Electronic Supplementary Material (ESI) for MedChemComm.

Novel hybrids derived from aspirin and chalcones potently suppress colorectal cancer in vitro and in vivo

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^{1}H NMR data of chalcones **6a-p**.

(*E*)-3-(2-hydroxyphenyl)-1-(p-tolyl)prop-2-en-1-one (**6a**). The title compound was prepared according to the general procedure in 68% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.49 (s, 1H), 8.23-8.13 (m, 3H), 8.00-7.97 (m, 2H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 6.8, 7.2 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 6.8, 7.2 Hz, 1H), 2.50 (s, 3H).

(*E*)-3-(2-hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (**6b**). The title compound was prepared according to the general procedure in 60% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 2H), 8.02 (d, *J* = 15.6 Hz, 1H), 7.88 (m, 2H), 7.26 (t, *J* = 8.0, 7.6 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.87 (t, *J* = 6.8, 7.2 Hz, 1H), 3.85 (s, 3H).

(*E*)-1-(4-chlorophenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one (**6c**). The title compound was prepared according to the general procedure in 65% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.39 (s, 1H), 8.10-8.07 (m, 3H), 7.86-7.80 (m, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.27 (t, *J* = 8.0, 6.8 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.86 (t, *J* = 7.2, 7.6 Hz, 1H).

(*E*)-1-(4-bromophenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one (**6d**). The title compound was prepared according to the general procedure in 55% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.34 (s, 1H), 8.09-8.05 (m, 3H), 7.90-7.78 (m, 4H), 7.29 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.89 (t, *J* = 6.8 Hz, 1H).

(*E*)-4-(3-(2-hydroxyphenyl)acryloyl)benzonitrile (**6e**). The title compound was prepared according to the general procedure in 50% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.39 (s, 1H), 8.25 (d, J = 7.6 Hz, 2H), 8.12-8.05 (m, 3H), 7.92-7.85 (m, 2H), 7.31 (t, J = 7.6, 8.0 Hz, 1H), 6.95 (d, J = 8.0Hz, 6.89 (7.6, 7.2 Hz, 1H).

(*E*)-3-(2-hydroxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one (**6f**). The title compound was prepared according to the general procedure in 44% yield. ^{1}H-NMR (400 MHz,

DMSO-d_6) δ 10.44 (s, 1H), 8.35-8.26 (m, 4H), 8.08 (d, *J* = 14.6 Hz, 1H), 7.86-7.82 (m, 2H), 7.29 (t, *J* = 6.4 Hz, 1H), 6.96-6.88 (m, 2H).

(*E*)-1-(4-chlorophenyl)-3-(2-hydroxy-4-methoxyphenyl)prop-2-en-1-one (**6g**). The title compound was prepared according to the general procedure in 47% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.43 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 2H), 8.0 (d, *J* = 15.6 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 15.6 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 2H), 6.49-6.47 (m, 2H), 3.75 (s, 3H).

(*E*)-1-(4-chlorophenyl)-3-(2-hydroxy-5-methoxyphenyl)prop-2-en-1-one (**6h**). The title compound was prepared according to the general procedure in 60% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 8.16 (d, *J* = 7.6 Hz, 2H), 8.07 (d, *J* = 15.6 Hz, 1H), 7.87 (d, *J* = 15.6 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.45 (s, 1H), 6.93-6.86 (m, 2H), 3.78 (s, 3H).

(*E*)-1-(4-chlorophenyl)-3-(5-fluoro-2-hydroxyphenyl)prop-2-en-1-one (**6i**). The title compound was prepared according to the general procedure in 65% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.30 (s, 1H), 8.17 (d, *J* = 7.6 Hz, 2H), 8.02 (d, *J* = 15.6 Hz, 1H), 7.91 (d, *J* = 15.6 Hz, 1H), 7.84 (m, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.14 (t, *J* = 8.0 Hz, 1H), 6.94-6.91 (m, 1H),

(*E*)-3-(5-chloro-2-hydroxyphenyl)-1-(4-chlorophenyl)prop-2-en-1-one (**6j**). The title compound was prepared according to the general procedure in 70% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 8.19 (d, *J* = 8.0 Hz, 2H), 8.07-8.04 (m, 1H), 8.00-7.94 (m, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H).

(*E*)-3-(5-bromo-2-hydroxyphenyl)-1-(4-chlorophenyl)prop-2-en-1-one (**6k**). The title compound was prepared according to the general procedure in 59% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.63 (s, 1H), 8.20-8.18 (m, 3H), 8.02-7.92 (m, 2H), 7.64 (d,

J = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H).

(*E*)-1-(4-chlorophenyl)-3-(2-hydroxy-3-methoxyphenyl)prop-2-en-1-one (**6l**). The title compound was prepared according to the general procedure in 67% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 9.51 (s, 1H), 8.13-8.07 (m, 3H), 7.82 (d, *J* = 15.6 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.84 (t, *J* = 8.0 Hz, 1H), 3.83 (s, 3H).

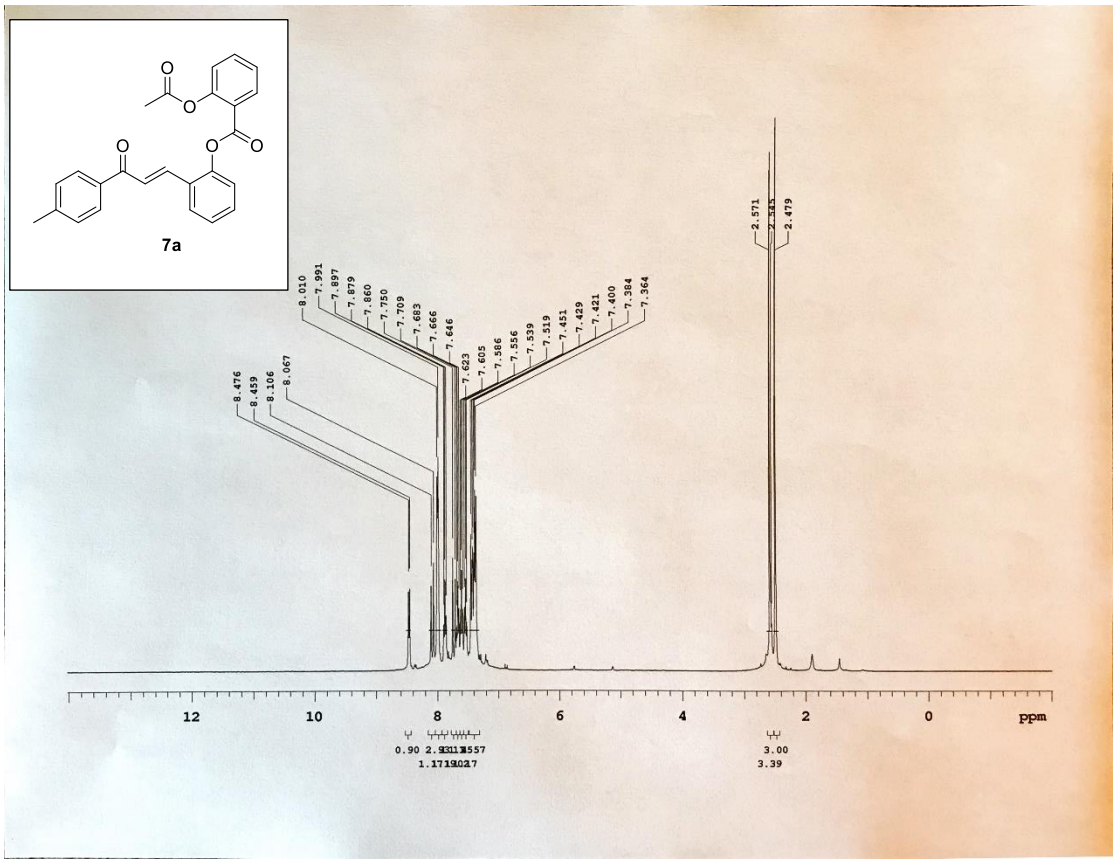
(*E*)-1-(4-chlorophenyl)-3-(2-hydroxy-5-methylphenyl)prop-2-en-1-one (**6m**). The title compound was prepared according to the general procedure in 65% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.11 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 2H), 8.04 (d, *J* = 15.6 Hz, 1H), 7.80 (d, *J* = 15.6 Hz, 1H), 7.69 (s, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 2.23 (s, 3H).

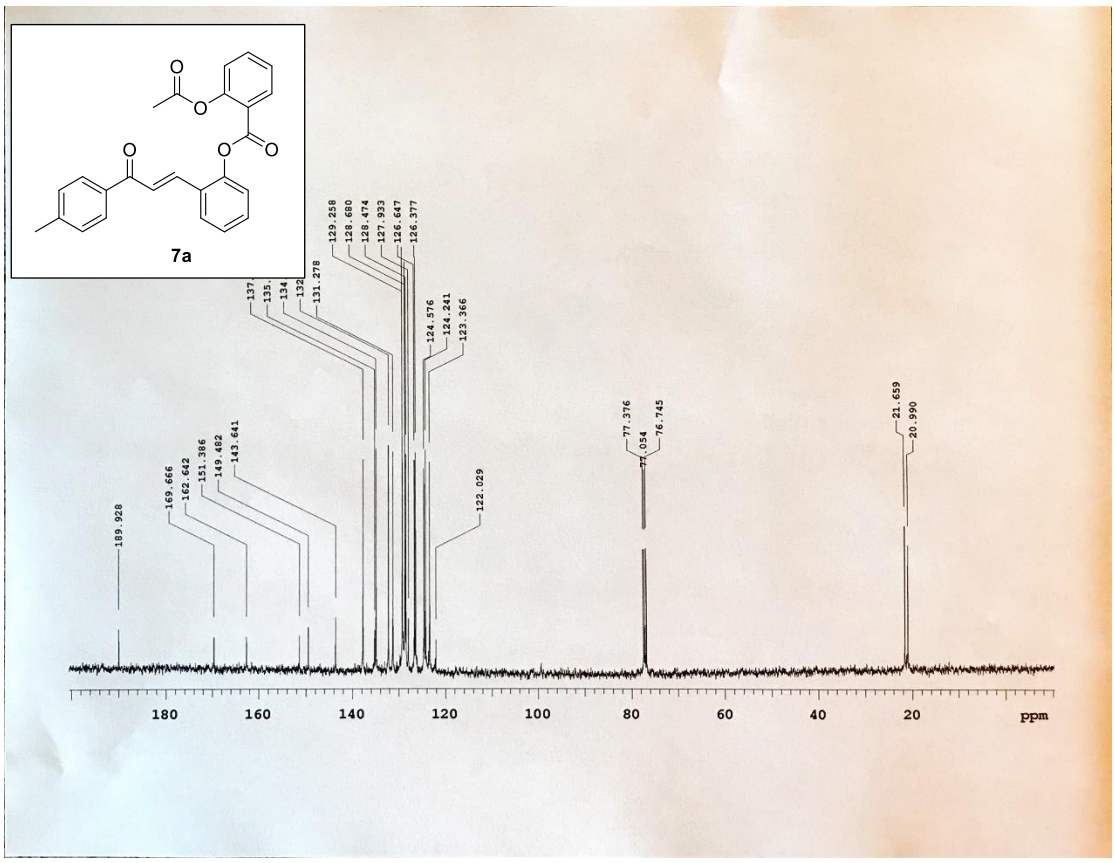
(*E*)-3-(2-hydroxy-5-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (**6n**). The title compound was prepared according to the general procedure in 70% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 9.81 (s, 1H), 8.13 (d, *J* = 8.8 Hz, 2H), 8.00 (d, *J* = 16.0 Hz, 1H), 7.85 (d, *J* = 16.0 Hz, 1H), 7.41 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.90-6.84 (m, 2H), 3.85 (s, 3H), 3.75 (s, 3H).

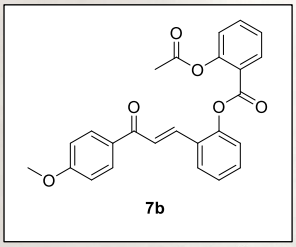
(*E*)-3-(5-bromo-2-hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (**6o**). The title compound was prepared according to the general procedure in 70% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 8.15-8.10 (m, 3H), 7.99-7.90 (m, 2H), 7.37 (d, *J* = 8.8 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 3.82 (s, 3H).

(*E*)-3-(5-chloro-2-hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (**6p**). The title compound was prepared according to the general procedure in 70% yield. ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10. 56 (s, 1H), 8.13 (d, *J* = 8.8 Hz, 2H), 8.00-7.89 (m, 3H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 1H), 3.81 (s, 3H).

