Supplementary Material (ESI) for Chemical Communications

Supporting Information

Dual Catalysis: Combining Photoredox and Lewis Base Catalysis for Direct Mannich Reactions

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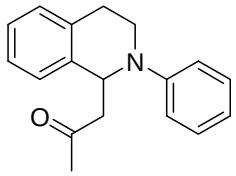
General: Unless otherwise noted, all commercially available compounds were used as provided without further purification. Solvents used in reactions were p.A. grade and dried only if indicated. Solvents for chromatography were technical grade and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminium plates with F-254 indicator, visualised by irradiation with UV light. Column chromatography was performed using silica gel Merck 60 (particle size 0.063 – 0.2 mm). Solvent mixtures are understood as volume/volume.
^{1}H-NMR and ^{13}C-NMR were recorded on a Bruker AV 300 spectrometer in $CDCl_3$. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated br (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartett), m (multiplet); coupling constants (*J*) are in Hertz (Hz). Mass spectra (MS-EI, 70 eV) were conducted on GC-MS Shimadzu QP2010 (column: Equity®-5, length × I.D. 30 m × 0.25 mm, d_f 0.25 µm, lot # 28089-U, Supelco). ESI spectra were conducted on a VG-Plattform II (Fisons Instruments). IR spectra were recorded on a Jasco FT/IR-420 and a Perkin Elmer Spectrum 100 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Melting points were measured on a Büchi 530 apparatus. Optical rotations were measured on a Perkin Elmer 241 polarimeter.

General procedure for the dual catalytic photooxidation-Mannich reaction

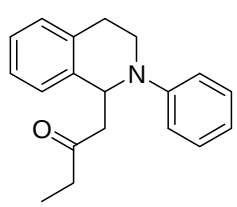
In a vial the appropriate photoredox catalyst, Lewis base and substrate were dissolved in the solvent indicated. Then 10 eq of the appropriate ketone were added via syringe and the reaction mixture was stirred for the time indicated under irradiation with the light source as indicated (distance app. 5 cm). The reaction was monitored via TLC (hexanes: ethylacetate). Upon consumption of starting material the crude mixture was purified by column chromatography (hexanes: ethylacetate) to yield the corresponding photooxidation-Mannich reaction products.

1-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (6)



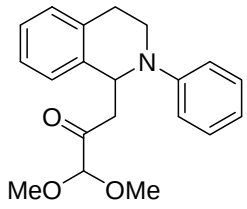
White solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28-7.22 (m, 2H), 7.17-7.15 (m, 4H), 6.94 (d, J = 8.1 Hz, 2H), 6.78 (t, J = 7.2 Hz, 1H), 5.40 (t, J = 6.4 Hz, 1H), 3.66 (dt, J = 12.5, 5.4 Hz, 1H), 3.53 (ddd, J = 13.5, 9.0, 4.8 Hz, 1H), 3.11-3.01 (m, 2H), 2.86-2.79 (m, 2H), 2.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.3, 148.8, 138.2, 134.4, 129.3, 128.6, 126.85, 126.79, 126.3, 118.3, 114.8, 54.8, 50.2, 42.1, 31.1, 27.2; IR (KBr): ν = 1701, 1595, 1499, 744 cm^{-1}; MS-EI: *m/z* (%) 256 (5), 208 (100), 115 (25), 104 (24), 77 (19).

1-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butan-2-one (7)



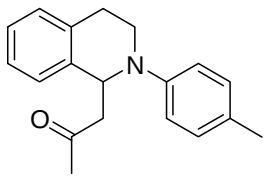
Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27-7.22 (m, 2H), 7.15-7.14 (m, 4H), 6.95 (d, J = 8.2 Hz, 2H), 6.77 (t, J = 7.2 Hz, 1H), 5.42 (t, J = 6.4 Hz, 1H), 3.65 (dt, J = 12.8, 5.5 Hz, 1H), 3.53 (ddd, J = 13.2, 8.7, 4.5 Hz, 1H), 3.11-3.01 (m, 2H), 2.88-2.74 (m, 2H), 2.40-2.21 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.9, 148.8, 138.3, 134.4, 129.3, 128.6, 126.8, 126.7, 126.2, 118.1, 114.6, 55.1, 48.9, 41.9, 37.2, 27.2, 7.5; IR (KBr): ν = 1710, 1597, 1499, 753 cm^{-1}; MS-EI: *m/z* (%) 279 (4), 208 (100), 115 (20), 104 (21), 77 (15).

1,1-dimethoxy-3-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (8)



Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27-7.22 (m, 2H), 7.17-7.15 (m, 4H), 6.95 (d, J = 8.1 Hz, 2H), 6.77 (t, J = 7.3 Hz, 1H), 5.48 (t, J = 6.5 Hz, 1H), 4.36 (s, 1H), 3.70-3.52 (m, 2H), 3.32 (s, 3H), 3.30 (s, 3H), 3.26 (dd, J = 17.0, 6.1 Hz, 1H), 3.06 (ddd, J = 14.8, 8.8, 5.9 Hz, 1H), 2.94 (dd, J = 17.0, 6.9 Hz, 1H), 2.84 (dt, J = 16.2, 4.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 148.8, 138.1, 134.5, 129.2, 128.6, 126.9, 126.8, 126.1, 118.1, 114.7, 103.8, 54.5, 54.40, 54.37, 44.5, 41.8, 27.0; IR (KBr): ν = 1728, 1599, 1496, 753 cm^{-1}; MS-EI: *m/z* (%) 325 (2), 208 (100), 103 (15), 77 (15), 75 (55).

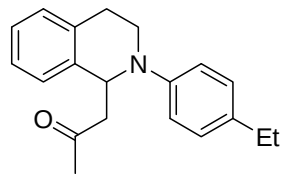
1-(2-*p*-tolyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (9)



Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.17-7.15 (m, 4H), 7.05 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 5.34 (t, J = 6.4 Hz, 1H), 3.63 (dt, J = 12.7, 5.0 Hz, 1H), 3.49 (ddd, J = 14.1, 9.6, 4.8 Hz, 1H), 3.09-2.99 (m, 2H), 2.84-2.74 (m, 2H), 2.25 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.3, 146.8, 138.2,

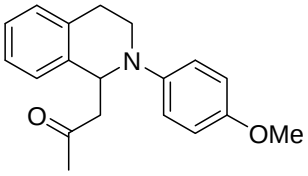
134.4, 132.4, 129.8, 128.8, 126.8, 126.7, 126.2, 115.7, 55.2, 50.0, 42.2, 31.0, 26.9, 20.3; IR (KBr): ν = 1712, 1615, 1516, 808, 755 cm^{-1}; MS-EI: *m/z* (%) 279 (4), 222 (100), 115 (20), 91 (25).

1-(2-(4-ethylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (10)



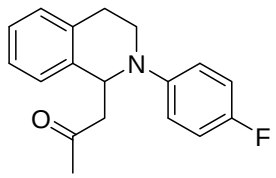
Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.17-7.12 (m, 4H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 5.36 (t, *J* = 6.4 Hz, 1H), 3.64 (dt, *J* = 12.6, 5.1 Hz, 1H), 3.50 (ddd, *J* = 14.0, 9.5, 4.6 Hz, 1H), 3.10-3.00 (m, 2H), 2.84-2.74 (m, 2H), 2.56 (q, *J* = 7.6 Hz, 2H), 2.07 (s, 3H), 1.2 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.4, 147.0, 138.3, 134.4, 128.7, 128.6, 126.8, 126.7, 126.2, 115.5, 55.2, 50.1, 42.1, 31.0, 27.8, 27.0, 15.8; IR (KBr): ν = 1710, 1625, 1596, 813, 752 cm^{-1}; MS-EI: *m/z* (%) 293 (3), 236 (100), 134 (15), 115 (13).

1-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (11)



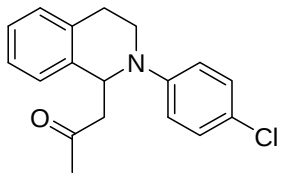
Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.17-7.11 (m, 4H), 6.92 (d, *J* = 9.0 Hz, 2H), 6.81 (d, *J* = 9.1 Hz, 2H), 5.25 (t, *J* = 6.4 Hz, 1H), 3.75 (s, 3H), 3.59-3.42 (m, 2H), 3.06-2.95 (m, 2H), 2.80-2.71 (m, 2H), 2.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.4, 153.3, 143.6, 138.2, 134.3, 128.9, 126.8, 126.6, 126.2, 118.4, 114.6, 56.0, 55.6, 49.9, 42.9, 30.9, 26.7; IR (KBr): ν = 1712, 1510, 1461, 823, 757 cm^{-1}; MS-EI: *m/z* (%) 295 (6), 238 (100), 195 (16).

1-(2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (12)



Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19-7.12 (m, 4H), 6.97-6.86 (m, 4H), 5.29 (t, *J* = 6.3 Hz, 1H), 3.62-3.45 (m, 2H), 3.07-2.97 (m, 2H), 2.83-2.73 (m, 2H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 156.5 (d, J_{C-F} = 237.8 Hz), 145.8, 138.0, 134.2, 128,9, 126.8, 126.3, 117.2 (d, J_{C-F} = 7.5 Hz), 115.6 (d, J_{C-F} = 22.0 Hz), 55.6, 50.1, 42.7, 31.0, 26.7; IR (KBr): ν = 1712, 1510, 1230, 817, 756 cm^{-1}; MS-EI: *m/z* (%) 283 (3), 226 (100), 211 (23), 122 (26), 115 (23).

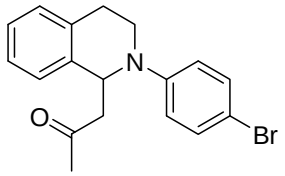
1-(2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (13)



Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.20-7.15 (m, 6H), 6.86 (d, *J* = 9.1 Hz, 2H), 5.34 (t, *J* = 6.3 Hz, 1H), 3.65-3.48 (m, 2H), 3.09-2.99 (m, 2H), 2.86-2.78 (m, 2H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 147.4, 137.9, 134.2, 129.1, 128.7, 126.9, 126.8, 126.4, 123.0, 115.8, 54.8, 50.1, 42.2, 31.1,

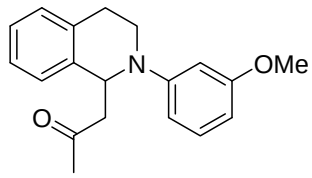
27.0; IR (KBr): ν = 1712, 1594, 1497, 813, 754 cm^{-1}; MS-EI: *m/z* (%) 299 (3), 244 (36), 242 (100), 115 (29).

1-(2-(4-bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (14)



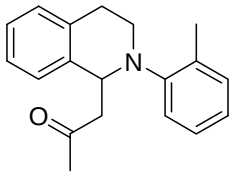
Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32 (d, J = 9.1 Hz, 2H), 7.17-7.14 (m, 4H), 6.83 (d, J = 9.0 Hz, 2H), 5.35 (t, J = 6.3 Hz, 1H), 3.64-3.47 (m, 2H), 3.09-2.99 (m, 2H), 2.89-2.79 (m, 2H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.9, 147.6, 140.6, 137.8, 134.1, 132.0, 128.7, 127.0, 126.8, 126.4, 116.4, 54.7, 50.0, 42.4, 31.0, 27.0; IR (KBr): ν = 1712, 1588, 1493, 811, 756 cm^{-1}; MS-EI: *m/z* (%) 345 (3), 343 (3), 288 (98), 286 (100), 207 (38), 206 (25), 117 (25), 115 (75).

1-(2-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (15)



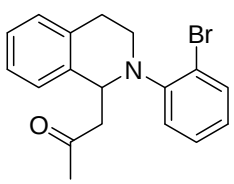
Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18-7.13 (m, 5H), 6.54 (dd, J = 8.2, 2.3 Hz, 1H), 6.49 (t, J = 2.3 Hz, 1H), 6.35 (dd, J = 8.1, 2.2 Hz, 1H), 5.39 (t, J = 6.3 Hz, 1H), 3.79 (s, 3H), 3.63 (dt, J = 15.6, 5.5 Hz, 1H), 3.52 (ddd, J = 13.4, 8.7, 4.6 Hz, 1H), 3.11-3.01 (m, 2H), 2.86-2.78 (m, 2H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 160.8, 150.2, 138.2, 134.4, 130.0, 128.6, 126.8, 126.3, 107.4, 103.2, 100.9, 55.1, 54.8, 50.3, 42.1, 31.1, 27.3; IR (KBr): ν = 1711, 1604, 1495, 756 cm^{-1}; MS-EI: *m/z* (%) 295 (4), 238 (100), 195 (20), 115 (15).

1-(2-o-tolyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (16)



Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21-7.11 (m, 5H), 7.06-6.95 (m, 2H), 6.83 (dd, J = 7.6, 1.1 Hz, 1H), 4.96 (dd, J = 8.5, 5.2 Hz, 1H), 3.46 (ddd, J = 13.4, 11.1, 4.1 Hz, 1H), 3.18 (ddd, J = 13.4, 5.6, 2.5 Hz, 1H), 3.01 (dd, J = 15.5, 8.7 Hz, 1H), 2.83 (ddd, J = 16.7, 11.1, 5.6 Hz, 1H), 2.7 (dd, J = 15.6, 5.1 Hz, 1H), 2.62 (dt, J = 16.6, 3.0 Hz, 1H), 2.27 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 149.7, 138.5, 135.0, 133.5, 131.1, 129.2, 126.5, 126.4, 126.3, 126.2, 123.2, 122.3, 57.1, 50.6, 43.7, 30.1, 26.1, 18.0; IR (KBr): ν = 1711, 1491, 760, 731 cm^{-1}; MS-EI: *m/z* (%) 279 (3), 222 (100), 118 (23), 115 (18), 91 (28).

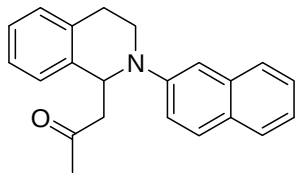
1-(2-(2-bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (17)



Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (dd, J = 7.9, 1.5 Hz, 1H), 7.22-7.09 (m, 5H), 6.93-6.85 (m, 2H), 5.02 (dd, J = 8.9, 4.8 Hz, 1H), 3.50 (dd, J = 8.4, 3.5 Hz, 2H), 3.09 (dd, J = 15.5, 9.0 Hz, 1H), 2.83-2.68 (m, 2H), 2.62 (dt, J = 16.7, 3.3 Hz,1H), 2.16 (s,

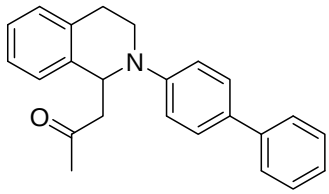
3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 149.1, 137.9, 134.9, 133.8, 129.3, 128.0, 126.6, 126.5, 126.4, 124.9, 124.3, 120.9, 57.6, 51.0, 43.9, 30.8, 25.6; IR (KBr): ν = 1713, 1582, 1472, 1028, 756 cm^{-1}; MS-EI: *m/z* (%) 345 (5), 343 (5), 288 (98), 286 (100), 206 (88), 130 (21), 115 (40).

1-(2-(naphthalen-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (18)



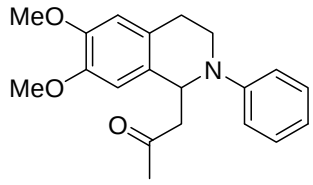
Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75-7.67 (m, 2H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.40-7.33 (m, 2H), 5.56 (t, *J* = 6.3 Hz, 1H), 3.82 (dt, *J* = 12.5, 5.1 Hz, 1H), 3.61 (dt, *J* = 12.9, 9.7, 4.6 Hz, 1H), 3.17-3.06 (m, 2H), 2.91-2.81 (m, 2H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 146.8, 138.2, 134.7, 134.3, 129.1, 128.8, 127.8, 127.4, 126.9, 126.8, 126.5, 126.3, 126.2, 122.9, 118.3, 109.5, 54.9, 50.2, 42.2, 31.0, 27.2; IR (KBr): ν = 1713, 1613, 1515, 820, 755 cm^{-1}; MS-EI: *m/z* (%) 315 (4), 258 (100), 127 (37), 115 (31).

