Supporting Information for

Cu(II)-catalyzed Cross Coupling Cyanomethylation of Tetrahydroisoquinolines with α-bromoalkylnitrile

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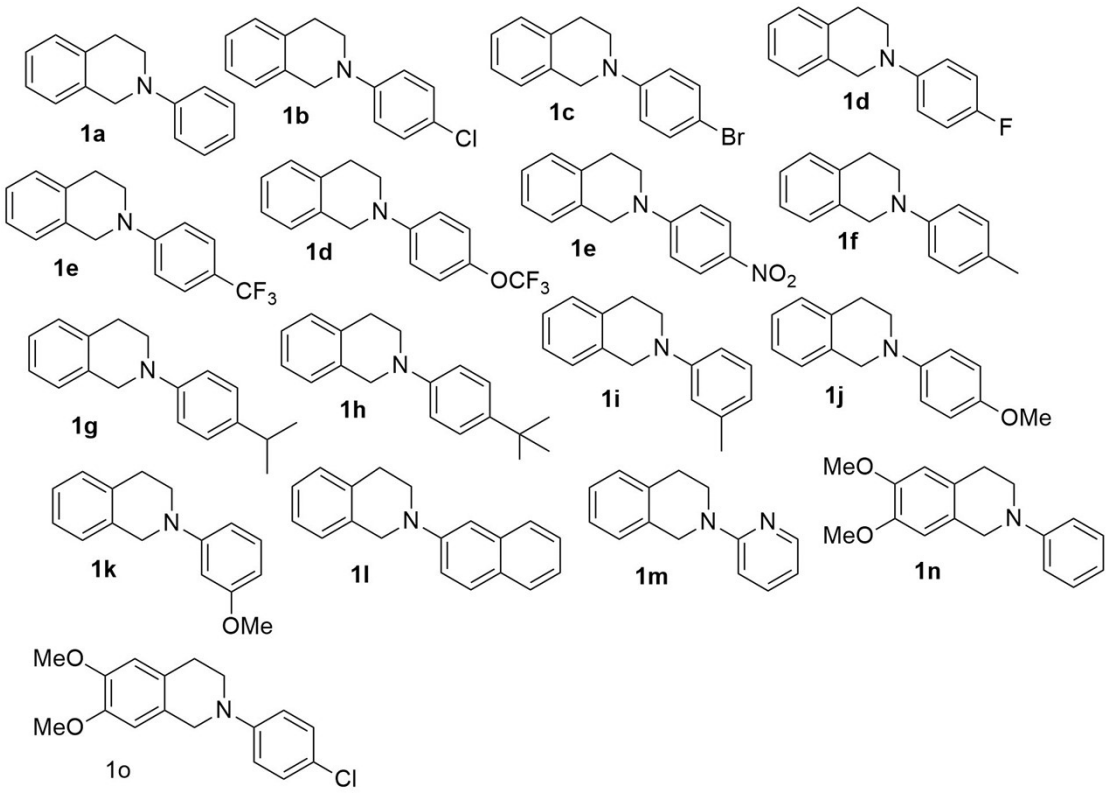
1. General procedure

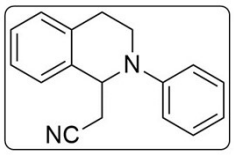
Experimental part: The reagents in the experiments were commercially available from the chemical company. All reagents were dried and distilled according to the standard reagent purification manual prior to use. The analyzed thin layer chromatography (TLC) was performed on a 60 F254 silica gel plate. TLC color development was developed by UV lamp (254 nm) and potassium permanganate. The ^1H NMR spectrum was obtained on a Mercury Plus-400(400 MHz). Chemical shifts are obtained as a residual solvent peak or trimethylsilane. The ^{13}C NMR spectrum was also obtained by Mercury Plus-400 (100 MHz). The chemical shift was obtained by calibrating the intermediate peak of the deuterated chloroform triplet to 77.0 ppm or the deuterated dimethyl sulfoxide intermediate peak to 39.5 ppm. High-resolution mass spectrometry (HRMS) was measured at the ACQUITYTM UPLC & Q-TOF MS Premier instrument at the Jinan University at Analytical Testing Center. Gas-mass chromatographic analysis was performed on a LECO Pegasus 4D GC x GC-TOFMS instrument. Gas chromatographic analysis was performed on a Shimadzu GC-2014 instrument.

2. Synthesis of substrates

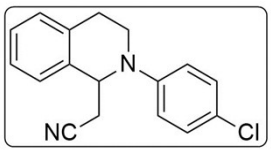
All these substrates were synthesized by following the procedure found in references 1-7.



5. NMR spectra information

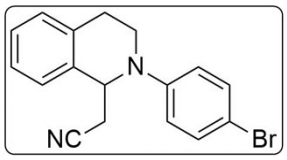


2-(2-Phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3a) Pale yellow solid, yield 89%; m.p. 87-89 ^{o}C; 1H NMR (400 MHz, $CDCl_3$) δ 2.66-2.72(m, 1H). 2.83-2.92 (m, 2H), 3.06-3.00 (m, 1H), 3.57-3.54 (m, 2H), 5.04 (t, J = 6.4 Hz, 1H), 6.84 (t, J = 6.8 Hz, 1H), 6.92 (d, J = 8.4 Hz, 2H), 7.29-7.21 (m, 6H). ^{13}C NMR (100MHz, $CDCl_3$) 134.8, 134.6, 129.6, 127.8, 126.6, 119.3, 118.2, 115.4, 57.3, 42.3, 27.6. IR (KBr): 749, 957, 1031, 1158, 1229, 1396, 1494, 1596, 2241, 2820, 3039cm^{-1}. HRMS (ESI-TOF) Calcd for C17H17N2 + $[M+H]^+$: 249.1350, found: 249.1339.

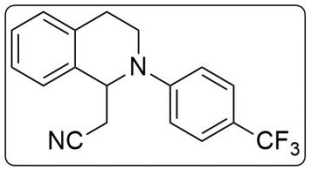


2-(2-(4-Chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3b): Yellow solid, yield 71%; m.p. 70-73 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.72-2.66 (m, 1H). 2.91-2.81 (m, 2H), 3.04-2.96 (m, 1H), 3.58-3.47 (m, 2H), 5.00 (t, J = 6.4 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 7.23-7.17 (m, 6H). ^{13}C NMR (100MHz, $CDCl_3$) 109.8, 56.2, 55.8, 42.3, 26.7, 24.2 IR (KBr): 2907, 2835, 2250, 1595,1497, 130, 860, 806, 512 cm^{-1}. HRMS (ESI-TOF) Calcd for

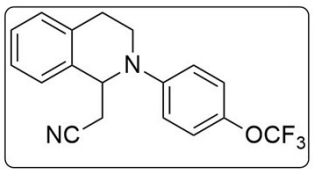
C19H20ClN2+[M+H]$^+$: 243.1206, found: 243.1220,



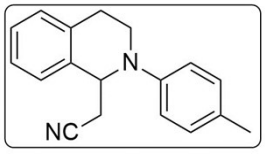
2-(2-(4-Bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3c): Pale yellow solid, yield 78%; m.p. 97-99 ^{o}C; 1H NMR (400 MHz, $CDCl_3$) δ 2.73-2.67(m, 1H), 2.92-2.83 (m, 2H), 3.04-2.97 (m, 1H), 3.58-3.47 (m, 2H), 5.00 (t, J = 6.0 Hz, 1H), 6.78 (d, 9.2 Hz, 2H), 7.20-7.16 (m, 1H), 7.26-7.22 (m, 3H), 7.34 (d, J = 8.8 Hz, 2H), ^{13}C NMR (100MHz, $CDCl_3$) 147.5,134.5,132.3, 128.8, 127.8, 126.5, 117.5, 166.8. IR (KBr): 2906, 2838, 2243, 1590,1494, 1335, 1225, 1150, 1150,798, 760, 583, 508 cm^{-1}. HRMS (ESI-TOF) Calcd for C17H16BrN2+ [M+H]$^+$: 327.0491, found: 327.0504.



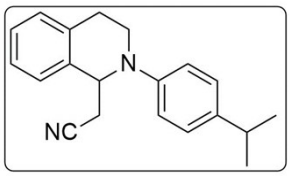
2-(2-(4-(Trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile(3d): Pale yellow oil, yield 47%; 1H NMR (400 MHz, CDCl3) δ2.79-2.73(m, 1H), 3.00-2.91 (m, 2H), 3.10-3.03 (m, 1H), 3.70-3.58 (m, 2H), 5.12 (t, J = 6.4 Hz, 1H), 6.93 (d, J = 8.8 Hz, 2H), 7.26-7.20 (m, 4H), 7.51 (d, J = 8.8 Hz, 2H), ^{13}C NMR (100MHz, $CDCl_3$) 150.5,134.5, 132.3, 129.8, 128.8, 127.5, 127.5, 127.2, 127.1, 124, 120.1, 117.9, 113.5, 56.1, 42.8. ^{19}FNMR (376MHz, $CDCl_3$) δ-179.6. IR (KBr): 2930, 2246, 1615,1515, 1395, 1327, 1075, 823, 760, 590, 515 cm^{-1}. HRMS (ESI-TOF) Calcd for C17H16F3N2+ [M+H]$^+$: 317.1260, found: 317.1275.



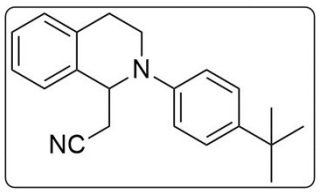
2-(2-(4-(Trifluoromethoxy)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3e): Pale yellow oil, yield 59%; 1H NMR (400 MHz, $CDCl_3$) δ 2.74-2.69 (m, 1H), 2.93-2.85 (m, 2H), 3.06-2.99 (m, 1H), 3.62-3.51 (m, 2H), 5.01 (t, J = 6.4 Hz, 1H), 6.89 (d, J = 9.2 Hz, 2H), 7.13 (d, J = 9.2 Hz, 2H), 7.21-7.17(m, 1H), 7.26-7.22 (m, 3H). ^{13}C NMR (100MHz, $CDCl_3$) 147.5,141.5, 134.3, 129.8, 128.8, 127.1, 127.0, 126.2, 126.1, 122.2, 120.1, ^{19}FNMR (376MHz, $CDCl_3$) δ-179.7 IR (KBr): 2927, 2242, 1613,1510, 1392, 1325, 1072, 1612,758,672, 530 cm^{-1}. HRMS (ESI-TOF) Calcd for C17H16F3N2O+ [M+H]$^+$: 333.1290, found: 333.1220.



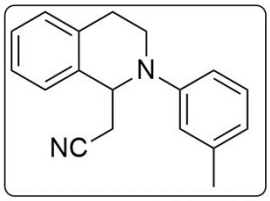
2-(2-(p-Tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3f): Yellow oil, yield: 86%; 1H NMR (400 MHz, $CDCl_3$) δ 2.26 (s, 3H); 7.27-7.21 (m, 3H), 2.73-2.67 (m, 1H), 2.91-2.81 (m, 2H), 3.05-2.98 (m, 1H), 3.54-3.51 (m, 2H), 5.00 (t, J = 5.6H, 1H), 6.86 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 7.18-7.16 (m, 1H),).^{13}C NMR (100MHz, $CDCl_3$) 146.4, 134.6, 129.7, 127.7, 126.8, 126.3, 116.2, 112.4, 56.3, 42.3, 27.7. IR (KBr):3049, 2977,2880,2240, 1601,1583,1493, 1413, 1229, 1040, 954, 855, 785, 725,695, 656 cm^{-1}. HRMS (ESI-TOF) Calcd for C18H19N2 + $[M+H]^+$: 263.1543, found: 263.1549.



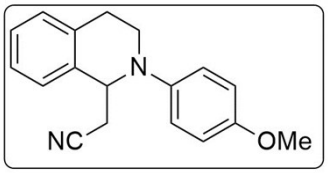
2-(2-(4-Isopropylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3g): Yellow solid, 50 mg, yield 79%; 68-74 ^oC; 1H NMR (400 MHz, $CDCl_3$) δ 1.21 (d, J = 6.8 Hz, 6H), 2.73-2.67 (m, 1H), 2.92-2.80 (m, 3H), 3.06-3.00 (m, 1H), 3.55-3.52 (m, 2H), 5.00 (t, J = 6.4 Hz, 1H),), 6.88 (d, J = 8.8 Hz, 2H), 7.18-7.14 (m, 3H), 7.27-7.21 (m, 3H).^{13}C NMR (100 MHz, $CDCl_3$) 148.4, 139.6, 134.7, 129.7, 128.8, 121.3, 120.2, 118.4, 116.3, 112.3, 56.7, 24.2. IR (KBr): 3149, 2984, 1737, 1518, 2240, 1601, 1583, 1493, 1518, 1129, 1040, 822, 572, 725, 812, 584, 556cm^{-1}. HRMS (ESI-TOF) Calcd for C18H19N2 + $[M+H]^+$: 291.1856, found: 263.1861.



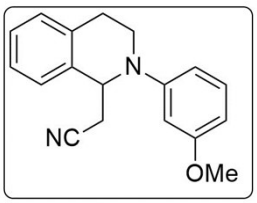
2-(2-(4-(tert-Butyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3h): White solid, yield 71%; m.p. 111-114 ^oC; 1H NMR (400 MHz, CDCl3) δ 1.30 (s, 9H). 2.75-2.69 (m, 1H), 2.94-2.85 (m, 2H), 3.08-3.00 (m, 1H), 3.58-3.54 (m, 2H), 5.04 (t, J = 5.6 Hz, 1H), 6.90 (d, J = 8.8 Hz, 2H), 7.19-7.17 (m, 1H), 7.29-7.23 (m, 3H), 7.33 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) 146.4, 142.6, 134.7, 129.7, 128.8, 121.3, 120.2, 118.4, 116.3, 112.3, 56.7, 24.2. IR (KBr): 3149, 2984, 1737, 1518, 2240, 1601, 1583, 1493, 1518, 1129, 1040, 822, 572, 725, 812, 584, 556cm^{-1}. HRMS (ESI-TOF) Calcd for C21H25N2 + $[M+H]^+$: 305.2012, found: 303.2016.



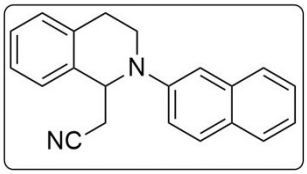
2-(2-(m-Tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3i): White solid, yield 62%; m.p. 67-70 ^{o}C; 1H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.75-2.69(m, 1H), 2.94-2.85 (m, 2H), 3.08-3.00 (m, 1H), 3.56 (t, J = 6.8 Hz, 2H), 5.06 (t, J = 6.0 Hz, 1H), 6.68 (d, J = 7.6 Hz, 1H), 6.74 (d, J = 8.0 Hz, 2H), 7.19-7.16 (m, 2H), 7.29-7.23 (m, 3H), ^{13}C NMR (100MHz, $CDCl_3$) 146.4, 134.6, 129.7, 127.7, 126.8, 126.3, 116.2, 112.4, 56.3, 42.3, 27.7. IR (KBr):3049, 2977,2880,2240, 1601,1583,1493, 1413,1229, 1040, 954, 855, 785, 725,695, 656cm^{-1}. HRMS (ESI-TOF) Calcd for C18H19N2 + $[M+H]^+$: 263.1543, found: 263.1549.