Spectral copies of ^{1}H NMR, and ^{13}C NMR of compounds **7a-p**







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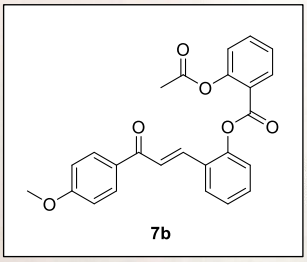

7b

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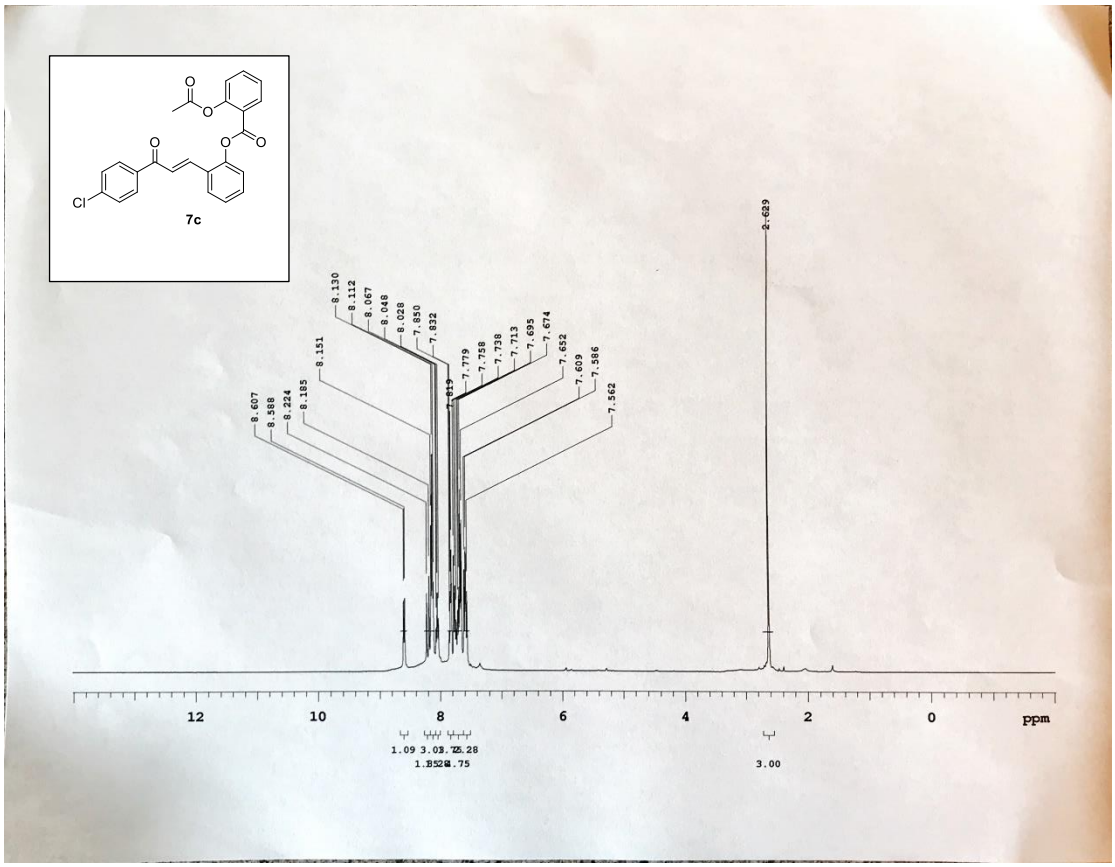
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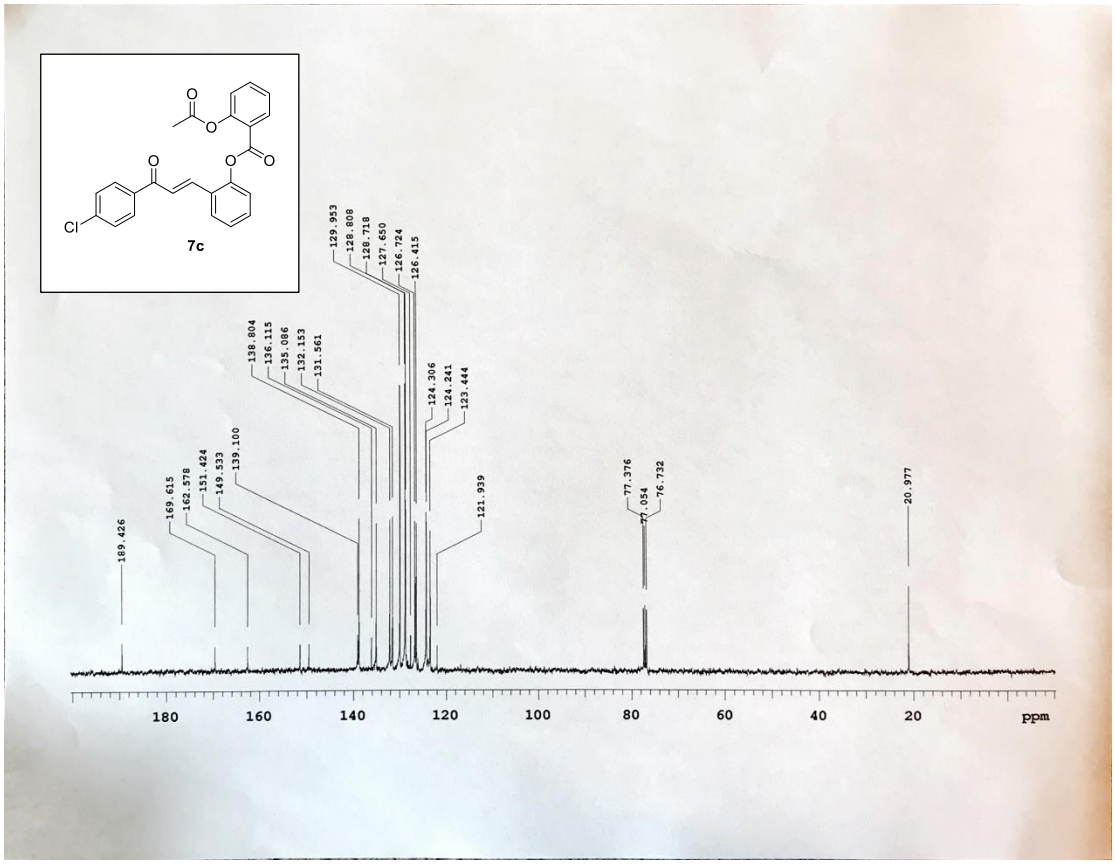
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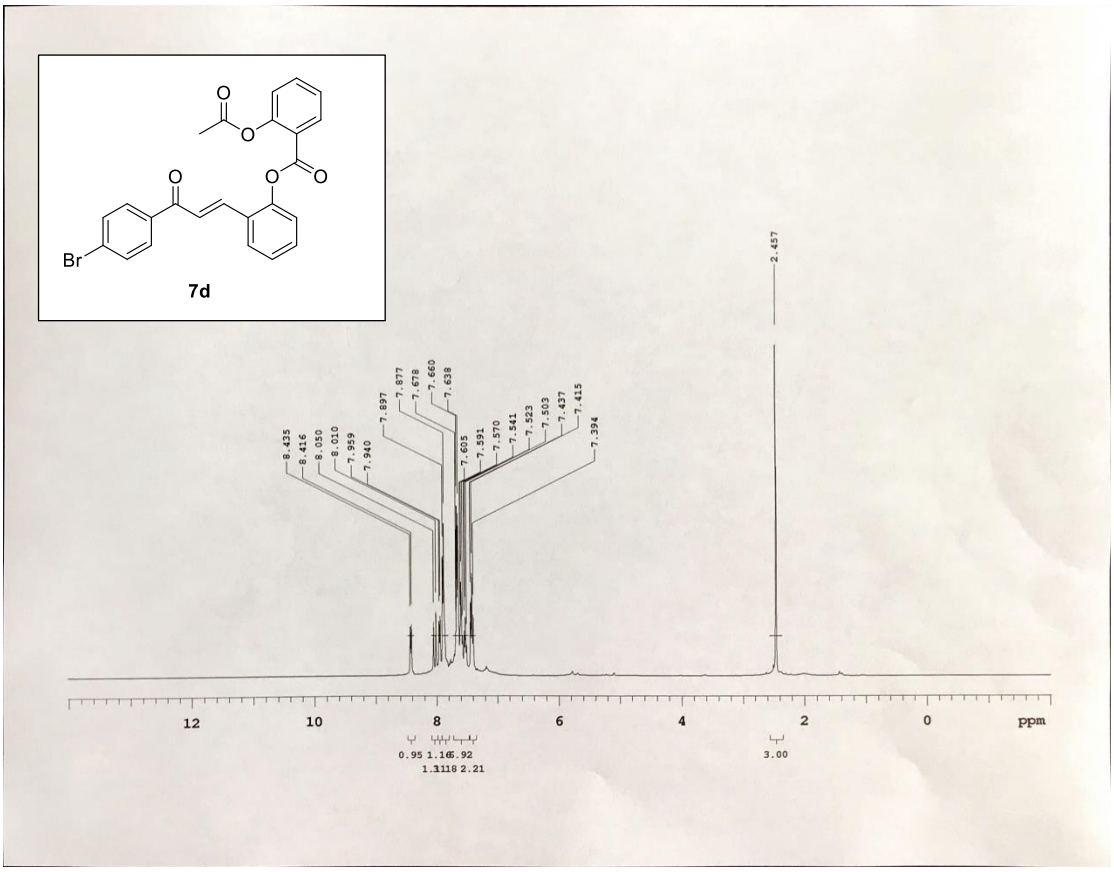
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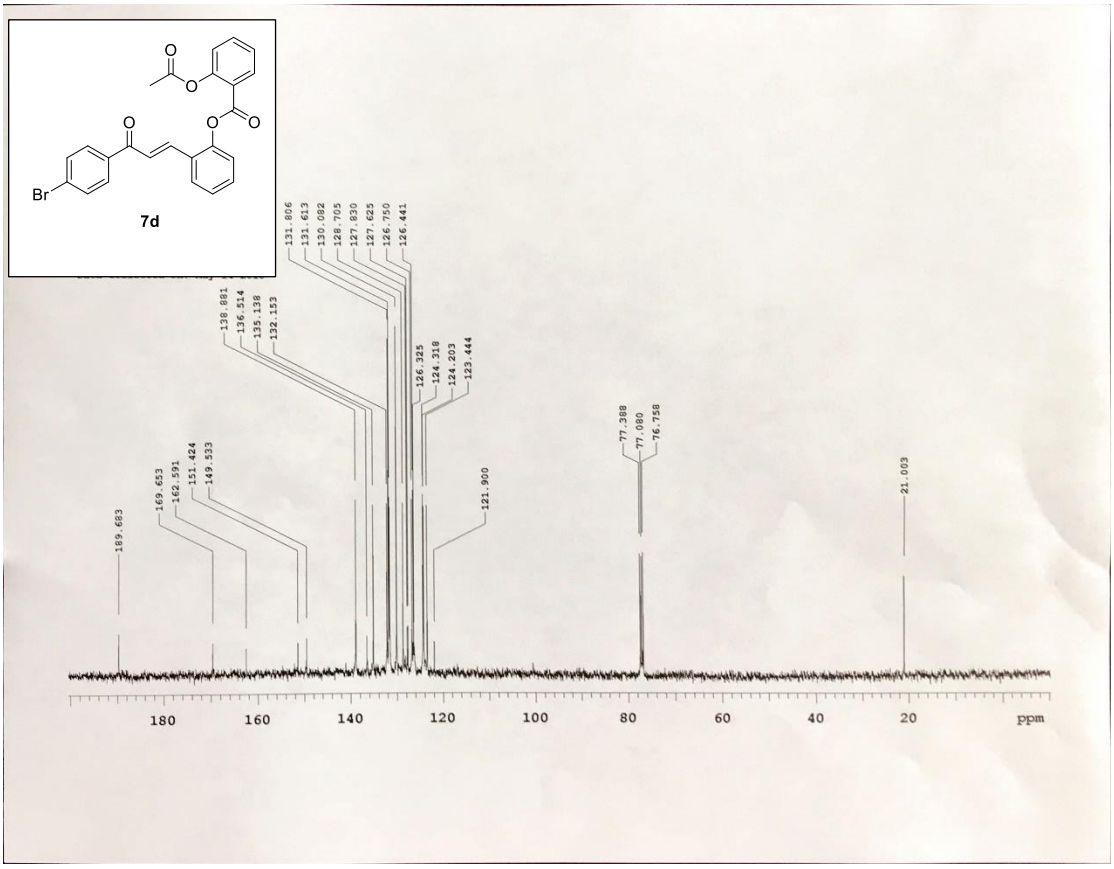
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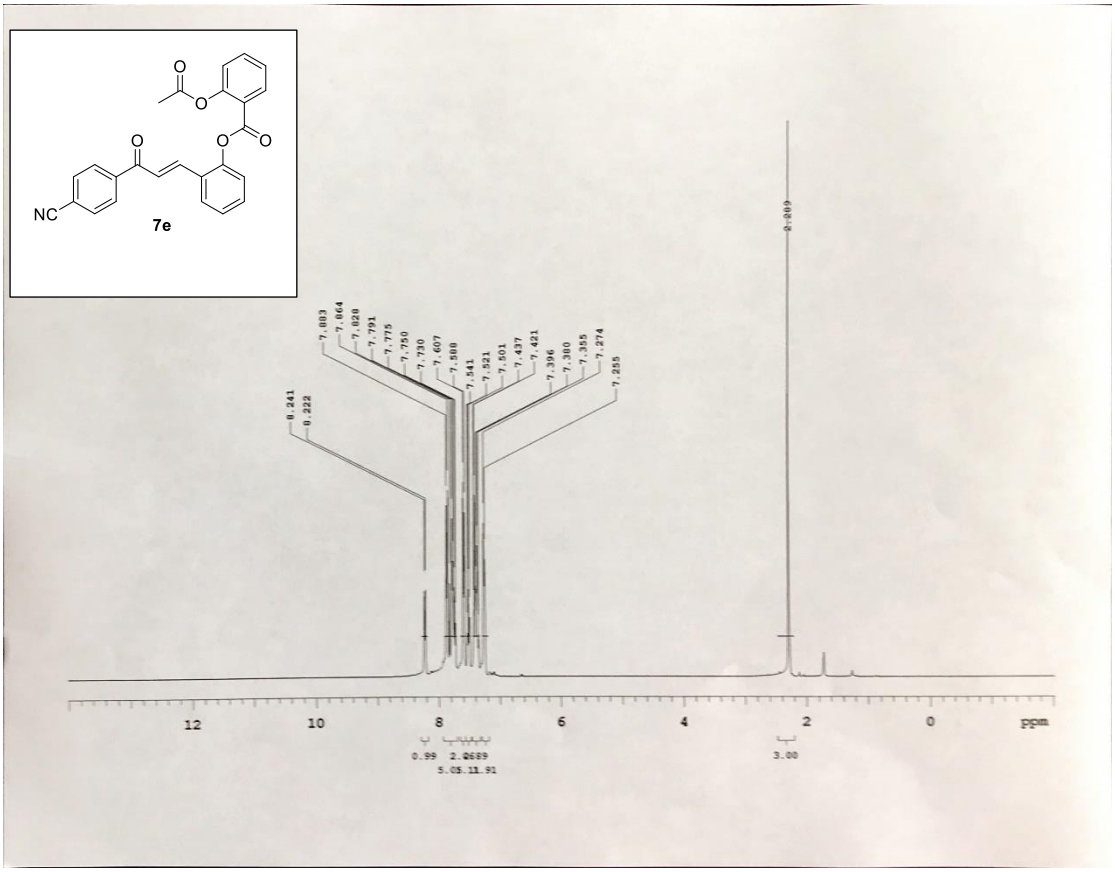
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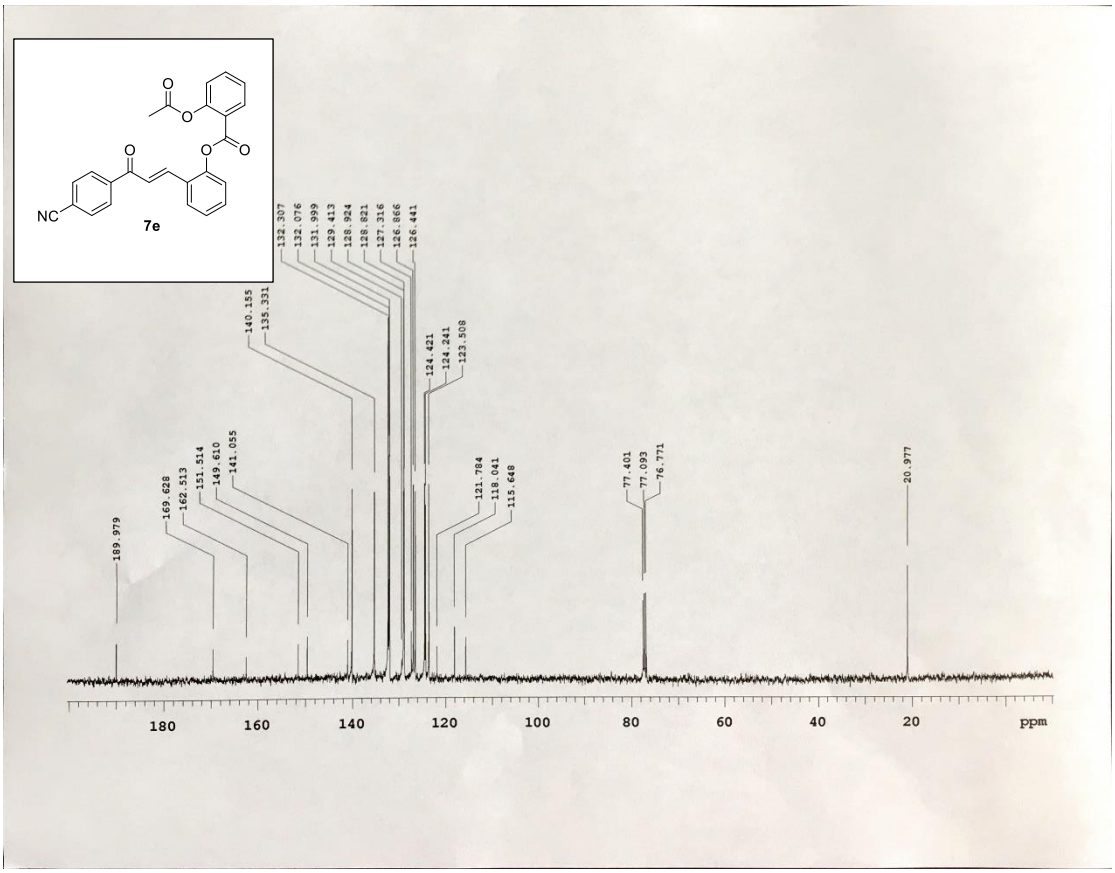
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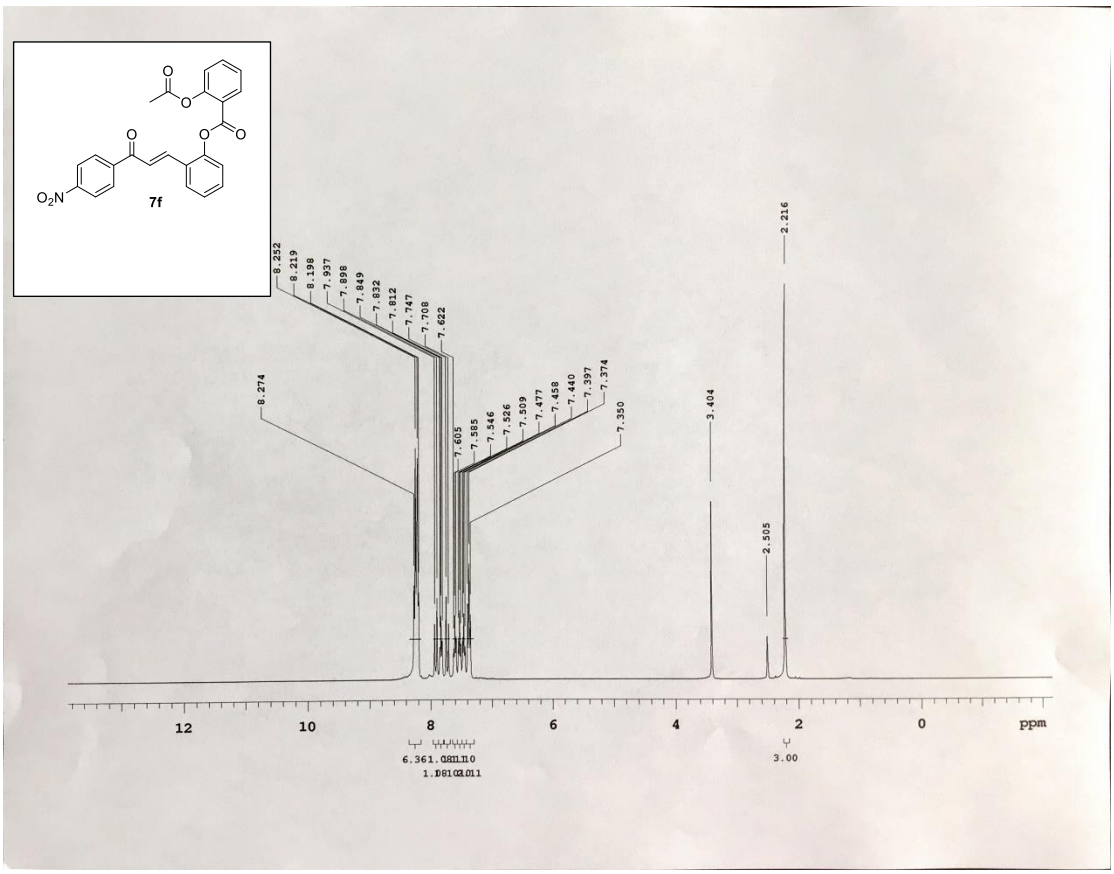
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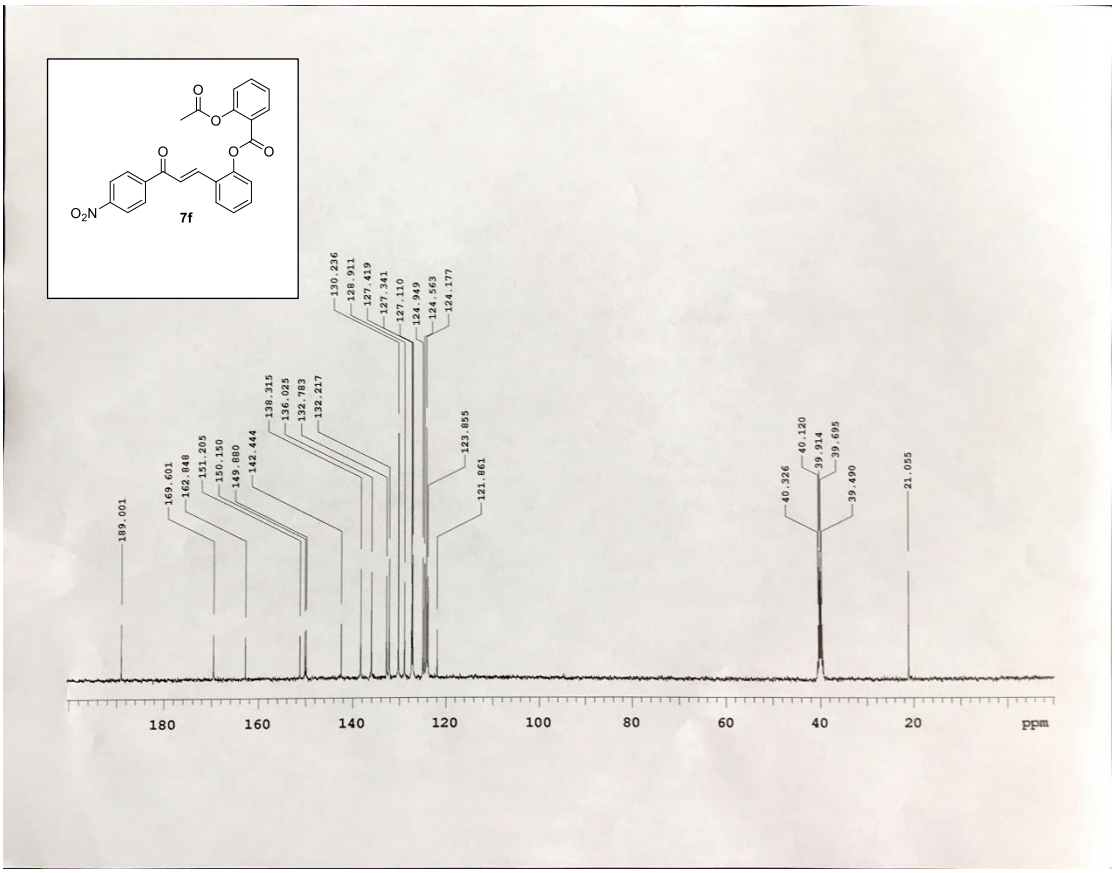
