Water mediated trapping of active methylene intermediates generated by IBX-induced oxidation of Baylis-Hillman adducts with nucleophiles

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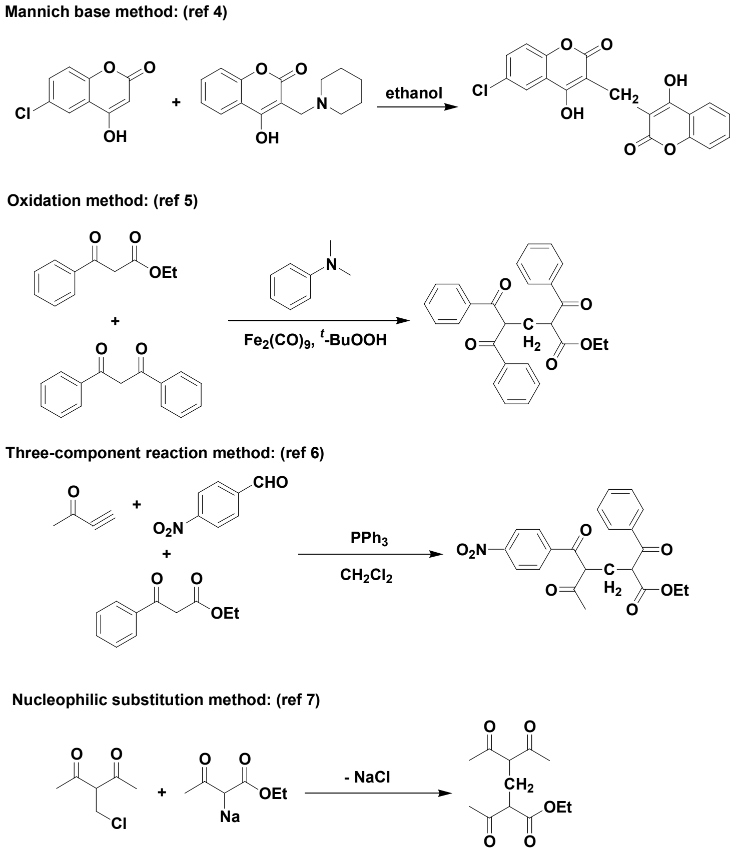
Electronic Supporting Information

General Remarks:
Tolualdehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde, 2-nitrobenzaldehyde, 4-trifluorobenzaldehyde, 3-phenylpropionaldehyde, thiophene-2-carboxaldehyde, 4-methylstyrene, 4-methoxystyrene, N-methyl-2-phenylindole, N-ethyl-2-phenylindole, 4-ethoxystyrene, 4-chlorostyrene, 4-fluoro-α-methylstyrene, 4-*tert*-butylstyrene, 4-chloro-α-methylstyrene, *n*-butyl vinyl ether, ethyl indole-2-carboxylate, ethyl benzoylacetate, ethyl 4-methoxybenzoylacetate, *tert*-butyl acrylate, cyclohexyl acrylate, and chloroform-*d* were purchased from Alfa Aesar Chemical Company. 2-ethylhexyl acrylate was obtained from TCI Chemical Company. Benzaldehyde, α-methylstyrene, nitromethane, furfural, IBX, benzamide, acetonitrile, toluene, 1,2-dichloroethane, ethyl acetate, *n*-heptane and petroether were purchased from Shanghai Chemical Compony. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-400. Chemical shifts are expressed in ppm relative to Me_4Si in $CDCl_3$. IR spectra were recorded on a FT-IR Bruker (VERTEX 70) using KBr technology. Elemental analysis was measured on a Vario Micro Cube (Elementar) Instrument. Baylis-Hillman adducts were prepared according to reported methods.[1, 2] Ionic liquid, $[BMIm]BF_4$, was synthesized according to our previous method.[3]

A typical procedure for IBX-induced oxidative *oxo* Diels-Alder reaction of Baylis-Hillman adducts with olefins: all reactions were conducted in a 10 mL of V-type flask equipped with triangle magnetic stirring. In a typical reaction, water (1.0 g) was mixed with ***2a*** (52 mg, 0.39 mmol), ***1a*** (62 mg, 0.30 mmol) and IBX (109 mg, 0.39 mmol) under air. The mixture was stirred for 3 hours at 90 °C. After reaction, the mixture was extracted with ethyl acetate (2 mL × 3). The obtained ester phases were then combined together and concentrated under reduced pressure. The product was obtained by preparation TLC using a mixed solution of ethyl acetate and petro ether as eluting solvent (normally, the ratio of ethyl acetate/petroether is 1/10). The generated 2-iodobenzoic acid could be recovered by filtration and regenerated by a known method.

A typical procedure for IBX-induced oxidative Michael reaction of Baylis-Hillman adducts with 1,3-dicarbonyl compounds: all reactions were conducted in a 10 mL of V-type flask equipped with triangle magnetic stirring. In a typical reaction, water (1.0 g) was mixed with ***4a*** (75.0 mg, 0.36 mmol), ***1a*** (62.0 mg, 0.30 mmol) and IBX (101.0 mg, 0.36 mmol) under air. The mixture was stirred for 3 hours at 90 °C. After reaction, the mixture was extracted with ethyl acetate (2 mL × 3). The obtained ester phases were then combined together and concentrated under reduced pressure. The product was obtained by preparation TLC using a mixed solution of ethyl acetate and petro ether as eluting solvent (normally, the ratio of ethyl acetate/petroether is 1/6).



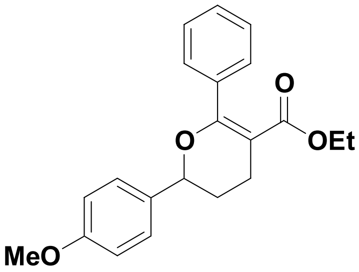
Scheme S1. Previous method to access skeleton of ***5a***-type axial-asymmetric polycarbonyl compounds.

A typical procedure for IBX-induced oxidative Michael reaction of Baylis-Hillman adducts with less-reactive indole: all reactions were conducted in a 10 mL of V-type flask equipped with triangle magnetic stirring. In a typical reaction, water (1.0 g) was mixed with ***1a*** (61.8 mg, 0.30 mmol), ***6a*** (62.4 mg, 0.33 mmol) and IBX (101.0 mg, 0.36 mmol) under air. The mixture was stirred for 10 hours at 90 °C. After reaction, the mixture was extracted with ethyl acetate (2 mL × 3). The obtained ester phases were then combined together and concentrated under reduced pressure. The product was obtained by preparation TLC using a mixed solution of ethyl acetate and petro ether as eluting solvent (normally, the ratio of ethyl acetate/petroether is 1/6).

A typical procedure for IBX-induced oxidative aza-Michael reaction of Baylis-Hillman adduct 1a with benzamide: the reactions was conducted in a 10 mL of V-type flask equipped with triangle magnetic stirring. In the beginning of the reaction, water (1.0 g) was mixed with ***1a*** (61.8 mg, 0.30 mmol), ***8a*** (39.9 mg, 0.33 mmol) and IBX (101.0 mg, 0.36 mmol) under air. The mixture was stirred for 4 hours at 90 °C. After reaction, the mixture was extracted with ethyl acetate (2 mL × 3). The obtained ester phases were then combined together and concentrated under reduced pressure. The product was obtained by preparation TLC using a mixed solution of ethyl acetate and petro ether as eluting solvent (the ratio of ethyl acetate/petroether is 1/4).

