Supplementary information

Direct Synthesis of 8-Acylated Quinoline N-Oxides via Palladium-Catalyzed Selective C-H Activation and C(sp2)-C(sp2) Cleavage

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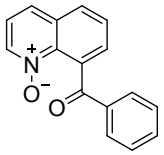
1. Instrument

NMR spectra were recorded at 500 MHz for protons on JOEL JNM-ECA spectrometers. ^{1}H NMR chemical shifts (δ) are given in ppm relative to TMS (δ = 0.0). Chemical shifts for ^{13}C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard. Data Reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad signal), integration, coupling constant (Hz) and identification. All major chemicals and solvents were obtained from commercial sources and used without further purification. The HRMS were measured by Thermo fisher, Exactive.

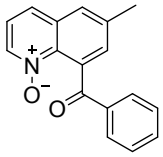
2. Typical procedure for the synthesis of 8-Acylated Quinoline N-Oxides: A sealable reaction tube equipped with a magnetic stirrer bar was charged with Quinoline N-Oxide (0.2 mmol), Dibenzoyl (2equiv.), $Pd(OAc)_2$(10mol%), TBHP(5.0-6.0 mol/L in decane, 2.5 equiv.),CH_2Cl_2 (1.5 ml). The reaction vessel was carried out 110℃. After completion, it was diluted with ethyl acetate, washed with water. After the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel to afford the corresponding product.

3. Characterization data of products:



8-benzoylquinoline 1-oxide(**3a**):

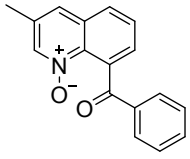
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 5.7 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.72 (t, *J* = 8.7 Hz, 3H), 7.63 (d, *J* = 6.9 Hz, 1H), 7.48 (t, *J* = 7.1 Hz, 1H), 7.33-7.40 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.56, 139.09, 138.53, 135.20, 134.02, 132.30, 131.00, 129.83, 129.18, 128.60, 128.37, 126.07, 121.99.


8-benzoyl-6-methylquinoline 1-oxide(**3b**):

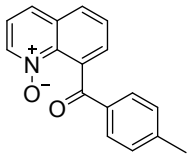
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, *J* = 5.2 Hz, 1H), 7.75 – 7.71 (m, 4H), 7.51 – 7.44 (m, 2H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.33-7.30 (m, 1H), 2.57 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.64, 139.09, 138.53, 137.72, 134.51, 133.91, 132.27, 131.86, 131.15, 128.65, 128.34, 127.97, 125.47, 121.93, 21.41.


8-benzoyl-6-fluoroquinoline 1-oxide(**3c**):

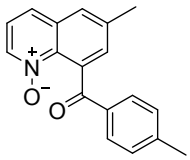
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.69 (t, *J* = 8.7 Hz, 1H), 7.65 (d, *J* = 6.6 Hz, 2H), 7.60 – 7.51 (m, 1H), 7.48 – 7.41 (m, 1H), 7.40 – 7.27 (m, 3H), 7.19 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.57, 160.22(d, J=253.7 Hz), 138.96, 136.74, 136.26, 135.28, 133.60, 131.62, 131.26, 127.64, 127.46, 124.17, 122.08, 121.82, 118.99, 118.77, 111.59, 111.41.


8-benzoyl-3-methylquinoline 1-oxide(**3d**):

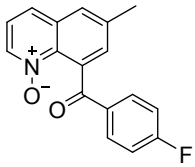
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 – 7.95 (m, 1H), 7.94 – 7.74 (m, 1H), 7.63 (dd, *J* = 8.8, 6.8 Hz, 3H), 7.55 (t, *J* = 7.7 Hz, 1H), 7.49 (dd, *J* = 14.8, 8.4 Hz, 1H), 7.42 (dd, *J* = 13.3, 6.4 Hz, 1H), 7.36 – 7.26 (m, 2H), 7.24 – 7.11 (m, 1H), 2.39 (t, *J* = 8.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.70, 137.53, 136.33, 135.56, 132.85, 131.42, 131.20, 129.67, 127.79, 127.58, 127.55 – 127.22, 124.55, 17.76. HRMS: m/z calcd for $C_{17}H_{13}O_2N[M+H]^+$: 264.10147; found:264.10179;


8-(4-methylbenzoyl)quinoline 1-oxide(**3e**):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 5.3 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.81 (t, *J* = 12.6 Hz, 1H), 7.80 – 7.67 (m, 1H), 7.61 (t, *J* = 7.0 Hz, 3H), 7.44 – 7.31 (m, 1H), 7.19 (d, *J* = 7.4 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.39, 142.99, 139.16, 136.09, 135.26, 134.29, 131.03, 129.79, 129.07, 128.77, 128.54, 125.88, 121.90, 21.67.

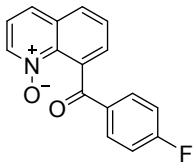

6-methyl-8-(4-methylbenzoyl)quinoline 1-oxide(**3f**):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, *J* = 4.0 Hz, 1H), 7.66 (s, 2H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.37 (s, 1H), 7.23 (s, 1H), 7.12 (d, *J* = 7.3 Hz, 2H), 2.50 (d, *J* = 13.6 Hz, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.53, 142.97, 139.04, 137.71, 136.10, 134.58, 134.09, 131.82, 131.16, 129.09, 128.79, 127.90, 125.44, 121.87, 21.67, 21.40. HRMS: m/z calcd for $C_{18}H_{163}O_2N[M+H]^+$: 278.11737; found:278.11756;



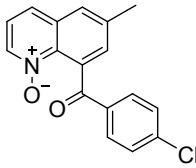
8-(4-fluorobenzoyl)-6-methylquinoline 1-oxide(**3g**):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 4H), 7.46 (s, 1H), 7.33 (d, *J* = 7.4 Hz, 1H), 7.19 – 6.90 (m, 2H), 2.58 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.19, 165.19(d, *J* = 251.3 Hz), 139.18, 137.59, 135.06, 134.56, 133.58, 131.84, 131.18, 131.14, 131.07, 128.13, 125.56, 122.00, 115.54, 115.37, 21.41. HRMS: m/z calcd for $C_{17}H_{13}O_2NF[M+H]^+$: 282.09222; found: 282.09248;



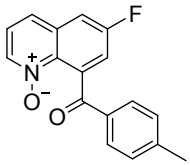
8-(4-fluorobenzoyl)quinoline 1-oxide(3**h**):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 5.4 Hz, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.76 – 7.73 (m, 3H), 7.64 (d, *J* = 6.6 Hz, 1H), 7.38 (t, *J* = 6.8 Hz, 1H), 7.07 (t, *J* = 8.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.05, 165.21(d, J=252.5), 139.05, 135.27, 135.02, 133.79, 131.26 – 130.92 , 129.83 , 129.25, 128.62, 126.03, 122.03, 115.57, 115.40.



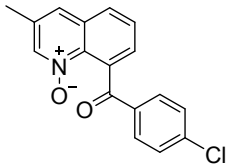
8-(4-chlorobenzoyl)-6-methylquinoline 1-oxide(**3i**):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 6.6 Hz, 2H), 7.60 – 7.51 (m, 1H), 7.44 (d, *J* = 6.4 Hz, 1H), 7.40 – 7.27 (m, 3H), 7.19 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.35, 139.22, 138.54, 137.59, 137.05, 134.60, 133.36, 131.91, 131.14, 129.88, 128.67, 128.21, 125.68, 122.04, 21.42. HRMS: m/z calcd for $C_{17}H_{13}O_2NCl[M+H]^+$: 298.06253; found:298.06293;

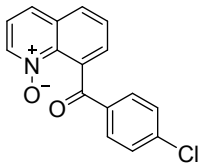


6-fluoro-8-(4-methylbenzoyl)quinoline 1-oxide(**3j**):

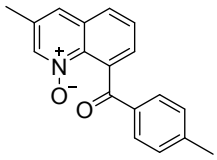
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 5.8 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 3H), 7.40 – 7.25 (m, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.52, 161.22(d, J=277.5), 143.48, 137.55, 136.35, 135.34, 134.76, 132.36, 129.24, 128.82, 125.22, 123.06, 120.31 – 120.09, 119.87, 112.55, 112.37, 21.70. HRMS: m/z calcd for $C_{17}H_{13}O_2NF[M+H]^+$: 282.09210; found:282.09248;


8-(4-chlorobenzoyl)-3-methylquinoline 1-oxide(**3k**):

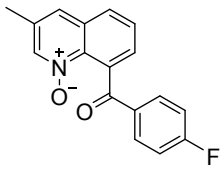
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.84 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.70 – 7.60 (m, 1H), 7.59 – 7.52 (m, 3H), 7.52 – 7.43 (m, 1H), 7.28 (d, *J* = 8.6 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.48, 138.51, 137.16, 136.62, 133.32, 132.63, 130.70, 129.83, 128.85, 128.66, 125.77, 18.79. HRMS: m/z calcd for $C_{17}H_{13}O_2NCl[M+H]^+$: 298.06256; found:298.06293;


8-(4-chlorobenzoyl)quinoline 1-oxide(**3l**):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 5.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.75 (t, *J* = 7.1 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 3H), 7.36 (d, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.21, 139.06, 138.58, 137.03, 135.25, 133.58, 131.01, 129.88, 129.33, 128.69, 126.11, 122.06.

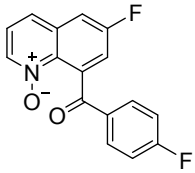

3-methyl-8-(4-methylbenzoyl)quinoline 1-oxide(**3m**):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.82 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.60 (dd, *J* = 8.1, 7.2 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 3H), 7.48 (dd, *J* = 7.0, 1.1 Hz, 1H), 7.11 (d, *J* = 7.9 Hz, 2H), 2.38 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.62, 142.92, 137.37, 136.64, 136.13, 134.07, 132.37, 130.71, 129.07, 128.76, 128.53, 128.32, 125.52, 21.66, 18.77. HRMS: m/z calcd for $C_{18}H_{16}O_2N[M+H]^+$: 278.11728; found:278.11756;


8-(4-fluorobenzoyl)-3-methylquinoline 1-oxide(**3n**):

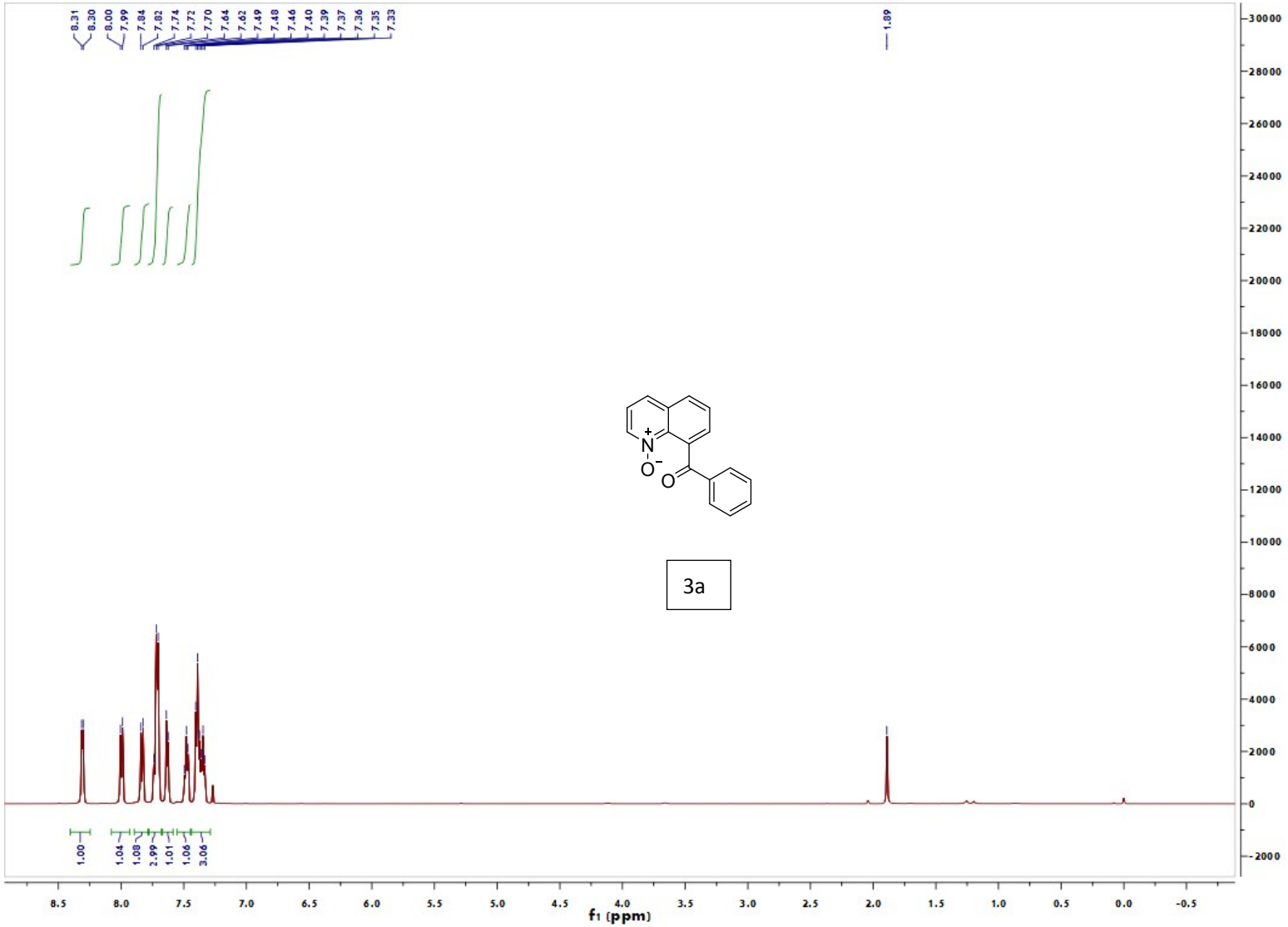
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.87 – 7.78 (m, 1H), 7.68 – 7.59 (m, 3H), 7.56 (s, 1H), 7.48 (d, *J* = 6.5 Hz, 1H), 6.98 (t, *J* = 8.7 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.30,

165.2(d, J=257.5), 137.25, 136.65, 135.10, 133.54, 132.58, 131.02, 130.78 – 130.33, 128.81, 128.60, 125.70, 115.47, 18.82. HRMS: m/z calcd for $C_{17}H_{13}O_2NF[M+H]^+$: 282.09216; found:282.09248;



6-fluoro-8-(4-fluorobenzoyl)quinoline 1-oxide(**3o**):

