Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Concise Synthesis of α-Cyano Tetrahydroisoquinolines with a Quaternary Center *via* Strecker Reaction

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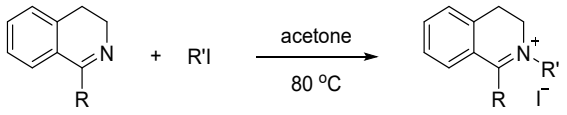
1. General

Commercially available reagents were used without further purification. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at room temperature in $CDCl_3$ on 400 MHz instrument with TMS (tetramethylsilane) as internal standard. Flash column chromatography was performed on neutral Al_2O_3 (200-300 mesh). The cyclic iminium salts **1** were prepared according to the known literature methods.[1]

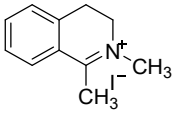
2. General Procedure for the Synthesis of Cyclic Iminium Salts



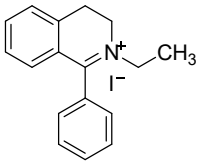
SM **1** **1**

General Procedure: A mixture of 1-substituted 3,4-dihydrosioquinoline (5.0 mmol) and alkyl iodide (15 mmol) in acetone (3.0 mL) was stirred at 80 °C overnight and the solid gradually formed. Afterwards the precipitate was filtered from the solution and washed with petroleum ether to give the corresponding cyclic iminium iodides **1**.

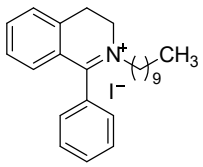
1,2-Dimethyl-3,4-dihydroisoquinolin-2-ium (1k): Yellow solid, 83% yield; m.p. = 191-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (m, 1H), 7.67 (dd, *J* = 7.5, 6.9 Hz, 1H), 7.48 (m, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 4.18 (t, *J* = 7.6 Hz, 2H), 3.96 (s, 3H), 3.36 (t, *J* = 7.6 Hz, 2H), 2.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 136.5, 136.5, 130.3, 128.5, 128.4, 127.5, 53.7, 47.4, 26.0, 20.8.



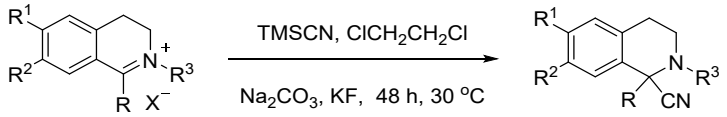
2-Ethyl-1-phenyl-3,4-dihydroisoquinolin-2-ium iodide (1l): Yellow solid, 82% yield; m.p. = 168-169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 6H), 7.45 (d, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 4.55 (t, *J* = 7.6 Hz, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 3.61 (t, *J* = 7.6 Hz, 2H), 1.47 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 137.6, 137.4, 134.1, 132.1, 129.4, 129.4, 128.5, 128.2, 128.1, 127.7, 54.8, 50.5, 26.3, 13.4.



2-Decyl-1-phenyl-3,4-dihydroisoquinolin-2-ium iodide (1m): Yellow solid, 94% yield; m.p. = 113-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (m, 6H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.31 (s, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 4.56 (t, *J* = 7.6 Hz, 2H), 4.19 – 3.96 (m, 2H), 3.59 (t, *J* = 7.6 Hz, 2H), 1.82 (m, 2H), 1.22 (m, 14H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 137.5, 137.3, 134.2, 132.0, 129.4, 129.4, 128.5, 128.4, 128.2, 127.7, 59.3, 50.9, 31.8, 29.3, 29.2, 29.2, 28.8, 27.8, 26.5, 26.3, 22.6, 14.1.



3. General Procedure for the Synthesis of α-Cyano Tetrahydroisoquinolines with a Quaternary Center *via* Strecker Reaction

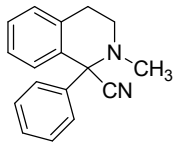


1 **2**

General Procedure: A mixture of TMSCN (99.2mg, 1 mmol) and potassium fluoride (58.1 mg, 1 mmol) in 1,2-dichloroethane (1.0 mL) were stirred in the schlenk tube at 30 °C for 30 min.

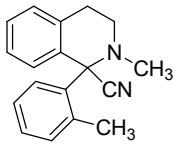
Then substrate **1** (0.5 mmol), sodium carbonate (26.5 mg, 0.25 mmol) and another 2 mL 1,2-dichloroethane were added into the reaction and stirred at 30°C for 48 h. After the completion, the reaction was quenched by saturated sodium bicarbonate solution. Subsequently, the mixture was extracted with dichloromethane twice and the combined organic extracts dried over sodium sulfate. The resulting residue was concentrated in vacuo and further purification was performed by a neutral Al_2O_3 column eluted with petroleum ether/ethyl acetate to give the products **2**.

2-Methyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2a): White solid, 93% yield, m.p. = 67-68 °C. R_f = 0.55 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$)

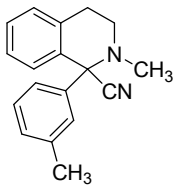


δ 7.56 (m, 2H), 7.43 – 7.27 (m, 3H), 7.22 – 7.09 (m, 2H), 7.07 – 6.94 (m, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 3.39 – 3.23 (m, 1H), 3.13 – 2.94 (m, 2H), 2.82 (dd, *J* = 16.2, 1.5 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 135.9, 134.0, 129.3, 128.9, 128.6, 128.6, 127.8, 127.8, 126.5, 117.1, 70.5, 49.6, 40.7, 29.1.

2-Methyl-1-(o-tolyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2b): the reaction temperature was raised up to 60°C; White solid, 85% yield, m.p. = 64-65 °C. R_f = 0.79 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 7.86 (m, 1H), 7.35 – 7.25 (m, 2H), 7.23 – 6.94 (m, 4H), 6.74 (d, *J* = 7.9 Hz, 1H), 3.33 – 3.19 (m, 1H), 3.16 – 2.93 (m, 2H), 2.84 (d, *J* = 16.0 Hz, 1H), 2.23 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1, 136.9, 135.0, 134.3, 133.1, 129.8, 128.7, 128.6, 127.8, 127.8, 126.8, 125.5, 117.0, 71.8, 49.7, 40.6, 28.7, 20.0.

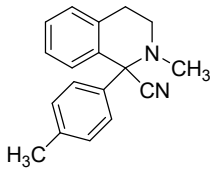


2-Methyl-1-(m-tolyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2c): White solid, 99% yield, m.p. = 89-90 °C. R_f = 0.55 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$)

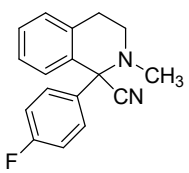


δ 7.36 (m, 2H), 7.25 (s, 1H), 7.21 – 7.09 (m, 3H), 7.03 (t, *J* = 6.9 Hz, 1H), 6.76 (m, 1H), 3.37 – 3.24 (m, 1H), 3.14 – 2.95 (m, 2H), 2.82 (d, *J* = 16.0 Hz, 1H), 2.34 (s, 3H), 2.26 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 138.4, 136.0, 133.9, 129.4, 129.3, 128.9, 128.4, 128.3, 127.8, 126.5, 125.0, 117.2, 70.5, 49.6, 40.8, 29.1, 21.5.

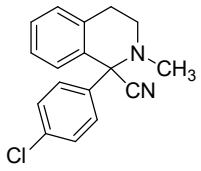
2-Methyl-1-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2d): White solid, 94% yield, m.p. = 113-114 °C. R_f = 0.56 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.8 Hz, 2H), 7.16 (m, 4H), 7.03 (m, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 3.37 – 3.23 (m, 1H), 3.14 – 2.95 (m, 2H), 2.81 (d, *J* = 16.0 Hz, 1H), 2.35 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 137.9, 136.1, 134.0, 129.3, 129.3, 128.9, 127.8, 127.7, 126.5, 117.3, 70.3, 49.6, 40.7, 29.1, 21.1.



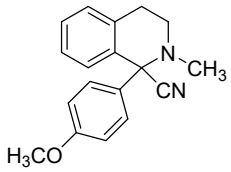
1-(4-Fluorophenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2e): Colorless liquid, 88% yield, m.p. = 95-96 °C. R_f = 0.54 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (m, 2H), 7.24 – 7.12 (m, 2H), 7.05 (m, 3H), 6.72 (d, *J* = 7.9 Hz, 1H), 3.35 – 3.23 (m, 1H), 3.13 – 2.95 (m, 2H), 2.82 (dd, *J* = 16.2, 1.4 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.71 (d, *J* = 248.2 Hz), 136.71 (d, *J* = 3.2 Hz), 135.64 (s), 133.96 (s), 129.60 (d, *J* = 8.3 Hz), 129.15 (s), 129.02 (s), 127.96 (s), 126.61 (s), 116.99 (s), 115.53 (d, *J* = 21.8 Hz), 69.89 (s), 49.56 (s), 40.65 (s), 29.00 (s); ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.1.



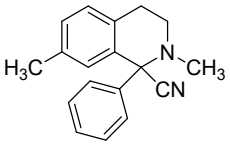
1-(4-Chlorophenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2f): White solid, 94% yield, m.p. = 124-125 °C. R_f = 0.56 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.34 (m, 2H), 7.22 – 7.10 (m, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 3.36 – 3.22 (m, 1H), 3.14 – 2.94 (m, 2H), 2.82 (dd, *J* = 16.2, 1.5 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 135.4, 134.6, 134.0, 129.2, 129.1, 129.1, 128.8, 128.0, 126.7, 116.8, 70.0, 49.5, 40.7, 29.0.



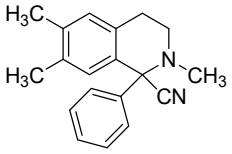
1-(4-Methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2g): White solid, 92% yield, m.p. = 79-80 °C. R_f = 0.45 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.22 – 7.10 (m, 2H), 7.09 – 6.98 (m, 1H), 6.88 (m, 2H), 6.76 (d, *J* = 7.9 Hz, 1H), 3.81 (s, 3H), 3.35 – 3.22 (m, 1H), 3.13 – 2.95 (m, 2H), 2.81 (m, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 136.1, 134.0, 132.8, 129.3, 129.0, 128.9, 127.8, 126.5, 117.3, 113.8, 69.9, 55.3, 49.6, 40.6, 29.1.



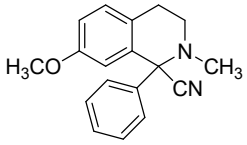
2,7-Dimethyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2h): Colorless liquid, 95% yield, m.p. = 57-58 °C. R_f = 0.58 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.48 (m, 2H), 7.36 (m, 3H), 7.01 (m, 2H), 6.53 (s, 1H), 3.32 – 3.19 (m, 1H), 3.12 – 2.92 (m, 2H), 2.78 (d, *J* = 15.8 Hz, 1H), 2.25 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 136.1, 135.6, 130.9, 129.5, 128.9, 128.8, 128.6, 128.5, 127.8, 117.3, 70.5, 49.7, 40.7, 28.7, 21.0.



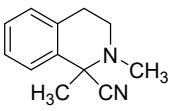
2,6,7-Trimethyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2i): White solid, 93% yield, m.p. = 108-109 °C. R_f = 0.50 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.48 (m, 2H), 7.46 – 7.28 (m, 3H), 6.92 (s, 1H), 6.48 (s, 1H), 3.30 – 3.16 (m, 1H), 3.02 (m, 2H), 2.74 (m, 1H), 2.24 (s, 3H), 2.18 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 136.6, 135.0, 133.2, 131.2, 129.9, 128.5, 128.5, 128.5, 127.8, 117.4, 70.3, 49.8, 40.7, 28.6, 19.4, 19.4.



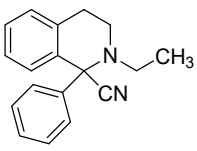
7-Methoxy-2-methyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2j): Colorless liquid, 86% yield. R_f = 0.50 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (m, 2H), 7.36 (m, 3H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.76 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.24 (d, *J* = 1.8 Hz, 1H), 3.59 (s, 3H), 3.29 – 3.17 (m, 1H), 3.12 – 2.93 (m, 2H), 2.76 (m, 1H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 140.7, 136.7, 129.9, 128.7, 128.6, 127.8, 126.1, 117.1, 114.3, 114.1, 70.6, 55.2, 49.8, 40.8, 28.3.



1,2-Dimethyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2k): Yellow oil, 87% yield. R_f = 0.30 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.37 (m, 1H), 7.26 – 7.20 (m, 2H), 7.12 (d, *J* = 6.2 Hz, 1H), 3.13 – 3.02 (m, 1H), 2.92 (m, 1H), 2.84 – 2.76 (m, 1H), 2.70 (m, 1H), 2.61 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.2, 134.3, 129.2, 127.9, 126.8, 126.7, 119.5, 60.2, 49.6, 40.6, 29.3, 26.5.

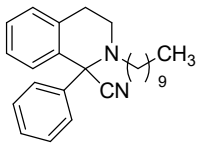


2-Ethyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2l): Colorless liquid, 85% yield. R_f = 0.67 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 6.2 Hz, 2H), 7.43 – 7.28 (m, 3H), 7.14 (d, *J* = 5.3 Hz, 2H), 7.07 – 6.93 (m, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 3.40 – 3.13 (m,

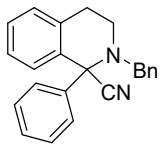


2H), 2.97 – 2.74 (m, 2H), 2.51 (m, 1H), 2.36 (m, 1H), 0.99 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 136.2, 134.3, 129.3, 128.9, 128.6, 128.5, 127.8, 127.7, 126.5, 118.0, 70.3, 45.9, 44.7, 29.4, 13.1.

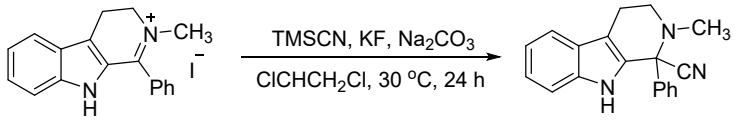
2-Decyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2m): Pale yellow liquid, 80% yield. R_f = 0.72 (petroleum ether/ethyl acetate 5:1).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 5.9 Hz, 2H), 7.33 (m, 3H), 7.13 (s, 2H), 7.02 (m, 1H), 6.73 (d, *J* = 7.9 Hz, 1H), 3.42 – 3.10 (m, 2H), 2.95 – 2.69 (m, 2H), 2.52 – 2.27 (m, 2H), 1.21 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 136.4, 134.4, 129.4, 128.9, 128.5, 128.4, 128.1, 127.6, 126.5, 117.9, 70.4, 51.3, 45.2, 31.9, 29.5, 29.5, 29.4, 29.3, 29.2, 27.4, 26.8, 22.7, 14.1.



2-Benzyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2n): Pale yellow solid, 85% yield, m.p. = 103-104 °C. R_f = 0.65 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (m, 2H), 7.43 – 7.22 (m, 8H), 7.20 – 7.09 (m, 2H), 7.04 (m, 1H), 6.79 (d, *J* = 7.9 Hz, 1H), 3.76 (d, *J* = 13.6 Hz, 1H), 3.36 (d, *J* = 13.6 Hz, 1H), 3.12 (m, 2H), 2.98 – 2.79 (m, 1H), 2.73 (d, *J* = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 138.2, 134.4, 129.5, 129.0, 128.8, 128.8, 128.4, 128.4, 128.0, 127.9, 127.3, 126.6, 117.6, 70.0, 55.8, 45.1, 29.2.



4. Synthesis of α-Cyano Tetrahydro-*β*-carboline with a Quaternary Center *via* Strecker Reaction

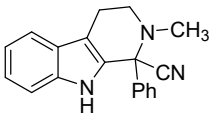


3 **4**

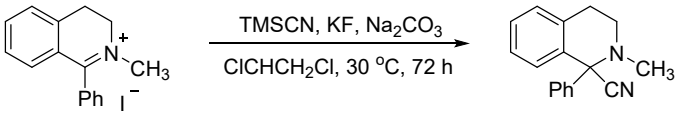
73% yield

A mixture of TMSCN (99.2mg, 1 mmol) and potassium fluoride (58.1 mg, 1 mmol) in 1,2-dichloroethane (1.0 mL) were stirred in the schlenk tube at 30 °C for 30 min. Then substrate **3** (0.5 mmol), sodium carbonate (26.5 mg, 0.25 mmol) and another 2 mL 1,2-dichloroethane was added into the reaction and stirred at 30°C for 24 h. After the completion, the reaction was quenched by saturated sodium bicarbonate solution. Subsequently, the mixture was extracted with dichloromethane twice and the combined organic extracts dried over sodium sulfate. The resulting residue was concentrated in vacuo and further purification was performed by a neutral Al_2O_3 column eluted with petroleum ether/ethyl acetate to give the product **4**.

2-Methyl-1-phenyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-1-carbonitrile (4): Pale yellow solid, 73% yield. R_f = 0.84 (petroleum ether/ethyl acetate 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.57 (m, 2H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.44 – 7.35 (m, 3H), 7.32 (s, 1H), 7.21 – 7.04 (m, 3H), 3.28 – 3.03 (m, 3H), 2.93 – 2.79 (m, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 136.9, 130.7, 129.6, 129.0, 127.56, 126.5, 123.1, 120.0, 119.1, 115.8, 111.4, 110.8, 67.2, 50.6, 39.8, 21.4.



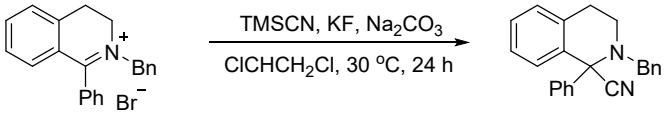
5. Synthesis of α-Cyano Tetrahydroisoquinolines at Gram Scale



1a **2a**

98% yield

A mixture of TMSCN (992.1mg, 10 mmol) and potassium fluoride (581.0 mg, 10 mmol) in 1,2-dichloroethane (10 mL) were stirred in the schlenk tube at 30 °C for 30 min. Then substrate **1a** (5 mmol, 1.7452), sodium carbonate (265.0 mg, 2.5 mmol) and another 10 mL 1,2-dichloroethane was added into the reaction and stirred at 30°C for 72 h. After the completion, the reaction was quenched by saturated sodium bicarbonate solution. Subsequently, the mixture was extracted with dichloromethane twice and the combined organic extracts dried over sodium sulfate. The resulting residue was concentrated in vacuo and further purification was performed by a neutral Al_2O_3 column eluted with petroleum ether/ethyl acetate to give the product **2a** in 98% yield.

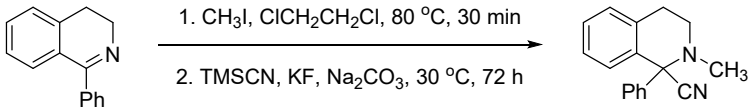


1n **2n**

81% yield

A mixture of TMSCN (793.7 mg, 8 mmol) and potassium fluoride (464.8 mg, 8 mmol) in 1,2-dichloroethane (10 mL) were stirred in the schlenk tube at 30 °C for 30 min. Then substrate **1n** (4 mmol, 1.5132 g), sodium carbonate (212.0 mg, 2 mmol) and another 12 mL 1,2-dichloroethane was added into the reaction and stirred at 30°C for 24 h. After the completion, the reaction was quenched by saturated sodium bicarbonate solution. Subsequently, the mixture was extracted with dichloromethane twice and the combined organic extracts dried over sodium sulfate. The resulting residue was concentrated in vacuo and further purification was performed by a neutral Al_2O_3 column eluted with petroleum ether/ethyl acetate to give the product **2n** in 81% yield.

6. Synthesis of 1-Cyano-1-phenyl-2-methyl-tetrahydroisoquinoline *via* One-pot Reaction with 1-Phenyl-3,4-dihydroisoquinoline as Starting Material



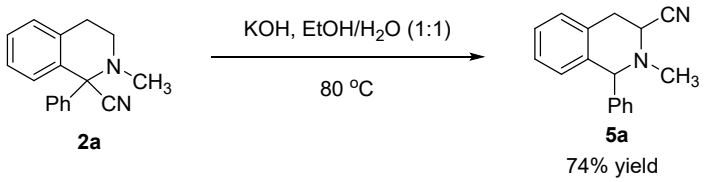
SM 1a **2a**

88% yield

A mixture of **SM 1a** (103.6mg, 0.5 mmol) and methyl iodide (212.9 mg, 1.5 mmol) in 1,2-dichloroethane (2.0 mL) were stirred in the sealed tube at 80 °C for 30 min. Then the sealed tube was cooled to room temperature, and TMSCN (99.2 mg, 1 mmol), potassium fluoride (58.1 mg, 1 mmol), sodium carbonate (26.5 mg, 0.25 mmol) and another 1 mL 1,2-dichloroethane were added into the sealed tube and stirred at 30 °C for 72 h. After the completion, the reaction was quenched by saturated sodium bicarbonate solution. Subsequently, the mixture was extracted with dichloromethane twice and the combined organic extracts dried over sodium sulfate. The resulting residue was concentrated in vacuo and further purification was performed by a neutral Al_2O_3

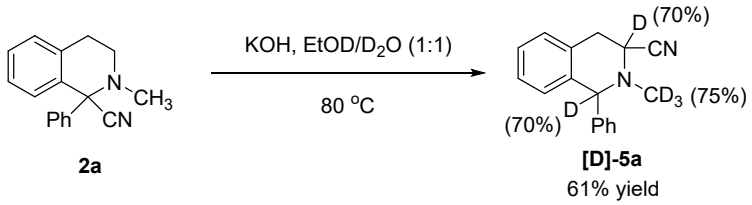
column eluted with petroleum ether/ethyl acetate to give the product **2a** in 88% yield.

7. Transformation of α-Cyano Tetrahydroisoquinoline



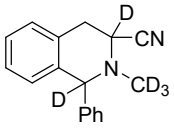
Procedure: A mixture of substrate **2a** (124.2 mg, 0.5 mmol) and KOH (673.2 mg, 12 mmol) in EtOH/H_2O (2.0 mL, v/v 1:1) were stirred in the schlenk tube at 80 °C for 4.5 h. After the completion, the reaction was quenched by 10% HCl solution with a pH of 5. Subsequently, the mixture was extracted with ethyl acetate twice and the combined organic extracts dried over sodium sulfate. The resulting mixture was concentrated in vacuo and further purification was performed by a neutral Al_2O_3 column eluted with petroleum ether/ethyl acetate to give the product **5a**.

2-Methyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-3-carbonitrile (5a): Yellow solid, 74% yield. R_f = 0.78 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 5H), 7.12 (m, 2H), 7.03 (m, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 4.52 (s, 1H), 4.17 (dd, *J* = 5.5, 1.8 Hz, 1H), 3.59 (dd, *J* = 16.0, 5.5 Hz, 1H), 3.06 (d, *J* = 16.0 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 137.0, 129.4, 129.3, 128.6, 128.6, 128.4, 127.8, 126.9, 126.6, 116.6, 67.3, 53.1, 42.1, 32.9.