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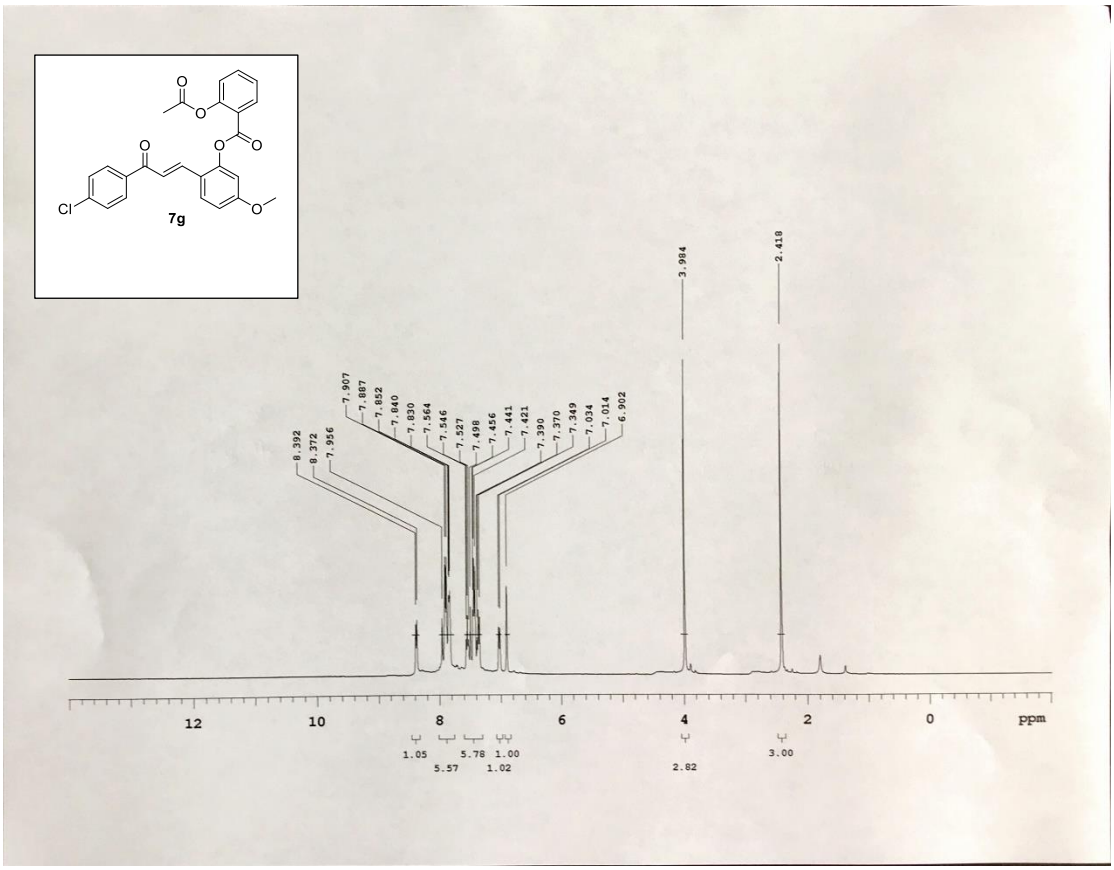
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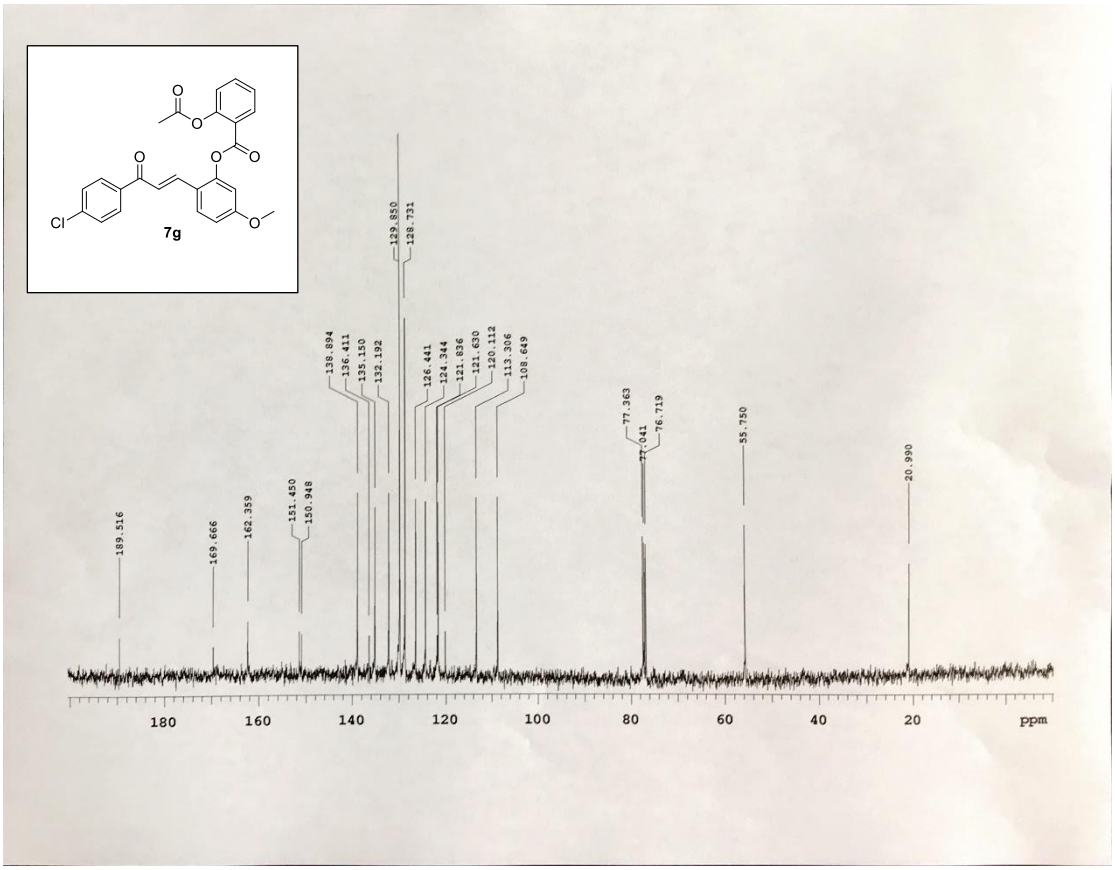
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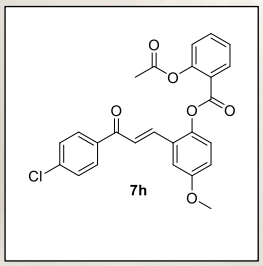
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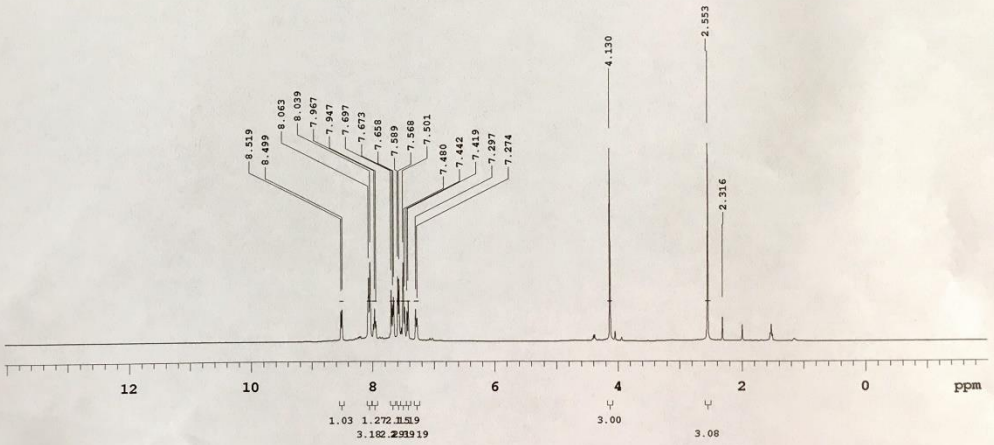
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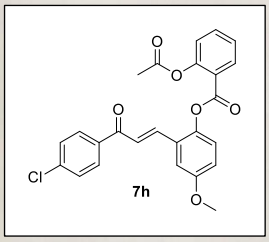
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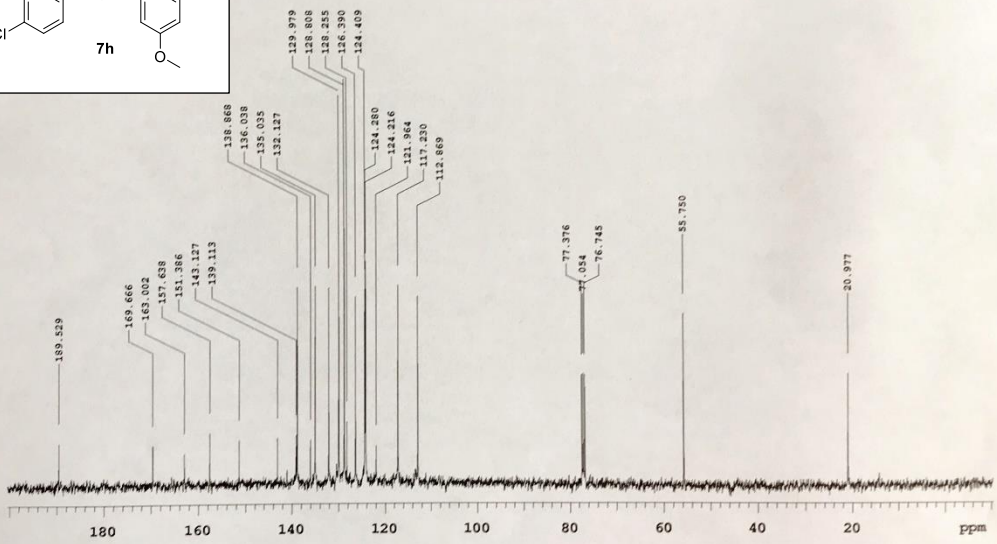
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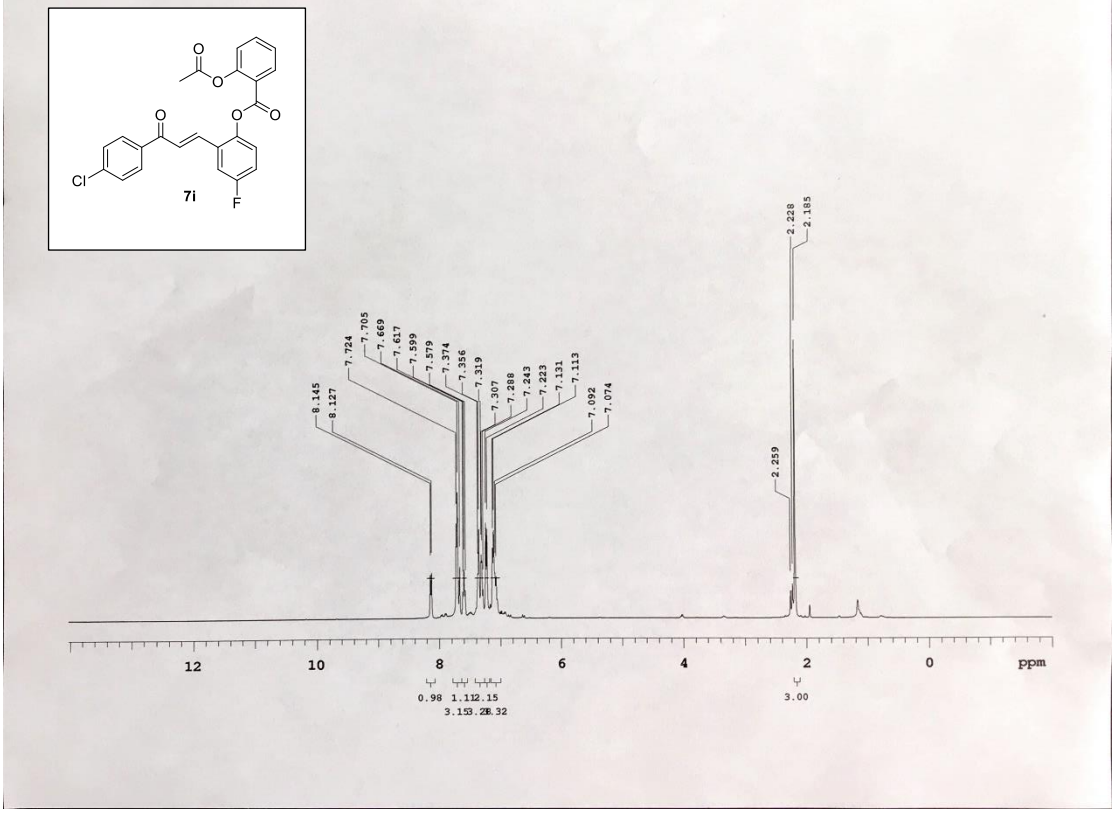
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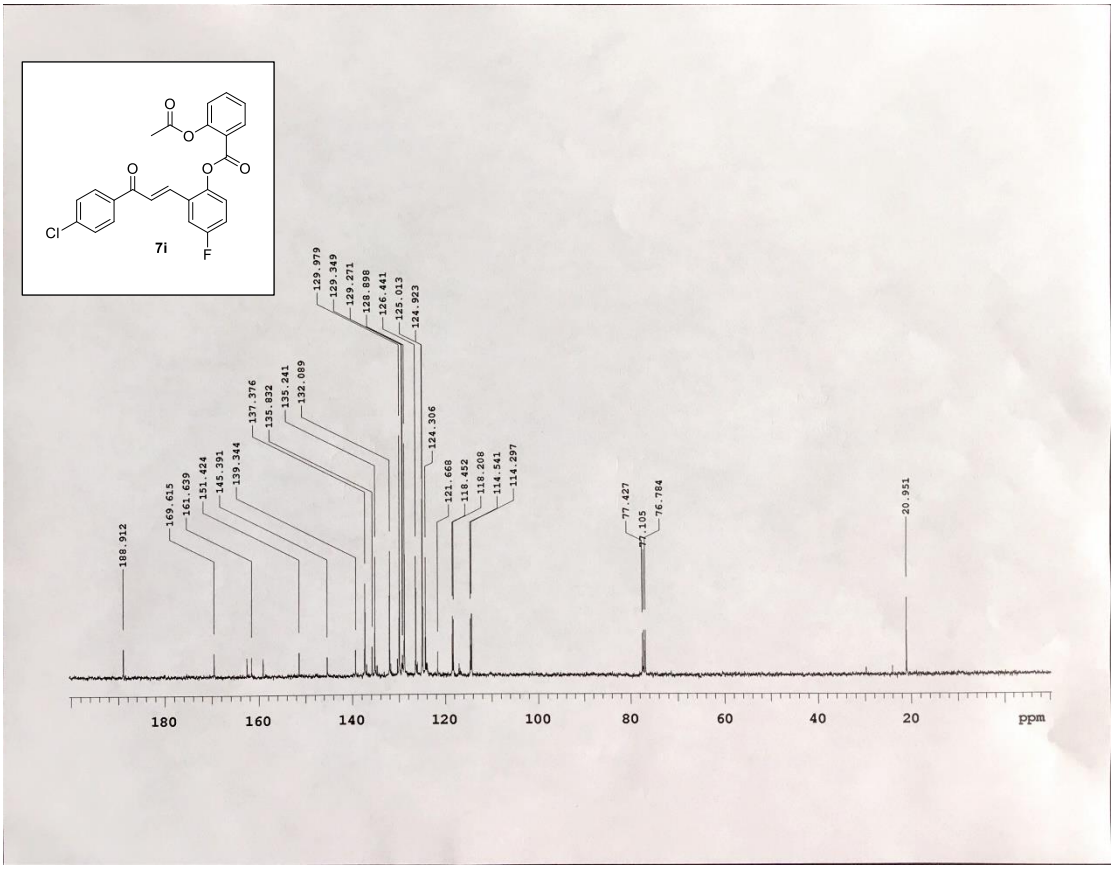
3.15
3.28
8.32
3.00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188.912
169.615
161.639
151.424
145.391
139.344
137.376
135.832
135.241
132.089
129.979
129.349
129.271
128.898
126.441
125.013
124.923
124.306
121.668
118.452