1-(2-(biphenyl-4-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (19)

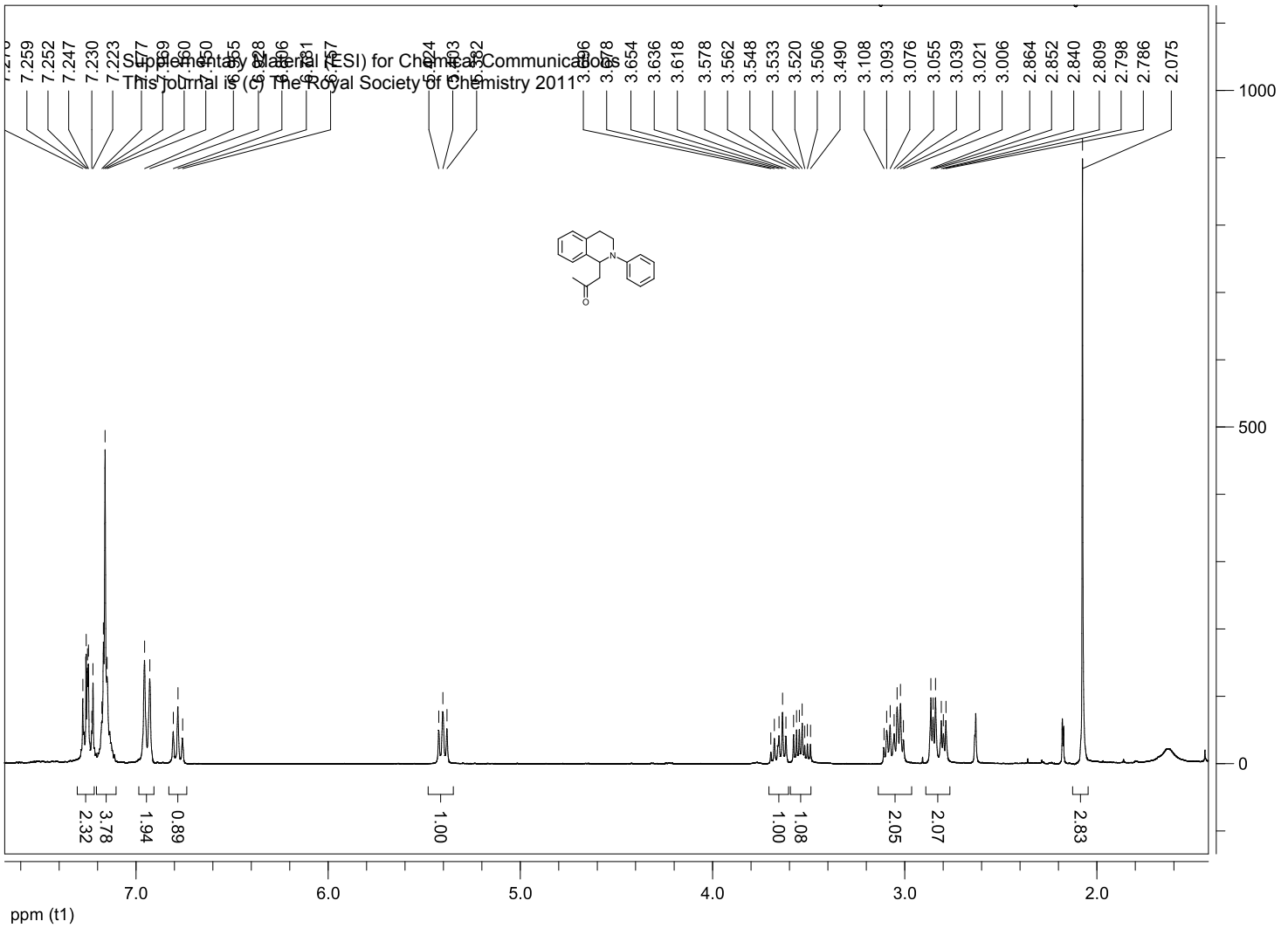


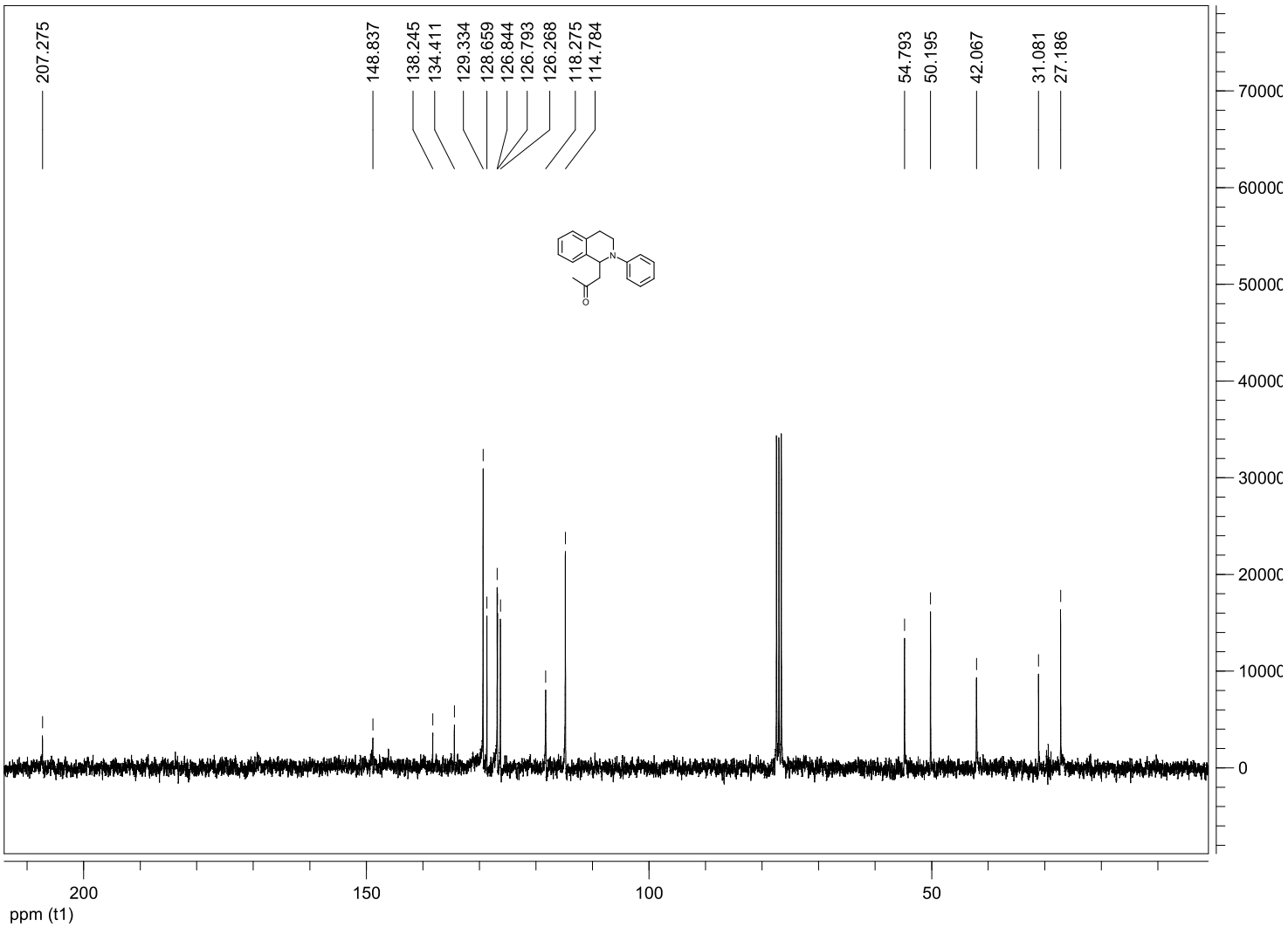
Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56-7.50 (m, 4H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.29-7.44 (m, 1H), 7.19-7.14 (m, 4H), 7.02 (d, *J* = 8.8 Hz, 2H), 5.47 (t, *J* = 6.3 Hz, 1H), 3.75-3.67 (m, 1H), 3.63-3.54 (m, 1H), 3.14-3.00 (m, 2H), 2.90-2.82 (m, 2H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 148.0, 140.9, 138.1, 134.4, 130.8, 128.6, 128.0, 127.9, 126.9, 126.3, 126.2, 114.7, 54.7, 50.2, 42.1, 31.2, 27.2; IR (KBr): ν = 1709, 1607, 1526, 1486, 913, 823, 759, 731 cm^{-1}; MS-EI: *m/z* (%) 341 (5), 284 (100), 153 (18), 115 (15).

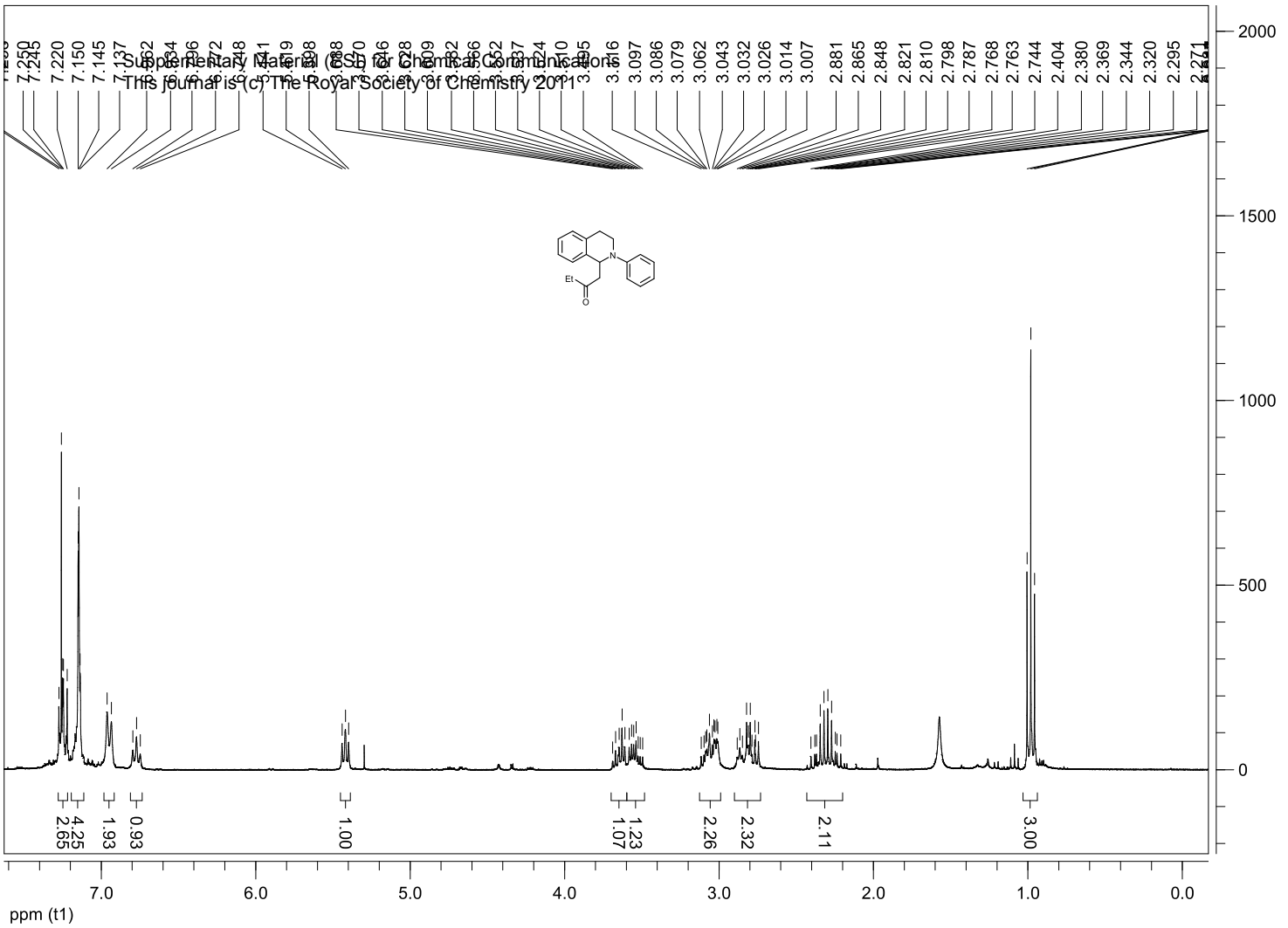
1-(6,7-dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-one (20)