References

1. V. K. Aggarwal, A. Mereu, *Chem. Commun*. **1999**, 2311-2312
2. Y. Song, H. Ke, N. Wang, L. Wang, G. Zou, *Tetrahedron*, **2009**, *65*, 9086-9090.
3. Y. Gu, F. Shi, Y. Deng, *J. Org. Chem.* **2004**, *69*, 391-394.
4. (a) R. A. Abramovitch, J. R. Gear, *Can. J. Chem.* **1958**, *36*, 1501-1510; (b) D. Molho, C. Mentzer, *Compt. rend*. **1959**, *248*, 1344-1347.
5. H. Li, Z. He, X. Guo, W. Li, X. Zhao, Z. Li, *Org. Lett*. **2009**, *11*, 4176-4179.
6. S. Xue, Q. -F. Zhou, L. –Z. Li, Q. –X. Guo, *Synlett* **2005**, *(19)* 2990-2992.
7. J. L. Simonsen, R. Storey, *Proceedings of the Chemical Society*, London, **1910**, *25*, 290.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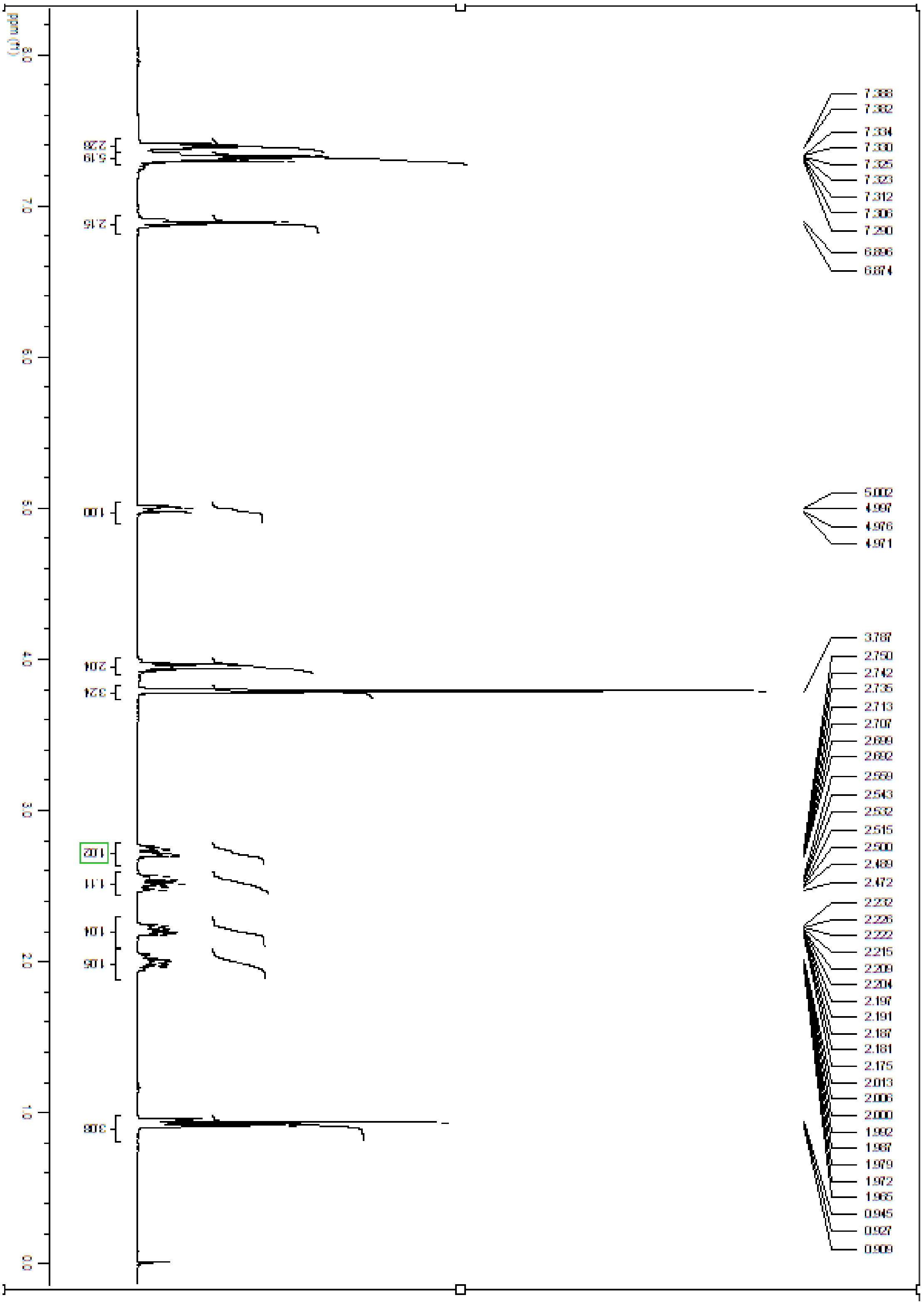
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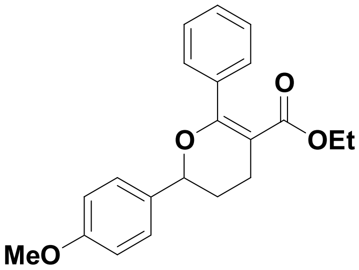
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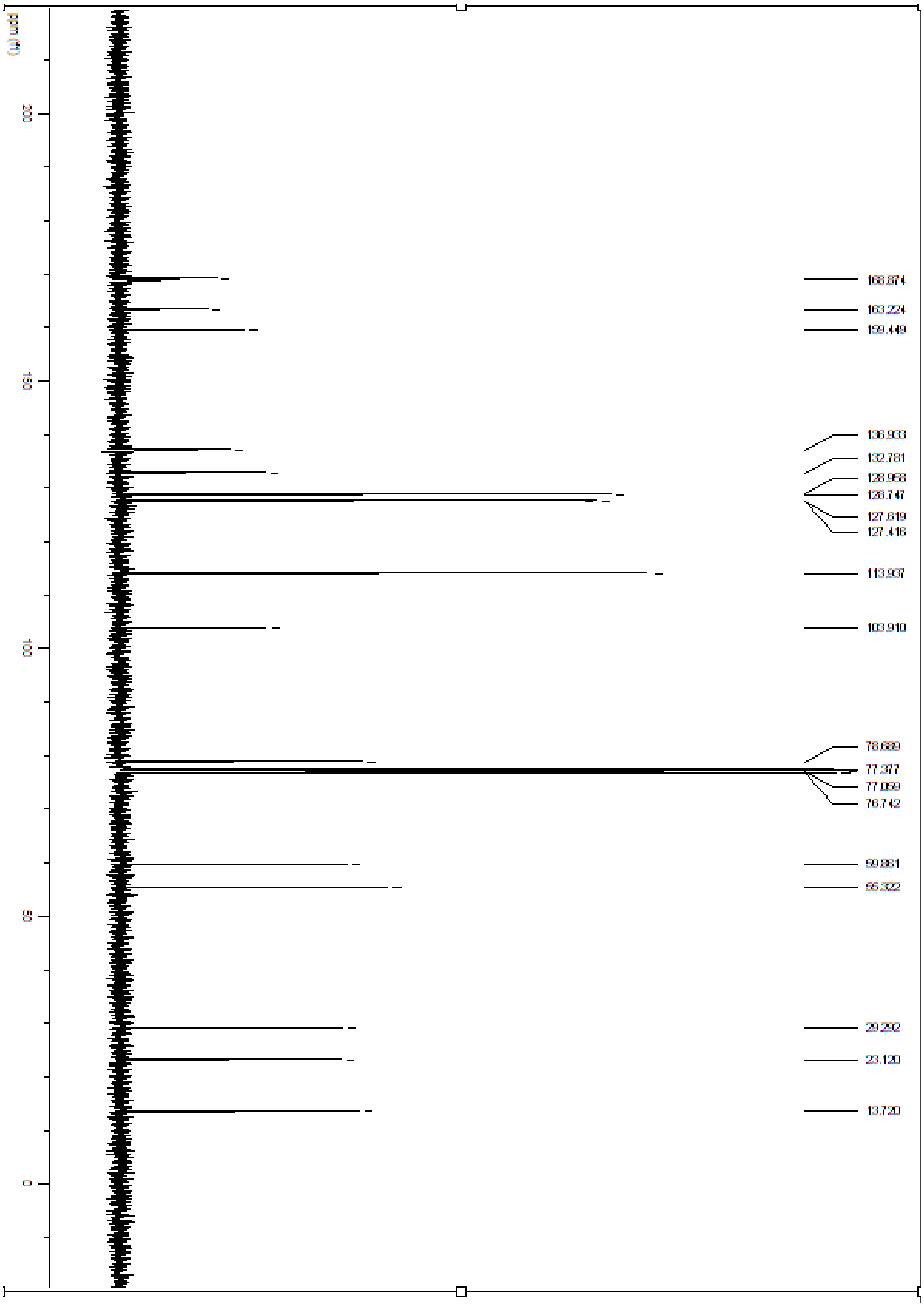
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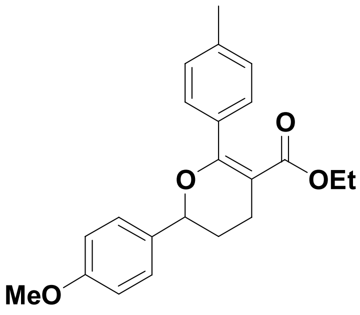
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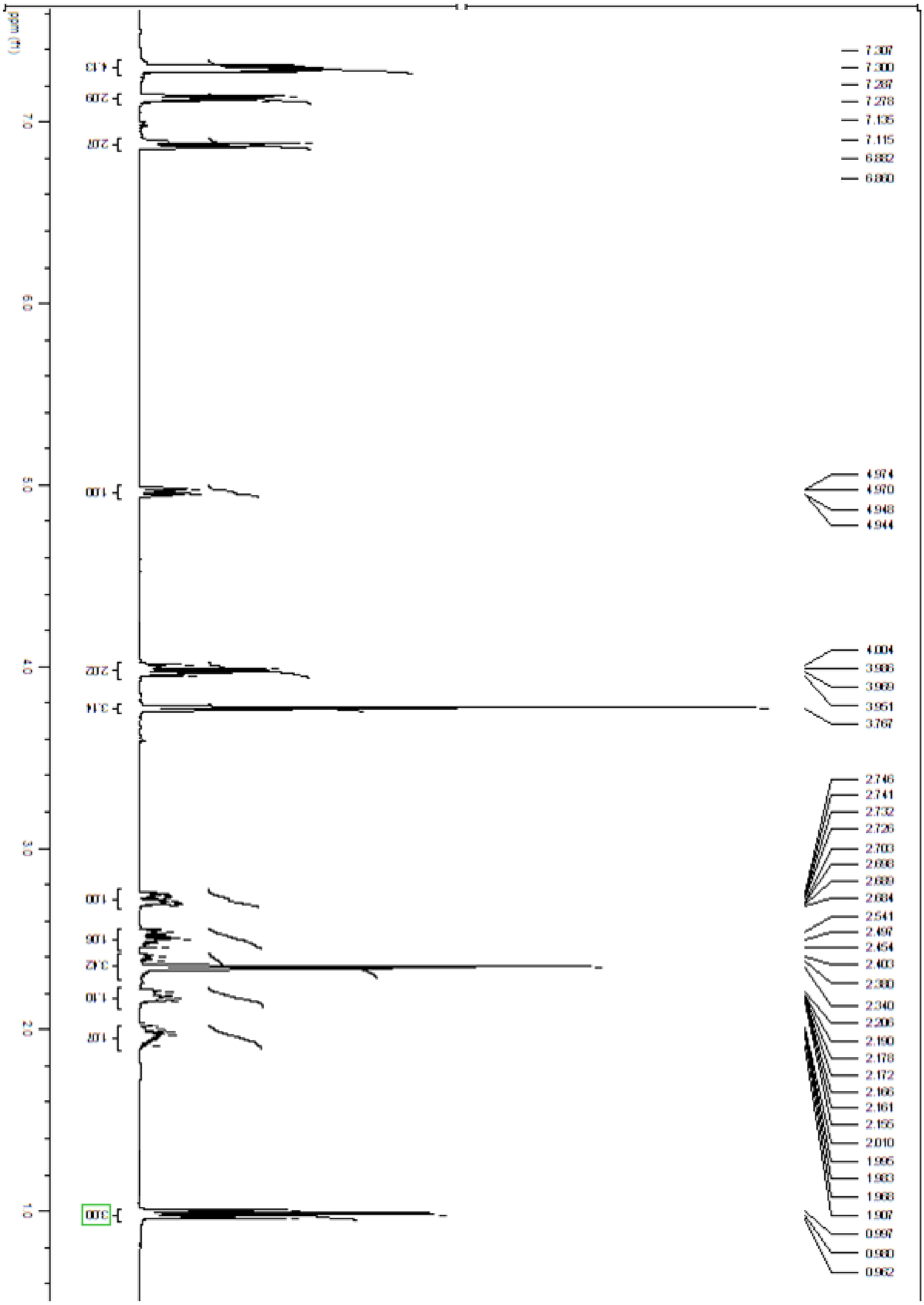
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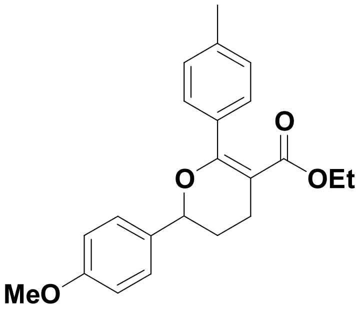
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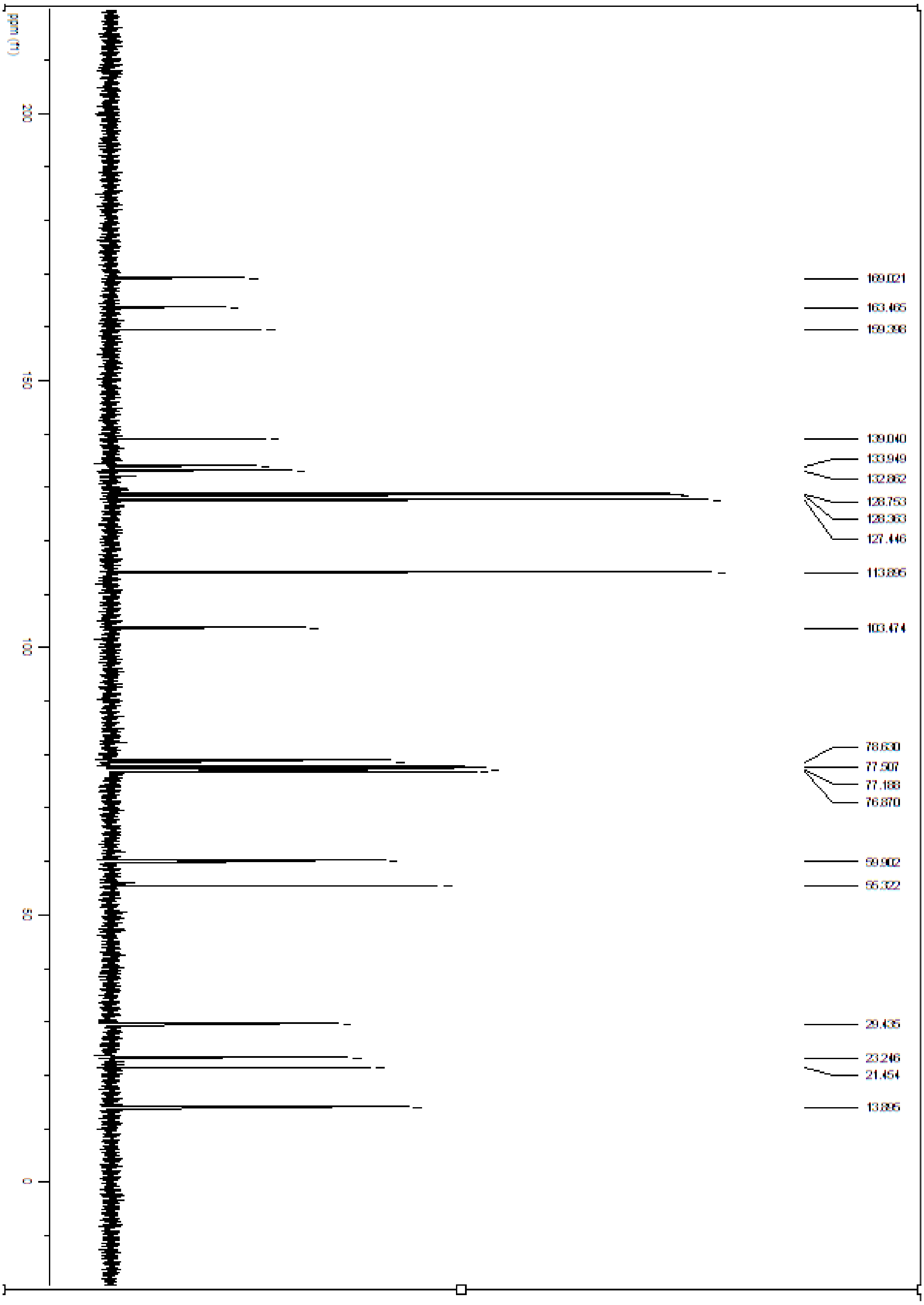
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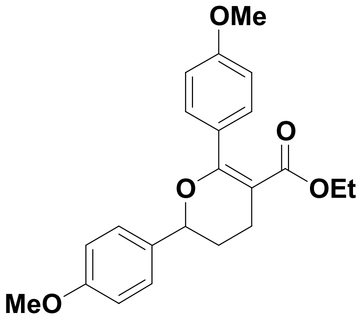
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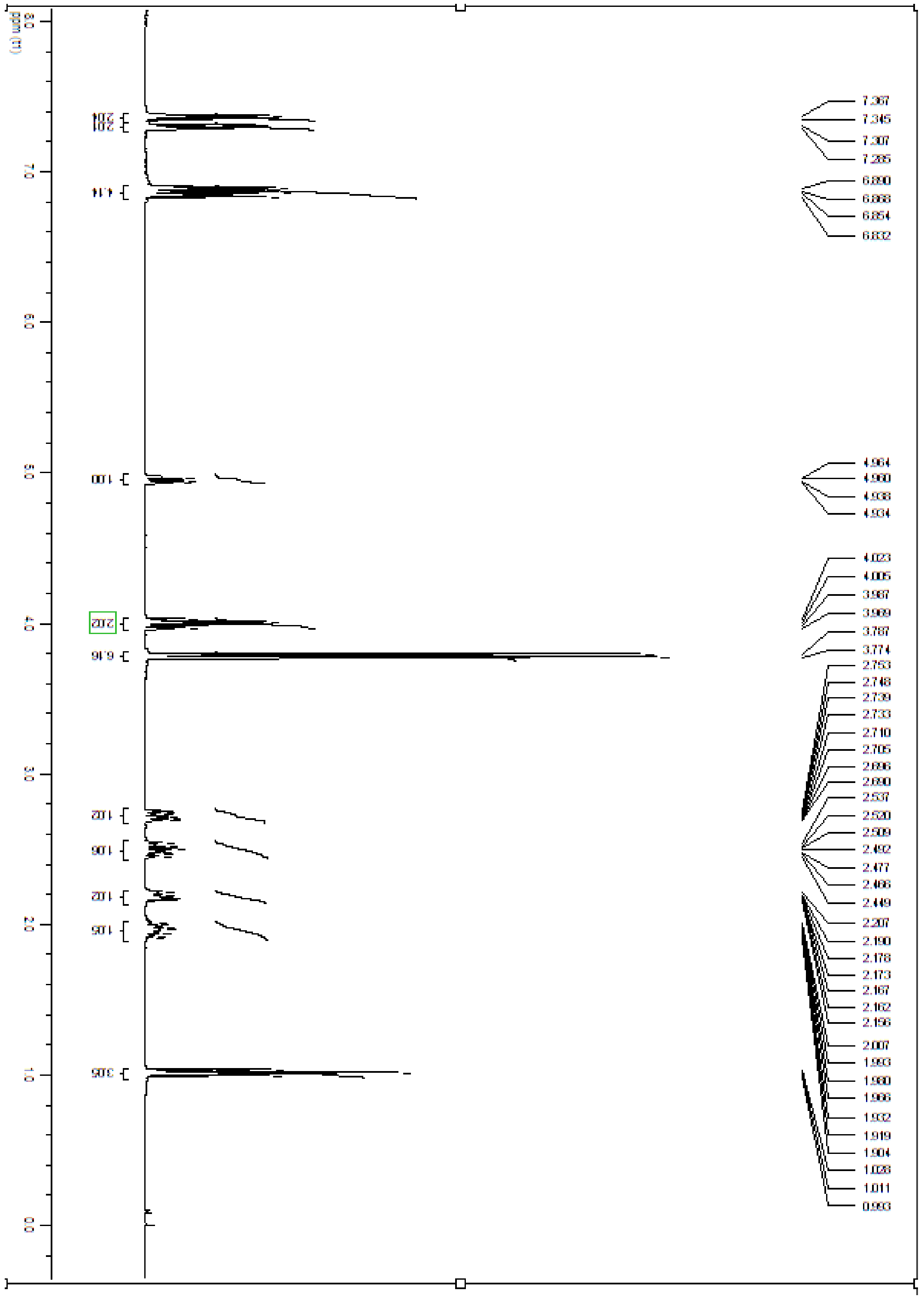
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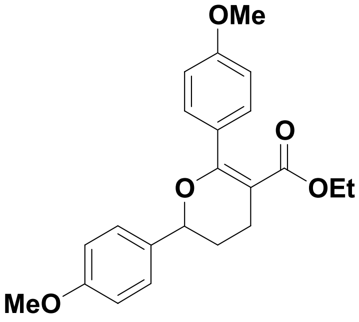
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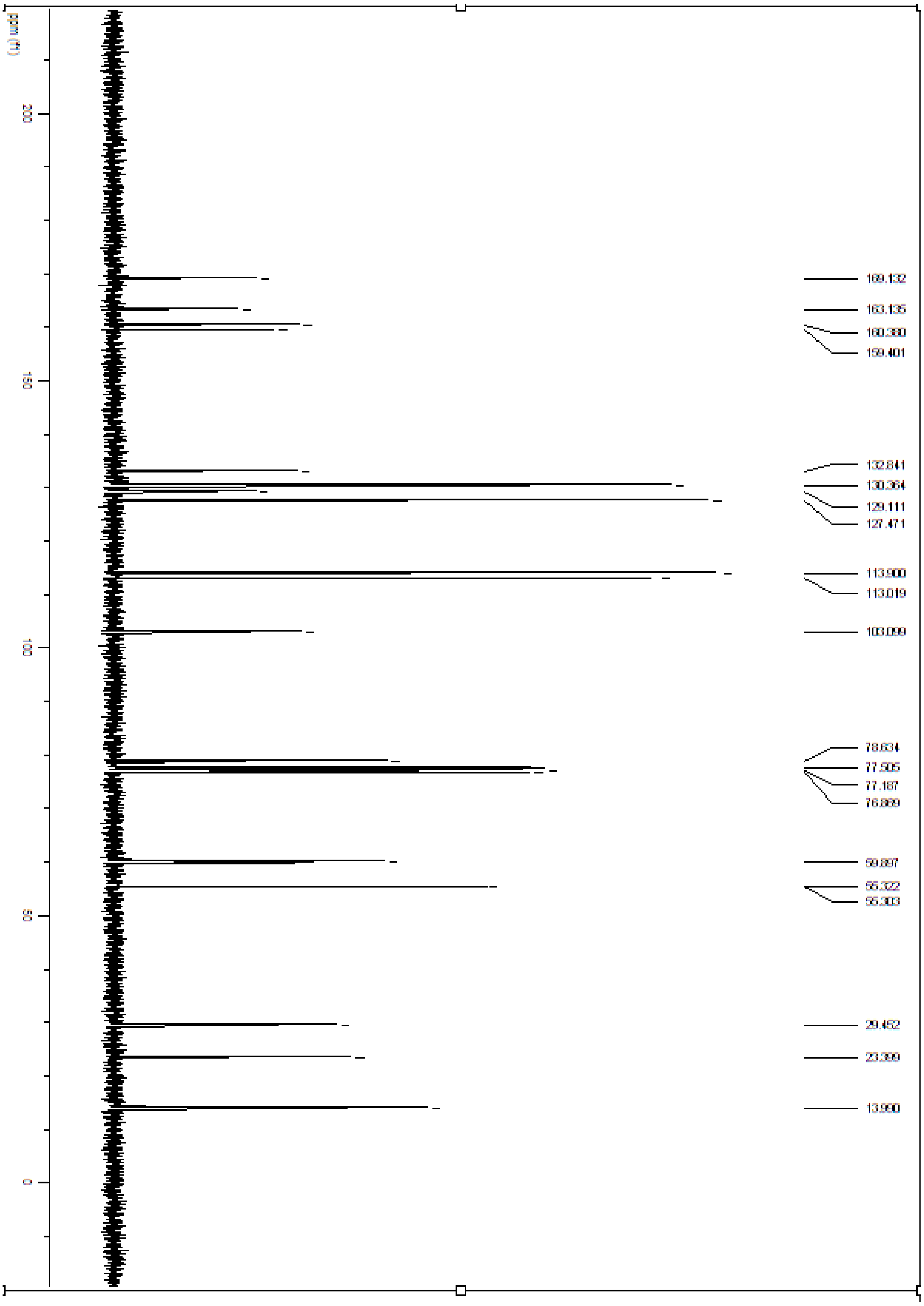
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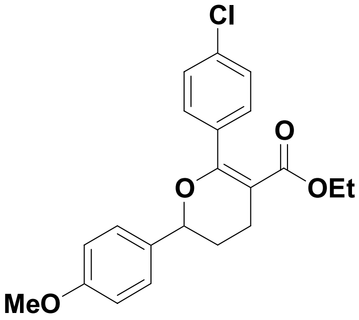
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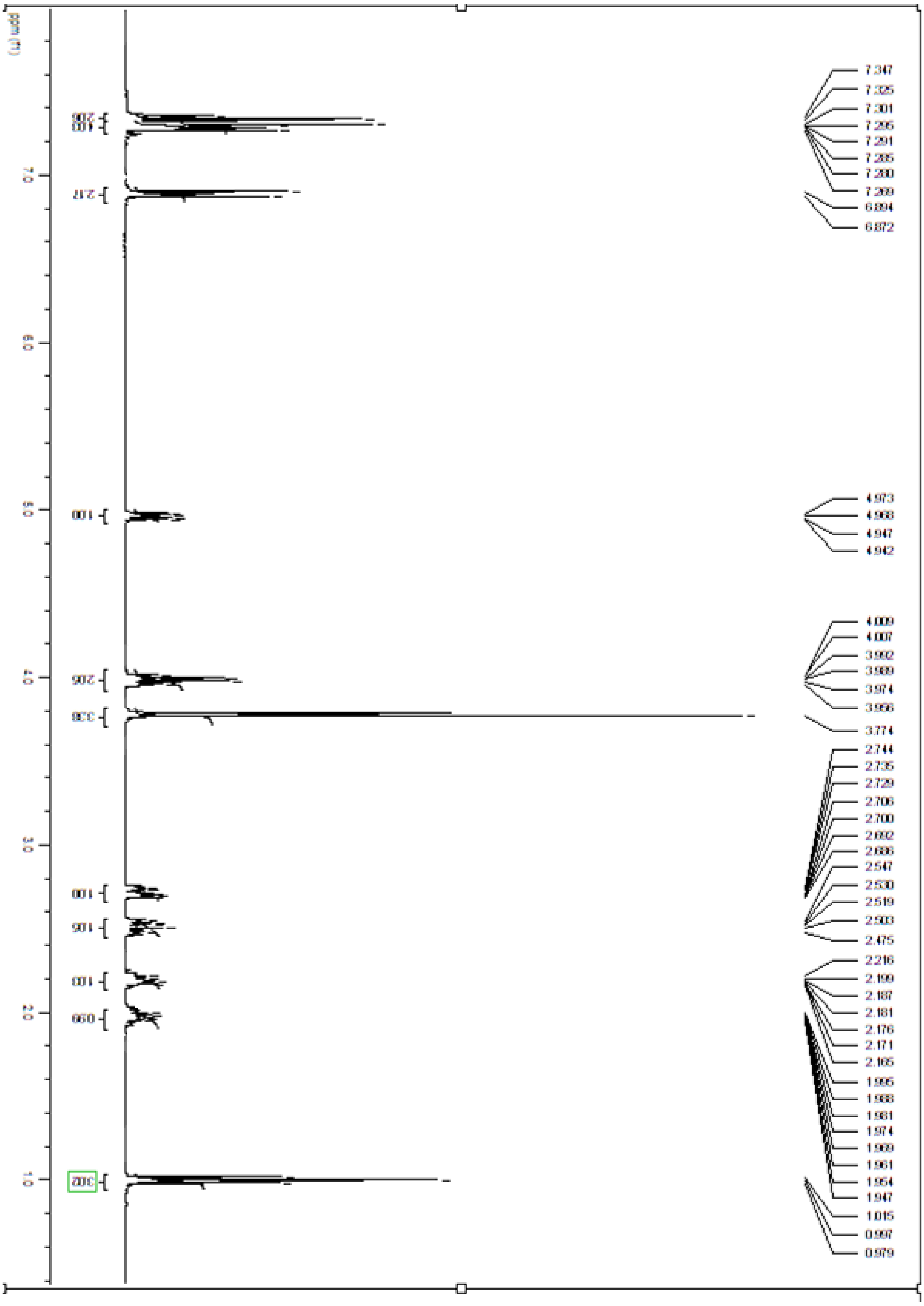
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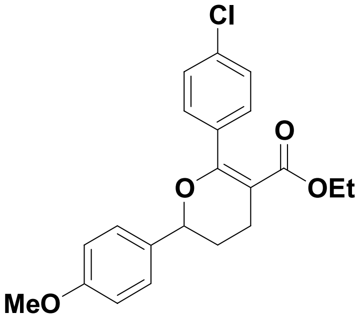
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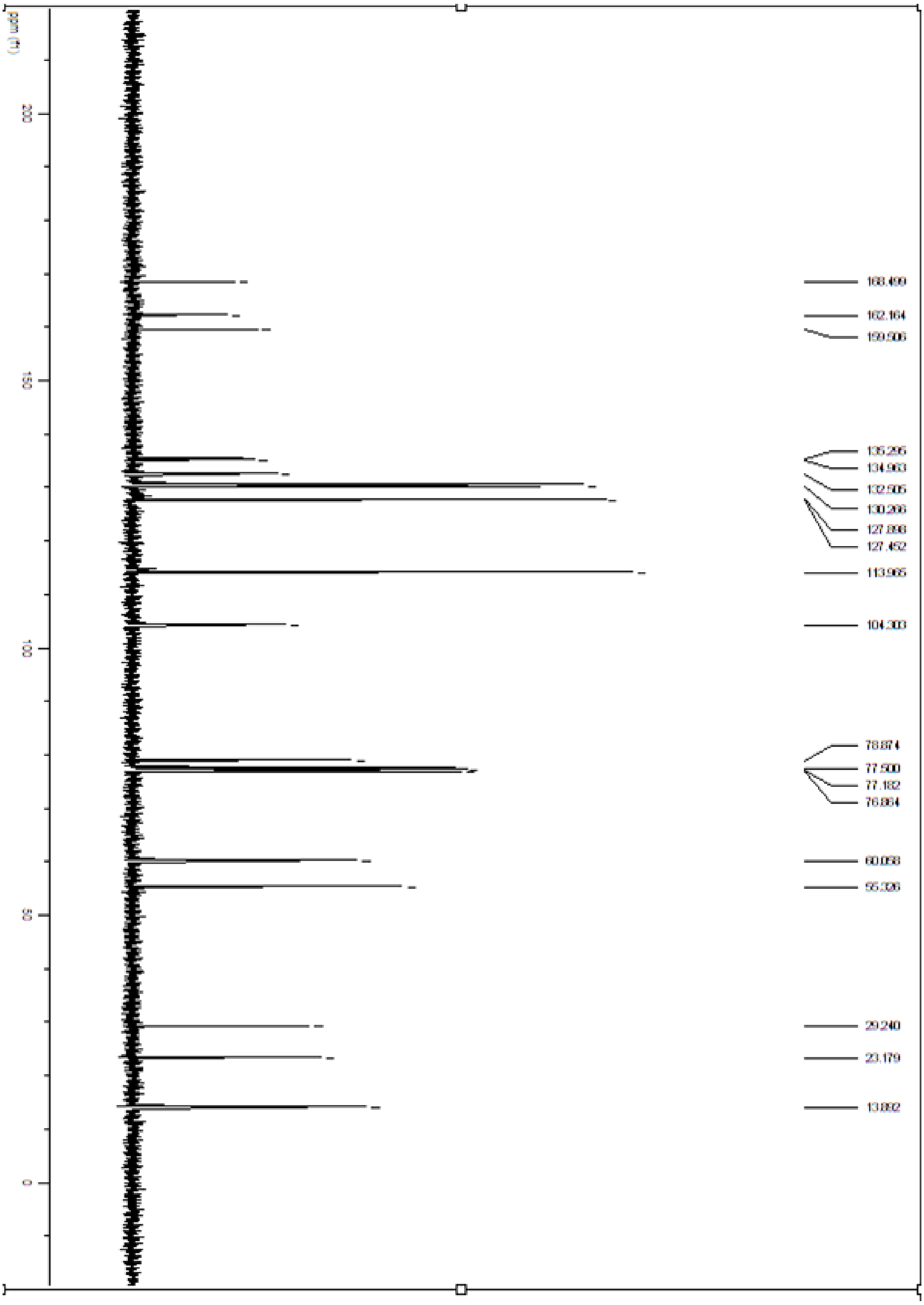
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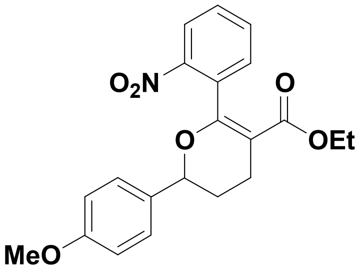
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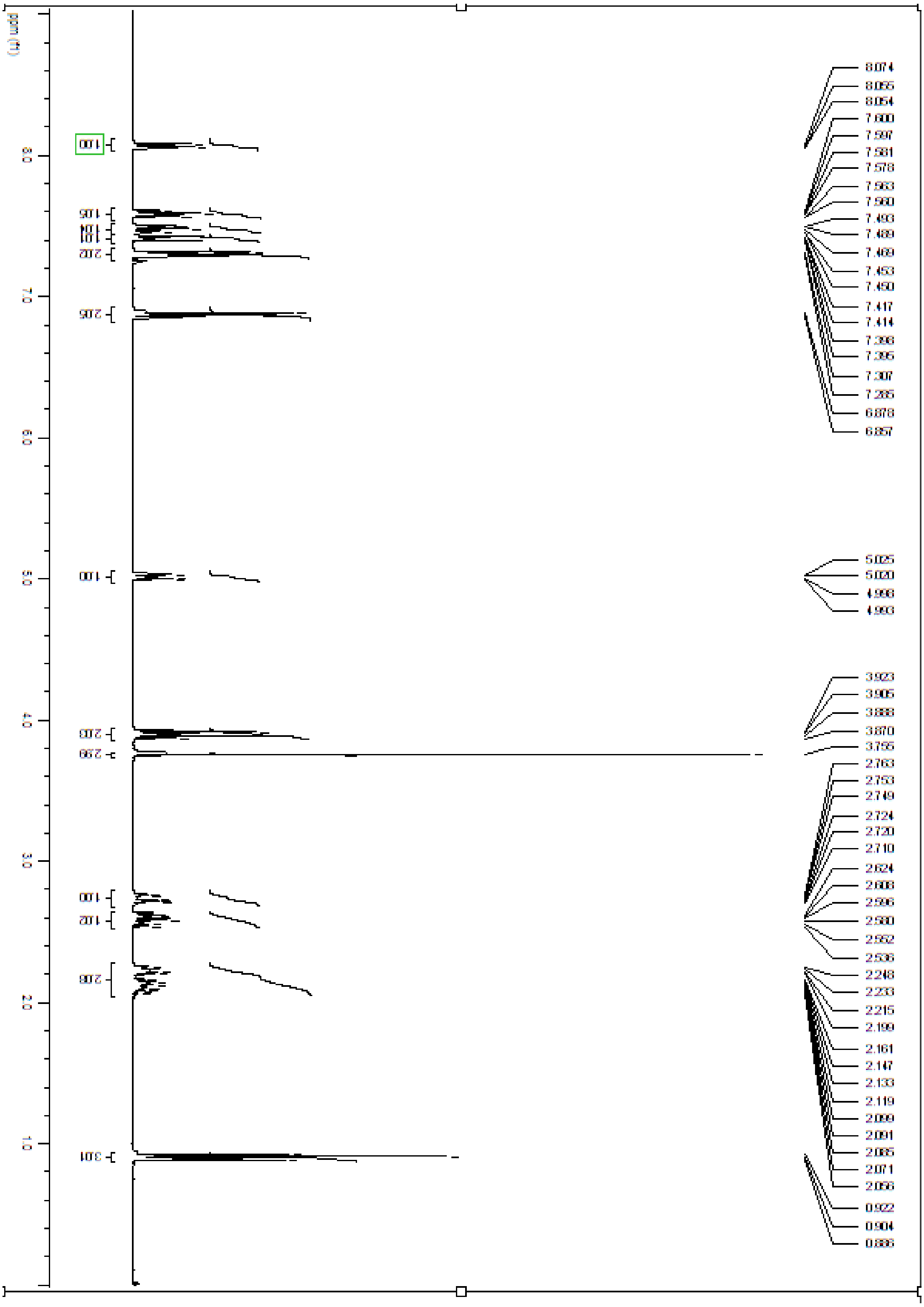
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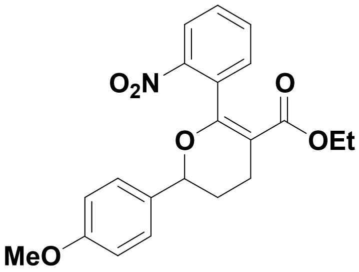
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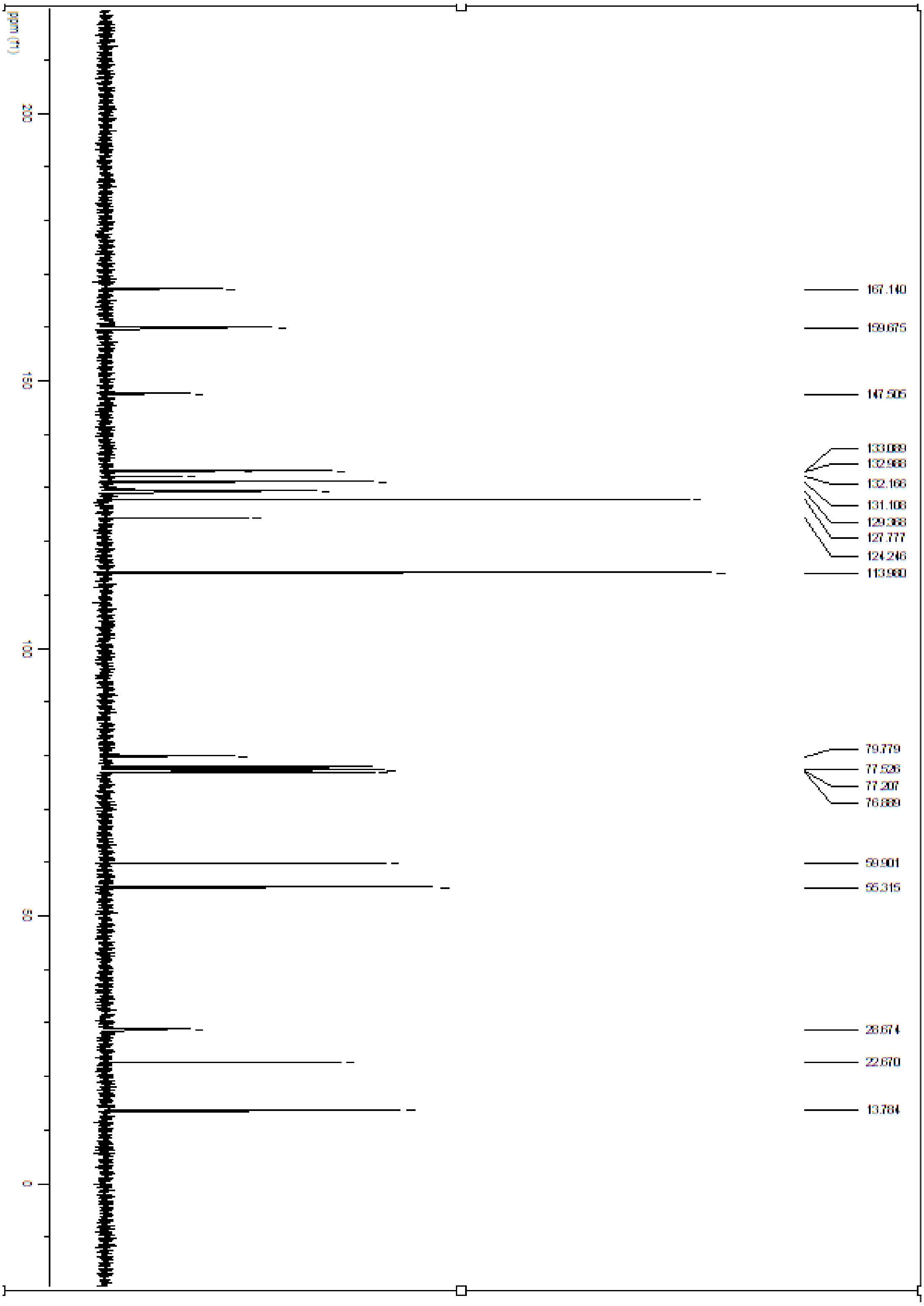
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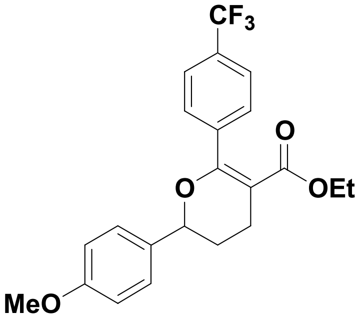
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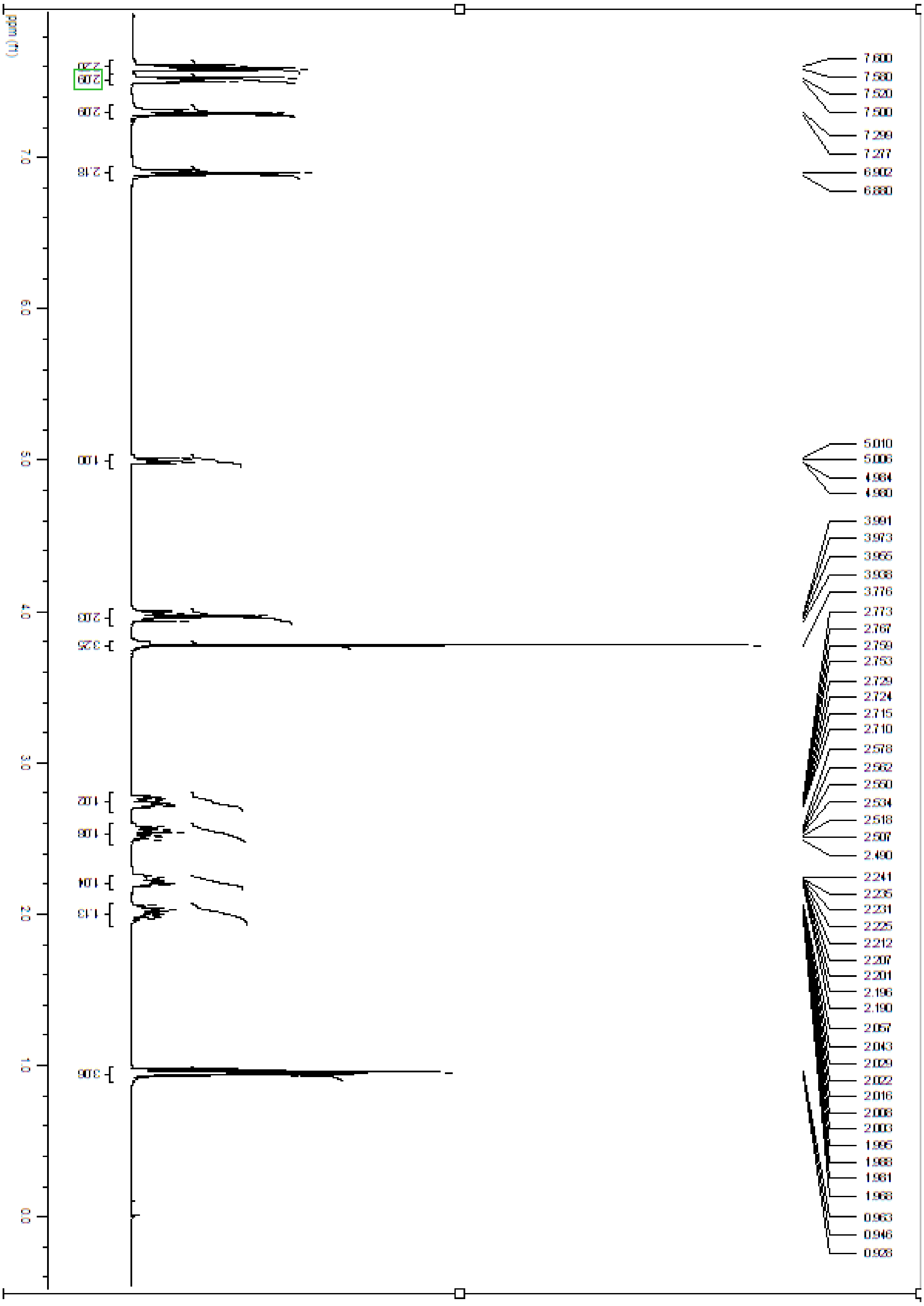
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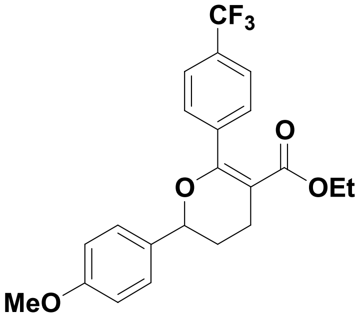
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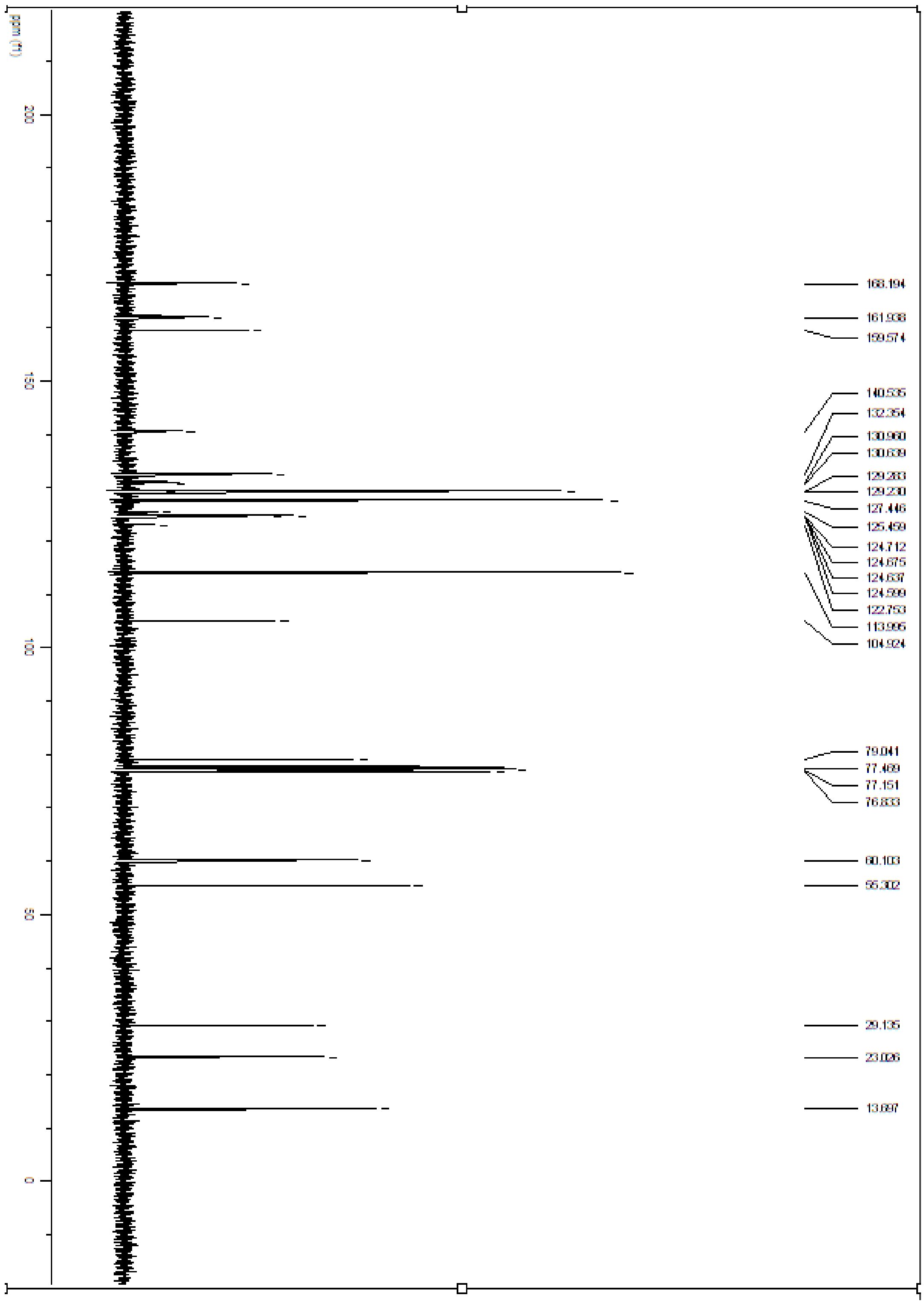
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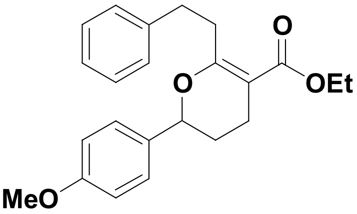
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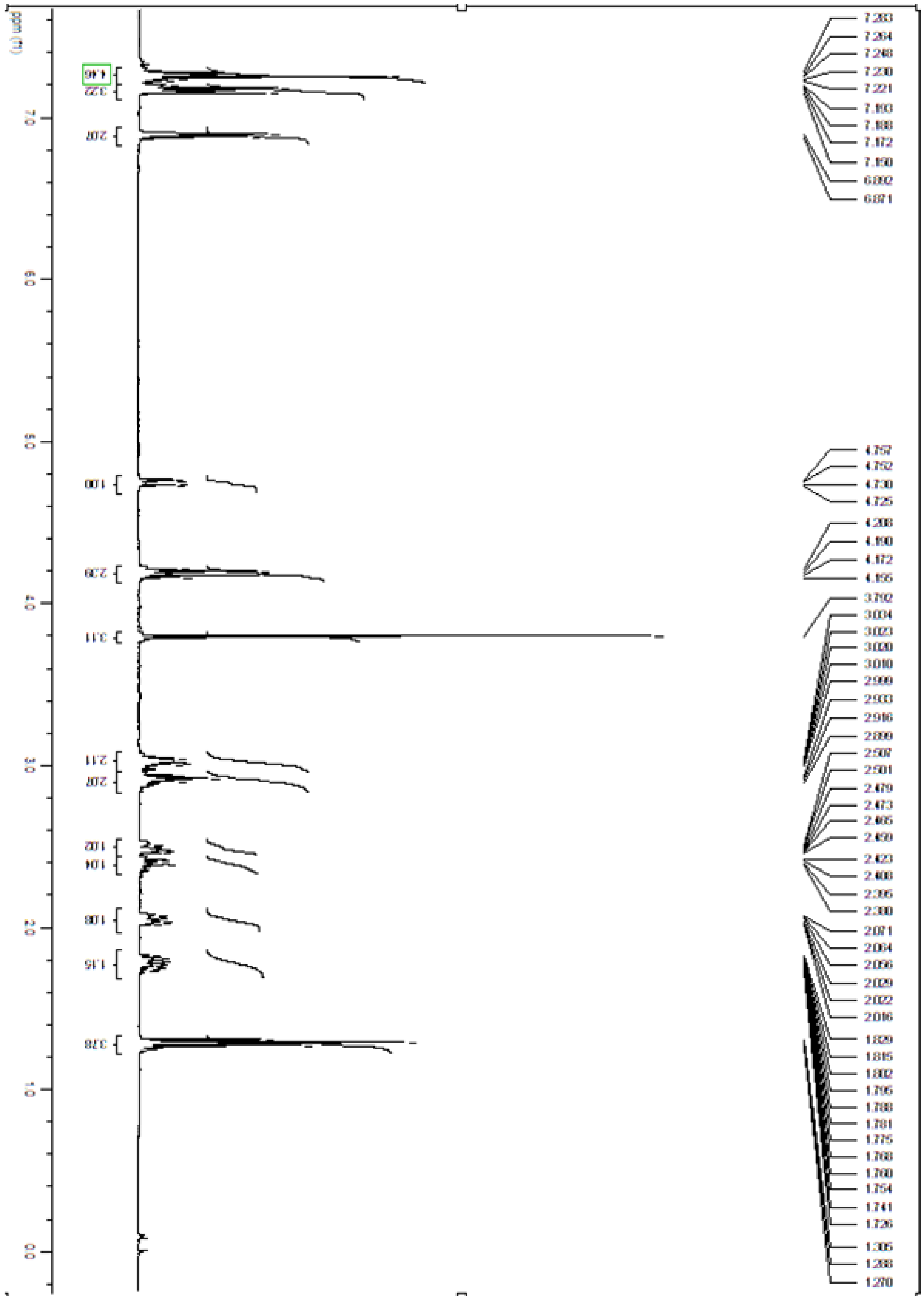
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1.802
1.795
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1.775
1.768
1.760
1.754
1.741
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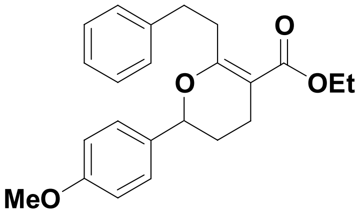
1.288
1.270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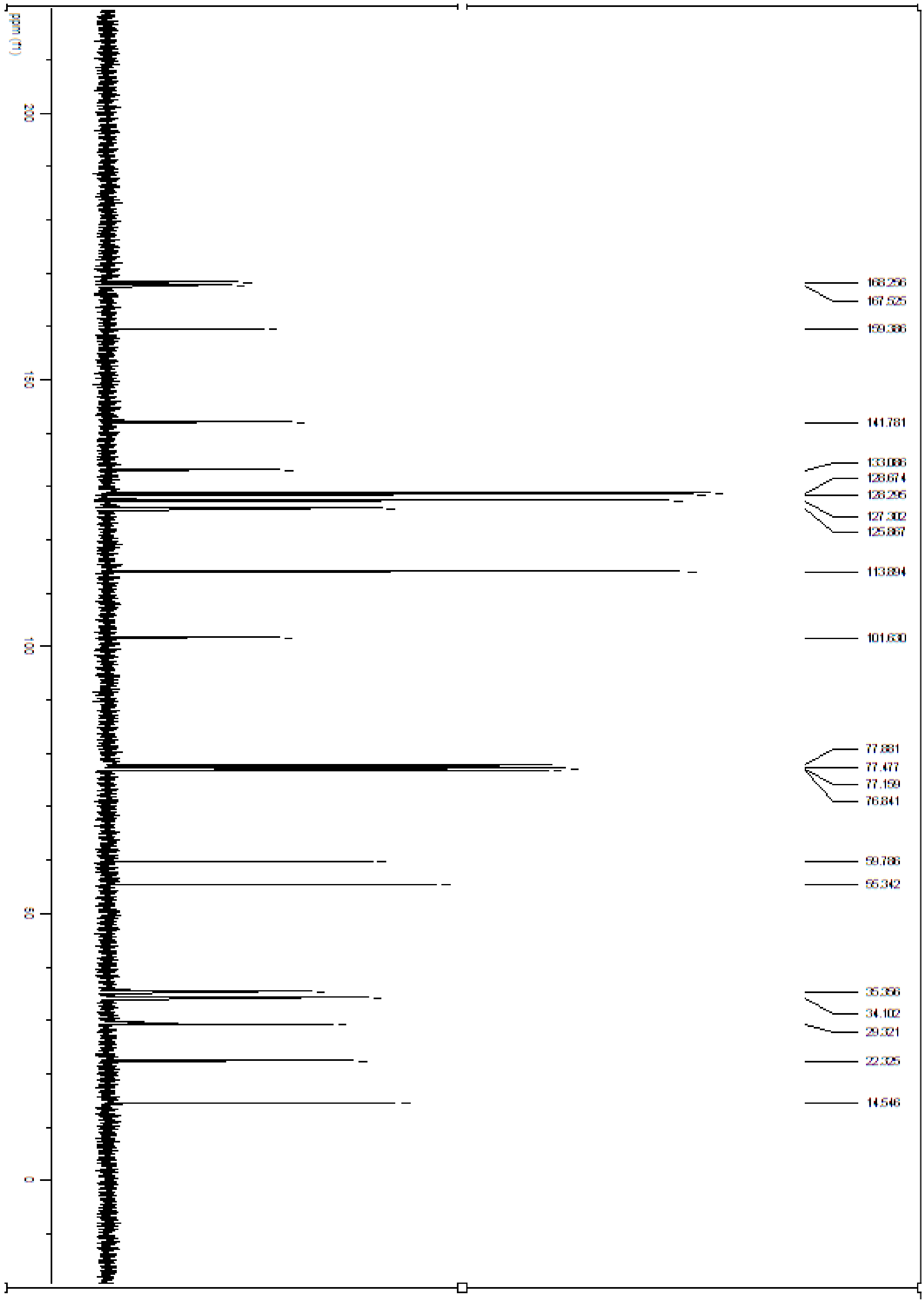
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127.302
125.867
113.894
101.630
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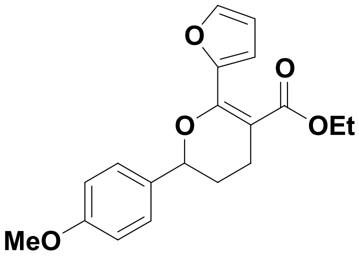
76.841
59.786
55.342
35.356
34.102
29.321
22.325
14.546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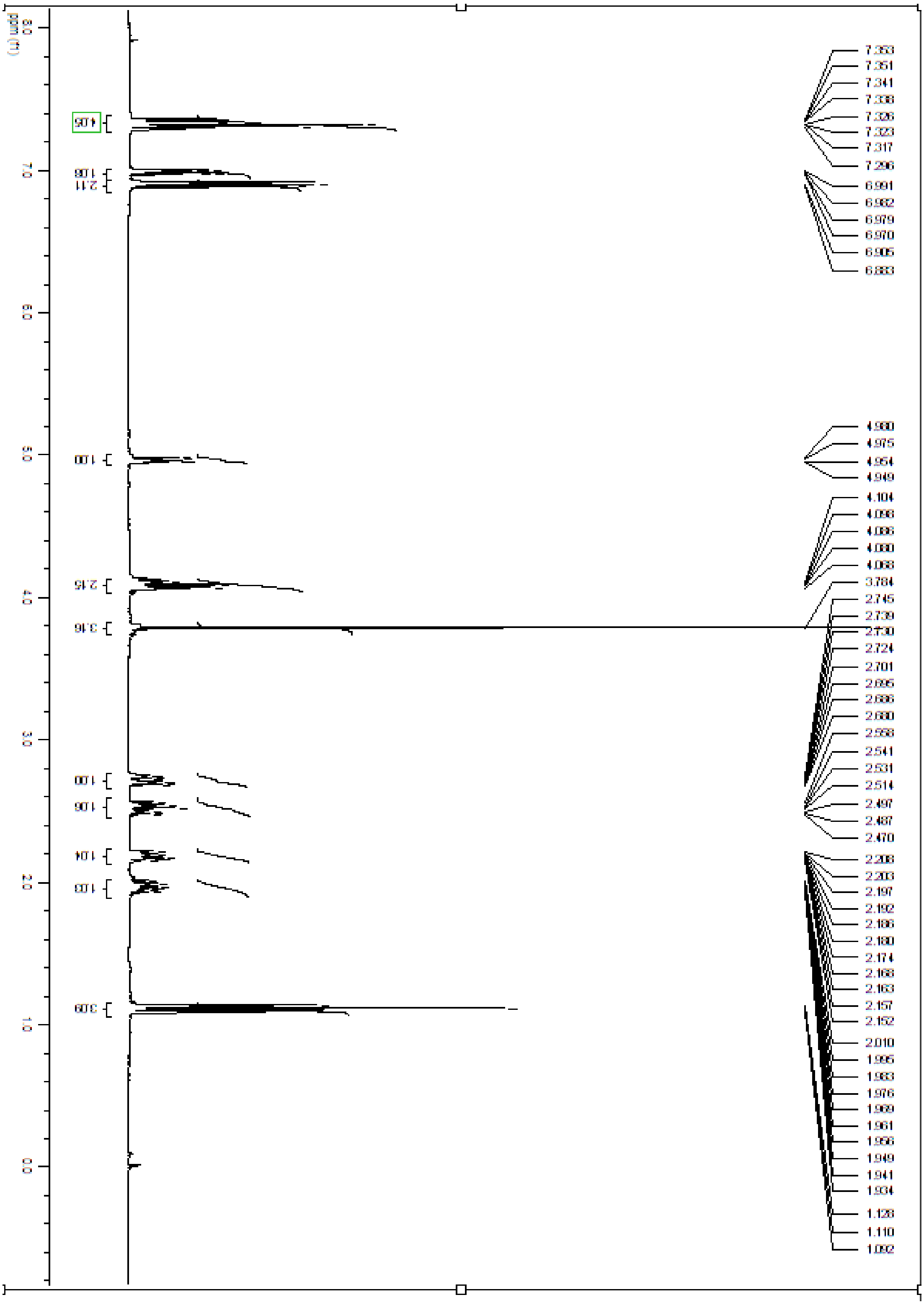
MeO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0.0
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2.11
1.00
2.15
3.16
1.00
1.06
1.04
1.03
3.09
7.353
7.351
7.341
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7.323
7.317
7.296
6.991
6.982
6.979
6.970
6.905
6.883
4.980
4.975
4.954
4.949
4.104
4.098
4.086
4.080
4.068
3.784
2.745
2.739
2.730
2.724
2.701
2.695
2.686
2.680
2.558
2.541
2.531
2.514
2.497
2.487
2.470
2.208
2.203
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2.192
2.186
2.180
2.174
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2.163
2.157
2.152
2.010
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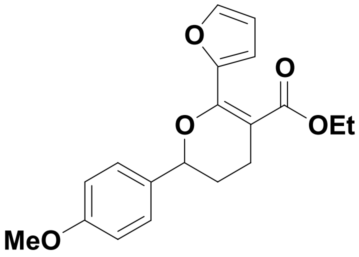
1.092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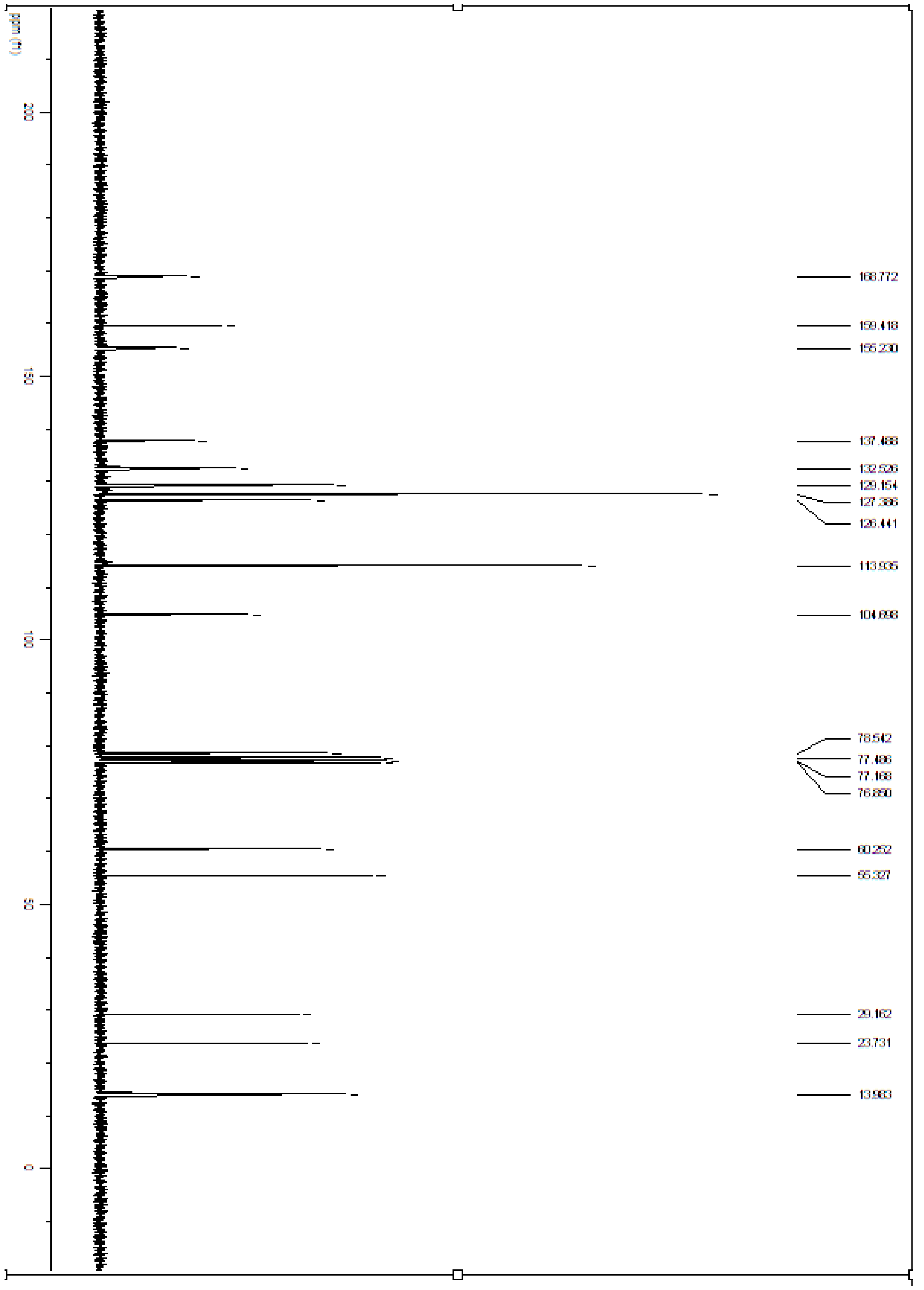
O
OEt
MeO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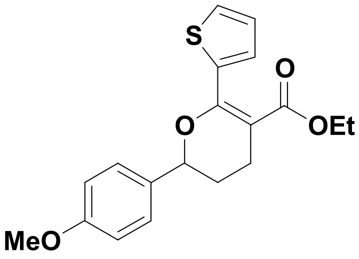
23.731
13.983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OEt
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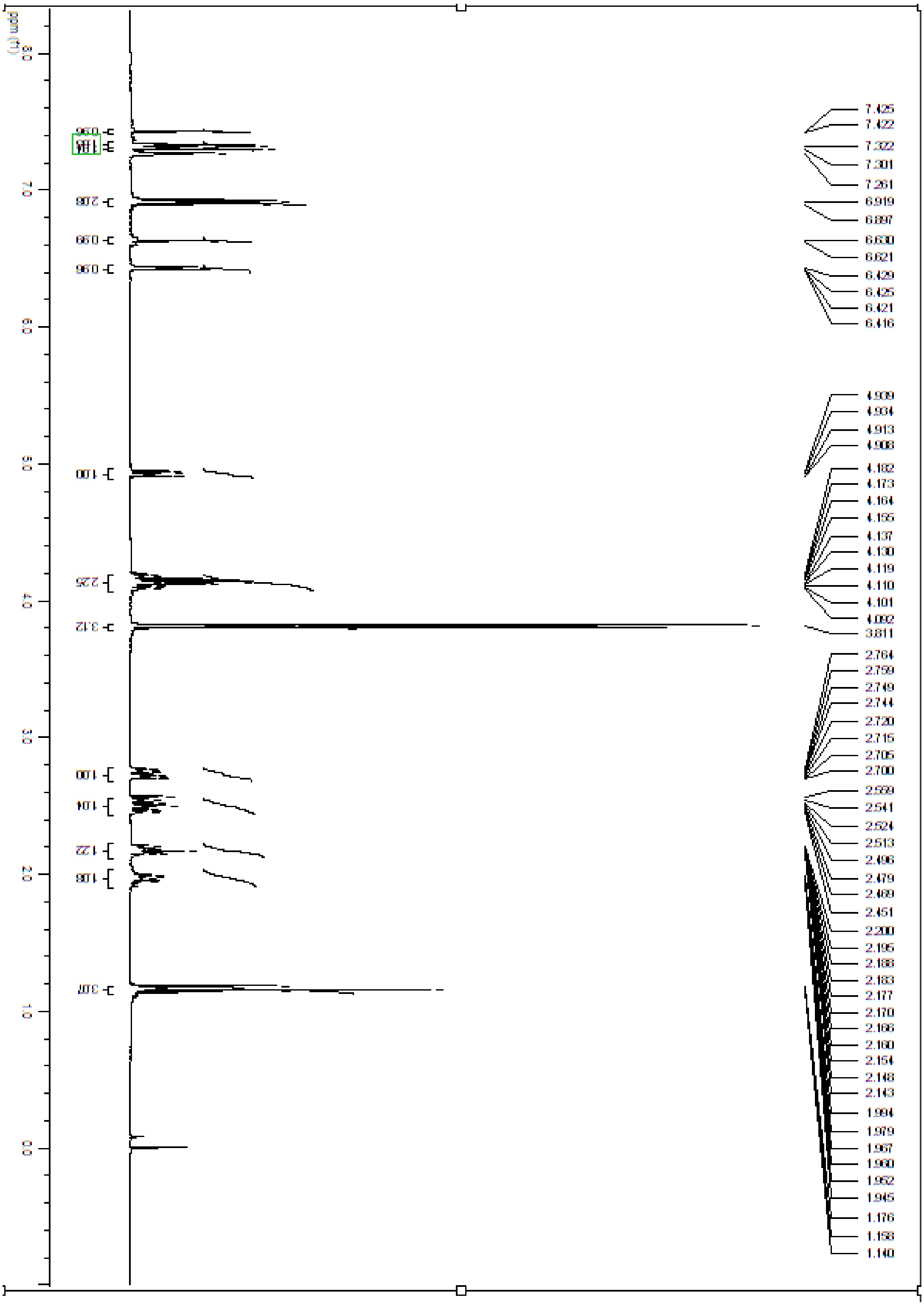
MeO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0.99
0.96
1.00
2.25
3.12
1.00
1.04
1.22
1.08
3.07
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7.422
7.322
7.301
7.261
6.919
6.897
6.630
6.621
6.429
6.425
6.421
6.416
4.939
4.934
4.913
4.908
4.182
4.173
4.164
4.155
4.137
4.130
4.119
4.110
4.101
4.092
3.811
2.764
2.759
2.749
2.744
2.720
2.715
2.705
2.700
2.559
2.541
2.524
2.513
2.496
2.479
2.469
2.451
2.200
2.195
2.188
2.183
2.177
2.170
2.166
2.160
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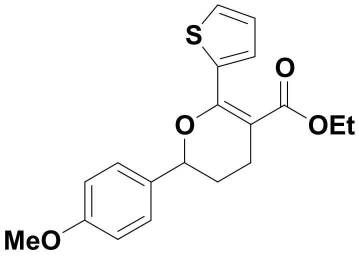
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OEt
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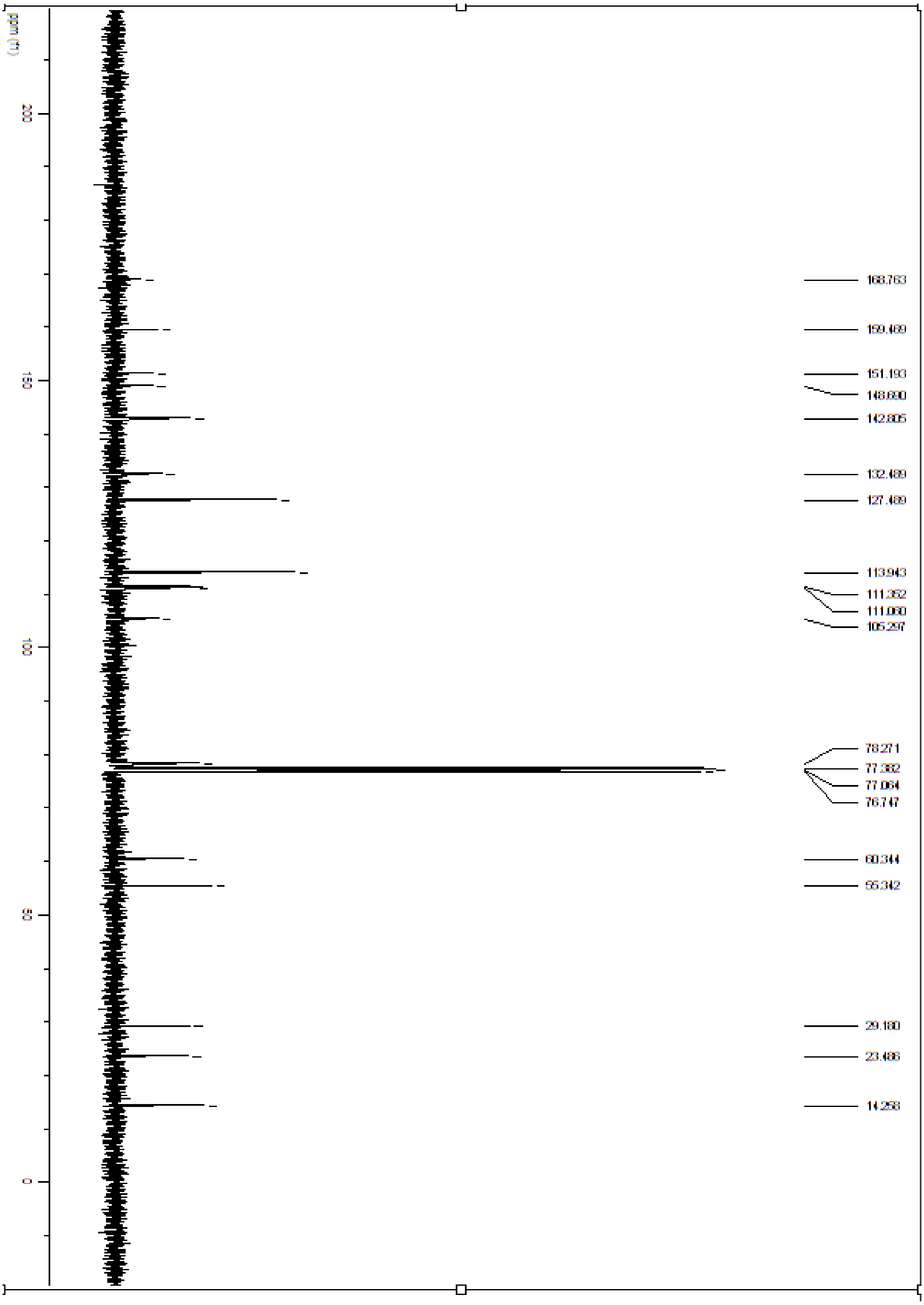
MeO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127.489
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111.080
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77.382
77.064
76.747
60.344
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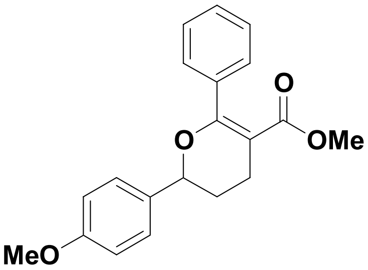
29.180
23.486
14.258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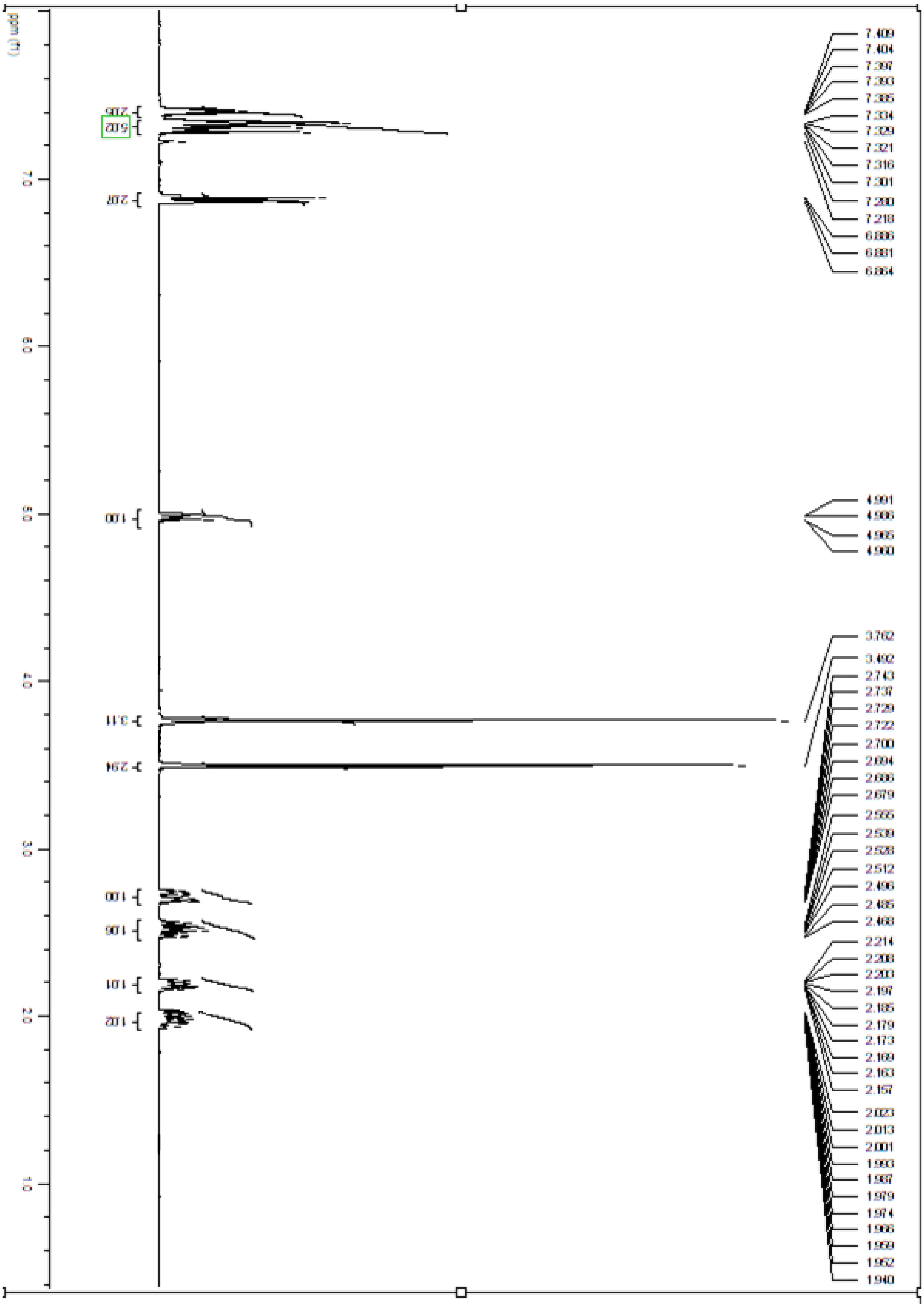
O
MeO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1.00
3.11
2.94
1.00
1.06
1.01
1.02
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7.404
7.397
7.393
7.385
7.334
7.329
7.321
7.316
7.301
7.280
7.218
6.896
6.881
6.864
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4.986
4.965
4.960
3.762
3.492
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2.737
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2.722
2.700
2.694
2.686
2.679
2.535
2.530
2.528
2.512
2.496
2.485
2.468
2.214
2.208
2.203
2.197
2.185
2.179
2.173
2.169
2.163
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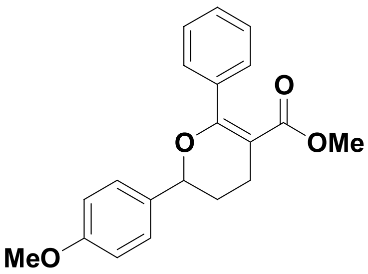
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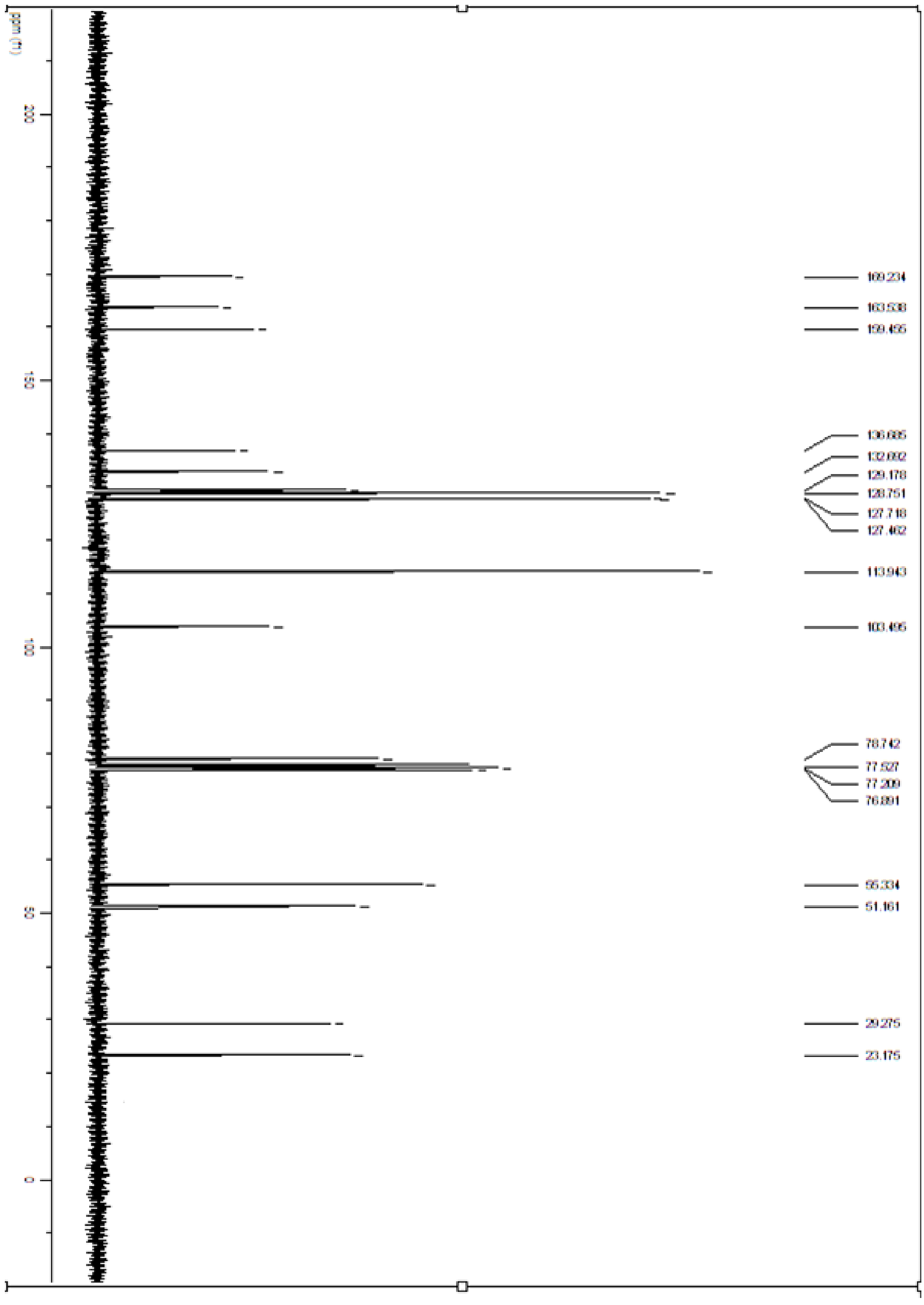
OMe
O
MeO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129.178
128.751
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127.462
