Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

The Application of NH_4SCN as Nontoxic Cyanide Source for Divergent Strecker Synthesis of Aminonitriles and Iminonitriles

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Supporting Information

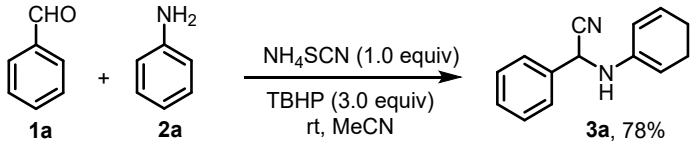
I. General Information

^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz or 600 MHz spectrometer at 25 ^{o}C. Chemical shifts values are given in ppm and referred as the internal standard to TMS: 0.00 ppm. Chemical shifts were expressed in parts per million (δ) downfield from the internal standard tetramethylsilane, and were reported as s (singlet), d (doublet), t (triplet), q (quadruple), dd (doublet of doublet), m (multiplet), etc. The coupling constants *J*, are reported in Hertz (Hz). High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro spectrometer. Melting points were determined with a Micromelting point apparatus. TLC plates were visualized by exposure to ultraviolet light.

Reagents and solvents were purchased as reagent grade and were used without further purification. All reactions were performed in standard glassware, heated at 70 ^{o}C for 3 h before used. Flash column chromatography was performed over silica gel (200-300 m) using a mixture of ethyl acetate (EtOAc) and petroleum ether (PE).

II. General Procedures and Characterization Data

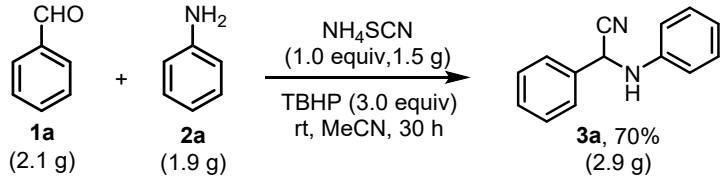
1. Procedure A for Synthesis of Aminonitrile 3a:



A mixture of ammonium thiocyanate (114 mg, 1.5 mmol, 1.0 equiv) and *tert*-butyl hydroperoxide (TBHP) (614 μL, 4.5 mmol, 3.0 equiv) were stirred at room temperature in MeCN (8 mL) for 18 h. Then aldehyde **1a** (153 μL, 1.5 mmol, 1.0 equiv) and amine **2a** (137 μL, 1.5 mmol, 1.0 equiv) were added to the solution. The mixture was stirred for another 12 h at room temperature.

When the reaction was completed, the reaction was quenched with aq. hydrogen peroxide solution (30% w/w, 2 mL) and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc/PE = 1:9) to give the desired product **3a** as a yellow solid (243.4 mg, 78%).

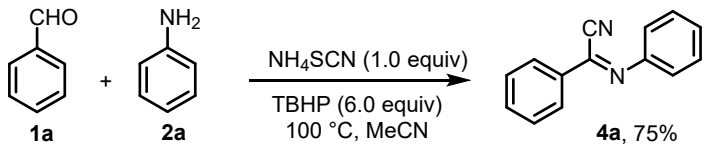
Gram-scale synthesis of product 3a:



A mixture of ammonium thiocyanate (1.5 g, 19.7 mmol, 1.0 equiv) and TBHP (8 mL, 59.1 mmol, 3.0 equiv) were stirred at room temperature in MeCN (60 mL) for 18 h. Aldehyde **1a** (2 mL, 19.7 mmol, 1.0 equiv) and amine **2a** (1.8 mL, 19.7 mmol, 1.0 equiv) were added to the solution. The mixture was stirred for another 12 h at room temperature.

When the reaction was completed, the reaction was quenched with aq. hydrogen peroxide solution (30% w/w, 10 mL) and the aqueous phase was extracted with DCM (3 x 60 mL). The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc/PE = 1:9) to give the desired product **3a** as a yellow solid (2.9 g, 70%).

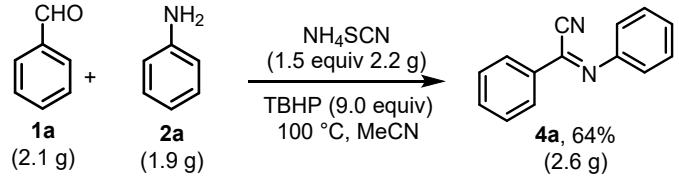
2. Procedure B for Synthesis of Iminonitrile 4a



A mixture of ammonium thiocyanate (114.2 mg, 1.5 mmol, 1.0 equiv) and TBHP (614 μL, 4.5 mmol, 3.0 equiv) were stirred at room temperature in MeCN (8 mL) for 18 h. Aldehyde **1a** (153 μL, 1.5 mmol, 1.0 equiv) and amine **2a** (137 μL, 1.5 mmol, 1.0 equiv) were added to the solution. The mixture was stirred for another 12 h at room temperature. To the resulting mixture was added TBHP (614 μL, 4.5 mmol, 3.0 equiv). The reaction mixture was stirred at 100 ºC (oil bath) for 6 h.

When the reaction was completed, the reaction was quenched with aq. hydrogen peroxide solution (30% w/w, 2 mL) and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (PE) to give the desired product **4a** as a brown solid (231.7 mg, 75%).

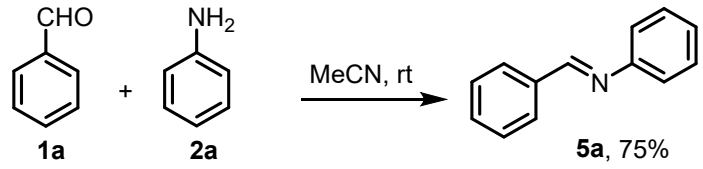
Gram-scale synthesis of product 4a:



A mixture of ammonium thiocyanate (2.2 g, 29.6 mmol, 1.5 equiv) and TBHP (12 mL, 88.7 mmol, 4.5 equiv) were stirred at room temperature in MeCN (80 mL) for 18 h. Aldehyde **1a** (2 mL, 19.7 mmol, 1.0 equiv) and amine **2a** (1.8 mL, 19.7 mmol, 1.0 equiv) were added to the solution. The mixture was stirred for another 12 h at room temperature. To the resulting mixture was added TBHP (12 mL, 88.7 mmol, 4.5 equiv). The reaction mixture was stirred at 100 ºC (oil bath) for 6 h.

When the reaction was completed, the reaction was quenched with aq. hydrogen peroxide solution (30% w/w, 10 mL) and the aqueous phase was extracted with DCM (3 x 60 mL). The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (PE) to give the desired product **4a** as a brown solid (2.6 g, 64%).

3. Procedure C for Synthesis of Imine 5a

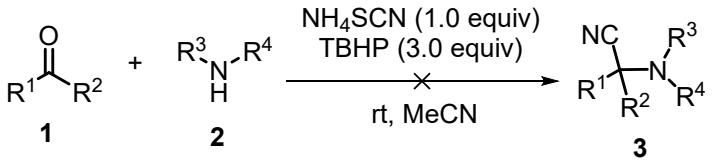


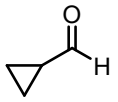
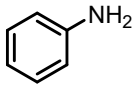
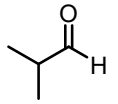
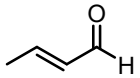
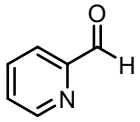
A mixture of aldehyde **1a** (1530 μL, 15 mmol, 1.0 equiv) and amine **2a** (1370 μL, 15 mmol, 1.0 equiv) in MeCN (20 mL) was stirred for 4 h at room temperature. When the reaction was completed, the reaction mixture was dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (PE) to give the desired product **5a** as a whited solid (2745 mg, 75%).

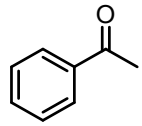
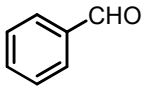
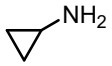
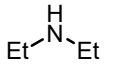
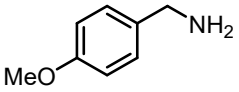
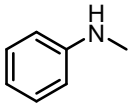
4. Further Investigations on Substrate Scopes

After investigating the substrate scopes of the method as shown in Table 2 and Table 3 of the text, we found it is somewhat narrow than that of the classic Strecker reaction. Representative examples were shown here. Actually, we have studied the reaction of many aliphatic aldehydes and aliphatic amines, including the pre-prepared imines. Unfortunately, none of them was suitable for this transformation.

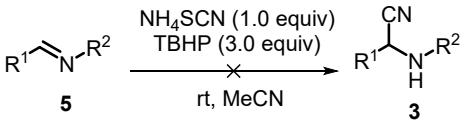
Here are some examples using aliphatic aldehydes or aliphatic amines.

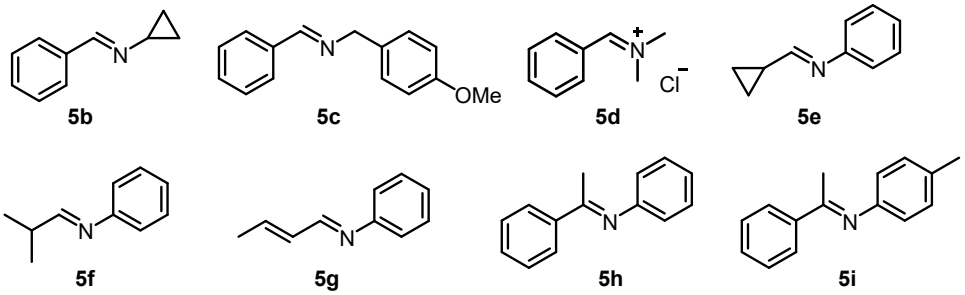


1	2
	
	
	
	

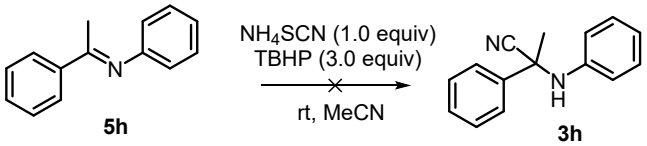
	
	
	
	
	

Here are some examples using pre-prepared imines derived from aliphatic aldehydes or aliphatic amines (**5b-g** were known compounds synthesized according to previous report[4]).



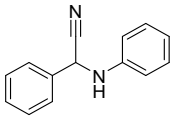


We also tried the reaction of acetophenone and aniline. Disappointingly, the reaction also did not provide the desired aminonitrile.



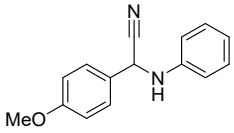
5. Characterization Data of 3a-t

2-Phenyl-2-(phenylamino)acetonitrile (3a)



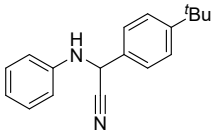
Following the general procedure **A**, **3a** was purified by silica gel chromatography (10% EtOAc/PE). A brown solid (243 mg, 78%); mp: 138 – 141 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 7.9 Hz, 2H), 7.44 (d, *J* = 6.0 Hz, 3H), 7.28 – 7.23 (m, 2H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.76 (d, *J* = 7.4 Hz, 2H), 5.41 (s, 1H), 4.01 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.8, 134.0, 129.70, 129.68, 129.5, 127.4, 120.4, 118.3, 114.3, 50.3. HRMS (ESI) calcd for $C_{14}H_{13}N_2^+$ [M + H$^+$] 209.1073, found 209.1075.

2-(4-Methoxyphenyl)-2-(phenylamino)acetonitrile (3b)



Following the general procedure **A**, **3b** was purified by silica gel chromatography (10% EtOAc/PE). A yellow solid (275 mg, 77%); mp: 123 – 124 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 8.7 Hz, 2H), 7.23 (d, *J* = 7.3 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.89 – 6.82 (m, 1H), 6.74 (d, *J* = 7.5 Hz, 2H), 5.33 (s, 1H), 3.98 (s, 1H), 3.80 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.4, 144.7, 129.5, 128.6, 125.9, 120.1, 118.4, 114.6, 114.1, 55.4, 49.6. HRMS (ESI) calcd for $C_{15}H_{15}N_2O^+$ [M + H$^+$] 239.1179, found 239.1172.

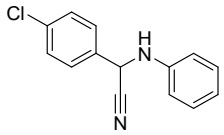
2-(4-(*tert*-Butyl)phenyl)-2-(phenylamino)acetonitrile (3c)



Following the general procedure **A**, **3c** was purified by silica gel chromatography (10% EtOAc/PE). A brown solid (320 mg, 81%); mp: 115 – 116 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 – 7.37 (m, 4H), 7.26 – 7.19 (m, 2H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.75

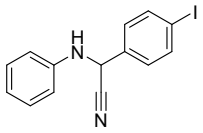
(d, *J* = 7.5 Hz, 2H), 5.35 (s, 1H), 4.13 (s, 1H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.0, 144.7, 131.0, 130.0, 127.2, 126.4, 120.4, 118.4, 114.3, 50.1, 34.9, 31.4. HRMS (ESI) calcd for $C_{18}H_{20}NaN_2^+$ [M + Na^+] 287.1519, found 287.1529.

2-(4-Chlorophenyl)-2-(phenylamino)acetonitrile (3d)



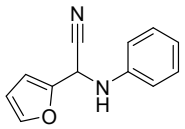
Following the general procedure **A**, **3d** was purified by silica gel chromatography (10% EtOAc/PE). A yellow solid (210 mg, 58%); mp: 131 – 133 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 6.5 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 7.3 Hz, 2H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 7.5 Hz, 2H), 5.38 (s, 1H), 4.03 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.5, 135.7, 132.5, 129.7, 129.6, 128.7, 120.7, 117.9, 114.4, 49.8. HRMS (ESI) calcd for $C_{14}H_{12}{}^{35}ClN_2^+$ [M + H^+] 243.0684, found 243.0687.

2-(4-Iodophenyl)-2-(phenylamino)acetonitrile (3e)



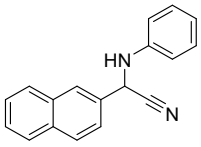
Following the general procedure **A**, **3e** was purified by silica gel chromatography (10% EtOAc/PE). A yellow solid (270 mg, 54%); mp: 125 – 127 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 8.1 Hz, 2H), 7.26 (s, 1H), 7.26 – 7.18 (m, 3H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 5.31 (d, *J* = 7.8 Hz, 1H), 4.14 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.3, 138.3, 133.5, 129.5, 129.0, 120.4, 117.9, 114.3, 95.4, 49.6. HRMS (ESI) calcd for $C_{14}H_{12}IN_2^+$ [M + H^+] 335.0040, found 335.0042.

2-(Furan-2-yl)-2-(phenylamino)acetonitrile (3f)



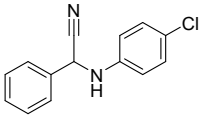
Following the general procedure **A**, **3f** was purified by silica gel chromatography (10% EtOAc/PE). A yellow solid (205 mg, 69%); mp: 102 – 103 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (s, 1H), 7.33 – 7.26 (m, 2H), 6.93 (t, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 7.5 Hz, 2H), 6.60 (d, *J* = 3.4 Hz, 1H), 6.44 (dd, *J* = 3.4, 1.9 Hz, 1H), 5.50 (s, 1H), 4.20 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.2, 144.1, 129.7, 120.8, 116.6, 114.6, 111.0, 109.8, 44.5. HRMS (ESI) calcd for $C_{12}H_{11}N_2O^+$ [M + H^+] 199.0866, found 199.0863.

2-(Naphthalen-2-yl)-2-(phenylamino)acetonitrile (3g)



Following the general procedure **A**, **3g** was purified by silica gel chromatography (10% EtOAc/PE). A brown solid (216 mg, 56%); mp: 144 – 145 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (s, 1H), 7.97 – 7.86 (m, 3H), 7.63 – 7.56 (m, 3H), 7.35 – 7.26 (m, 2H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 7.4 Hz, 2H), 5.59 (s, 1H), 4.16 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.6, 133.4, 133.0, 131.1, 129.6, 129.4, 128.2, 127.7, 127.1, 127.0, 126.6, 124.4, 120.3, 118.2, 114.2, 50.3. HRMS (ESI) calcd for $C_{18}H_{15}N_2^+$ [M + H^+] 259.1230, found 259.1235.

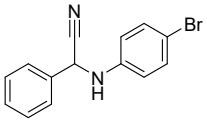
2-((4-Chlorophenyl)amino)-2-phenylacetonitrile (3h)



Following the general procedure **A**, **3h** was purified by silica gel chromatography (10% EtOAc/ PE). A yellow solid (315.8 mg, 87%); mp: 129 – 131 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.55 (m, 2H), 7.46 (d, *J* = 7.1 Hz, 3H), 7.23 (d, *J* = 8.7 Hz, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 5.39 (s, 1H), 4.11 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*)

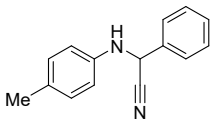
δ 143.3, 133.6, 129.8, 129.6, 129.5, 127.3, 125.2, 118.0, 115.5, 50.4. HRMS (ESI) calcd for $C_{14}H_{12}{}^{35}ClN_2^+$ [M + H^+] 243.0684, found 243.0682.

2-((4-Bromophenyl)amino)-2-phenylacetonitrile (3i)



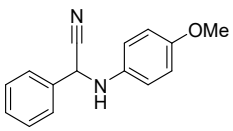
Following the general procedure **A**, **3i** was purified by silica gel chromatography (10% EtOAc/ PE). A yellow solid (369 mg, 86%); mp: 117 – 119 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.53 (m, 2H), 7.46 (dd, *J* = 5.1, 1.9 Hz, 3H), 7.36 (d, *J* = 8.9 Hz, 2H), 6.65 (d, *J* = 8.9 Hz, 2H), 5.39 (s, 1H), 4.12 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.7, 133.5, 132.5, 129.8, 129.5, 127.3, 118.0, 115.9, 112.4, 50.2. HRMS (ESI) calcd for $C_{14}H_{11}{}^{79}BrNaN_2^+$ [M + Na^+] 308.9998, found 309.0008.

2-Phenyl-2-(p-tolylamino)acetonitrile (3j)



Following the general procedure **A**, **3j** was purified by silica gel chromatography (10% EtOAc/ PE). A yellow solid (239 mg, 72%); mp: 125 – 127 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 7.8 Hz, 2H), 7.49 – 7.42 (m, 3H), 7.09 (d, *J* = 8.3 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 5.41 (s, 1H), 3.92 (s, 1H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.5, 134.2, 130.2, 129.9, 129.6, 129.4, 127.4, 118.5, 114.6, 50.8, 20.6. HRMS (ESI) calcd for $C_{15}H_{15}N_2^+$ [M + H^+] 223.1230, found 223.1233.

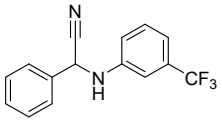
2-((4-Methoxyphenyl)amino)-2-phenylacetonitrile (3k)



Following the general procedure **A**, **3k** was purified by silica gel chromatography (10% EtOAc/ PE). A yellow solid (290 mg, 81%); mp: 127 – 128 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 5.8 Hz, 2H), 7.45 (d, *J* = 6.7 Hz, 3H), 6.94 – 6.65 (m, 4H), 5.35 (s, 1H), 4.10 (s, 1H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.2,

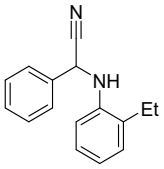
138.7, 134.3, 129.6, 129.4, 127.4, 118.6, 116.4, 115.1, 55.8, 51.7. HRMS (ESI) calcd for $C_{15}H_{15}N_2O^+$ [M + H^+] 239.1179, found 239.1180.

2-Phenyl-2-((3-(trifluoromethyl)phenyl)amino)acetonitrile (3l)



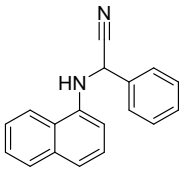
Following the general procedure **A**, **3l** was purified by silica gel chromatography (10% EtOAc/ PE). A brown solid (199 mg, 48%); mp: 129 – 130 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 3.7 Hz, 2H), 7.48 (d, *J* = 6.4 Hz, 3H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 5.46 (s, 1H), 4.33 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 145.0, 133.3, 132.0 (q, $^2J_{C\text{-}F}$ = 32.3 Hz), 130.2, 129.9, 129.6, 127.3, 124.1 (q, $^1J_{C\text{-}F}$ = 273.7 Hz), 117.8, 116.9, 116.8 (q, $^3J_{C\text{-}F}$ = 3.0 Hz), 110.8, 50.0. HRMS (ESI) calcd for $C_{15}H_{12}F_3N_2^+$ [M + H^+] 277.0947, found 277.0952.

2-((2-Ethylphenyl)amino)-2-phenylacetonitrile (3m)



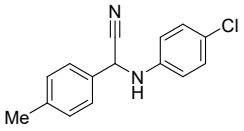
Following the general procedure **A**, **3m** was purified by silica gel chromatography (10% EtOAc/ PE). A yellow solid (280 mg, 79%); mp: 138 – 139 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 6.1 Hz, 2H), 7.48 (d, *J* = 6.9 Hz, 3H), 7.23 – 7.16 (m, 2H), 6.98 – 6.80 (m, 2H), 5.48 (s, 1H), 3.96 (s, 1H), 2.50 (q, *J* = 7.5 Hz, 2H), 1.24 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.3, 134.3, 129.7, 129.5, 129.4, 128.6, 127.3, 127.3, 120.3, 118.5, 112.0, 50.3, 23.9, 13.2. HRMS (ESI) calcd for $C_{16}H_{17}N_2^+$ [M + H^+] 237.1386, found 237.1388.

2-(Naphthalen-1-ylamino)-2-phenylacetonitrile (3n)



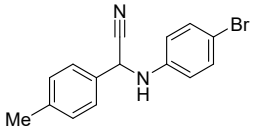
Following the general procedure **A**, **3n** was purified by silica gel chromatography (10% EtOAc/PE). A yellow solid (158 mg, 41%); mp: 144 – 146 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 9.7 Hz, 2H), 7.58 – 7.41 (m, 7H), 6.93 (d, *J* = 6.5 Hz, 1H), 5.59 (s, 1H), 4.66 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.0, 134.4, 134.1, 129.8, 129.6, 129.0, 127.5, 126.3, 126.3, 125.7, 124.1, 120.8, 119.9, 118.3, 107.5, 50.4. HRMS (ESI) calcd for $C_{18}H_{15}N_2^+$ [M + H$^+$] 259.1230, found 259.1234.

2-((4-Chlorophenyl)amino)-2-(*p*-tolyl)acetonitrile (3o)



Following the general procedure **A**, **3o** was purified by silica gel chromatography (10% EtOAc/PE). A brown solid (288 mg, 75%); mp: 133 – 134 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 2.7 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 5.33 (s, 1H), 4.06 (s, 1H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.4, 139.9, 130.7, 130.2, 129.6, 127.2, 125.1, 118.2, 115.5, 50.1, 21.3. HRMS (ESI) calcd for $C_{15}H_{14}{}^{35}ClN_2^+$ [M + H$^+$] 257.0840, found 257.0844.

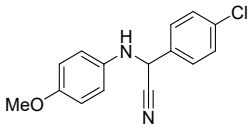
2-((4-Bromophenyl)amino)-2-(*p*-tolyl)acetonitrile (3p)



Following the general procedure **A**, **3p** was purified by silica gel chromatography (10% EtOAc/PE). A brown solid (324 mg, 72%); mp: 157 – 158 °C. ^{1}H NMR (400 MHz,

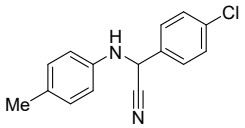
Chloroform-*d*) δ 7.44 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 5.9 Hz, 2H), 6.64 (d, *J* = 8.8 Hz, 2H), 5.32 (s, 1H), 4.04 (s, 1H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.7, 139.9, 132.5, 130.6, 130.2, 127.3, 118.1, 116.0, 112.5, 50.1, 21.3. HRMS (ESI) calcd for $C_{15}H_{13}{}^{79}BrNaN_2^+$ [M + Na^+] 323.0154, found 323.0152.

2-(4-Chlorophenyl)-2-((4-methoxyphenyl)amino)acetonitrile (3q)



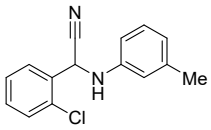
Following the general procedure **A**, **3q** was purified by silica gel chromatography (10% EtOAc/PE). A brown solid (184 mg, 45%); mp: 117 – 119 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 6.75 (d, *J* = 8.9 Hz, 2H), 5.33 (s, 1H), 4.00 – 3.78 (s, 1H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.4, 138.3, 135.6, 132.7, 129.6, 128.7, 118.2, 116.7, 115.1, 55.8, 51.2. HRMS (ESI) calcd for $C_{15}H_{14}{}^{35}ClN_2O^+$ [M + H^+] 273.0789, found 273.0792.

2-(4-Chlorophenyl)-2-(*p*-tolylamino)acetonitrile (3r)



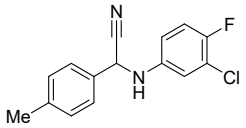
Following the general procedure **A**, **3r** was purified by silica gel chromatography (10% EtOAc/PE). A brown solid (307 mg, 80%); mp: 135 – 136 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 2H), 6.69 (d, *J* = 8.4 Hz, 2H), 5.39 (s, 1H), 3.96 (s, 1H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.0, 135.6, 132.6, 130.3, 130.2, 129.6, 128.7, 118.0, 114.9, 50.2, 20.6. HRMS (ESI) calcd for $C_{15}H_{14}{}^{35}ClN_2^+$ [M + H^+] 257.0840, found 257.0842.

2-(2-Chlorophenyl)-2-(*m*-tolylamino)acetonitrile (3s)



Following the general procedure **A**, **3s** was purified by silica gel chromatography (10% EtOAc/PE). A yellow solid (238 mg, 62%); mp: 122 – 124 °C. ^{1}H NMR (400 MHz, Chloroform-*d*)δ 7.79 – 7.71 (m, 1H), 7.52 – 7.46 (m, 1H), 7.43 – 7.36 (m, 2H), 7.17 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 8.2 Hz, 2H), 5.73 (s, 1H), 3.98 (s, 1H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.7, 139.6, 133.7, 132.0, 131.1, 130.6, 129.6, 129.2, 127.9, 121.5, 118.0, 115.2, 111.5, 48.2, 21.7. HRMS (ESI) calcd for $C_{15}H_{14}{}^{35}ClN_2^+$ [M + H$^+$] 257. 0840, found 257.0844.

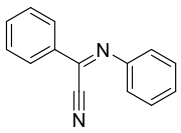
2-((3-Chloro-4-fluorophenyl)amino)-2-(*p*-tolyl)acetonitrile (3t)



Following the general procedure **A**, **3t** was purified by silica gel chromatography (10% EtOAc/PE). A brown solid (230 mg, 56%); mp: 125 – 126 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 7.6 Hz, 2H), 7.02 (t, J = 8.7 Hz, 1H), 6.78 (dd, J = 6.0, 2.9 Hz, 1H), 6.62 – 6.56 (m, 1H), 5.28 (d, J = 6.4 Hz, 1H), 3.97 (s, 1H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ152.7 (d, $^1J_{C\text{-}F}$ = 242.2 Hz), 141.6 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 140.0, 130.5, 130.2, 127.2, 121.8 (d, $^2J_{C\text{-}F}$ = 19.0 Hz), 118.0, 117.3 (d, $^2J_{C\text{-}F}$ = 22.4 Hz), 116.0, 113.7 (d, $^3J_{C\text{-}F}$ = 6.6 Hz), 50.5, 21.33. HRMS (ESI) calcd for $C_{15}H_{13}{}^{35}ClFN_2^+$ [M + H$^+$] 275.0746, found 275.0748.

6. Characterization Data of 4a-h

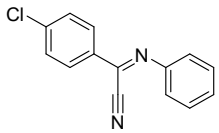
(*Z*)-*N*-Phenylbenzimidoyl cyanide (4a)



Following the general procedure **B**, **4a** was purified by silica gel chromatography (PE). A yellow solid (231 mg, 75%); mp: 108 – 110 °C. ^{1}H NMR (400 MHz, Chloroform-*d*)

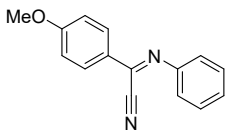
δ 8.08 (d, *J* = 7.3 Hz, 2H), 7.48 (dt, *J* = 14.8, 7.2 Hz, 3H), 7.39 (t, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 149.1, 139.8, 133.6, 132.8, 129.2, 129.0, 128.2, 127.3, 120.3, 110.8. HRMS (ESI) calcd for $C_{14}H_{11}N_2^+$ [M + H^+] 207.0917, found 207.0916.

(*Z*)-4-Chloro-*N*-phenylbenzimidoyl cyanide (4b)



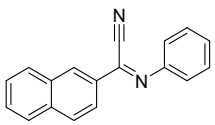
Following the general procedure **B**, **4b** was purified by silica gel chromatography (PE). A yellow solid (209 mg, 58%); mp: 132 – 133 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.1 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 7.7 Hz, 2H). HRMS (ESI) calcd for $C_{14}H_{10}{}^{35}ClN_2^+$ [M + H^+] 241.0527, found 241.0529.

(*Z*)-4-Methoxy-*N*-phenylbenzimidoyl cyanide (4c)



Following the general procedure **B**, **4c** was purified by silica gel chromatography (PE). Yellow oil (226 mg, 64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 8.8 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.26 – 7.18 (m, 1H), 7.11 (d, *J* = 7.8 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d)δ 163.6, 149.6, 139.3, 130.3, 129.4, 127.0, 126.7, 120.5, 114.6, 111.1, 55.8. HRMS (ESI) calcd for $C_{15}H_{13}N_2O^+$ [M + H^+] 237.1022, found 237.1025.

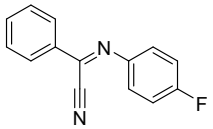
(*Z*)-*N*-Phenyl-2-naphthimidoyl cyanide (4d)



Following the general procedure **B**, **4d** was purified by silica gel chromatography (PE). Yellow oil (200 mg, 52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.60 (s, 1H), 8.27 (dd,

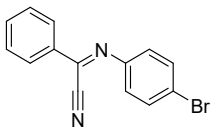
J = 8.7, 1.9 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.58 (m , 2H), 7.52 – 7.48 (m, 2H), 7.37 – 7.32 (m, 1H), 7.25 (dt, *J* = 7.3, 1.2 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 149.4, 139.9, 135.6, 132.8, 131.5, 131.2, 129.5, 129.5, 129.2, 128.8, 128.1, 127.5, 127.4, 123.0, 120.6, 111.2. HRMS (ESI) calcd for $C_{18}H_{13}N_2^+$ [M + H$^+$] 257.1073, found 257.1079.

(*Z*)-*N*-(4-Fluorophenyl)benzimidoyl cyanide (4e)



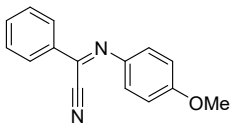
Following the general procedure **B**, **4e** was purified by silica gel chromatography (PE). A yellow solid (181 mg, 54%); mp: 122 – 124 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.23 (d, *J* = 4.9 Hz, 2H), 7.17 (t, *J* = 8.5 Hz, 2H).^{13}C NMR (101 MHz, Chloroform-d) δ 162.0 (d, $^1J_{C\text{-}F}$ = 248.5 Hz), 145.1 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 139.8, 133.7, 133.1, 129.2, 128.4, 122.6 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 116.4 (d, $^2J_{C\text{-}F}$ = 22.2 Hz), 111.1. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -114.36. HRMS (ESI) calcd for $C_{14}H_9FN_2^+$ [M + H$^+$] 225.0823, found 225.0833.

(*Z*)-*N*-(4-Bromophenyl)benzimidoyl cyanide (4f)



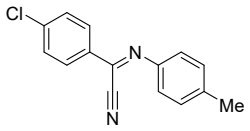
Following the general procedure **B**, **4f** was purified by silica gel chromatography (PE). Yellow oil (324 mg, 76%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 7.6 Hz, 2H), 7.60 (dd, *J* = 7.9, 5.8 Hz, 3H), 7.56 (d, *J* = 7.6 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 148.1, 140.4, 133.5, 133.3, 132.6, 129.3, 128.4, 122.3, 121.1, 110.8. HRMS (ESI) calcd for $C_{14}H_9{}^{79}BrNaN_2^+$ [M + Na$^+$] 306.9841, found 306.9849.

(*Z*)-*N*-(4-Methoxyphenyl)benzimidoyl cyanide (4g)



Following the general procedure **B**, **4g** was purified by silica gel chromatography (PE). A yellow solid (209 mg, 59%); mp: 128 – 130 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 7.9 Hz, 3H), 7.34 (d, *J* = 8.9 Hz, 2H), 7.00 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 159.5, 141.9, 137.0, 134.2, 132.5, 129.1, 128.0, 123.2, 114.6, 111.8, 55.7. HRMS (ESI) calcd for $C_{15}H_{12}NaN_2O^+$ [M + Na^+] 259.0842, found 259.0854.