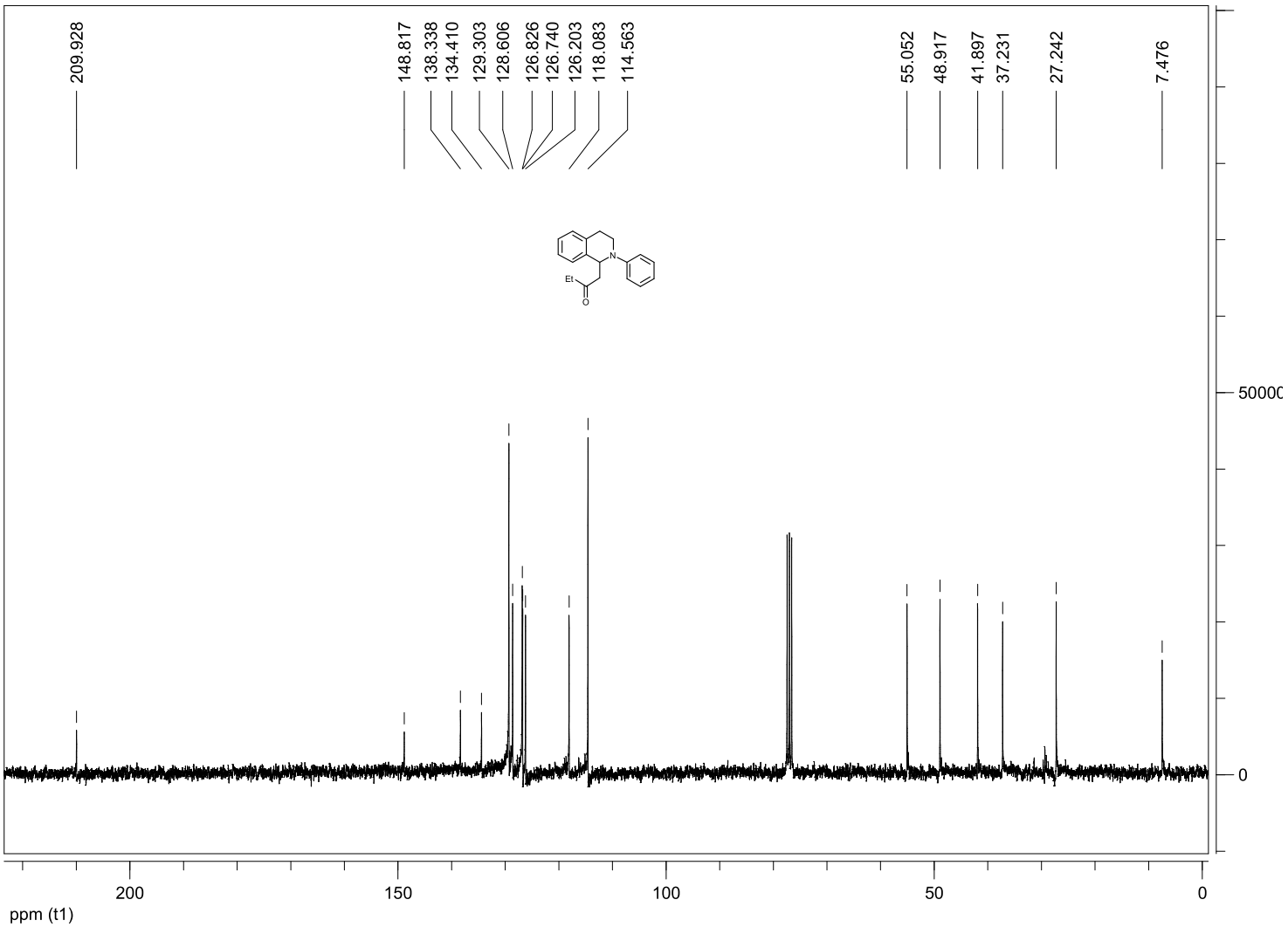


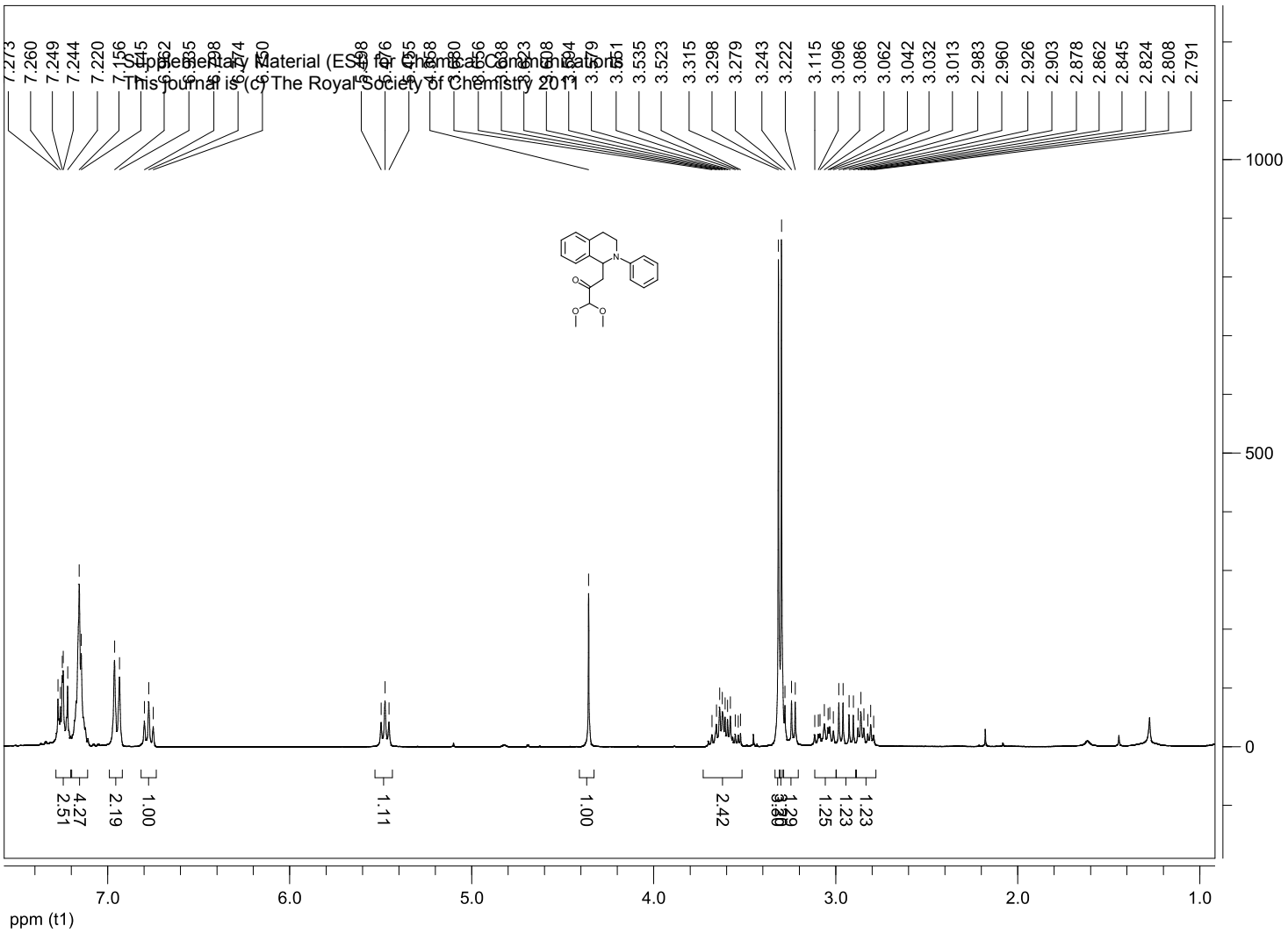
Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.24 (dd, *J* = 8.7, 7.3 Hz, 2H), 6.94 (d, t, *J* = 8.0 Hz, 2H), 6.78 (t, *J* = 7.3 Hz, 1H), 6.69 (s, 1H), 6.61 (s, 1H), 5.30 (t, *J* = 6.3 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.67 (dt, *J* = 12.8, 5.0 Hz, 1H), 3.50 (ddd, *J* = 12.9, 9.6, 4.6 Hz, 1H), 3.05 (dd, *J* = 16.2, 5.7 Hz, 1H), 2.99 (m, 1H), 2.82 (dd, *J* = 16.3, 6.9 Hz, 1H), 2.70 (dt, *J* = 16.21 4.5 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.6, 145.0, 147.8, 147.4, 130.1, 129.3, 126.3, 118.4, 115.1, 111.3, 109.7, 56.0, 55.9, 54.6, 50.1, 42.0, 31.2, 26.6; IR (KBr): ν = 1710, 1599, 1509, 1114, 753 cm^{-1}; MS-EI: *m/z* (%) 325 (3), 267 (100), 252 (32), 224 (19).

