Electronic Supplementary Material (ESI) for RSC Advances.

Mild and Highly Efficient Metal-Free Oxidative α-Cyanation of *N*-Acyl/Sulfonyl Tetrahydroisoquinolines

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Supporting Information

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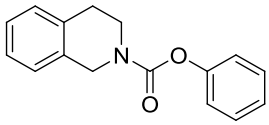
General Information: All reagents were used as received. Acetonitrile was distilled on phosphorus pentoxide. ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker Avance 400 Ultrashield NMR spectrometers. Chemical shifts (δ) were given in parts per million (ppm) and were measured downfield from internal tetramethylsilane. High-resolution mass spectrometry (HRMS) data were obtained on an FTICR-MS instrument (Ionspec 7.0 T). The melting points were determined on an X-4 microscope melting point apparatus and are uncorrected. Conversion was monitored by thin layer chromatography (TLC). Flash column chromatography was performed over silica gel (100-200 mesh). 2,2,6,6-tetramethylpiperidine *N*-oxide fluoroborate salt ($T^{+}BF_4^{-}$) was synthesized with a described procedure previously.[S1]

Characterization of starting materials

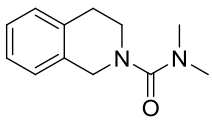
To a solution of tetrahydroisoquinoline (THIQ, 1mmol, 1 equiv.) in CH_2Cl_2 (20 mL) was added triethylamine (0.17 mL, 1.2 equiv.). The mixture was cooled to 0 ºC, and acyl chloride or anhydride (1.2 equiv.) was added slowly. The mixture was stirred 10 min at 0 ºC and then 1 h at rt. The solution was washed with water and brine, then dried over $MgSO_4$ and concentrated. The crude product was purified by flash column chromatography (elution: PE:EA = 5:1), and **1** was obtained in the yield of 75-99%. Characterization of non-previously reported compounds is given.

phenyl 3,4-dihydroisoquinoline-2(1*H*)-carboxylate (1d)



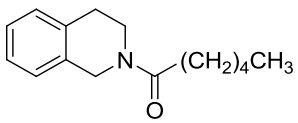
White solid, Mp: 90-91 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.35 (t, J = 6.8 Hz, 2H), 7.29 – 7.05 (m, 7H), 4.82 and 4.69 (s, 2H), 3.93 – 3.71 (m, 2H), 3.02 – 2.83 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 154.0, 151.5, 134.6, 134.4, 133.3, 132.9, 129.4, 129.0, 128.7, 126.8, 126.6, 126.5, 126.3, 125.4, 121.9, 46.3, 46.0, 42.4, 41.7, 29.2, 28.8. HRMS (ESI) calcd for $C_{14}H_{18}NO_2$ $[M+H]^{+}$ 234.1489, found 234.1489.

***N*,*N*-dimethyl-3,4-dihydroisoquinoline-2(1*H*)-carboxamide (1f)**



Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 – 7.05 (m, 4H), 4.40 (s, 2H), 3.47 (t, J = 6.0 Hz, 2H), 2.90 (t, J = 6.0 Hz, 2H), 2.86 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 134.6, 134.0, 128.9, 126.4, 126.3, 126.1, 48.8, 44.8, 38.5, 28.7. HRMS (ESI) calcd for $C_{12}H_{17}N_2O$ $[M+H]^{+}$ 205.1335, found 205.1340.

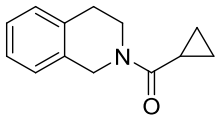
1-(3,4-dihydroisoquinolin-2(1*H*)-yl)hexan-1-one (1h)



Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.25 – 7.02 (m, 4H), 4.72 and 4.60 (s, 2H), 3.81 and 3.66 (t, J = 6.0 Hz, 2H), 2.88 and 2.82 (t, J = 6.0, 2H), 2.45 – 2.34 (m, 2H), 1.75

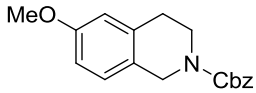
– 1.58 (m, 2H), 1.43 – 1.27 (m, 4H), 0.98 – 0.82 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 172.2, 172.1, 135.1, 134.1, 133.6, 132.7, 128.9, 128.3, 126.8, 126.6, 126.5, 126.4, 126.3, 126.0, 47.4, 44.2, 43.2, 39.6, 33.8, 33.6, 31.7, 31.6, 29.6, 28.5, 25.0, 24.9, 22.5, 14.0. HRMS (ESI) calcd for $C_{15}H_{22}NO$ $[M+H]^+$ 232.1696, found 232.1698.

cyclopropyl(3,4-dihydroisoquinolin-2(1*H*)-yl)methanone (1m)



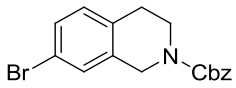
Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.35 – 7.14 (m, 4H), 4.95 and 4.82 (s, 2H), 4.05 – 3.85 (m, 2H), 3.11 – 2.85 (m, 2H), 2.02 – 1.85 (m, 2H), 1.16 – 1.05 (m, 2H), 0.98 – 0.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 172.4, 135.3, 134.5, 133.9, 132.9, 128.9, 128.2, 126.7, 126.6, 126.4, 126.2, 47.2, 44.7, 43.3, 40.1, 29.6, 28.7, 12.6, 11.6, 11.4, 8.4, 7.6, 7.4. HRMS (ESI) calcd for $C_{13}H_{16}NO$ $[M+H]^+$ 202.1226, found 202.1230.

benzyl 6-methoxy-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (1p)



Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.27 (m, 5H), 7.00 (d, J = 12.8 Hz, 1H), 6.74 (d, J = 8.4 Hz, 1H), 6.70 – 6.63 (m, 1H), 5.17 (s, 2H), 4.58 (s, 2H), 3.77 (s, 3H), 3.74 – 3.64 (m, 2H), 2.88 – 2.75 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 158.2, 155.6, 136.8, 135.9, 128.5, 128.1, 128.0, 127.4, 127.2, 125.7, 125.2, 113.4, 112.6, 67.2, 55.3, 45.3, 41.6, 41.4, 29.3, 29.1. HRMS (ESI) calcd for $C_{17}H_{26}NO_3$ $[M+H]^+$ 292.1907, found 292.1903.

benzyl 7-bromo-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (1s)



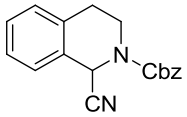
Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.44 – 7.33 (m, 5H), 7.33 – 7.22 (m, 2H), 7.03 (d, J = 8.0 Hz, 1H), 5.22 (s, 2H), 4.64 and 4.62 (s, 2H), 3.78 – 3.69 (m, 2H), 2.88 – 2.76 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 155.4, 136.6, 135.6, 135.2, 133.6, 133.4, 130.5, 130.3, 129.6, 129.5, 129.2, 129.1, 128.6, 128.4, 128.2, 128.1, 120.1, 119.9, 67.4, 45.4, 41.5, 41.2, 28.6, 28.3. HRMS (ESI) calcd for $C_{15}H_{21}N_2O_4$ $[M+H]^+$ 293.1496, found 293.1498.

General procedure to synthesize 2a-t and 4

An oven dried Schlenk tube was charged with substrate **1** or **3** (0.4 mmol) and $T^+BF_4^-$ (146 mg, 0.6 mmol). The tube was evacuated and backfilled with nitrogen (this process was repeated three times) and then CH_3CN (2 mL), TMSCN (75 μL, 0.6 mmol) and AcOH (23 μL, 0.4 mmol) were added successively by syringe. The reaction mixture was stirred at rt for 2-16 h. Upon consumption of the starting material, the reaction mixture was concentrated in vacuo to give the crude product, which was purified by flash column chromatography (elution: PE:EA = 5:1) to give the desired compound **2** or **4**.

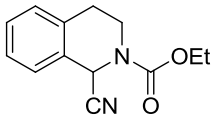
Characterization of products

benzyl 1-cyano-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2a)



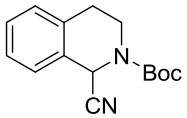
Yield: 97%. White solid, Mp: 88-89 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.47 – 7.34 (m, 5H), 7.33 – 7.26 (m, 3H), 7.24 – 7.15 (m, 1H), 6.13 and 5.97 (s, 1H), 5.28 – 5.19 (m, 2H), 4.33 and 4.17 (d, J = 12.4 Hz, 1H), 3.49 and 3.38 (t, J = 10.0 Hz, 1H), 3.04 – 2.91 (m, 1H), 2.88 and 2.84 (t, J = 3.6, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 154.9, 154.2, 135.7, 135.6, 134.5, 134.2, 129.6, 129.4, 129.0, 128.7, 128.5, 128.3, 128.2, 127.9, 127.9, 127.3, 127.1, 127.1, 118.0, 68.5, 68.3, 46.2, 40.1, 39.6, 29.7, 28.1, 28.0. HRMS (ESI) calcd for $C_{18}H_{17}N_2O_2$ $[M+H]^+$ 293.1285, found 293.1286.

ethyl 1-cyano-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2b)



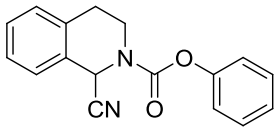
Yield: 93%. White solid, Mp: 93-94 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.34 – 7.26 (m, 3H), 7.24 – 7.17 (m, 1H), 6.12 and 5.98 (s, 1H), 4.38 – 4.08 (m, 3H), 3.44 and 3.35 (t, J = 8.8 Hz, 1H), 2.99 and 2.95 (dd, J = 10.8, 5.6 Hz, 1H), 2.87 and 2.83 (t, J = 3.6 Hz, 1H), 1.39 – 1.27 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 155.0, 154.3, 134.5, 134.3, 129.6, 129.4, 128.9, 128.5, 128.0, 127.3, 127.1, 118.1, 62.7, 46.2, 46.1, 39.9, 39.3, 28.0, 14.6. HRMS (ESI) calcd for $C_{13}H_{15}N_2O_2$ $[M+H]^+$ 231.1128, found 231.1123.

tert-butyl 1-cyano-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2c)



Yield 78%. White solid, Mp: 88-89 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.37 – 7.29 (m, 3H), 7.26 – 7.19 (m, 1H), 6.10 and 5.87 (s, 1H), 4.37 – 3.98 (m, 1H), 3.52 – 3.18 (m, 1H), 2.98 and 2.94 (dd, J = 10.8, 5.6 Hz, 1H), 2.86 and 2.82 (t, J = 3.6 Hz, 1H), 1.55 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 153.9, 153.3, 134.6, 134.5, 129.4, 128.8, 128.1, 127.2, 127.1, 118.2, 82.2, 81.8, 46.6, 45.6, 40.1, 38.7, 28.3, 28.1. HRMS (ESI) calcd for $C_{15}H_{19}N_2O_2$ $[M+H]^+$ 259.1441, found 259.1435.

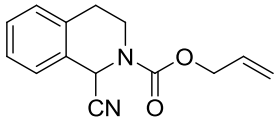
phenyl 1-cyano-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2d)



Yield 89%. White solid, Mp: 119-120 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.43 (t, J = 7.6 Hz, 2H), 7.40 – 7.33 (m, 3H), 7.33 – 7.26 (m, 2H), 7.21 (t, J = 8.4 Hz, 2H), 6.25 and 6.21 (s, 1H), 4.45 – 4.35 (m, 1H), 3.76 – 3.45 (m, 1H), 3.19 – 2.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$,

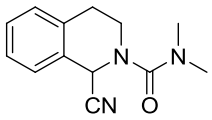
rotomers seen) δ 153.5, 152.8, 150.9, 150.7, 134.4, 134.1, 129.7, 129.5, 129.4, 129.2, 128.3, 127.7, 127.5, 127.2, 127.1, 126.1, 126.0, 121.7, 121.6, 117.8, 46.7, 46.3, 40.7, 39.9, 28.1, 27.9. HRMS (ESI) calcd for $C_{17}H_{15}N_2O_2$ $[M+H]^+$ 279.1128, found 279.1123.

allyl 1-cyano-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2e)



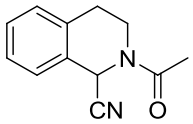
Yield: 93%. Colorless Oil. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.34 – 7.24 (m, 3H), 7.24 – 7.16 (m, 1H), 6.18 – 5.88 (m, 2H), 5.42 – 5.30 (m, 1H), 5.26 (d, J = 10.4 Hz, 1H), 4.80 – 4.62 (m, 2H), 4.30 and 4.17 (d, J = 11.6 Hz, 1H), 3.47 and 3.34 (t, J = 9.2 Hz, 1H), 2.98 and 2.94 (dd, J = 10.6, 5.6 Hz, 1H), 2.90 – 2.80 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 154.7, 153.9, 134.5, 134.8, 132.2, 129.6, 129.4, 129.0, 128.4, 128.0, 127.3, 127.1, 118.6, 118.4, 118.0, 67.2, 46.2, 40.0, 39.5, 28.0. HRMS (ESI) calcd for $C_{14}H_{15}N_2O_2$ $[M+H]^+$ 243.1128, found 243.1133.

1-cyano-*N*,*N*-dimethyl-3,4-dihydroisoquinoline-2(1*H*)-carboxamide (2f)



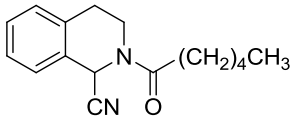
Yield:81%. White solid, Mp: 120-121 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.33 – 7.24 (m, 3H), 7.22 – 7.17 (m, 1H), 5.58 (s, 1H), 3.82 – 3.74 (m, 1H), 3.48 and 3.45 (dd, J = 12.0, 4.0 Hz, 1H), 3.16 – 3.05 (m, 1H), 2.93 (s, 6H), 2.92 – 2.80 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 134.1, 129.5, 129.2, 128.7, 127.3, 127.1, 118.8, 48.6, 43.5, 38.3, 28.0. HRMS (ESI) calcd for $C_{13}H_{16}N_3O$ $[M+H]^+$ 230.1288, found 230.1287.

2-acetyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2g)



Yield: 86%. White solid, Mp: 107-108 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.37 – 7.26 (m, 3H), 7.25 – 7.18 (m, 1H), 6.45 (s, 1H), 3.95 and 3.92 (t, J = 4.8 Hz, 1H), 3.70 and 3.66 (dd, J = 8.8, 5.2 Hz, 1H), 3.04 – 2.90 (m, 2H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 169.8, 169.2, 133.9, 129.7, 129.2, 129.0, 128.5, 127.6, 127.3, 126.9, 117.9, 117.5, 48.3, 43.5, 42.2, 37.5, 28. 5, 27.6, 21.8, 21.4. HRMS (ESI) calcd for $C_{12}H_{13}N_2O$ $[M+H]^+$ 201.1022, found 201.1024.

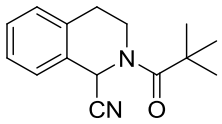
2-hexanoyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2h)



Yield: 87%. Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.36 – 7.26 (m, 3H), 7.24 – 7.18 (m, 1H), 6.48 (s, 1H), 4.00 and 3.96 (t, J = 4.4 Hz, 1H), 3.67 and 3.65 (dd, J = 13.6, 5.6 Hz, 1H), 3.03 – 2.93 (m, 2H), 2.53 – 2.30 (m, 2H), 1.77 – 1.61 (m, 2H), 1.39 – 1.30 (m, 4H),

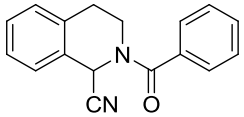
0.91 (t, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 172.4, 135.0, 133.9, 129.8, 129.2, 129.0, 128.7, 127.9, 127.6, 127.4, 127.0, 118.1, 117.6, 47.7, 43.6, 41.5, 37.6, 33.6, 33.4, 31.5, 31.3, 28.6, 27.7, 24.6, 22.5, 14.0. HRMS (ESI) calcd for $C_{16}H_{21}N_2O$ $[M+H]^+$ 257.1648, found 257.1654.

2-pivaloyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2i)



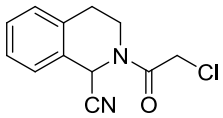
Yield 83%. White solid, Mp: 128-129 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.34 – 7.21 (m, 3H), 7.18 – 7.12 (m, 1H), 6.35 (s, 1H), 4.40 and 4.37 (d, J = 4.4 Hz, 1H), 3.62 – 3.49 (m, 1H), 3.02 and 2.98 (dd, J = 11.6, 5.2 Hz, 1H), 2.88 – 2.78 (m, 1H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 133.6, 129.3, 128.8, 128.6, 127.4, 127.3, 118.3, 45.7, 42.2, 39.0, 28.5, 28.0. HRMS (ESI) calcd for $C_{15}H_{19}N_2O$ $[M+H]^+$ 243.1492, found 243.1496.

2-benzoyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2j)



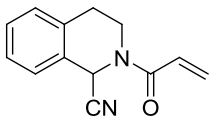
Yield 86%. White solid, Mp: 95-96 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.53 – 7.43 (m, 5H), 7.42 – 7.27 (m, 3H), 7.25 – 7.19 (m, 1H), 6.58 – 5.41 (m, 1H), 5.05 – 3.88 (m, 1H), 3.66 – 3.42 (m, 1H), 3.13 – 2.97 (m, 1H), 2.92 – 2.78 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 171.0, 134.0, 133.7, 131.0, 129.6, 129.1, 128.9, 128.1, 127.5, 127.2, 117.9, 44.6, 43.3, 28.6. HRMS (ESI) calcd for $C_{17}H_{15}N_2O$ $[M+H]^+$ 263.1179, found 263.1184.

2-(2-chloroacetyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2k)



Yield 83%. White solid, Mp: 109-110 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.30 – 7.20 (m, 3H), 7.17 – 7.11 (m, 1H), 6.28 (s, 1H), 4.11 (dd, J = 32.7, 12.5 Hz, 2H), 4.00 – 3.92 (m, 1H), 3.67 and 3.64 (dd, J = 10.4, 3.6 Hz, 1H), 3.07 and 3.03 (dd, J = 10.8, 5.4 Hz, 1H), 2.92 and 2.88 (t, J = 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 166.1, 133.6, 129.3, 129.2, 127.7, 127.6, 127.3, 117.4, 44.2, 42.1, 40.8, 28.4. HRMS (ESI) calcd for $C_{12}H_{12}ClN_2O$ $[M+H]^+$ 235.0633, found 235.0635.

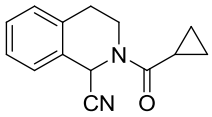
2-acryloyl-1,2,3,4-tetrahydronaphthalene-1-carbonitrile (2l)



Yield: 82%. White solid, Mp: 104-105 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.21 (m, 3H), 7.19 – 7.09 (m, 1H), 6.57 and 6.53 (d, J = 10.4 Hz, 1H), 6.40 and 6.36 (s, 2H), 5.78 (d, J = 10.4 Hz, 1H), 4.11 – 3.91 (m, 1H), 3.75 – 3.54 (m, 1H), 3.00 – 2.83 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 133.9, 130.5, 129.2, 129.1, 128.5, 127.6, 127.4, 126.3, 117.7, 44.0, 41.8, 28.6.

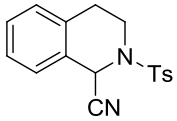
HRMS (ESI) calcd for $C_{13}H_{13}N_2O$ $[M+H]^+$ 213.1022, found 213.1018.

2-(cyclopropanecarbonyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2m)



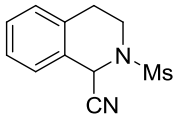
Yield: 86%. White solid, Mp: 117-118 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.40 – 7.28 (m, 3H), 7.23 (d, J = 6.8 Hz, 1H), 6.37 and 6.11 (s, 1H), 4.68 – 4.15 (m, 1H), 3.91 – 3.66 (m, 1H), 3.14 – 2.82 (m, 2H), 1.90 – 1.78 (m, 1H), 1.28 – 1.01 (m, 2H), 1.00 – 0.78 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 173.0, 134.3, 129.7, 129.2, 129.0, 128.9, 127.5, 127.3, 127.0, 118.0, 47.4, 44.1, 41.6, 38.1, 28.6, 27.8, 11.3, 8.6, 8.1. HRMS (ESI) calcd for $C_{14}H_{15}N_2O$ $[M+H]^+$ 227.1179, found 227.1184.

2-tosyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2n)



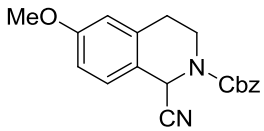
Yield: >99%. White solid, Mp: 114-115 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.80 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.4 Hz, 2H), 7.32 – 7.22 (m, 3H), 7.18 – 7.13 (m, 1H), 5.89 (s, 1H), 4.11 – 4.03 (m, 1H), 3.23 – 3.04 (m, 2H), 2.87 – 2.79 (m, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 134.3, 133.1, 130.0, 129.7, 129.2, 128.0, 127.8, 127.4, 127.0, 116.1, 47.1, 40.8, 28.1, 21.7. HRMS (ESI) calcd for $C_{17}H_{17}N_2O_2S$ $[M+H]^+$ 313.1005, found 313.1009.

2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2o)



Yield: >99%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.31 – 7.21 (m, 3H), 7.17 (d, J = 7.2 Hz, 1H), 5.80 (s, 1H), 4.00 and 3.97 (d, J = 6.0 Hz, 1H), 3.33 and 3.30 (dd, J = 12.4, 3.6 Hz, 1H), 3.11 and 3.07 (dd, J = 11.6, 6.0 Hz, 1H), 3.02 (s, 3H), 2.90 – 2.82 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.1, 129.8, 129.3, 127.5, 127.3, 127.1, 117.0, 47.1, 40.7, 37.7, 28.3. HRMS (ESI) calcd for $C_{10}H_{12}NO_2S$ $[M-CN]^+$ 210.0583, found 210.0584.

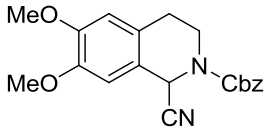
benzyl 1-cyano-6-methoxy-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2p)



Yield: 83%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.45 – 7.28 (m, 5H), 7.23 – 7.14 (m, 1H), 6.81 (dd, J = 8.4, 2.0 Hz, 1H), 6.74 – 6.65 (m, 1H), 6.06 and 5.92 (s, 1H), 5.21 (s, 2H), 4.27 and 4.11 (d, J = 12.4 Hz, 1H), 3.77 (s, 3H), 3.47 and 3.36 (t, J = 10.0 Hz, 1H), 2.99 – 2.86 (m, 1H), 2.83 and 2.79 (t, J = 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 159.8, 154.9, 154.2, 136.0, 135.8, 135.7, 128.7, 128.5, 128.3, 128.3, 120.5, 120.0, 118.2, 114.1, 113.6, 113.5, 68.4, 68.3, 55.5, 45.9, 40.0, 39.6, 28.4, 28.3. HRMS (ESI) calcd for $C_{19}H_{19}N_2O_3$

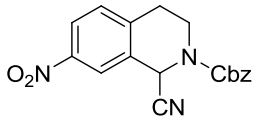
$[M+H]^+$ 323.1390, found 323.1396.

benzyl 1-cyano-6,7-dimethoxy-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2q)



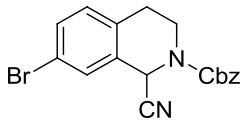
Yield 86%. White solid, Mp: 129-130 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.49 – 7.31 (m, 5H), 6.73 (d, *J* = 16.4 Hz, 1H), 6.64 (s, 1H), 6.06 and 5.90 (s, 1H), 5.22 (s, 2H), 4.36 and 4.21 (d, *J* = 12.4 Hz, 1H), 3.87 (s, 6H), 3.43 and 3.33 (t, *J* = 10.4 Hz, 1H), 2.99 – 2.83 (m, 1H), 2.81 – 2.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 154.9, 154.1, 149.4, 148.4, 135.8, 128.7, 128.5, 128.4, 128.2, 126.7, 126.4, 119.8, 119.2, 118.1, 111.5, 109.2, 109.1, 68.5, 68.3, 56.1, 56.0, 46.0, 40.0, 39.5, 27.6. HRMS (ESI) calcd for $C_{20}H_{21}N_2O_4$ $[M+H]^+$ 353.1496, found 353.1499.

benzyl 1-cyano-7-nitro-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2r)



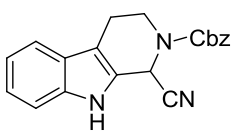
Yield 97%. White solid, Mp: 156-157 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 8.23 (d, *J* = 20.0 Hz, 1H), 8.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.47 – 7.30 (m, 6H), 6.31 and 6.12 (s, 1H), 5.25 (s, 2H), 4.43 and 4.29 (d, *J* = 10.8 Hz, 1H), 3.50 and 3.38 (t, *J* = 8.4 Hz, 1H), 3.15 – 2.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 154.7, 153.8, 146.9, 142.0, 141.8, 135.4, 135.3, 130.9, 130.7, 130.0, 129.5, 128.8, 128.4, 123.8, 122.6, 116.9, 68.7, 46.0, 39.3, 38.8, 28.3. HRMS (ESI) calcd for $C_{18}H_{16}N_3O_4$ $[M+H]^+$ 338.1135, found 338.1134.

benzyl 7-bromo-1-cyano-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (2s)



Yield >99%. White solid, Mp: 124-125 ºC. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.53 – 7.30 (m, 7H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.11 and 5.94 (s, 1H), 5.22 (s, 2H), 4.34 and 4.19 (d, *J* = 11.6 Hz, 1H), 3.43 and 3.32 (t, *J* = 9.6 Hz, 1H), 2.97 – 2.74 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 154.7, 153. 9, 135.5, 135.4, 133.4, 133.1, 132.1, 131.1, 131.0, 130.2, 129.9, 128.7, 128.5, 128.2, 120.6, 117.3, 68.4, 45.7, 39.7, 39.2, 27.6. HRMS (ESI) calcd for $C_{18}H_{16}BrN_2O_2$ $[M+H]^+$ 371.0390, found 371.0381.

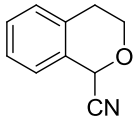
benzyl 1-cyano-3,4-dihydro-1*H*-pyrido[3,4-b]indole-2(9*H*)-carboxylate (2t)



Yield 41%. Pale yellow dope . ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 8.27 and 8.17 (s, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.43 – 7.31 (m, 6H), 7.28 – 7.21 (m, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 6.25

and 6.07 (s, 1H), 5.26 (s, 2H), 4.65 and 4.51 (dd, J = 12.4, 2.8 Hz, 1H), 3.45 – 3.24 (m, 1H), 2.95 – 2.74 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rotomers seen) δ 155.3, 154.2, 136.6, 135.6, 128.7, 128.6, 128.4, 128.2, 126.1, 123.5, 123.0, 120.3, 118.8, 116.4, 111.5, 111.1, 68.6, 43.1, 40.6, 40.2, 21.0, 20.7. HRMS (ESI) calcd for $C_{20}H_{16}N_3O_2$ $[M-H]^-$ 330.1248, found 330.1247.

isochroman-1-carbonitrile (4)

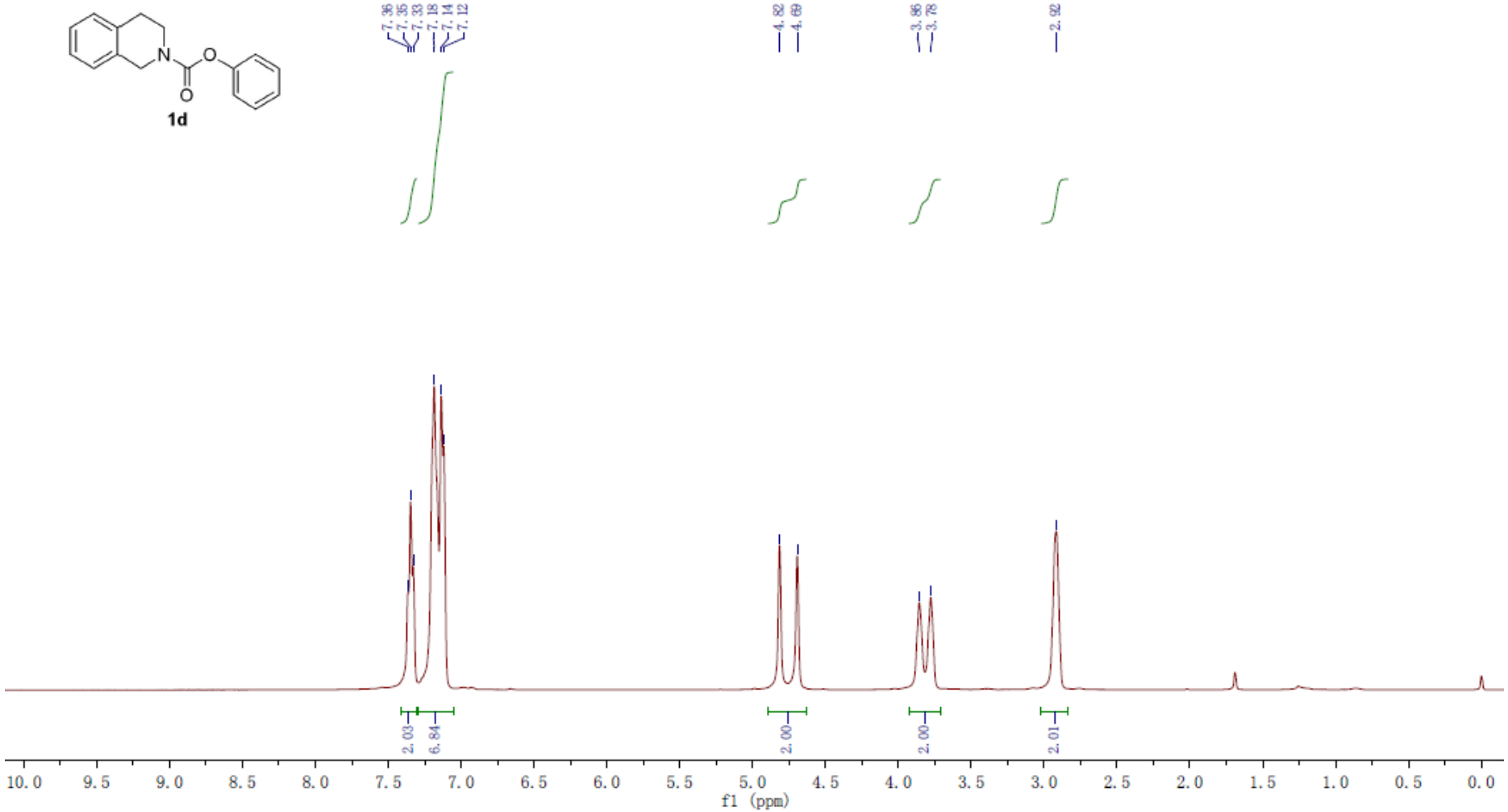


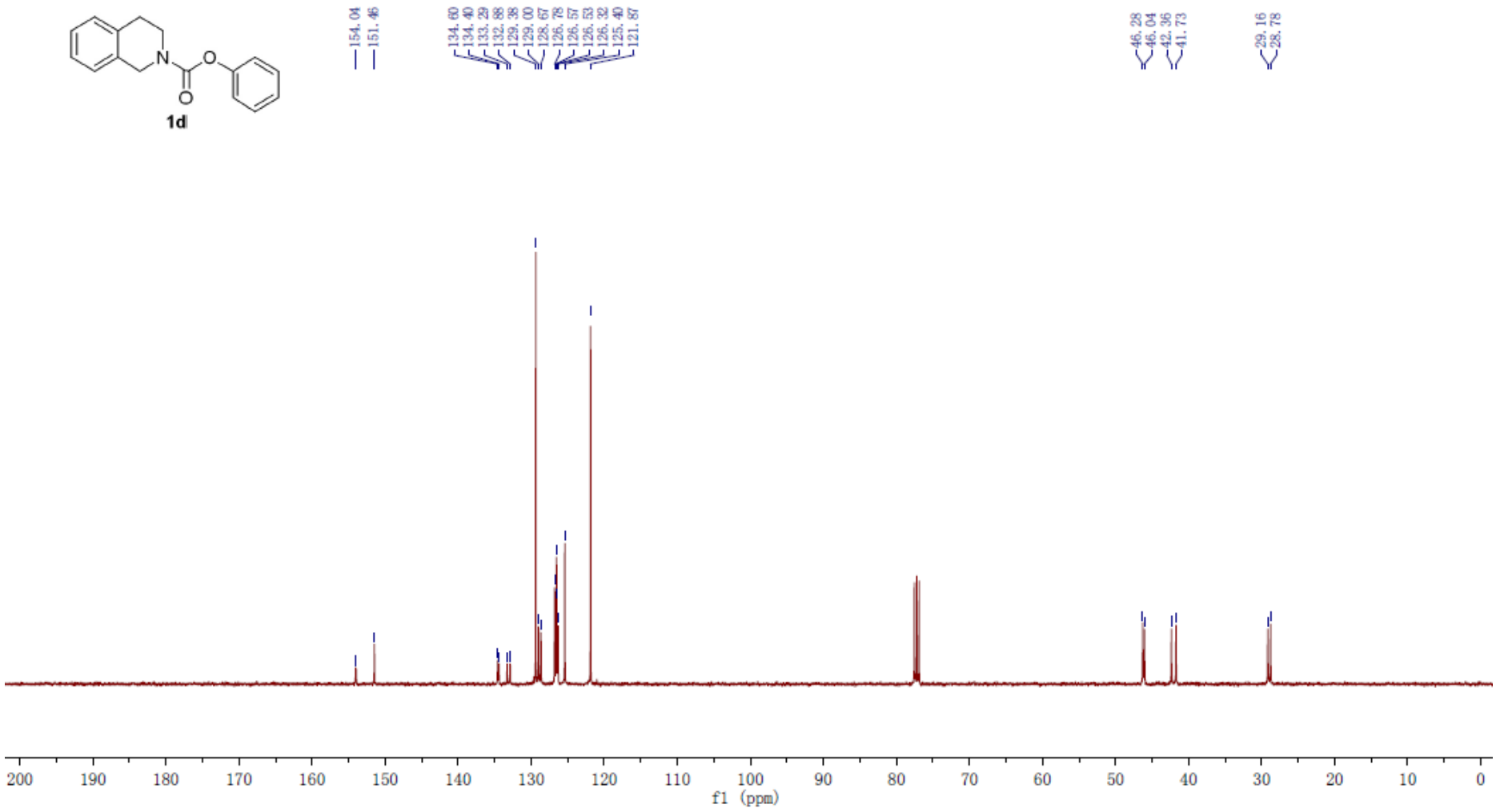
Yield: 79%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, rotomers seen) δ 7.33 – 7.26 (m, 2H), 7.23 – 7.16 (m, 2H), 5.65 (s, 1H), 4.22 – 4.08 (m, 2H), 3.07 and 3.03 (dd, J = 10.0, 6.4 Hz, 1H), 2.79 and 2.75 (t, J = 3.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.0, 129.5, 129.1, 128.7, 127.1, 125.5, 118.1, 65.3, 63.3, 27.2. HRMS (ESI) calcd for $C_{10}H_{10}NO$ $[M+H]^+$ 160.0757, found.160.0757

References

[S1] Richter, H.; Mancheno, O. G. *Eur. J. Org. Chem.* **2010**, 4460.