Procedure: A mixture of substrate **2a** (124.2 mg, 0.5 mmol) and KOH (673.2 mg, 12 mmol) in EtOD/D_2O (2.0 mL, v/v 1:1) were stirred in the schlenk tube at 80 °C for 4.5 h. After the completion, the reaction was quenched by 10% HCl solution with a pH of 5. Subsequently, the mixture was extracted with ethyl acetate twice and the combined organic extracts dried over sodium sulfate. The resulting mixture was concentrated in vacuo and further purification was performed by a neutral Al_2O_3 column eluted with petroleum ether/ethyl acetate to give the deuterated product **[D]-5a**.

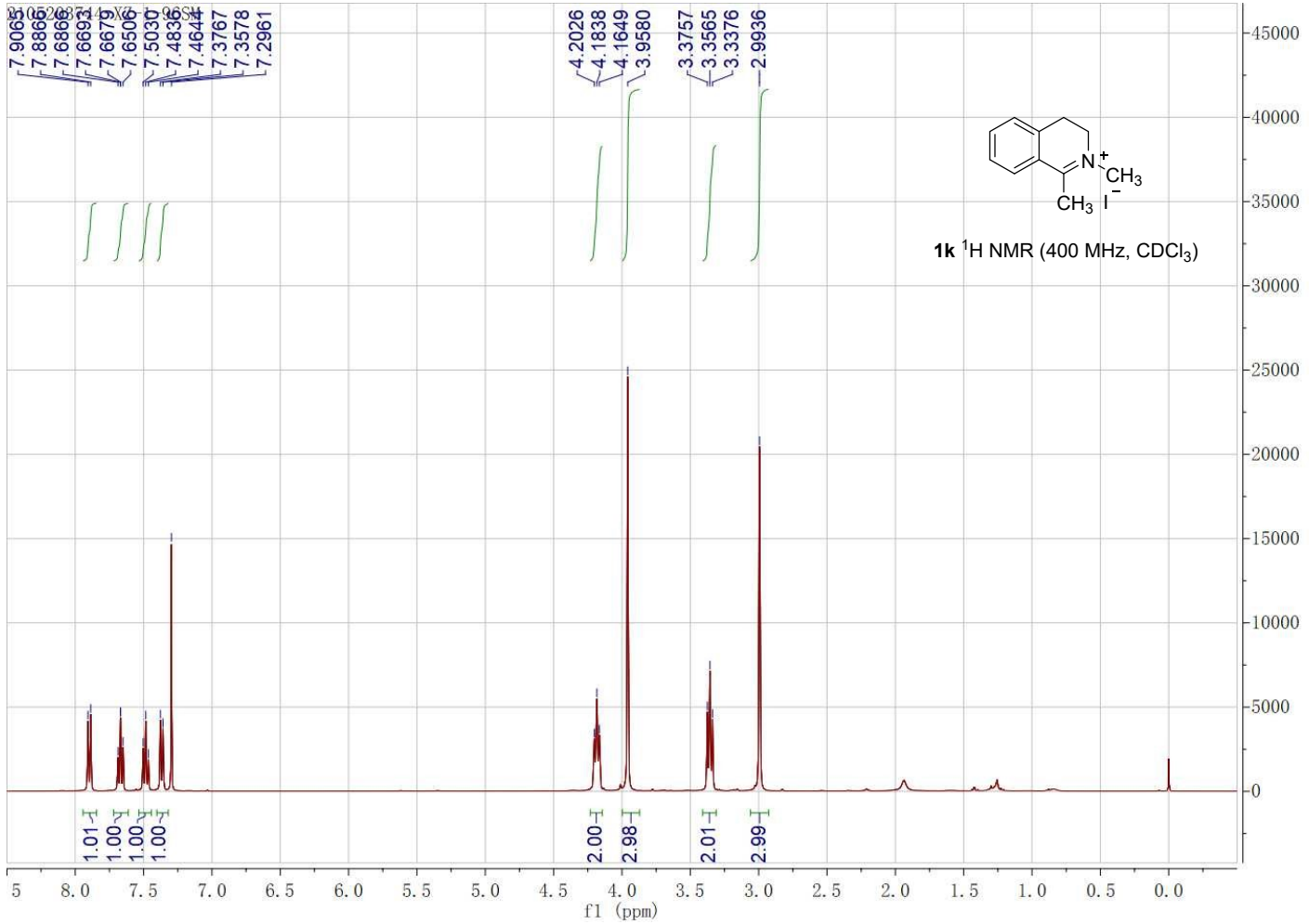
2-(Methyl-d3)-1-phenyl-1,2,3,4-tetrahydroisoquinoline-3-carbonitrile-1,3-d2 ([D]-5a): Yellow solid, 61% yield. R_f = 0.78 (petroleum ether/ethyl acetate 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 5H), 7.13 (d, *J* = 4.0 Hz, 2H), 7.04 (td, *J* = 8.1, 4.0 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 4.52 (s, 0.30H), 4.17 (d, *J* = 3.9 Hz, 0.30H), 3.59 (dd, *J* = 16.1, 5.9 Hz, 1H), 3.06 (d, *J* = 16.1 Hz, 1H), 2.35 – 2.25 (m, 0.75H).



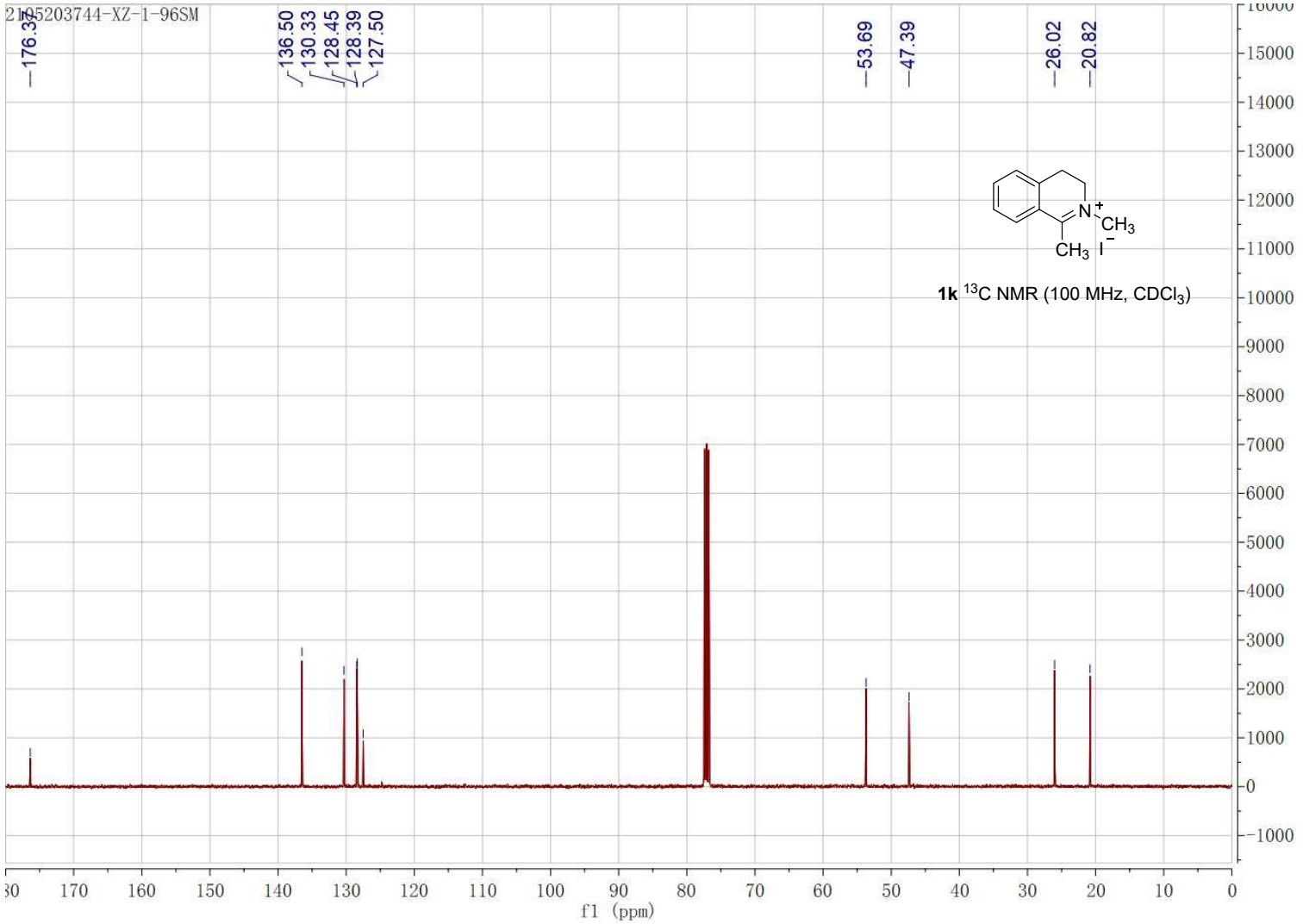
8. Reference

[1]. Ji, Y.; Feng, G.-S.; Chen, M.-W.; Shi, L.; Du, H.; Zhou, Y.-G. *Org. Chem. Front.* **2017**, *4,* 1125-1129.

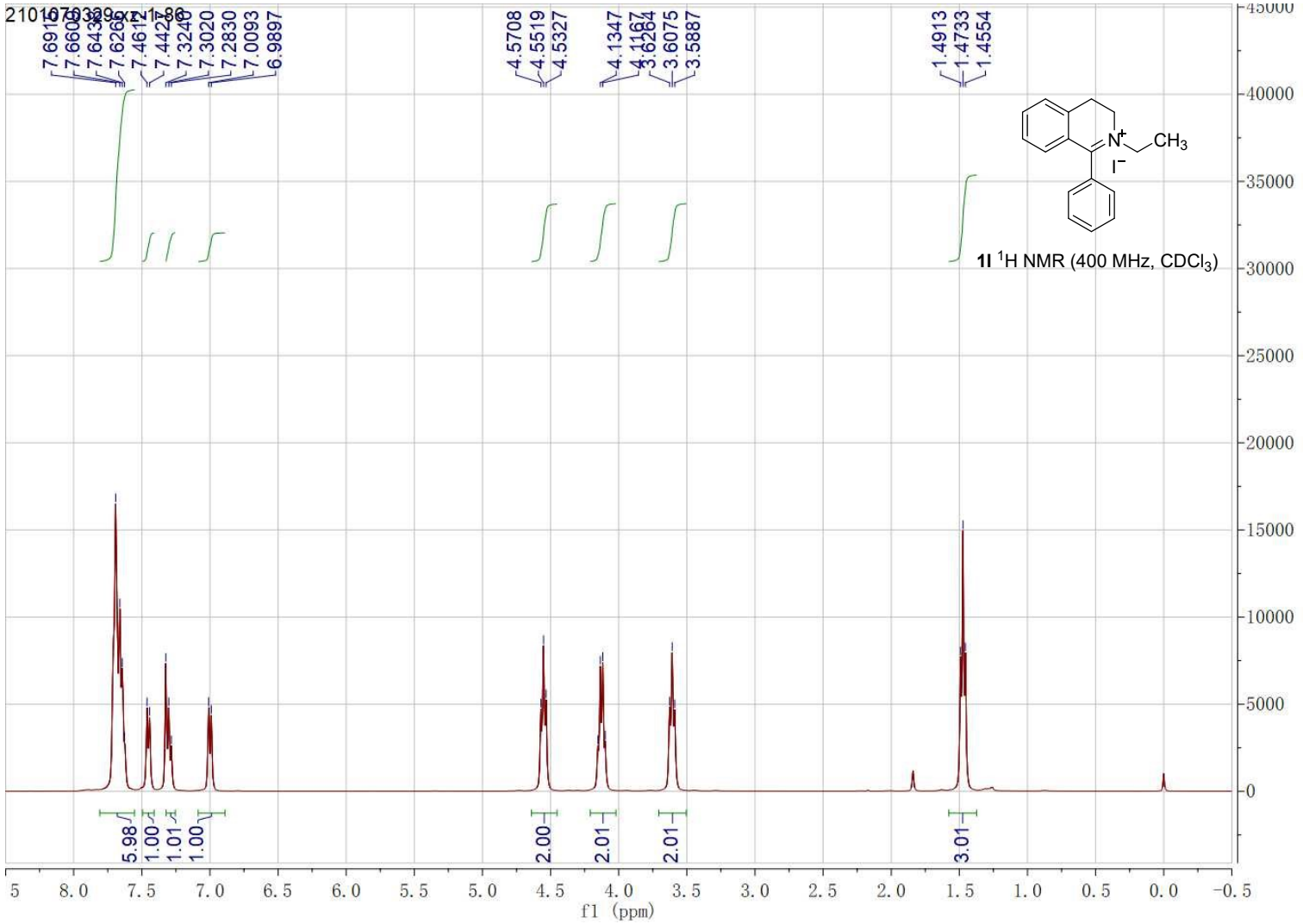
9. Copy of NMR for compounds



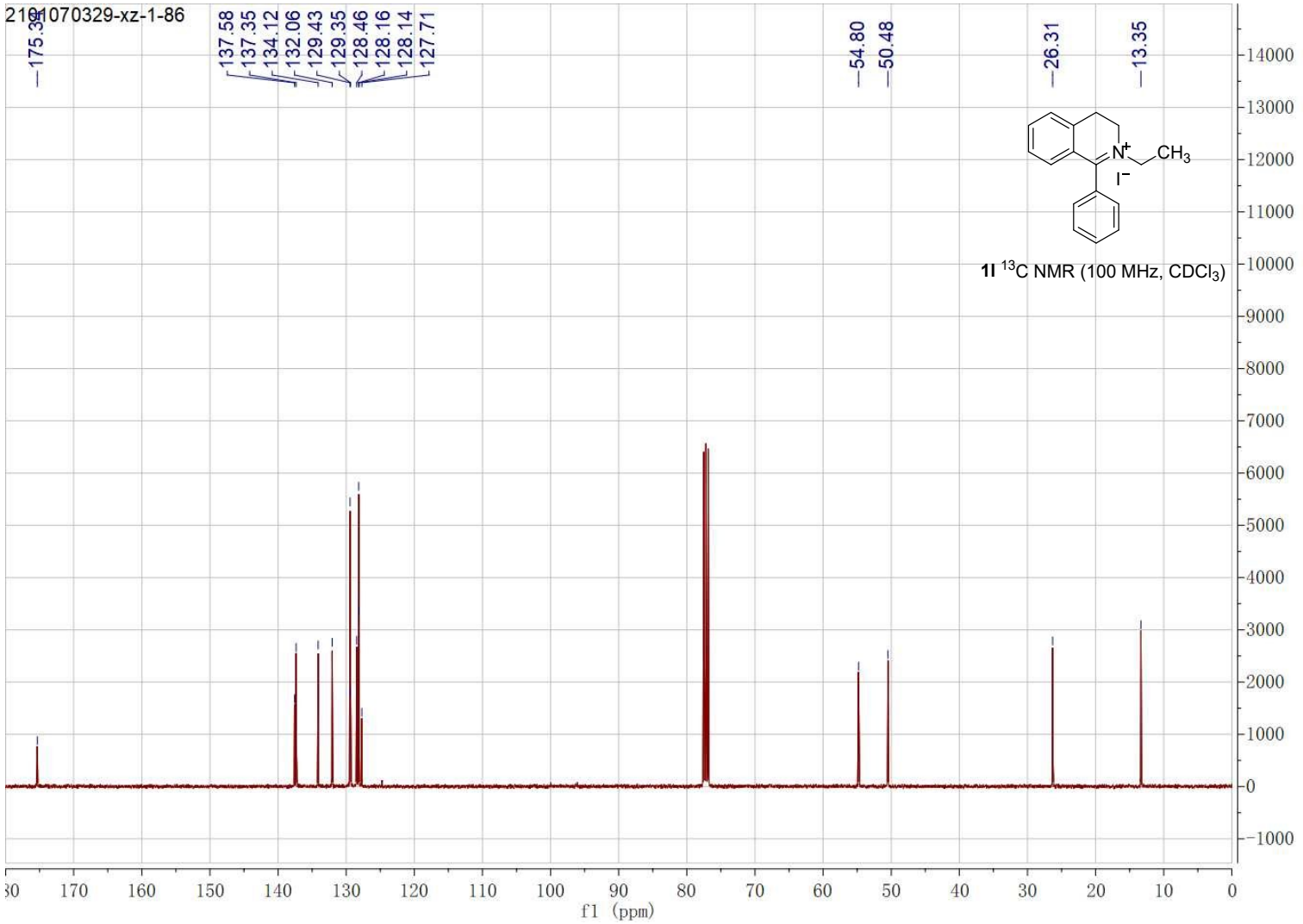
1k ^{1}H NMR (400 MHz, $CDCl_3$)

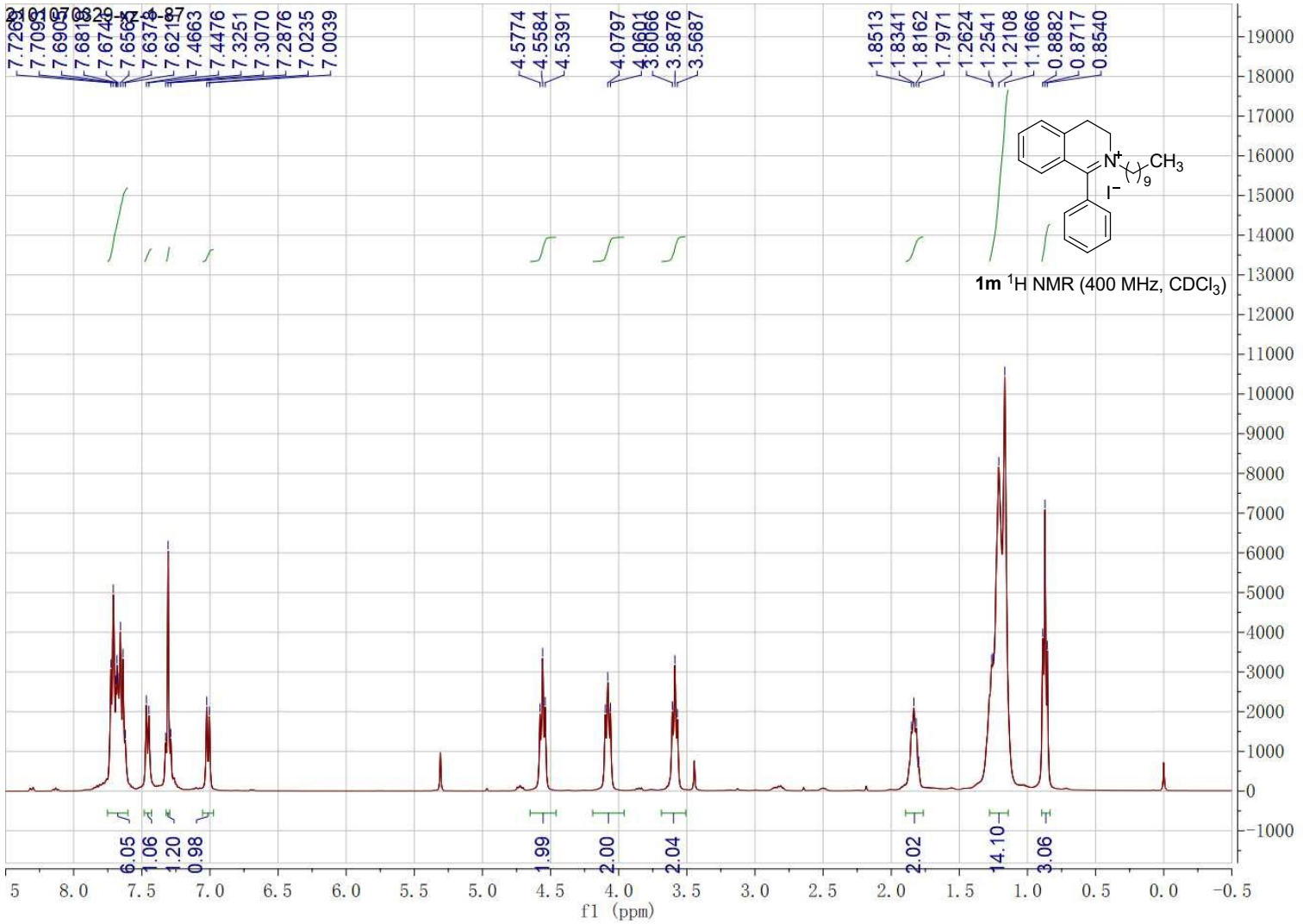


1k ^{13}C NMR (100 MHz, $CDCl_3$)

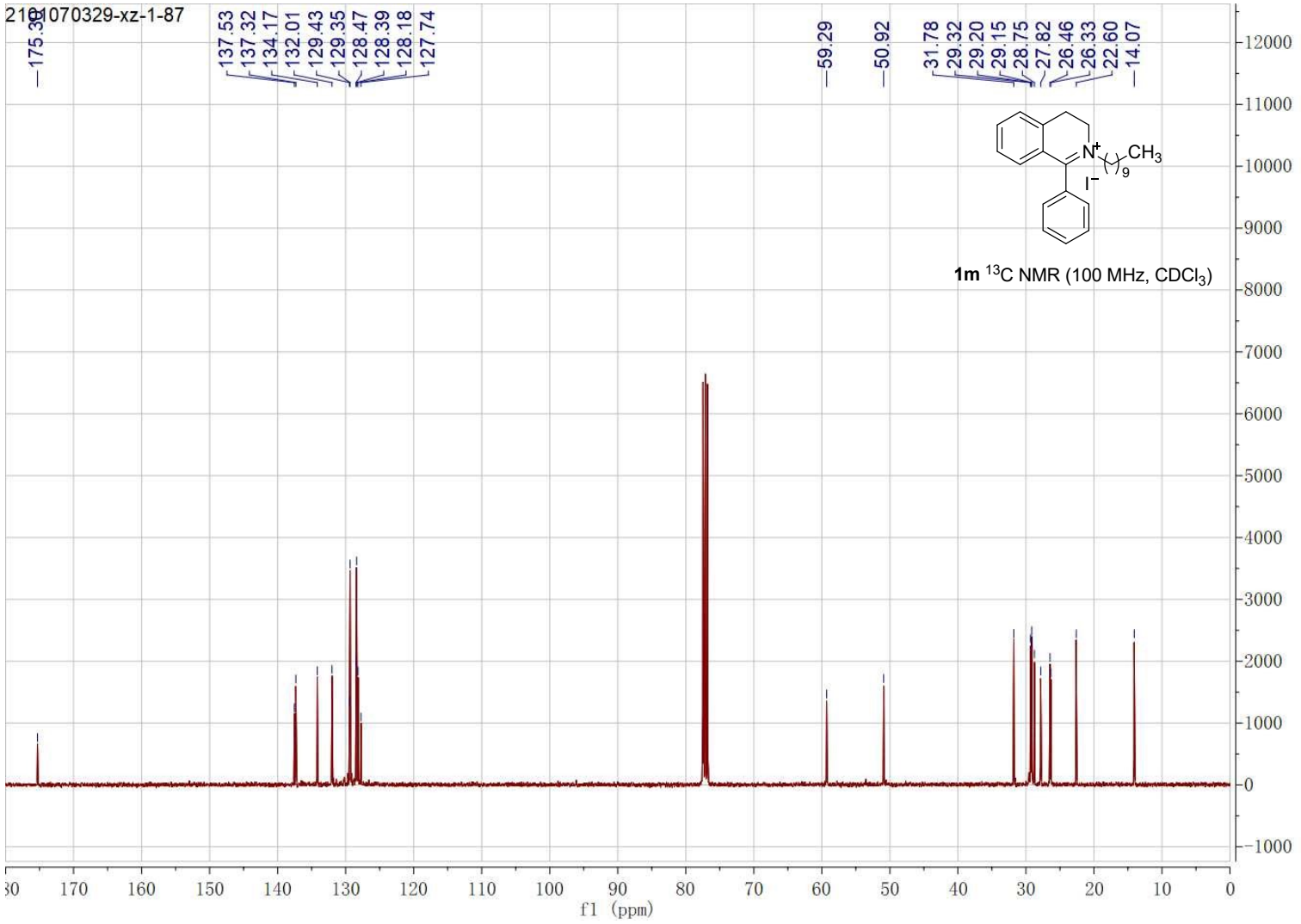


1l ^{1}H NMR (400 MHz, $CDCl_3$)