118.208
114.541
114.297
77.427
77.105
76.784
20.951
180
160
140
120
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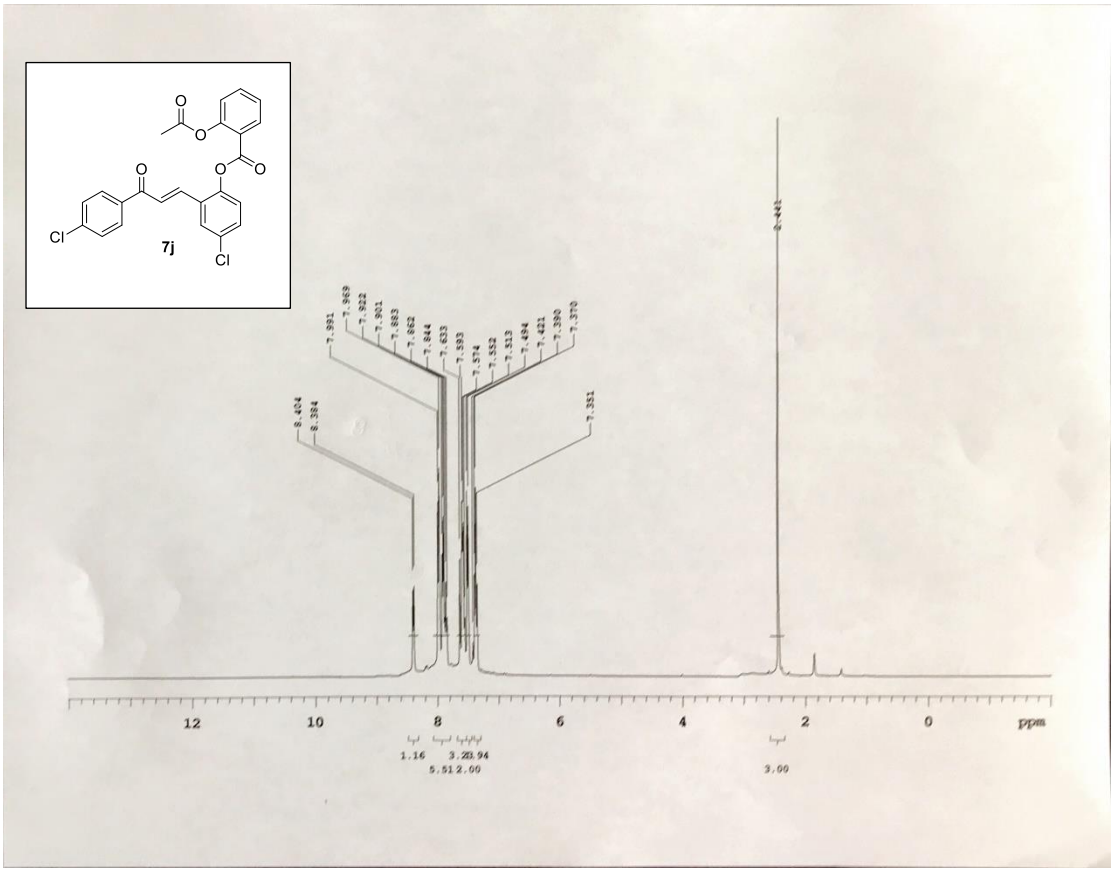
80
60
40
20
ppm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Cl
Cl
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7.922
7.901
7.883
7.862
7.844
7.633
7.593
7.574
7.552
7.513
7.494
7.421
7.390
7.370
8.404
8.384
7.351
12
10
8
6
4
2
0
ppm
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3.28
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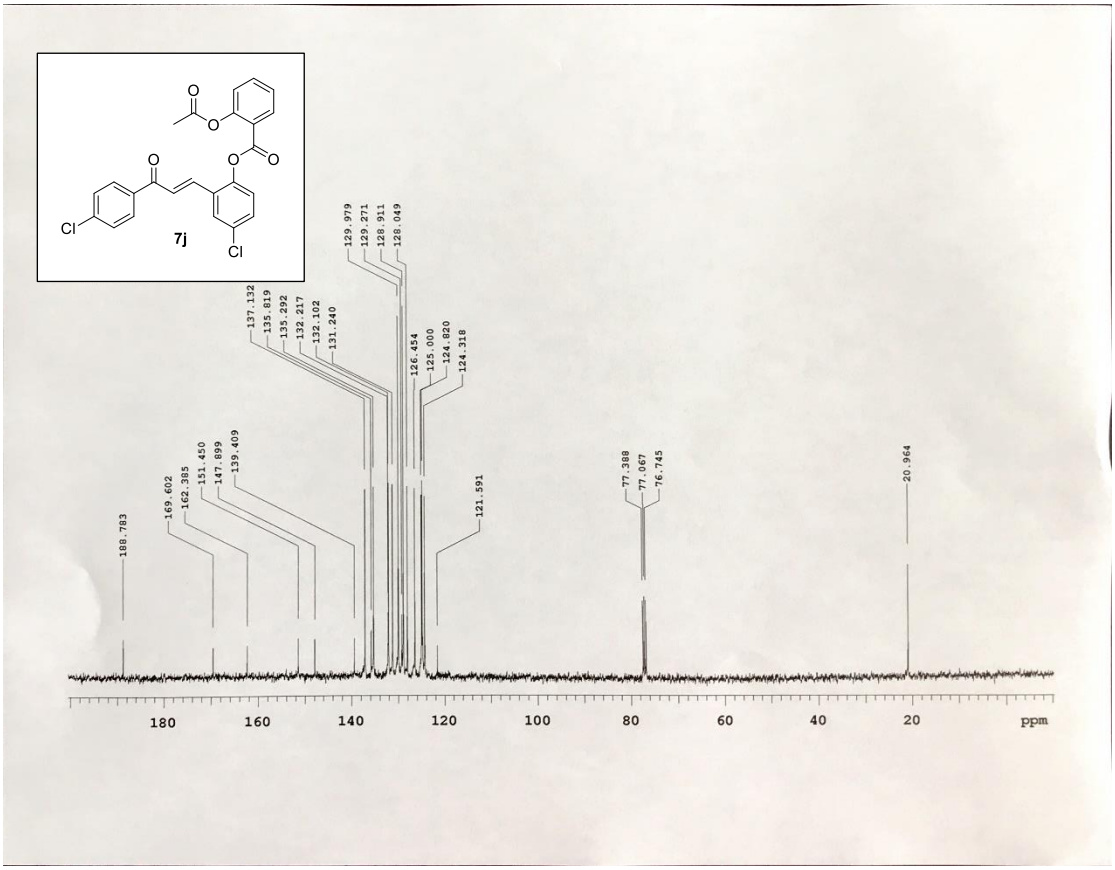
5.51
2.00
3.00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Cl
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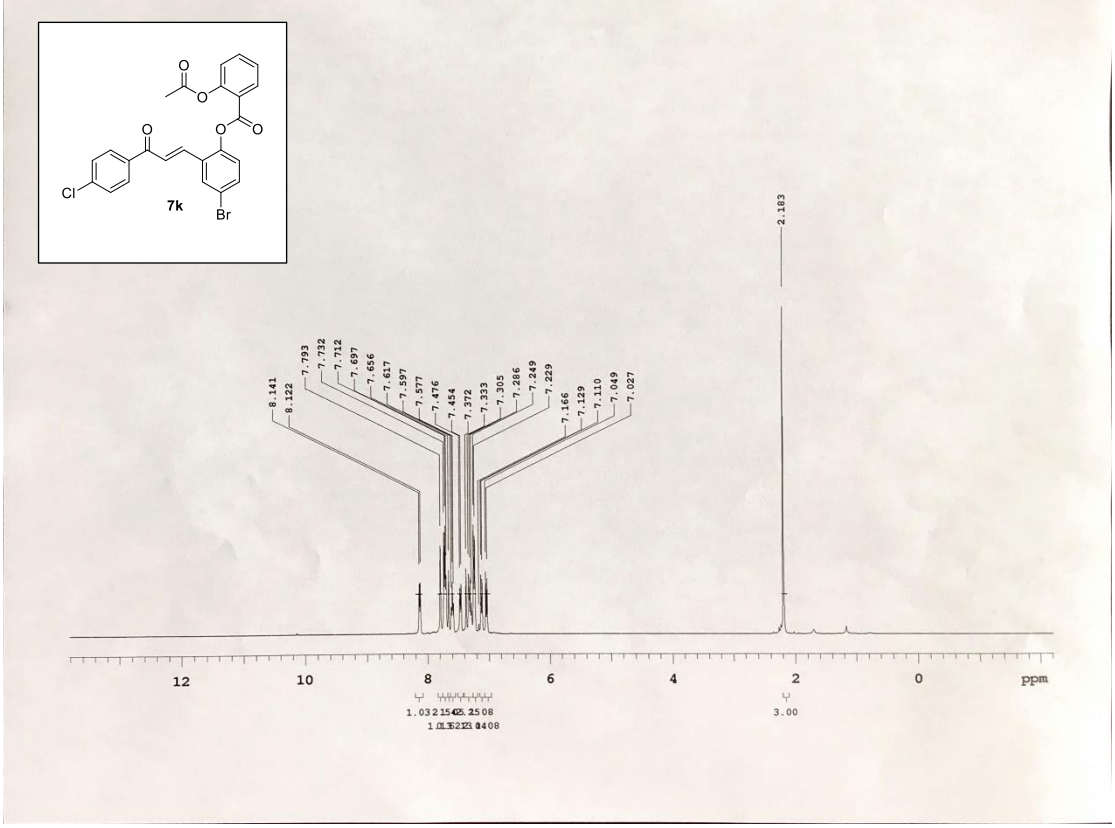
129.271
128.911
128.049
137.132
135.819
135.292
132.217
132.102
131.240
126.454
125.000
124.820
124.318
121.591
77.388
77.067
76.745
20.964
169.602
162.385
151.450
147.899
139.409
188.783
180
160
140
120
100
80
60
40
20
ppm