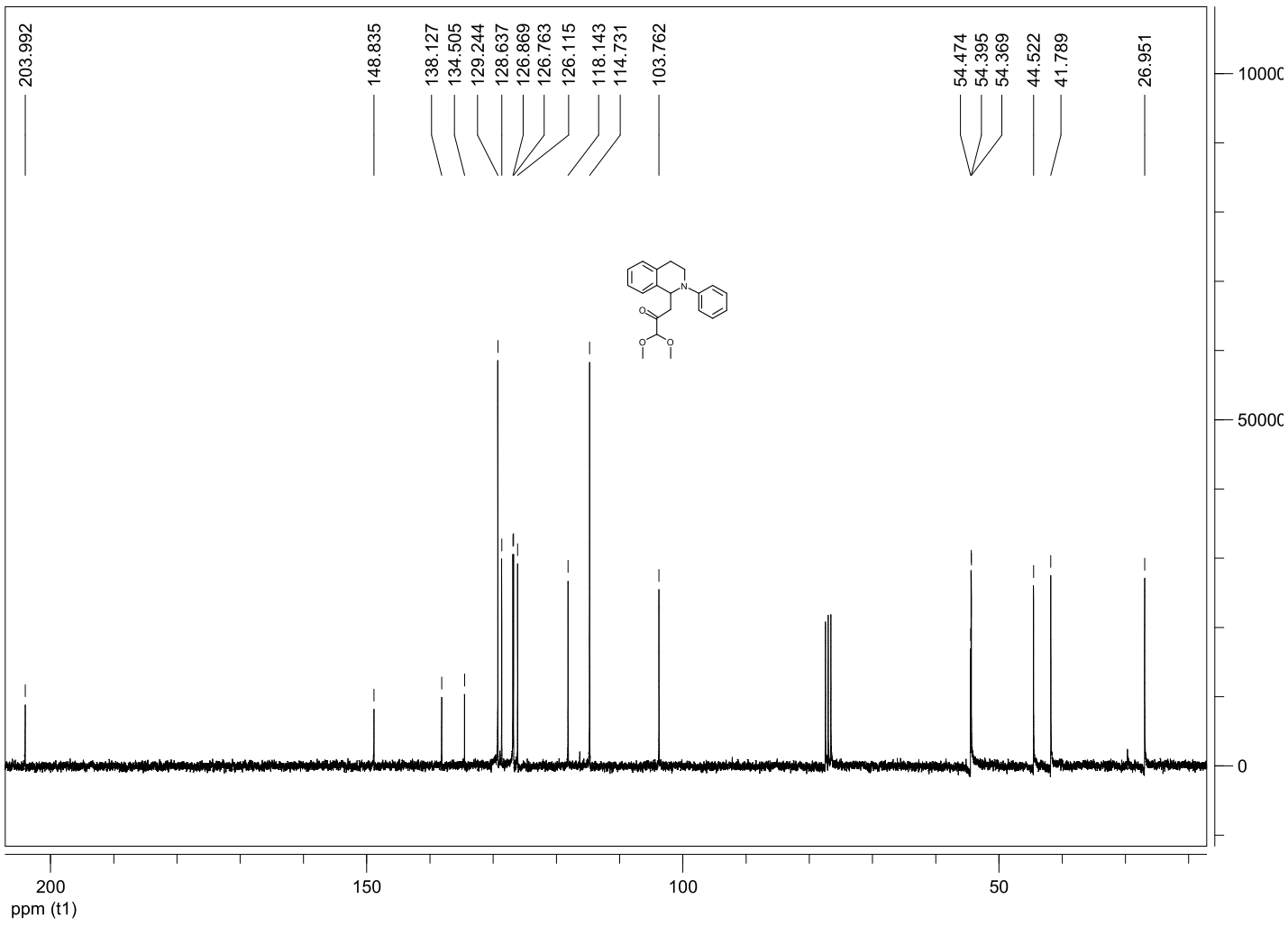


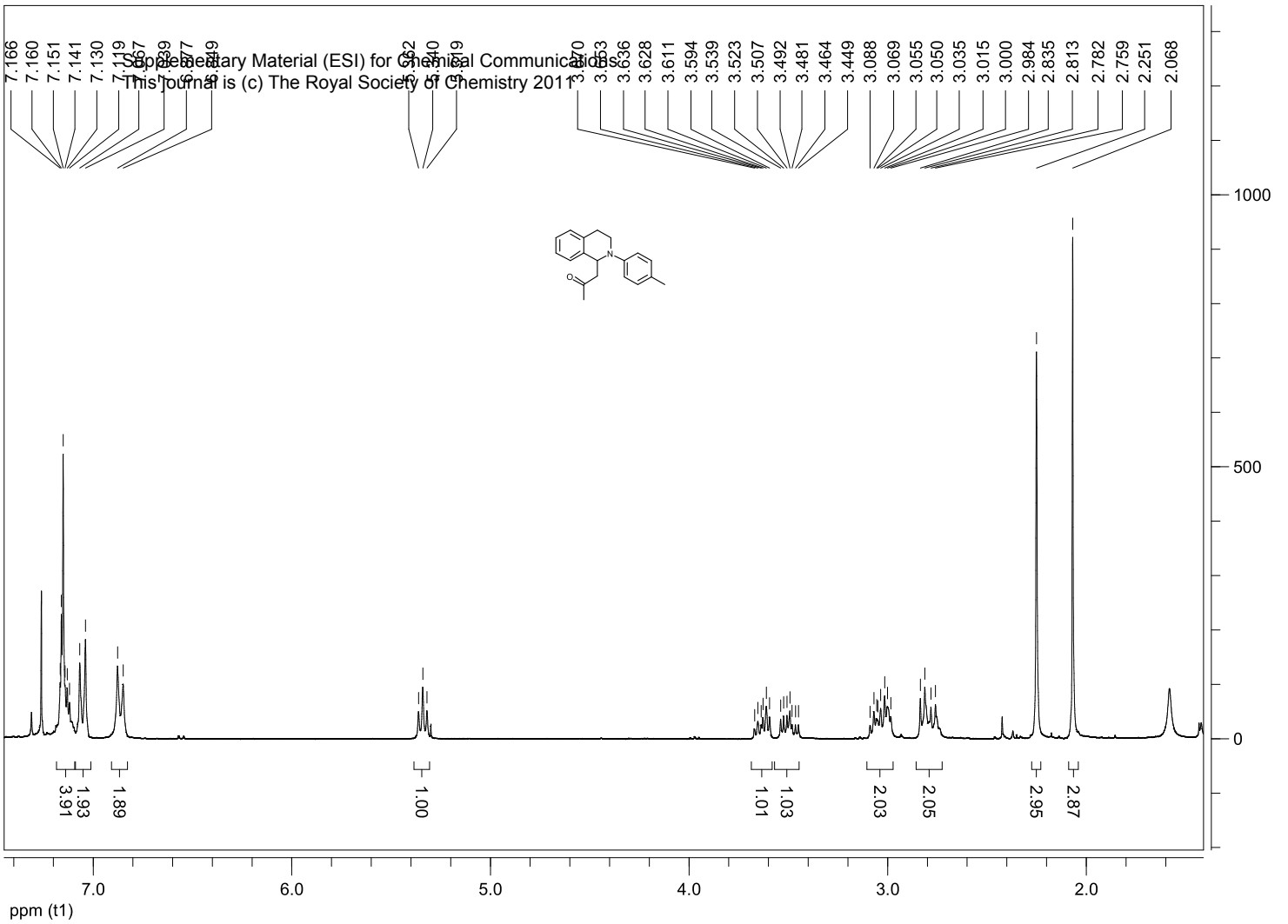


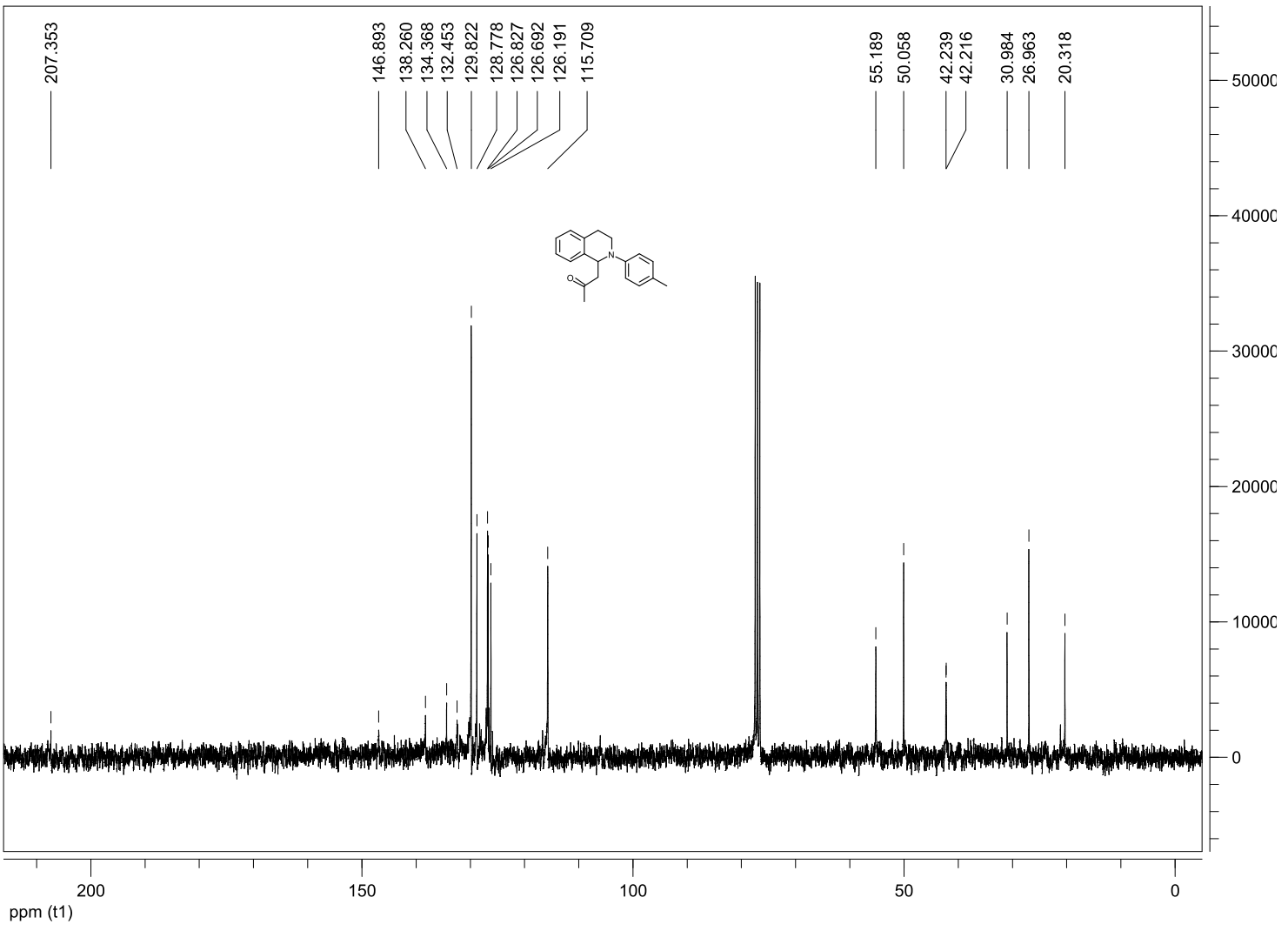


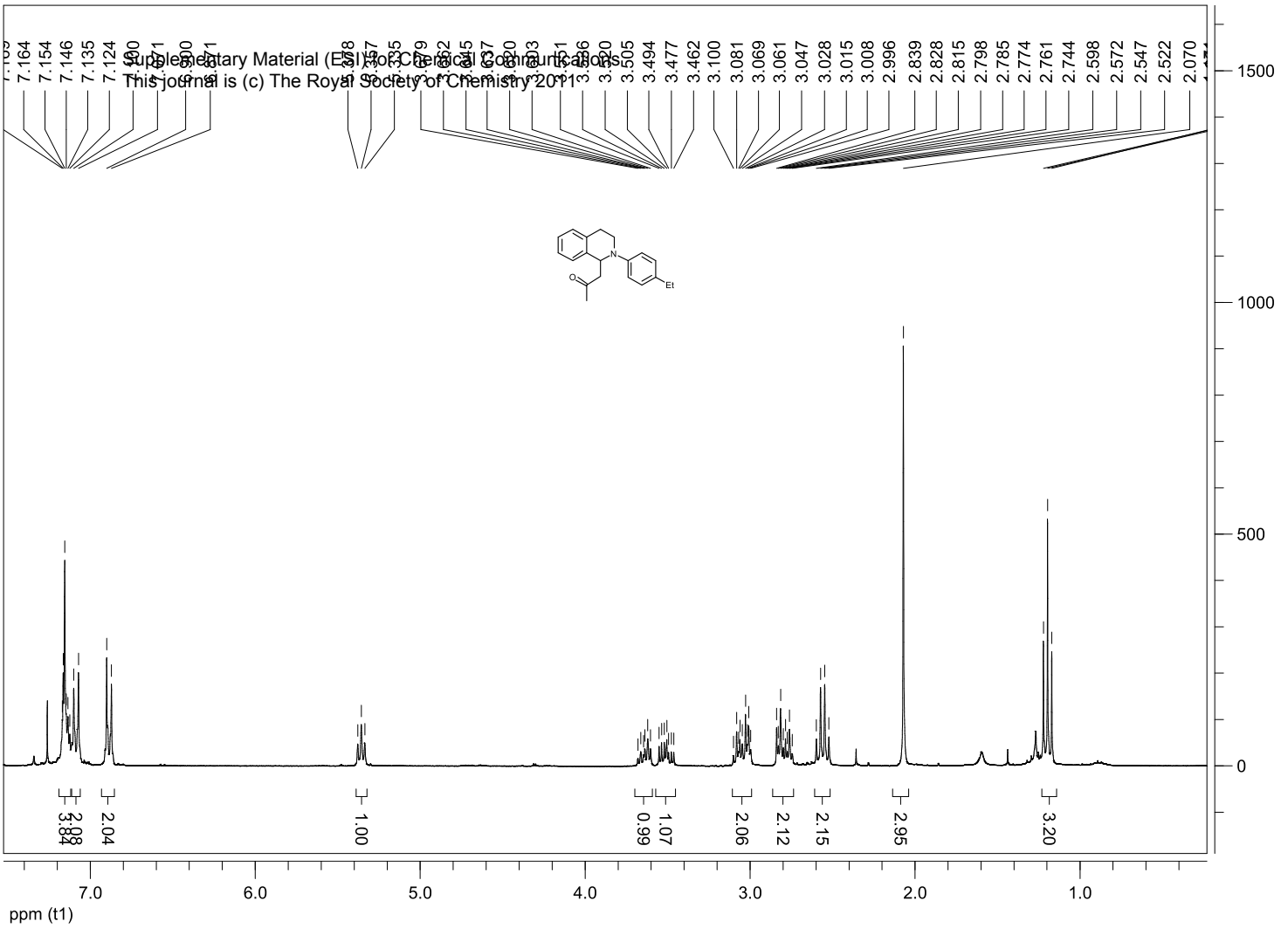


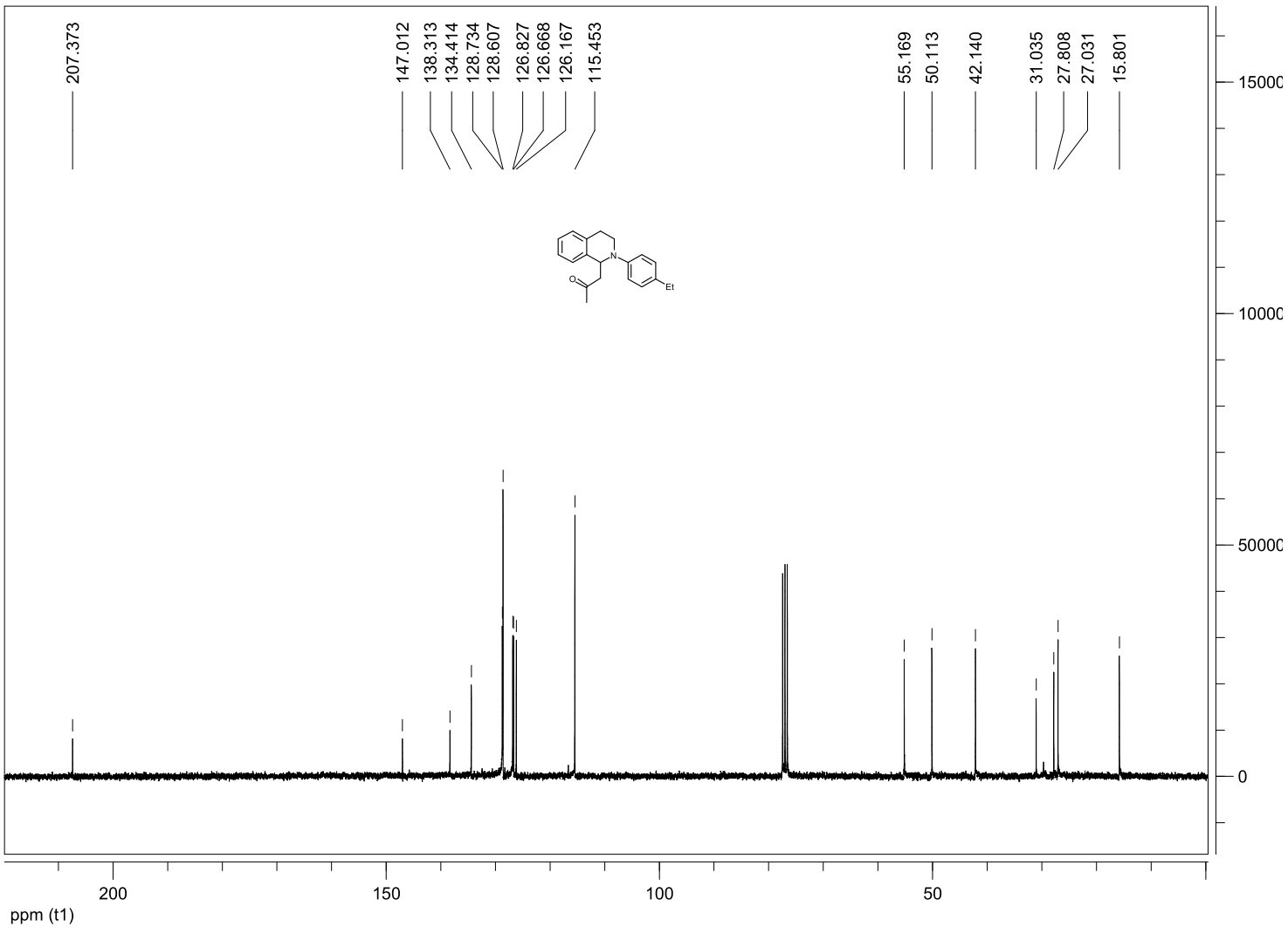


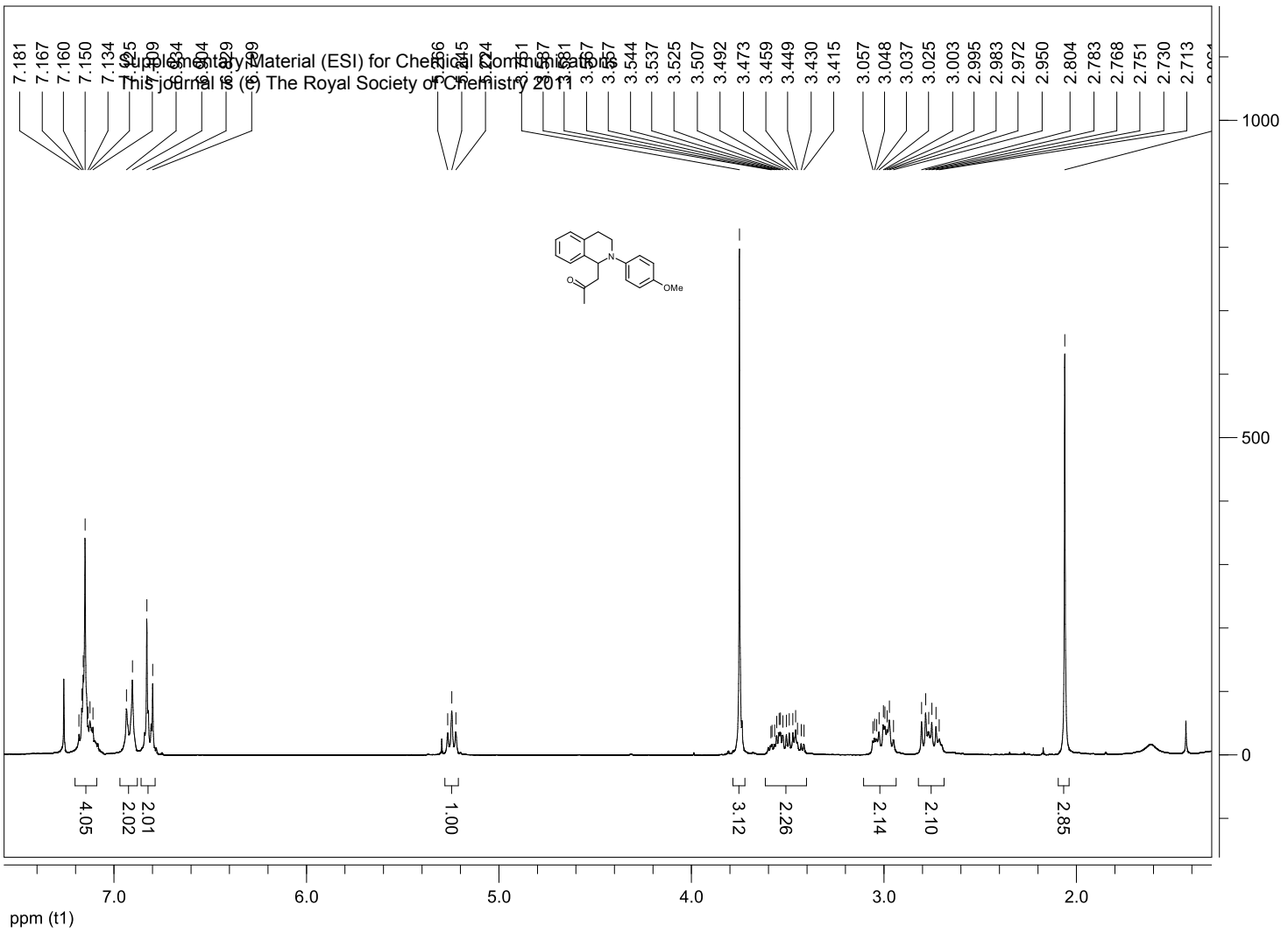


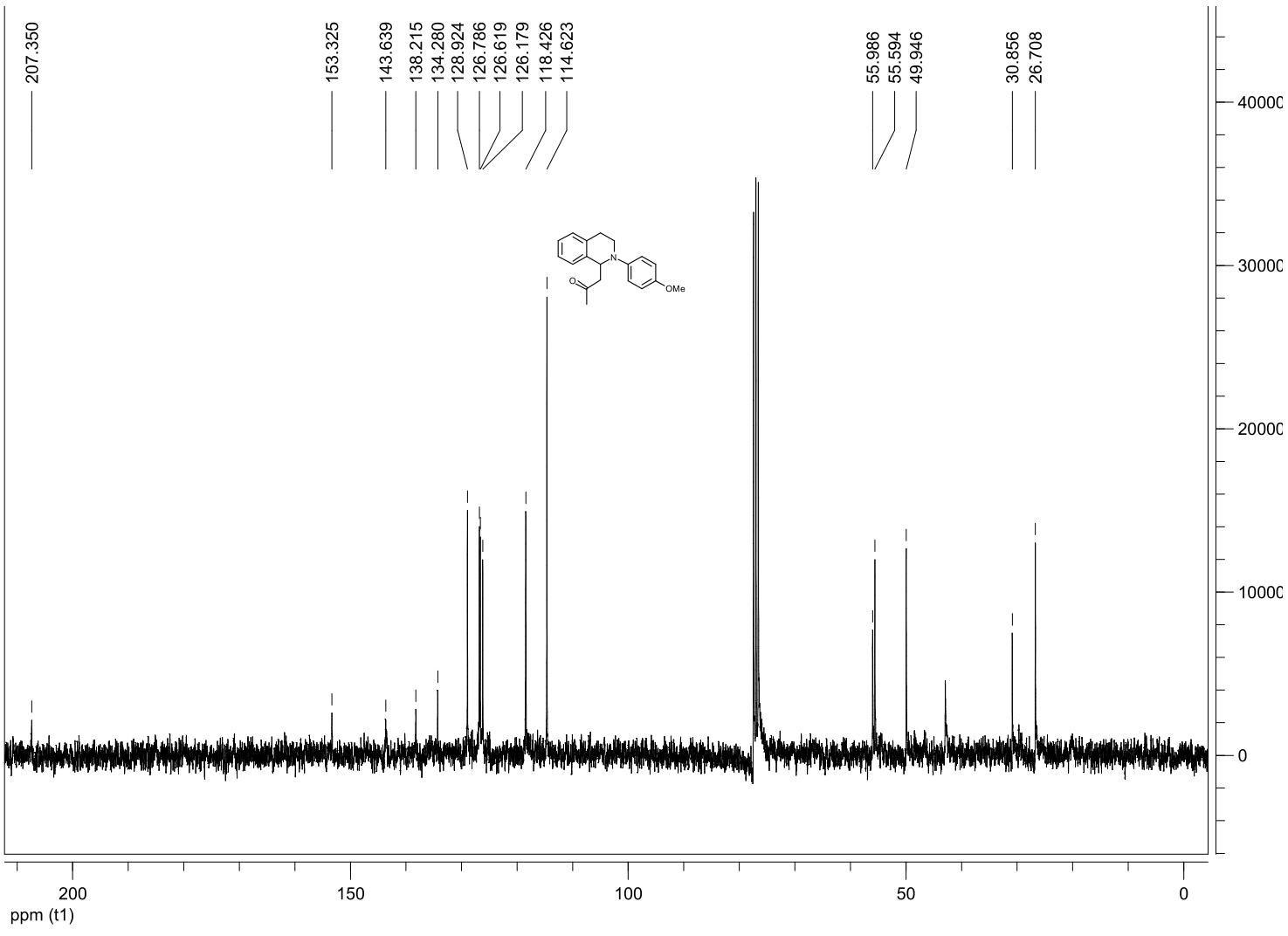