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103.495
78.742
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77.209
76.891
55.334
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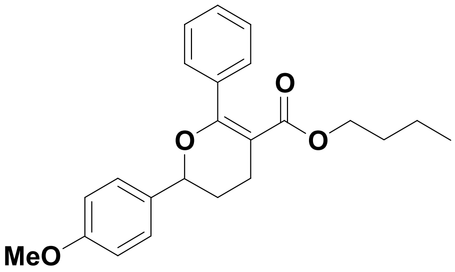
23.175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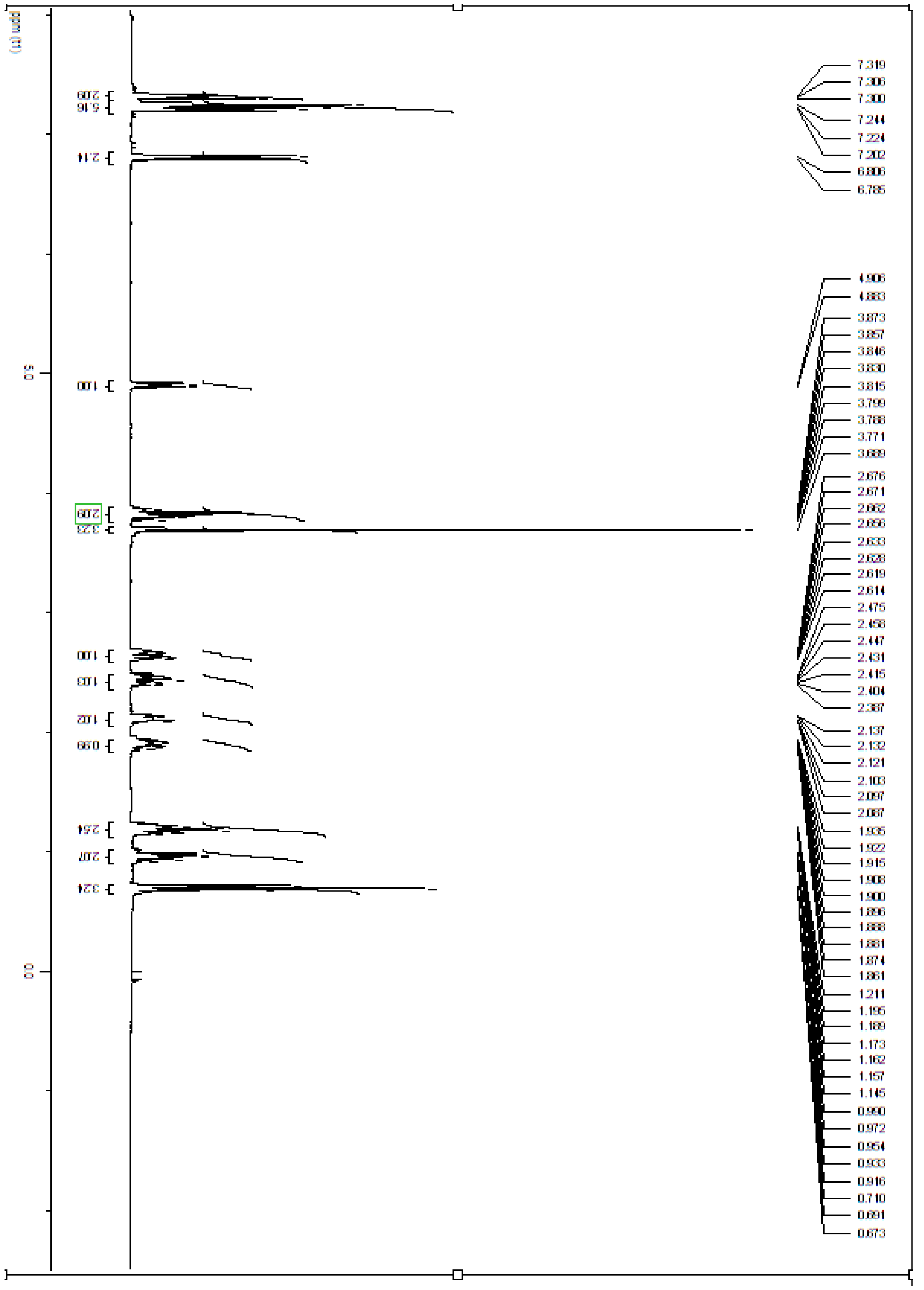
O
O
MeO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1.00
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2.07
3.24
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7.300
7.244
7.224
7.202
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6.785
4.906
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3.873
3.857
3.846
3.830
3.815
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3.788
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2.671
2.662
2.656
2.633
2.628
2.619
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2.475
2.458
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2.137
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2.121
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2.097
2.087
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1.922
1.915
1.908
1.900
1.896
1.888
1.881
1.874
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1.189
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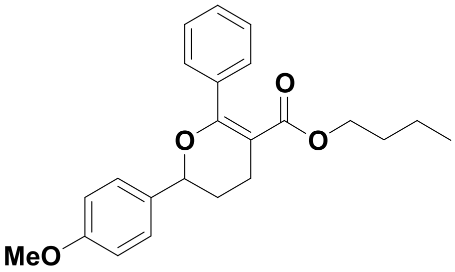
0.673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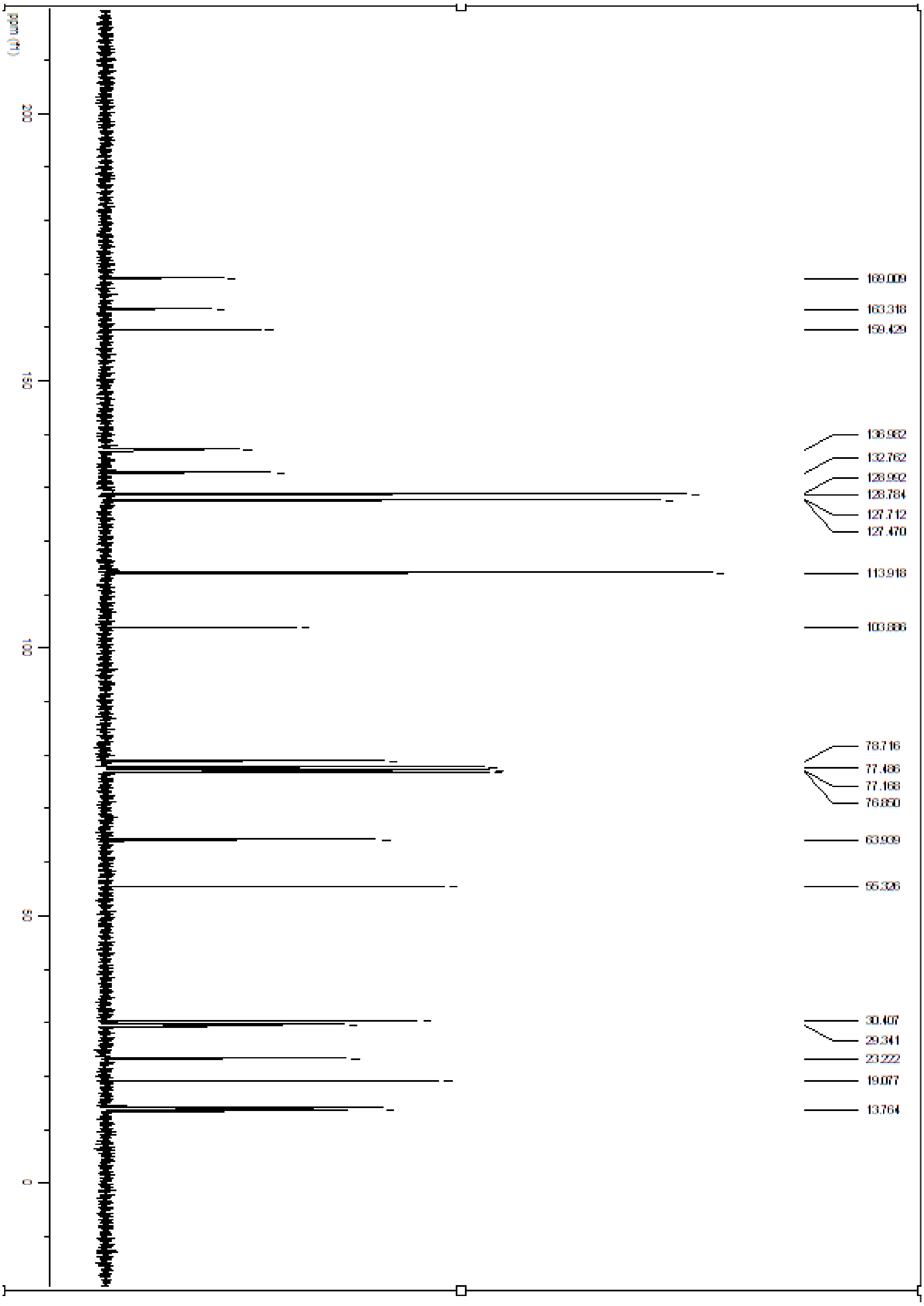
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127.712
127.470
113.918
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76.850
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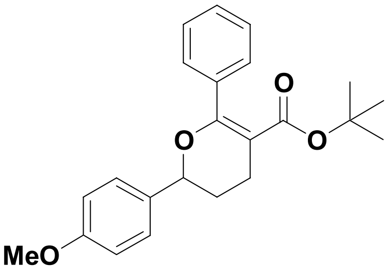
13.764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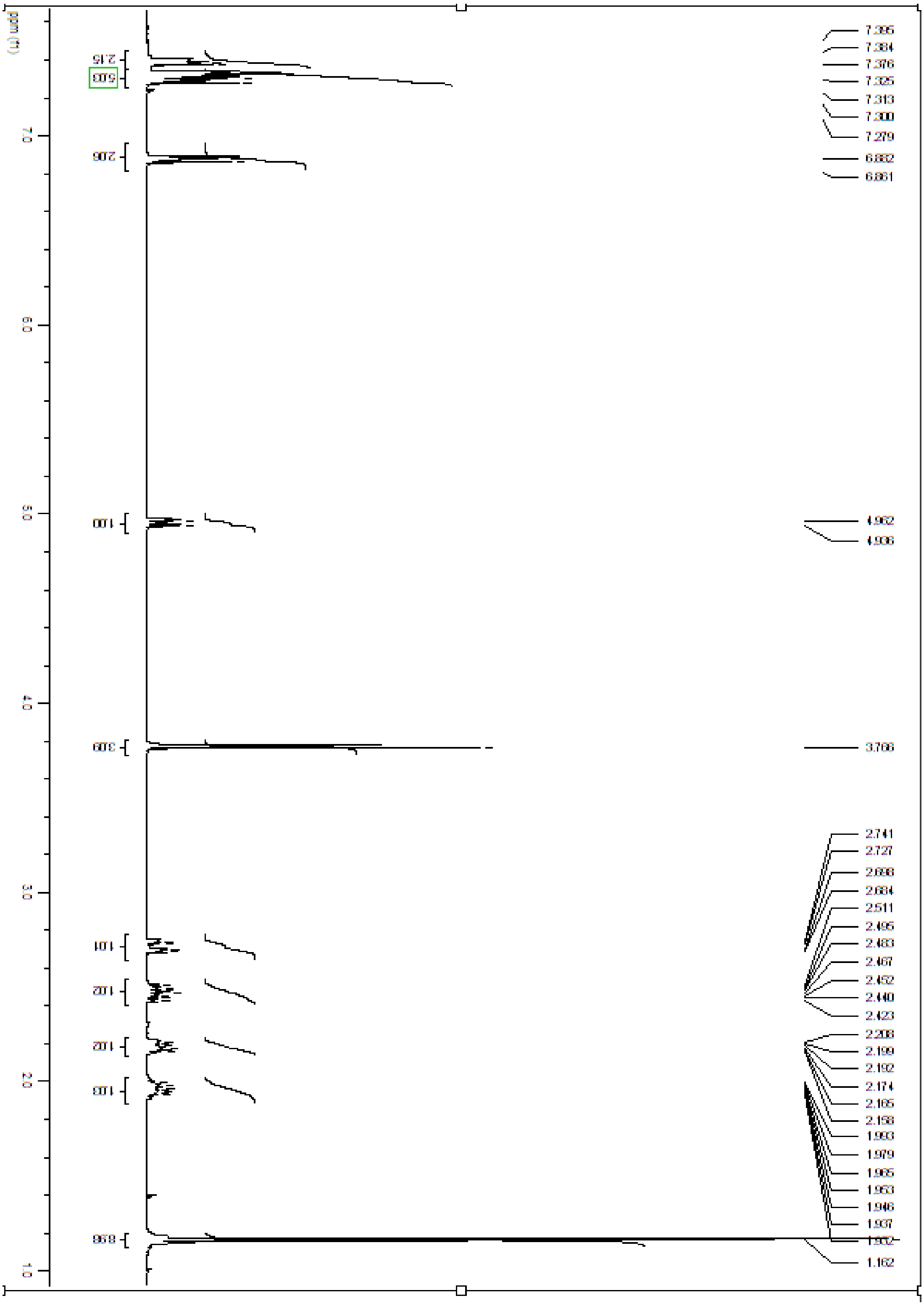
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3.09
1.01
1.02
1.02
1.03
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7.300
7.279
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6.861
4.962
4.936
3.766
2.741
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2.495
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2.192
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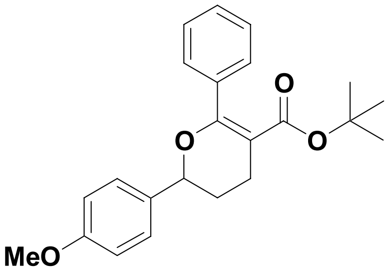
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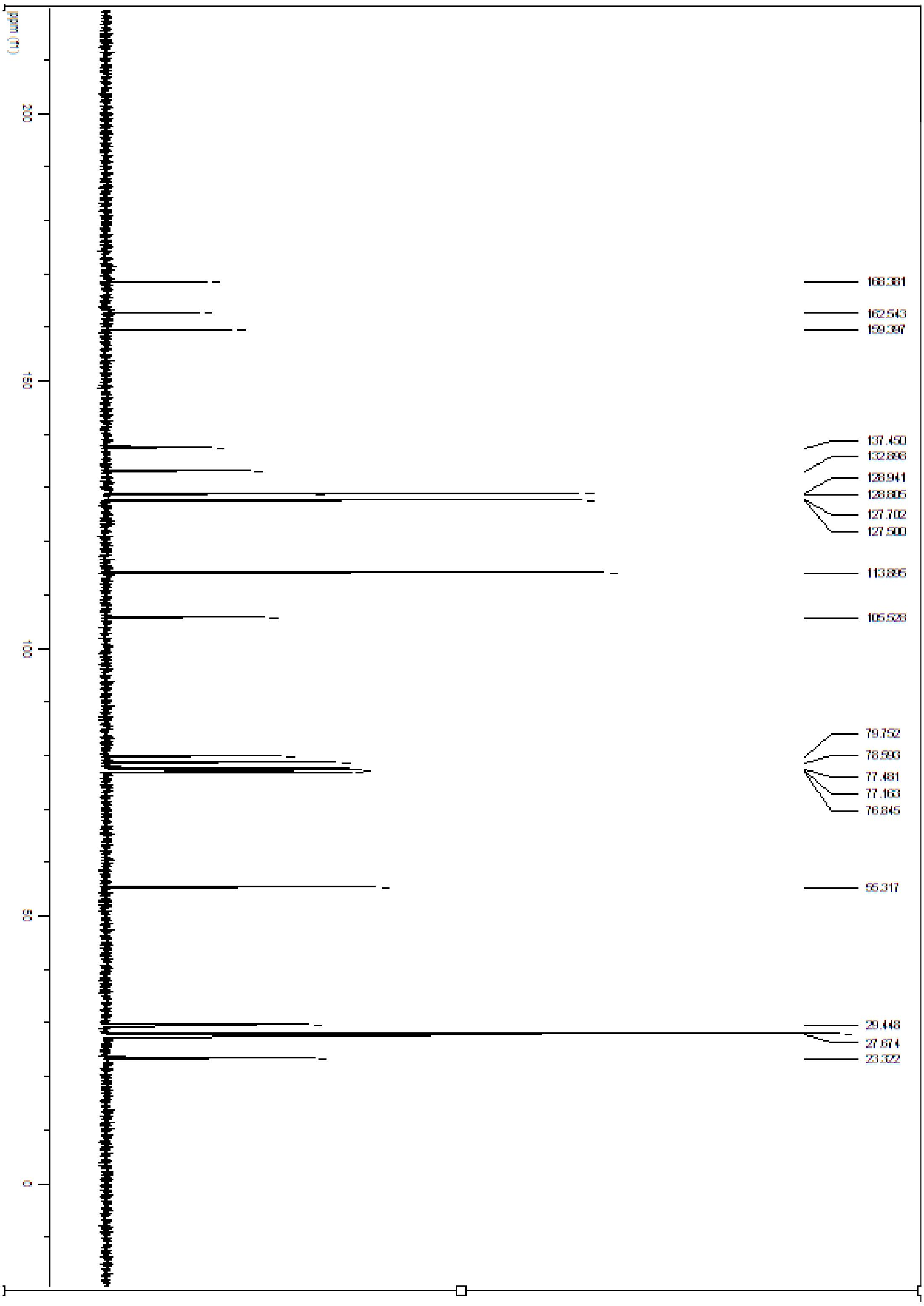
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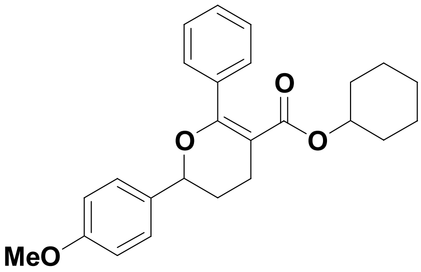
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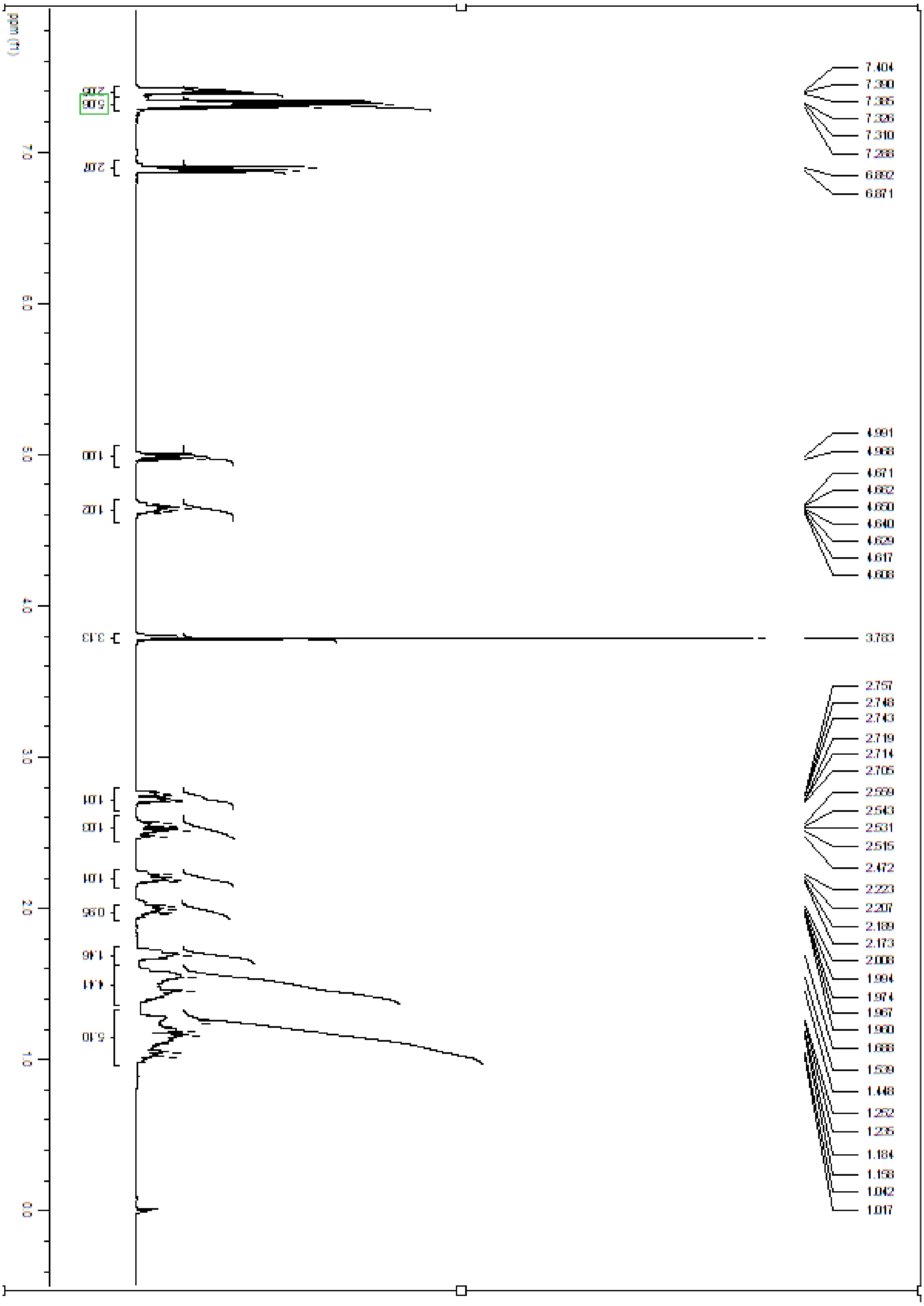
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1.02
3.13
1.01
1.03
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7.310
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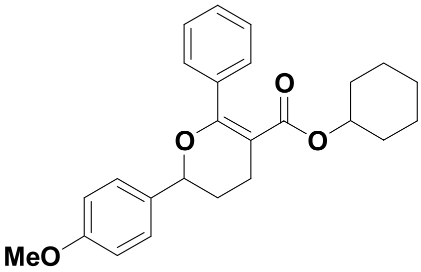
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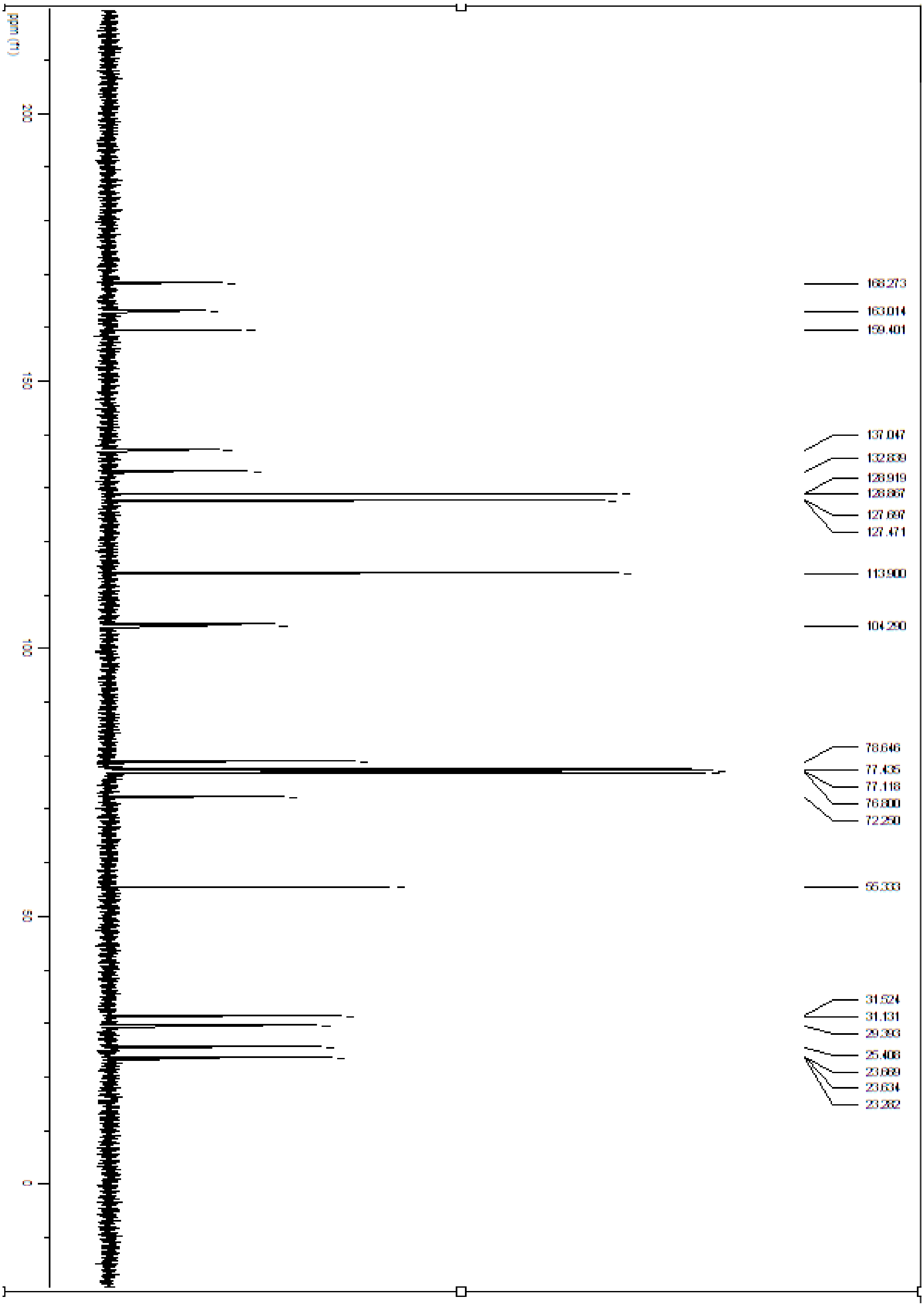
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23.634
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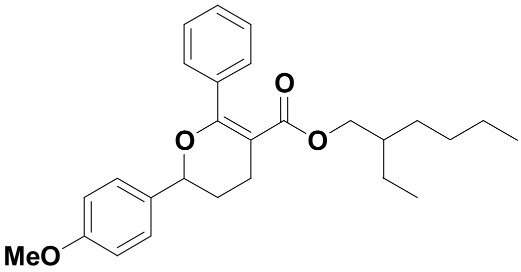
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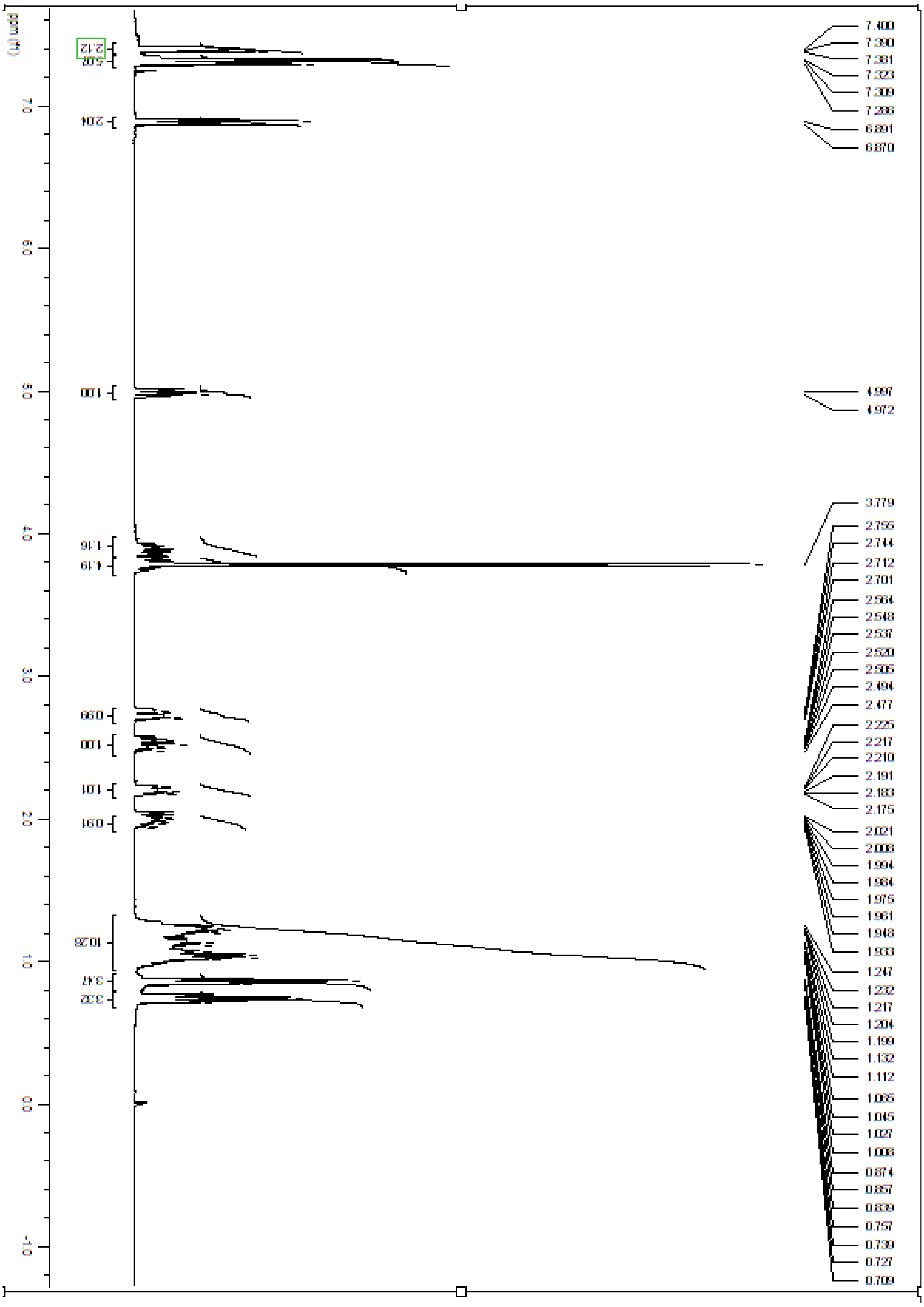
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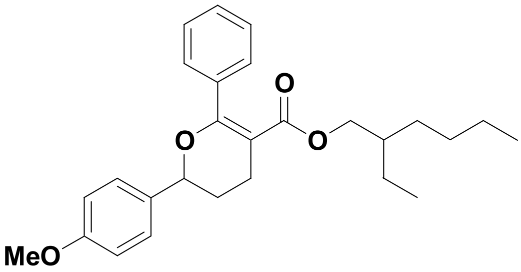
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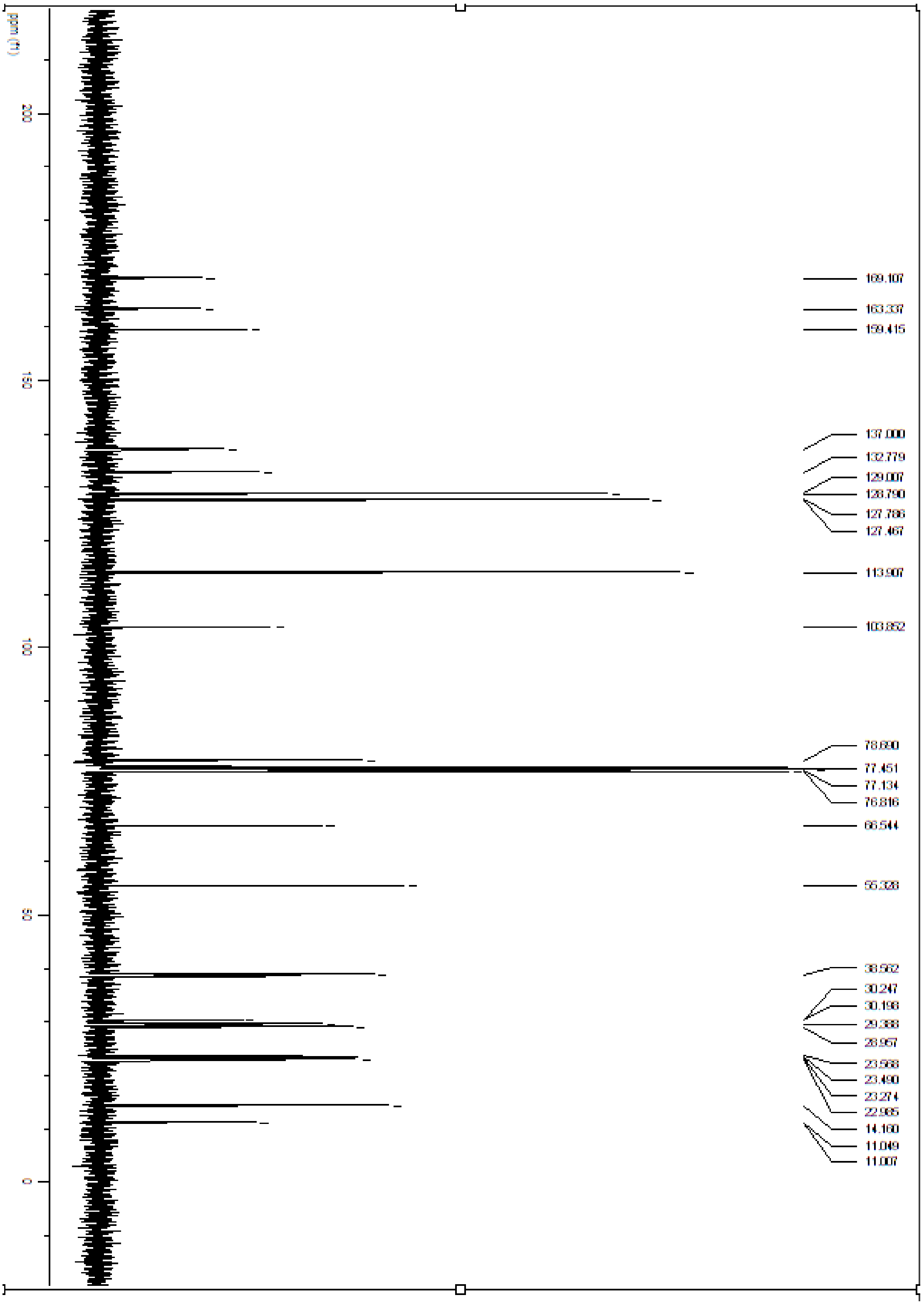
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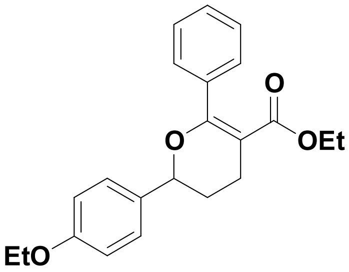
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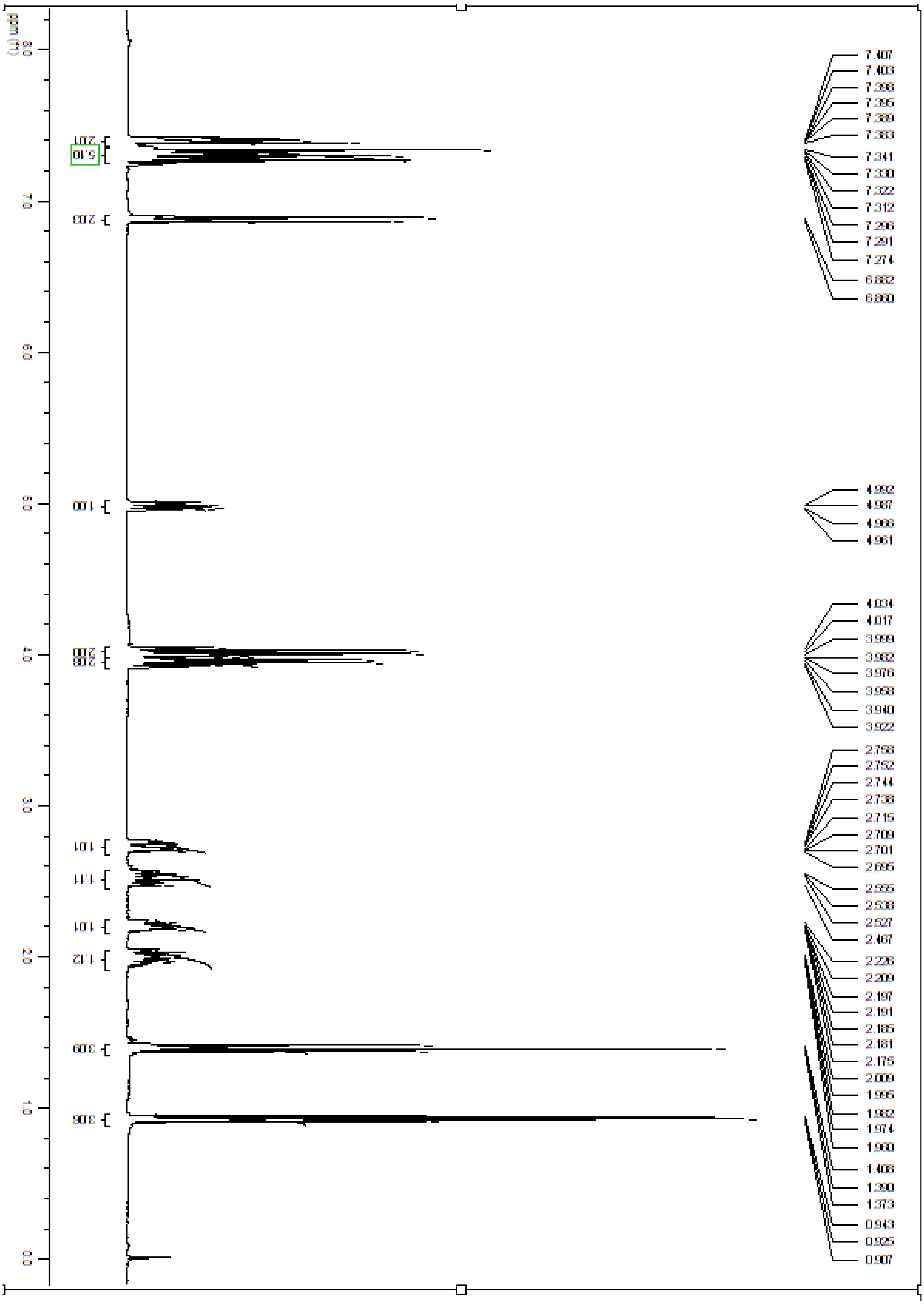
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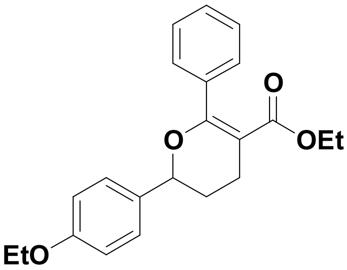
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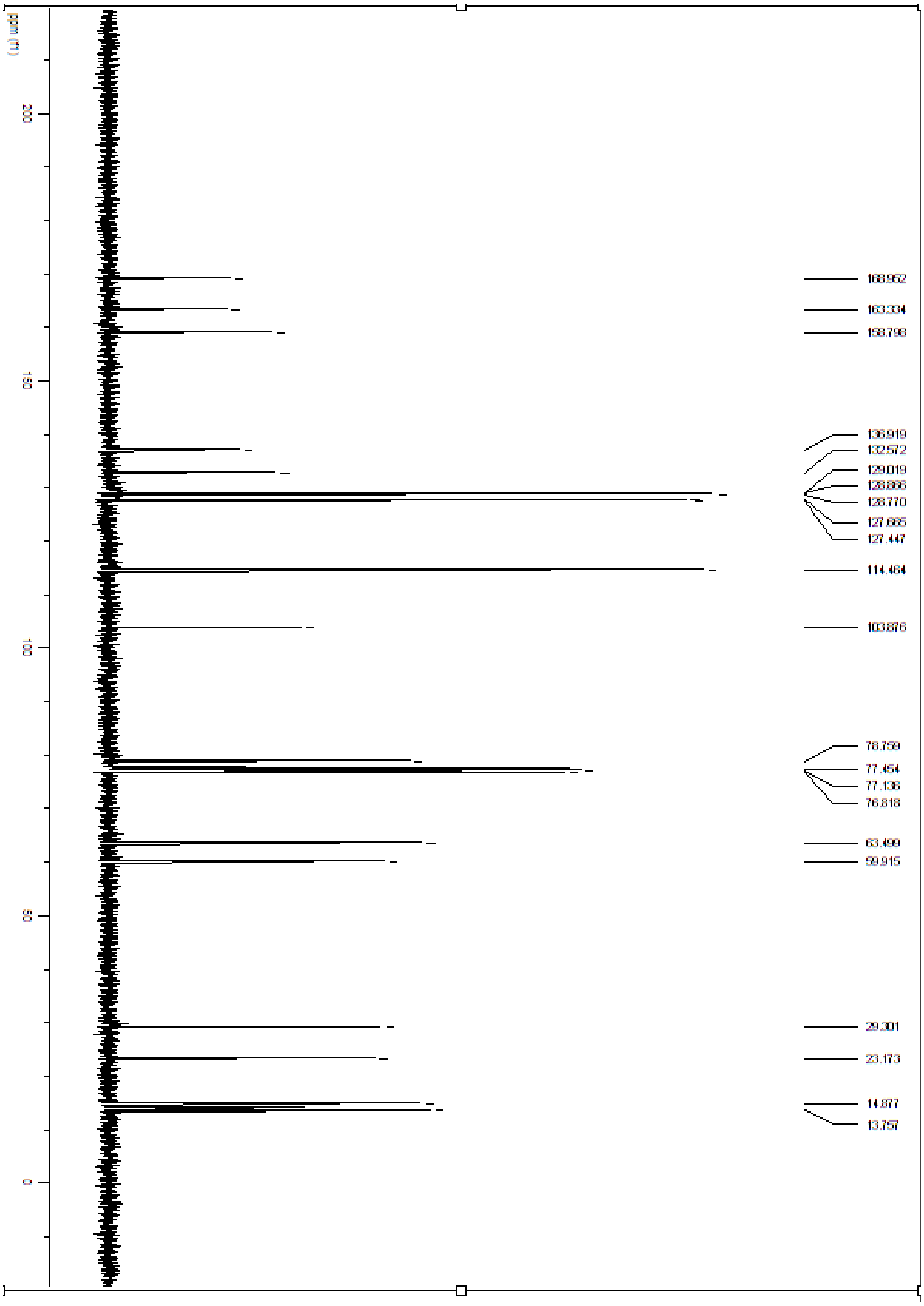
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127.447
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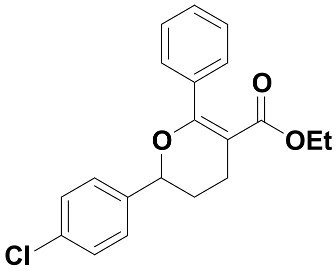
77.136
76.818
63.499
59.915
29.301
23.173
14.877
13.757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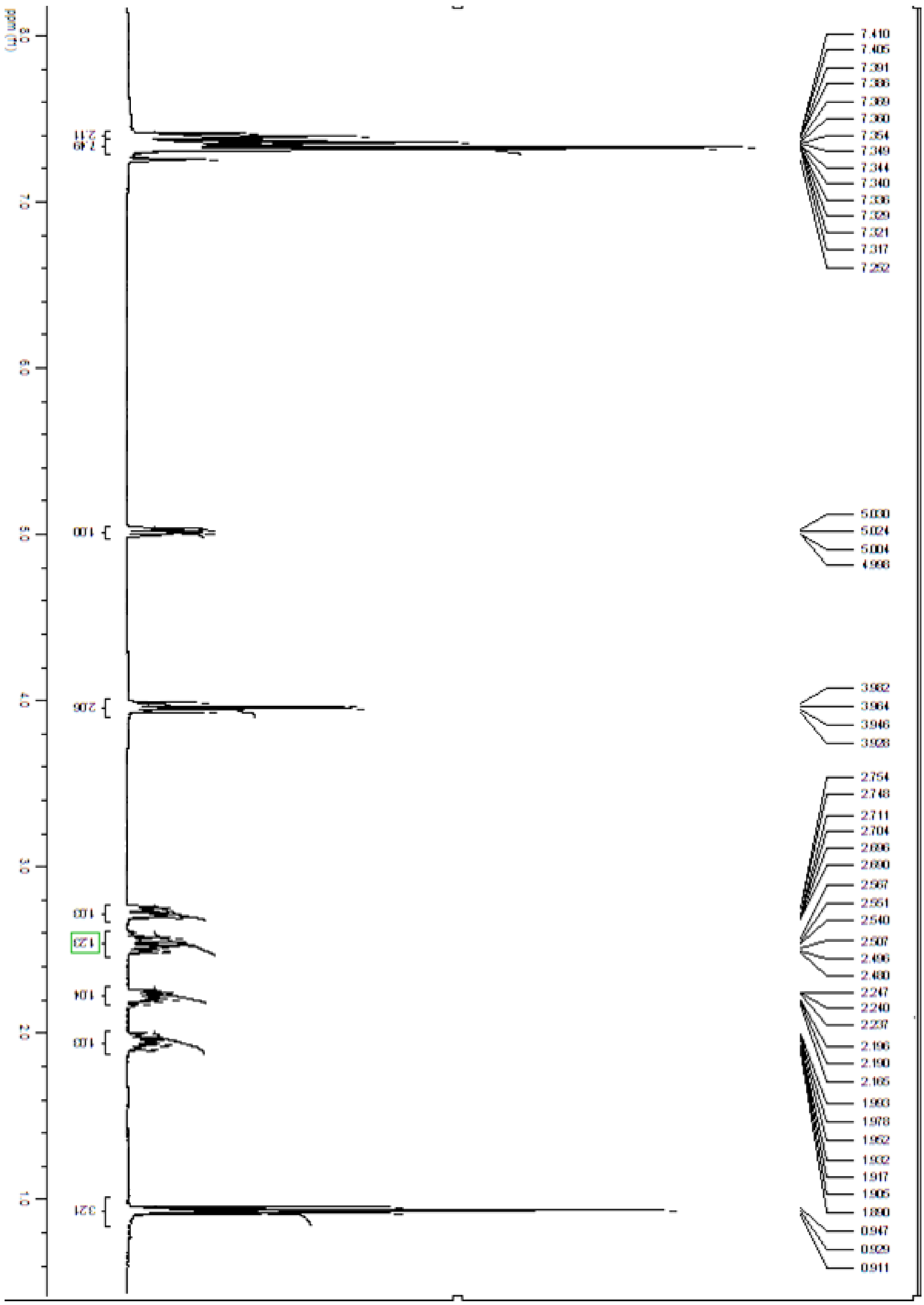
OEt
O
Cl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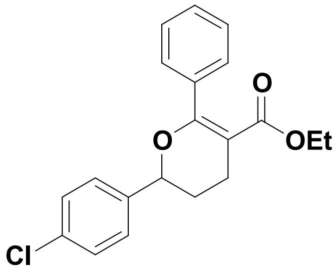
2.06
1.00
1.20
1.04
1.00
3.21
7.410
7.405
7.391
7.386
7.369
7.360
7.354
7.349
7.344
7.340
7.336
7.329
7.321
7.317
7.252
5.030
5.024
5.004
4.998
3.982
3.964
3.946
3.928
2.754
2.748
2.711
2.704
2.696
2.690
2.567
2.551
2.540
2.507
2.496
2.480
2.247
2.240
2.237
2.196
2.190
2.165
1.993
1.978
1.962
1.932
1.917
1.905
1.890
0.947
0.929
0.911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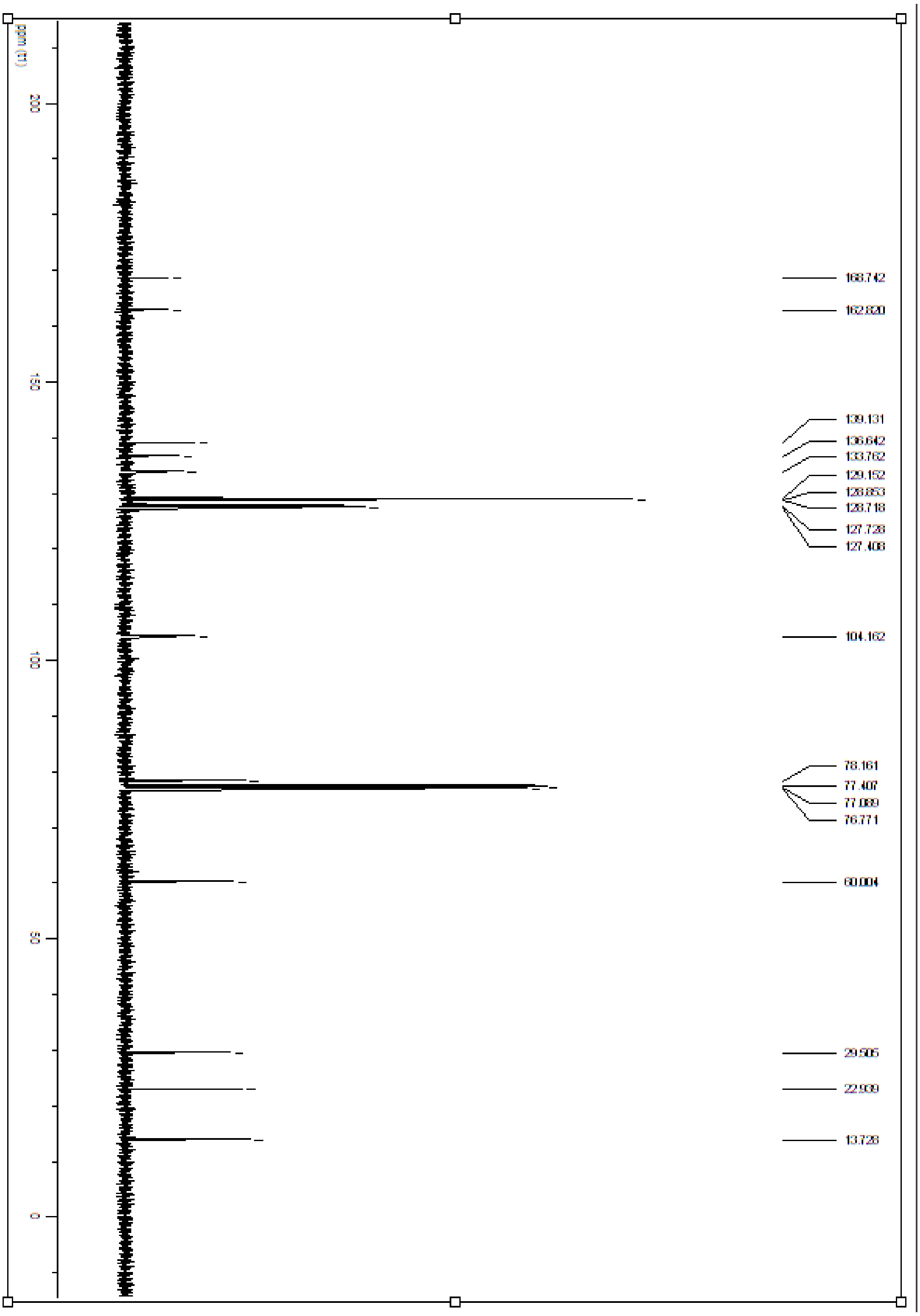
O
OEt
Cl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100
50
0
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162.820
139.131
136.642
133.762
129.152
128.853
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127.728
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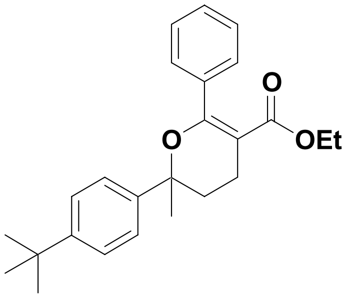
104.162
78.161
77.407
77.089
76.771
60.004
29.505
22.939
13.728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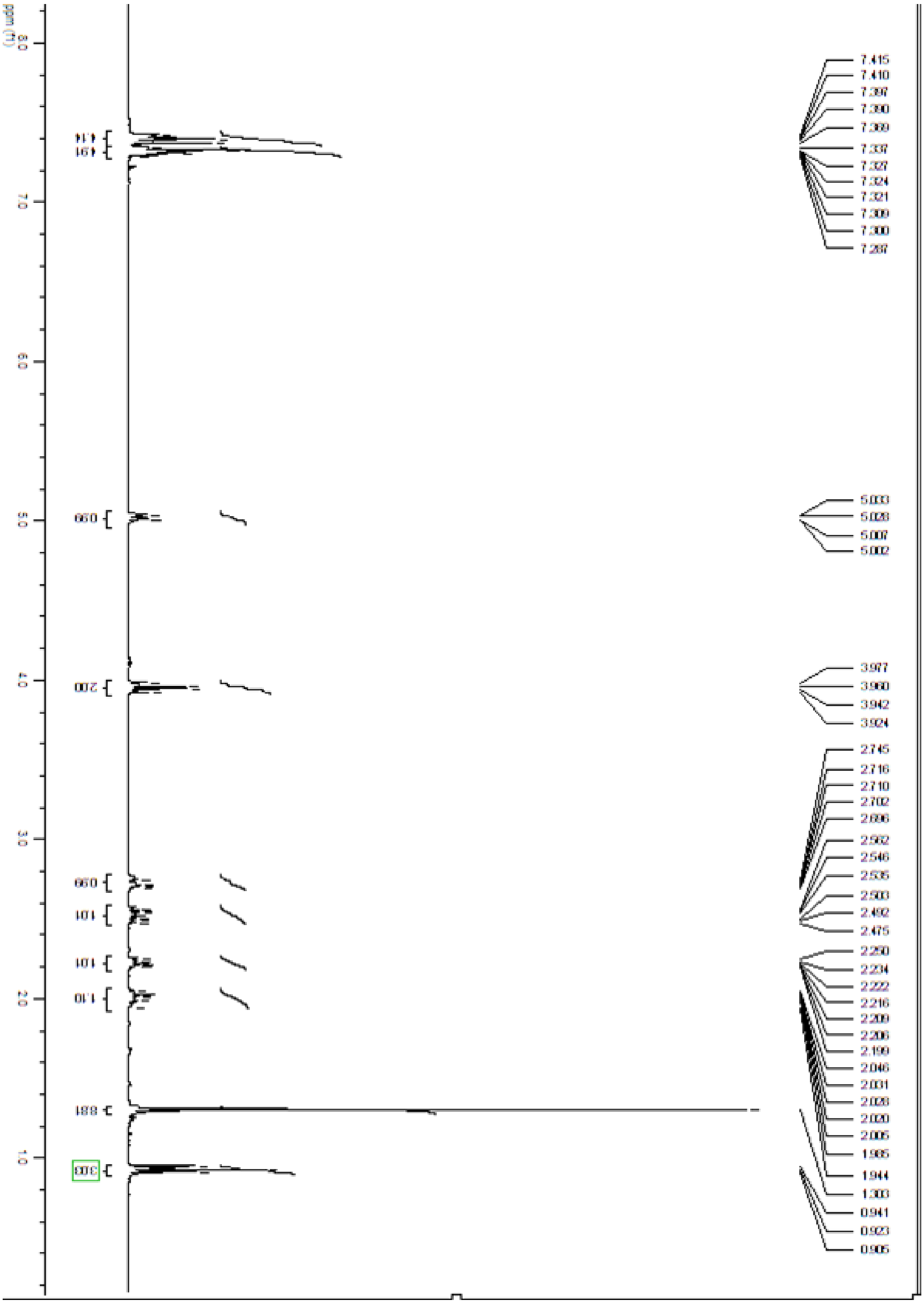
OEt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4.0
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4.14
4.91
0.99
2.00
0.99
1.01
1.01
1.10
8.81
3.00
7.415
7.410
7.397
7.390
7.369
7.337
7.327
7.324
7.321
7.309
7.300
7.287
5.033
5.028
5.007
5.002
3.977
3.960
3.942
3.924
2.745
2.716
2.710
2.702
2.686
2.562
2.546
2.536
2.503
2.492
2.475
2.250
2.234
2.222
2.216
2.209
2.206
2.190
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2.031
2.028
2.020
2.006
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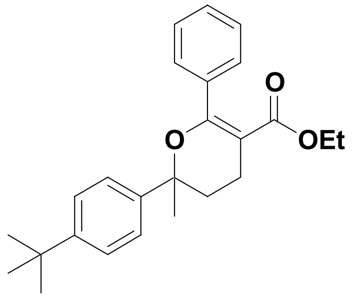
1.944
1.303
0.941
0.923
0.905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OEt
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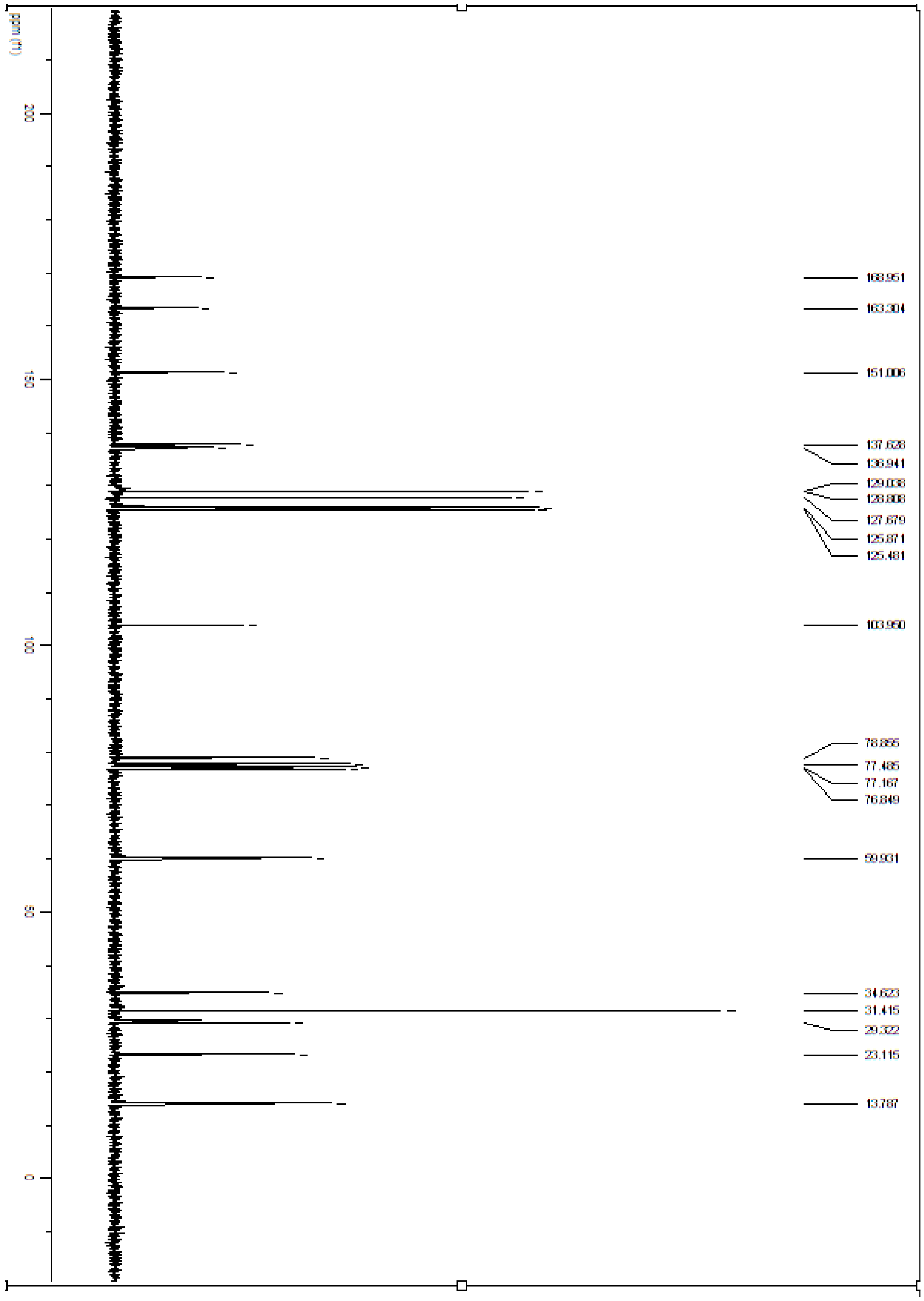
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150
100
50
0
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163.304
151.006
137.628
136.941
129.038
128.808
127.679
125.871
125.481
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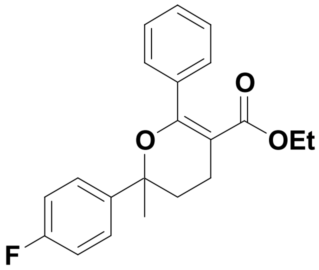
78.855
77.485
77.167
76.849
59.931
34.623
31.415
29.322
23.115
13.787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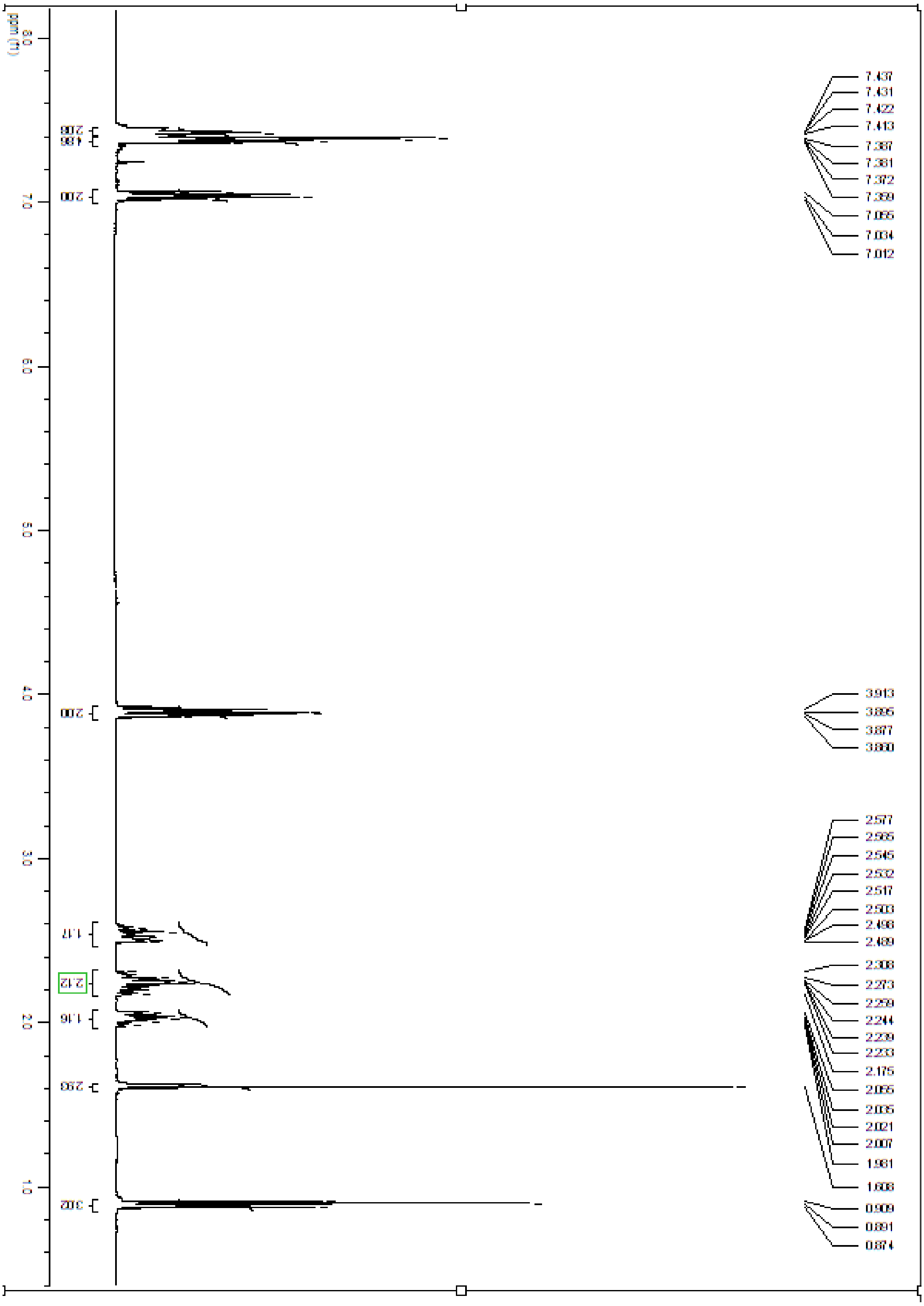
OEt
O
F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1.0
2.06
4.86
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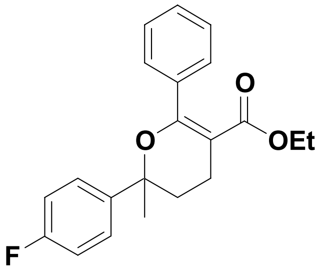
2.00
1.17
2.12
1.16
2.93
3.02
7.437
7.431
7.422
7.413
7.387
7.381
7.372
7.369
7.055
7.034
7.012
3.913
3.895
3.877
3.860
2.577
2.565
2.545
2.532
2.517
2.503
2.498
2.489
2.308
2.273
2.259
2.244
2.239
2.233
2.175
2.055
2.035
2.021
2.007
1.981
1.608
0.909
0.891
0.874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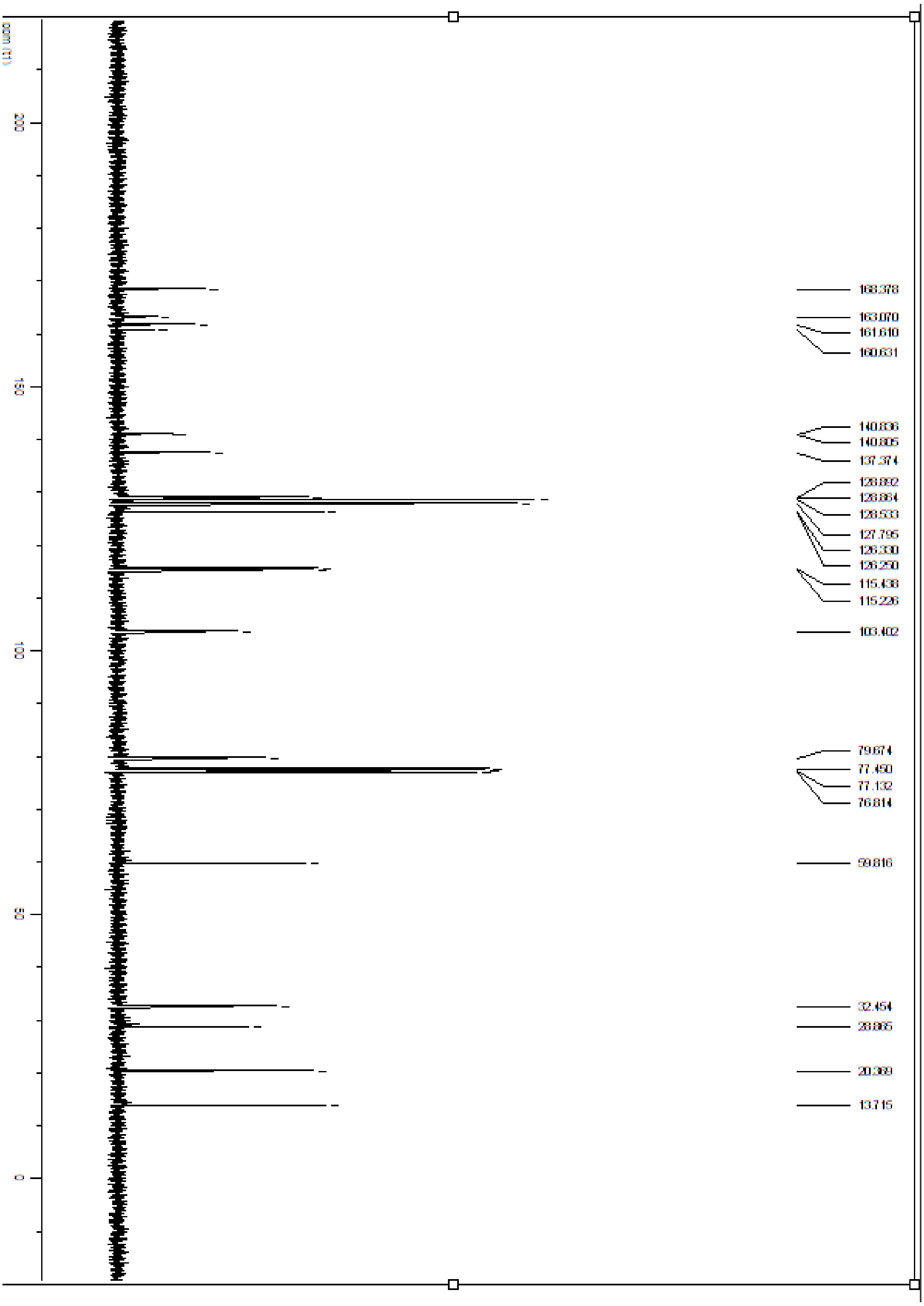
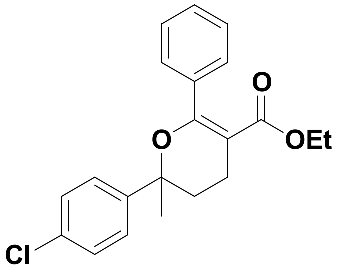
OEt
O
F