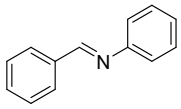
(*Z*)-4-Chloro-*N*-(*p*-tolyl)benzimidoyl cyanide (4h)



Following the general procedure **B**, **4h** was purified by silica gel chromatography (PE). A yellow solid (301 mg, 79%); mp: 132 – 134 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 – 8.04 (m, 2H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.29 (s, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 146.3, 139.2, 138.2, 137.5, 132.5, 130.1, 129.5, 129.4, 120.9, 111.2, 21.4. HRMS (ESI) calcd for $C_{15}H_{12}{}^{35}ClN_2^+$ [M + H^+] 255.0684, found 255.0688.

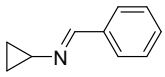
7. Characterization Data of 5a-b

(*E*)-*N*,*1*-Diphenylmethanimine (5a)



Following the general procedure **C**, **5a** was purified by silica gel chromatography (PE). A white solid (2450 mg, 98%); mp: 92 – 94 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 (s, 1H), 7.93 (d, *J* = 3.6 Hz, 2H), 7.54 – 7.46 (m, 3H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.26 – 7.20 (m, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 160.6, 152.2, 136.3, 131.6, 129.3, 129.0, 128.9, 126.1, 121.0. HRMS (ESI) calcd for $C_{13}H_{12}N^+$ [M + H^+] 182.0964, found 182.0966.

(*E*)-*N*-Cyclopropyl-1-phenylmethanimine (5b)



Following the general procedure **C**, **5b** was purified by silica gel chromatography (PE). A gray solid (387 mg, 88%); mp: 78 – 80 °C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.46 (s, 1H), 7.68 (dd, J = 6.7, 3.0 Hz, 2H), 7.42 – 7.33 (m, 3H), 3.03 (tt, J = 6.8, 3.4 Hz, 1H), 1.04 – 0.97 (m, 2H), 0.96 – 0.90 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 158.52, 136.61, 130.17, 128.64, 127.64, 42.07, 8.92. HRMS (ESI) calcd for $C_{10}H_{12}N^{+}$ [M + H^{+}] 146.0964, found 146.0961.

III. X-ray Crystal Structure and Data of 4h

Single crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a DCM solution of **4h**. Crystal data collection and refinement parameters of **4h** are summarized in Table S2. Intensity data were collected at 160 K on a ROD, Synergy Custom system, HyPix diffractometer using mirror-monochromated Cu Kα radiation, λ = 1.54184 Å. The data were corrected for decay, Lorentz, and polarization effects as well as absorption and beam corrections based on the multi-scan technique. The structure was solved by the ShelXT [2] structure solution program using Intrinsic Phasing and refined with the ShelXL [3] refinement package using Least Squares minimisation.

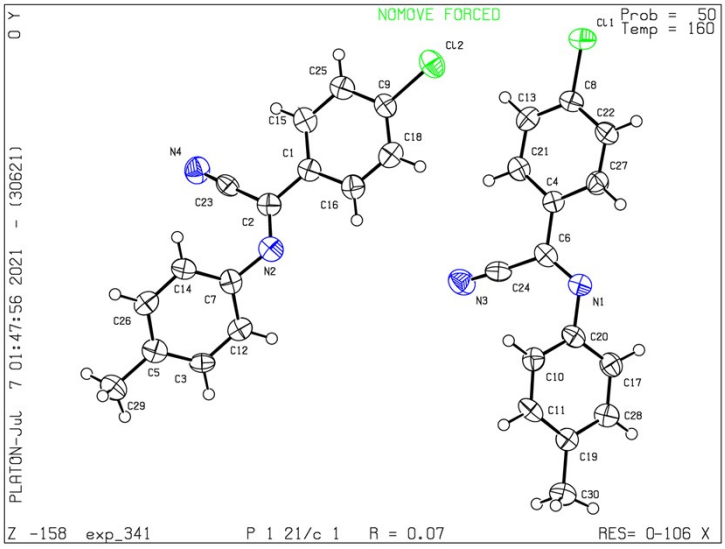


Figure S1 X-ray Crystal Structure of **4h** with 50% ellipsoid probability

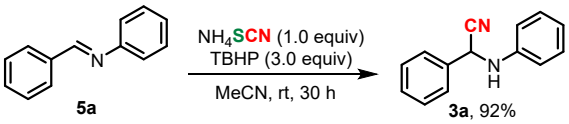
Table S1 Crystal Data and Structure Refinement for **4h**

Identification code	4h
Empirical formula	$C_{15}H_{11}ClN_2$
Formula weight	254.70
Temperature/K	159.99(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	21.7065(16)
b/Å	3.9870(2)

c/Å	30.5412(18)
α/°	90
β/°	110.142(8)
γ/°	90
Volume/Å3	2481.5(3)
Z	4
ρ_{calc}g/cm^3	1.364
μ/mm^{-1}	2.560
F(000)	1056.0
Crystal size/mm^3	0.05 × 0.05 × 0.05
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.164 to 100.852
Index ranges	-20 ≤ h ≤ 21, -3 ≤ k ≤ 3, -30 ≤ l ≤ 30
Reflections collected	8134
Independent reflections	2429 [R_{int} = 0.0454, R_{sigma} = 0.0435]
Data/restraints/parameters	2429/0/327
Goodness-of-fit on F^2	1.081
Final R indexes [I>=2σ (I)]	R^1 = 0.0707, wR^2 = 0.1944
Final R indexes [all data]	R^1 = 0.0857, wR^2 = 0.2053
Largest diff. peak/hole / e Å^{-3}	0.45/-0.45

IV. Mechanistic Investigation

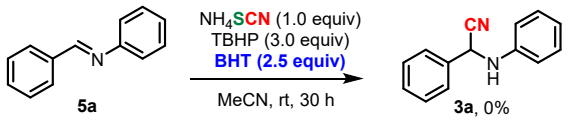
1. NH_4SCN/TBHP-Mediated Cyanation of Imine



A mixture of ammonium thiocyanate (114 mg, 1.5 mmol, 1.0 equiv) and TBHP (614 μL, 4.5 mmol, 3.0 equiv) in MeCN (8 mL) was stirred at room temperature for 18 h. To the solution was then added imine **5a** (270 mg, 1.5 mmol, 1.0 equiv), stirred the mixture for another 12 h at room temperature.

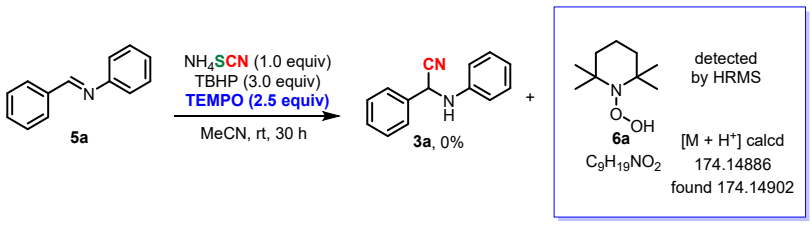
When the reaction was completed, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc/PE = 1:9) to give the desired product **3a** as a yellow solid (280.4 mg, 92%).

2. BHT Inhibiting and TEMPO Trapping Experiments



A mixture of ammonium thiocyanate (114 mg, 1.5 mmol, 1.0 equiv) and TBHP (614 μL, 4.5 mmol, 3.0 equiv) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) (826.3 mg, 3.75 mmol, 2.5 quiv) in MeCN (8 mL)were stirred at room temperature for 18 h.[1] To the solution was then added imine **5a** (270 mg, 1.5 mmol, 1.0 equiv), stirred the mixture for another 12 h at room temperature.

No **3a** was monitored by TLC.



A mixture of ammonium thiocyanate (114 mg, 1.5 mmol, 1.0 equiv) and TBHP (614 μL, 4.5 mmol, 3.0 equiv) and 2,2,6,6-tetramethylpiperidinooxy (TEMPO) (585.0 mg, 3.75 mmol, 2.5 quiv) in MeCN was stirred at room temperature (8 mL) for 18 h.[2-3] To

the solution was added imine **5a** (270 mg, 1.5 mmol, 1.0 equiv), then stirred the mixture for another 12 h at room temperature.

No **3a** was monitored by TLC. The HRMS spectrum (Figure S2) showed the formation of **6a** (adduct of TEMPO-OH).

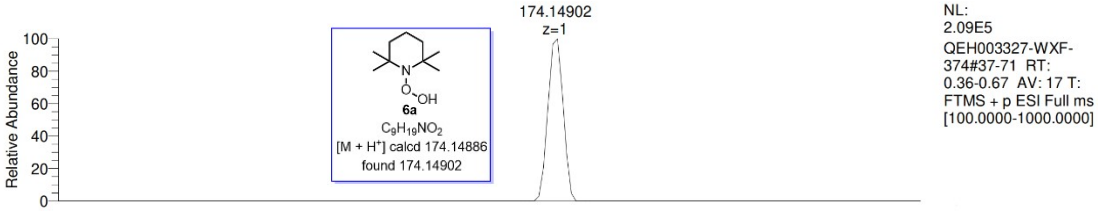
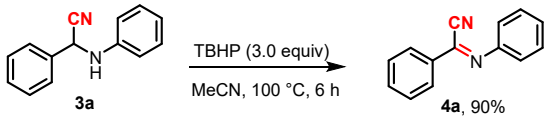


Figure S2

3. Oxidation of α-Aminonitrile



To a solution of **3a** (312 mg, 1.5 mmol, 1.0 equiv) in MeCN (8 mL) was added TBHP (614 μL, 4.5 mmol, 3.0 equiv). The resulting mixture was stirred at 100 ºC for 6 h.

When the reaction was completed, the reaction was quenched with sat. aq. $NaHCO_3$ (10 mL) and the aqueous phase was extracted with DCM (3 x 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography (PE) to give the desired product **4a** as a brown solid (268.1 mg, 90%).

4. Precipitation of $BaSO_4$

A mixture of ammonium thiocyanate (114 mg, 1.5 mmol, 1.0 equiv) and *tert*-butyl hydroperoxide (TBHP) (614 mL, 4.5 mmol, 3.0 equiv) were stirred at room temperature in MeCN (8 mL) for 18 h. Then aldehyde **1a** (153 mL, 1.5 mmol, 1.0 equiv) and amine **2a** (137 mL, 1.5 mmol, 1.0 equiv) were added to the solution. The mixture was stirred for another 12 h at room temperature.

When the reaction was completed, the reaction mixture was poured into deionized water (20 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The aqueous layer was transferred into a 100 mL Erlenmeyer flask, to which was added aq. solution of $BaCl_2$ (2 M, 3 mL), Then the precipitate generated was separated by filtration and dried at 67 °C to give a white powder (328 mg).[5] The powder was further analyzed by FT-IR

spectra using a FTIR, TENSOR II spectrometer (Bruker Technology Co., Ltd.) by incorporating samples in KBr disks to confirm the characteristic vibrational bands. Reflections (SI, Figure S3) of the precipitated solid agreed the IR spectra reported previously for $BaSO_4$.[6]

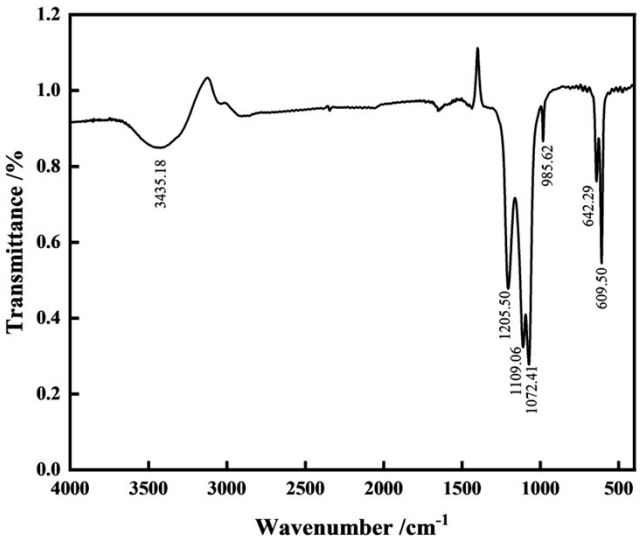


Figure S3 FTIR spectra of precipitated solid

V. References

(1) R. H. Matjie, R. Singh and C. A. Strydom, Oxidation of sodium thiocyanate (NaSCN) in stretford aqueous liquor using air and commercial hydrogen peroxide (H_2O_2), *Energ. Fuel.,* 2016, **30**, 2345-2355.

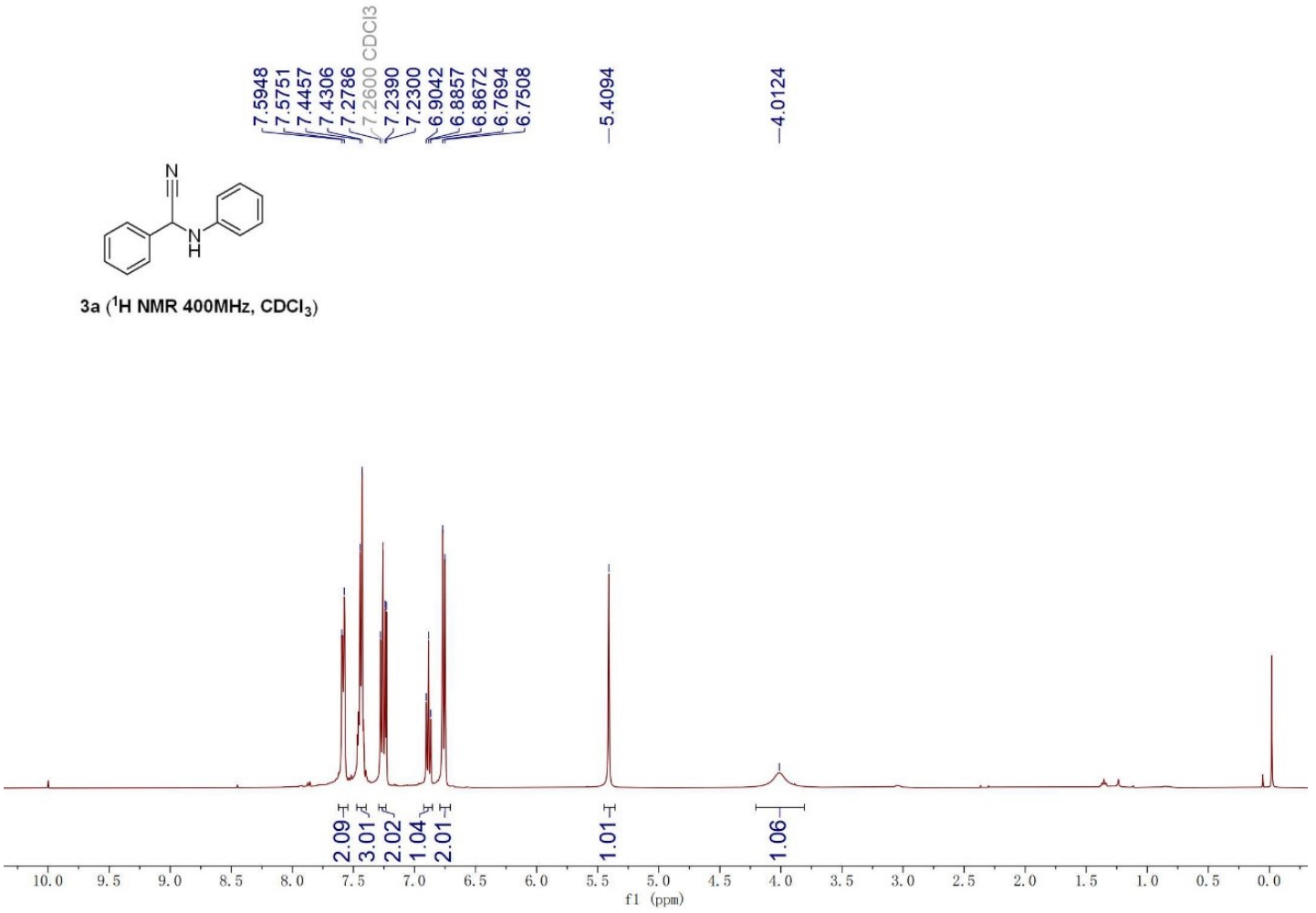
(2) Q. Yang, X. Yan, C. Feng, D. Chen, Z. Yan and K. Xu, Tandem Strecker/C(sp3)–H amination reactions for the construction of cyanide-functionalized imidazo[1,5-α]pyridines with NH_4SCN as a cyanating agent, *Org. Chem. Front.,* 2021, **8**, 6384-6389. (3) Y. Li, X. Liang, K. Niu, J. Gu, F. Liu, Q. Xia, Q. Wang and W. Zhang, Visible-light-induced photocatalyst-free radical trifluoromethylation, *Org. Lett.,* 2022, **24**, 5918–5923.

(4) N. Boyer, P. Gloanec, G. De Nanteuil, P. Jubault and J.-C. Quirion, Synthesis of α,α-difluoro-β-amino esters or *gem*-difluoro-β-lactams as potential metallocarboxypeptidase inhibitors, *Eur. J. Org. Chem.,* 2008, **25**, 4277-4295.

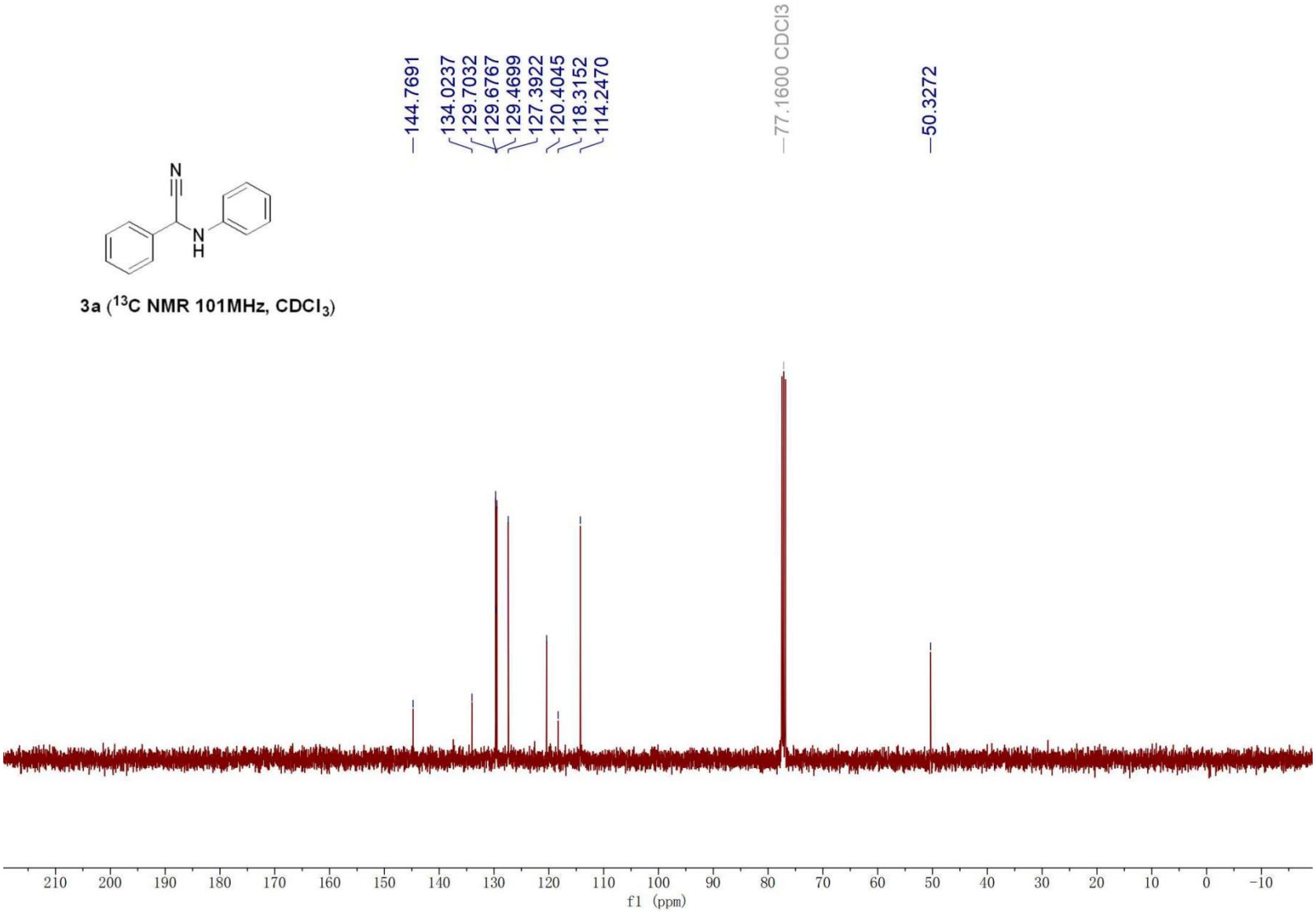
(5) A. Wagner and A. R. Ofial, Potassium thiocyanate as source of cyanide for the oxidative α-cyanation of tertiary amines, *J. Org. Chem.,* 2015, **80**, 2848-2854

(6) M. Zhang, B. Zhang, X. Li, Z. Yin, and X. Guo, Synthesis and surface properties of submicron barium sulfate particles. *Appl. Surf. Sci.*, 2011, **258**, 24-29.

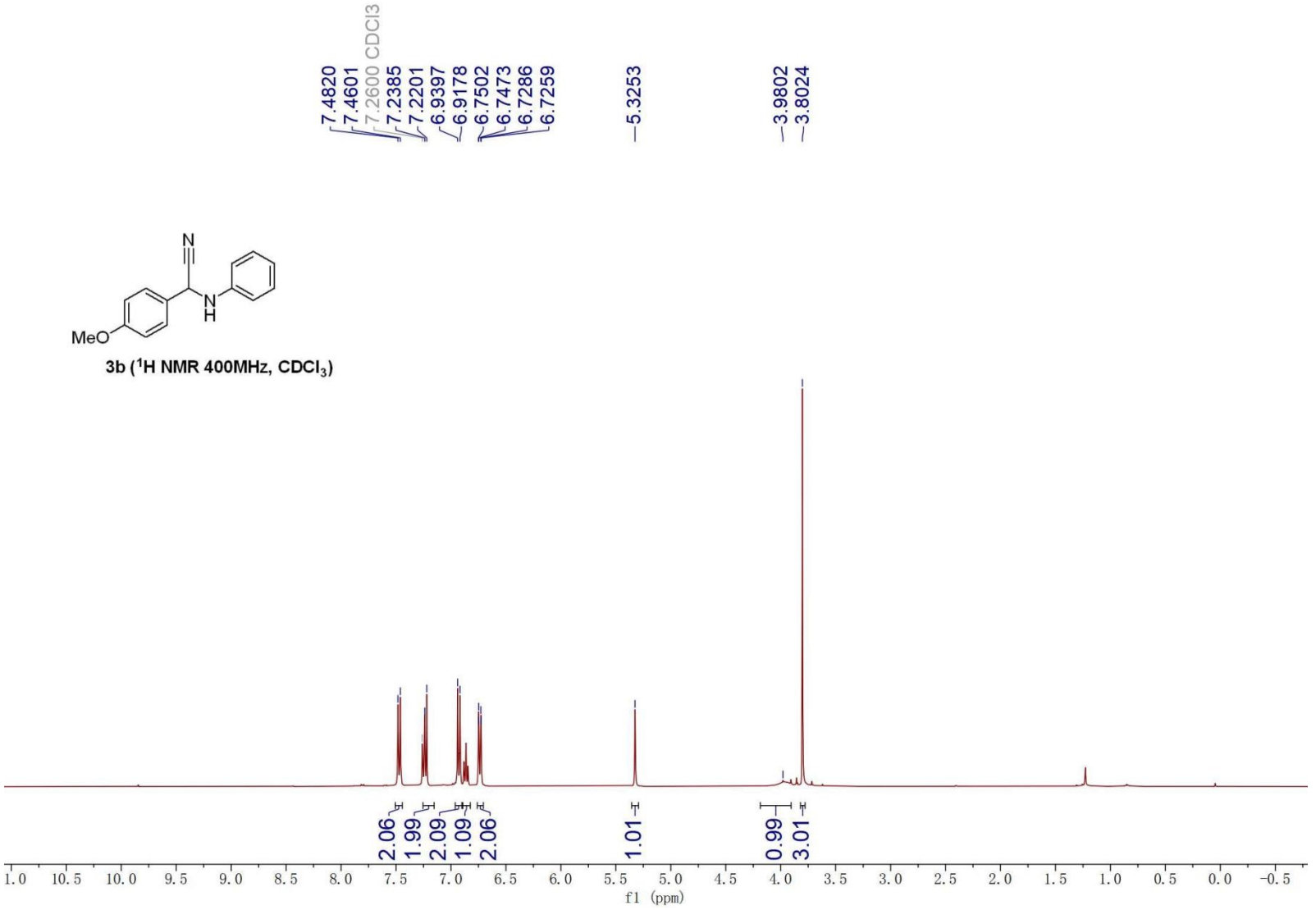
VI. MNR Spectra



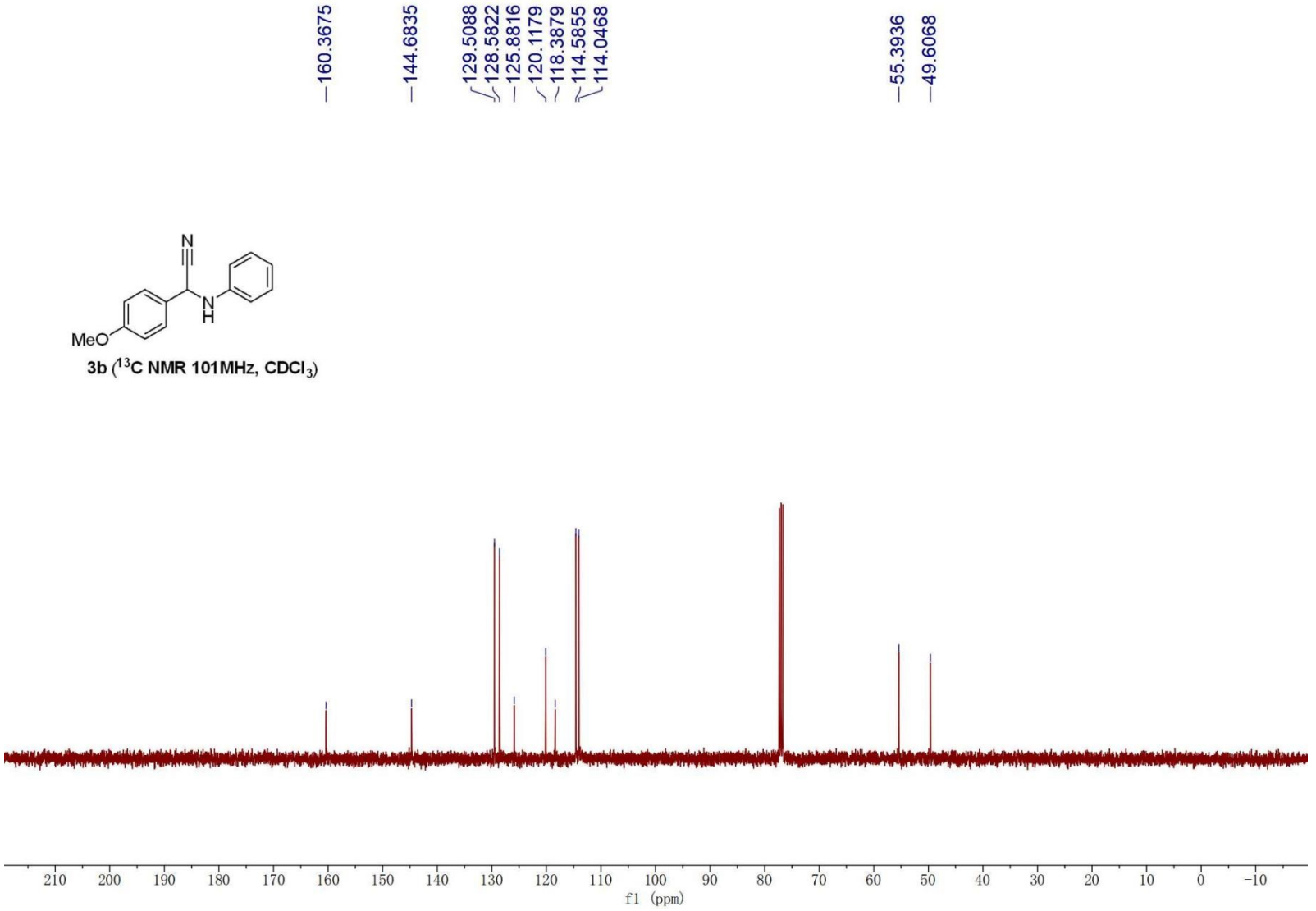
3a (^{1}H NMR 400MHz, $CDCl_3$)



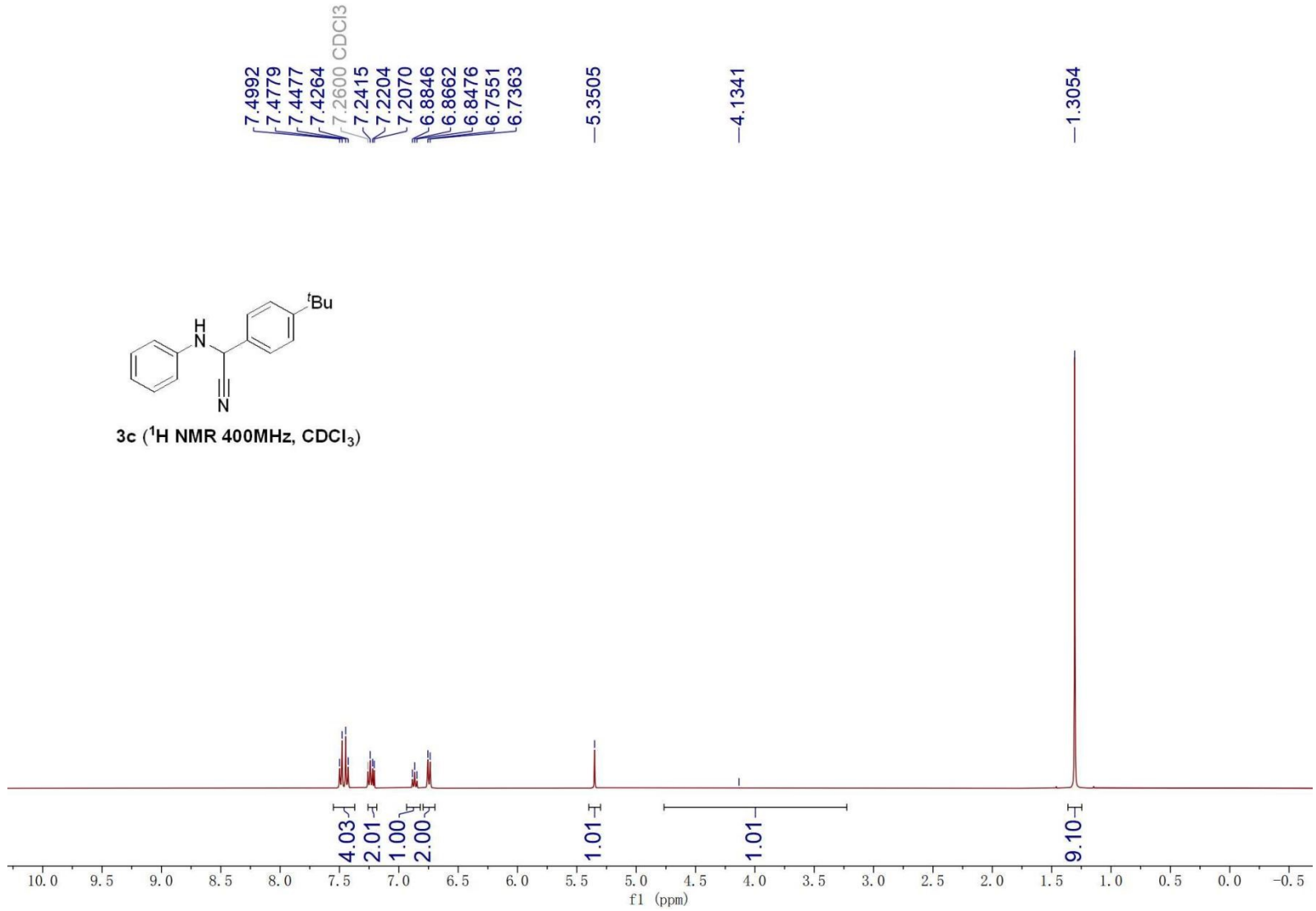
3a (^{13}C NMR 101MHz, $CDCl_3$)