^{1}H NMR (500 MHz, DMSO- *d*6) δ 8.01 (dd, *J* = 7.9, 5.6 Hz, 2H), 7.72 – 7.47 (m, 1H), 7.45 – 7.20 (m, 5H), 2.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.14, 165.39(d, J=252.5), 161.25(d, J=252.5), 136.92, 136.19, 134.71, 134.31, 132.34, 131.16, 125.31, 123.19, 120.26 – 120.05, 119.92, 115.75, 115.57, 112.82, 112.71. HRMS: m/z calcd for $C_{16}H_{10}O_2NF_2[M+H]^+$: 286.06689; found:286.06741;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8.30
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7.82
7.74
7.72
7.70
7.64
7.62
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7.48
7.46
7.40
7.39
7.37
7.36
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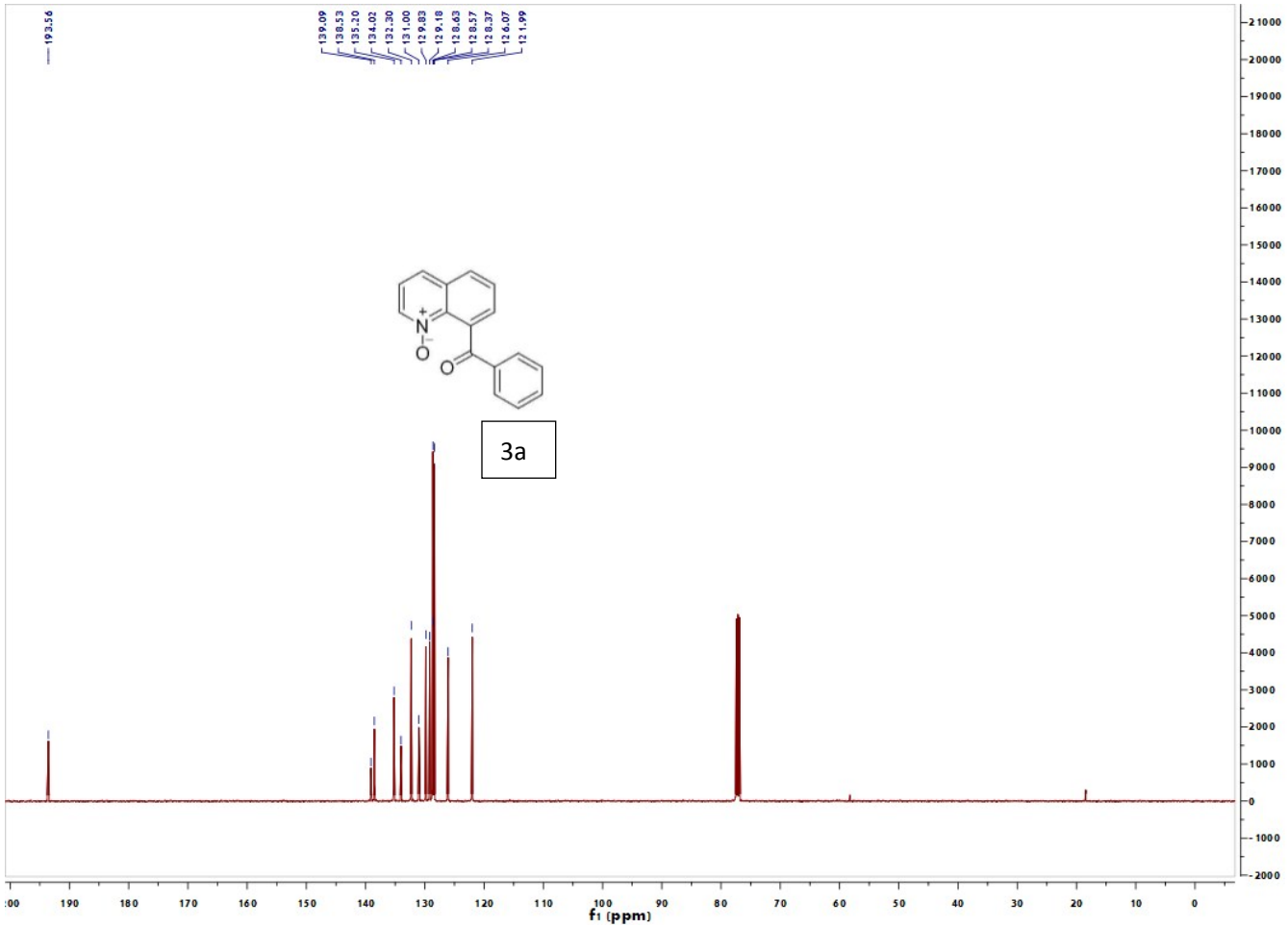
2.99
1.01
1.06
3.06
f1 (ppm)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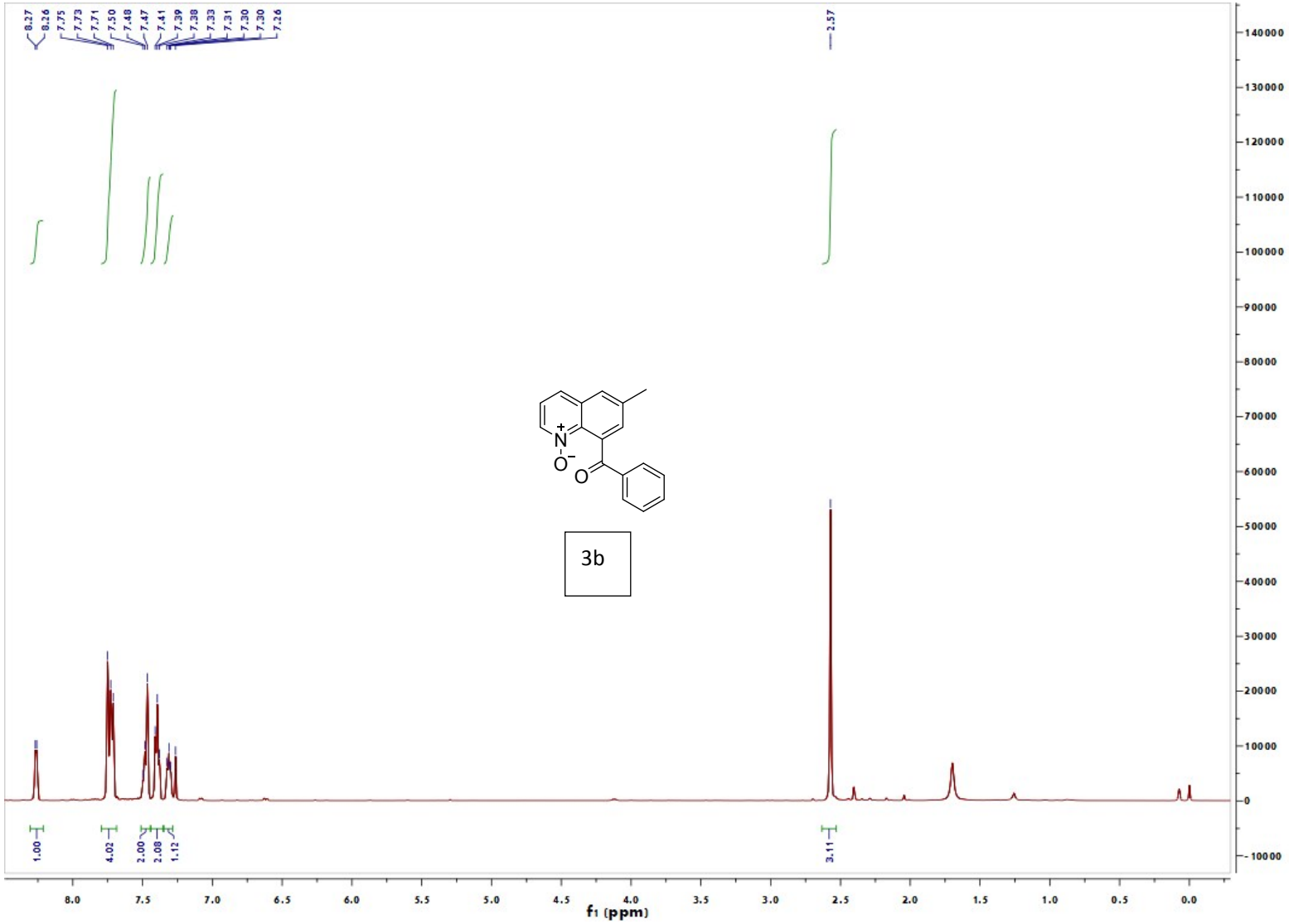
f1 (ppm)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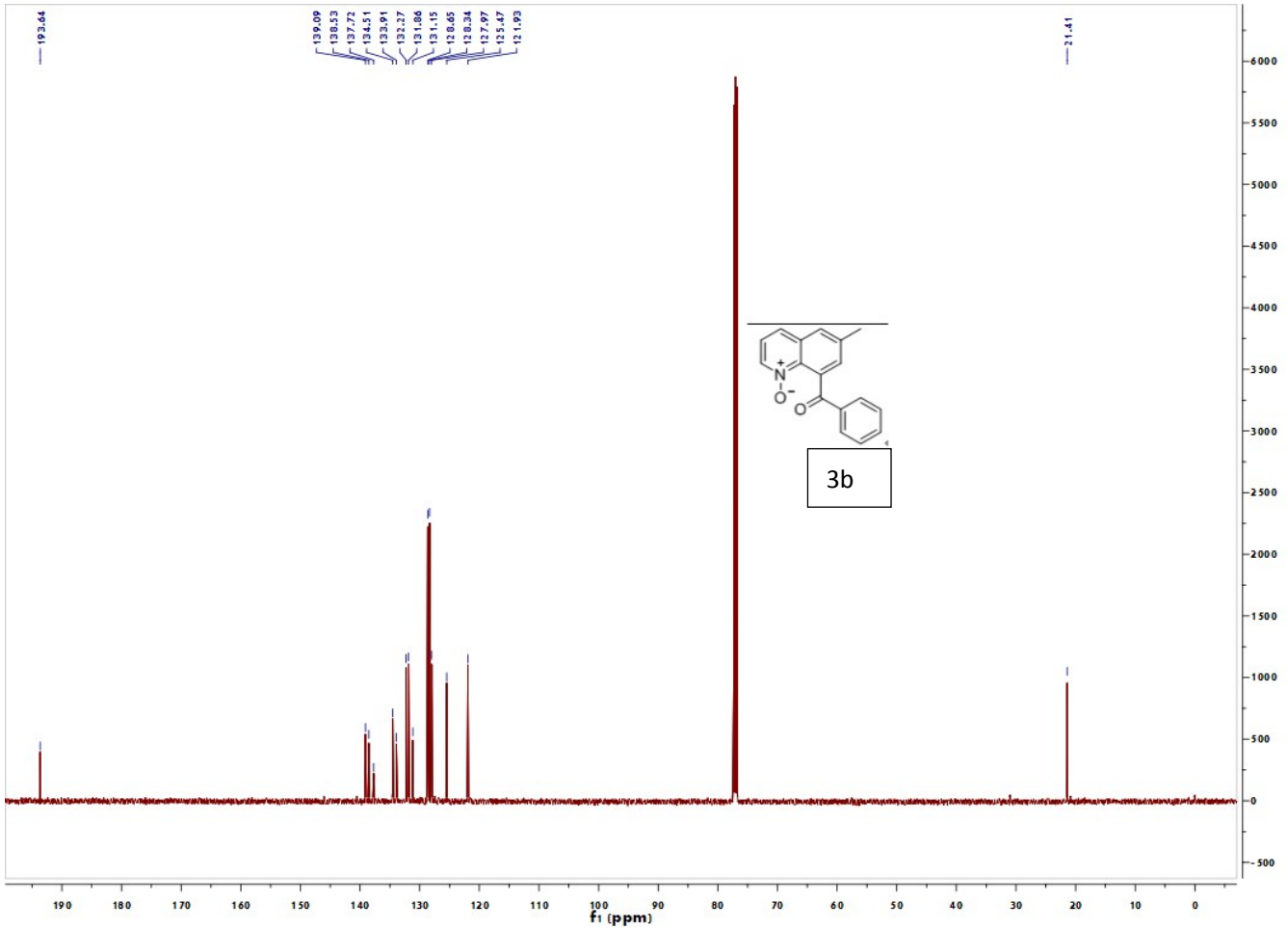
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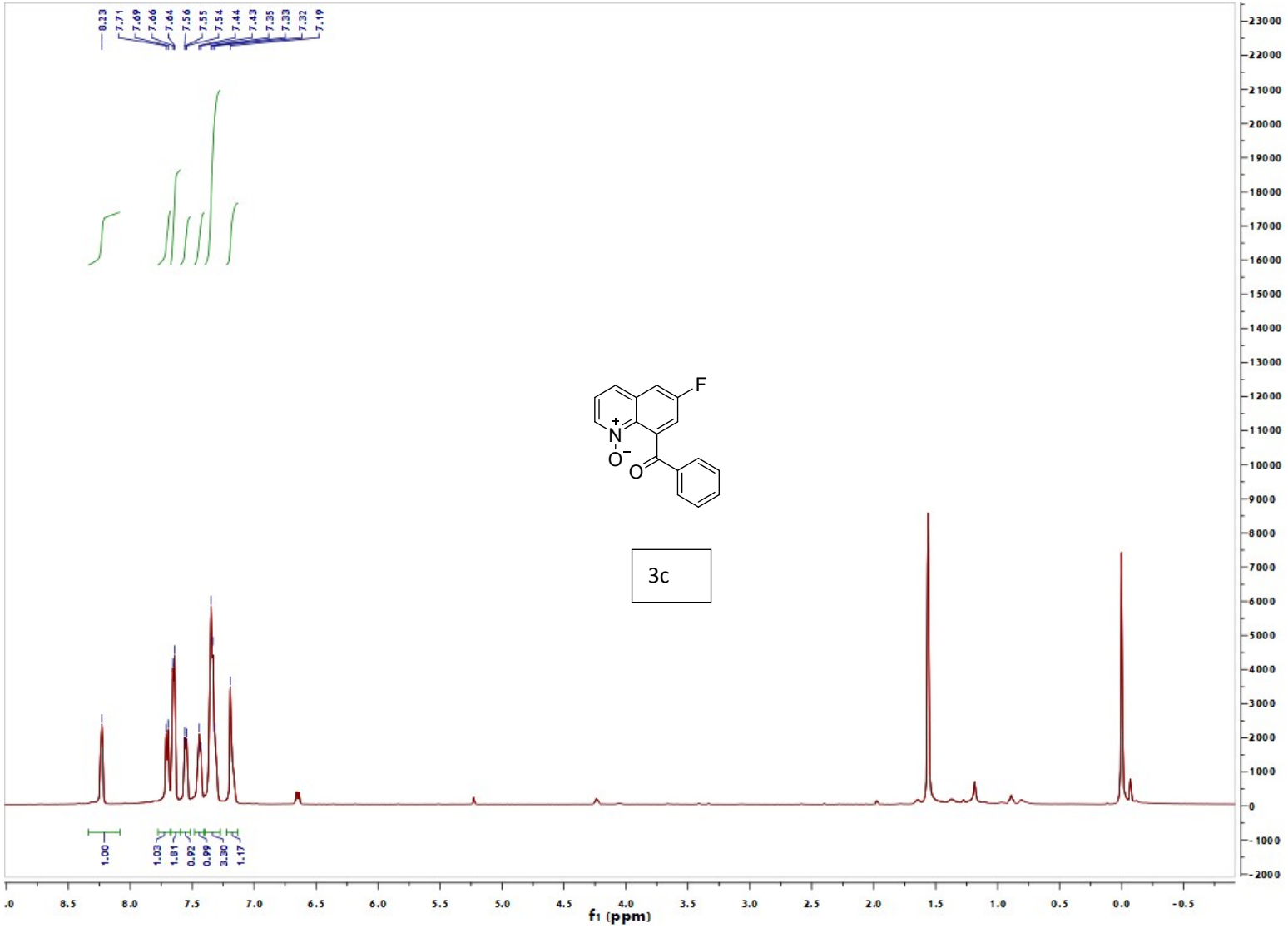
3b