ppm (t1)
200
150
100
50
0
168.378
163.070
161.610
160.631
140.836
140.805
137.374
128.882
128.864
128.533
127.795
126.330
126.250
115.438
115.226
103.402
79.674
77.450
77.132
76.814
59.816
32.454
28.865
20.369
13.715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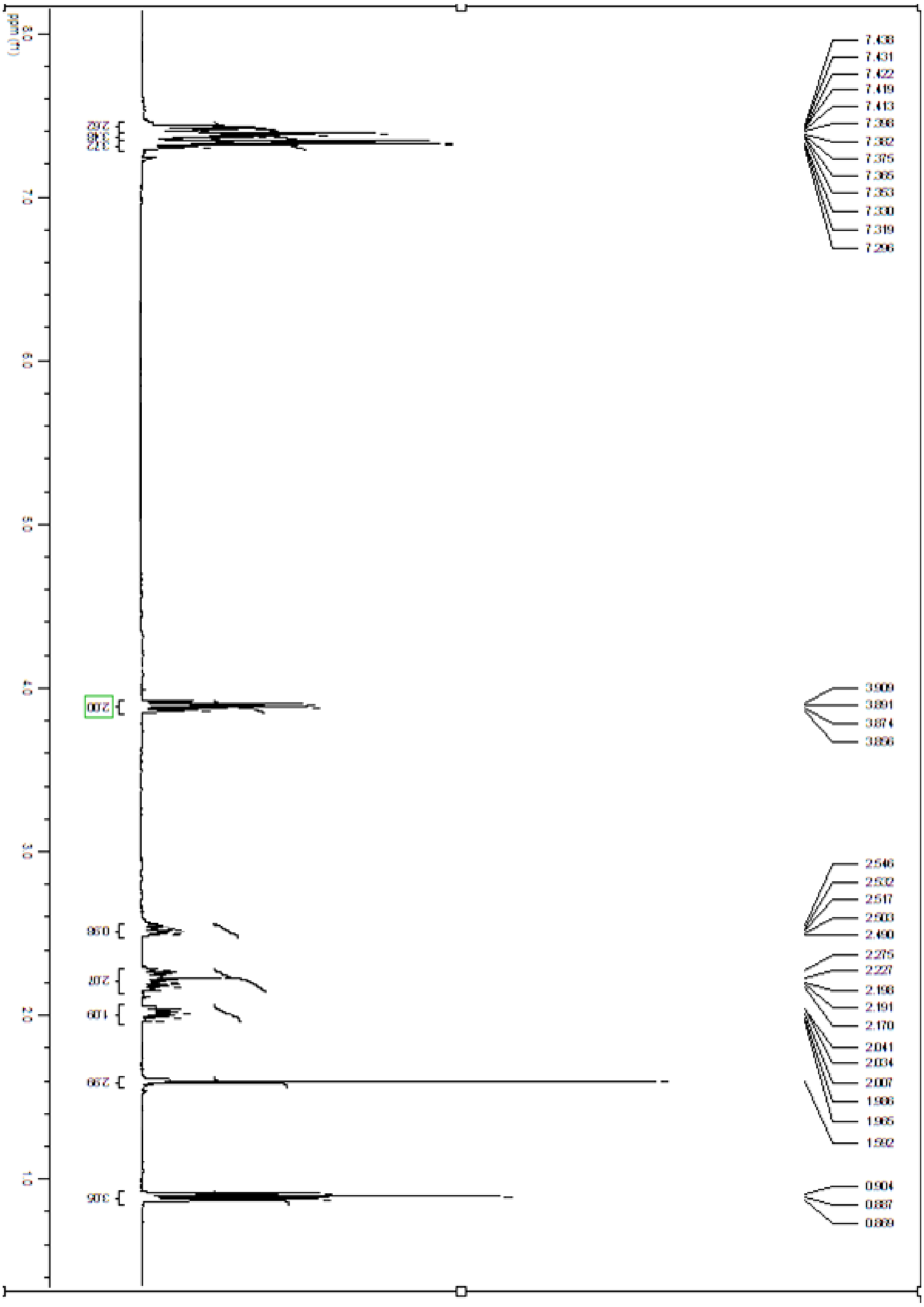
OEt
O
Cl