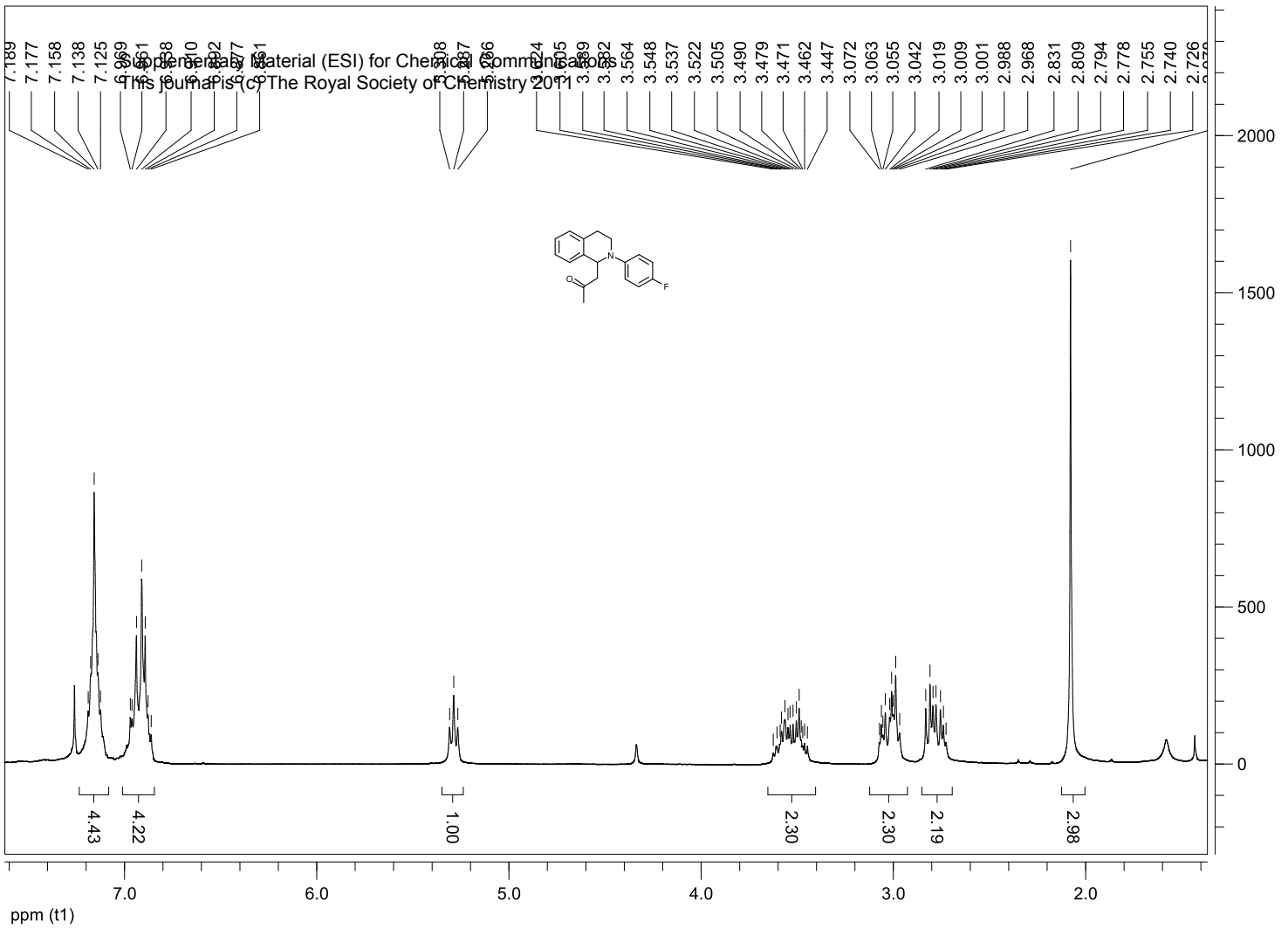


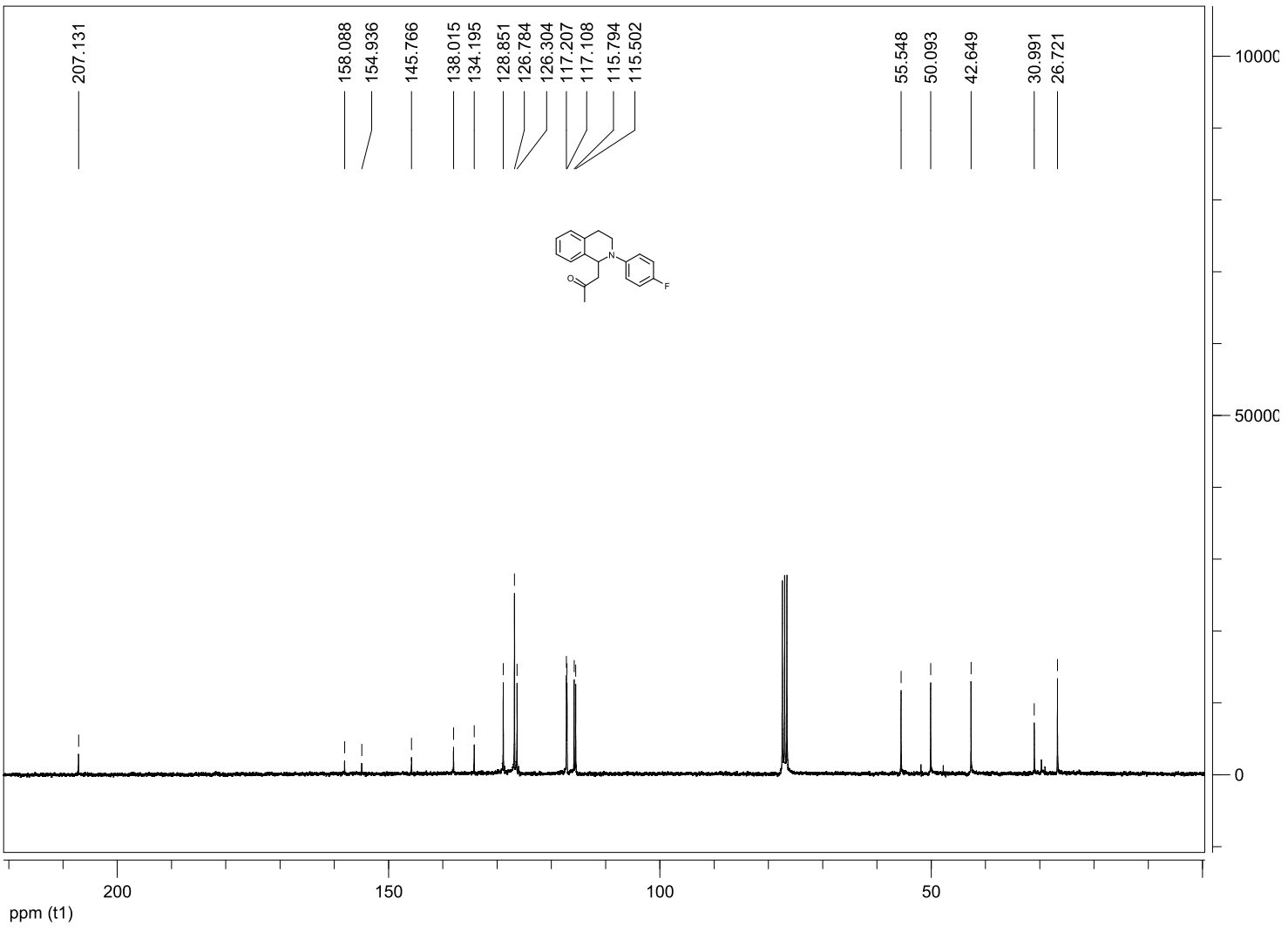


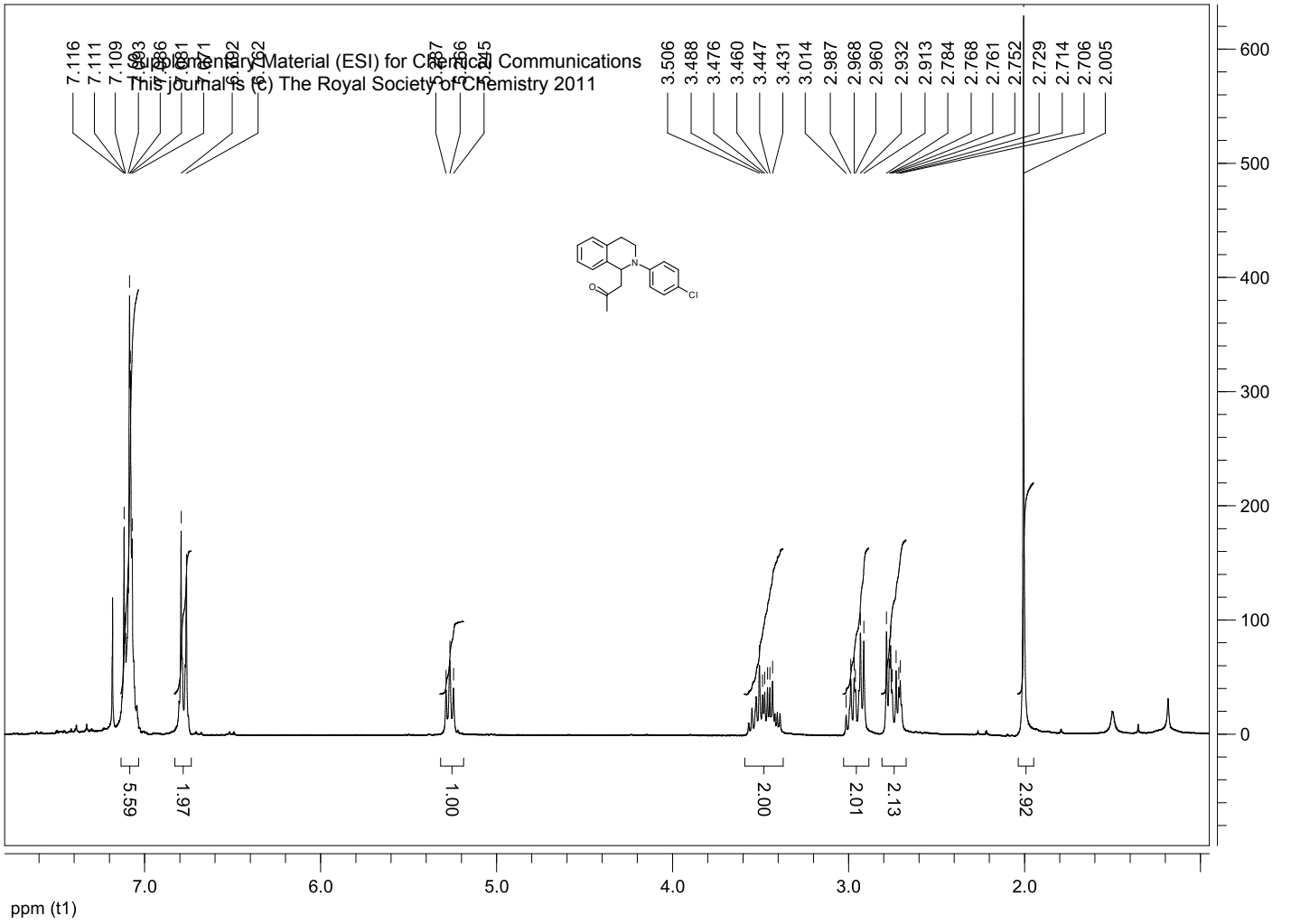


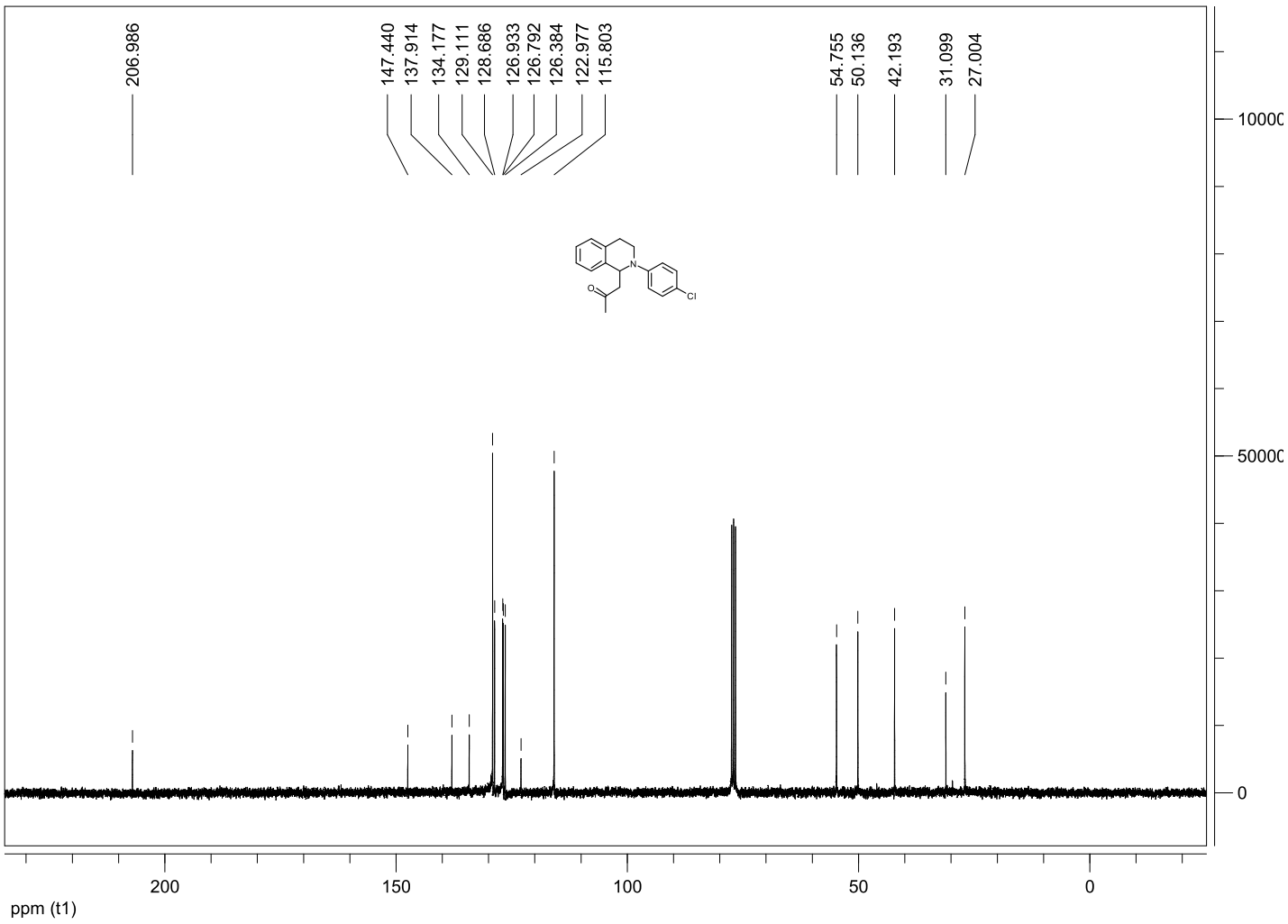

7.181
7.167
7.160
7.150
7.134
3.057
3.048
3.037
3.025
3.003
2.995
2.983
2.972
2.950
2.804
2.783
2.768
2.751
2.730
2.713
OMe
4.05
2.02
2.01
1.00
3.12
2.26