f1 (ppm)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O
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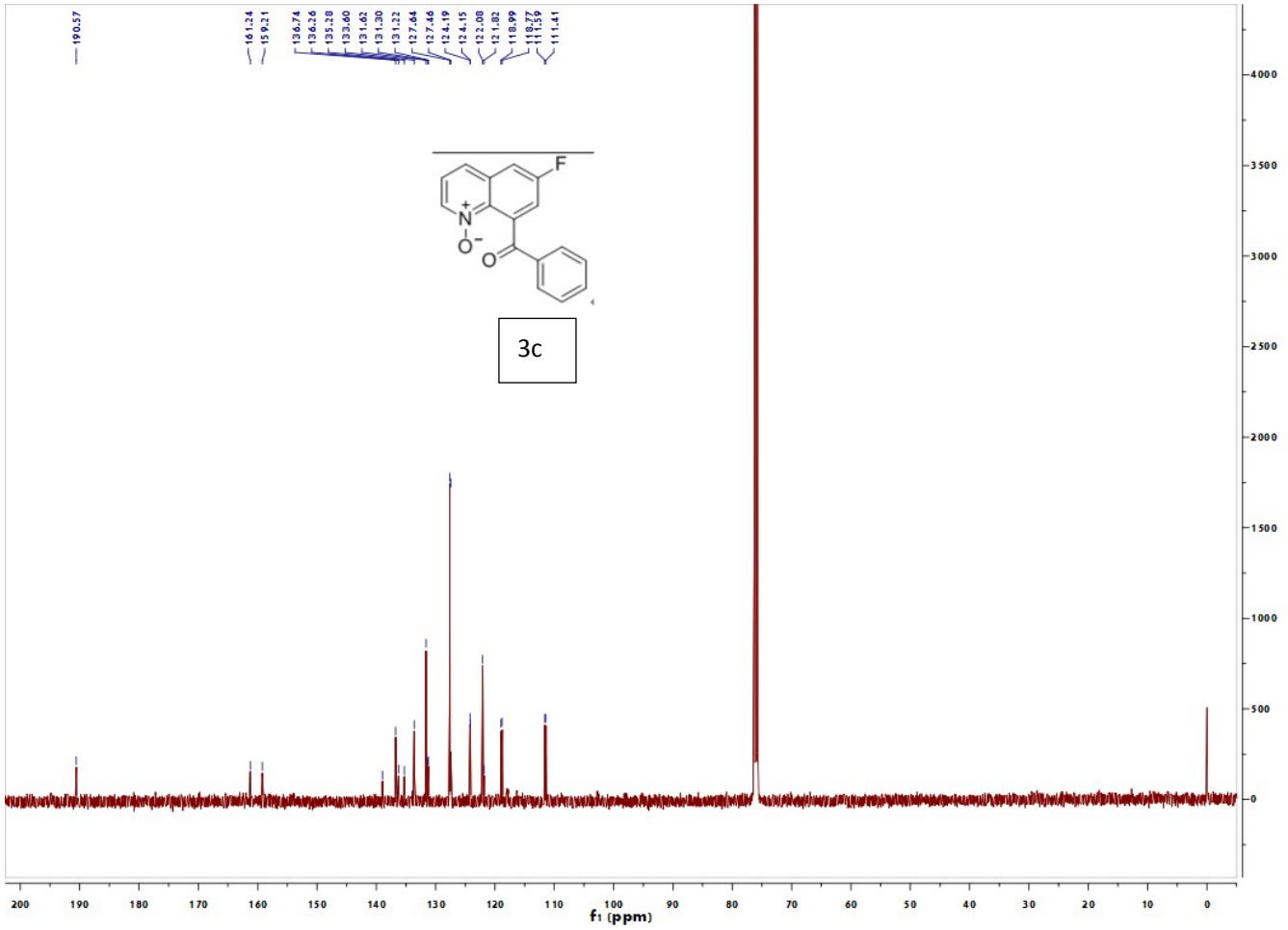
f1 (ppm)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118.77
111.59
111.41
F
N+
O-
O
3c
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3500
3000
2500
2000
1500
1000
500
0
200
190
180
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100
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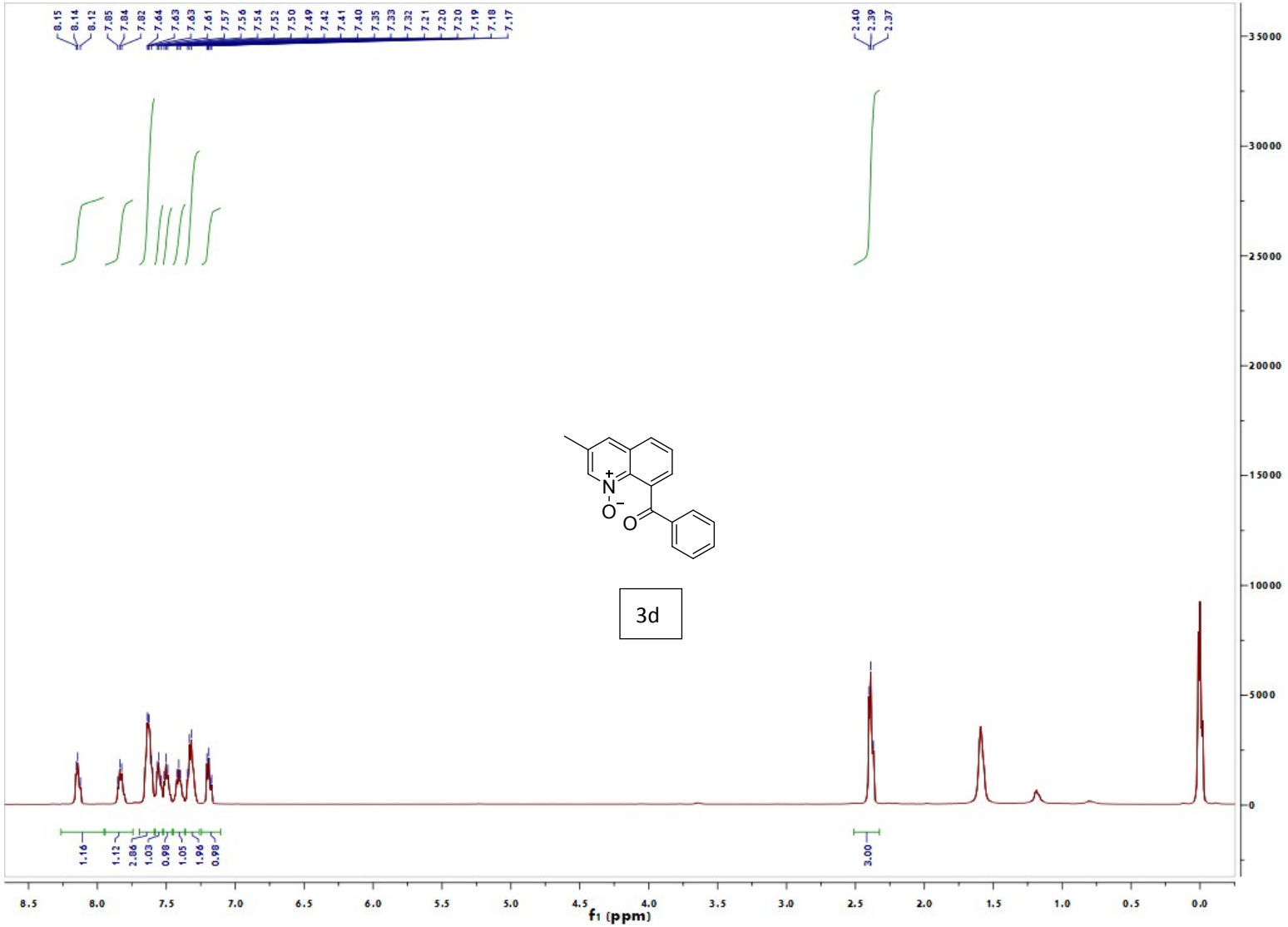
0
f1 (ppm)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7.32
7.21
7.20
7.20
7.19
7.18
7.17
2.40
2.39
2.37
35000
30000
25000
20000
15000
10000
5000
0
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1.12
2.86
1.03
0.98
1.05
1.96
0.98
3.00
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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2.0
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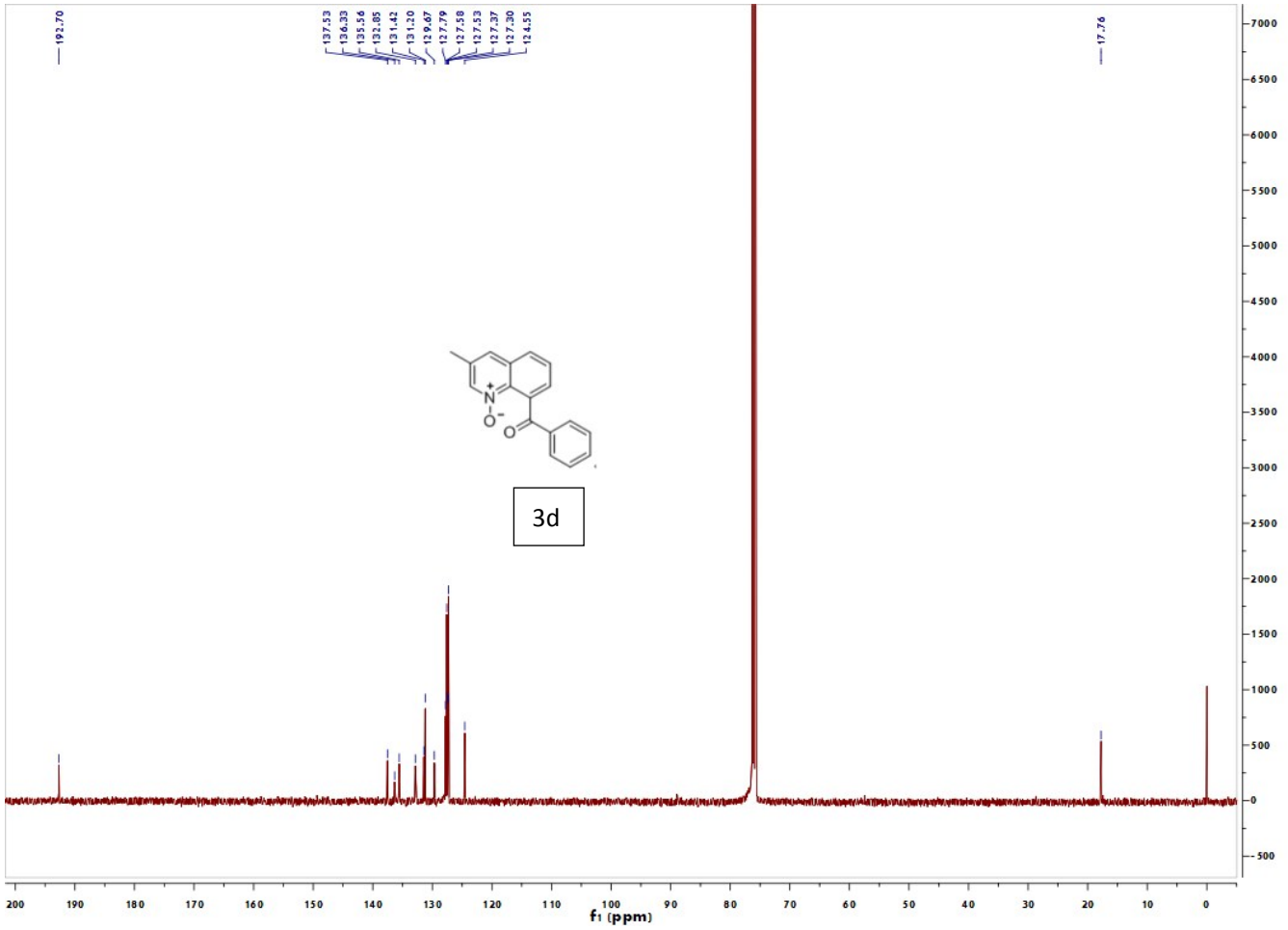
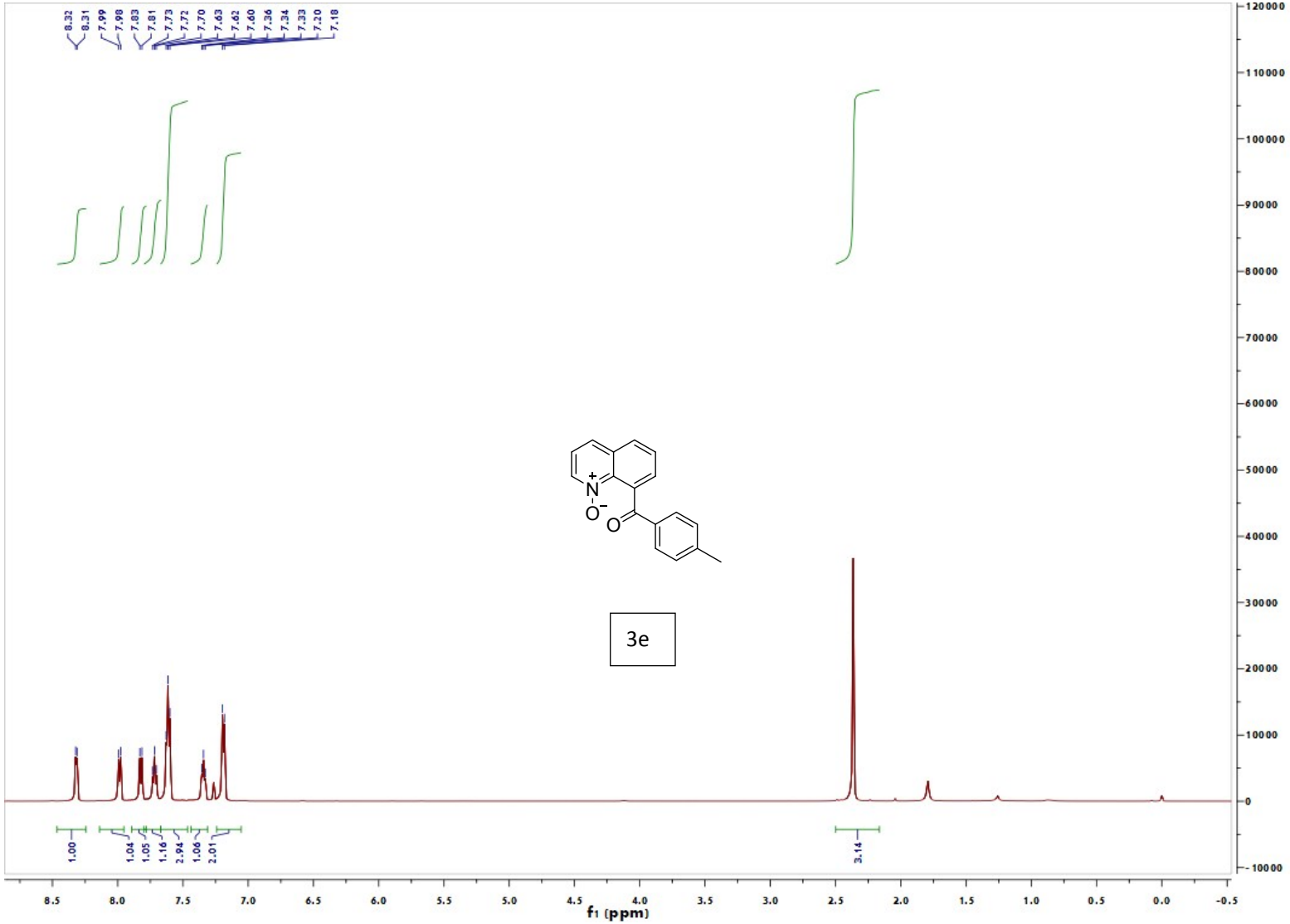
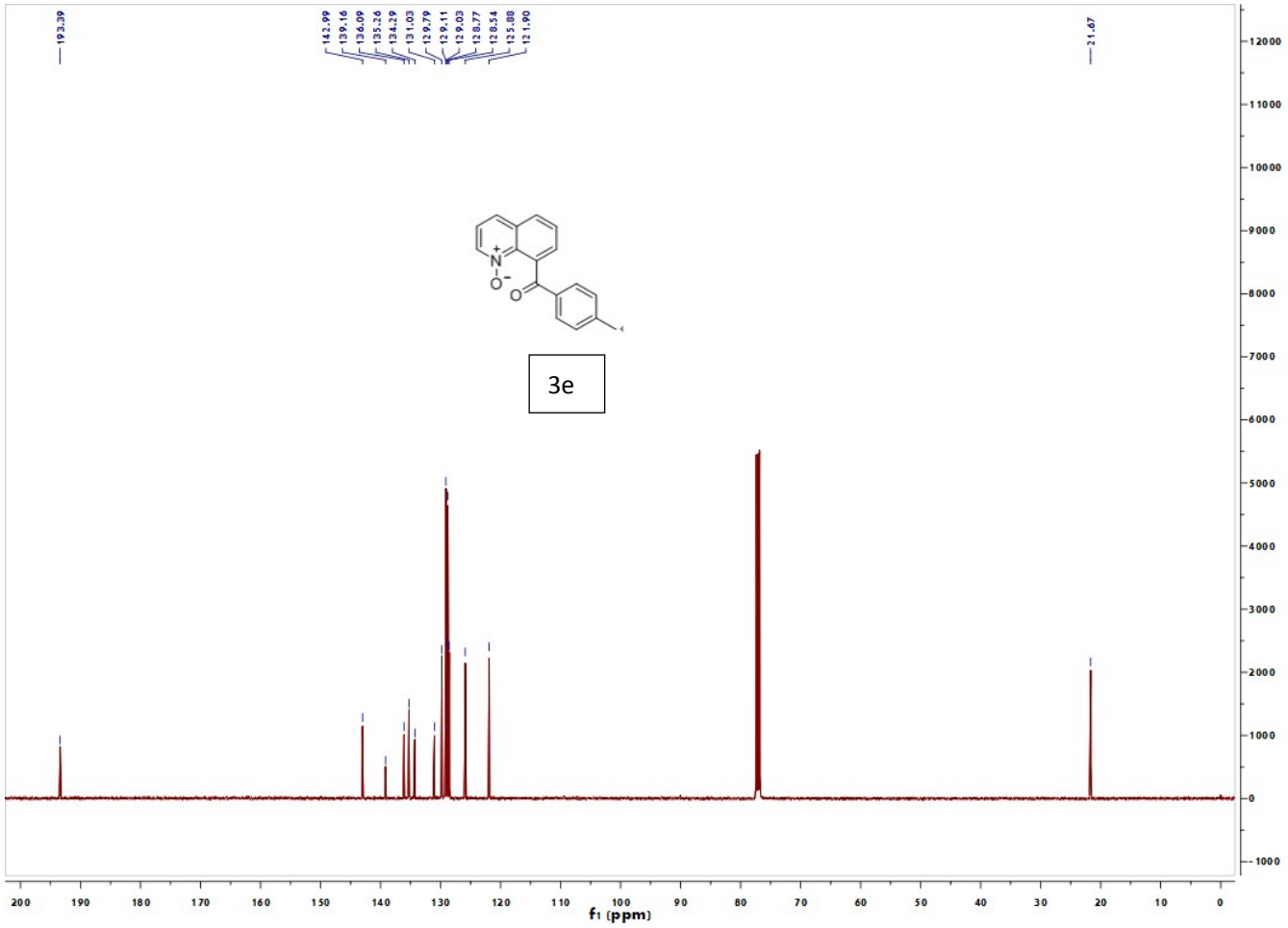
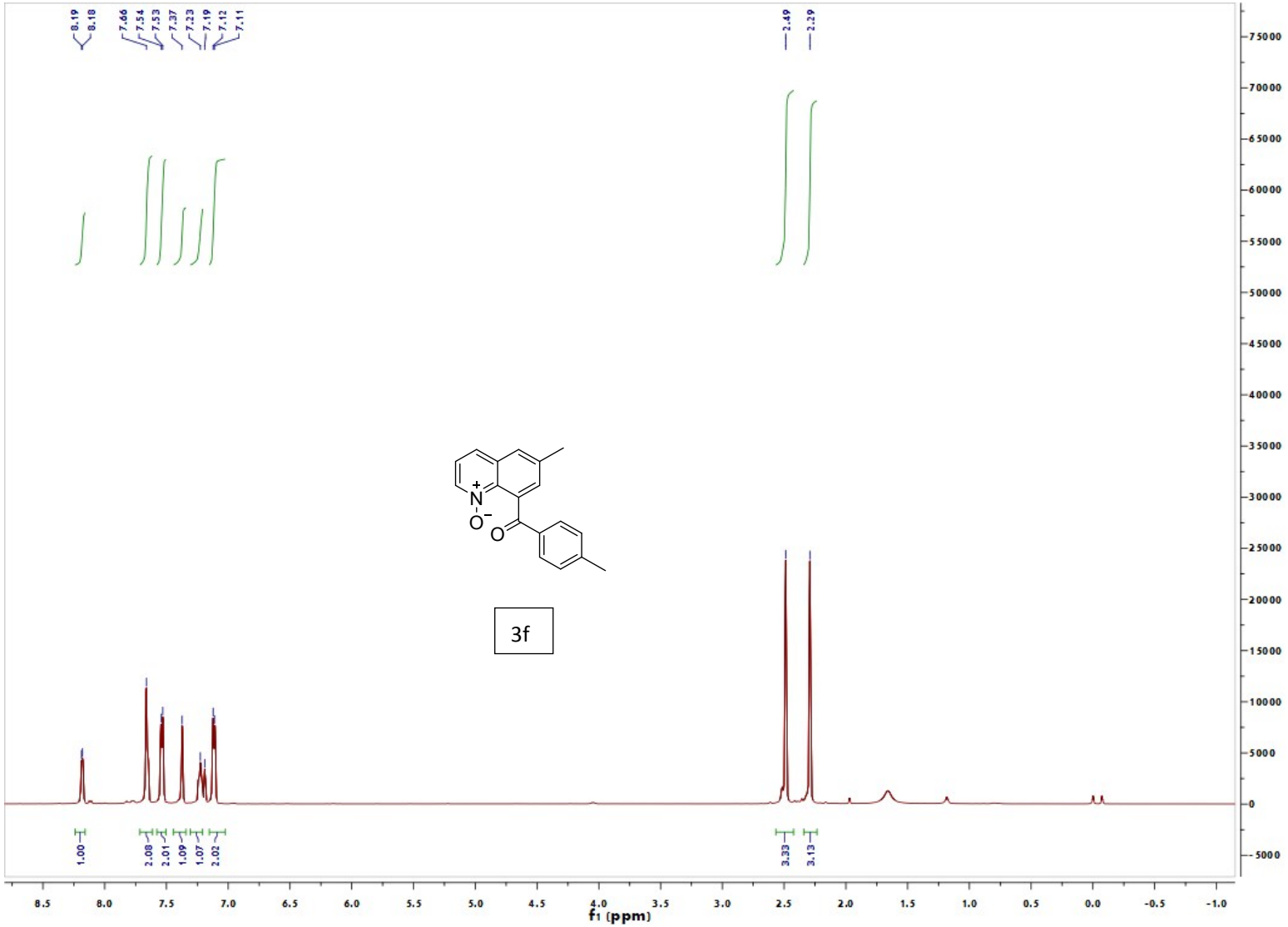
1.0
0.5
0.0
f1 (ppm)