ppm (t1)
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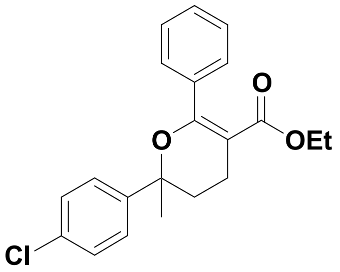
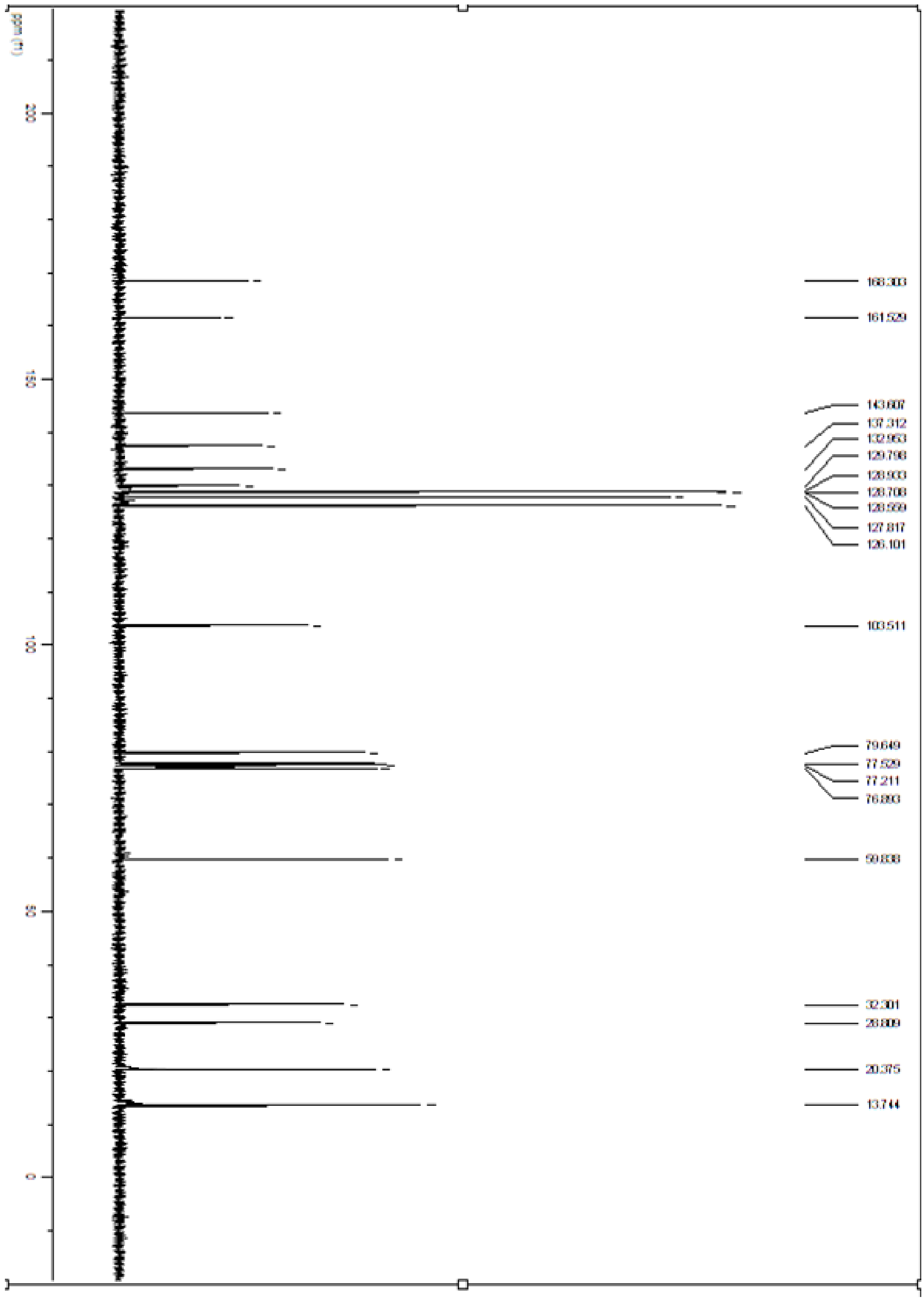
5.0
4.0
3.0
2.0
1.0
2.00
0.98
2.07
1.09
2.99
3.06
7.438
7.431
7.422
7.419
7.413
7.398
7.382
7.375
7.365
7.353
7.330
7.319
7.296
3.909
3.891
3.874
3.856
2.546
2.532
2.517
2.503
2.490
2.275
2.227
2.198
2.191
2.170
2.041
2.034
2.007
1.986
1.965
1.592
0.904
0.887
0.869


O
OEt
O
Cl


ppm (f1)
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150
100
50
0
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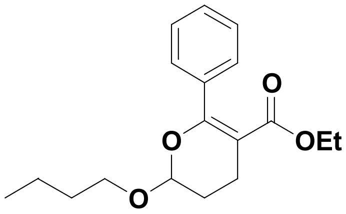
137.312
132.953
129.798
128.903
128.708
128.559
127.817
126.101
103.511
79.649
77.529
77.211
76.893
60.838
32.301
28.809
20.375
13.744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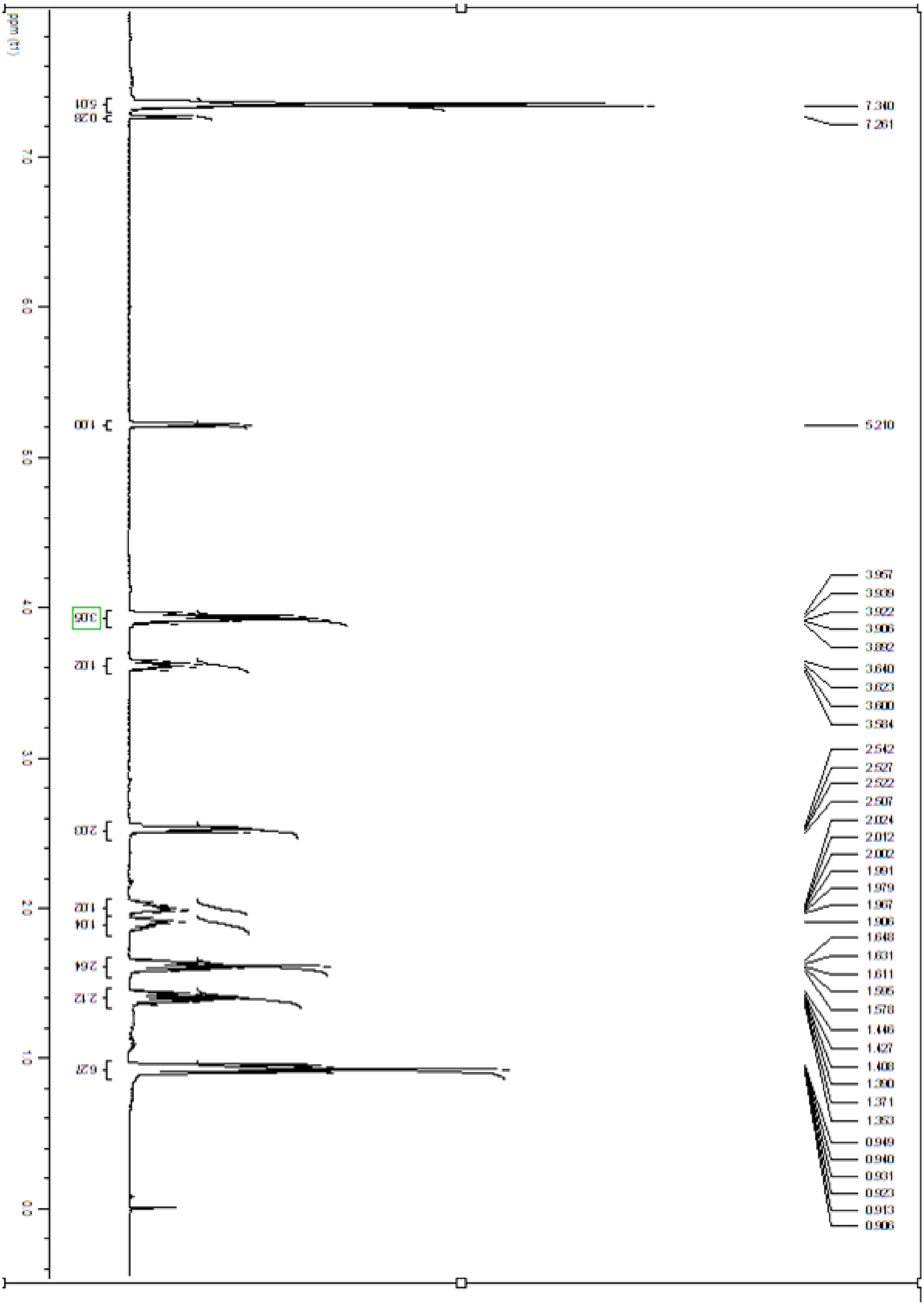
OEt
O
O


ppm (t1)
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4.0
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2.0
1.0
0.0
5.01
0.28
1.00
3.05
1.02
2.00
1.02
1.04
2.64
2.12
6.27
7.340
7.261
5.210
3.957
3.939
3.922
3.906
3.892
3.640
3.623
3.600
3.584
2.542
2.527
2.522
2.507
2.024
2.012
2.002
1.991
1.979
1.967
1.906
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1.631
1.611
1.595
1.578
1.446
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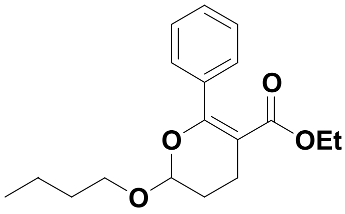
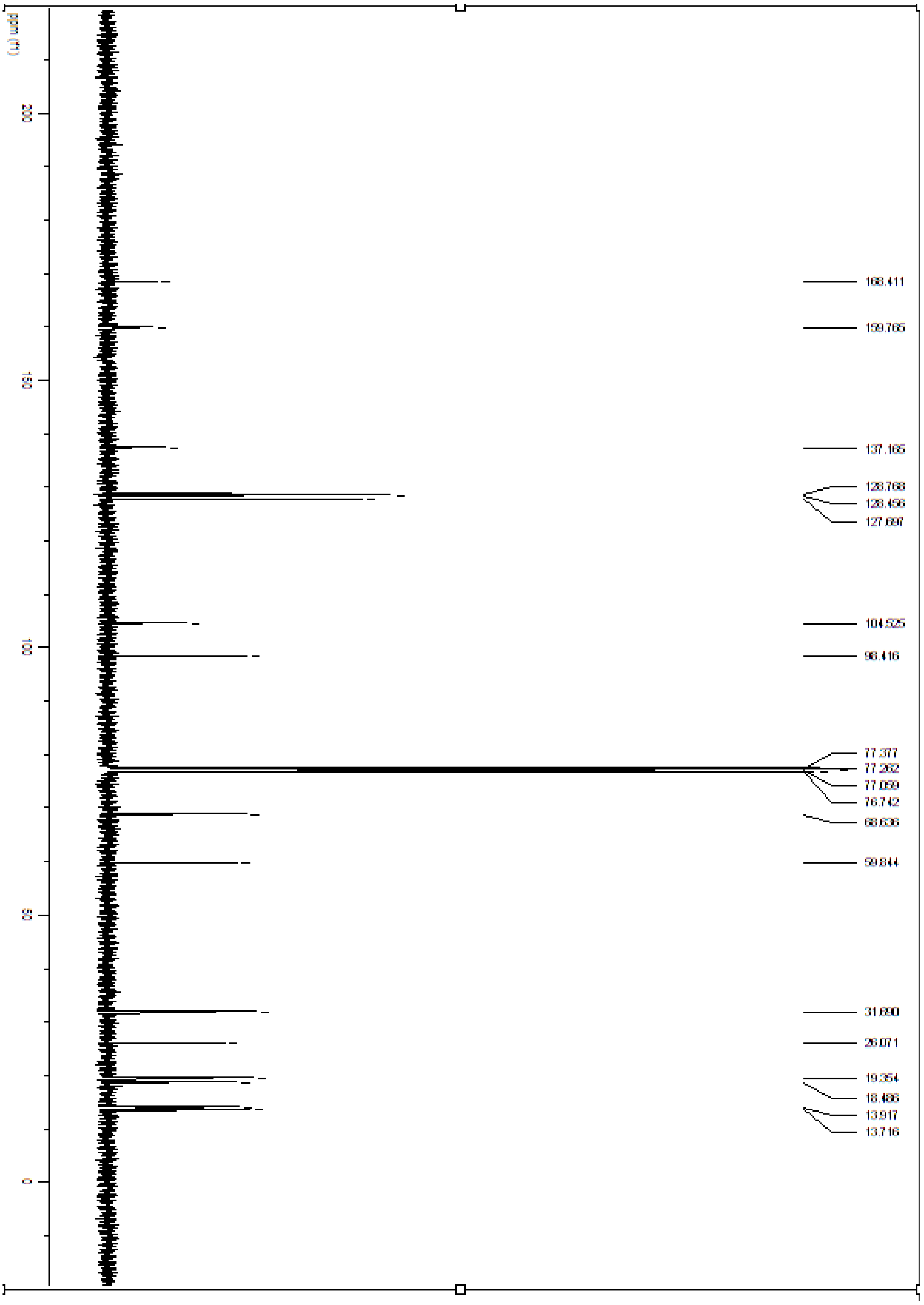
1.390
1.371
1.353
0.949
0.940
0.931
0.923
0.913
0.906


O
OEt
O
O


ppm (f1)
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100
50
0
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159.765
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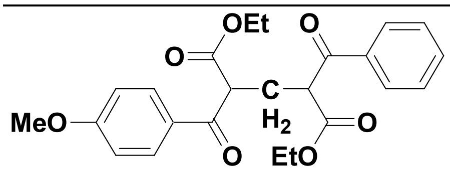
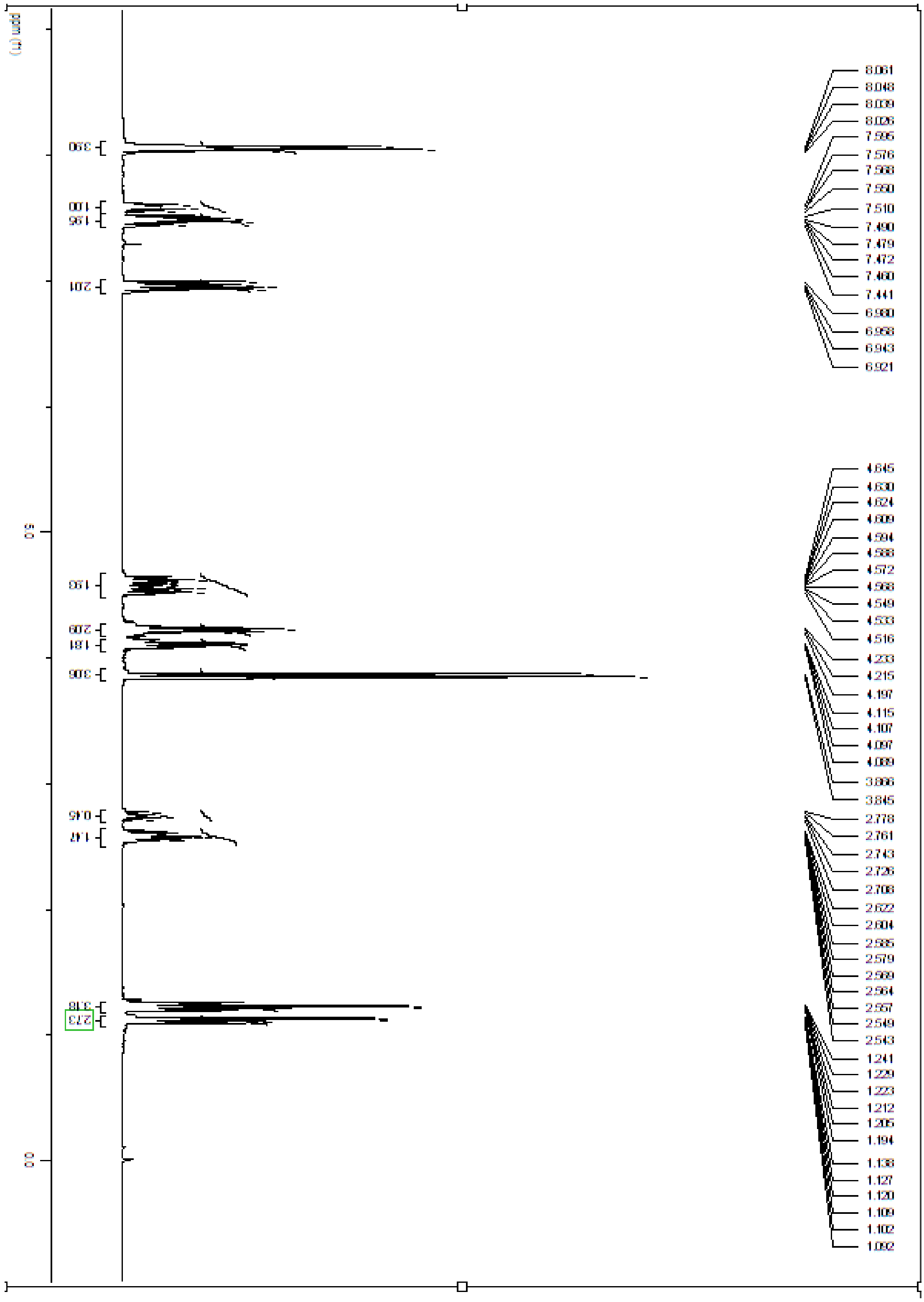
128.456
127.697
104.525
98.416
77.377
77.262
77.059
76.742
68.636
59.844
31.690
26.071
19.354
18.486
13.917
13.716


OEt
O
O
C
H2
MeO
O
EtO
O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1.81
3.06
0.46
1.47
3.18
2.73
8.061
8.048
8.039
8.026
7.595
7.576
7.568
7.550
7.510
7.490
7.479
7.472
7.460
7.441
6.980
6.958
6.943
6.921
4.645
4.630
4.624
4.609
4.594
4.588
4.572
4.568
4.549
4.533
4.516
4.233
4.215
4.197
4.115
4.107
4.097
4.089
3.866
3.845
2.778
2.761
2.743
2.726
2.708
2.622
2.604
2.585
2.579
2.569
2.564
2.557
2.549
2.543
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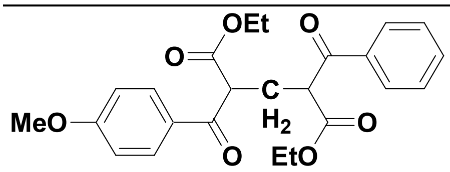
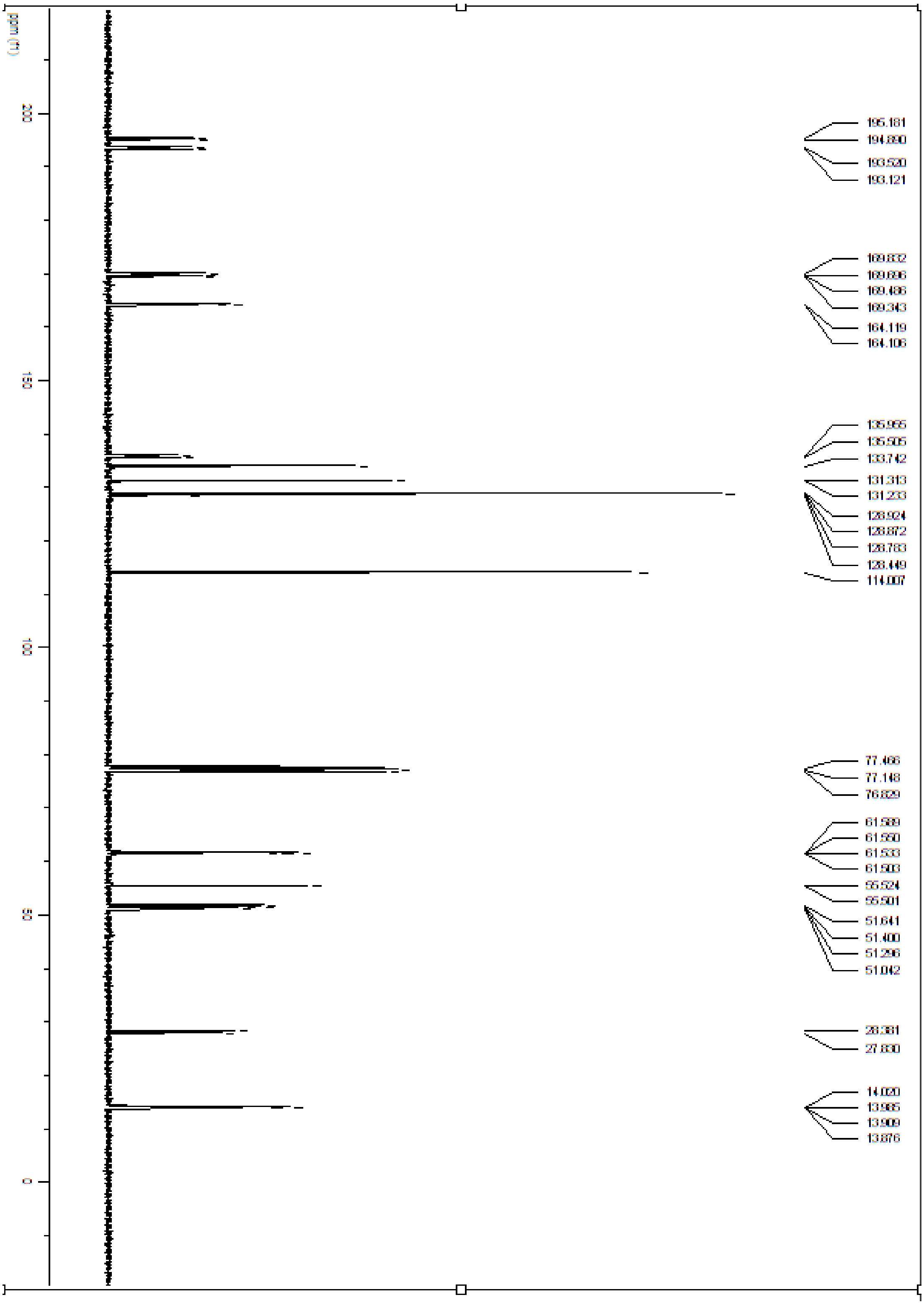
1.229
1.223
1.212
1.205
1.194
1.138
1.127
1.120
1.109
1.102
1.092


