Supporting Information

TMEDA-Catalyzed Synthesis of Pentasubstituted 2-Aminopyrroles from Ynehydrazides and Dialkyl Acetylenedicarboxylates

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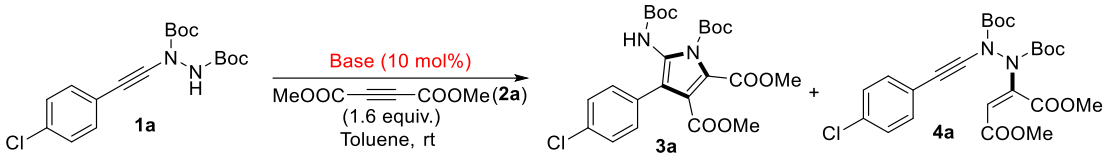
I. General considerations

Reagents. Unless otherwise indicated, all reactions were carried out in Schlenk tube under an argon atmosphere with dry solvents. Anhydrous MeCN was purchased from Alfa Aesar and used as received. Ether/THF was dried and purified by distillation from sodium/benzophenone. CH_2Cl_2 were distilled from CaH_2. $CuCl_2$ was purchased from Aladdin. Other copper catalysts were purchased from Alfa Aesar, Strem, Aladdin or JK Chemical and used as received. All other reagents were purchased from commercial sources and used as received. For reactions that require heating, oil bath was used as the heat source. All ynehydrazides were synthesized according to our previously reported procedure and Batey's conditions, the NMR data were consistant with the related literature.[1],[2]

Analytical Methods. All new compounds were characterized by ^1H NMR, ^{13}C NMR, and HRMS. NMR spectra were recorded on a Bruker AV-400 instrument in $CDCl_3$. All ^1H NMR spectra are reported in ppm downfield from tetramethylsilane (0 ppm). All ^{13}C NMR spectra are reported in ppm relative to residual $CHCl_3$ (77.0 ppm). Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Flash column chromatography was performed over silica gel (200-300 mesh) using petroleum ether and ethyl acetate as the eluent. Reactions were monitored by thin-layer chromatography (TLC) carried out on commercial silica gel plates (GF254) using UV light as a visualizing agent. Flash chromatography was performed on silica gel 60 (200-300 mesh). High-resolution mass spectra (HRMS; (ESI)) were acquired with quadrupole and time-of-flight (TOF) mass spectrometers.

II. Optimization of reaction conditions

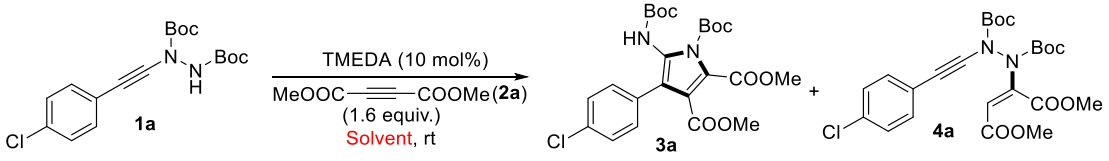
Table S1. Catalyst screening



Entry	Catalyst	Reaction time (h)	Yield of **3a**(**4a**)[a]
1	DABCO	1	47%(10%)
2	**TMEDA**	**1**	**85%(7%)**
3	NEt_3	3	trace
4	DMAP	3	26%(28%)
5	K_2CO_3	3	trace
6	NaOAc	3	16%(10%)
7	-	1	0

[a]0.2 mmol scale experiment, yields were determined by ^{1}H NMR using 4-nitroacetophenone as internal standard, the yield of **4a** in parentheses.

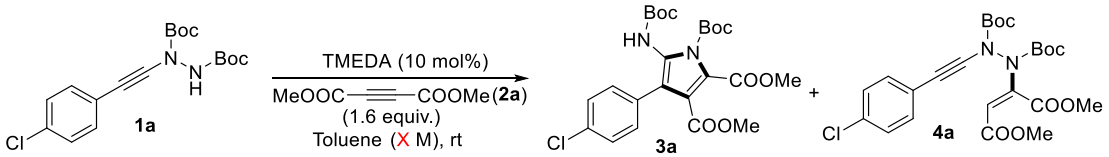
Table S2. Solvent screening



Entry	Solvent	Reaction time (h)	Yield of **3a**(**4a**)[a]
1	DCM	1	79%(7%)
2	Xylene	1	83%(7%)
3	MeCN	1	38%(32%)
4	**Toluene**	**1**	**85%(7%)**
5	THF	2.5	70%(8%)

[a]0.2 mmol scale experiment, yields were determined by ^{1}H NMR using 4-nitroacetophenone as internal standard, the yield of **4a** in parentheses.

Table S3. Reaction concentration

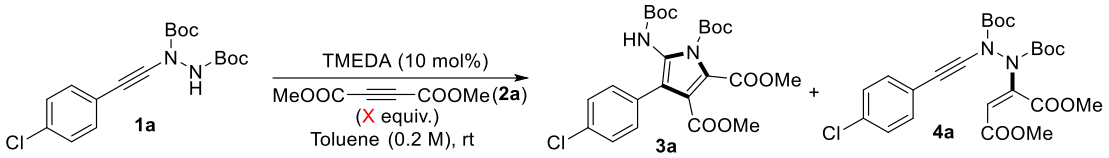


Entry	X	Reaction time (h)	Yield of **3a**(**4a**)[a]
1	0.4	1	84%(7%)

2	**0.2**	**1**	**85%(7%)**
3	0.1	2.5	83%(10%)

[a]0.2 mmol scale experiment, yields were determined by ^{1}H NMR using 4-nitroacetophenone as internal standard, the yield of **4a** in parentheses.

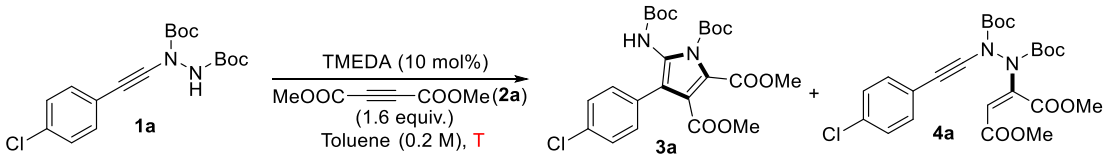
Table S4. Equivalent of dimethyl acetylenedicarboxylate



Entry	X	Reaction time (h)	Yield of **3a**(**4a**)[a]
1	0.8	1	56%(6%)
2	1.4	1	81%(7%)
3	**1.6**	**1**	**85%(7%)**
4	2.0	1	82%(10%)

[a]0.2 mmol scale experiment, yields were determined by ^{1}H NMR using 4-nitroacetophenone as internal standard, the yield of **4a** in parentheses.

Table S5. Reaction temperature



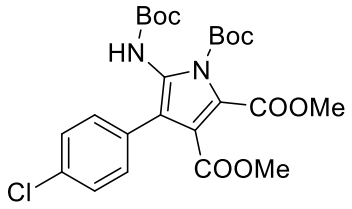
Entry	T (°C)	Reaction time (h)	Yield of **3a**(**4a**)[a]
1	50	1	80%(12%)
2	**rt**	**1**	**85%(7%)**
3	0	5	84%(7%)

[a]0.2 mmol scale experiment, yields were determined by ^{1}H NMR using 4-nitroacetophenone as internal standard, the yield of **4a** in parentheses.

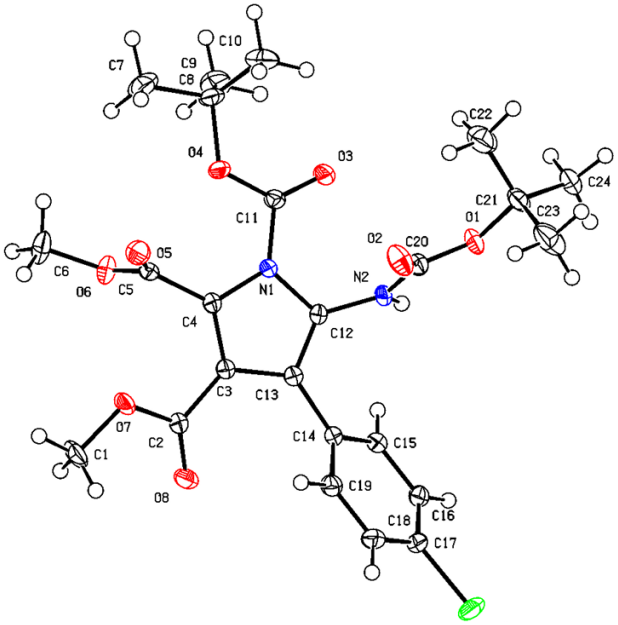
III. General procedure for the synthesis of pentasubstituted 2-aminopyrroles

General Procedure: In a 15 mL resealable screw-cap test tube, ynehydrazide (0.2 mmol, 1.0 equiv.), toluene (1.0 mL), dimethyl acetylenedicarboxylate (45.5 mg, 0.32 mmol, 1.6 equiv.), *N*,*N*,*N*',*N*'-tetramethylethylenediamine (TMEDA, 2.3 mg, 0.02 mmol, 10 mol%) were added successively. The reaction mixture is stirred rapidly at room temperature until completion, subsequently diluted with ethyl acetate (4.0 mL), followed by the addition of saturated aqueous water (4.0 mL). The aqueous layer was extracted with ethyl acetate (3 × 6 mL). The combined organic layer was washed with brine (5.0 mL), dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography (silica gel, 200~300 mesh) or preparative TLC to afford the related pentasubstituted 2-aminopyrroles.

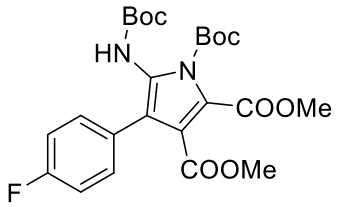
IV. Characterization data for the products



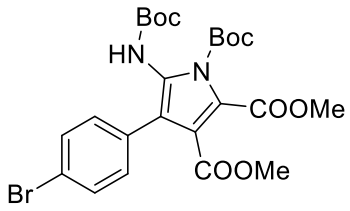
1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3a): The representative procedure was followed using di-*tert*-butyl 1-((4-chlorophenyl)ethynyl)hydrazine-1,2-dicarboxylate (73.4 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3a** (84.6 mg, 83% yield) as a white solid, m.p. 146.4-148.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.28 (s, 1H, -N*H*), 3.92 (s, 3H), 3.68 (s, 3H), 1.58 (s, 9H), 1.33 (br s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.4, 162.0, 153.0, 147.2, 133.4, 131.0, 130.4, 128.0, 125.7, 125.3, 121.0, 116.9, 86.9, 81.4, 52.8, 51.9, 27.9, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{30}ClN_2O_8$ 509.1685, found 509.1688.



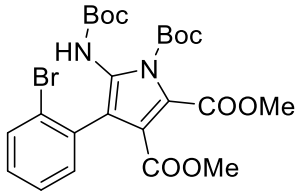
X-Ray structure of 4a (CCDC 2502084)



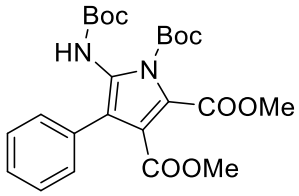
1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-fluorophenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3b): The representative procedure was followed using di-*tert*-butyl 1-((4-fluorophenyl)ethynyl)hydrazine-1,2-dicarboxylate (70.1 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3b** (74.2 mg, 75% yield) as a white solid, m.p. 156.2-157.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 2H), 7.03 (dd, *J* = 8.4, 8.4 Hz, 2H), 6.30 (s, 1H, -N*H*), 3.91 (s, 3H), 3.67 (s, 3H), 1.57 (s, 9H), 1.32 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.5, 162.2 (d, *J* = 244.8 Hz), 162.1, 153.1, 147.2, 131.4 (d, *J* = 8.1 Hz), 127.8 (d, *J* = 3.3 Hz), 125.6, 125.3, 121.2, 117.1, 114.8 (d, *J* = 21.3 Hz), 86.9, 81.3, 52.8, 51.9, 28.0, 27.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.83 (s); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{30}FN_2O_8$ 493.1981, found 493.1982.



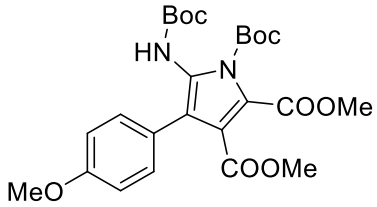
2,3-Dibenzyl 1-(*tert*-butyl) 4-(4-bromophenyl)-5-((*tert*-butoxycarbonyl)amino)-1*H*-pyrrole-1,2,3-tricarboxylate (3c): The representative procedure was followed using di-*tert*-butyl 1-((4-bromophenyl)ethynyl)hydrazine-1,2-dicarboxylate (82.3 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3c** (90.7 mg, 82% yield) as a white solid, m.p. 140.6-141.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 6.32 (s, 1H, -N*H*), 3.91 (s, 3H), 3.67 (s, 3H), 1.56 (s, 9H), 1.32 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.4, 162.0, 153.0, 147.1, 131.3, 130.93, 130.86, 125.7, 125.2, 121.6, 120.9, 116.8, 86.9, 81.4, 52.8, 51.9, 27.9, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{30}BrN_2O_8$ 553.1180, found 553.1184.



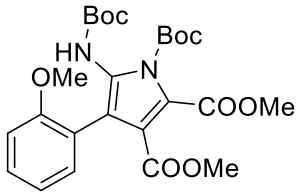
1-(*tert*-Butyl) 2,3-dimethyl 4-(2-bromophenyl)-5-((*tert*-butoxycarbonyl)amino)-1*H*-pyrrole-1,2,3-tricarboxylate (3d): The representative procedure was followed using di-*tert*-butyl 1-((2-bromophenyl)ethynyl)hydrazine-1,2-dicarboxylate (82.3 mg, 0.2 mmol). Upon stirring at room temperature for 2 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 8:1 petroleum ether:ethyl acetate) to afford **3d** (90.3 mg, 81% yield) as a white solid, m.p. 132.7-134.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.0 Hz, 1H), 7.33-7.27 (m, 2H), 7.22-7.13 (m, 1H), 6.16 (s, 1H, -N*H*), 3.93 (s, 3H), 3.60 (s, 3H), 1.57 (s, 9H), 1.33 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.9, 162.4, 153.2, 147.0, 133.3, 132.1, 132.0, 129.1, 126.8, 126.7, 125.0, 124.6, 121.6, 115.9, 86.7, 81.1, 52.9, 51.7, 28.0, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{30}BrN_2O_8$ 553.1180, found 553.1183.



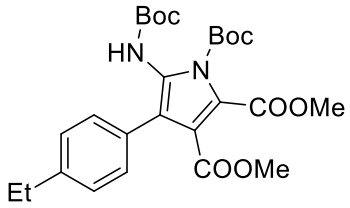
1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-phenyl-1*H*-pyrrole-1,2,3-tricarboxylate (3e): The representative procedure was followed using di-*tert*-butyl 1-(phenylethynyl)hydrazine-1,2-dicarboxylate (66.5 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 12:1 petroleum ether:ethyl acetate) to afford **3e** (70.0 mg, 74% yield) as a white solid. m.p. 147.6-149.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.27 (m, 5H), 6.25 (s, 1H, -N*H*), 3.91 (s, 3H), 3.66 (s, 3H), 1.57 (s, 9H), 1.31 (br s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.7, 162.1, 153.2, 147.3, 131.8, 129.6, 127.9, 127.4, 125.2, 122.0, 117.6, 86.7, 81.2, 52.8, 51.9, 28.0, 27.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{31}N_2O_8$ 475.2075, found 475.2074.



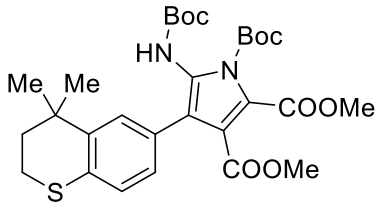
1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-methoxyphenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3f): The representative procedure was followed using di-*tert*-butyl 1-((4-methoxyphenyl)ethynyl)hydrazine-1,2-dicarboxylate (72.5 mg, 0.2 mmol). Upon stirring at room temperature for 1.5 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 8:1 petroleum ether:ethyl acetate) to afford **3f** (81.1 mg, 80% yield) as a white solid, m.p. 141.5-143.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.0 Hz, 2H), 6.23 (s, 1H, -N*H*), 3.91 (s, 3H), 3.81 (s, 3H), 3.68 (s, 3H), 1.57 (s, 9H), 1.34 (br s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.8, 162.1, 158.9, 153.3, 147.2, 130.8, 125.2, 125.0, 124.0, 121.8, 117.5, 113.3, 86.5, 81.1, 55.2, 52.7, 51.8, 27.9, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{32}N_2O_9$ 505.2181, found 505.2179.



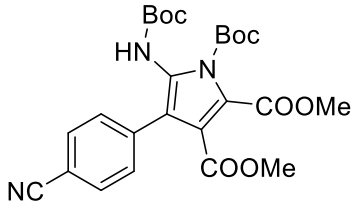
1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(2-methoxyphenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3g): The representative procedure was followed using di-*tert*-butyl 1-((2-methoxyphenyl)ethynyl)hydrazine-1,2-dicarboxylate (72.5 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 4:1 petroleum ether:ethyl acetate) to afford **3g** (80.3 mg, 79% yield) as a yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (ddd, *J* = 8.4, 8.4, 2.0 Hz, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 6.89 (dd, *J* = 8.4, 8.4, 2.0 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.16 (s, 1H, -N*H*), 3.83 (s, 3H), 3.68 (s, 3H), 3.56 (s, 3H), 1.49 (s, 9H), 1.28 (br s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.6, 162.2, 156.8, 153.5, 147.1, 131.3, 129.0, 125.4, 125.3, 120.7, 120.2, 117.7, 110.6, 86.1, 80.9, 55.4, 52.6, 51.5, 28.0, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{33}N_2O_9$ 505.2181, found 505.2183.



1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-ethylphenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3h): The representative procedure was followed using di-*tert*-butyl 1-((4-ethylphenyl)ethynyl)hydrazine-1,2-dicarboxylate (72.1 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 9:1 petroleum ether:ethyl acetate) to afford **3h** (82.7 mg, 82% yield) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.26 (s, 1H), 3.91 (s, 3H), 3.68 (s, 3H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.57 (s, 9H), 1.36-1.28 (m, 9H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.8, 162.0, 153.3, 147.2, 143.3, 129.4, 128.9, 127.3, 125.1, 125.0, 121.9, 117.6, 86.5, 81.1, 52.7, 51.8, 28.6, 27.9, 27.5, 15.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{35}N_2O_8$ 503.2388, found 503.2396.

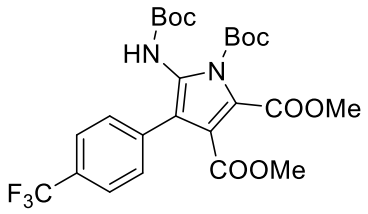


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4,4-dimethylthiochroman-6-yl)-1*H*-pyrrole-1,2,3-tricarboxylate (3i): The representative procedure was followed using di-*tert*-butyl 1-((4,4-dimethylthiochroman-6-yl)ethynyl)hydrazine-1,2-dicarboxylate (86.5 mg, 0.2 mmol). Upon stirring at room temperature for 40 min, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3i** (86.8 mg, 75% yield) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 1.6 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.99 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.16 (s, 1H, -N*H*), 3.89 (s, 3H), 3.68 (s, 3H), 3.06-2.97 (m, 2H), 1.99-1.92 (m, 2H), 1.56 (s, 9H), 1.39-1.25 (m, 15H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.0, 161.9, 153.5, 147.2, 141.3, 131.0, 128.1, 127.3, 127.1, 126.0, 125.1, 121.9, 117.9, 86.5, 81.3, 52.7, 51.9, 37.7, 33.0, 30.3, 29.7, 28.0, 27.5, 23.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{29}H_{39}N_2O_8S$ 575.2422, found 575.2424.

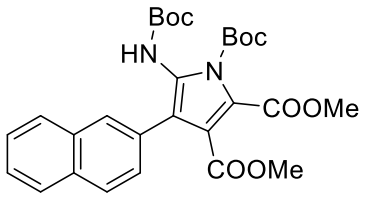


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-cyanophenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3j): The representative procedure was followed using di-*tert*-butyl 1-((4-cyanophenyl)ethynyl)hydrazine-1,2-dicarboxylate (71.5 mg, 0.2 mmol). Upon stirring at room temperature for 50 min, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 4:1 petroleum ether:ethyl acetate) to afford **3j** (33.2 mg, 33% yield) as a white solid, m.p. 178.8-179.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 6.53 (s, 1H, -N*H*), 3.91 (s, 3H), 3.67 (s, 3H), 1.57 (s, 9H), 1.29 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1, 162.0, 152.5, 147.1, 137.3,

131.5, 130.5, 126.1, 125.8, 119.9, 119.0, 116.4, 110.9, 87.5, 81.6, 52.9, 52.0, 27.9, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{30}N_3O_8$ 500.2027, found 500.2029.

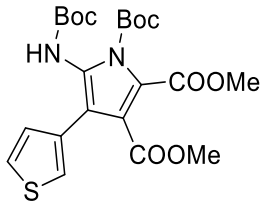


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-(trifluoromethyl)phenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3k): The representative procedure was followed using di-*tert*-butyl 1-((4-(trifluoromethyl)phenyl)ethynyl)hydrazine-1,2-dicarboxylate (80.1 mg, 0.2 mmol). Upon stirring at room temperature for 50 min, the reaction mixture was worked up and purified by preparative TLC (silica gel, eluted with 3:1 petroleum ether:ethyl acetate) to afford **3k** (64.0 mg, 59% yield) as a white solid, m.p. 142.3-144.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 6.47 (s, 1H, -N*H*), 3.93 (s, 3H), 3.68 (s, 3H), 1.58 (s, 9H), 1.30 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.3, 162.0, 152.8, 147.1, 135.9, 130.1, 129.3 (q, J = 32.3 Hz), 125.9, 125.6, 124.7 (q, J = 3.7 Hz), 124.2 (q, J = 270.3 Hz), 120.6, 116.7, 87.2, 81.4, 52.8, 51.9, 27.8, 27.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.56 (s); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{30}F_3N_2O_8$ 543.1949, found 543.1951.

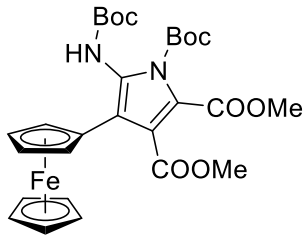


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(naphthalen-2-yl)-1*H*-pyrrole-1,2,3-tricarboxylate (3l): The representative procedure was followed using di-*tert*-butyl 1-(naphthalen-2-ylethynyl)hydrazine-1,2-dicarboxylate (76.5 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 8:1 petroleum ether:ethyl acetate) to afford **3l** (82.0 mg, 78% yield) as a white solid, m.p. 155.6-156.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.77 (m, 4H), 7.53-7.37 (m, 3H), 6.27 (s, 1H, -N*H*), 3.93 (s, 3H), 3.65 (s, 3H), 1.59 (s, 9H), 1.29 (br s,

9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.7, 162.1, 153.4, 147.3, 133.1, 132.6, 129.4, 128.4, 128.1, 127.9, 127.6, 127.2, 126.0, 125.9, 125.6, 125.4, 122.2, 117.5, 86.8, 81.3, 52.8, 51.9, 28.0, 27.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{33}N_2O_8$ 525.2231, found 525.2232.

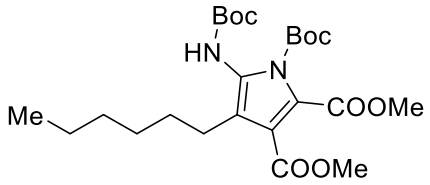


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(thiophen-3-yl)-1*H*-pyrrole-1,2,3-tricarboxylate (3m): The representative procedure was followed using di-*tert*-butyl 1-(thiophen-2-ylethynyl)hydrazine-1,2-dicarboxylate (67.7 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 12:1 petroleum ether:ethyl acetate) to afford **3m** (66.4 mg, 69% yield) as a white solid, m.p. 138.0-139.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.32-7.24 (m, 1H), 7.14 (d, J = 4.8 Hz, 1H), 6.37 (s, 1H, -N*H*), 3.90 (s, 3H), 3.73 (s, 3H), 1.57 (s, 9H), 1.35 (br s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.8, 161.8, 153.1, 147.2, 131.3, 128.8, 125.4, 124.8, 124.3, 123.9, 117.8, 116.8, 86.7, 81.3, 52.7, 52.0, 28.0, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{29}N_2O_8S$ 481.1639, found 481.1642.

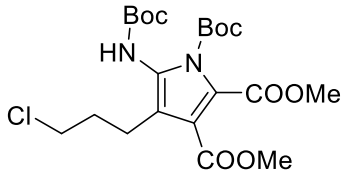


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-ferrocenyl-1*H*-pyrrole-1,2,3-tricarboxylate (3n): The representative procedure was followed using di-*tert*-butyl 1-(ferrocenylethynyl)hydrazine-1,2-dicarboxylate (88.1 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3n** (96.7 mg, 83% yield) as a brown solid, m.p. 167.7-169.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.52 (br s, 1H, -N*H*), 4.55 (s, 2H), 4.23 (s, 2H), 4.08 (s, 5H), 3.89 (s, 3H), 3.86 (s, 3H), 1.71-1.09 (m, 18H); $^{13}C\{^{1}H\}$ NMR

(100 MHz, $CDCl_3$) δ 165.1, 161.0, 152.8, 147.3, 125.3, 122.2, 120.7, 116.7, 86.2, 81.4, 76.4, 70.4, 69.1, 68.2, 52.4, 52.2, 28.1, 27.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{35}FeN_2O_8$ 583.1737, found 583.1734.

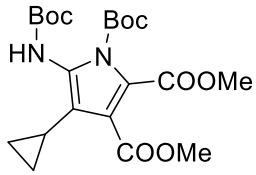


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-hexyl-1*H*-pyrrole-1,2,3-tricarboxylate (3o): The representative procedure was followed using di-*tert*-butyl 1-(oct-1-yn-1-yl)hydrazine-1,2-dicarboxylate (102.1 mg, 0.3 mmol). Upon stirring at room temperature for 1.5 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3o** (118.2 mg, 82% yield) as a colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 6.19 (br s, 1H, -N*H*), 3.88 (s, 3H), 3.78 (s, 3H), 2.54 (t, *J* = 7.6 Hz, 2H), 1.54 (s, 9H), 1.50-1.38 (m, 11H), 1.33-1.21 (m, 6H), 0.86 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.6, 163.0, 153.7, 147.2, 127.2, 124.1, 123.4, 115.5, 86.2, 81.0, 52.7, 51.6, 31.6, 29.7, 29.2, 28.1, 27.6, 24.2, 22.6, 14.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{39}N_2O_8$ 483.2701, found 483.2711.

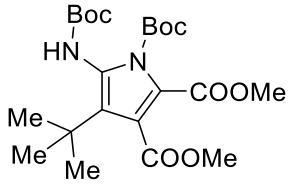


2,3-Dibenzyl 1-(*tert*-butyl) 5-((*tert*-butoxycarbonyl)amino)-4-(3-chloropropyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3p): The representative procedure was followed using di-*tert*-butyl 1-(5-chloropent-1-yn-1-yl)hydrazine-1,2-dicarboxylate (66.6 mg, 0.2 mmol). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 8:1 petroleum ether:ethyl acetate) to afford **3p** (78.8mg, 83% yield) as a colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 6.31 (br s, 1H, -N*H*), 3.88 (s, 3H), 3.78 (s, 3H), 3.50 (t, *J* = 6.4 Hz, 2H), 2.71 (t, *J* = 6.4 Hz, 2H), 1.99 (tt, *J* = 6.4, 6.4 Hz, 2H), 1.53 (s, 9H), 1.45 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.4, 162.8, 153.7, 147.0,

127.6, 124.7, 121.3, 115.0, 86.5, 81.2, 52.8, 51.7, 44.8, 32.0, 28.1, 27.5, 21.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{32}ClN_2O_8$ 475.1842, found 475.1845.

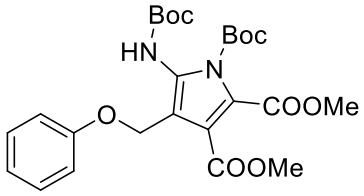


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-cyclopropyl-1*H*-pyrrole-1,2,3-tricarboxylate (3q): The representative procedure was followed using di-*tert*-butyl 1-(cyclopropylethynyl)hydrazine-1,2-dicarboxylate (88.9 mg, 0.3 mmol). Upon stirring at room temperature for 1.5 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 8:1 petroleum ether:ethyl acetate) to afford **3q** (114.1 mg, 87% yield) as a white solid, m.p. 119.4-121.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (br s, 1H, -N*H*), 3.88 (s, 3H), 3.83 (s, 3H), 1.84-1.75 (m, 1H), 1.55 (s, 9H), 1.49 (s, 9H), 0.81-0.72 (m, 2H), 0.52-0.48 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.8, 162.5, 152.7, 147.5, 126.2, 124.5, 120.3, 119.0, 86.5, 81.0, 52.6, 51.7, 28.1, 27.5, 6.9, 5.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{31}N_2O_8$ 439.2075, found 439.2076.

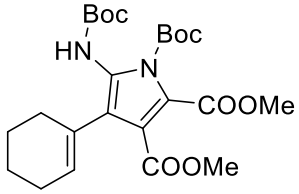


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(*tert*-butyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3r): The representative procedure was followed using 1-(3,3-dimethylbut-1-yn-1-yl)hydrazine-1,2-dicarboxylate (62.5 mg, 0.2 mmol) and dimethyl acetylenedicarboxylate (71.0 mg, 0.5 mmol, 2.5 equiv.). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3r** (75.8 mg, 83% yield) as a white solid, m.p. 176.1-177.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.09 (br s, 1H, -N*H*), 3.84 (s, 3H), 3.81 (s, 3H), 1.54 (s, 9H), 1.45 (s, 9H), 1.31 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.3, 160.1, 153.9,

147.6, 128.1, 124.5, 122.4, 120.3, 85.6, 81.1, 52.4, 52.1, 32.4, 30.4, 28.1, 27.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{35}N_2O_8$ 455.2388, found 455.2390.

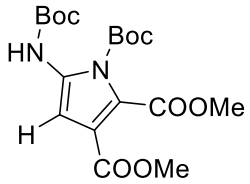


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(phenoxymethyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3s): The representative procedure was followed using di-*tert*-butyl 1-(3-phenoxyprop-1-yn-1-yl)hydrazine-1,2-dicarboxylate (72.5 mg, 0.2 mmol). Upon stirring at room temperature for 40 min, the reaction mixture was worked up and purified by preparative TLC (silica gel, eluted with 3:1 petroleum ether:ethyl acetate) to afford **3s** (49.4 mg, 49% yield) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, J = 7.2, 7.2 Hz, 2H), 7.02-6.75 (m, 4H), 5.07 (s, 2H), 3.87 (s, 3H), 3.71 (s, 3H), 1.54 (s, 9H), 1.42 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2, 162.2, 158.7, 152.9, 147.3, 129.3, 127.0, 126.3, 120.7, 116.2, 114.8, 114.6, 87.0, 81.5, 60.7, 52.8, 51.9, 28.1, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{33}N_2O_9$ 505.2181, found 505.2179.

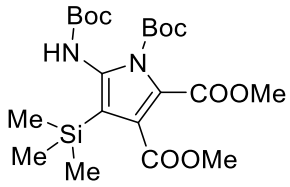


1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(cyclohex-1-en-1-yl)-1*H*-pyrrole-1,2,3-tricarboxylate (3t): The representative procedure was followed using di-*tert*-butyl 1-(cyclohex-1-en-1-ylethynyl)hydrazine-1,2-dicarboxylate (67.3 mg, 0.2 mmol). Upon stirring at room temperature for 1.5 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3t** (86.7 mg, 91% yield) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (s, 1H, -N*H*), 5.57 (s, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 2.21-2.12 (m, 2H), 2.12-2.03 (m, 2H), 1.73-1.56 (m, 4H), 1.52 (s, 9H), 1.42 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.6, 162.5, 153.3, 147.3,

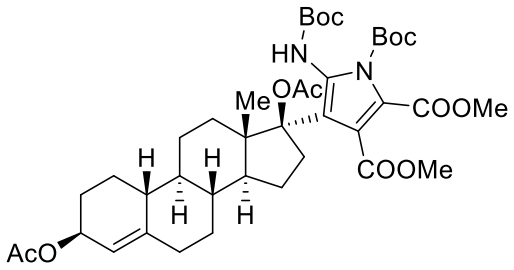
129.9, 127.2, 125.5, 124.6, 124.0, 116.7, 86.3, 80.8, 52.7, 51.8, 28.6, 28.1, 27.5, 25.5, 22.9, 22.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{35}N_2O_8$ 479.2388, found 479.2385.