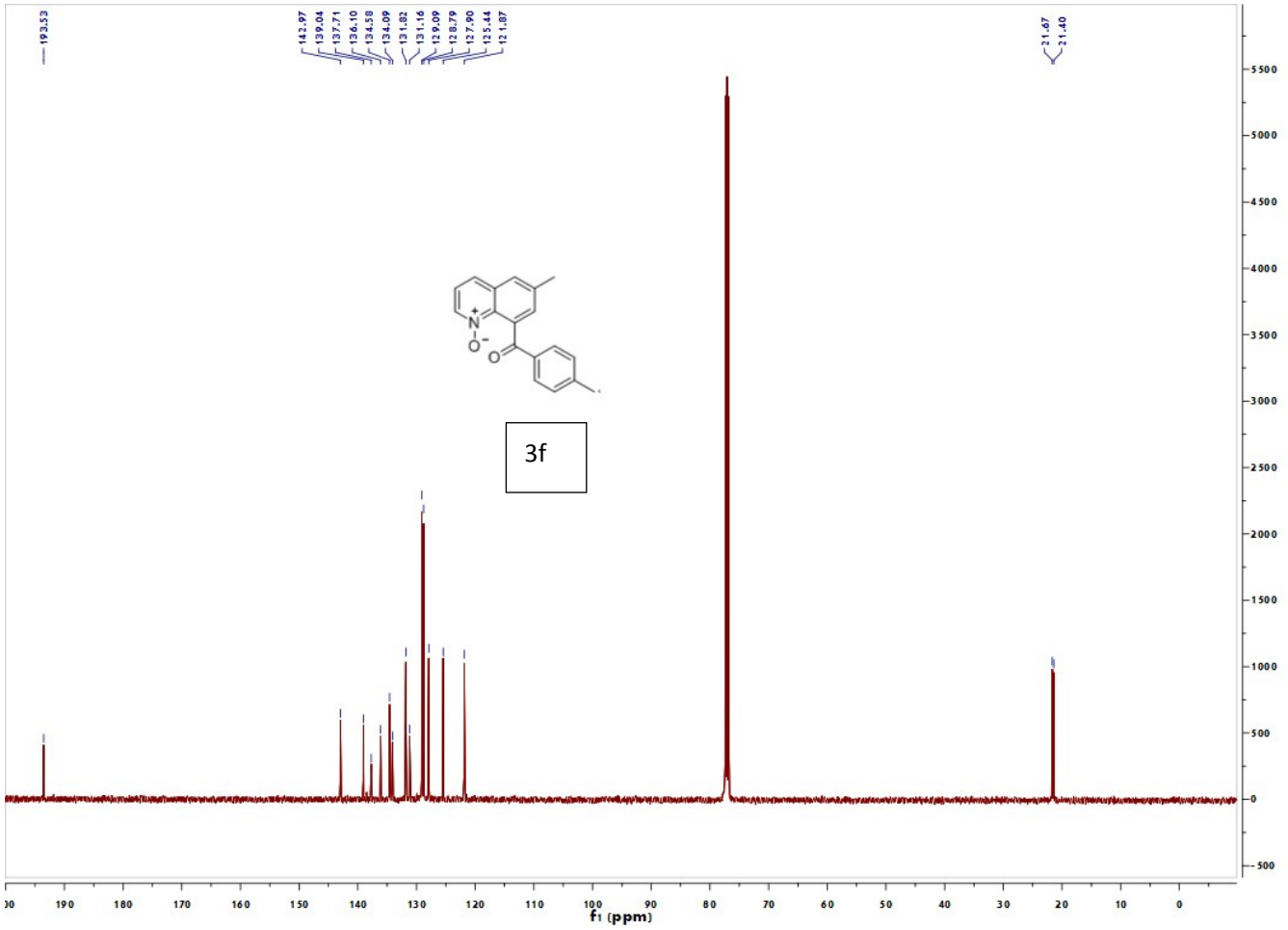
3d

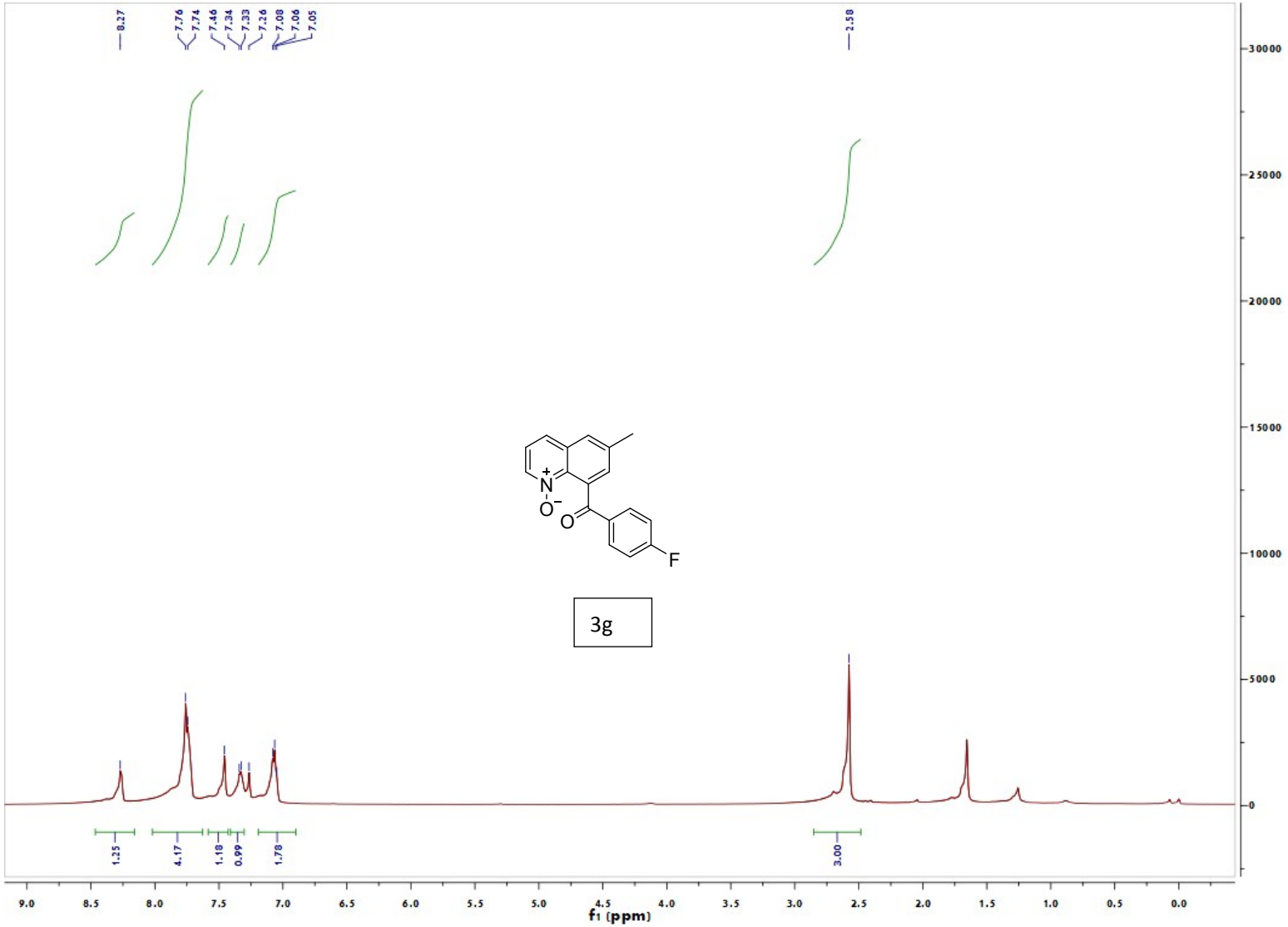

192.70
137.53
136.33
135.56
132.85
131.42
131.20
129.67
127.79
127.58
127.53
127.37
127.30
124.55
17.76
3d
f1 (ppm)


8.32
8.31
7.99
7.98
7.83
7.81
7.73
7.72
7.70
7.63
7.62
7.60
7.36
7.34
7.33
7.20
7.18
3e
1.00
1.04
1.05
1.16
2.94
1.06
2.01
3.14
f1 (ppm)