OEt
O
O
C
H2
MeO
O
EtO
O


ppm (f1)
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150
100
50
0
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194.890
193.520
193.121
169.832
169.696
169.486
169.343
164.119
164.106
135.965
135.505
133.742
131.313
131.233
128.924
128.872
128.783
128.449
114.007
77.466
77.148
76.829
61.589
61.560
61.533
61.503
55.524
55.501
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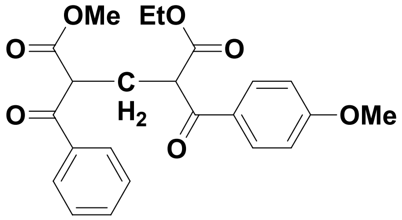
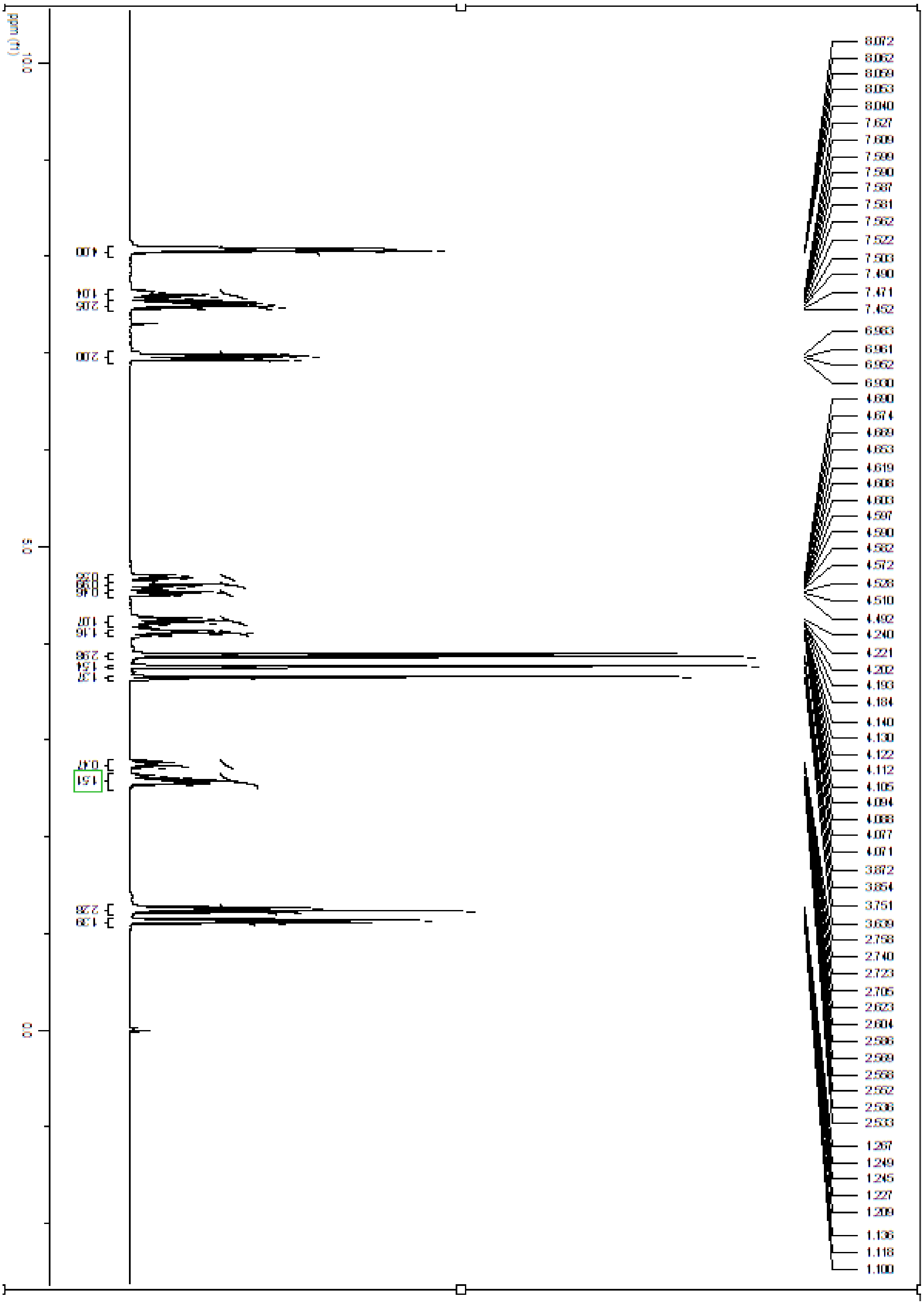
51.400
51.296
51.042
28.381
27.830
14.020
13.985
13.909
13.876


OMe
EtO
O
O
C
H2
O
O
OMe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2.00
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1.16
2.98
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1.37
0.47
1.51
2.28
1.38
8.072
8.062
8.059
8.053
8.040
7.627
7.609
7.599
7.590
7.587
7.581
7.562
7.522
7.503
7.490
7.471
7.452
6.983
6.961
6.952
6.930
4.690
4.674
4.669
4.653
4.619
4.608
4.603
4.597
4.590
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4.492
4.240
4.221
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4.193
4.184
4.140
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4.122
4.112
4.105
4.094
4.088
4.077
4.071
3.872
3.854
3.751
3.639
2.758
2.740
2.723
2.705
2.623
2.604
2.586
2.569
2.558
2.552
2.536
2.533
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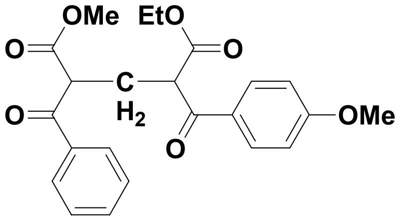
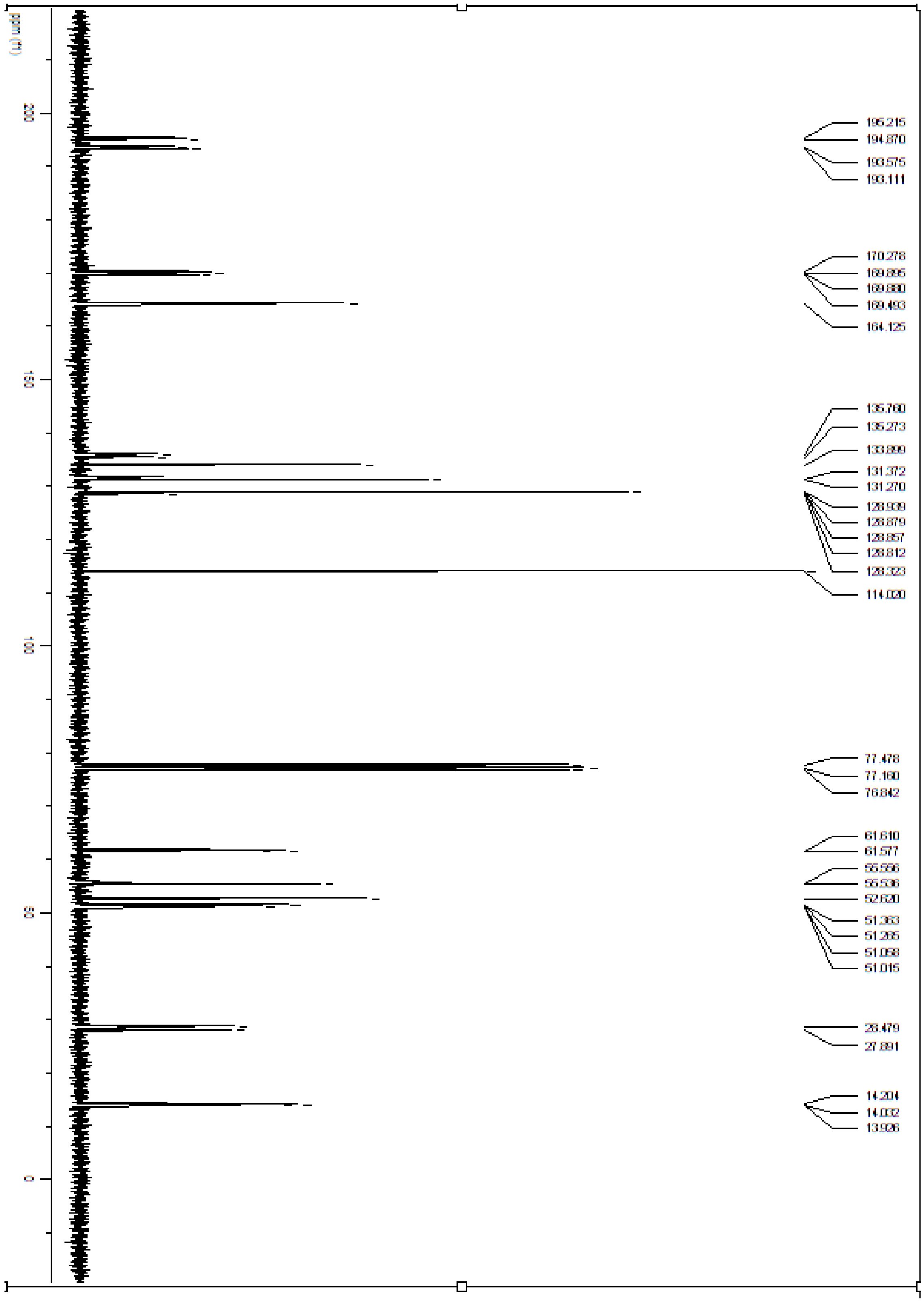
1.249
1.245
1.227
1.209
1.136
1.118
1.100

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100
50
0
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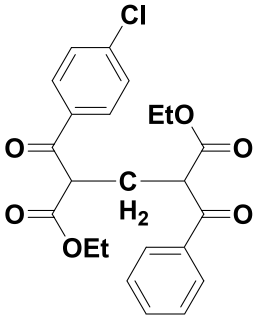
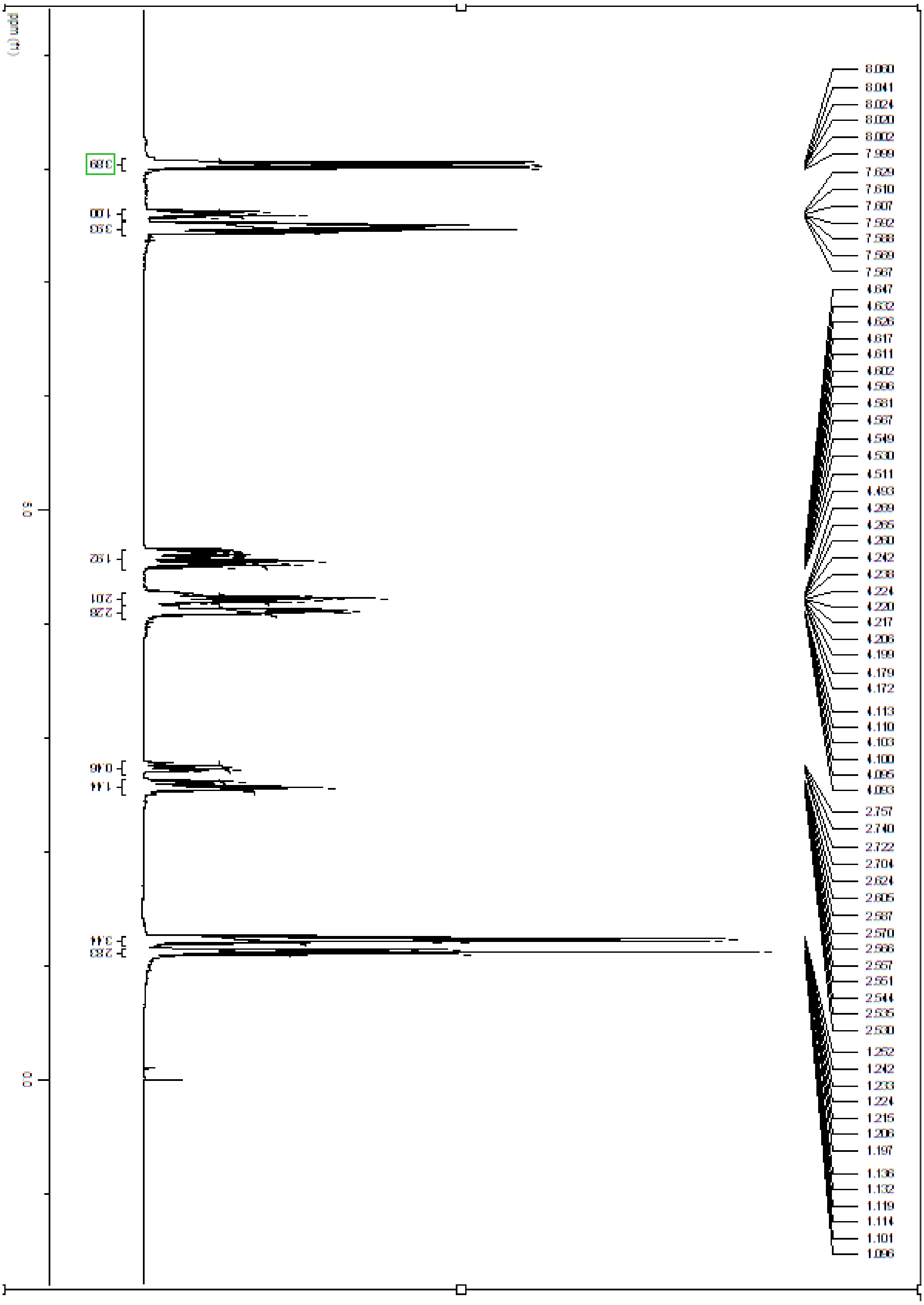
193.111
170.278
169.895
169.880
169.493
164.125
135.760
135.273
133.899
131.372
131.270
128.909
128.879
128.857
128.812
128.323
114.020
77.478
77.160
76.842
61.610
61.577
55.596
55.536
52.620
51.363
51.285
51.058
51.015
28.479
27.891
14.204
14.032
13.926


Cl
EtO
O
O
C
H2
O
O
OEt


ppm (f1)
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3.93
1.92
2.01
2.28
0.46
1.44
3.44
2.83
8.060
8.041
8.024
8.020
8.002
7.999
7.629
7.610
7.607
7.592
7.588
7.569
7.567
4.647
4.632
4.626
4.617
4.611
4.602
4.596
4.581
4.567
4.549
4.530
4.511
4.493
4.269
4.265
4.260
4.242
4.238
4.224
4.220
4.217
4.206
4.199
4.179
4.172
4.113
4.110
4.103
4.100
4.095
4.093
2.757
2.740
2.722
2.704
2.624
2.605
2.587
2.570
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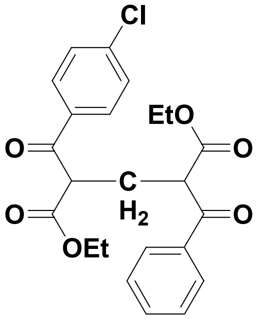
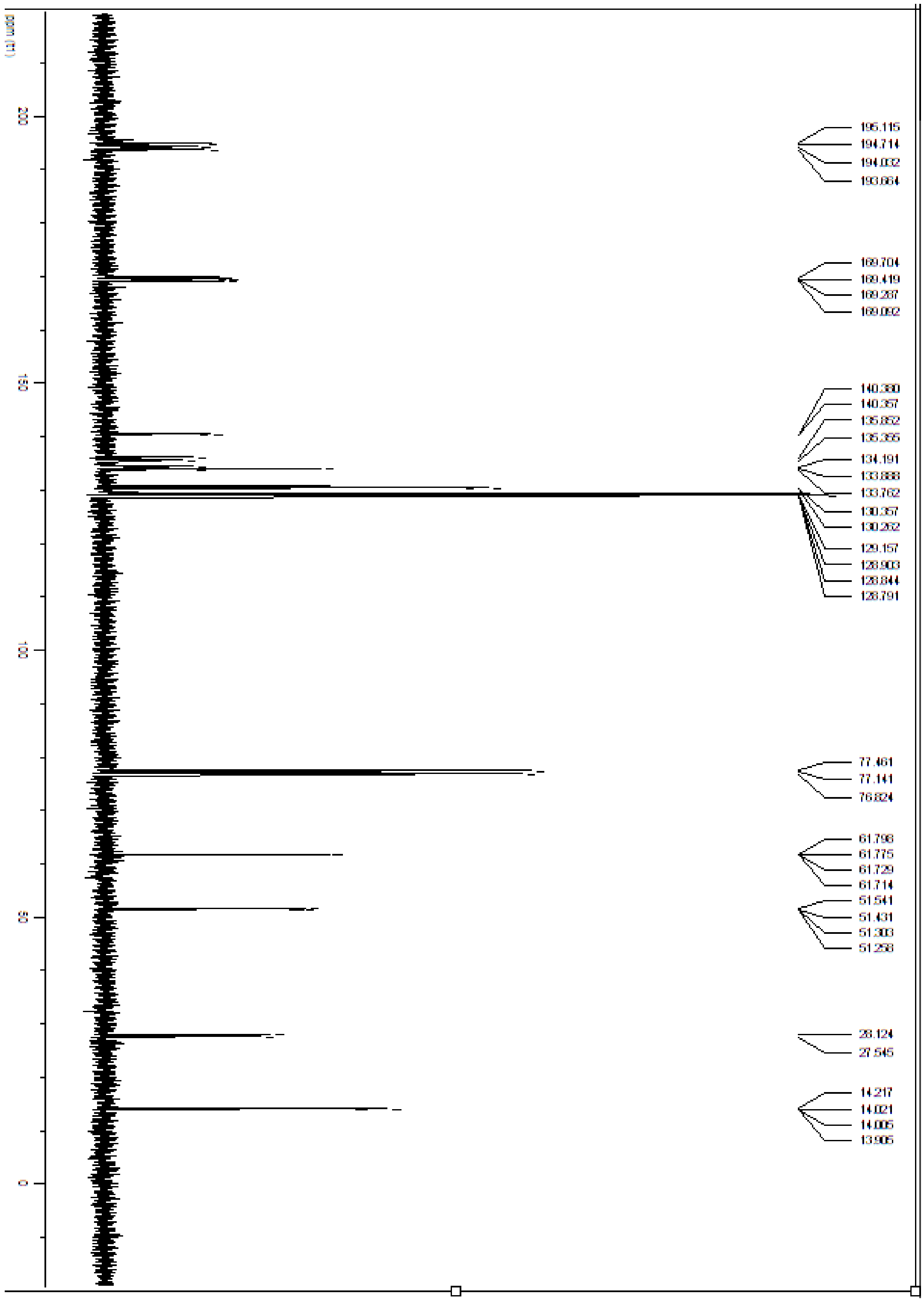
2.557
2.551
2.544
2.535
2.530
1.252
1.242
1.233
1.224
1.215
1.206
1.197
1.136
1.132
1.119
1.114
1.101
1.096


Cl
EtO
O
O
C
H2
O
O
OEt


ppm (t1)
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100
50
0
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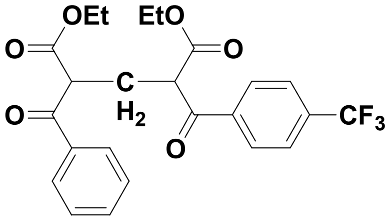
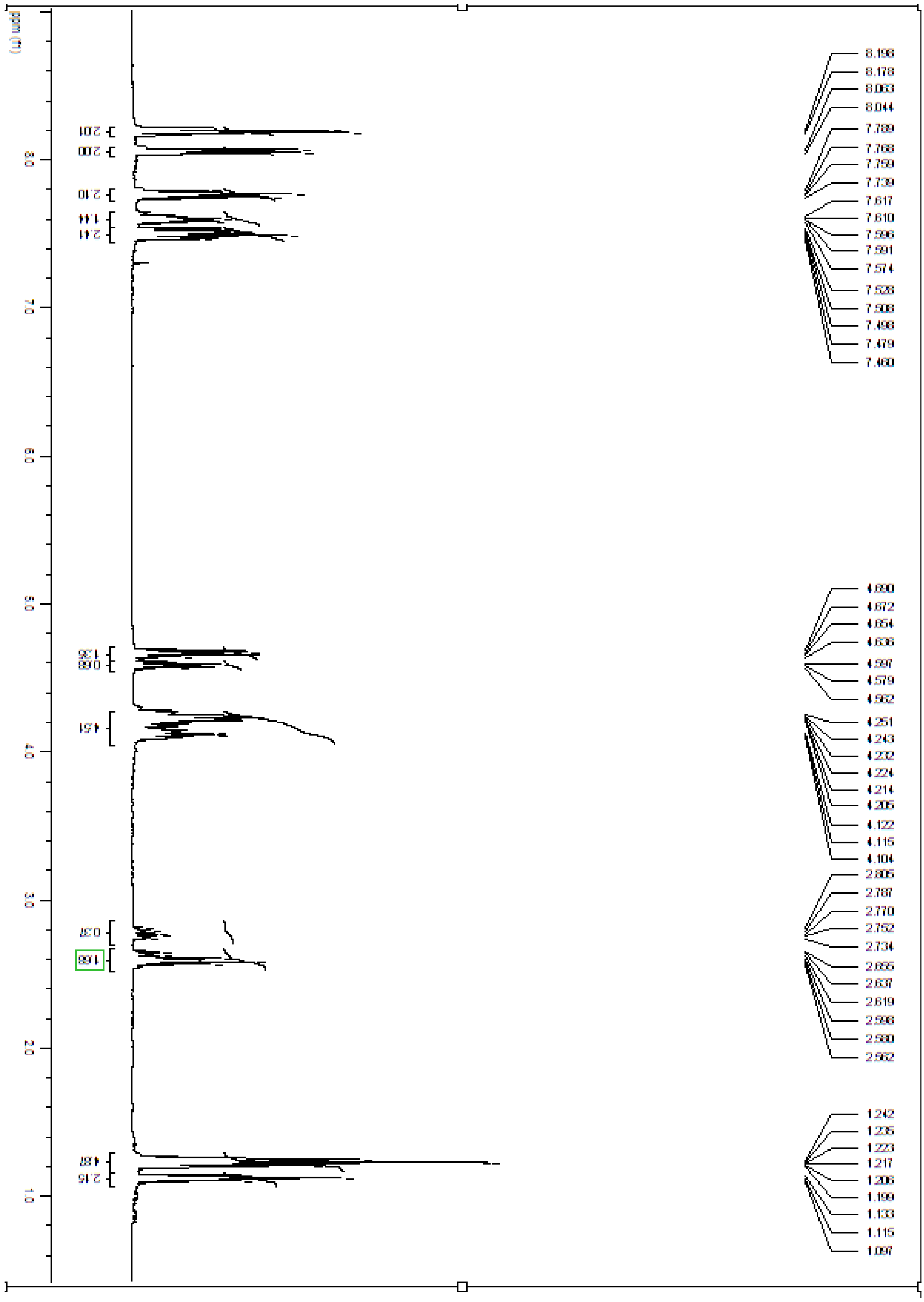
194.714
194.032
193.684
169.704
169.419
169.287
169.092
140.380
140.357
135.852
135.355
134.191
133.888
133.762
130.357
130.262
129.157
128.903
128.844
128.791
77.461
77.141
76.824
61.798
61.775
61.729
61.714
51.541
51.431
51.303
51.258
28.124
27.545
14.217
14.021
14.005
13.905


OEt
EtO
O
O
O
O
C
H2
CF3


ppm (f1)
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4.0
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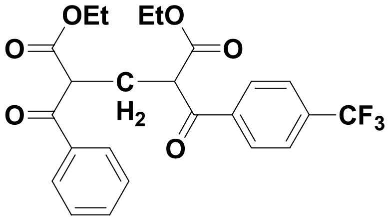
2.0
1.0
2.01
2.00
2.10
1.44
2.41
1.26
0.88
4.51
0.37
1.68
4.87
2.15
8.198
8.178
8.063
8.044
7.789
7.768
7.759
7.739
7.617
7.610
7.596
7.591
7.574
7.528
7.508
7.496
7.479
7.460
4.690
4.672
4.654
4.636
4.597
4.579
4.562
4.251
4.243
4.232
4.224
4.214
4.205
4.122
4.115
4.104
2.805
2.787
2.770
2.752
2.734
2.655
2.637
2.619
2.598
2.580
2.562
1.242
1.235
1.223
1.217
1.206
1.199
1.133
1.115
1.097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EtO
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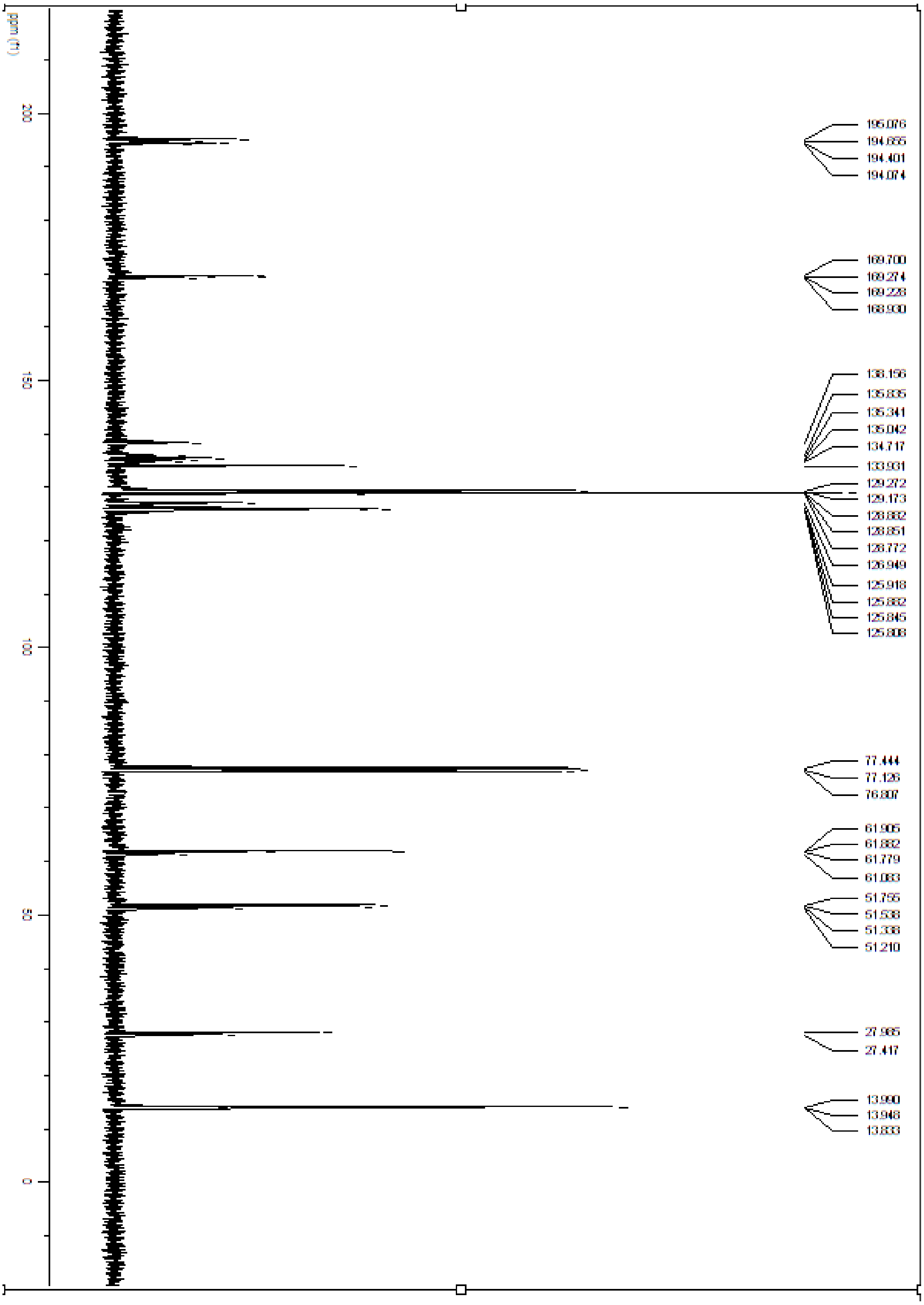
O
O
O
C
H2
CF3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100
50
0
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194.655
194.401
194.074
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169.274
169.228
168.930
138.156
135.835
135.341
135.042
134.717
133.931
129.272
129.173
128.882
128.851
128.772
126.949
125.918
125.882
125.845
125.808
77.444
77.126
76.807
61.905
61.882
61.779
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51.755
51.538
51.336
51.210
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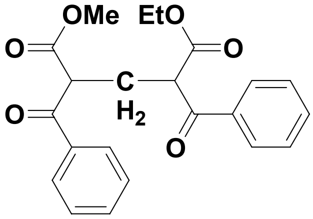
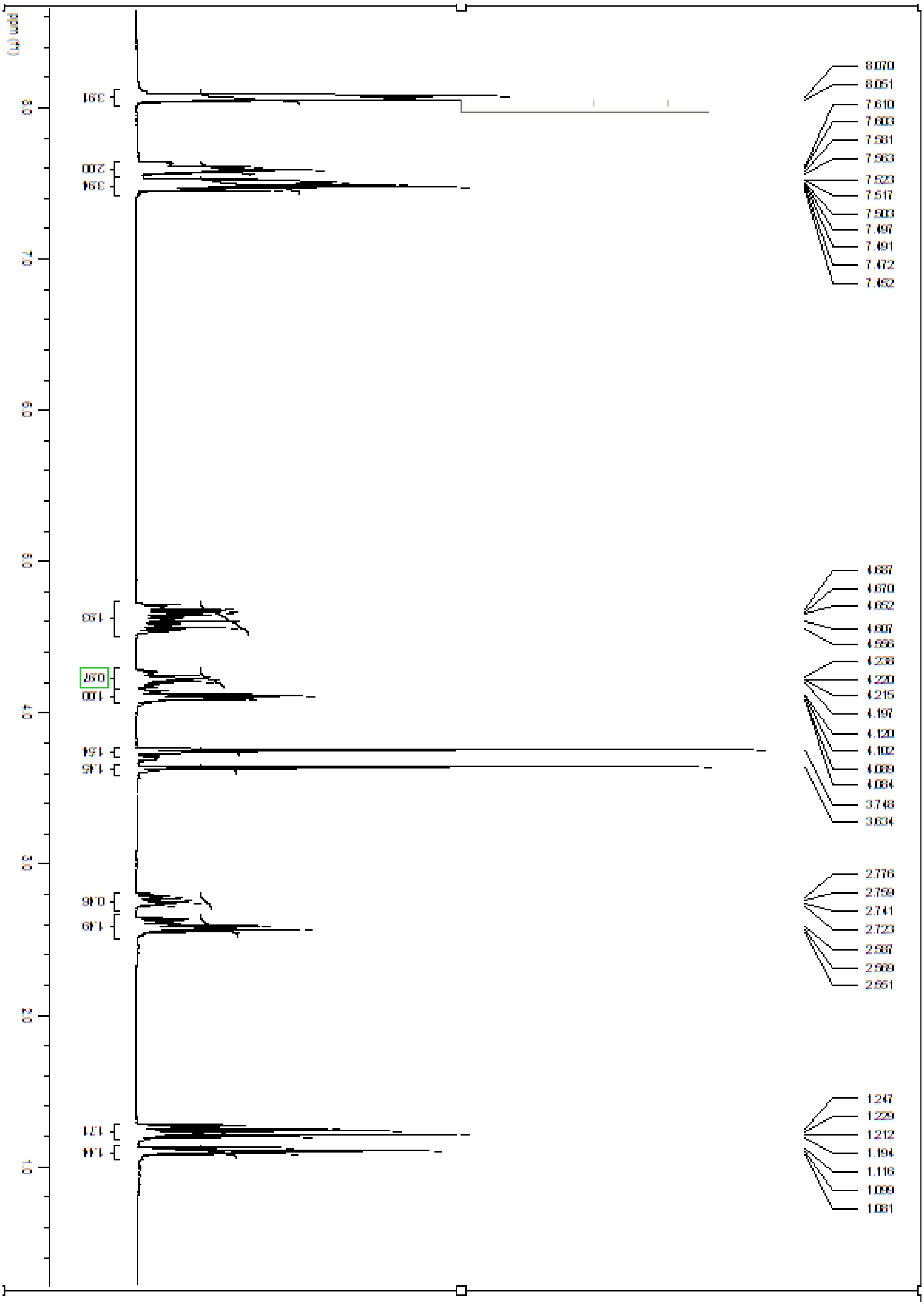
13.990
13.948
13.833