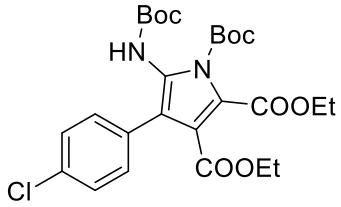
1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-1*H*-pyrrole-1,2,3-tricarboxylate (3u): The representative procedure was followed using di-*tert*-butyl 1-ethynylhydrazine-1,2-dicarboxylate (76.9 mg, 0.3 mmol). Upon stirring at room temperature for 40 min, the reaction mixture was worked up and purified by preparative TLC (silica gel, 12:1 petroleum ether:ethyl acetate) to afford **3u** (61.2 mg, 51% yield) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H, -N*H*), 6.65 (s, 1H), 3.88 (s, 3H), 3.77 (s, 3H), 1.55 (s, 9H), 1.49 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.2, 162.7, 151.2, 149.2, 131.8, 122.4, 118.5, 96.7, 87.8, 81.3, 52.7, 51.7, 28.1, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{27}N_2O_8$ 399.1762, found 399.1765.



1-(*tert*-Butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(trimethylsilyl)-1*H*-pyrrole-1,2,3-tricarboxylate (3v): The representative procedure was followed using di-*tert*-butyl 1-((trimethylsilyl)ethynyl)hydrazine-1,2-dicarboxylate (65.7 mg, 0.2 mmol). Upon stirring at room temperature for 2 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **3v** (75.2 mg, 80% yield) as a white solid, m.p. 133.2-134.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 1H, -N*H*), 3.87 (s, 3H), 3.80 (s, 3H), 1.55 (s, 9H), 1.47 (s, 9H), 0.24 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.6, 162.4, 153.7, 147.5, 132.4, 126.7, 122.5, 115.3, 86.4, 81.1, 52.6, 51.6, 28.2, 27.5, -0.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{35}N_2O_8Si$ 471.2157, found 471.2156.

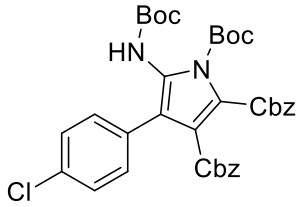


Ethynodiol diacetate derivative (3w): The representative procedure was followed using ethynodiol diacetate derivatived ynehydrazide (123 mg, 0.2 mmol). Upon stirring at room temperature for 4 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 2:1 petroleum ether:ethyl acetate) to afford **3w** (103.6 mg, 68% yield) as a white solid, m.p. 148.2-149.6 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.32-5.85 (m, 1H, -N*H*), 5.35-5.23 (m, 1H), 5.23-5.12 (m, 1H), 3.79 (br s, 6H), 3.05-2.73 (m, 1H), 2.33-2.13 (m, 1H), 2.11-0.82 (m, 44H), 0.71-0.46 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.8, 169.9, 165.9, 159.9, 154.3, 147.1, 144.9, 125.4, 122.3, 121.9, 121.7, 119.6, 90.2, 85.7, 81.0, 70.4, 52.2, 52.1, 49.3, 48.1, 45.6, 41.7, 41.3, 35.7, 35.0, 33.2, 31.2, 28.3, 27.7, 27.5, 27.2, 25.7, 24.8, 24.3, 21.5, 21.4, 14.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{40}H_{56}N_2O_{12}$ 757.3906, found 757.3908.

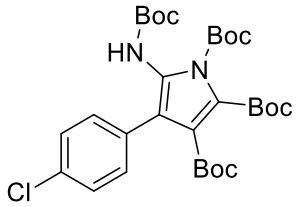


1-(*tert*-Butyl) 2,3-diethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (5a): The representative procedure was followed using di-*tert*-butyl 1-((4-chlorophenyl)ethynyl)hydrazine-1,2-dicarboxylate (73.4 mg, 0.2 mmol) and diethyl acetylenedicarboxylate (54.5 mg, 0.32 mmol, 1.6 equiv.). Upon stirring at room temperature for 1.5 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **5a** (88.3 mg, 82% yield) as a white solid, m.p. 136.5-137.7 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 6.28 (s, 1H), 4.36 (q, J = 7.2 Hz, 2H), 4.13 (q, J = 7.2 Hz, 2H), 1.57 (s, 9H), 1.37 (d, J = 7.2 Hz, 3H), 1.32 (s, 9H), 1.13 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)

δ 163.0, 161.5, 153.1, 147.2, 133.3, 131.1, 130.6, 128.0, 125.8, 125.0, 121.0, 117.2, 86.8, 81.3, 61.9, 60.8, 27.9, 27.5, 13.9, 13.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{34}ClN_2O_8$ 537.1998, found 537.1996.

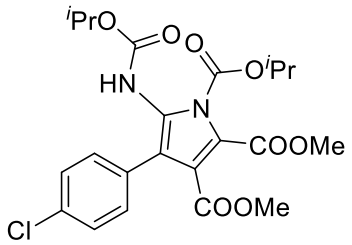


2,3-Dibenzyl 1-(*tert*-butyl) 5-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (5b): The representative procedure was followed using di-*tert*-butyl 1-((4-chlorophenyl)ethynyl)hydrazine-1,2-dicarboxylate (73.4 mg, 0.2 mmol), TMEDA (4.6 mg, 0.04 mmol, 0.2 equiv.) and dibenzyl acetylenedicarboxylate (94.2 mg, 0.32 mmol, 1.6 equiv.). Upon stirring at room temperature for 30 min, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 15:1 petroleum ether:ethyl acetate) to afford **5b** (97.2mg, 73% yield) as a brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.12 (m, 12H), 7.02-6.97 (m, 2H), 6.23 (s, 1H, -N*H*), 5.04 (s, 2H), 4.92 (s, 2H), 1.45 (s, 9H), 1.24 (br s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 161.2, 153.0, 147.2, 135.1, 134.9, 133.3, 131.0, 130.3, 128.4, 128.34, 128.31, 128.2, 128.1, 128.0, 125.4, 125.2, 121.1, 117.3, 86.9, 81.3, 67.8, 66.7, 27.9, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{36}H_{38}ClN_2O_8$ 661.2311, found 661.2310.



Tri-*tert*-butyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (5c): The representative procedure was followed using di-*tert*-butyl 1-((4-chlorophenyl)ethynyl)hydrazine-1,2-dicarboxylate (73.4 mg, 0.2 mmol), TMEDA (6.9 mg, 0.06 mmol, 0.3 equiv.) and di-*tert*-butyl acetylenedicarboxylate (72.4 mg, 0.32 mmol, 1.6 equiv.). Upon stirring at room temperature for 24 h, the reaction mixture was worked up and

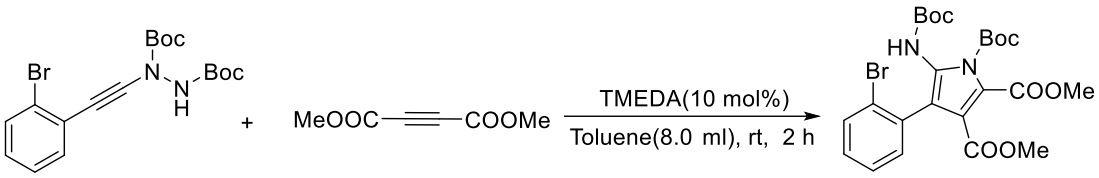
purified by flash chromatography (silica gel, eluted with 15:1 petroleum ether:ethyl acetate) to afford **5c** (47.5 mg, 40% yield) as a white solid, m.p. 172.6-173.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 6.20 (s, 1H, -N*H*), 1.59 (s, 9H), 1.58 (s, 9H), 1.35 (br s, 9H), 1.30 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6, 159.4, 153.3, 147.7, 133.1, 131.1, 131.0, 127.9, 124.7, 124.5, 121.0, 120.3, 86.1, 82.7, 81.5, 81.2, 28.0, 27.8, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{30}H_{42}ClN_2O_8$ 593.2624, found 593.2623.



2,3-Dimethyl 1-propyl 4-(4-chlorophenyl)-5-((propoxycarbonyl)amino)-1*H*-pyrrole-1,2,3-tricarboxylate (5d): The representative procedure was followed using dipropyl 1-((4-chlorophenyl)ethynyl)hydrazine-1,2-dicarboxylate (67.8 mg, 0.2 mmol) and TMEDA (2.3 mg, 0.02 mmol, 0.1 equiv.). Upon stirring at room temperature for 1 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 8:1 petroleum ether:ethyl acetate) to afford **5d** (70.4 mg, 73% yield) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 2H), 6.48 (s, 1H, -N*H*), 5.15 (hept, *J* = 6.4 Hz, 1H), 4.81 (hept, *J* = 6.4 Hz, 1H), 3.91 (s, 3H), 3.66 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 6H), 1.20-1.05 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1, 162.0, 153.9, 148.2, 133.5, 131.0, 130.0, 128.0, 126.4, 124.7, 121.8, 116.8, 74.2, 69.8, 52.9, 51.8, 21.7, 21.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{26}ClN_2O_8$ 481.1372, found 481.1381.

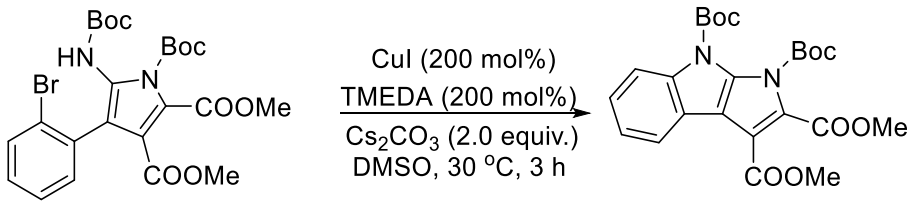
V. Synthetic applications

a. Gram-scale experiment:



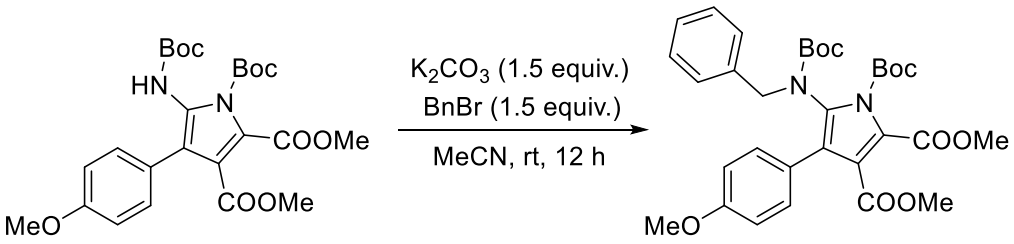
In a 25 mL round-bottomed flask, di-*tert*-butyl 1-((2-bromophenyl)ethynyl)hydrazine-1,2-dicarboxylate (658.1 mg, 1.6 mmol, 1.0 equiv.), toluene (8.0 ml), dimethyl acetylenedicarboxylate (363.8 mg, 2.56 mmol, 1.6 equiv.), TMEDA (18.5 mg, 0.16 mmol, 10 mol%) were added successively. The reaction mixture is stirred rapidly at room temperature for 2 h and diluted with ethyl acetate (15.0 mL), then saturated aq. water (20.0 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with brine (15.0 mL), dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography (eluted with 8:1 petroleum ether:ethyl acetate) to afford the **3d** (669 mg, 75%) as a white solid.

b. Synthetic applications:

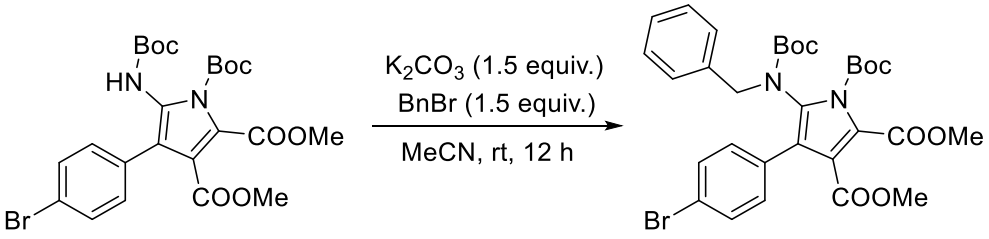


1,8-Di-*tert*-butyl 2,3-dimethyl pyrrolo[2,3-b]indole-1,2,3,8-tetracarboxylate (6): In a 15 mL oven-dried resealable screw-cap test tube, **3d** (110.7 mg, 0.2 mmol), cuprous iodide (76.2 mg, 0.4 mmol, 200 mol%) and cesium carbonate (130.4 mg, 0.4 mmol, 2.0 equiv.) were added. The tube was evacuated and backfilled with argon. Dimethyl sulfoxide (2.0 mL), TMEDA (46.4 mg, 0.4 mmol, 200 mol%) were added via syringe. The reaction mixture was stirred at 30 °C for 3 h, then quenched with water (6.0 mL) and extracted with ethyl acetate (3×10 mL). The combined organic phases were washed with brine (3×10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, eluted with 15:1 petroleum ether:ethyl acetate) to afford **6** (79.5 mg, 84% yield) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.95 (m, 1H), 7.92-7.85 (m, 1H), 7.28-7.19 (m, 2H),

3.90 (s, 6H), 1.58 (s, 9H), 1.54 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.5, 162.1, 149.5, 147.0, 139.8, 134.7, 128.5, 124.4, 123.6, 122.6, 121.2, 115.5, 111.4, 110.4, 86.7, 84.8, 52.9, 51.9, 28.1, 27.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{29}N_2O_8$ 473.1918, found 473.1924.

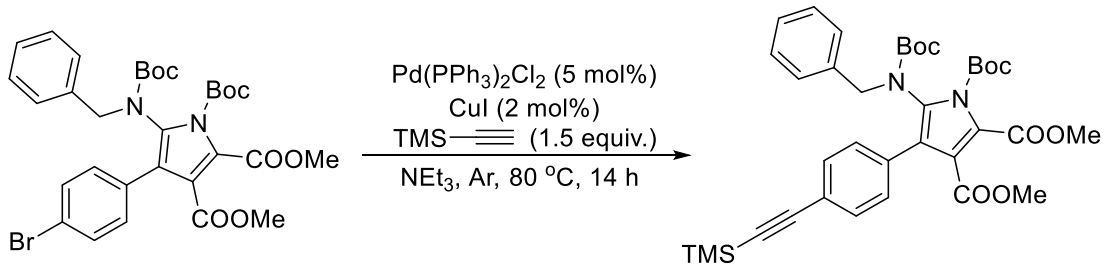


1-(*tert*-butyl) 2,3-dimethyl 5-(benzyl(*tert*-butoxycarbonyl)amino)-4-(4-methoxyphenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (7a): In a 15 mL oven-dried resealable screw-cap test tube, a mixture of **3f** (100.9 mg, 0.2 mmol) and benzyl bromide (51.3 mg, 0.3 mmol, 1.5 equiv.), potassium carbonate (41.5 mg, 0.3 mmol, 1.5 equiv.) in acetonitrile (1.0 mL) was prepared. The reaction was stirred at room temperature for 12 h. The reaction was diluted with water (5.0 mL) and extracted with ethyl acetate (3 ×10 mL). The combined organic phases were washed with brine (3×10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, eluted with 6:1 petroleum ether:ethyl acetate) to afford **7a** (105.4 mg, 88% yield) as a white solid, m.p. 144.5-146.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-6.67 (m, 9H), 4.62-4.50 (m, 1H), 4.23-4.09 (m, 1H), 3.93-3.88 (m, 3H), 3.83-3.78 (m, 3H), 3.63 (s, 3H), 1.52 (s, 9H), 1.50-1.43 (m, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.6, 162.4, 158.8, 155.1, 146.6, 136.0, 130.8, 130.5, 129.0, 128.3, 127.9, 127.8, 127.1, 126.9, 126.5, 123.6, 122.6, 116.6, 133.1, 86.3, 81.2, 55.1, 53.2, 52.7, 51.7, 28.3, 27.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{32}H_{39}N_2O_9$ 595.2650, found 595.2649.



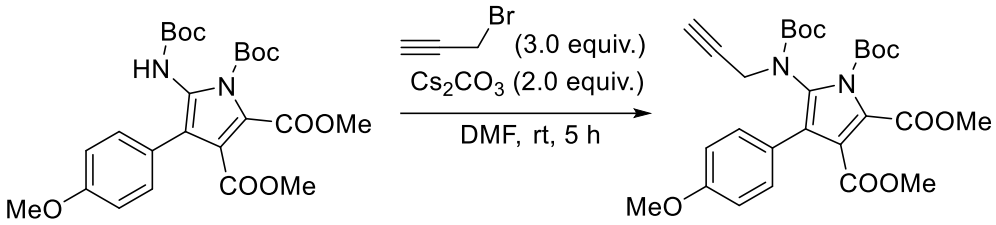
1-(*tert*-butyl) 2,3-dimethyl 5-(benzyl(*tert*-butoxycarbonyl)amino)-4-(4-bromophenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (7b): In a 15 mL oven-dried resealable screw-cap test tube, a mixture of **3c** (442.7 mg, 0.8 mmol) and benzyl bromide (205.2 mg, 1.2 mmol, 1.5 equiv.),

potassium carbonate (165.9 mg, 1.2 mmol, 1.5 equiv.) in acetonitrile (4.0 mL) was prepared. The reaction was stirred at room temperature for 12 h. The reaction was diluted with water (10.0 mL) and extracted with ethyl acetate (3 ×15 mL). The combined organic phases were washed with brine (3×10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, eluted with 9:1 petroleum ether:ethyl acetate) to afford **7b** (459.9 mg, 89% yield) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.19 (m, 2H), 7.16-7.06 (m, 1H), 7.06-6.97 (m, 2H), 6.87-6.79 (m, 2H), 6.71 (d, *J* = 8.4 Hz, 2H), 4.88-4.68 (m, 1H), 4.07-3.99 (m, 1H), 3.96-3.89 (m, 3H), 3.62 (s, 3H), 1.60-1.54 (m, 9H), 1.52-1.44 (m, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2, 162.3, 154.9, 146.6, 135.8, 131.3, 130.9, 130.6, 128.9, 128.3, 128.0, 127.9, 127.2, 122.2, 121.5, 115.8, 86.8, 81.4, 53.3, 52.9, 51.7, 28.3, 27.6; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{31}H_{35}BrN_2NaO_8$ 665.1469, found 665.1463.

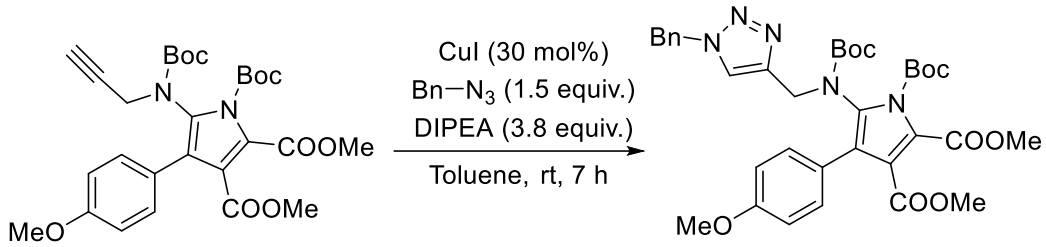


1-(*tert*-butyl) 2,3-dimethyl 5-(benzyl(*tert*-butoxycarbonyl)amino)-4-(4-((trimethylsilyl)ethynyl)phenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (8): In a 15 mL oven-dried resealable screw-cap test tube, **7b** (64.4 mg, 0.1 mmol), cuprous iodide (0.38 mg, 0.002 mmol, 2 mol%) and bis(triphenylphosphine)palladium(II) dichloride (3.5 mg, 0.005 mmol, 5 mol%) were added. The tube was evacuated and backfilled with argon. Triethylamine (1.0 mL) and ethynyltrimethylsilane (14.7 mg, 0.15 mmol, 1.5 equiv.) were added via syringe. The reaction mixture was stirred at 80 °C for 14 h, The reaction mixture was carefully filtered through the Celite, and washed with ethyl acetate (30 mL). The combined filtrates were concentrated under reduced pressure to obtain a crude product. The crude product was purified by flash chromatography (silica gel, eluted with 40:1 petroleum ether:ethyl acetate) to afford **8** (50.3 mg, 76% yield) as a yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.21 (m, 2H), 7.16 -7.08 (m, 1H), 7.07-6.98 (m, 2H), 6.97-6.69 (m, 4H), 4.73-4.54 (m, 1H), 4.12 (d, *J* = 14.4 Hz,

1H), 3.97-3.87 (m, 3H), 3.59 (s, 3H), 1.57-1.52 (m, 9H), 1.52-1.42 (m, 9H), 0.31-0.22 (m, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.3, 162.2, 155.3, 154.9, 146.6, 135.7, 131.8, 131.1, 129.5, 129.2, 129.1, 128.1, 127.3, 122.4, 121.9, 116.2, 105.1, 94.3, 86.6, 81.4, 53.2, 52.8, 51.7, 28.3, 27.6, 0.0; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{36}H_{44}N_2NaO_8Si$ 683.2759, found 683.2758.

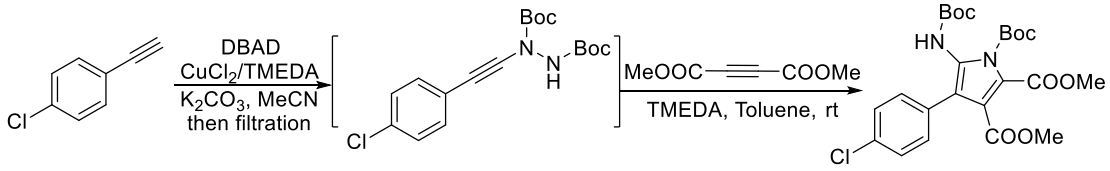


1-(*tert*-butyl) 2,3-dimethyl 5-((*tert*-butoxycarbonyl)(prop-2-yn-1-yl)amino)-4-(4-methoxyphenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (9): In a 15 mL oven-dried resealable screw-cap test tube, a mixture of **3f** (201.8 mg, 0.4 mmol) and propargyl bromide (142.7 mg, 1.2 mmol, 3.0 equiv.), cesium carbonate (260.6 mg, 0.8 mmol, 2.0 equiv.) in N,N-dimethylformamide (2.0 mL) was prepared. The reaction was stirred at room temperature for 5 h. The reaction was diluted with water (10 mL) and extracted with EtOAc (3 ×10 mL). The combined organic phases were washed with brine (3×10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, eluted with 8:1 petroleum ether:ethyl acetate) to afford **9** (181.7 mg, 83% yield) as a white solid, m.p. 110.3-111.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 2H), 6.91-6.83 (m, 2H), 4.28-4.00 (m, 1H), 3.97-3.85 (m, 4H), 3.82 (s, 3H), 3.71-3.65 (m, 3H), 2.07-1.95 (m, 1H, -C≡C*H*), 1.62-1.53 (m, 9H), 1.52-1.36 (m, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.5, 162.5, 159.1, 153.9, 146.8, 130.7, 127.8, 127.1, 123.6, 123.4, 116.0, 113.3, 86.4, 81.6, 77.6, 73.2, 55.1, 52.8, 51.7, 38.5, 28.2, 27.6; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{34}N_2NaO_9$ 565.2157, found 565.2157.



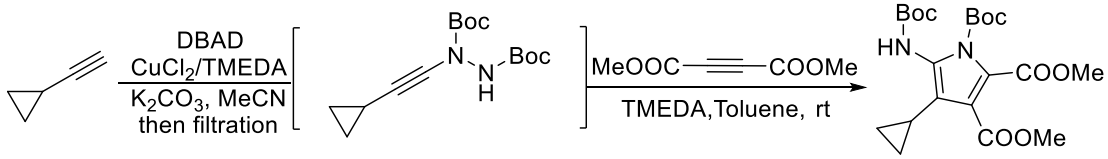
1-(*tert*-butyl) 2,3-dimethyl 5-(((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)(*tert*-butoxycarbonyl)amino)-4-(4-methoxyphenyl)-1*H*-pyrrole-1,2,3-tricarboxylate (10): In a 15 mL oven-dried resealable screw-cap test tube, a mixture of **9** (54.3 mg, 0.1 mmol) and benzyl azide (20.0 mg, 0.15 mmol, 1.5 equiv.), N,N-diisopropylethylamine (DIPEA, 49.1 mg, 0.38 mmol, 3.8 equiv.), cuprous iodide (5.7 mg, 0.03 mmol, 30 mol%) in toluene (1.0 mL) was prepared. The reaction was stirred at room temperature for 7 h. The reaction mixture was diluted with aqueous sodium bicarbonate solution (10 mL) and extracted with ethyl acetate (3 ×10 mL). The combined organic phases were washed with brine (3×10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, eluted with 2:1 petroleum ether:ethyl acetate) to afford **10** (57.9 mg, 85% yield) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 3H), 7.19-6.93 (m, 4H), 6.84-6.73 (m, 2H), 6.72-6.15 (m, 1H), 5.45-5.37 (m, 1H), 5.15-5.05 (m, 1H), 4.85-4.69 (m, 1H), 4.35-4.19 (m, 1H), 3.97-3.89 (m, 3H), 3.86-3.81 (m, 3H), 3.64 (s, 3H), 1.55 (s, 9H), 1.48-1.29 (m, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2, 162.3, 158.7, 154.9, 146.7, 143.8, 134.8, 134.6, 130.7, 128.9, 128.5, 127.8, 127.2, 124.0, 122.9, 122.8, 116.0, 112.9, 86.5, 81.5, 55.1, 53.7, 52.8, 51.7, 45.2, 28.3, 27.6; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{41}N_5NaO_9$ 698.2796, found 698.2788.

c. Direct synthesis of pyrrole from terminal alkynes:



In a 15 mL resealable screw-cap test tube, potassium carbonate (11.0 mg, 0.08 mmol, 0.2 equiv.), di-*tert*-butyl azodicarboxylate (138.4 mg, 0.6 mmol, 1.5 equiv.), 1-chloro-4-ethynylbenzene (54.6 mg, 0.4 mmol), cupric chloride anhydrous (10.8 mg, 0.08 mmol, 20 mol%) were added successively. The tube was evacuated and backfilled with argon (this

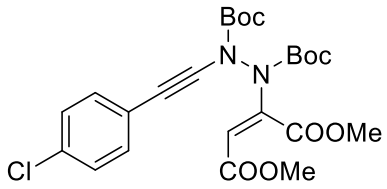
process was repeated for 3 times). Anhydrous MeCN (1.0 mL), TMEDA (9.3 mg, 0.08 mmol, 20 mol%) were added under argon atmosphere. The reaction mixture was stirred vigorously at 30 ºC for 6 h. The reaction mixture was carefully filtered through the silica gel under vacuum conditions, and washed with ethyl acetate (20 mL). The combined filtrates were concentrated under reduced pressure to obtain a crude product. The crude product was placed in a new tube, toluene (1.0 mL), dimethyl acetylenedicarboxylate (79.6 mg, 0.56 mmol, 1.4 equiv.), TMEDA (4.6 mg, 0.04 mmol, 10 mol%) were added successively. The reaction mixture is stirred rapidly at room temperature until the end of the reaction and diluted with ethyl acetate (4 mL), then saturated aq. water (4.0 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 6 mL). The combined organic layer was washed with brine (15.0 mL), dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by flash chromatography (eluted with 8:1 petroleum ether:ethyl acetate) to afford the **3a** (101.7 mg, 49%) as a white solid.



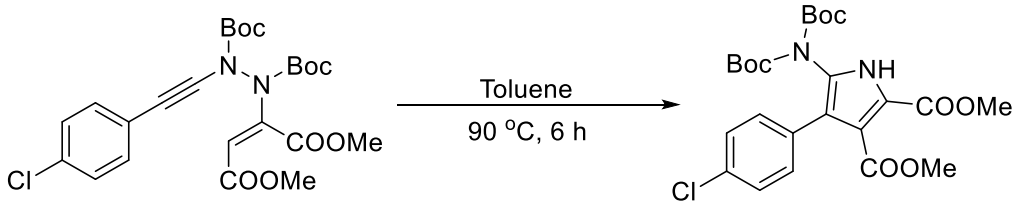
In a 15 mL resealable screw-cap test tube, potassium carbonate (11.0 mg, 0.08 mmol, 0.2 equiv.), di-*tert*-butyl azodicarboxylate (138.4 mg, 0.6 mmol, 1.5 equiv.), ethynylcyclopropane (26.4 mg, 0.4 mmol), cupric chloride anhydrous (10.8 mg, 0.08 mmol, 0.2 equiv.) were added successively. The tube was evacuated and backfilled with argon (this process was repeated for 3 times). Anhydrous MeCN (1.0 mL), TMEDA (9.3 mg 0.08 mmol, 20 mol%) were added under argon atmosphere. The reaction mixture was stirred vigorously at 30 ºC for 6 h. The reaction mixture was carefully filtered through the silica gel under vacuum conditions, and washed with ethyl acetate (20 mL). The combined filtrates were concentrated under reduced pressure to obtain a crude product. The crude product was placed in a new tube, toluene (1.0 mL), dimethyl acetylenedicarboxylate (79.6 mg, 0.56 mmol, 1.4 equiv.), TMEDA (4.6 mg, 0.04 mmol, 10 mol%) were added successively. The reaction mixture is stirred rapidly at room temperature until the end of the reaction and diluted with ethyl acetate (4.0 mL), then saturated aq. water (4.0 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 6 mL). The combined organic layer was washed with brine (15 mL), dried over Na_2SO_4, filtered, and

concentrated. The crude product was purified by flash chromatography (eluted with 8:1 petroleum ether:ethyl acetate) to afford the **3q** (84.9 mg, 48%) as a white solid.

VI. Mechanism studies

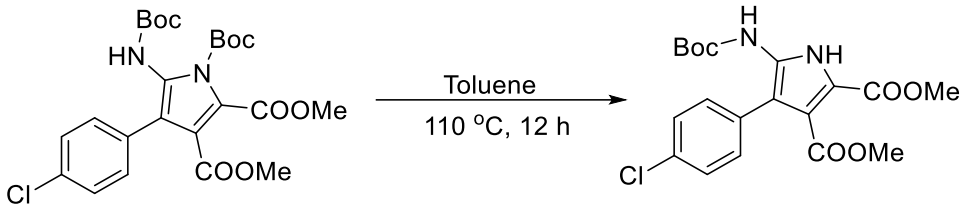


Di-*tert*-butyl (*E*)-1-((4-chlorophenyl)ethynyl)-2-(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)hydrazine-1,2-dicarboxylate (4a): The representative procedure was followed with the following modifications: di-*tert*-butyl 1-((4-chlorophenyl)ethynyl)hydrazine-1,2-dicarboxylate (73.4 mg, 0.2 mmol), cesium carbonate (6.5 mg, 0.02 mmol, 0.1 equiv.), ethyl acetate (1.0 mL) and dimethyl acetylenedicarboxylate (45.5 mg, 0.32 mmol, 1.6 equiv.). Upon stirring at room temperature for 3 h, the reaction mixture was worked up and purified by flash chromatography (silica gel, eluted with 10:1 petroleum ether:ethyl acetate) to afford **4a** (59 mg, 58% yield) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.18 (m, 4H), 5.69-5.53 (m, 1H), 3.85 (s, 3H), 3.65 (s, 3H), 1.56-1.35 (m, 18H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 165.4, 162.4, 150.5, 148.8, 144.0, 134.2, 132.8, 128.6, 120.4, 102.3, 85.7, 85.6, 80.3, 72.4, 53.0, 51.8, 27.8, 27.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{30}ClN_2O_8$ 509.1685, found 509.1692.

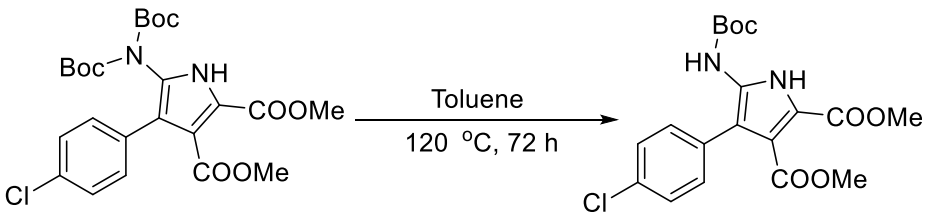


1,2-Bis(*tert*-butoxycarbonyl)-5-(4-chlorophenyl)-3,4-bis(methoxycarbonyl)-1*H*-pyrrole (11): In a 15 mL oven-dried resealable screw-cap test tube, **4a** (50.9 mg, 0.1 mmol) and toluene (1.0 mL) were mixed. The reaction was stirred at 90 °C for 6 h. After the reaction mixture was cooled to room temperature, the crude product was concentrated in vacuo and purified by flash

chromatography (silica gel, eluted with 4:1 petroleum ether:ethyl acetate) to afford **11** (33 mg, 65% yield) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18 (s, 1H, -N*H*), 7.33 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 3.91 (s, 3H), 3.76 (s, 3H), 1.32 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.5, 160.8, 150.0, 133.4, 130.5, 129.7, 128.7, 126.5, 120.4, 120.2, 117.9, 83.9, 52.5, 52.2, 27.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{30}ClN_2O_8$ 509.1685, found 509.1695.



Dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-1*H*-pyrrole-2,3-dicarboxylate (12): In a 15 mL oven-dried resealable screw-cap test tube, **3a** (50.9 mg, 0.1 mmol) and toluene (1.0 mL) were mixed. The reaction was stirred at 110 °C for 12 h. After the reaction mixture was cooled to room temperature, the crude product was concentrated in vacuo and purified by flash chromatography (silica gel, eluted with 6:1 petroleum ether:ethyl acetate) to afford **12** (33 mg, 81% yield) as a white solid, m.p. 147.5-149.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.68 (s, 1H, -N*H*), 7.39 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.84 (s, 1H, -N*H*Boc), 3.85 (s, 3H), 3.76 (s, 3H), 1.51 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7, 159.7, 152.5, 133.4, 130.4, 130.1, 129.3, 128.8, 120.8, 114.3, 108.1, 82.9, 52.3, 51.8, 28.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}ClN_2O_6$ 409.1161, found 409.1156.



Dimethyl 5-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-1*H*-pyrrole-2,3-dicarboxylate (12): In a 15 mL oven-dried resealable screw-cap test tube, **11** (10.2 mg, 0.02 mmol) and toluene (0.5 mL) were mixed. The reaction was stirred at 120 °C for 72 h. After the

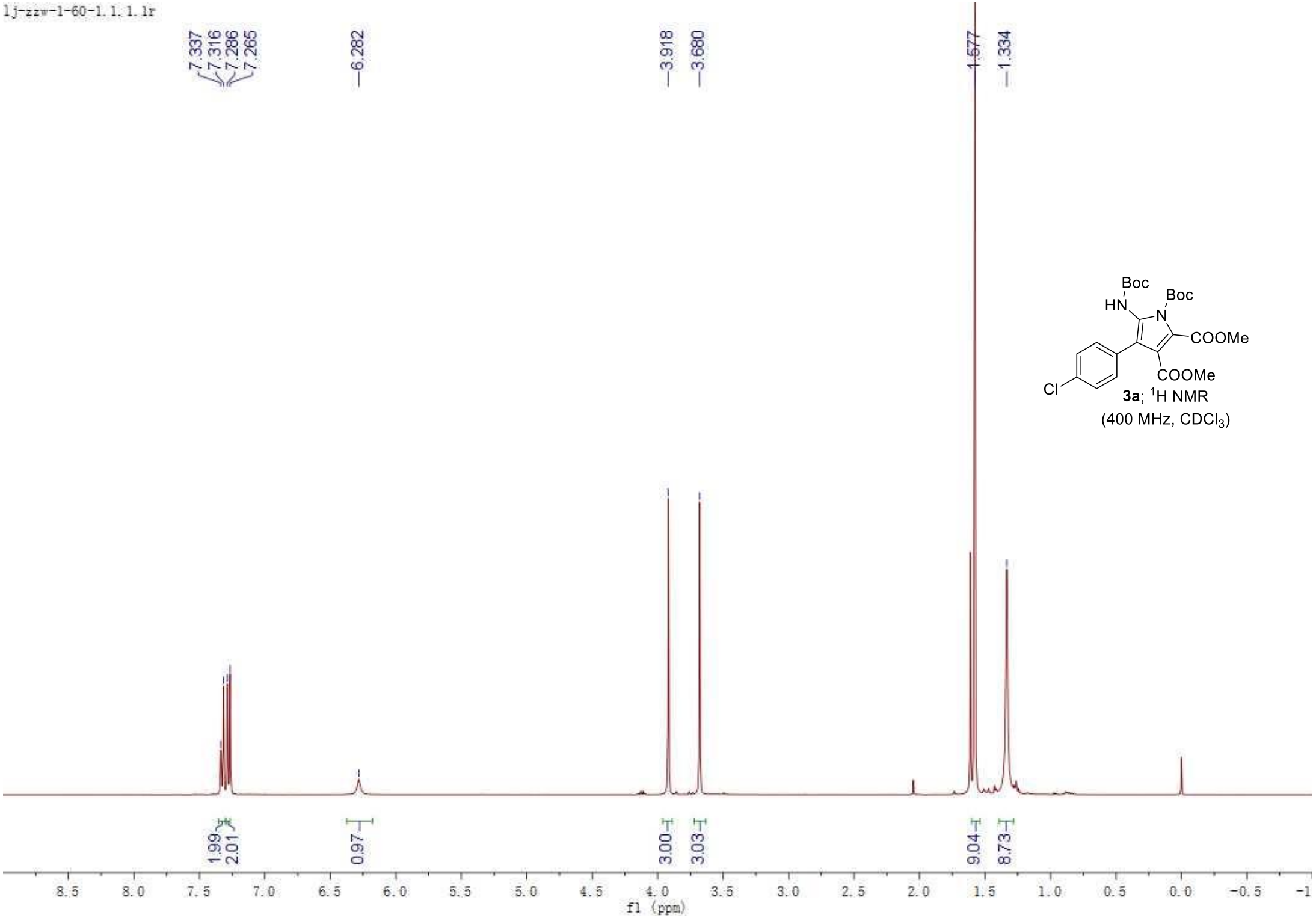
reaction mixture was cooled to room temperature, the mixture was diluted with ethyl acetate (15 mL) and 4-nitroacetophenone (3.3 mg, 0.02 mmol) was added. Crude ^{1}H NMR analysis indicated the formation of **9** in 74% yield.

VII. References

[1] Lei, J.; Sha, W.; Xie, X.; Weng, W.-T. *Org. Lett.* **2023**, *25*, 320.

[2] Beveridge, E. R.; Batey, R. A. *Org. Lett.* **2012**, *14*, 540.

VIII. Copies of NMR spectra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7.316
7.286
7.265
6.282
3.918
3.680
1.677
1.334
1.99
2.01
0.97
3.00
3.03
9.04
8.73
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
-1
f1 (ppm)
Boc
HN
Boc
N
COOMe
COOMe
Cl
3a; 1H NMR
(400 MHz, CDCl3)

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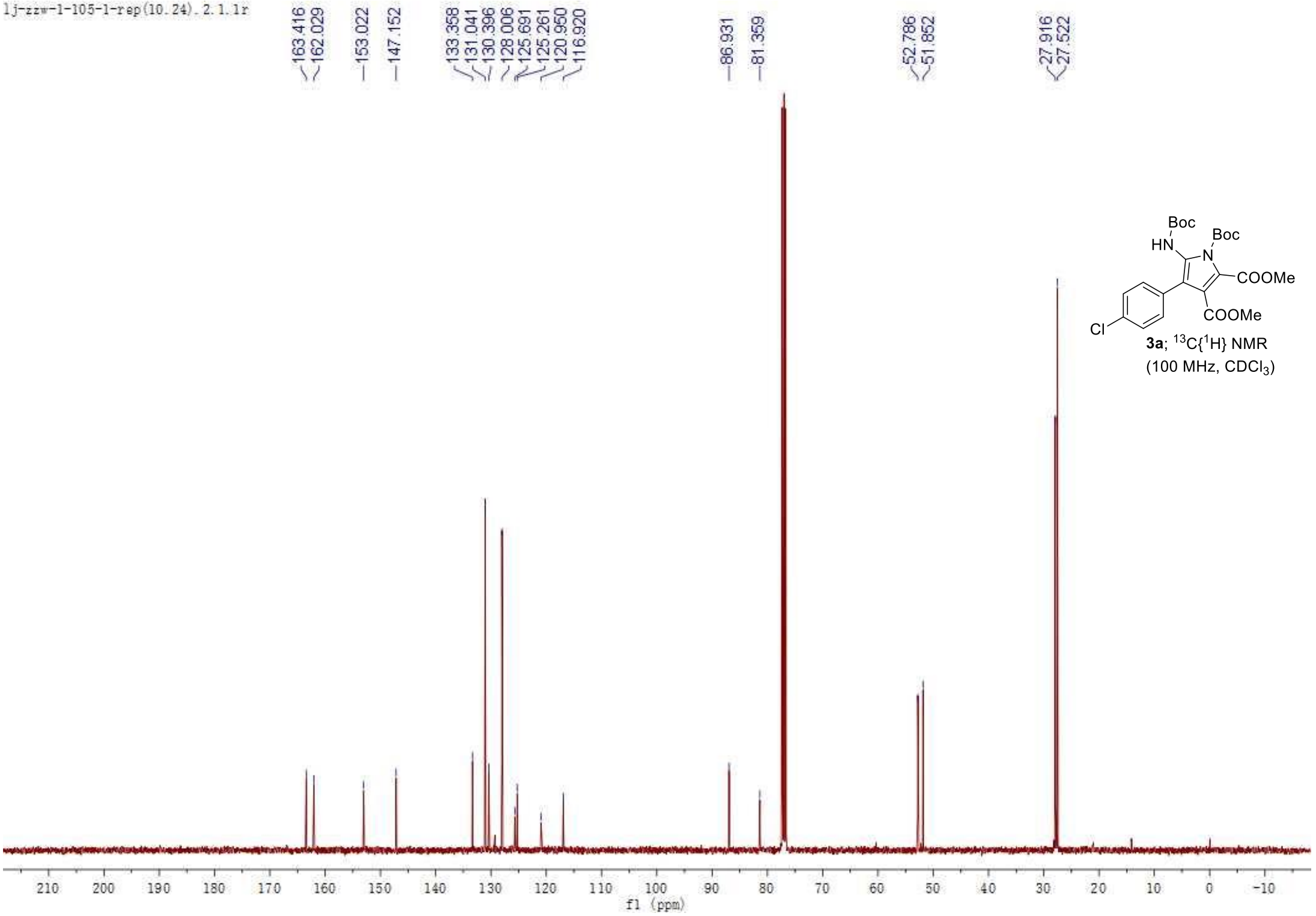
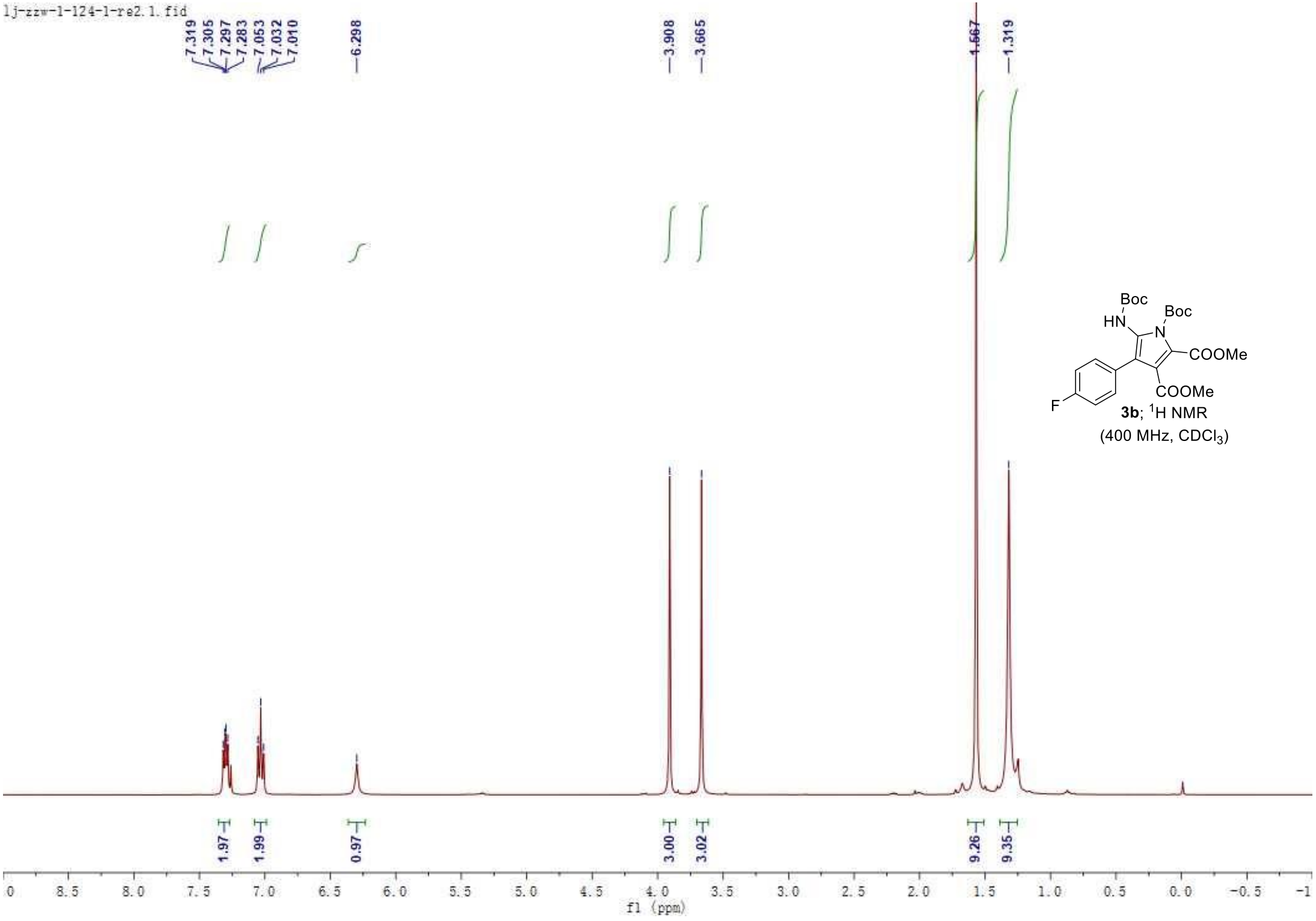


3a; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)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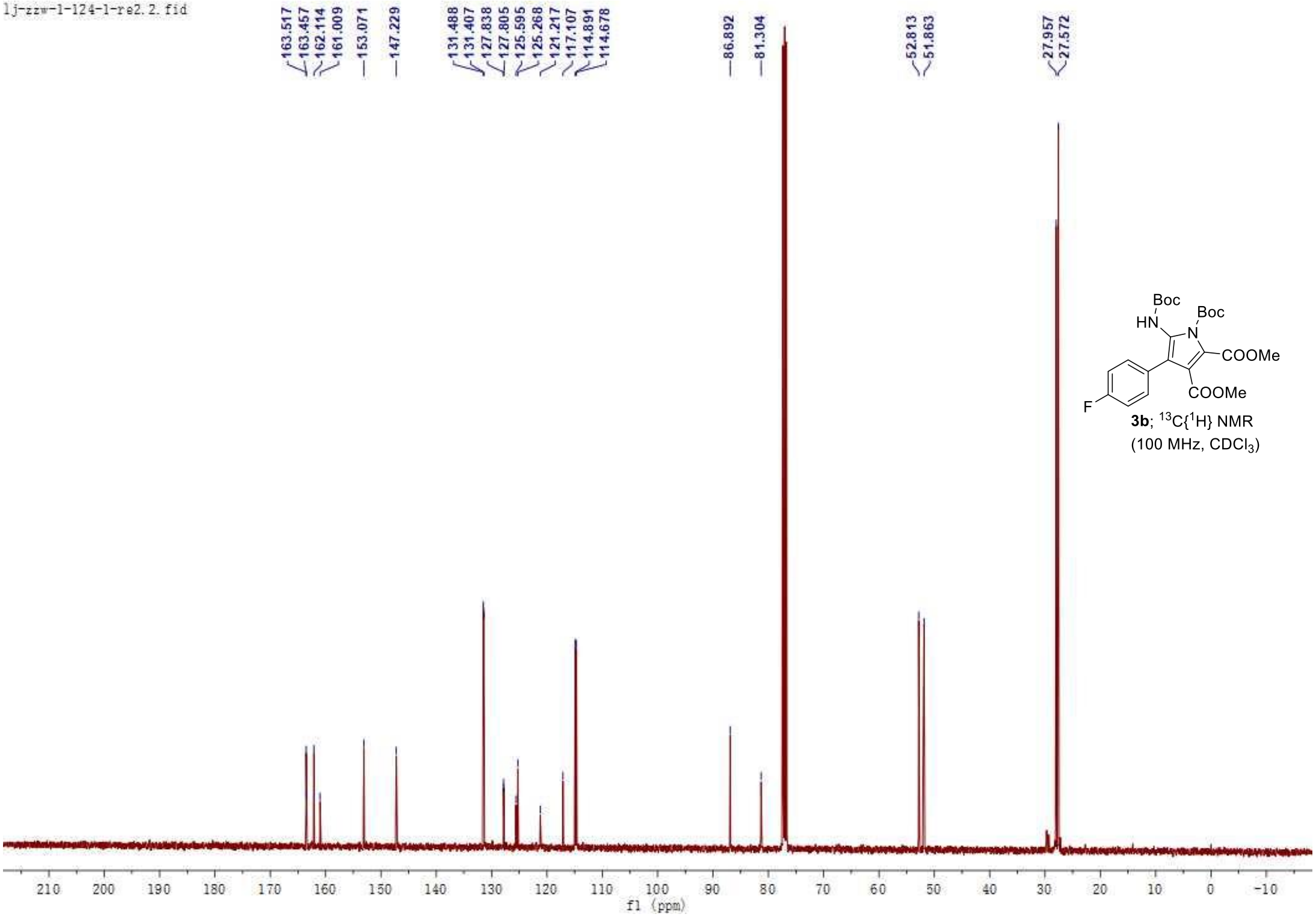
7.305
7.297
7.283
7.053
7.032
7.010
6.298
3.908
3.665
1.667
1.319
1.97
1.99
0.97
3.00
3.02
9.26
9.35
f1 (ppm)
Boc
HN
Boc
N
COOMe
COOMe
F
3b; 1H NMR
(400 MHz, CDCl3)

lj-zzw-1-124-1-re2.2.fid



3b; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

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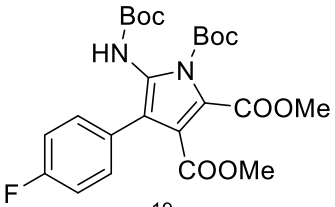
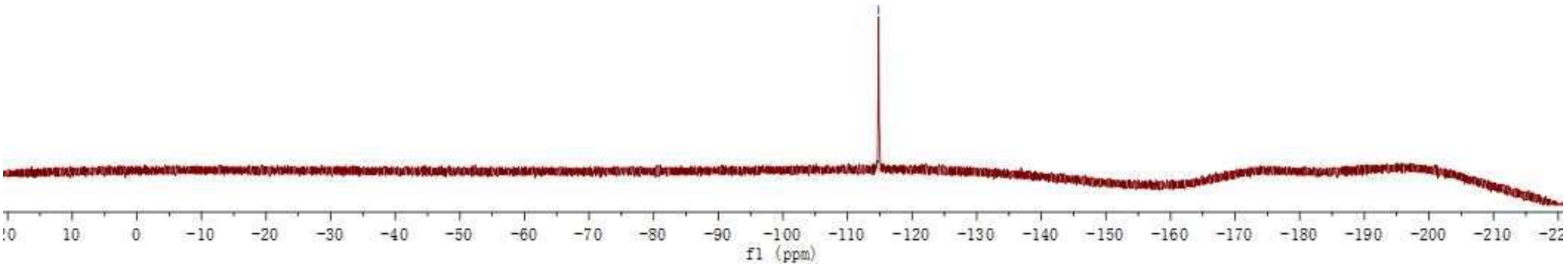
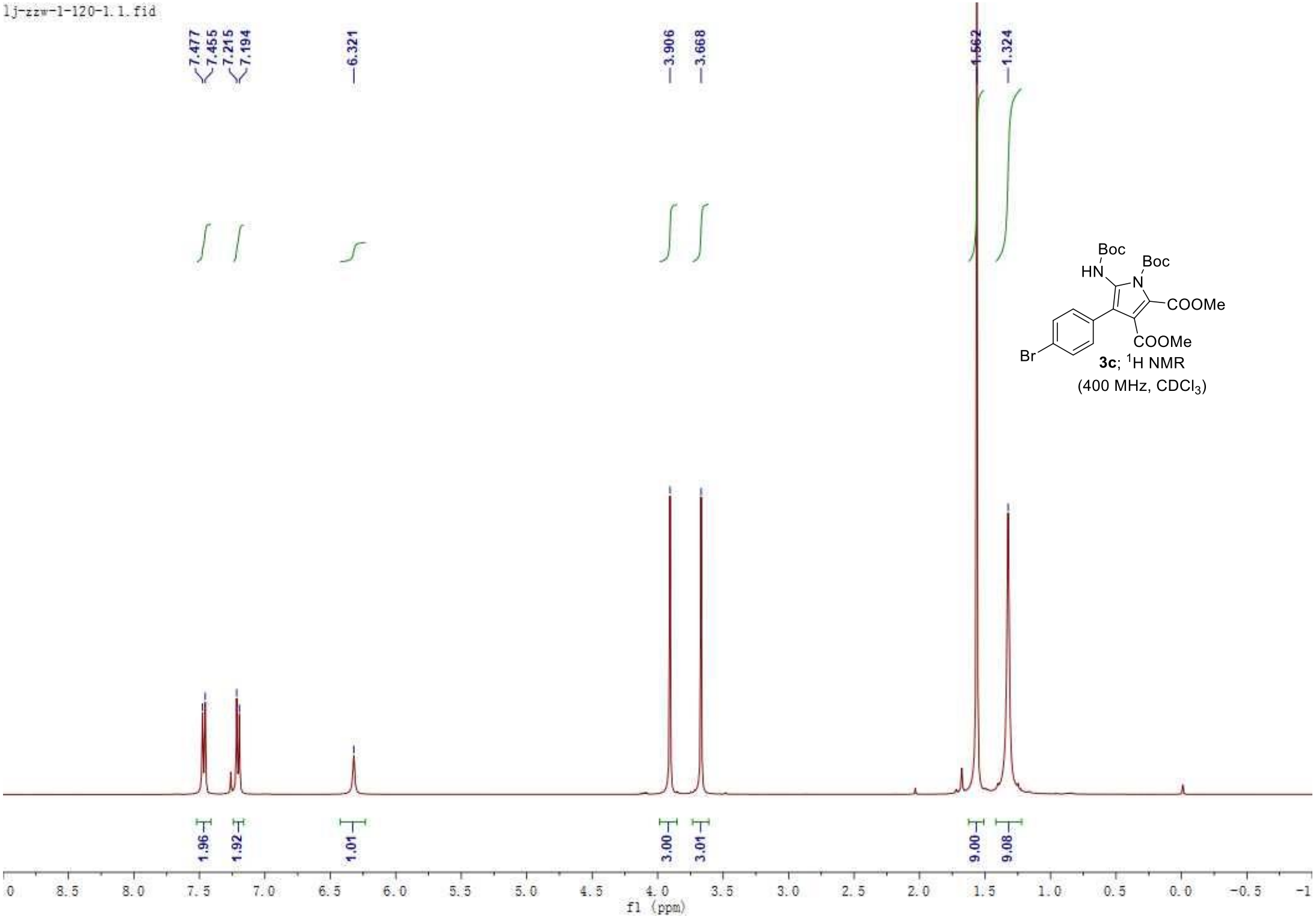


3b; ^{19}F NMR
(376 MHz, $CDCl_3$)




lj-zzw-1-120-1.1.fid
7.477
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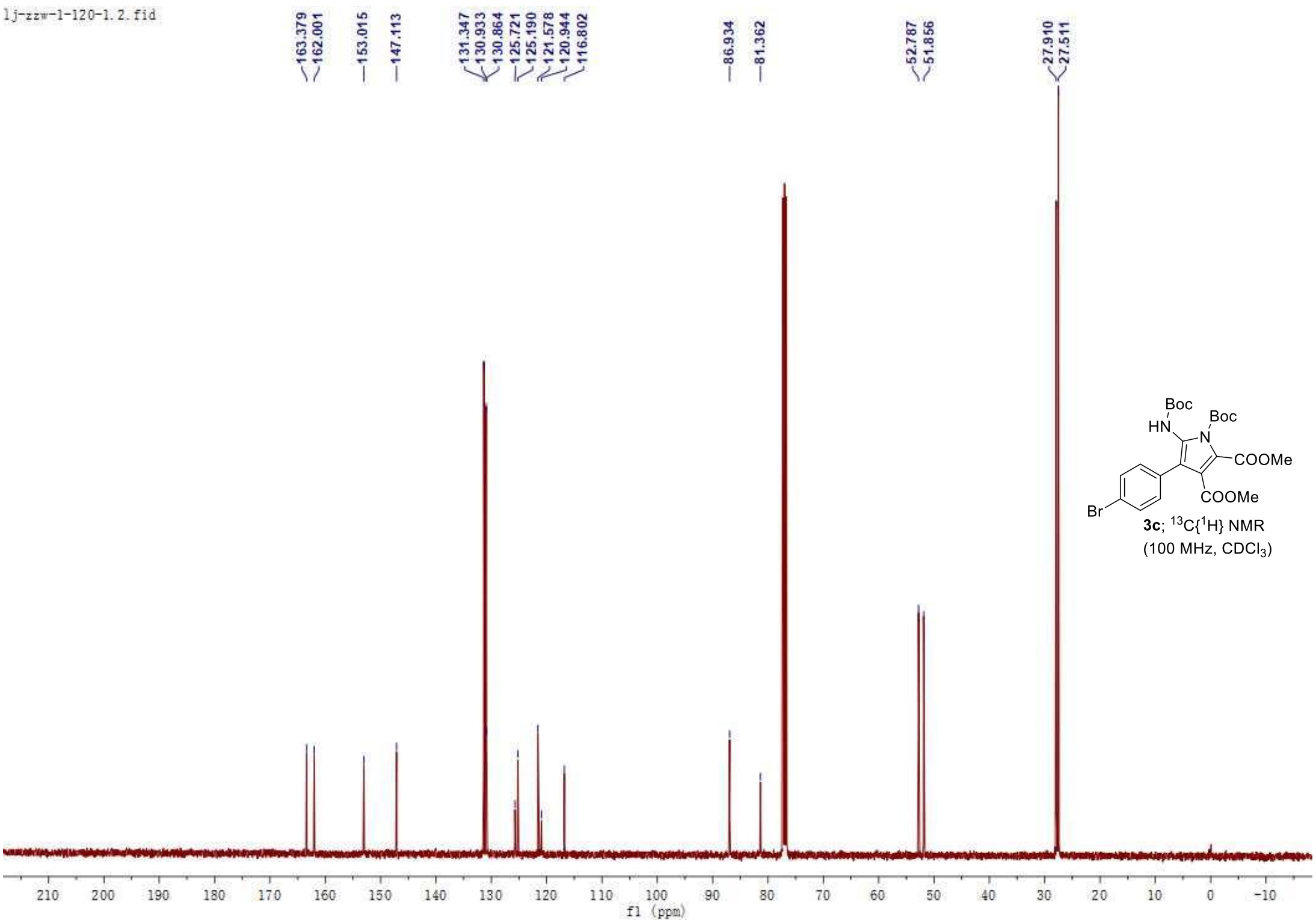
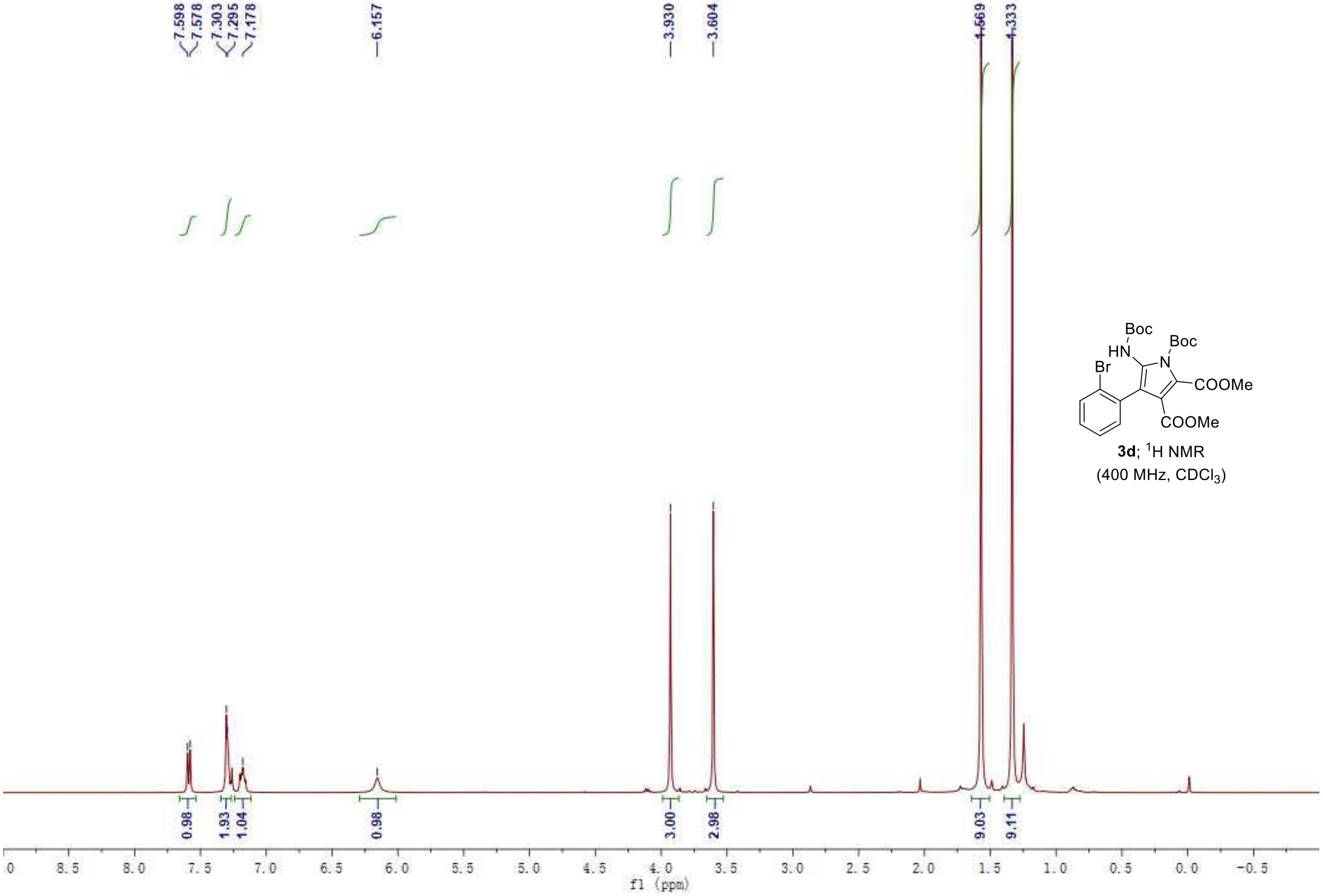
7.215
7.194
6.321
3.906
3.668
1.562
1.324
Boc
HN
Boc
N
COOMe
COOMe
Br
3c; 1H NMR
(400 MHz, CDCl3)
1.96
1.92
1.01
3.00
3.01
9.00
9.08
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