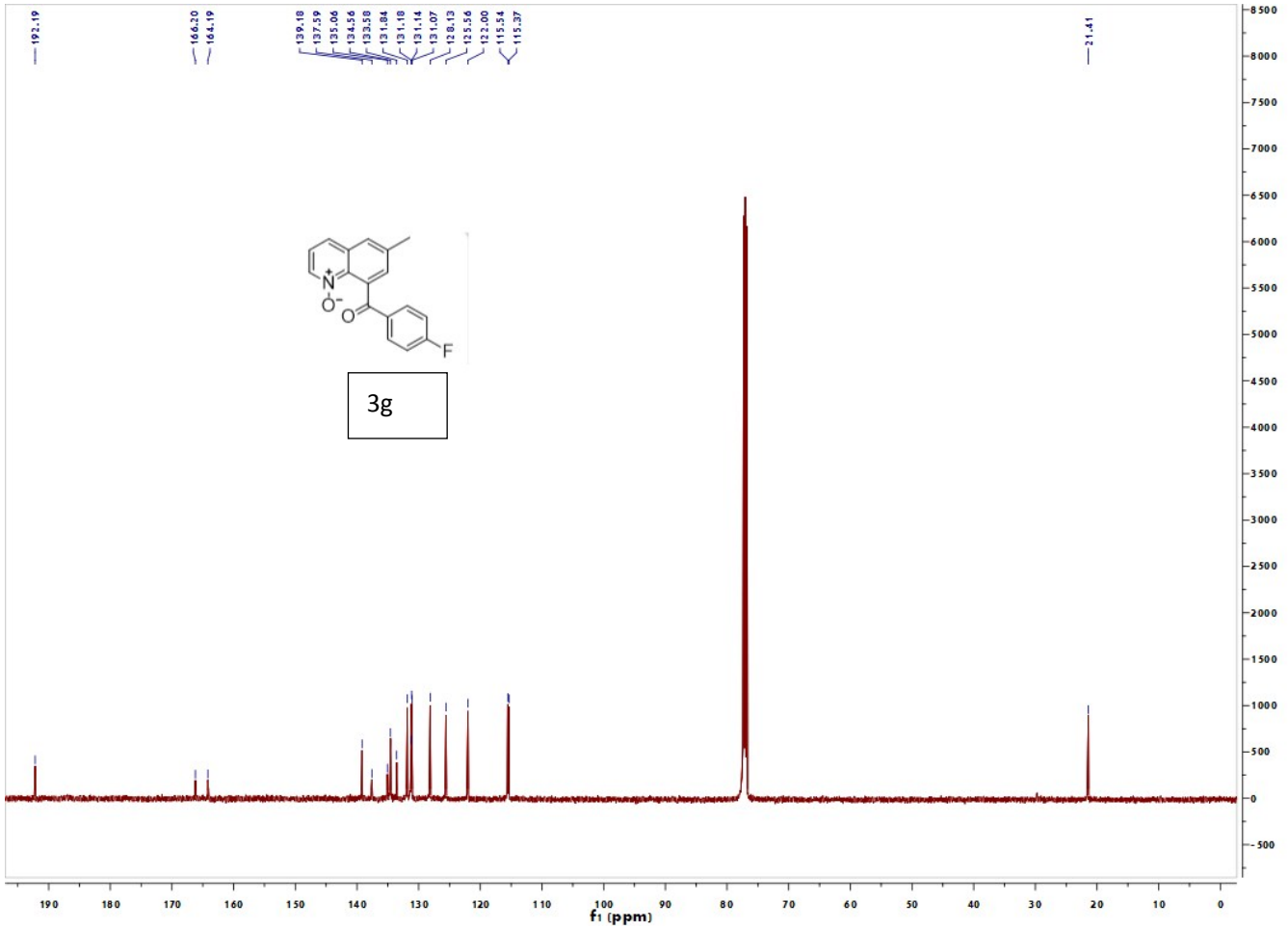

193.39
142.99
139.16
136.09
135.26
134.29
131.03
129.79
129.11
129.03
128.77
128.54
125.88
121.90
21.67
3e
f1 (ppm)

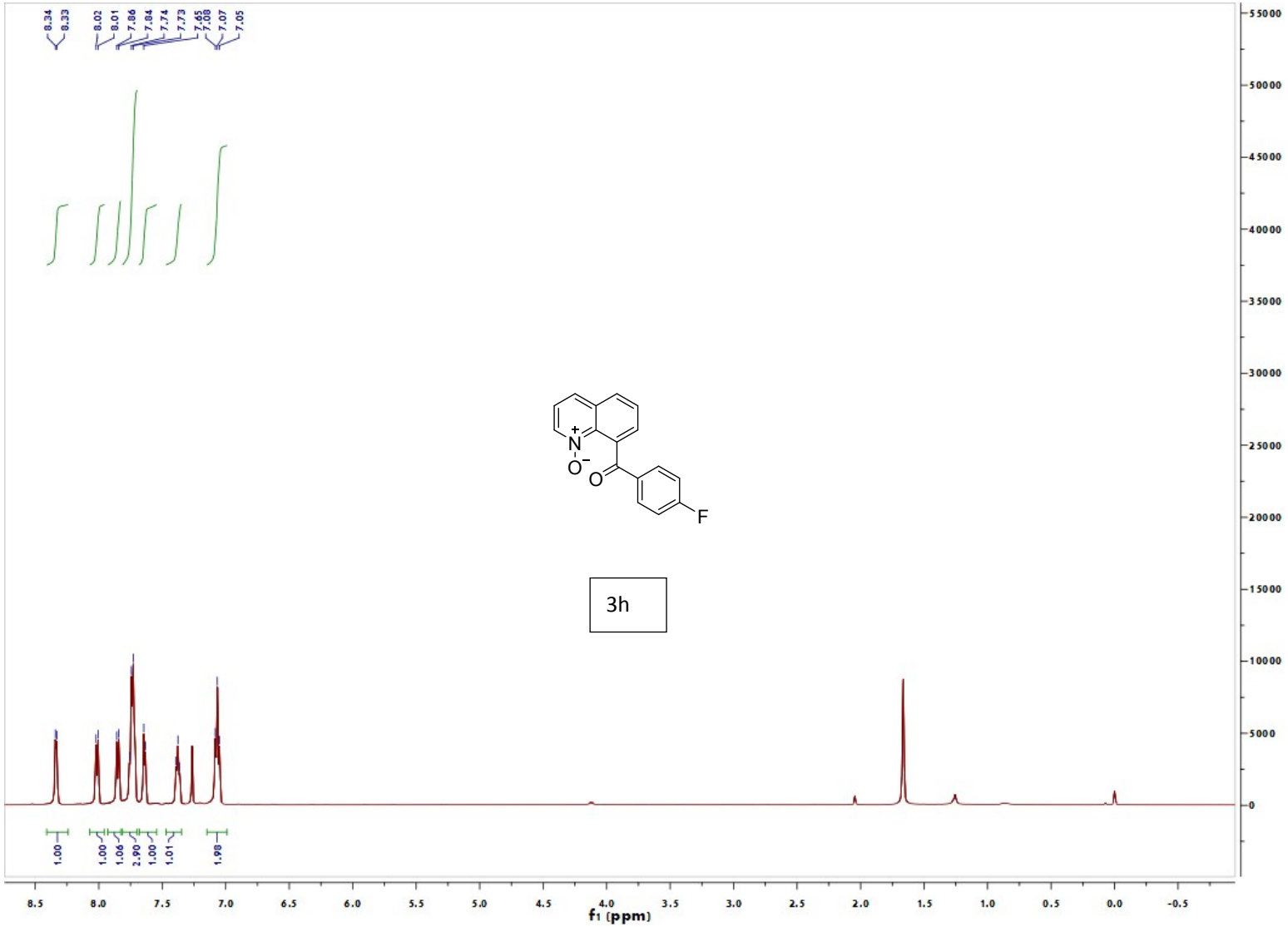

8.19
8.18
7.66
7.54
7.53
7.37
7.23
7.19
7.12
7.11
2.49
2.29
3f
1.00
2.08
2.01
1.09
1.07
2.02
3.33
3.13
f1 (ppm)

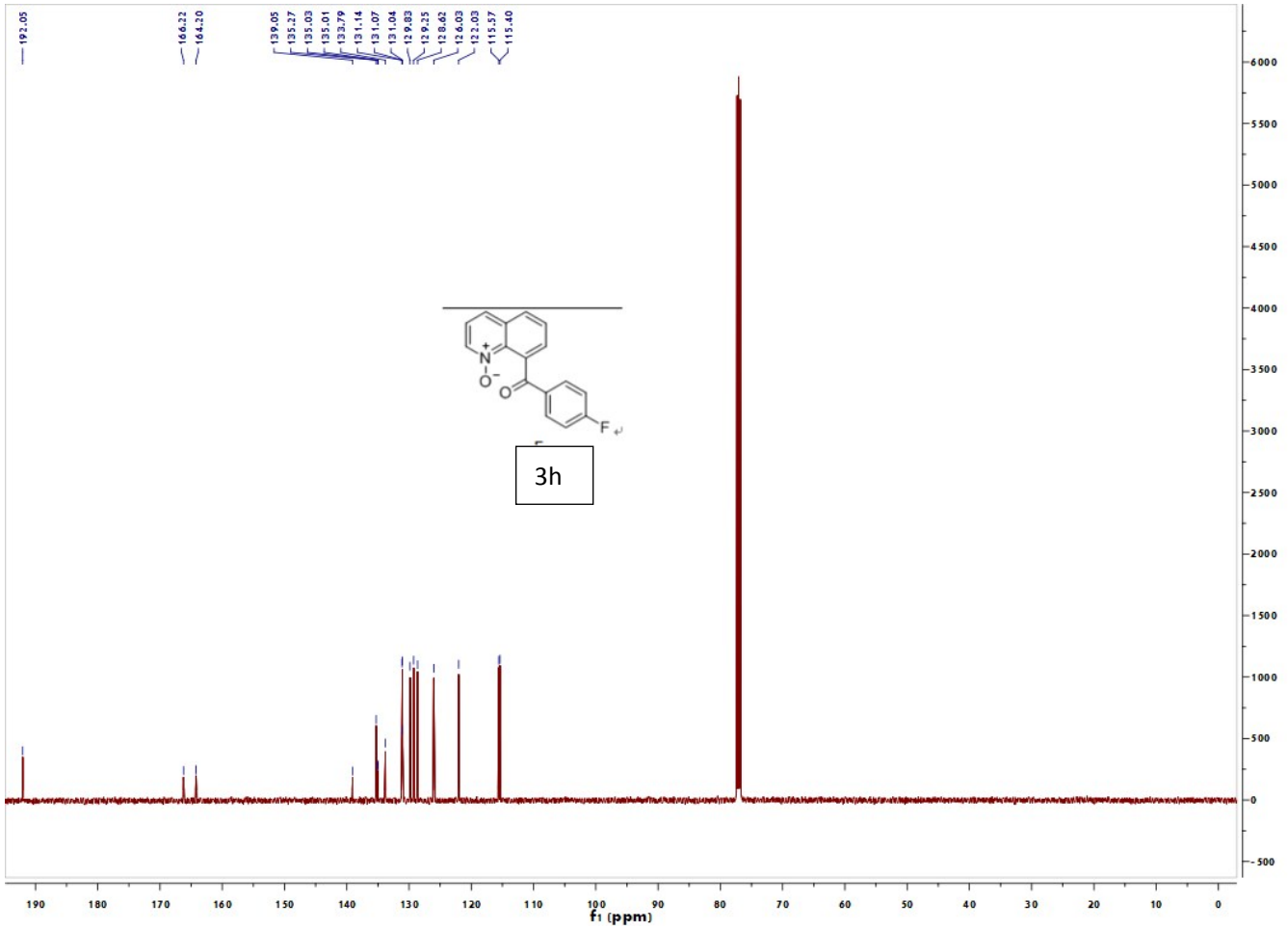

193.53
142.97
139.04
137.71
136.10
134.58
134.09
131.82
131.16
129.09
128.79
127.90
125.44
121.87
21.67
21.40
3f
f1 (ppm)

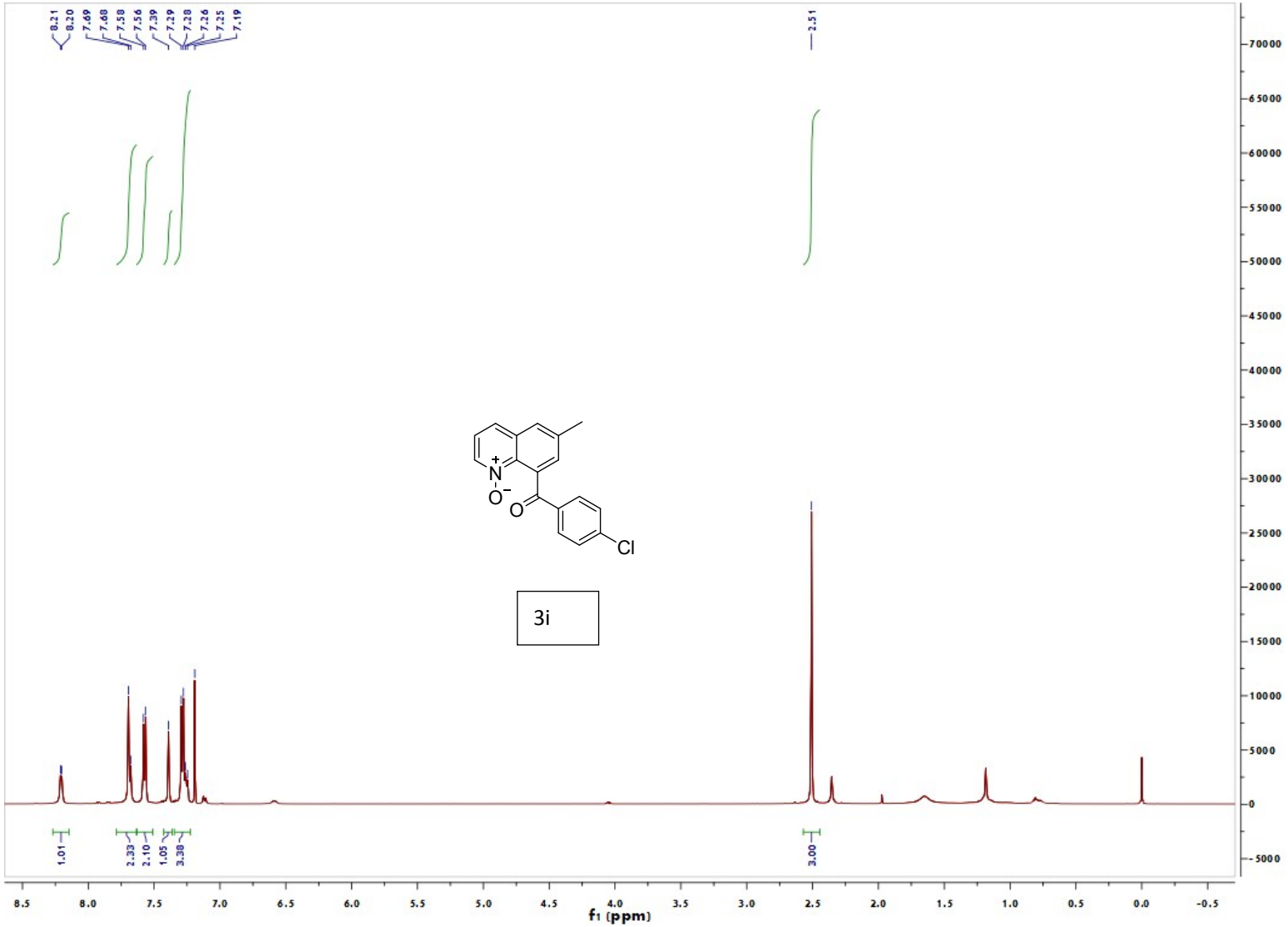

8.27
7.76
7.74
7.46
7.34
7.33
7.26
7.08
7.06
7.05
2.58
30000
25000
20000
15000
10000
5000
0
1.25
4.17
1.18
0.99
1.78
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
N
O
O
F