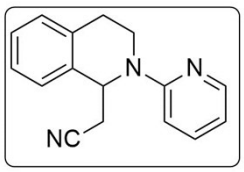
2-(2-(4-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3j): Pale yellow solid, yield 75%; m.p. 94-99 ^{o}C; 1H NMR (400 MHz, $CDCl_3$) δ 2.70-2.64 (m, 1H), 2.89-2.75 (m, 2H), 3.02-2.94 (m, 1H), 3.48-3.44 (m, 2H), 4.88 (t, J = 6 Hz, 1H) 6.84 (d, J = 8.8 Hz, 2H), 3.75 (s, 3H), 6.94 (d, J = 8.8 Hz, 2H), 7.18-7.14 (m, 1H), 7.25-7.20 (m, 3H), ^{13}C NMR (100MHz, CDCl3) 15.4, 143.6, 134.7, 134.9, 129.1, 127.7, 126.8, 126.3,119.6,118.3, 114.2, 57.3, 55.3, 43.5, 27.7. IR (KBr):3034, 2997, 1720, 1513,1493, 1213, 1031, 596, 560cm^{-1}. HRMS (ESI-TOF) Calcd for C18H19N2 O+ $[M+H]^+$: 279.1492, found: 279.1499.



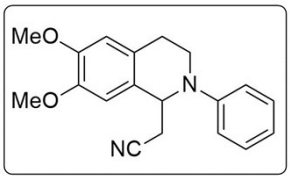
2-(2-(3-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3k) Yellow oil, yield 69%; 1H NMR (400 MHz, $CDCl_3$) δ 2.69-2.72 (m, 1H). 2.96-2.87 (m, 2H), 3.08-3.01 (m, 1H), 3.59-3.55 (m, 2H), 3.80 (s, 3H), 7.28-7.18 (m, 5H), 5.04 (t, J = 6.8 Hz, 1H), 6.54 (dd, J1 = 8.4 Hz, J2 = 2.4 Hz, 1H), 6.44 (dd, J1 = 8.0 Hz, J2 = 2.0 Hz, 1H), 6.47 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100MHz, CDCl3) 15.4, 143.6, 134.7, 134.9, 129.1, 127.7, 126.8, 126.3,119.6,118.3, 114.2, 57.3, 55.3, 43.5, 27.7. IR (KBr):3034, 2997, 1720, 1513,1493, 1213, 1031, 596, 560cm^{-1}. HRMS (ESI-TOF) Calcd for C18H19N2 O+ $[M+H]^+$: 279.1492, found: 279.1499.



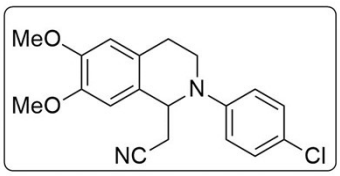
2-(2-(Naphthalen-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3l): Pale yellow solid, yield 67%; m.p. 130-133 ^{o}C; 1H NMR (400 MHz, CDCl3) δ 2.77-2.68 (m, 1H). 2.90-2.82 (m, 2H), 3.08-3.00 (m, 1H), 3.70-3.57 (m, 2H), 5.16 (t, J = 6.8 Hz, 1H), 7.11 (s, 1H), 7.27-7.15 (m, 6H), 7.37 (t, J = 6.8 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.8 Hz, 1H). HRMS (ESI-TOF) Calcd for C21H19N2 + [M+H]+ : 299.1550, found: 299.15439, IR (KBr): 471, 756, 838, 959,1109, 1176, 1291, 1469, 1508, 1593, 1628, 2244, 2910cm^{-1}. HRMS (ESI-TOF) Calcd for C21H19N2+ [M+H]+ : 299.1550, found: 299.15439.



2-(2-(Pyridin-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3m); Pale yellow solid, yield 47%; m.p. 52-56 ^{o}C; 1H NMR (400 MHz, CDCl3) δ 3.01-3.25 (m, 3H), 3.19-3.11 (m, 1H), 3.61-3.55 (m, 1H), 3.76-3.70 (m, 1H), 5.78 (t, J = 6 Hz, 1H), 6.67-6.62 (m, 2H), 7.28-7.20 (m, 4H), 7.52-7.48 (m, 1H), 8.21 (dd, J1 = 4.8 Hz, J2 = 1.2 Hz, 1H),). ^{13}C NMR (100MHz, $CDCl_3$) 157.8, 147.6, 137.6, 135.1, 135.0, 129.6, 127.8, 126.6, 118.3, 113.2, 57.3, 42.3, 27.6. IR (KBr): 749, 957, 1031, 1158, 1229, 1396, 1494, 1596, 2241, 2820, 3039cm^{-1}. HRMS (ESI-TOF) Calcd for C17H17N2 + $[M+H]^+$: 250.1339, found: 249.1340.



2-(6,7-Dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3n); Pale yellow solid, yield 70%; m.p. 138-140 ^{o}C; 1H NMR (400 MHz, $CDCl_3$) δ 2.71-2.65(m, 1H), 2.86-2.74 (m, 2H), 3.00-2.92 (m, 1H), 3.58-3.43(m, 2H), 3.82 (s, 3H), 3.84 (s, 3H), 5.00 (t, J = 6.8 Hz, 1H), 6.61 (s, 1H), 6.76 (s, 1H), 6.83 (t, J = 7.2 Hz, 1H), 6.92 (d, J = 8.4 Hz, 2H), 7.26(t, J = 8.4 Hz, 2H). ^{13}C NMR (100MHz, $CDCl_3$) 148.4, 147.6, 129.7, 126.9, 126.7, 119.7, 118.8, 115.3,111.6,108.3, 56.3, 55.3, 43.0, 23.7. IR (KBr):3034, 2629 , 1720, 1593, 1143, 831, 754, 693 cm^{-1}. HRMS (ESI-TOF) Calcd for C19H21N2 O2+ $[M+H]^+$: 309.1498, found: 279.1609.



2-(2-(4-Chlorophenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3o) Yellow solid, yield 47%; m.p. 173-177 ^{o}C; 1H NMR (400 MHz, CDCl3) δ 2.70-2.62 (m, 1H). 2.87-2.71 (m, 2H), 3.02-2.91 (m, 1H), 3.60-3.48 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 4.93 (t, J

= 6.4 Hz, 1H), 6.63 (s, 1H), 6.75 (s, 1H), 6.85 (d, J = 8.4 Hz, 2H), 7.21(d, J = 8.4 Hz, 2H). ^{13}C NMR (100MHz, CDCl3) 148.3, 147.6, 129.7, 126.9, 126.7, 119.7, 118.8, 115.3,111.6,108.3, 56.3, 55.3, 43.0, 23.7. IR (KBr):3034, 2629, 1720, 1593, 1143, 831, 754, 693 cm^{-1}. HRMS (ESI-TOF) Calcd for C19H20N2Cl O2+ $[M+H]^+$: 343.1208, found: 343.1220.

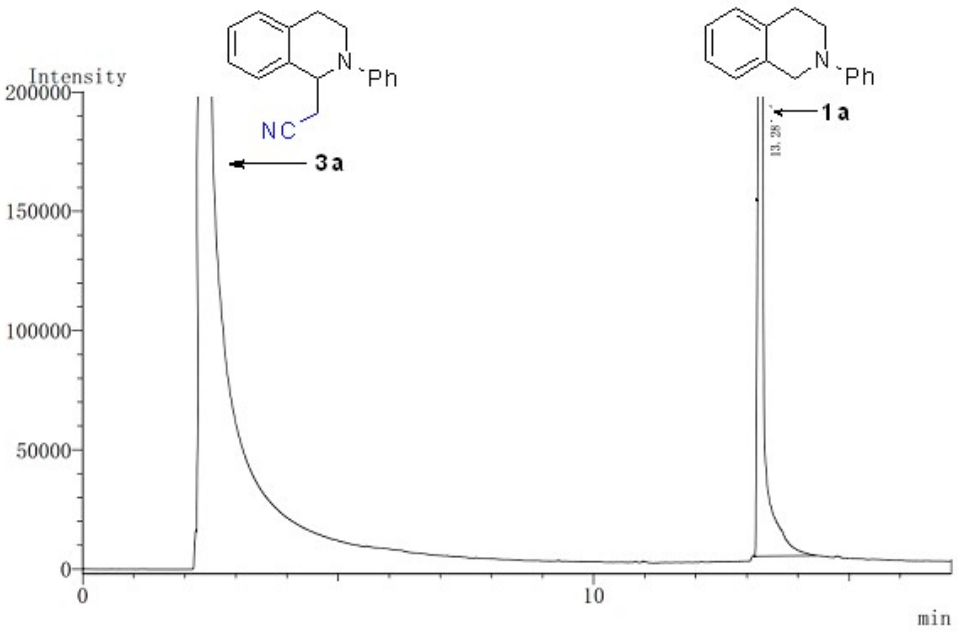


Figure. S_1. GC spectrum of product **2a**.

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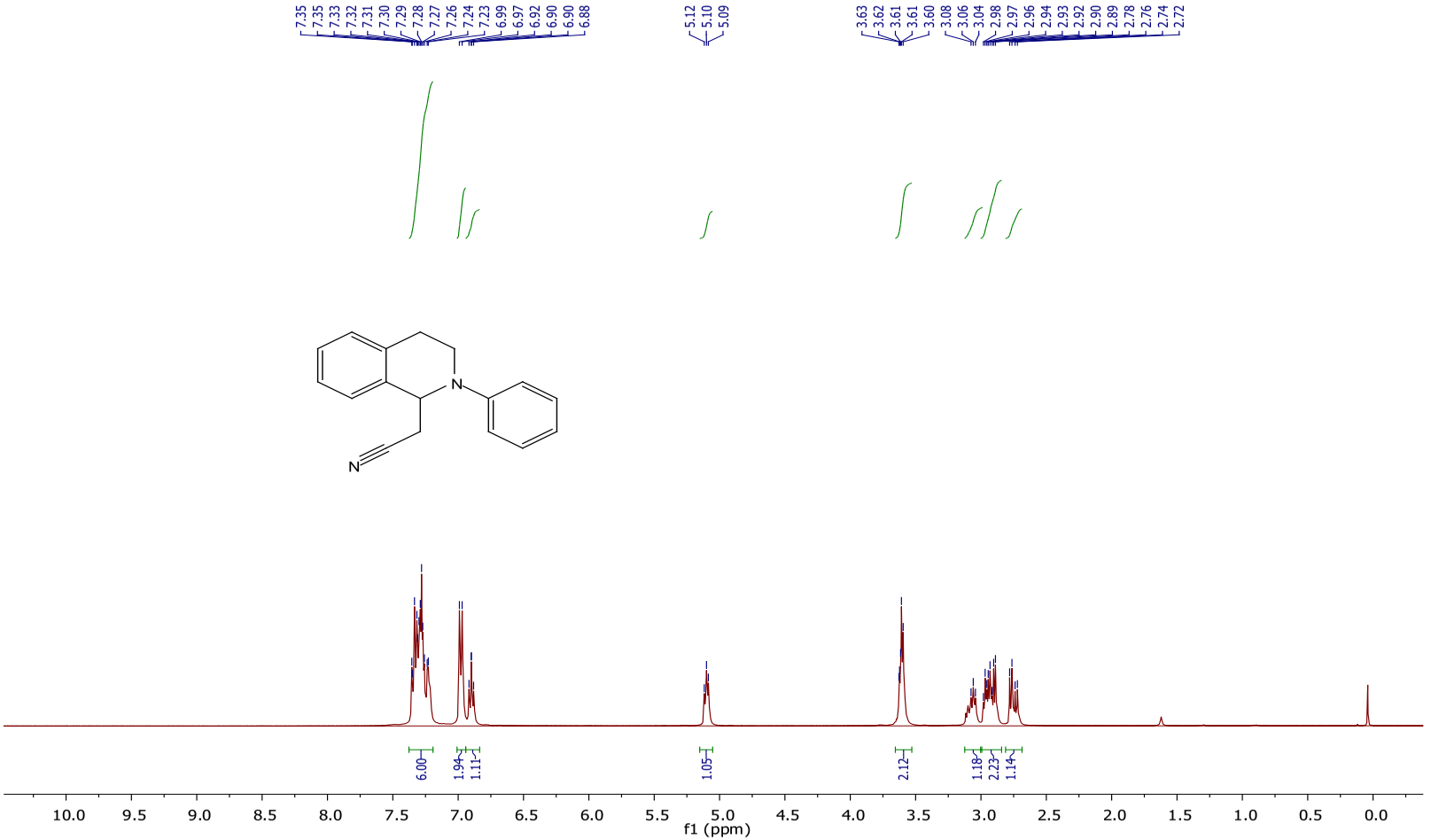
[6] X. Wu, D.-F. Chen, S.-S. Chen, Y.-F, Zhu, *Eur. J. Org. Chem*. **2015**, 468-473.

[7] G. Bergonzini, C. S. Schindler, C.-J. Wallentin, E. N. Jacobsen, C. R. J. Stephenson, *Chem. Sci.***2014**, *5*, 112-116.