7k
Cl
Br
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8.122
7.793
7.732
7.712
7.697
7.656
7.617
7.597
7.577
7.476
7.454
7.372
7.333
7.305
7.286
7.249
7.229
7.166
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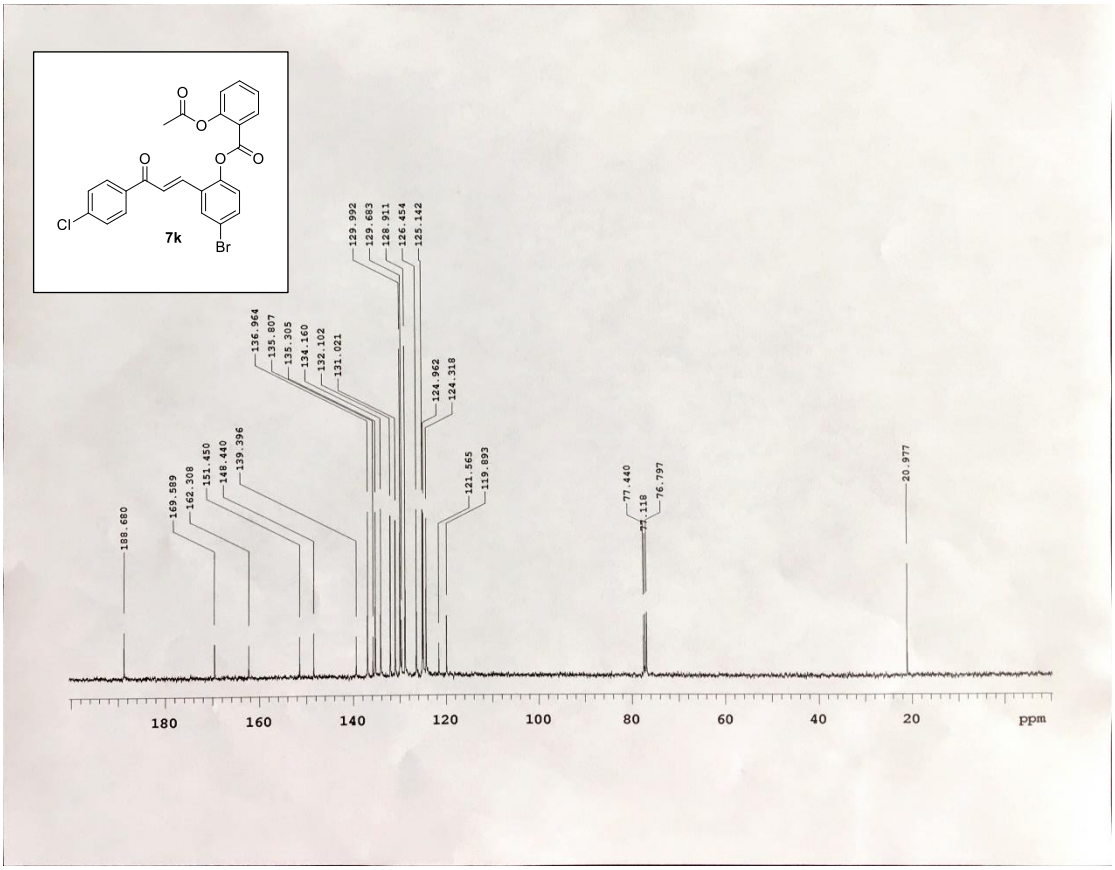
7.110
7.049
7.027
2.183
12
10
8
6
4
2
0
ppm
3.00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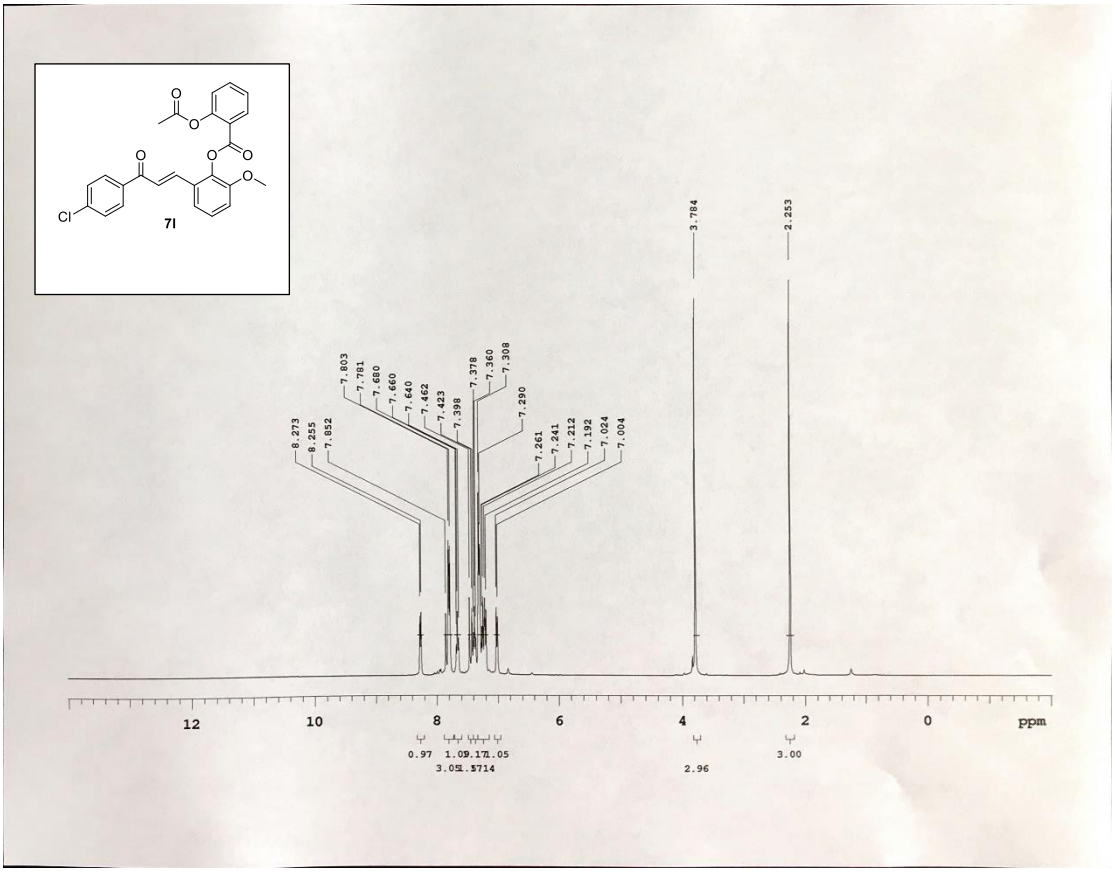
162.308
151.450
148.440
139.396
136.964
135.807
135.305
134.160
132.102
131.021
129.992
129.683
128.911
126.454
125.142
124.962
124.318
121.565
119.893
77.440
77.118
76.797
20.977
180
160
140
120
100
80
60
40
20
ppm