Copies of ^{1}H NMR and ^{13}C NMR spectra for new compounds

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129.38
129.00
128.67
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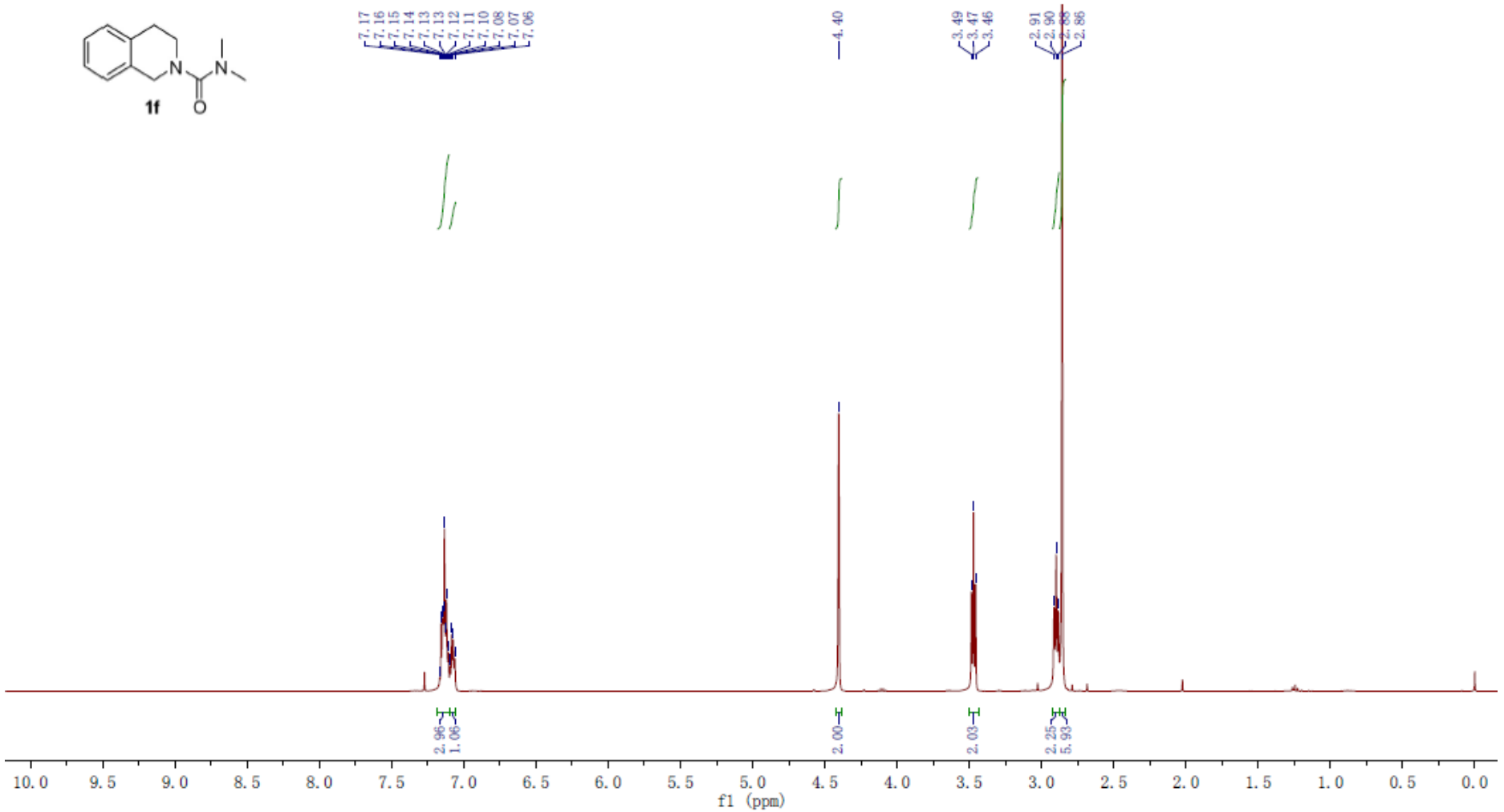
126.53
126.32
125.40
121.87
46.28
46.04
42.36
41.73
29.16
28.78
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.13
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7.12
7.11
7.10
7.08
7.07
7.06
4.40
3.49
3.47
3.46
2.91
2.90
2.88
2.86
2.96
1.06
2.00
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7.5
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6.0
5.5
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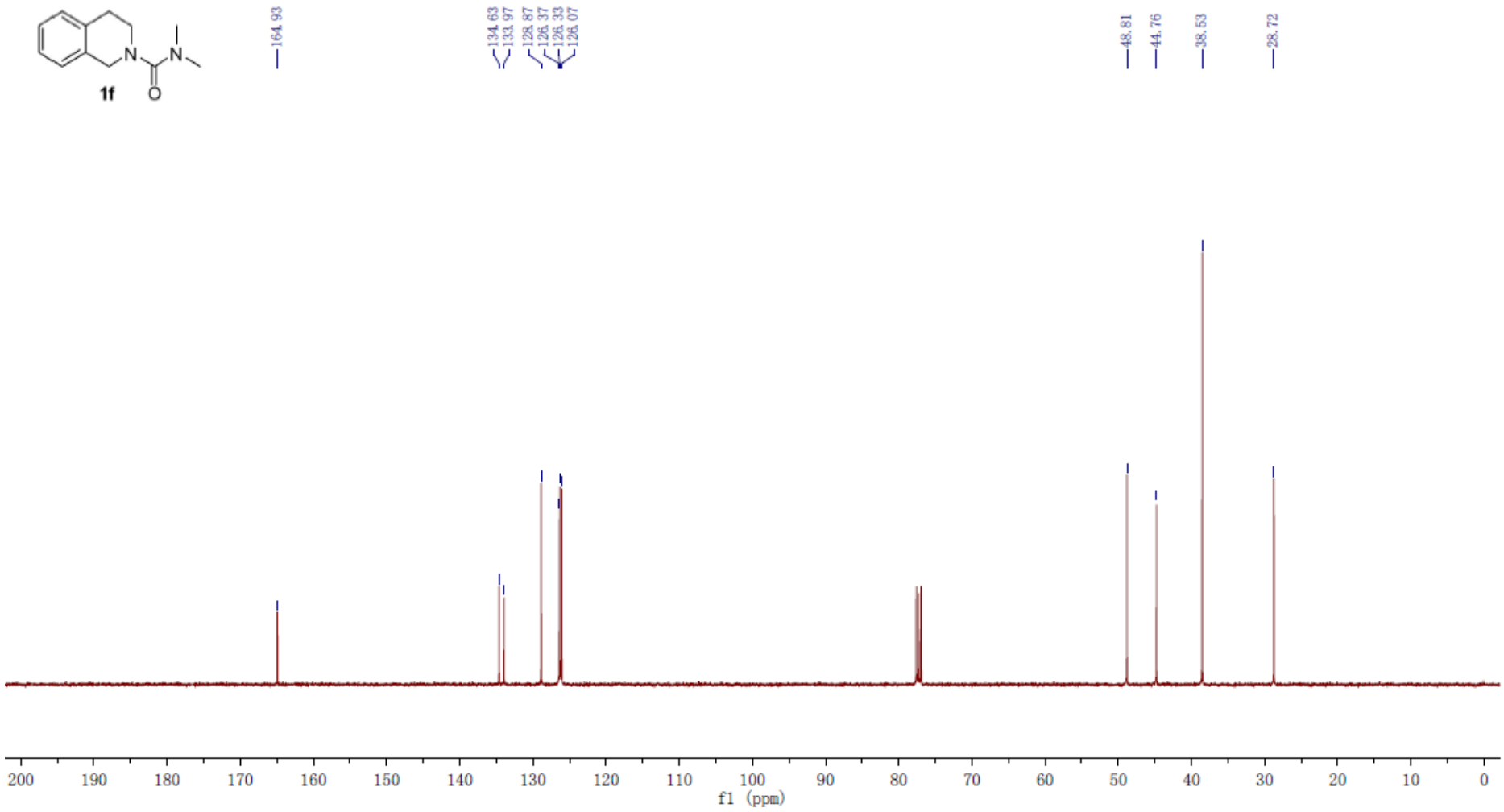
f1 (ppm)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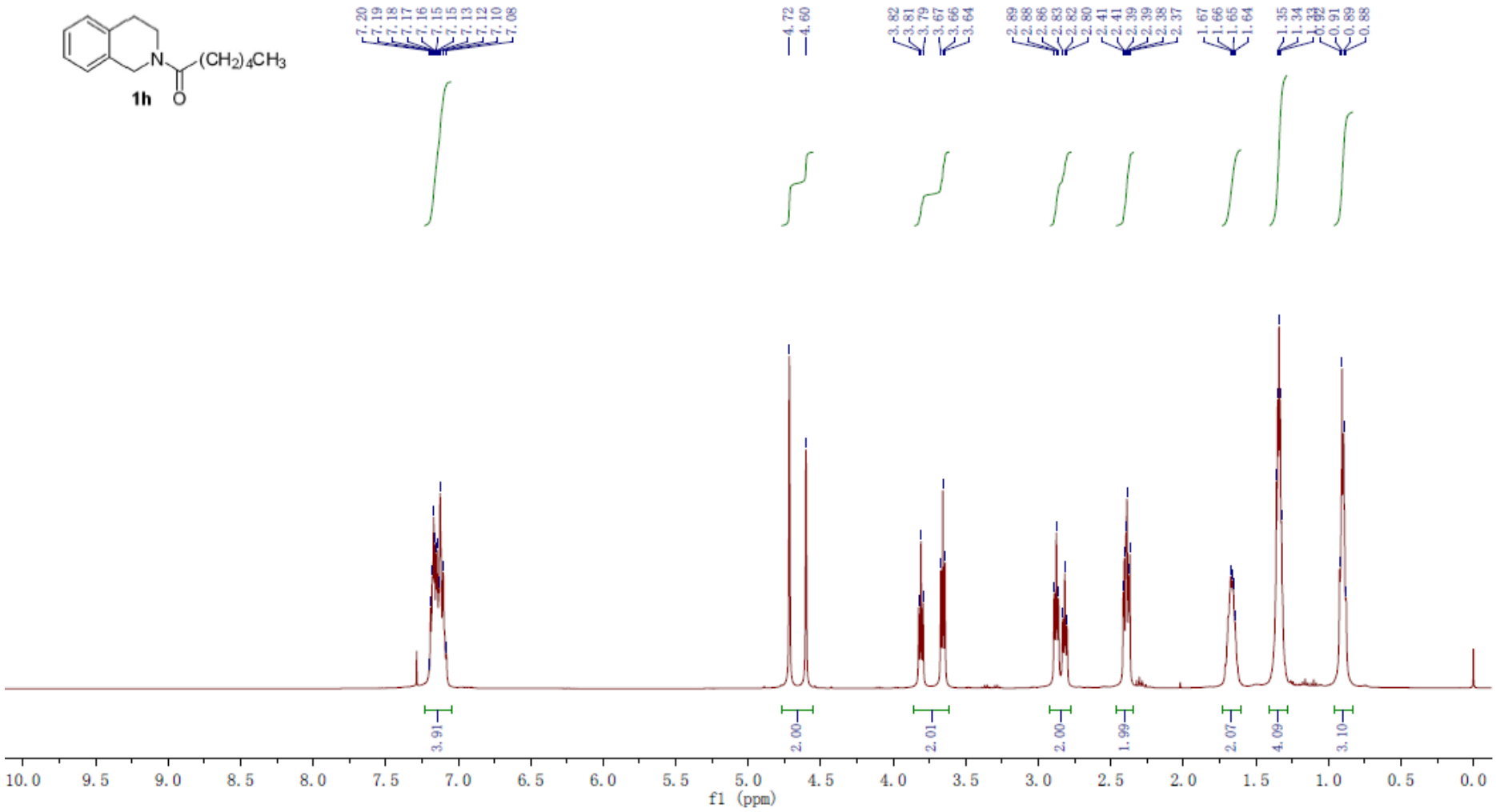
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2.38
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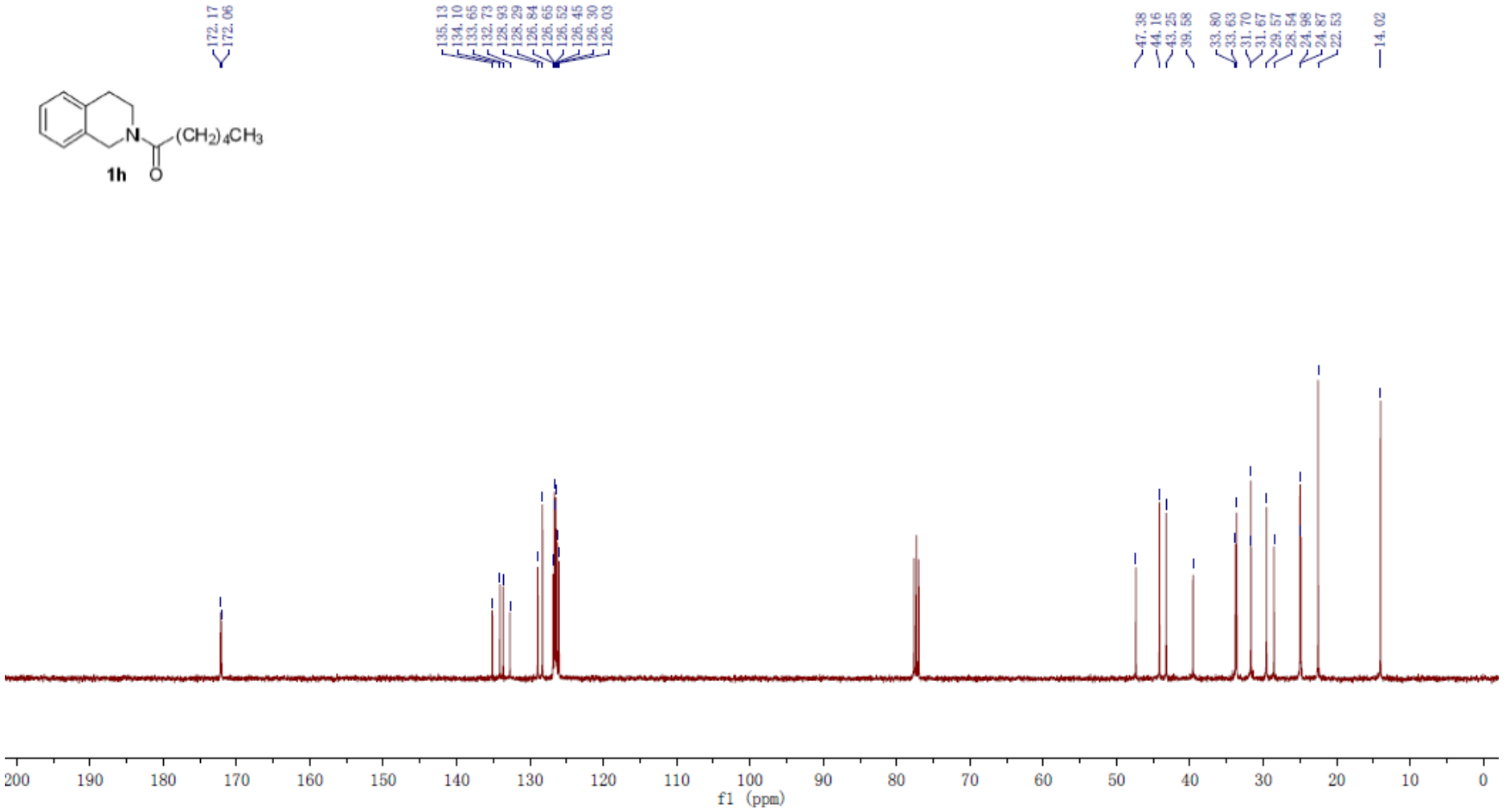
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126.03
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14.02
N
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O
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180
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90
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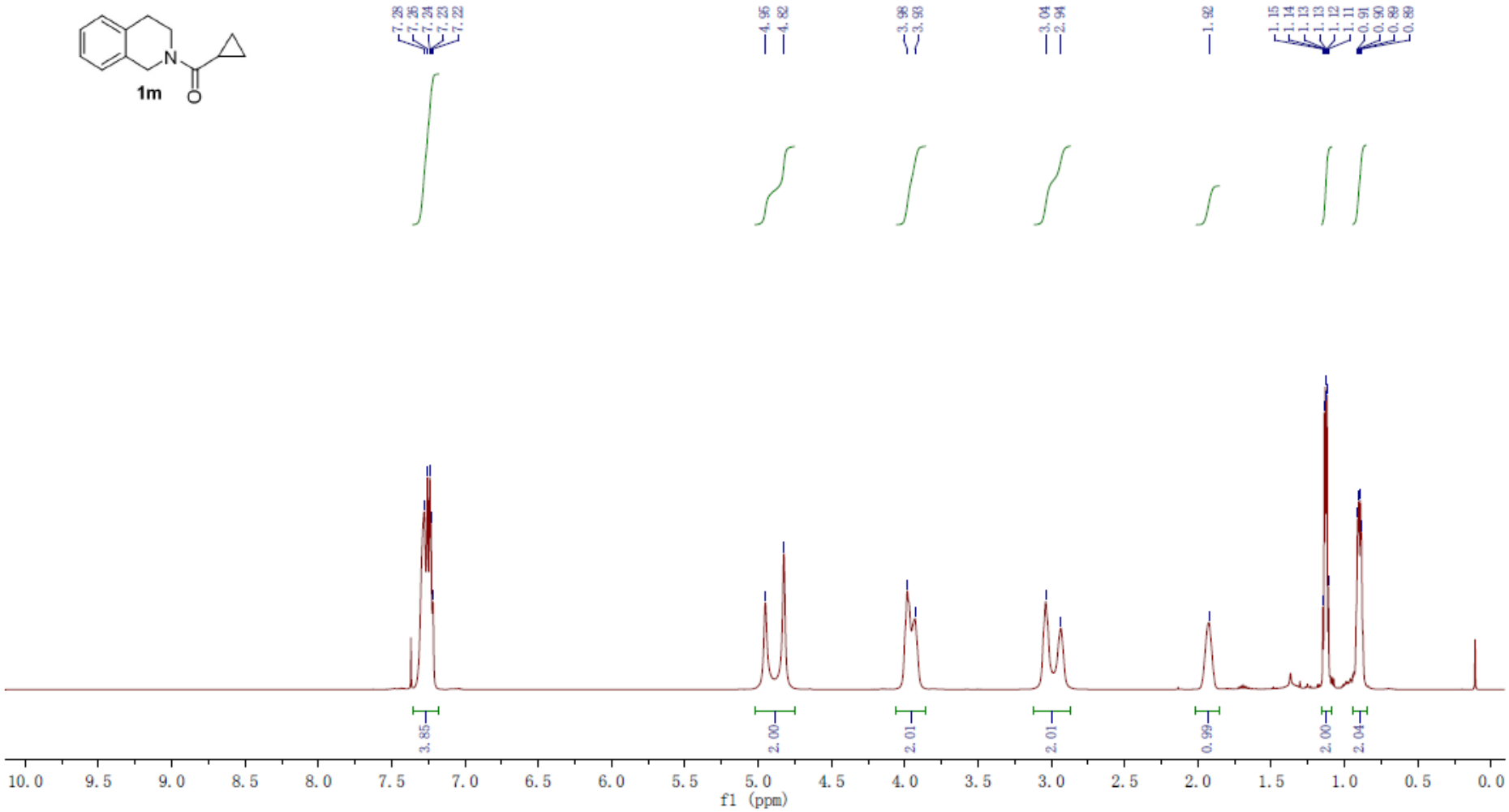
10
0
f1 (ppm)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1.15
1.14
1.13
1.12
1.11
0.91
0.90
0.89
0.89
3.85
2.00
2.01
2.01
0.99
2.00
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6.0
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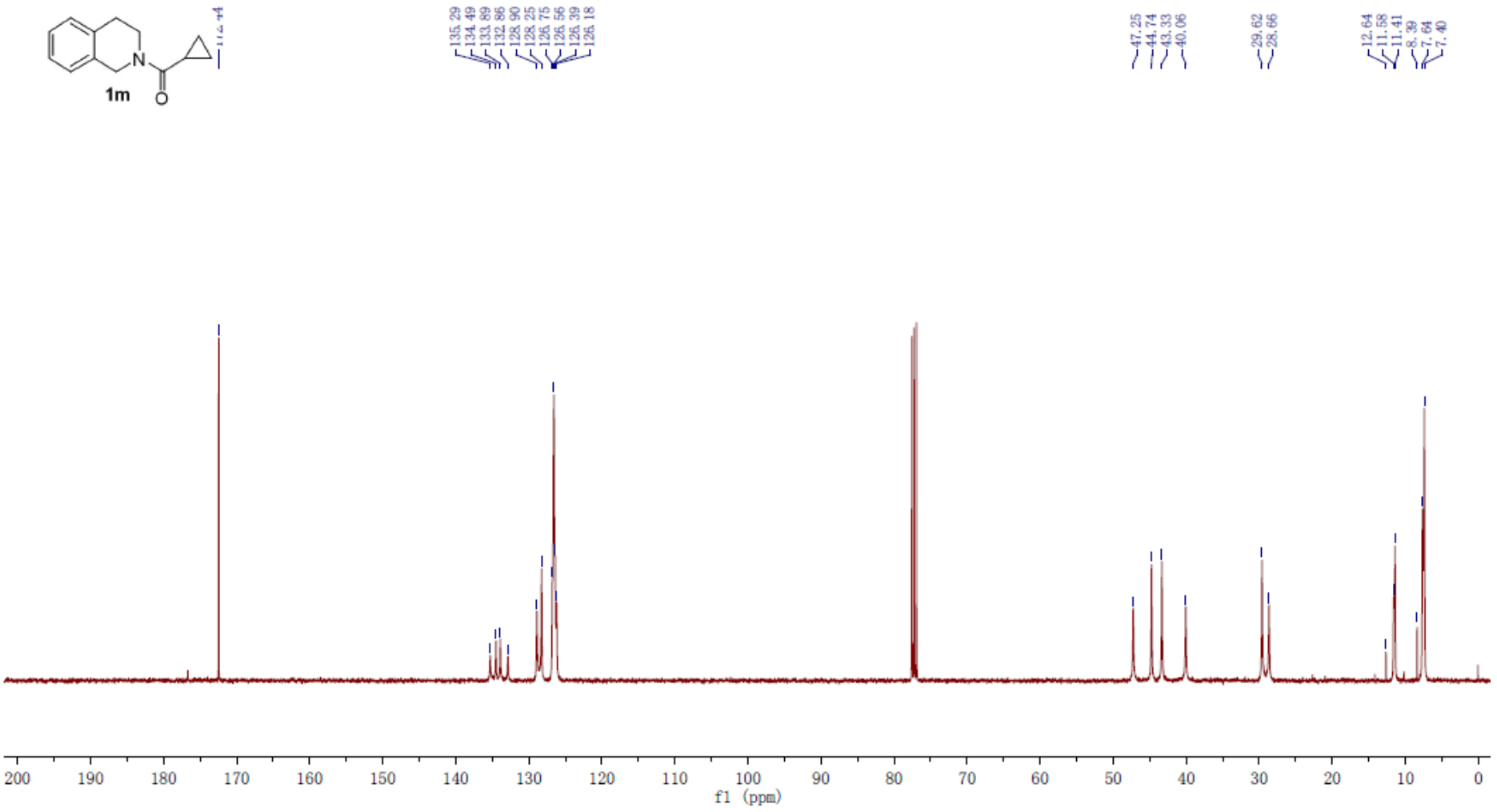
f1 (ppm)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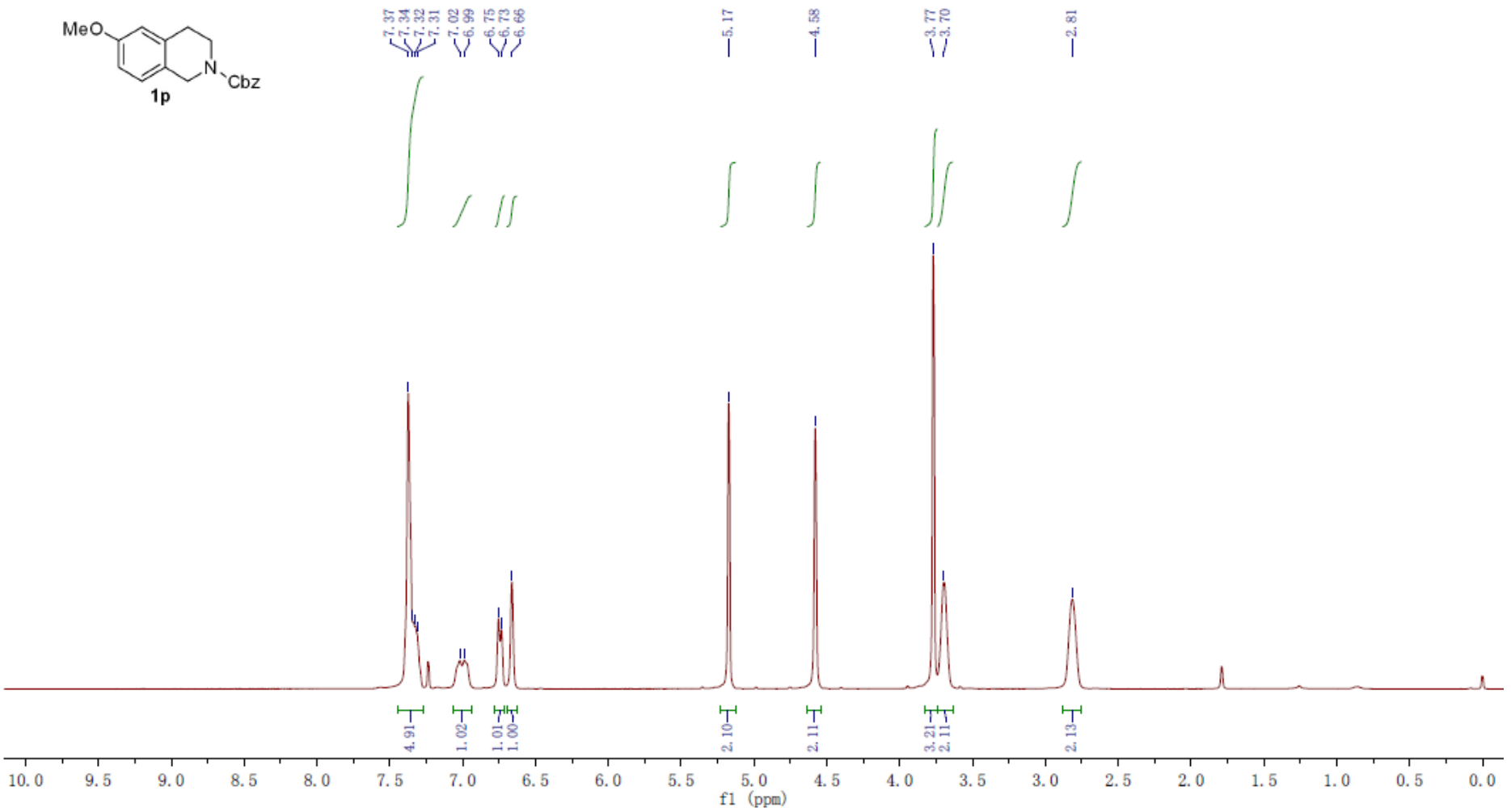
f1 (ppm)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Cbz
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2.81
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1.01
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5.5
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4.5
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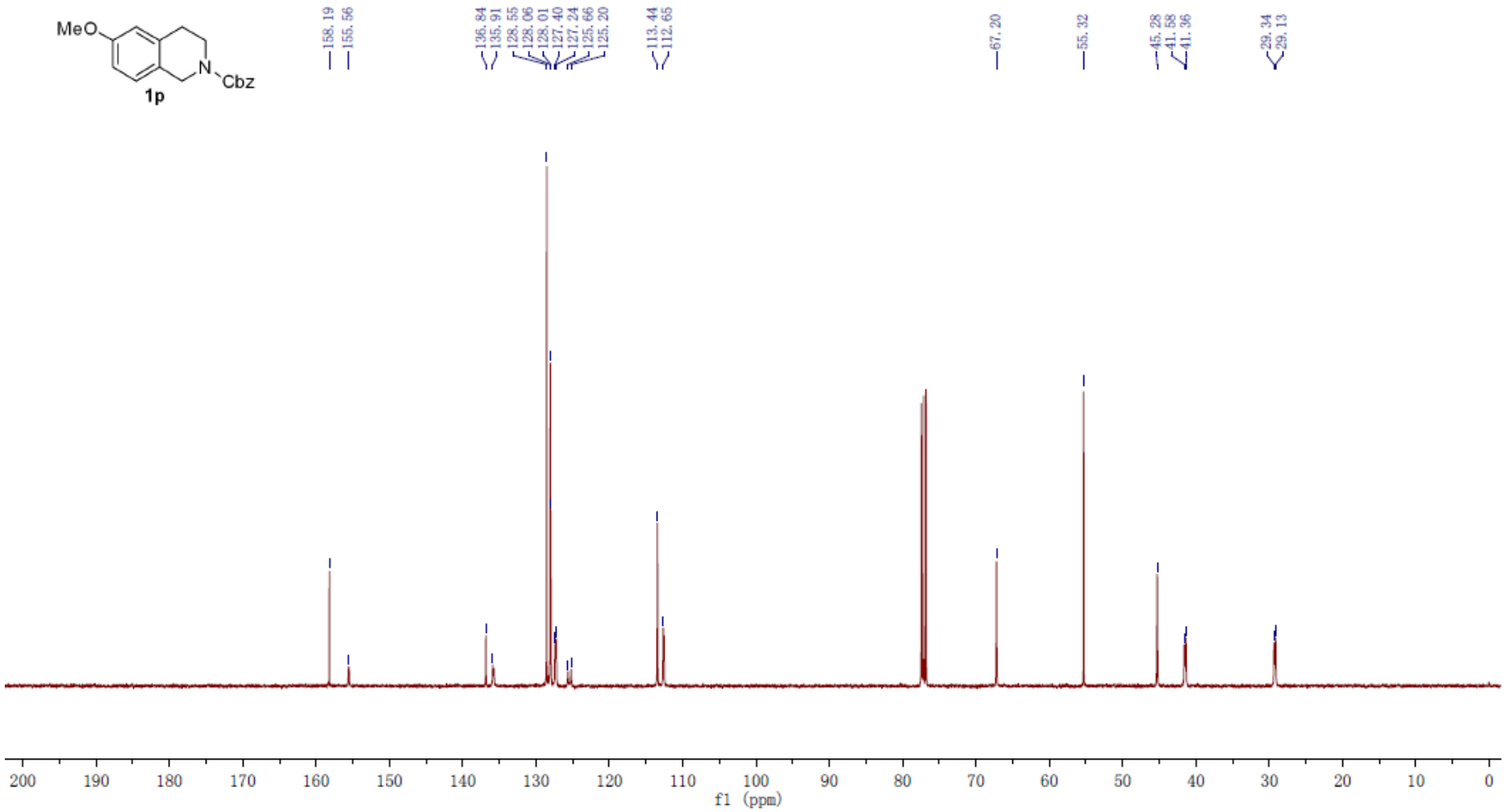
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