6. Copies of ^{1}H/^{13}C NMR spectra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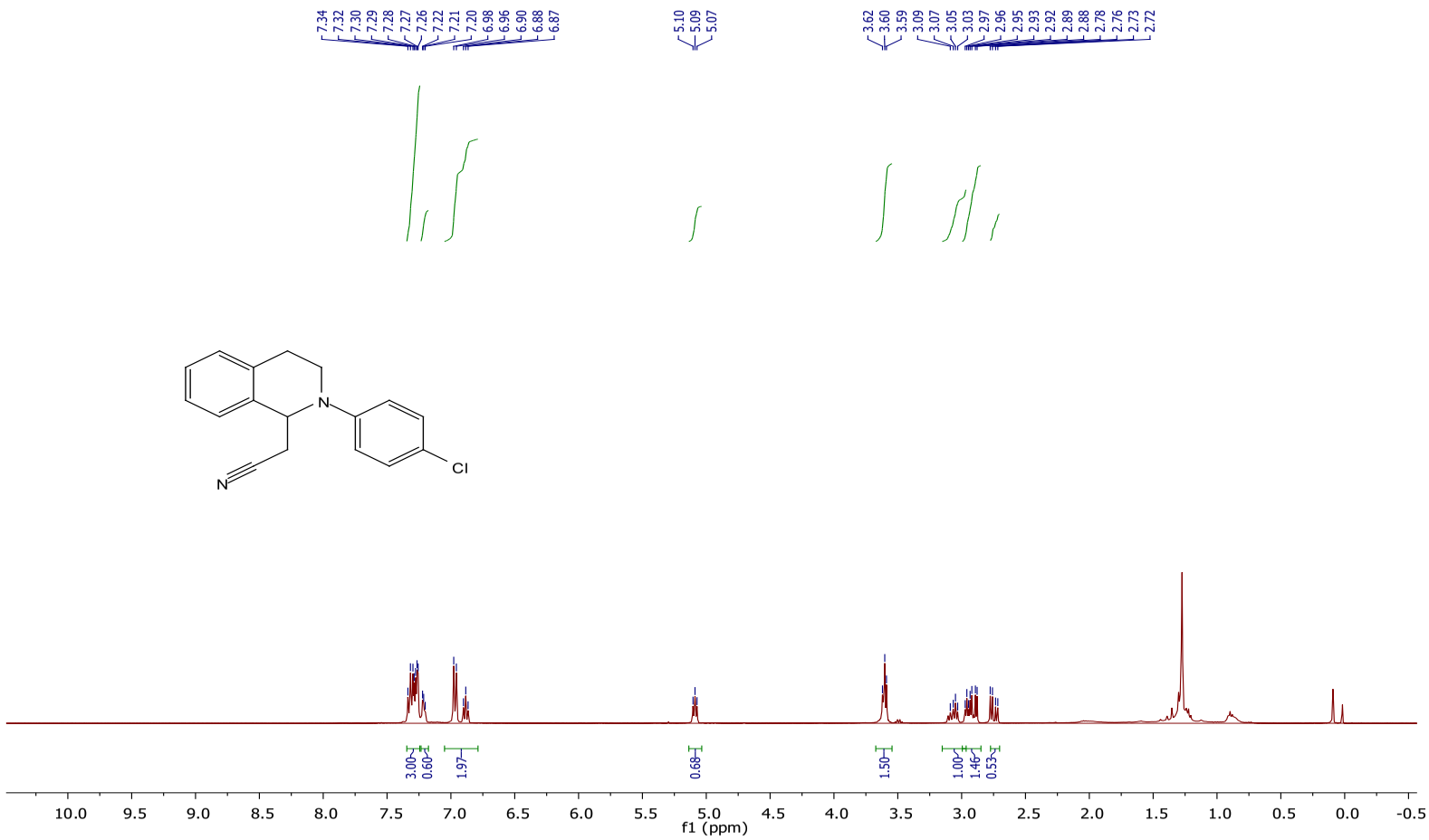
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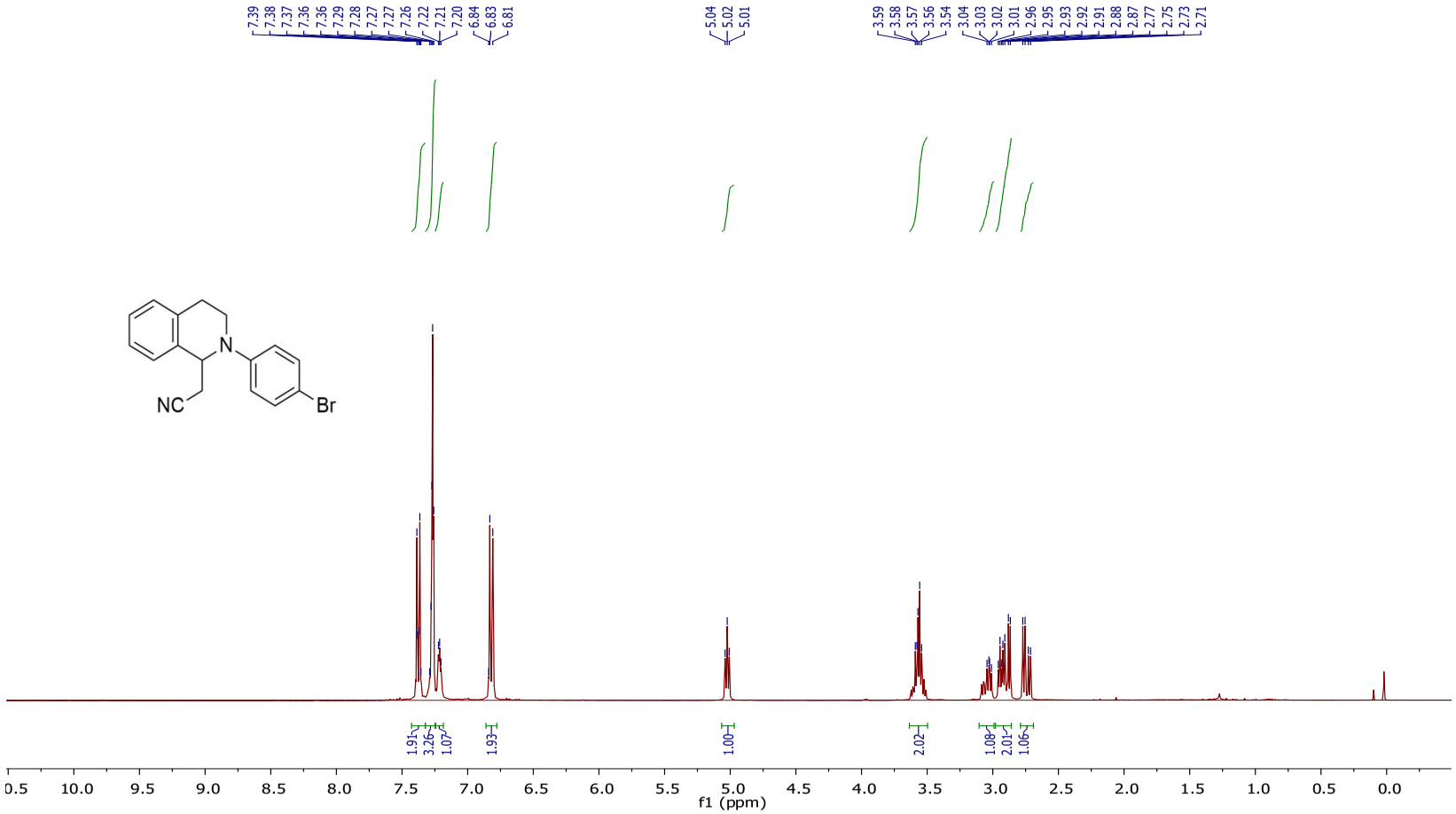
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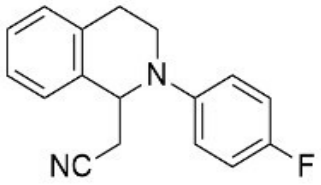
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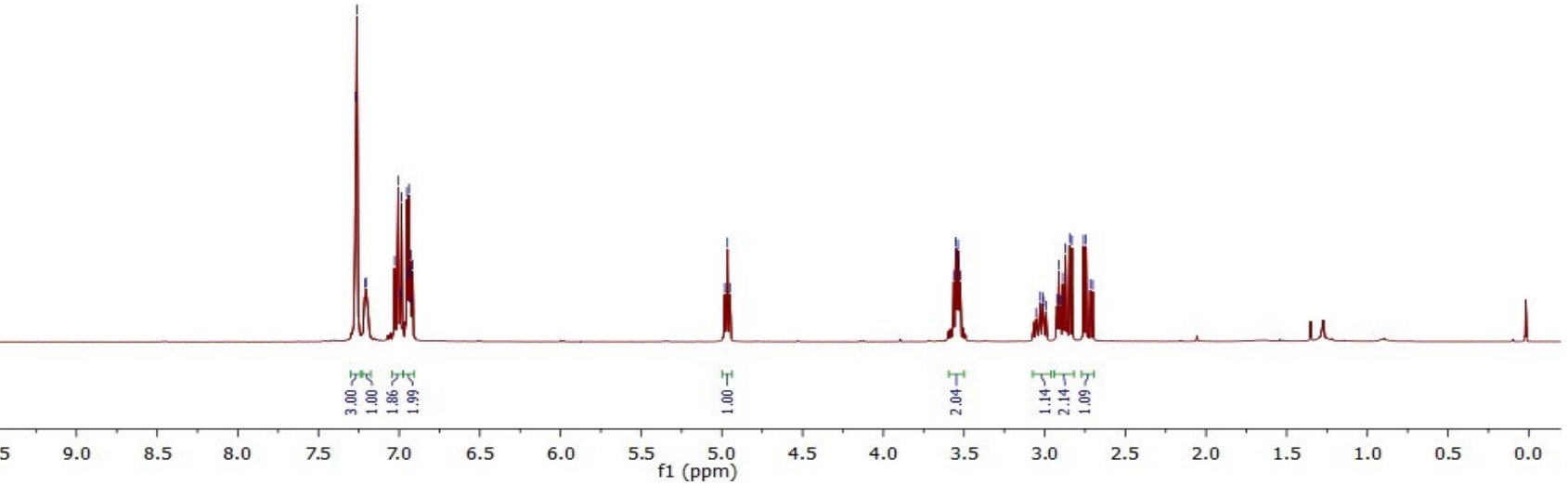
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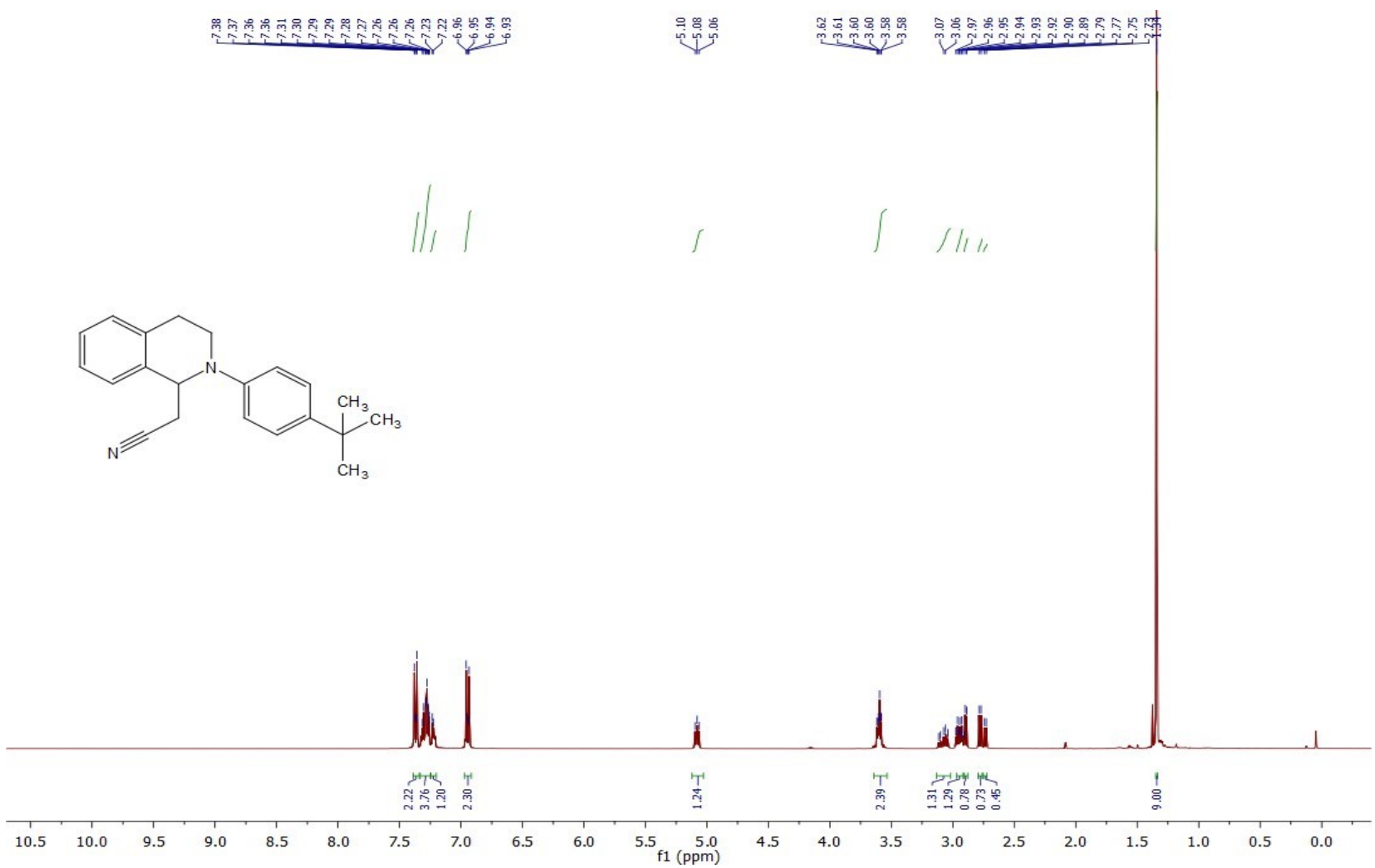
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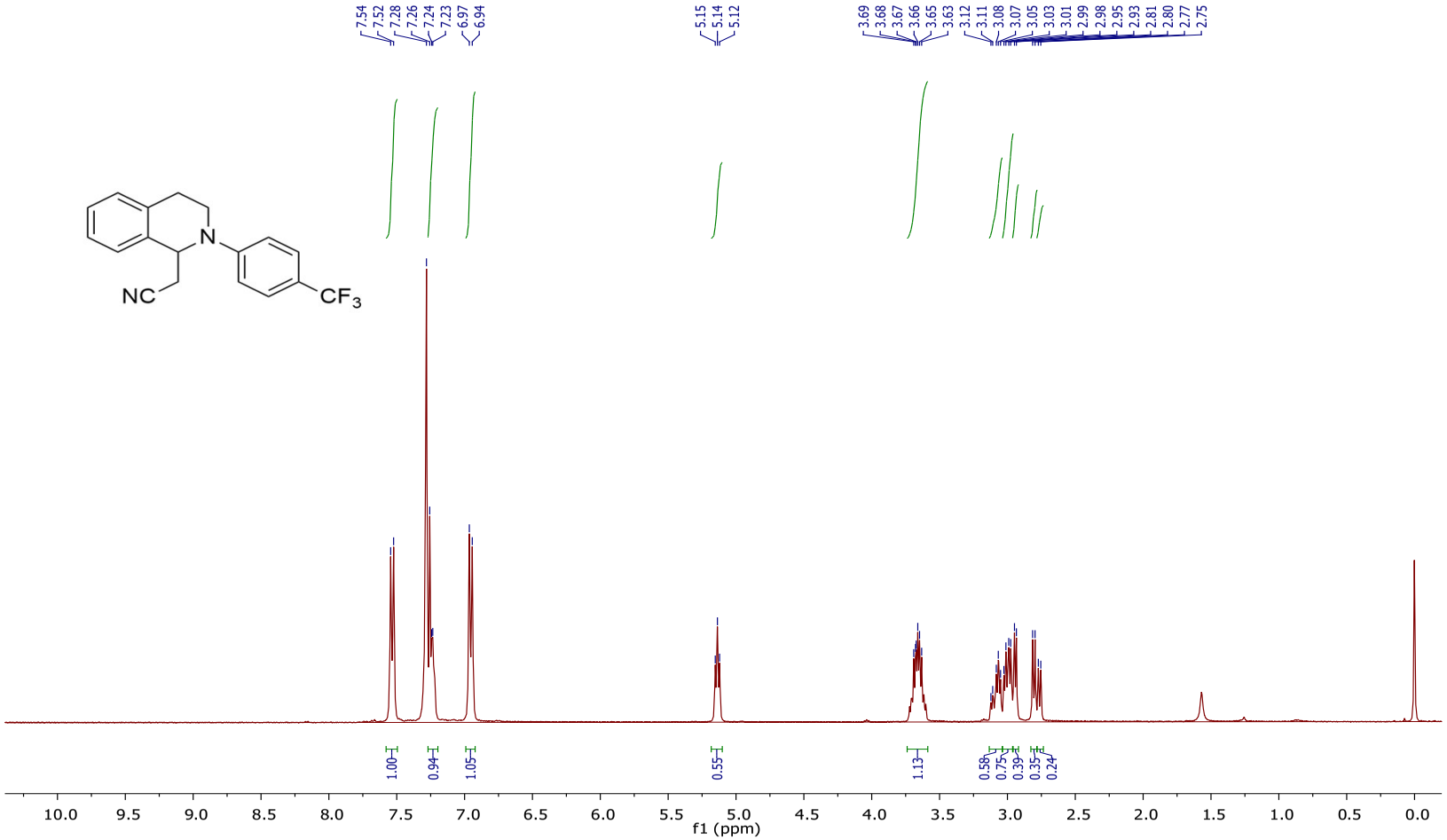
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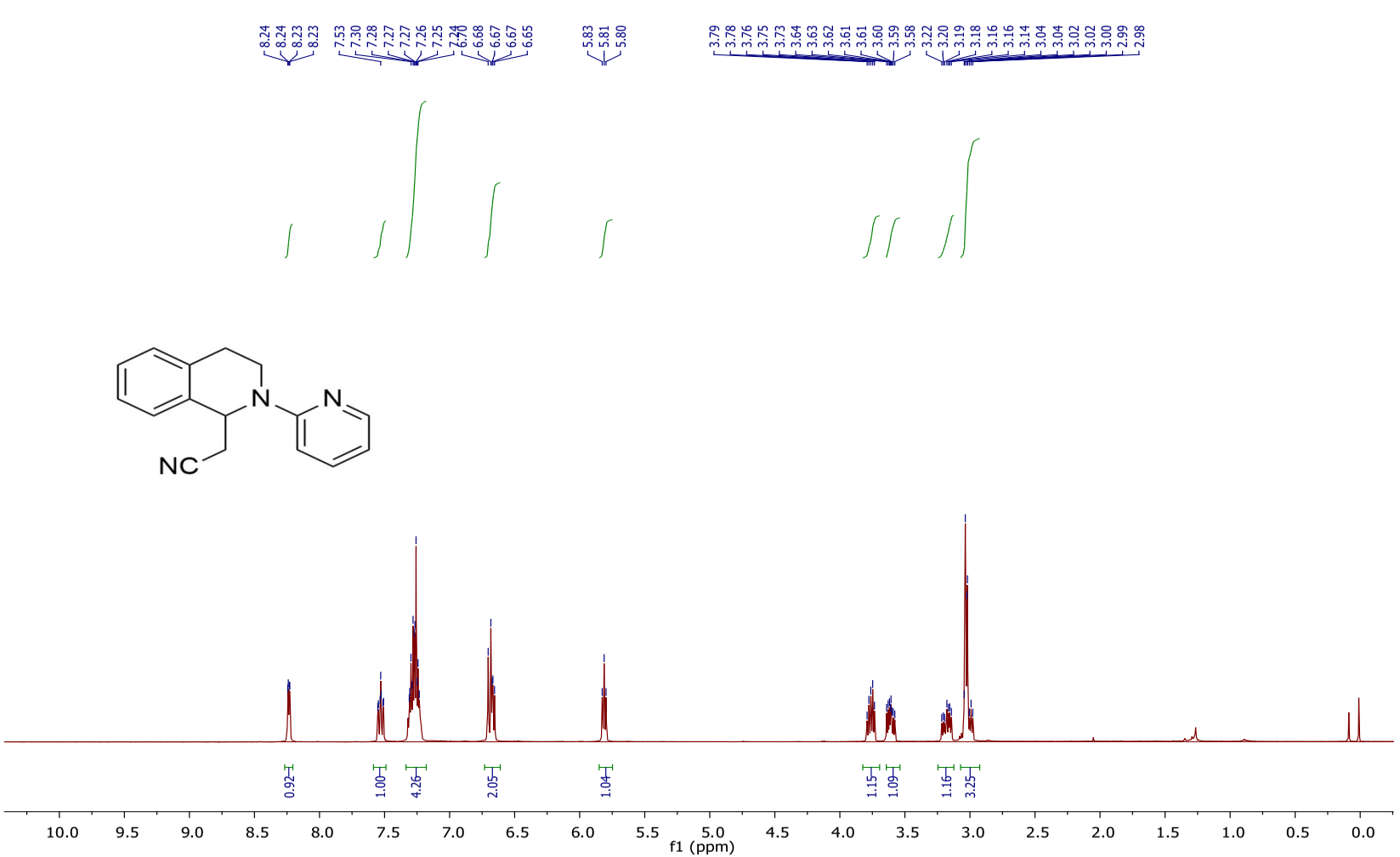
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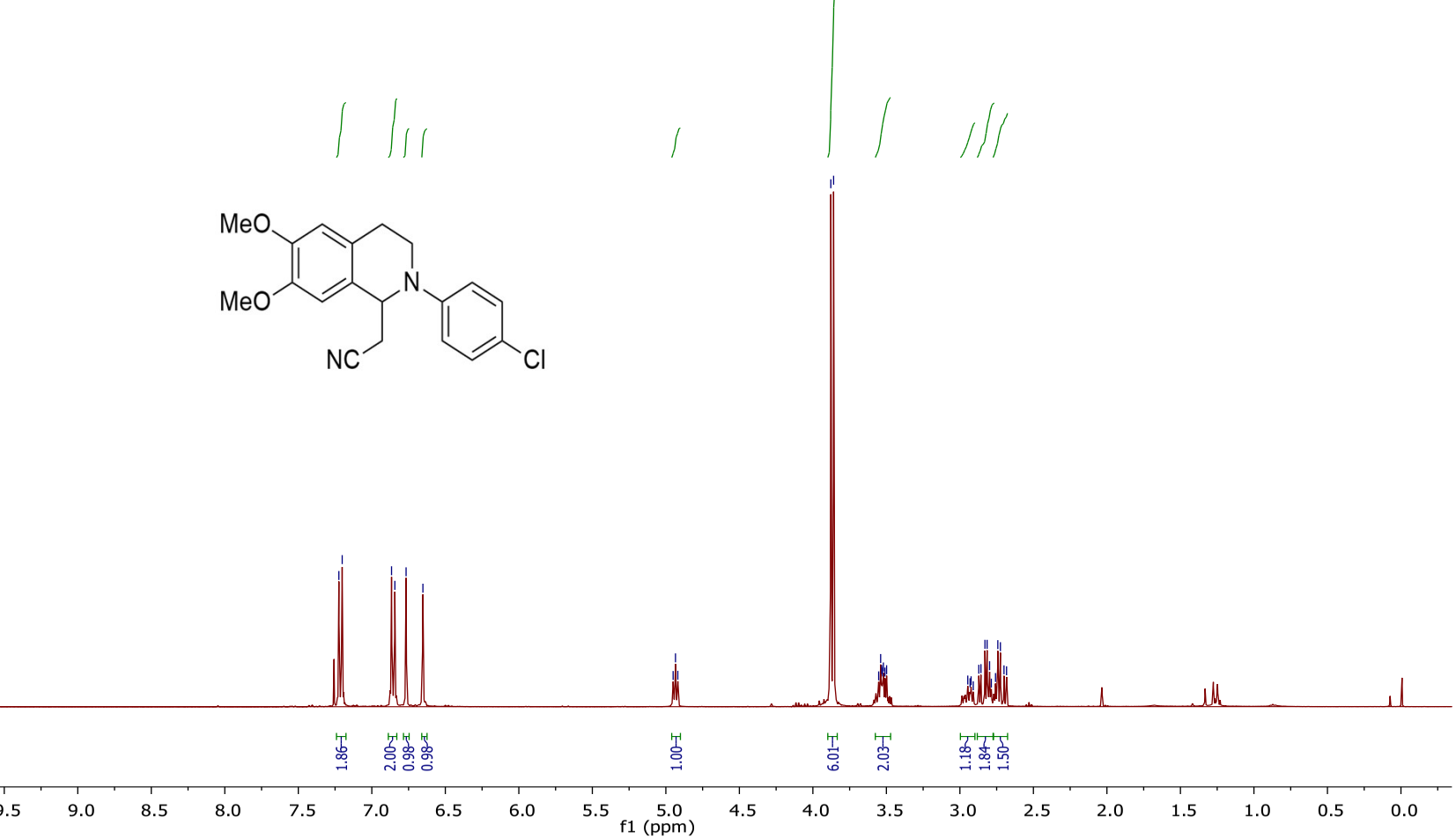
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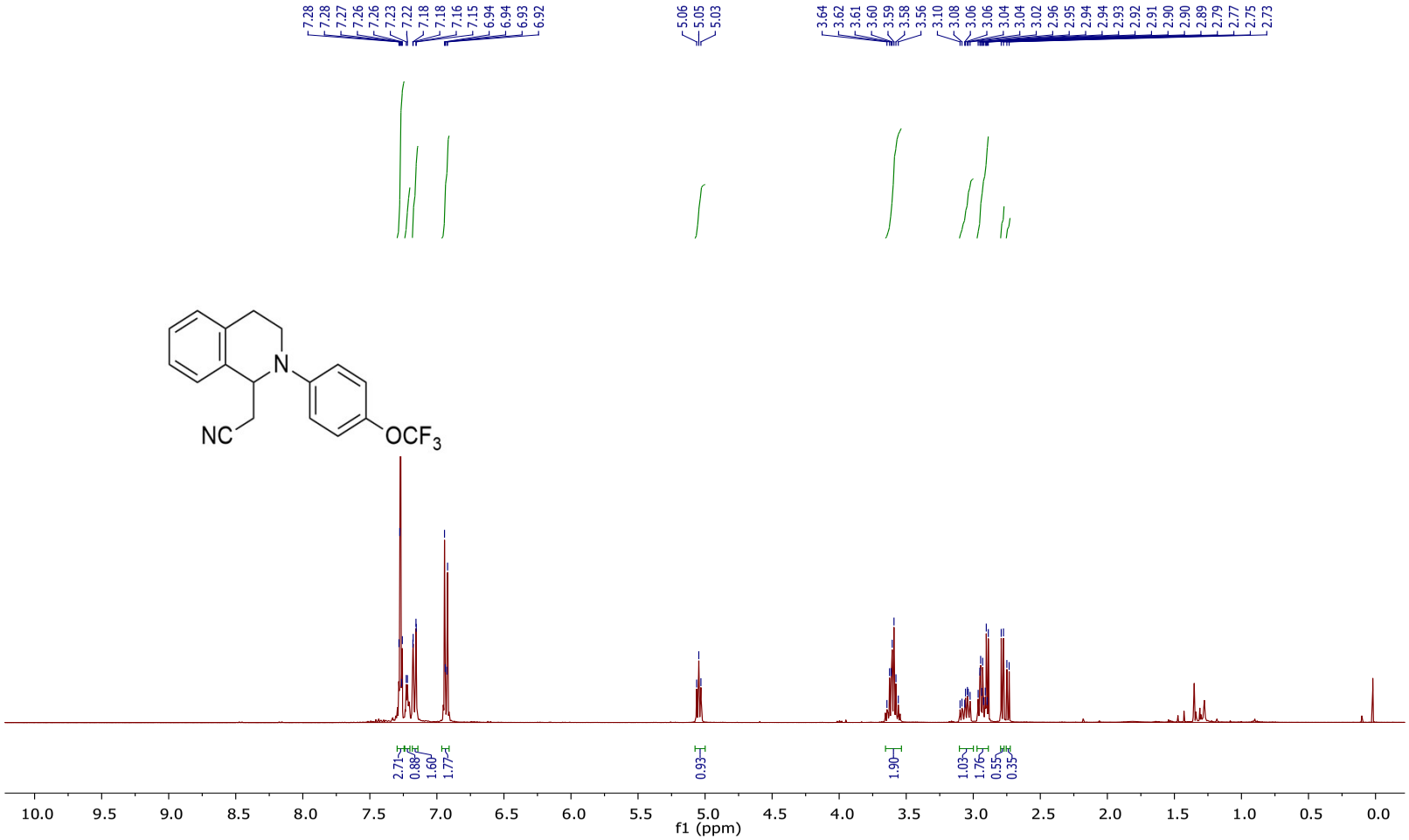
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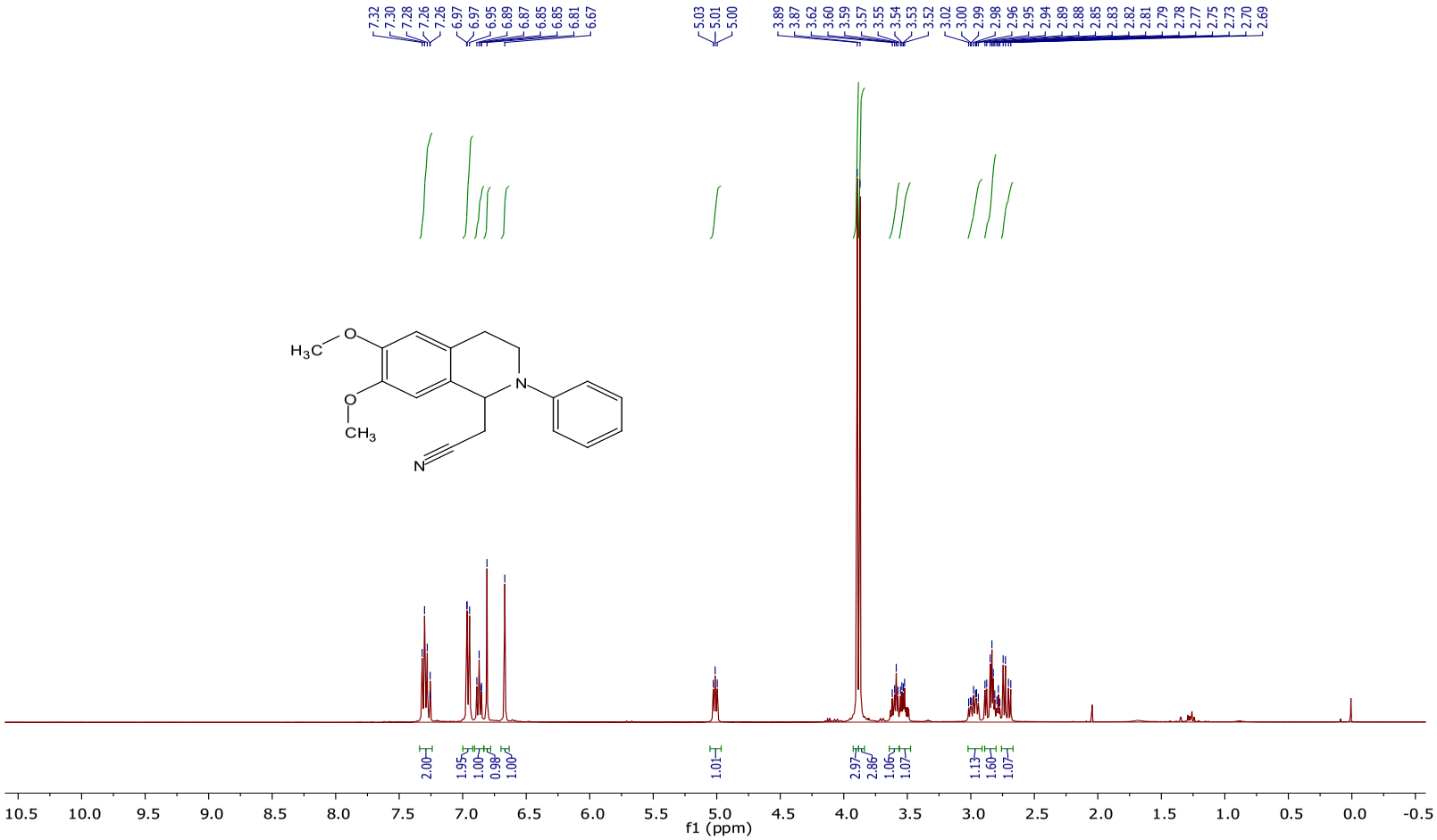
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f1 (ppm)
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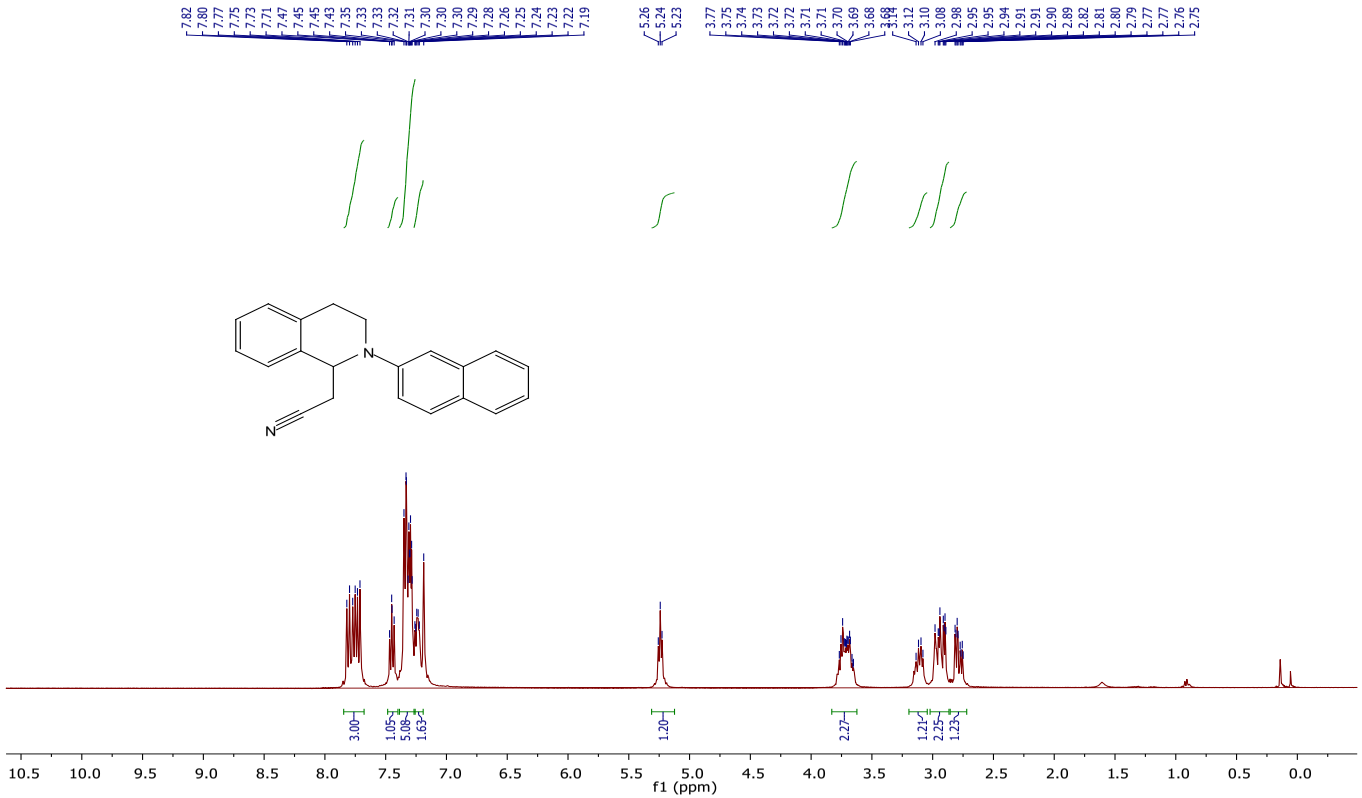
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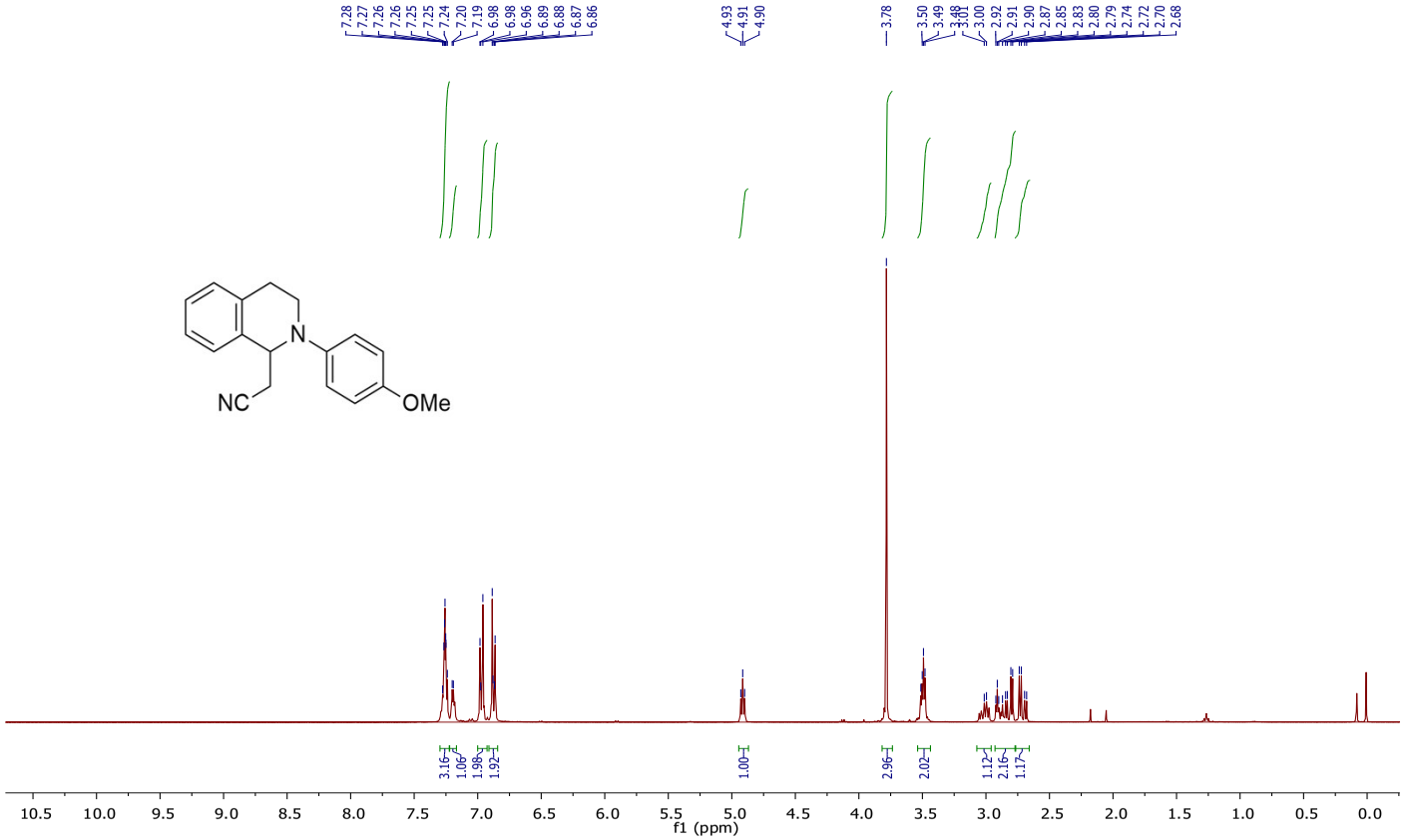
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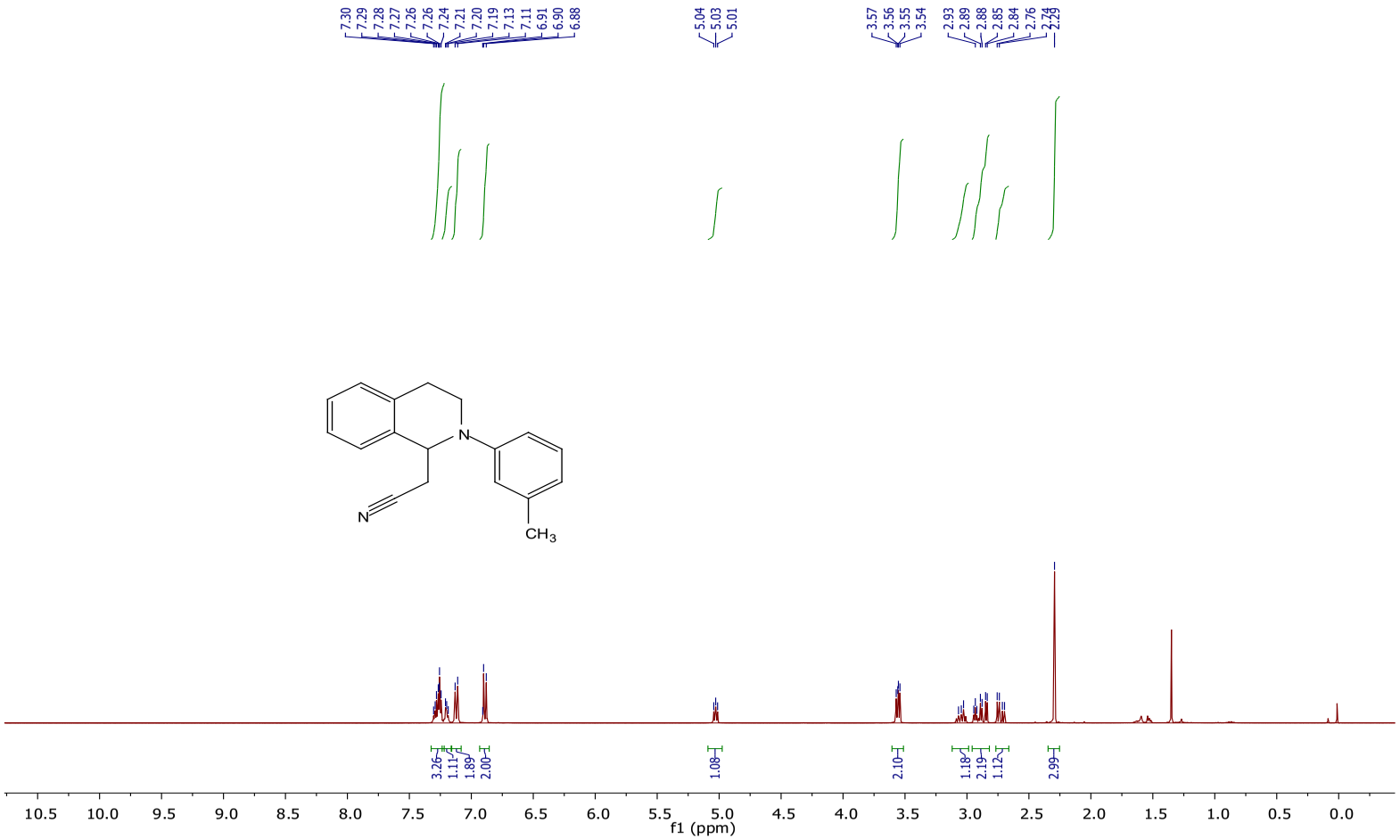
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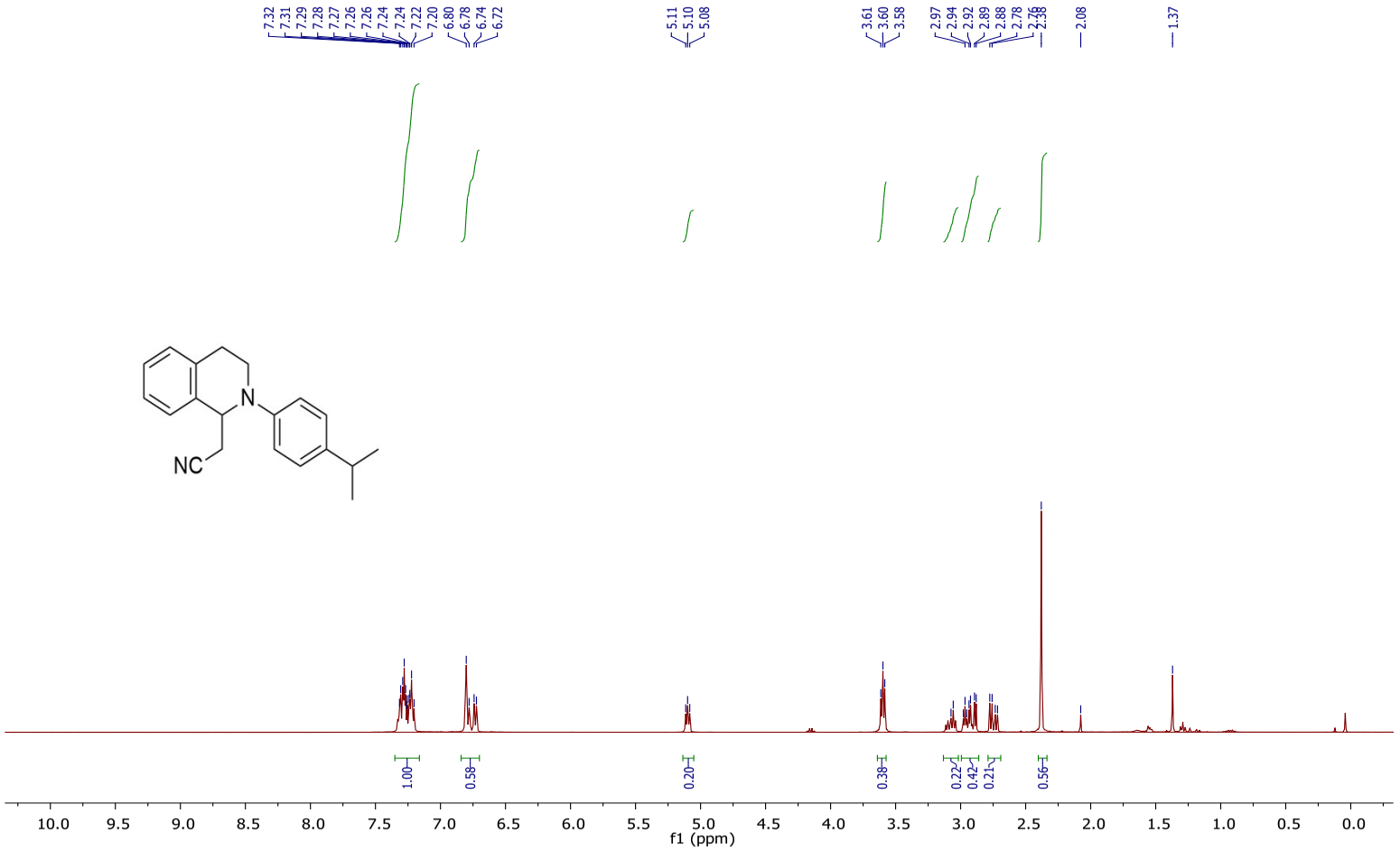
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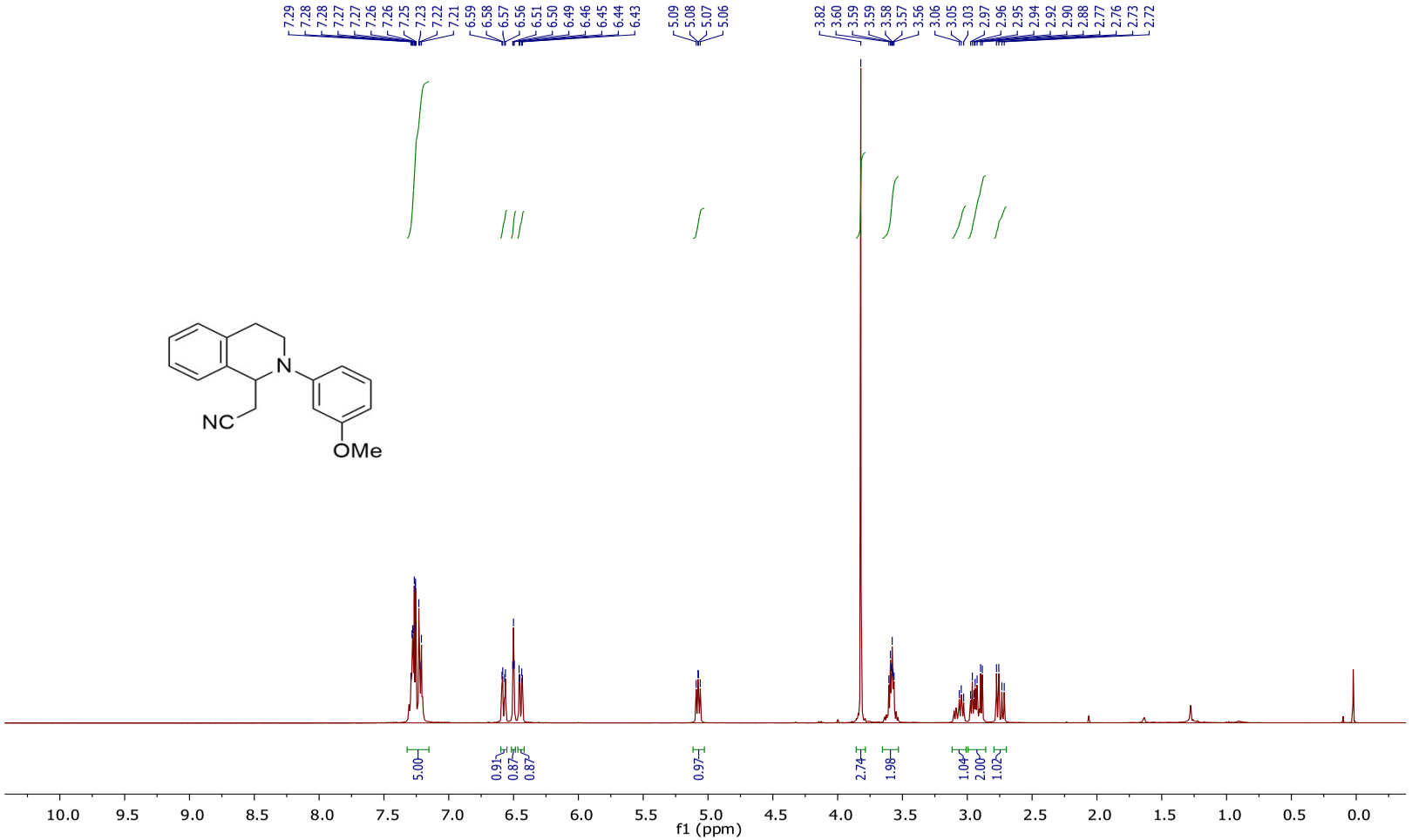
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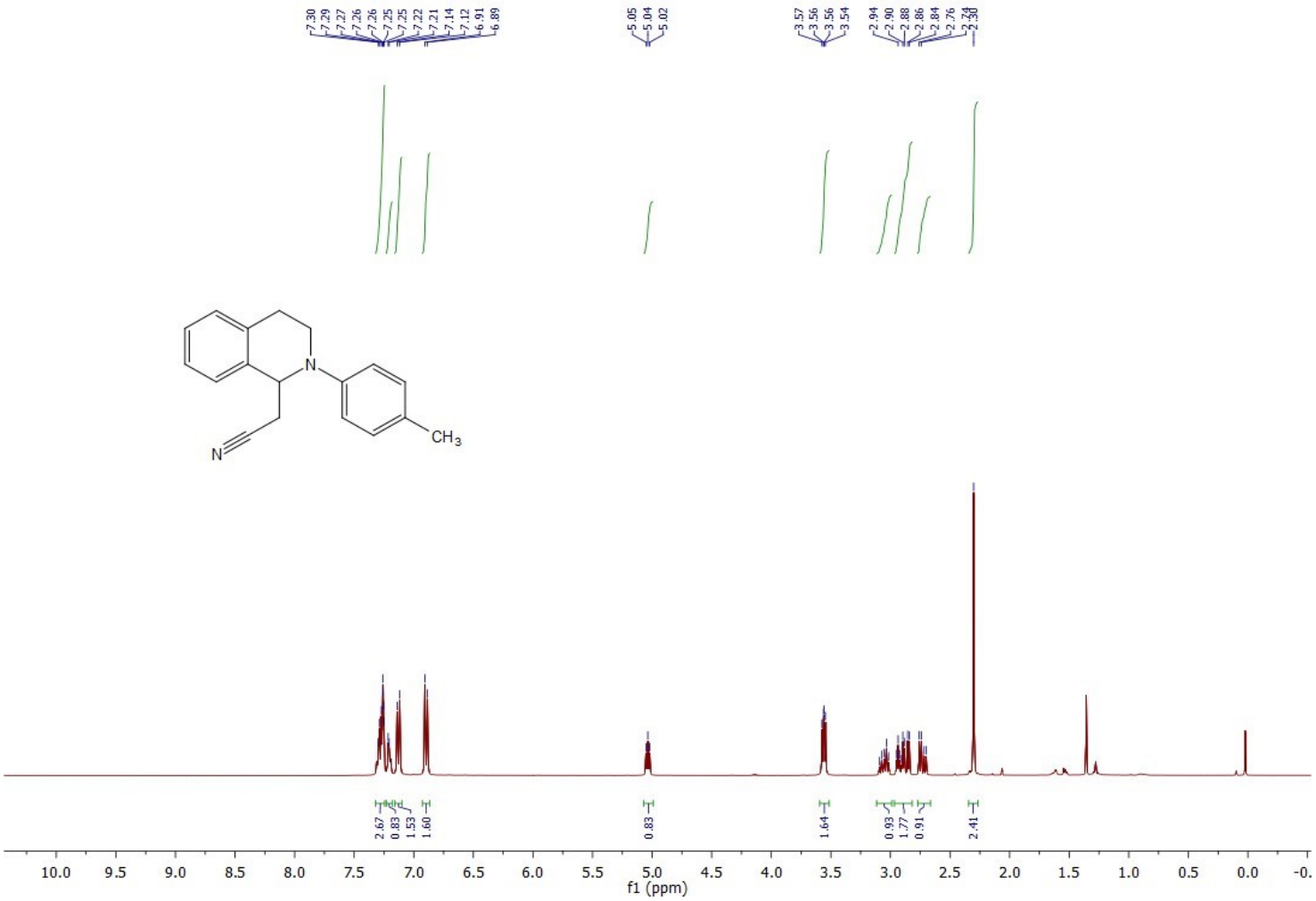
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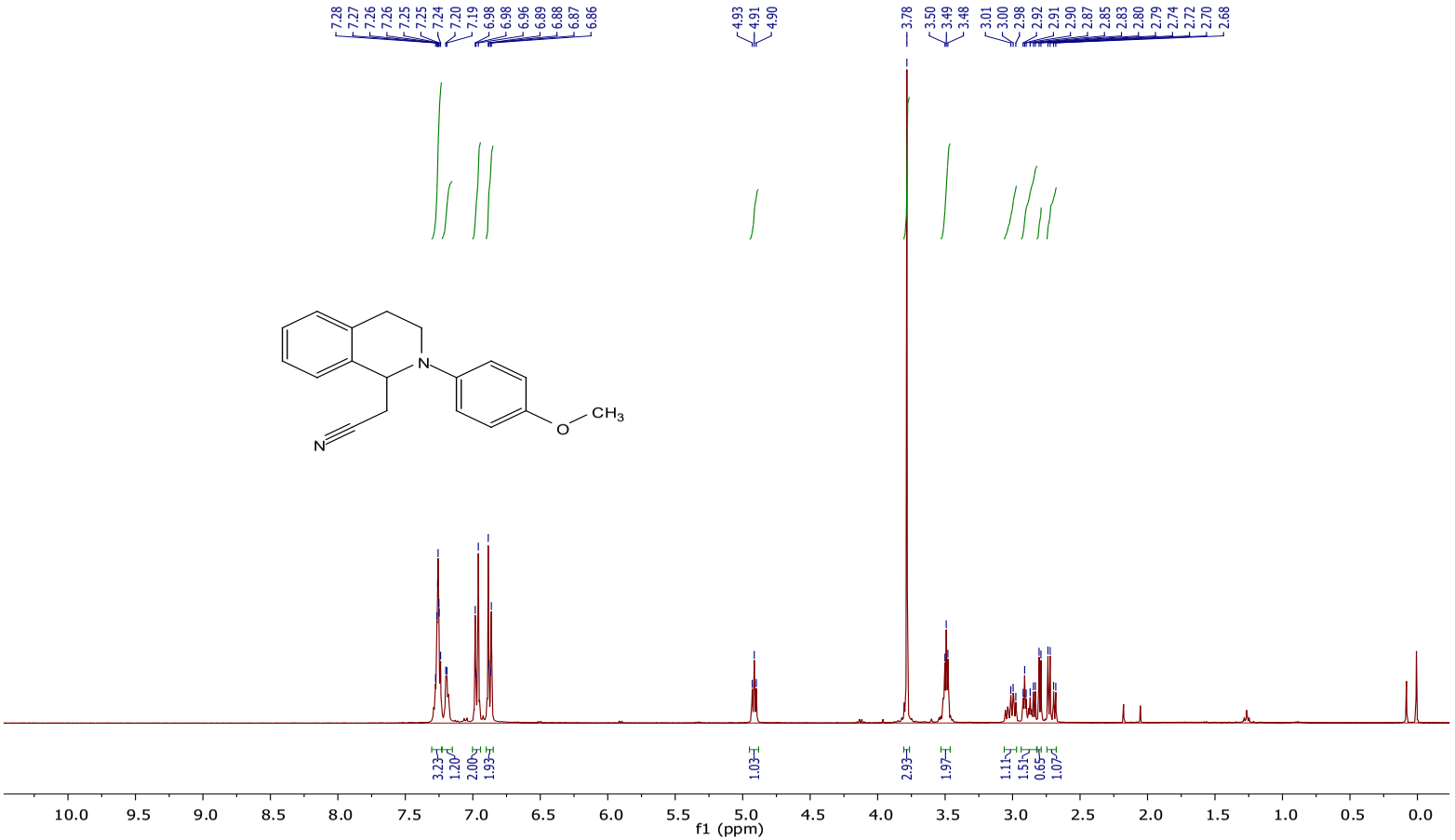
-0.
f1 (ppm)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6.89
6.88
6.87
6.86
4.93
4.91
4.90
3.78
3.50
3.49
3.48
3.01
3.00
2.98
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2.91
2.90
2.87
2.85
2.83
2.80
2.79
2.74
2.72
2.70
2.68
N
O
CH3
N
3.23
1.20
2.00
1.93
1.03
2.93
1.97
1.11
1.51
0.65
1.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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4.5
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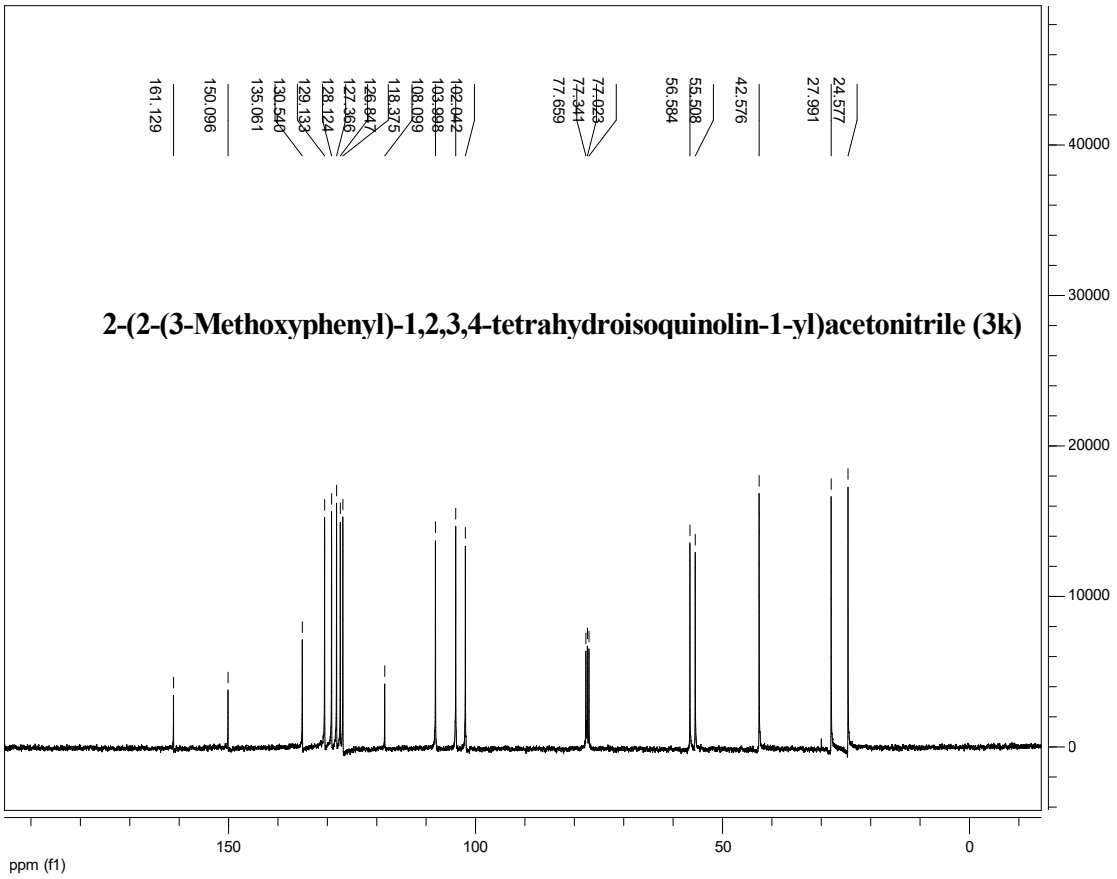
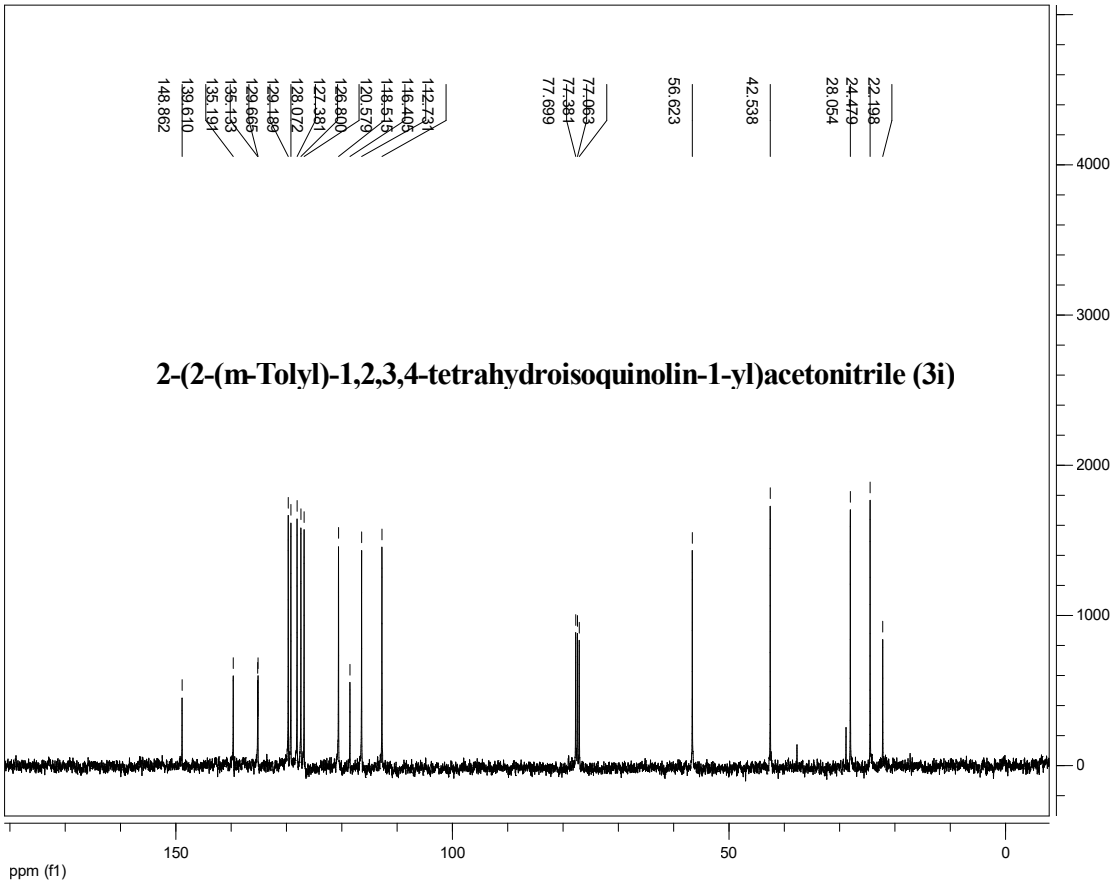
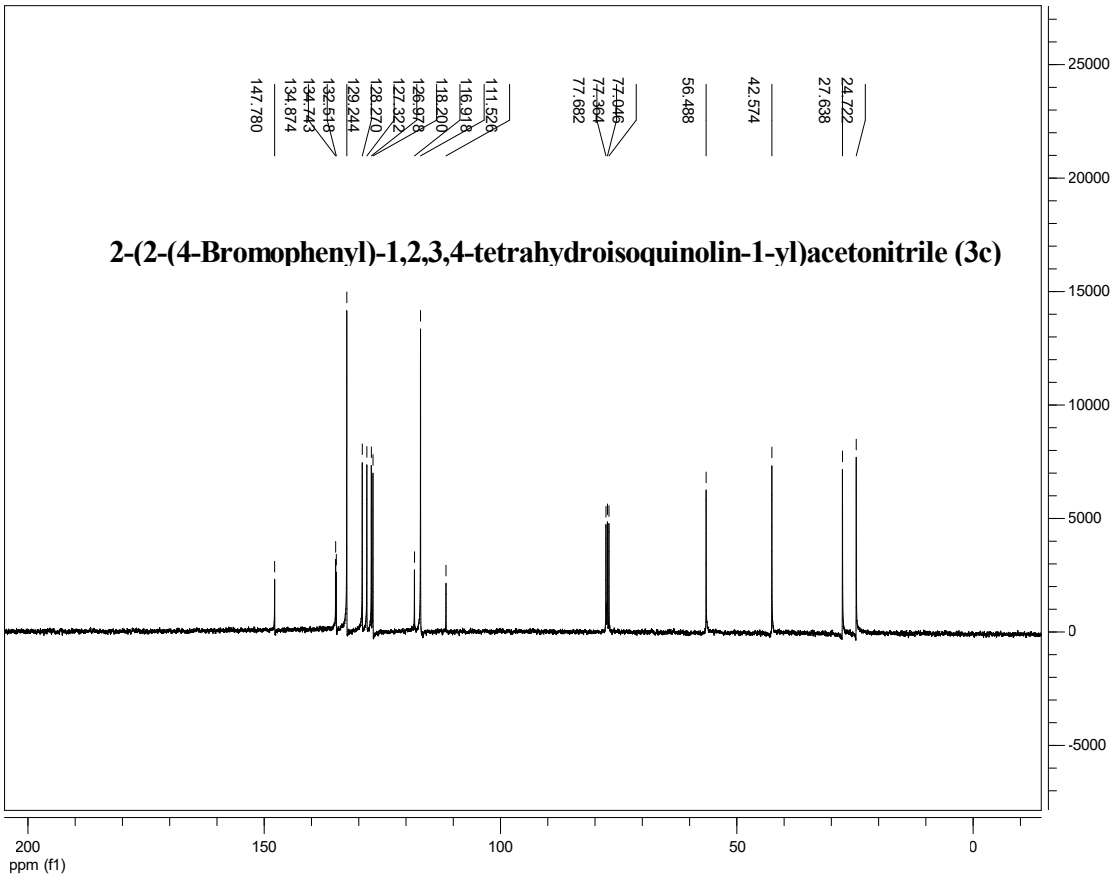
f1 (ppm)