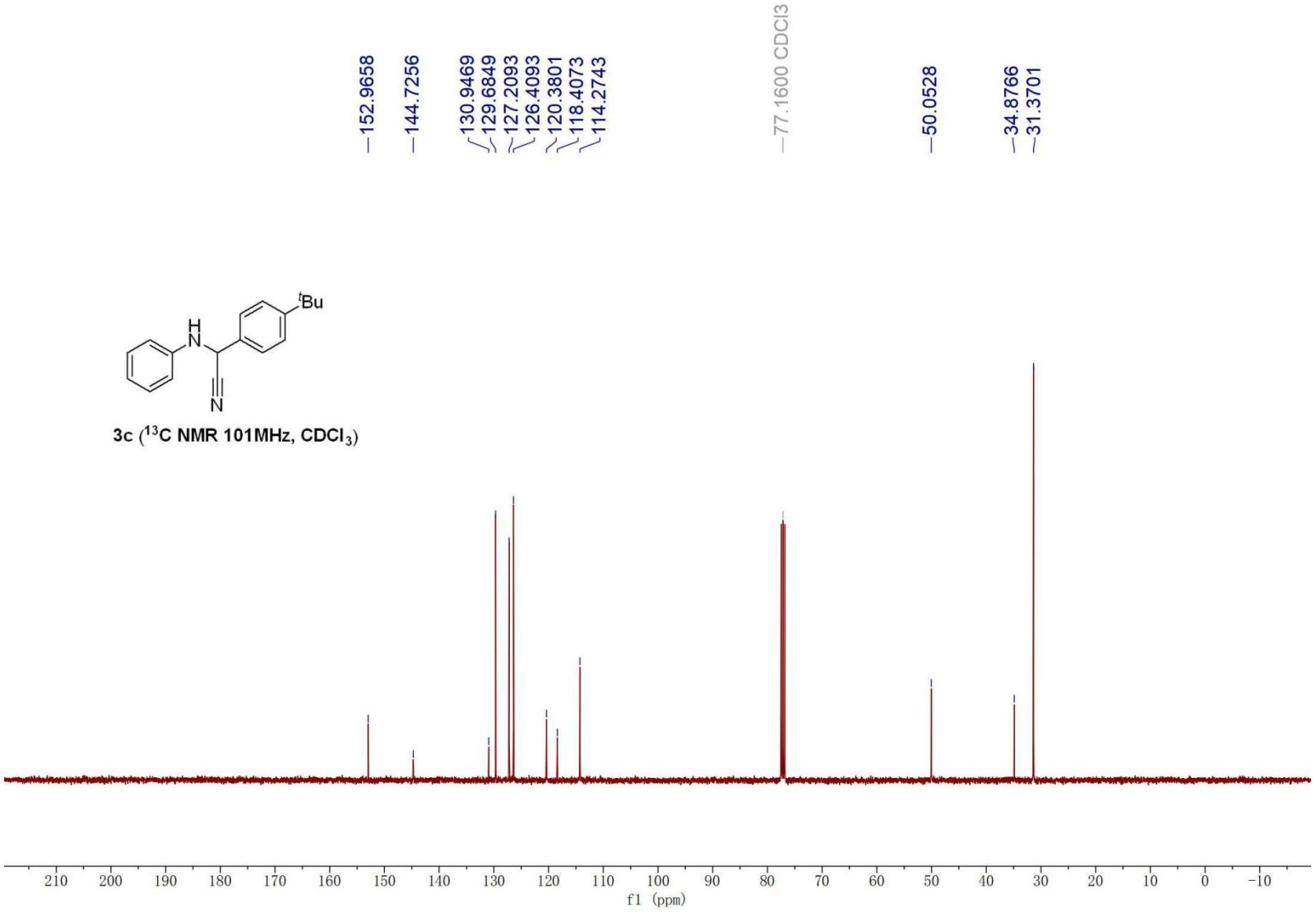
3b (^{1}H NMR 400MHz, $CDCl_3$)

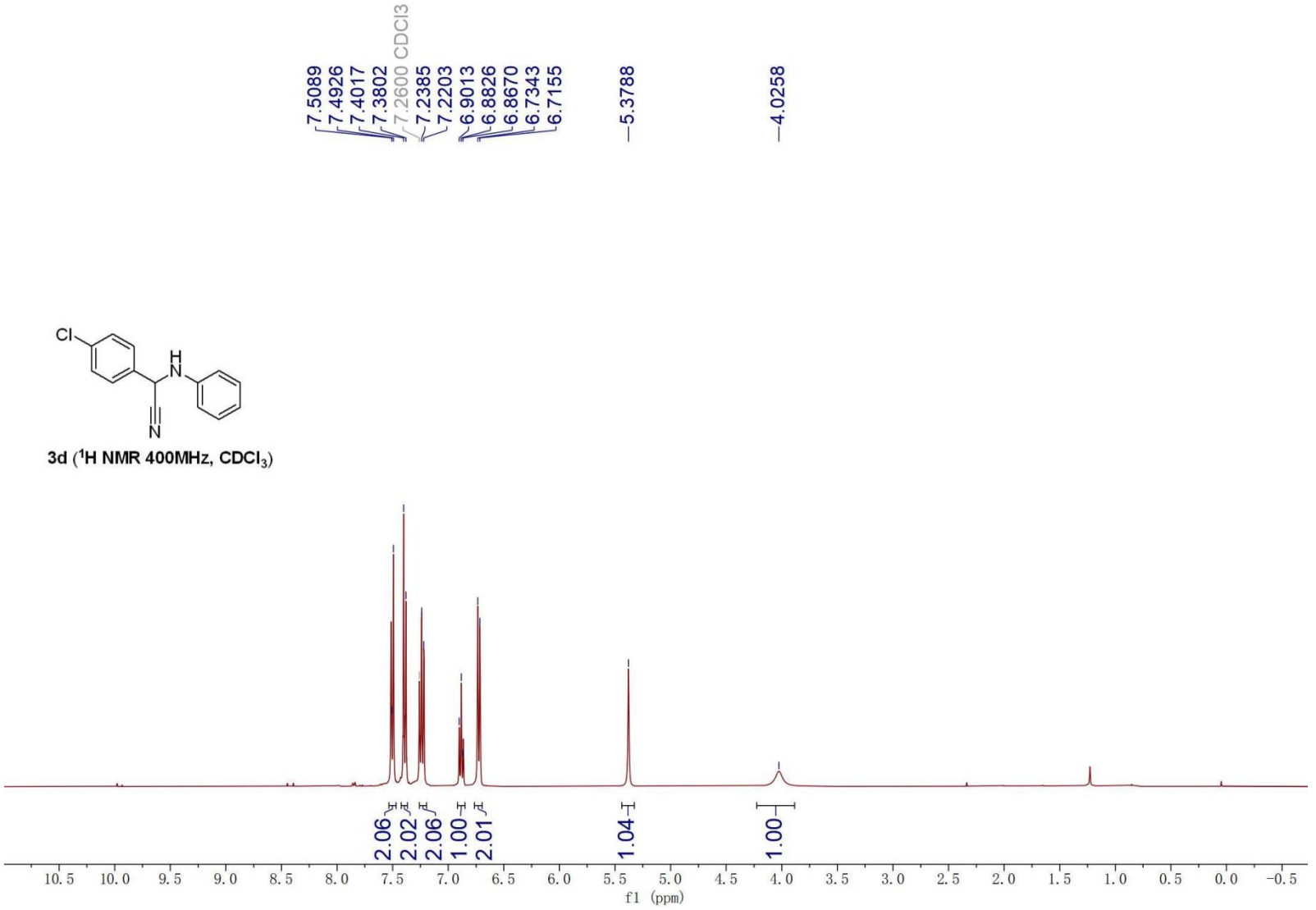


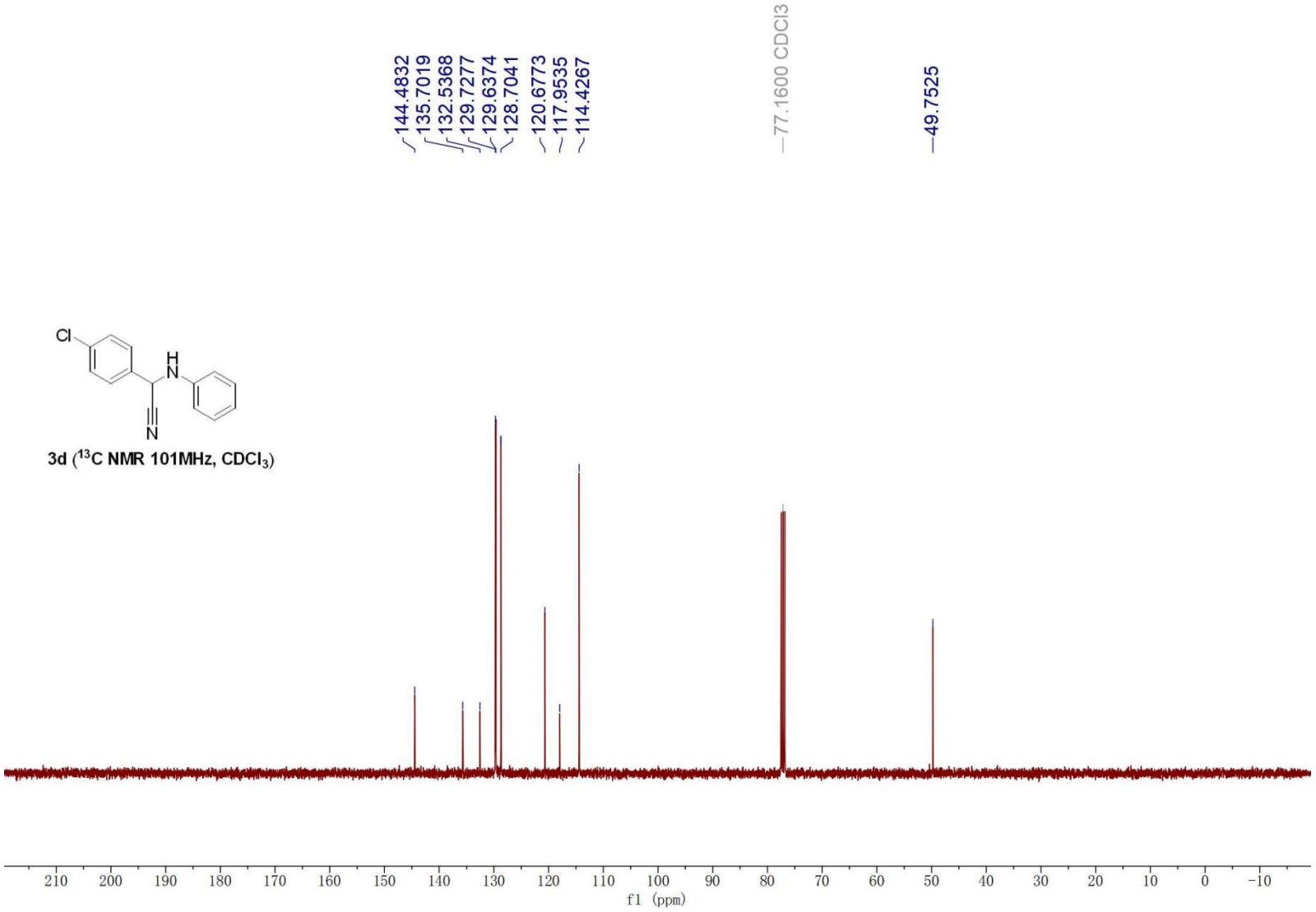
3b (^{13}C NMR 101MHz, $CDCl_3$)

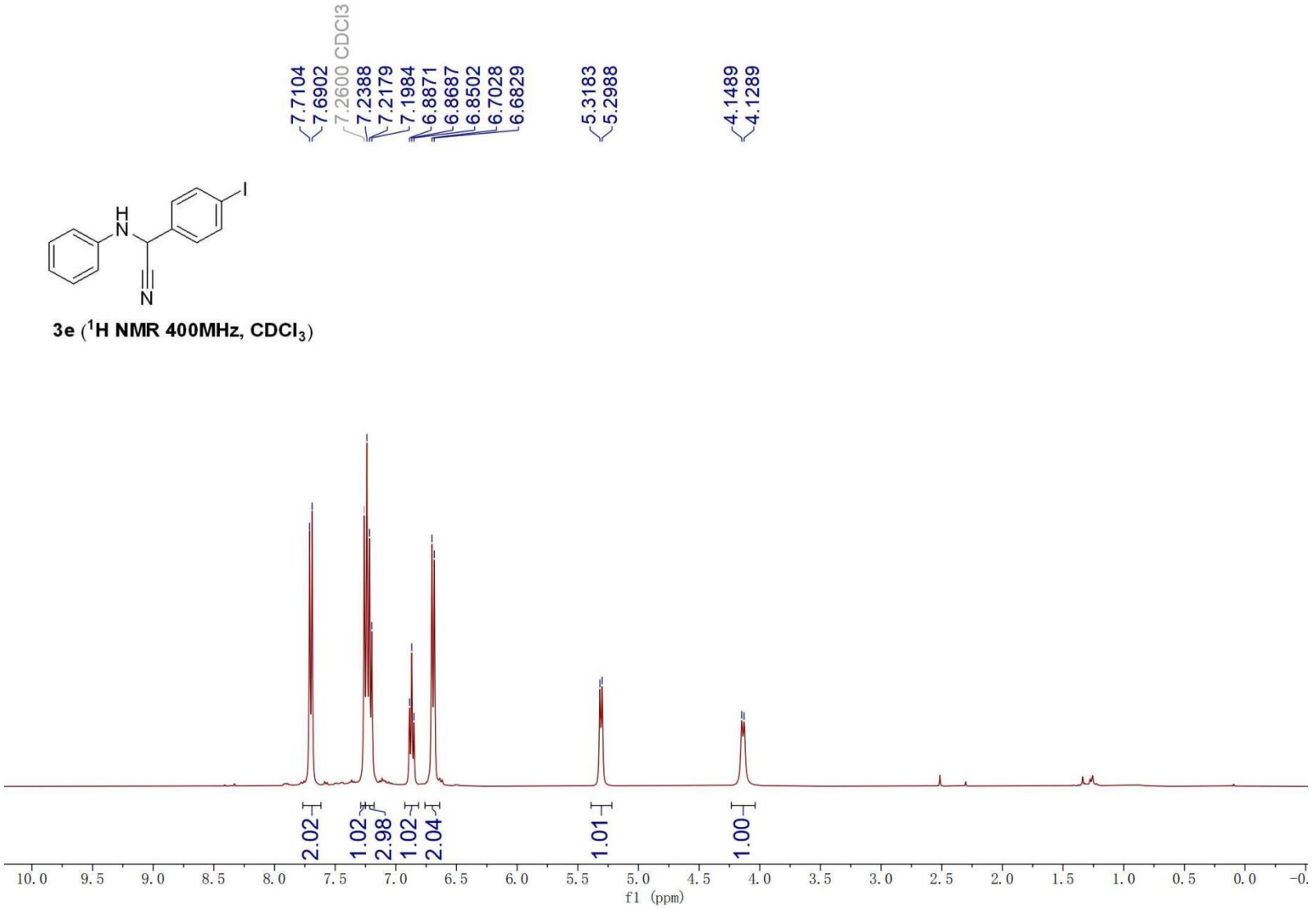


3c (^{1}H NMR 400MHz, $CDCl_3$)

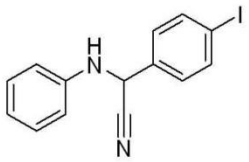

152.9658
144.7256
130.9469
129.6849
127.2093
126.4093
120.3801
118.4073
114.2743
77.1600 CDCl3
50.0528
34.8766
31.3701
tBu
H
N
N
3c (13C NMR 101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.5089
7.4926
7.4017
7.3802
7.2600 CDCl3
7.2385
7.2203
6.9013
6.8826
6.8670
6.7343
6.7155
5.3788
4.0258
Cl
H
N
N
3d (1H NMR 400MHz, CDCl3)
2.06
2.02
2.06
1.00
2.01
1.04
1.00
10.5 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 -0.5
f1 (ppm)

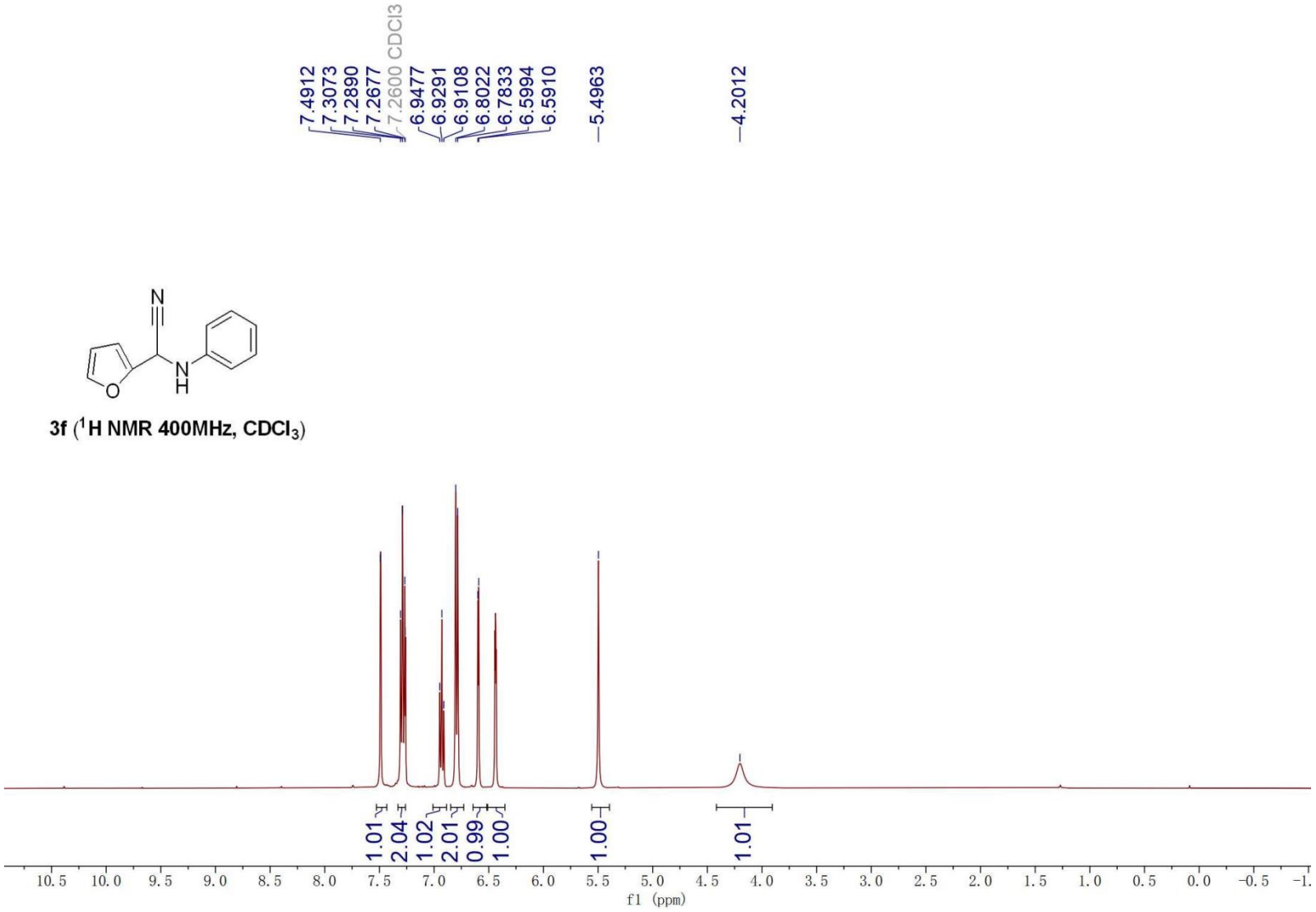

144.4832
135.7019
132.5368
129.7277
129.6374
128.7041
120.6773
117.9535
114.4267
77.1600 CDCl3
49.7525
Cl
H
N
N
3d (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



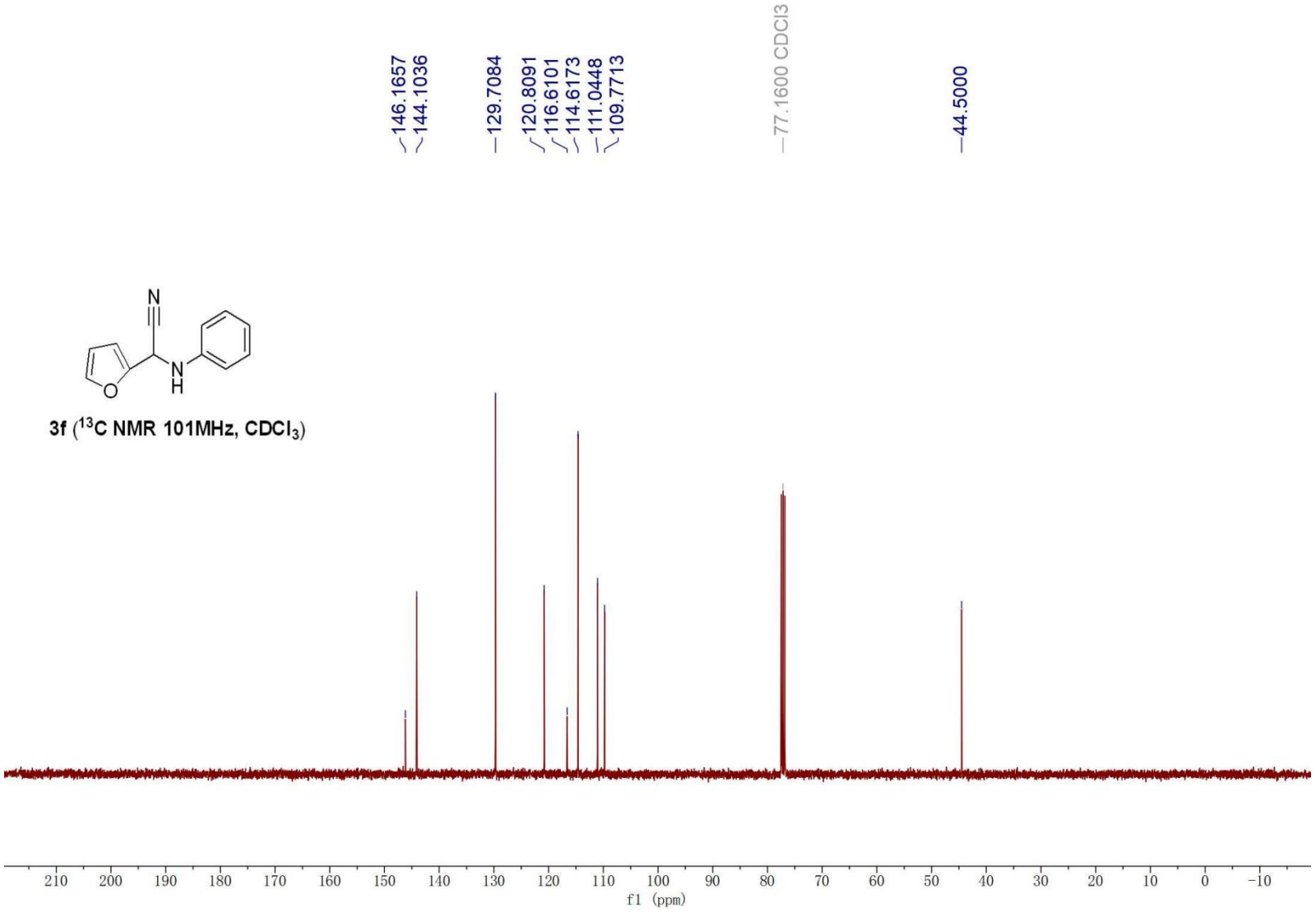
3e (^{1}H NMR 400MHz, $CDCl_3$)

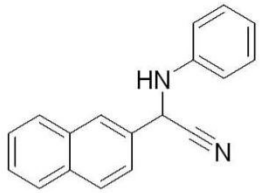


3e (^{13}C NMR 101MHz, $CDCl_3$)

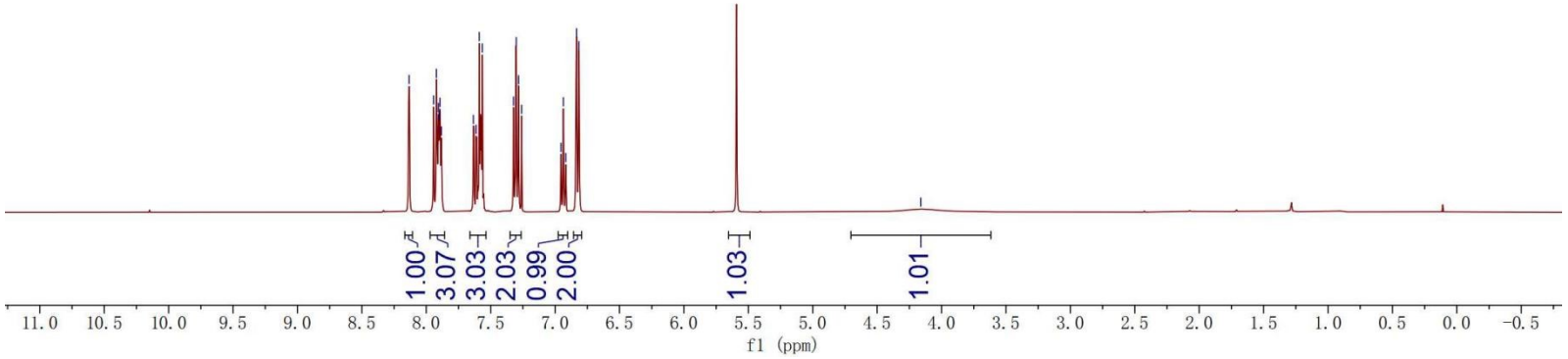


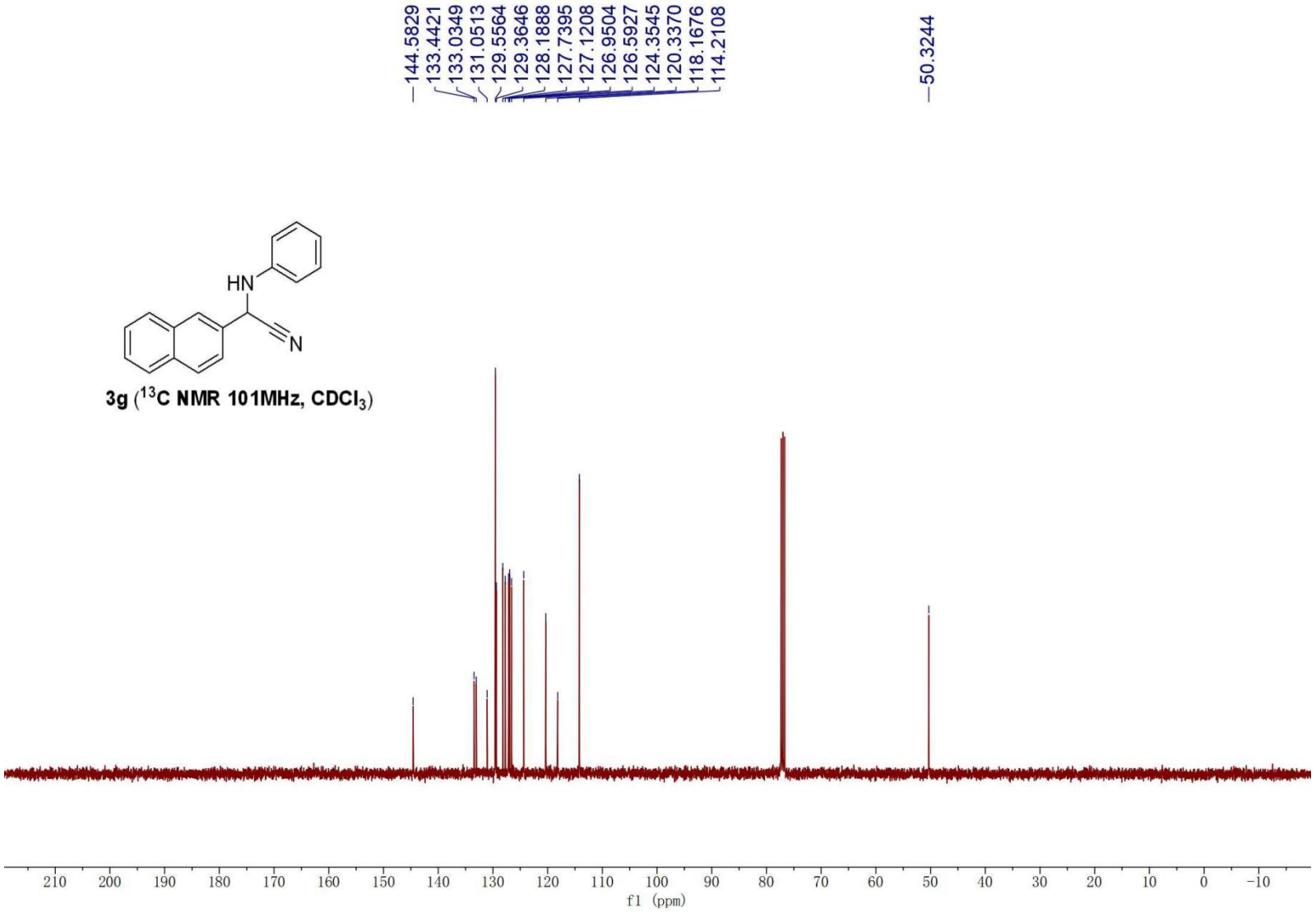
3f (^{1}H NMR 400MHz, $CDCl_3$)

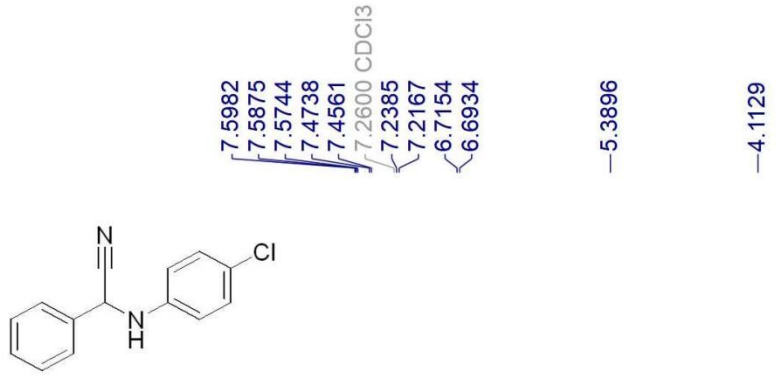

146.1657
144.1036
129.7084
120.8091
116.6101
114.6173
111.0448
109.7713
77.1600 CDCl3
44.5000
N
N
H
O
3f (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



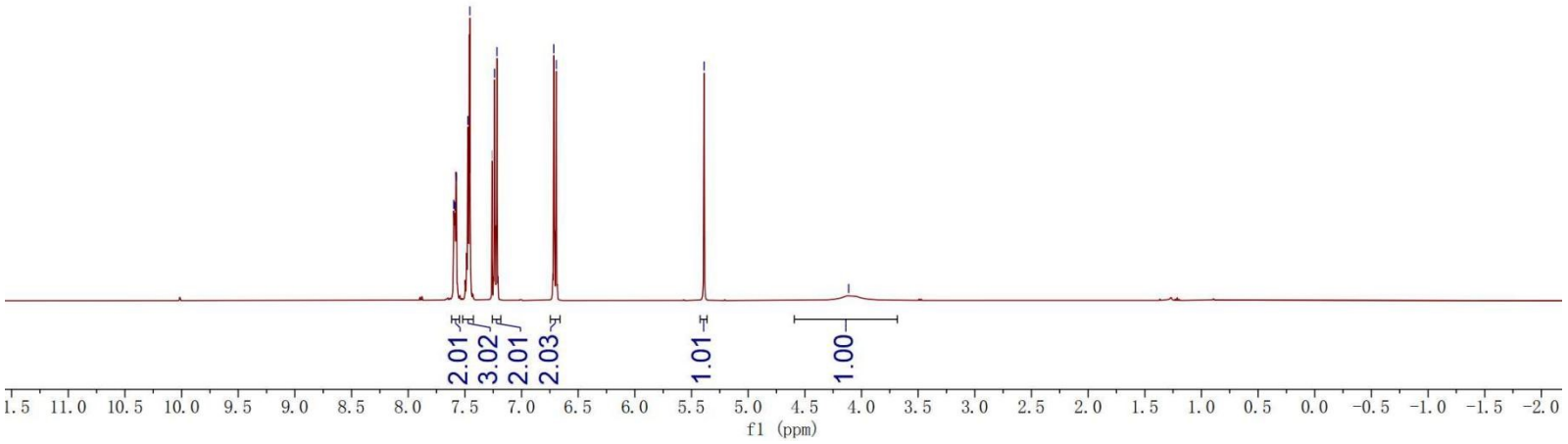
3g (^{1}H NMR 400MHz, $CDCl_3$)