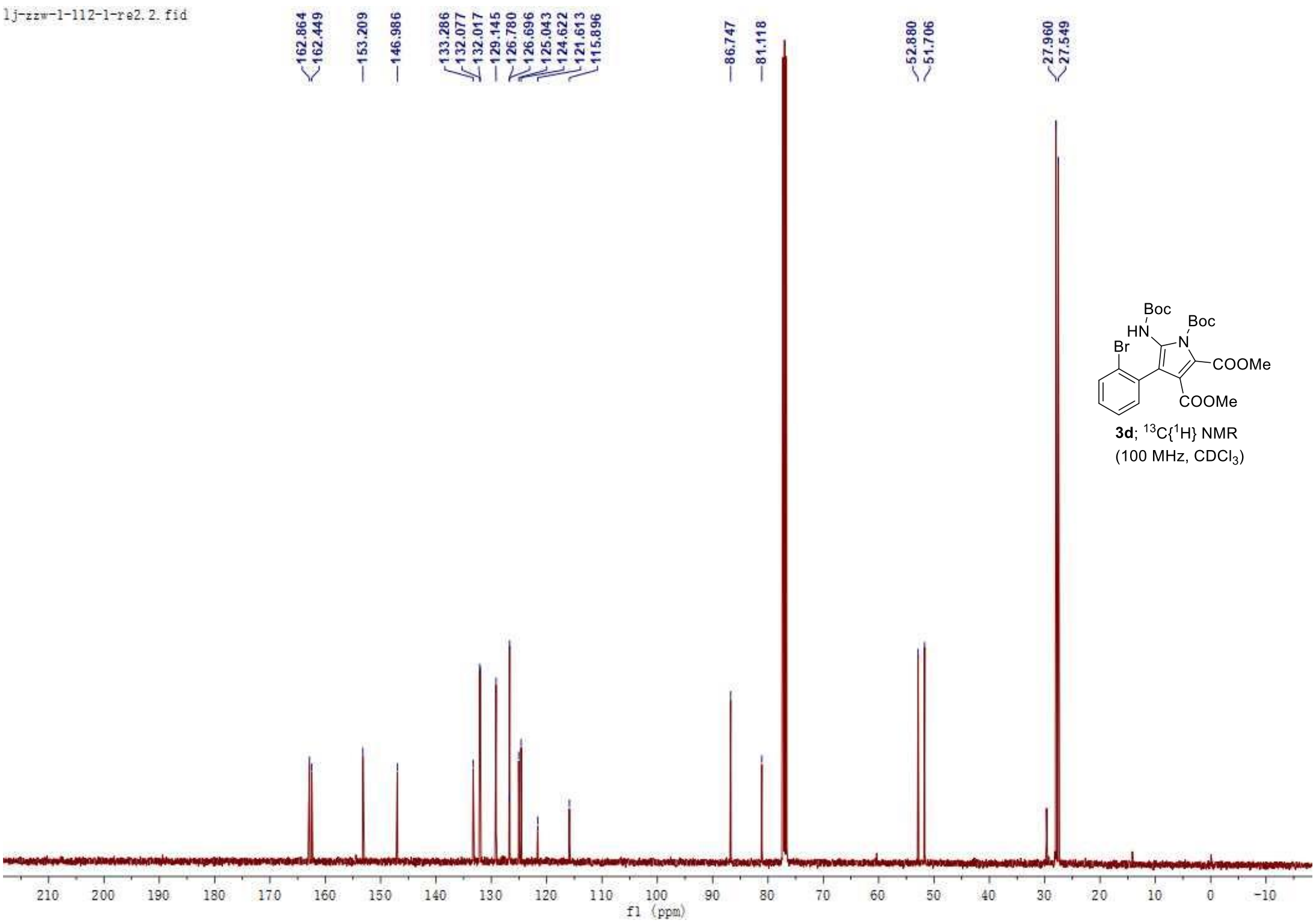


3c; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

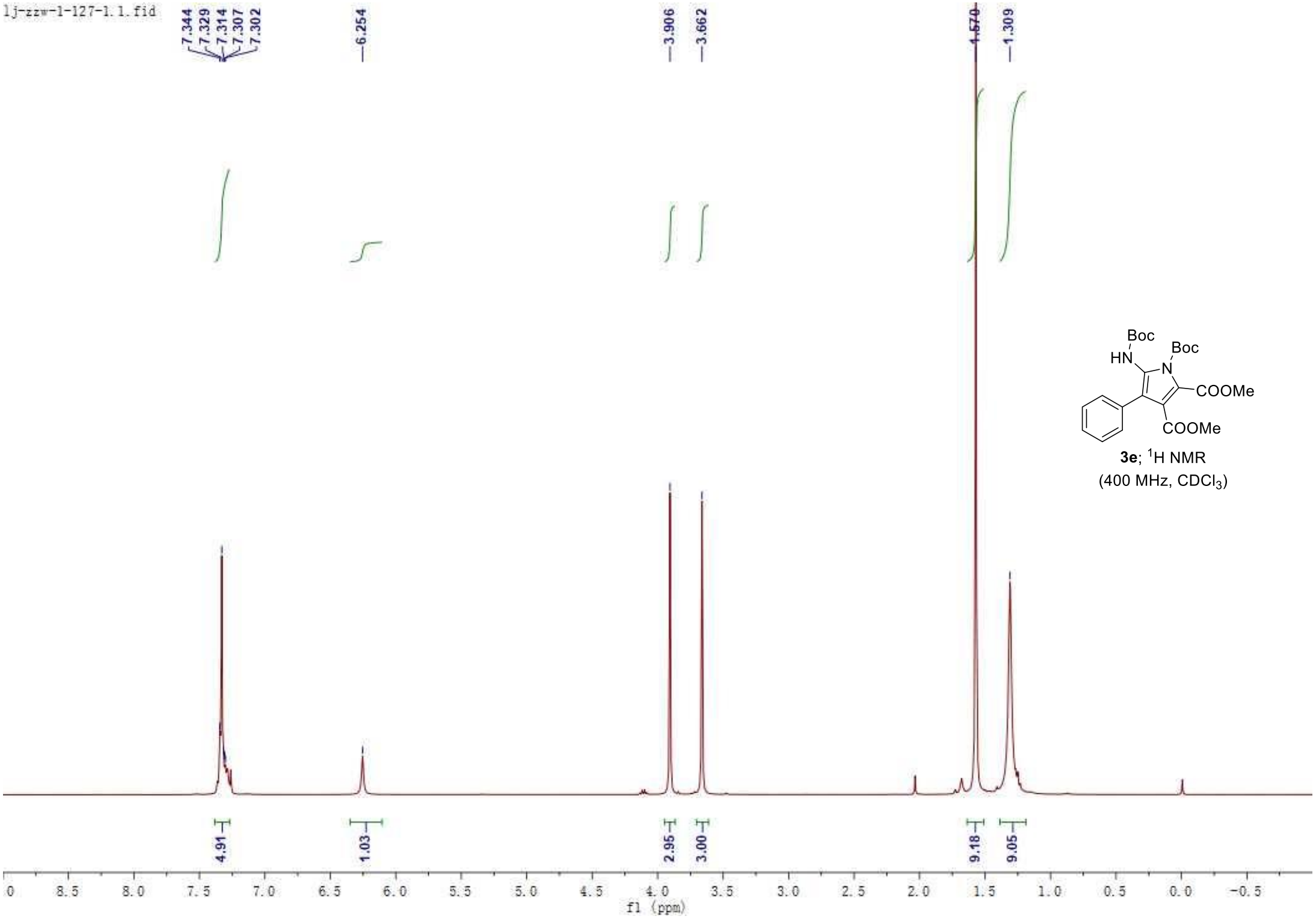
lj-zzw-1-112-1-re2.1.fid



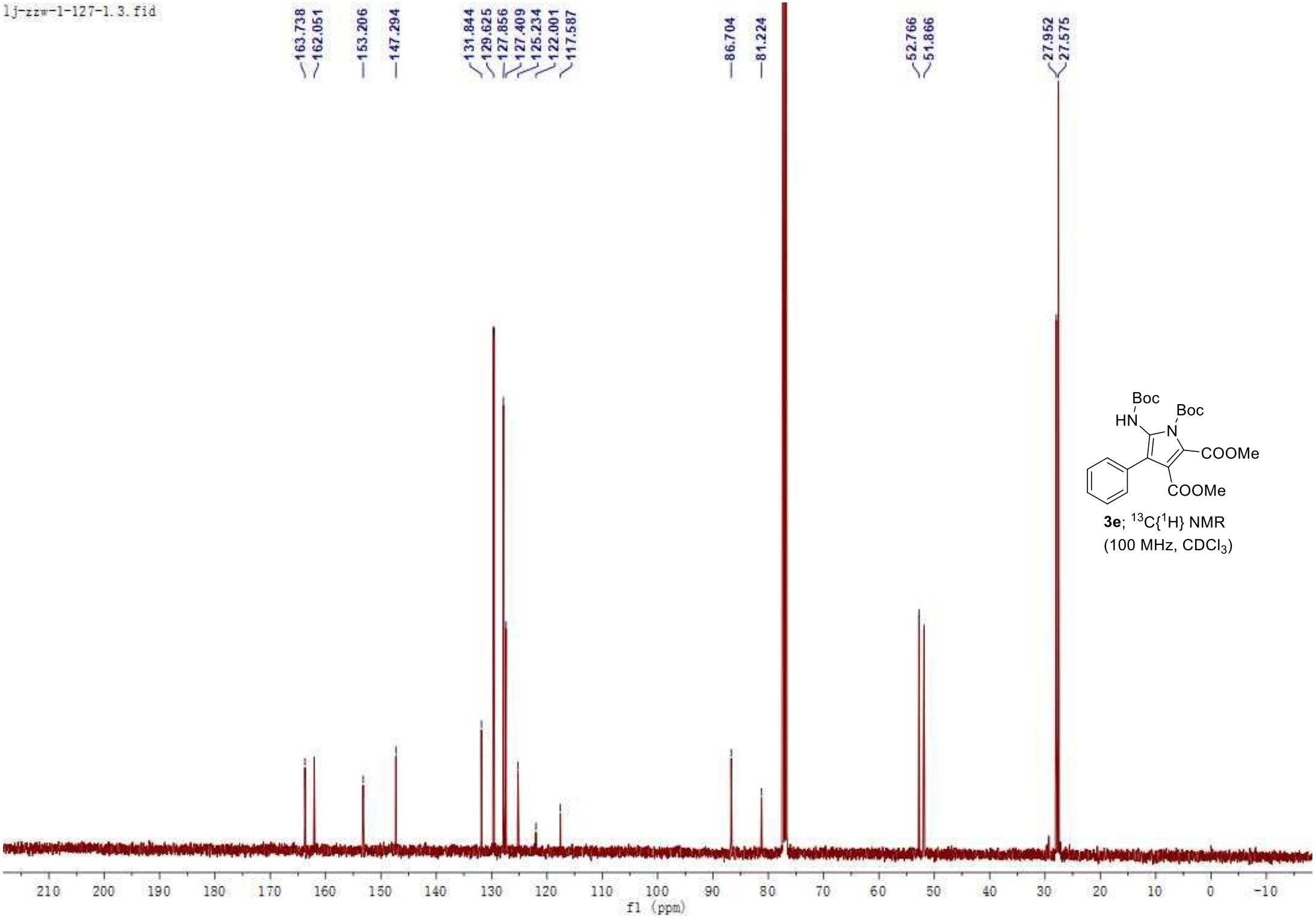
3d; ^{1}H NMR
(400 MHz, $CDCl_3$)



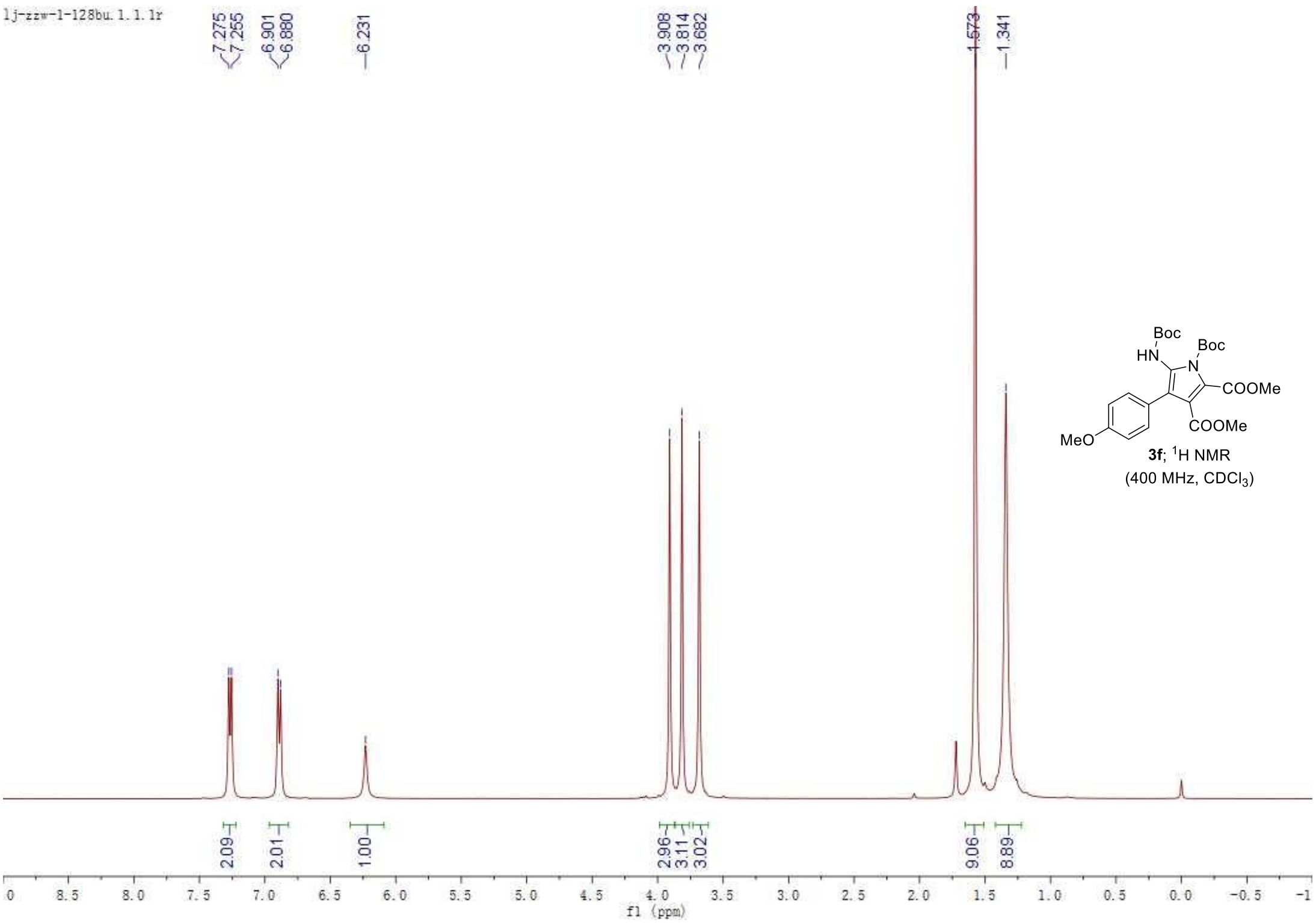
3d; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)



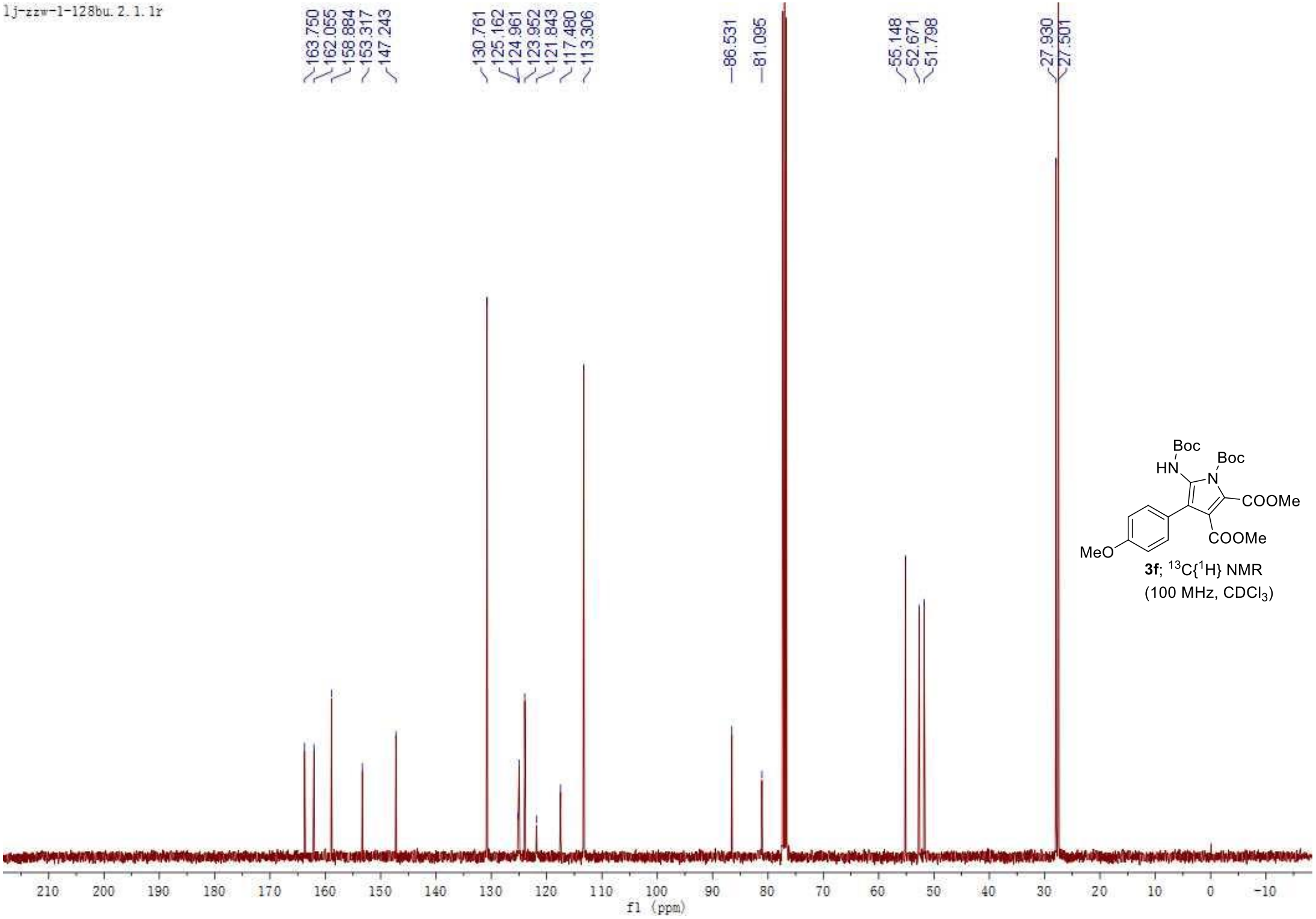
3e; ^{1}H NMR
(400 MHz, $CDCl_3$)



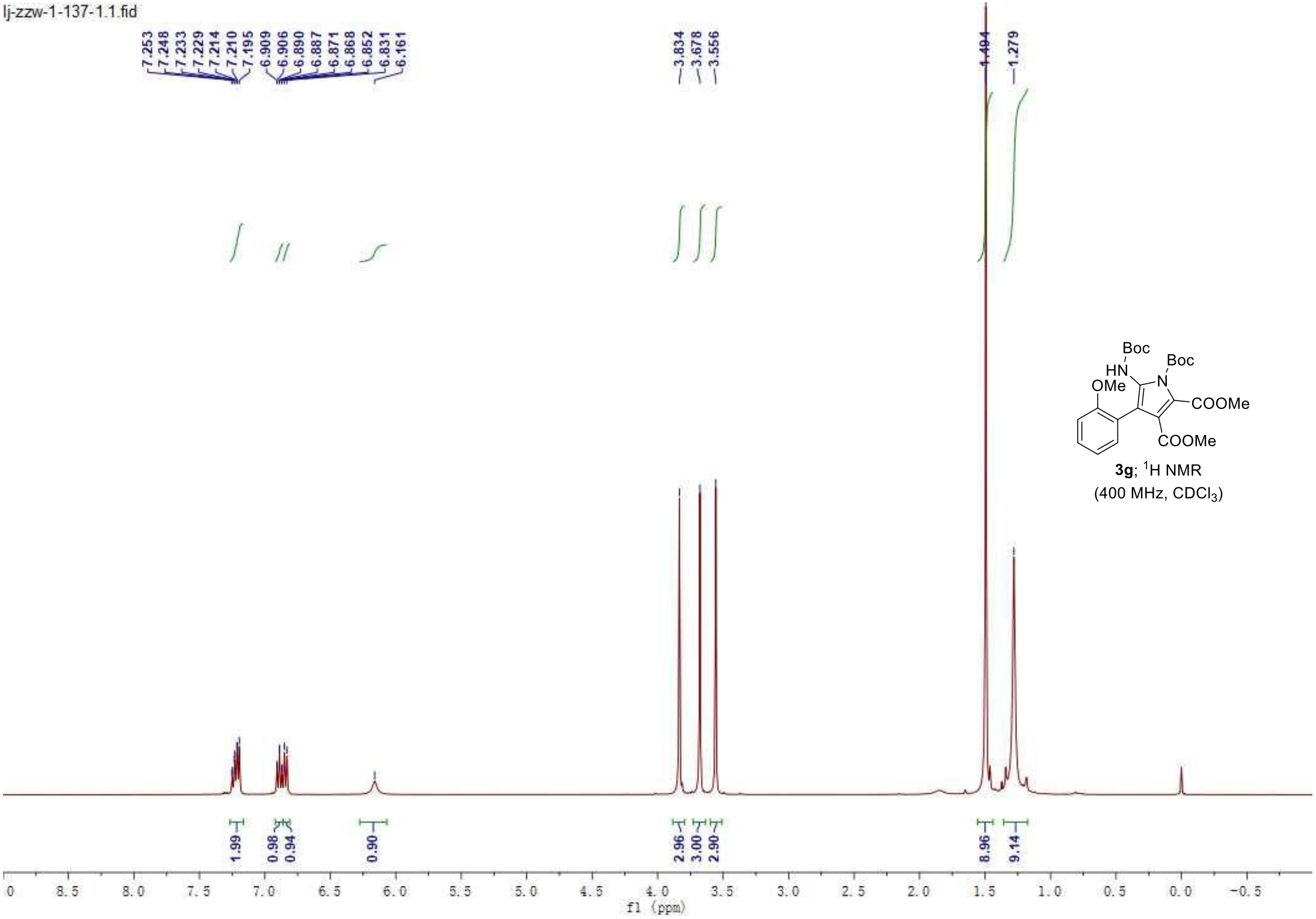
3e; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)



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



3f; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)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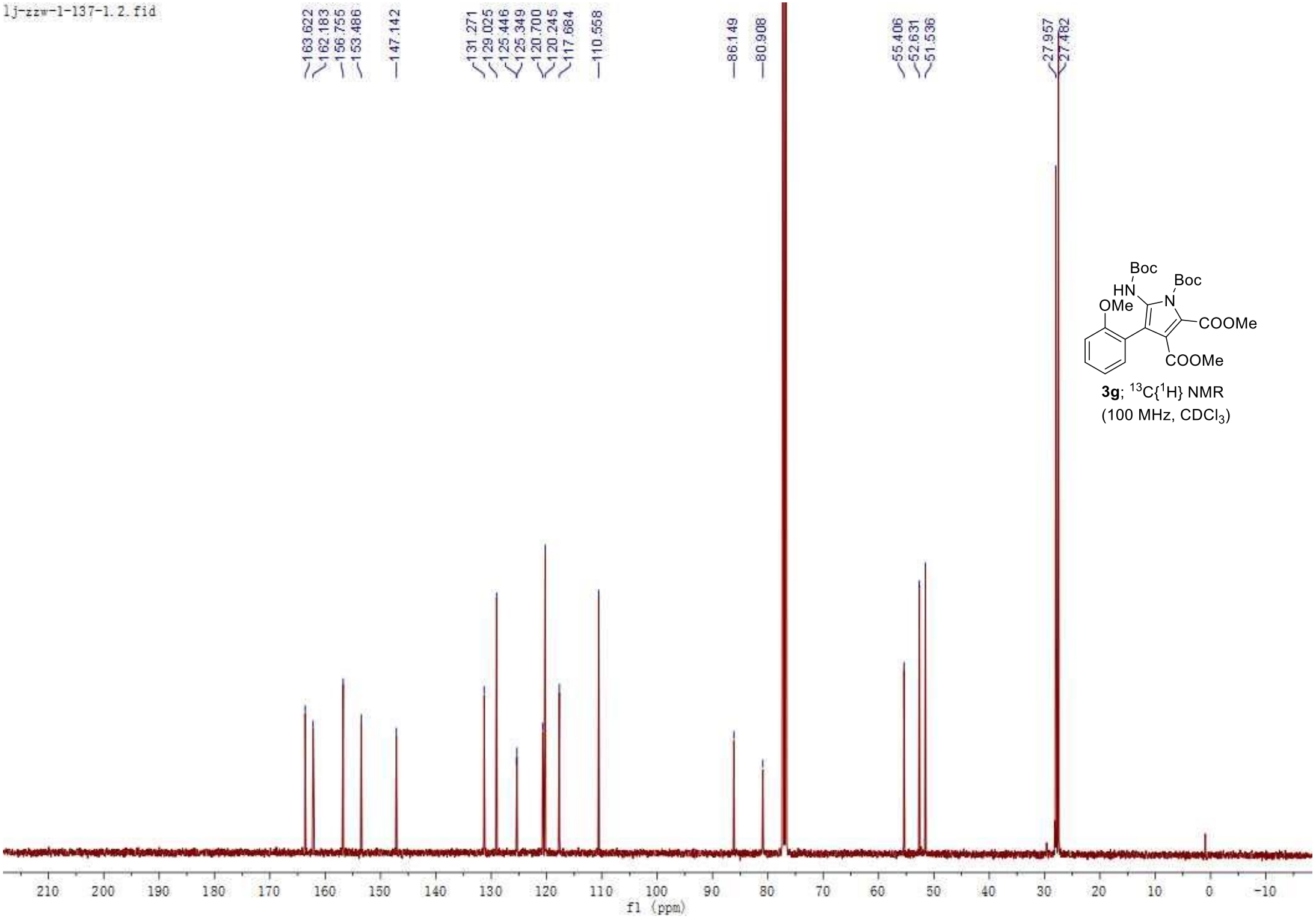
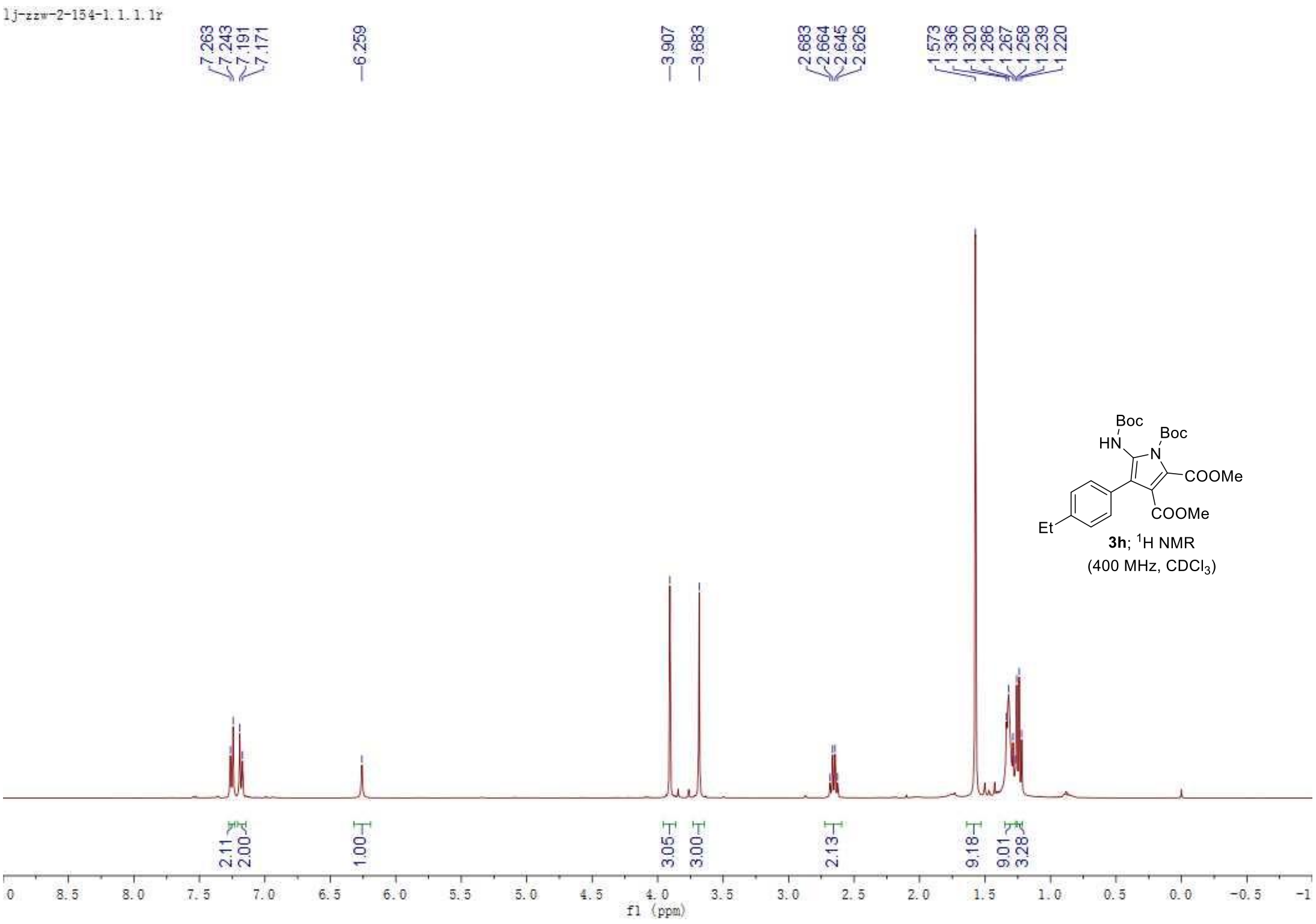
6.852
6.831
6.161
3.834
3.678
3.556
1.494
1.279
1.99
0.98
0.94
0.90
2.96
3.00
2.90
8.96
9.14
f1 (ppm)
Boc
HN
Boc
N
OMe
COOMe
COOMe
3g; 1H NMR
(400 MHz, CDCl3)