7l
8.273
8.255
7.852
7.803
7.781
7.680
7.660
7.640
7.462
7.423
7.398
7.378
7.360
7.308
7.290
7.261
7.241
7.212
7.192
7.024
7.004
3.784
2.253
12
10
8
6
4
2
0
ppm
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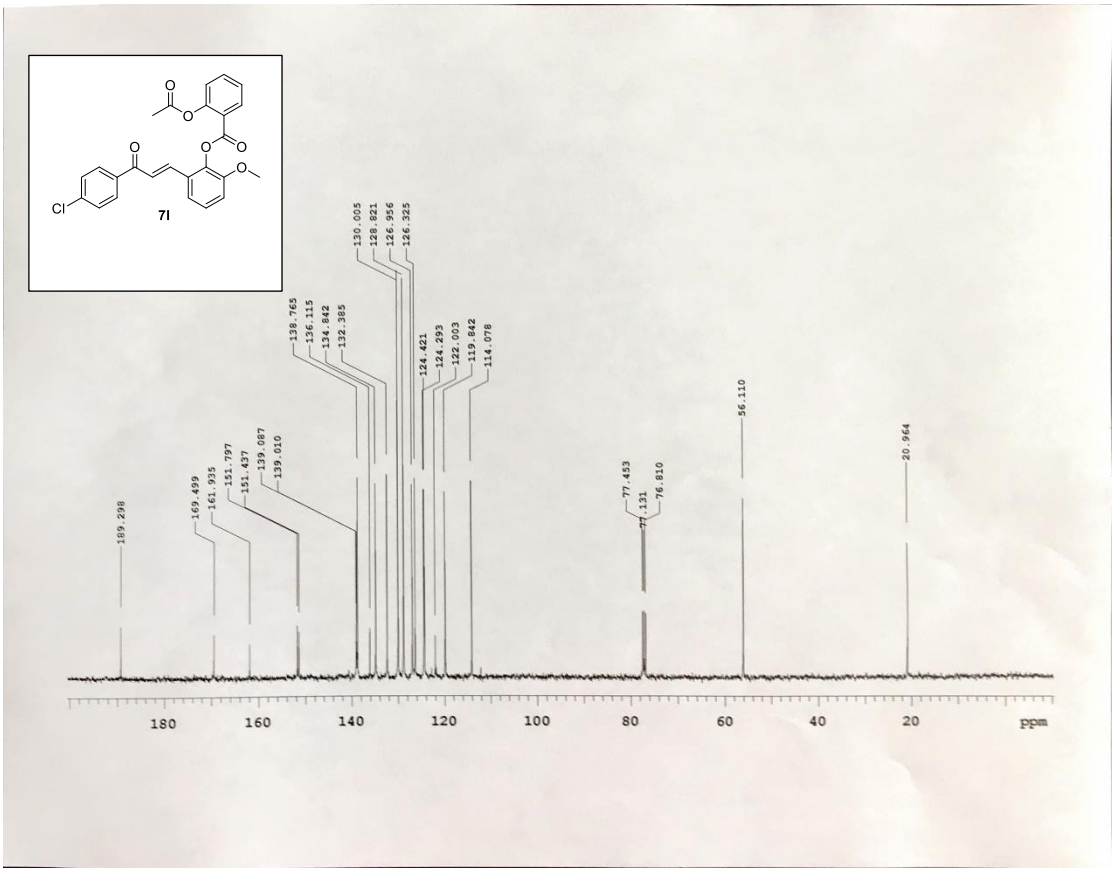
1.17
1.05
3.05
1.5714
2.96
3.00