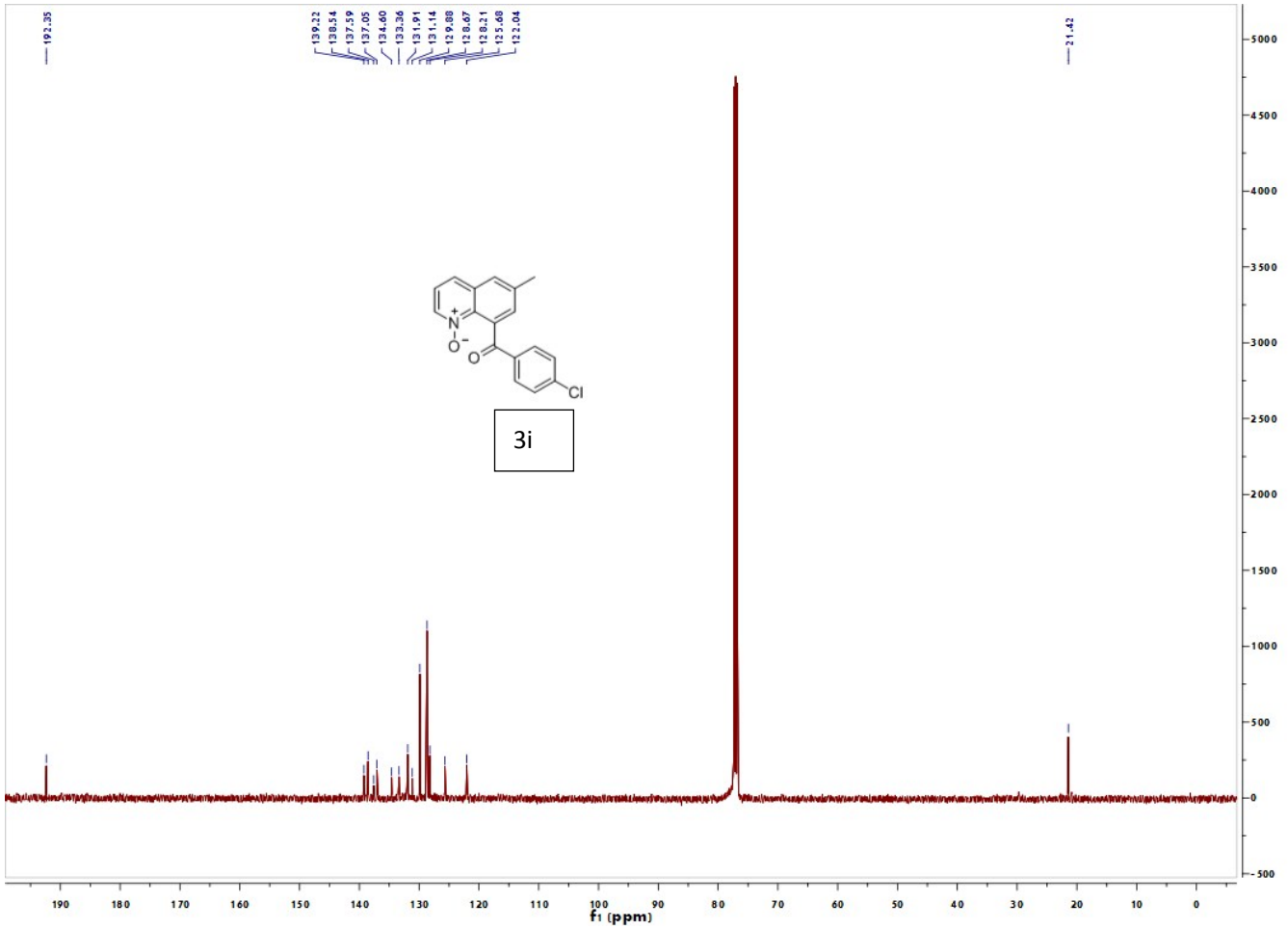
3g

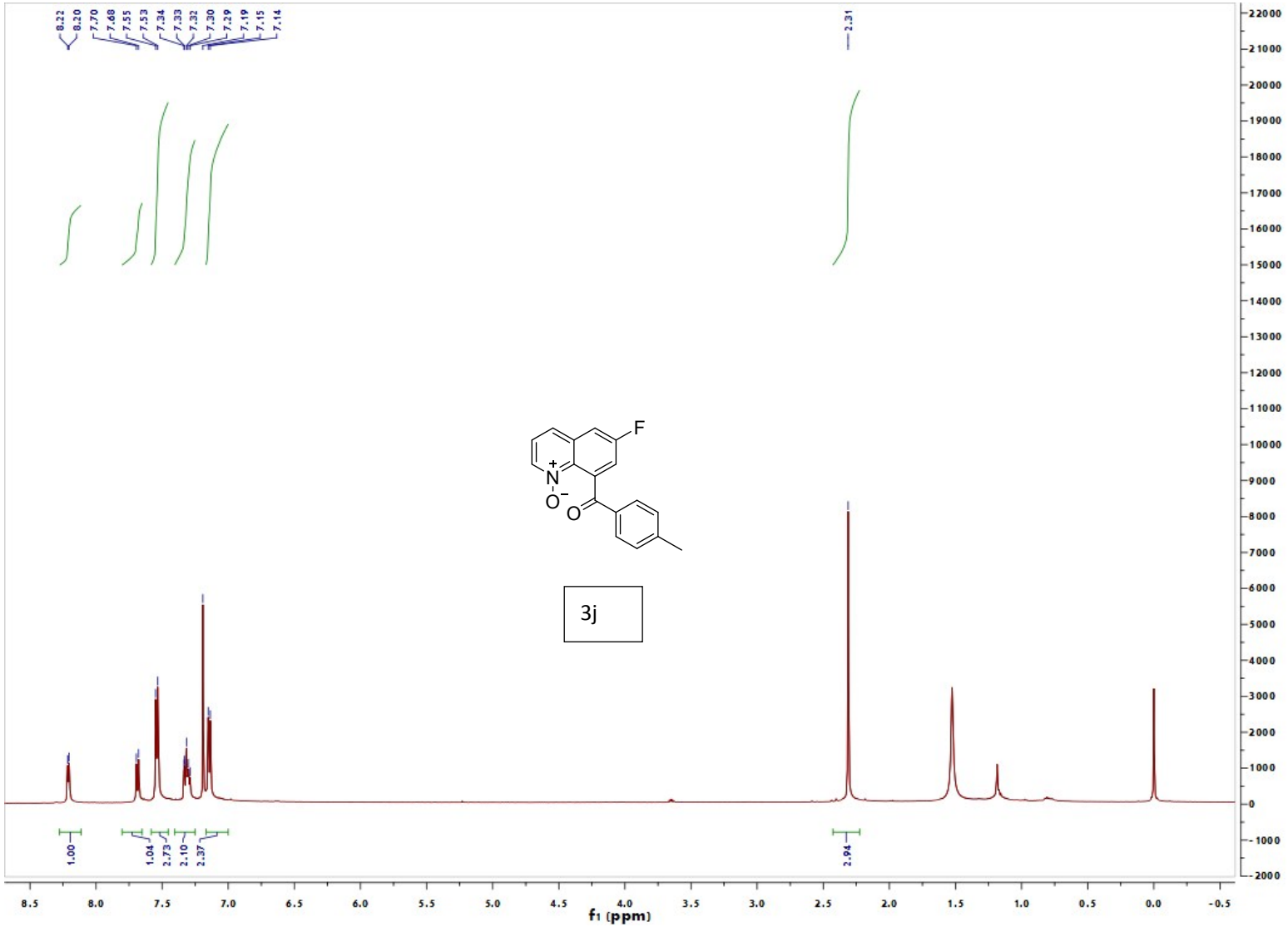

192.19
166.20
164.19
139.18
137.59
135.06
134.56
133.58
131.84
131.18
131.14
131.07
128.13
125.56
122.00
115.54
115.37
21.41
O
N
O
F
3g
f1 (ppm)

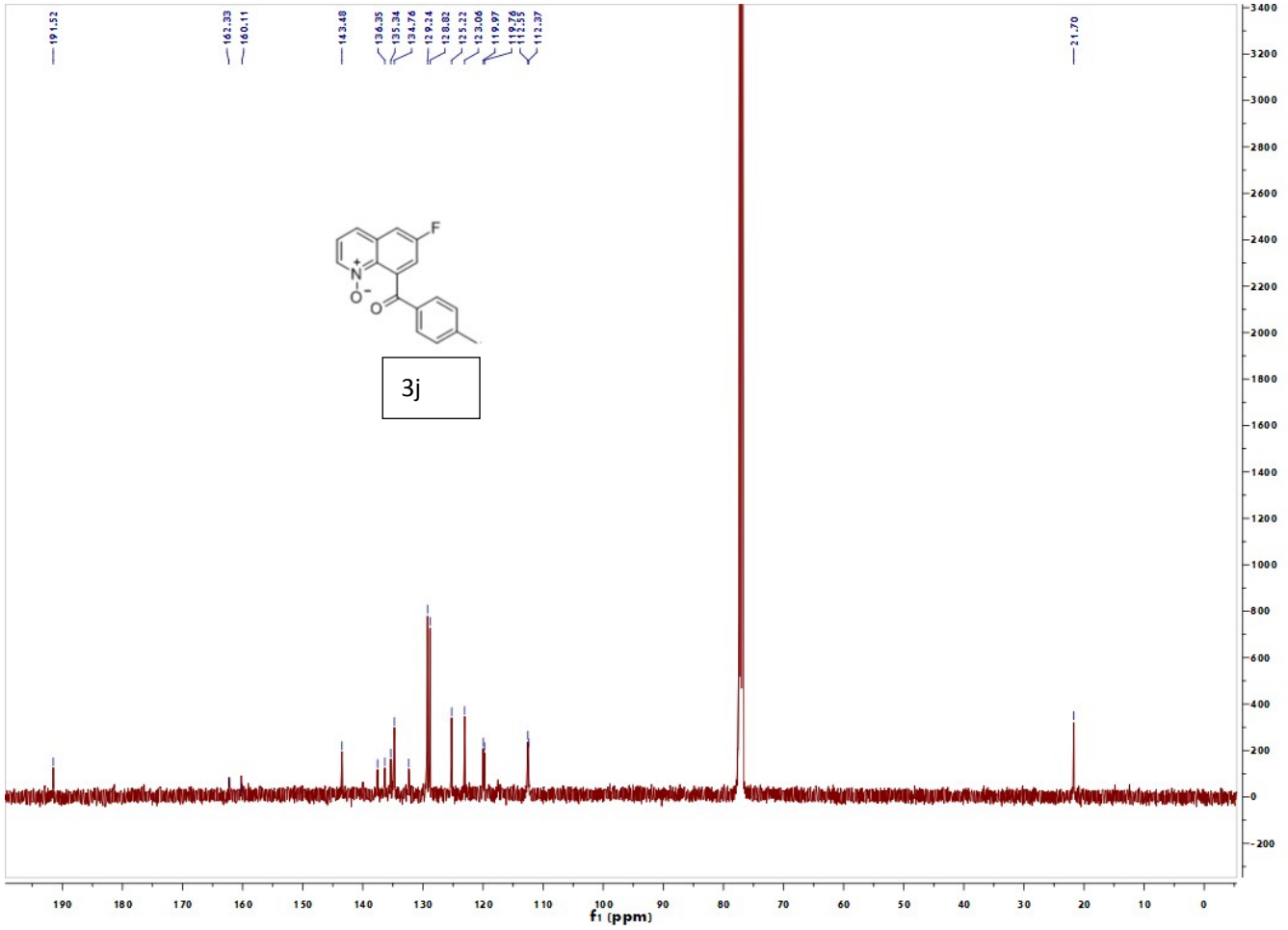

8.34
8.33
8.02
8.01
7.86
7.84
7.74
7.73
7.65
7.08
7.07
7.05
O
F
3h
1.00
1.00
1.06
2.90
1.00
1.01
1.98
f1 (ppm)

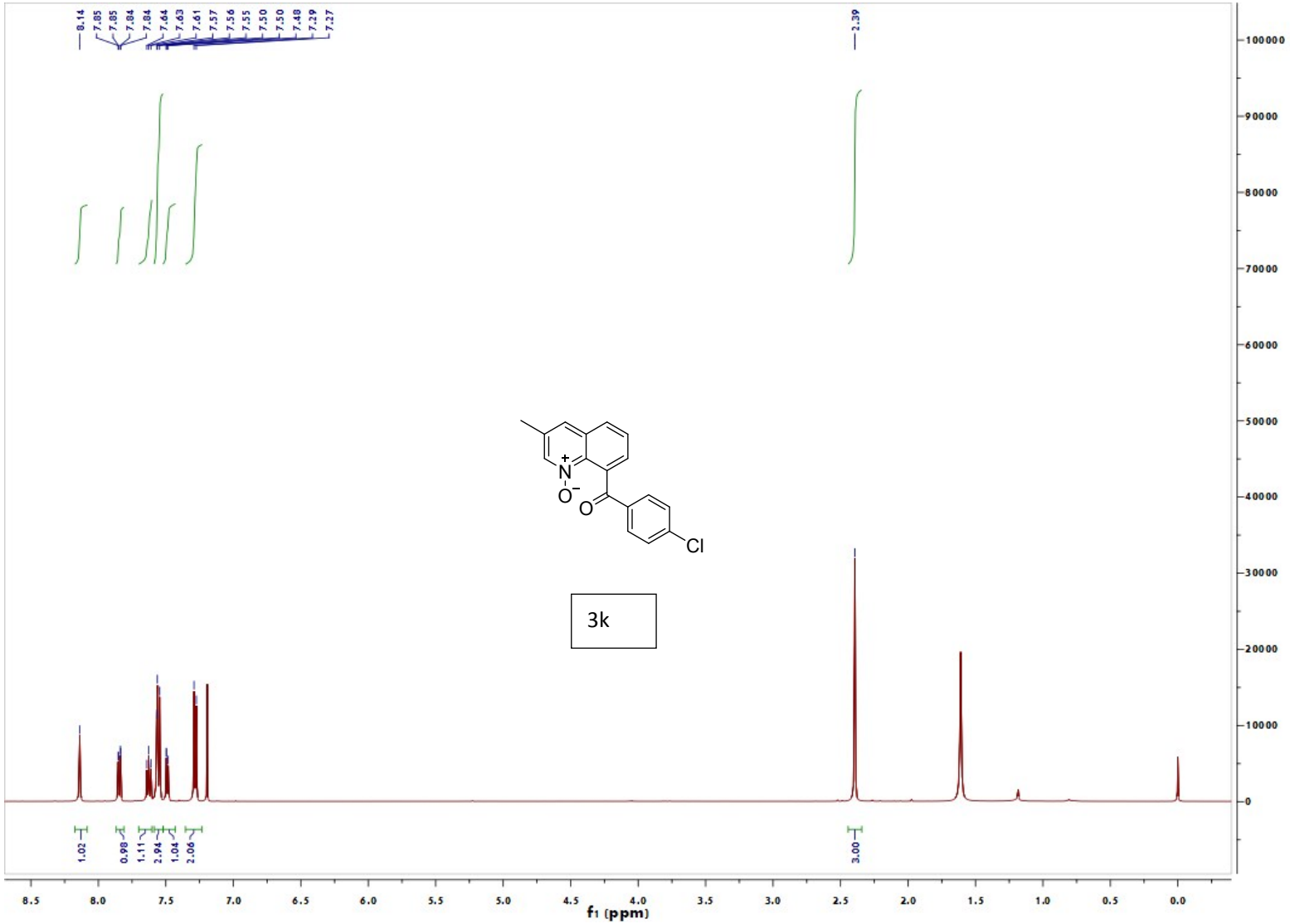

192.05
166.22
164.20
139.05
135.27
135.03
135.01
133.79
131.14
131.07
131.04
129.83
129.25
128.62
126.03
122.03
115.57
115.40
3h
f1 (ppm)