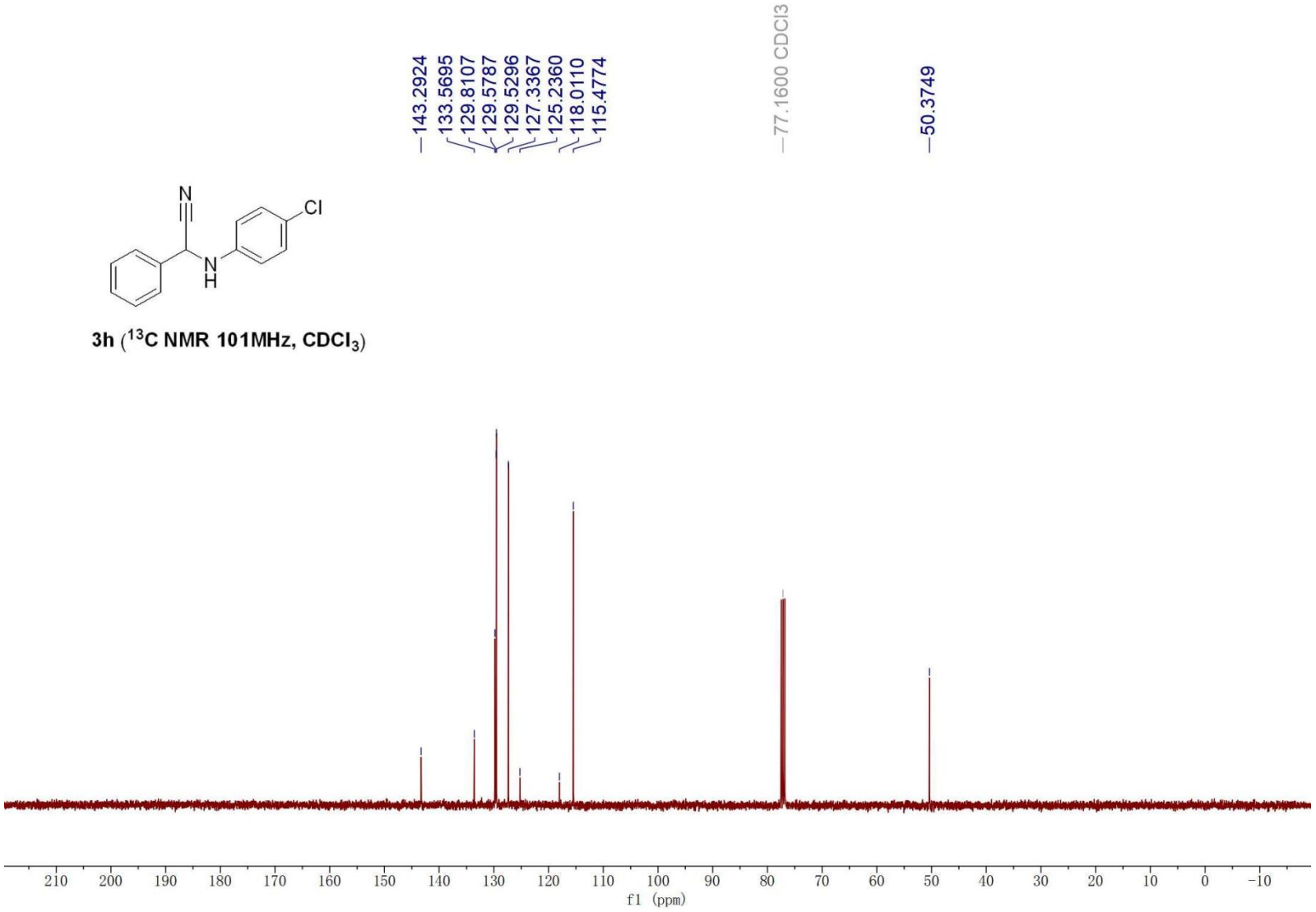



144.5829
133.4421
133.0349
131.0513
129.5564
129.3646
128.1888
127.7395
127.1208
126.9504
126.5927
124.3545
120.3370
118.1676
114.2108
50.3244
HN
N
3g (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

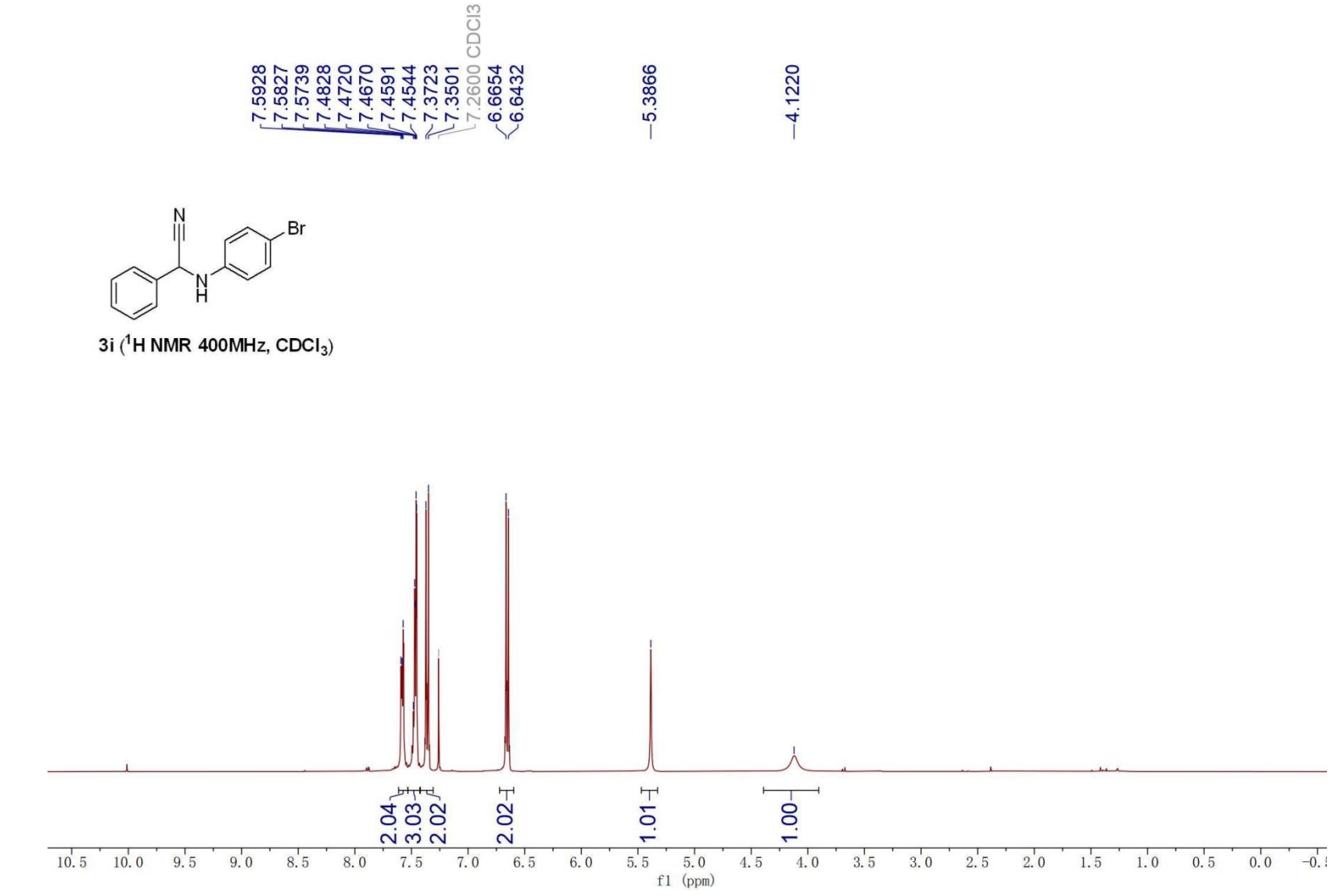


3h (^{1}H NMR 400MHz, $CDCl_3$)

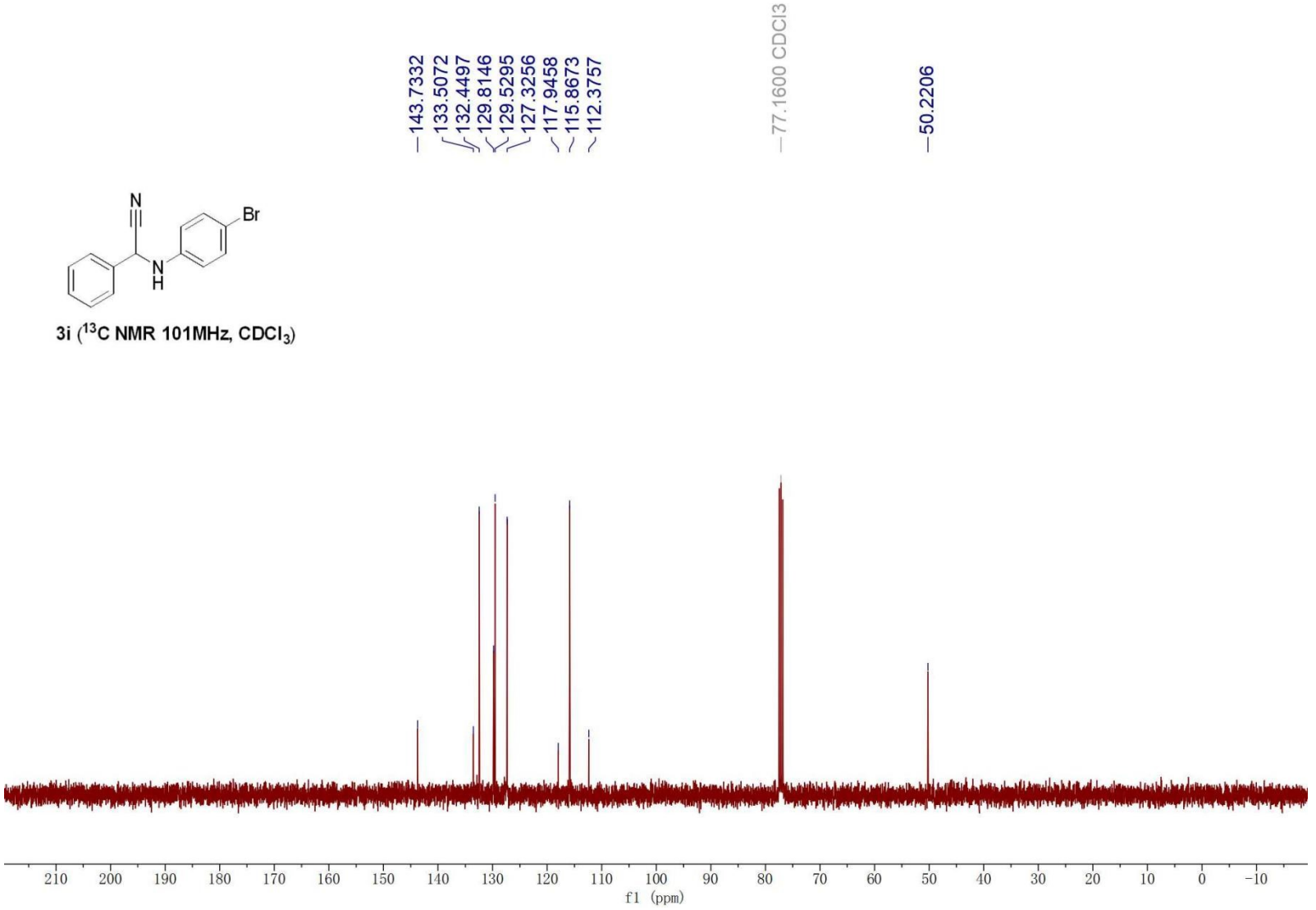


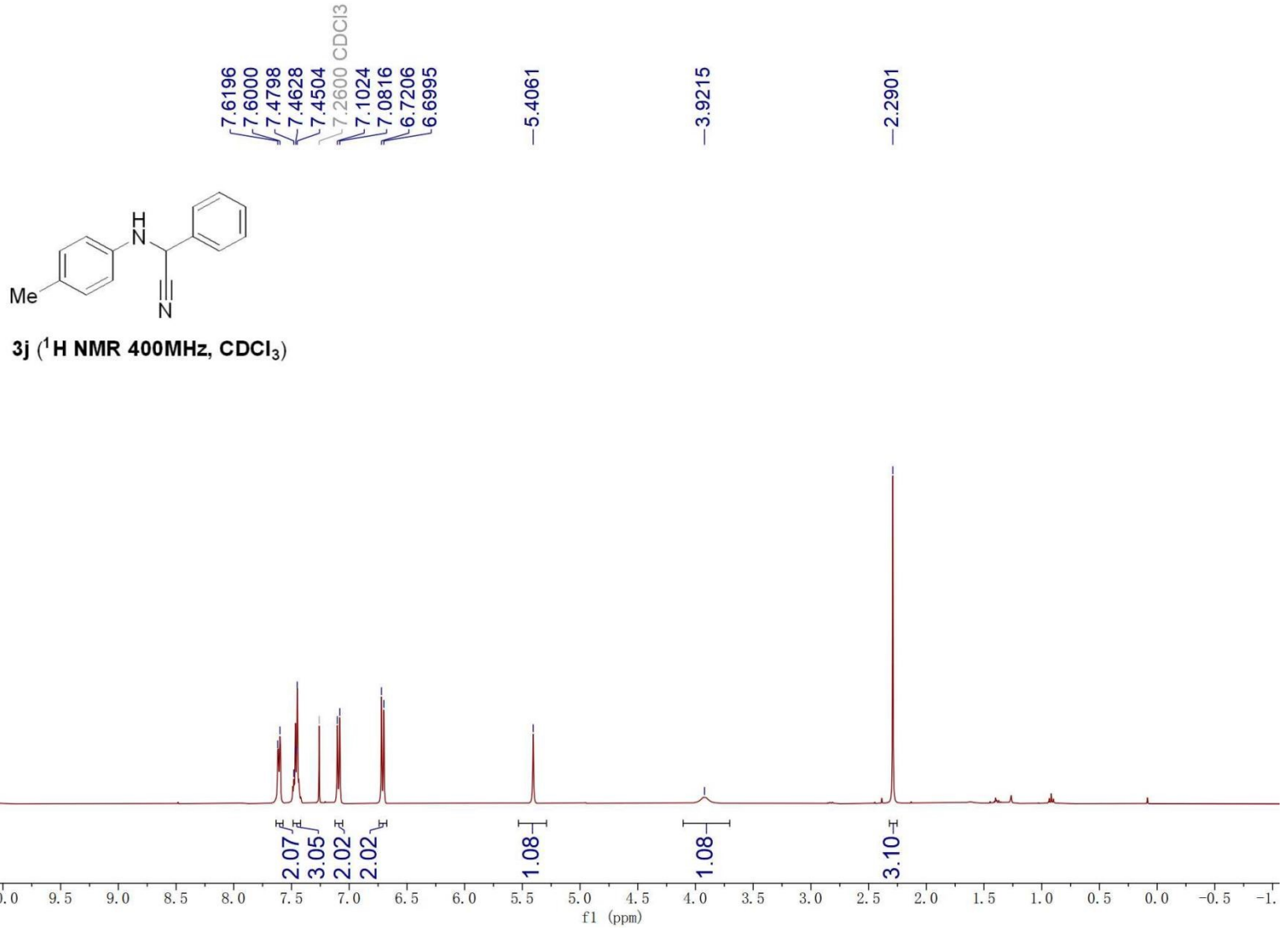


3h (^{13}C NMR 101MHz, $CDCl_3$)

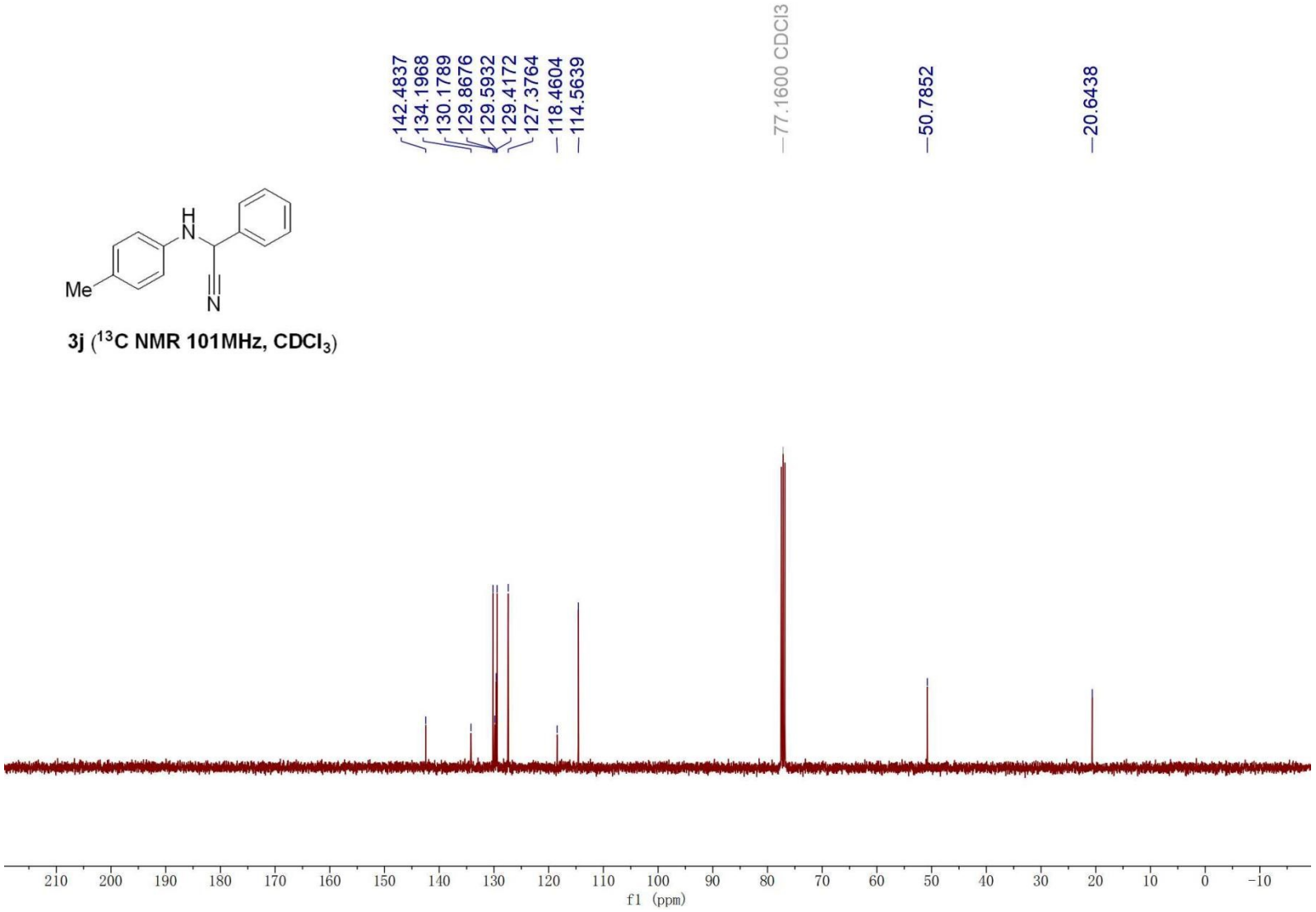


3i (^{1}H NMR 400MHz, $CDCl_3$)

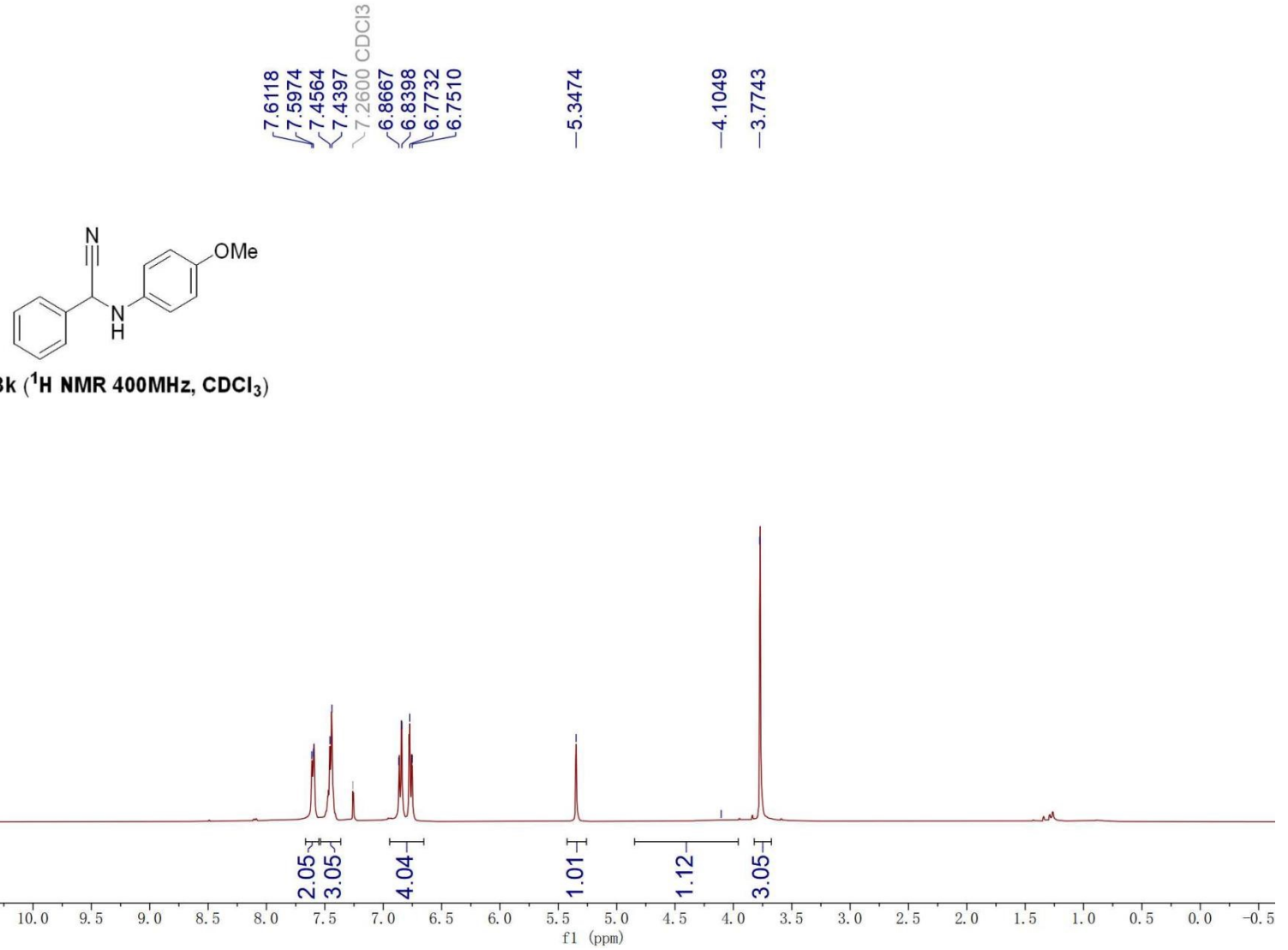

143.7332
133.5072
132.4497
129.8146
129.5295
127.3256
117.9458
115.8673
112.3757
77.1600 CDCl3
50.2206
N
Br
N
H
3i (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



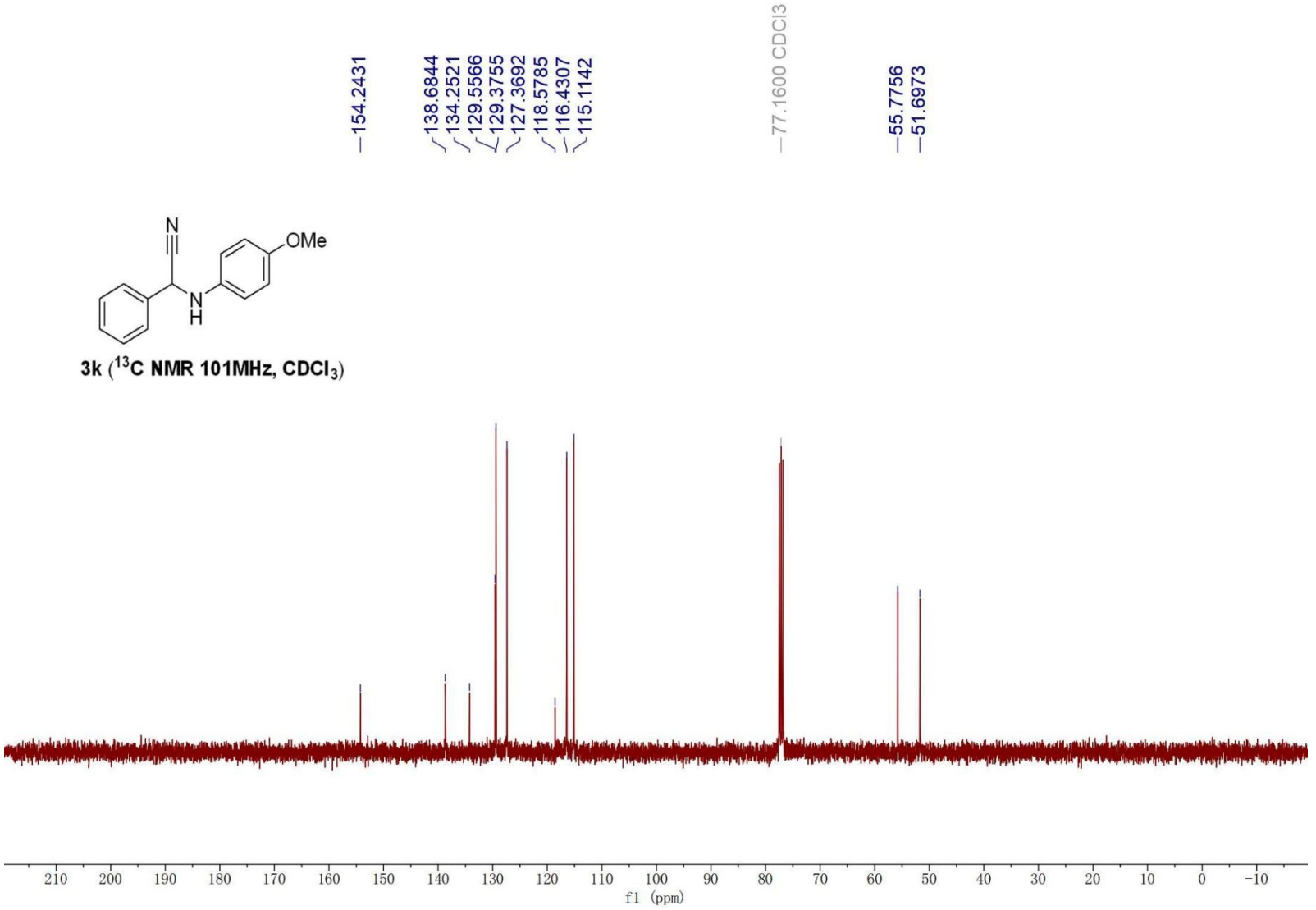
3j (^{1}H NMR 400MHz, $CDCl_3$)

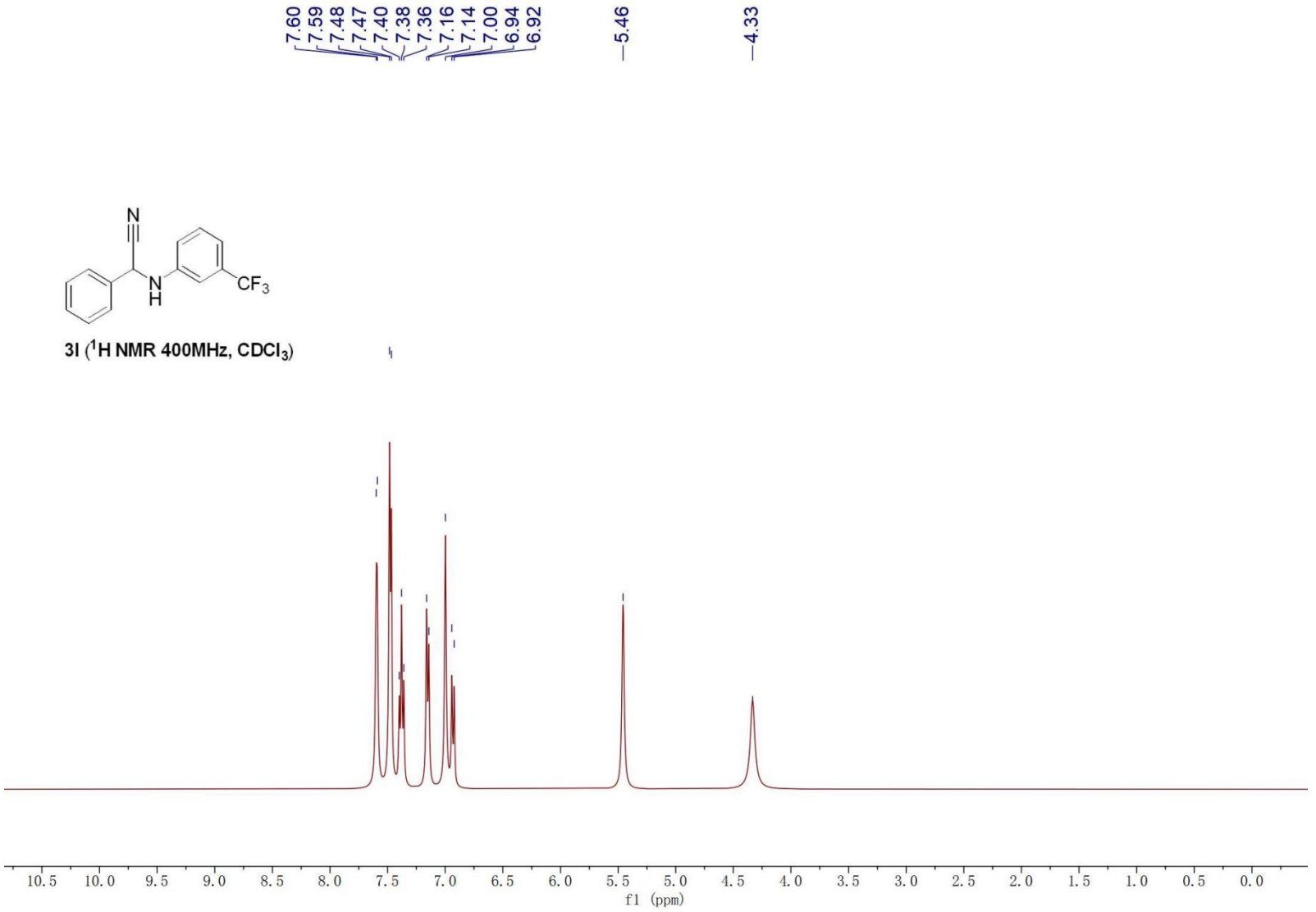


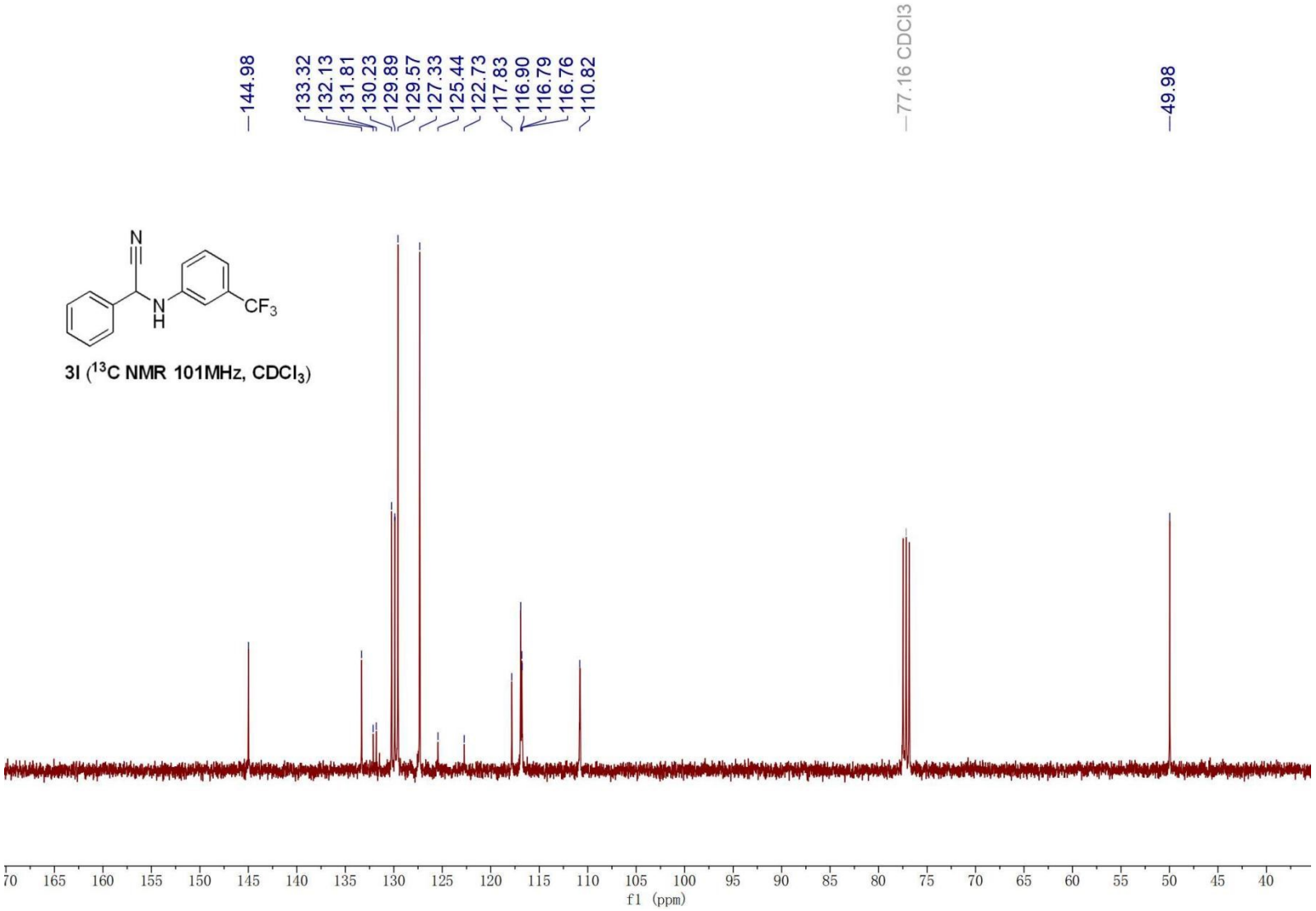
3j (^{13}C NMR 101MHz, $CDCl_3$)