MeO
N
Cbz
1p
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135.91
128.55
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128.01
127.40
127.24
125.66
125.20
113.44
112.65
67.20
55.32
45.28
41.58
41.36
29.34
29.13
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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50
40
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20
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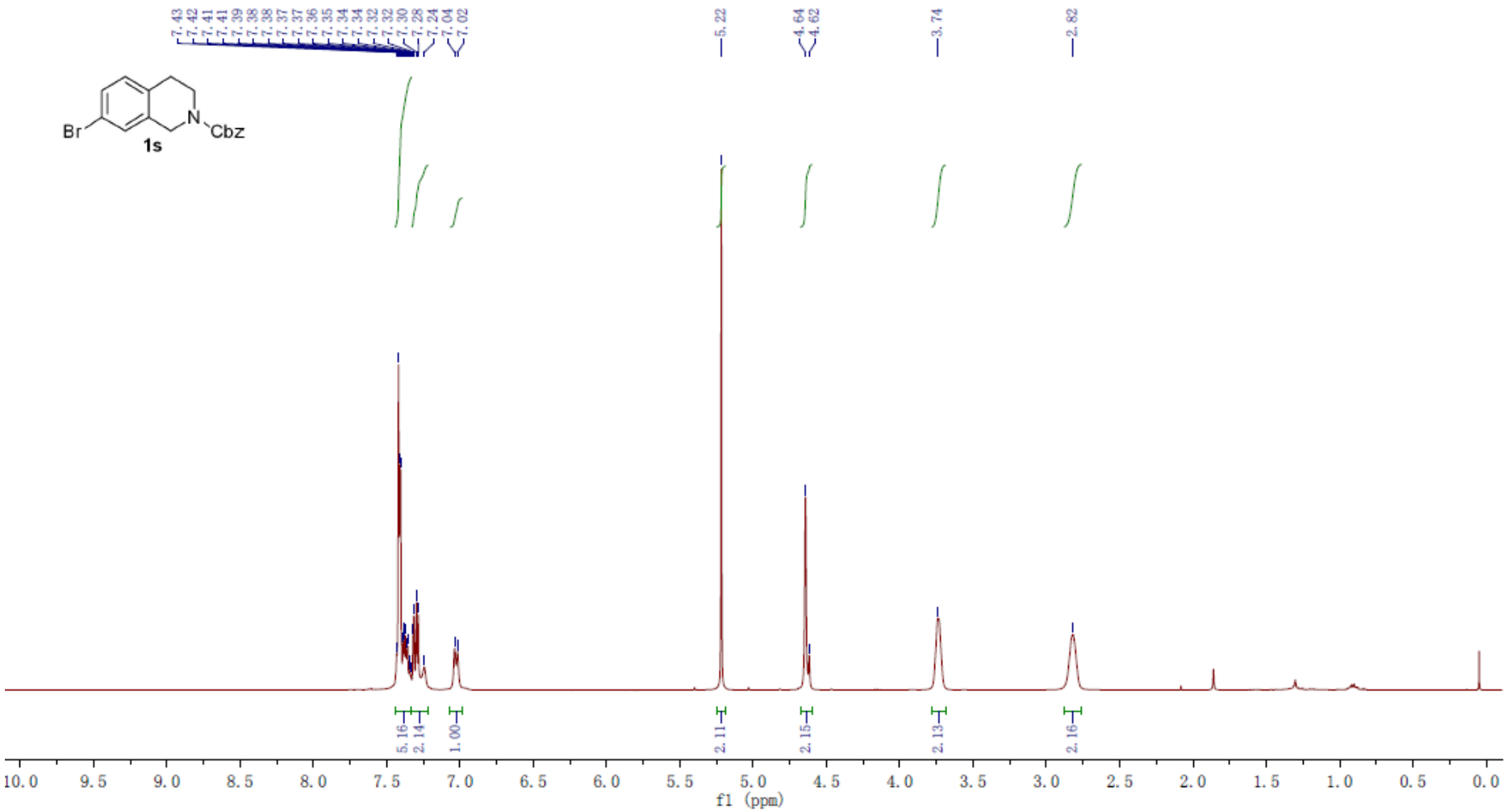
0
f1 (ppm)


7.43
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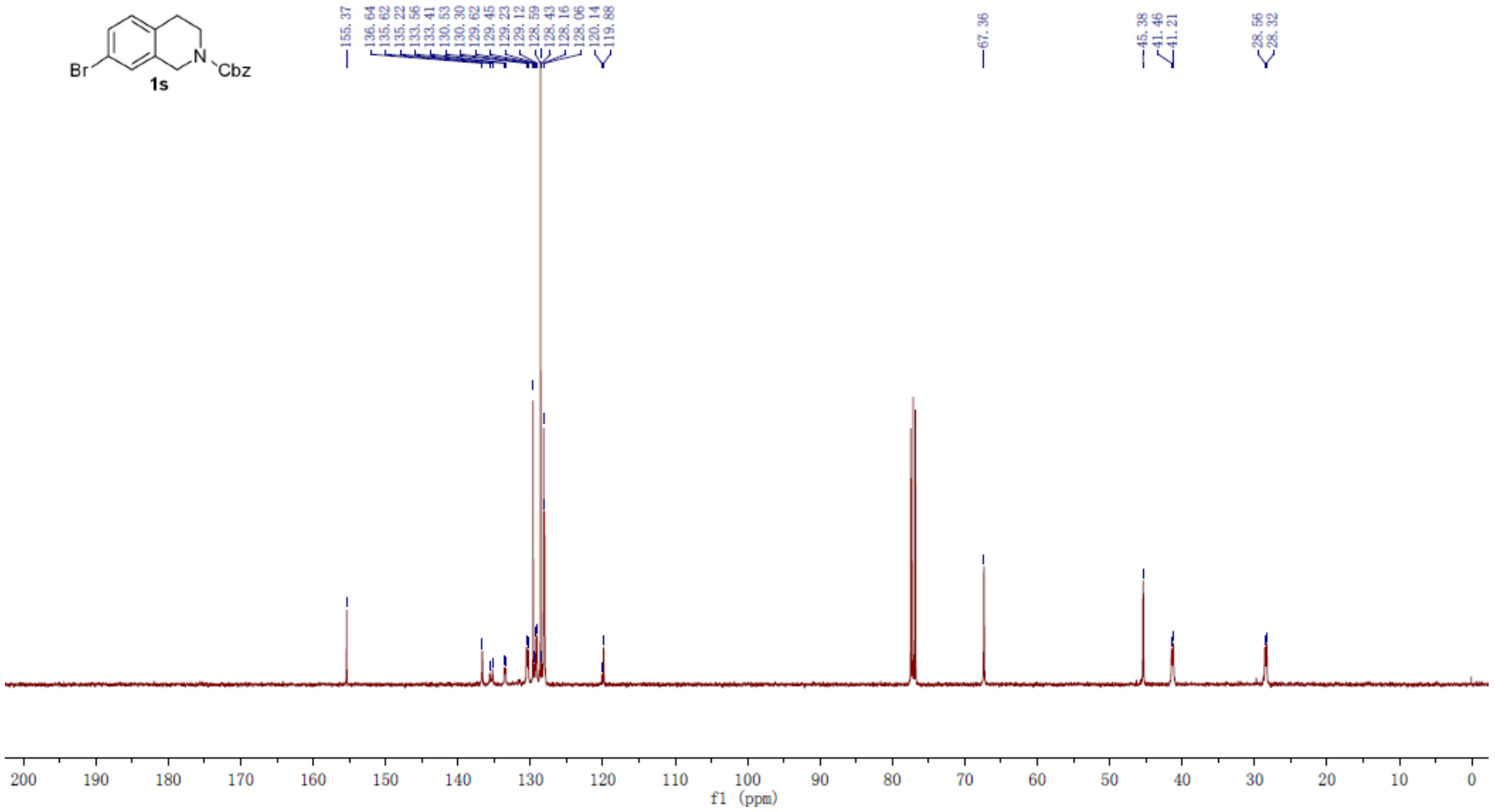
7.41
7.41
7.39
7.38
7.38
7.37
7.37
7.36
7.35
7.34
7.34
7.32
7.32
7.30
7.28
7.24
7.04
7.02
5.22
4.64
4.62
3.74
2.82
Br
N
Cbz
1s
5.16
2.14
1.00
2.11
2.15
2.13
2.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Br
N
Cbz
1s
155.37
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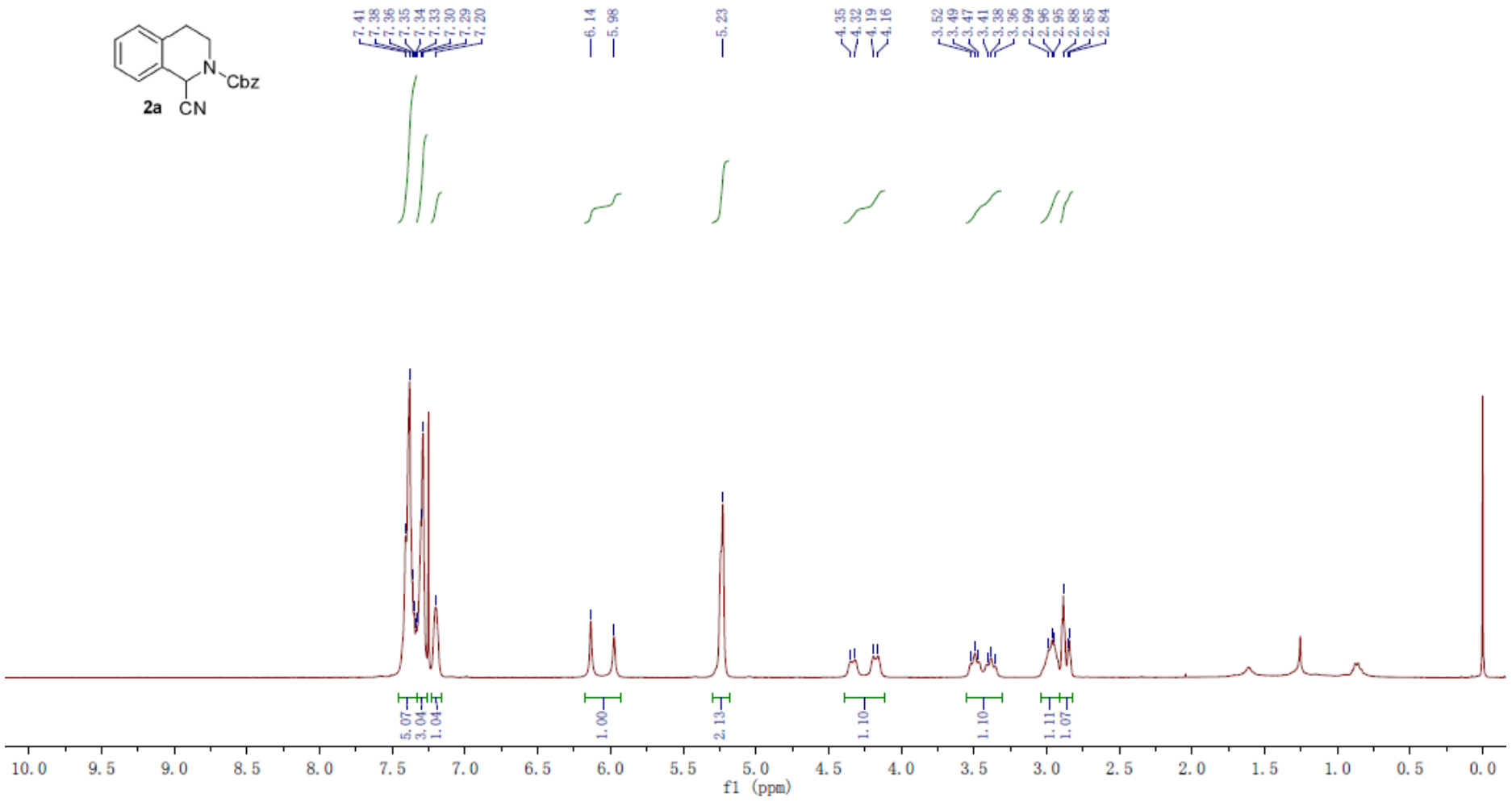
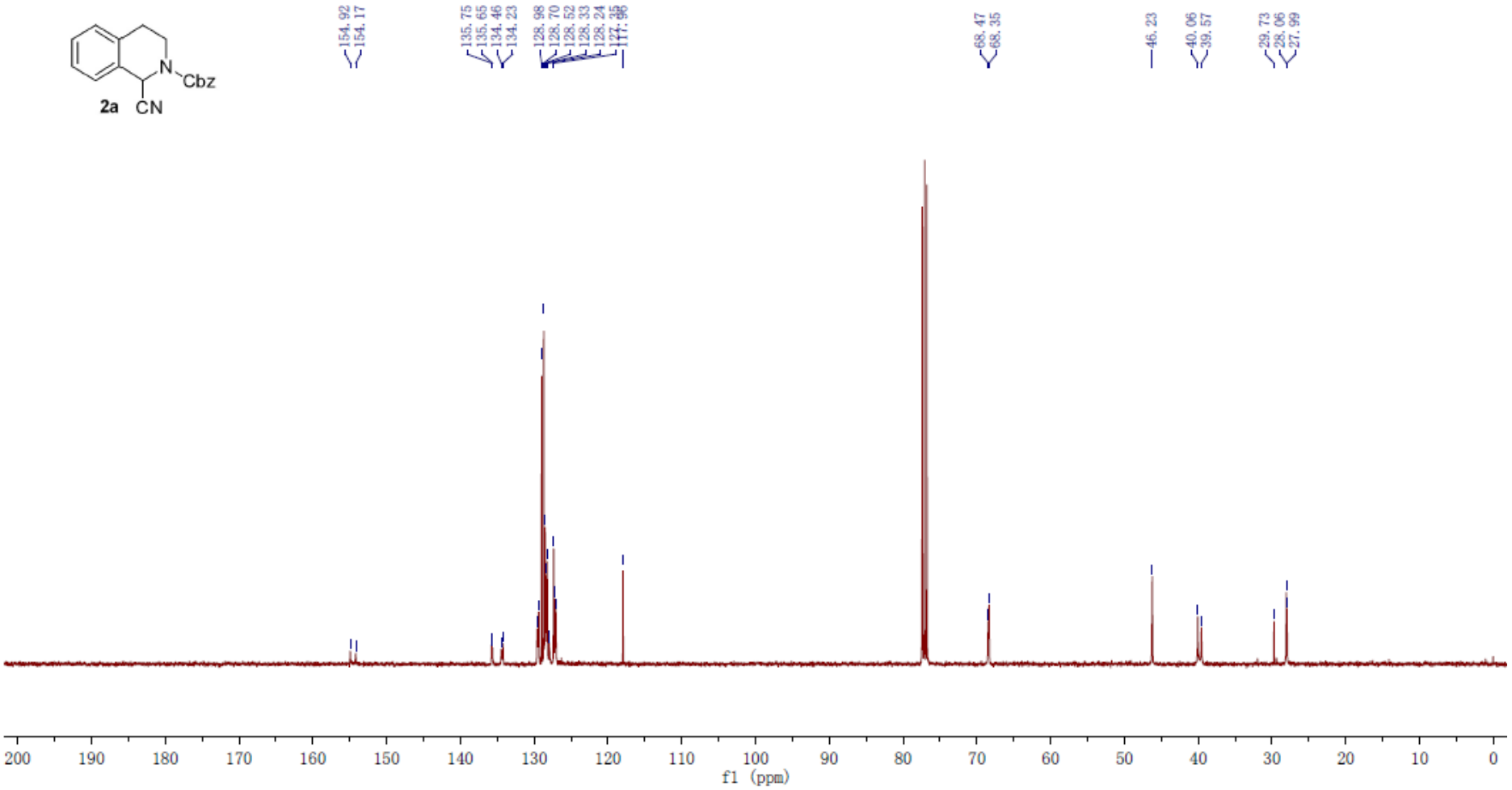
135.62
135.22
133.56
133.41
130.53
130.30
129.62
129.45
129.23
129.12
128.59
128.43
128.16
128.06
120.14
119.88
67.36
45.38
41.46
41.21
28.56
28.32
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
Cbz
2a CN
7.41
7.38
7.36
7.35
7.34
7.33
7.30
7.29
7.20
6.14
5.98
5.23
4.35
4.32
4.19
4.16
3.52
3.49
3.47
3.41
3.38
3.36
2.99
2.96
2.95
2.88
2.85
2.84
5.07
3.04
1.04
1.00
2.13
1.10
1.10
1.11
1.07
10.0
9.5
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
Cbz
2a CN
154.92
154.17
135.75
135.65
134.46
134.23
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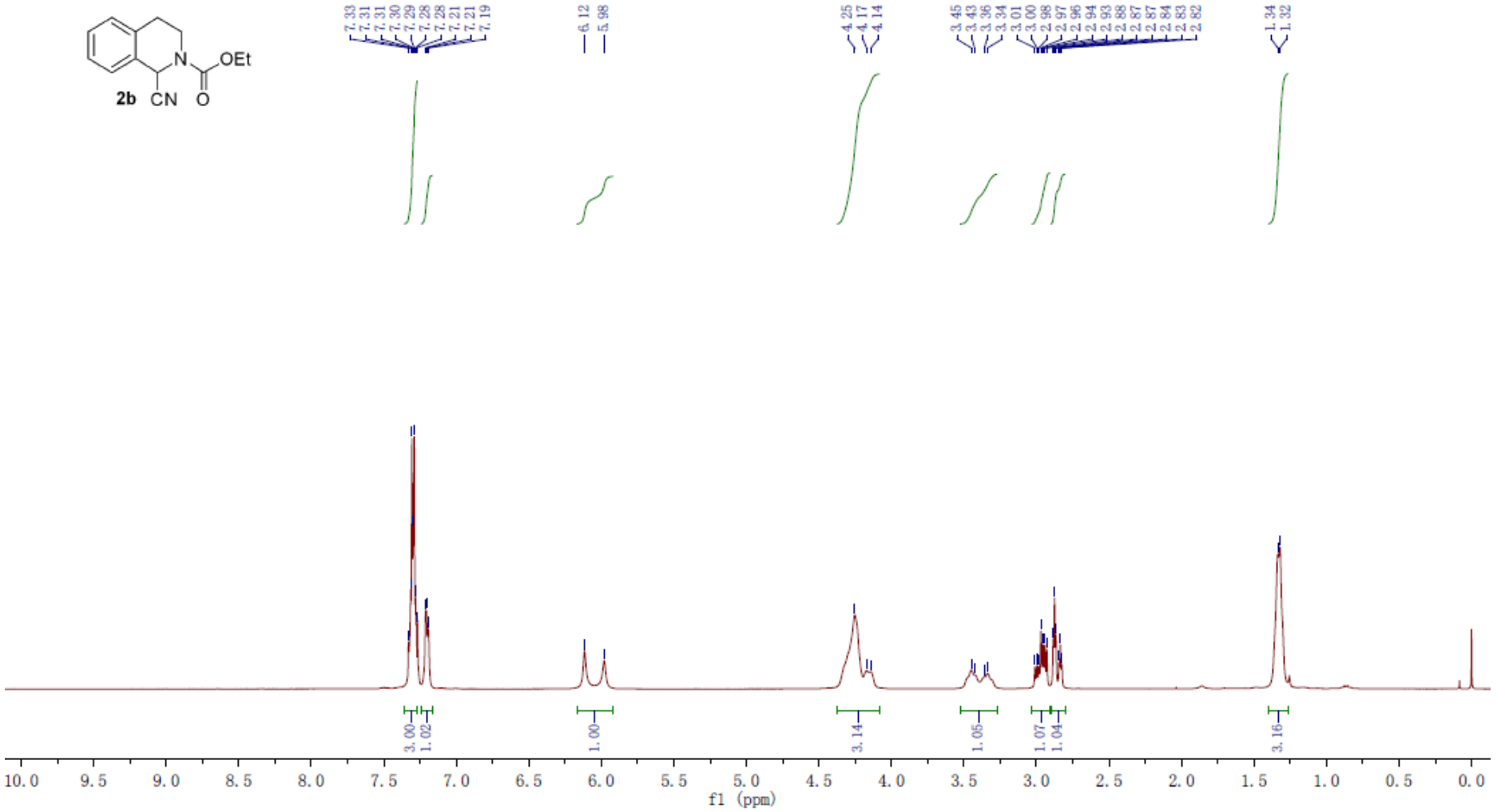
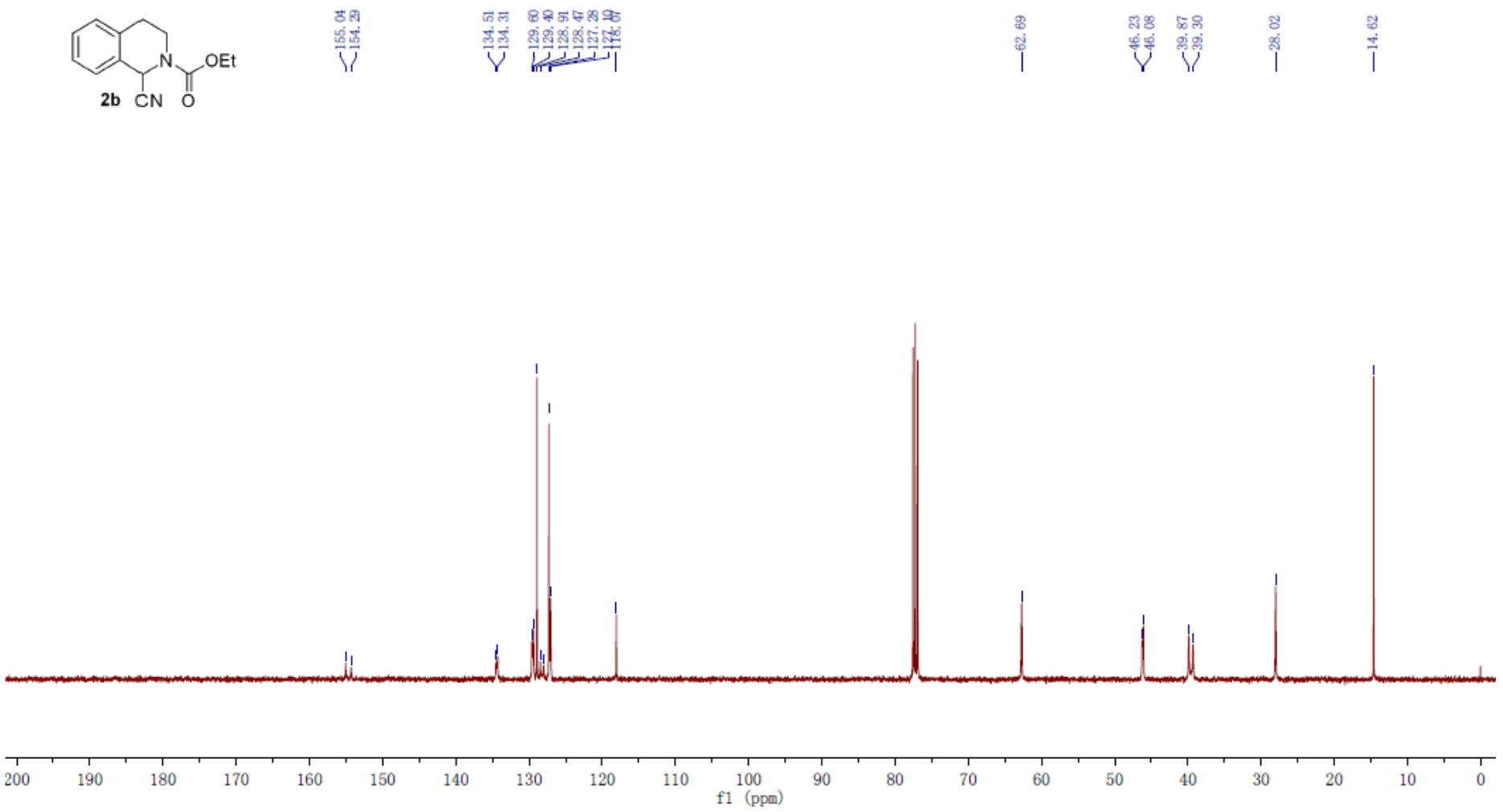
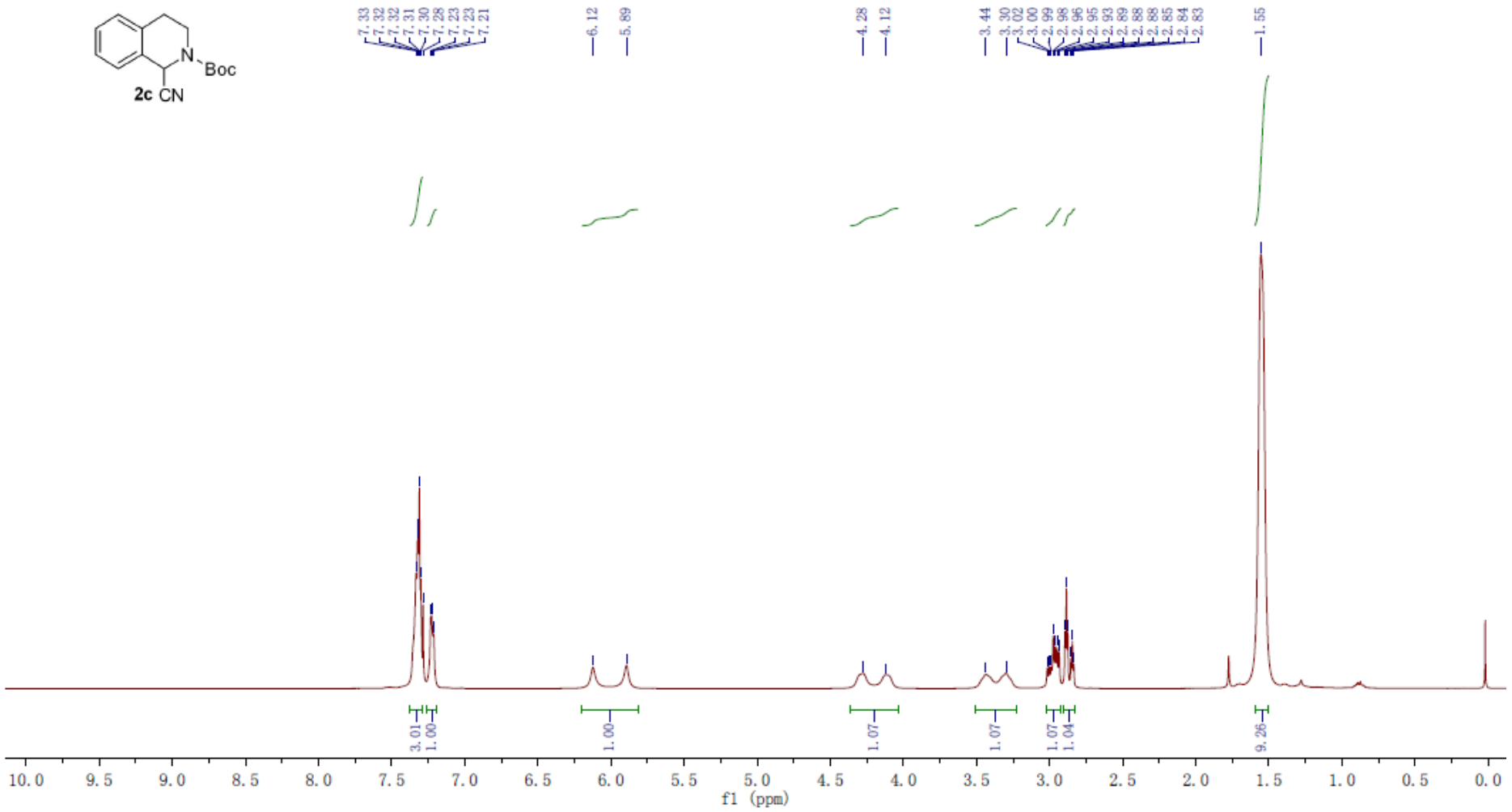
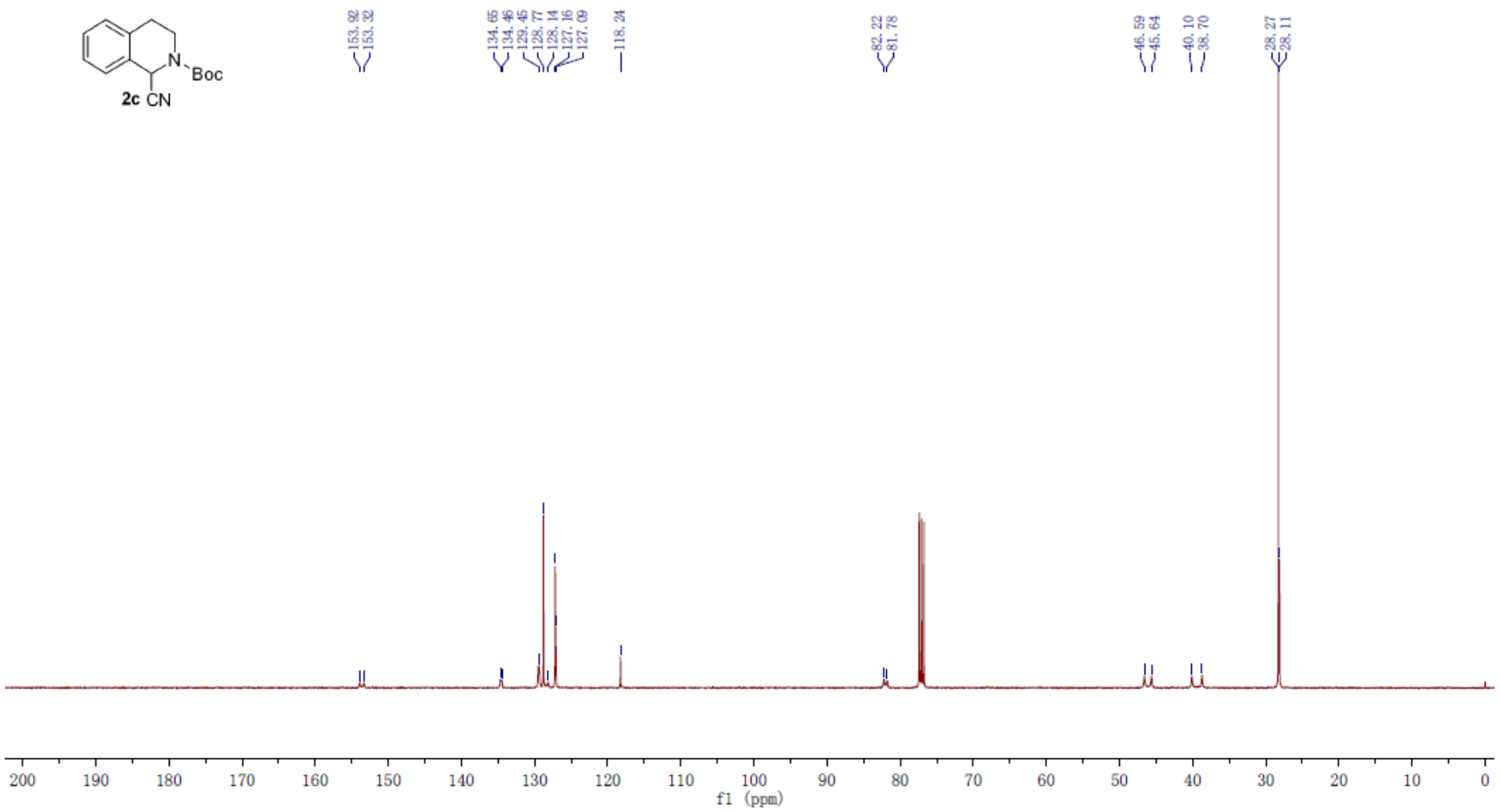
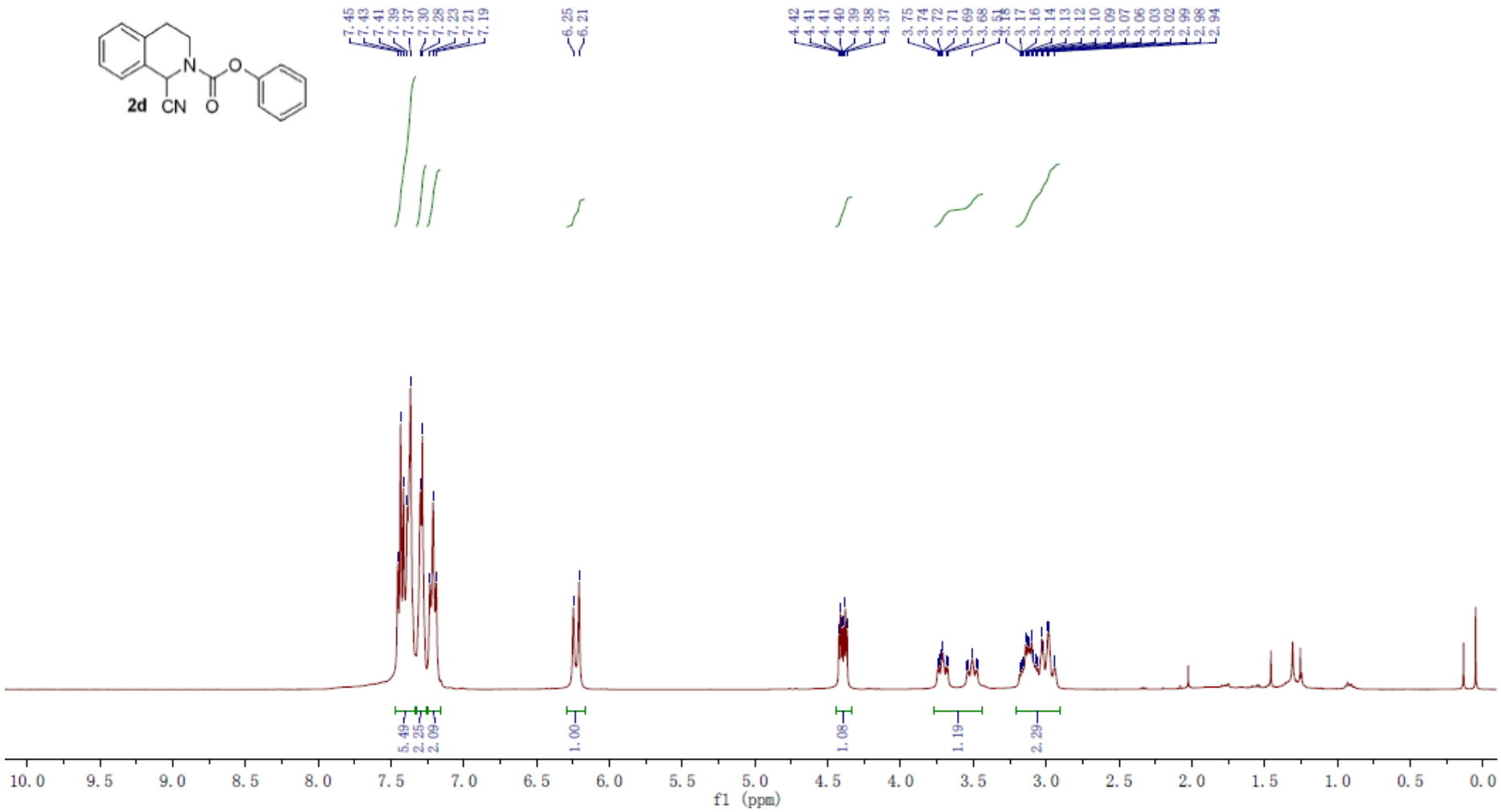
128.70
128.52
128.33
128.24
68.47
68.35
46.23
40.06
39.57
29.73
28.06
27.99
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