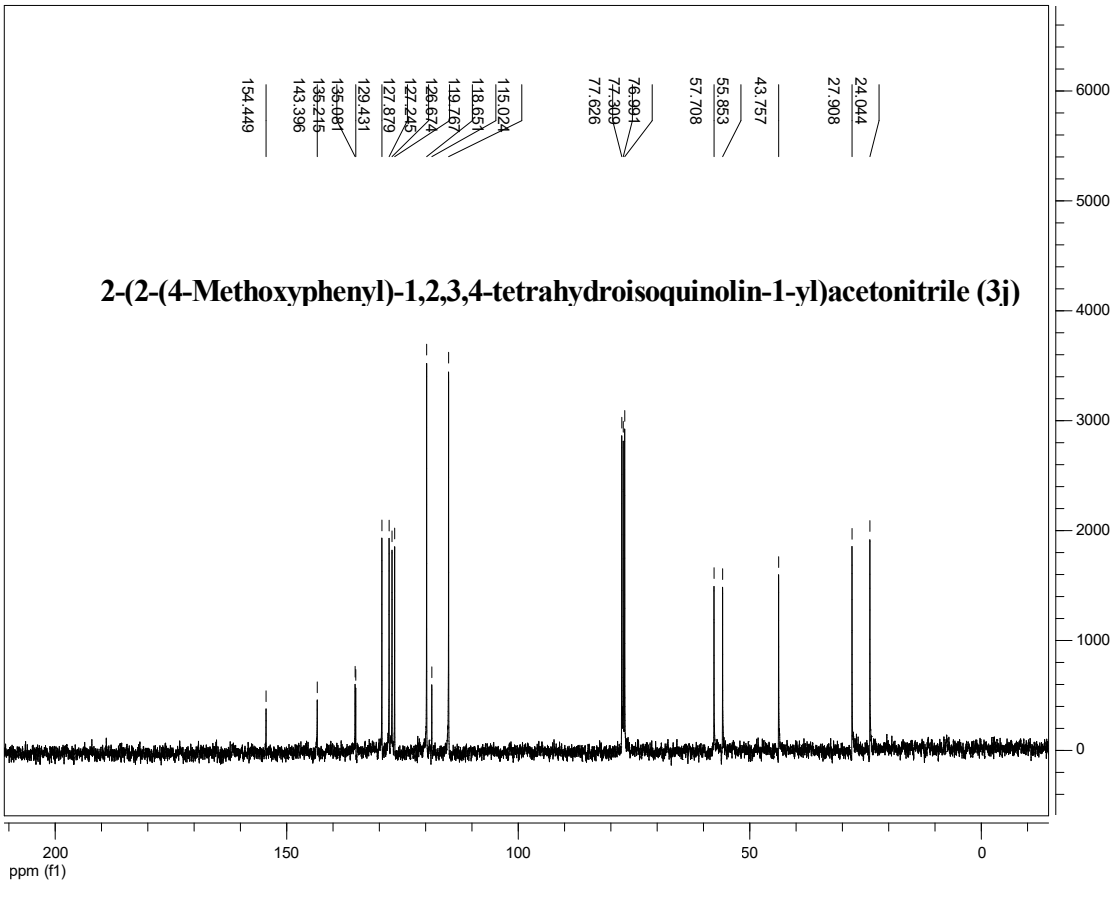
2-(2-(3-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3k)