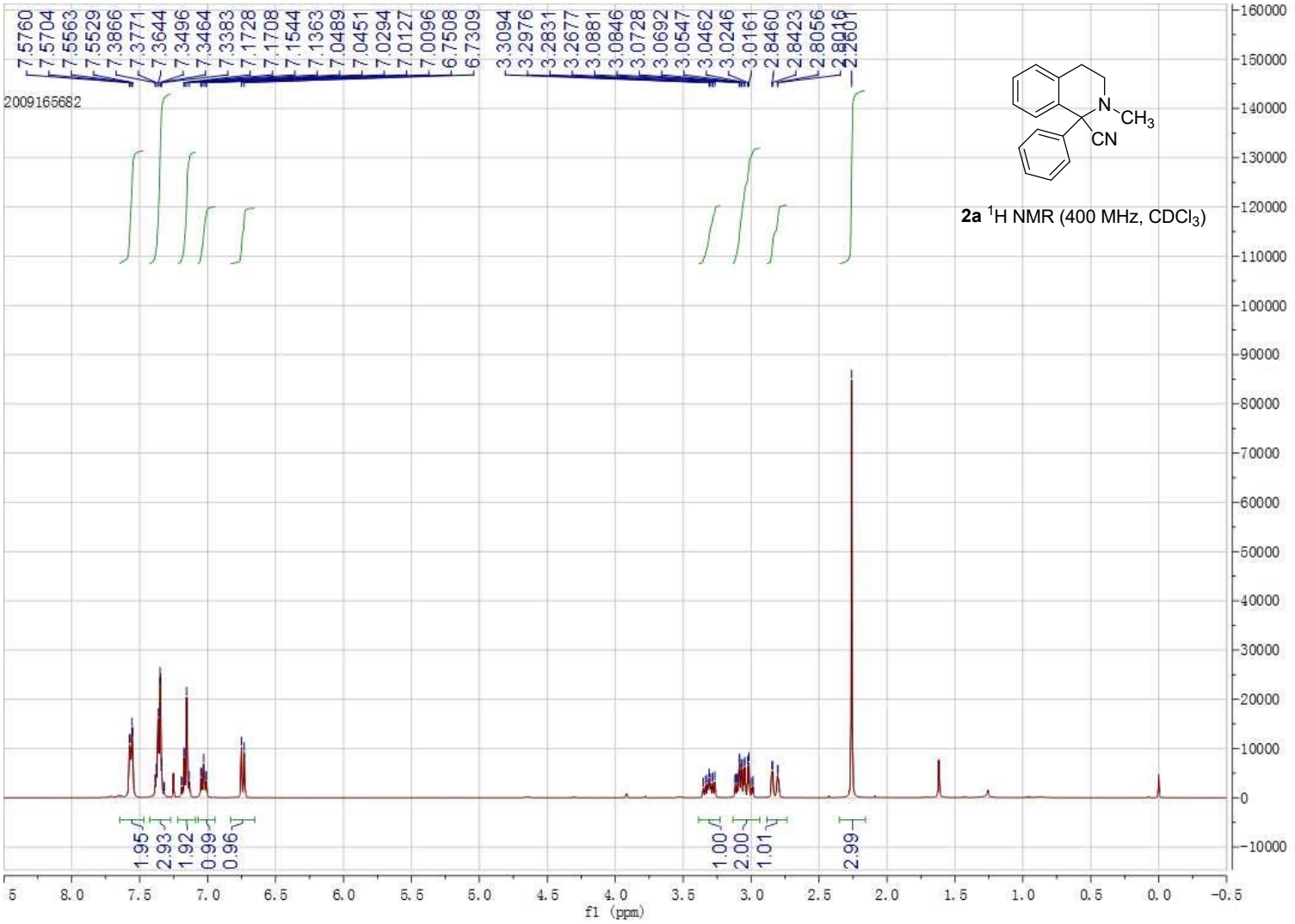

2101070329-xz-1-86
175.39
137.58
137.35
134.12
132.06
129.43
129.35
128.46
128.16
128.14
127.71
54.80
50.48
26.31
13.35
N+
CH3
I−
1l 13C NMR (100 MHz, CDCl3)
f1 (ppm)

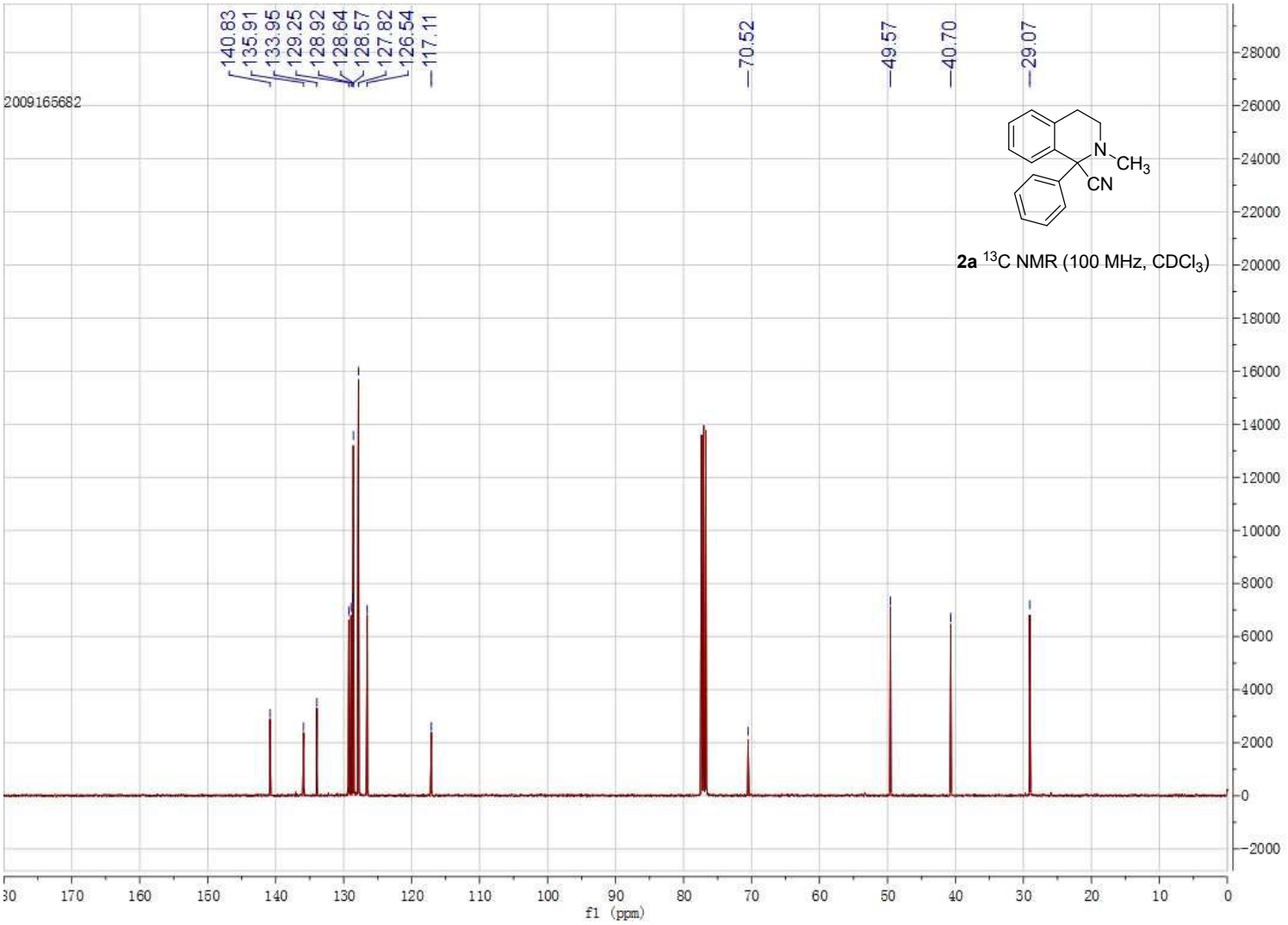


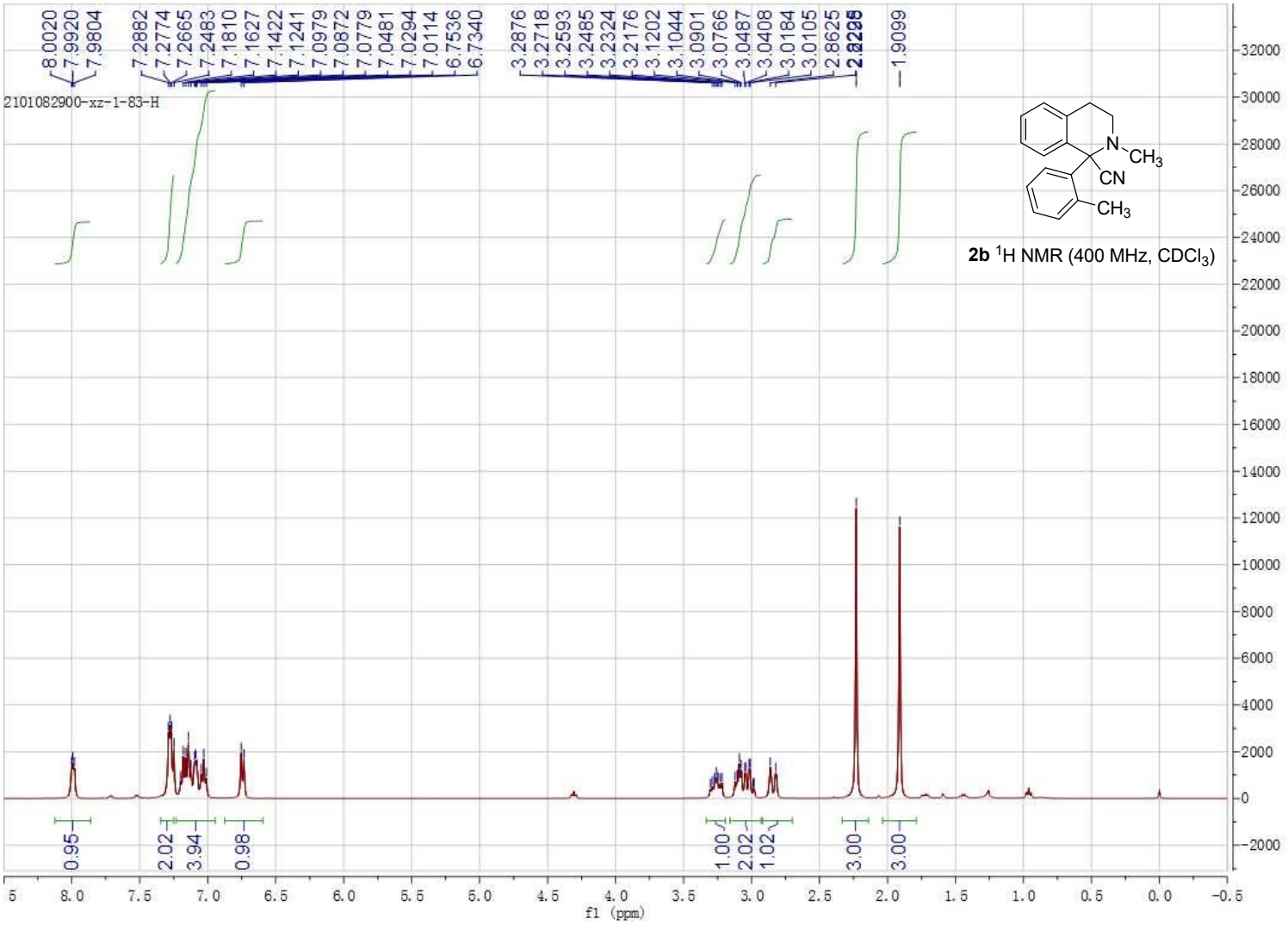
1m ^{1}H NMR (400 MHz, $CDCl_3$)



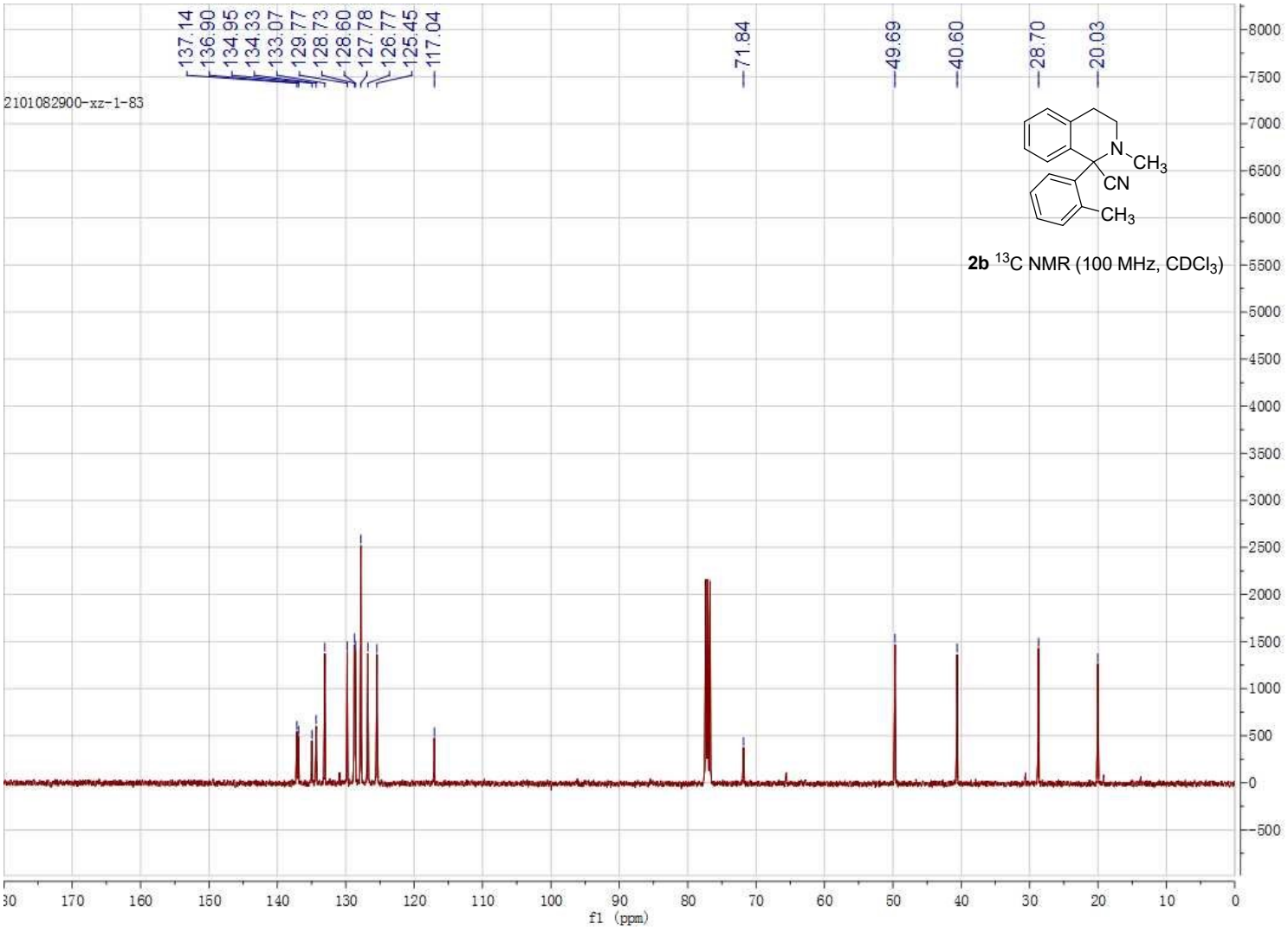
1m ^{13}C NMR (100 MHz, $CDCl_3$)


7.5760
7.5704
7.5563
7.5529
7.3866
7.3771
7.3644
7.3496
7.3464
7.3383
7.1728
7.1708
7.1544
7.1363
7.0489
7.0451
7.0294
7.0127
7.0096
6.7508
6.7309
3.3094
3.2976
3.2831
3.2677
3.0881
3.0846
3.0728
3.0692
3.0547
3.0462
3.0246
3.0161
2.8460
2.8423
2.8056
2009165682
N
CH3
CN
2a 1H NMR (400 MHz, CDCl3)
1.95
2.93
1.92
0.99
0.96
1.00
2.00
1.01
2.99
f1 (ppm)

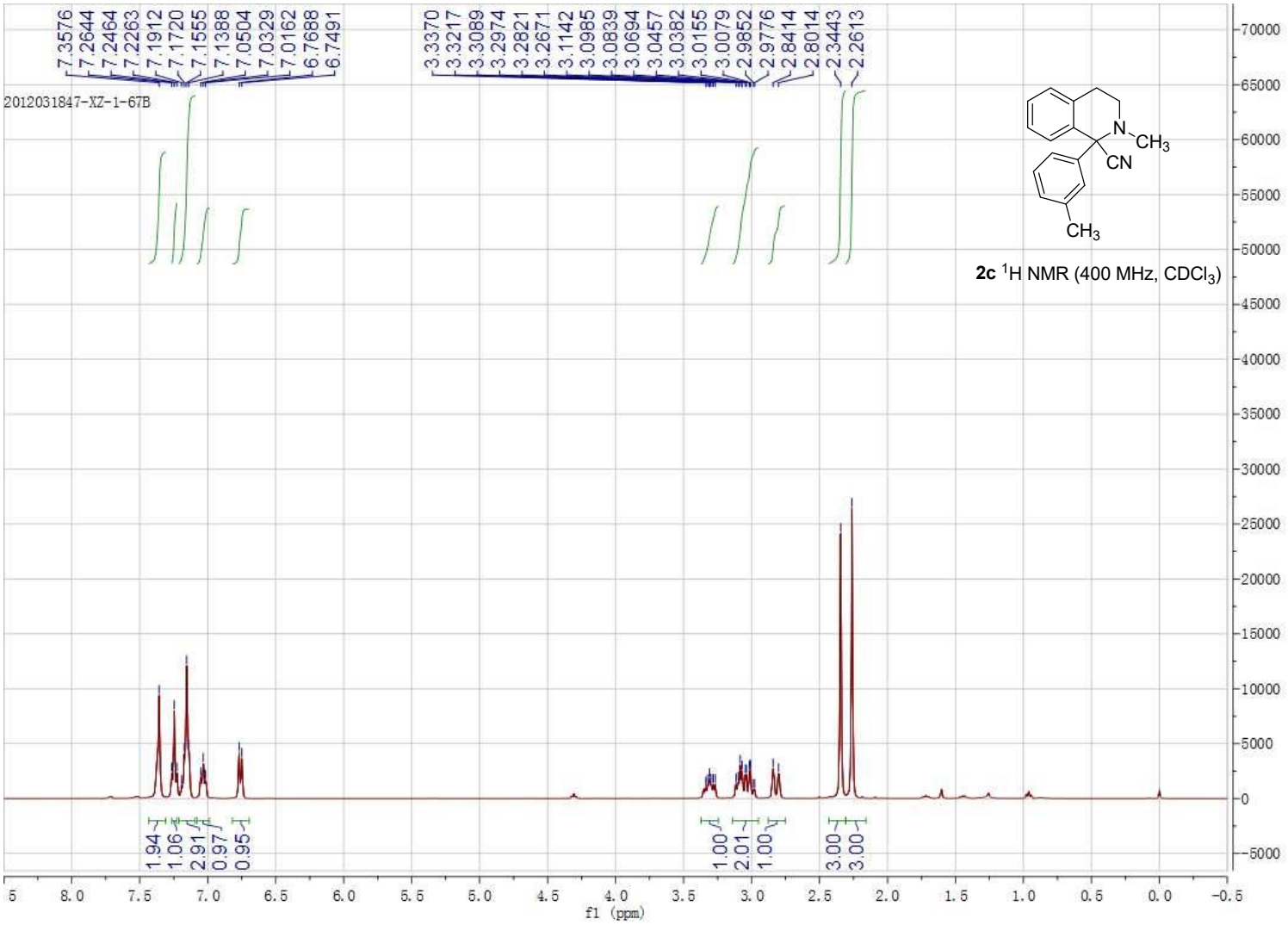

140.83
135.91
133.95
129.25
128.92
128.64
128.57
127.82
126.54
117.11
70.52
49.57
40.70
29.07
2009165682
N
CH3
CN
2a 13C NMR (100 MHz, CDCl3)
f1 (ppm)