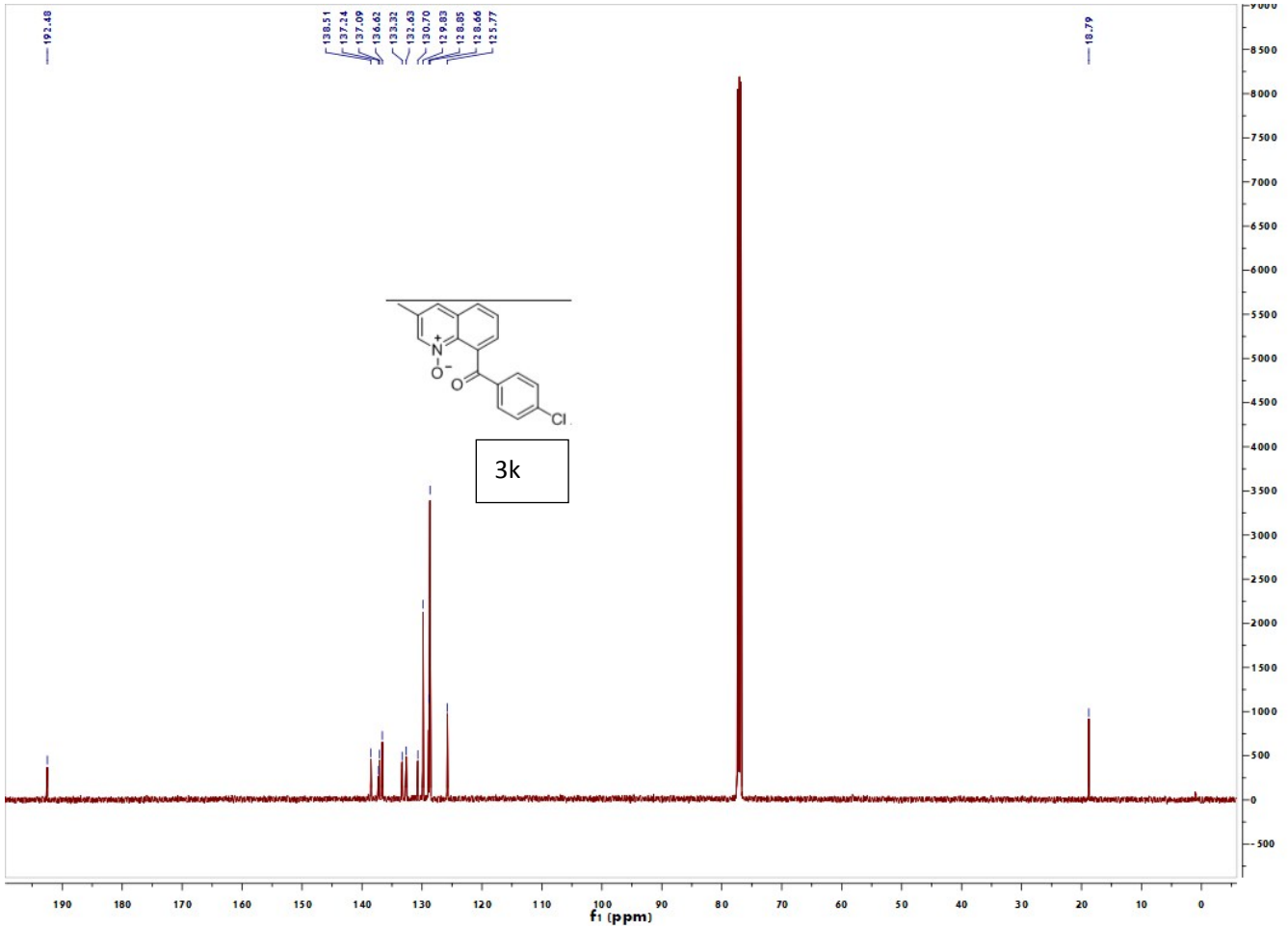

8.21
8.20
7.69
7.68
7.58
7.56
7.39
7.29
7.28
7.26
7.25
7.19
2.51
N
O
O
Cl
3i
1.01
2.33
2.10
1.05
3.38
3.00
f1 (ppm)


192.35
139.22
138.54
137.59
137.05
134.60
133.36
131.91
131.14
129.88
128.67
128.21
125.68
122.04
21.42
Cl
3i
f1 (ppm)

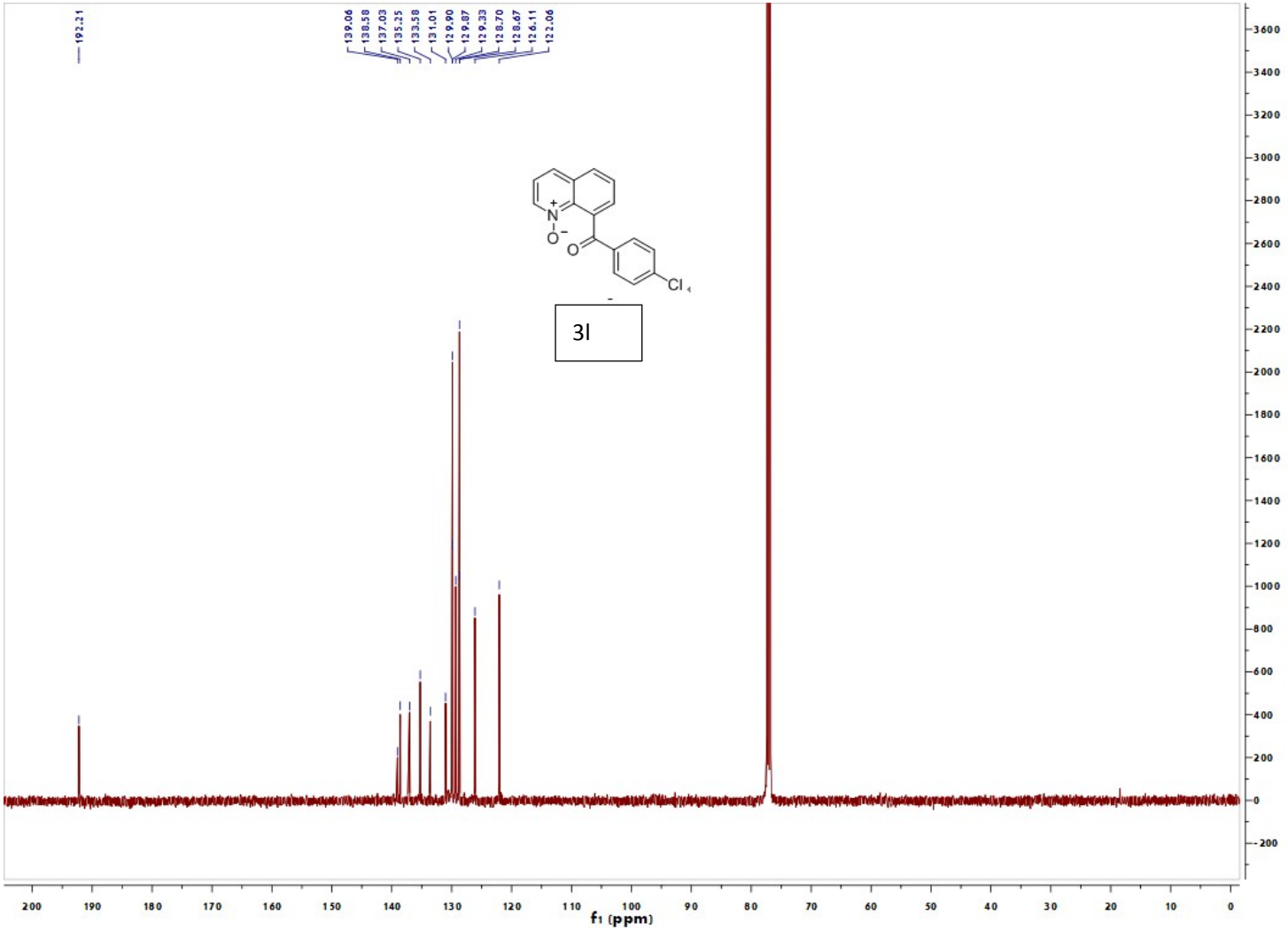

8.22
8.20
7.70
7.68
7.55
7.53
7.34
7.33
7.32
7.30
7.29
7.19
7.15
7.14
2.31
F
N
O
O
3j
1.00
1.04
2.73
2.10
2.37
2.94
f1 (ppm)

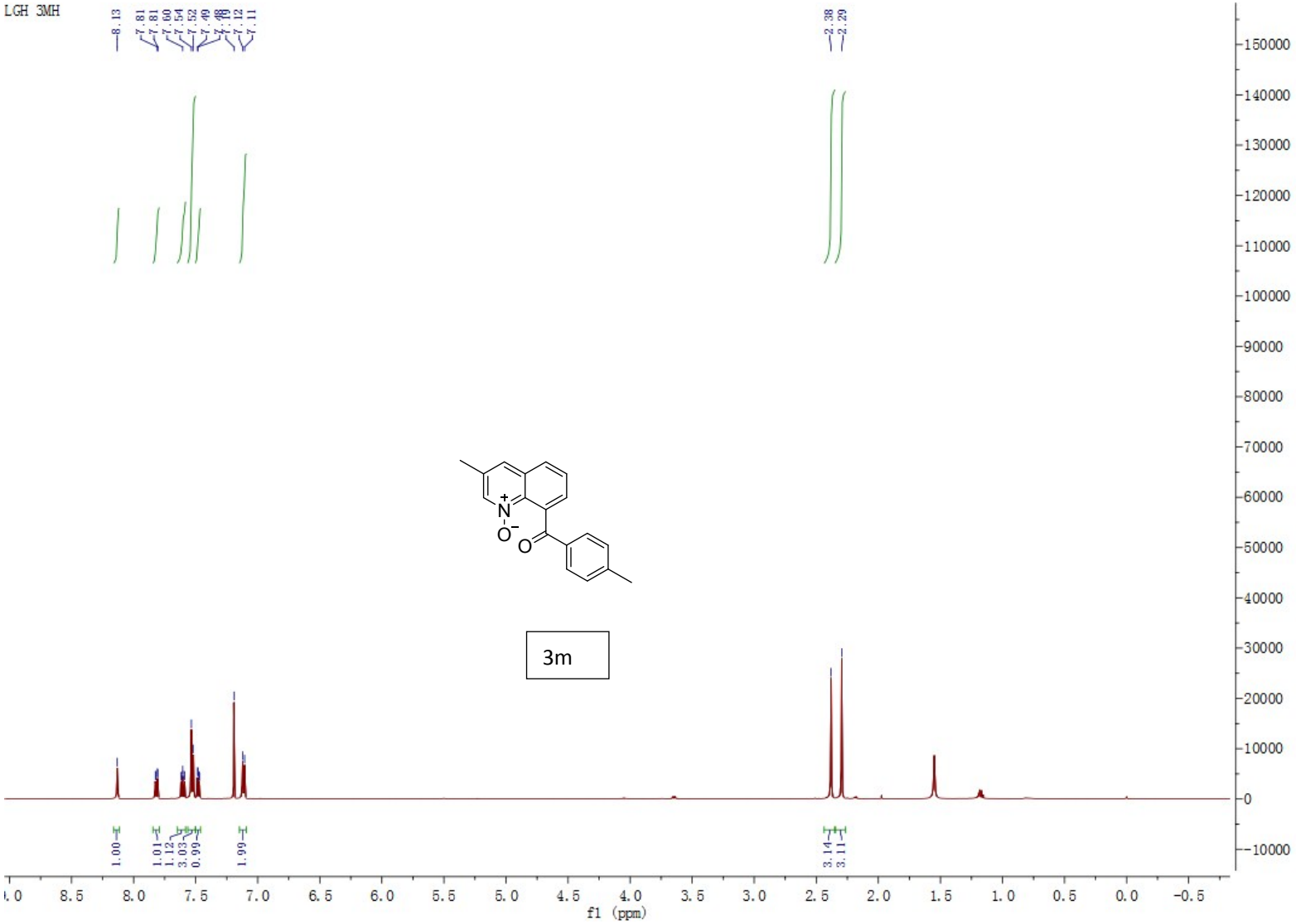

191.52
162.33
160.11
143.48
136.35
135.34
134.76
129.24
128.82
125.22
123.06
119.97
119.76
112.55
112.37
21.70
F
O
O
3j
f1 (ppm)

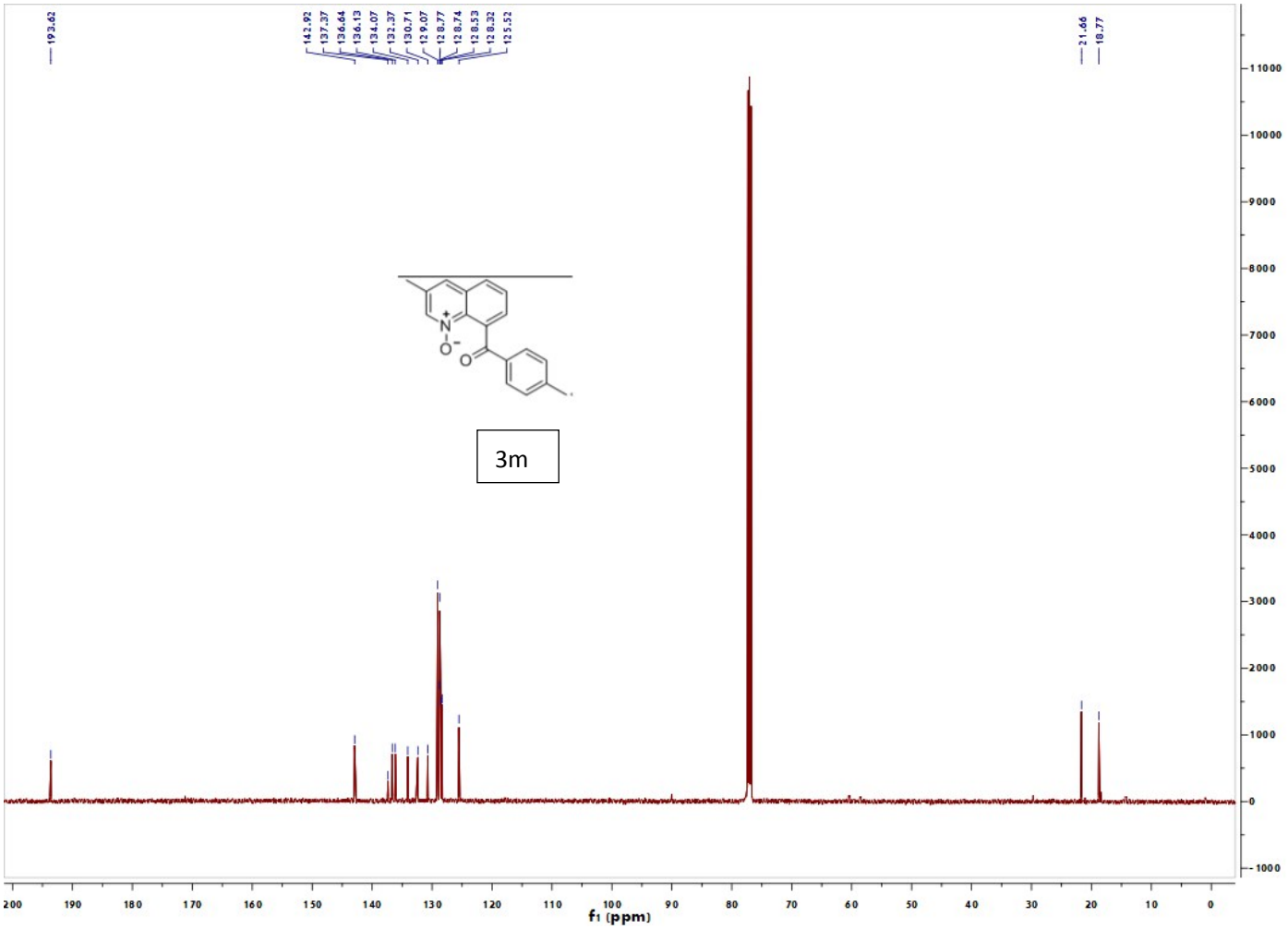

8.14
7.85
7.85
7.84
7.84
7.64
7.63
7.61
7.57
7.56
7.55
7.50
7.50
7.48
7.29
7.27
2.39
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
N
O
O
Cl
3k
1.02
0.98
1.11
2.94
1.04
2.06
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