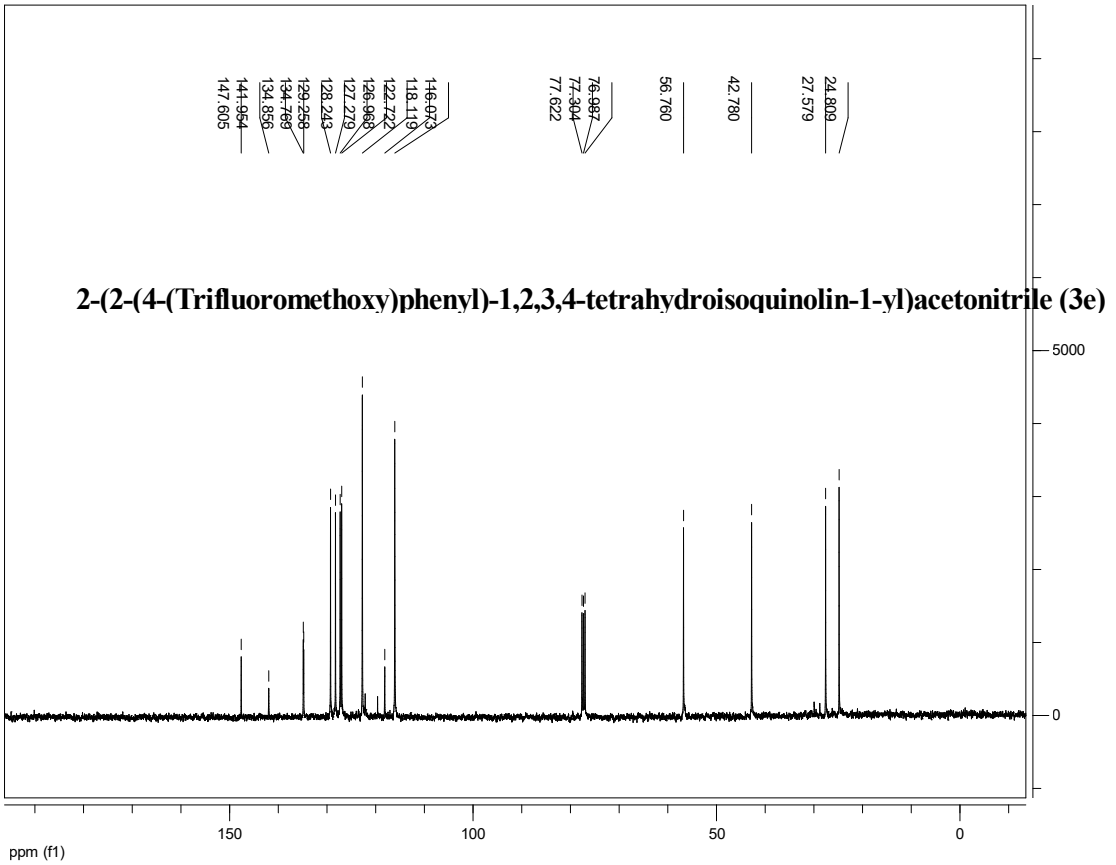
2-(2-(m-Tolyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3i)