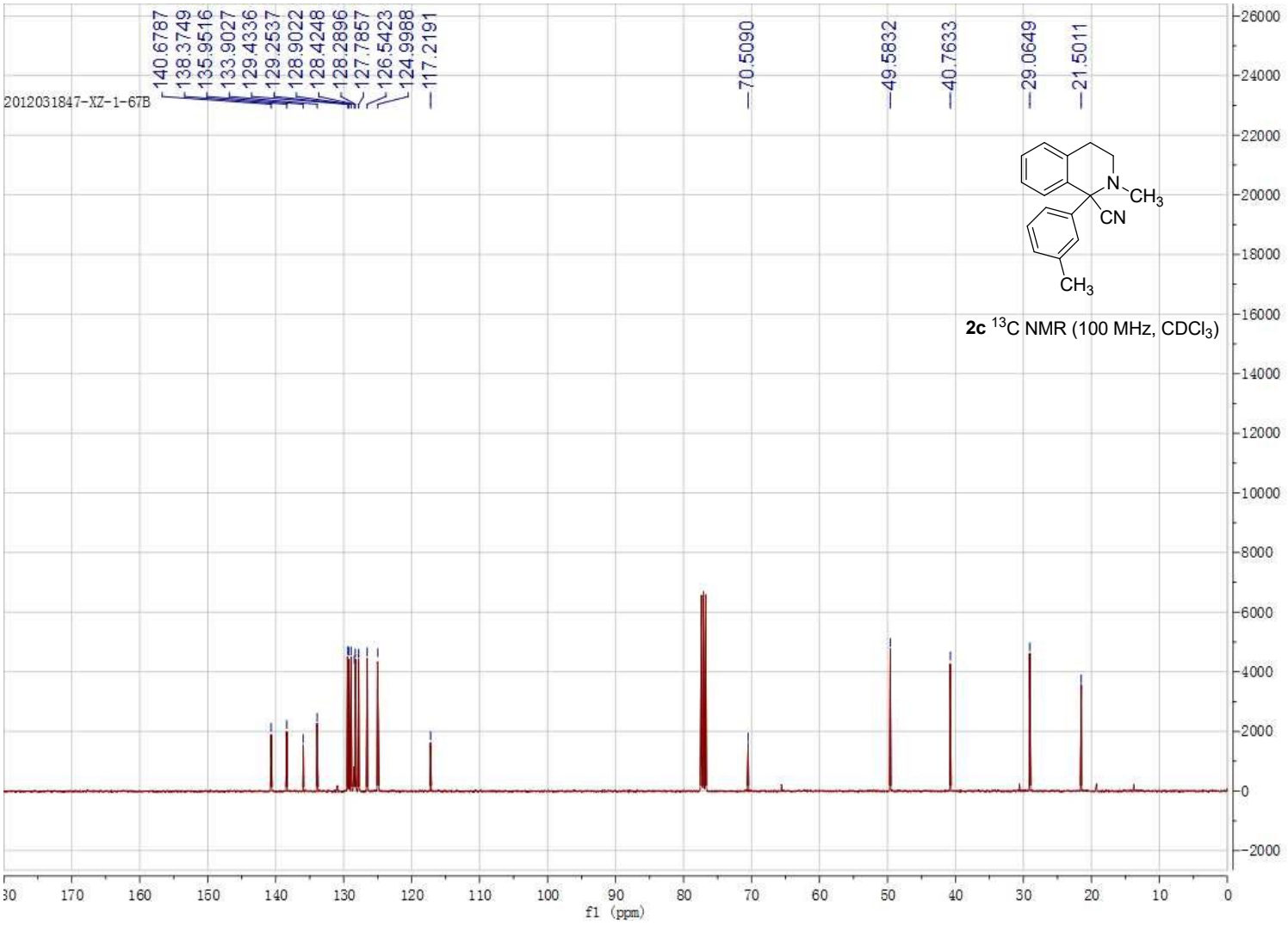
2b ^{1}H NMR (400 MHz, $CDCl_3$)



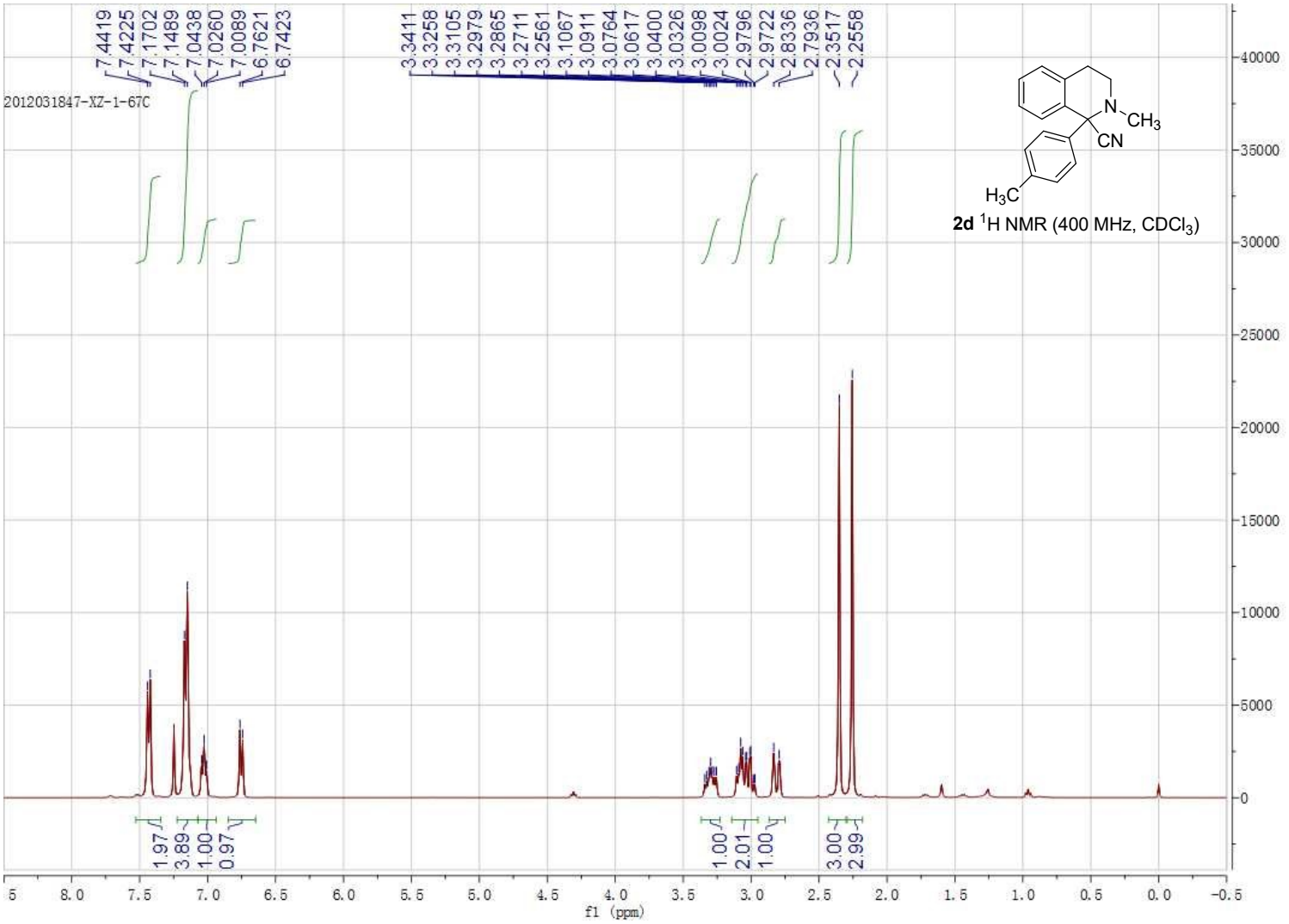
2b ^{13}C NMR (100 MHz, $CDCl_3$)



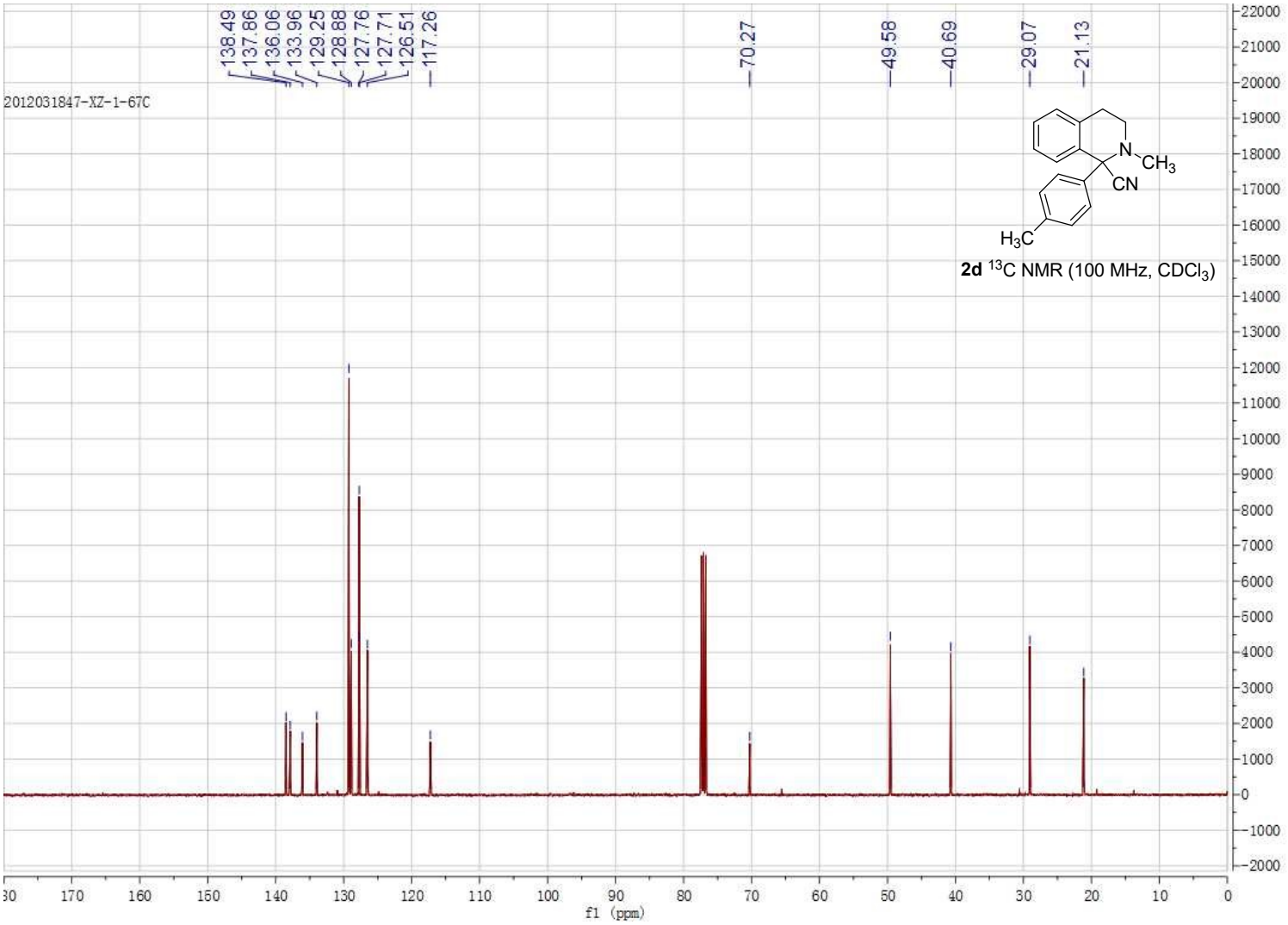
2c ^{1}H NMR (400 MHz, $CDCl_3$)



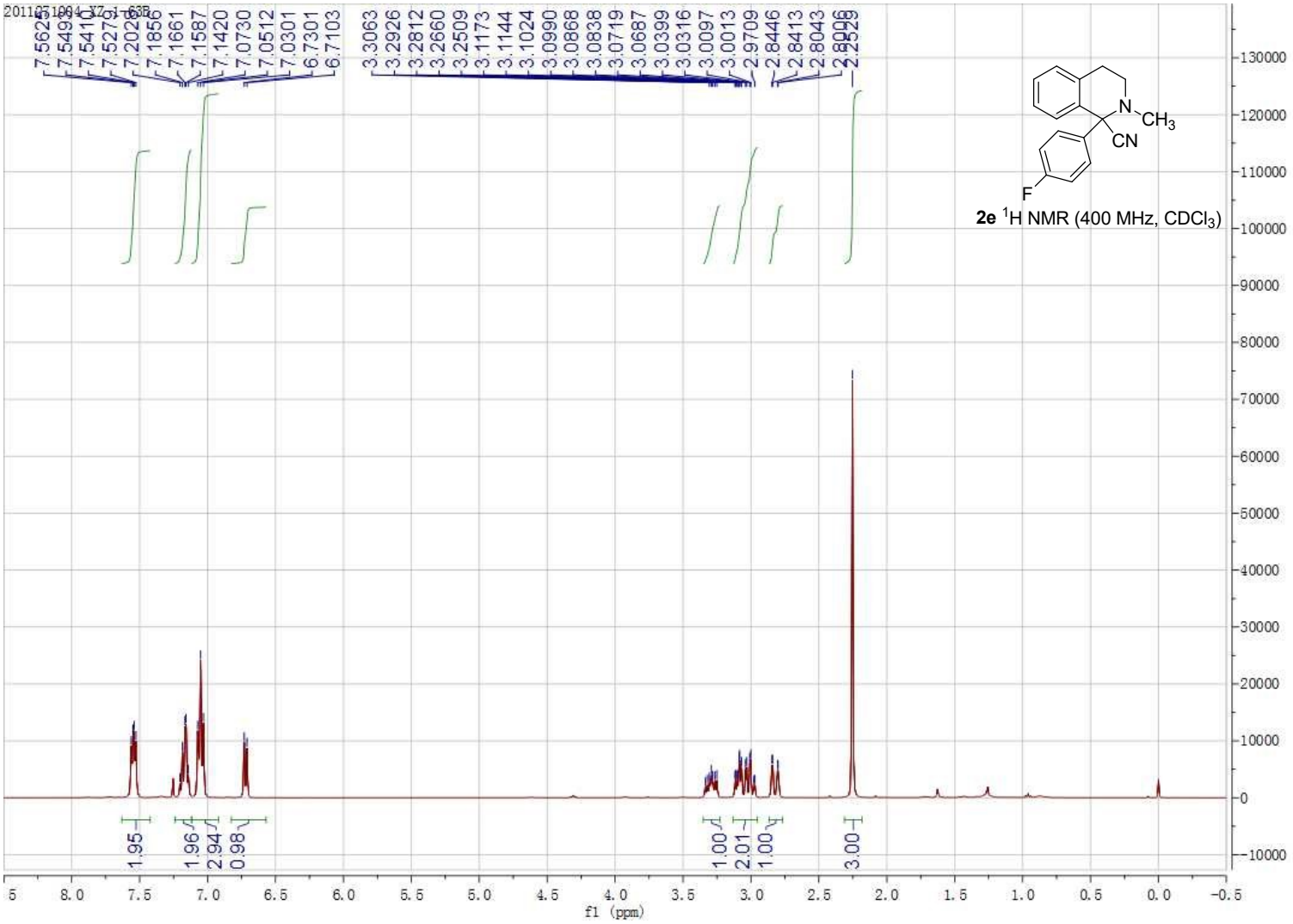
2c ^{13}C NMR (100 MHz, $CDCl_3$)



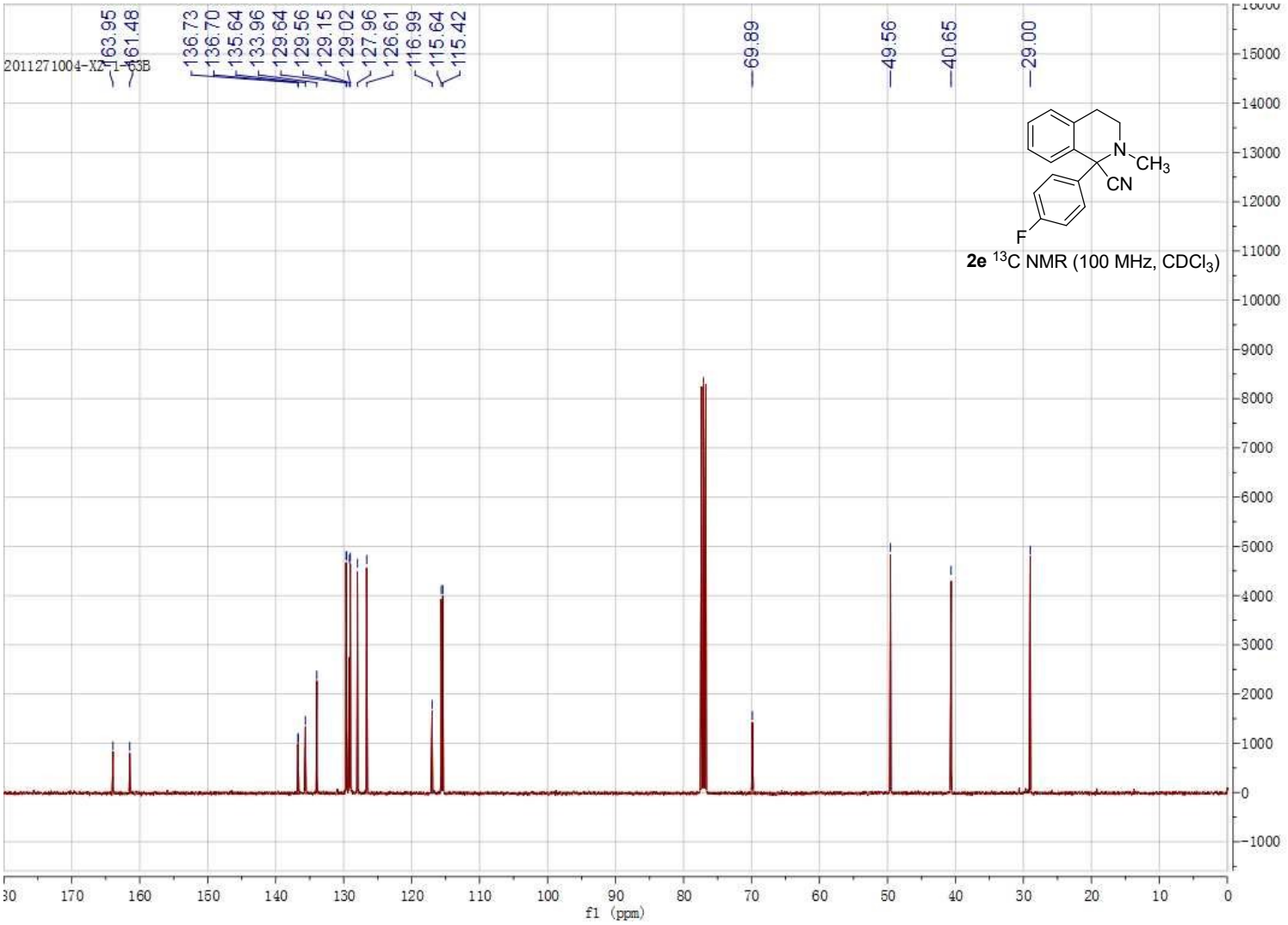
2d ^{1}H NMR (400 MHz, $CDCl_3$)



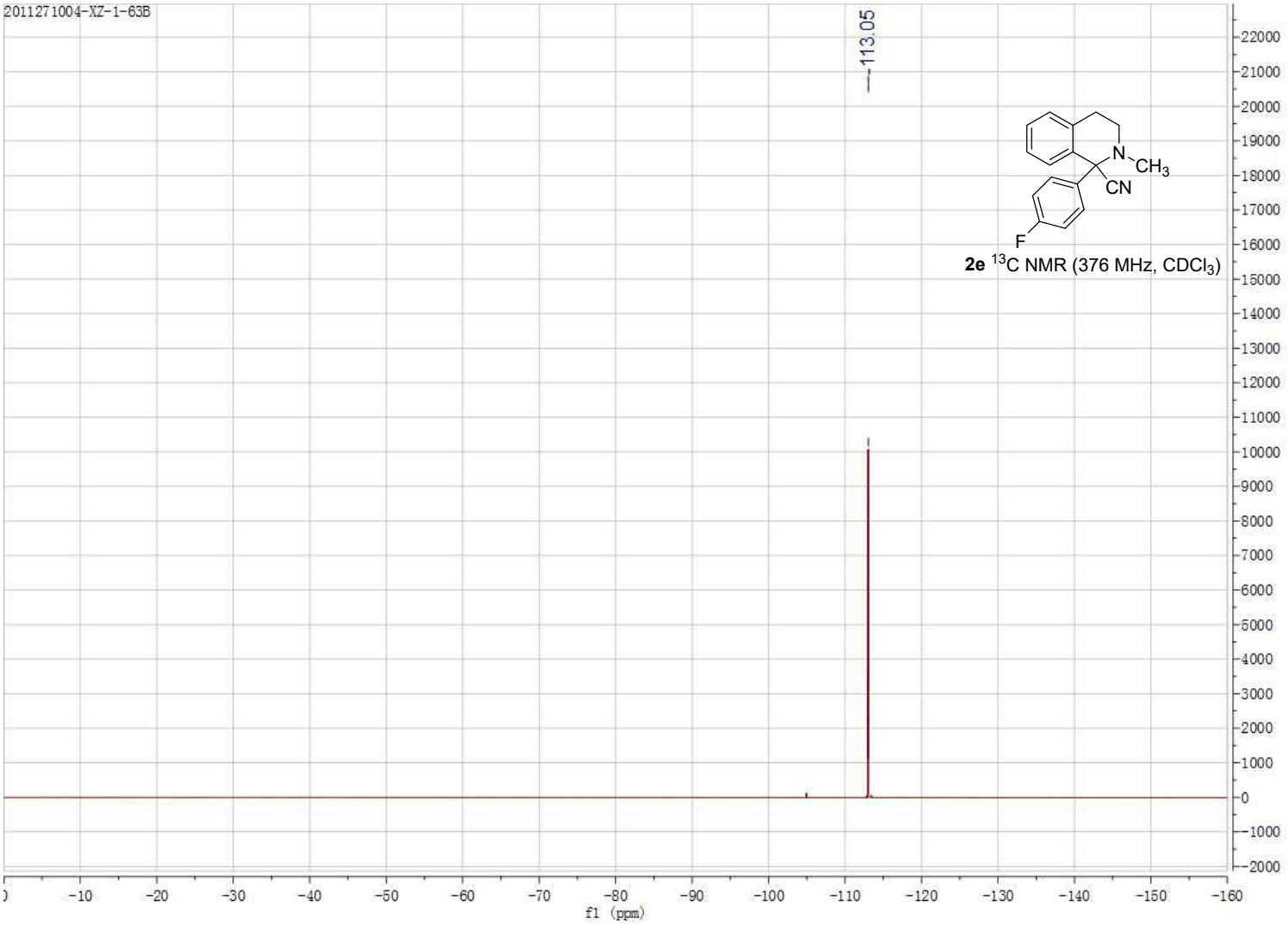
2d ^{13}C NMR (100 MHz, $CDCl_3$)