7l
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151.797
151.437
139.087
139.010
138.765
136.115
134.842
132.385
130.005
128.821
126.956
126.325
124.421
124.293
122.003
119.842
114.078
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77.131
76.810
56.110
20.964
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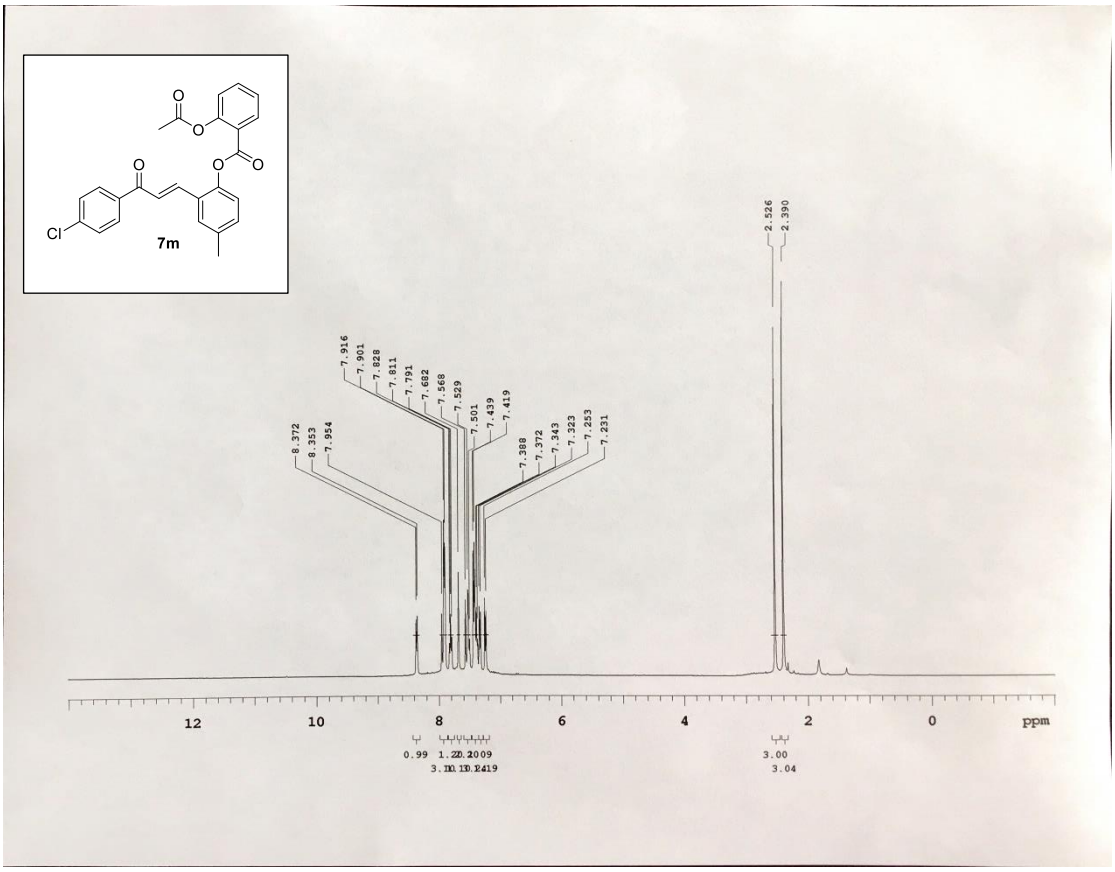
140
120
100
80
60
40
20
ppm


7m
Cl
2.526
2.390
7.916
7.901
7.828
7.811
7.791
7.682
7.568
7.529
7.501
7.439
7.419
7.388
7.372
7.343
7.323
7.253
7.231
8.372
8.353
7.954
12
10
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6
4
2
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ppm
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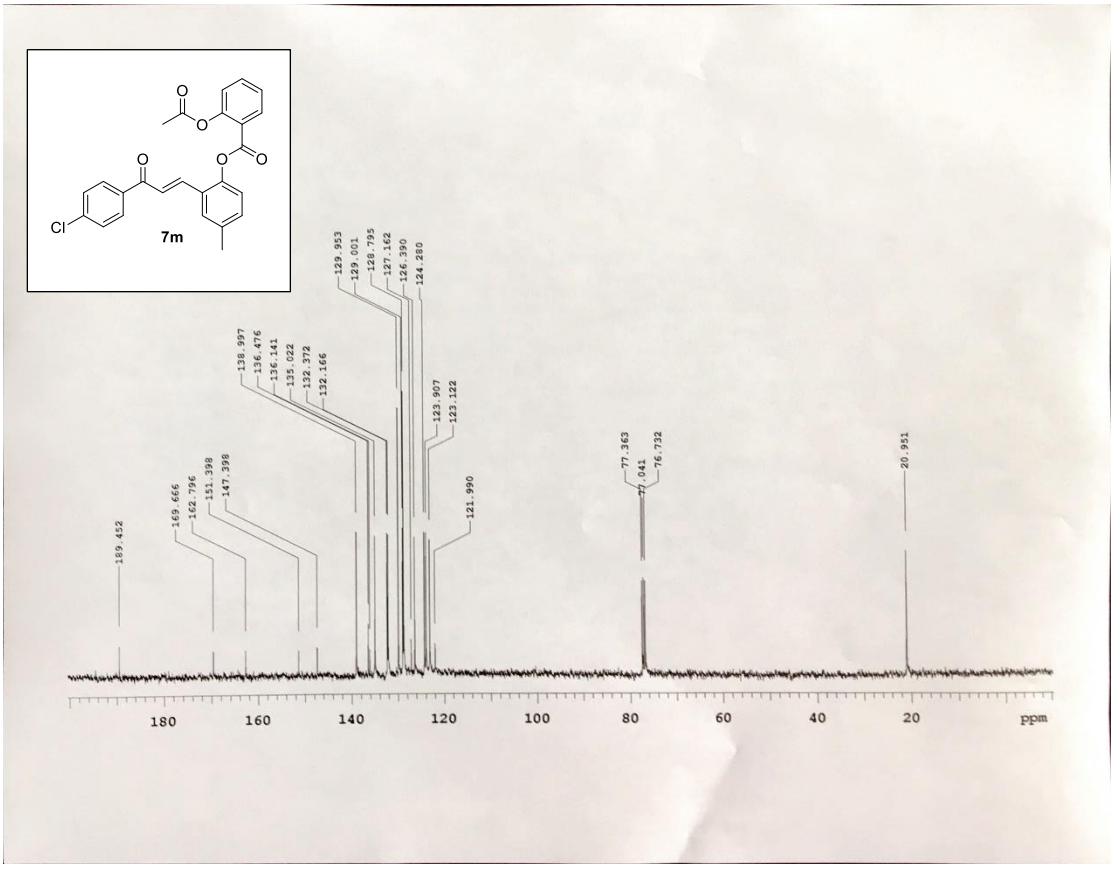
3.00
3.04


7m
Cl
189.452
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162.796
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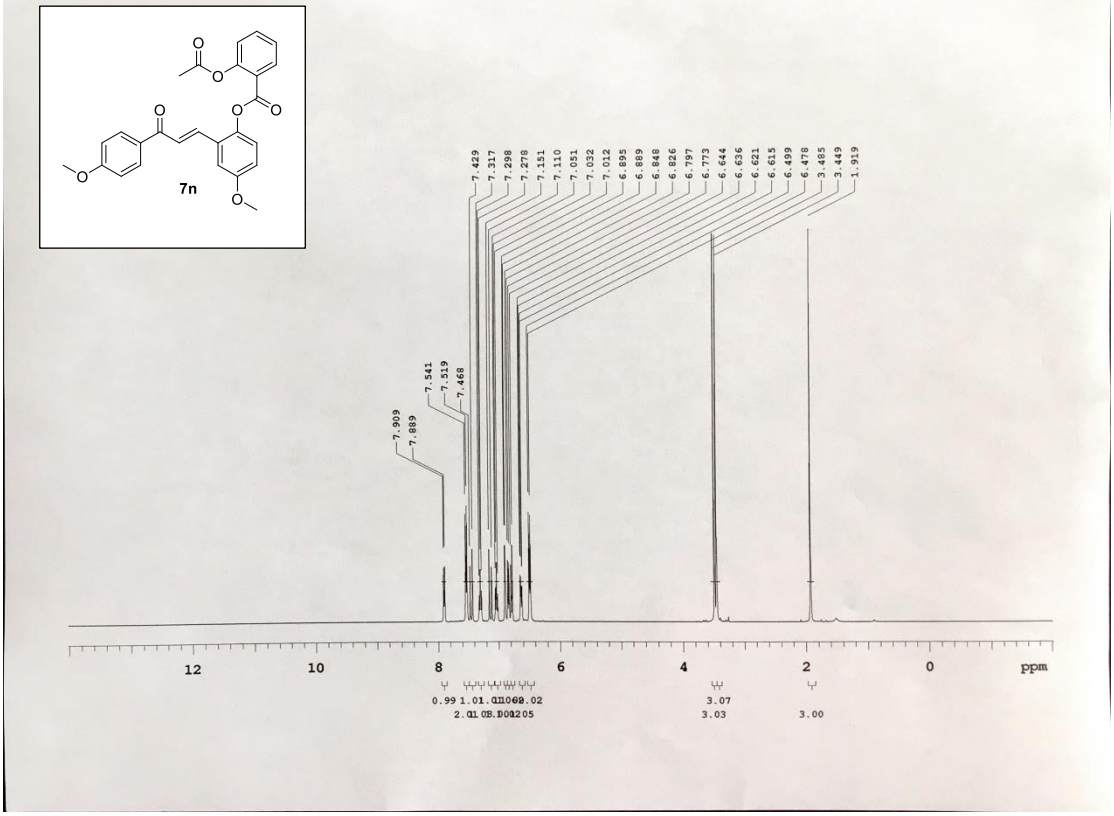
147.398
138.997
136.476
136.141
135.022
132.372
132.166
129.953
129.001
128.795
127.162
126.390
124.280
123.907
123.122
121.990
77.363
77.041
76.732
20.951
180
160
140
120
100
80
60
40
20
ppm


7n
7.909
7.889
7.541
7.519
7.468
7.429
7.317
7.298
7.278
7.151
7.110
7.051
7.032
7.012
6.895
6.889
6.848
6.826
6.797
6.773
6.644
6.636
6.621
6.615
6.499
6.478
3.485
3.449
1.919
12
10
8
6
4
2
0
ppm
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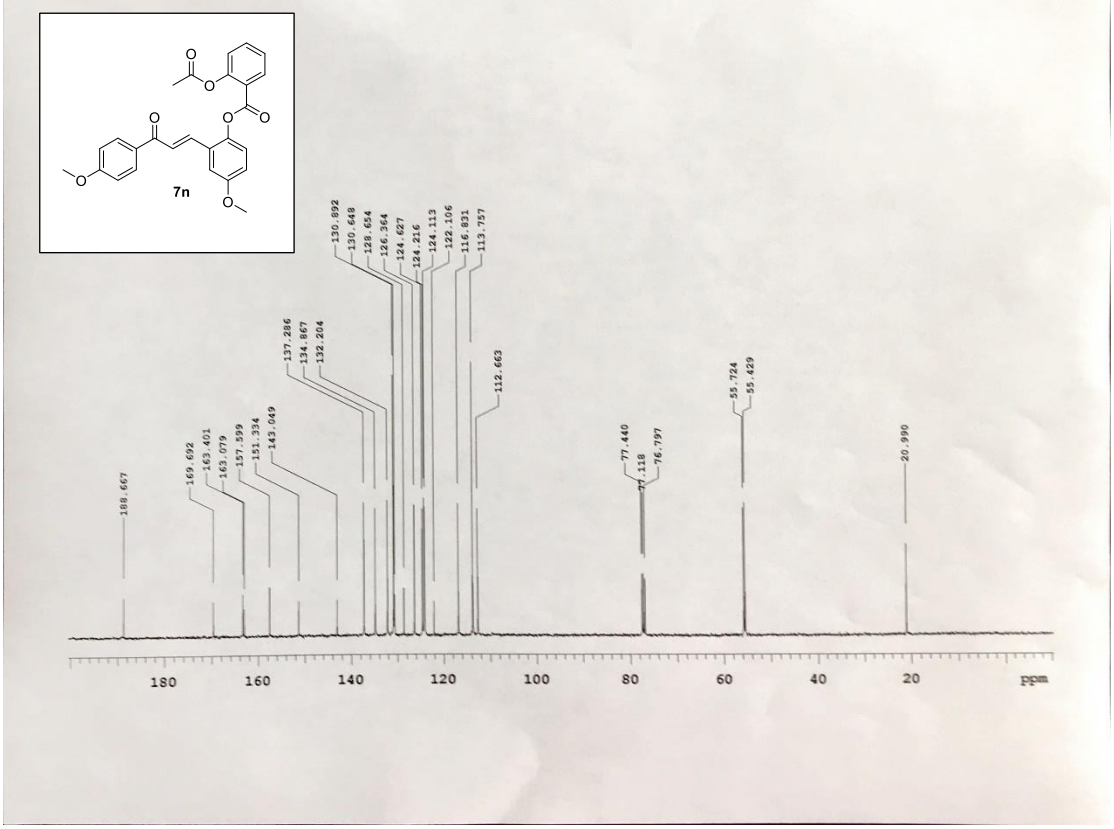
1.01
1.00
3.02
3.07
3.03
3.00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163.401
163.079
157.599
151.334
143.049
137.286
134.867
132.204
130.892
130.648
128.654
126.364
124.627
124.216
124.113
122.106
116.831
113.757
112.663
77.440
77.118
76.797
55.724
55.429
20.990
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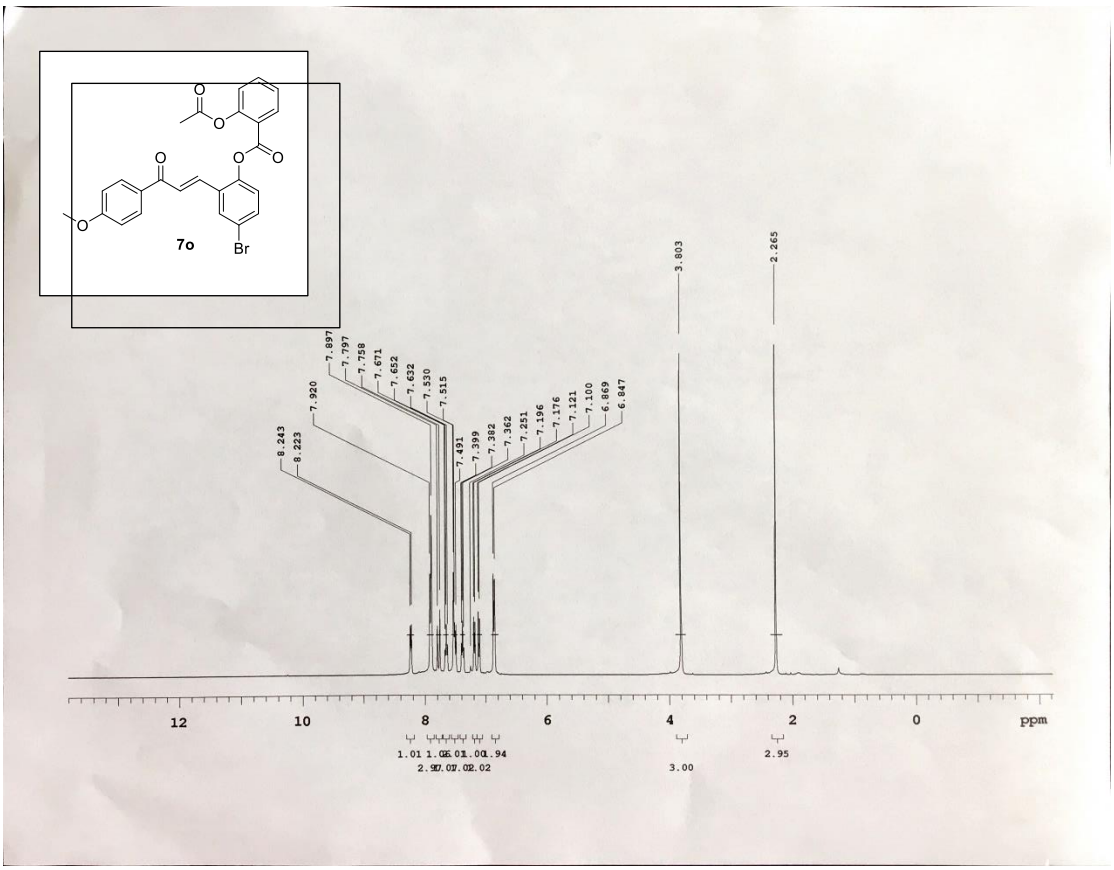
160
140
120
100
80
60
40
20
ppm