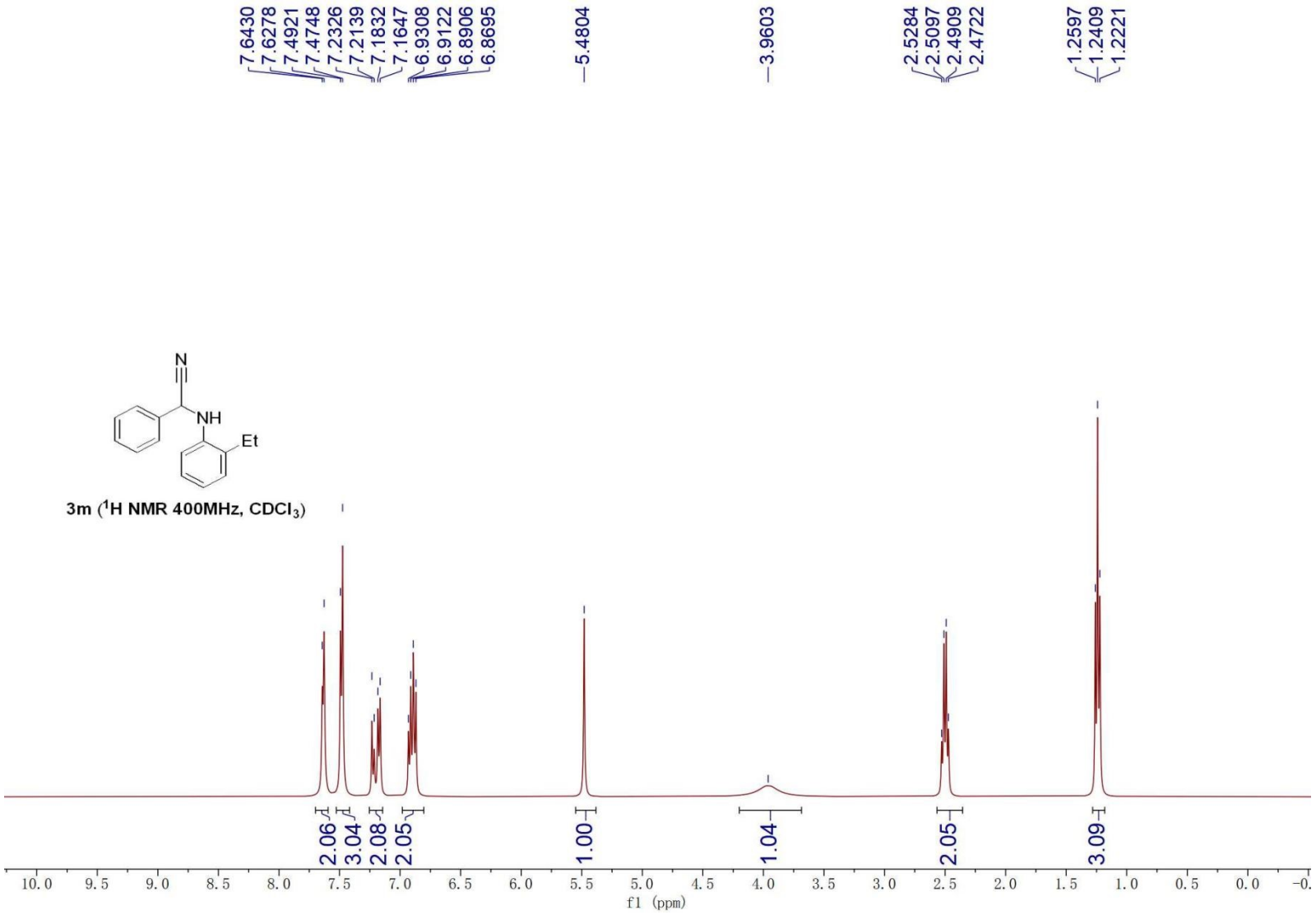


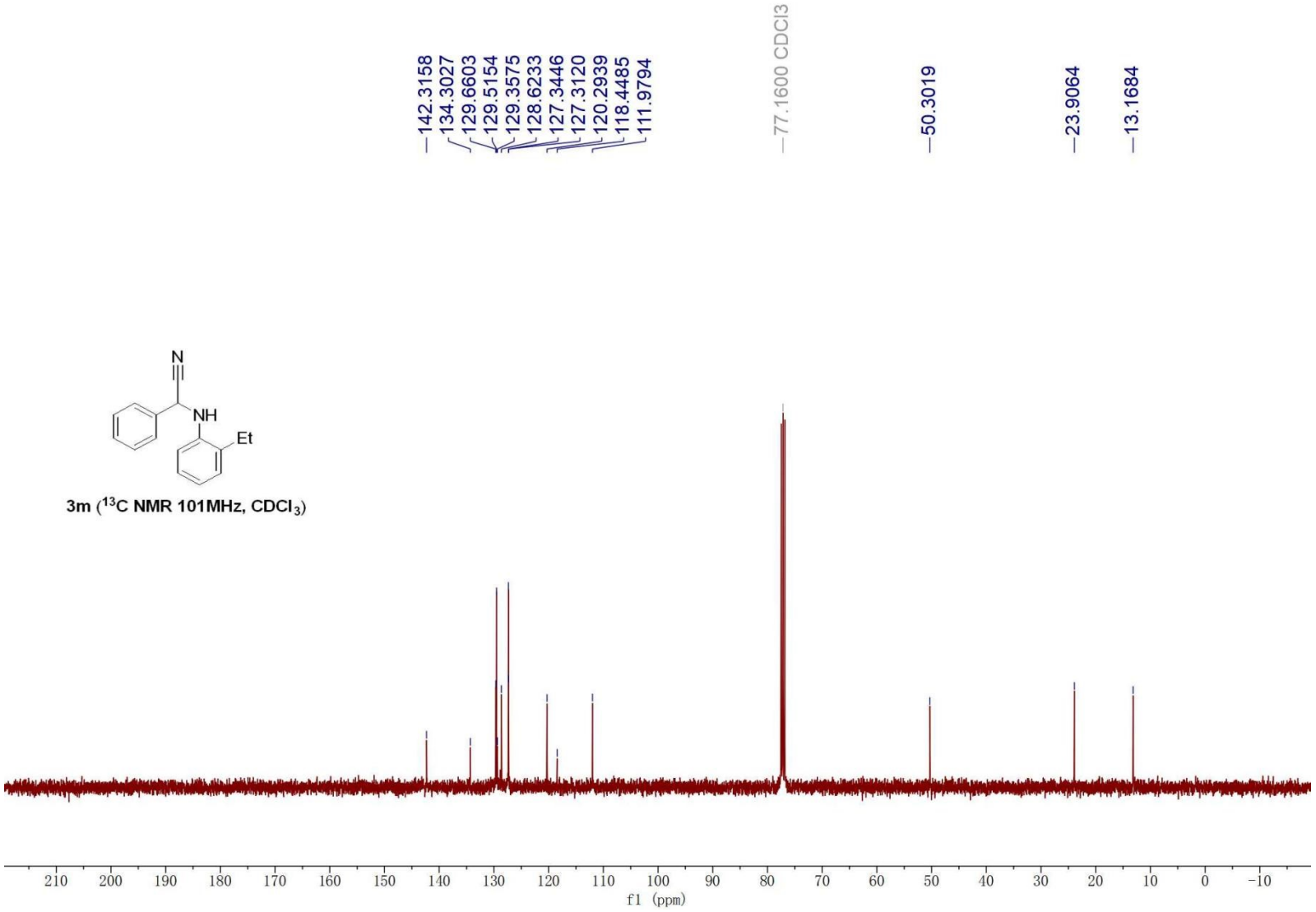
3k (^{1}H NMR 400MHz, $CDCl_3$)

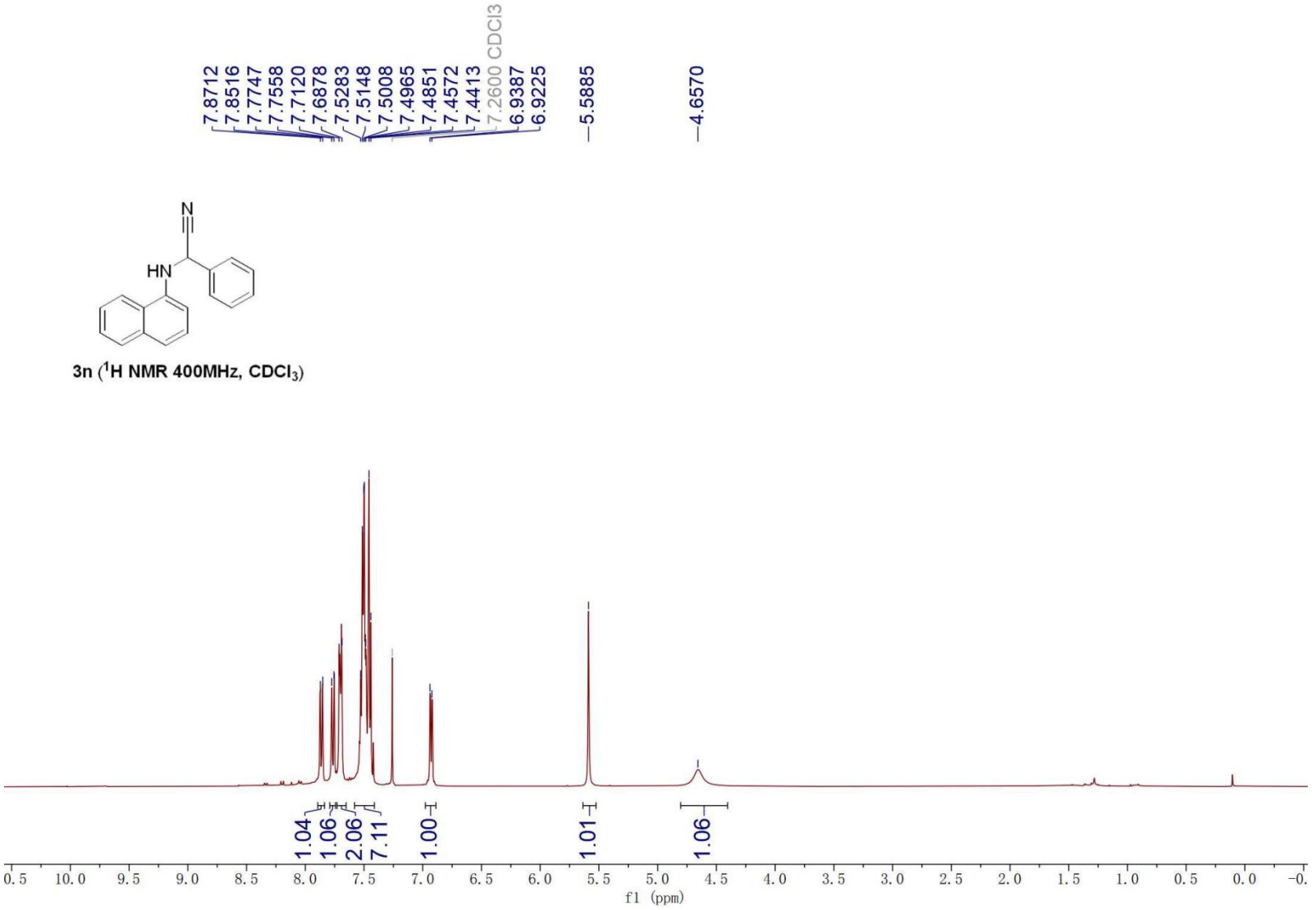

154.2431
138.6844
134.2521
129.5566
129.3755
127.3692
118.5785
116.4307
115.1142
77.1600 CDCl3
55.7756
51.6973
N
OMe
N
H
3k (13C NMR 101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.60
7.59
7.48
7.47
7.40
7.38
7.36
7.16
7.14
7.00
6.94
6.92
5.46
4.33
N
N
H
CF3
3l (1H NMR 400MHz, CDCl3)
10.5
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)

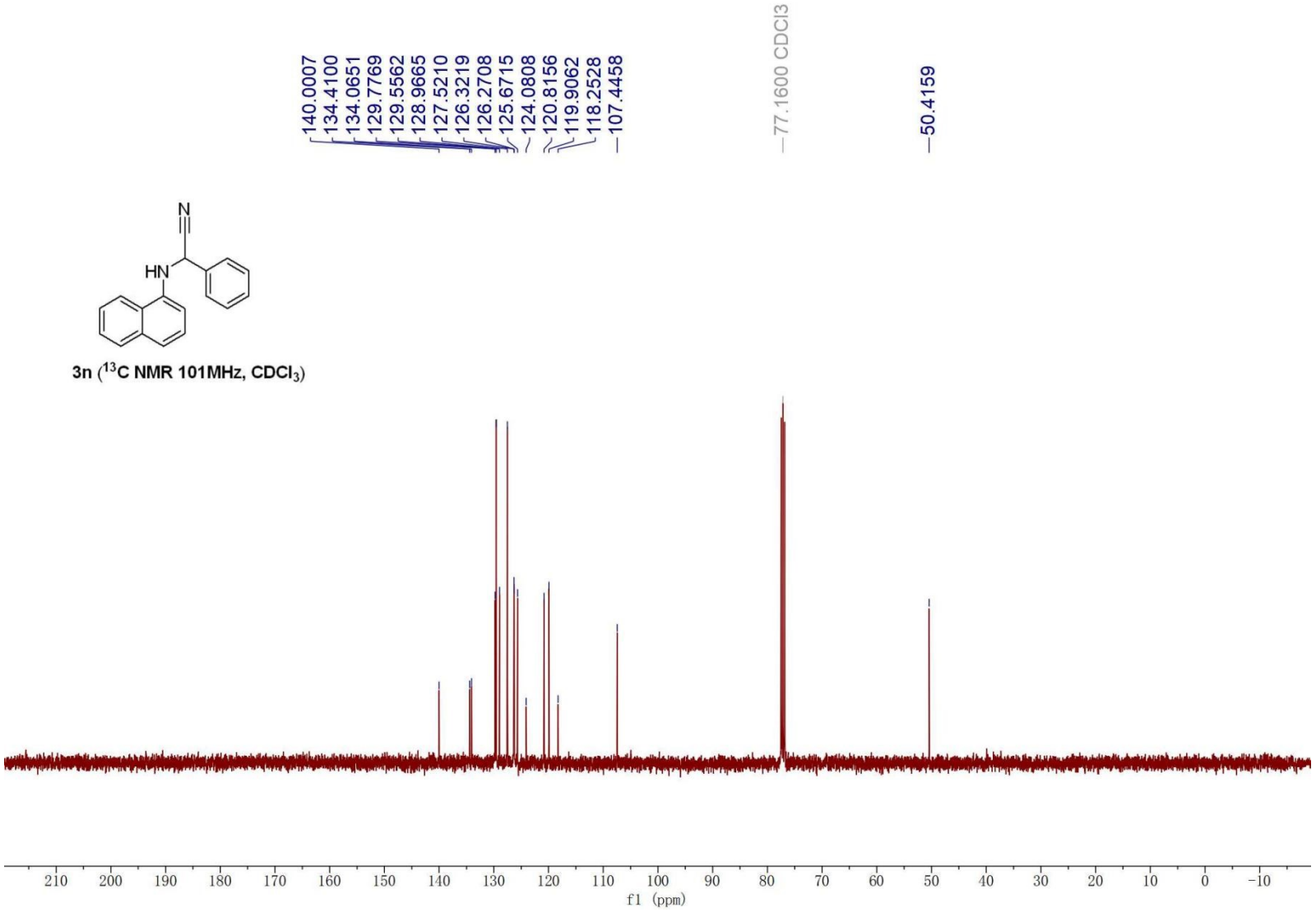

144.98
133.32
132.13
131.81
130.23
129.89
129.57
127.33
125.44
122.73
117.83
116.90
116.79
116.76
110.82
77.16 CDCl3
49.98
N
N
H
CF3
3l (13C NMR 101MHz, CDCl3)
f1 (ppm)

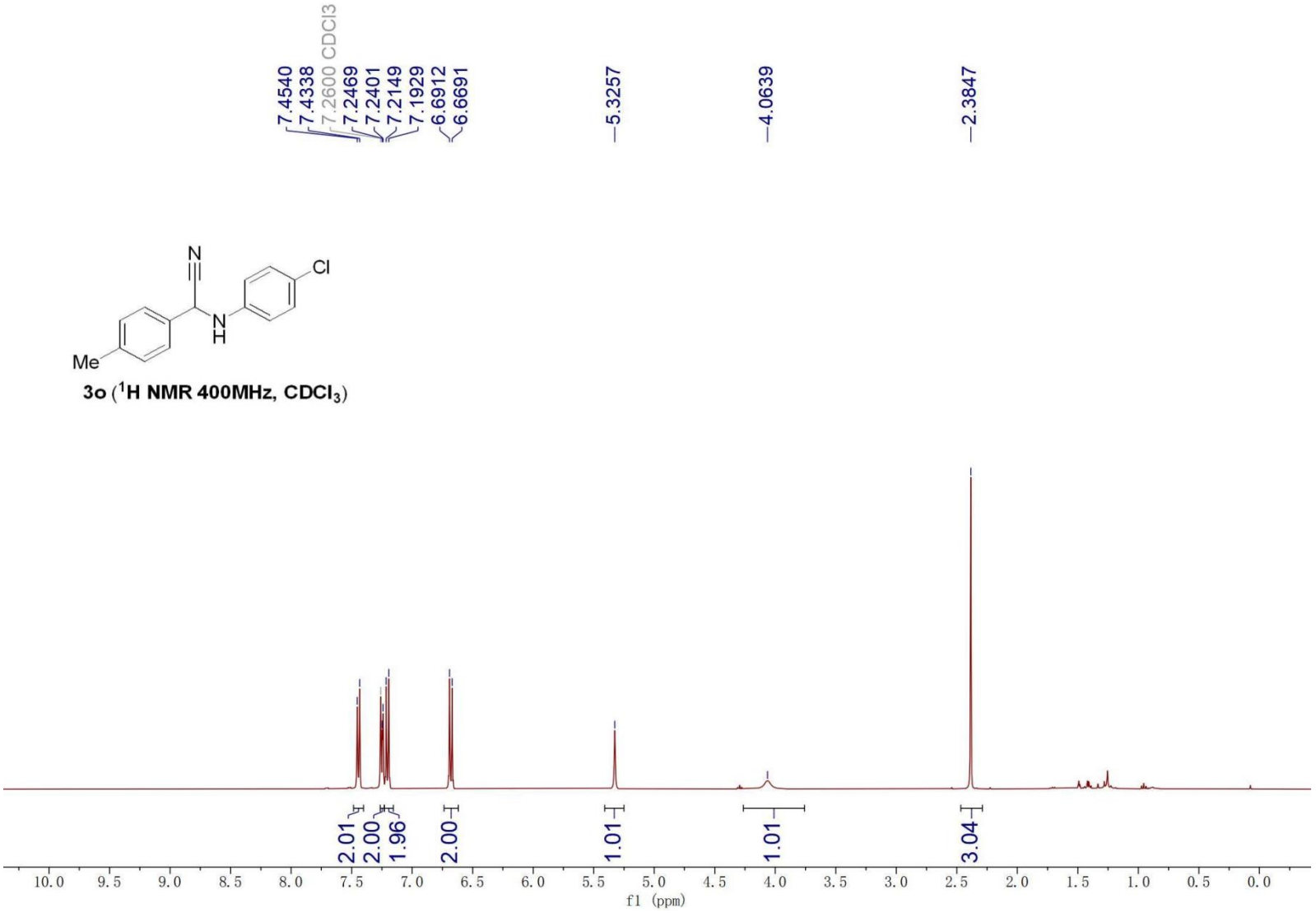

7.6430
7.6278
7.4921
7.4748
7.2326
7.2139
7.1832
7.1647
6.9308
6.9122
6.8906
6.8695
5.4804
3.9603
2.5284
2.5097
2.4909
2.4722
1.2597
1.2409
1.2221
N
NH
Et
3m (1H NMR 400MHz, CDCl3)
2.06
3.04
2.08
2.05
1.00
1.04
2.05
3.09
f1 (ppm)


142.3158
134.3027
129.6603
129.5154
129.3575
128.6233
127.3446
127.3120
120.2939
118.4485
111.9794
77.1600 CDCl3
50.3019
23.9064
13.1684
N
NH
Et
3m (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

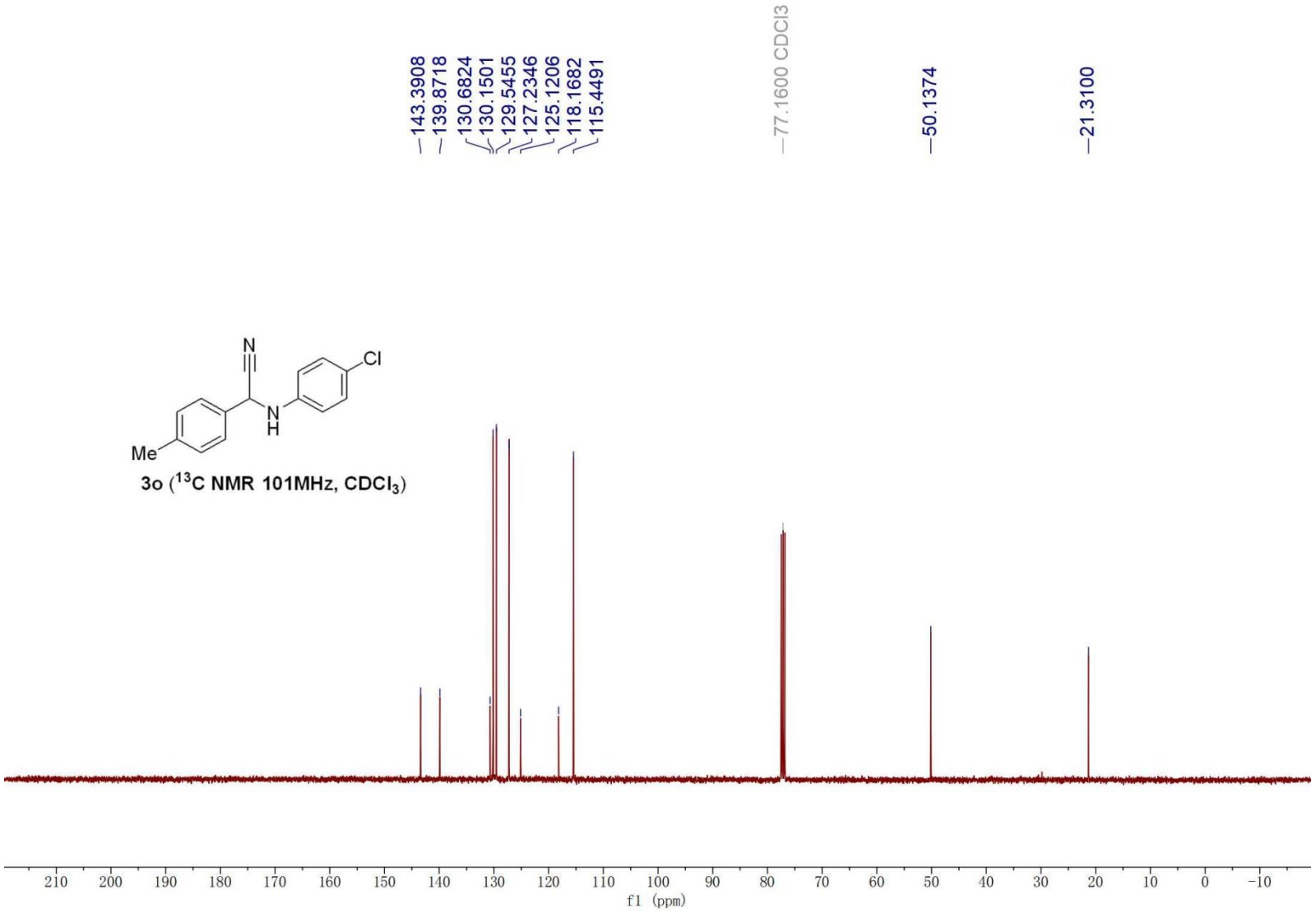


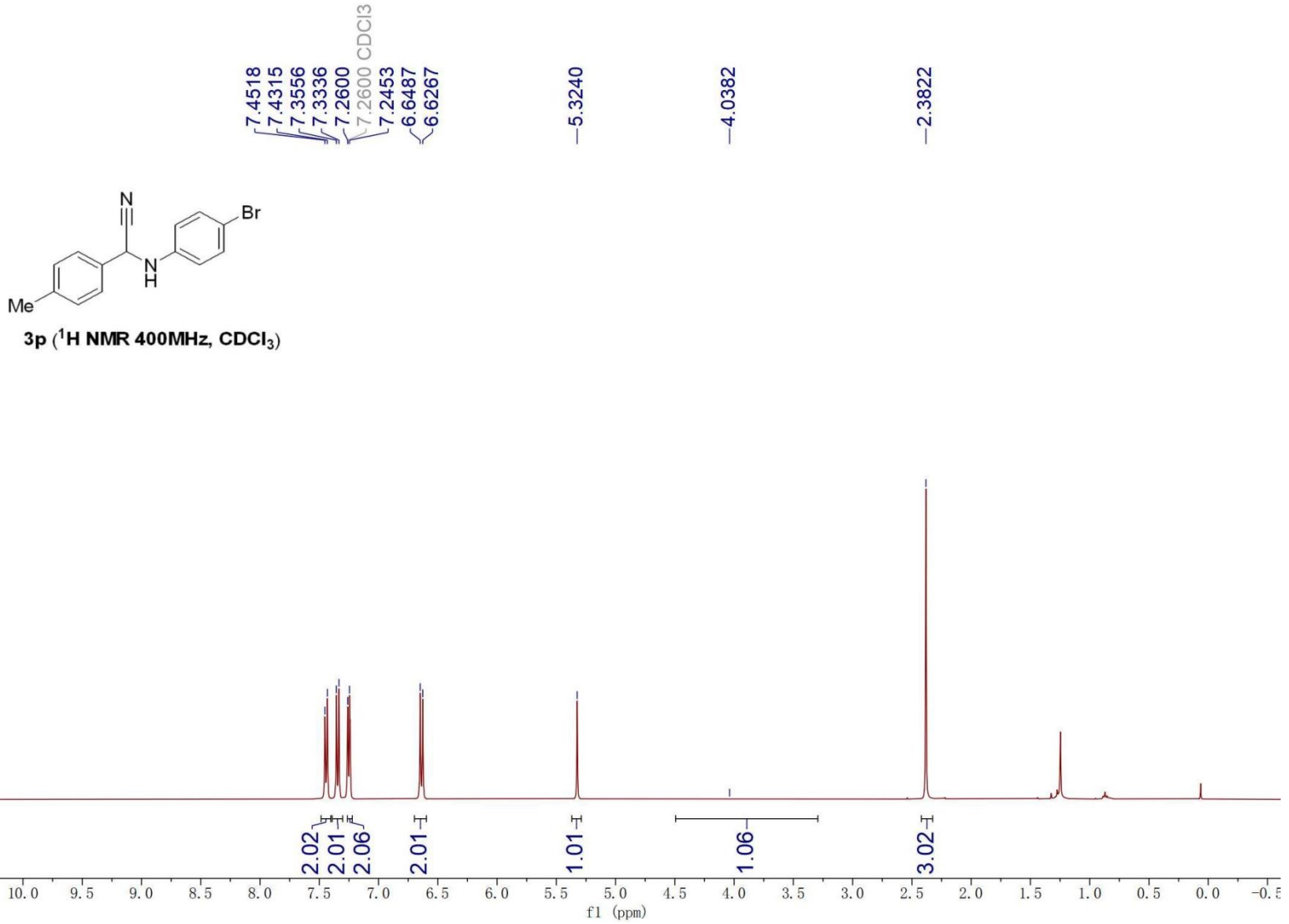
3n (^{1}H NMR 400MHz, $CDCl_3$)


140.0007
134.4100
134.0651
129.7769
129.5562
128.9665
127.5210
126.3219
126.2708
125.6715
124.0808
120.8156
119.9062
118.2528
107.4458
77.1600 CDCl3
50.4159
N
HN
3n (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

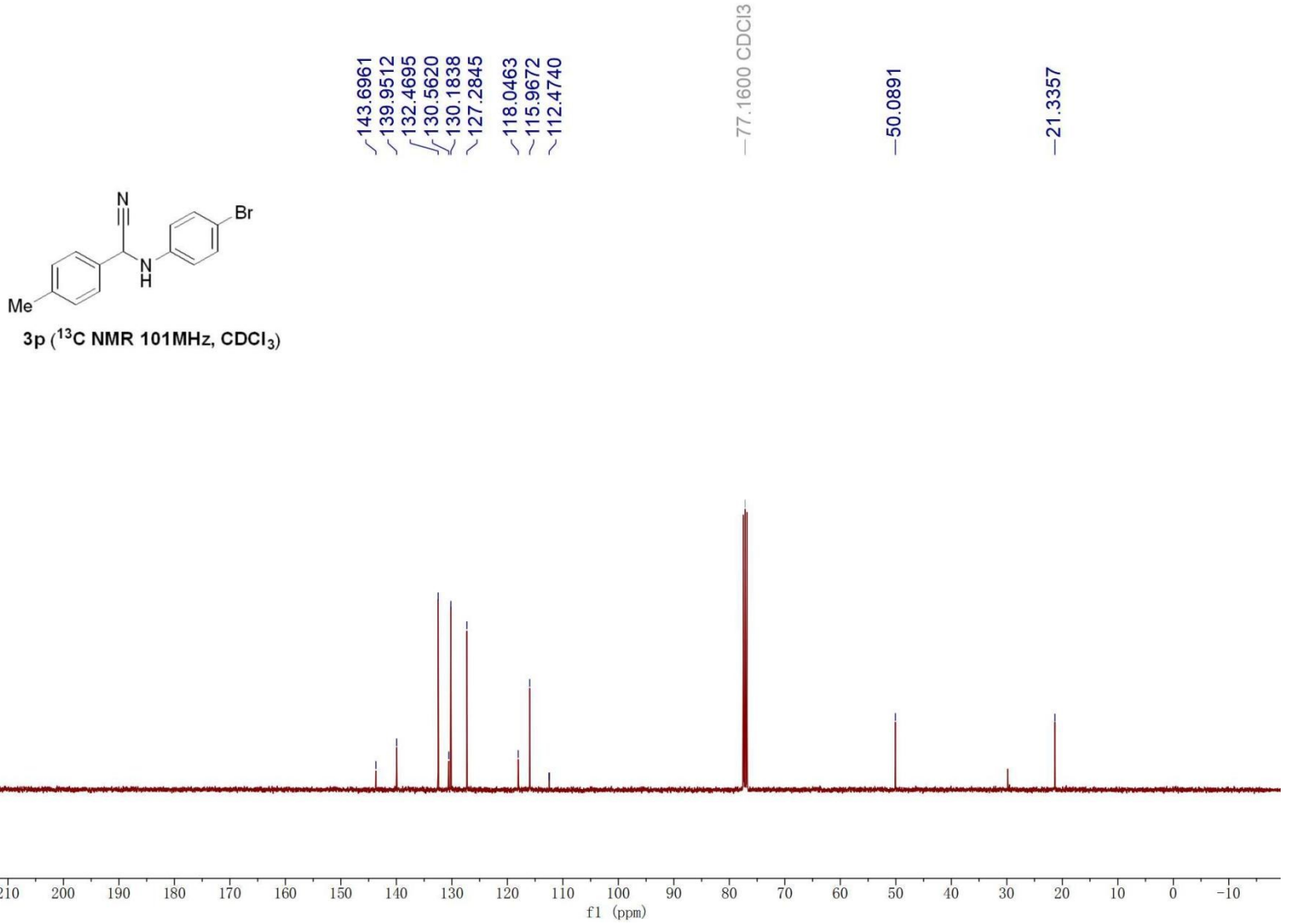


3o (^{1}H NMR 400MHz, $CDCl_3$)