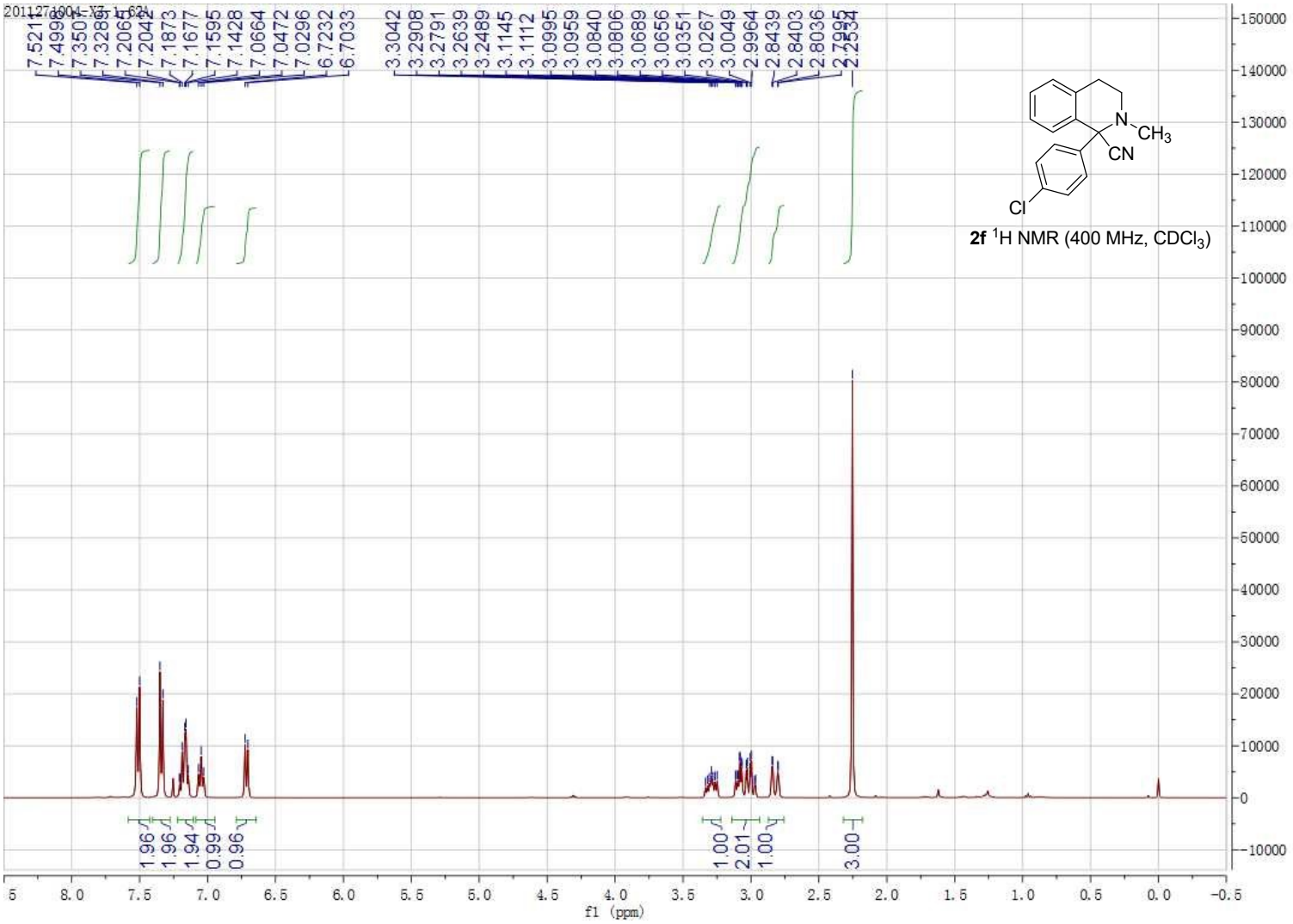
2e ^{1}H NMR (400 MHz, $CDCl_3$)



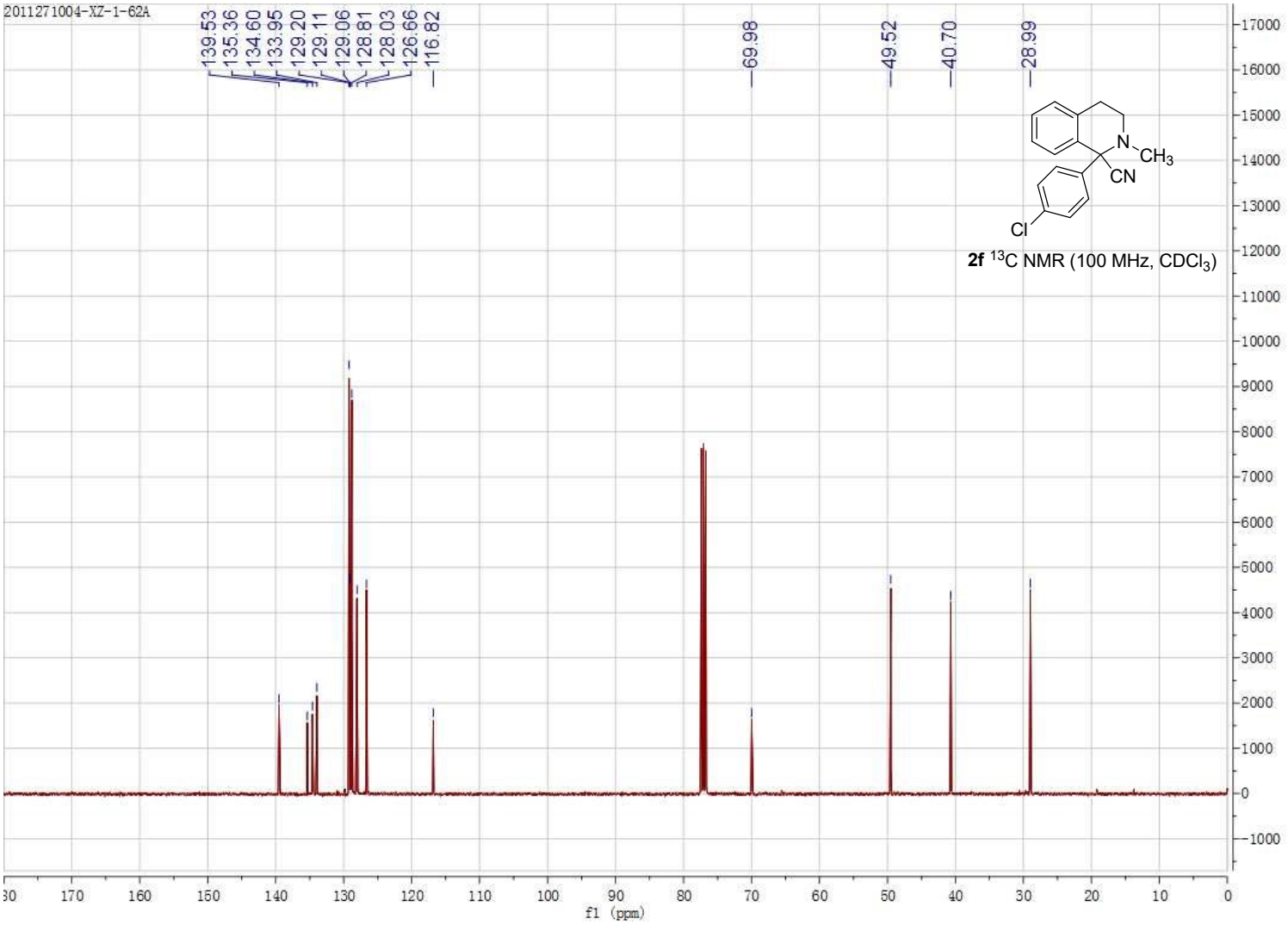
2e ^{13}C NMR (100 MHz, $CDCl_3$)



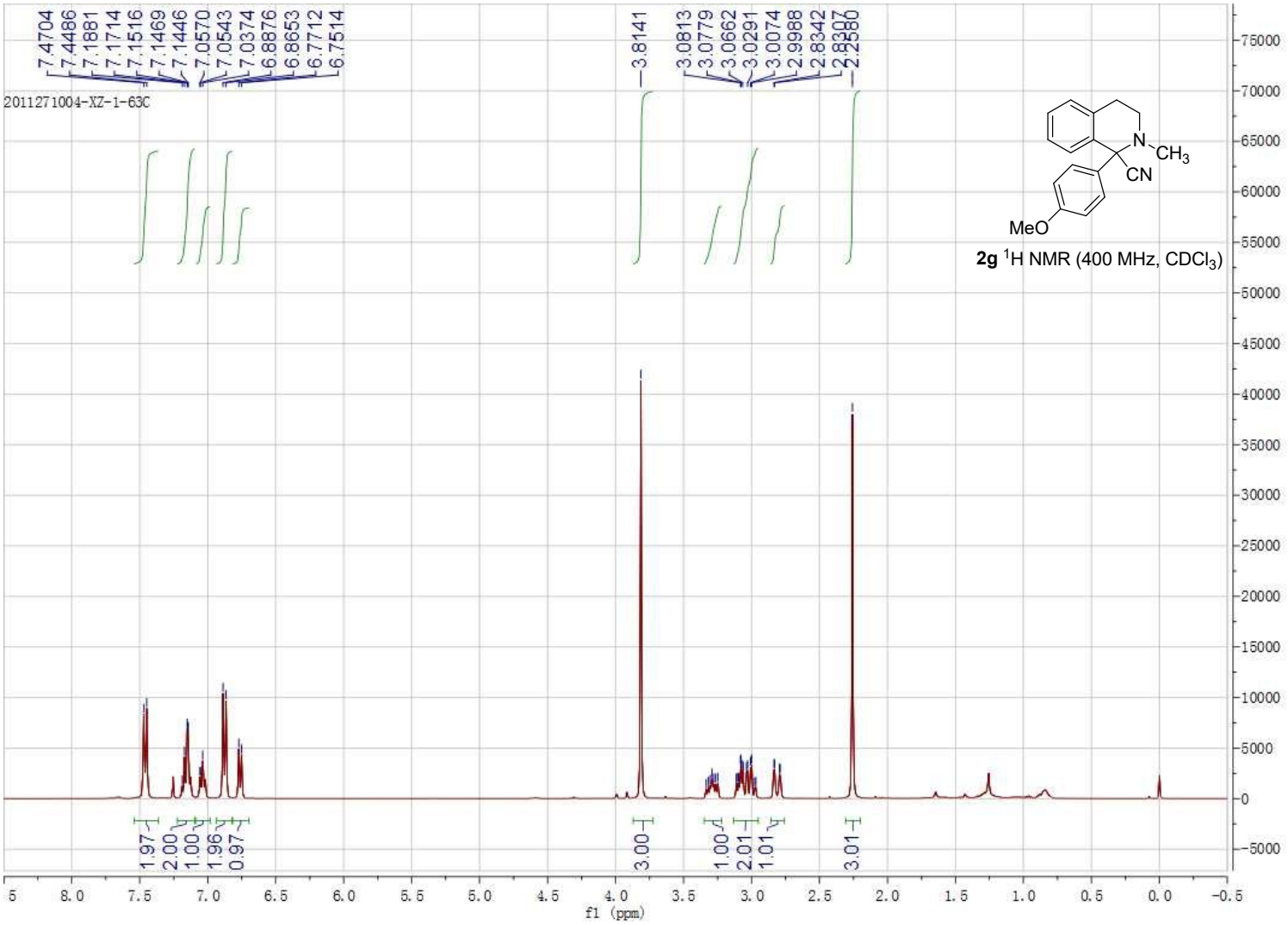
2e ^{13}C NMR (376 MHz, $CDCl_3$)



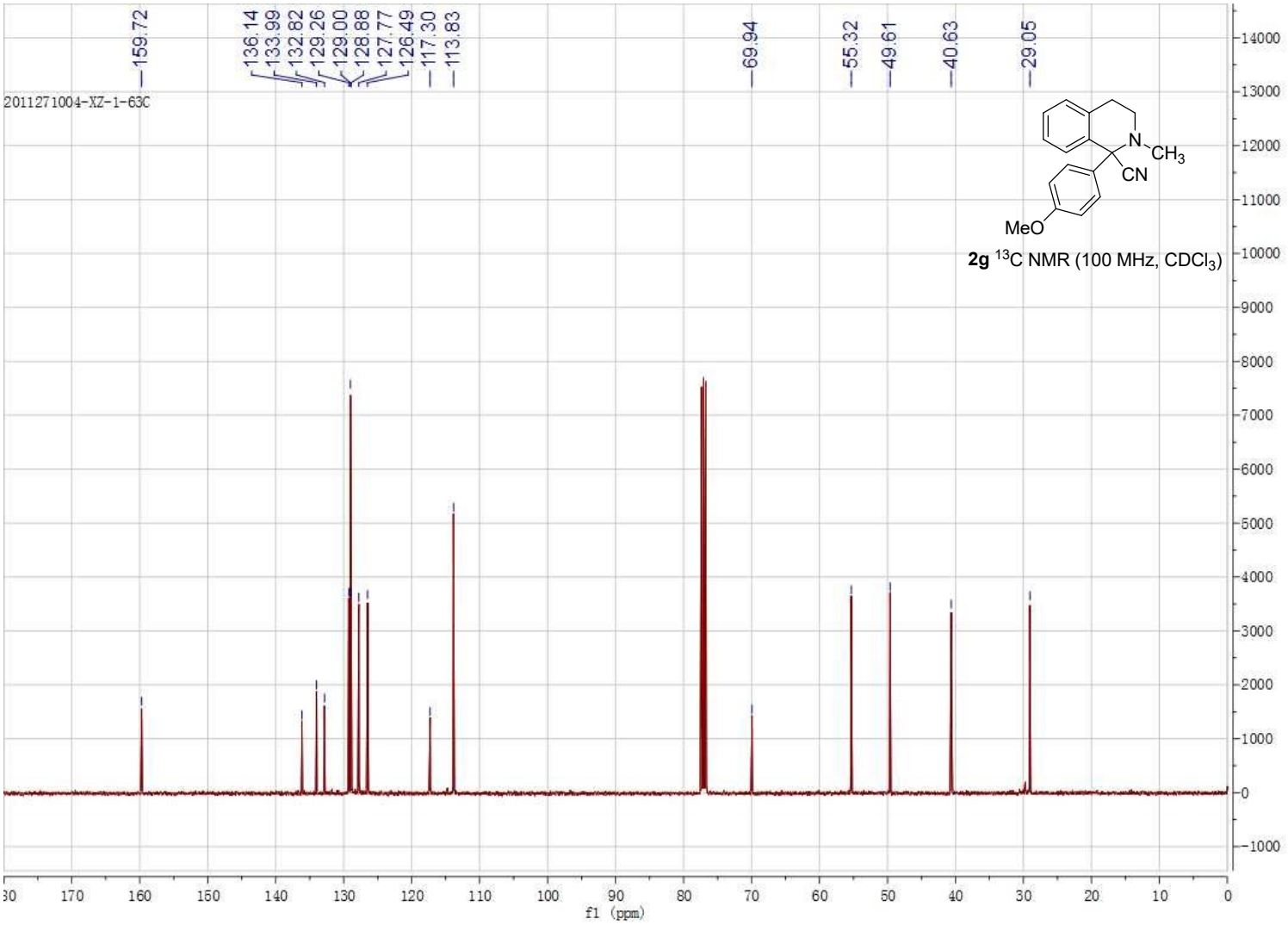
2f ^{1}H NMR (400 MHz, $CDCl_3$)



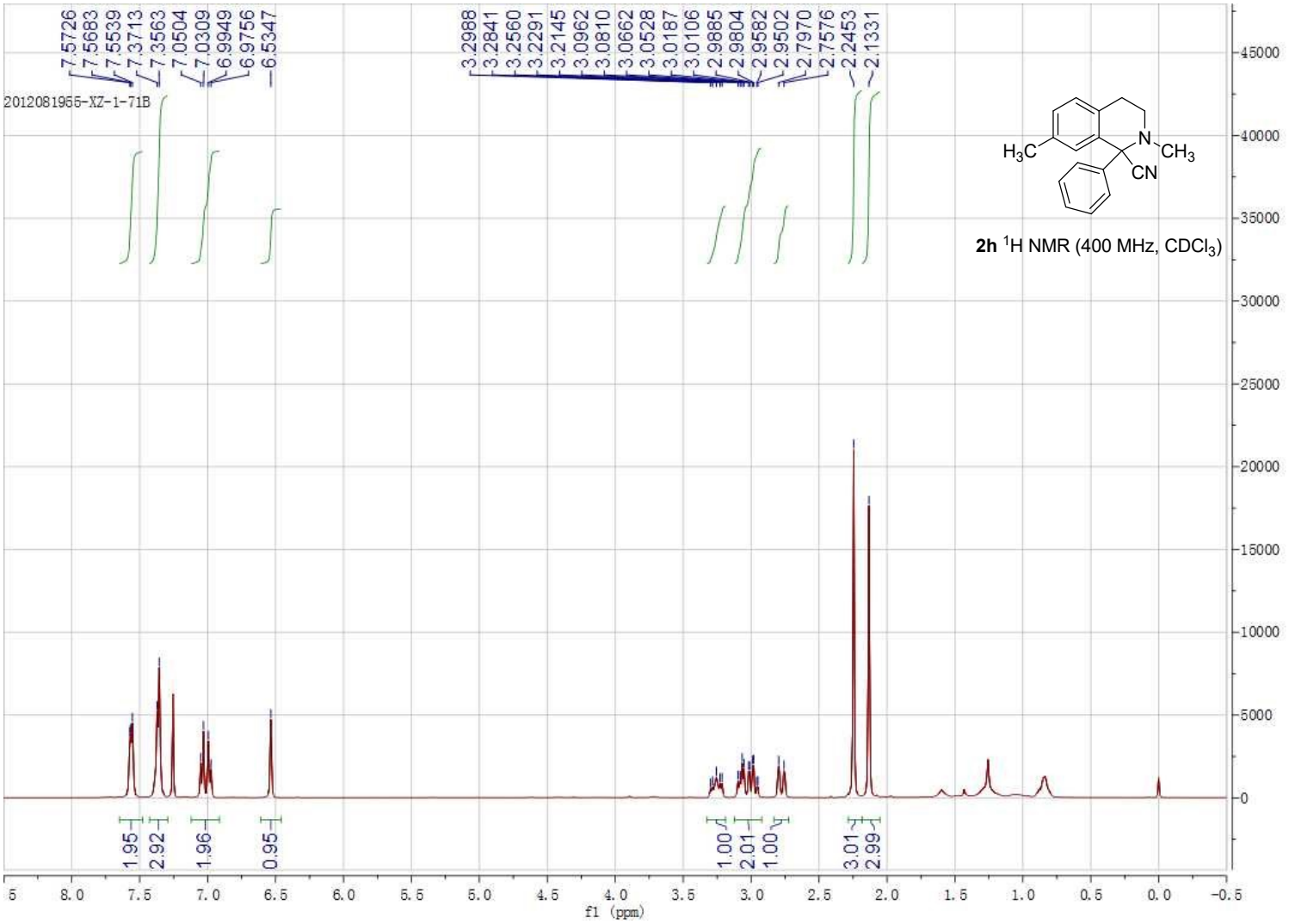
2f ^{13}C NMR (100 MHz, $CDCl_3$)



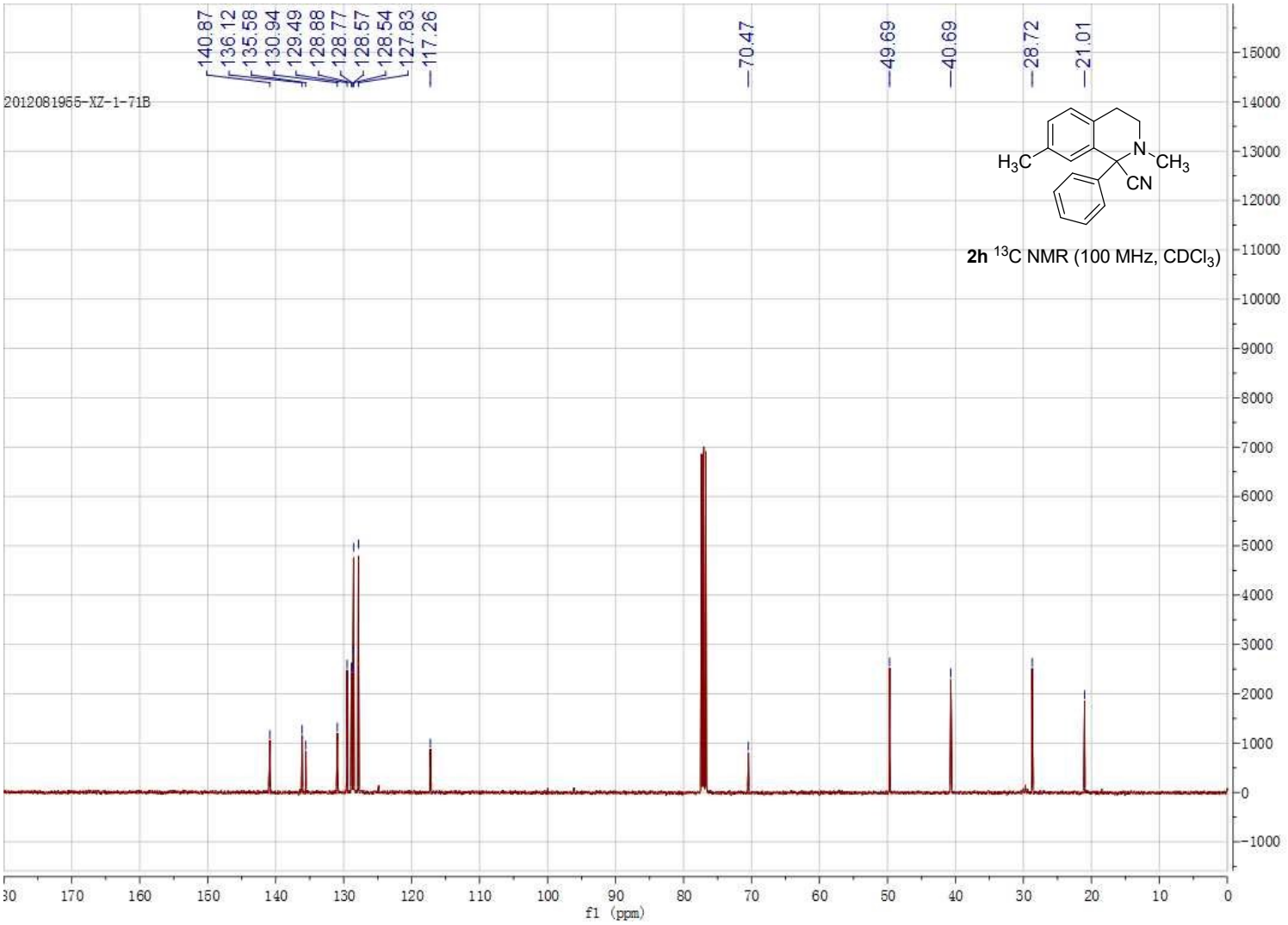
2g ^{1}H NMR (400 MHz, $CDCl_3$)



2g ^{13}C NMR (100 MHz, $CDCl_3$)



2h ^{1}H NMR (400 MHz, $CDCl_3$)