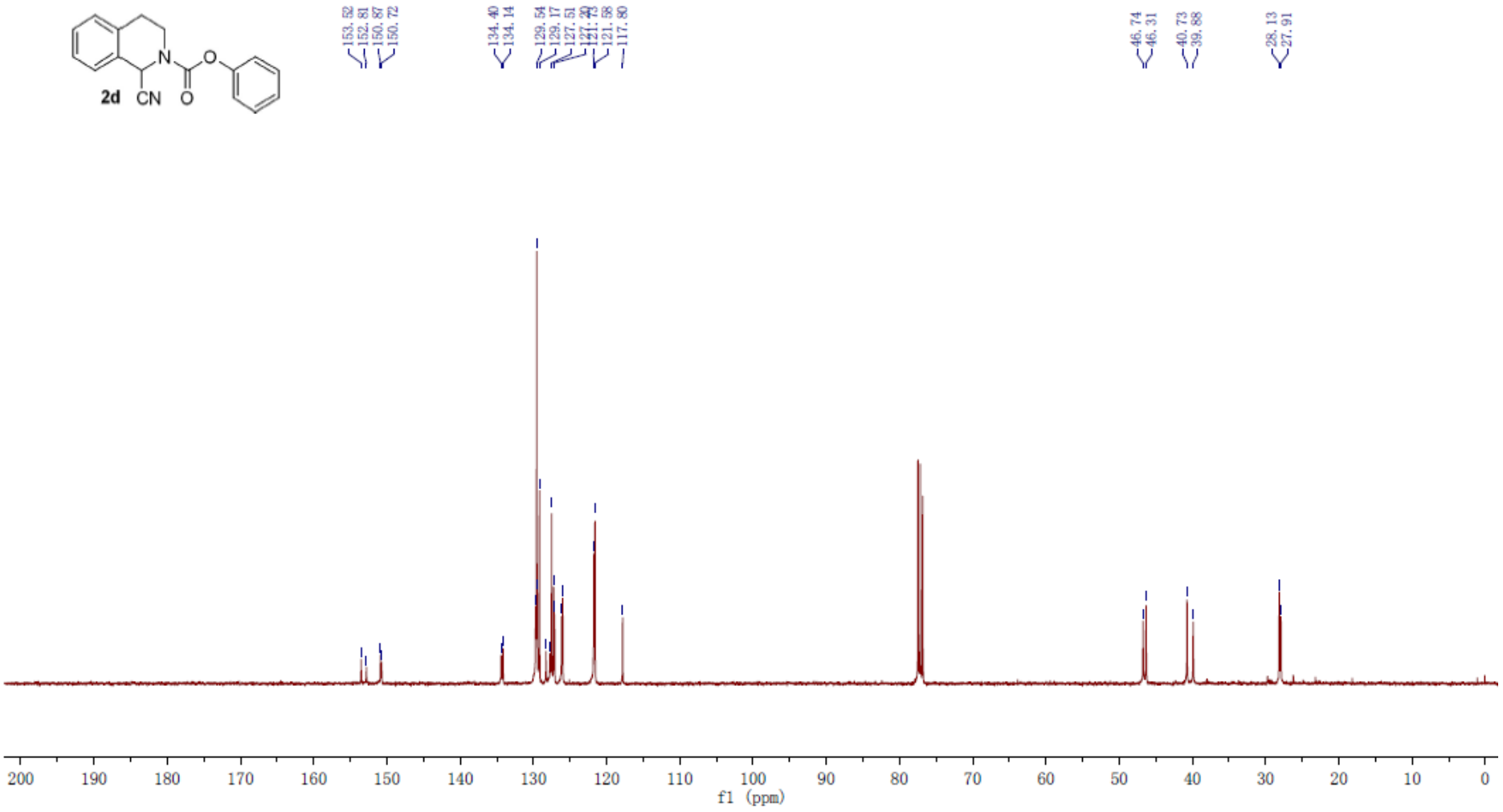

2b
CN
O
OEt
7.33
7.31
7.31
7.30
7.29
7.28
7.28
7.21
7.21
7.19
6.12
5.98
4.25
4.17
4.14
3.45
3.43
3.36
3.34
3.01
3.00
2.98
2.97
2.96
2.94
2.93
2.88
2.87
2.87
2.84
2.83
2.82
1.34
1.32
3.00
1.02
1.00
3.14
1.05
1.07
1.04
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


2b
CN
O
N
OEt
155.04
154.29
134.51
134.31
129.60
129.40
128.91
128.47
127.28
122.10
118.07
62.69
46.23
46.08
39.87
39.30
28.02
14.62
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


2c CN
Boc
7.33
7.32
7.32
7.31
7.30
7.28
7.23
7.23
7.21
6.12
5.89
4.28
4.12
3.44
3.30
3.02
3.00
2.99
2.98
2.96
2.95
2.93
2.89
2.88
2.88
2.85
2.84
2.83
1.55
3.01
1.00
1.00
1.07
1.07
1.07
1.04
9.26
10.0
9.5
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)


2c CN
Boc
153.92
153.32
134.65
134.46
129.45
128.77
128.14
127.16
127.09
118.24
82.22
81.78
46.59
45.64
40.10
38.70
28.27
28.11
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


2d
CN
7.45
7.43
7.41
7.39
7.37
7.30
7.28
7.23
7.21
7.19
6.25
6.21
4.42
4.41
4.41
4.40
4.39
4.38
4.37
3.75
3.74
3.72
3.71
3.69
3.68
3.17
3.16
3.14
3.13
3.12
3.10
3.09
3.07
3.06
3.03
3.02
2.99
2.98
2.94
5.49
2.25
2.09
1.00
1.08
1.19
2.29
10.0
9.5
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)


2d
CN
O
153.52
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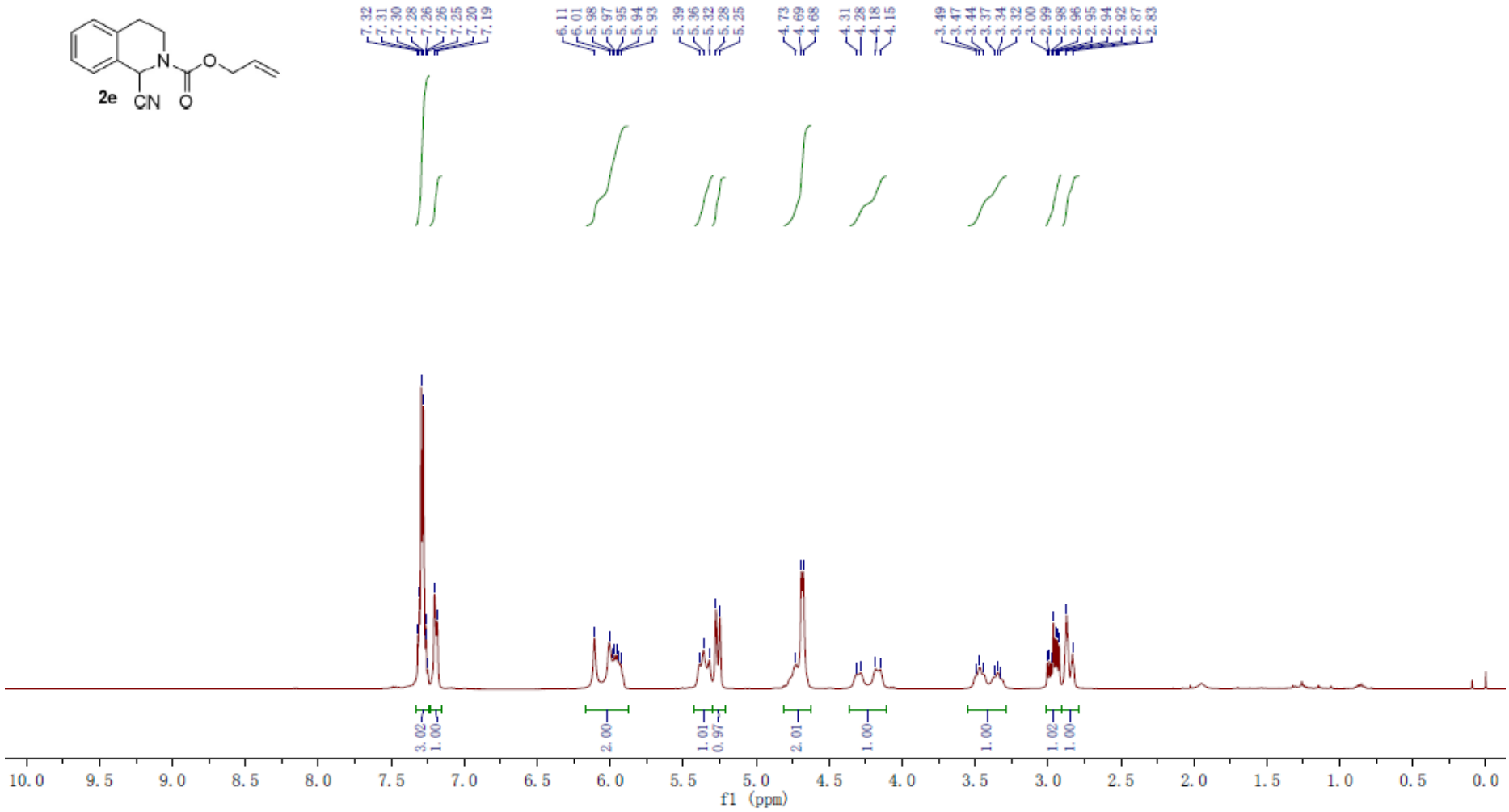
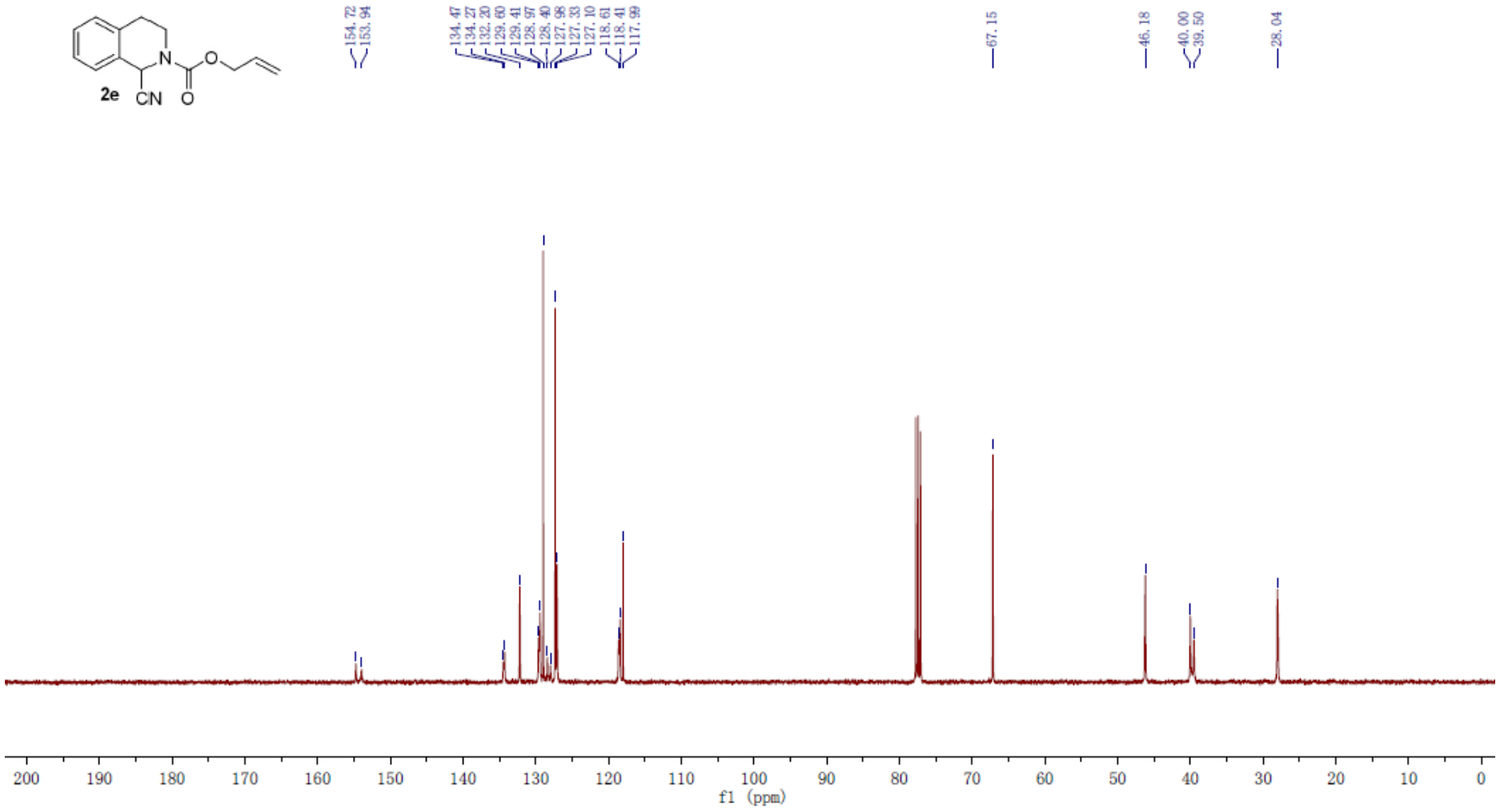
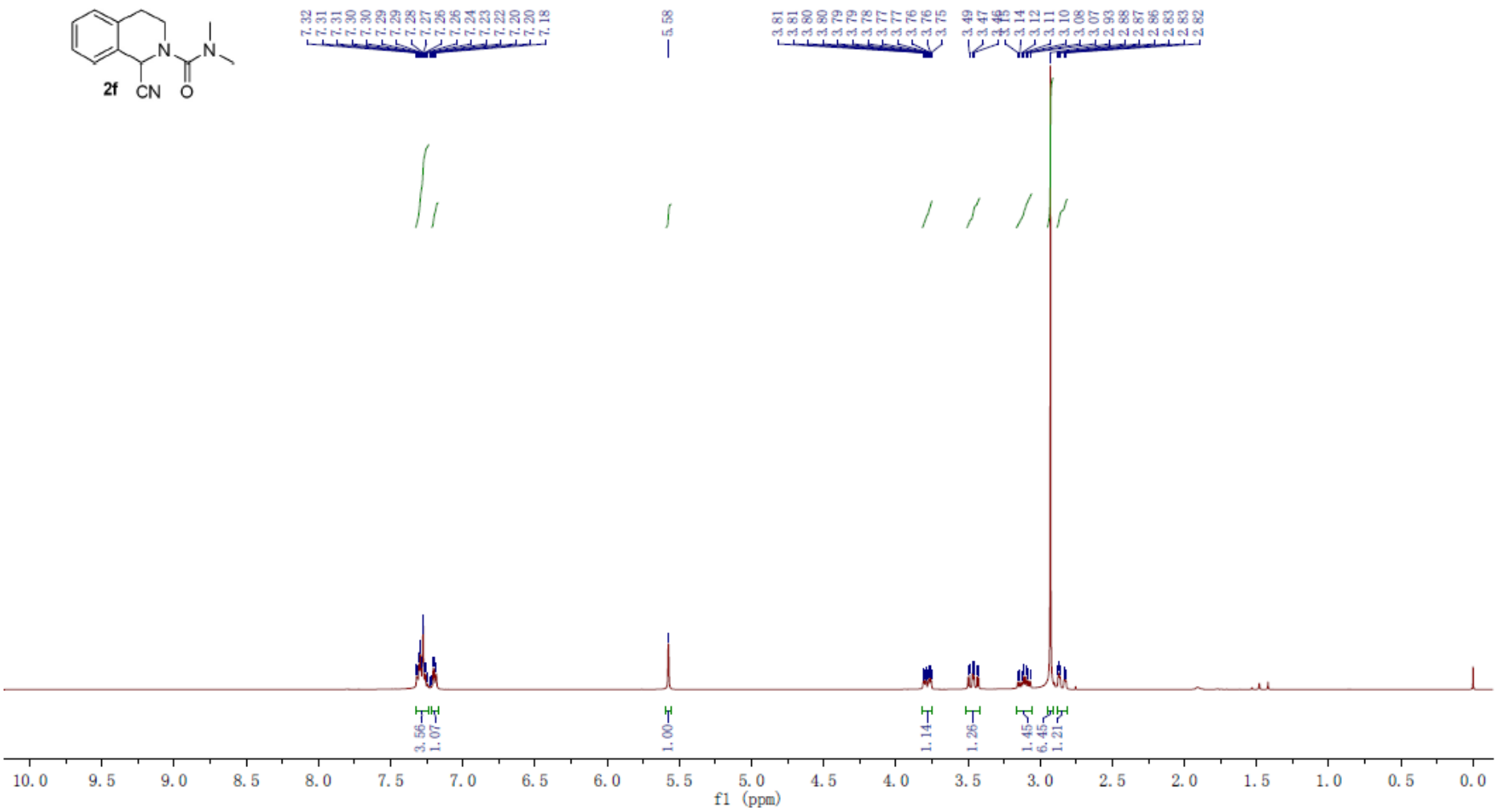
150.87
150.72
134.40
134.14
129.54
129.17
127.51
121.58
117.80
46.74
46.31
40.73
39.88
28.13
27.91
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


2e
CN
O
7.32
7.31
7.30
7.28
7.26
7.26
7.25
7.20
7.19
6.11
6.01
5.98
5.97
5.95
5.94
5.93
5.39
5.36
5.32
5.28
5.25
4.73
4.69
4.68
4.31
4.28
4.18
4.15
3.49
3.47
3.44
3.37
3.34
3.32
3.00
2.99
2.98
2.96
2.95
2.94
2.92
2.87
2.83
3.02
1.00
2.00
1.01
0.97
2.01
1.00
1.00
1.02
1.00
10.0
9.5
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)


2e
CN
O
154.72
153.94
134.47
134.27
132.20
129.60
129.41
128.97
128.40
127.98
127.33
127.10
118.61
118.41
117.99
67.15
46.18
40.00
39.50
28.04
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


