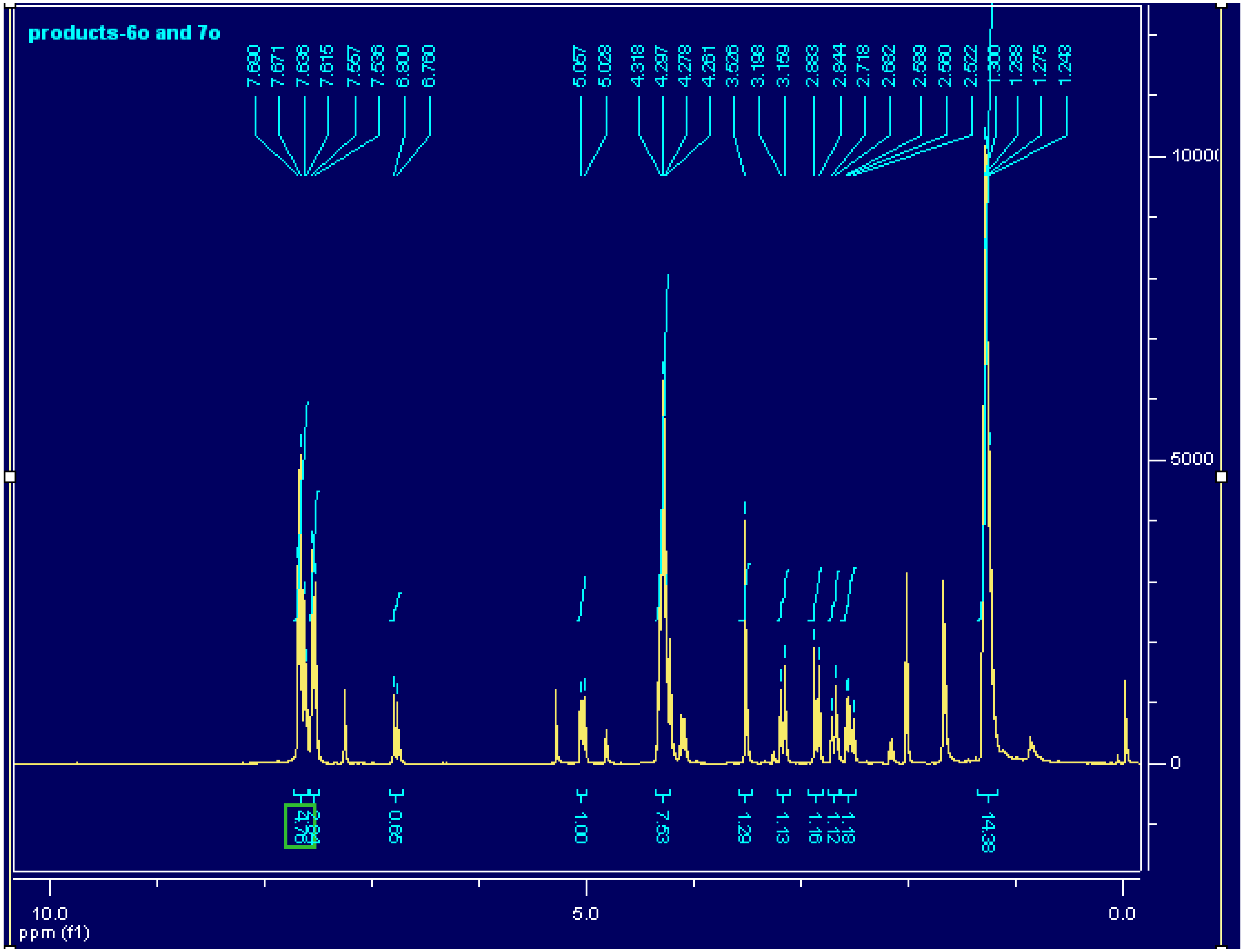
135.167
130.381
130.294
127.800
127.718
125.471
116.241
116.022
115.645
115.430
82.132
77.317
77.000
76.807
76.682
74.923
62.647
62.607
47.777
45.025
44.128
13.925
13.867
Products-6l and 7l
2500
2000
1500
1000
500
0
200
150
100
50
0
ppm (f1)