140.87
136.12
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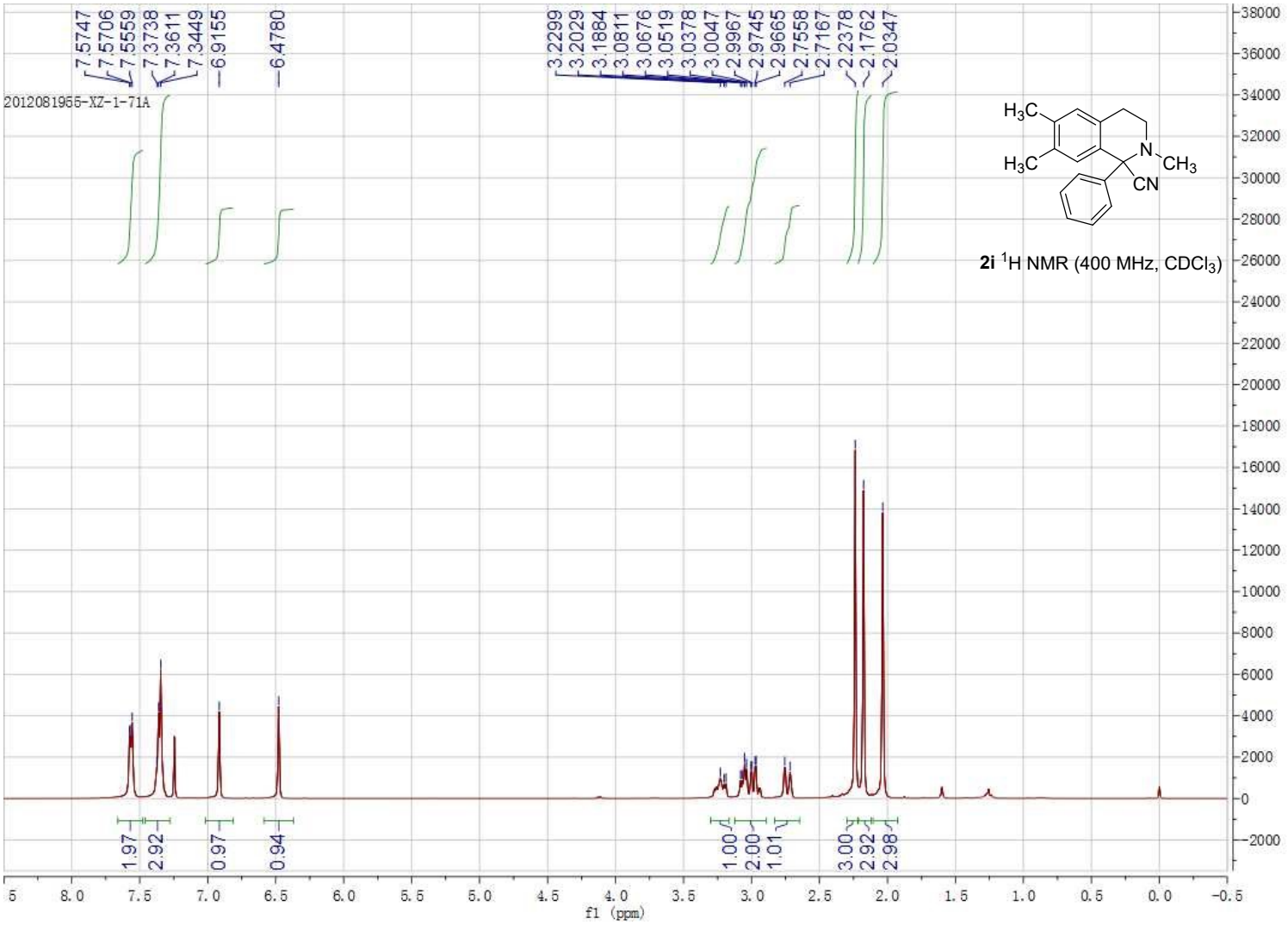
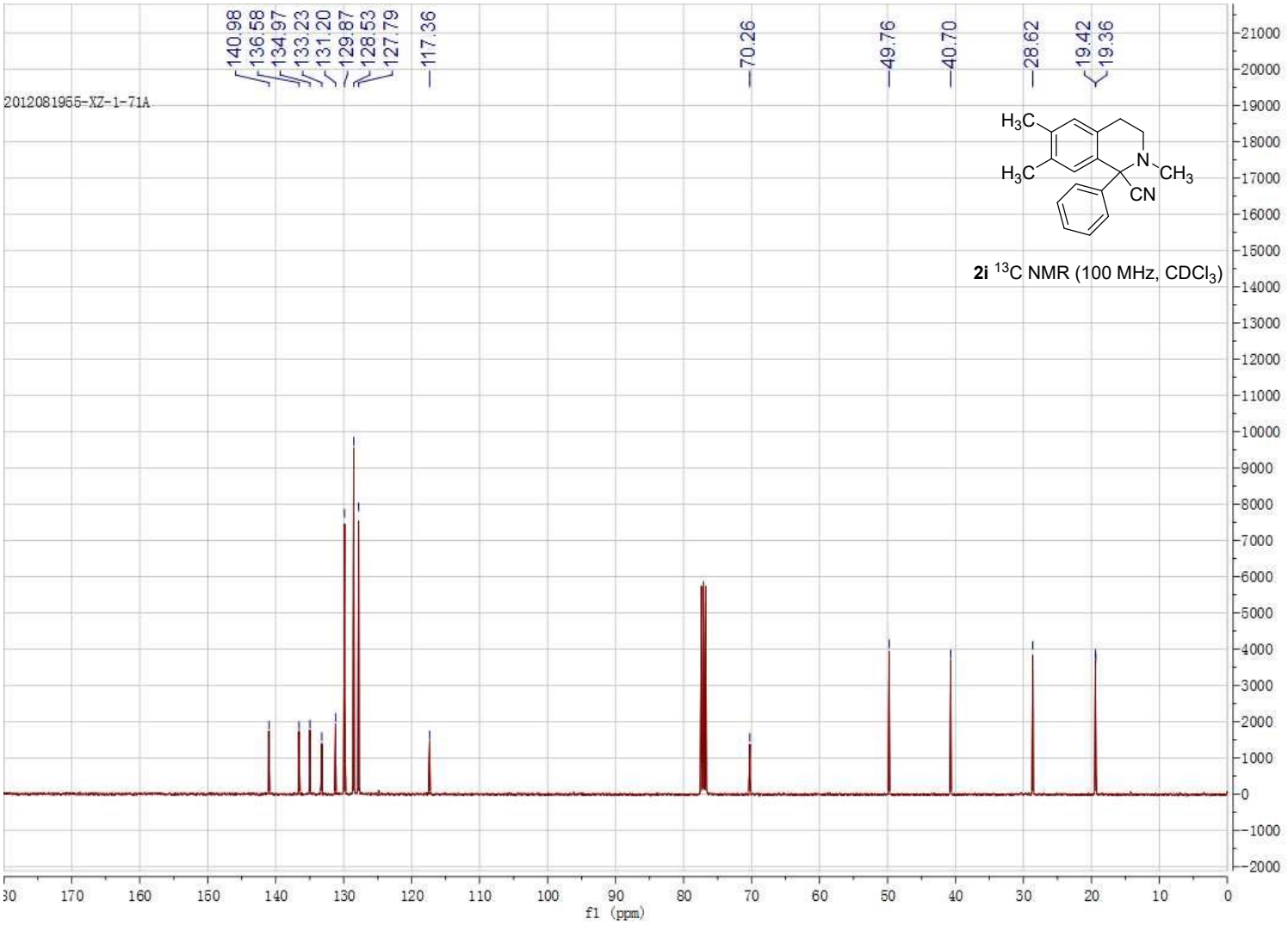
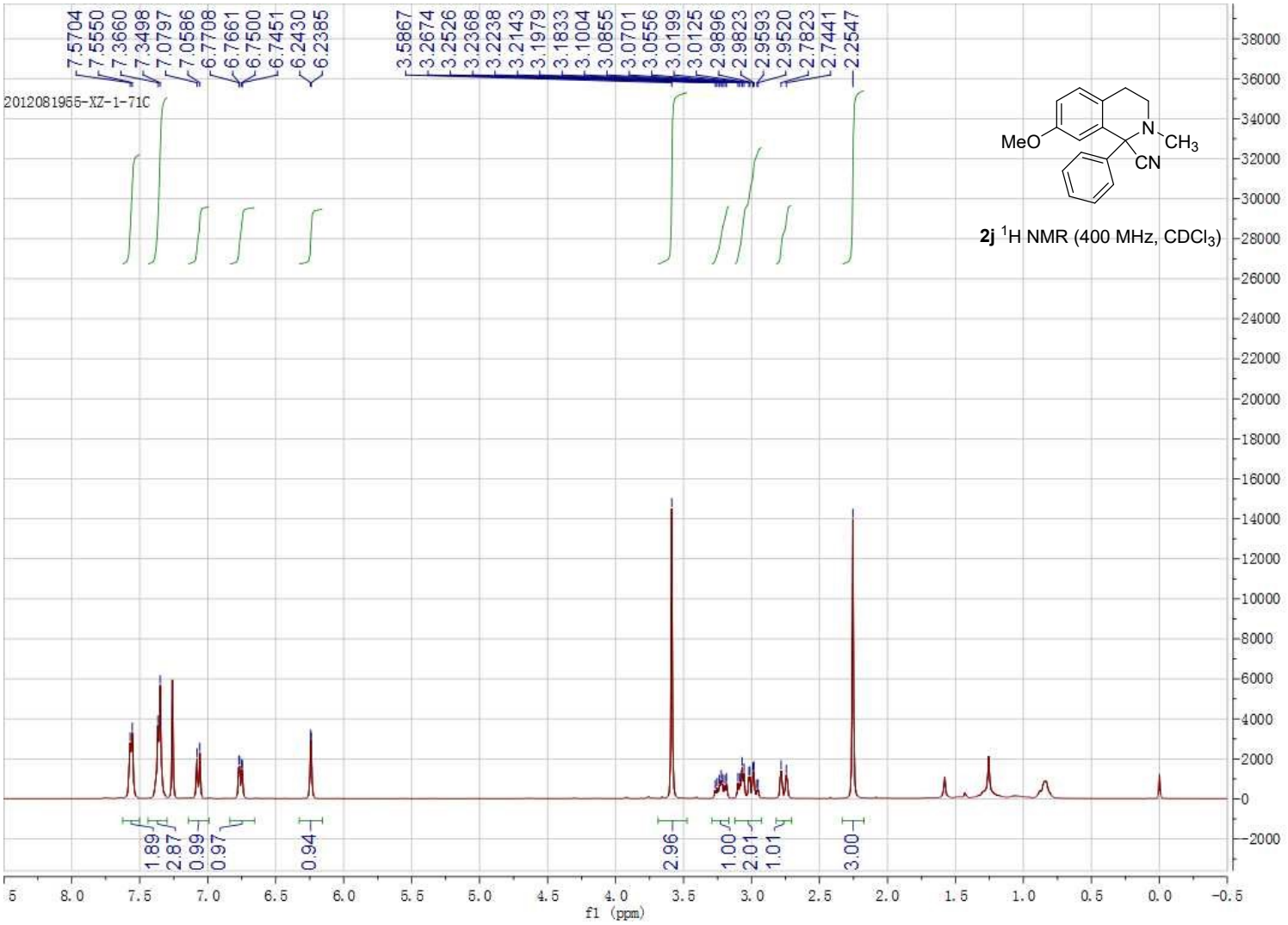
130.94
129.49
128.88
128.77
128.57
128.54
127.83
117.26
70.47
49.69
40.69
28.72
21.01
2012081965-XZ-1-71B
H3C
N
CH3
CN
2h 13C NMR (100 MHz, CDCl3)
f1 (ppm)



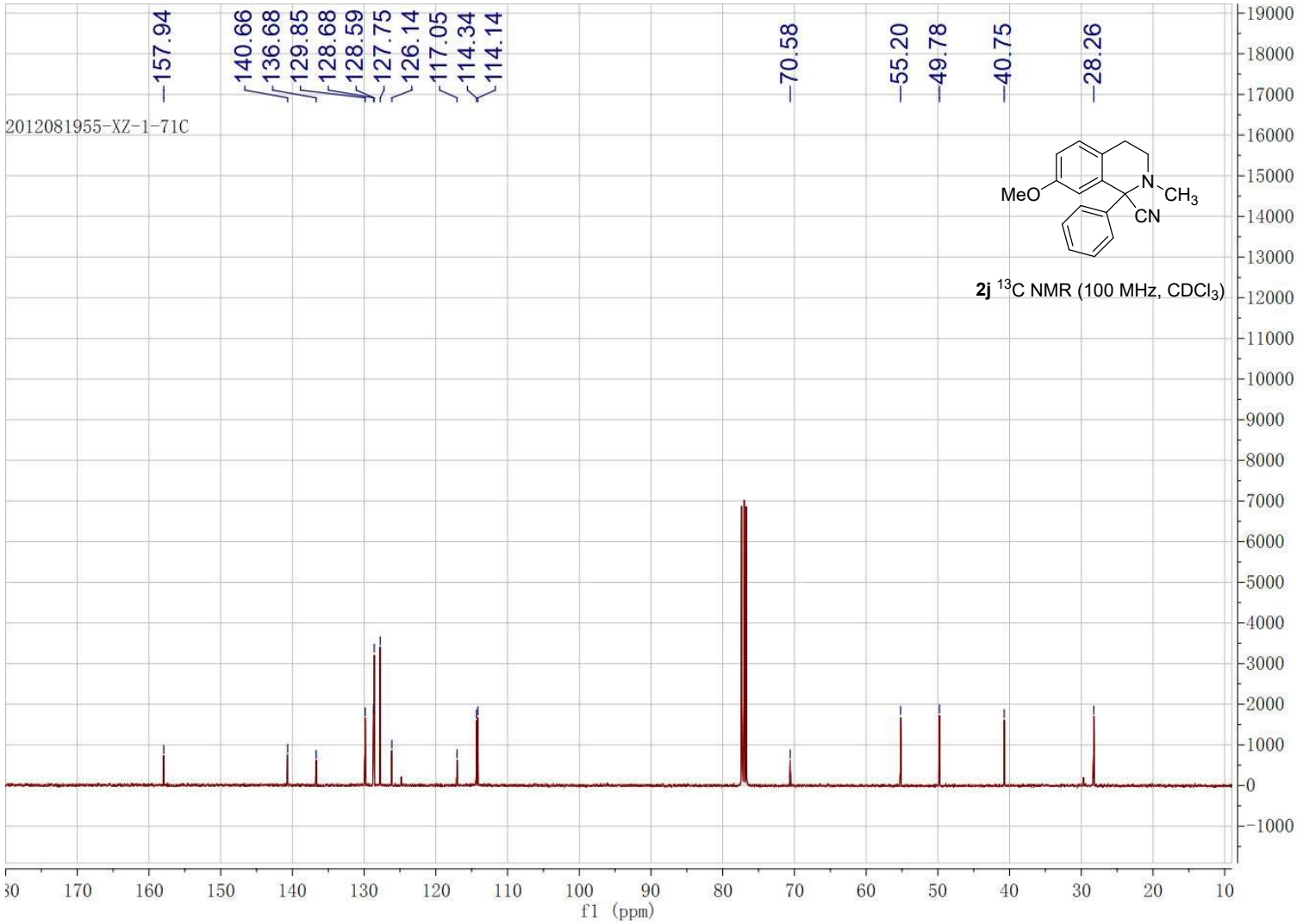
2i ^{1}H NMR (400 MHz, $CDCl_3$)



2i ^{13}C NMR (100 MHz, $CDCl_3$)



2j ^{1}H NMR (400 MHz, $CDCl_3$)


157.94
140.66
136.68
129.85
128.68
128.59
127.75
126.14
117.05
114.34
114.14
70.58
55.20
49.78
40.75
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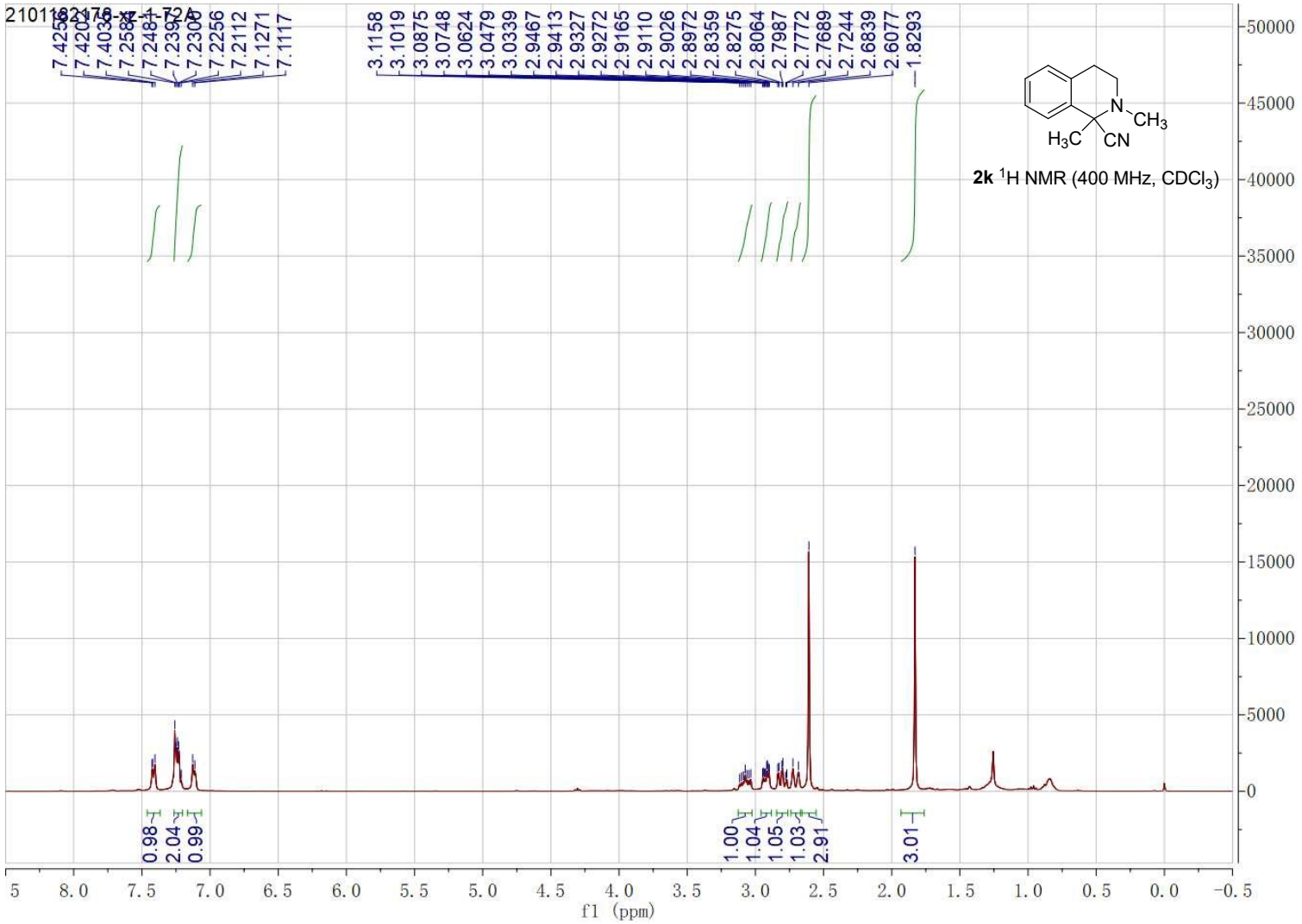
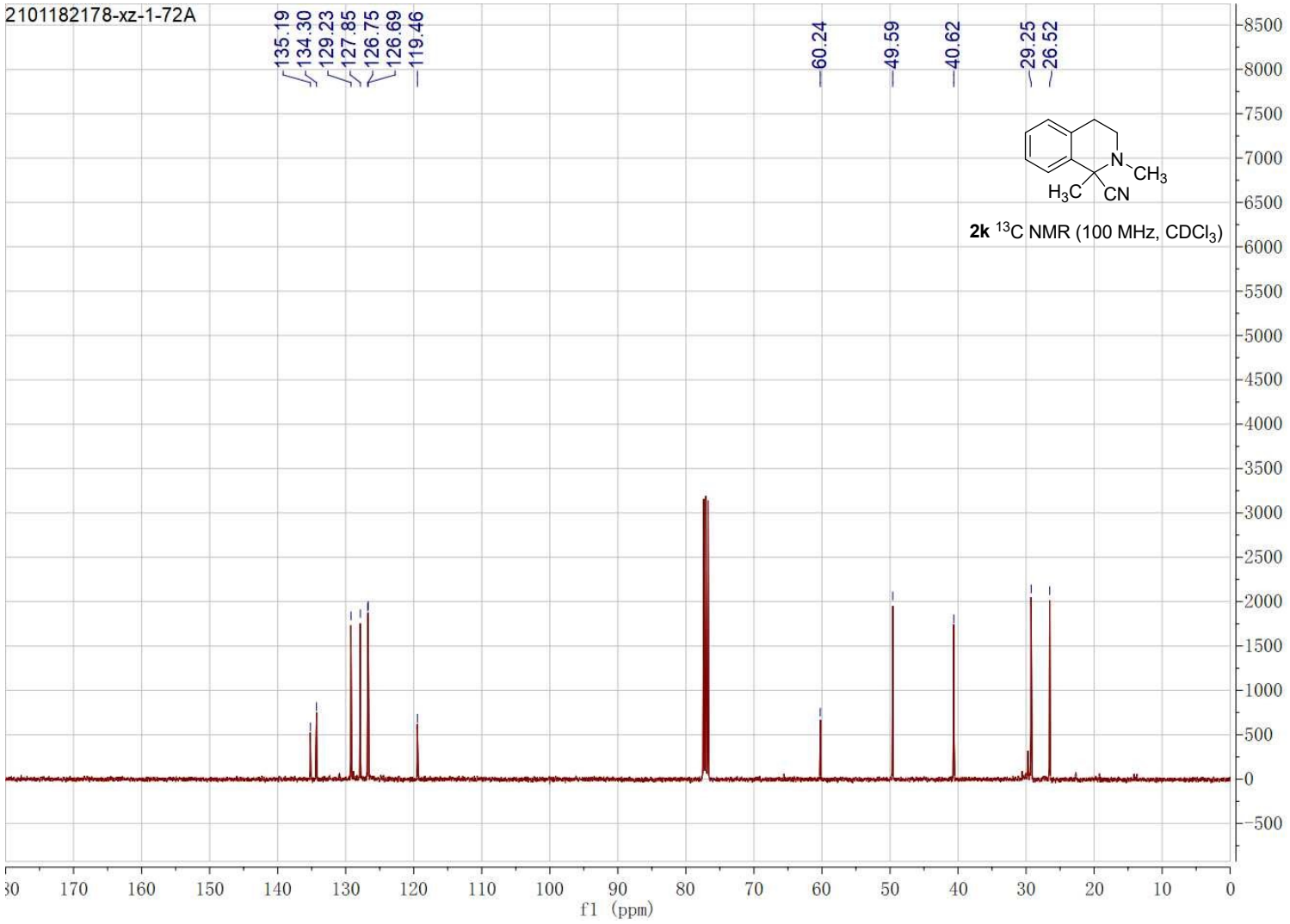
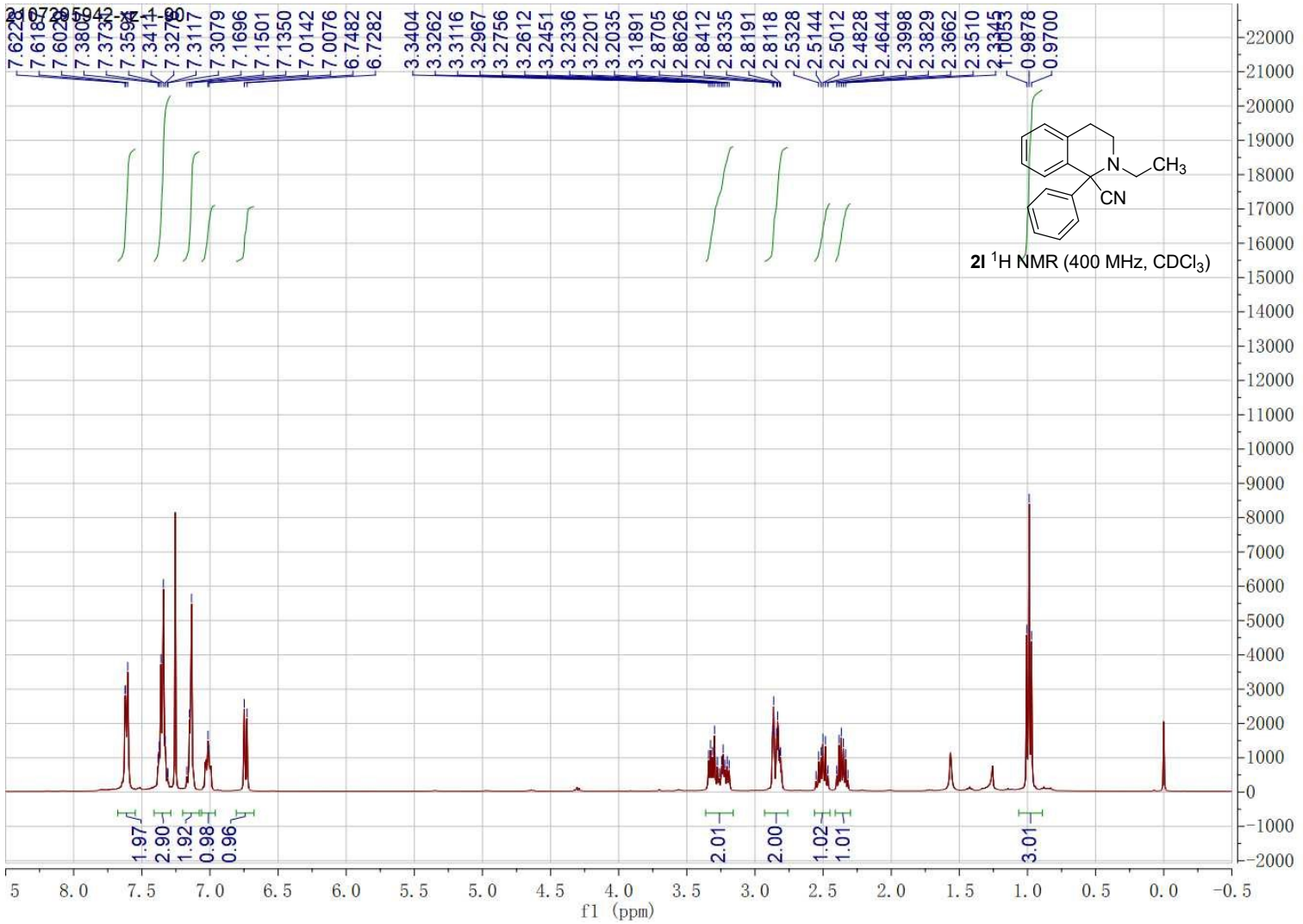
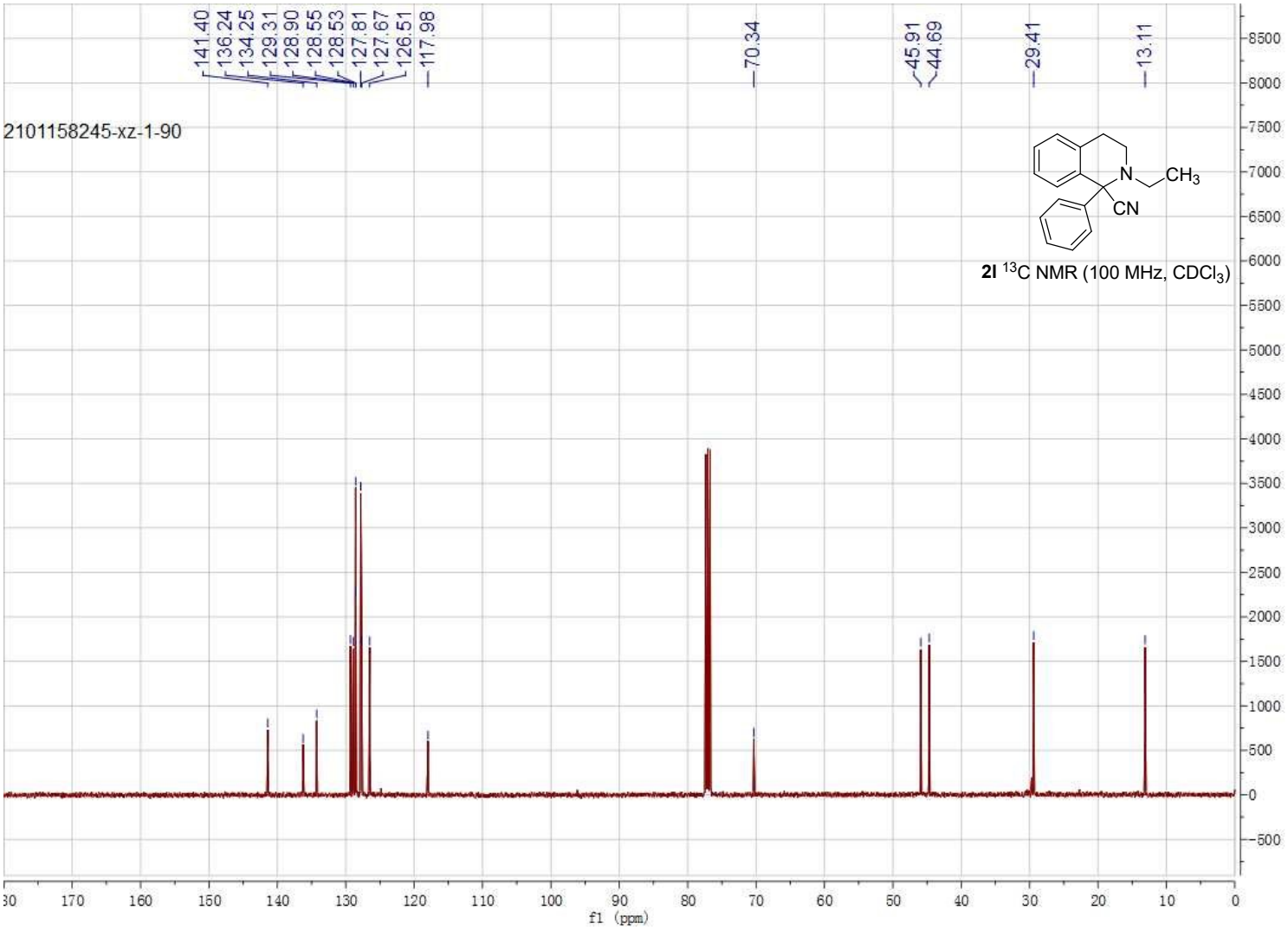
2012081955-XZ-1-71C
MeO
N
CH3
CN
2j 13C NMR (100 MHz, CDCl3)
f1 (ppm)