2.14
2.10
2.85
1000
500
0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

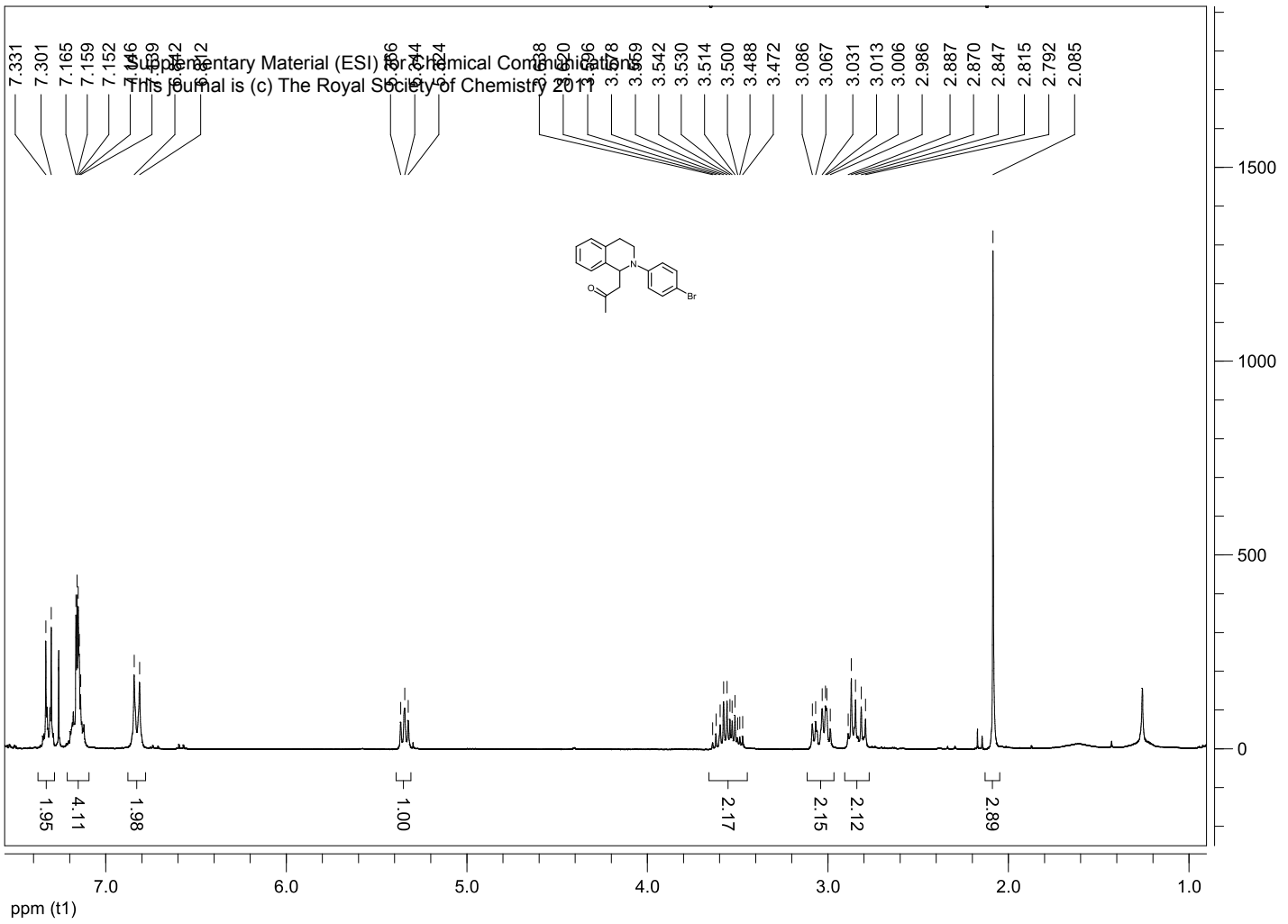

207.350
153.325
143.639
138.215
134.280
128.924
126.786
126.619
126.179
118.426
114.623
55.986
55.594
49.946
30.856
26.708
OMe
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)