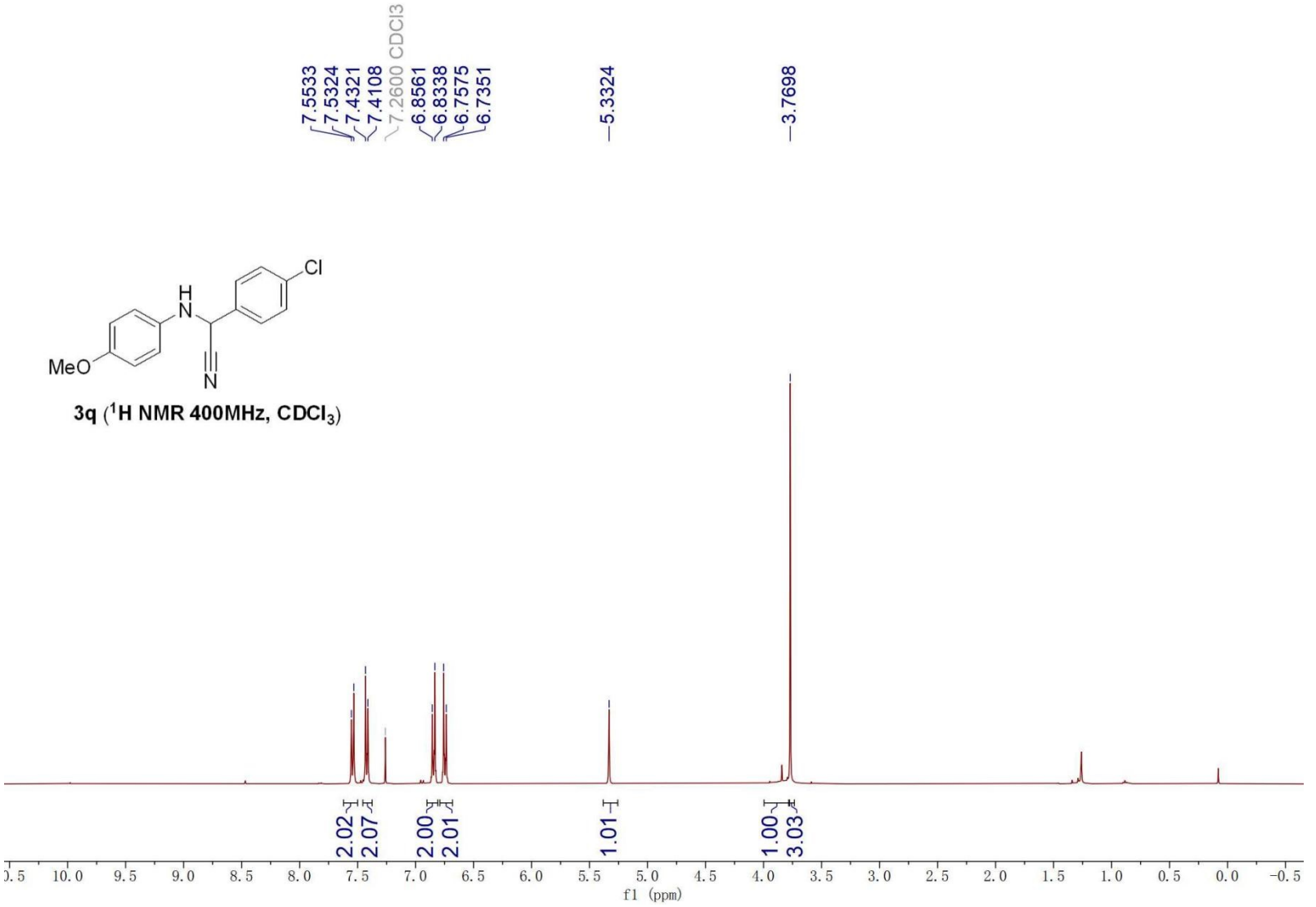

143.3908
139.8718
130.6824
130.1501
129.5455
127.2346
125.1206
118.1682
115.4491
77.1600 CDCl3
50.1374
21.3100
N
Cl
N
H
Me
3o (13C NMR 101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



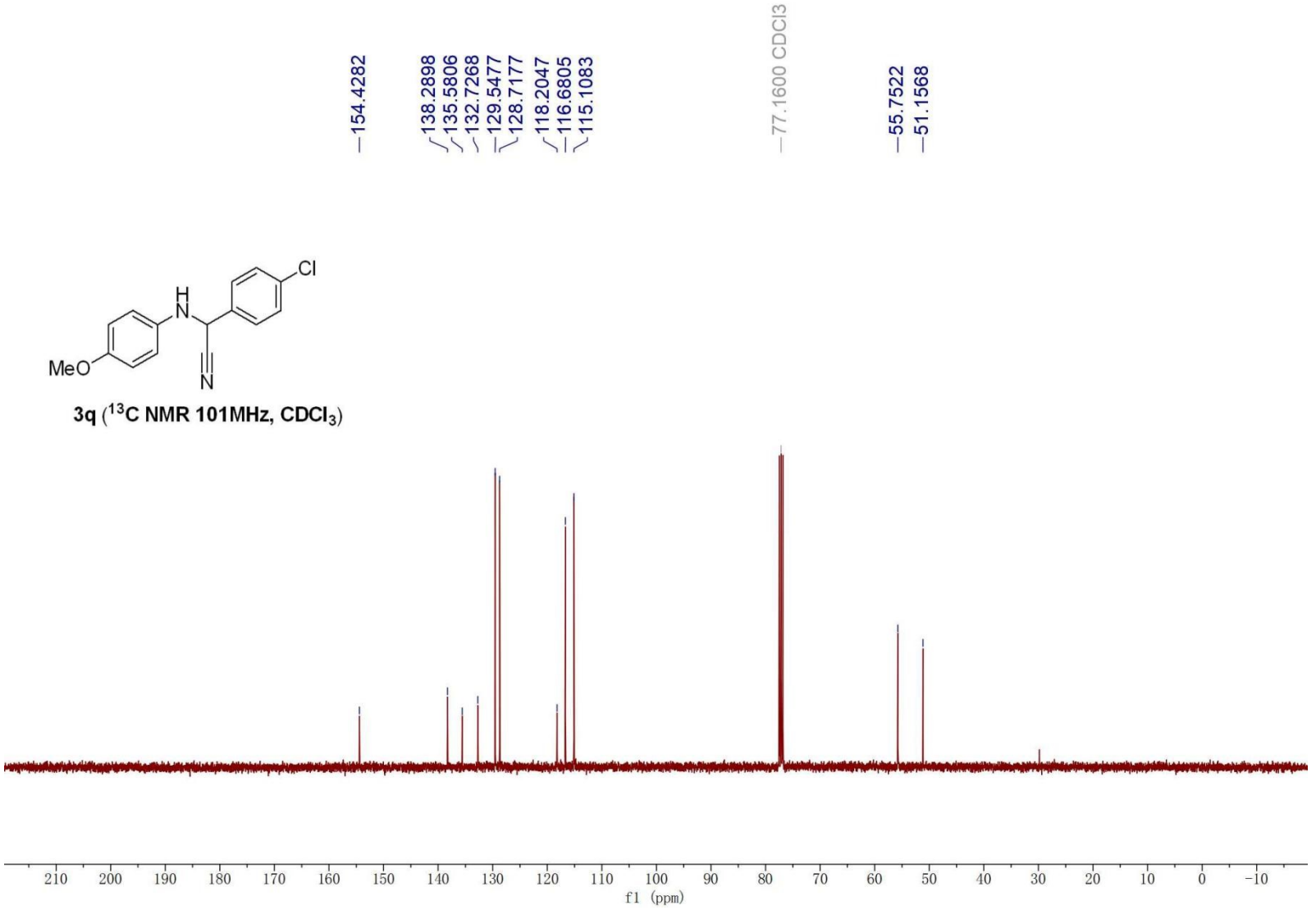
3p (^{1}H NMR 400MHz, $CDCl_3$)

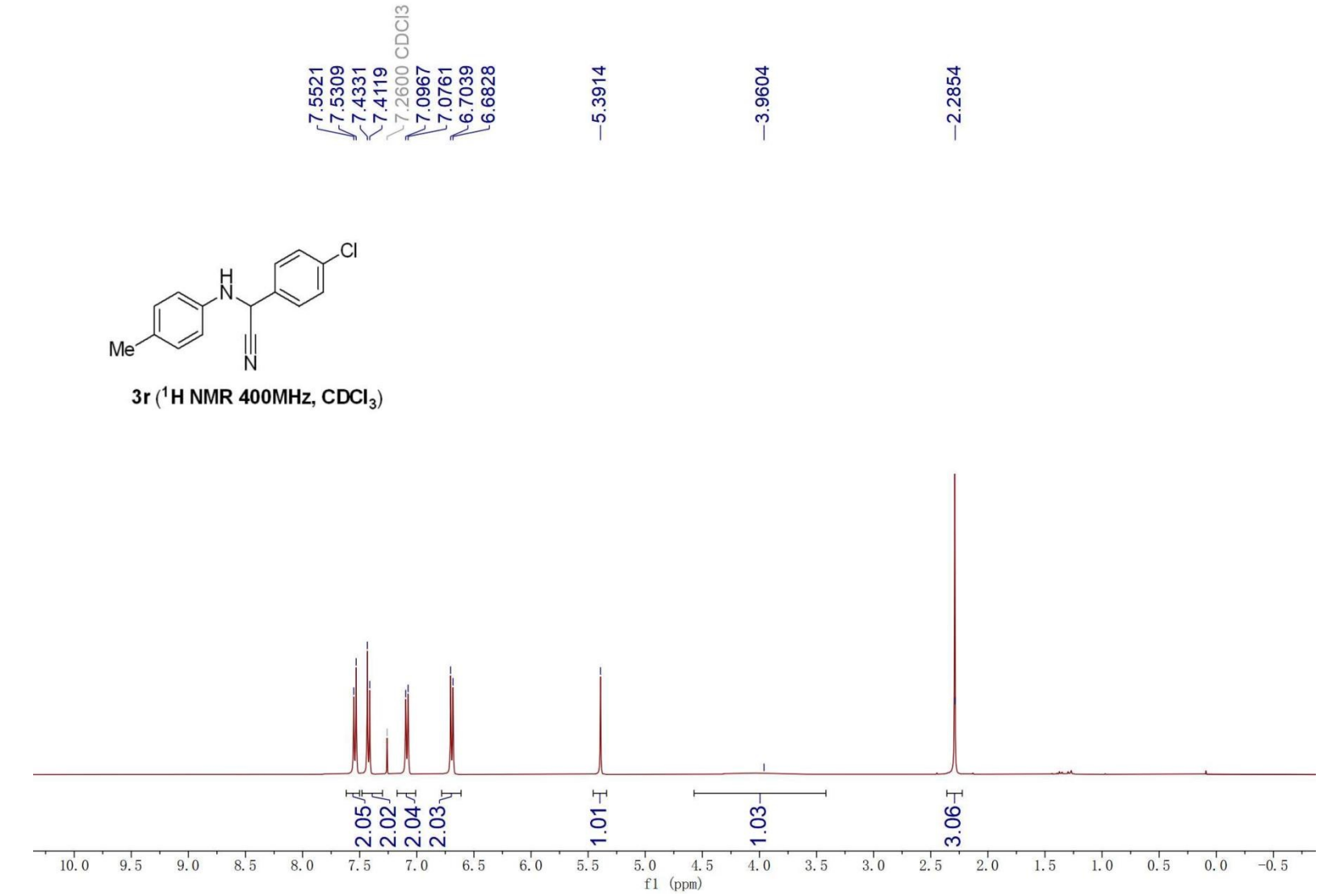


3p (^{13}C NMR 101MHz, $CDCl_3$)

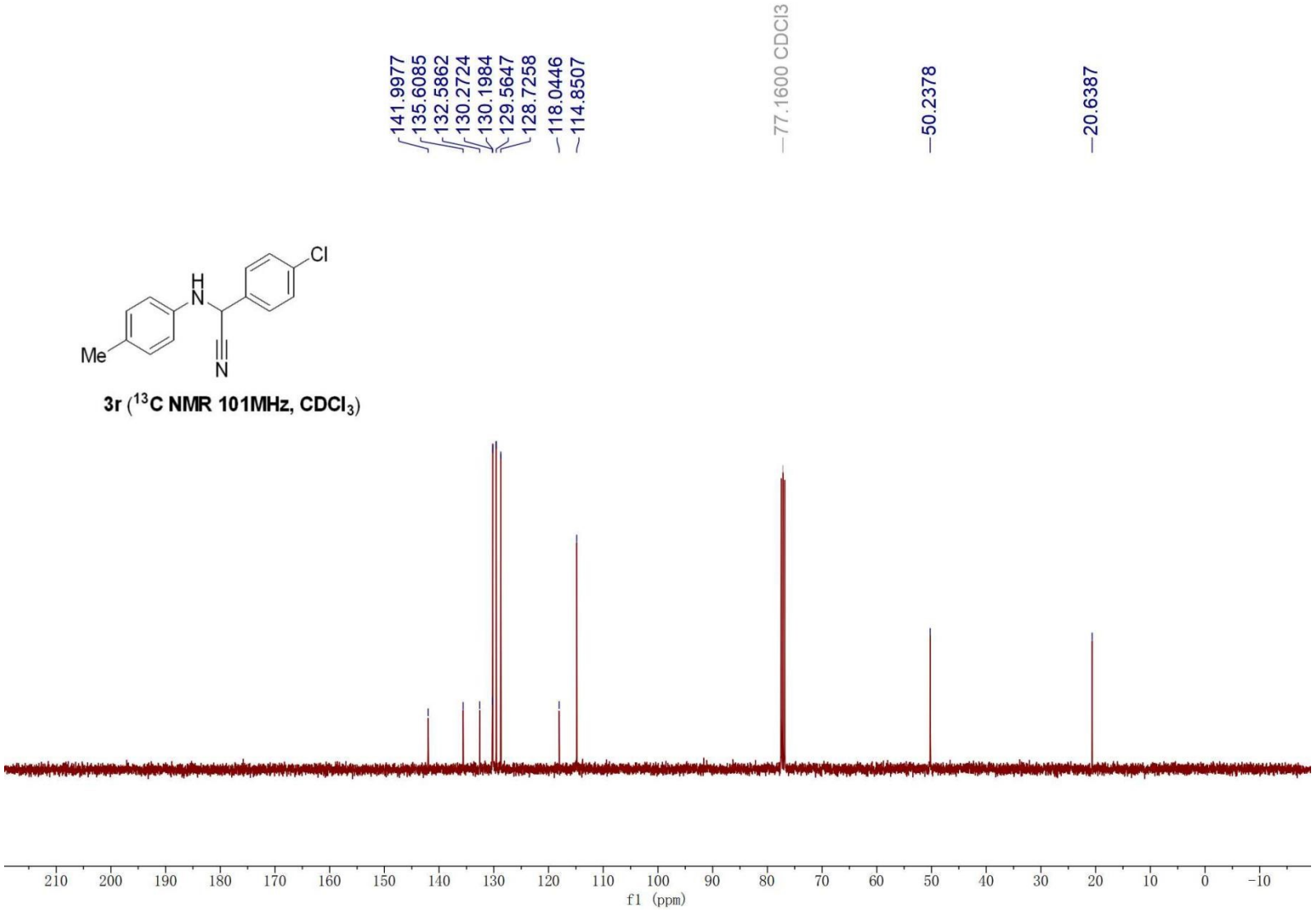


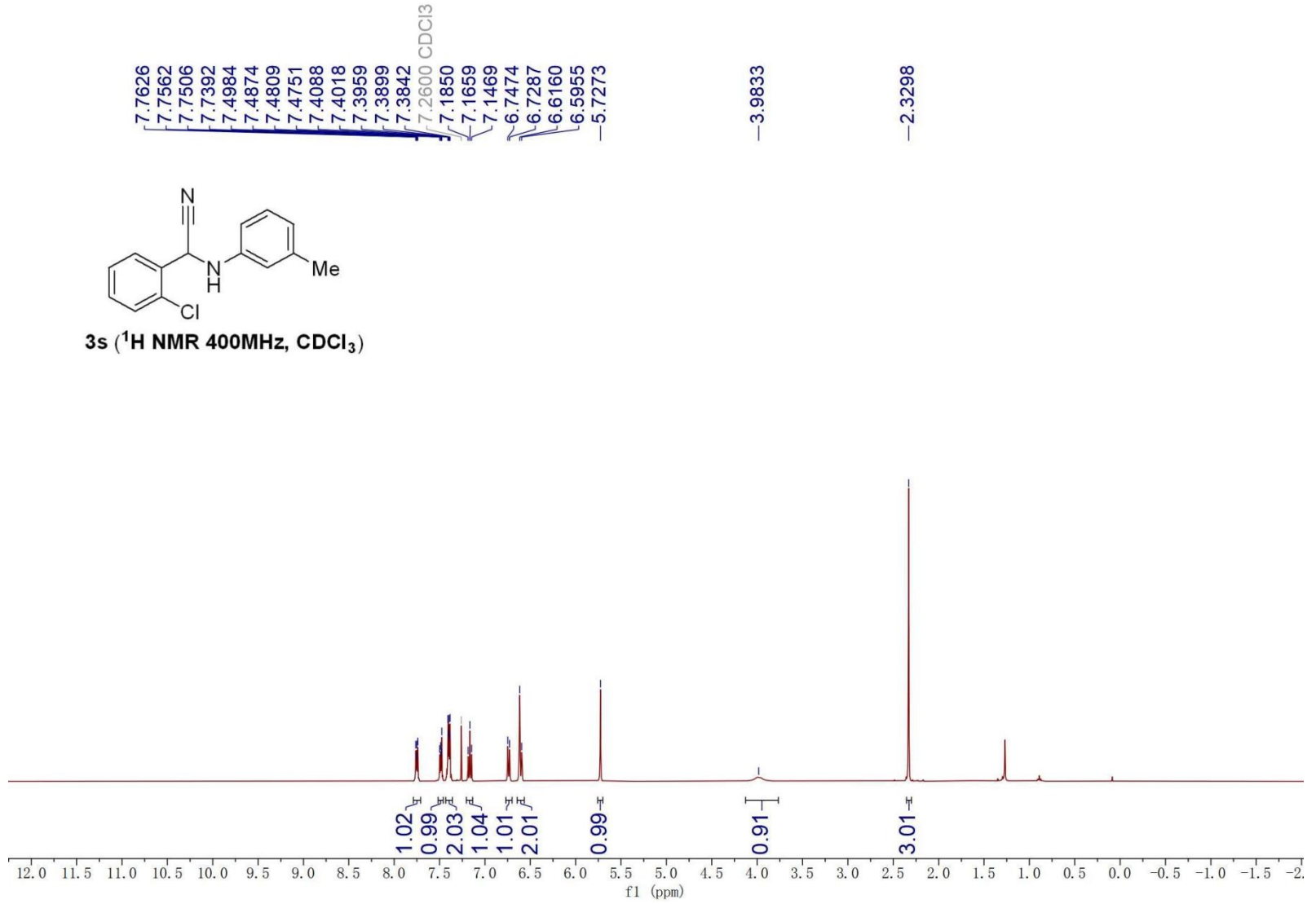
3q (**^{1}H NMR 400MHz, $CDCl_3$**)


154.4282
138.2898
135.5806
132.7268
129.5477
128.7177
118.2047
116.6805
115.1083
77.1600 CDCl3
55.7522
51.1568
Cl
H
N
MeO
N
3q (13C NMR 101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

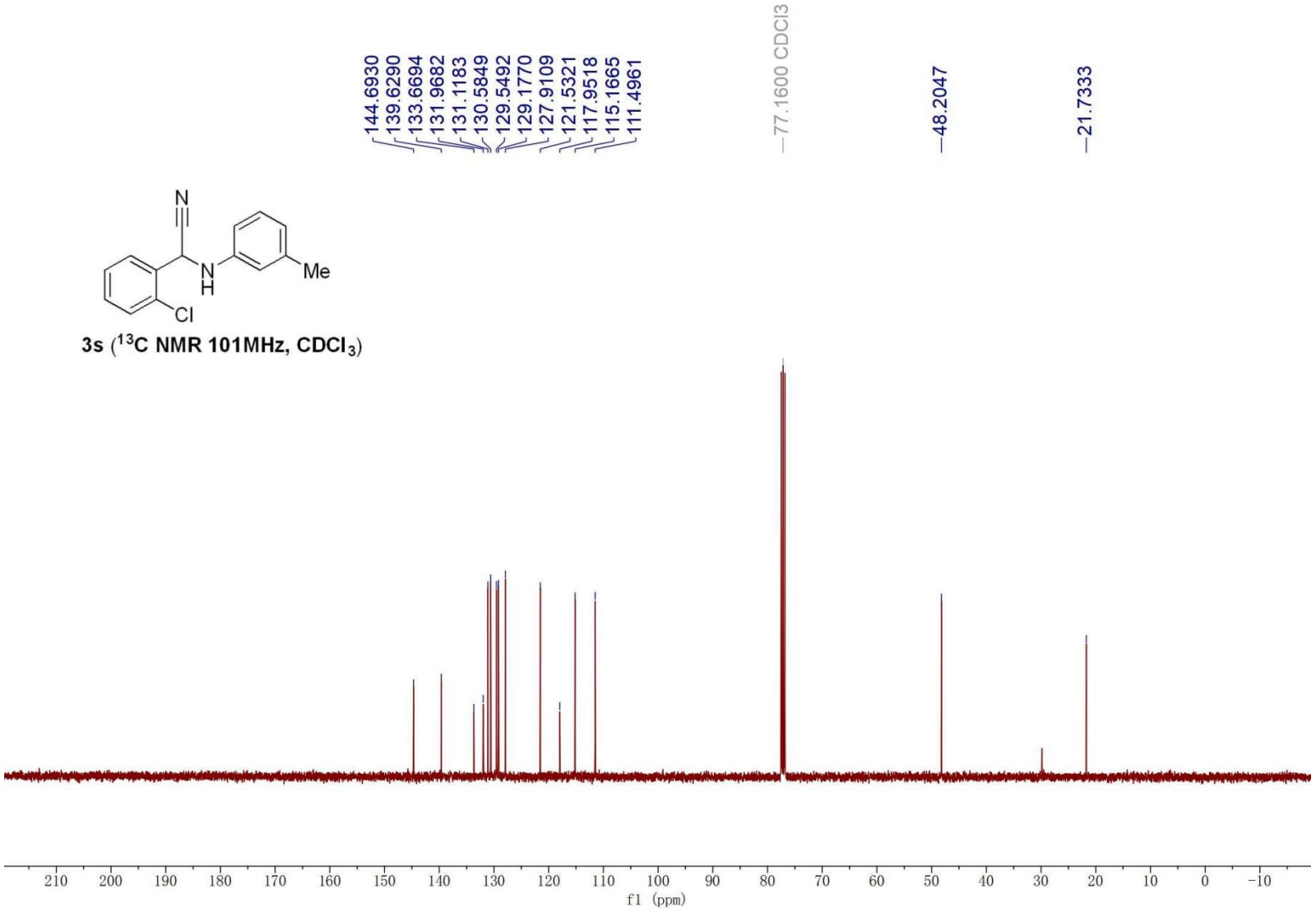


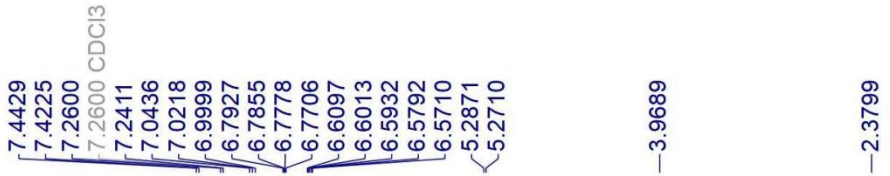
3r (^{1}H NMR 400MHz, $CDCl_3$)

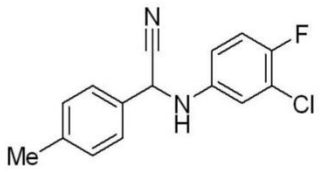

141.9977
135.6085
132.5862
130.2724
130.1984
129.5647
128.7258
118.0446
114.8507
77.1600 CDCl3
50.2378
20.6387
Cl
H
N
Me
N
3r (13C NMR 101MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



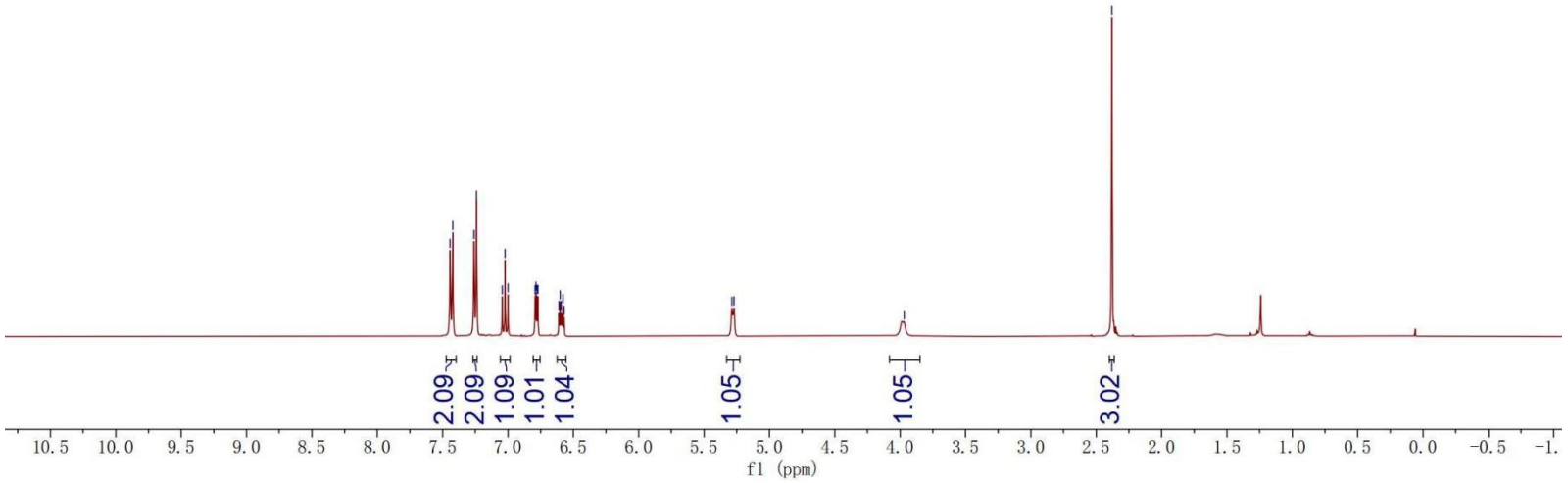
3s (^{1}H NMR 400MHz, $CDCl_3$)

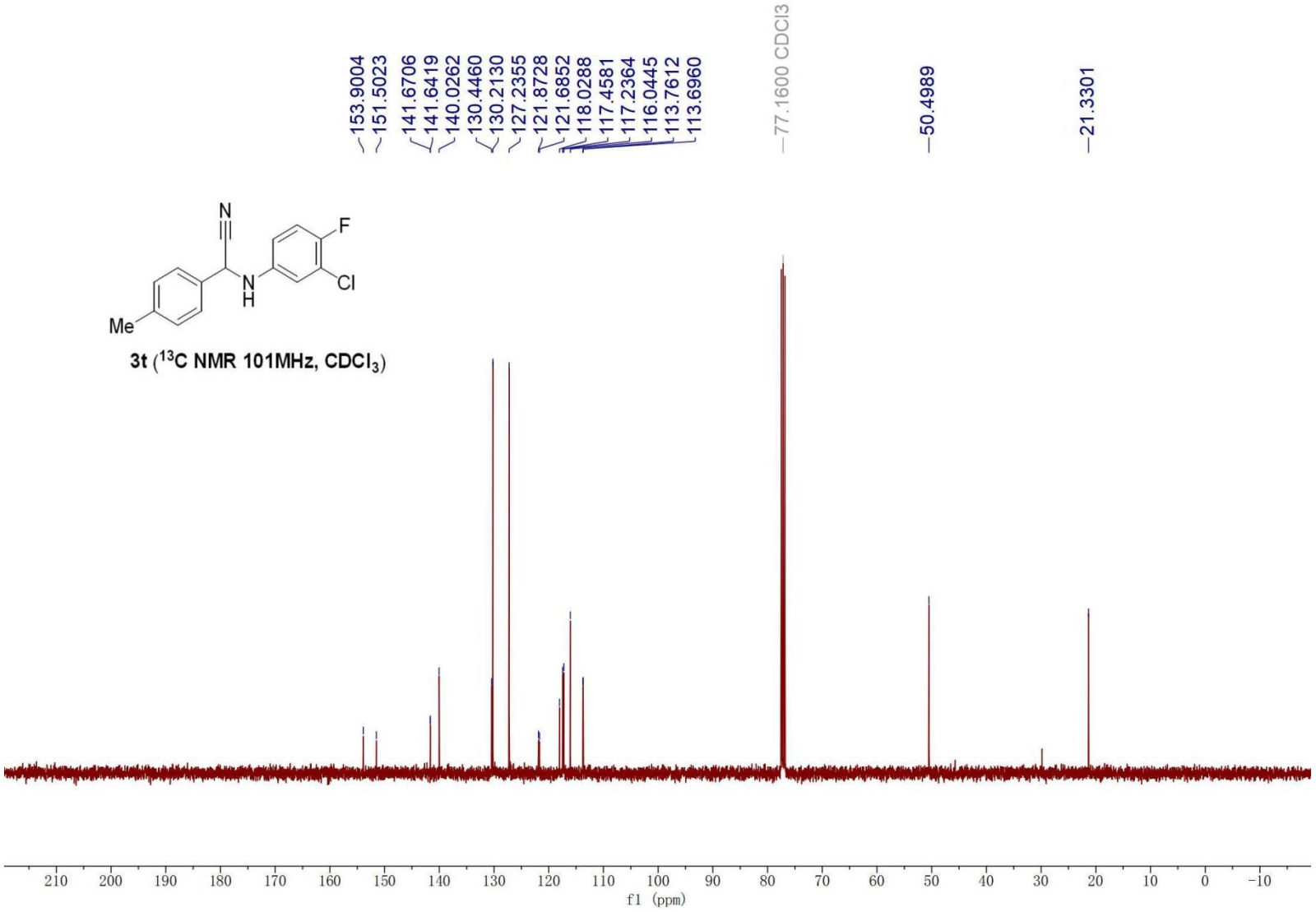

144.6930
139.6290
133.6694
131.9682
131.1183
130.5849
129.5492
129.1770
127.9109
121.5321
117.9518
115.1665
111.4961
77.1600 CDCl3
48.2047
21.7333
N
N
H
Me
Cl
3s (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

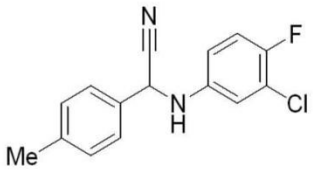




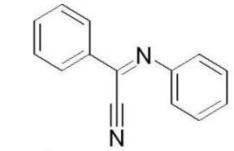
3t (^{1}H NMR 400MHz, $CDCl_3$)



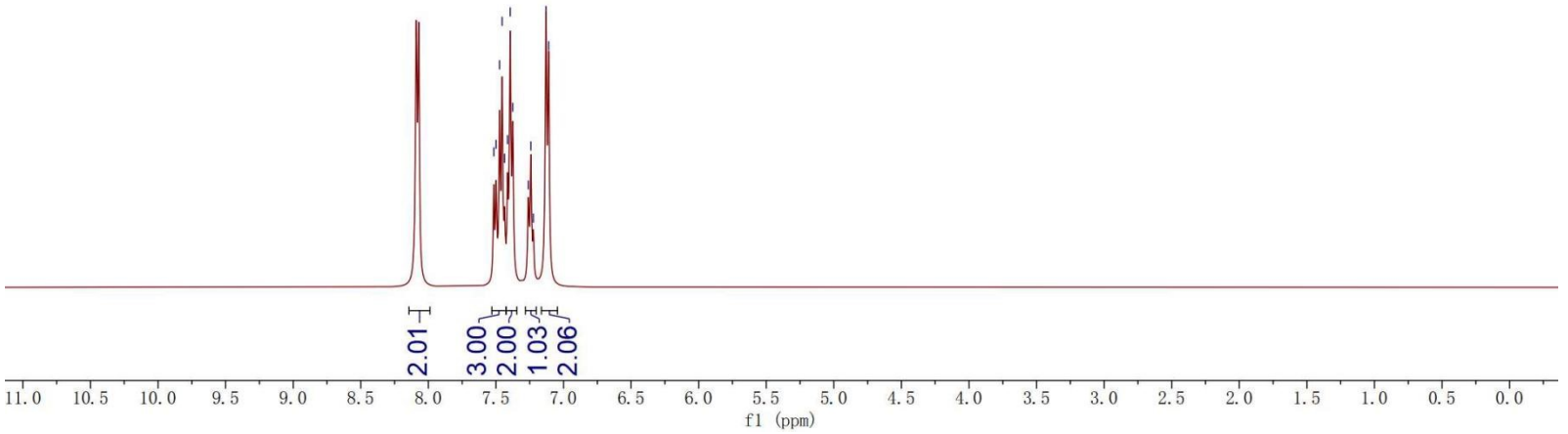

153.9004
151.5023
141.6706
141.6419
140.0262
130.4460
130.2130
127.2355
121.8728
121.6852
118.0288
117.4581
117.2364
116.0445
113.7612
113.6960
77.1600 CDCl3
50.4989
21.3301
N
F
Cl
N
H
Me
3t (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