3g; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)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1.320
1.286
1.267
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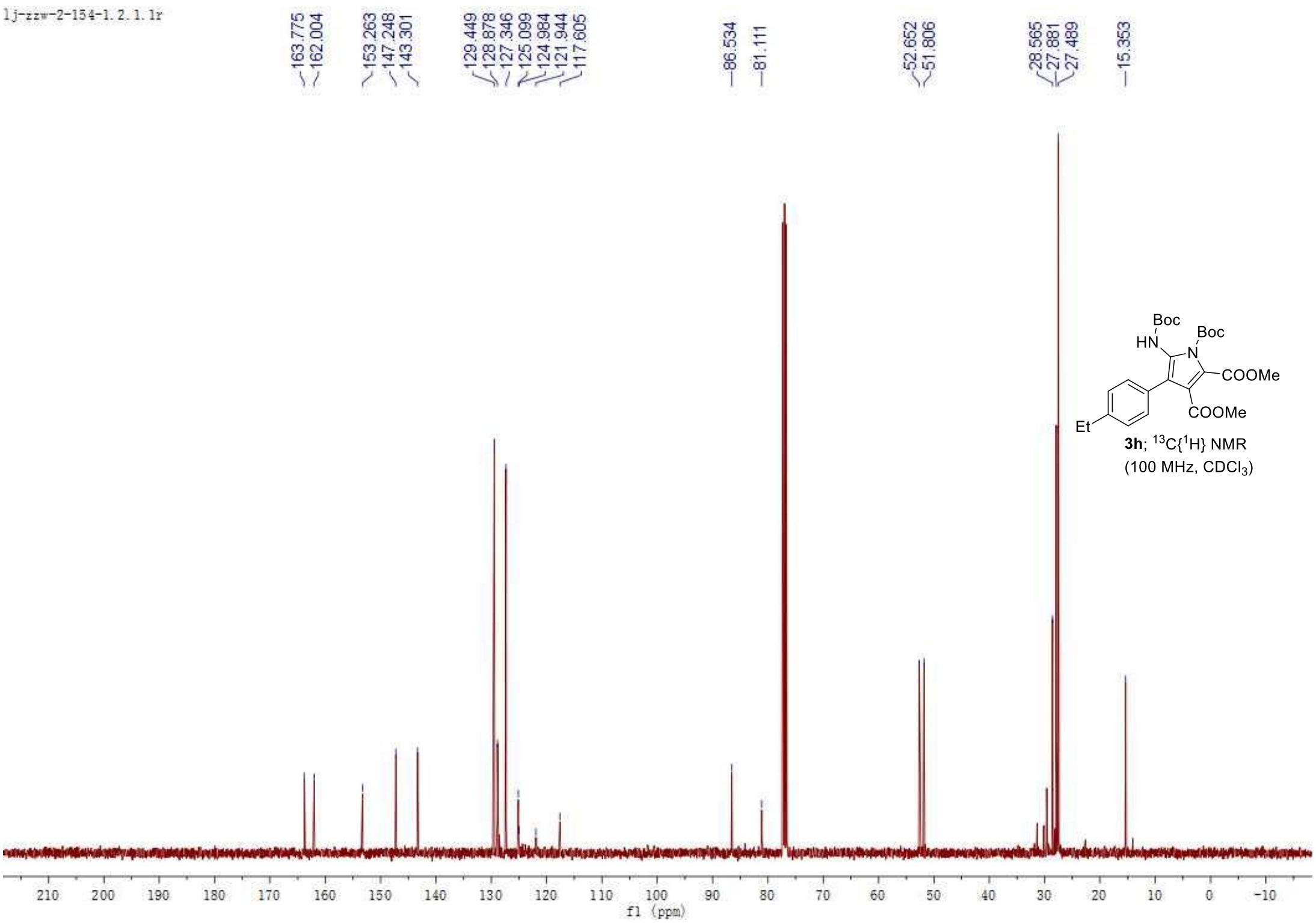
COOMe
Et
3h; 1H NMR
(400 MHz, CDCl3)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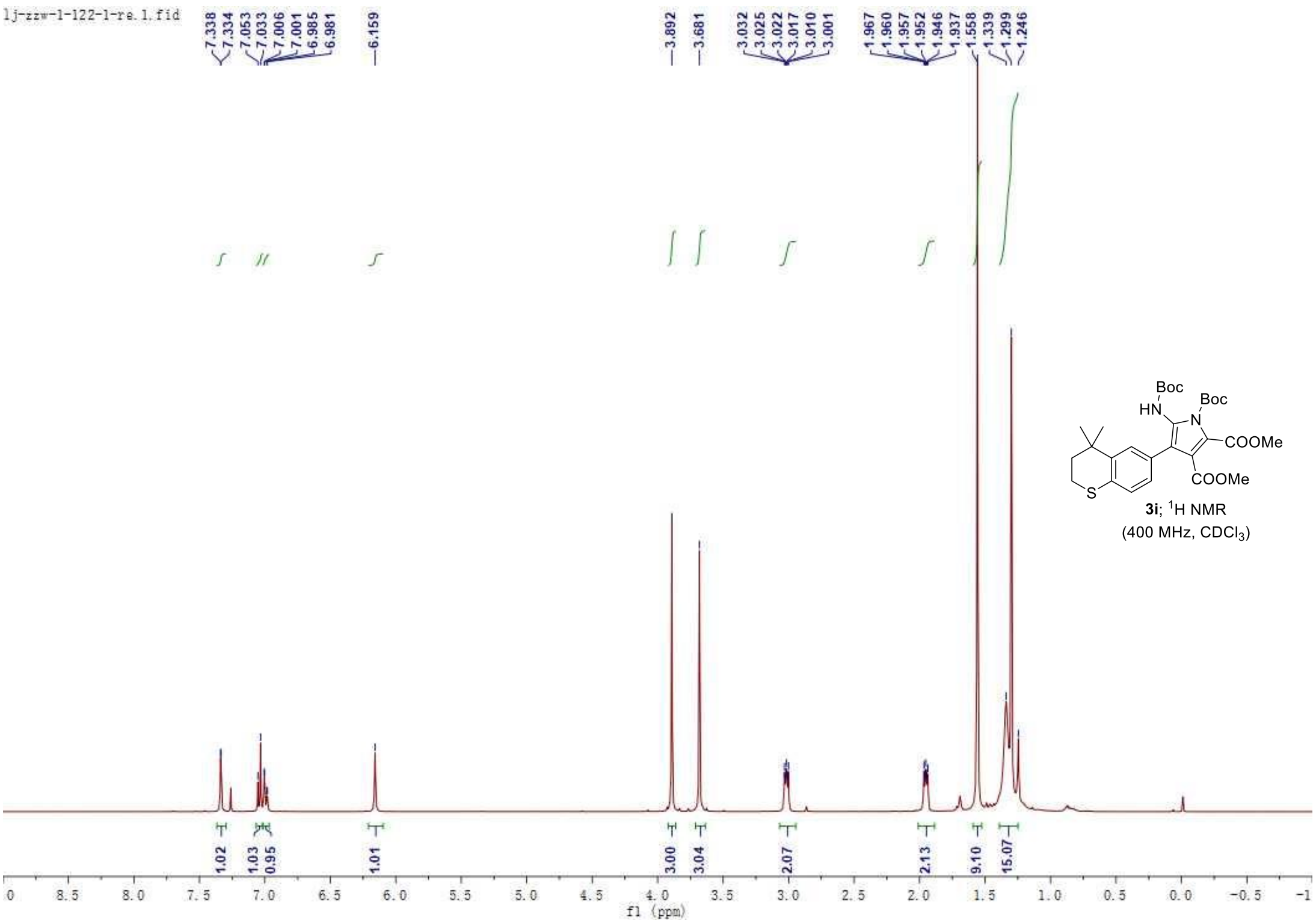
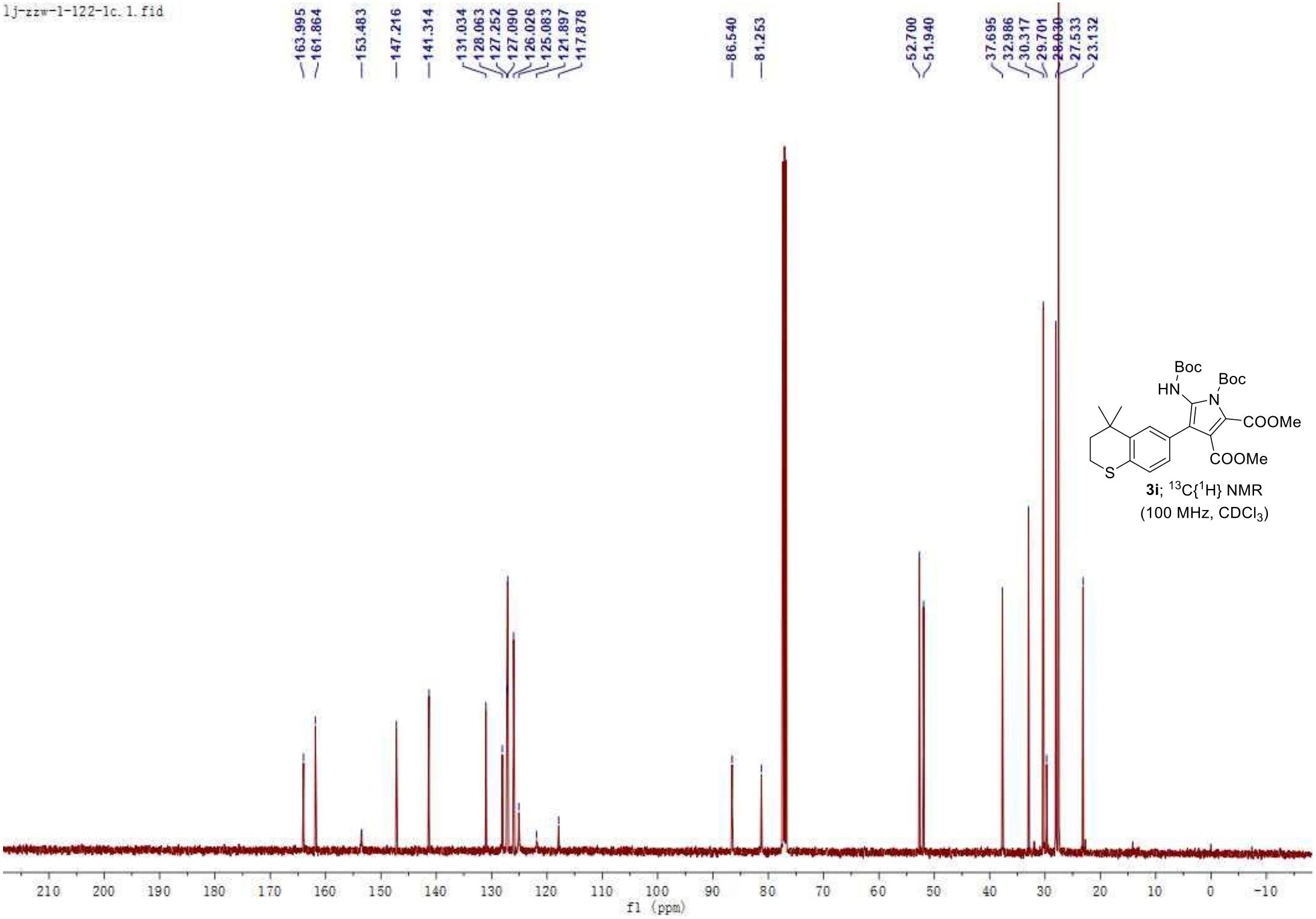
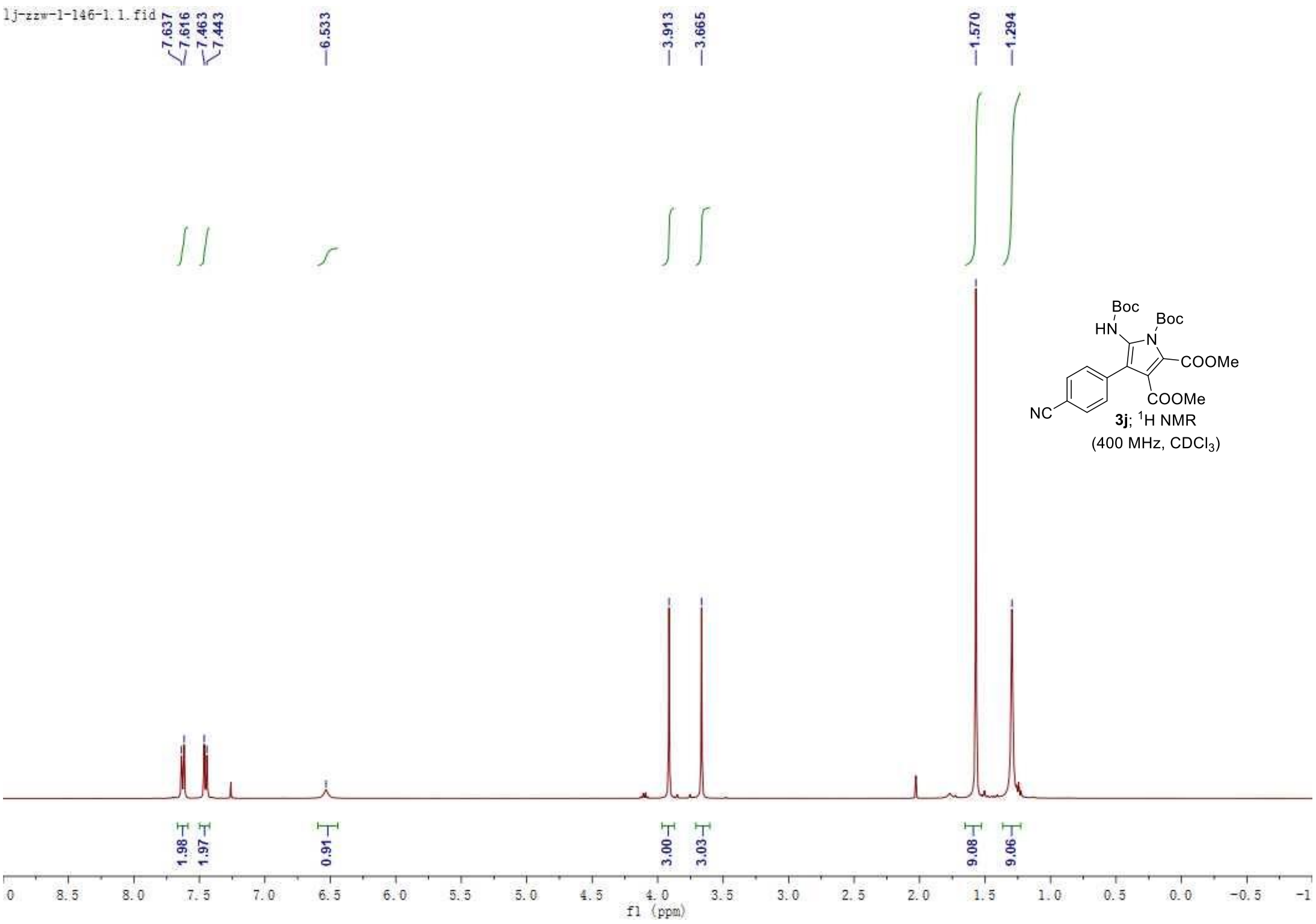
86.534
81.111
52.652
51.806
28.565
27.881
27.489
15.353
Boc
HN
Boc
N
COOMe
COOMe
Et
3h; 13C{1H} NMR
(100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

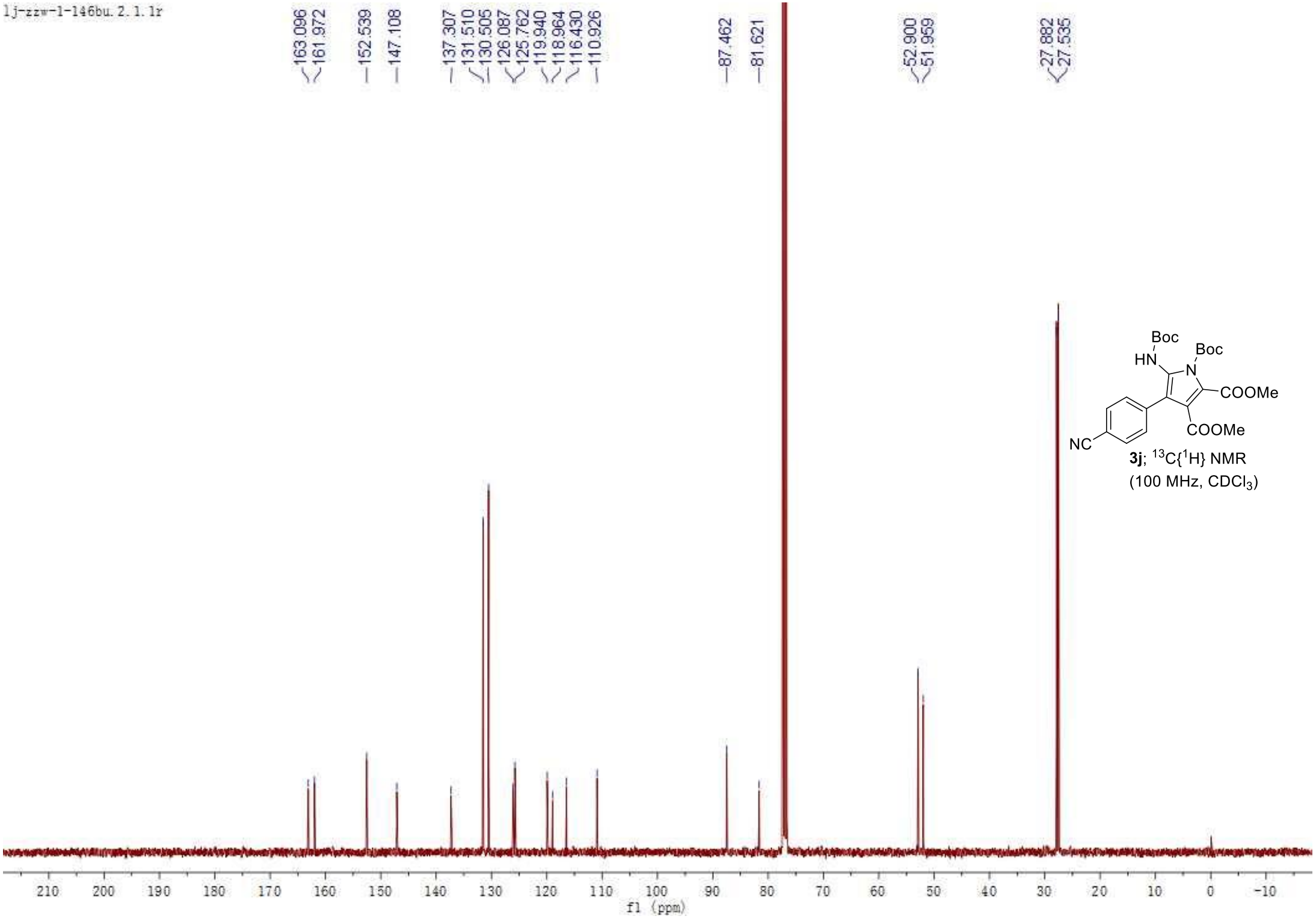


3i; ^{1}H NMR
(400 MHz, $CDCl_3$)

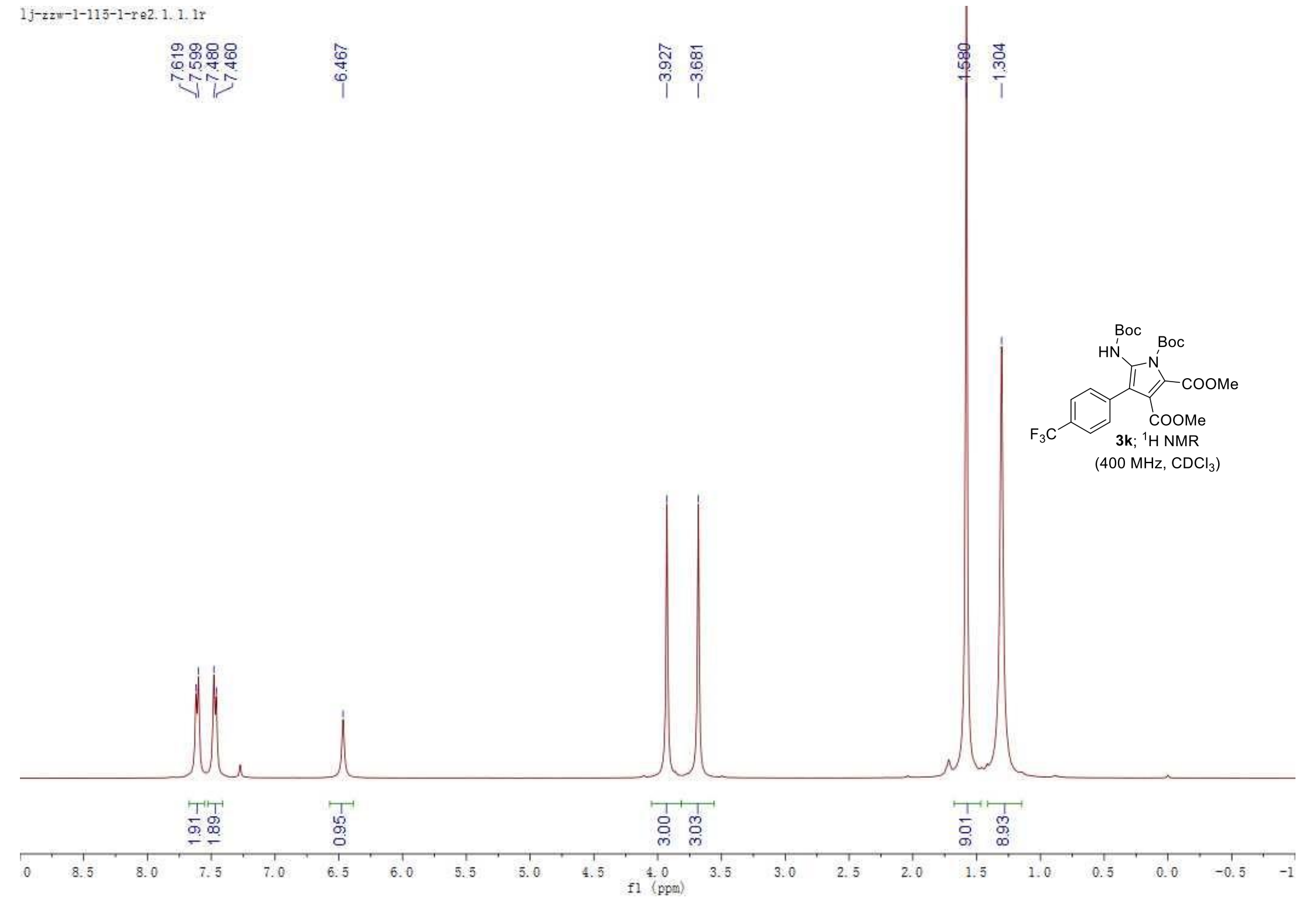


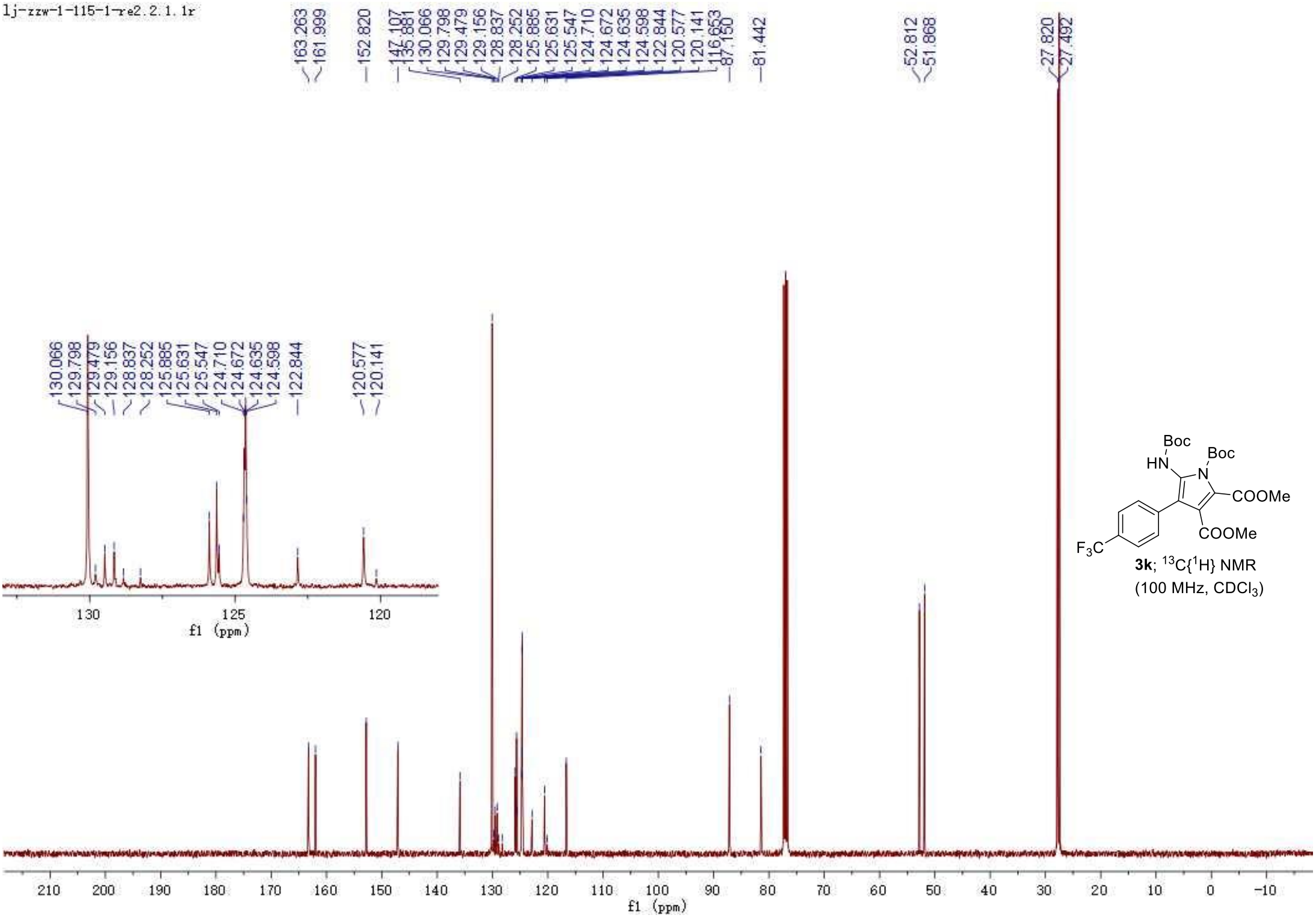
3i; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)


lj-zzw-1-146-1.1.fid
7.637
7.616
7.463
7.443
6.533
3.913
3.665
1.570
1.294
1.98
1.97
0.91
3.00
3.03
9.08
9.06
f1 (ppm)
Boc
HN
N
Boc
COOMe
COOMe
NC
3j; 1H NMR
(400 MHz, CDCl3)

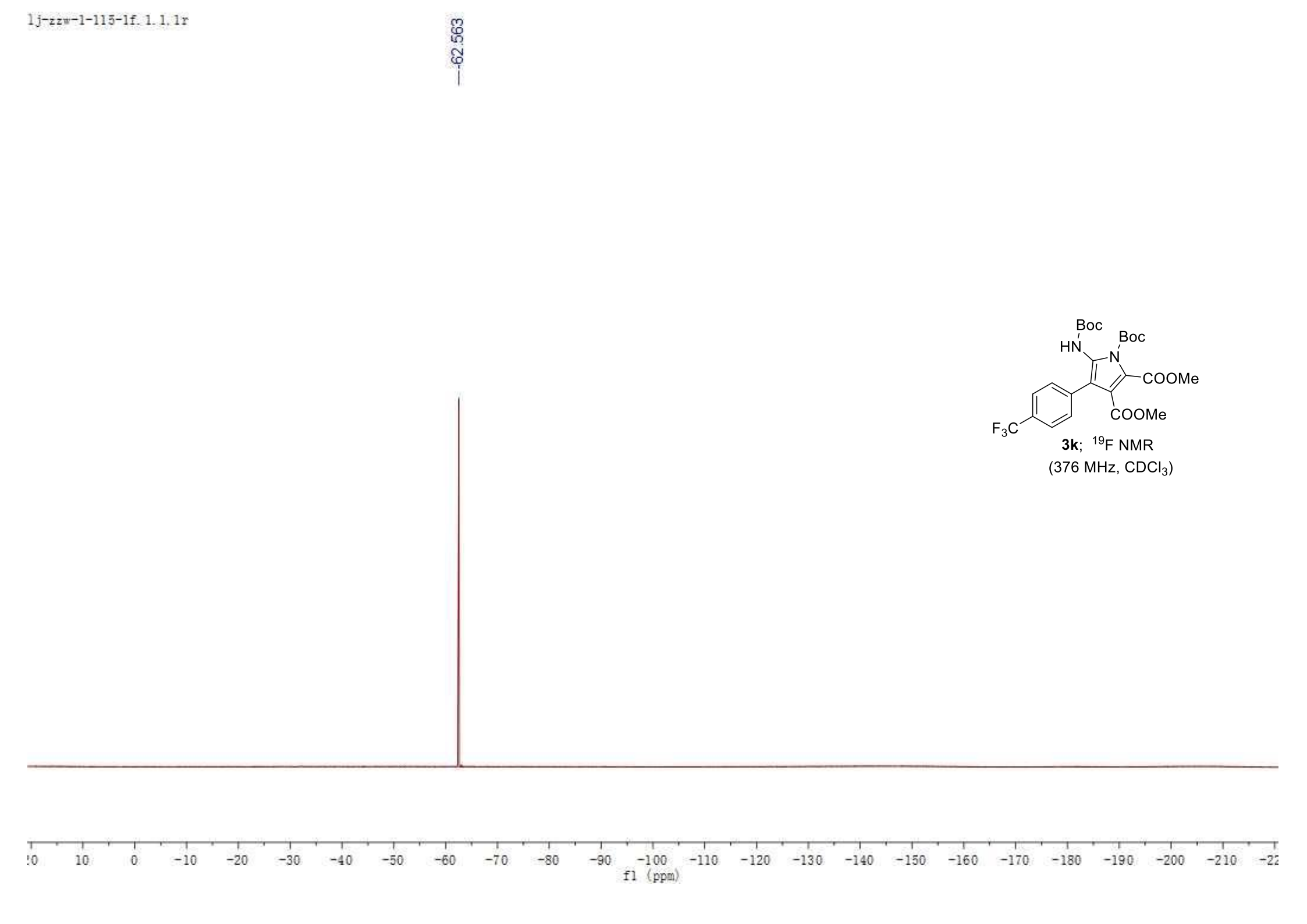


3j; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

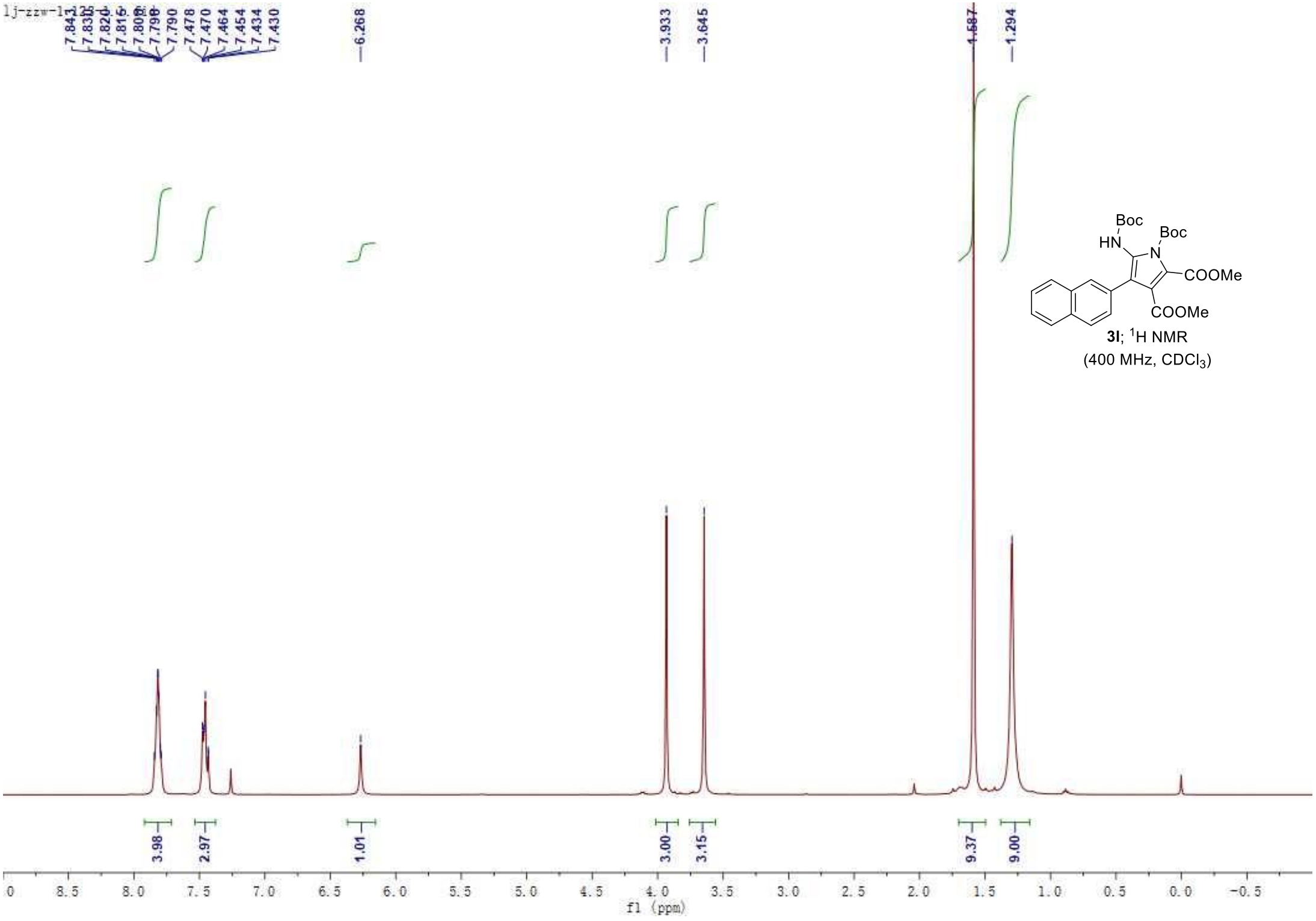

lj-zzw-1-115-1-re2.1.1.1r
7.619
7.599
7.480
7.460
6.467
3.927
3.681
1.580
1.304
1.91
1.89
0.95
3.00
3.03
9.01
8.93
f1 (ppm)
Boc
HN
Boc
N
COOMe
COOMe
F3C
3k; 1H NMR
(400 MHz, CDCl3)



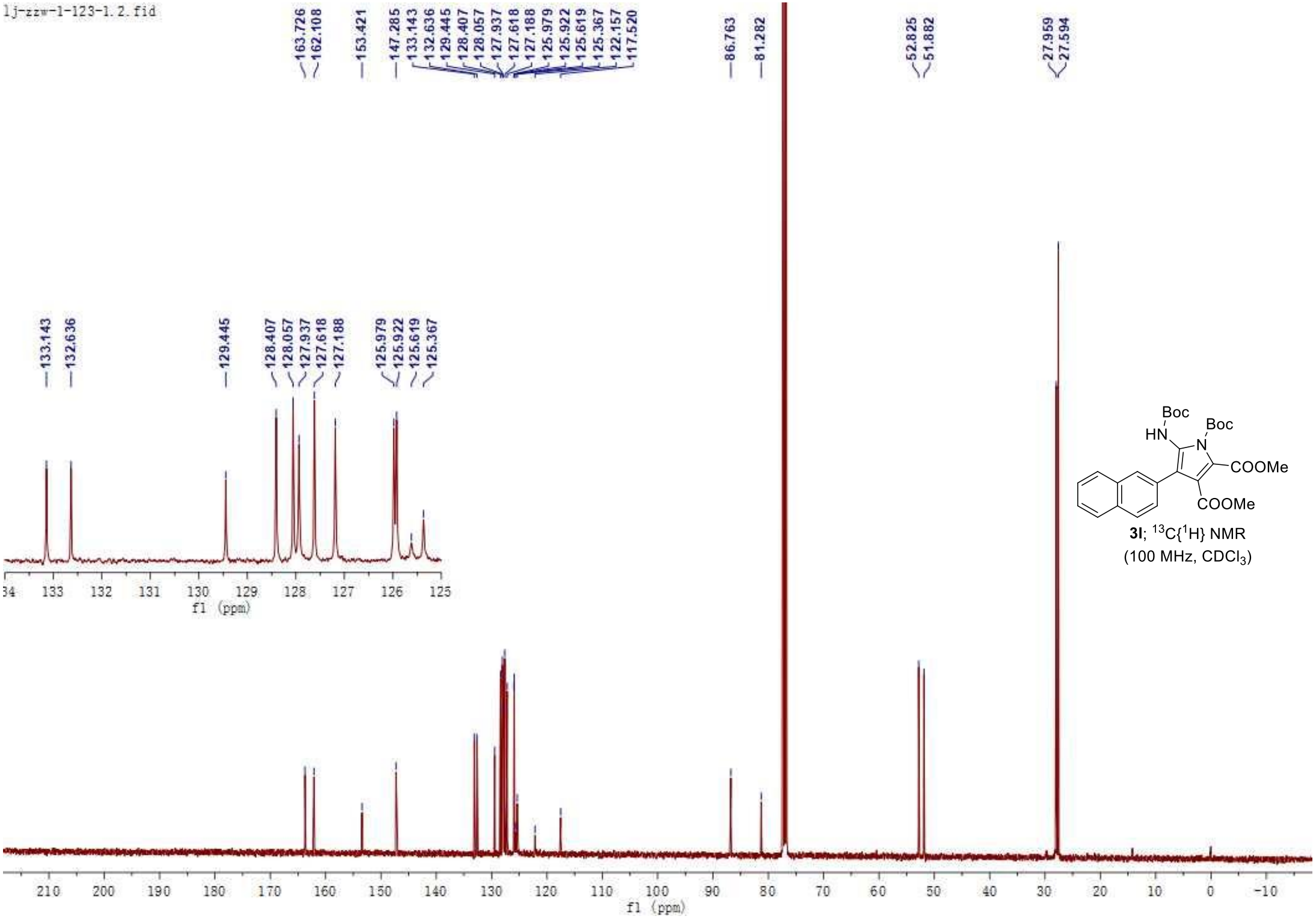
3k; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)