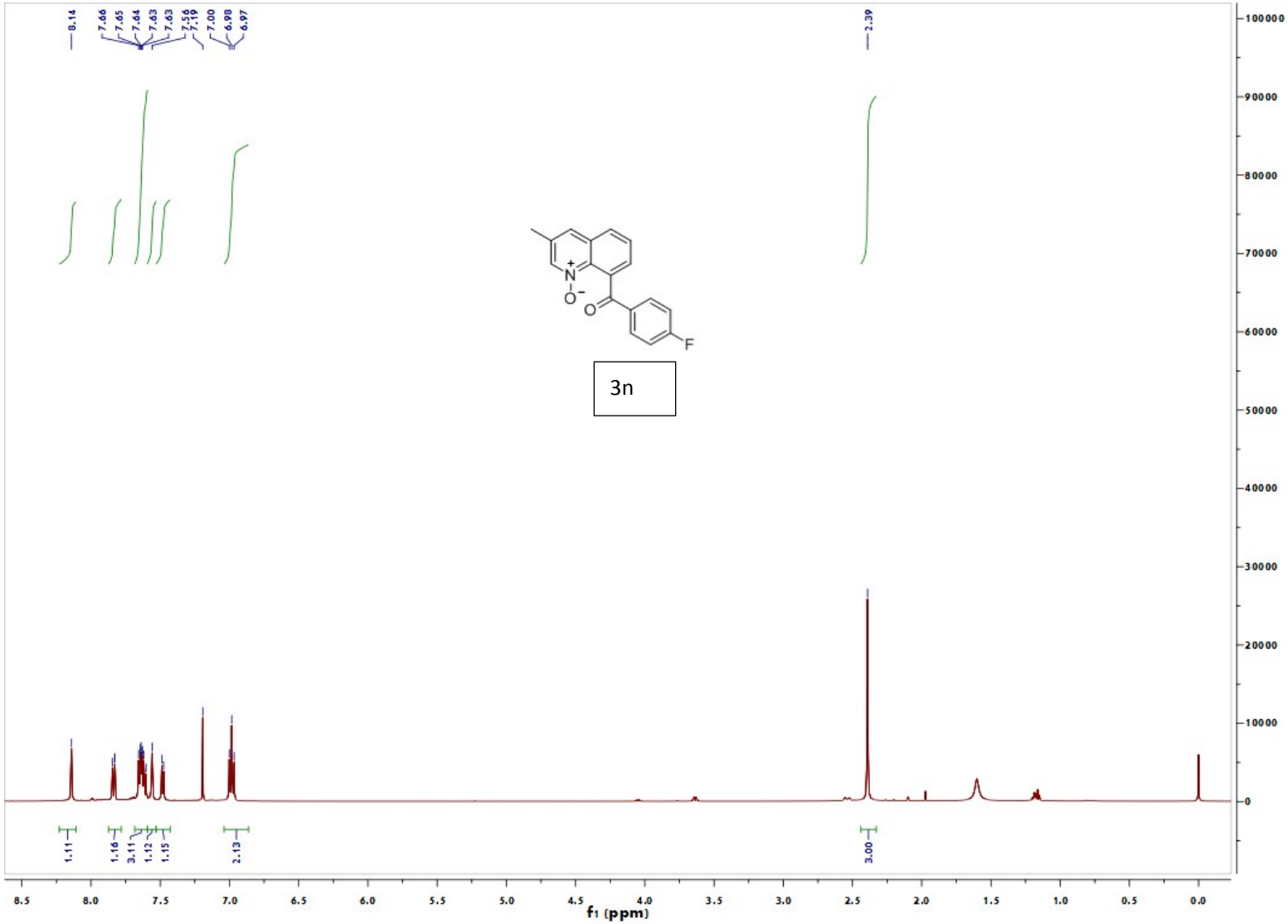

192.48
138.51
137.24
137.09
136.62
133.32
132.63
130.70
129.83
128.85
128.66
125.77
18.79
3k
f1 (ppm)


8.34
8.33
8.01
7.84
7.75
7.65
7.63
7.37
7.36
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
1.00
1.10
1.08
1.16
2.74
2.80
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
N
O
O
Cl
3l

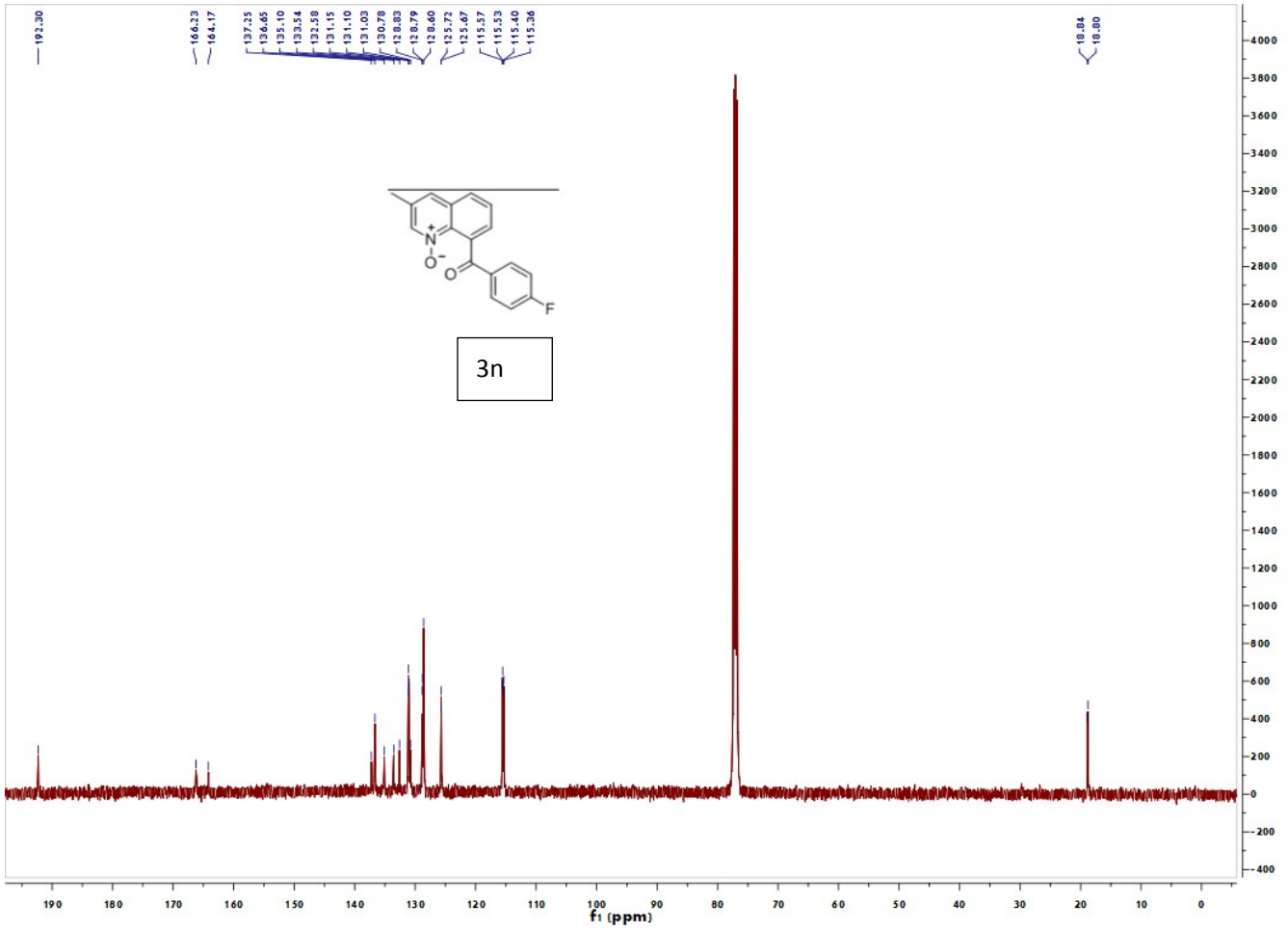

192.21
139.06
138.58
137.03
135.25
133.58
131.01
129.90
129.87
129.33
128.70
128.67
126.11
122.06
Cl
3l
f1 (ppm)


LGH 3MH
8.13
7.81
7.81
7.60
7.54
7.52
7.49
7.12
7.11
2.38
2.29
3m
1.00
1.01
1.12
3.03
0.99
1.99
3.14
3.11
f1 (ppm)


193.62
142.92
137.37
136.64
136.13
134.07
132.37
130.71
129.07
128.77
128.74
128.53
128.32
125.52
21.66
18.77
3m
f1 (ppm)


8.14
7.66
7.65
7.64
7.63
7.63
7.16
7.15
7.00
6.98
6.97
2.39
O
N
O
F
1.11
1.16
3.11
1.12
1.15
2.13
3.00
f1 (ppm)

3n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164.17
137.25
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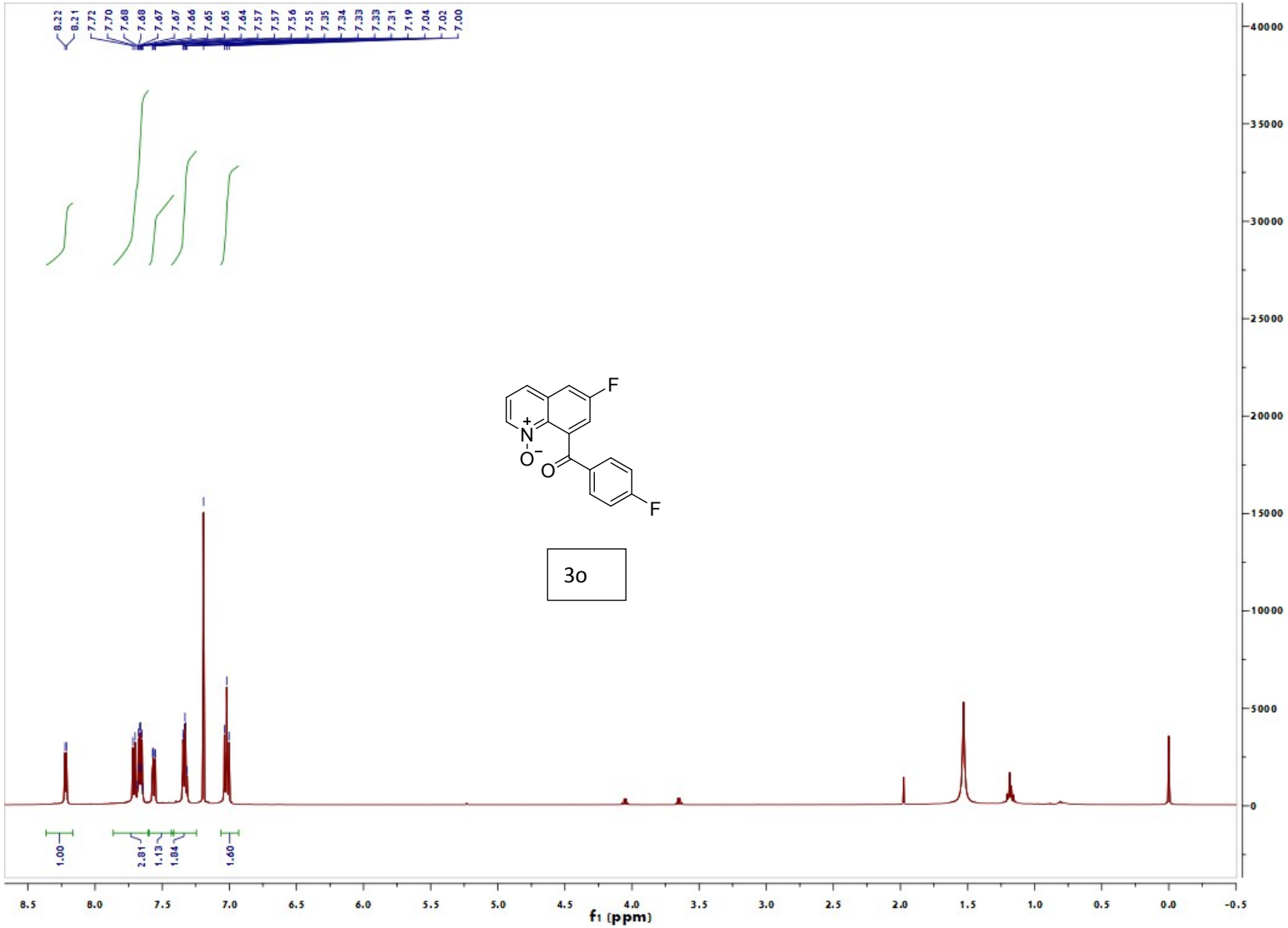
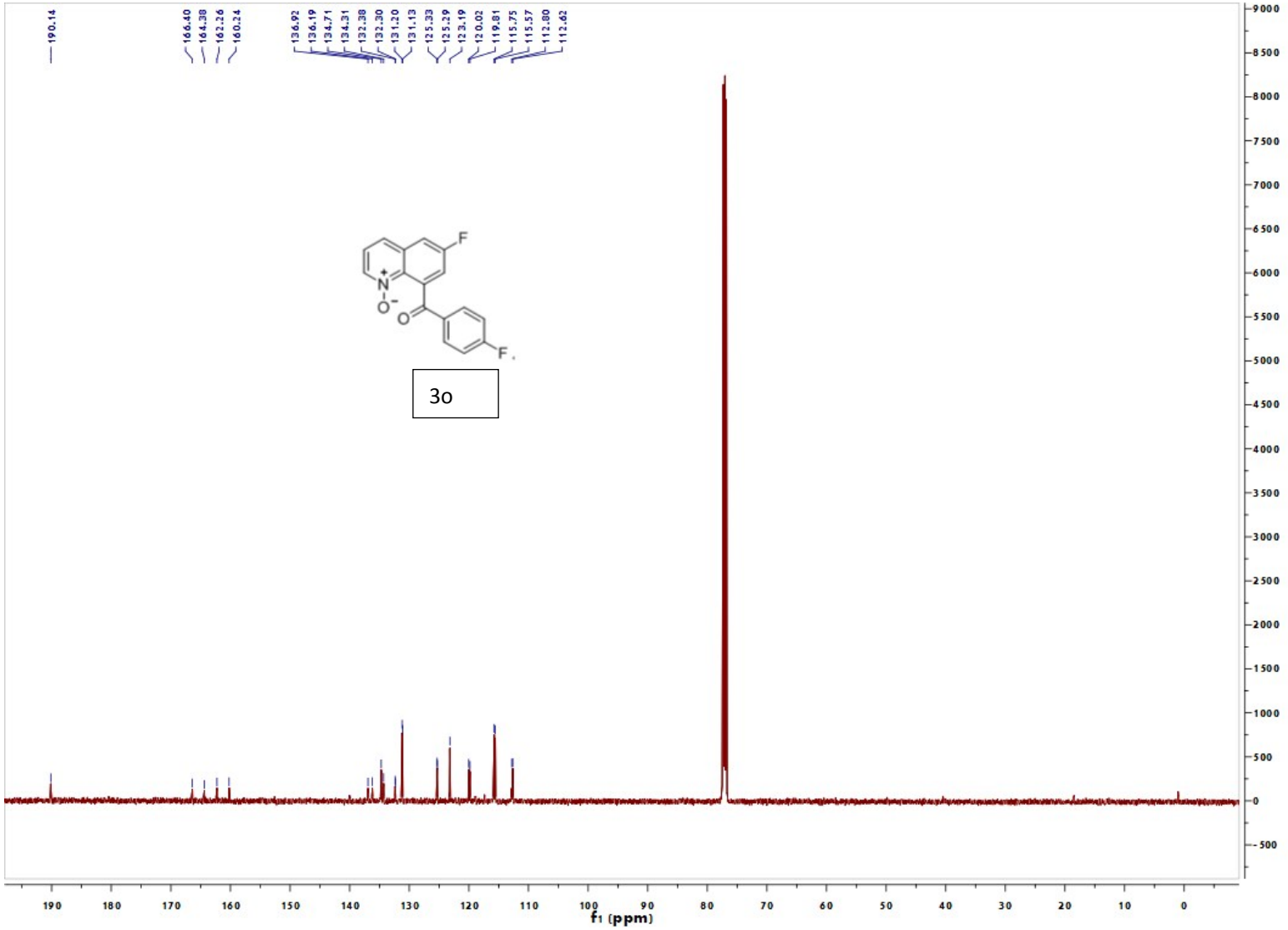
135.10
133.54
132.58
131.15
131.10
131.03
130.78
128.83
128.79
128.60
125.72
125.67
115.57
115.53
115.40
115.36
18.84
18.80
3n
f1 (ppm)


8.22
8.21
7.72
7.70
7.68
7.68
7.67
7.67
7.66
7.65
7.65
7.64
7.57
7.57
7.56
7.55
7.35
7.34
7.33
7.33
7.31
7.19
7.04
7.02
7.00
F
N
O
O
F
1.00
2.81
1.13
1.84
1.60
f1 (ppm)

3o


190.14
166.40
164.38
162.26
160.24
136.92
136.19
134.71
134.31
132.38
132.30
131.20
131.13
125.33
125.29
123.19
120.02
119.81
115.75
115.57
112.80
112.62
F
N
O
O
F
3o
f1 (ppm)