7.331
7.301
7.165
7.159
7.152
3.086
3.067
3.031
3.013
3.006
2.986
2.887
2.870
2.847
2.815
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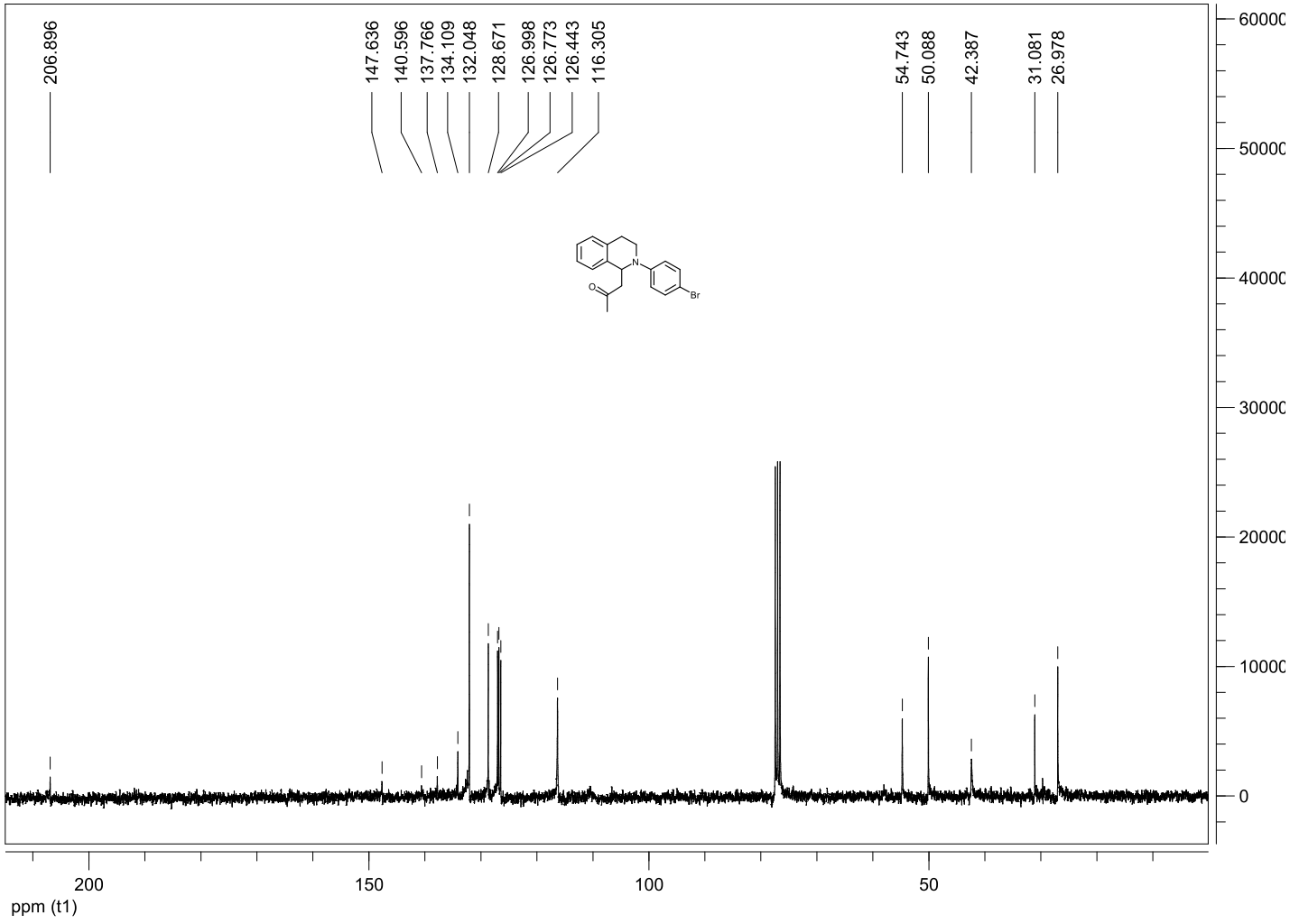
1.65
4.11
1.98
1.00
2.17
2.15
2.12
2.89
ppm (t1)


206.896
147.636
140.596
137.766
134.109
132.048
128.671
126.998
126.773
126.443
116.305
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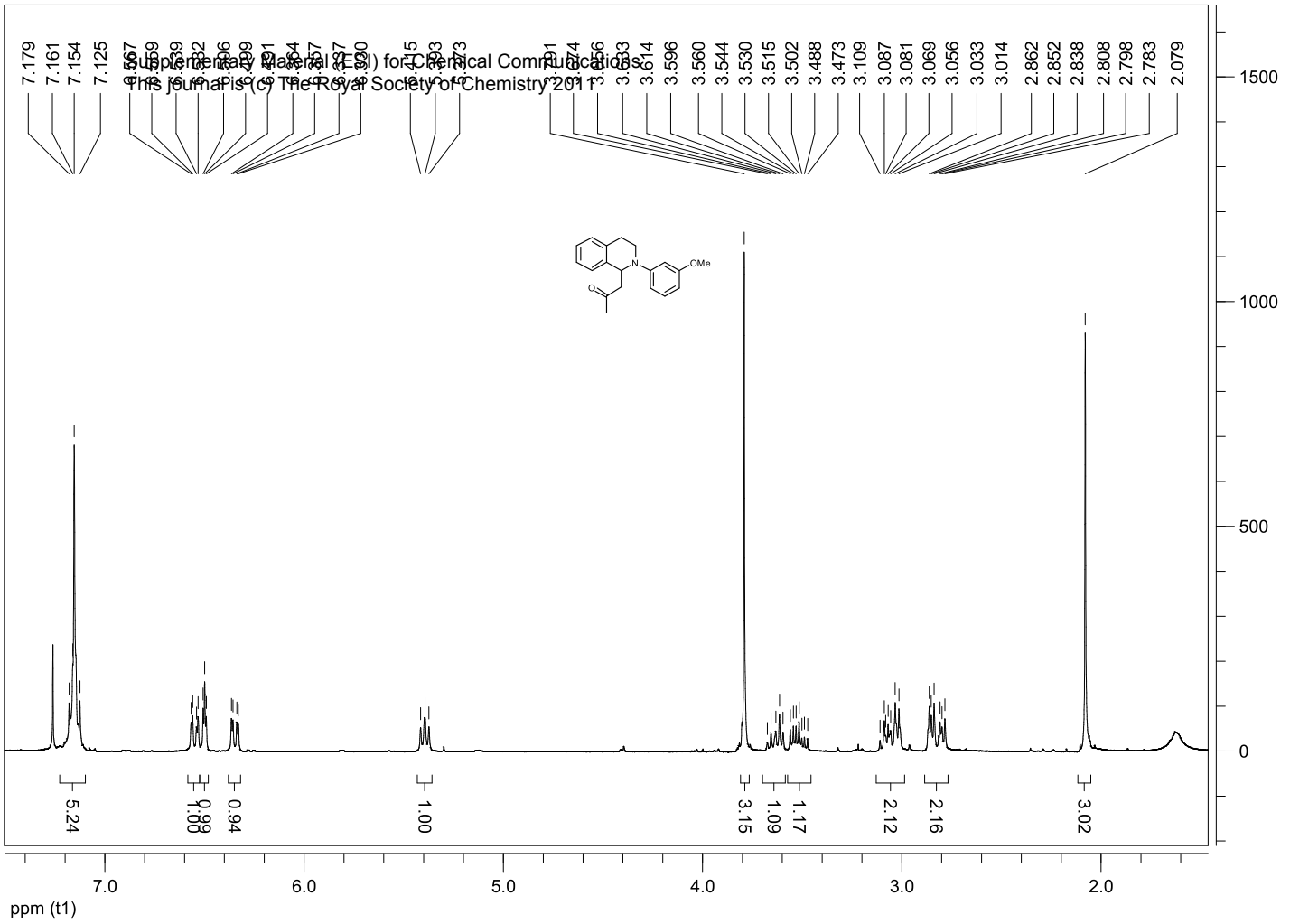
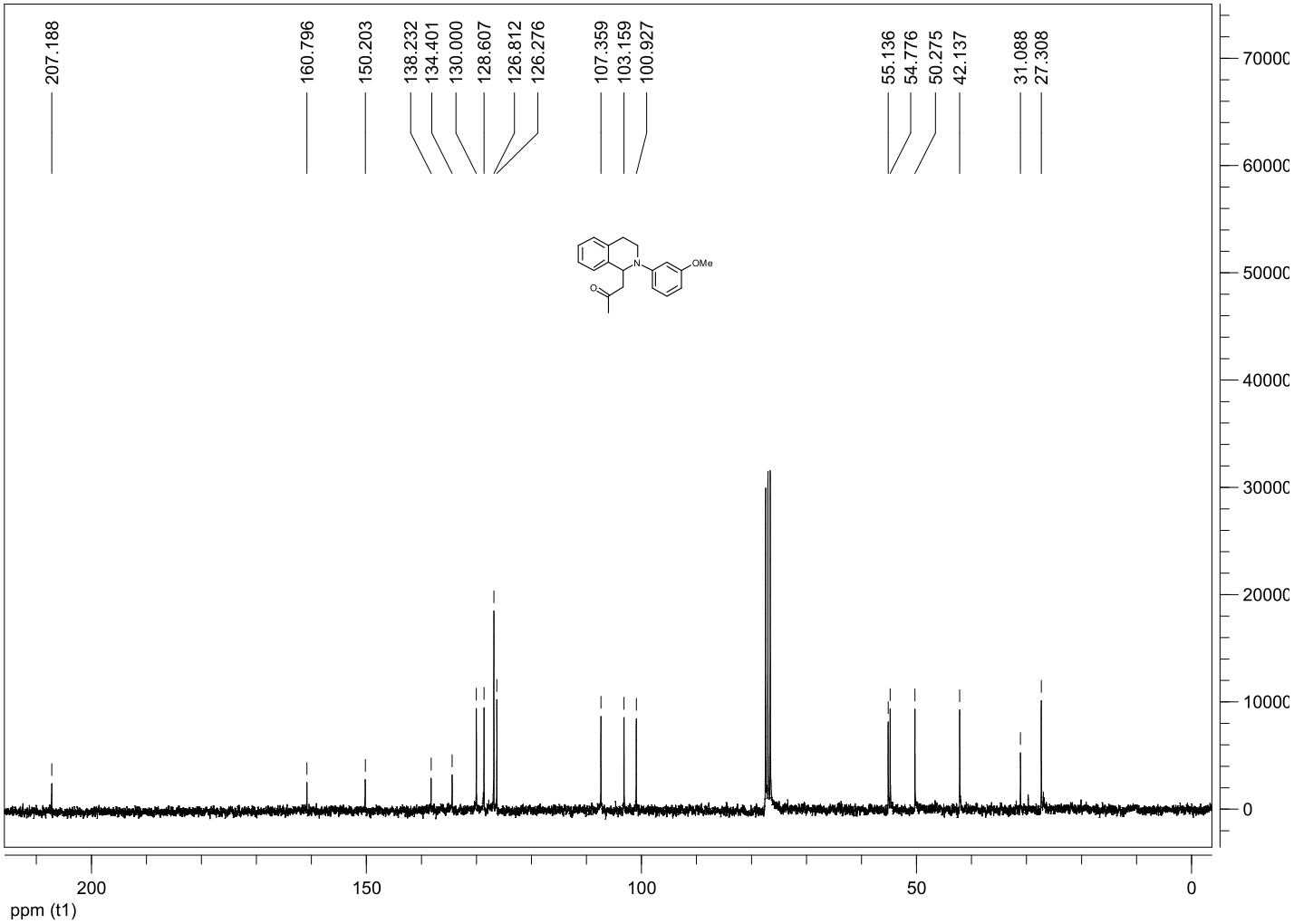
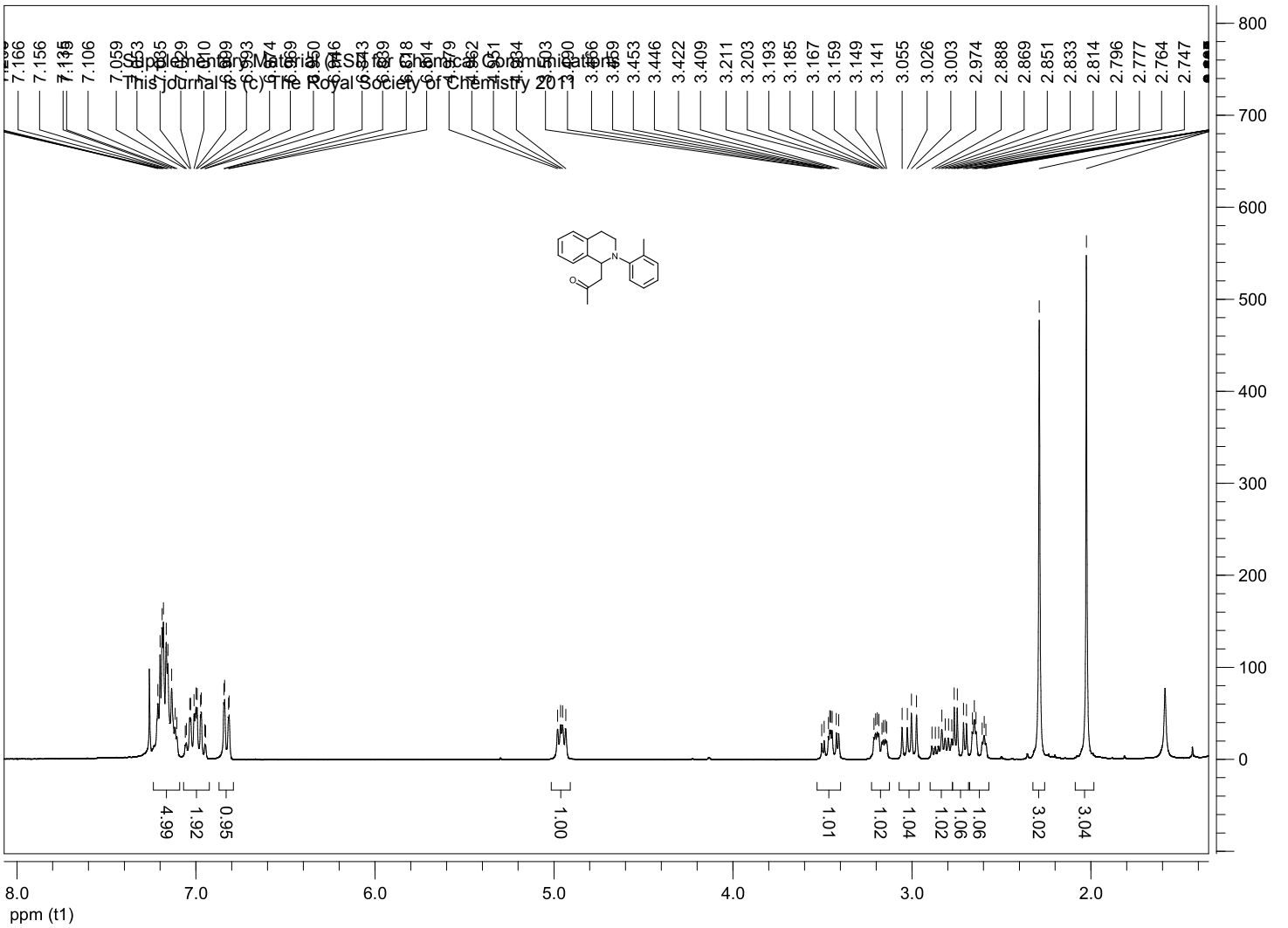
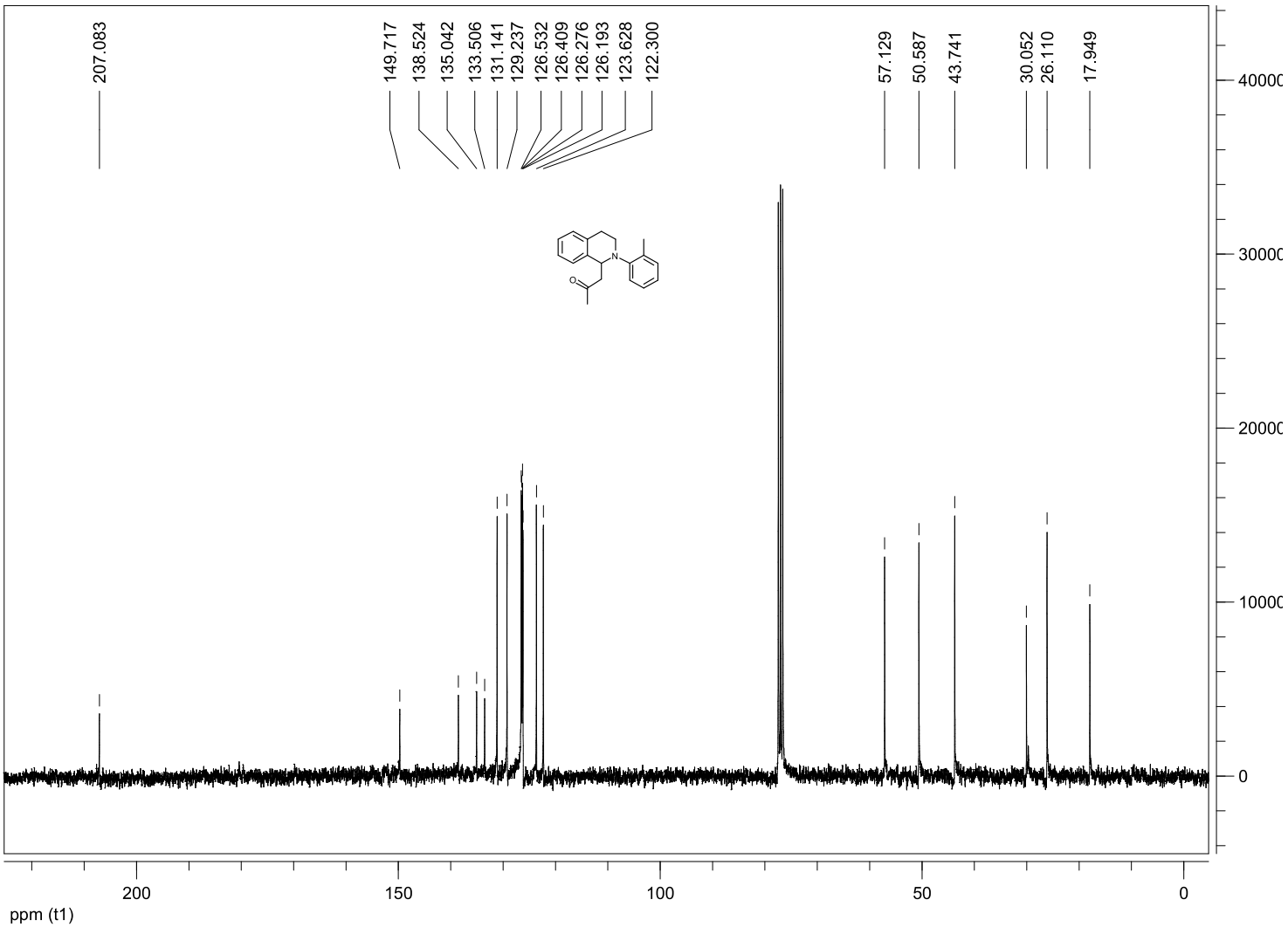
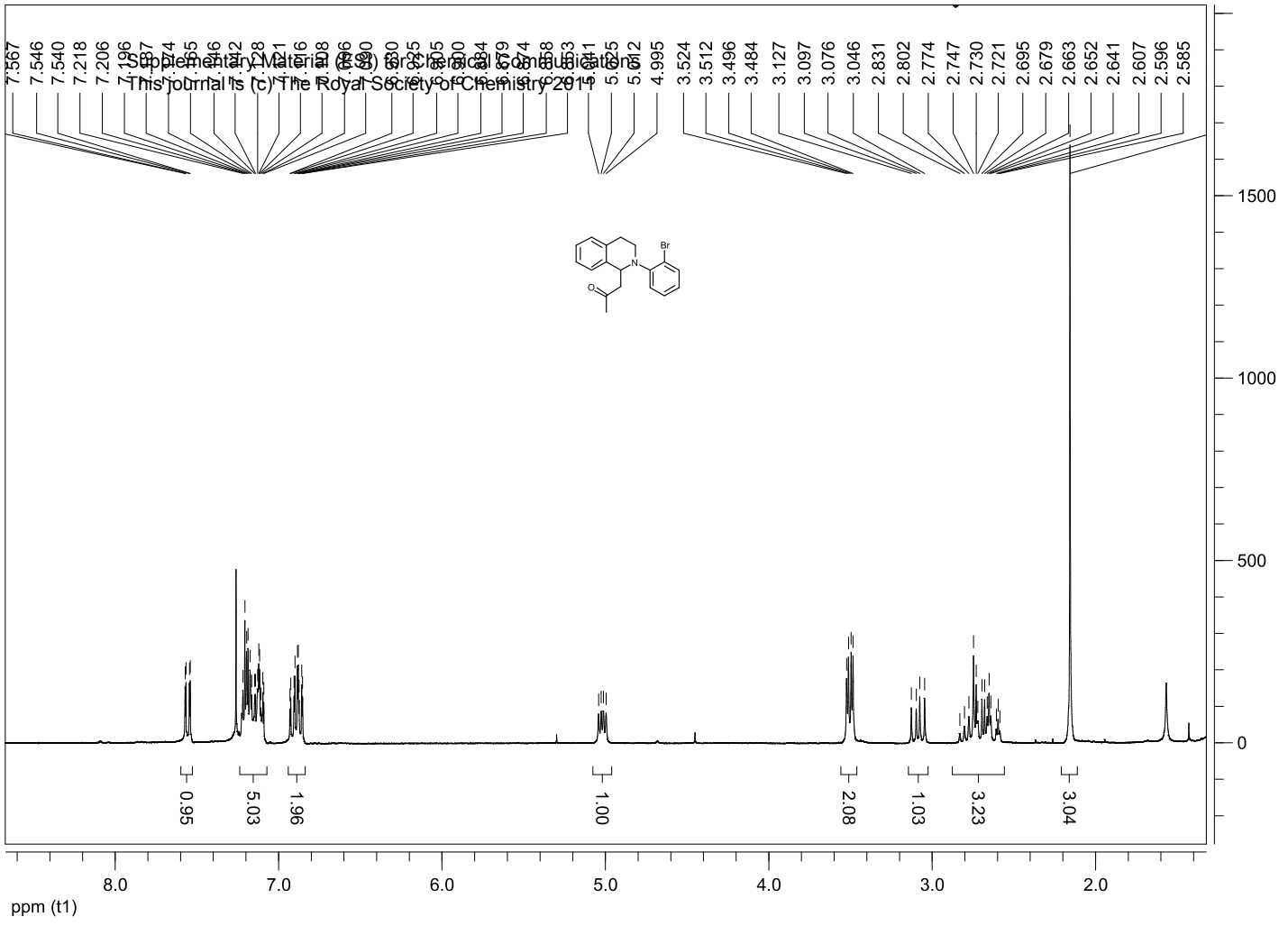
50.088
42.387
31.081
26.978
ppm (t1)