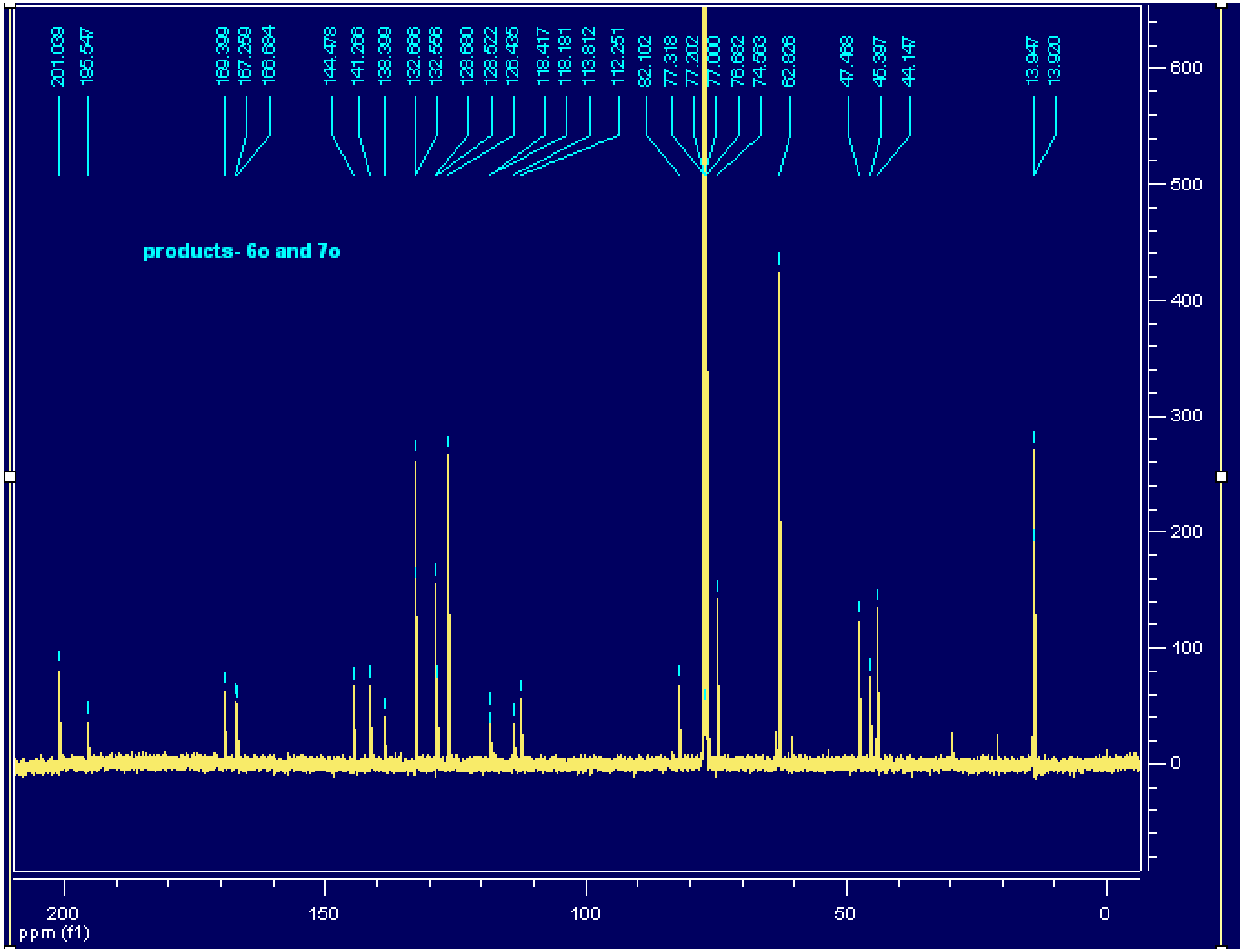

products-6m and 7m
7.532
7.491
7.466
7.446
7.356
7.335
7.261
6.694
6.665
4.946
4.938
4.919
4.910
4.279
4.262
4.244
3.400
3.172
3.133
2.850
2.812
2.632
2.624
2.615
2.587
2.015
1.291
1.273
1.255
1.231
2000
1500
1000
500
0
4.24
8.24
1.19
1.00
10.47
2.40
1.08
1.10
2.24
16.43
10.0
5.0
0.0
ppm (f1)