OMe
EtO
O
O
O
O
C
H2


ppm (f1)
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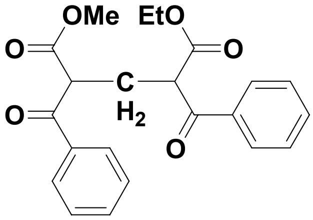
7.0
6.0
5.0
4.0
3.0
2.0
1.0
3.91
2.00
3.94
1.93
0.97
1.00
1.54
1.45
0.46
1.49
1.71
1.44
8.070
8.051
7.610
7.603
7.581
7.563
7.523
7.517
7.503
7.497
7.491
7.472
7.452
4.687
4.670
4.652
4.607
4.596
4.238
4.220
4.215
4.197
4.120
4.102
4.089
4.084
3.748
3.634
2.776
2.759
2.741
2.723
2.587
2.569
2.551
1.247
1.229
1.212
1.194
1.116
1.099
1.081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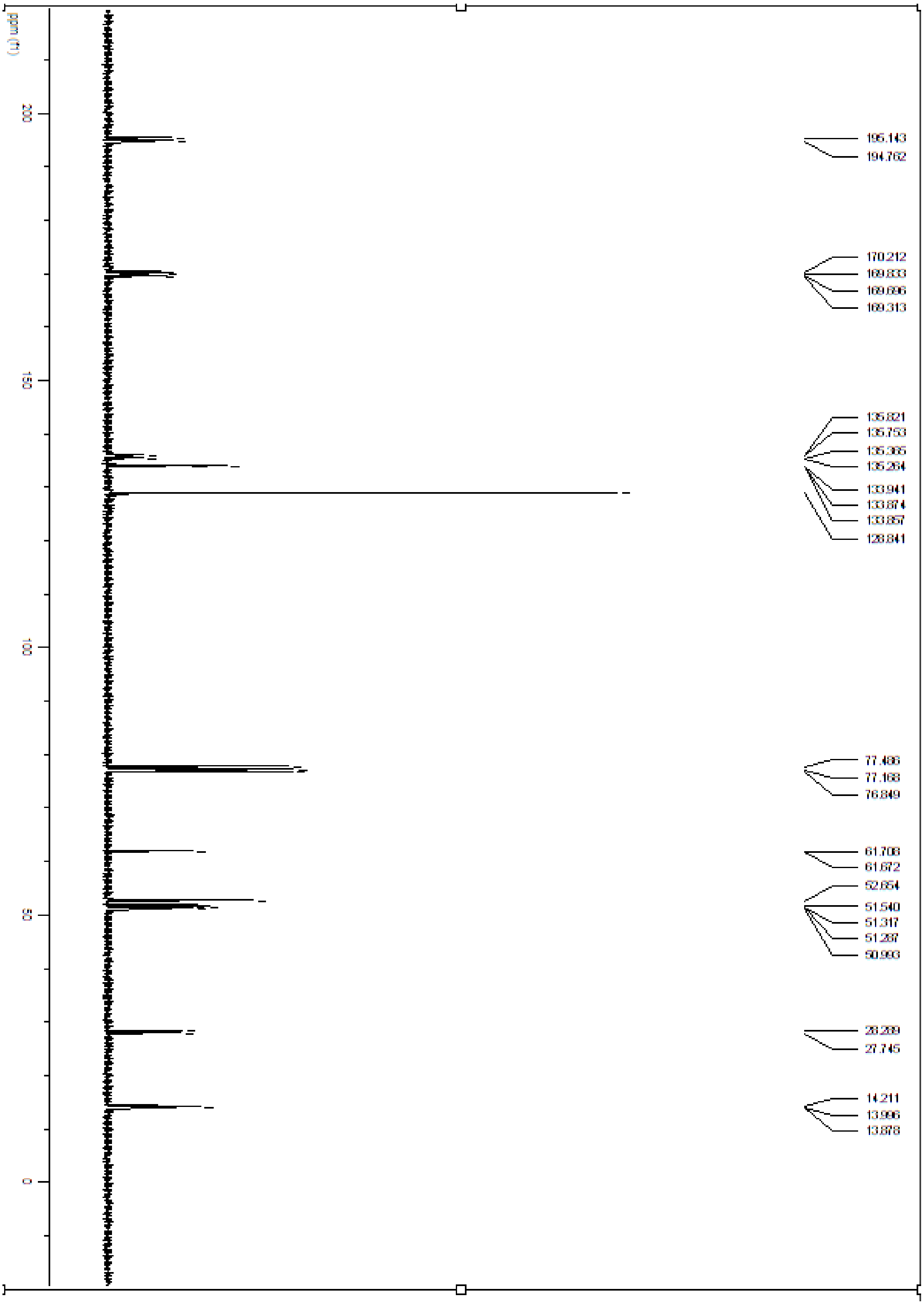
EtO
O
O
O
O
C
H2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100
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0
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169.833
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169.313
135.821
135.753
135.365
135.264
133.941
133.874
133.857
128.841
77.486
77.168
76.849
61.708
61.672
52.654
51.540
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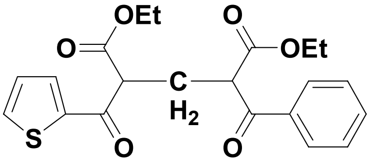
51.287
50.993
28.289
27.745
14.211
13.996
13.878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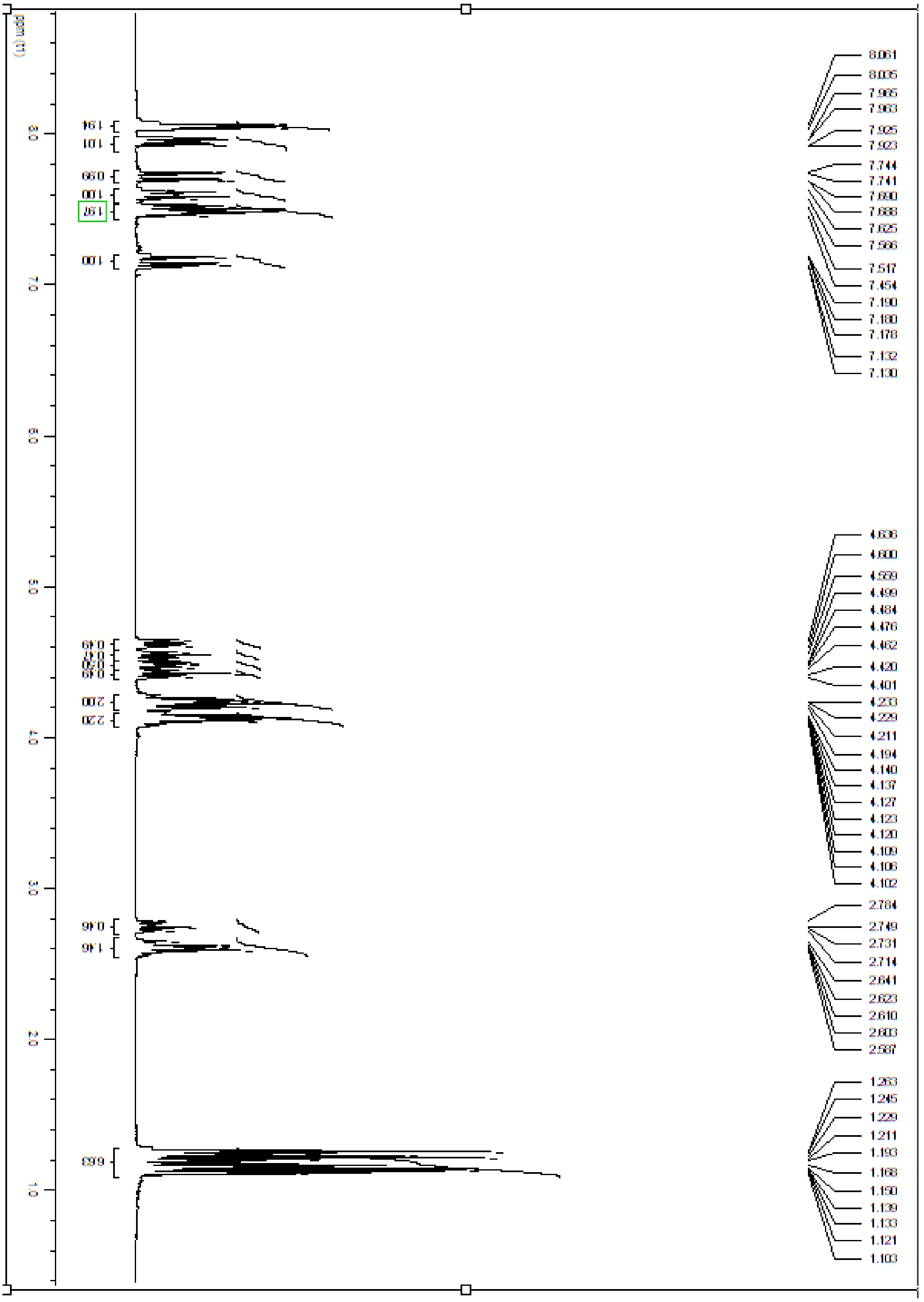
O
O
OEt
C
H2
S
O
O


ppm (t1)
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7.0
6.0
5.0
4.0
3.0
2.0
1.0
1.94
1.01
0.99
1.00
1.97
1.00
0.49
2.00
2.20
0.46
1.46
6.63
8.061
8.035
7.965
7.963
7.925
7.923
7.744
7.741
7.690
7.688
7.625
7.586
7.517
7.454
7.190
7.180
7.178
7.132
7.130
4.636
4.600
4.559
4.499
4.484
4.476
4.462
4.420
4.401
4.233
4.229
4.211
4.194
4.140
4.137
4.127
4.123
4.120
4.109
4.106
4.102
2.784
2.749
2.731
2.714
2.641
2.623
2.610
2.603
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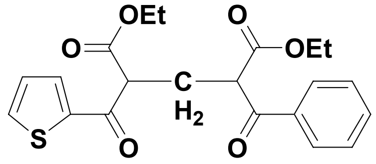
1.245
1.229
1.211
1.193
1.168
1.150
1.139
1.133
1.121
1.103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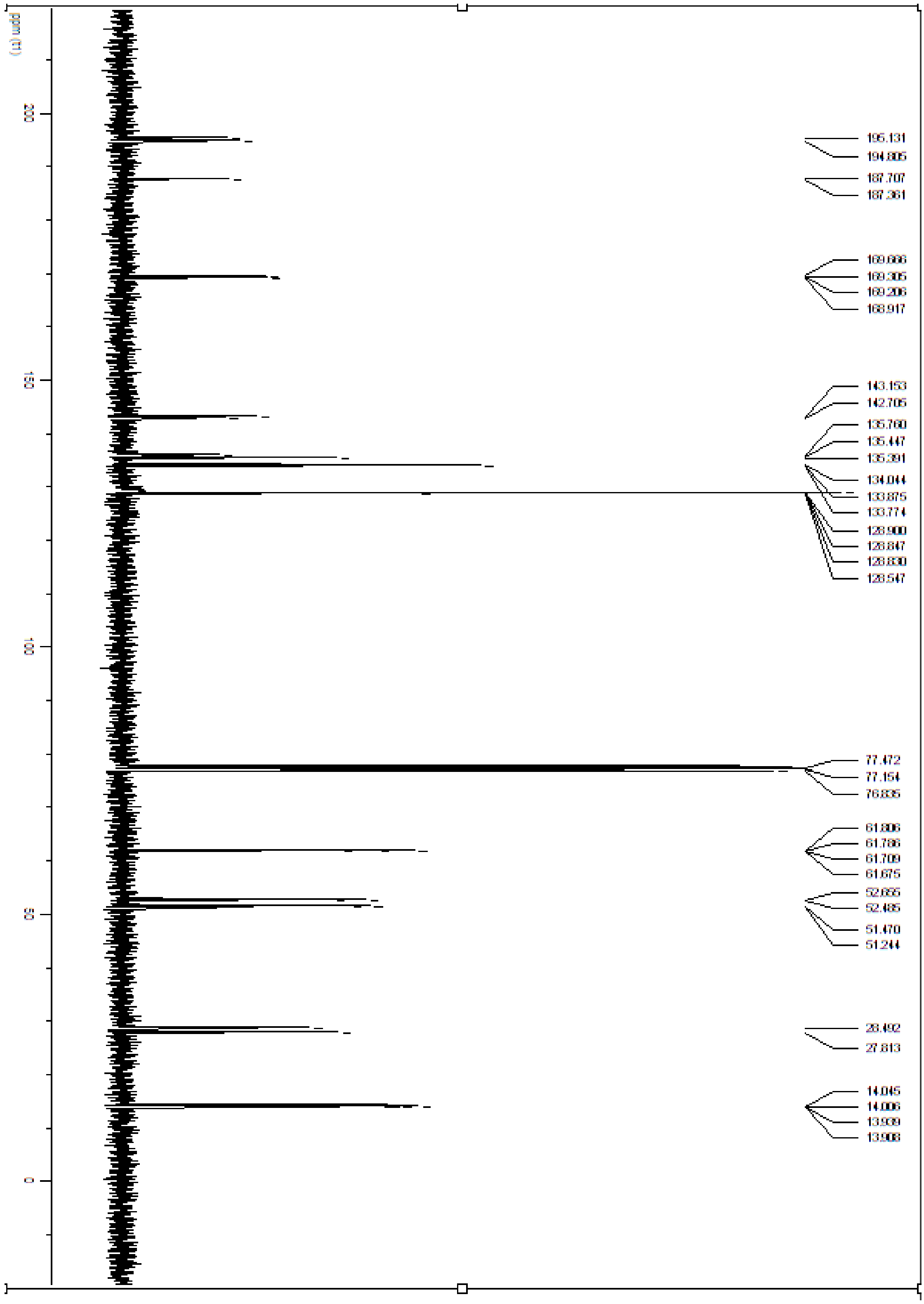
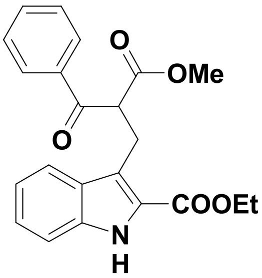
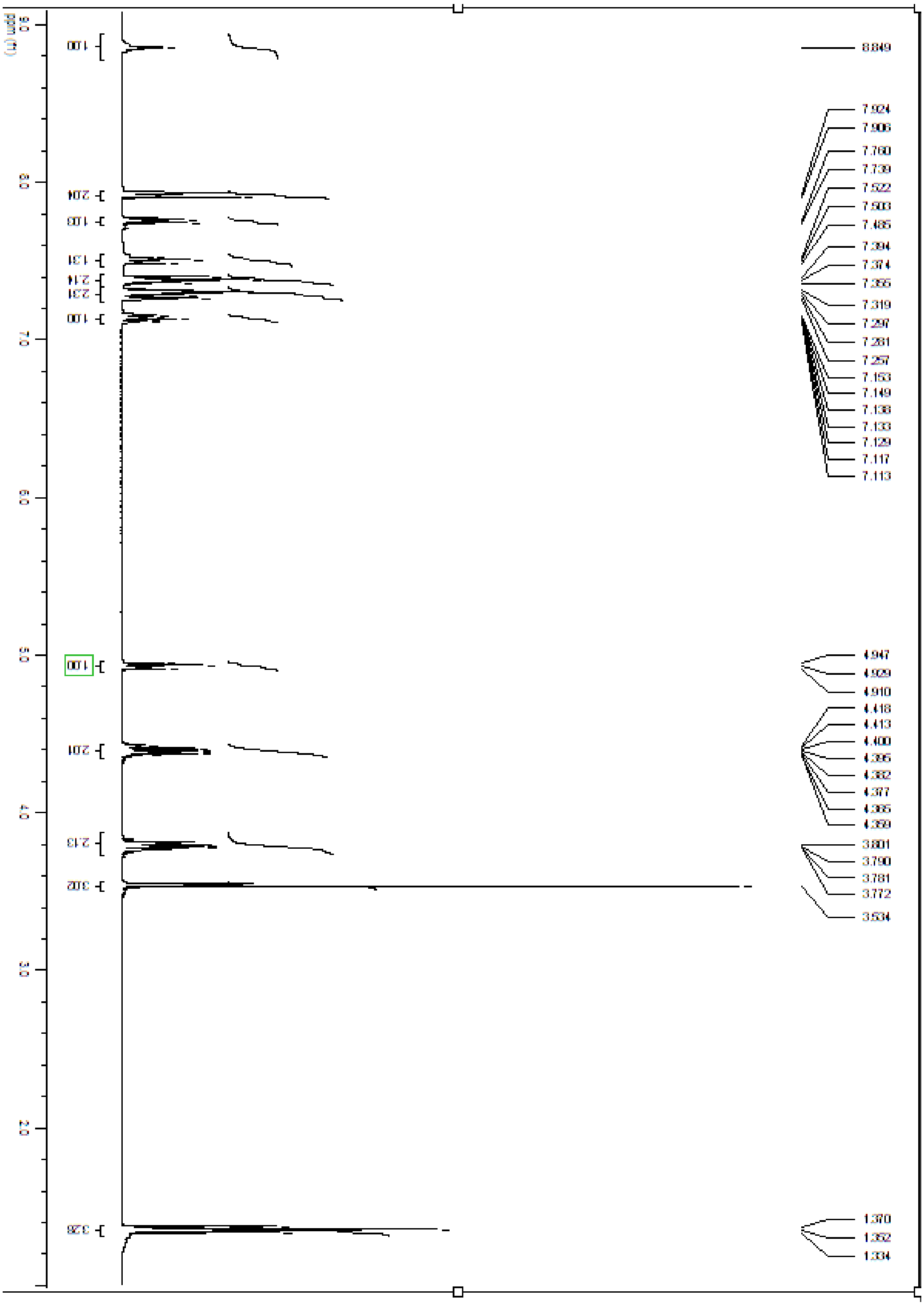
O
O
OEt
C
H2
S
O
O


ppm (t1)
200
150
100
50
0
195.131
194.805
187.707
187.361
169.666
169.305
169.206
168.917
143.153
142.705
135.760
135.447
135.391
134.044
133.875
133.774
128.900
128.847
128.830
128.547
77.472
77.154
76.835
61.806
61.786
61.709
61.675
52.655
52.485
51.470
51.244
28.492
27.813
14.045
14.006
13.939
13.908


O
OMe
O
COOEt
N
H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7.0
6.0
5.0
4.0
3.0
2.0
1.00
2.04
1.00
1.31
2.14
2.31
1.00
1.00
2.01
2.13
3.02
3.26
8.849
7.924
7.906
7.760
7.739
7.522
7.503
7.485
7.394
7.374
7.355
7.319
7.297
7.281
7.257
7.153
7.149
7.138
7.133
7.129
7.117
7.113
4.947
4.929
4.910
4.418
4.413
4.400
4.395
4.382
4.377
4.365
4.359
3.801
3.790
3.781
3.772
3.534
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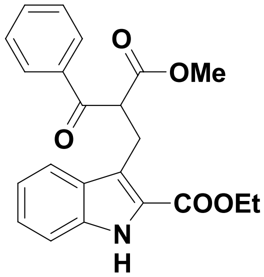
1.352
1.334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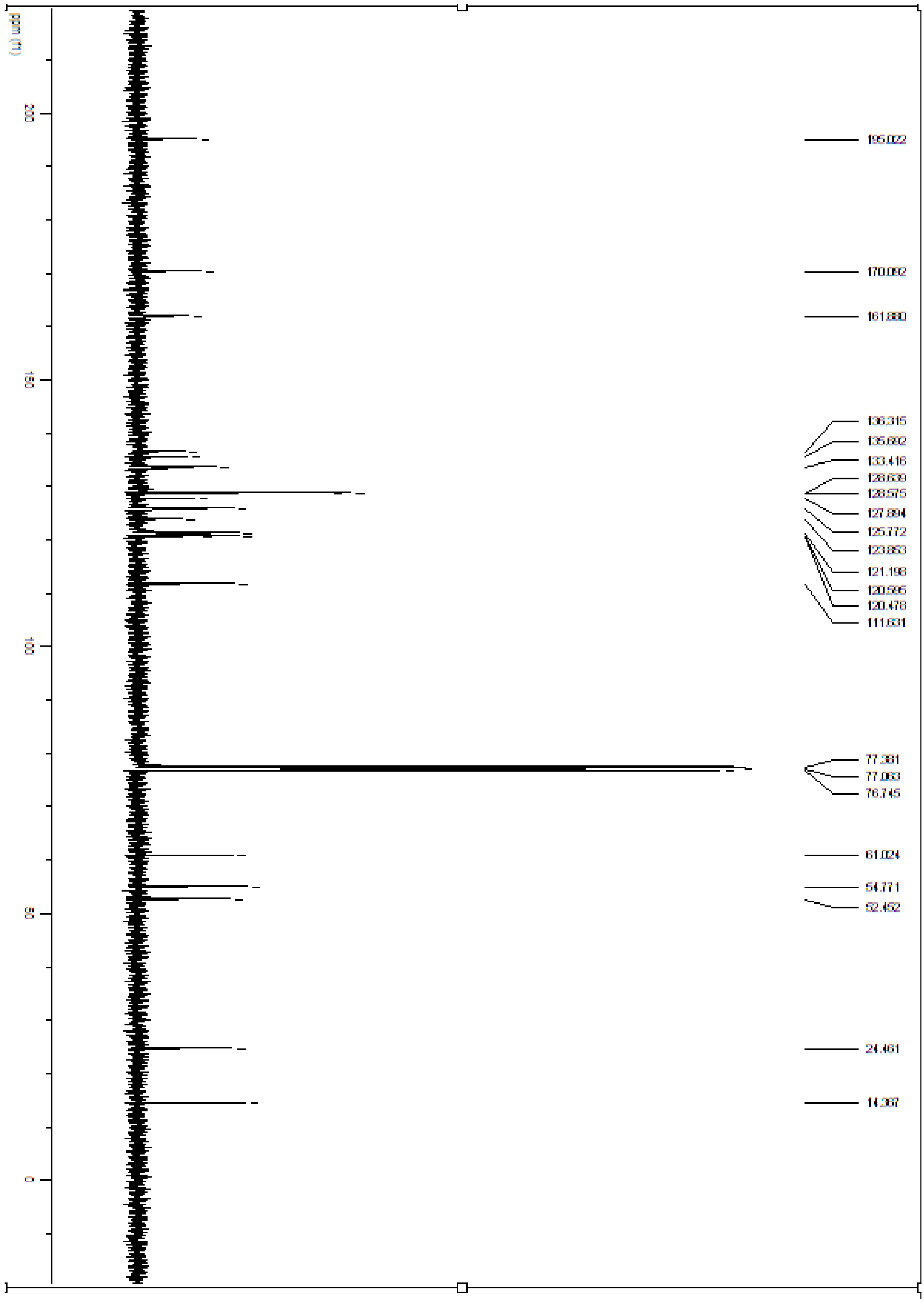
OMe
O
COOEt
N
H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100
50
0
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170.092
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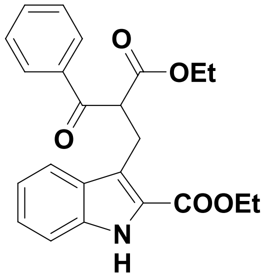
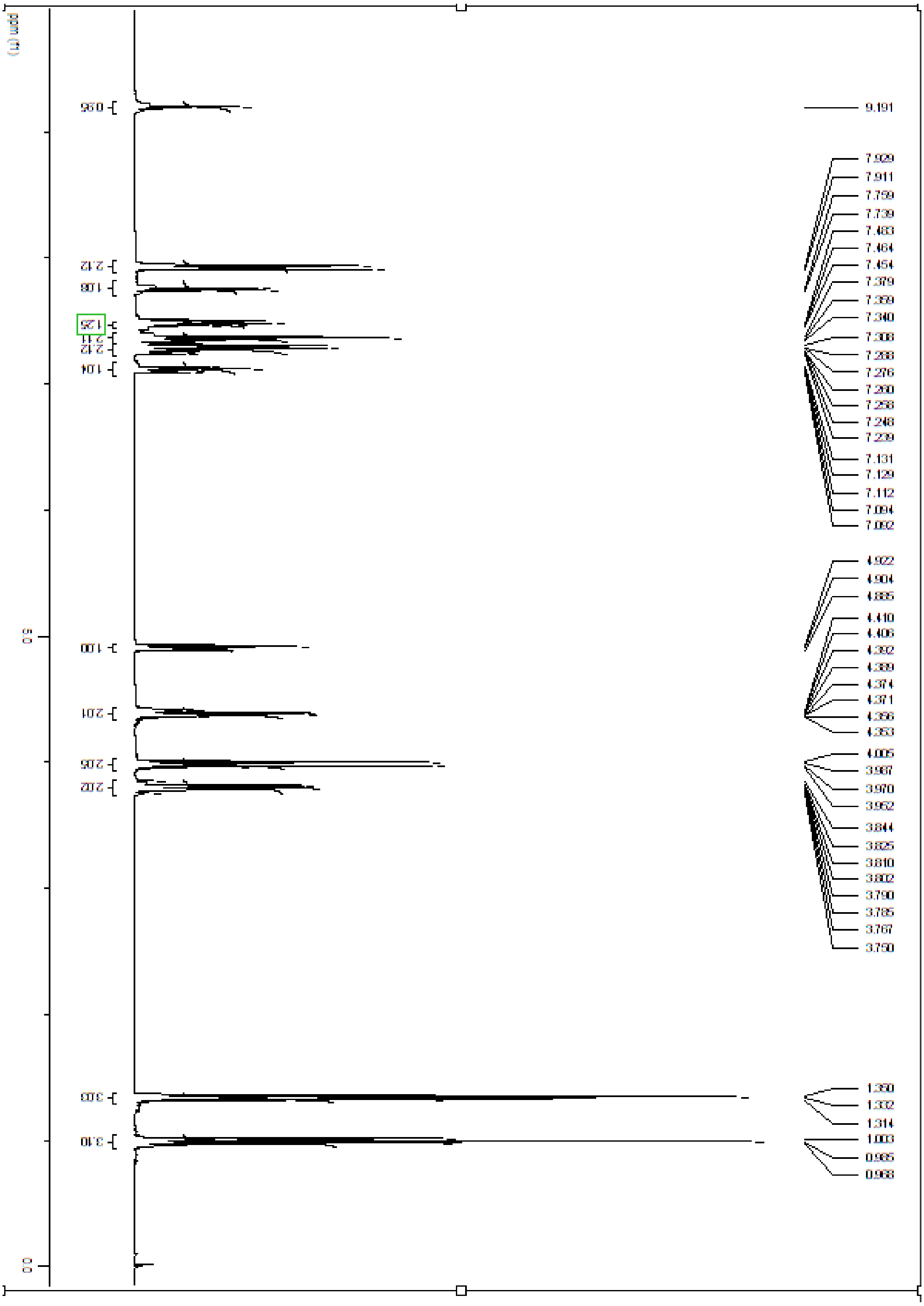
136.315
135.692
133.416
128.639
128.575
127.894
125.772
123.853
121.198
120.596
120.478
111.631
77.381
77.063
76.745
61.024
54.771
52.452
24.461
14.367


O
OEt
O
COOEt
N
H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0.56
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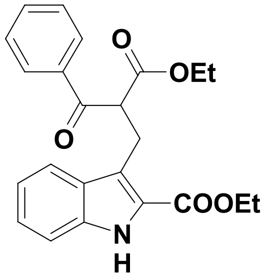
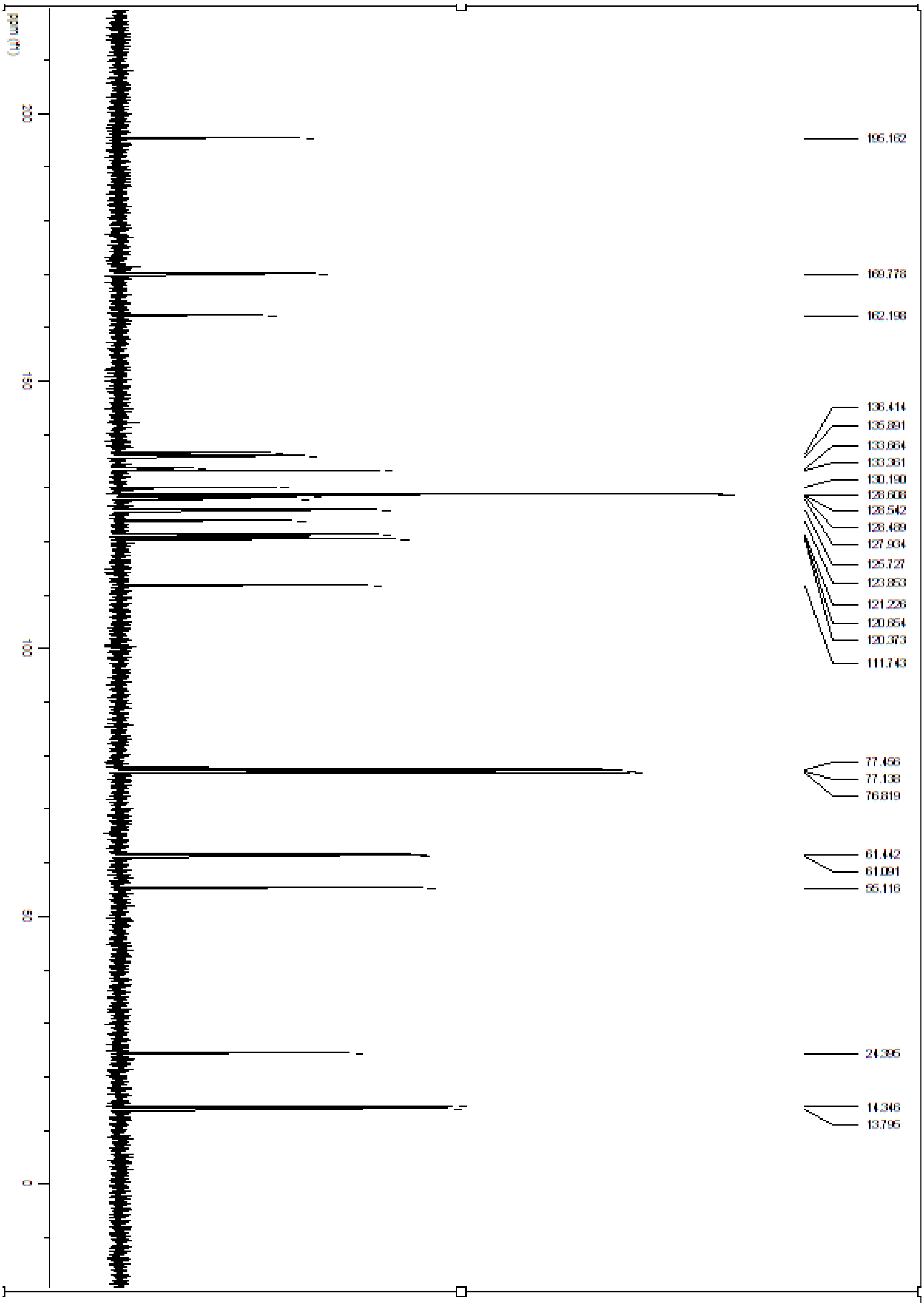
1.08
1.25
2.11
2.12
1.04
1.00
2.01
2.05
2.02
3.03
3.10
9.191
7.929
7.911
7.759
7.739
7.483
7.464
7.454
7.379
7.359
7.340
7.308
7.288
7.276
7.260
7.258
7.248
7.239
7.131
7.129
7.112
7.094
7.092
4.922
4.904
4.885
4.410
4.406
4.392
4.389
4.374
4.371
4.356
4.353
4.005
3.987
3.970
3.952
3.844
3.825
3.810
3.802
3.790
3.785
3.767
3.750
1.350
1.332
1.314
1.003
0.985
0.968


O
OEt
O
COOEt
N
H


ppm (f1)
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100
50
0
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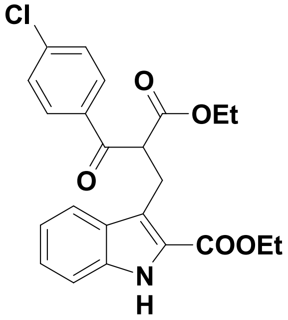
162.198
136.414
135.891
133.664
133.361
130.190
128.608
128.542
128.489
127.934
125.727
123.853
121.226
120.654
120.373
111.743
77.456
77.138
76.819
61.442
61.091
55.116
24.395
14.346
13.796


Cl
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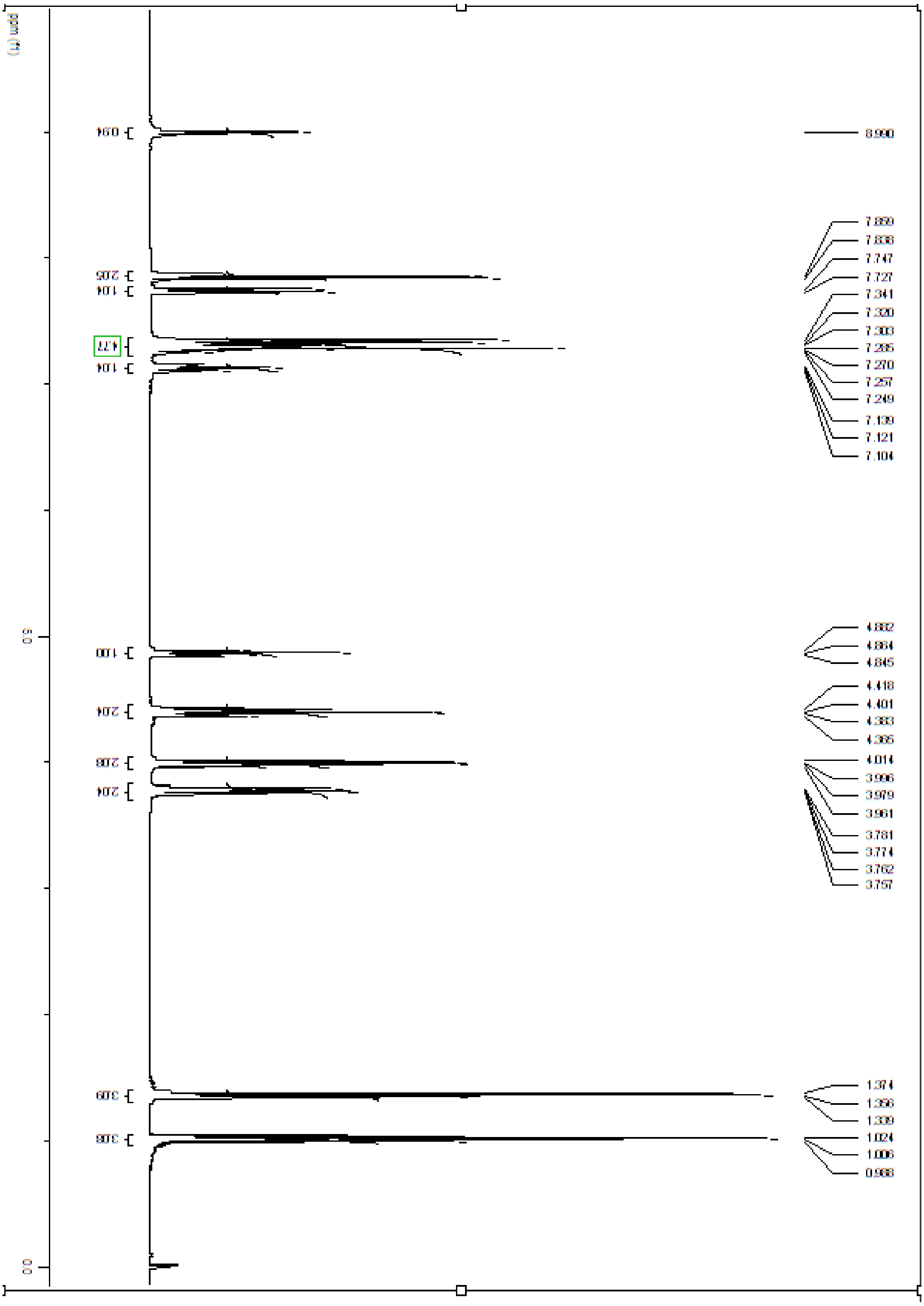
O
COOEt
N
H


ppm (t1)
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0.94
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1.00
2.04
2.08
2.04
3.09
3.08
8.990
7.859
7.838
7.747
7.727
7.341
7.320
7.303
7.285
7.270
7.257
7.249
7.139
7.121
7.104
4.882
4.864
4.845
4.418
4.401
4.383
4.365
4.014
3.996
3.979
3.961
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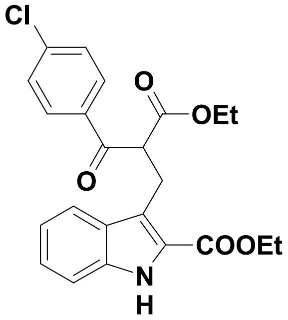
3.774
3.762
3.757
1.374
1.356
1.339
1.024
1.006
0.988