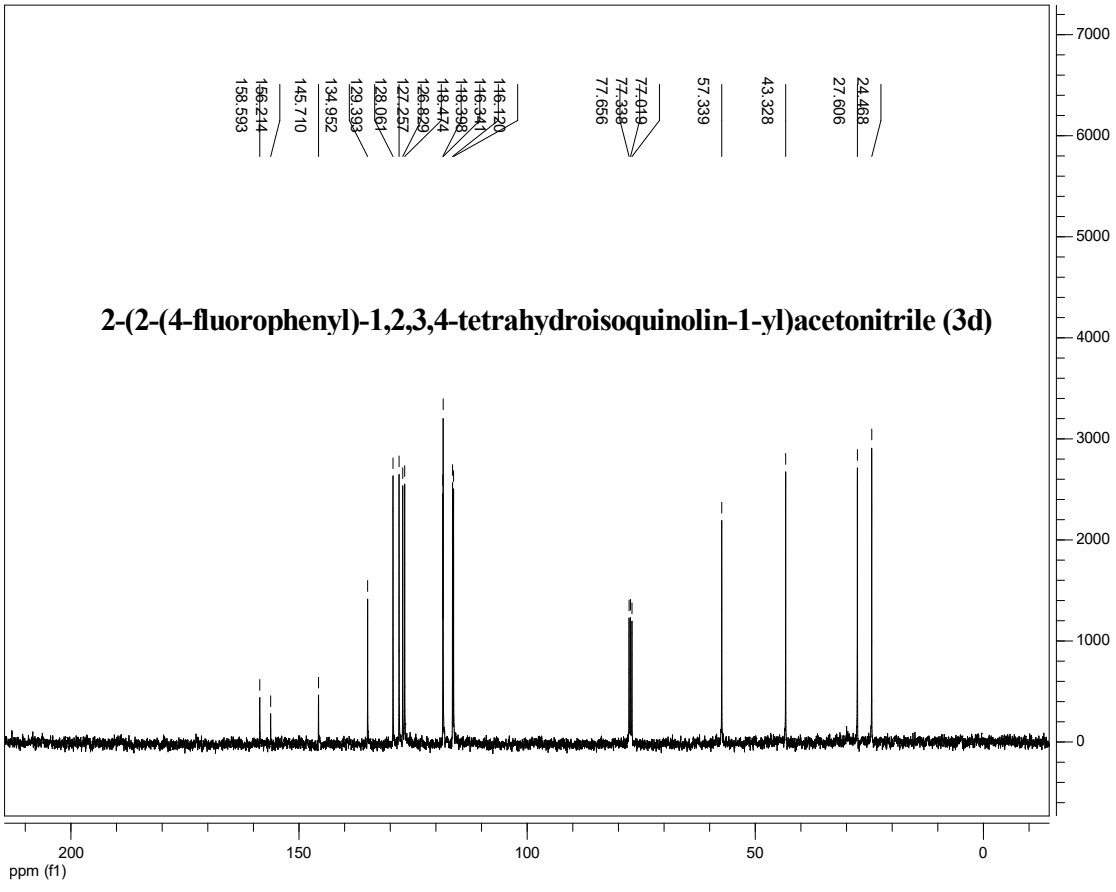
2-(2-(4-Bromophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3c)