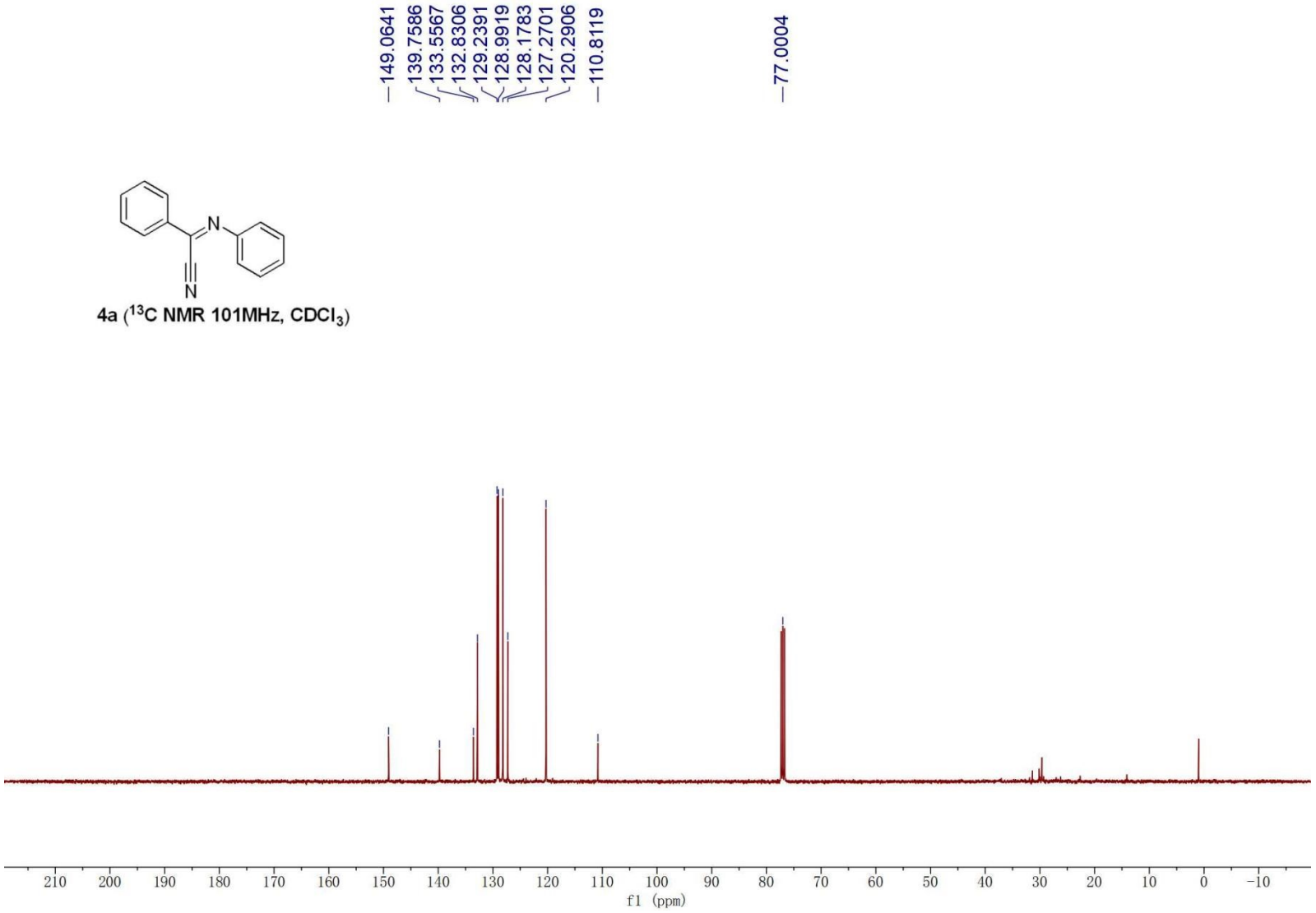


3t (^{19}F NMR 376MHz, $CDCl_3$)

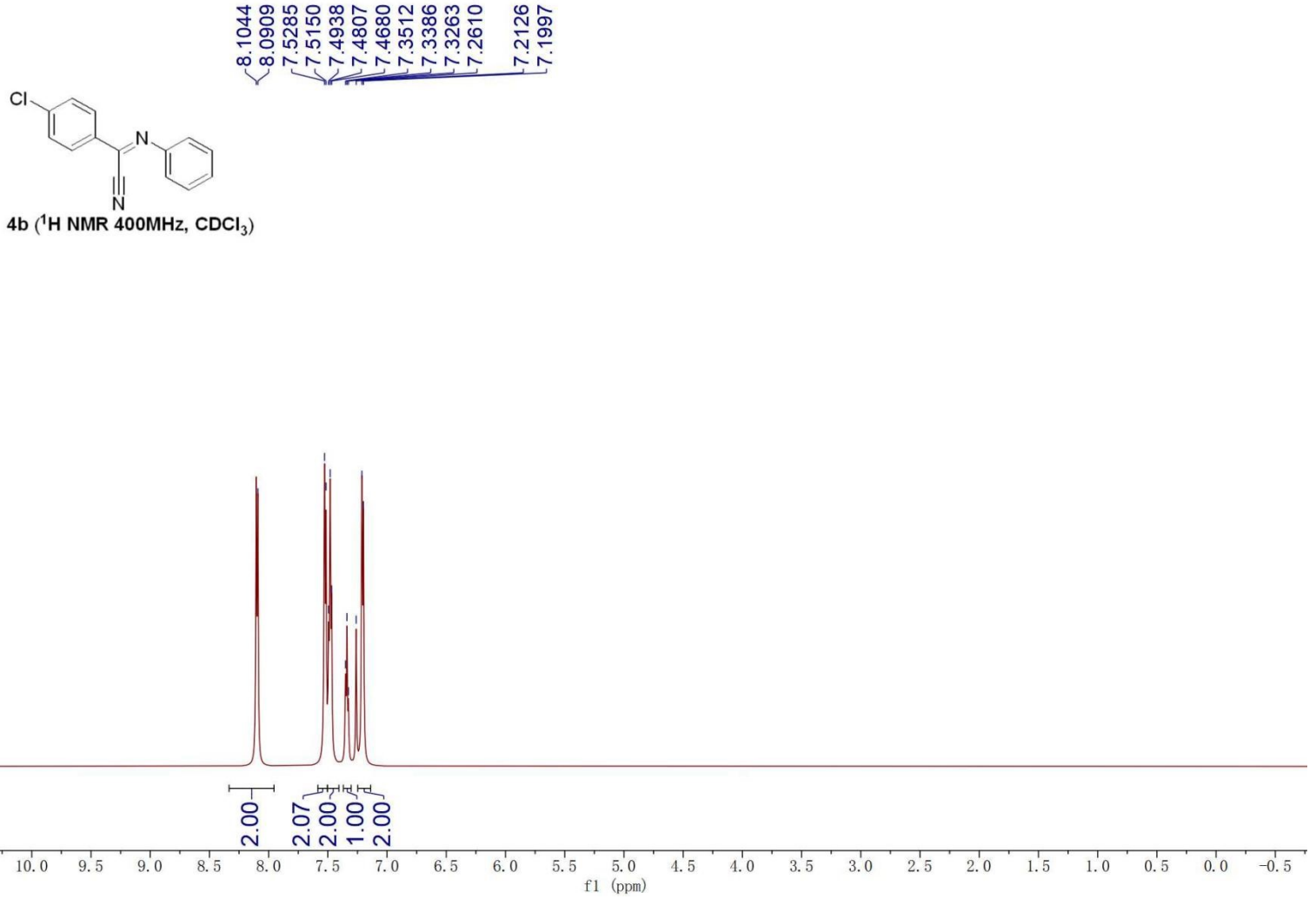


4a (^{1}H NMR 400MHz, $CDCl_3$)

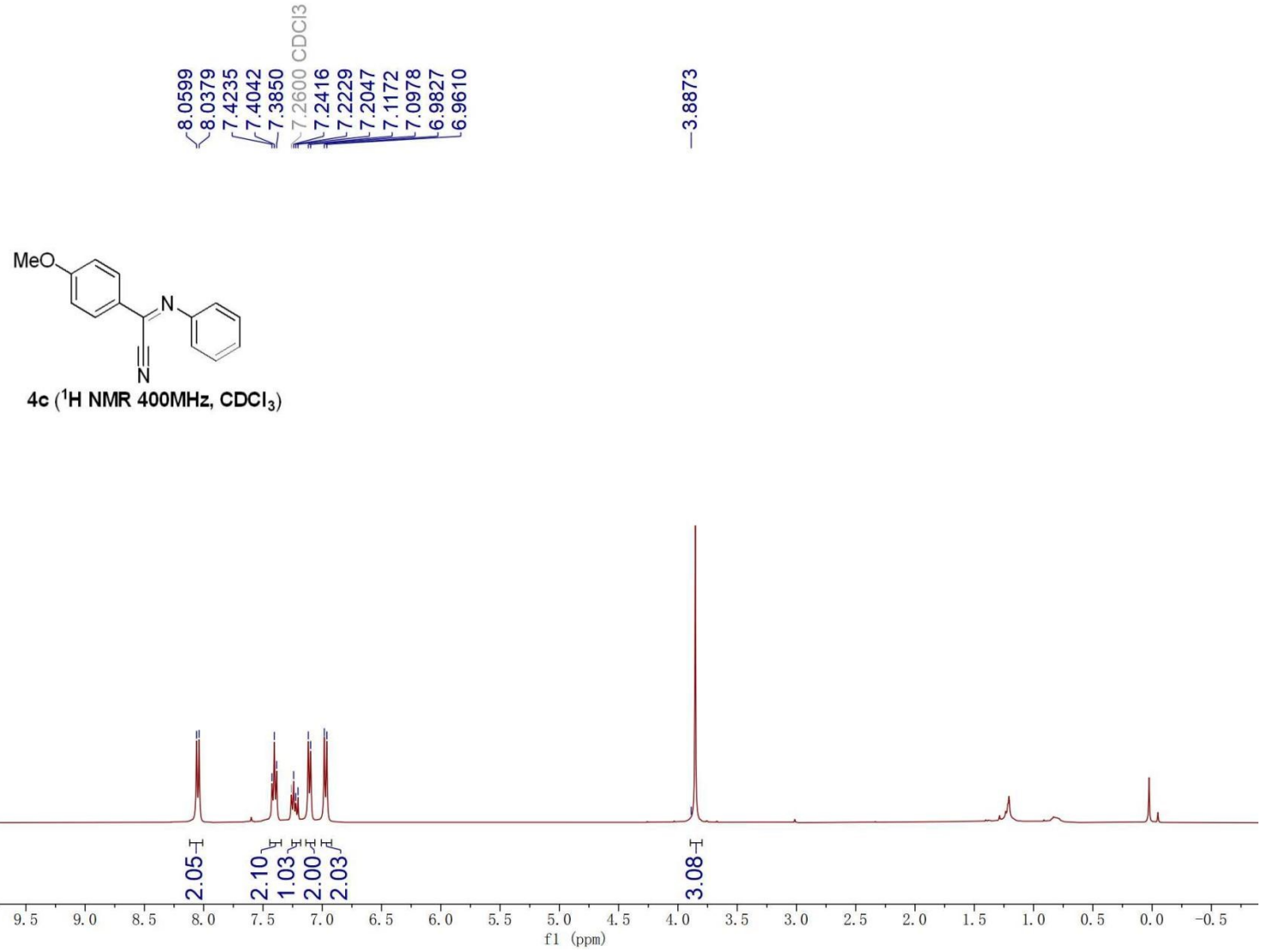




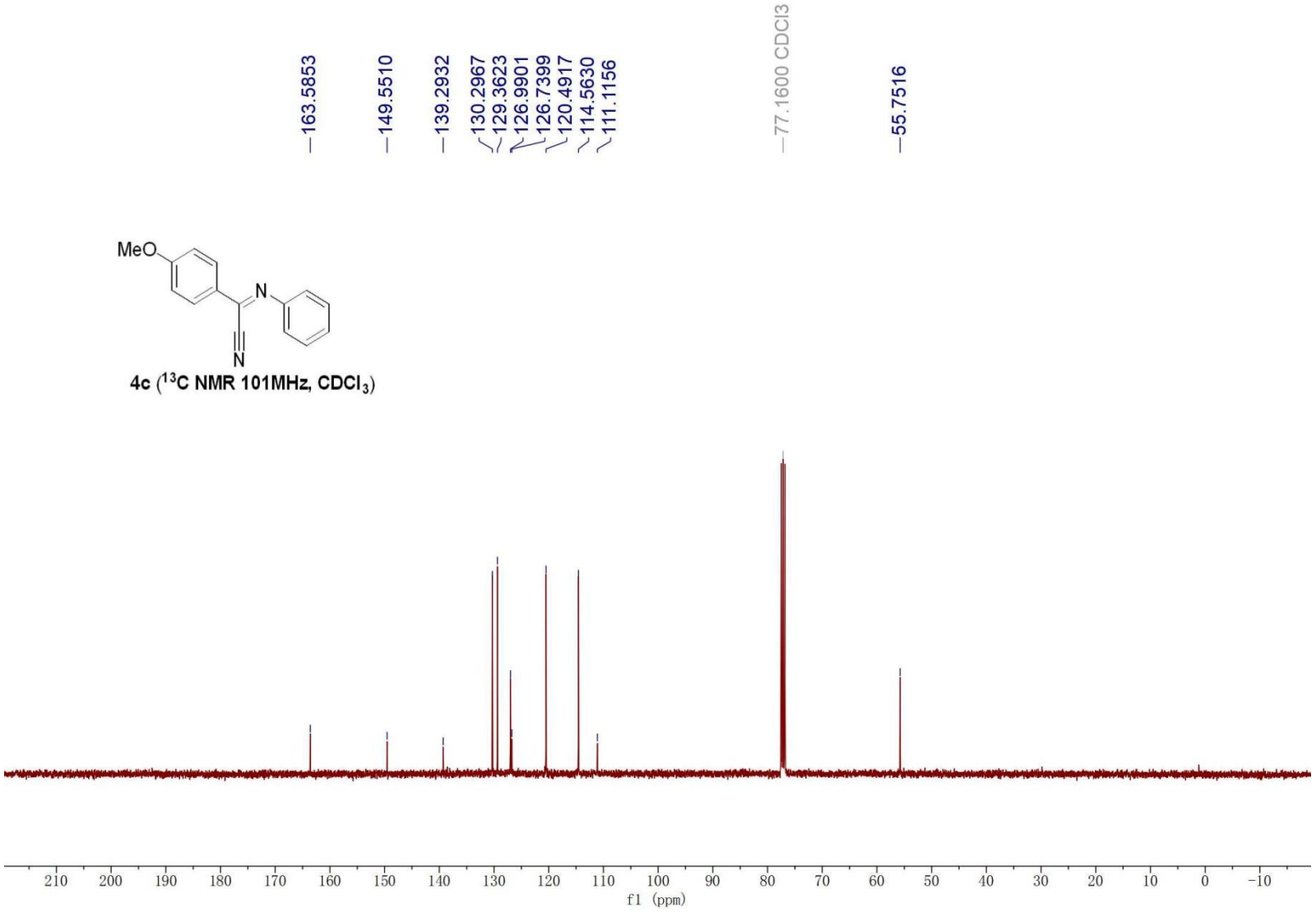
4a (^{13}C NMR 101MHz, $CDCl_3$)



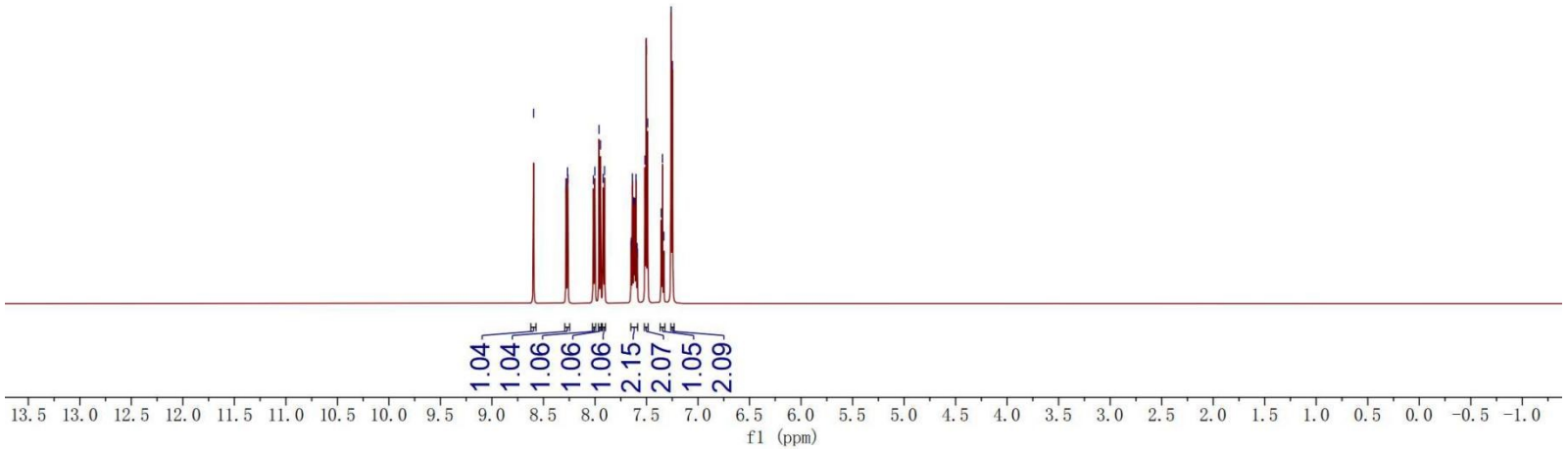
4b (^{1}H NMR 400MHz, $CDCl_3$)

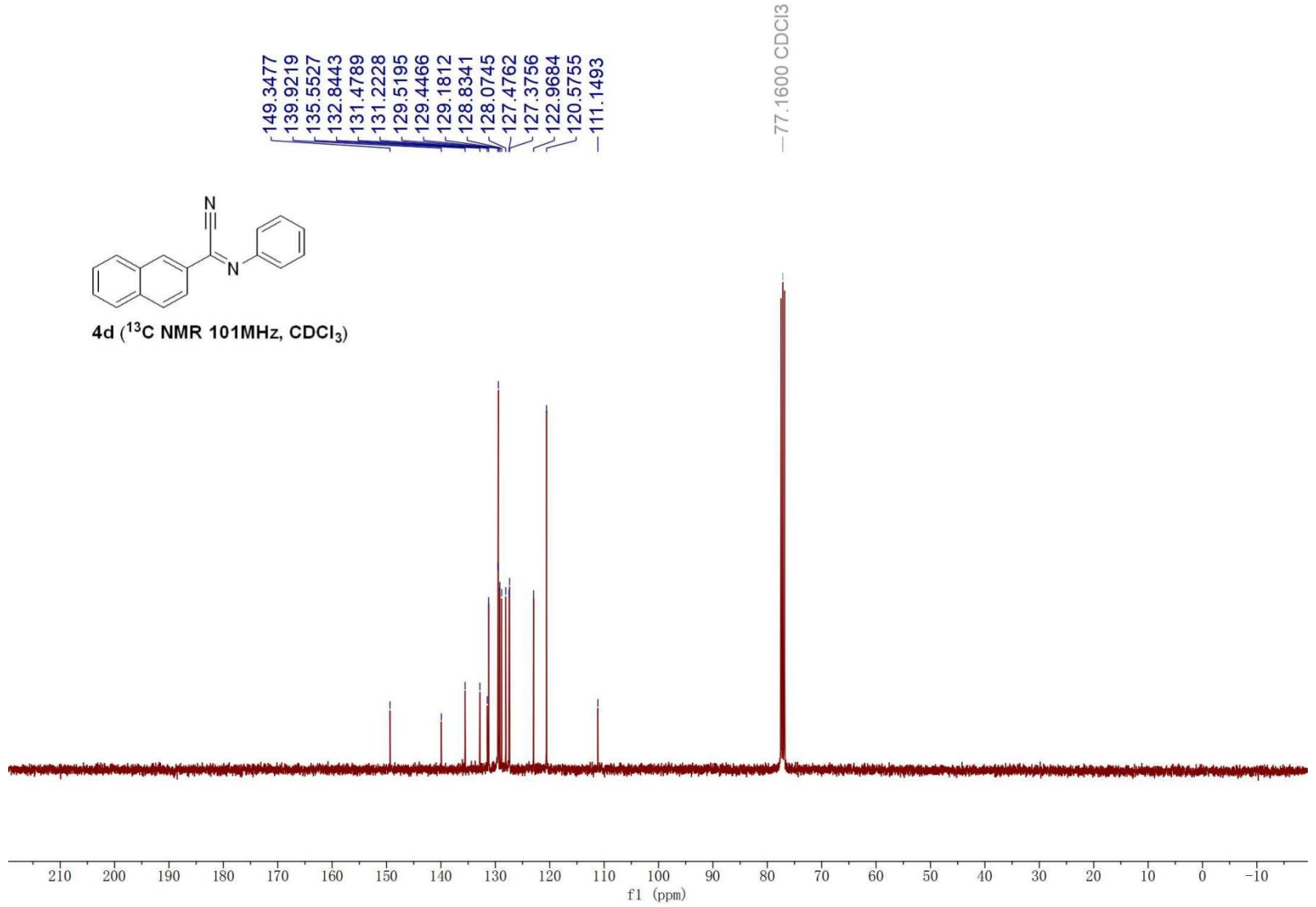


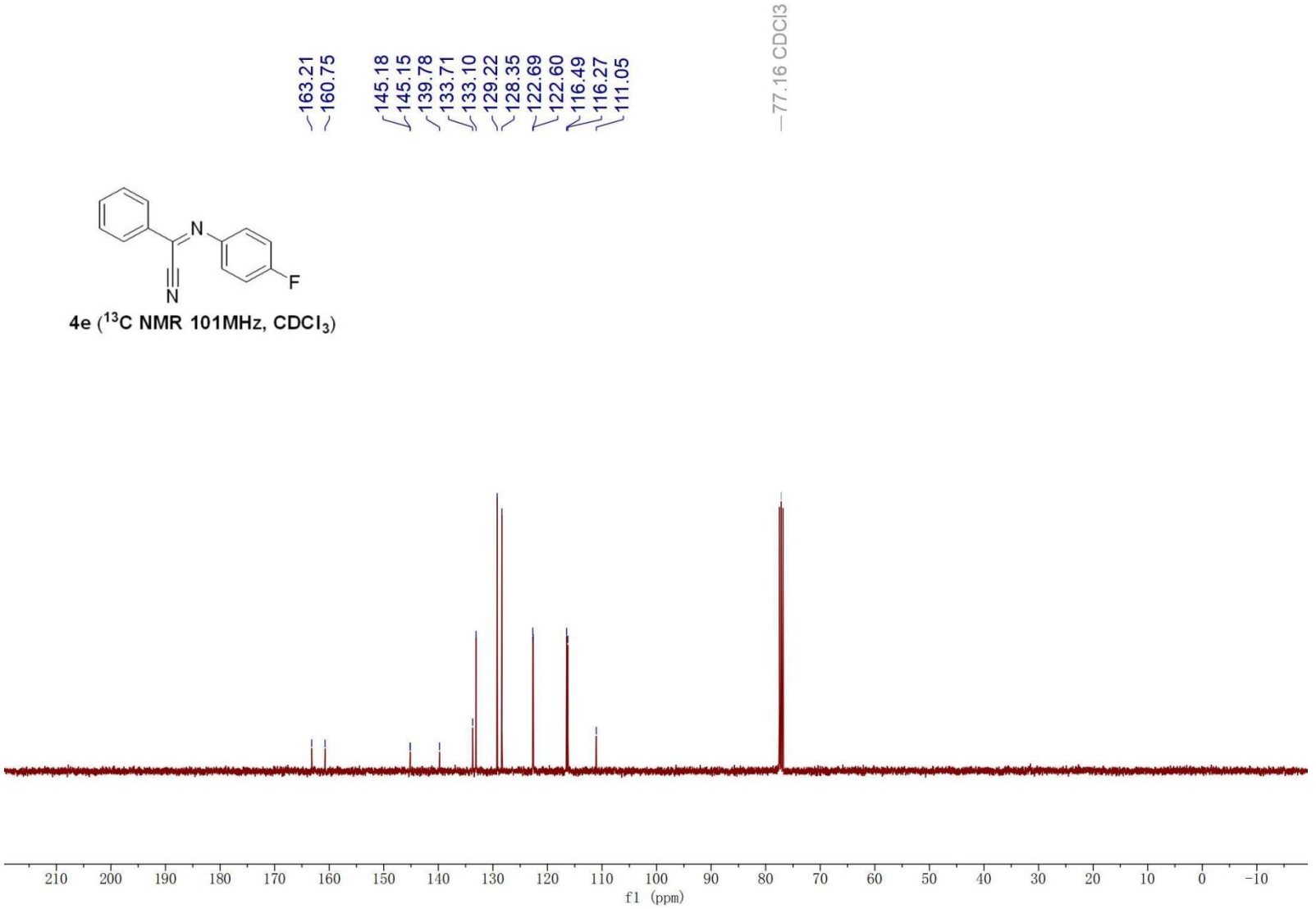
4c (^{1}H NMR 400MHz, $CDCl_3$)

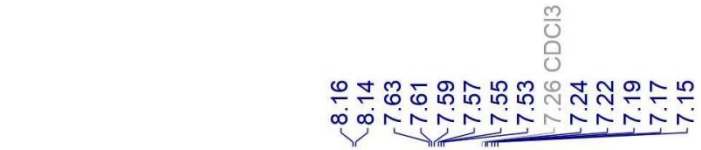

163.5853
149.5510
139.2932
130.2967
129.3623
126.9901
126.7399
120.4917
114.5630
111.1156
77.1600 CDCl3
55.7516
MeO
N
N
4c (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

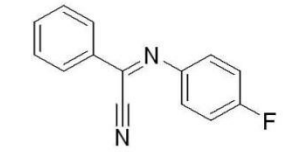
4d (^{1}H NMR 400MHz, $CDCl_3$)



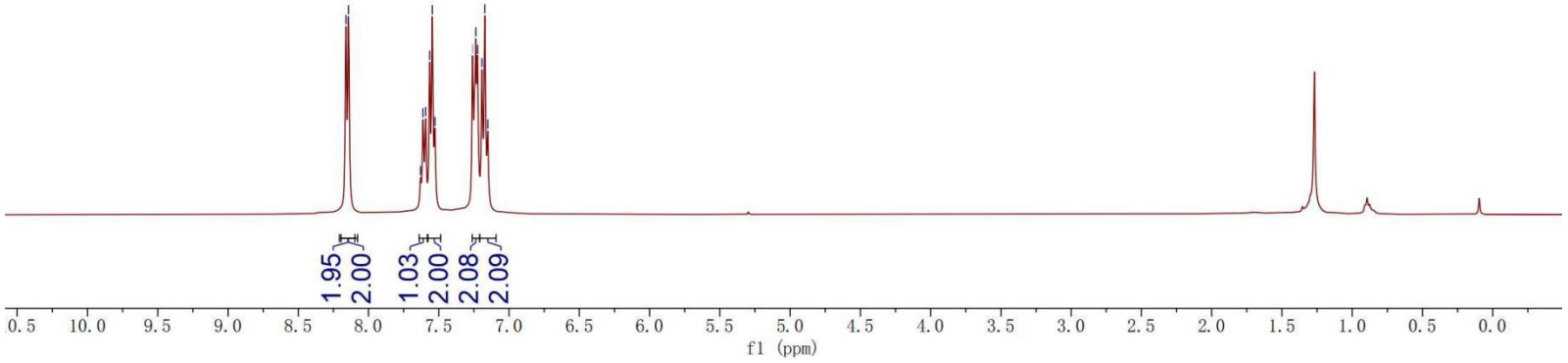

149.3477
139.9219
135.5527
132.8443
131.4789
131.2228
129.5195
129.4466
129.1812
128.8341
128.0745
127.4762
127.3756
122.9684
120.5755
111.1493
77.1600 CDCl3
N
N
4d (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

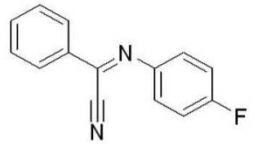

163.21
160.75
145.18
145.15
139.78
133.71
133.10
129.22
128.35
122.69
122.60
116.49
116.27
111.05
77.16 CDCl3
N
N
F
4e (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



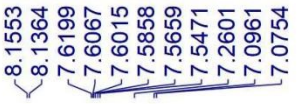


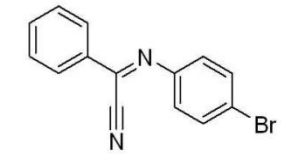
4e (^{1}H NMR 400MHz, $CDCl_3$)



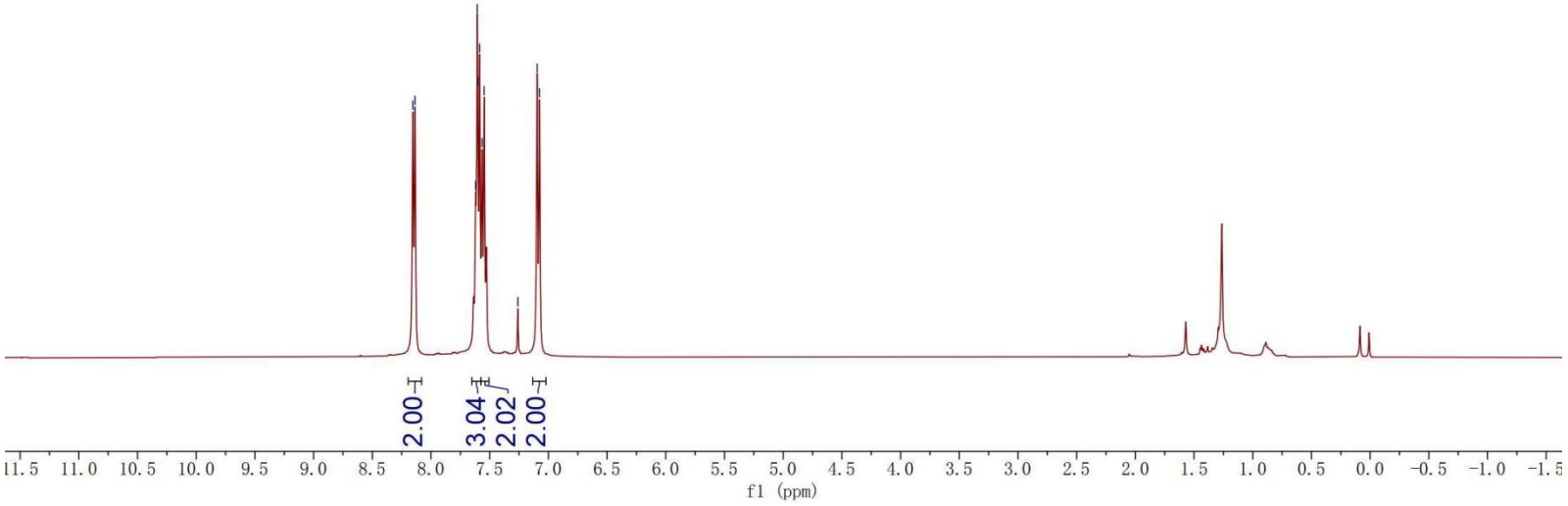


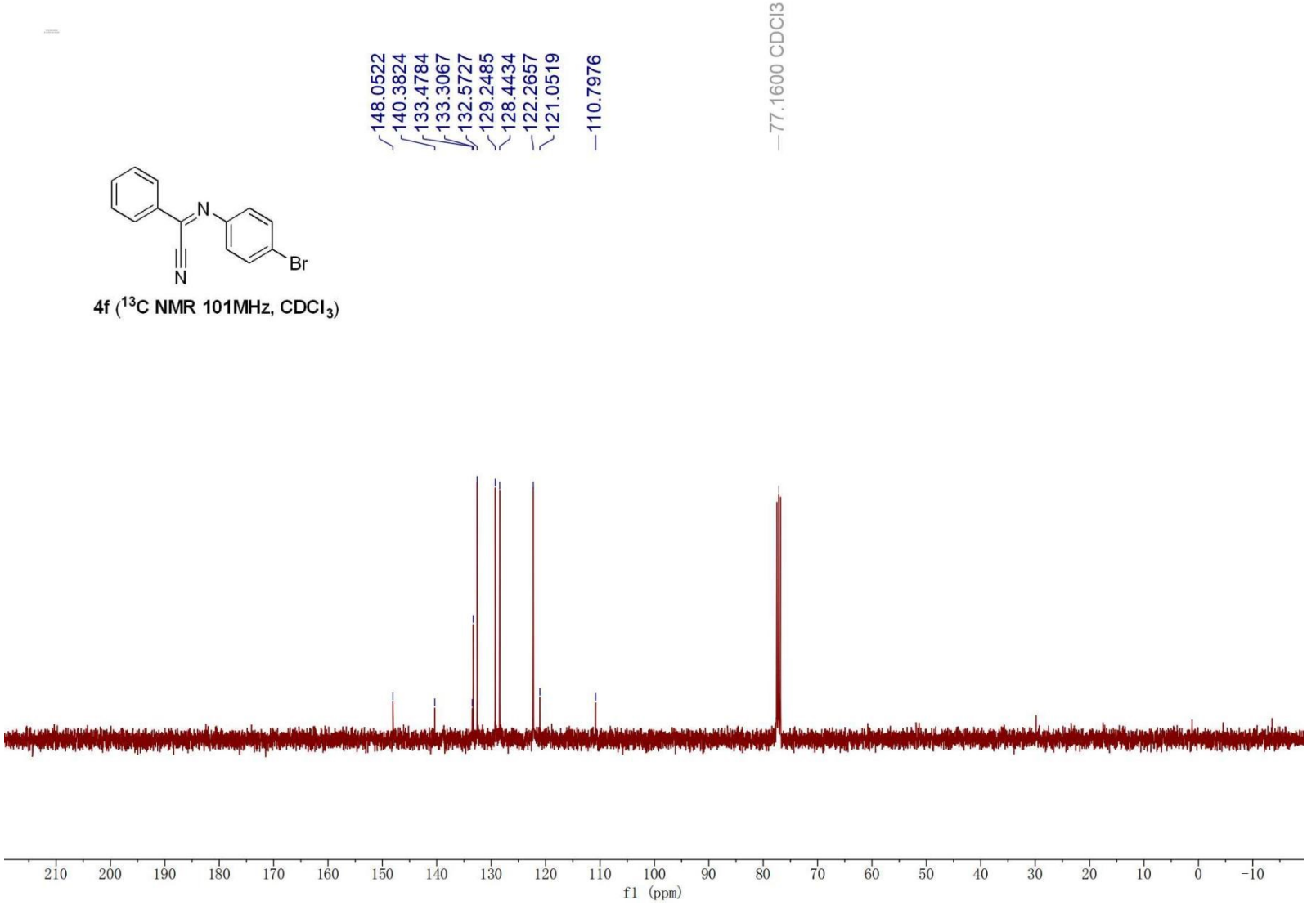
4e (^{19}F NMR 376MHz, $CDCl_3$)