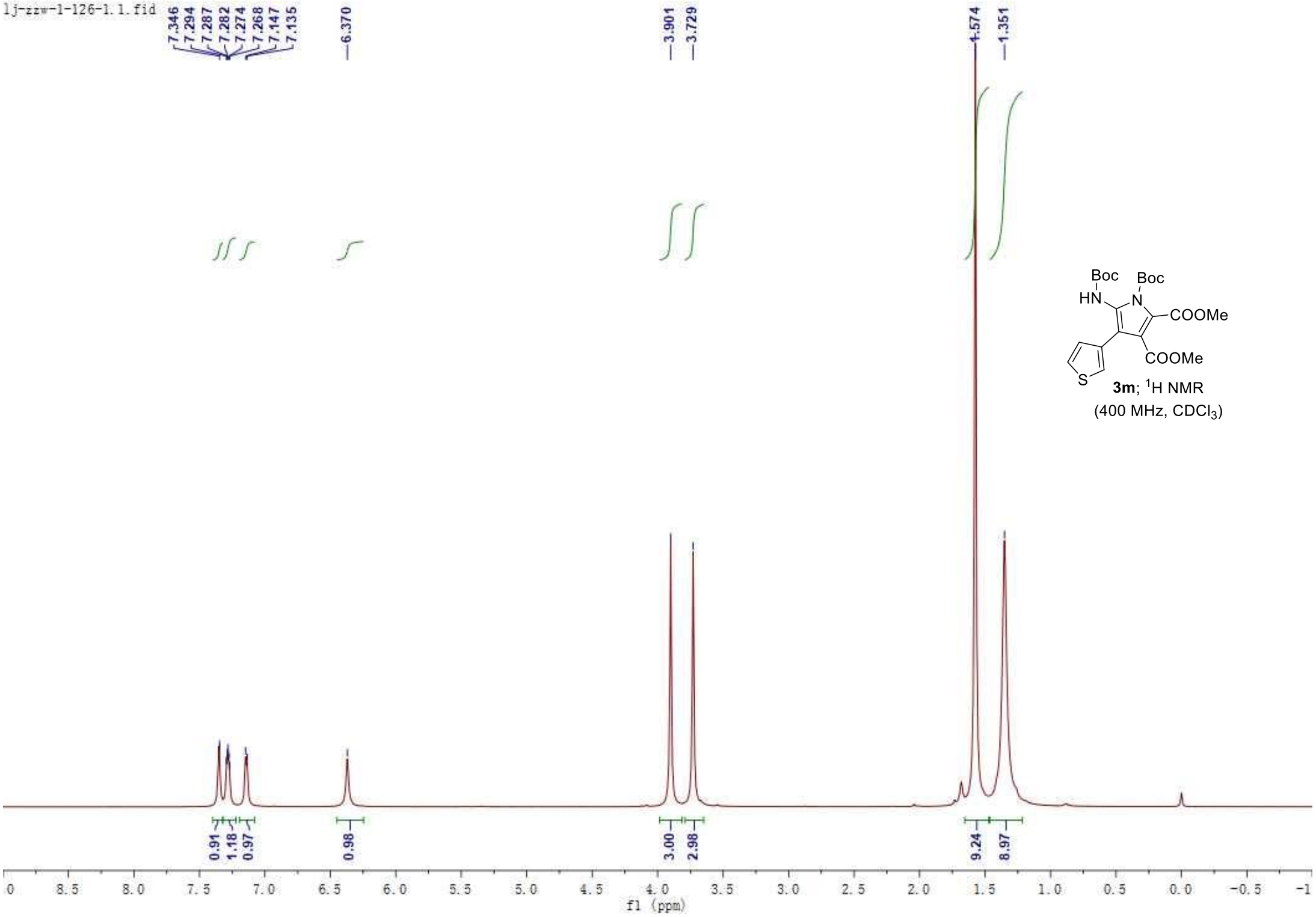
3k; ^{19}F NMR
(376 MHz, $CDCl_3$)



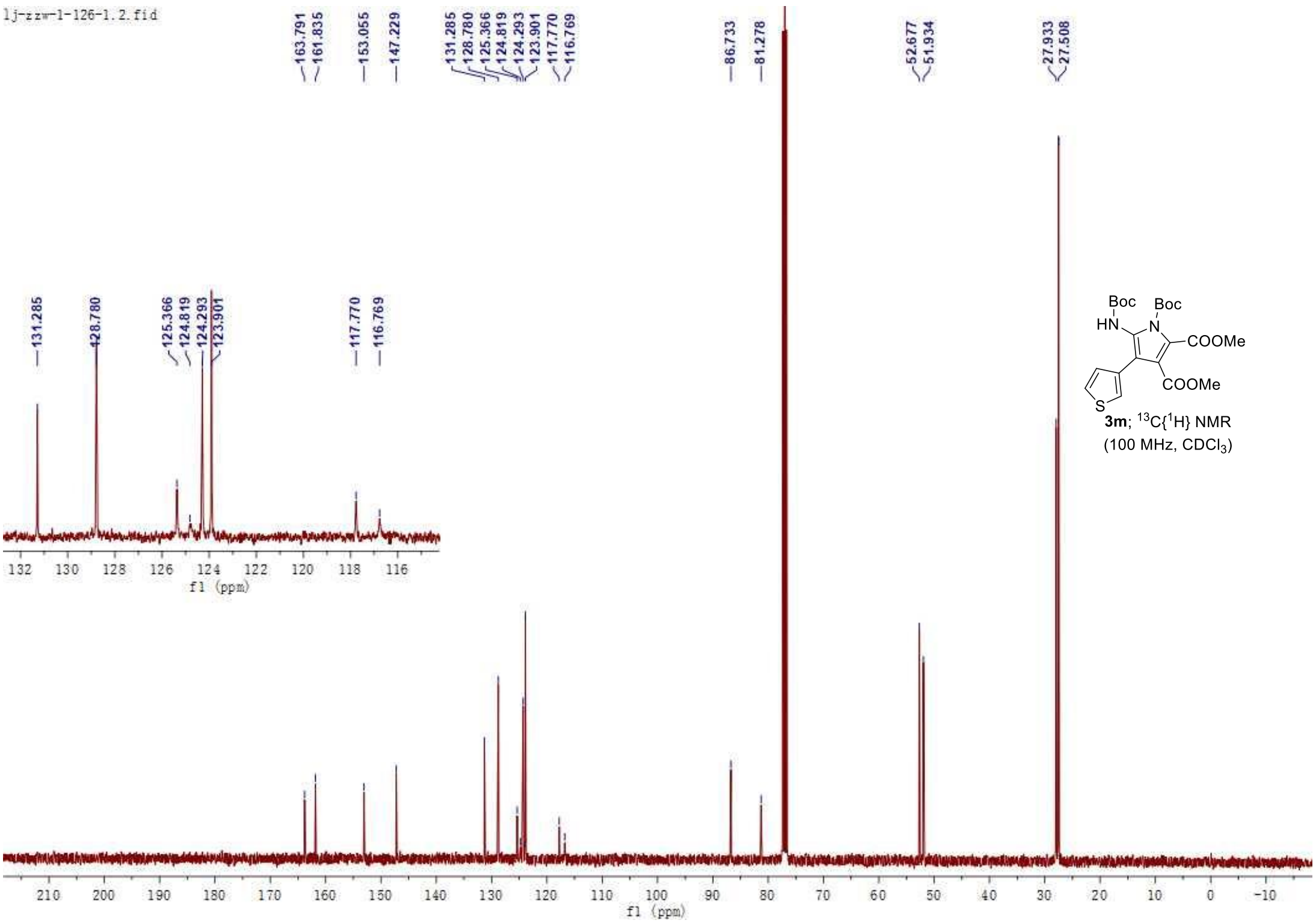
3l; ^{1}H NMR
(400 MHz, $CDCl_3$)

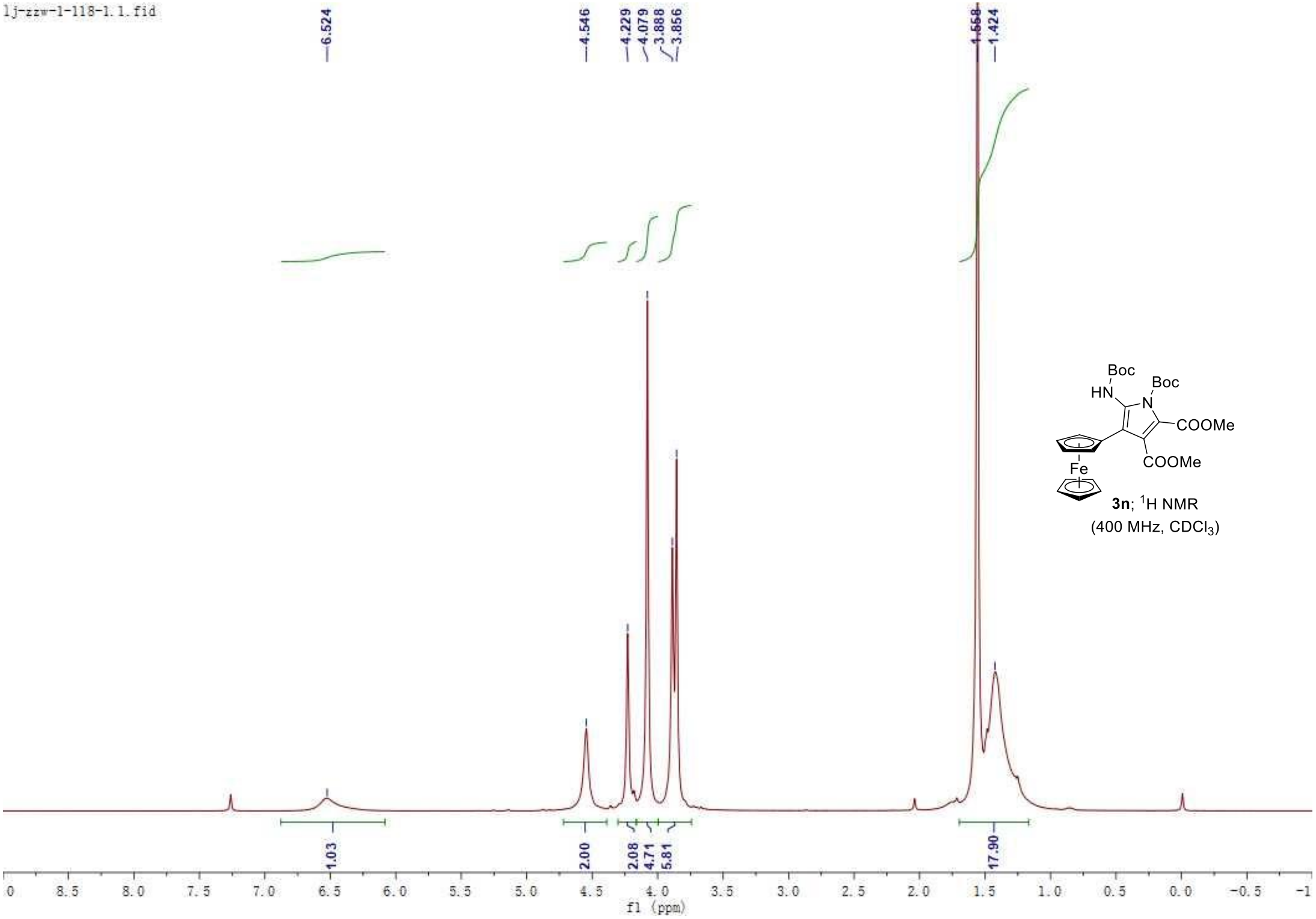


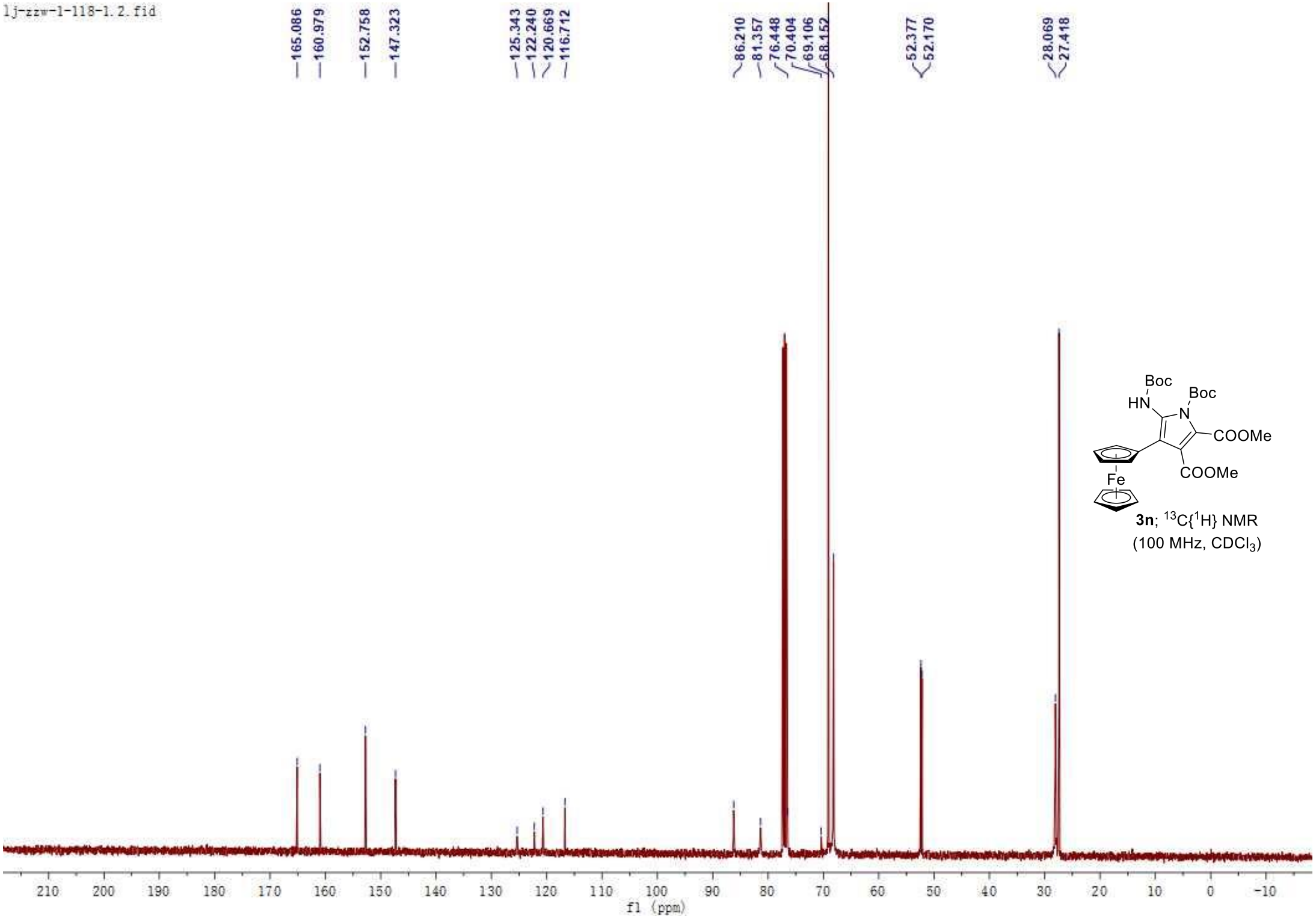
3l; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)



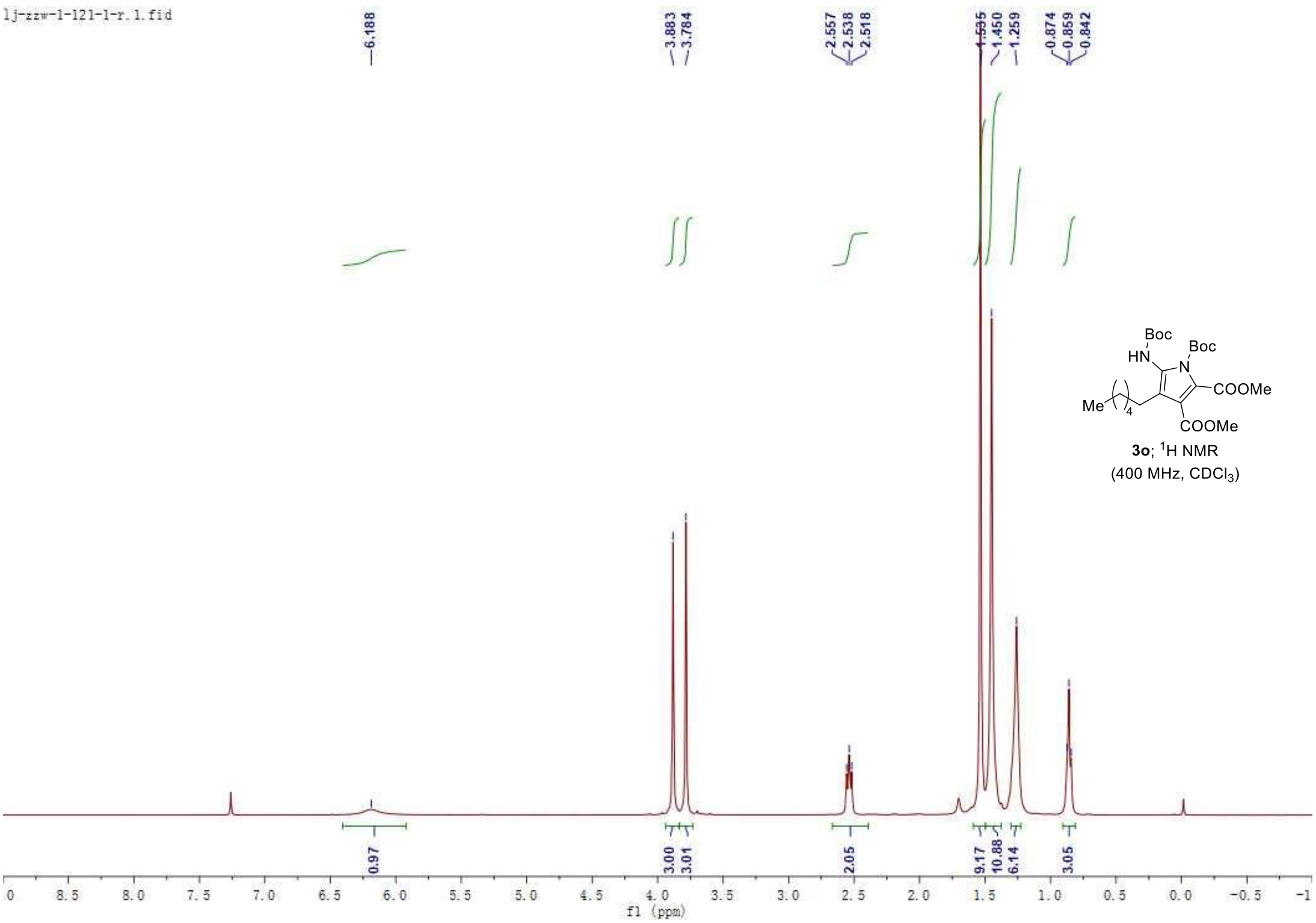
3m; ^{1}H NMR
(400 MHz, $CDCl_3$)


lj-zzw-1-126-1.2.fid
163.791
161.835
153.055
147.229
131.285
128.780
125.366
124.819
124.293
123.901
117.770
116.769
86.733
81.278
52.677
51.934
27.933
27.508
f1 (ppm)
Boc
Boc
HN
N
COOMe
COOMe
S
3m; 13C{1H} NMR
(100 MHz, CDCl3)

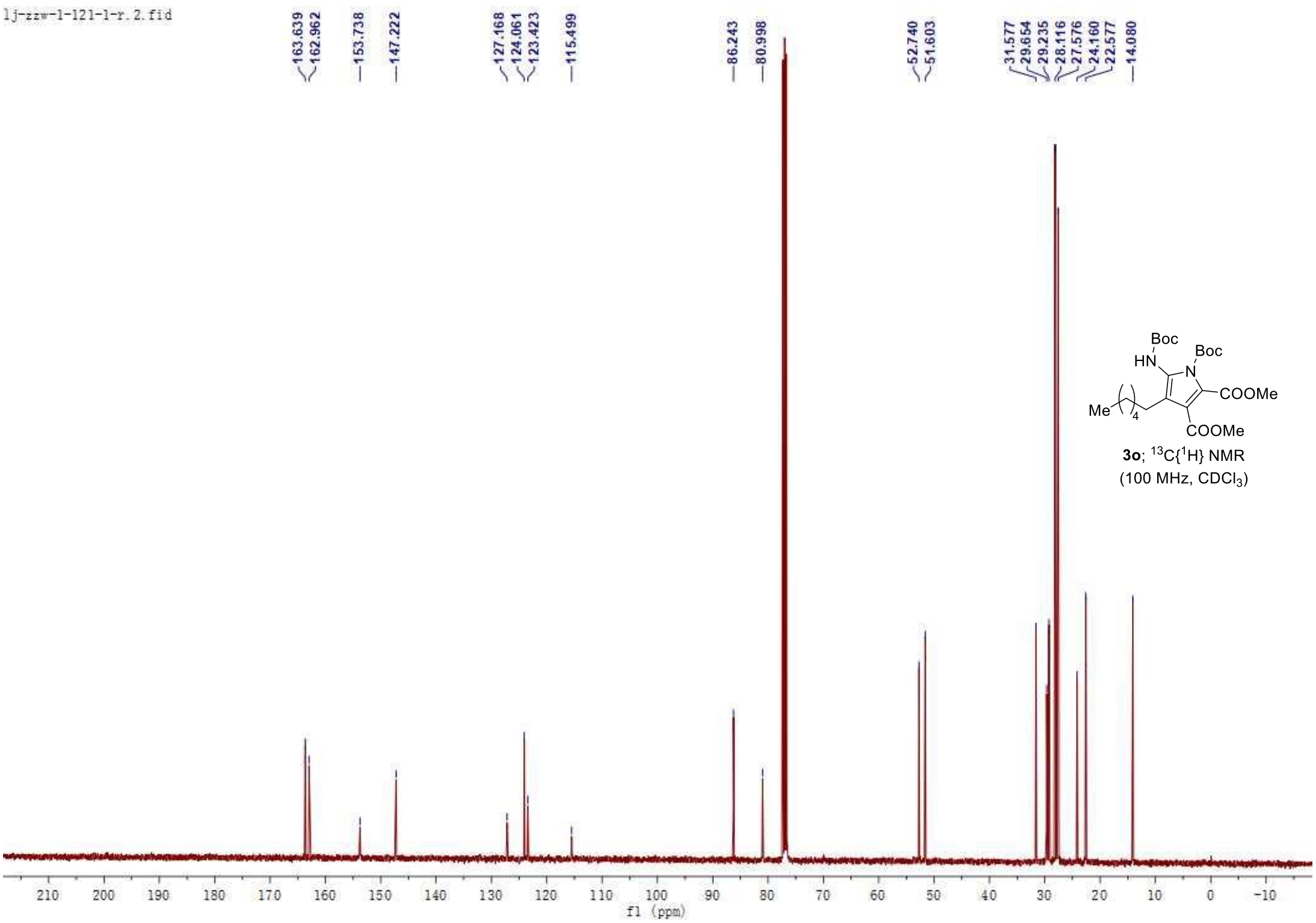

lj-zzw-1-118-1.1.fid
6.524
4.546
4.229
4.079
3.888
3.856
1.568
1.424
1.03
2.00
2.08
4.71
5.81
17.90
f1 (ppm)
Boc
HN
Boc
N
COOMe
COOMe
Fe
3n; 1H NMR
(400 MHz, CDCl3)



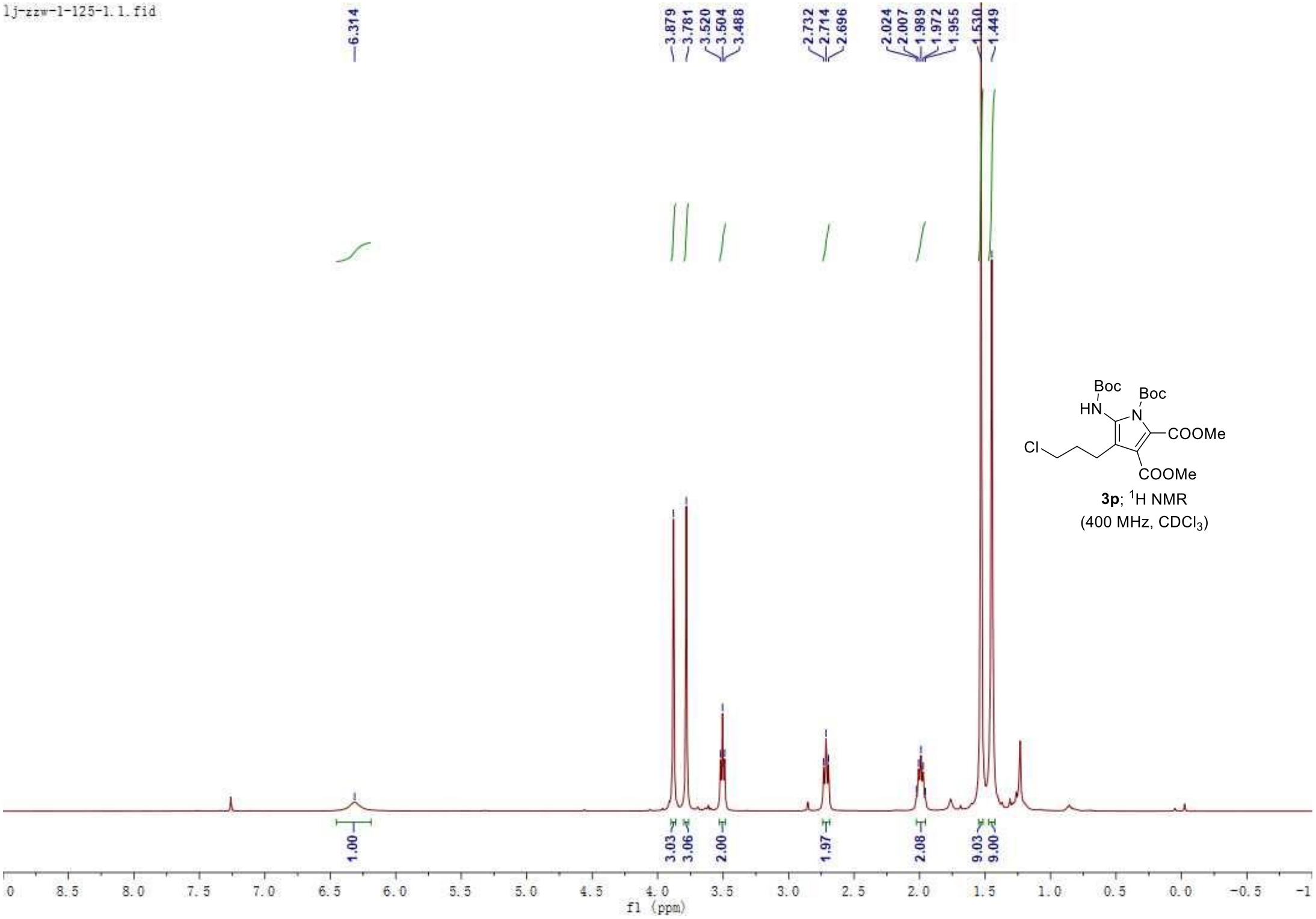
3n; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)