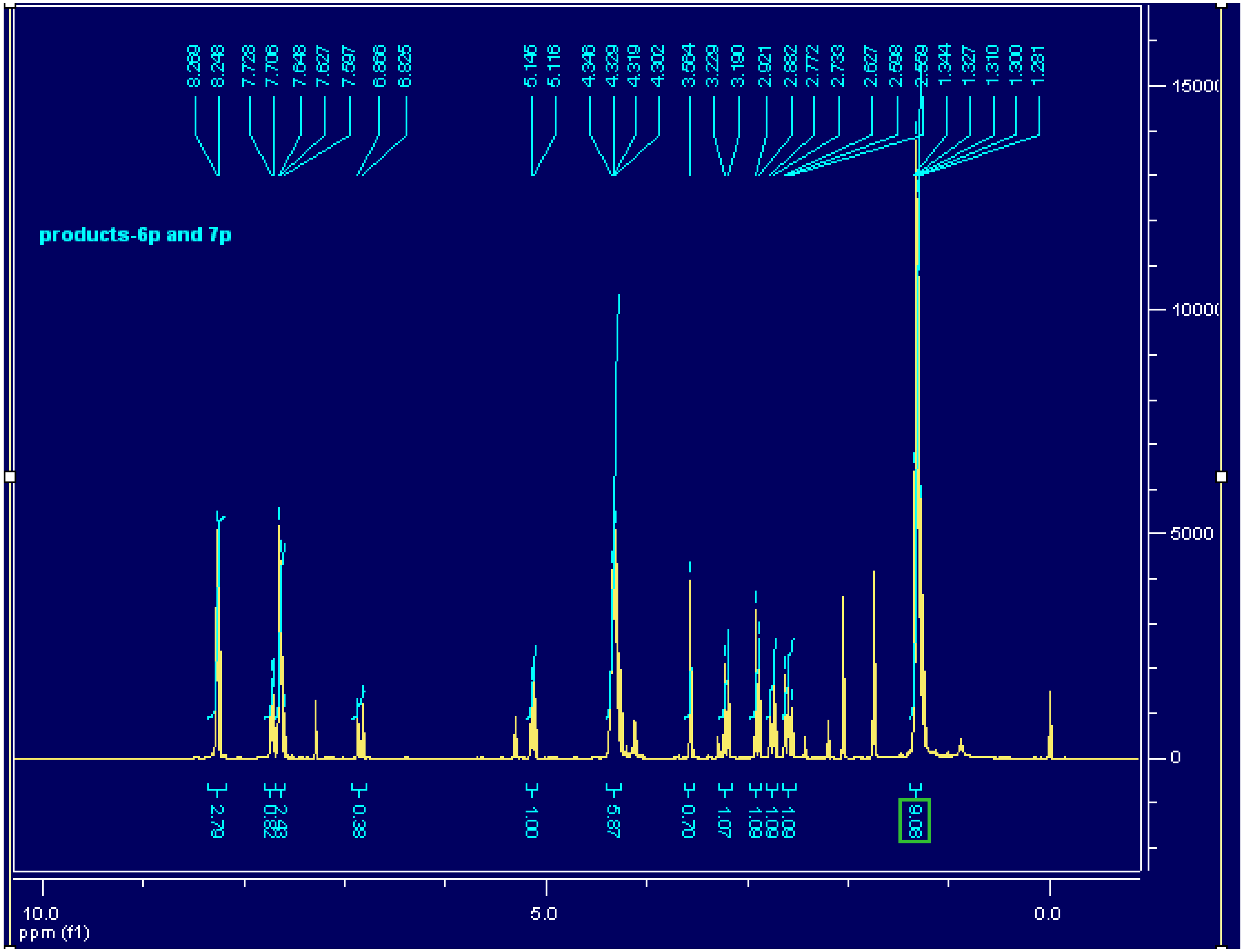

201.722
195.882
168.444
167.428
166.841
142.463
137.858
136.703
134.170
132.541
129.519
129.210
128.790
127.261
126.103
82.103
77.318
77.000
76.761
76.682
74.806
62.654
62.621
47.636
45.081
44.114
13.915
13.886
products-6m and 7m
200
150
100
50
0
200
150
100
50
0
ppm (f1)