2f
CN
O
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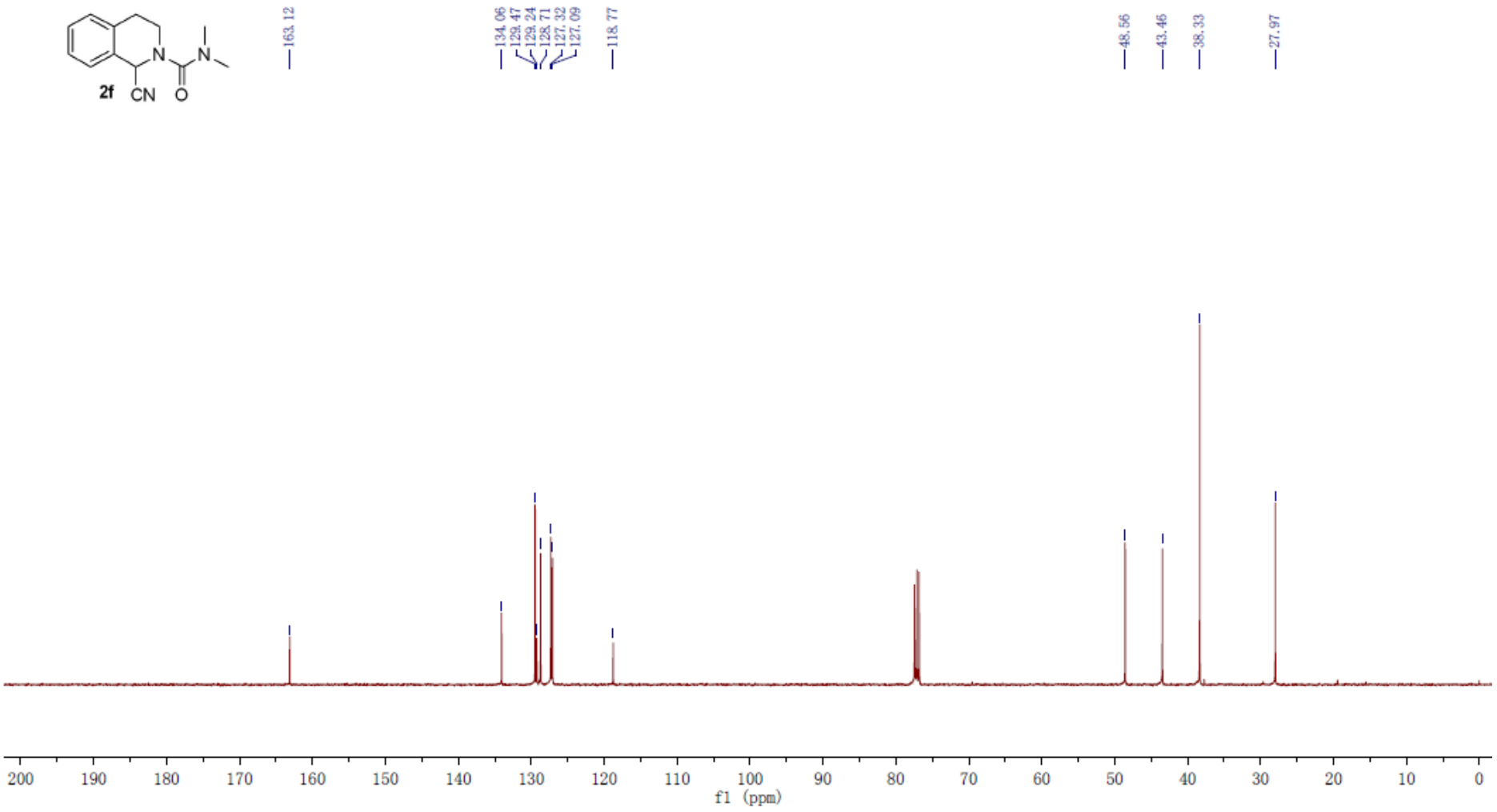
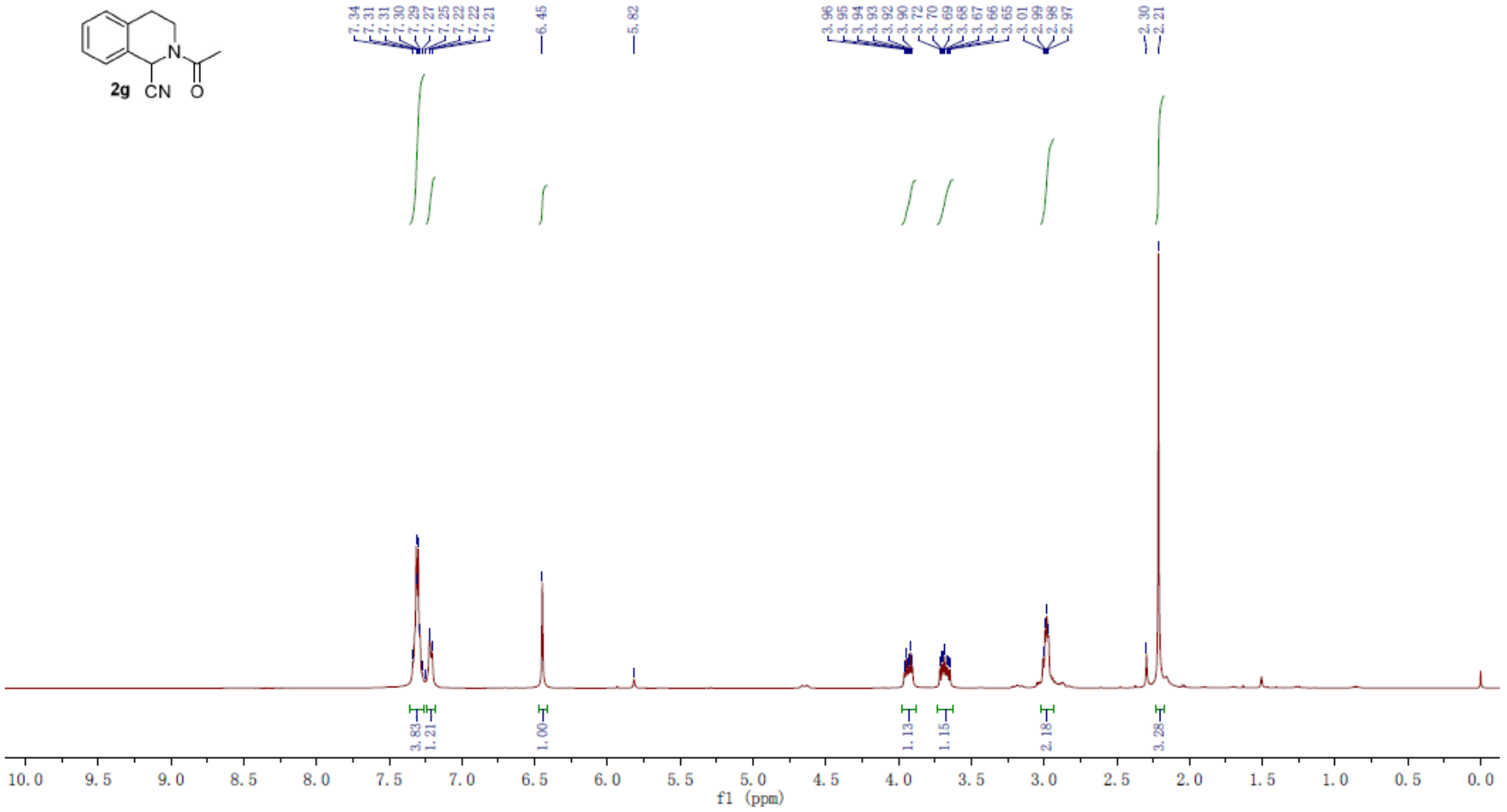
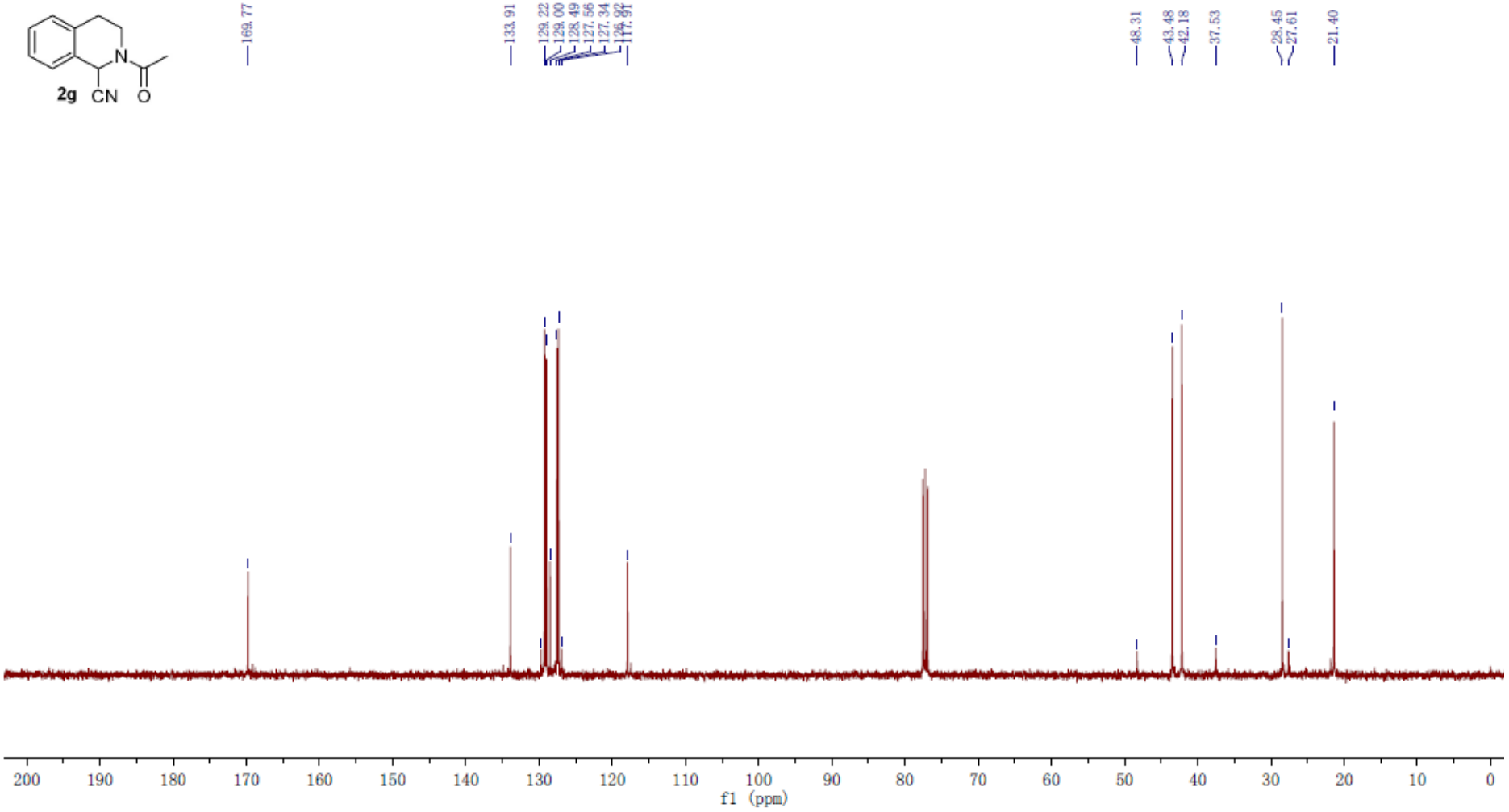
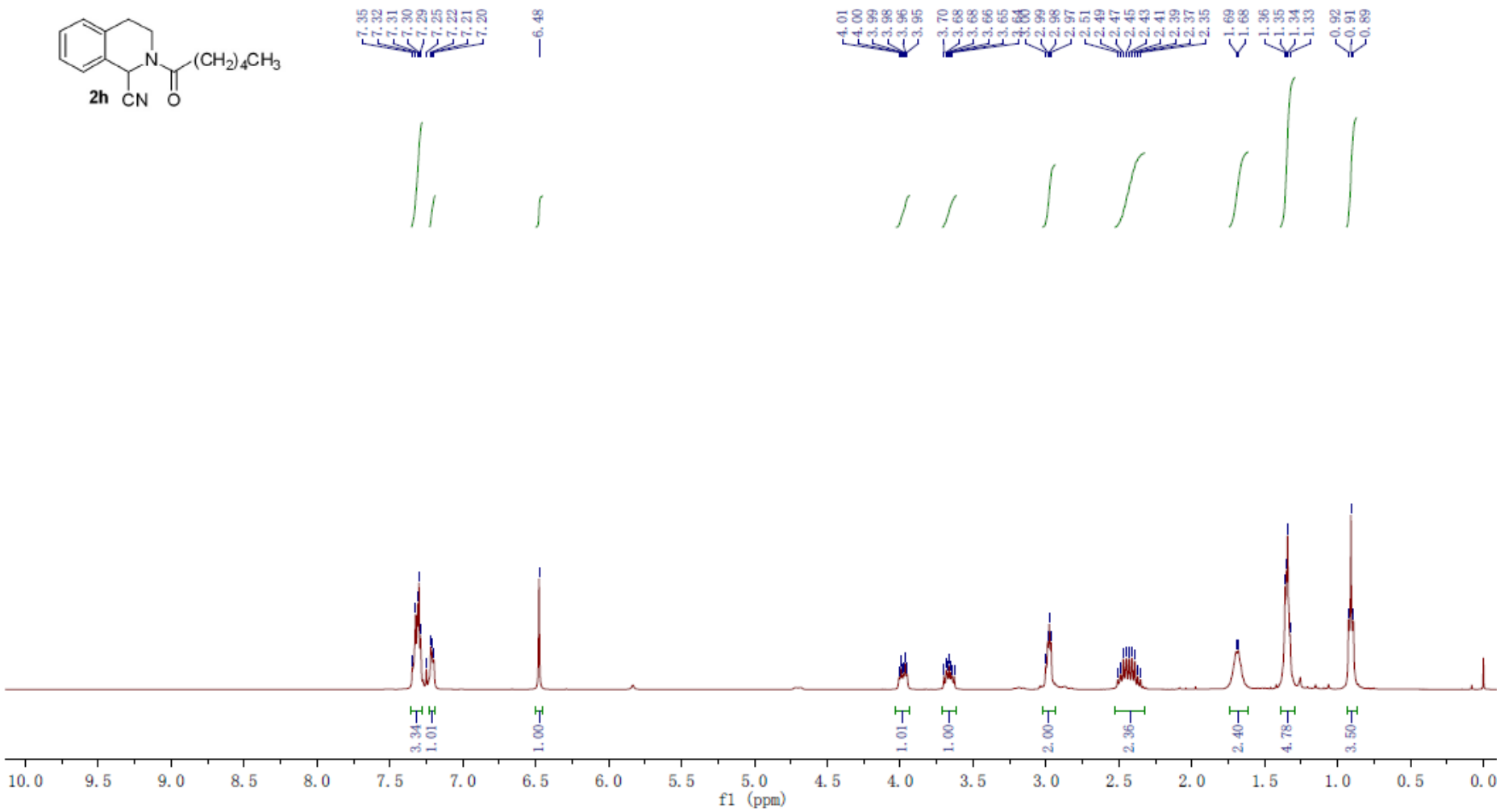
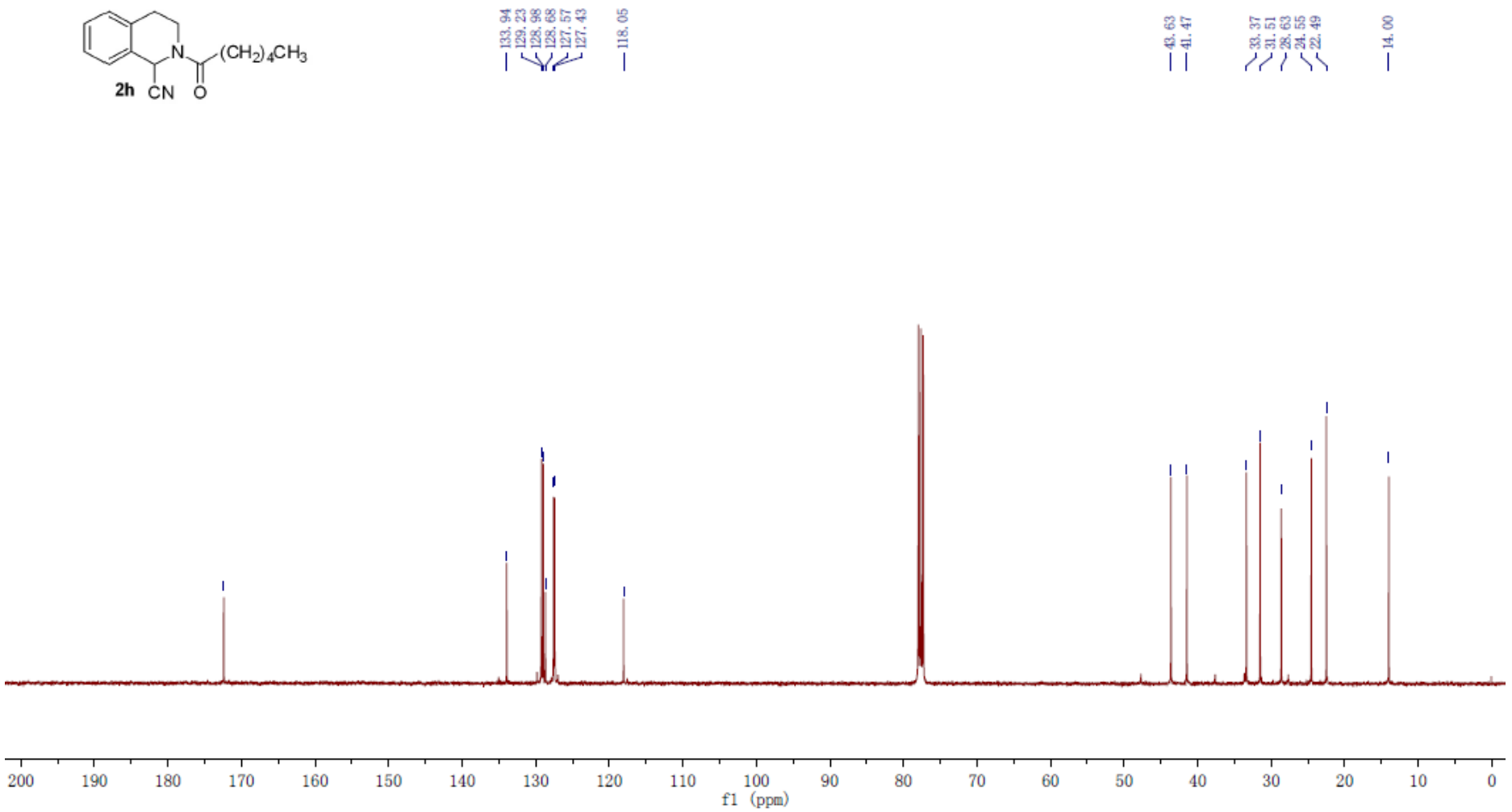
7.31
7.31
7.30
7.30
7.29
7.29
7.28
7.27
7.26
7.26
7.24
7.23
7.22
7.20
7.20
7.18
5.58
3.81
3.81
3.80
3.80
3.79
3.79
3.78
3.77
3.77
3.76
3.76
3.75
3.49
3.47
3.46
3.45
3.14
3.12
3.11
3.10
3.08
3.07
2.93
2.88
2.87
2.86
2.83
2.83
2.82
3.56
1.07
1.00
1.14
1.26
1.45
6.45
1.21
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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)

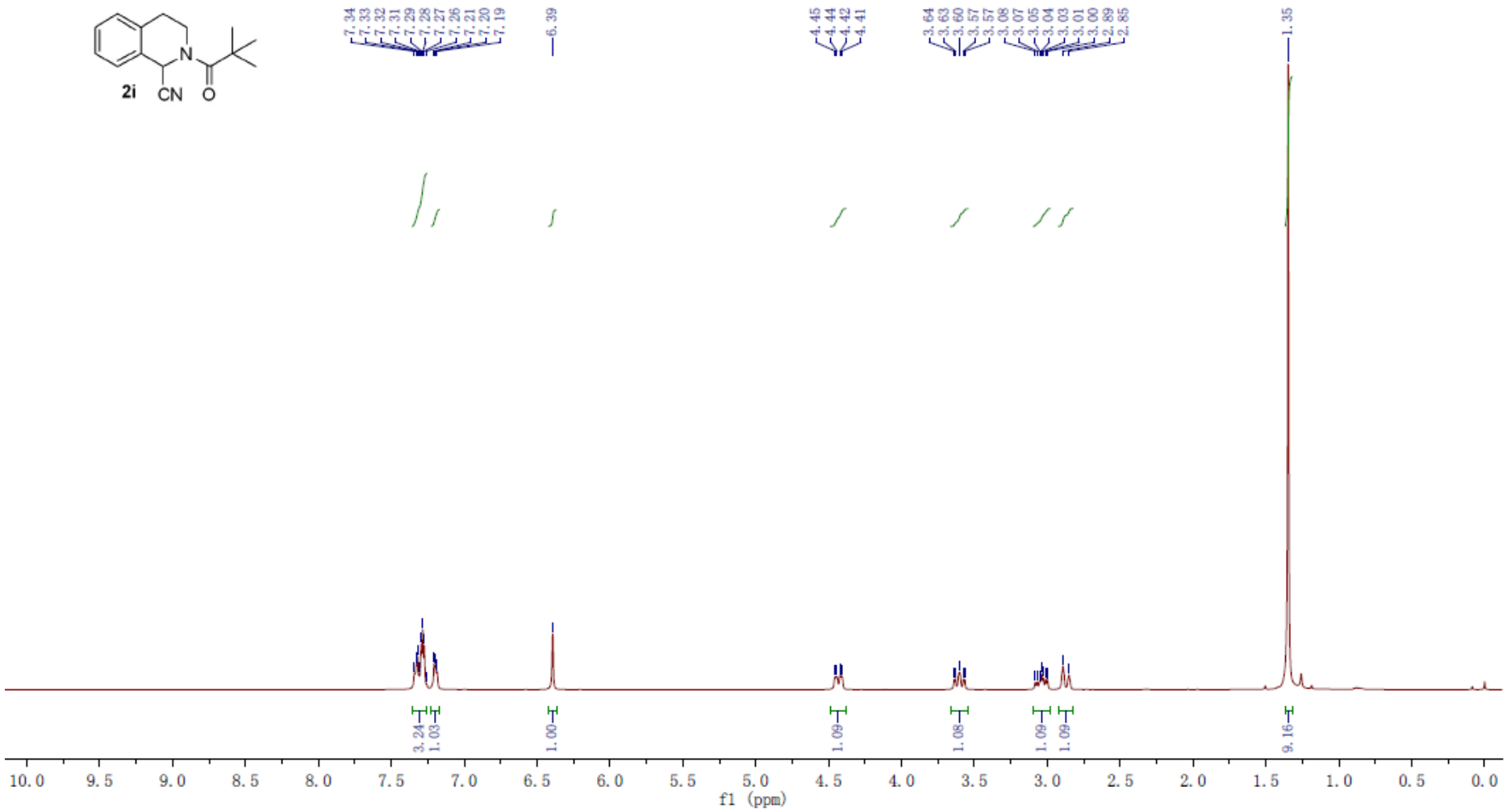

2f
CN
O
163.12
134.06
129.47
129.24
128.71
127.32
127.09
118.77
48.56
43.46
38.33
27.97
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

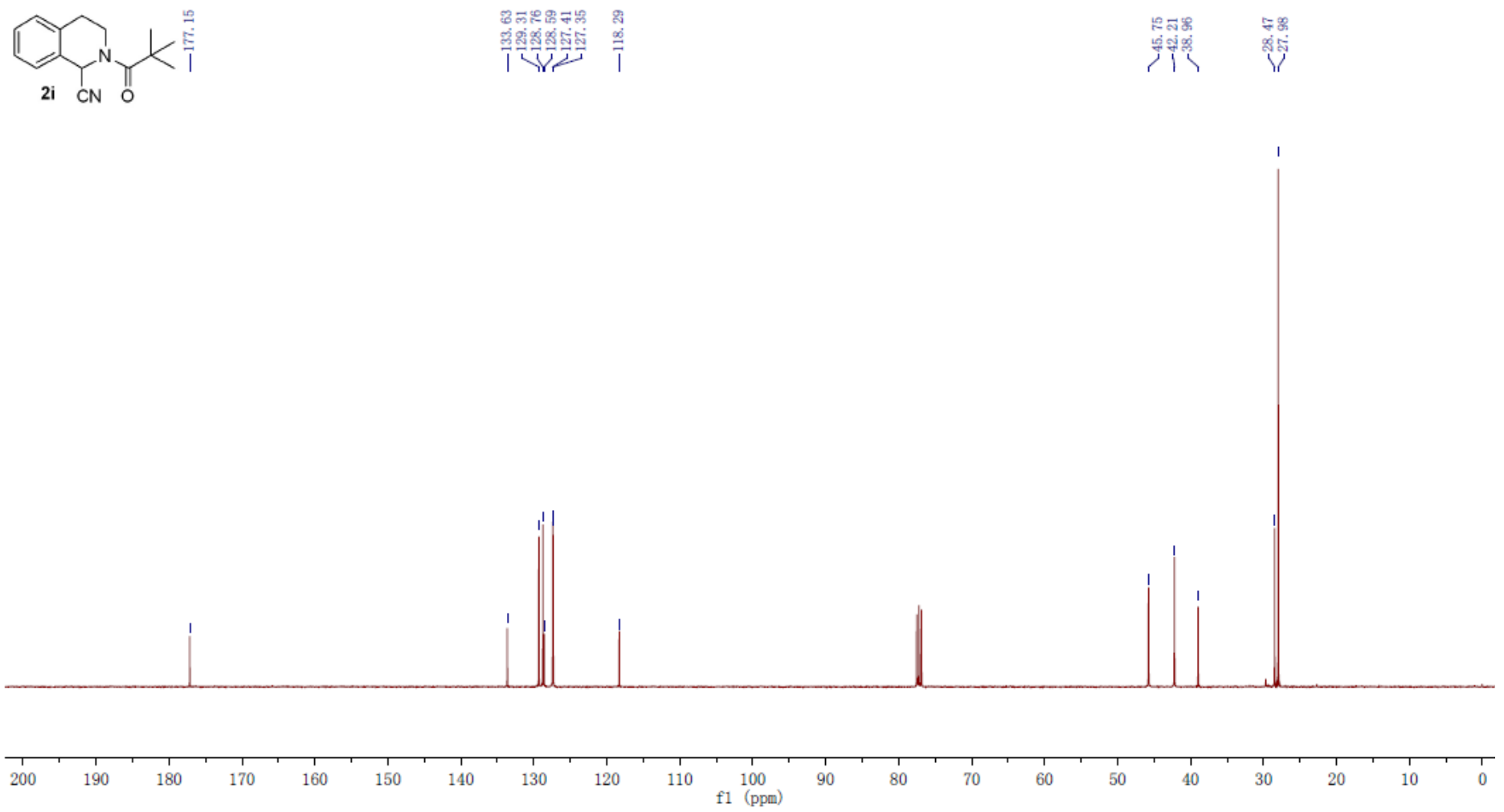

2g
CN
O
7.34
7.31
7.31
7.30
7.29
7.27
7.25
7.22
7.22
7.21
6.45
5.82
3.96
3.95
3.94
3.93
3.92
3.90
3.72
3.70
3.69
3.68
3.67
3.66
3.65
3.01
2.99
2.98
2.97
2.30
2.21
3.83
1.21
1.00
1.13
1.15
2.18
3.28
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

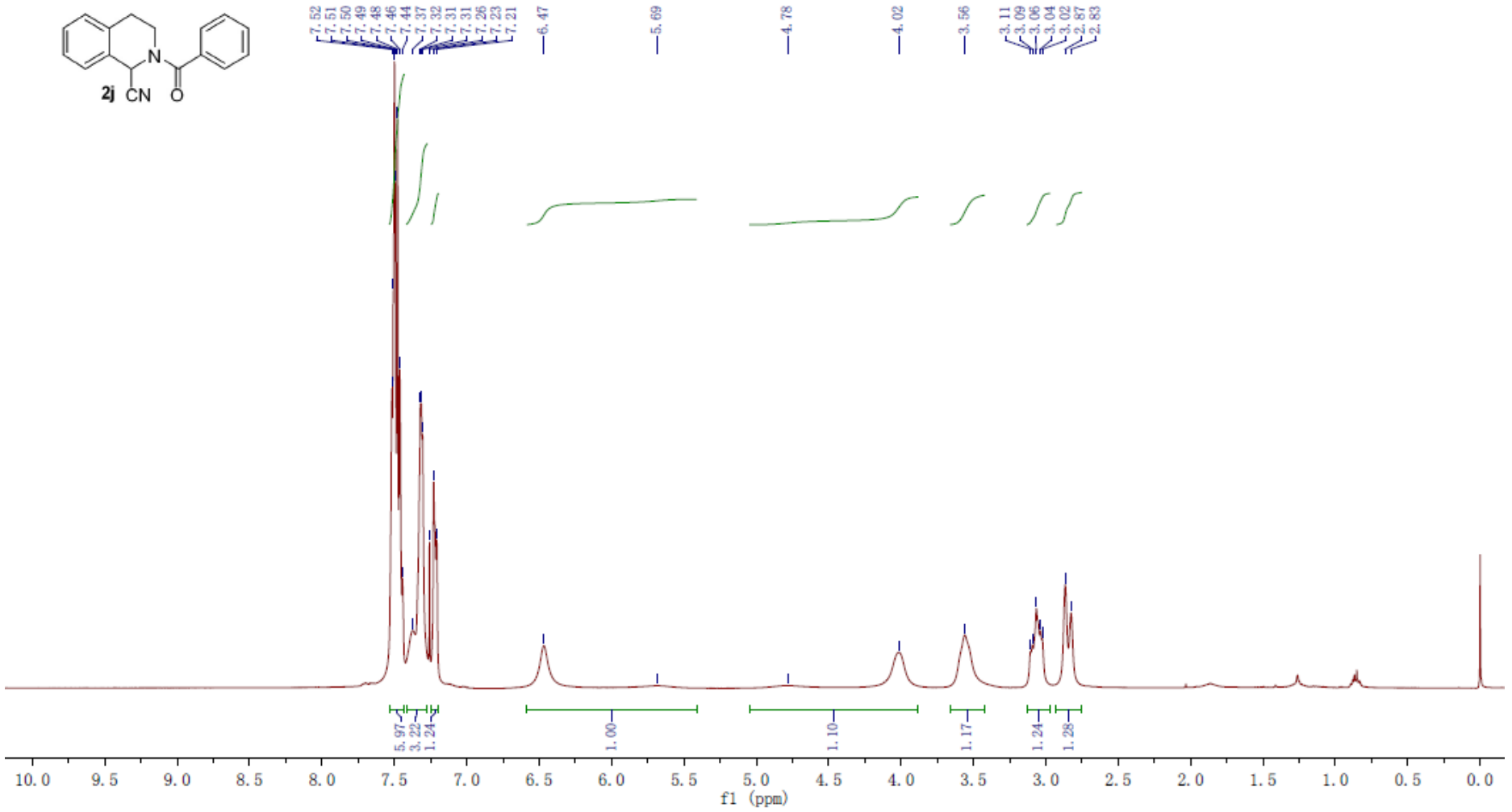

2g
CN
O
169.77
133.91
129.22
129.00
128.49
127.56
127.34
48.31
43.48
42.18
37.53
28.45
27.61
21.40
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


2h
CN
O
(CH2)4CH3
7.35
7.32
7.31
7.30
7.29
7.25
7.22
7.21
7.20
6.48
4.01
4.00
3.99
3.98
3.96
3.95
3.70
3.68
3.68
3.66
3.65
2.99
2.98
2.97
2.51
2.49
2.47
2.45
2.43
2.41
2.39
2.37
2.35
1.69
1.68
1.36
1.35
1.34
1.33
0.92
0.91
0.89
3.34
1.01
1.00
1.01
1.00
2.00
2.36
2.40
4.78
3.50
10.0
9.5
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)


2h
CN
O
N
(CH2)4CH3
133.94
129.23
128.98
128.68
127.57
127.43
118.05
43.63
41.47
33.37
31.51
28.63
24.55
22.49
14.00
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


2i
CN
O
7.34
7.33
7.32
7.31
7.29
7.28
7.27
7.26
7.21
7.20
7.19
6.39
4.45
4.44
4.42
4.41
3.64
3.63
3.60
3.57
3.57
3.08
3.07
3.05
3.04
3.03
3.01
3.00
2.89
2.85
1.35
3.24
1.03
1.00
1.09
1.08
1.09
1.09
9.16
10.0
9.5
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)


2i
CN
O
177.15
133.63
129.31
128.76
128.59
127.41
127.35
118.29
45.75
42.21
38.96
28.47
27.98
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