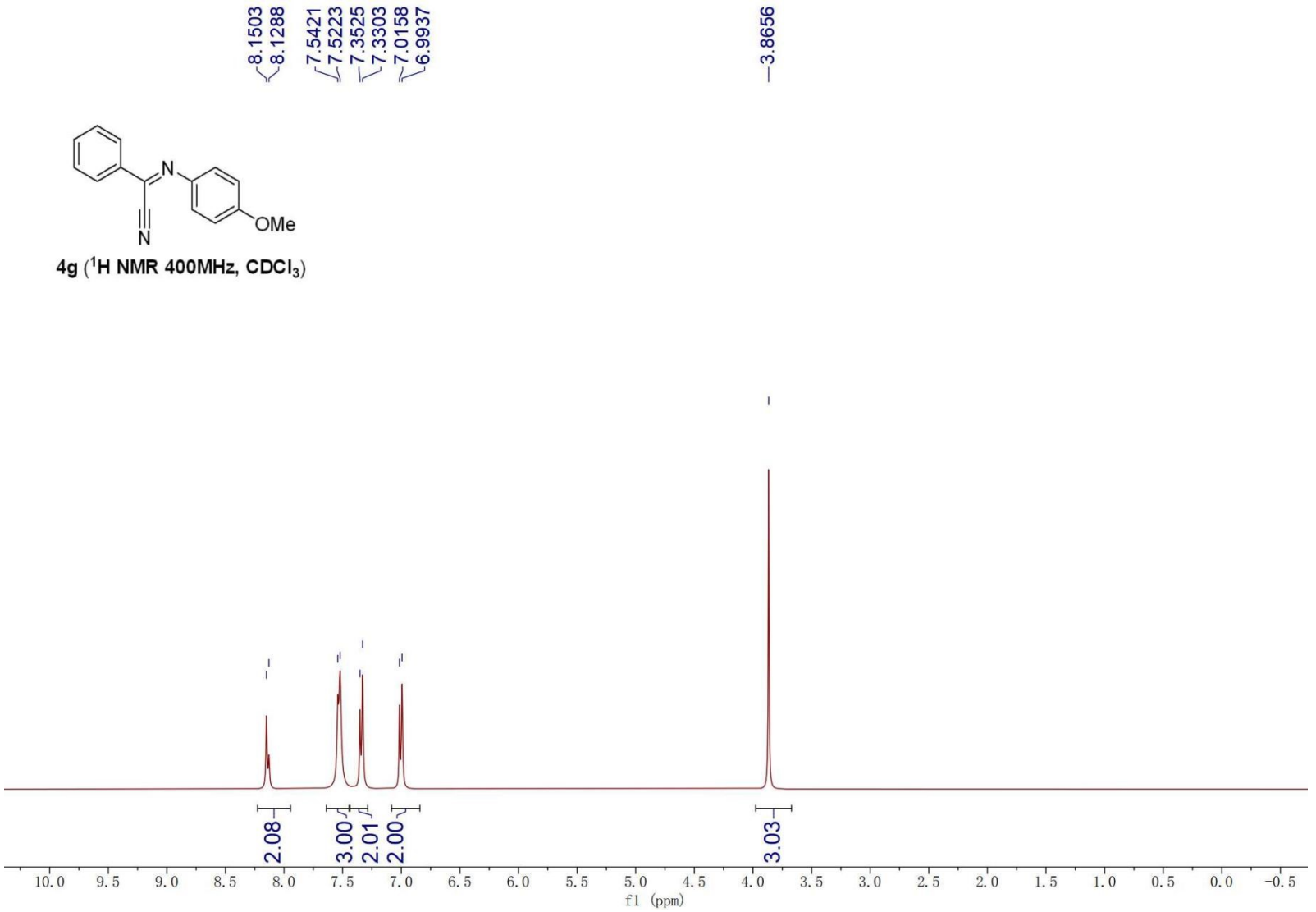


4f (^{1}H NMR 400MHz, $CDCl_3$)

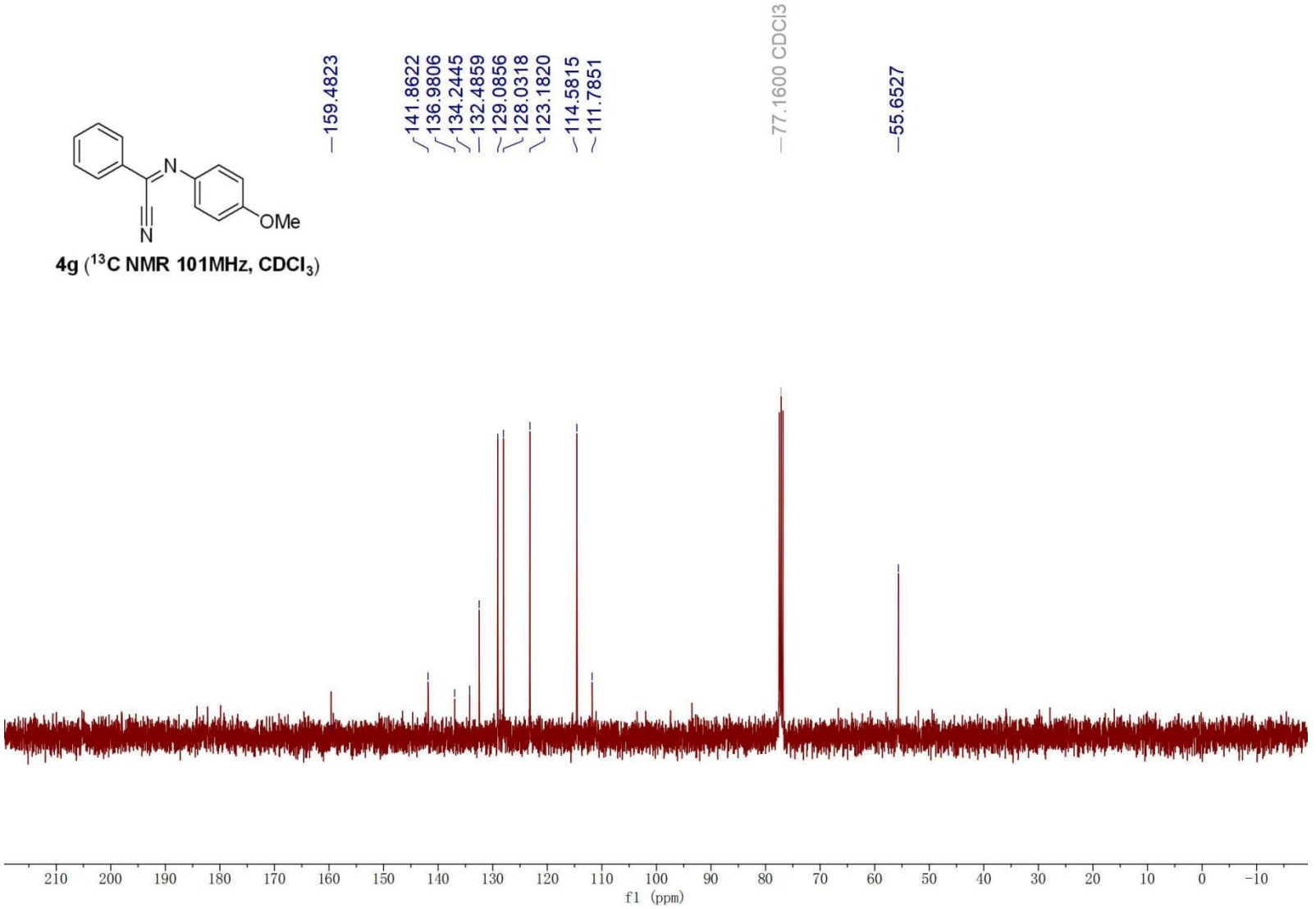




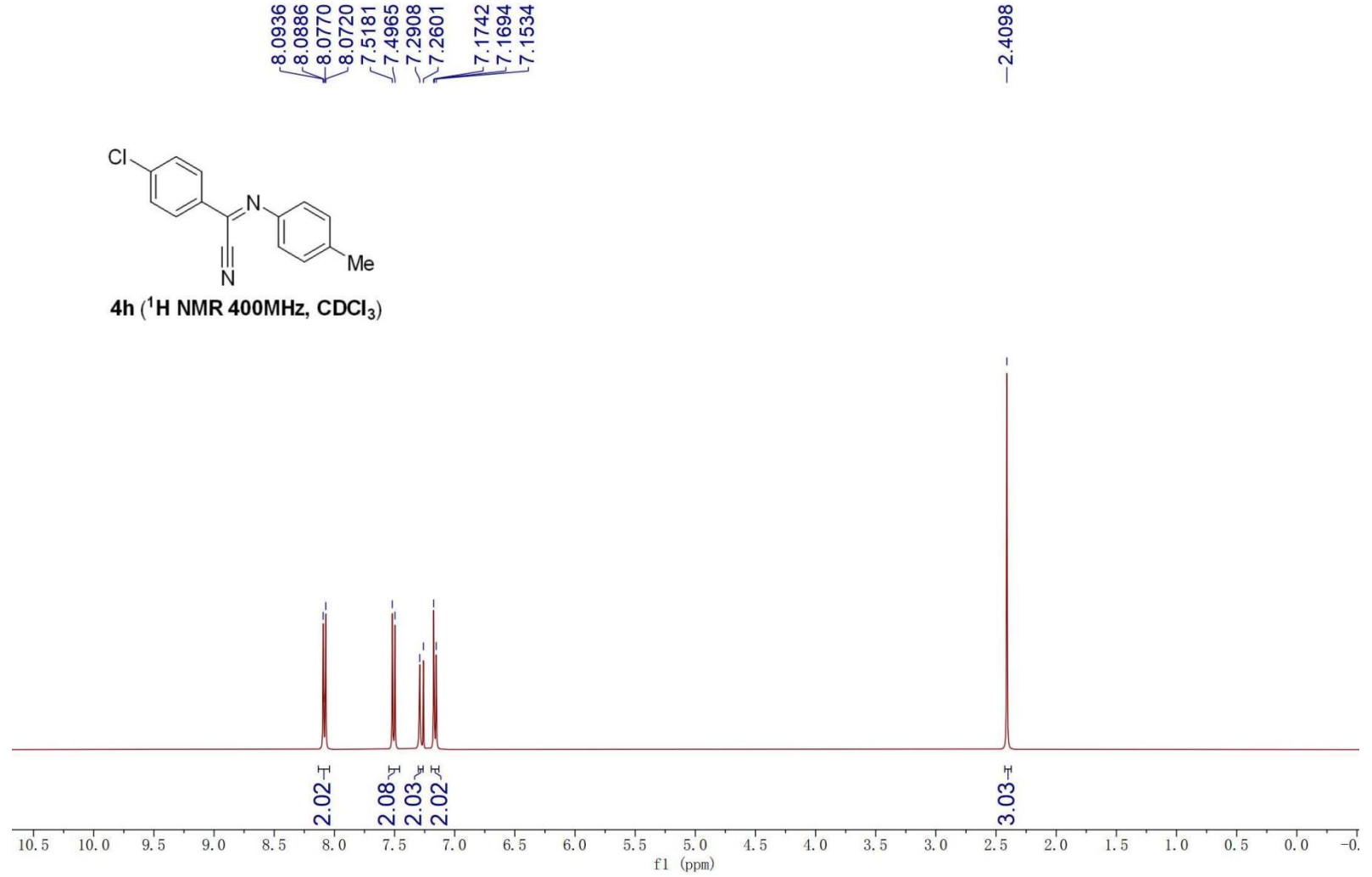
4f (^{13}C NMR 101MHz, $CDCl_3$)

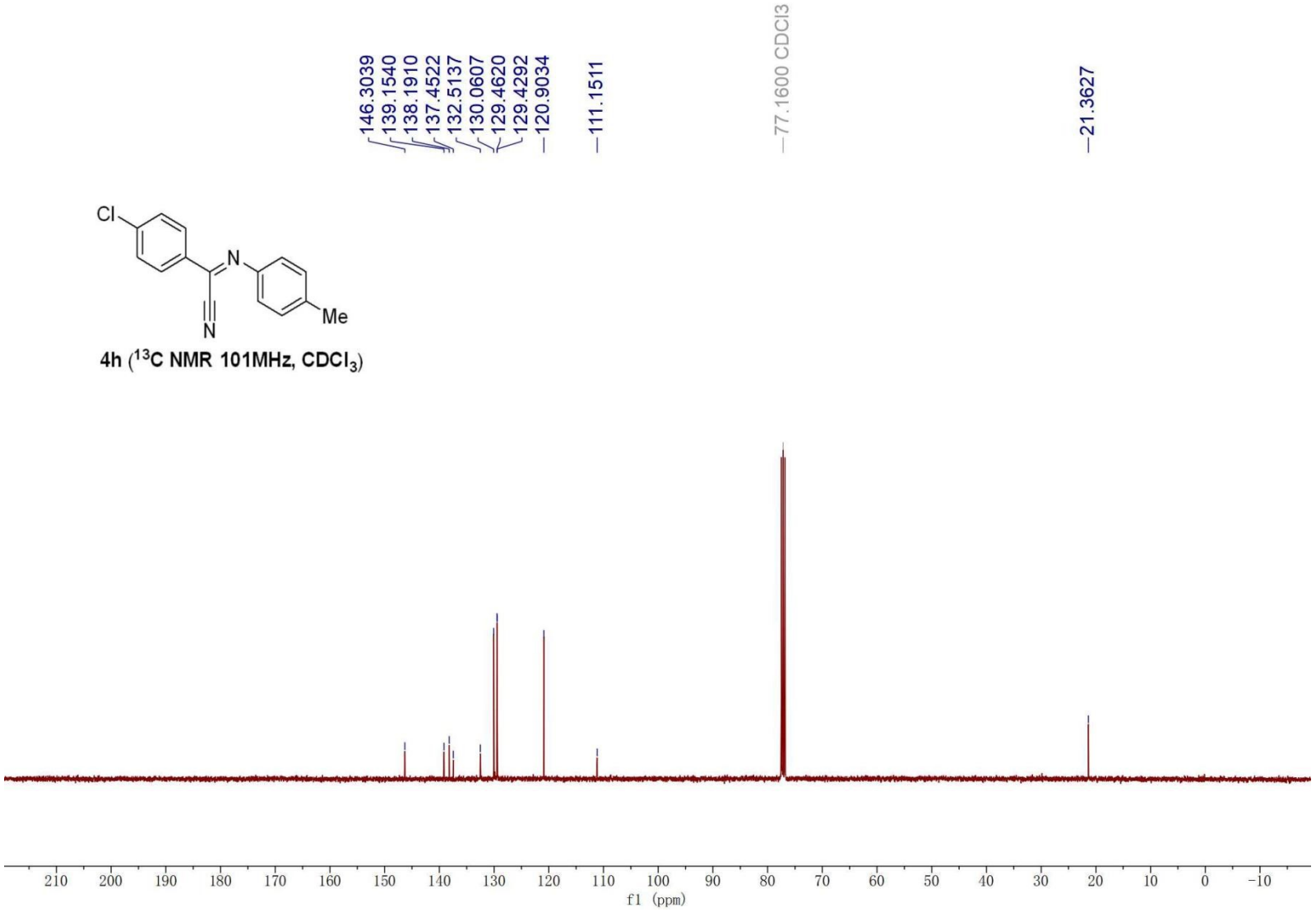


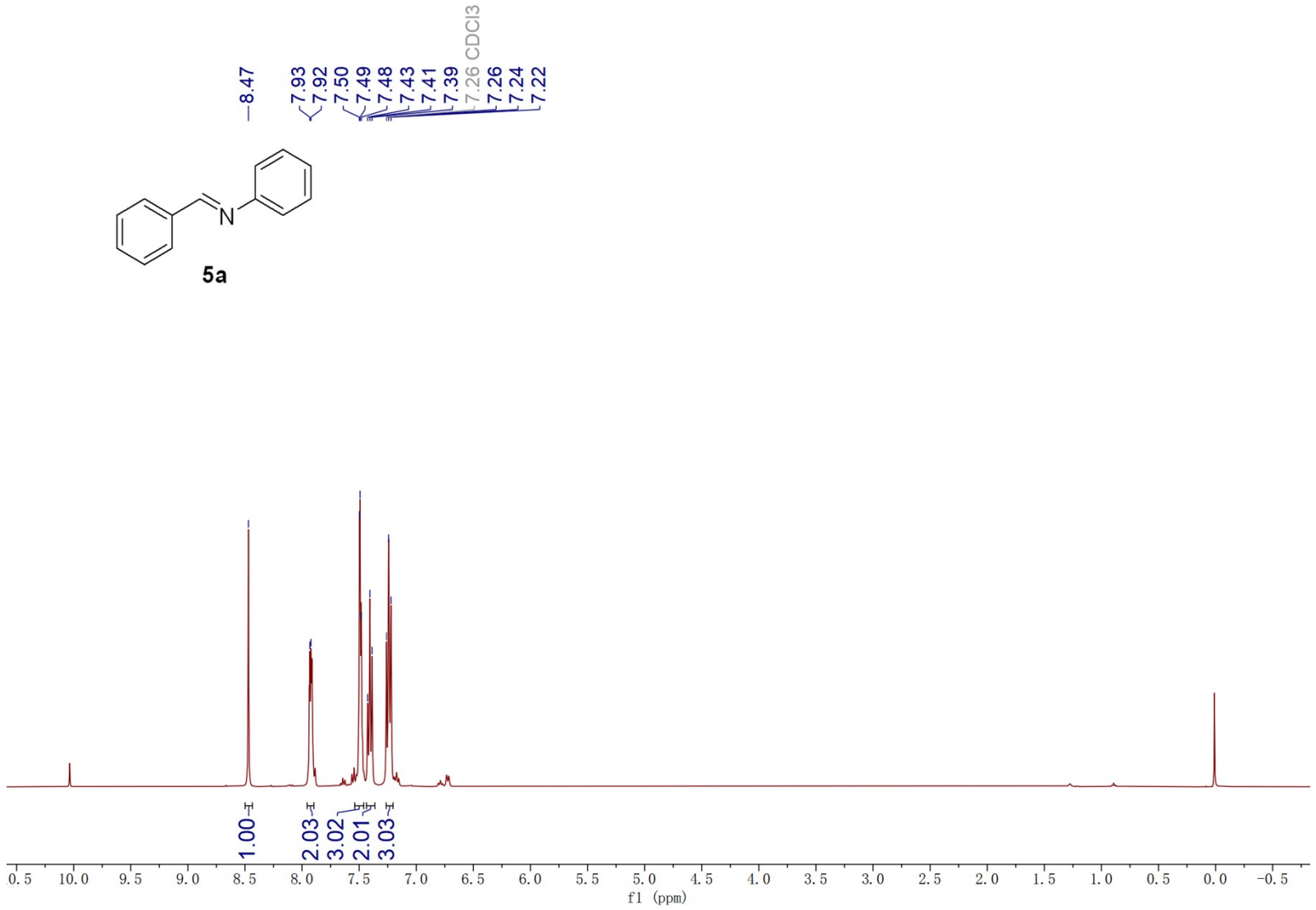
4g (^{1}H NMR 400MHz, $CDCl_3$)

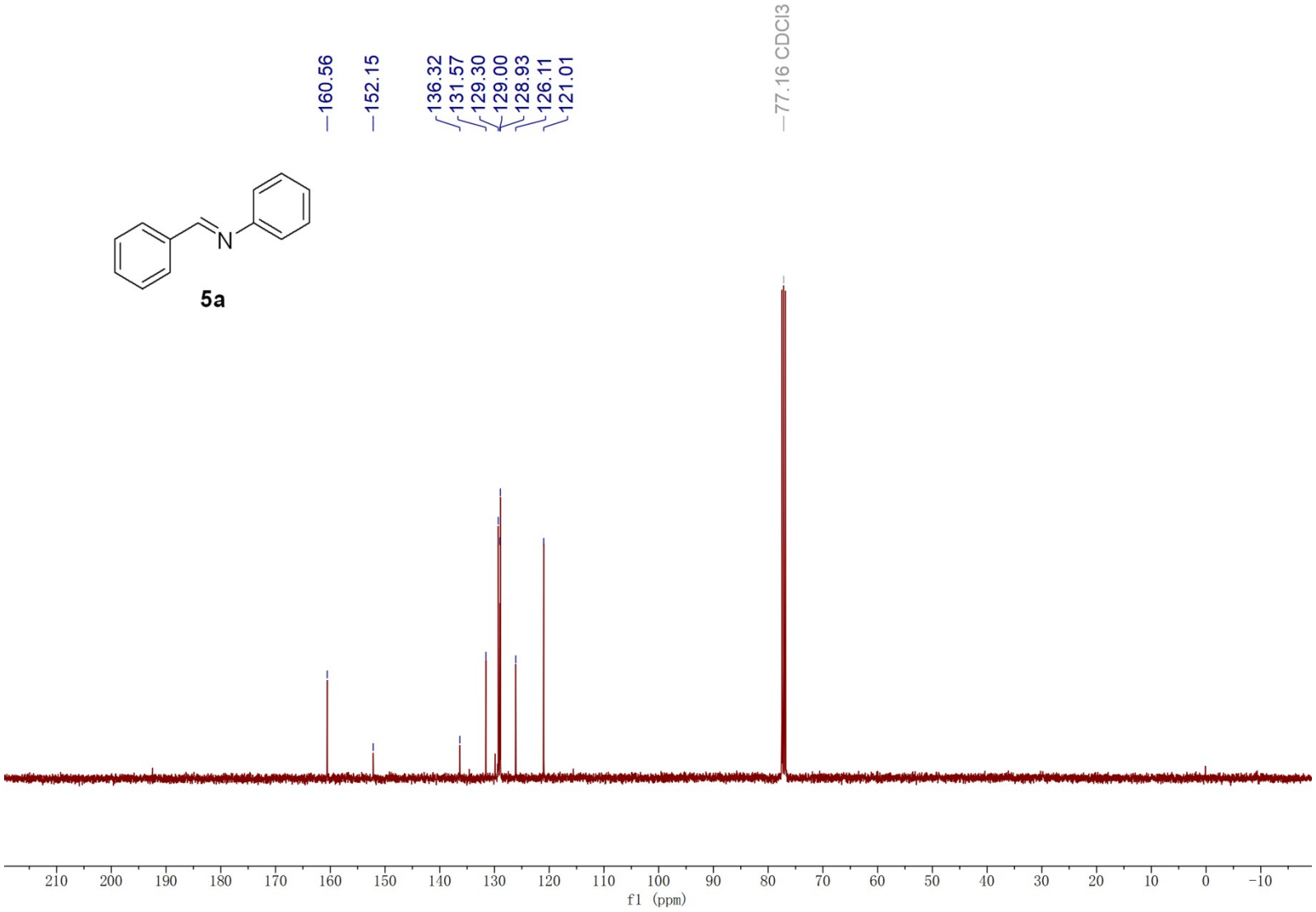


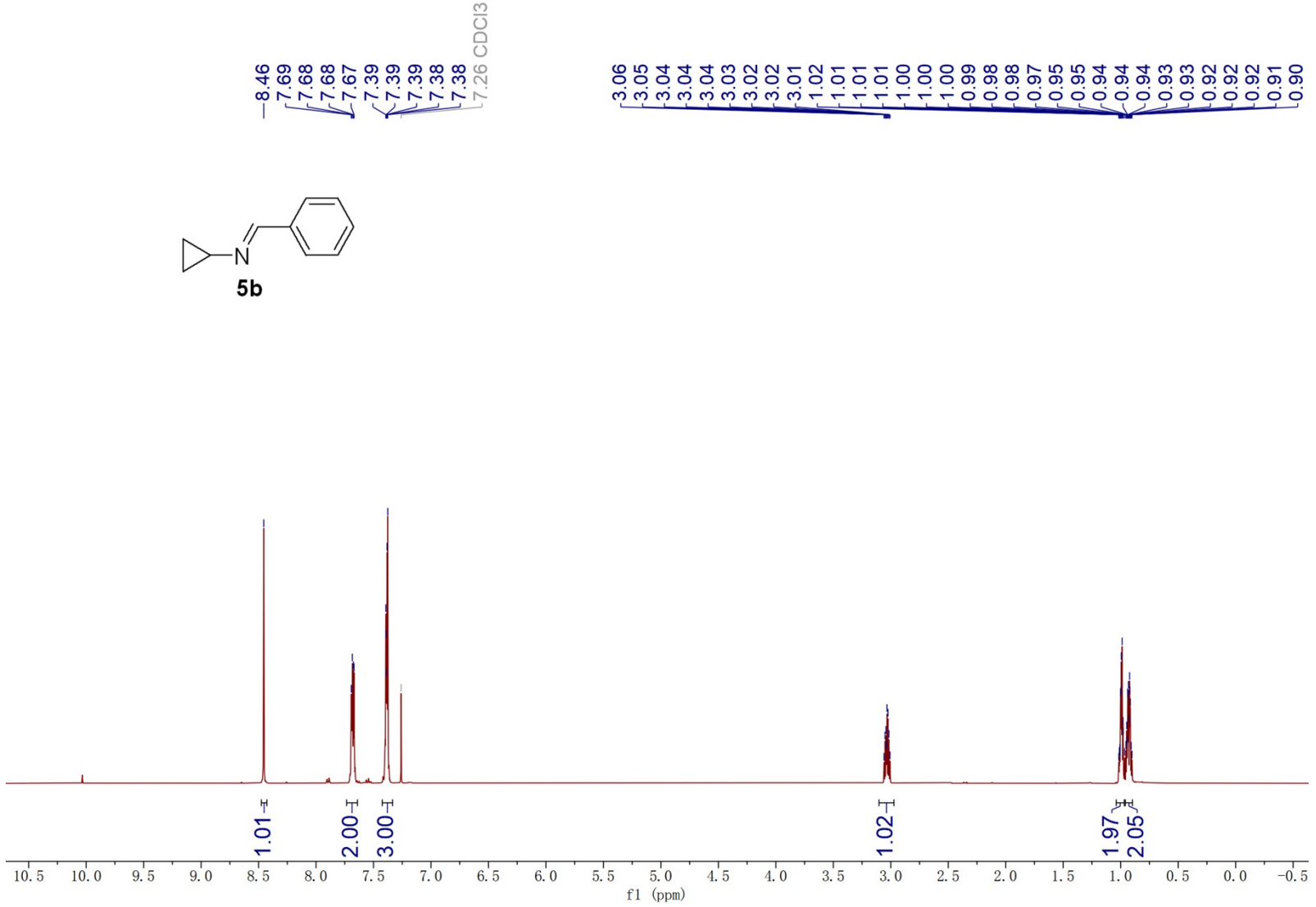
4g (^{13}C NMR 101MHz, $CDCl_3$)

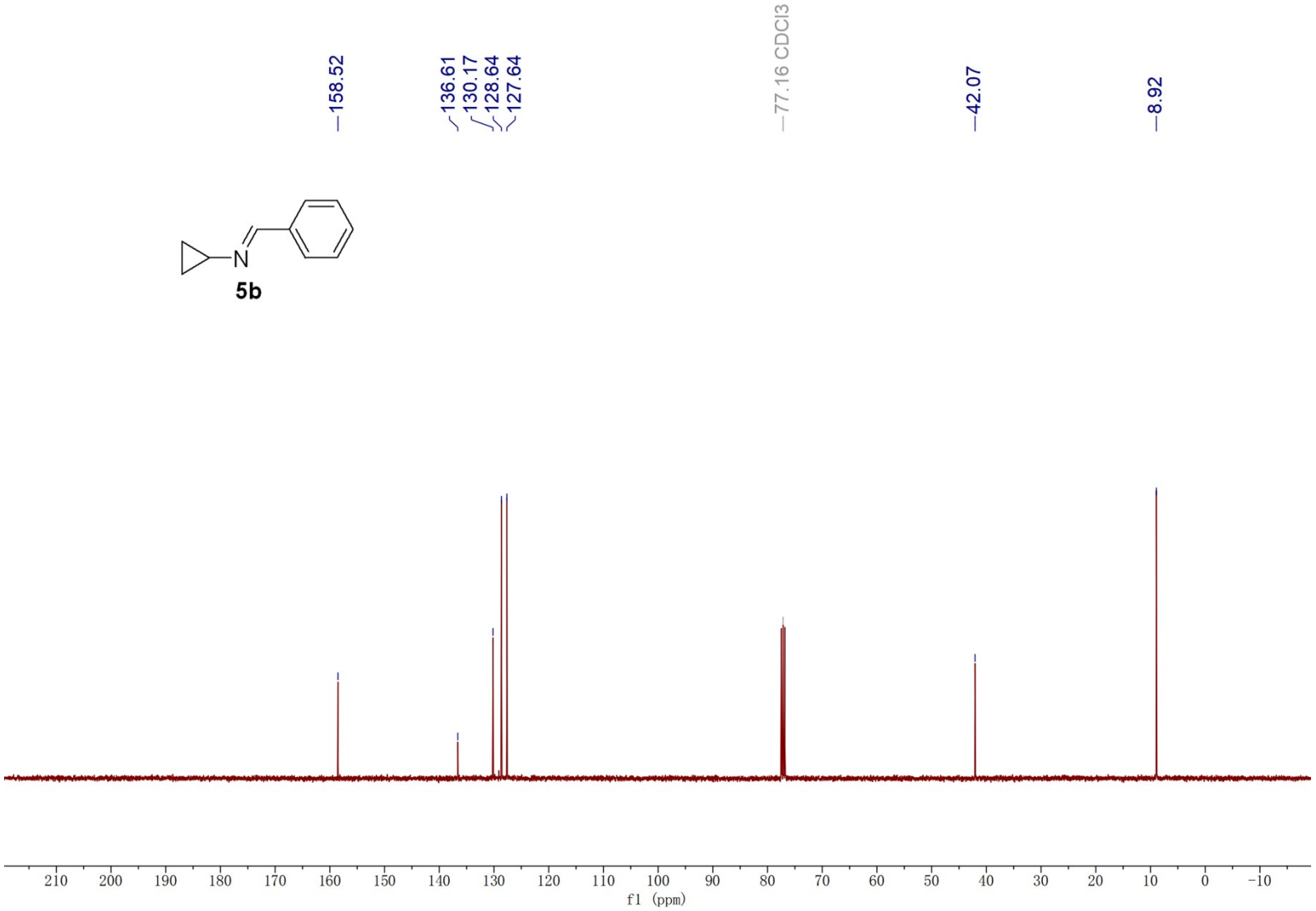

8.0936
8.0886
8.0770
8.0720
7.5181
7.4965
7.2908
7.2601
7.1742
7.1694
7.1534
2.4098
Cl
N
N
Me
4h (1H NMR 400MHz, CDCl3)
2.02
2.08
2.03
2.02
3.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)


146.3039
139.1540
138.1910
137.4522
132.5137
130.0607
129.4620
129.4292
120.9034
111.1511
77.1600 CDCl3
21.3627
Cl
N
N
Me
4h (^{13}C NMR 101MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


8.47
7.93
7.92
7.50
7.49
7.48
7.43
7.41
7.39
7.26 CDCl3
7.26
7.24
7.22
N
5a
1.00
2.03
3.02
2.01
3.03
f1 (ppm)


160.56
152.15
136.32
131.57
129.30
129.00
128.93
126.11
121.01
77.16 CDCl3
N
5a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.46
7.69
7.68
7.68
7.67
7.39
7.39
7.39
7.38
7.38
7.26 CDCl3
3.06
3.05
3.04
3.04
3.04
3.03
3.02
3.02
3.01
1.02
1.01
1.01
1.01
1.00
1.00
1.00
0.99
0.98
0.98
0.97
0.95
0.95
0.94
0.94
0.94
0.93
0.93
0.92
0.92
0.92
0.91
0.90
N
5b
1.01
2.00
3.00
1.02
1.97
2.05
10.5 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 −0.5
f1 (ppm)


158.52
136.61
130.17
128.64
127.64
77.16 CDCl3
42.07
8.92
N
5b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)