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

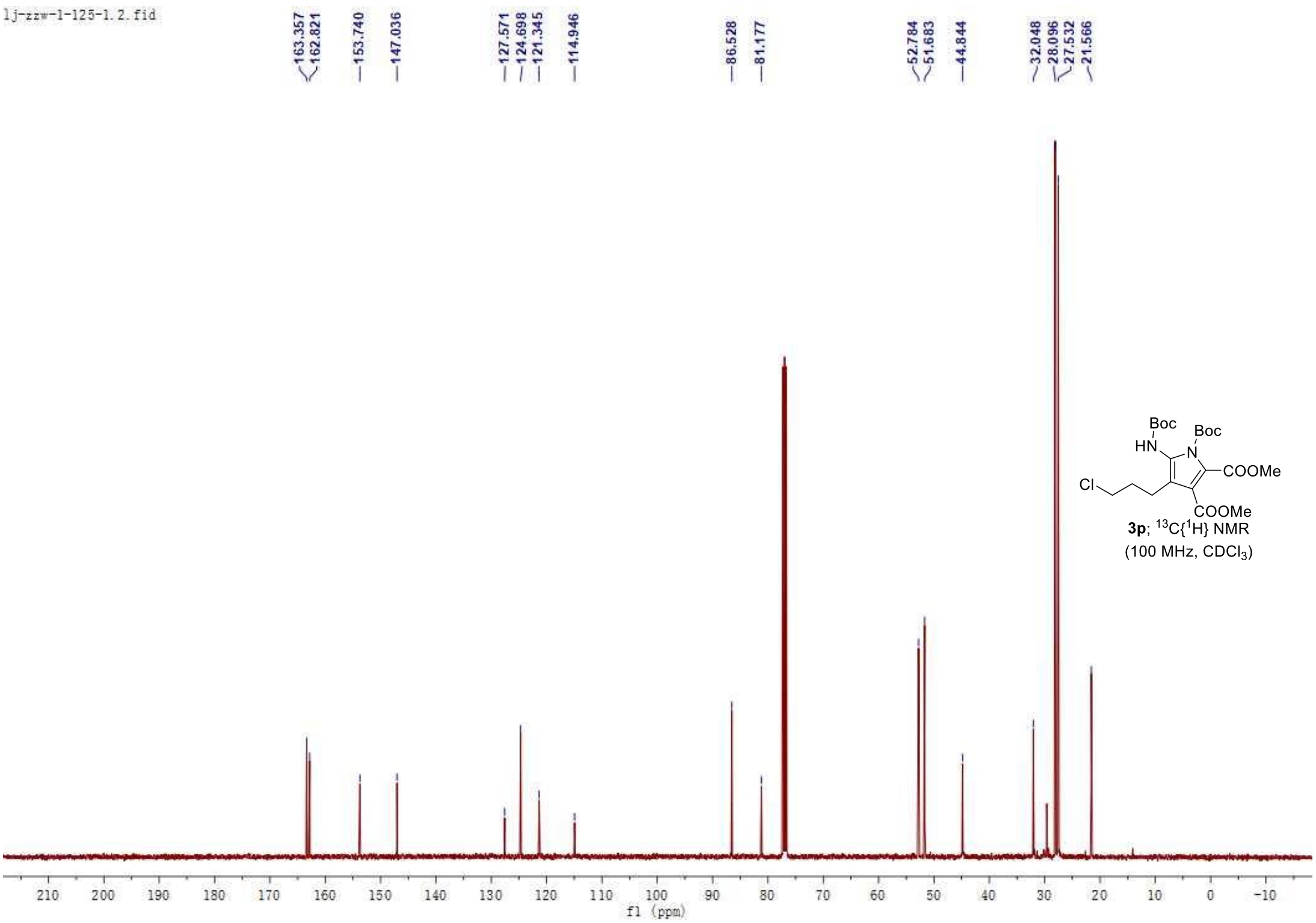


3o; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

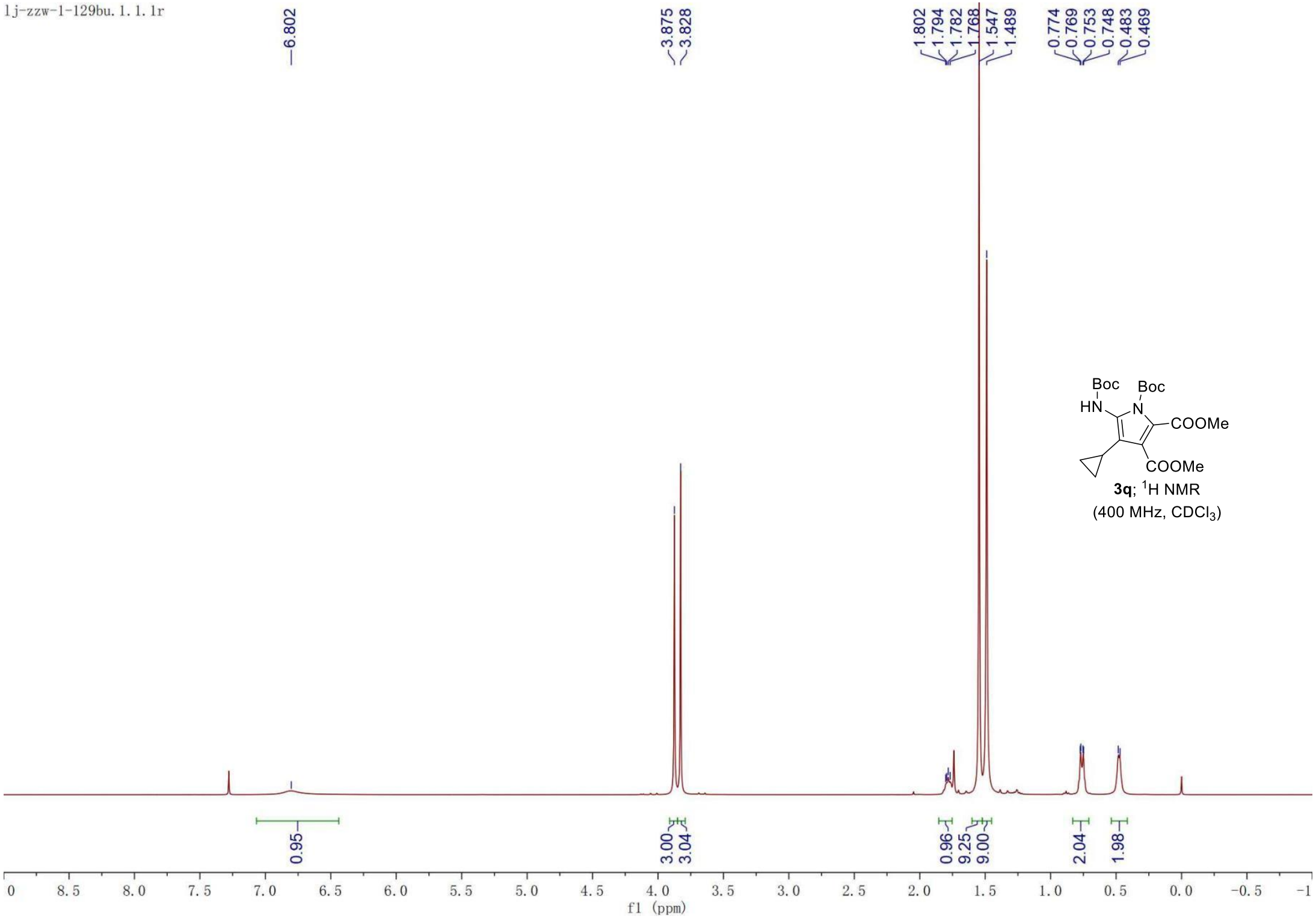


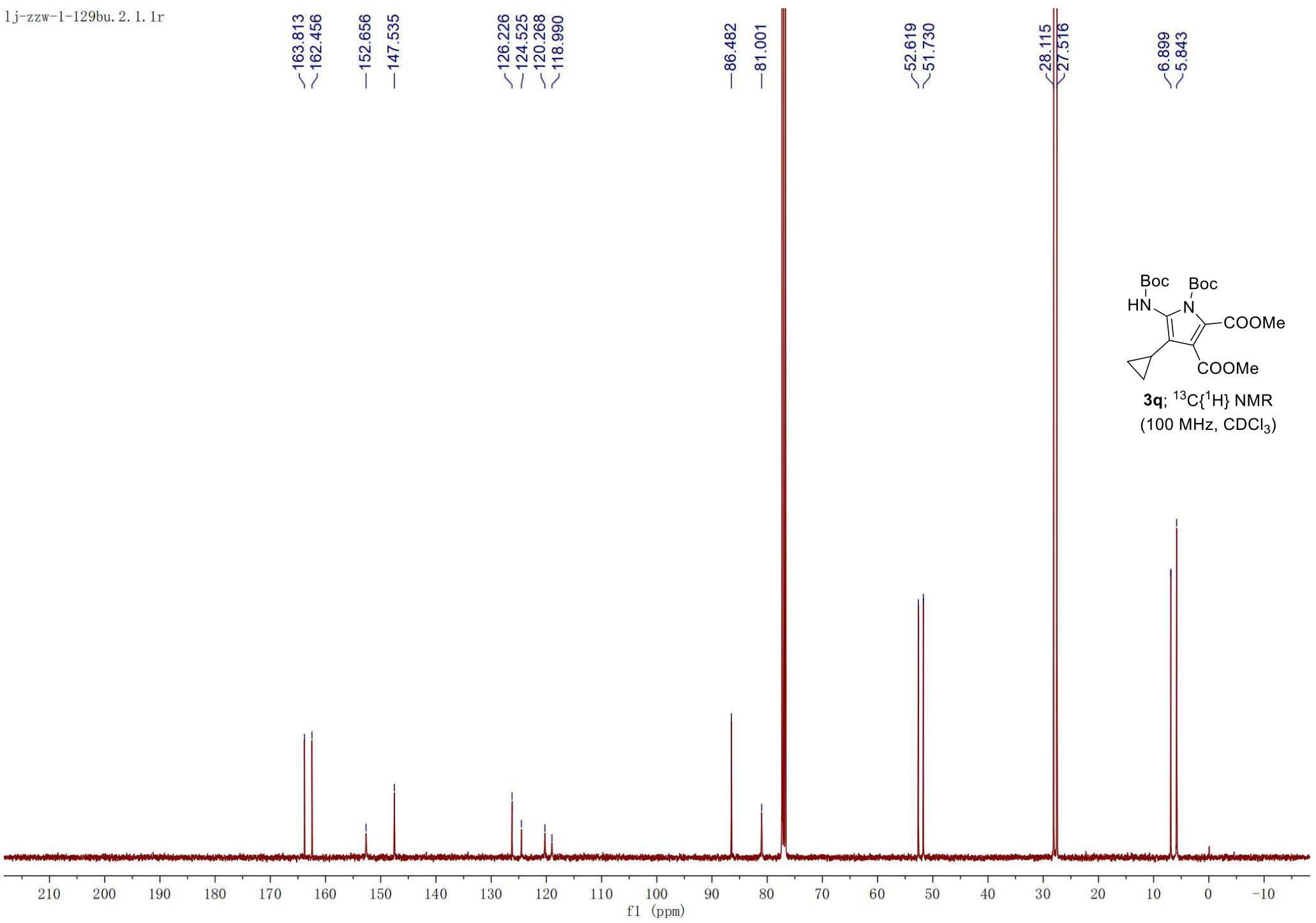
3p; ^{1}H NMR
(400 MHz, $CDCl_3$)

lj-zzw-1-125-1.2.fid

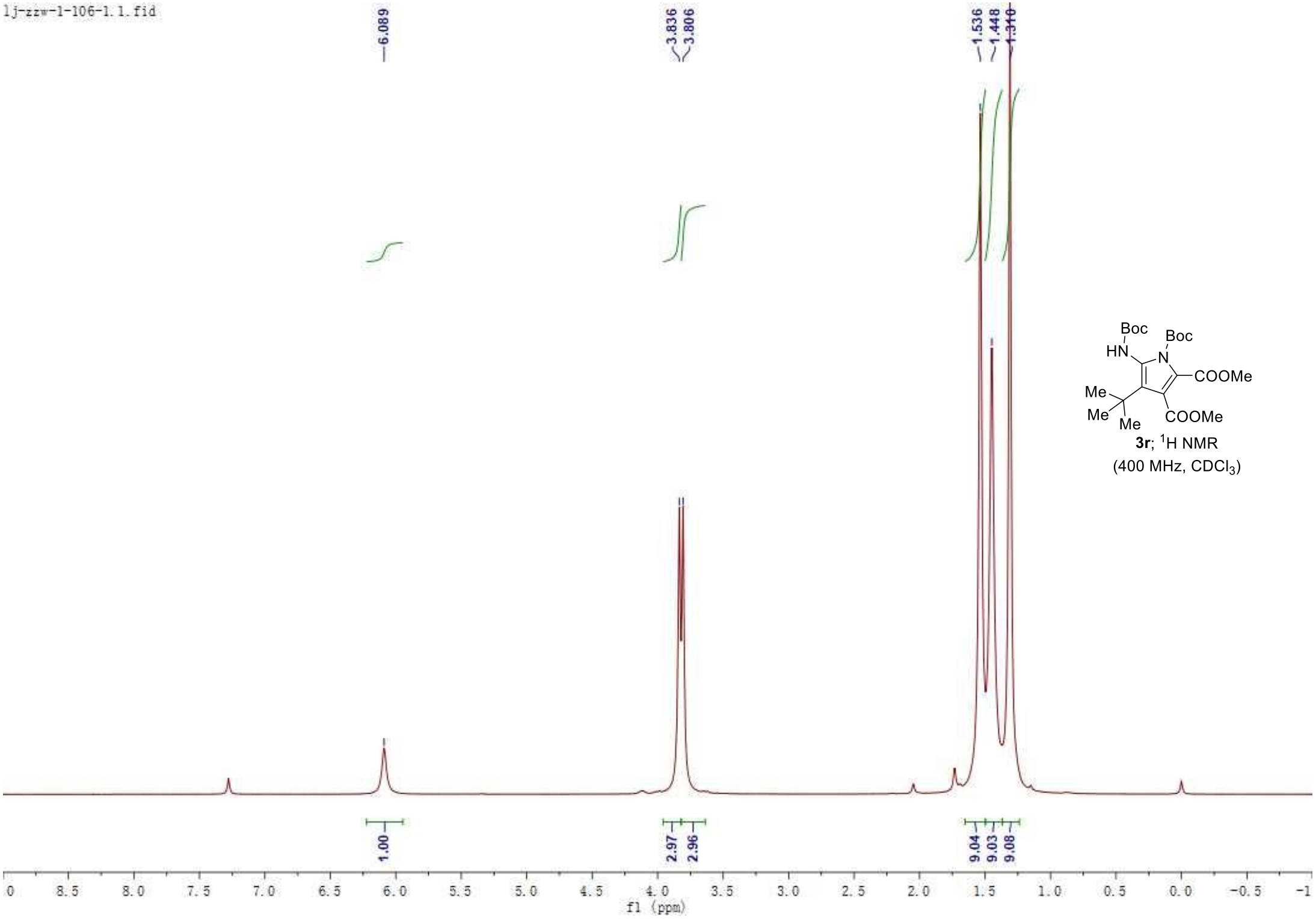


3p; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

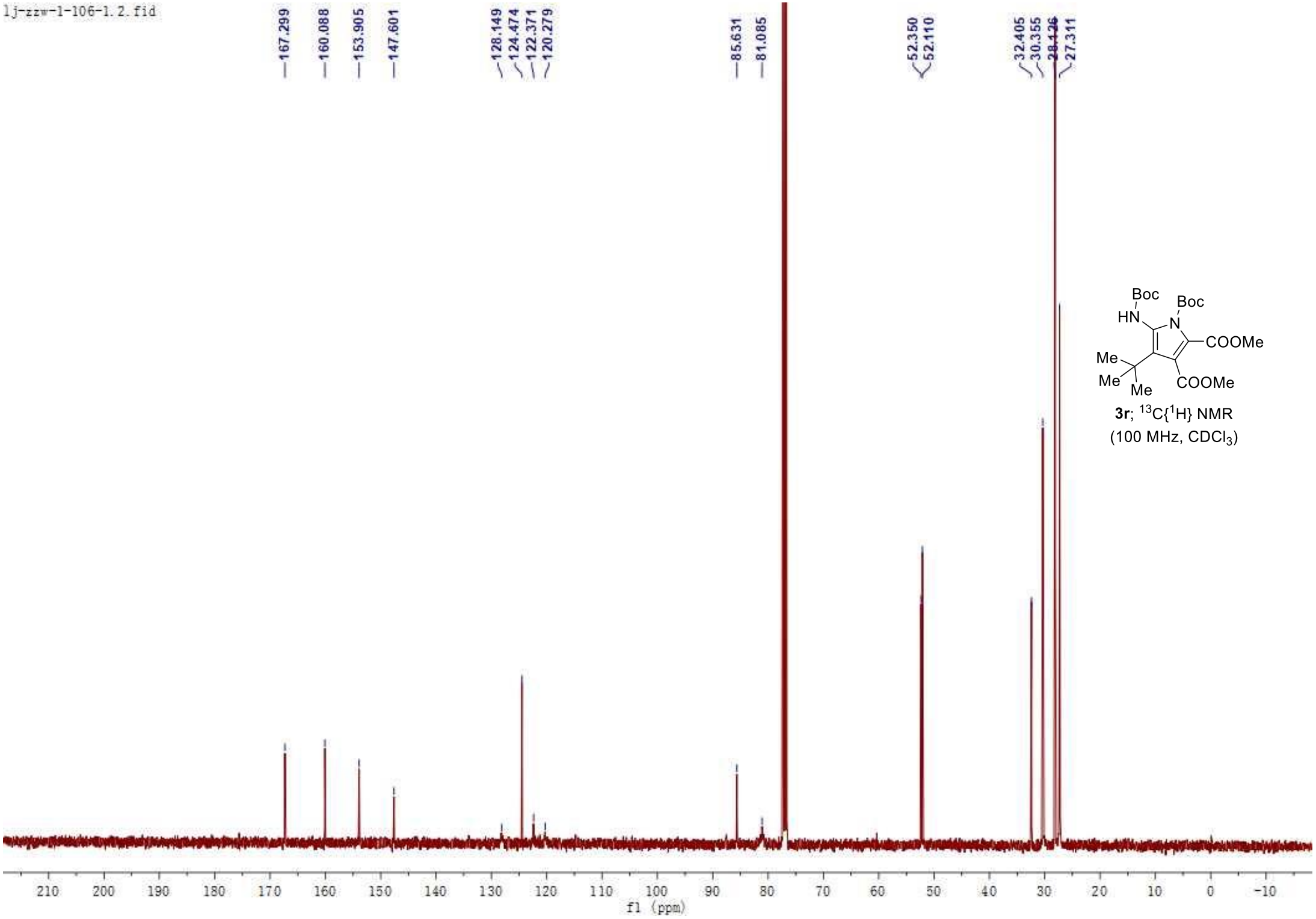

1j-zzw-1-129bu.1.1.1r
6.802
3.875
3.828
1.802
1.794
1.782
1.768
1.547
1.489
0.774
0.769
0.753
0.748
0.483
0.469
Boc
Boc
HN
N
COOMe
COOMe
3q; 1H NMR
(400 MHz, CDCl3)
0.95
3.00
3.04
0.96
9.25
9.00
2.04
1.98
f1 (ppm)

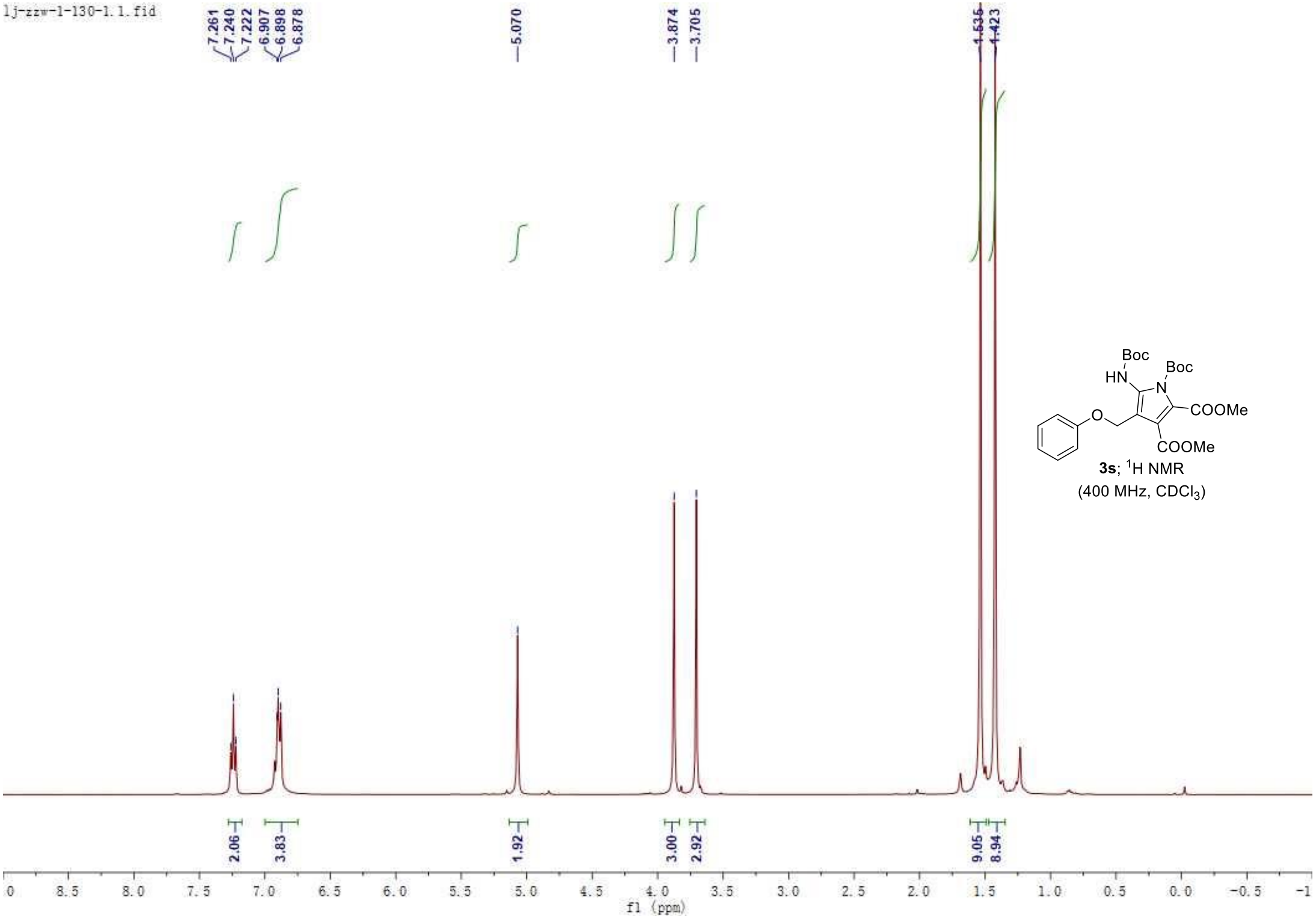


3q; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

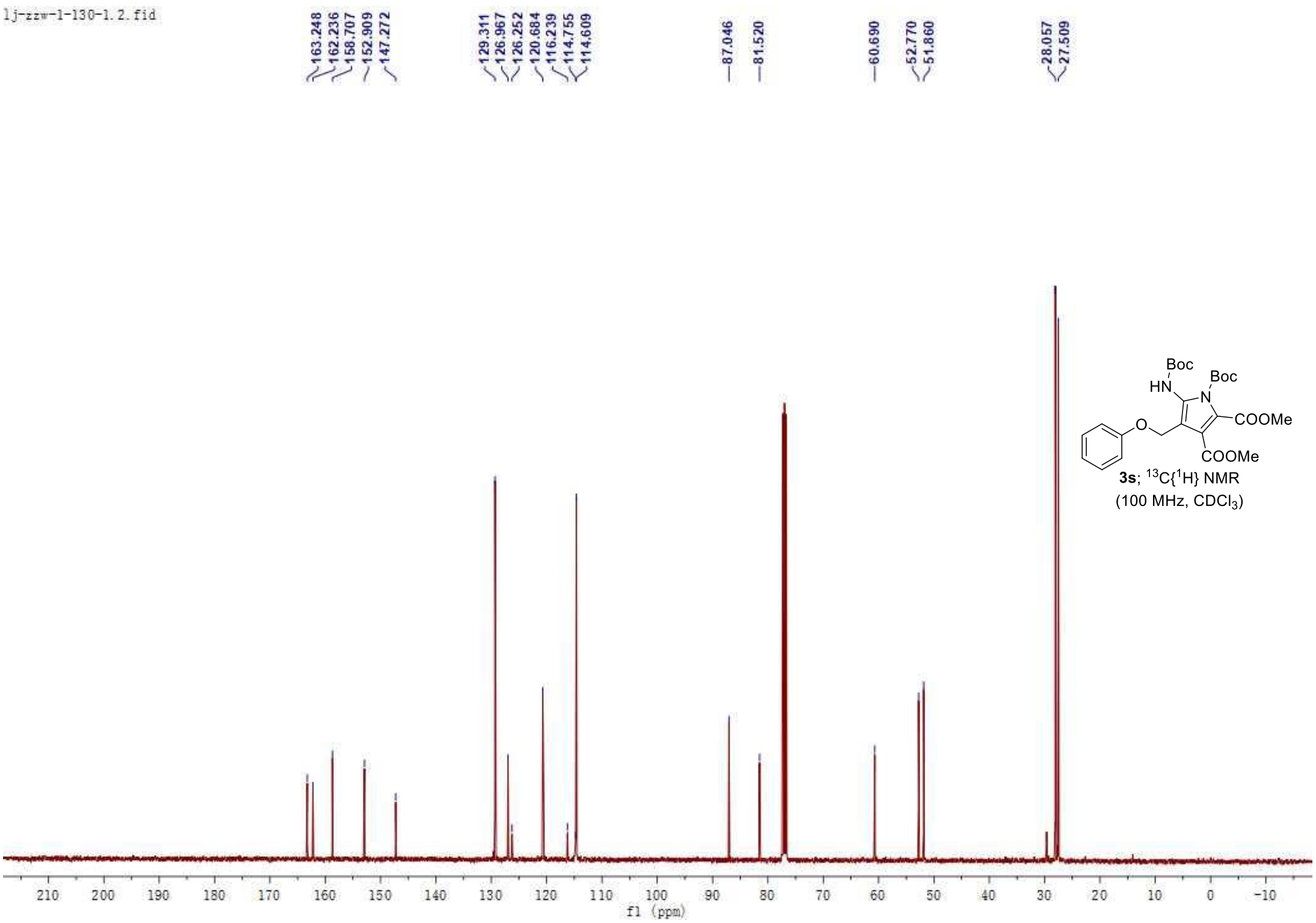


3r; ^{1}H NMR
(400 MHz, $CDCl_3$)

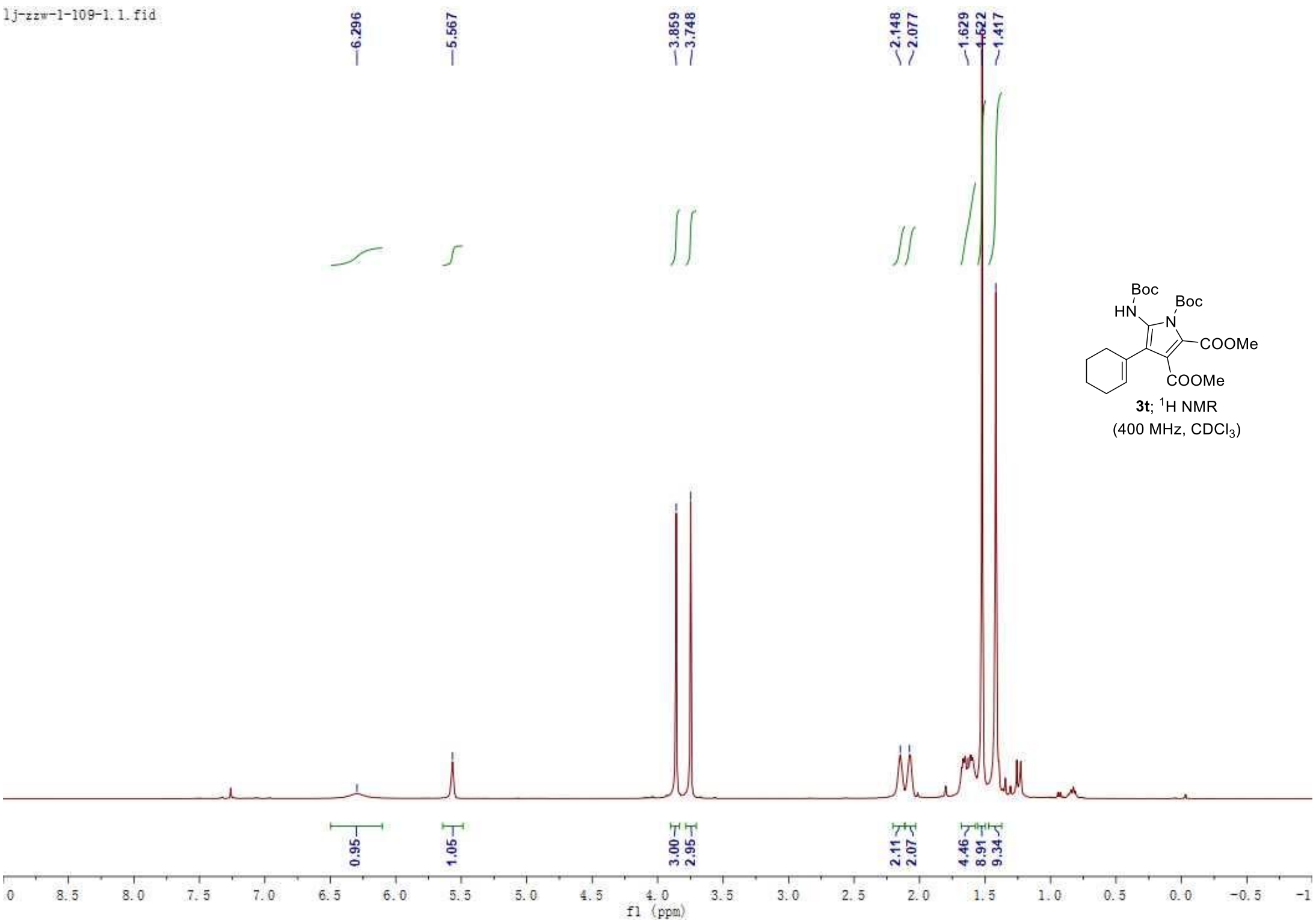

lj-zzw-1-106-1.2.fid
167.299
160.088
153.905
147.601
128.149
124.474
122.371
120.279
85.631
81.085
52.350
52.110
32.405
30.355
28.126
27.311
Boc
HN
Boc
N
COOMe
Me
Me
Me
COOMe
3r; 13C{1H} NMR
(100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


lj-zzw-1-130-1.1.fid
7.261
7.240
7.222
6.907
6.898
6.878
5.070
3.874
3.705
1.535
1.423
2.06
3.83
1.92
3.00
2.92
9.05
8.94
f1 (ppm)
Boc
HN
Boc
N
O
COOMe
COOMe
3s; 1H NMR
(400 MHz, CDCl3)

lj-zzw-1-130-1.2.fid



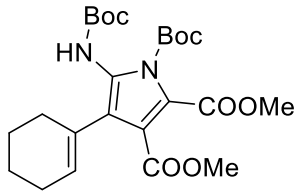
3s; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)



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

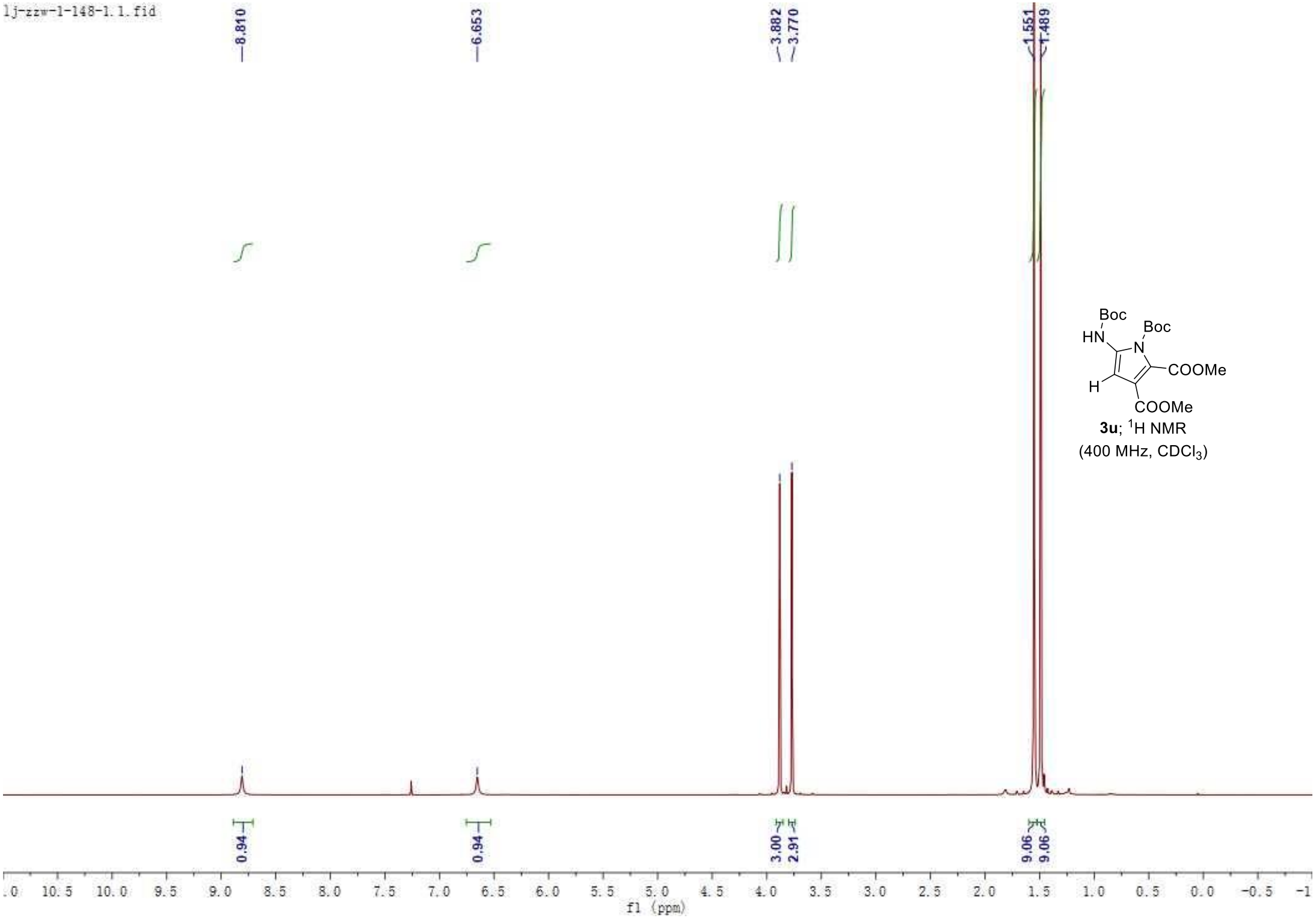
lj-zzw-1-109-1-re(two).2.1.1r

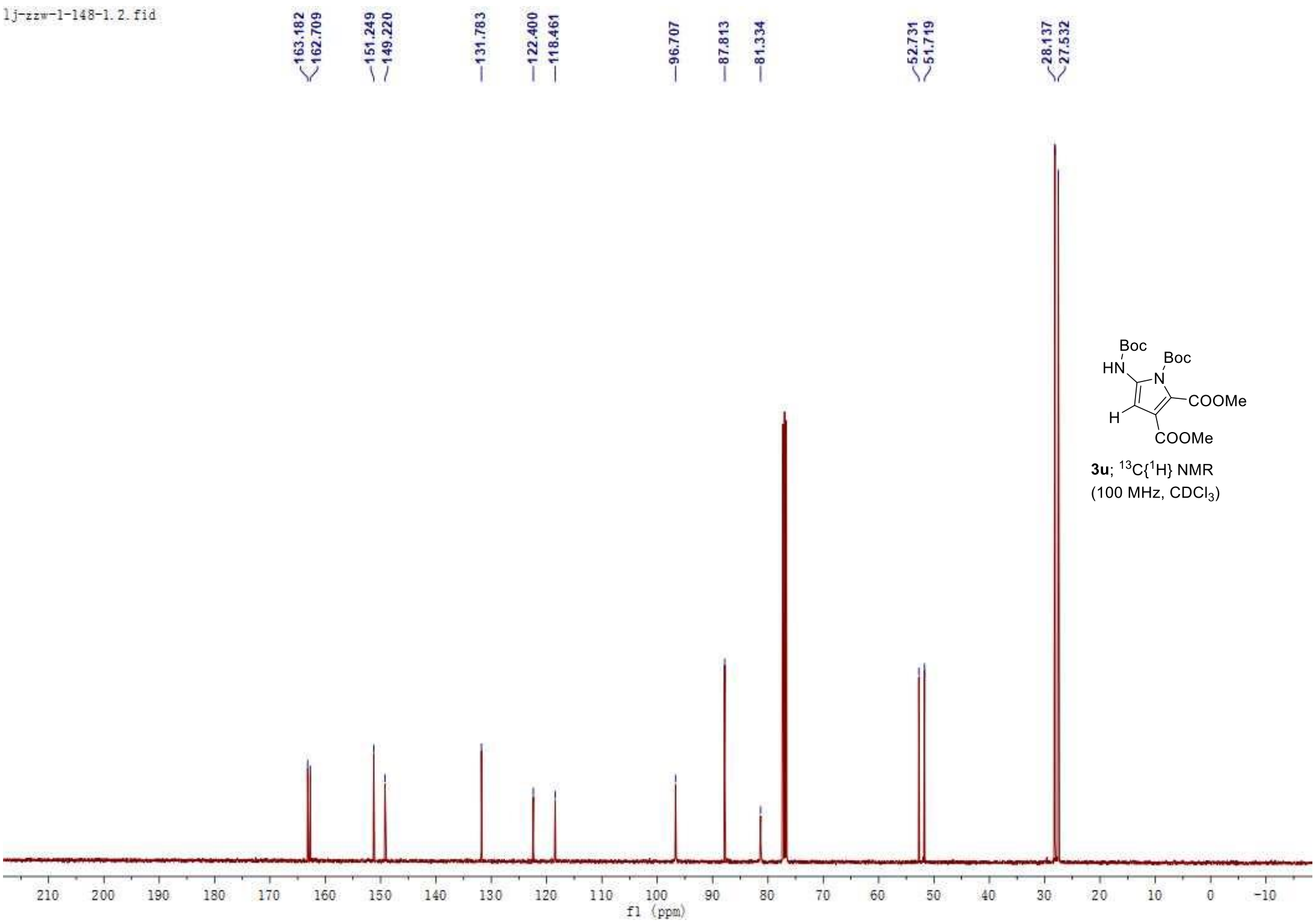
163.605
162.463
153.311
147.342
129.936
127.243
125.498
124.622
124.006
116.706
86.287
80.783
52.663
51.776
28.619
28.079
27.524
25.478
22.926
21.990