2j
CN
O
N
7.52
7.51
7.50
7.49
7.48
7.46
7.44
7.37
7.32
7.31
7.31
7.26
7.23
7.21
6.47
5.69
4.78
4.02
3.56
3.11
3.09
3.06
3.04
3.02
2.87
2.83
5.97
3.22
1.24
1.00
1.10
1.17
1.24
1.28
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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1.0
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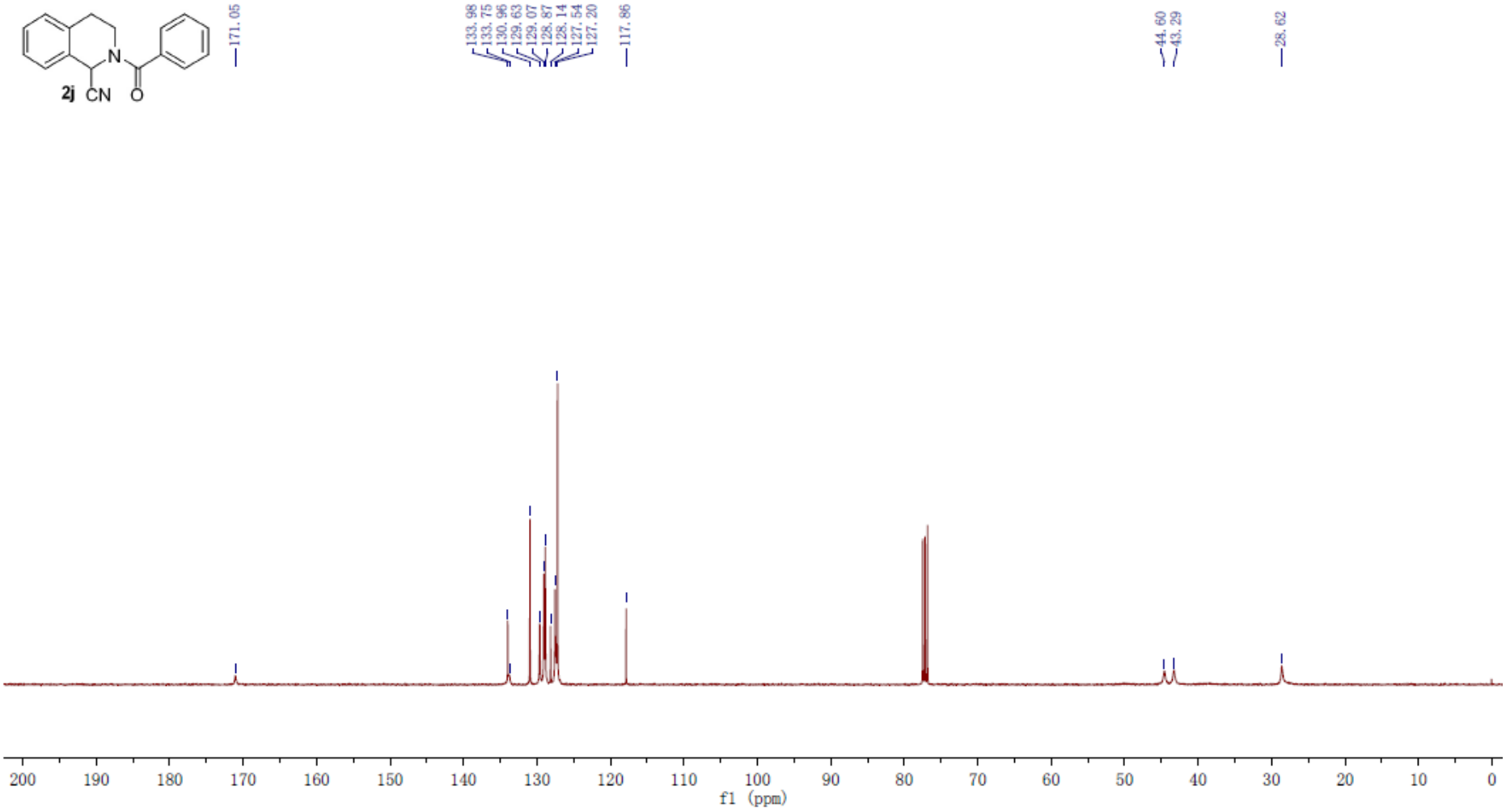
0.0
f1 (ppm)


2j
CN
O
171.05
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129.63
129.07
128.87
128.14
127.54
127.20
117.86
44.60
43.29
28.62
200
190
180
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130
120
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90
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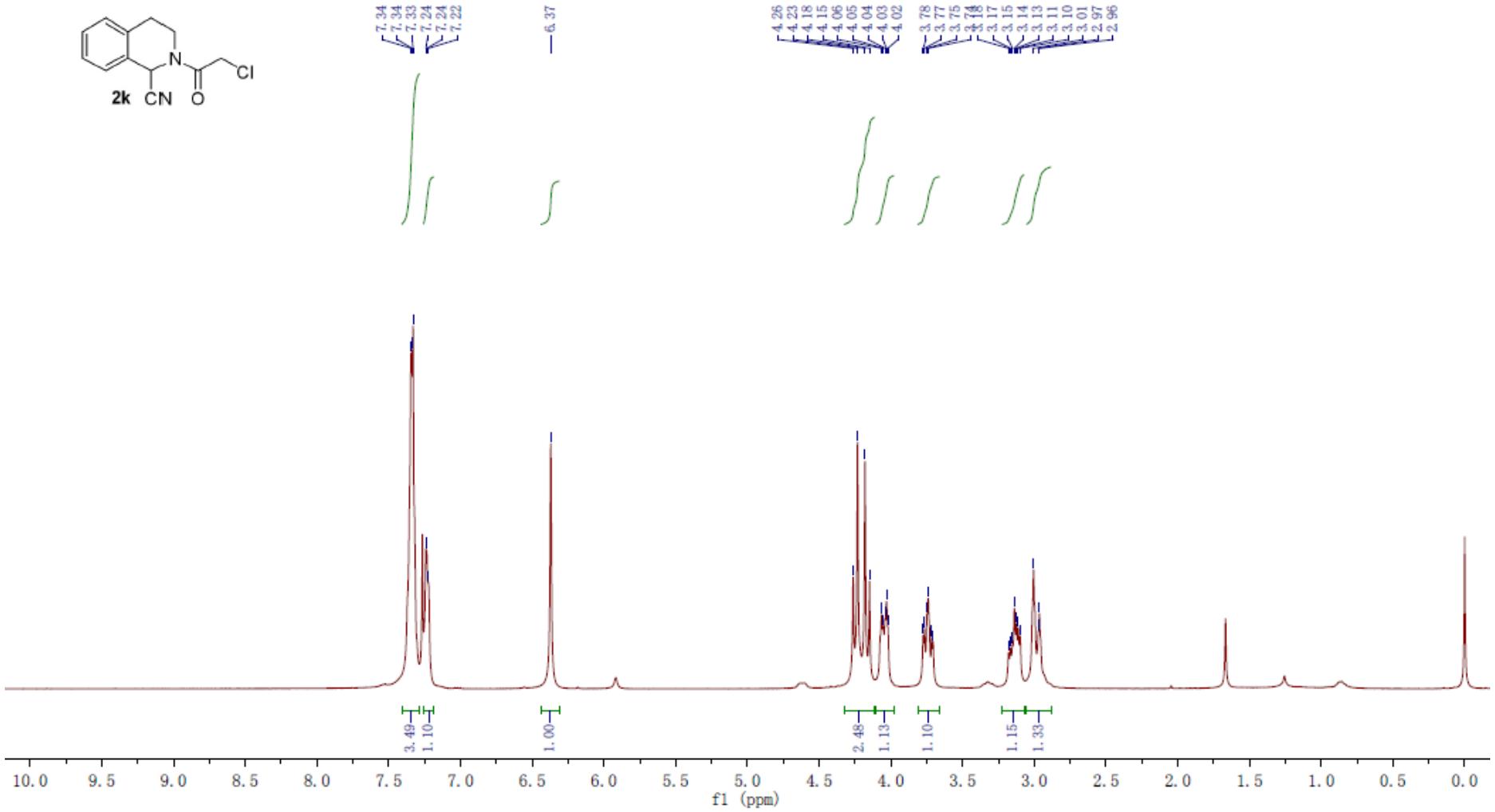
f1 (ppm)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CN
O
N
Cl
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7.33
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7.24
7.22
6.37
4.26
4.23
4.18
4.15
4.06
4.05
4.04
4.03
4.02
3.78
3.77
3.75
3.74
3.18
3.17
3.15
3.14
3.13
3.11
3.10
3.01
2.97
2.96
3.49
1.10
1.00
2.48
1.13
1.10
1.15
1.33
10.0
9.5
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
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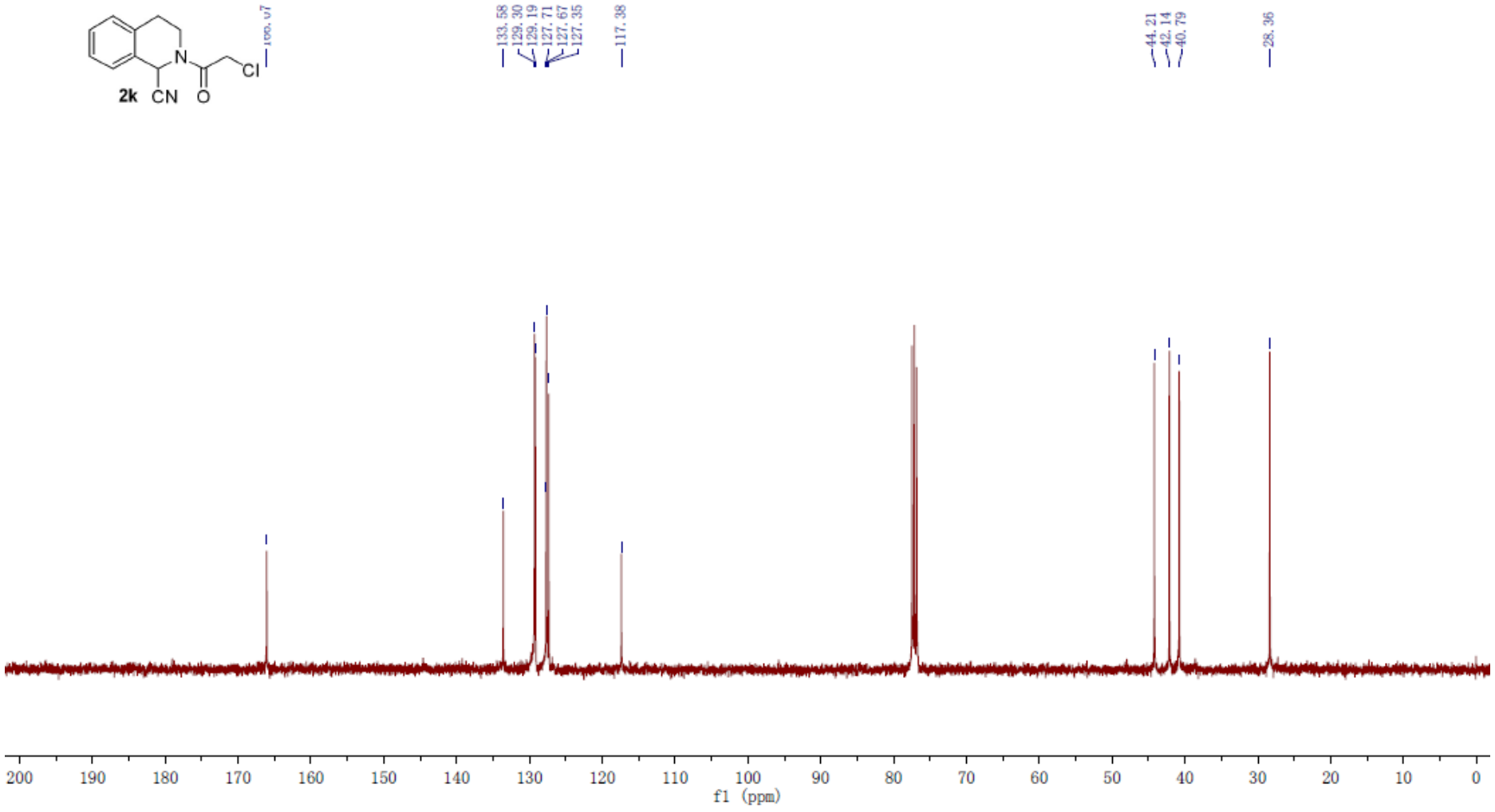
0.0
f1 (ppm)


2k
CN
O
N
Cl
133.58
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129.19
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127.67
127.35
117.38
44.21
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40.79
28.36
200
190
180
170
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150
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130
120
110
100
90
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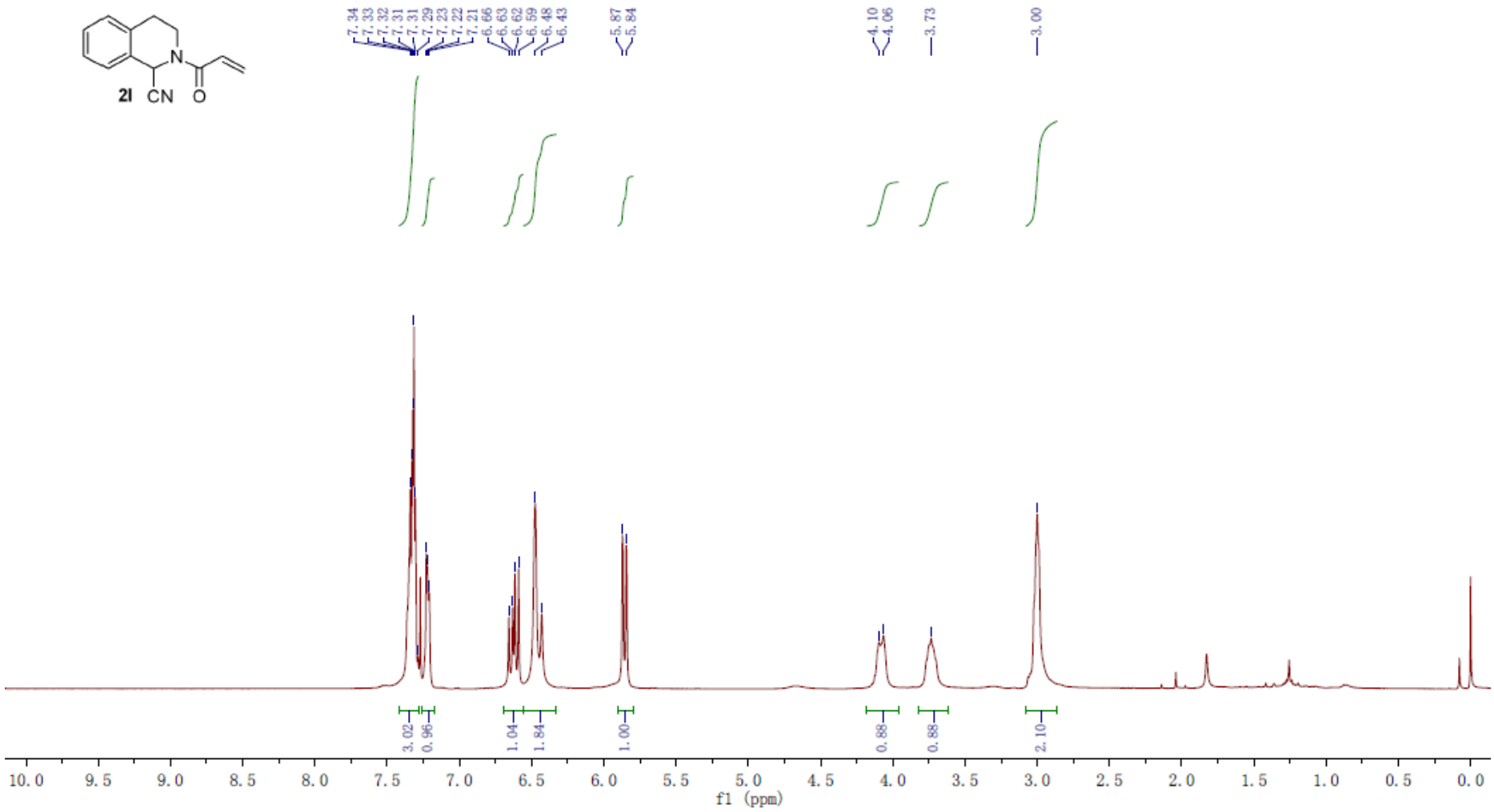
70
60
50
40
30
20
10
0
f1 (ppm)


2l
CN
O
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7.33
7.32
7.31
7.31
7.29
7.23
7.22
7.21
6.66
6.63
6.62
6.59
6.48
6.43
5.87
5.84
4.10
4.06
3.73
3.00
3.02
0.96
1.04
1.84
1.00
0.88
0.88
2.10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
1.5
1.0
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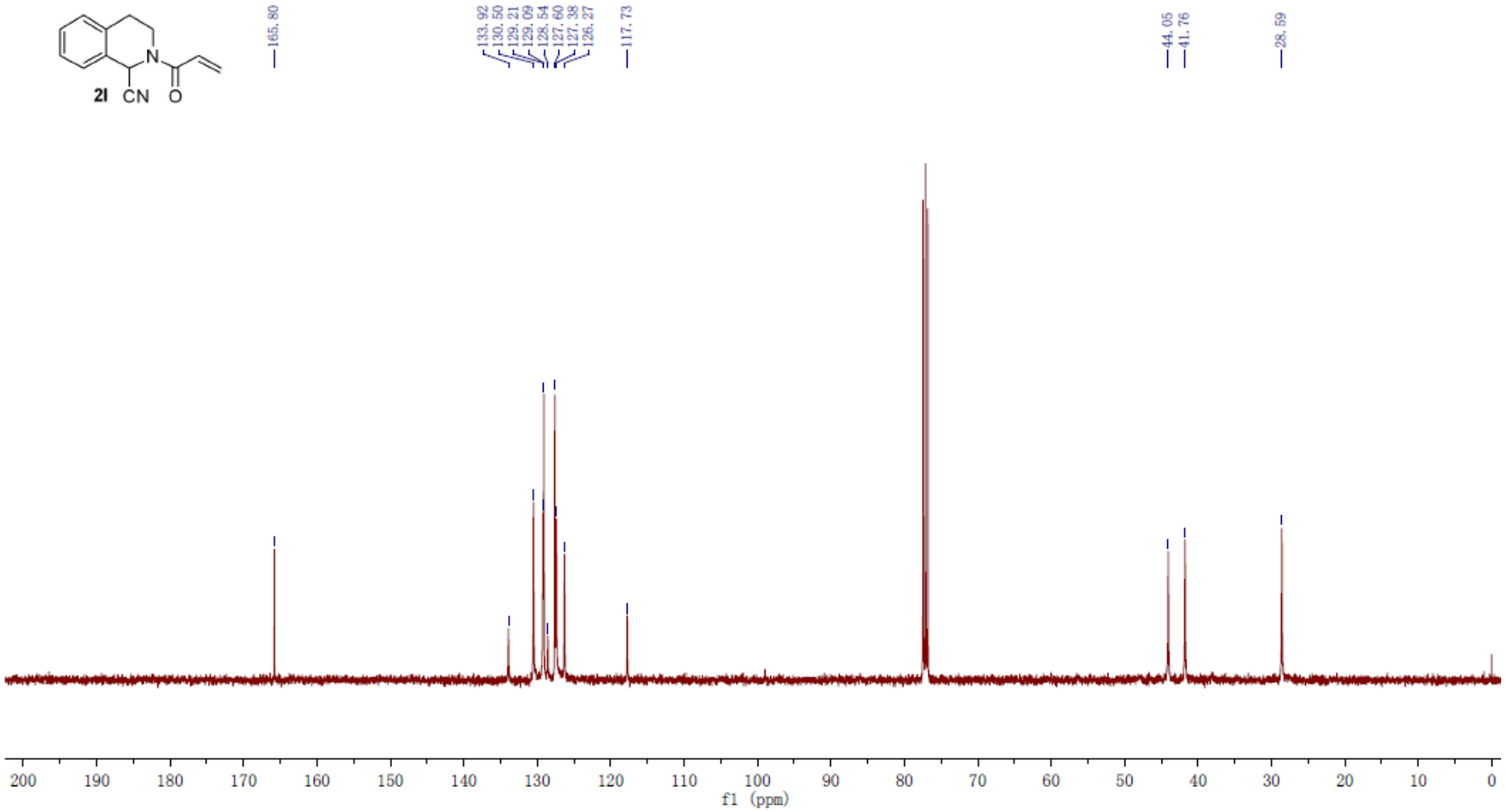
0.0
f1 (ppm)


2l
CN
O
165.80
133.92
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129.21
129.09
128.54
127.60
127.38
126.27
117.73
44.05
41.76
28.59
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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50
40
30
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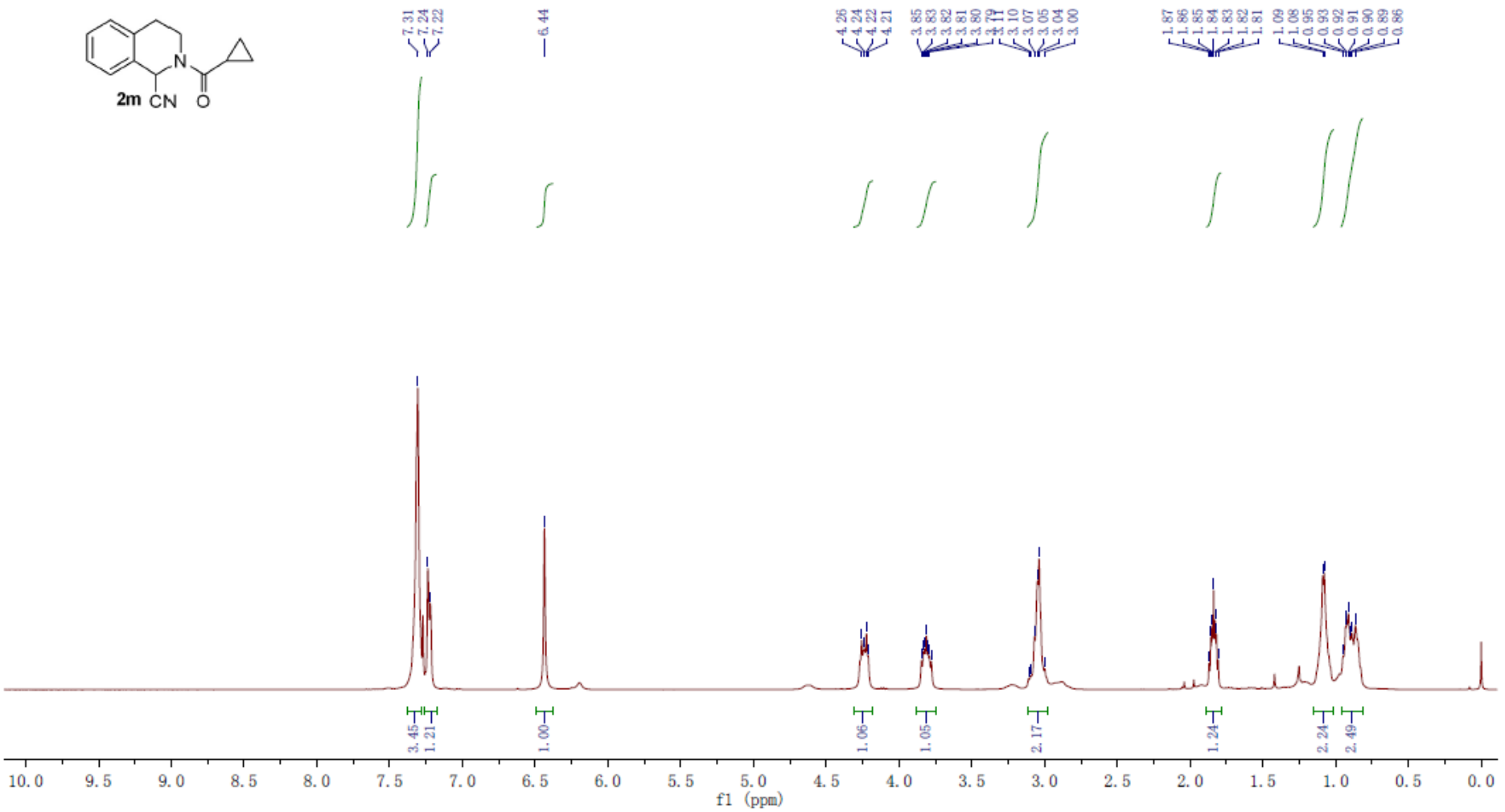
f1 (ppm)


2m
CN
O
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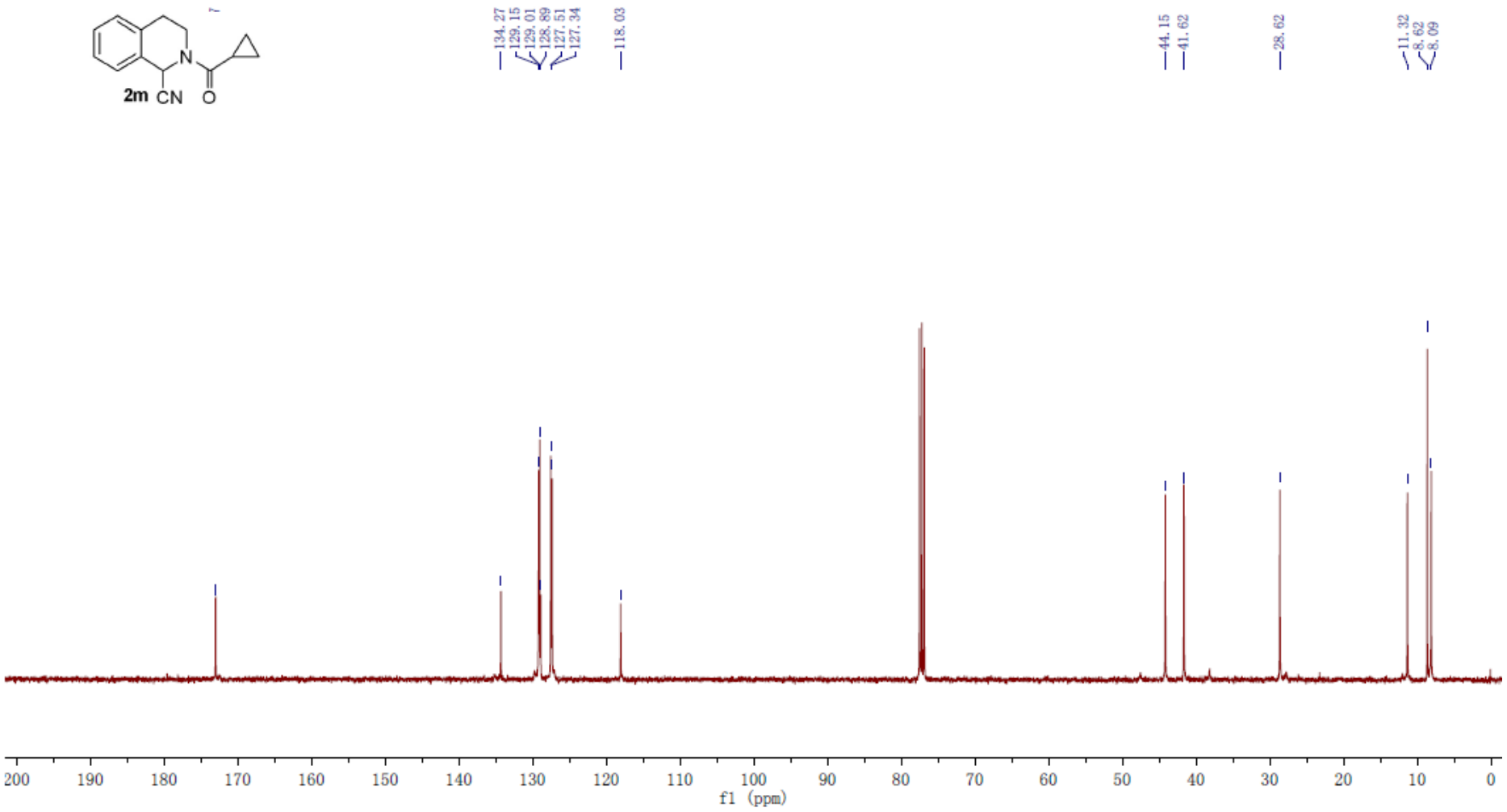
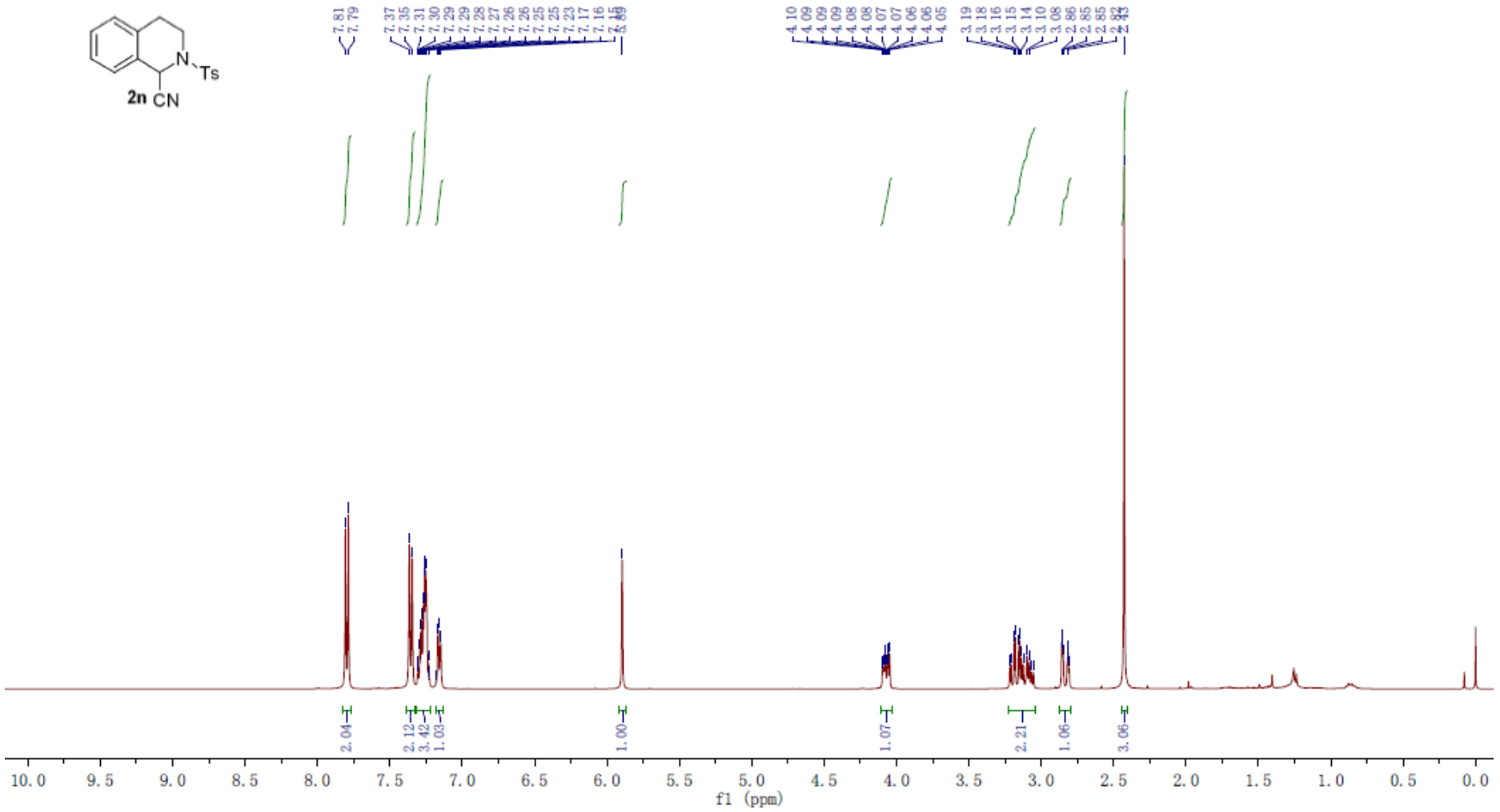
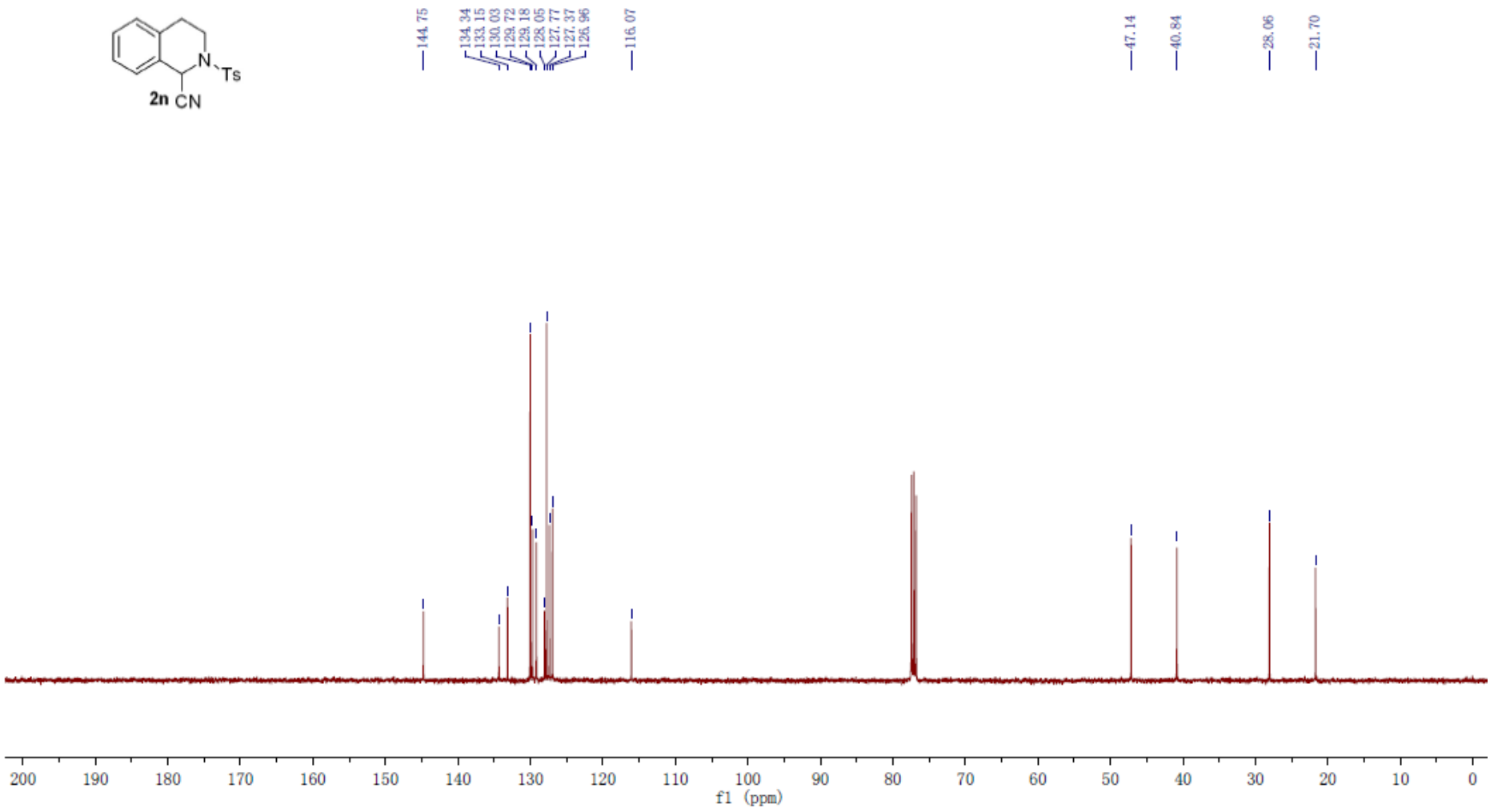
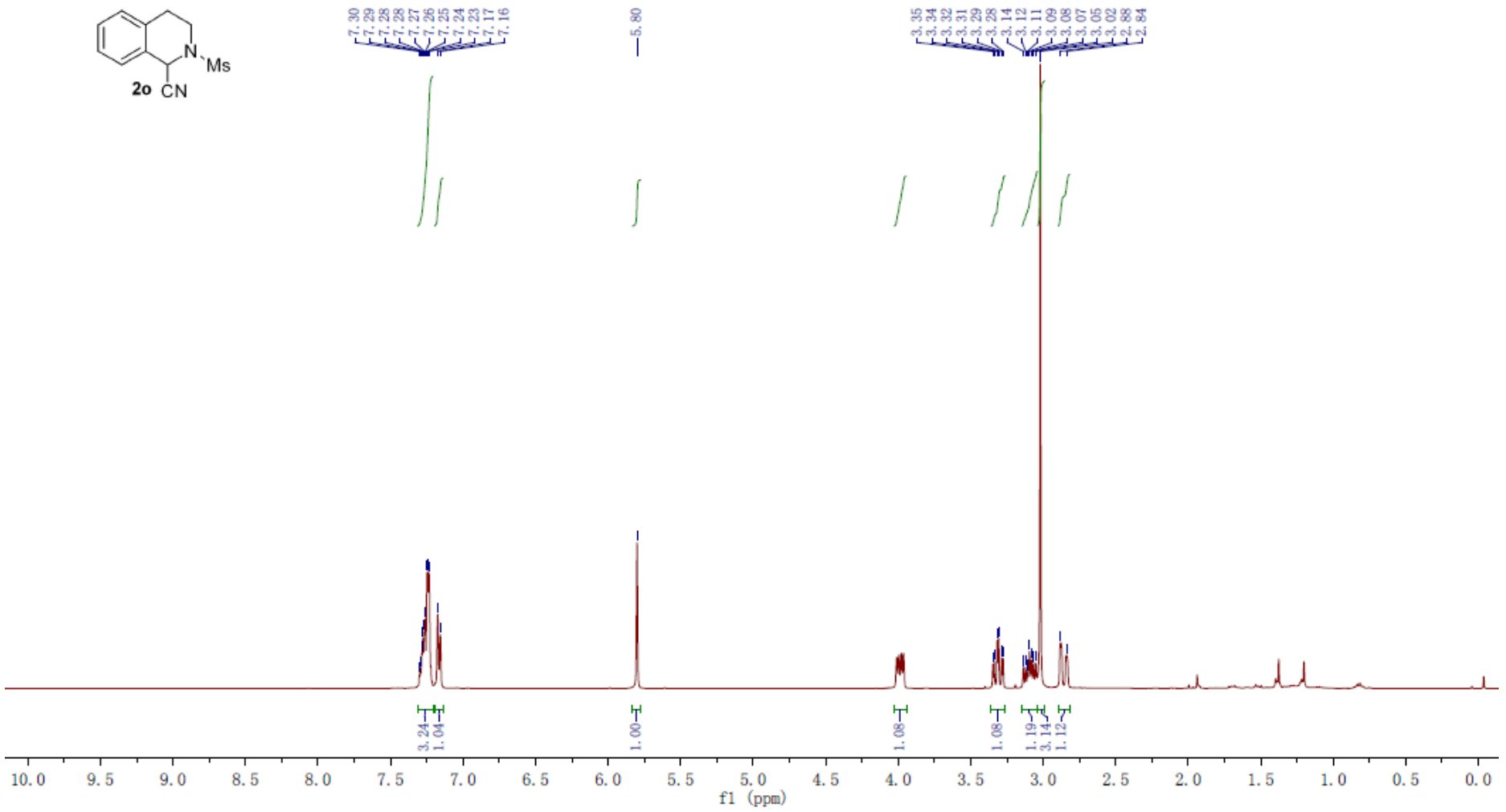
7.24
7.22
6.44
4.26
4.24
4.22
4.21
3.85
3.83
3.82
3.81
3.80
3.07
3.05
3.04
3.00
1.87
1.86
1.85
1.84
1.83
1.82
1.81
1.09
1.08
0.95
0.93
0.92
0.91
0.90
0.89
0.86
3.45
1.21
1.00
1.06
1.05
2.17
1.24
2.24
2.49
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