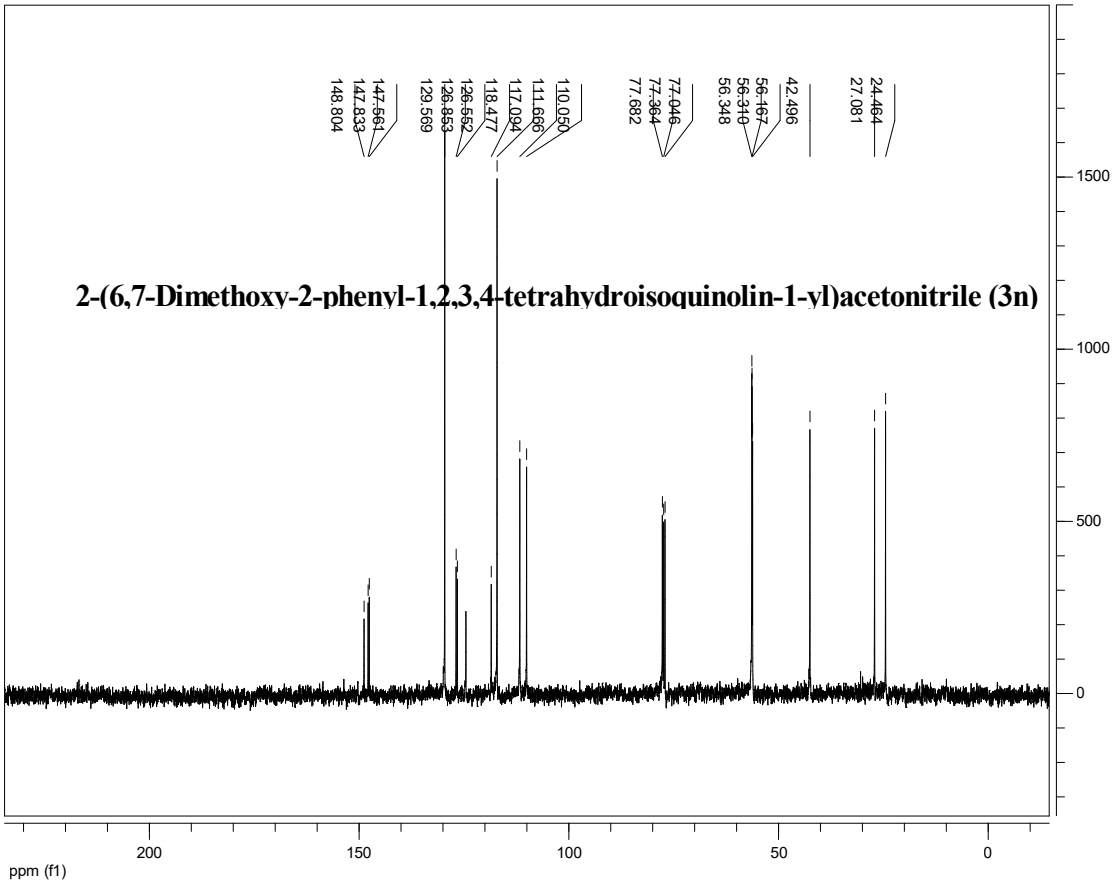
2-(2-(4-Methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3j)