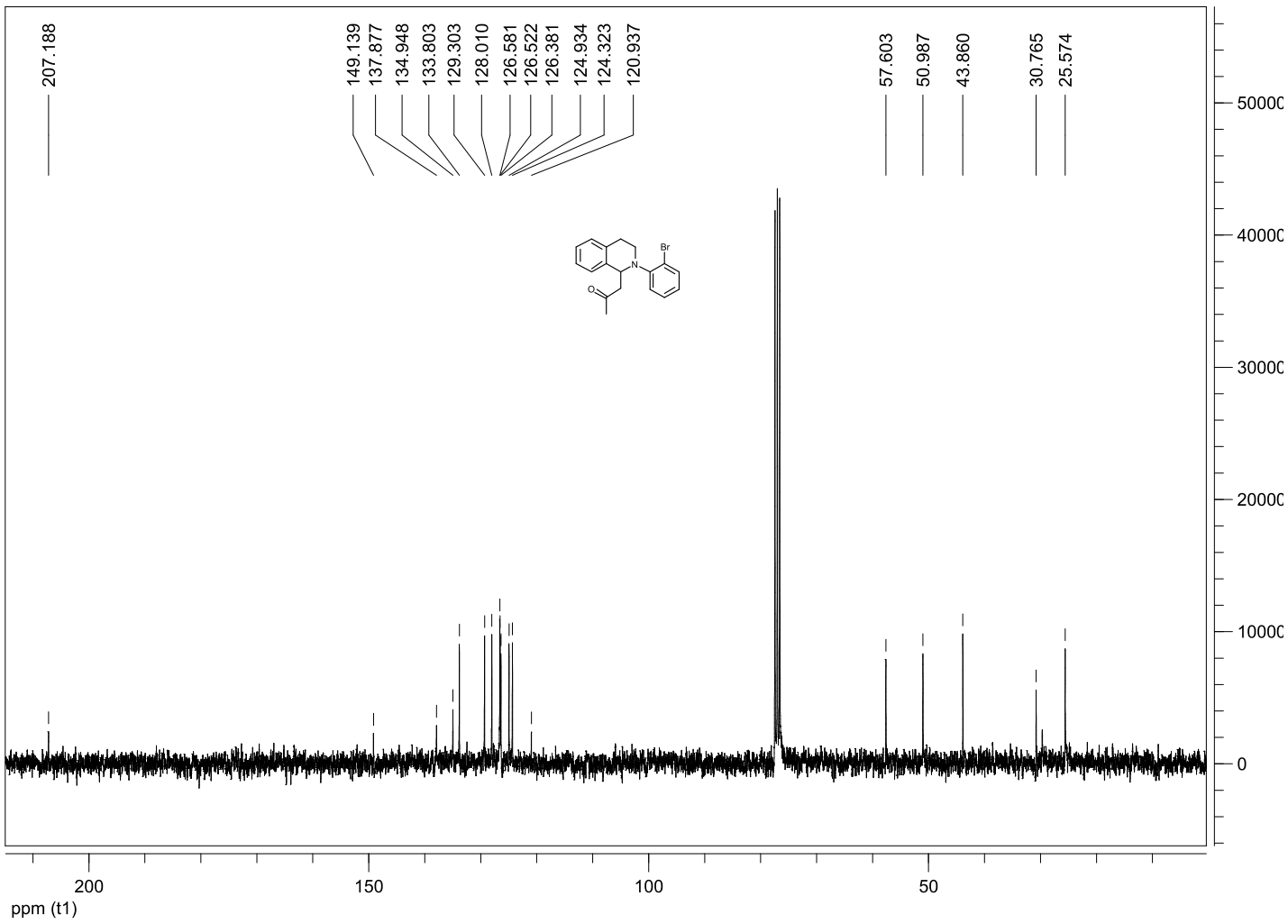


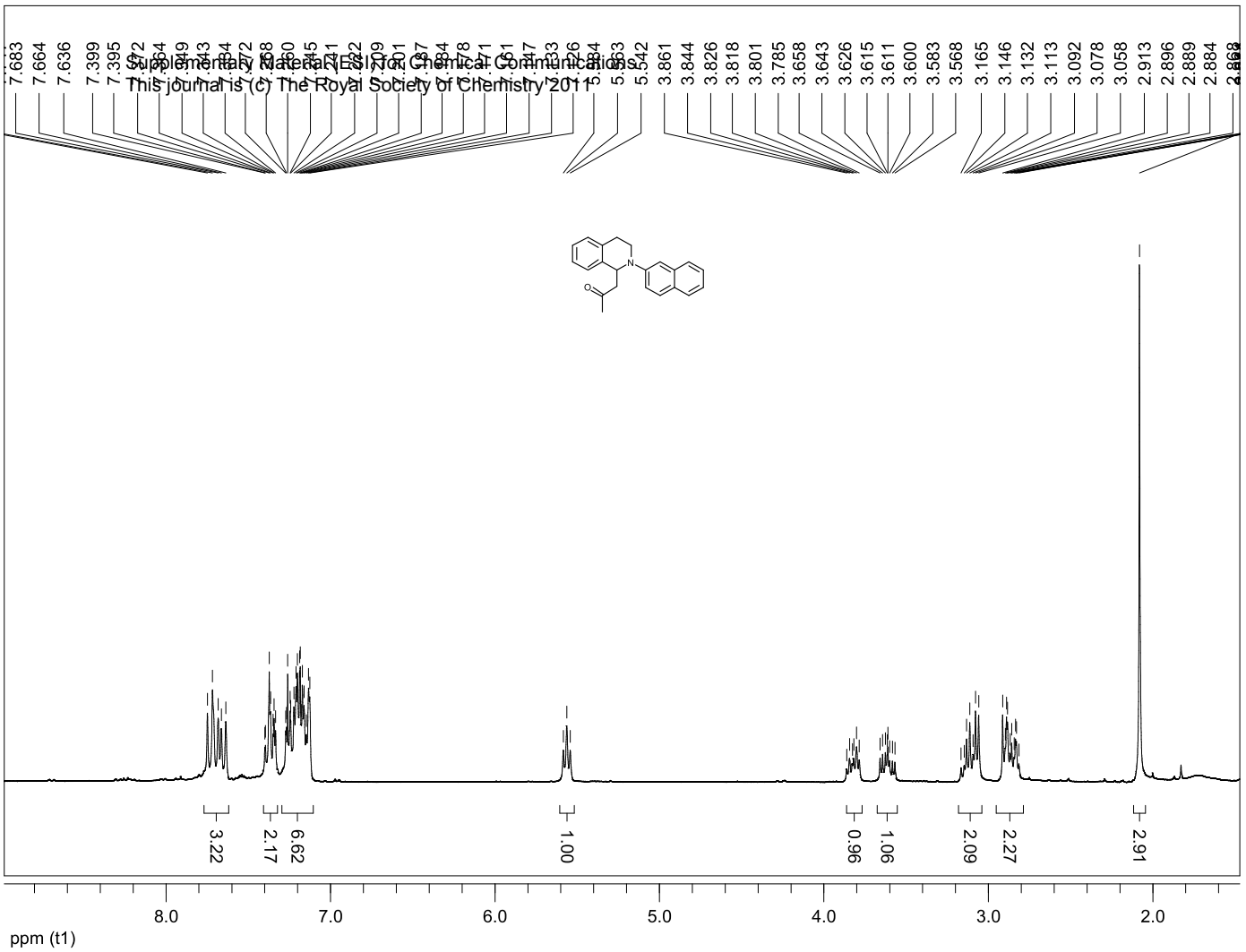


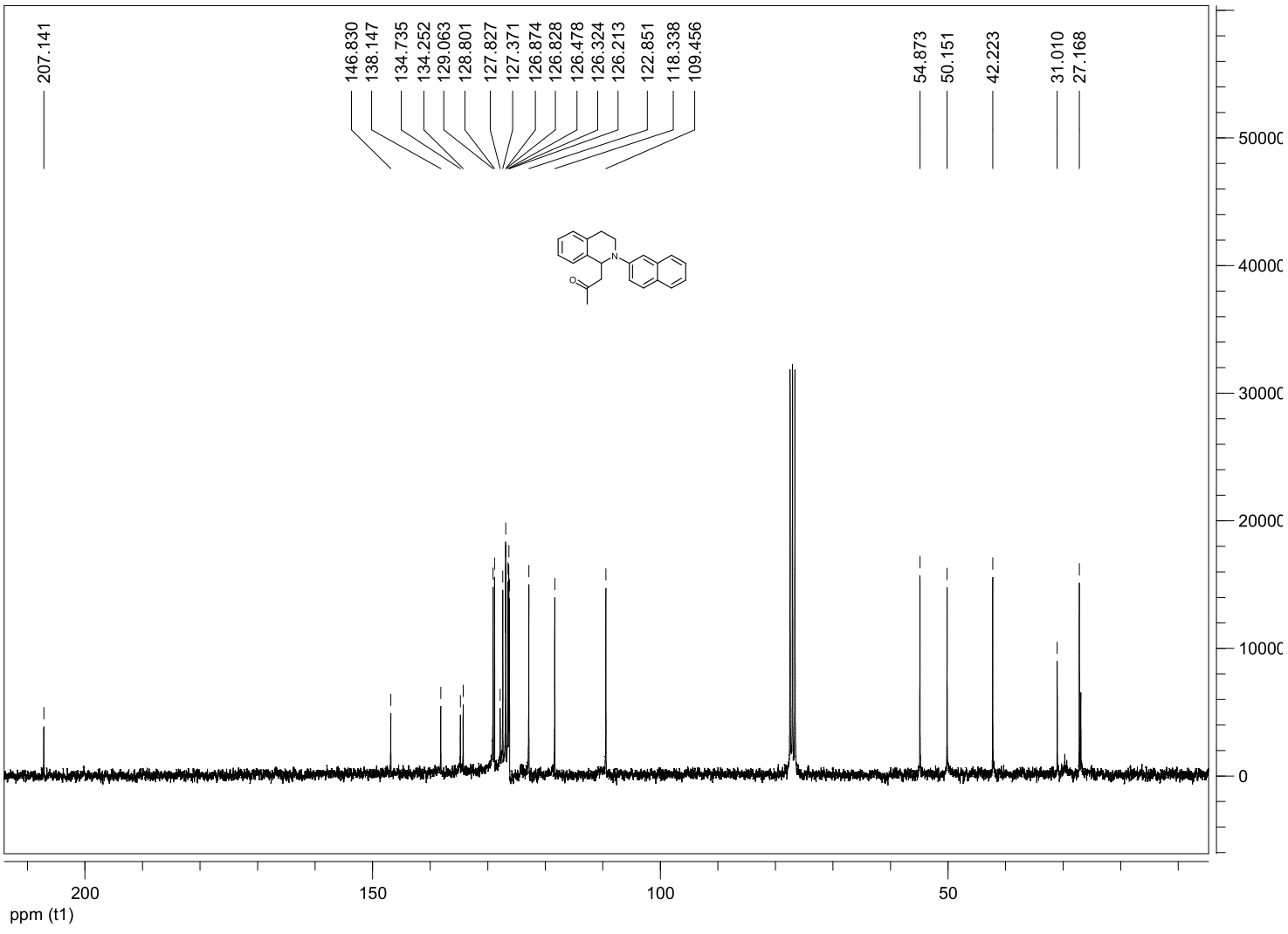


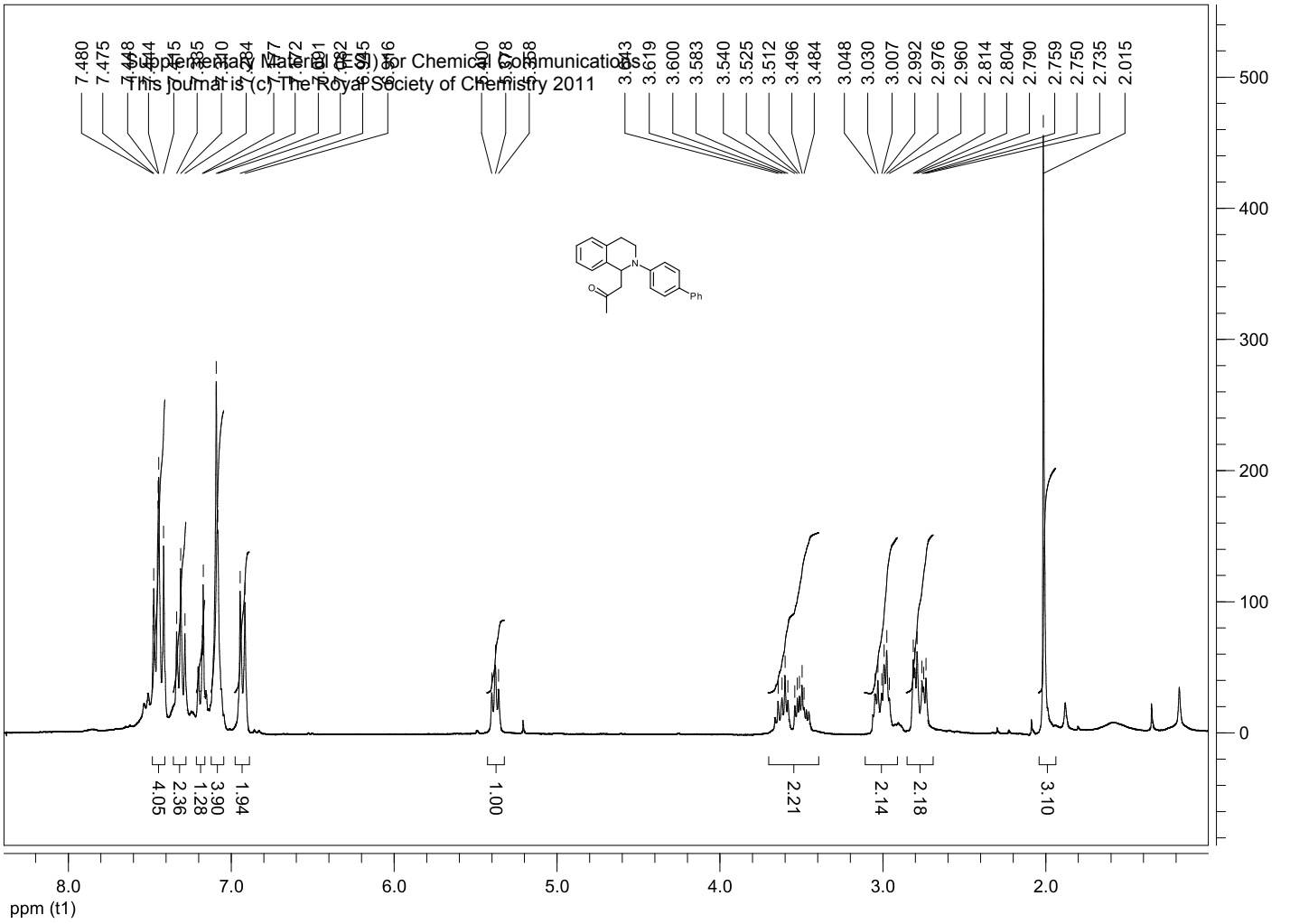


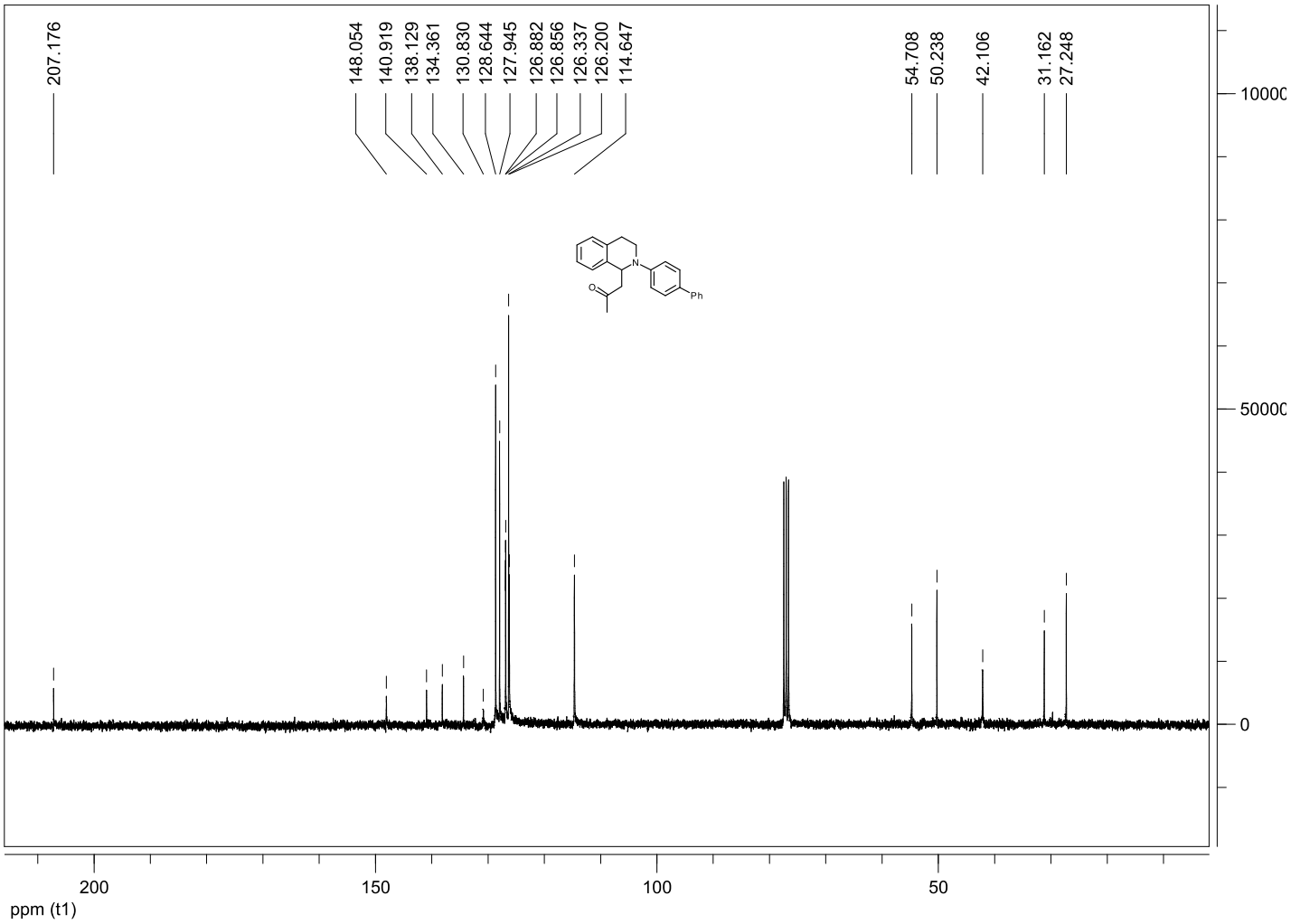


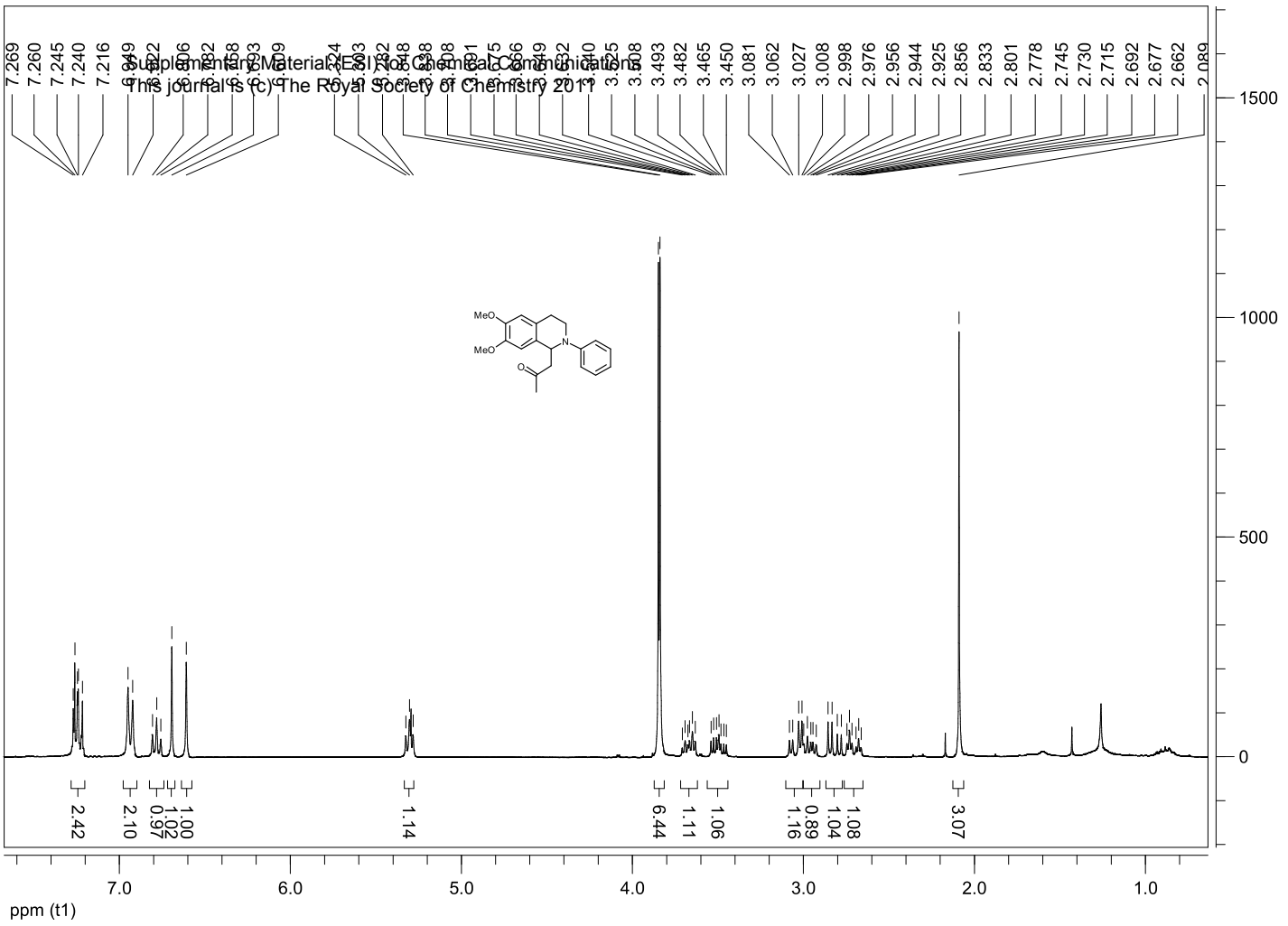


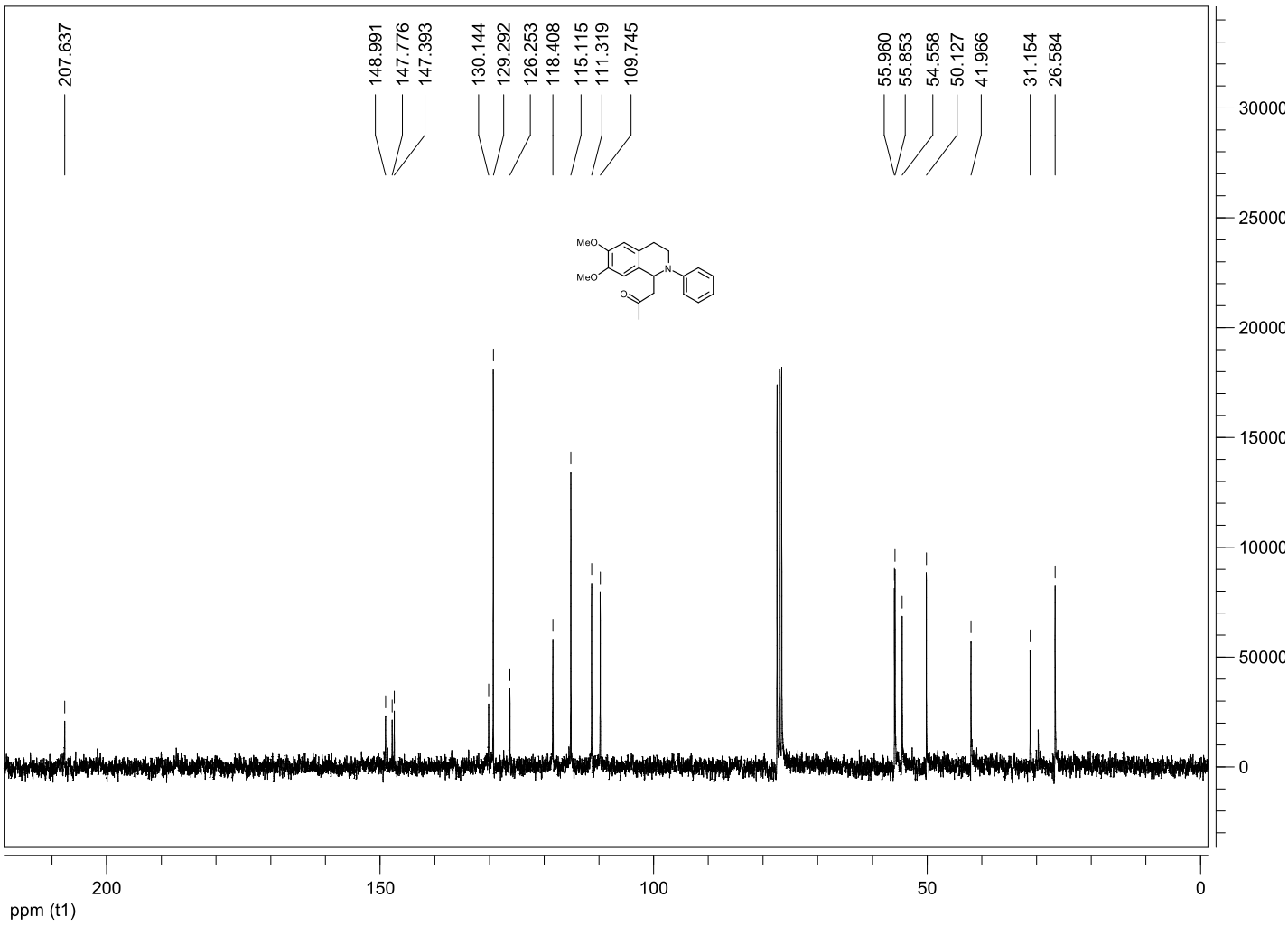









7.269
7.260
7.245
7.240
7.216
3.493
3.482
3.465
3.450
3.081
3.062
3.027
3.008
2.998
2.976
2.956
2.944
2.925
2.856
2.833
2.801
2.778
2.745
2.730
2.715
2.692
2.677
2.662
MeO
MeO
N
O
2.42
2.10
0.97
1.02
1.00
1.14
6.44
1.11
1.00
1.16
0.89
1.04
1.08
3.07
1500
1000
500
0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


207.637
148.991
147.776
147.393
130.144
129.292
126.253
118.408
115.115
111.319
109.745
55.960
55.853
54.558
50.127
41.966
31.154
26.584
MeO
MeO
N
O
30000
25000
20000
15000
10000
5000
0
200
150
100
50
0
ppm (t1)