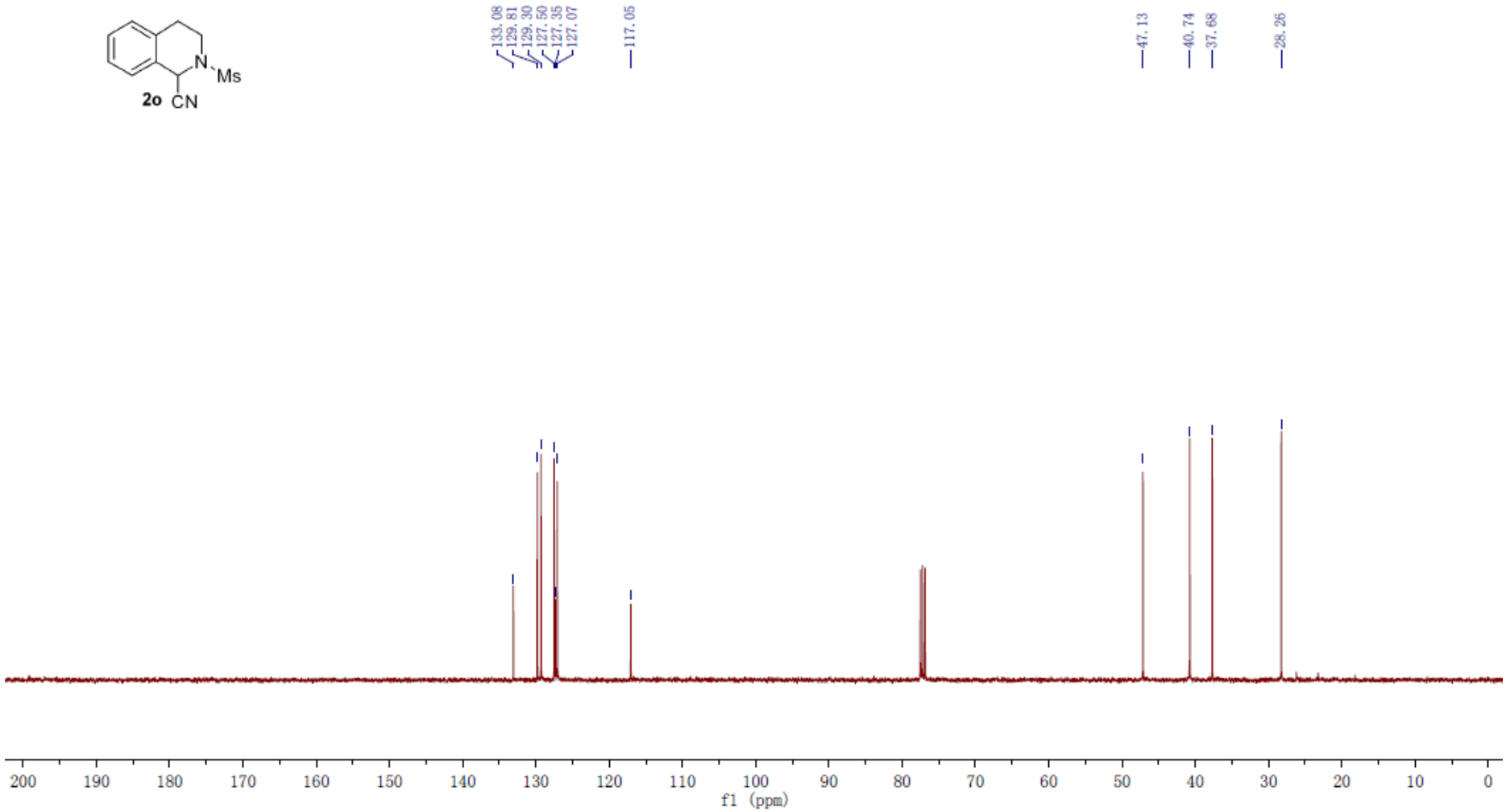

2m
CN
O
134.27
129.15
129.01
128.89
127.51
127.34
118.03
44.15
41.62
28.62
11.32
8.62
8.09
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

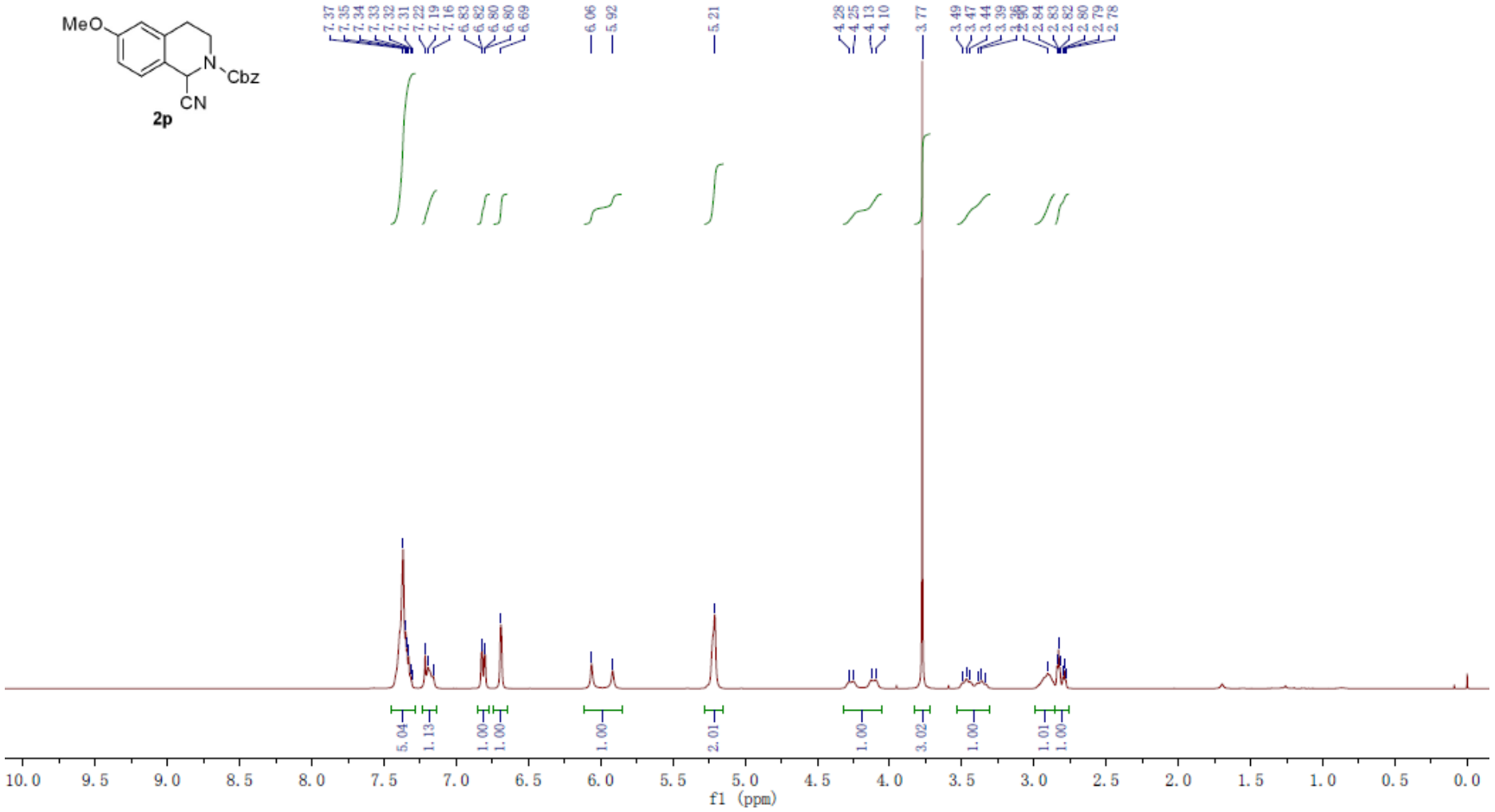

2n
CN
N
Ts
7.81
7.79
7.37
7.35
7.31
7.30
7.29
7.29
7.28
7.27
7.26
7.26
7.25
7.25
7.23
7.17
7.16
4.10
4.09
4.09
4.09
4.08
4.08
4.07
4.07
4.06
4.06
4.05
3.19
3.18
3.16
3.15
3.14
3.10
3.08
2.86
2.85
2.85
2.84
2.83
2.04
2.12
3.42
1.03
1.00
1.07
2.21
1.06
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

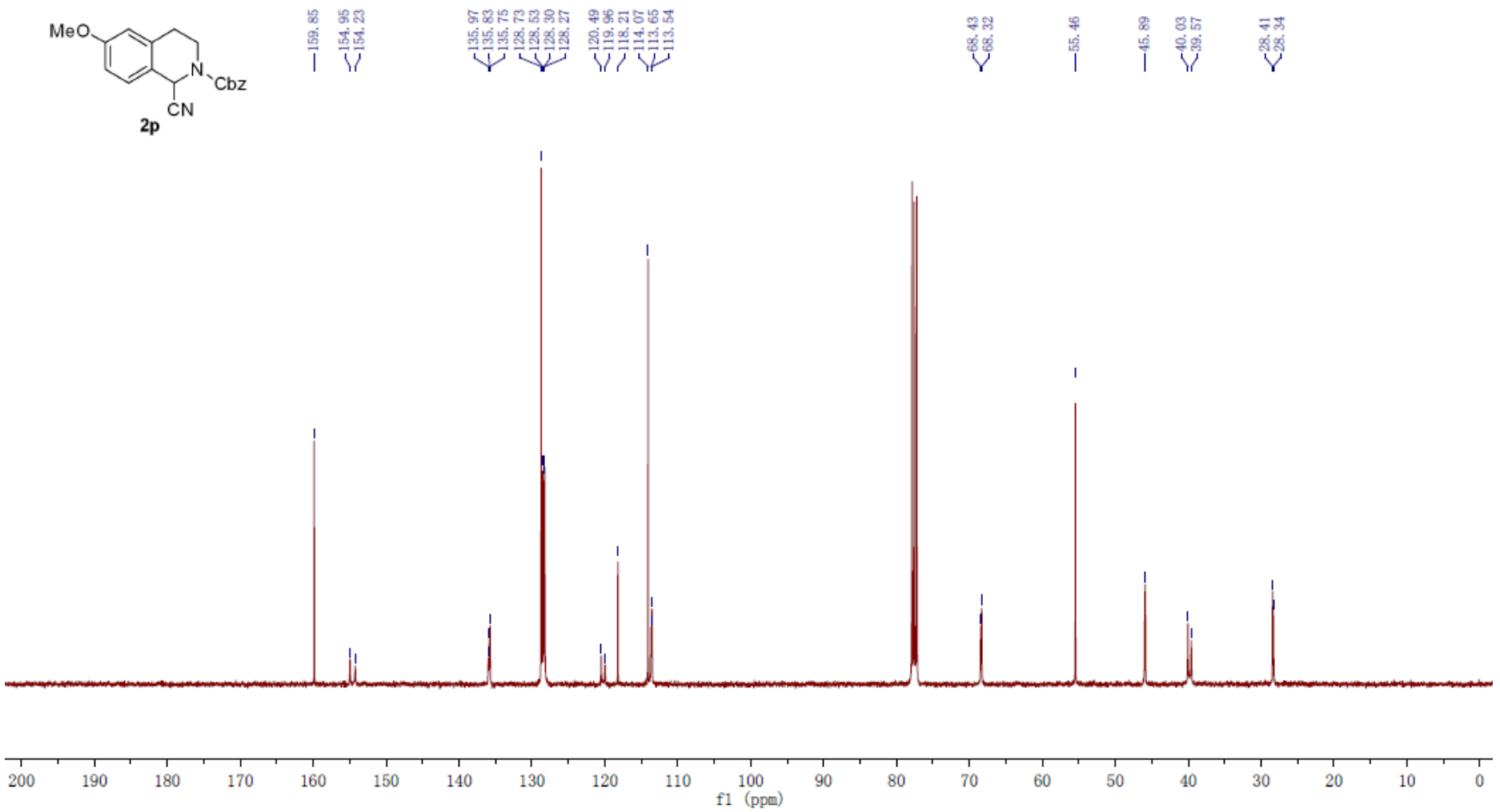

2n
CN
N
Ts
144.75
134.34
133.15
130.03
129.72
129.18
128.05
127.77
127.37
126.96
116.07
47.14
40.84
28.06
21.70
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N
Ms
2o CN
7.30
7.29
7.28
7.28
7.27
7.26
7.25
7.24
7.23
7.17
7.16
5.80
3.35
3.34
3.32
3.31
3.29
3.28
3.14
3.12
3.11
3.09
3.08
3.07
3.05
3.02
2.88
2.84
3.24
1.04
1.00
1.08
1.08
1.19
3.14
1.12
10.0
9.5
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
Ms
2o CN


133.08
129.81
129.30
127.50
127.35
127.07
117.05
47.13
40.74
37.68
28.26
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


MeO
N
Cbz
CN
2p
7.37
7.35
7.34
7.33
7.32
7.31
7.22
7.19
7.16
6.83
6.82
6.80
6.80
6.69
6.06
5.92
5.21
4.28
4.25
4.13
4.10
3.77
3.49
3.47
3.44
3.39
2.84
2.83
2.82
2.80
2.79
2.78
5.04
1.13
1.00
1.00
1.00
2.01
1.00
3.02
1.00
1.01
1.00
10.0
9.5
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)


MeO
N
Cbz
CN
2p
159.85
154.95
154.23
135.97
135.83
135.75
128.73
128.53
128.30
128.27
120.49
119.96
118.21
114.07
113.65
113.54
68.43
68.32
55.46
45.89
40.03
39.57
28.41
28.34
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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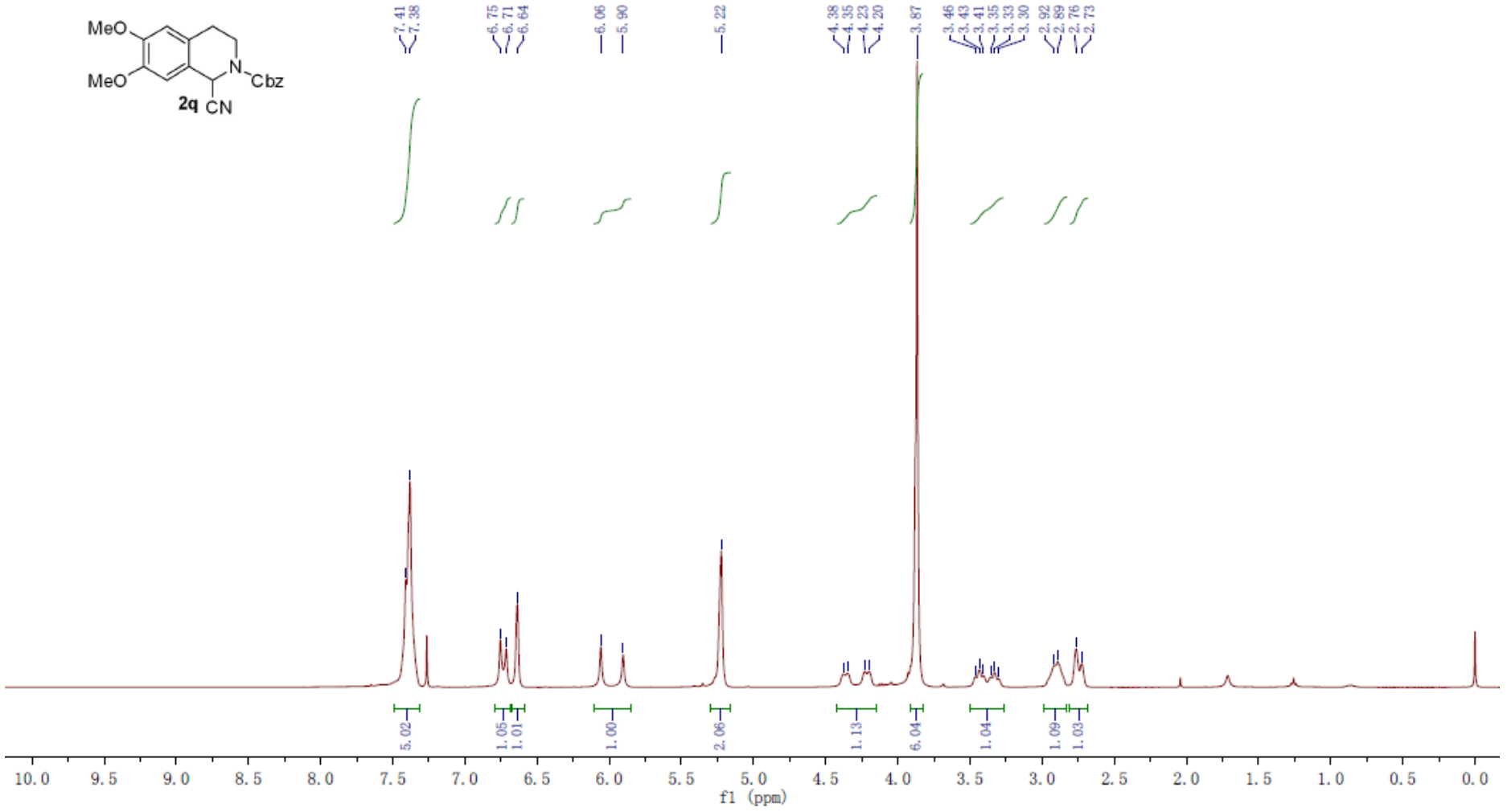
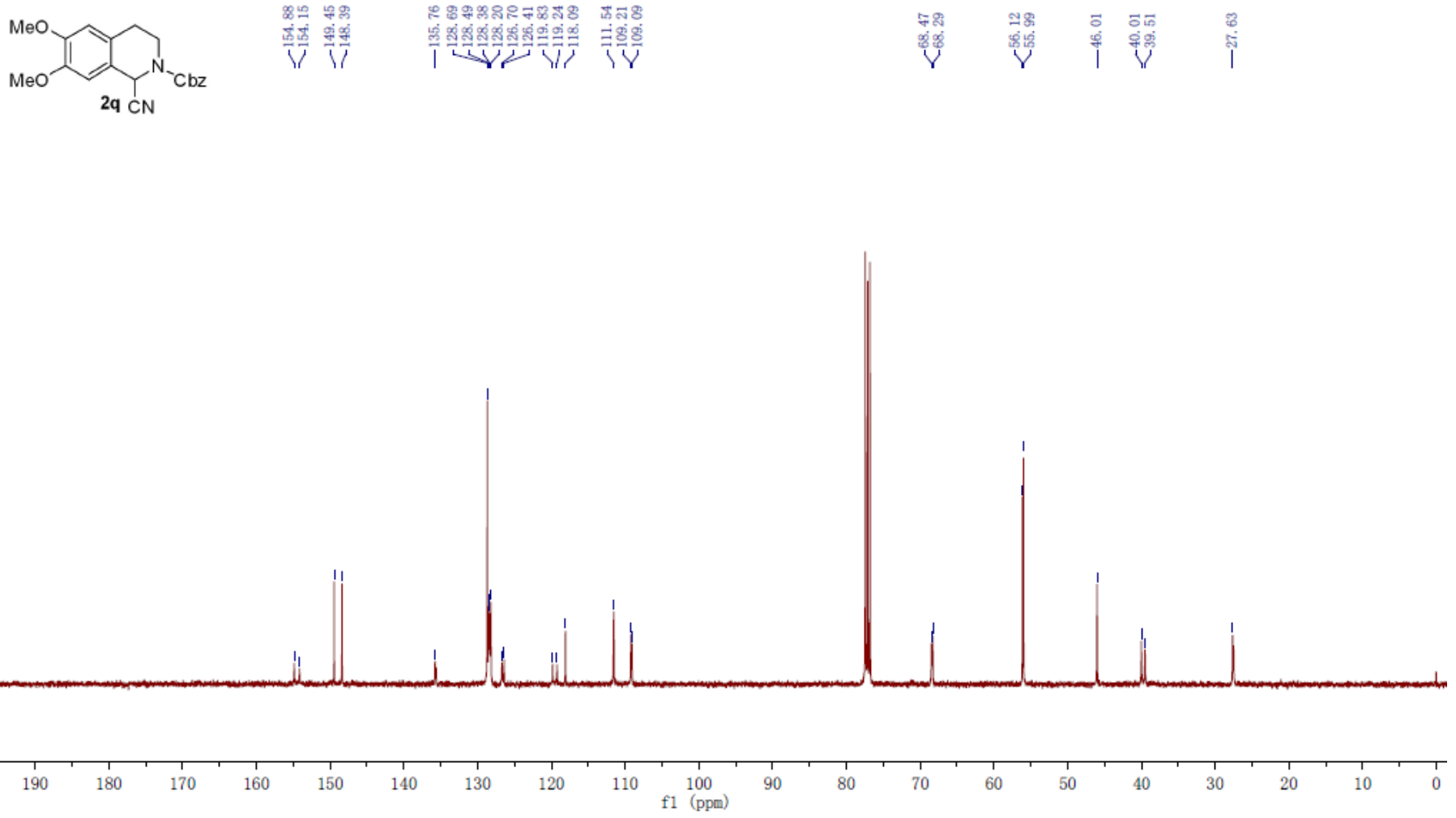
50
40
30
20
10
0
f1 (ppm)


MeO
MeO
N
Cbz
2q CN
7.41
7.38
6.75
6.71
6.64
6.06
5.90
5.22
4.38
4.35
4.23
4.20
3.87
3.46
3.43
3.41
3.35
3.33
3.30
2.92
2.89
2.76
2.73
5.02
1.05
1.01
1.00
2.06
1.13
6.04
1.04
1.09
1.03
10.0 9.5 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)