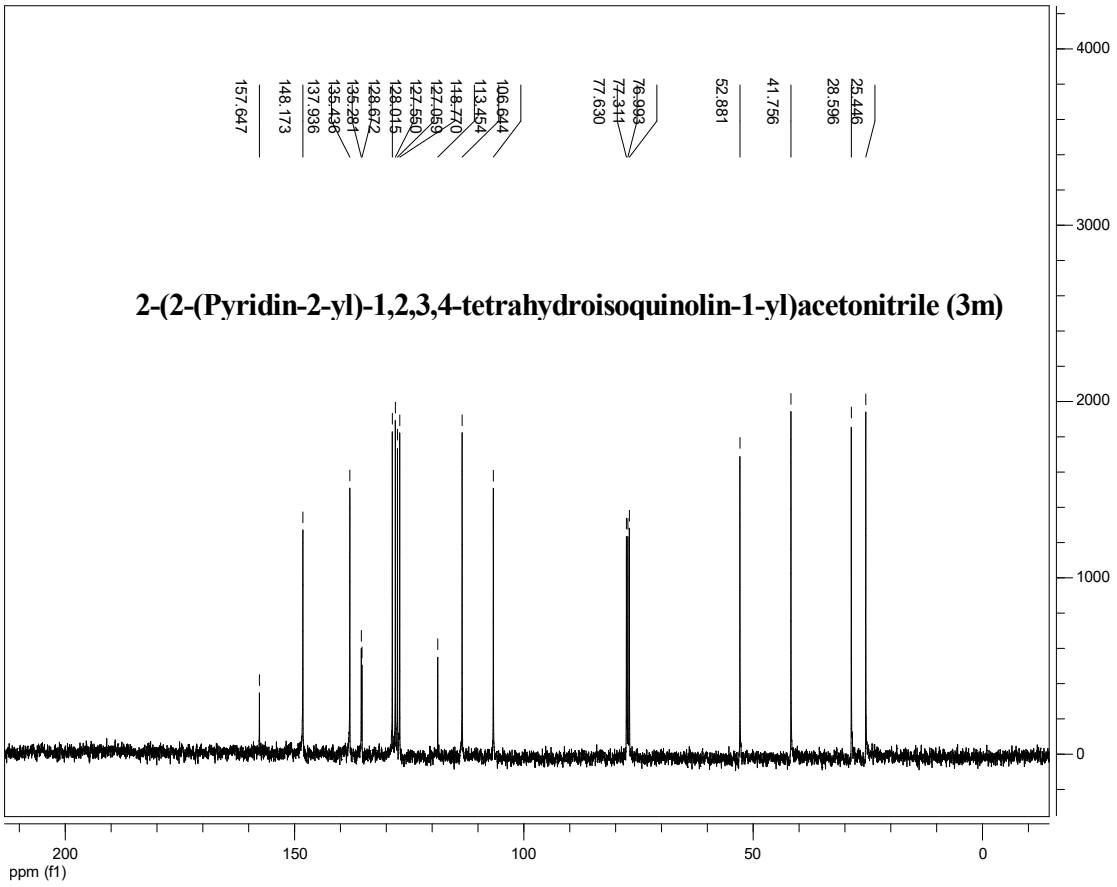
2-(2-(4-(Trifluoromethoxy)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3e)



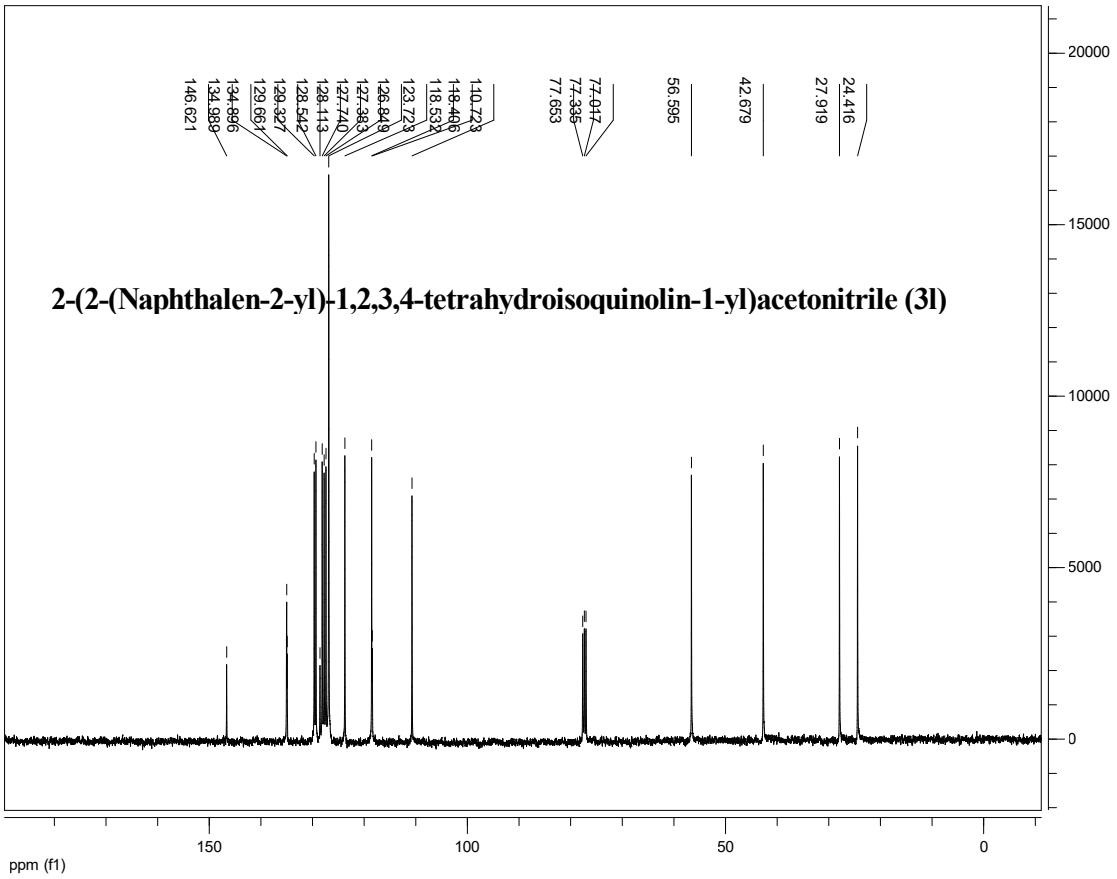
2-(2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3d)



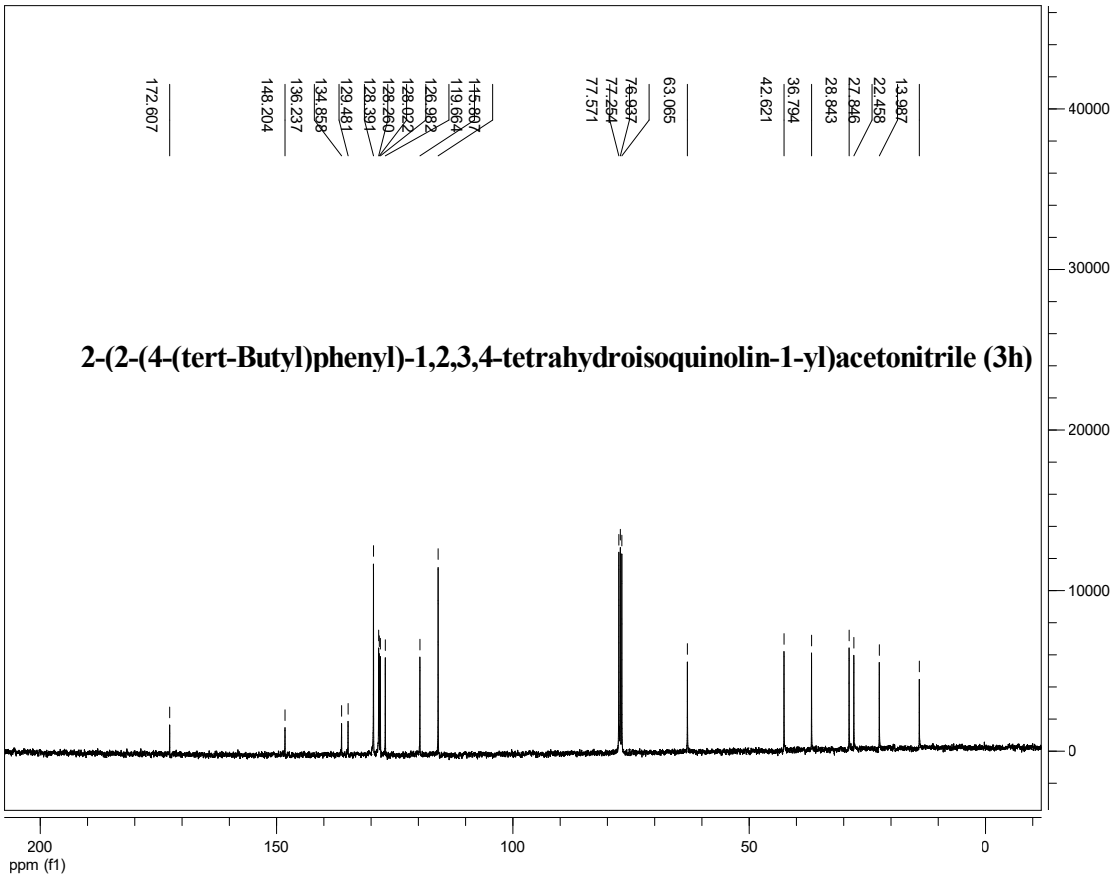
2-(6,7-Dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3n)



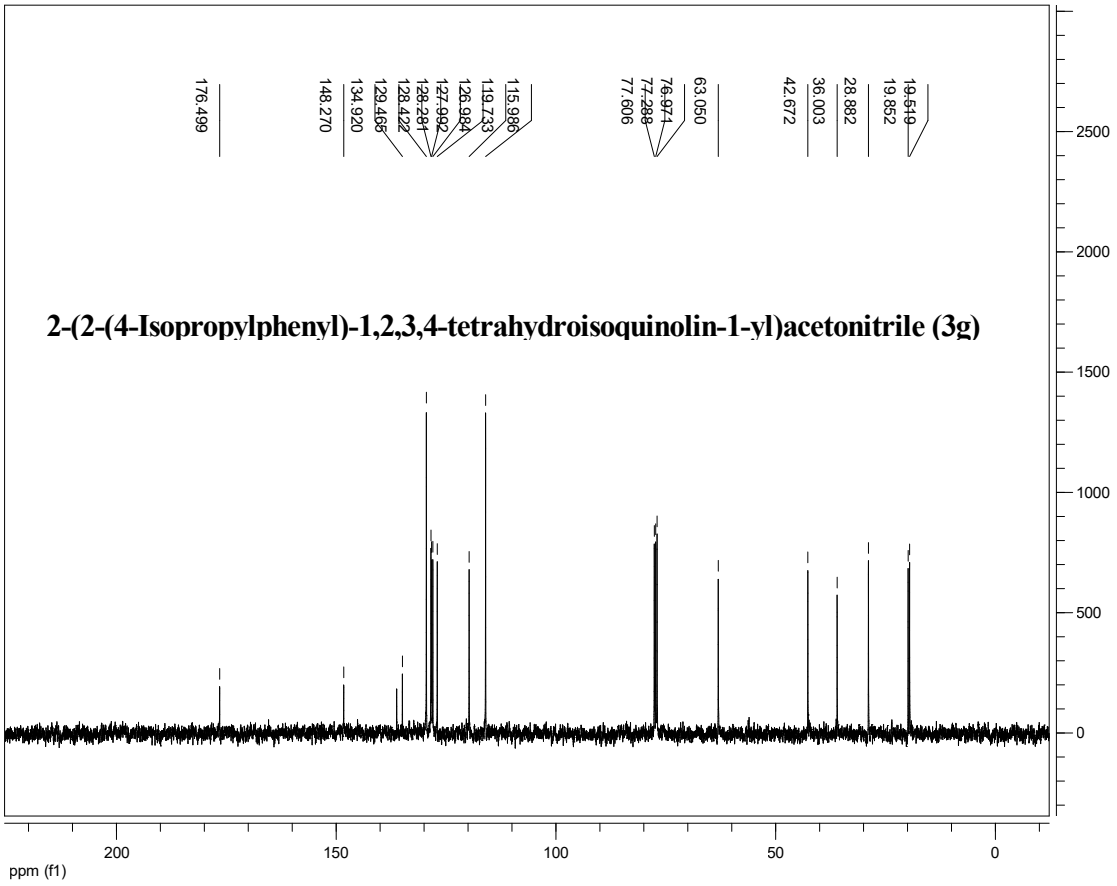
2-(2-(Pyridin-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3m)



2-(2-(Naphthalen-2-yl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3l)



2-(2-(4-(tert-Butyl)phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3h)



2-(2-(4-Isopropylphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (3g)