7o
Br
8.243
8.223
7.920
7.897
7.797
7.758
7.671
7.652
7.632
7.530
7.515
7.491
7.399
7.382
7.362
7.251
7.196
7.176
7.121
7.100
6.869
6.847
3.803
2.265
12
10
8
6
4
2
0
ppm
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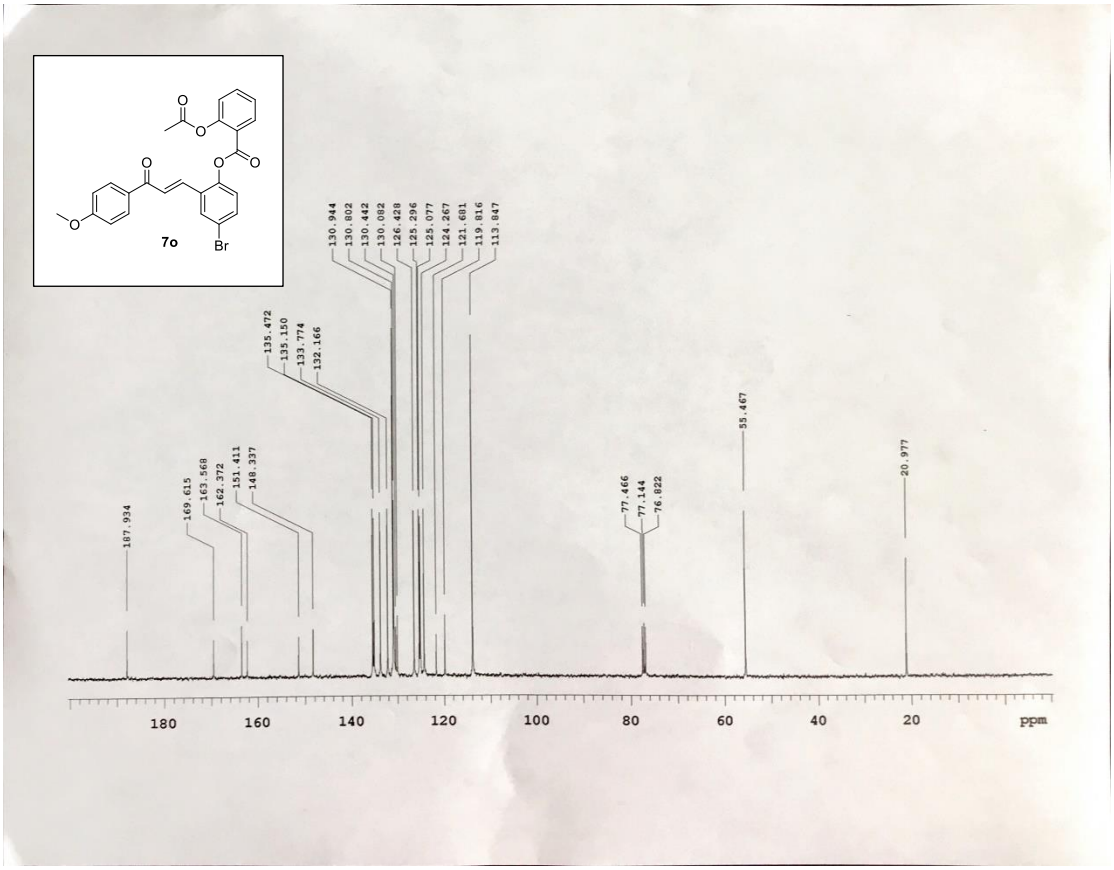
1.02
1.01
1.00
1.94
2.95
3.00
2.95


7o
Br
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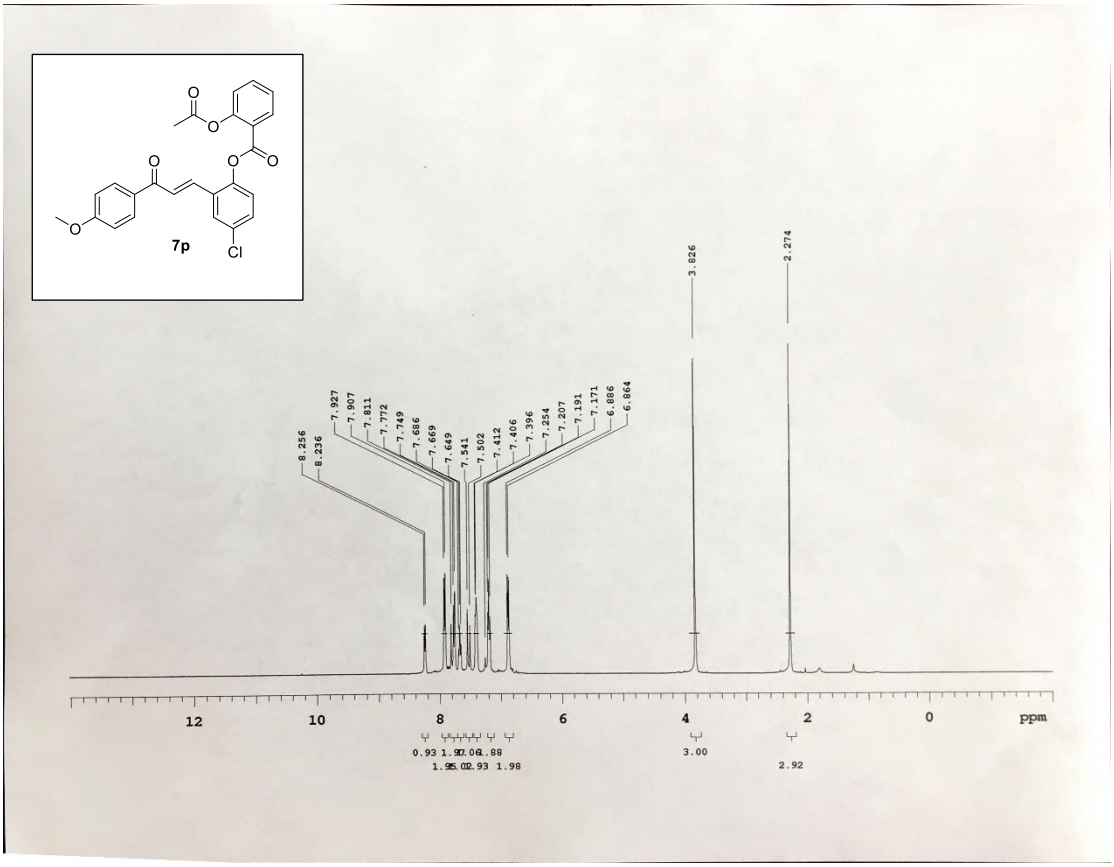
162.372
151.411
148.337
135.472
135.150
133.774
132.166
130.944
130.802
130.442
130.082
126.428
125.296
125.077
124.267
121.681
119.816
113.847
77.466
77.144
76.822
55.467
20.977
180
160
140
120
100
80
60
40
20
ppm


7p
Cl
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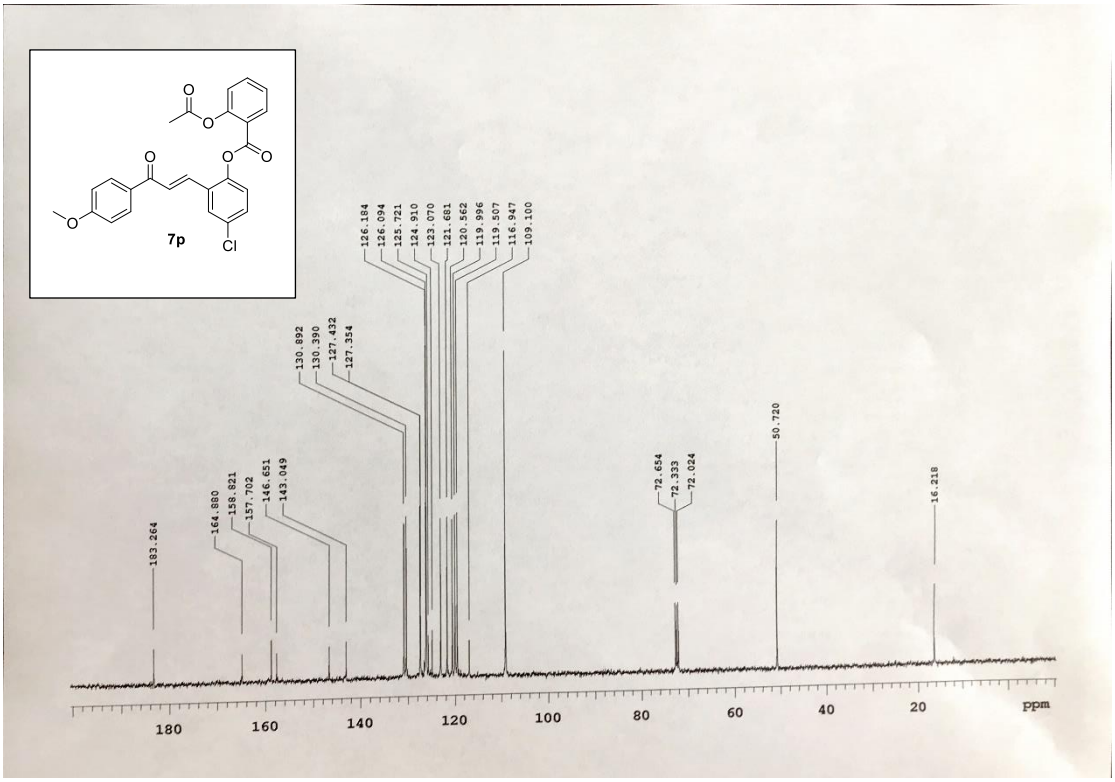
7.907
7.811
7.772
7.749
7.686
7.669
7.649
7.541
7.502
7.412
7.406
7.396
7.254
7.207
7.191
7.171
6.886
6.864
3.826
2.274
12
10
8
6
4
2
0
ppm
0.93
1.95
2.02
2.93
1.98
3.00
2.92


7p
Cl
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123.070
121.681
120.562
119.996
119.507
116.947
109.100
130.892
130.390
127.432
127.354
72.654
72.333
72.024
50.720
16.218
183.264
164.880
158.821
157.702
146.651
143.049
180
160
140
120
100
80
60
40
20
ppm