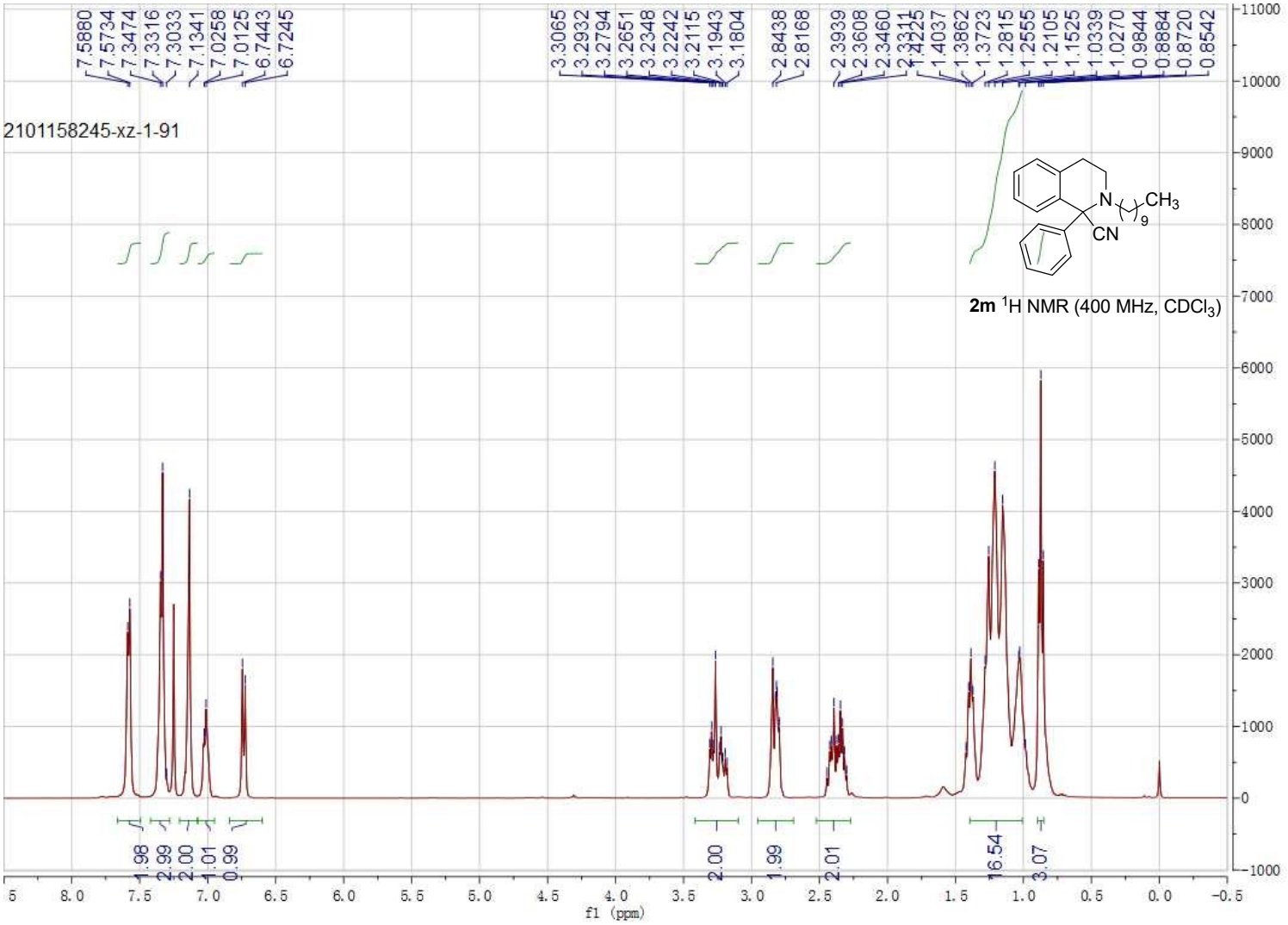
2k ^{1}H NMR (400 MHz, $CDCl_3$)


2101182178-xz-1-72A
135.19
134.30
129.23
127.85
126.75
126.69
119.46
60.24
49.59
40.62
29.25
26.52
N
CH3
H3C
CN
2k 13C NMR (100 MHz, CDCl3)
f1 (ppm)

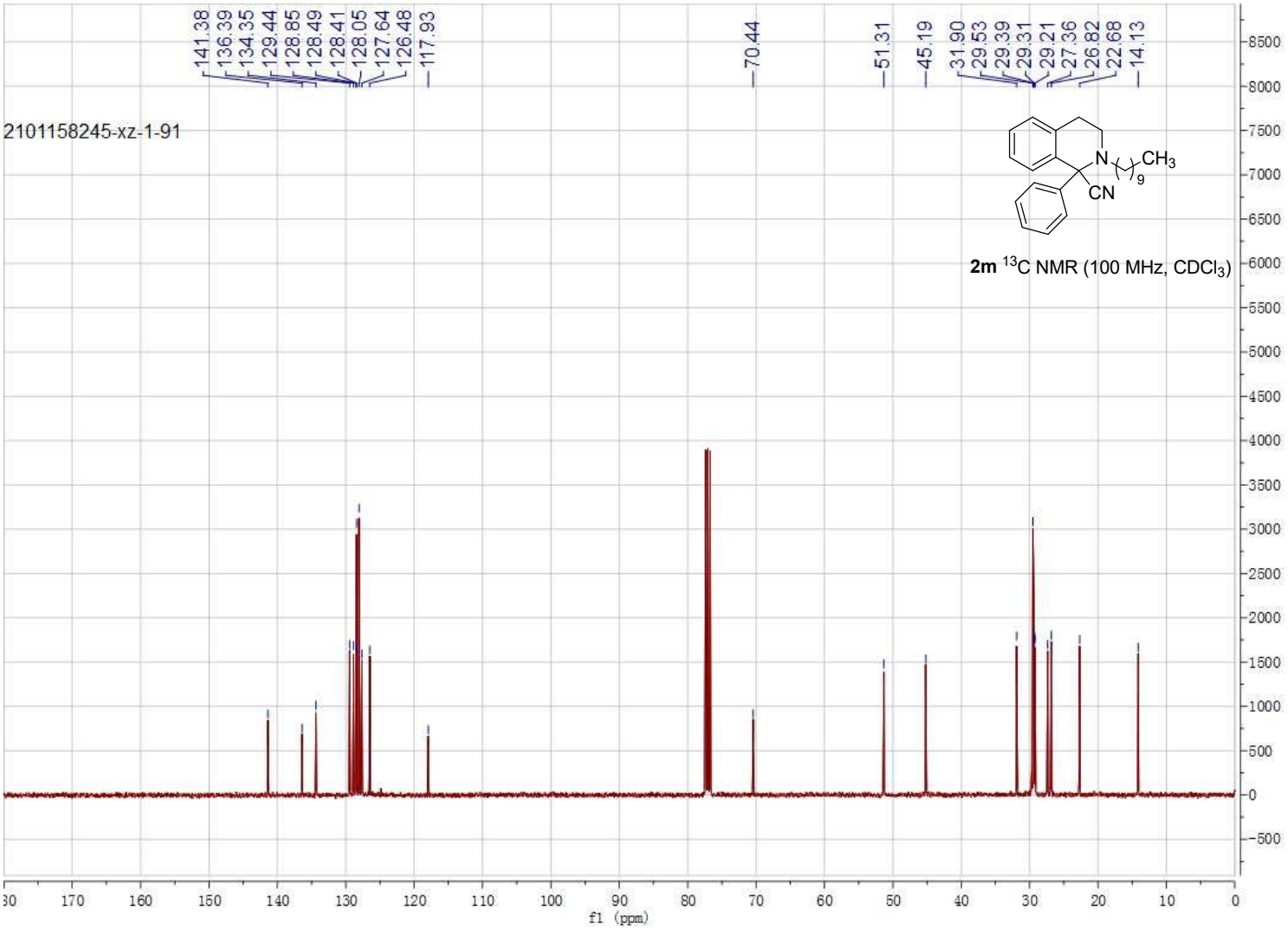

2107295942-xz-1-90
7.6225
7.6185
7.6022
7.3805
7.3731
7.3598
7.3412
7.3276
7.3117
7.3079
7.1696
7.1501
7.1350
7.0142
7.0076
6.7482
6.7282
3.3404
3.3262
3.3116
3.2967
3.2756
3.2612
3.2451
3.2336
3.2201
3.2035
3.1891
2.8705
2.8626
2.8412
2.8335
2.8191
2.8118
2.5328
2.5144
2.5012
2.4828
2.4644
2.3998
2.3829
2.3662
2.3510
2.3345
1.0053
0.9878
0.9700
N
CH3
CN
2I 1H NMR (400 MHz, CDCl3)
1.97
2.90
1.92
0.98
0.96
2.01
2.00
1.02
1.01
3.01
f1 (ppm)



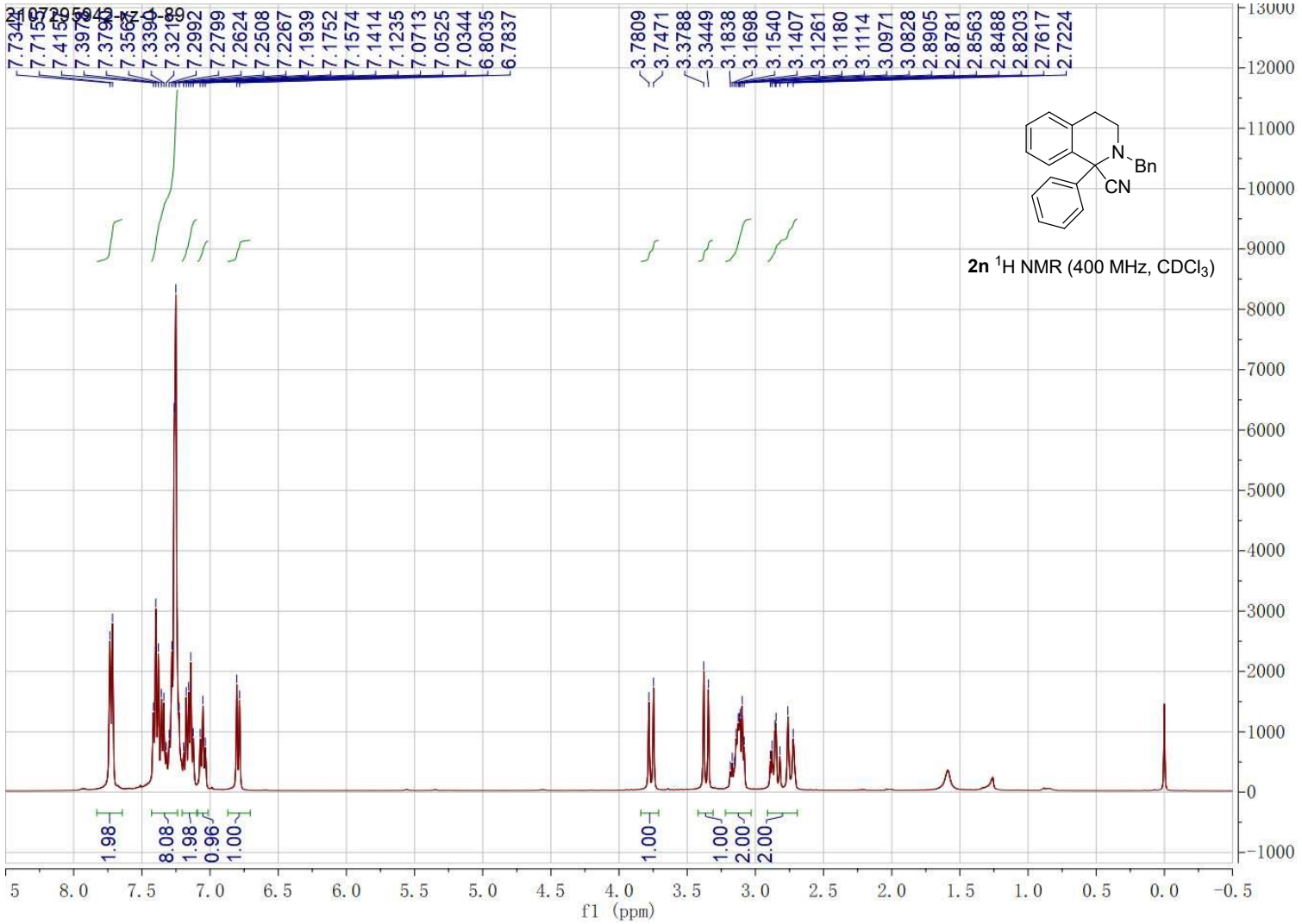
2l ^{13}C NMR (100 MHz, $CDCl_3$)