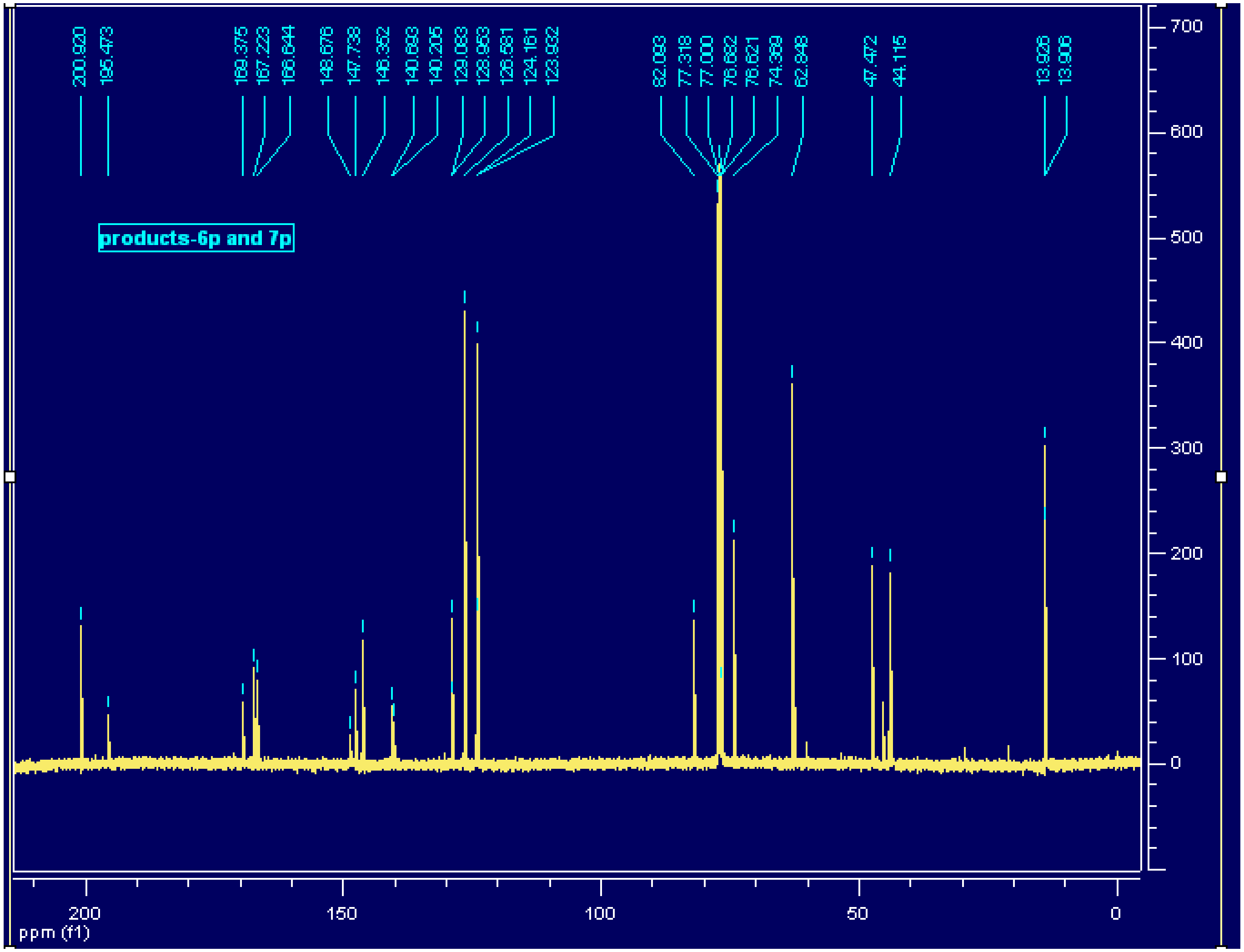

products-6n and 7n
7.525
7.504
7.494
7.402
7.382
7.301
7.279
6.715
6.675
4.935
4.927
4.908
4.899
4.289
4.272
3.504
3.176
3.136
2.852
2.813
2.668
2.639
2.615
2.587
1.289
1.281
1.270
1.263
0.33
1.00
6.13
0.88
1.14
1.15
2.38
9.64
6000
5000
4000
3000
2000
1000
0
10.0
5.0
0.0
ppm (f1)


201.705
195.914
169.455
167.423
166.844
142.581
138.378
132.967
132.204
131.777
129.730
127.570
126.180
125.134
122.334
82.114
77.318
77.000
76.763
76.682
74.862
62.668
47.633
45.102
44.141
13.948
13.896
products-6n and 7n
2000
1500
1000
500
0
200
150
100
50
ppm (f1)


products-6o and 7o
7.690
7.671
7.638
7.615
7.557
7.536
6.800
6.780
5.057
5.028
4.318
4.297
4.278
4.261
3.528
3.198
3.159
2.883
2.844
2.718
2.682
2.589
2.560
2.522
1.300
1.288
1.275
1.248
10000
5000
0
4.78
2.84
0.86
1.00
7.53
1.29
1.13
1.16
1.12
1.18
14.38
10.0
5.0
0.0
ppm (f1)


201.039
195.547
169.399
167.259
166.684
144.478
141.266
138.399
132.686
132.566
128.880
128.522
128.435
118.417
118.181
113.812
112.251
82.102
77.318
77.202
77.000
76.682
74.563
62.826
47.488
45.397
44.147
13.947
13.920
products- 6o and 7o
600
500
400
300
200
100
0
200
150
100
50
0
ppm (f1)


8.269
8.248
7.728
7.706
7.648
7.627
7.597
6.866
6.825
5.145
5.116
4.346
4.329
4.319
4.302
3.564
3.229
3.190
2.921
2.882
2.772
2.733
2.627
2.588
2.569
1.344
1.327
1.310
1.300
1.281
products-6p and 7p
15000
10000
5000
0
2.79
0.82
2.43
0.38
1.00
5.87
0.70
1.07
1.08
1.08
1.08
9.08
10.0
ppm (f1)
5.0
0.0


200.900
195.473
169.375
167.223
166.644
148.676
147.738
146.362
140.683
140.205
129.083
128.963
126.581
124.161
123.932
82.093
77.318
77.000
76.682
76.621
74.369
62.848
47.472
44.115
13.926
13.906
products-6p and 7p
700
600
500
400
300
200
100
0
200
150
100
50
0
ppm (f1)