MeO
MeO
N
Cbz
2q CN
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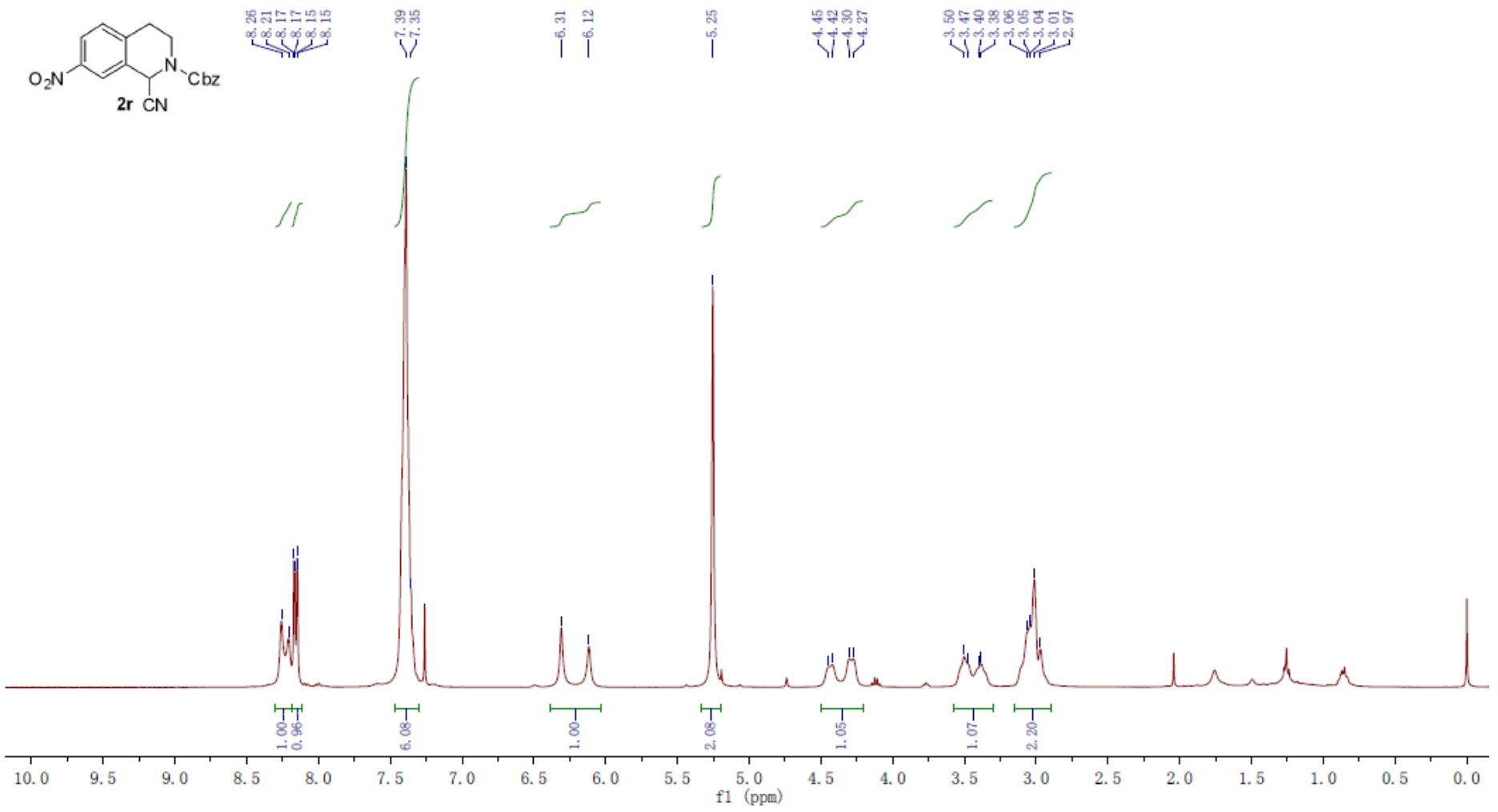
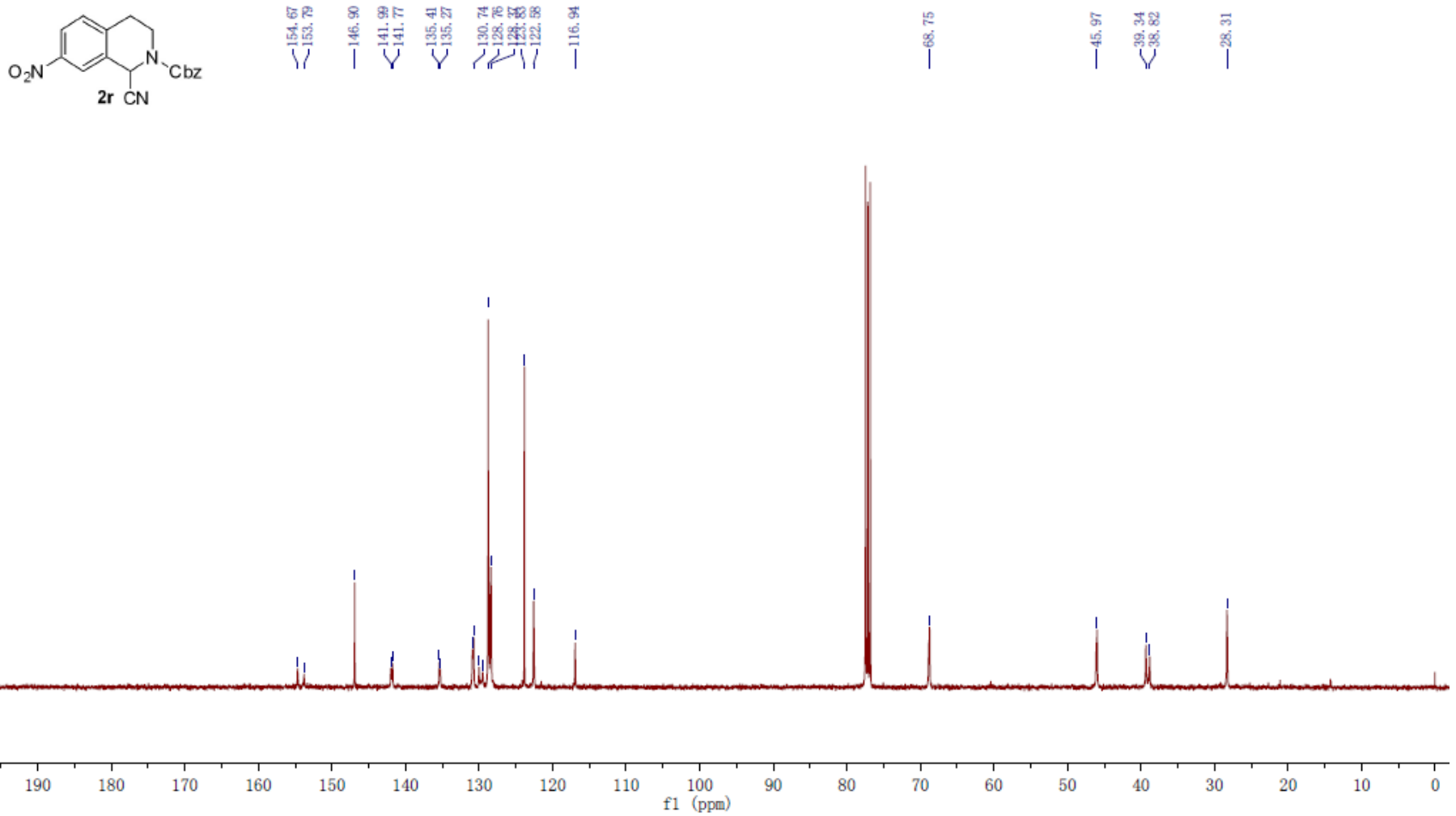
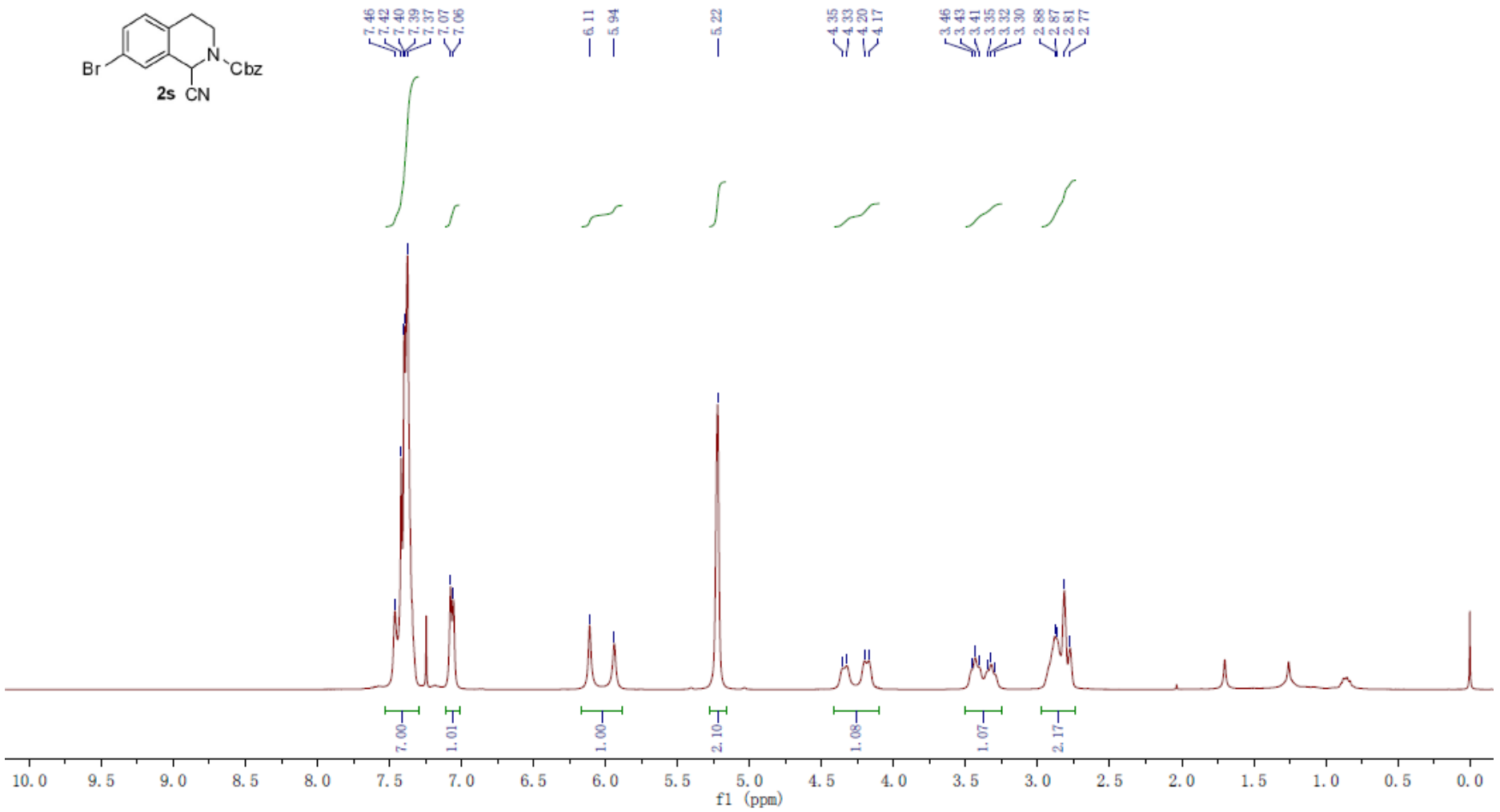
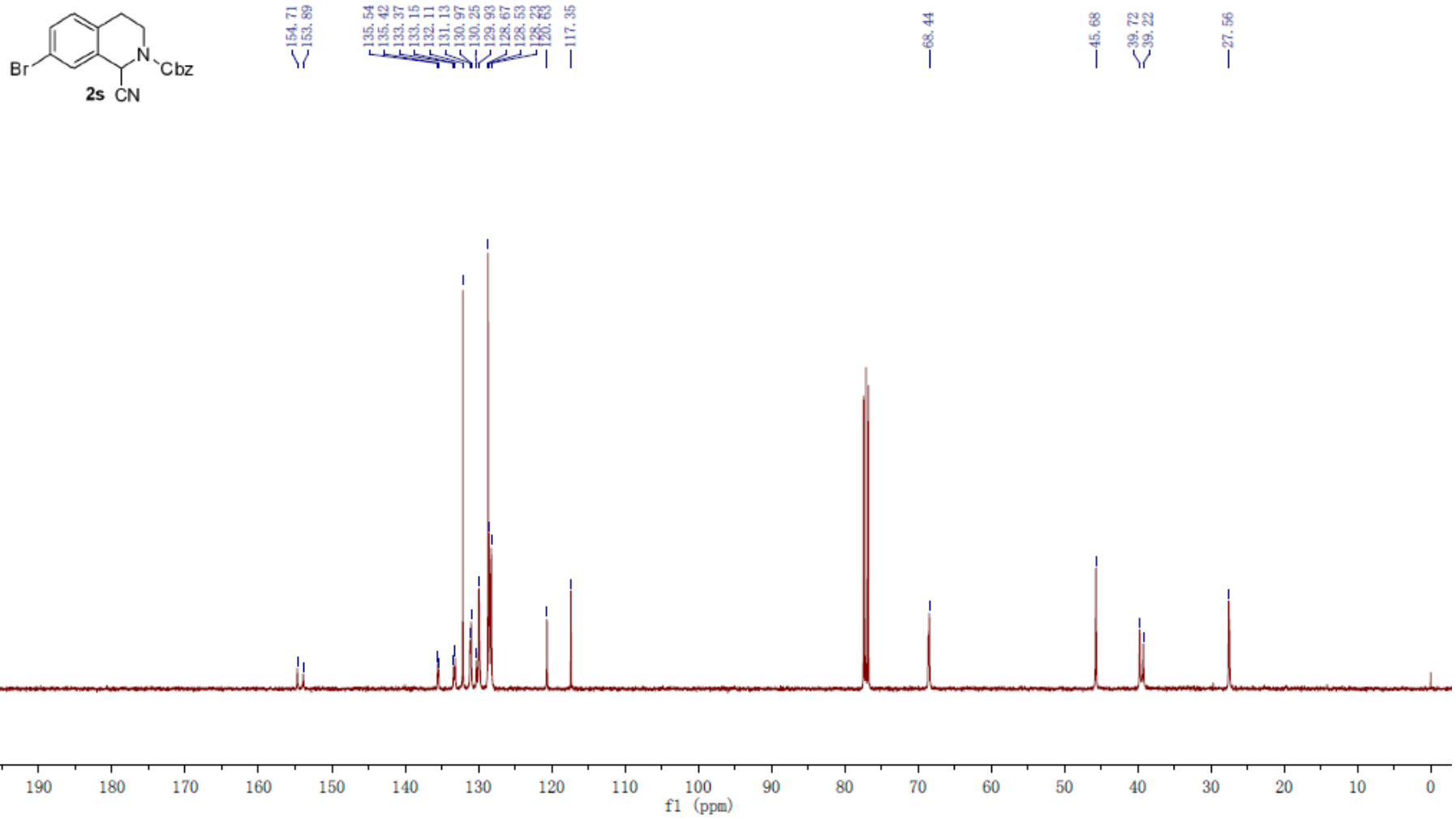
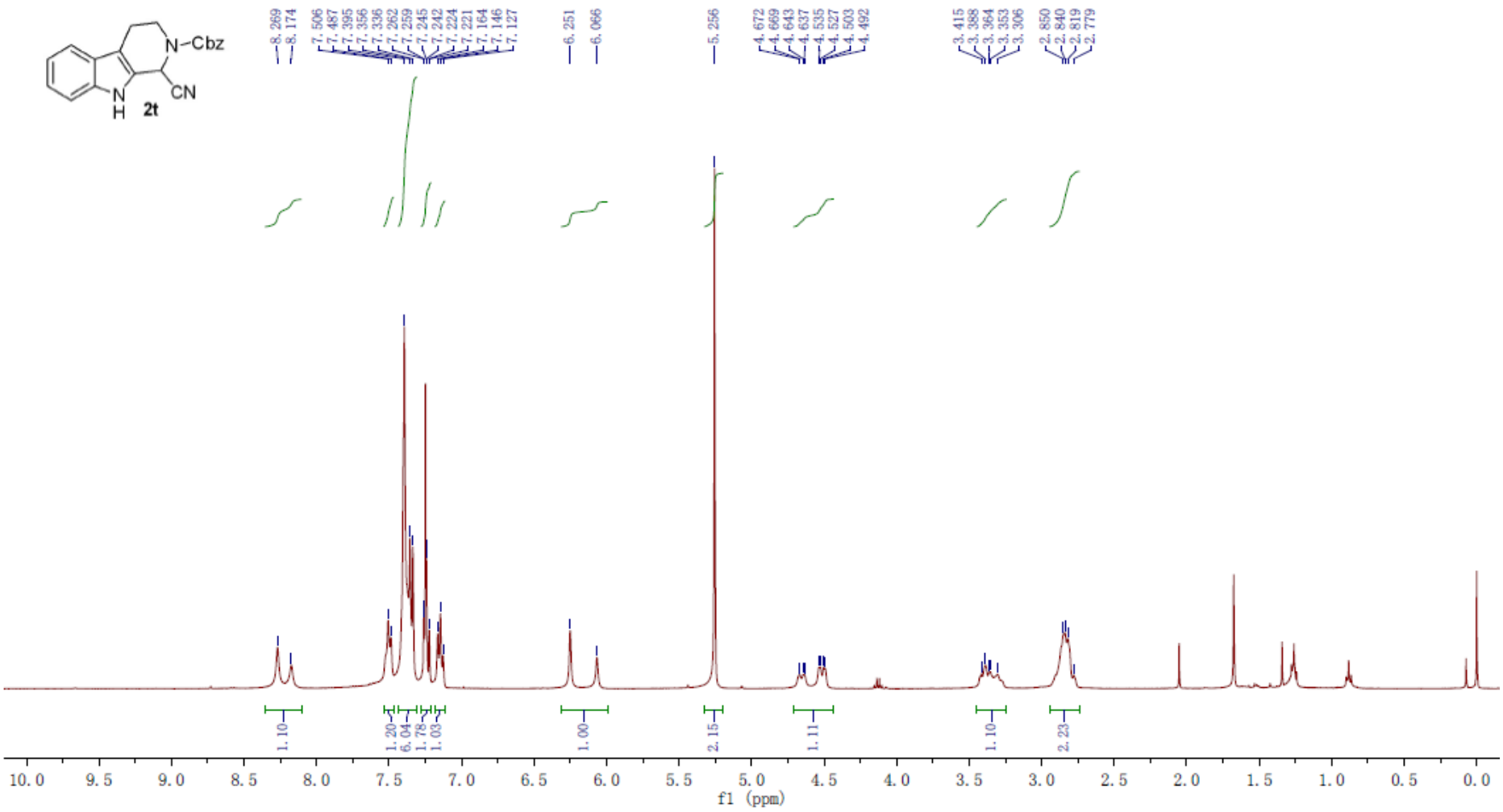
154.15
149.45
148.39
135.76
128.69
128.49
128.38
128.20
126.70
126.41
119.83
119.24
118.09
111.54
109.21
109.09
68.47
68.29
56.12
55.99
46.01
40.01
39.51
27.63
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O2N
N
Cbz
2r CN
8.26
8.21
8.17
8.17
8.15
8.15
7.39
7.35
6.31
6.12
5.25
4.45
4.42
4.30
4.27
3.50
3.47
3.40
3.38
3.06
3.05
3.04
3.01
2.97
1.00
0.96
6.08
1.00
2.08
1.05
1.07
2.20
10.0
9.5
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)


O2N
N
Cbz
2r CN
154.67
153.79
146.90
141.99
141.77
135.41
135.27
130.74
128.76
122.58
116.94
68.75
45.97
39.34
38.82
28.31
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Br
N
Cbz
2s CN
7.46
7.42
7.40
7.39
7.37
7.07
7.06
6.11
5.94
5.22
4.35
4.33
4.20
4.17
3.46
3.43
3.41
3.35
3.32
3.30
2.88
2.87
2.81
2.77
7.00
1.01
1.00
2.10
1.08
1.07
2.17
10.0
9.5
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)


Br
N
Cbz
2s CN
154.71
153.89
135.54
135.42
133.37
133.15
132.11
131.13
130.97
130.25
129.93
128.67
128.53
120.63
117.35
68.44
45.68
39.72
39.22
27.56
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


N-Cbz
CN
N
H
2t
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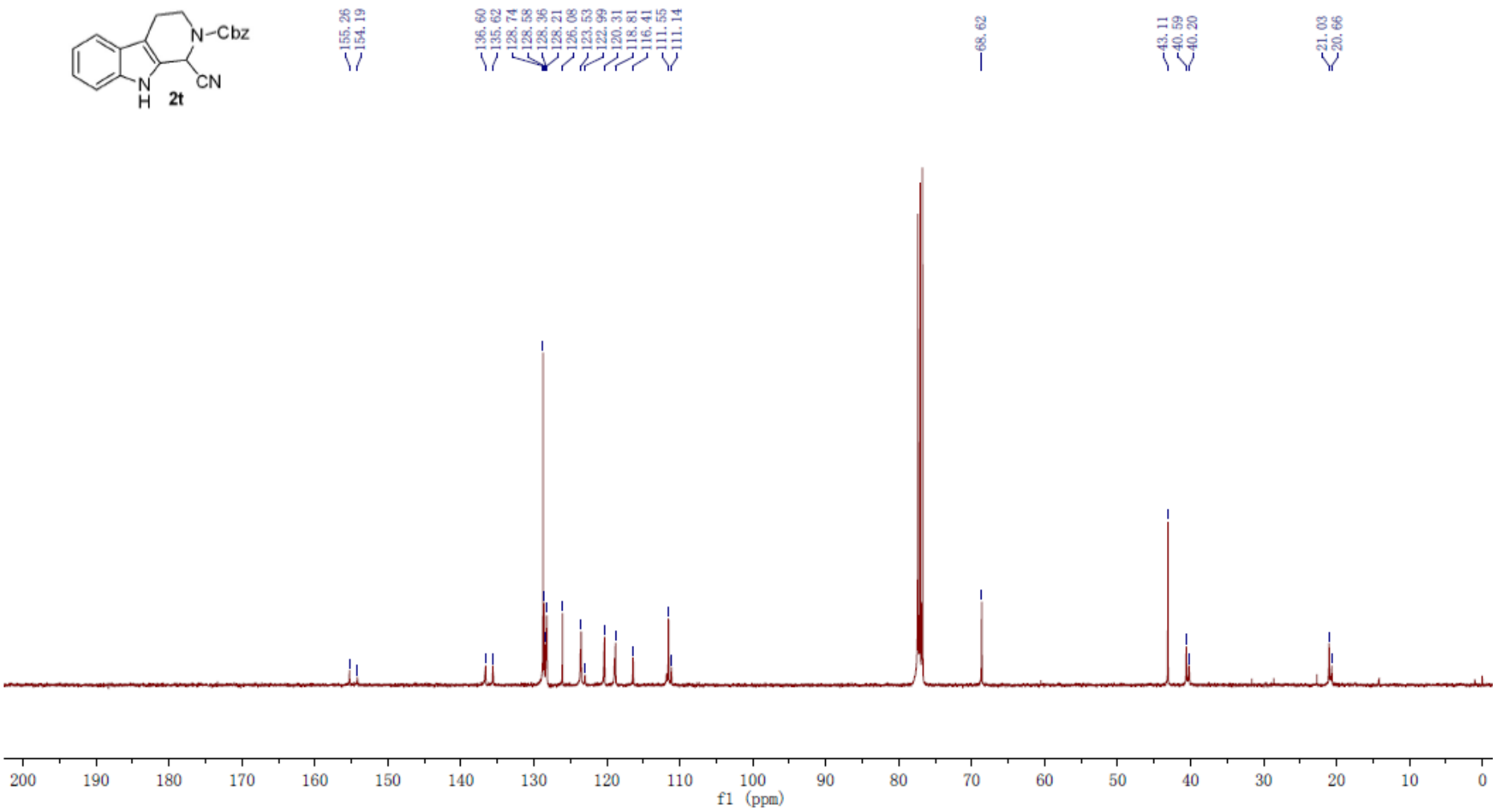
8.174
7.506
7.487
7.395
7.356
7.336
7.262
7.259
7.245
7.242
7.224
7.221
7.164
7.146
7.127
6.251
6.066
5.256
4.672
4.669
4.643
4.637
4.535
4.527
4.503
4.492
3.415
3.388
3.364
3.353
3.306
2.850
2.840
2.819
2.779
1.10
1.20
6.04
1.78
1.03
1.00
2.15
1.11
1.10
2.23
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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-Cbz
CN
N
H
2t
155.26
154.19
136.60
135.62
128.74
128.58
128.36
128.21
126.08
123.53
122.99
120.31
118.81
116.41
111.55
111.14
68.62
43.11
40.59
40.20
21.03
20.66
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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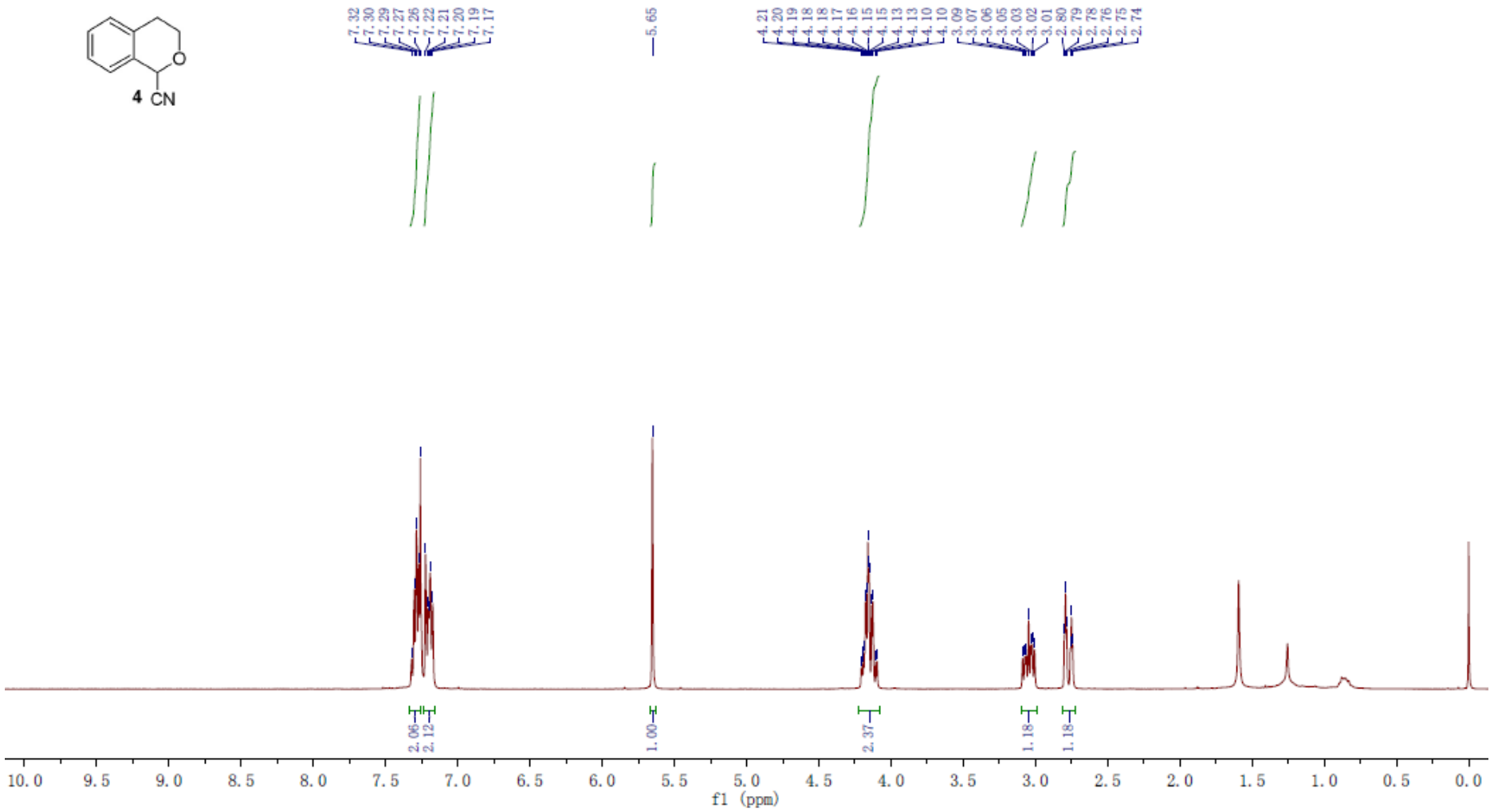
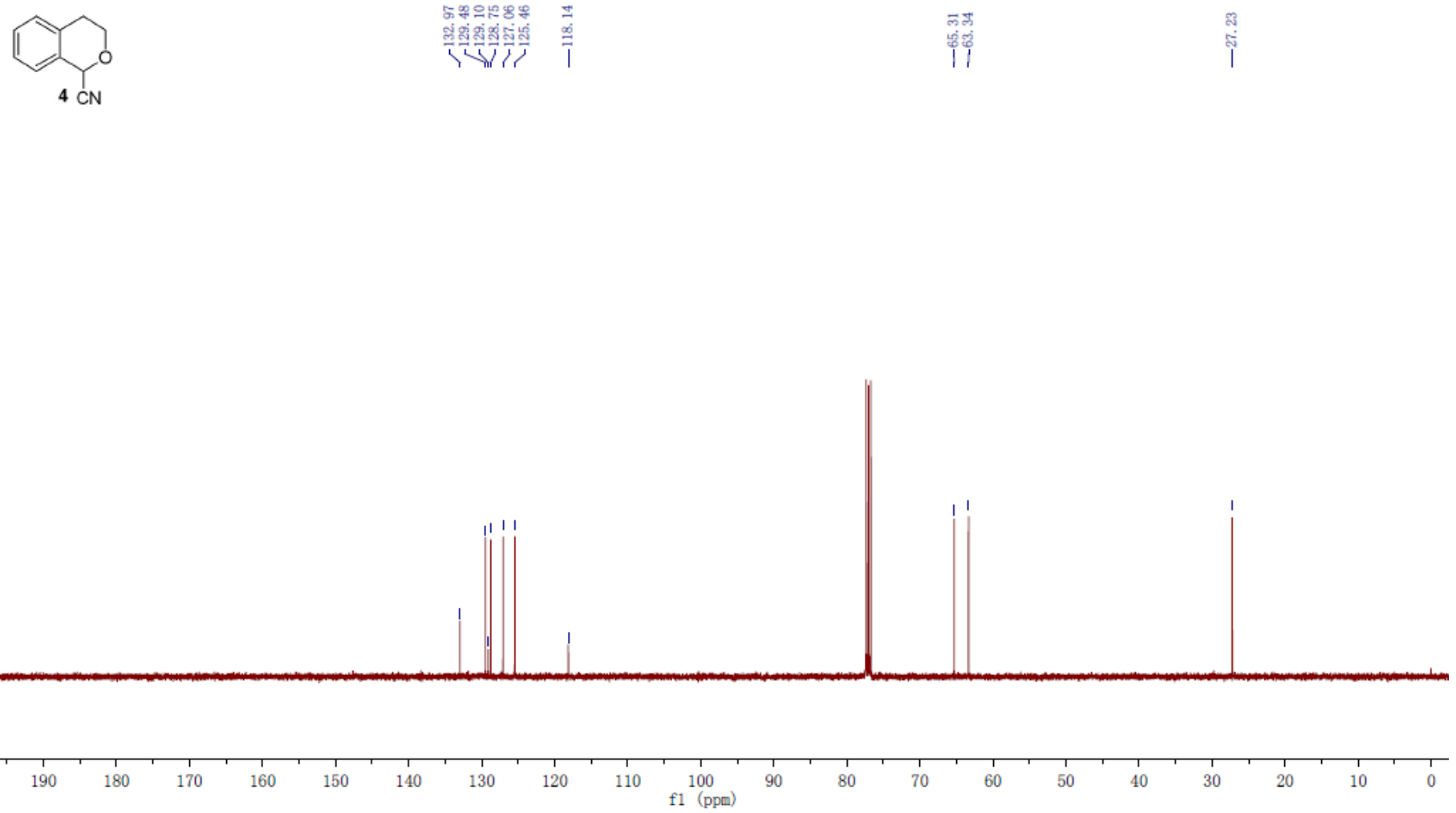
50
40
30
20
10
0
f1 (ppm)


4 CN
7.32
7.30
7.29
7.27
7.26
7.22
7.21
7.20
7.19
7.17
5.65
4.21
4.20
4.19
4.18
4.18
4.17
4.16
4.15
4.15
4.13
4.13
4.10
4.10
3.09
3.07
3.06
3.05
3.03
3.02
3.01
2.80
2.79
2.78
2.76
2.75
2.74
2.06
2.12
1.00
2.37
1.18
1.18
10.0
9.5
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)


4 CN
132.97
129.48
129.10
128.75
127.06
125.46
118.14
65.31
63.34
27.23
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)