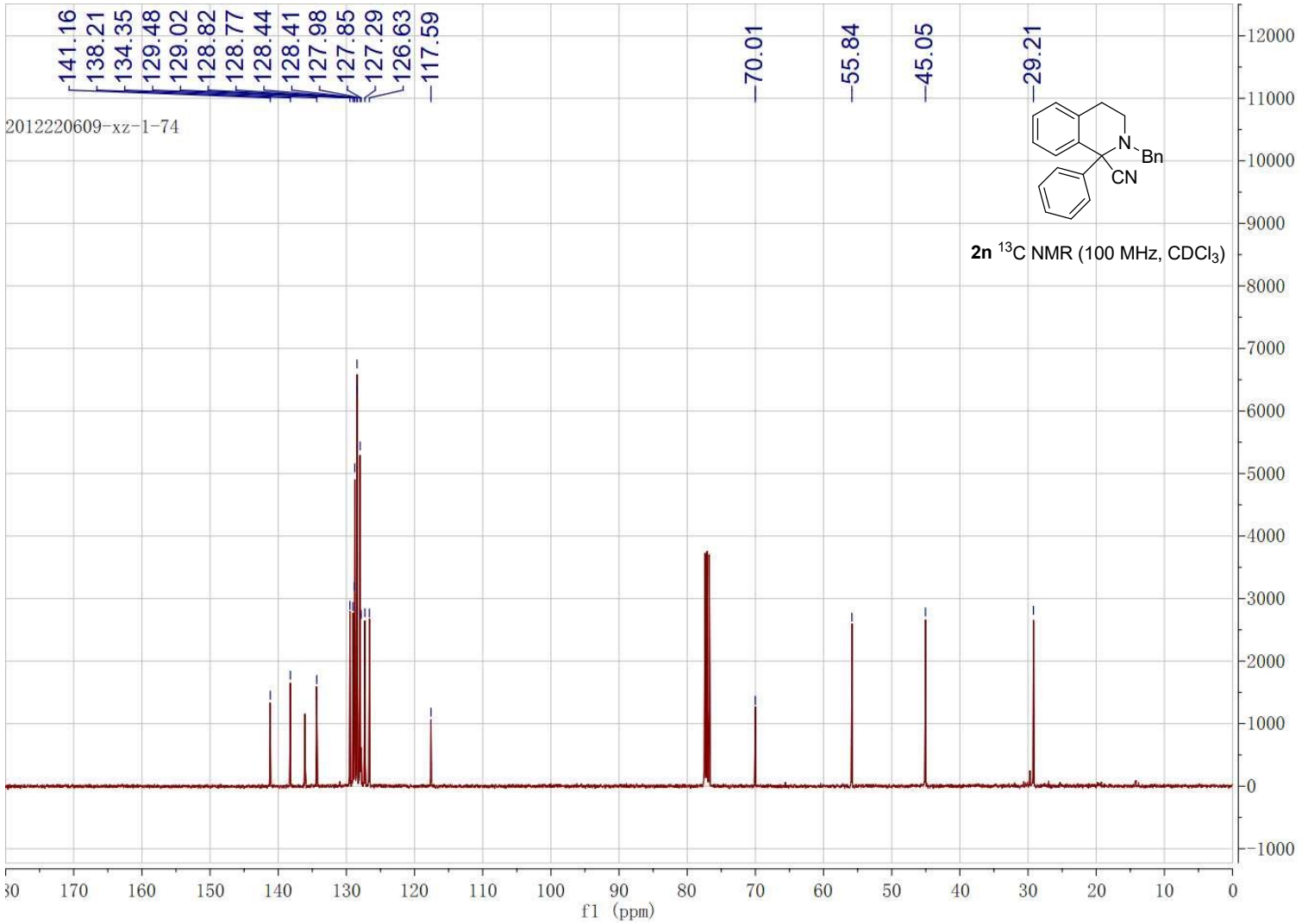


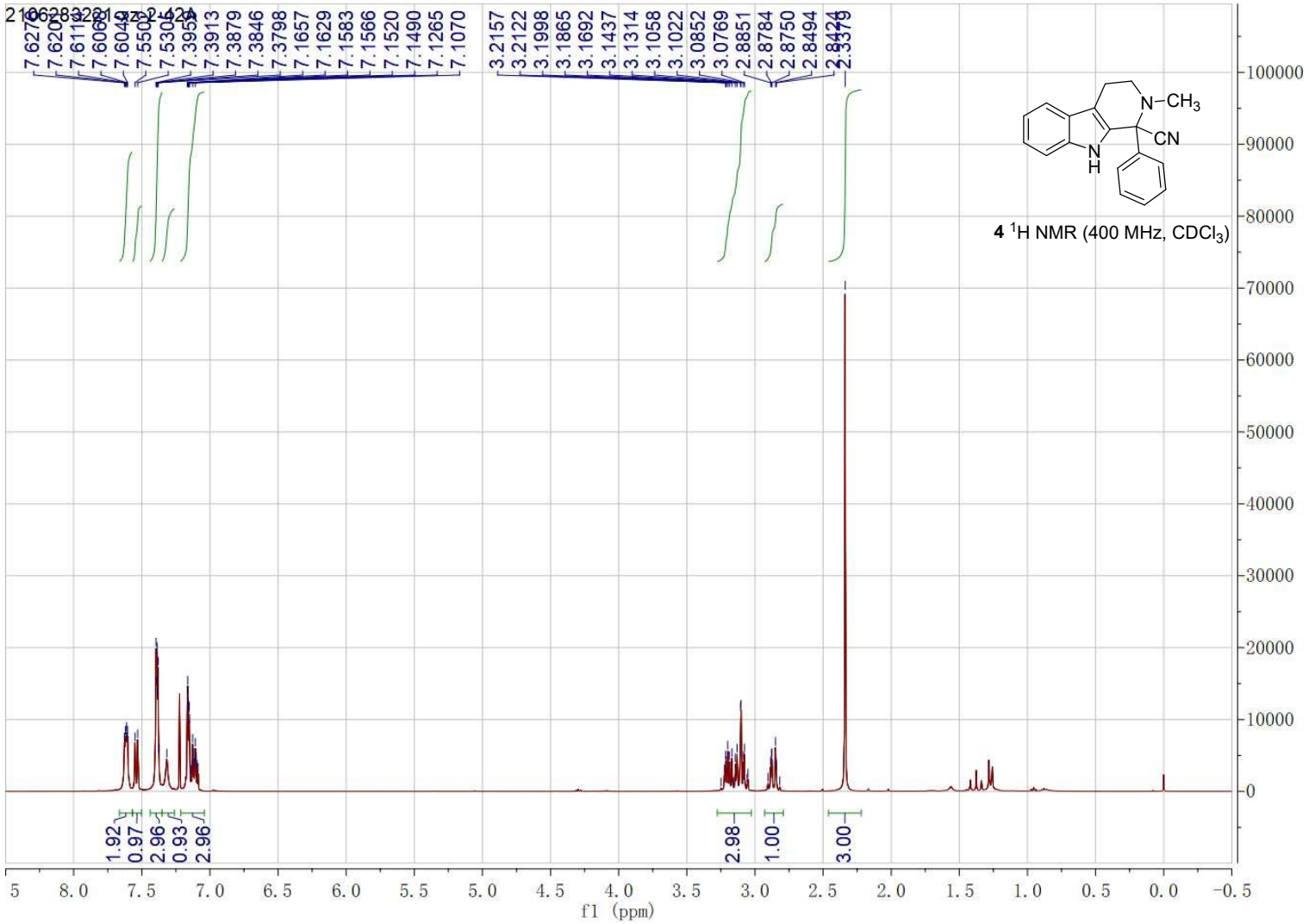
2m ^{1}H NMR (400 MHz, $CDCl_3$)

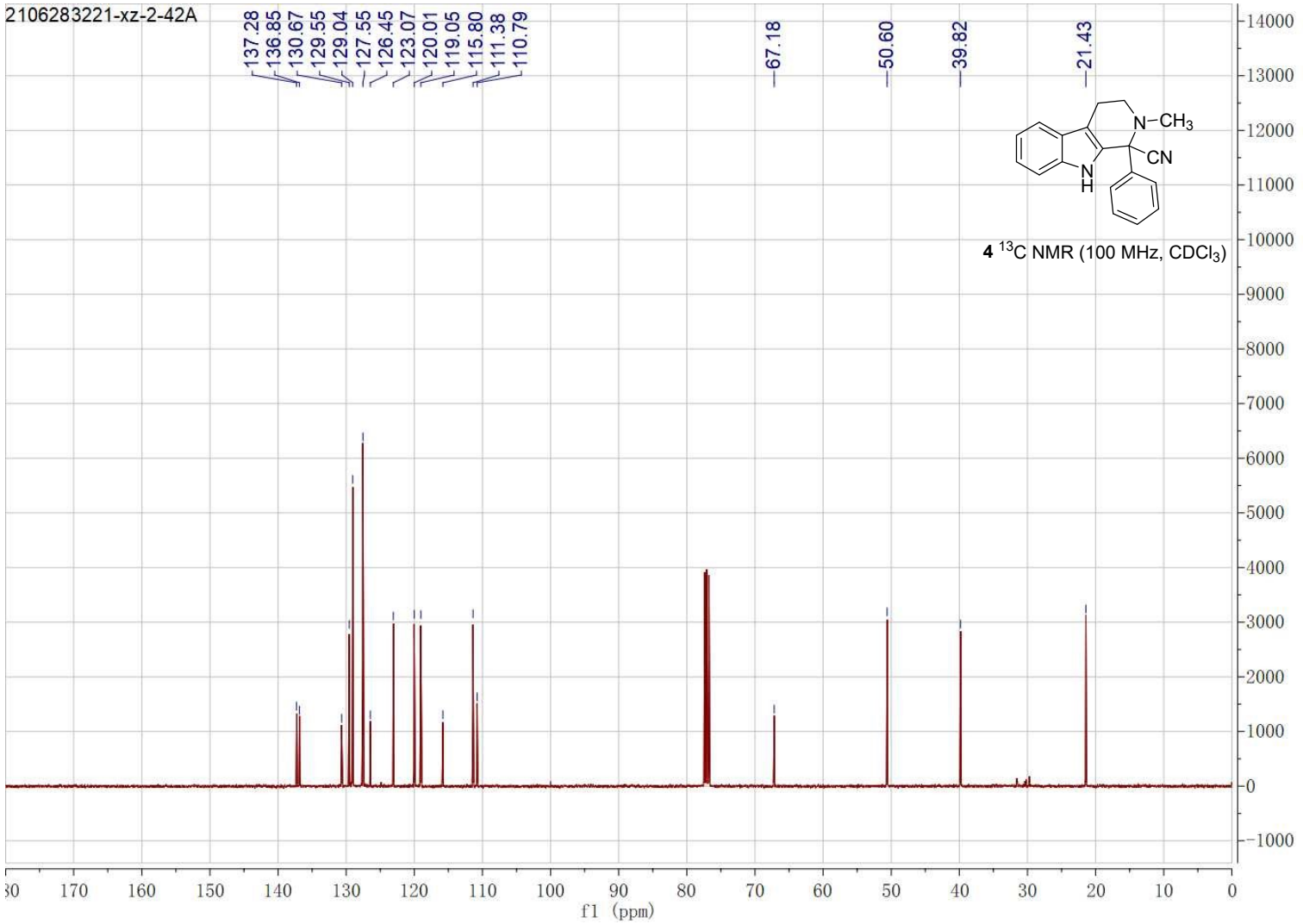


2m ^{13}C NMR (100 MHz, $CDCl_3$)

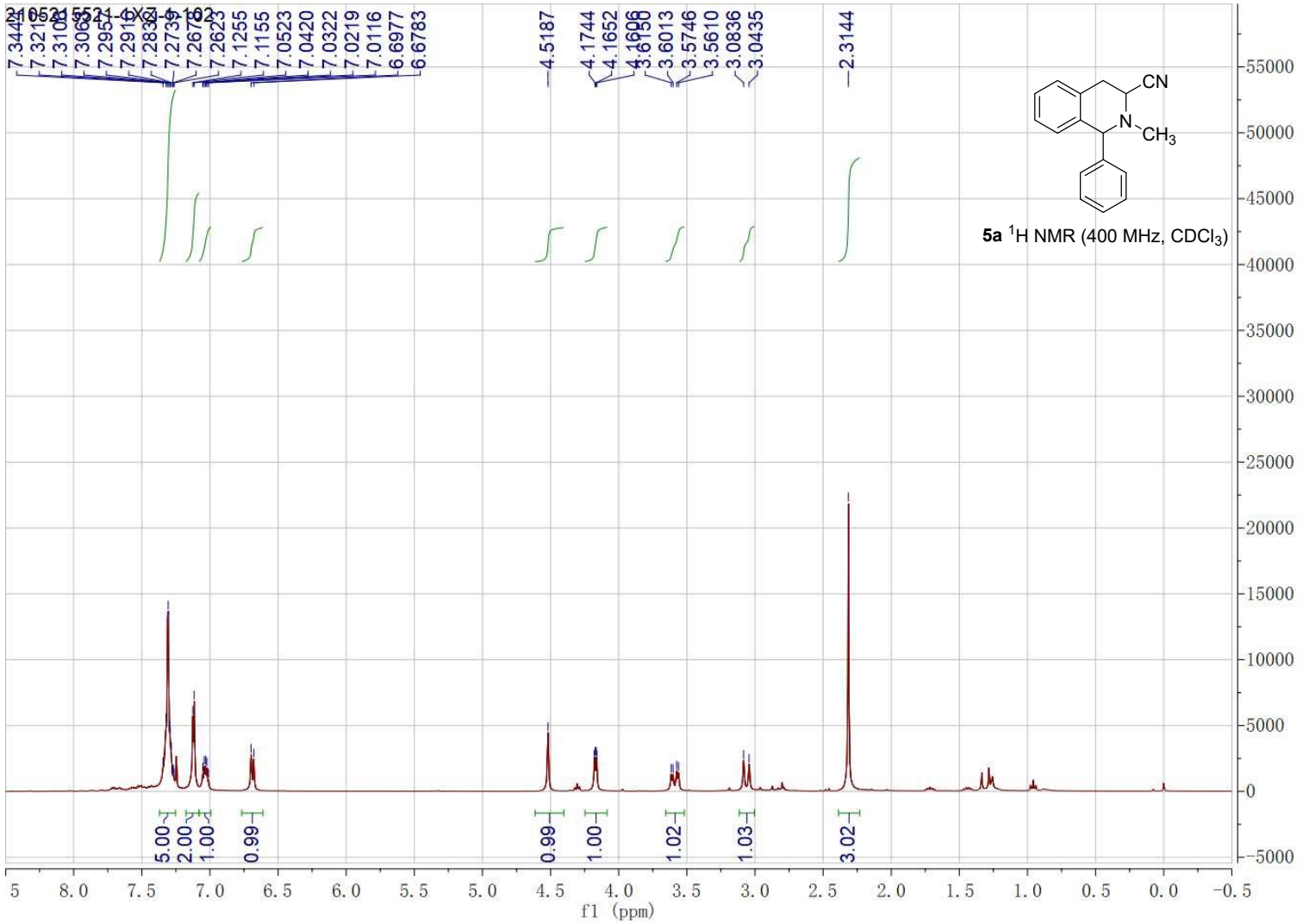

2107295942-kzl-89
7.7345
7.7155
7.4154
7.3978
7.3794
7.3566
7.3390
7.3210
7.2992
7.2799
7.2624
7.2508
7.2267
7.1939
7.1752
7.1574
7.1414
7.1235
7.0713
7.0525
7.0344
6.8035
6.7837
3.7809
3.7471
3.3788
3.3449
3.1838
3.1698
3.1540
3.1407
3.1261
3.1180
3.1114
3.0971
3.0828
2.8905
2.8781
2.8563
2.8488
2.8203
2.7617
2.7224
N
Bn
CN
2n 1H NMR (400 MHz, CDCl3)
1.98
8.08
1.98
0.96
1.00
1.00
1.00
2.00
2.00
f1 (ppm)

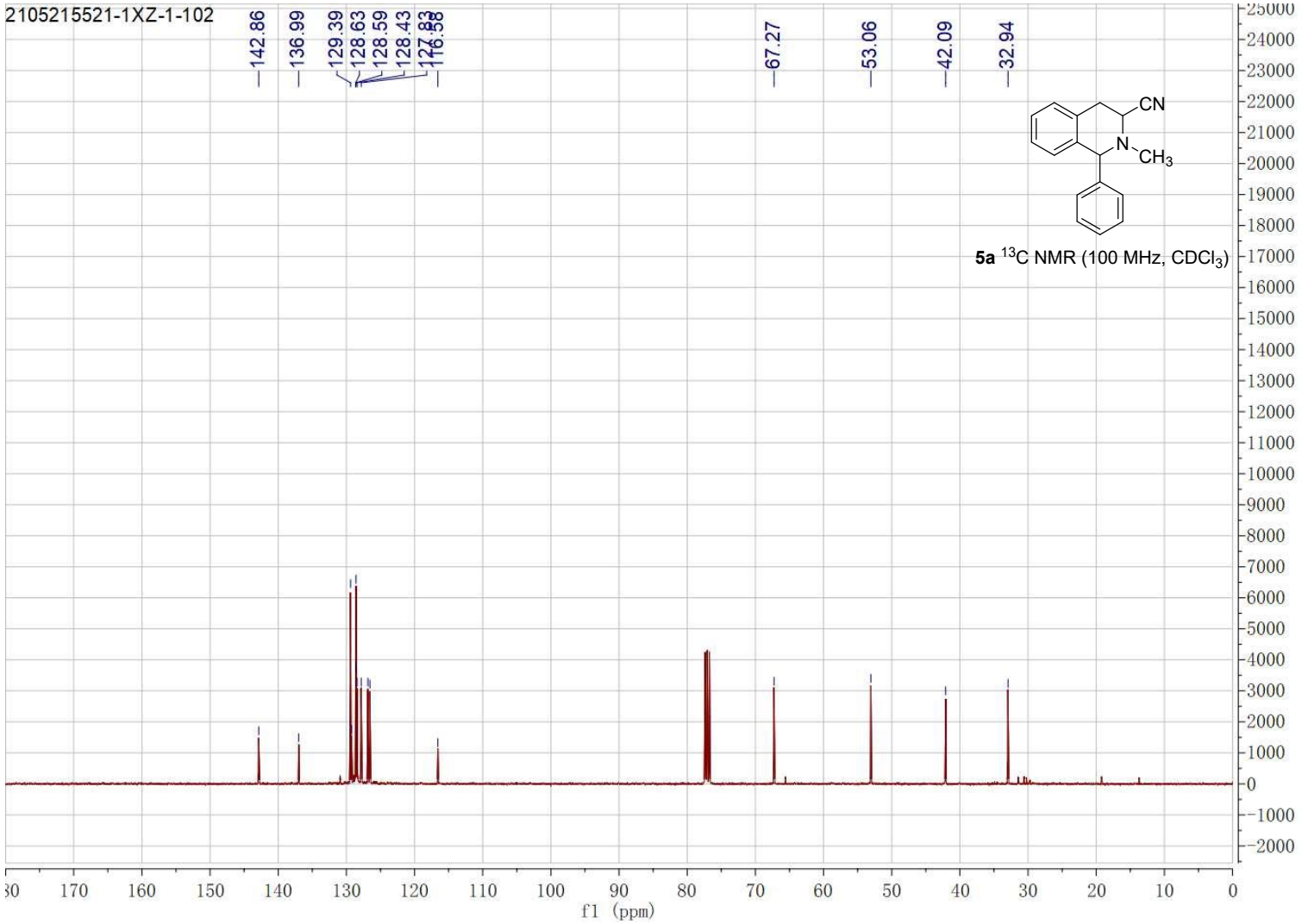

141.16
138.21
134.35
129.48
129.02
128.82
128.77
128.44
128.41
127.98
127.85
127.29
126.63
117.59
70.01
55.84
45.05
29.21
2012220609-xz-1-74
N
Bn
CN
2n ^{13}C NMR (100 MHz, $CDCl_3$)
f1 (ppm)


7.6276
7.6202
7.6111
7.6066
7.6044
7.5502
7.5305
7.3953
7.3913
7.3879
7.3846
7.3798
7.1657
7.1629
7.1583
7.1566
7.1520
7.1490
7.1265
7.1070
3.2157
3.2122
3.1998
3.1865
3.1692
3.1437
3.1314
3.1058
3.1022
3.0852
3.0769
2.8851
2.8784
2.8750
2.8494
2.3379
1.92
0.97
2.96
0.93
2.96
2.98
1.00
3.00
f1 (ppm)
N–CH3
CN
N
H
4 1H NMR (400 MHz, CDCl3)

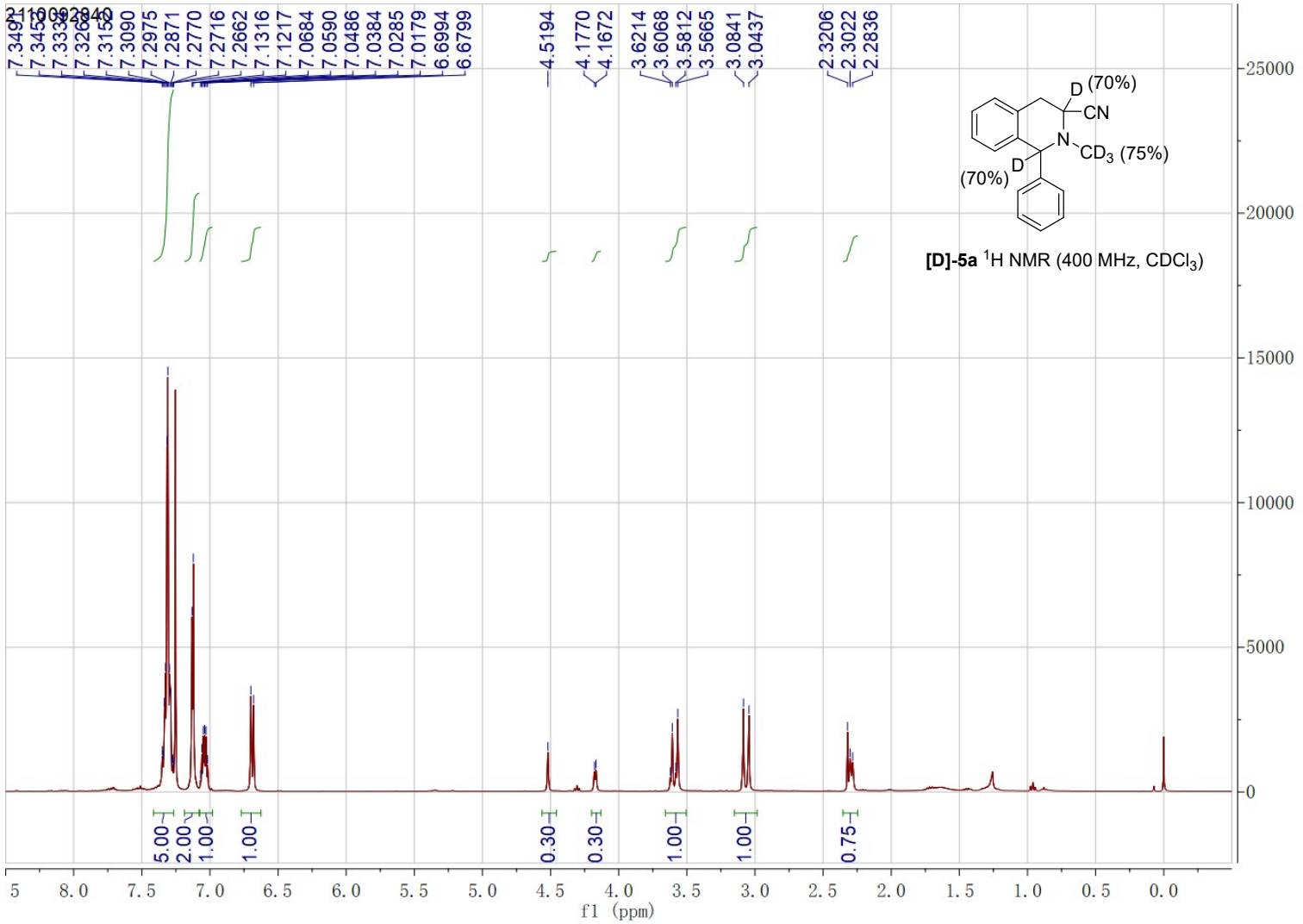


4 ^{13}C NMR (100 MHz, $CDCl_3$)


7.3445
7.3216
7.3102
7.3063
7.2951
7.2916
7.2839
7.2739
7.2678
7.2623
7.1255
7.1155
7.0523
7.0420
7.0322
7.0219
7.0116
6.6977
6.6783
4.5187
4.1744
4.1652
4.1606
4.1550
3.6150
3.6013
3.5746
3.5610
3.0836
3.0435
2.3144
CN
N
CH3
5a 1H NMR (400 MHz, CDCl3)
5.00
2.00
1.00
0.99
0.99
1.00
1.02
1.03
3.02
f1 (ppm)



5a ^{13}C NMR (100 MHz, $CDCl_3$)


7.3491
7.3455
7.3338
7.3268
7.3152
7.3090
7.2975
7.2871
7.2770
7.2716
7.2662
7.1316
7.1217
7.0684
7.0590
7.0486
7.0384
7.0285
7.0179
6.6994
6.6799
4.5194
4.1770
4.1672
3.6214
3.6068
3.5812
3.5665
3.0841
3.0437
2.3206
2.3022
2.2836
D (70%)
CN
N
CD3 (75%)
D
(70%)
[D]-5a 1H NMR (400 MHz, CDCl3)
25000
20000
15000
10000
5000
0
5.00
2.00
1.00
1.00
0.30
0.30
1.00
1.00
0.75
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)