Cl
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COOEt
N
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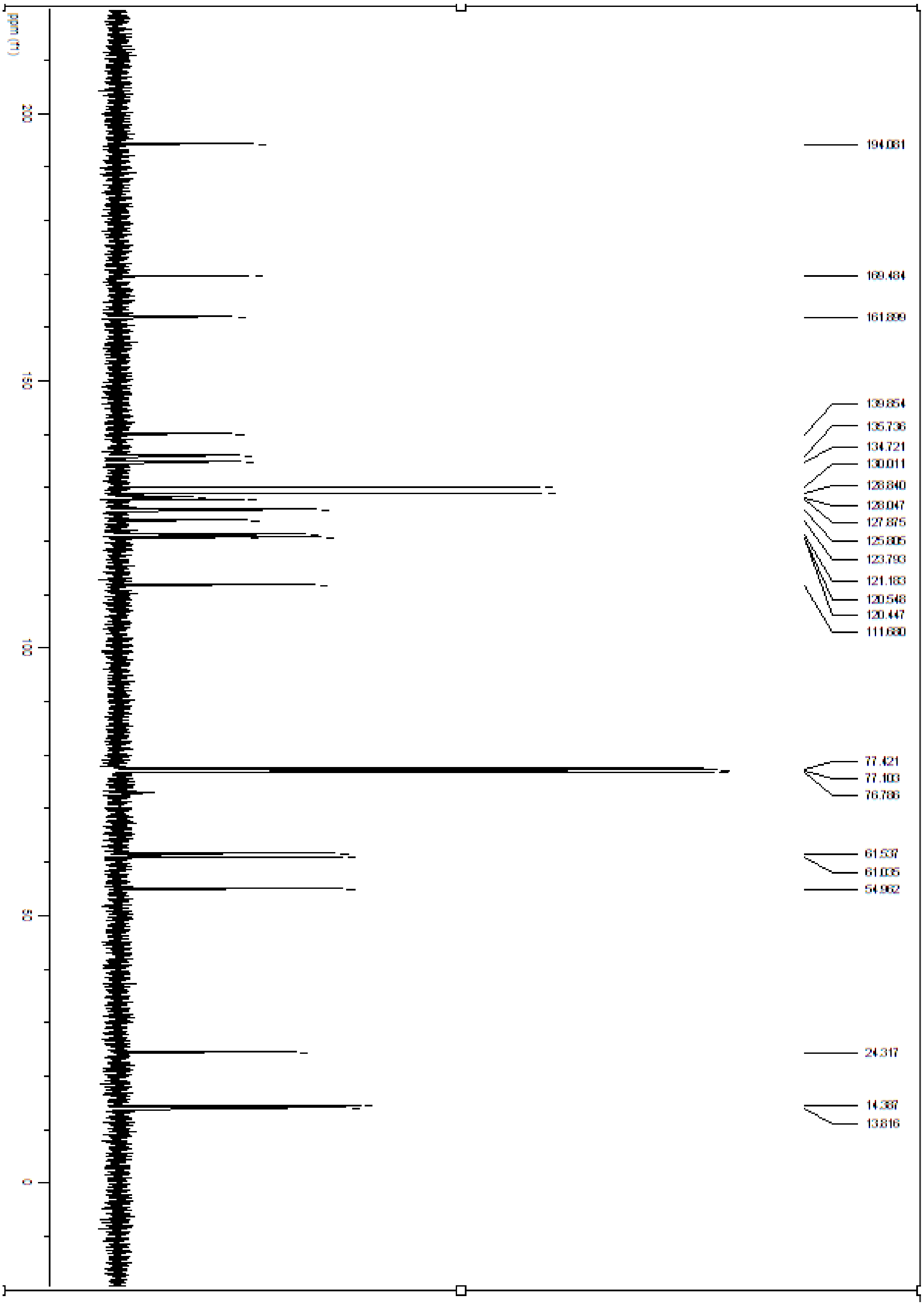
ppm (f1)
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135.736
134.721
130.011
128.840
128.047
127.875
125.805
123.793
121.183
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120.447
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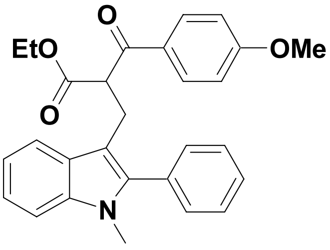
77.421
77.103
76.786
61.537
61.035
54.962
24.317
14.387
13.816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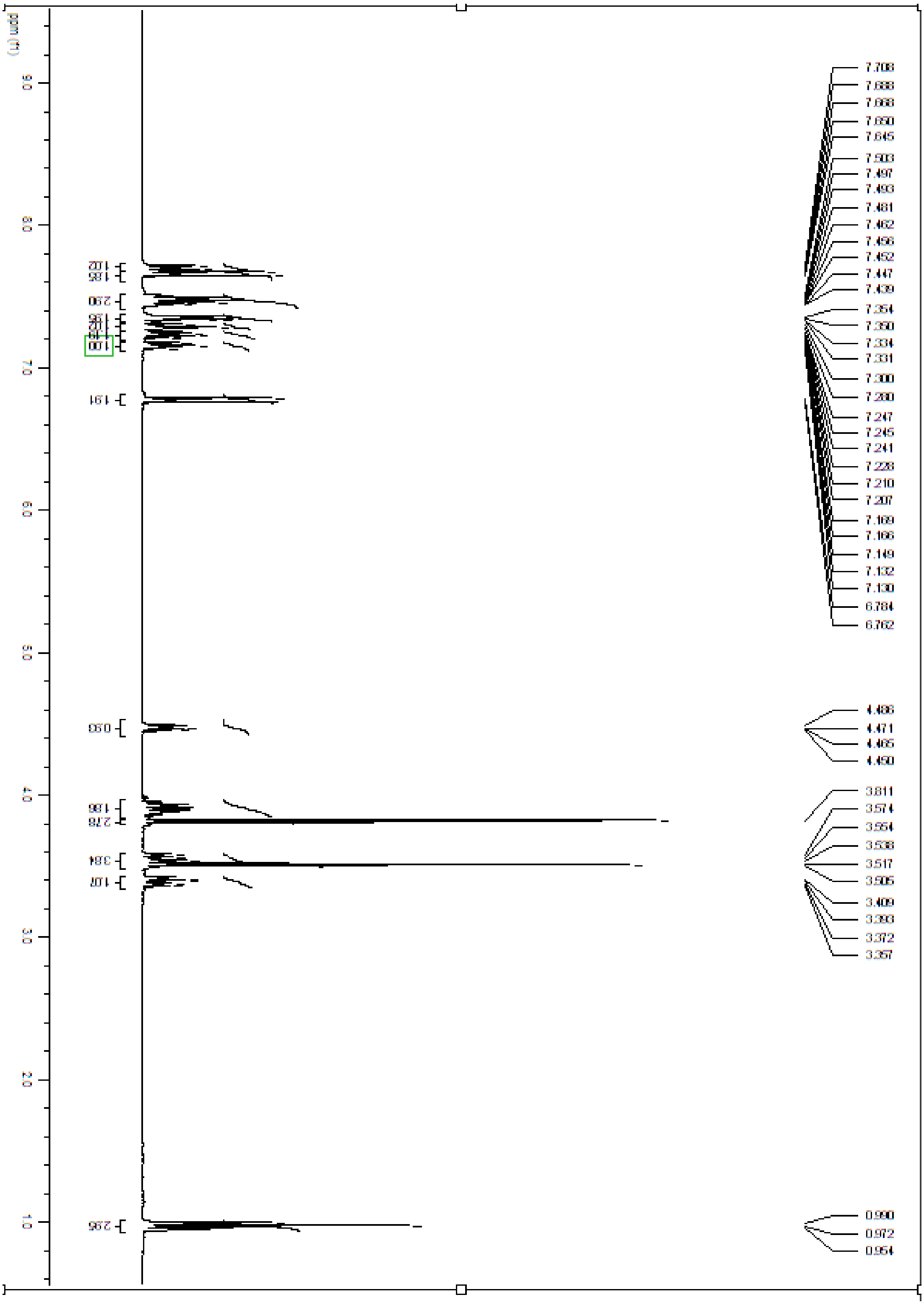
O
OMe
N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1.0
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2.90
1.00
1.91
0.59
1.86
2.78
3.84
1.07
2.96
7.708
7.688
7.668
7.650
7.645
7.503
7.497
7.493
7.481
7.462
7.456
7.452
7.447
7.439
7.354
7.350
7.334
7.331
7.300
7.280
7.247
7.245
7.241
7.228
7.210
7.207
7.169
7.166
7.149
7.132
7.130
6.784
6.762
4.486
4.471
4.465
4.450
3.811
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3.554
3.538
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3.505
3.409
3.393
3.372
3.357
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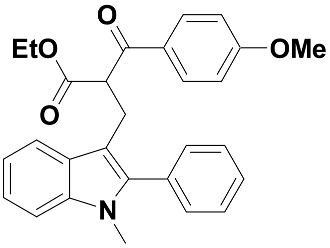
0.972
0.954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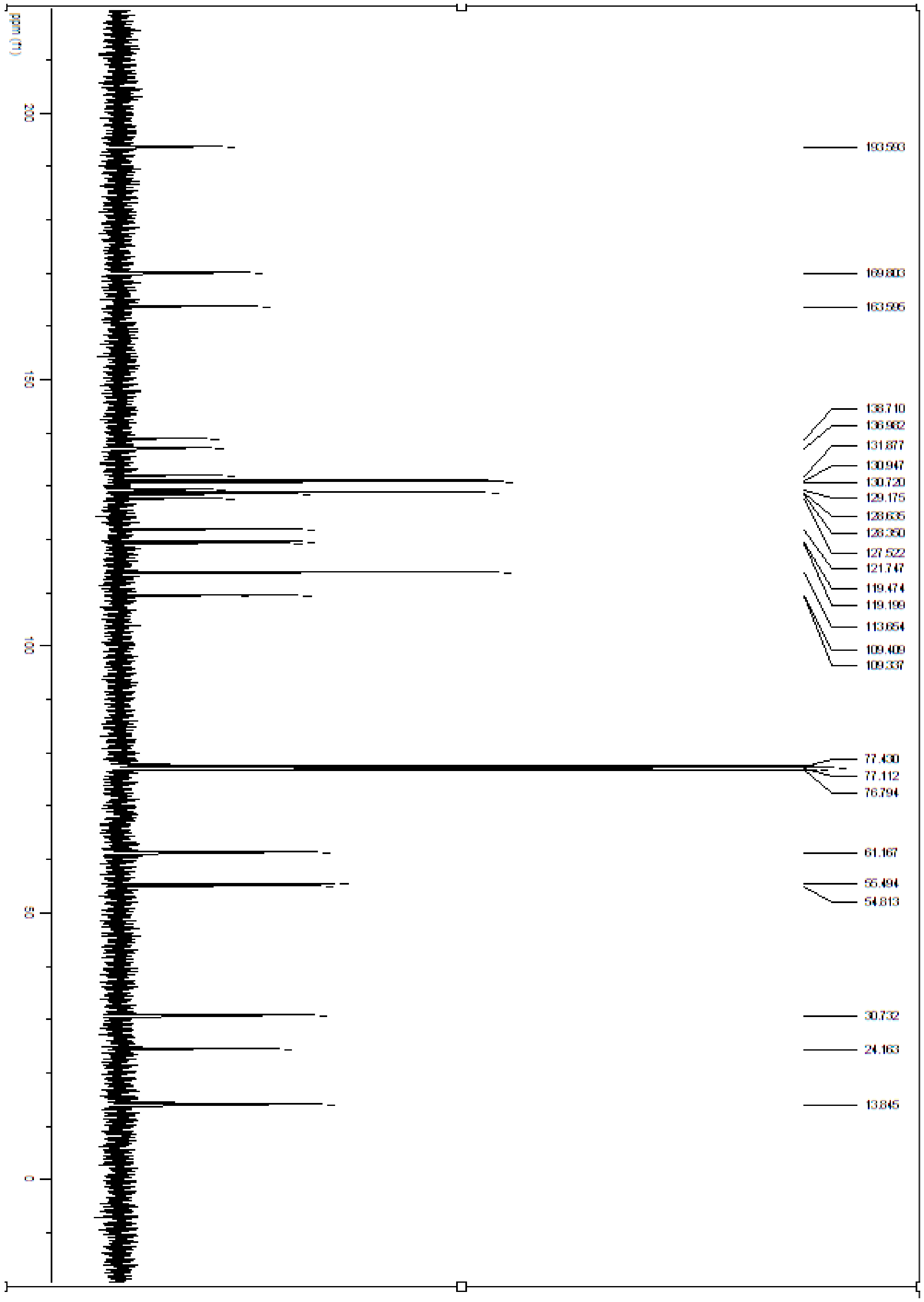
EtO
OMe
O
N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130.720
129.175
128.636
128.350
127.522
121.747
119.474
119.199
113.654
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77.430
77.112
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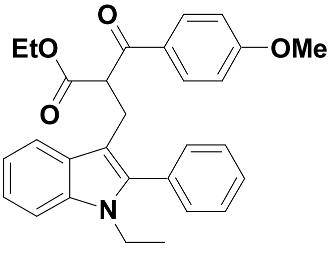
55.494
54.813
30.732
24.163
13.845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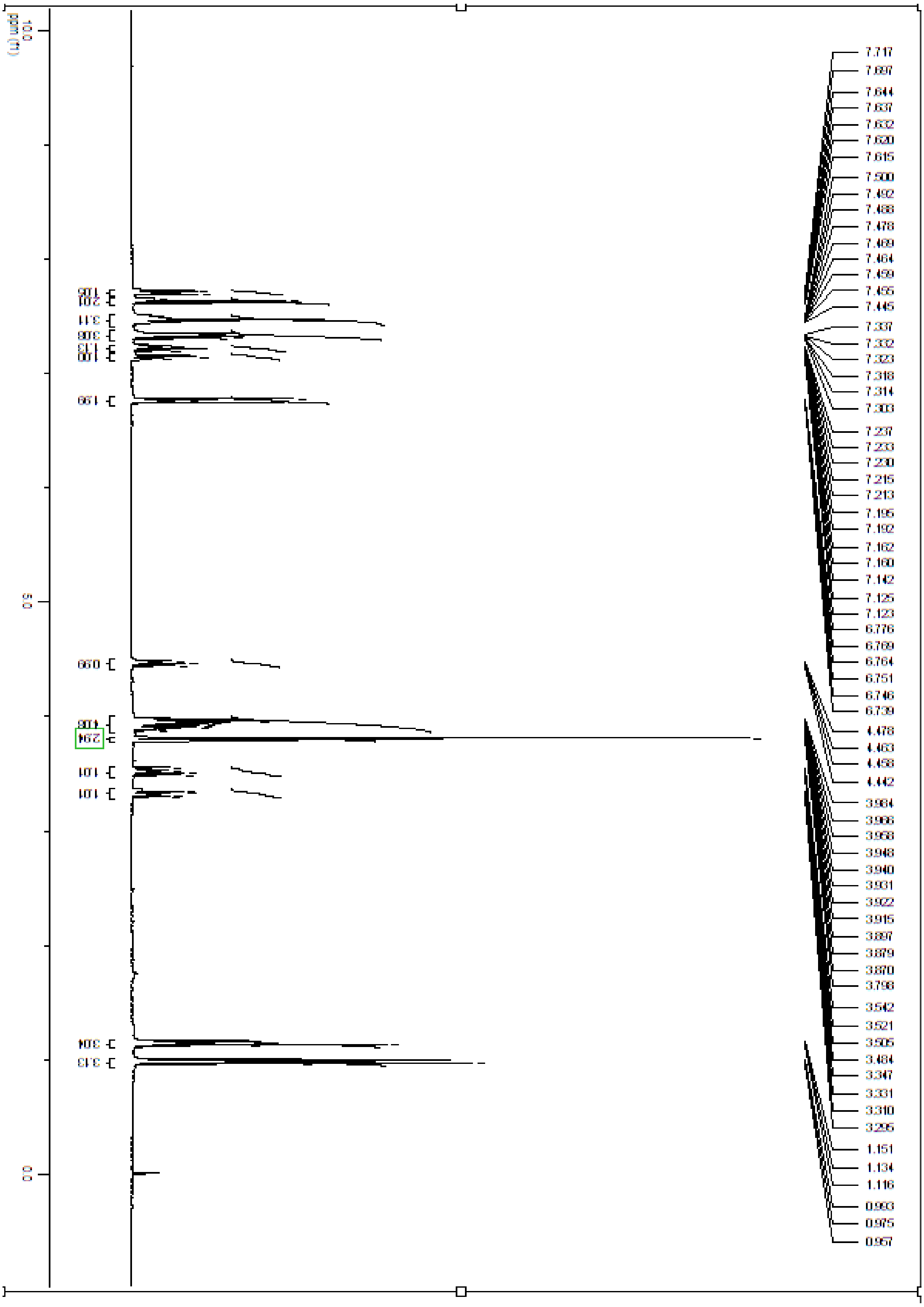
EtO
O
OMe
N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0.0
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3.08
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1.00
1.99
0.99
1.08
2.94
1.01
1.01
3.04
3.13
7.717
7.697
7.644
7.637
7.632
7.620
7.615
7.500
7.492
7.488
7.478
7.469
7.464
7.459
7.455
7.445
7.337
7.332
7.323
7.318
7.314
7.303
7.237
7.233
7.230
7.215
7.213
7.195
7.192
7.162
7.160
7.142
7.125
7.123
6.776
6.769
6.764
6.751
6.746
6.739
4.478
4.463
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4.442
3.984
3.966
3.958
3.948
3.940
3.931
3.922
3.915
3.897
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3.870
3.798
3.542
3.521
3.505
3.484
3.347
3.331
3.310
3.296
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1.134
1.116
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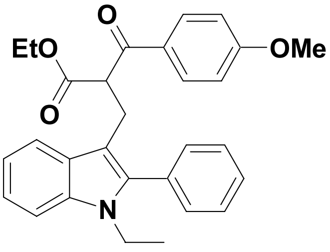
0.975
0.957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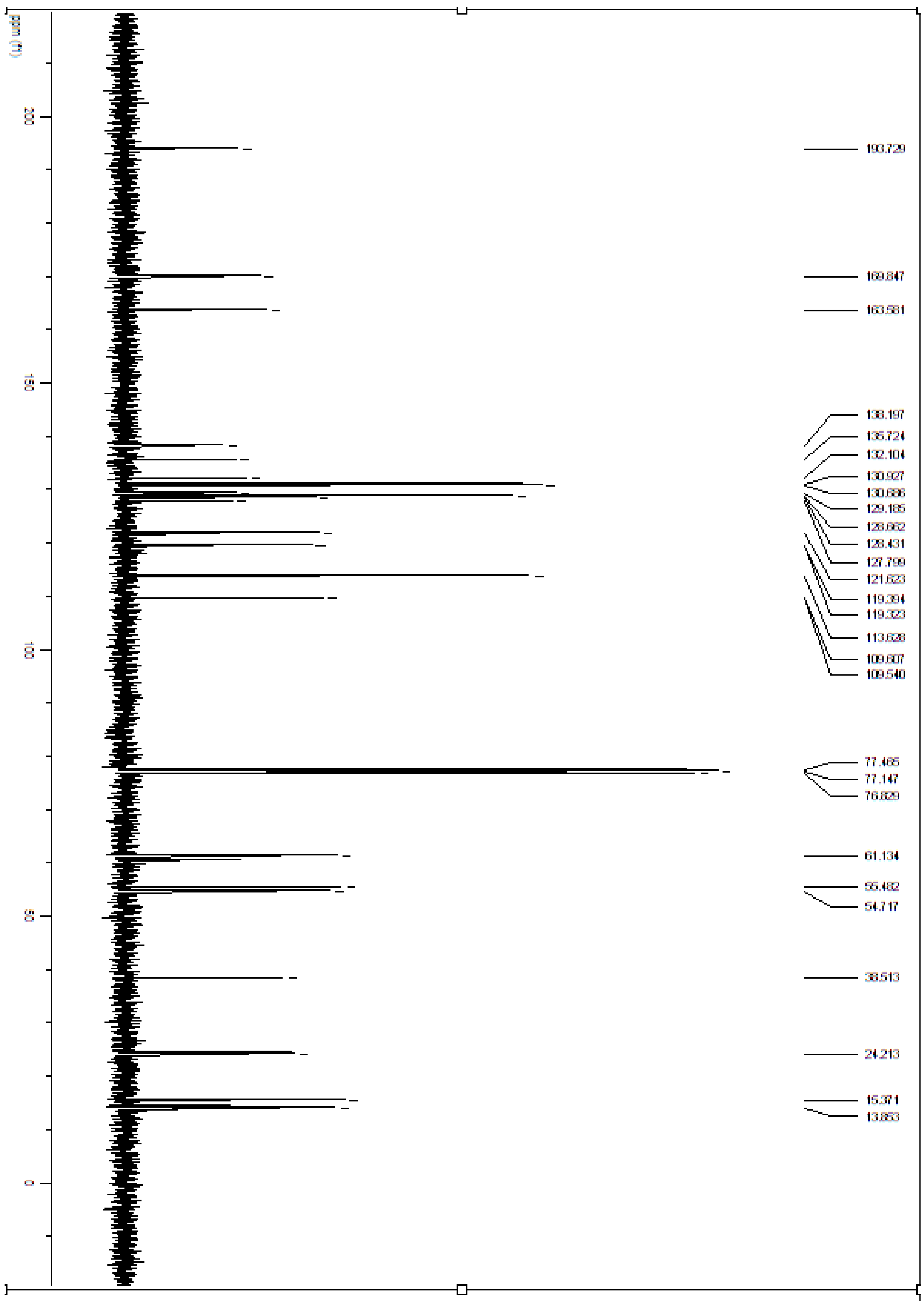
O
OMe
N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132.104
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130.686
129.185
128.662
128.431
127.799
121.623
119.394
119.323
113.628
109.607
109.540
77.465
77.147
76.829
61.134
55.482
54.717
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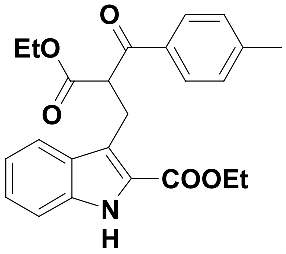
24.213
15.371
13.853


O
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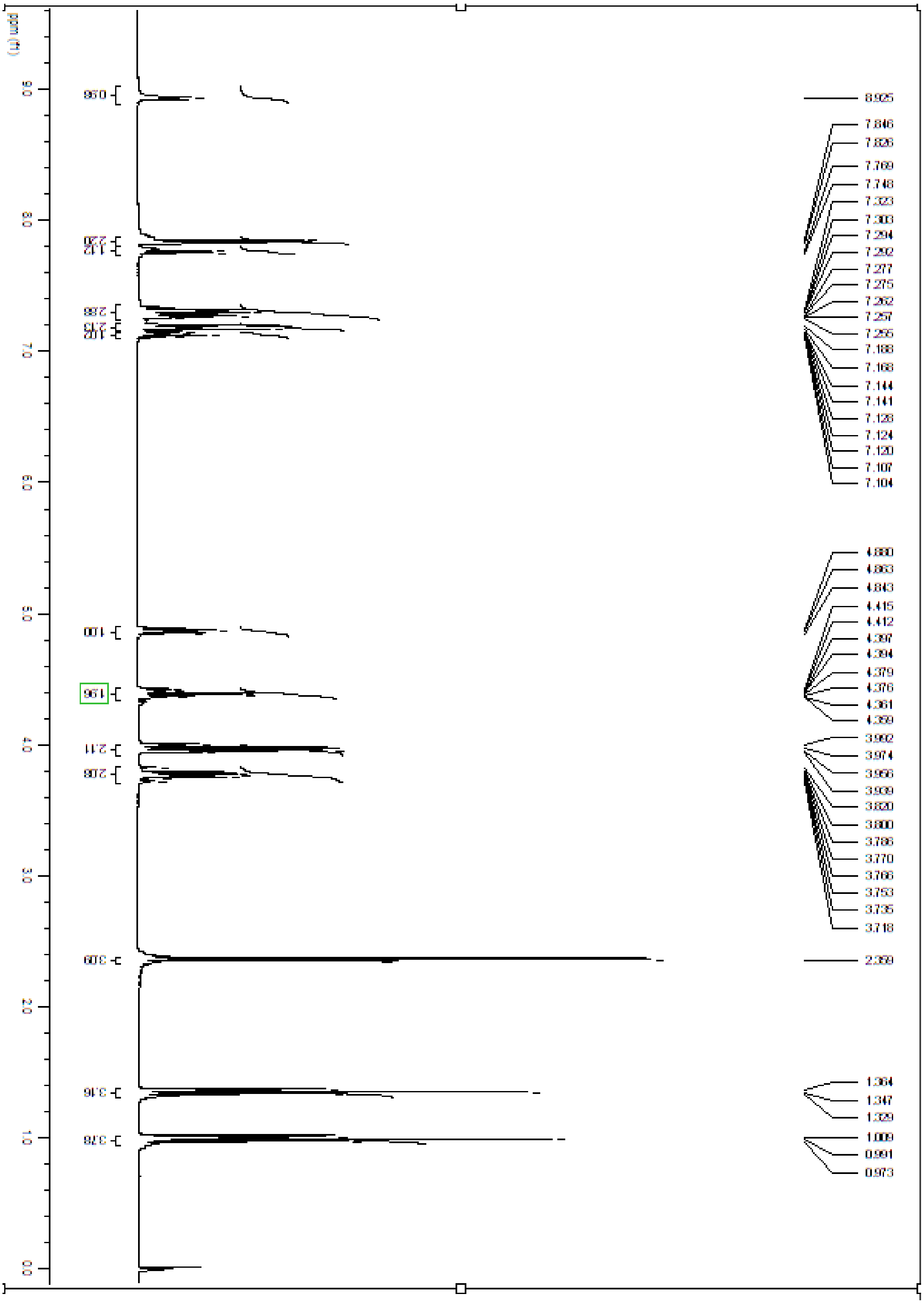
O
COOEt
N
H


ppm (f1)
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7.0
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1.0
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1.12
2.88
2.15
1.05
1.00
1.96
2.11
2.08
3.09
3.16
3.78
8.925
7.846
7.826
7.769
7.748
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7.294
7.292
7.277
7.275
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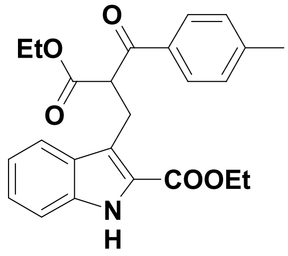
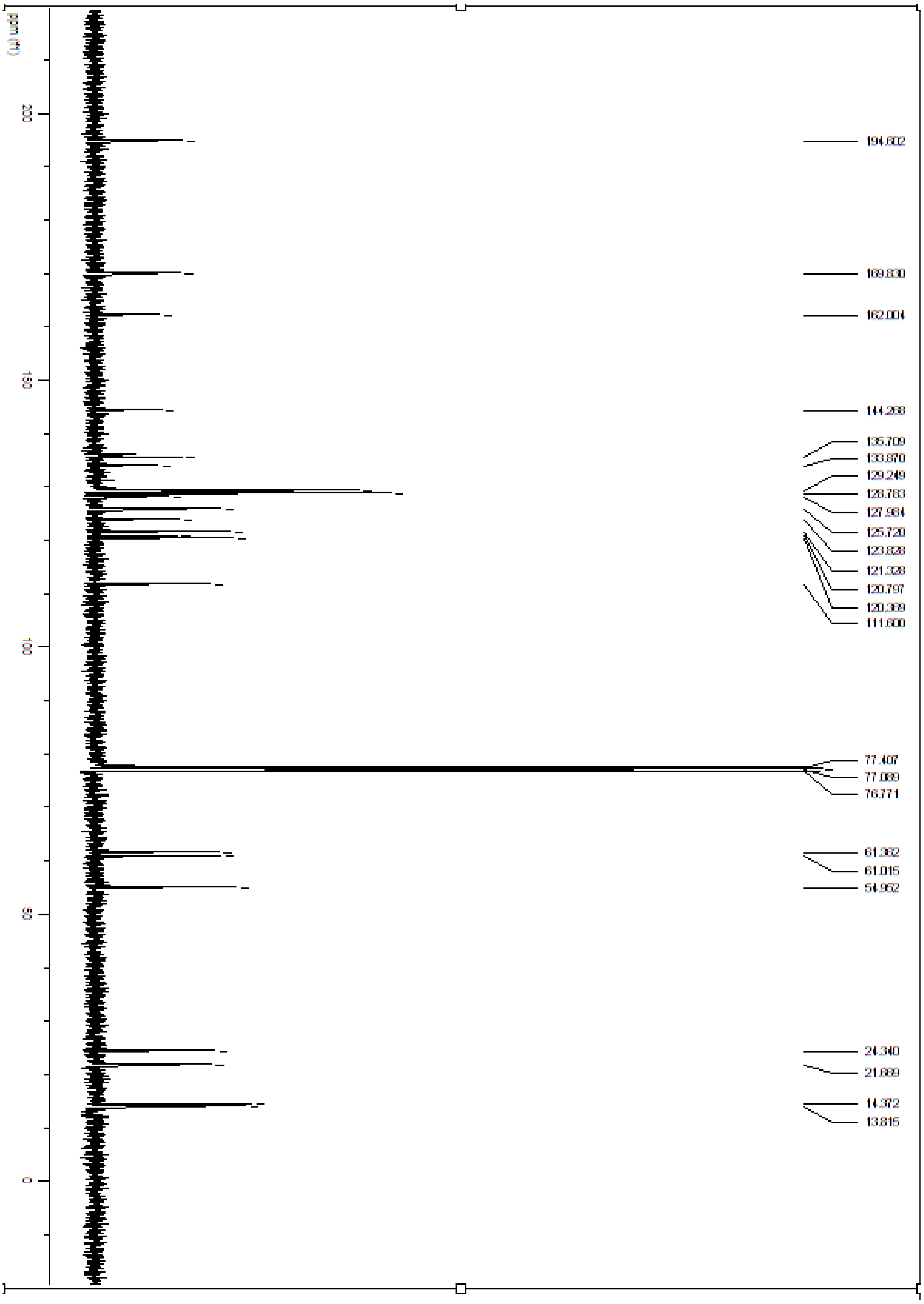
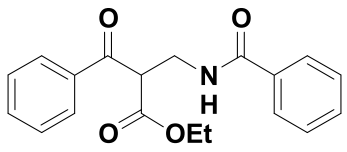
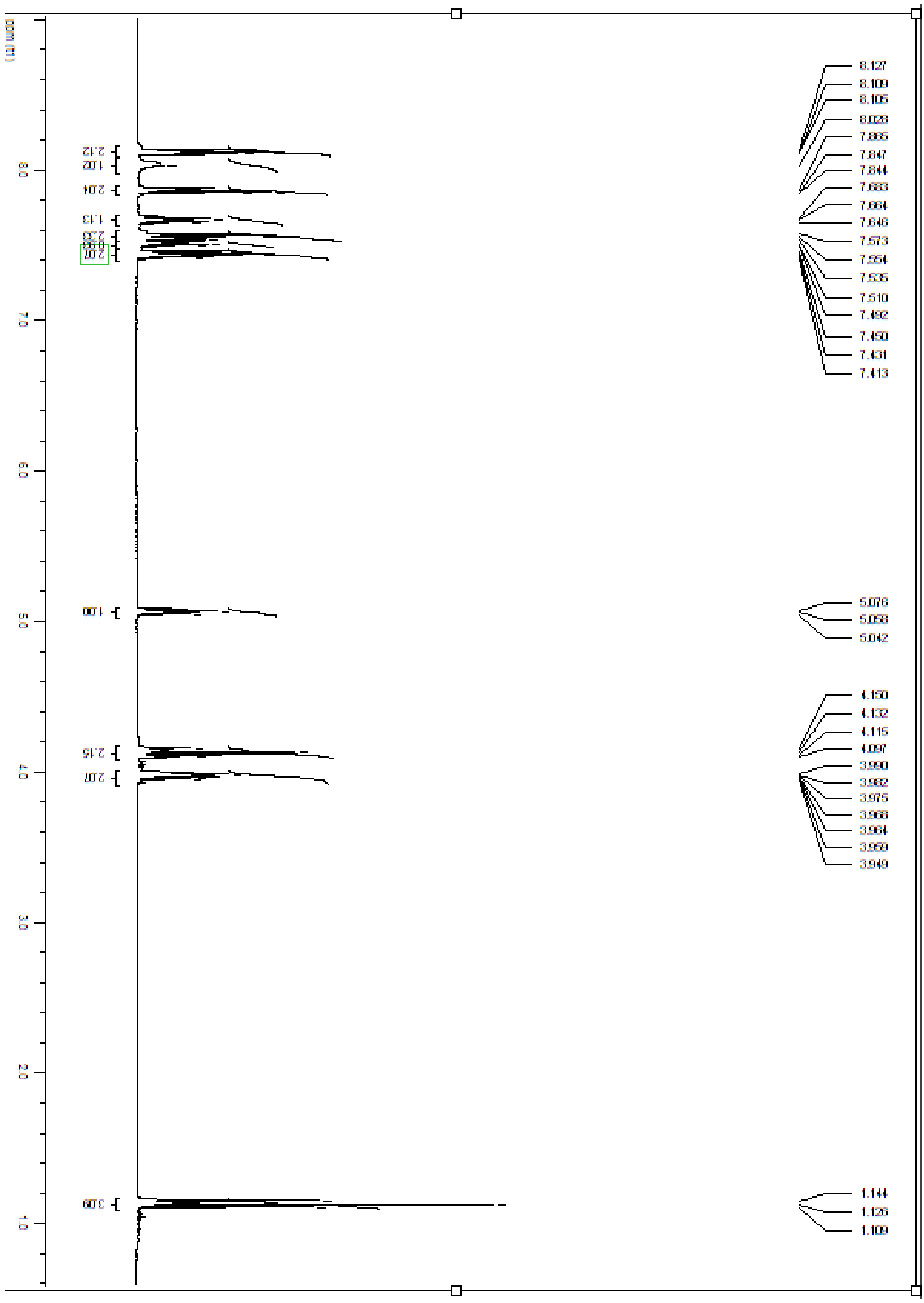
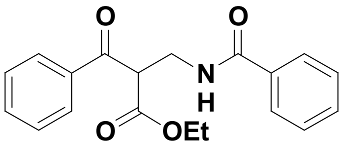
7.257
7.255
7.188
7.168
7.144
7.141
7.128
7.124
7.120
7.107
7.104
4.880
4.863
4.843
4.415
4.412
4.397
4.394
4.379
4.376
4.361
4.359
3.992
3.974
3.956
3.939
3.820
3.800
3.786
3.770
3.766
3.753
3.735
3.718
2.359
1.364
1.347
1.329
1.009
0.991
0.973

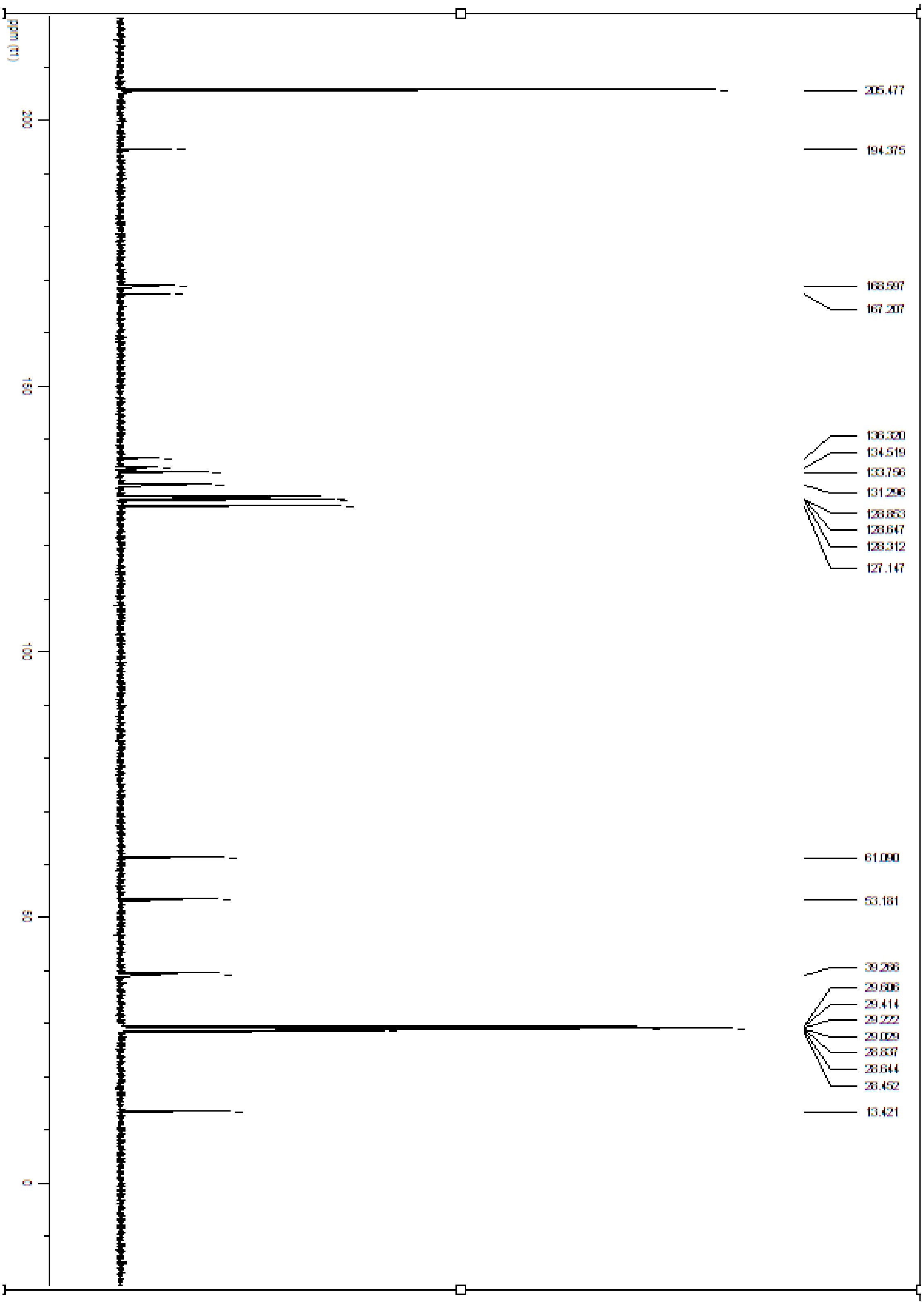

EtO
O
O
COOEt
N
H


ppm (f1)
200
150
100
50
0
194.602
169.830
162.004
144.268
135.709
133.870
129.249
128.763
127.984
125.720
123.828
121.328
120.797
120.369
111.600
77.407
77.089
76.771
61.362
61.015
54.952
24.340
21.659
14.372
13.815


O
O
N
H
O
OEt


ppm (t1)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
2.12
1.02
2.04
1.13
2.07
1.00
2.15
2.07
3.09
8.127
8.109
8.105
8.028
7.866
7.847
7.844
7.683
7.664
7.646
7.573
7.554
7.536
7.510
7.492
7.450
7.431
7.413
5.076
5.058
5.042
4.150
4.132
4.115
4.097
3.990
3.982
3.975
3.968
3.964
3.959
3.949
1.144
1.126
1.109


O
O
N
H
O
OEt


ppm (t1)
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150
100
50
0
205.477
194.375
168.597
167.207
136.320
134.519
133.796
131.296
128.853
128.647
128.312
127.147
61.090
53.181
39.266
29.606
29.414
29.222
29.029
28.837
28.644
28.452
13.421