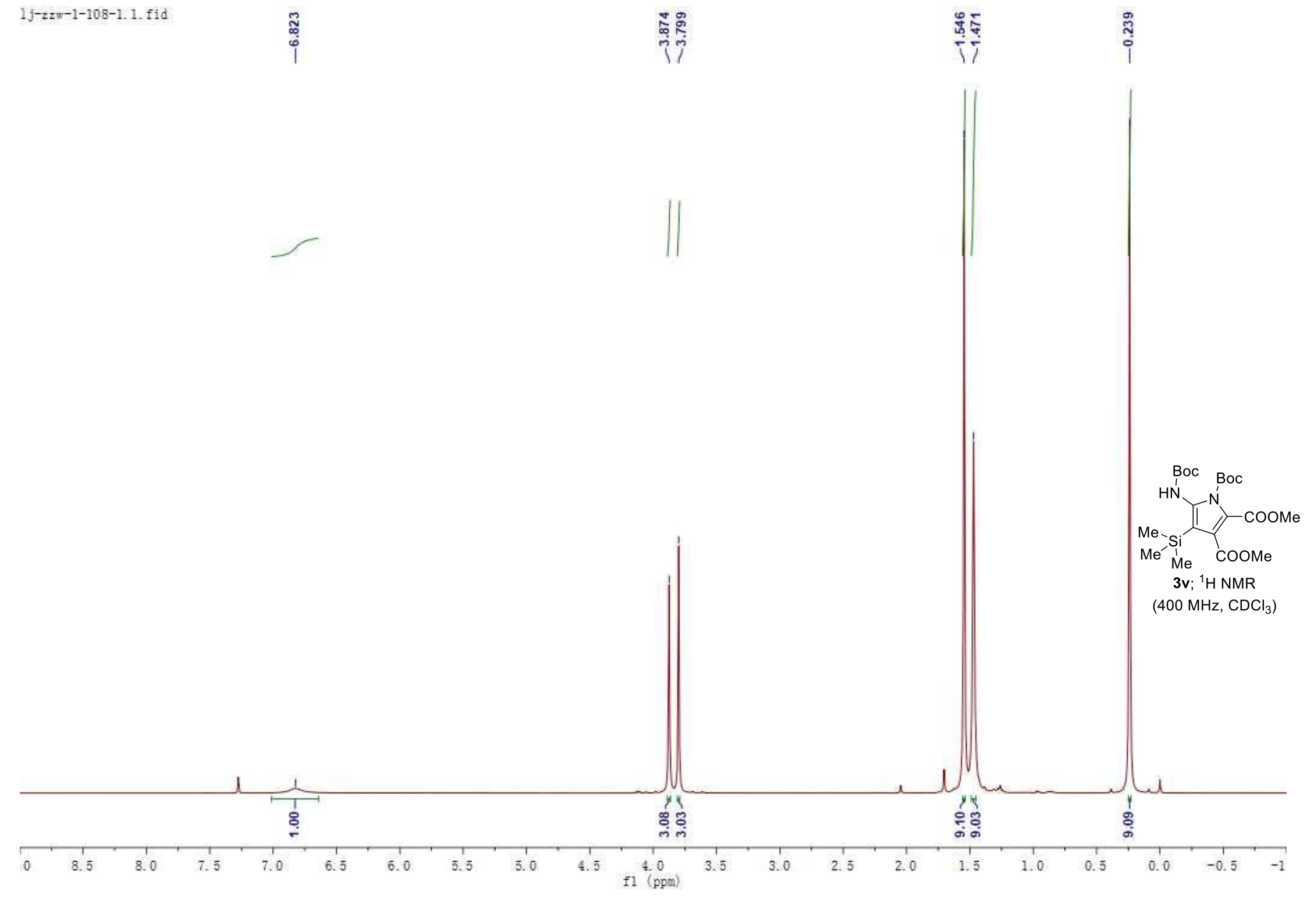


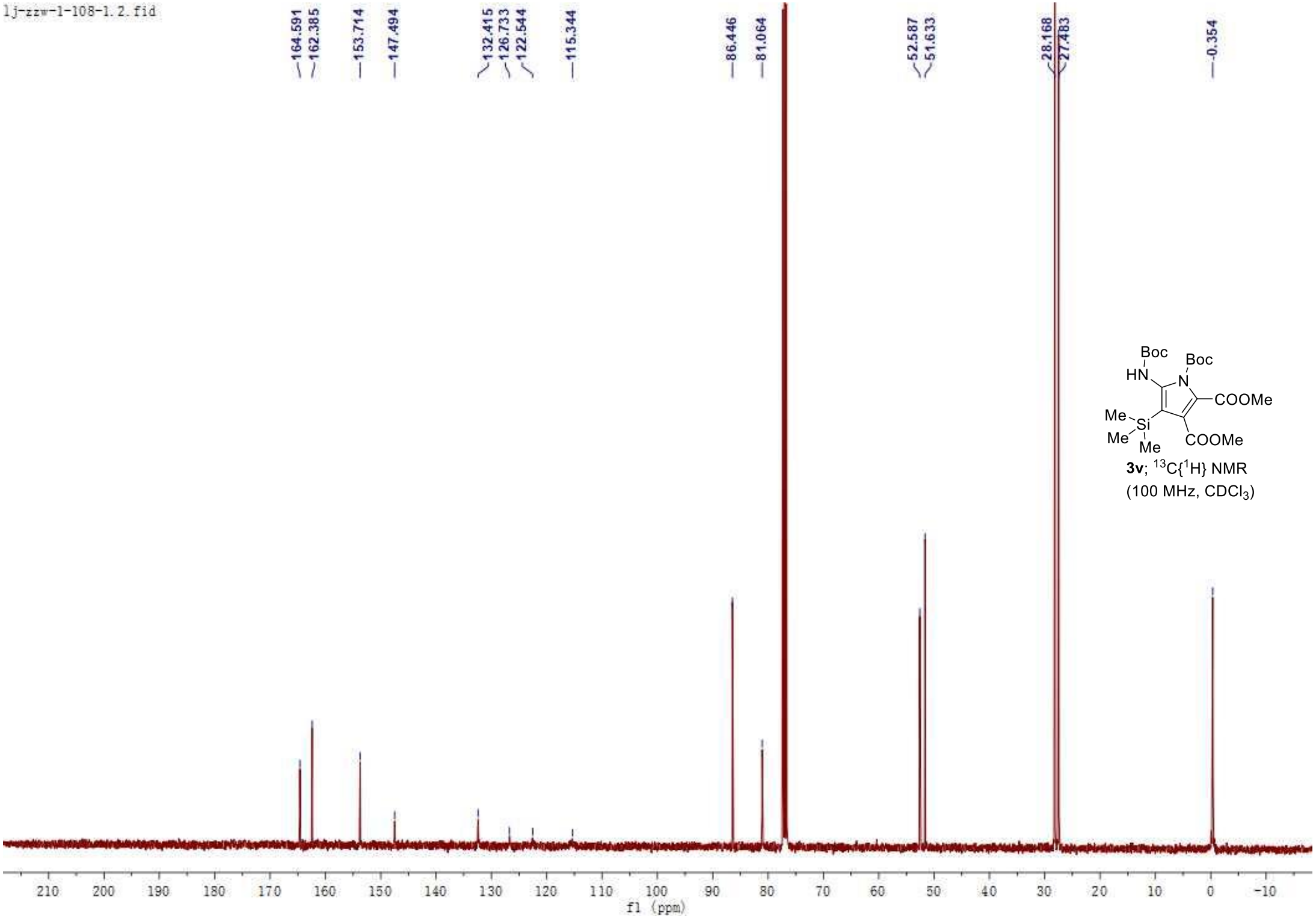
3t; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

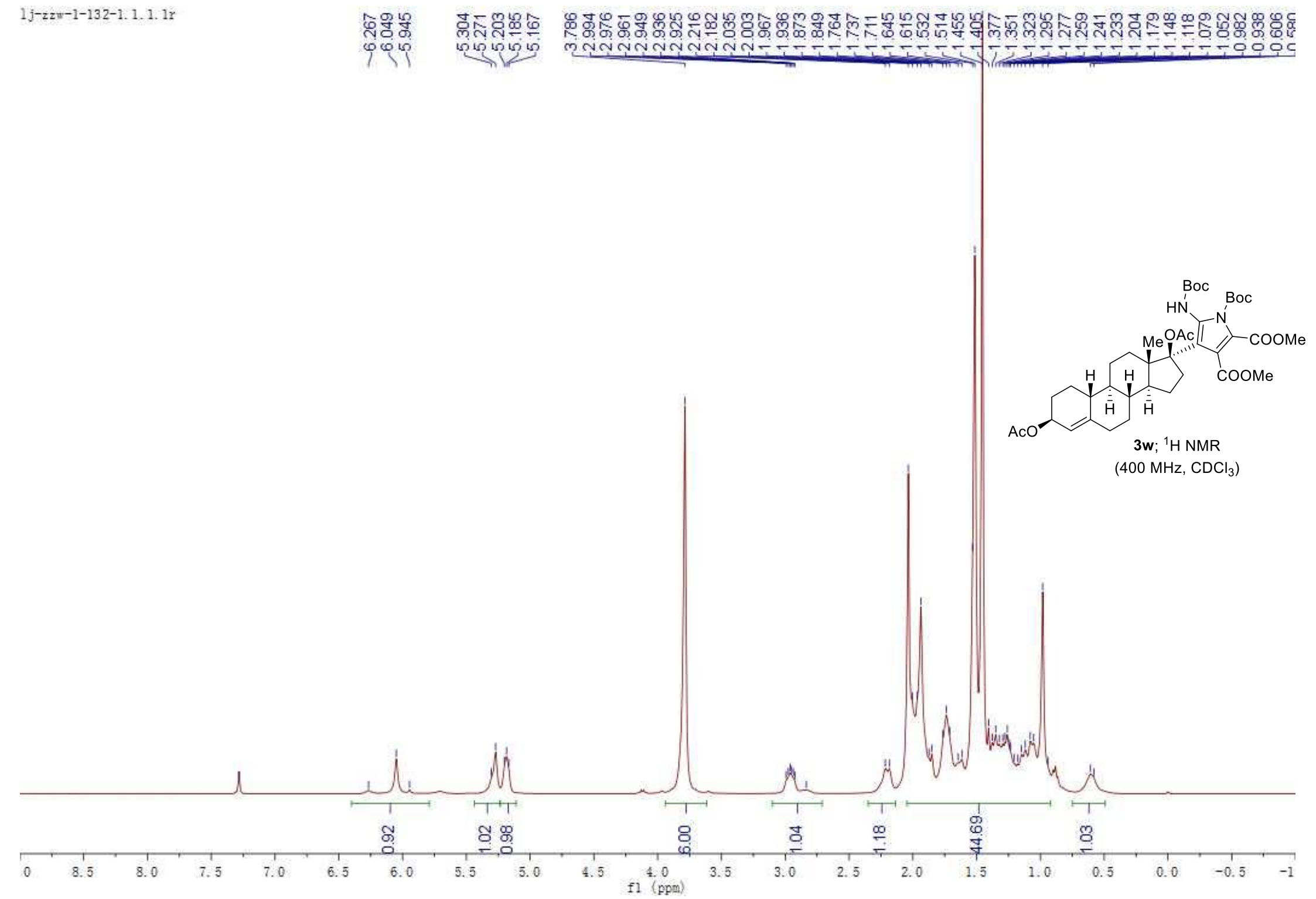
f1 (ppm)


lj-zzw-1-148-1.1.fid
8.810
6.653
3.882
3.770
1.551
1.489
0.94
0.94
3.00
2.91
9.06
9.06
f1 (ppm)
Boc
HN
Boc
N
COOMe
H
COOMe
3u; 1H NMR
(400 MHz, CDCl3)

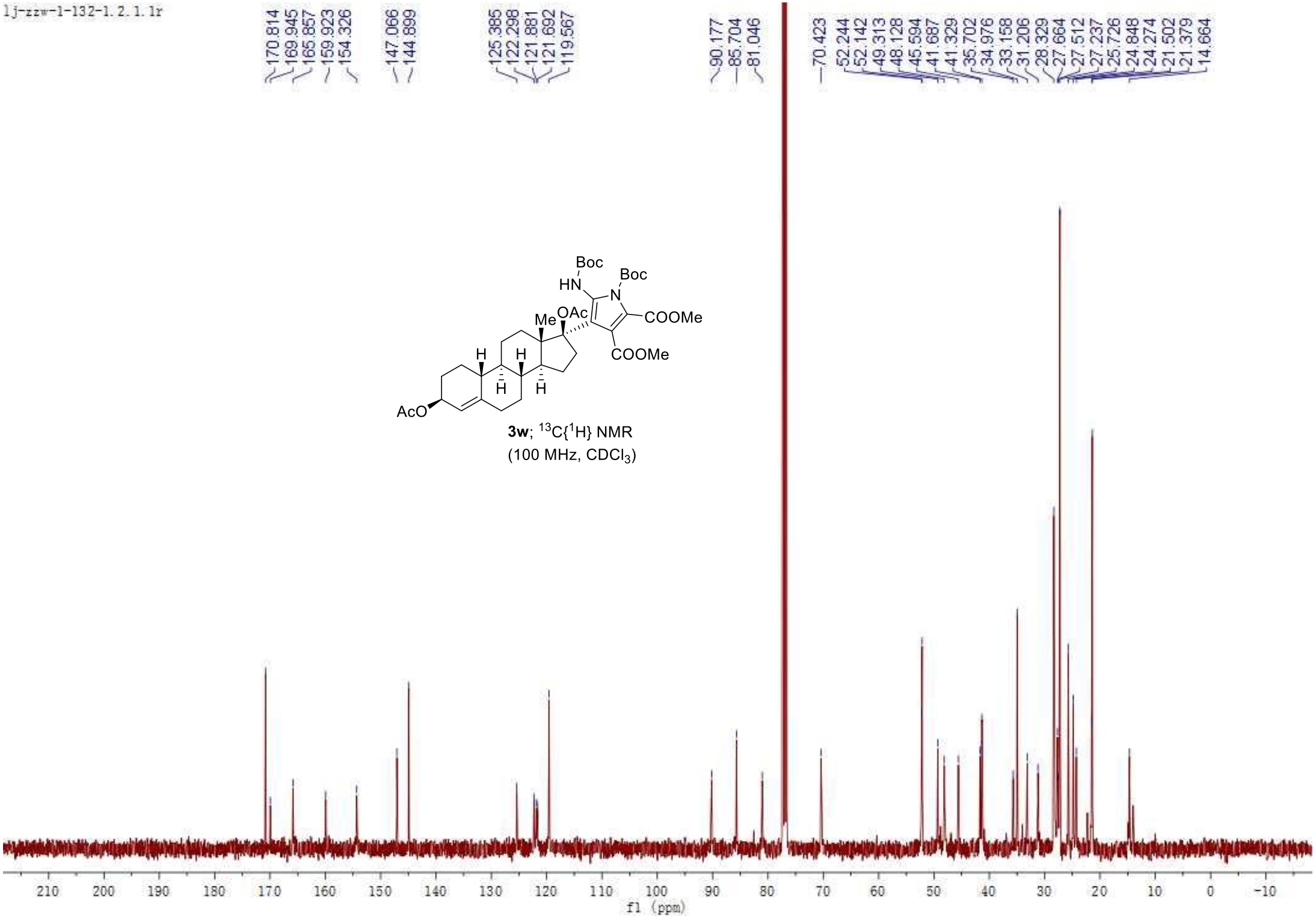

lj-zzw-1-148-1.2.fid
163.182
162.709
151.249
149.220
131.783
122.400
118.461
96.707
87.813
81.334
52.731
51.719
28.137
27.532
Boc
HN
Boc
N
COOMe
H
COOMe
3u; 13C{1H} NMR
(100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

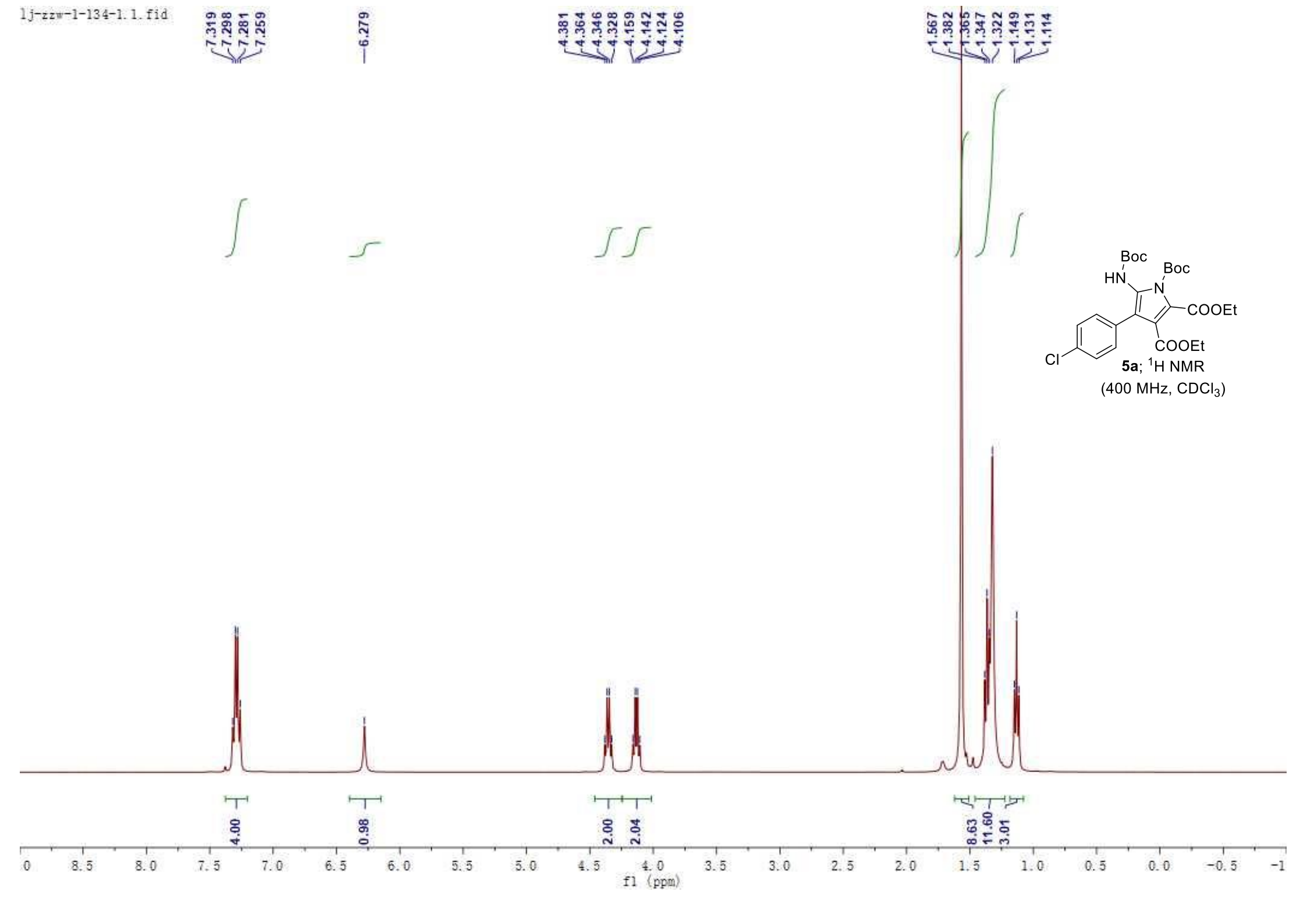

lj-zzw-1-108-1.1.fid
6.823
3.874
3.799
1.546
1.471
0.239
1.00
3.08
3.03
9.10
9.03
9.09
f1 (ppm)
Boc
Boc
HN
N
COOMe
Me
Si
Me
Me
COOMe
3v; 1H NMR
(400 MHz, CDCl3)


lj-zzw-1-108-1.2.fid
164.591
162.385
153.714
147.494
132.415
126.733
122.544
115.344
86.446
81.064
52.587
51.633
28.168
27.483
-0.354
Boc
HN
Boc
N
COOMe
Me
Si
Me
Me
COOMe
3v; 13C{1H} NMR
(100 MHz, 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)

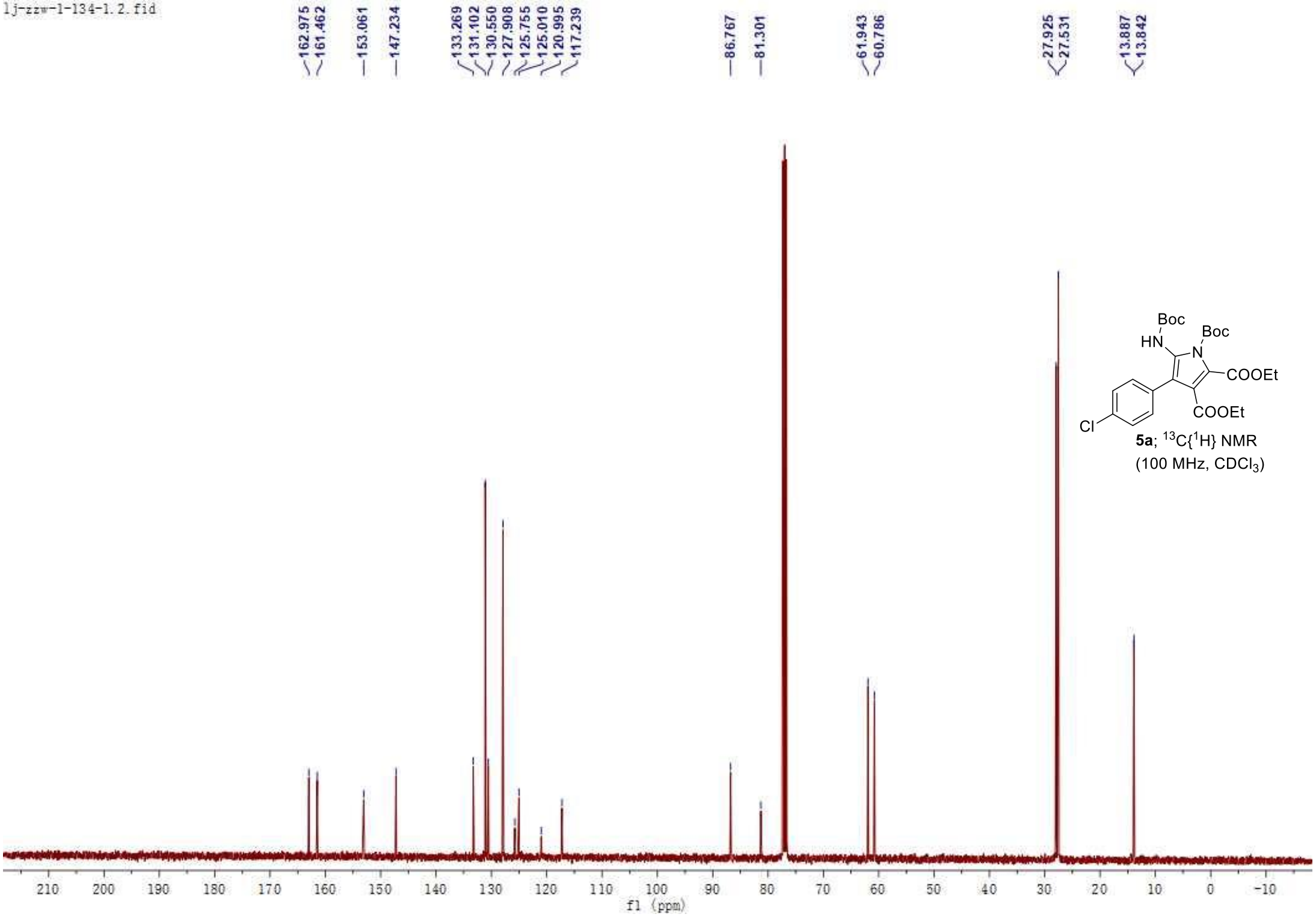


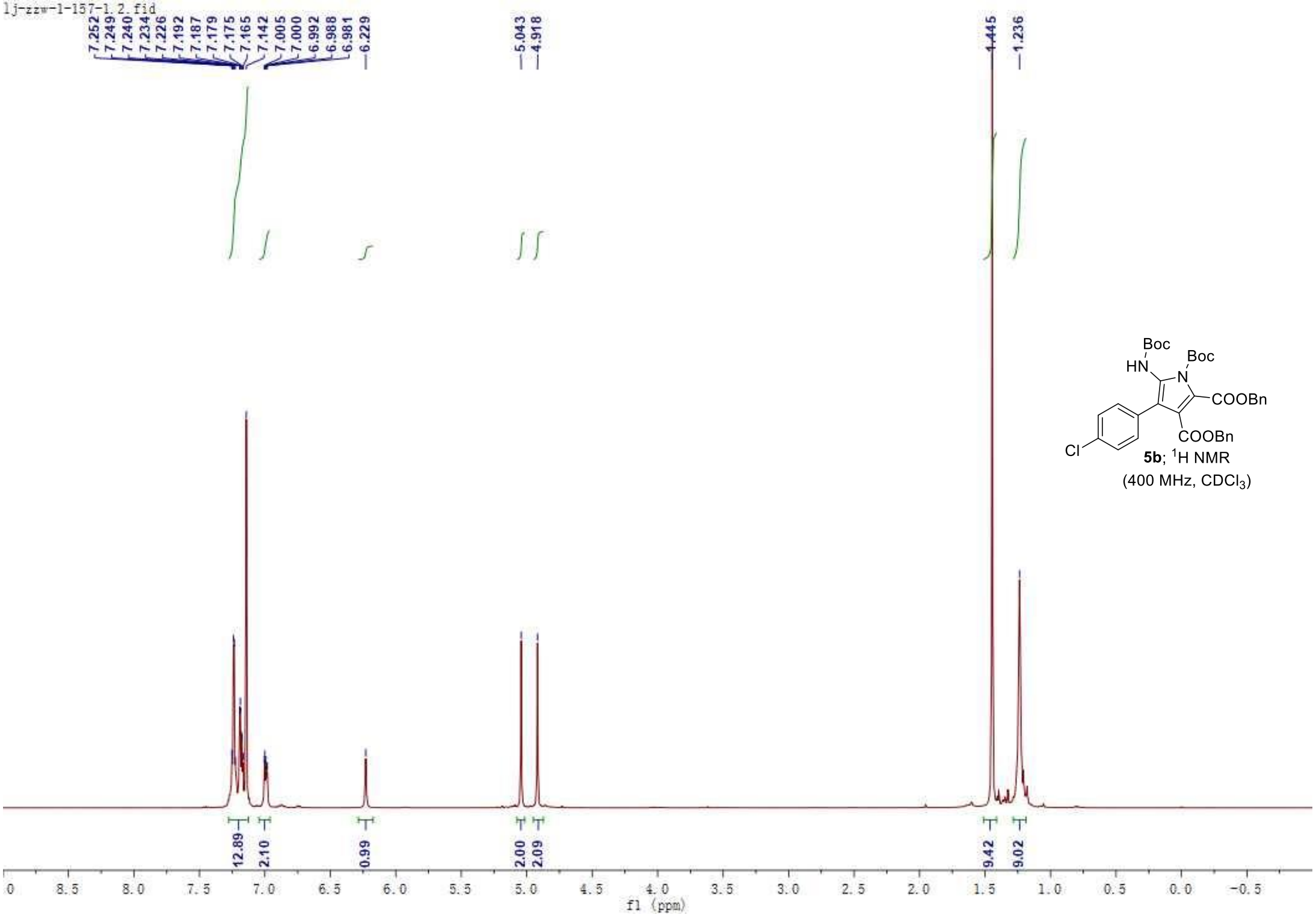
3w; ^{1}H NMR
(400 MHz, $CDCl_3$)

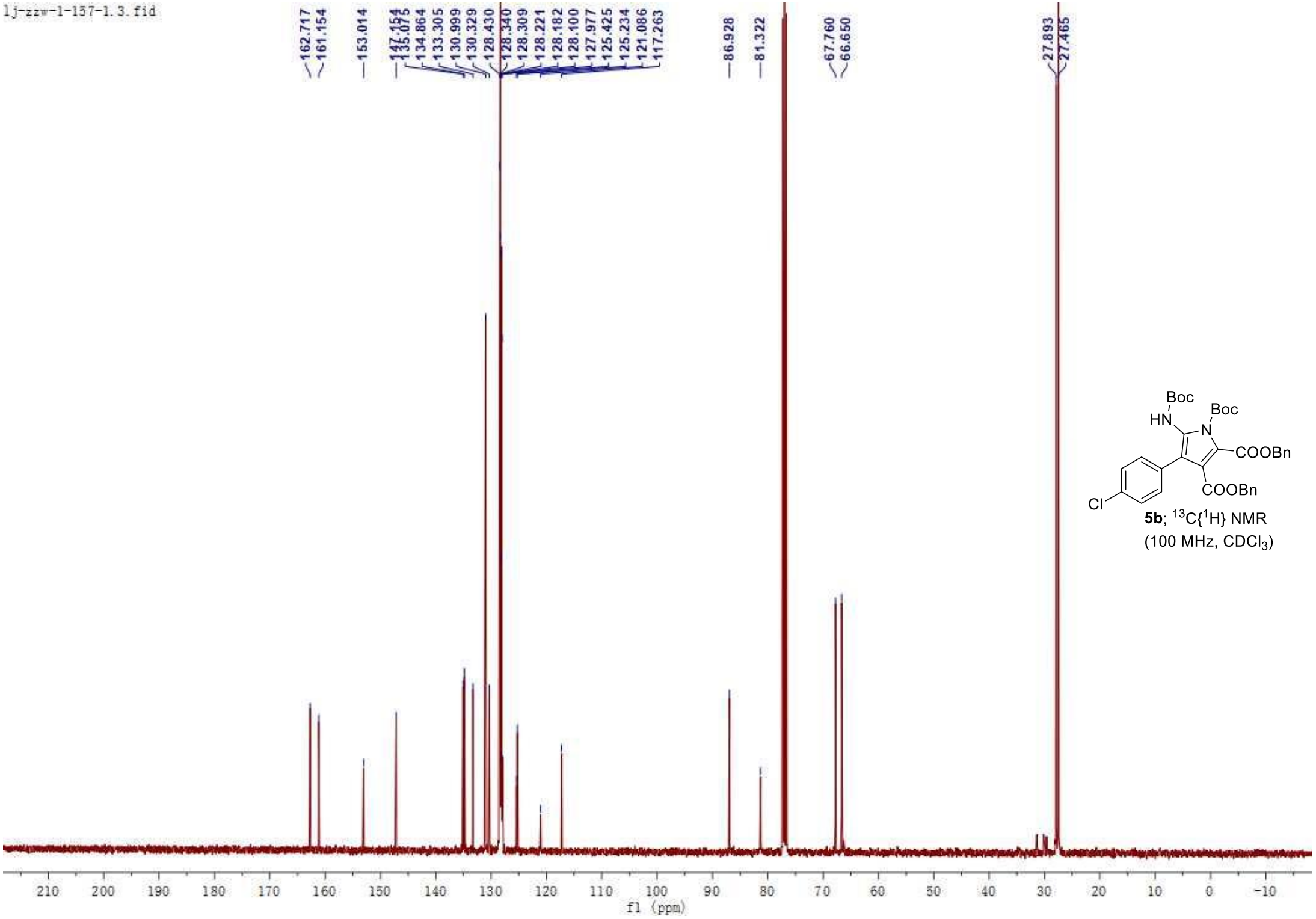

lj-zzw-1-132-1.2.1.1r
170.814
169.945
165.857
159.923
154.326
147.066
144.899
125.385
122.298
121.881
121.692
119.567
90.177
85.704
81.046
70.423
52.244
52.142
49.313
48.128
45.594
41.687
41.329
35.702
34.976
33.158
31.206
28.329
27.664
27.512
27.237
25.726
24.848
24.274
21.502
21.379
14.664
Boc
HN
Boc
N
Me
OAc
COOMe
COOMe
H
H
H
H
AcO
3w; 13C{1H} NMR
(100 MHz, 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)


lj-zzw-1-134-1.1.fid
7.319
7.298
7.281
7.259
6.279
4.381
4.364
4.346
4.328
4.159
4.142
4.124
4.106
1.567
1.382
1.365
1.347
1.322
1.149
1.131
1.114
Boc
HN
Boc
N
COOEt
COOEt
Cl
5a; 1H NMR
(400 MHz, CDCl3)
4.00
0.98
2.00
2.04
8.63
11.60
3.01
f1 (ppm)

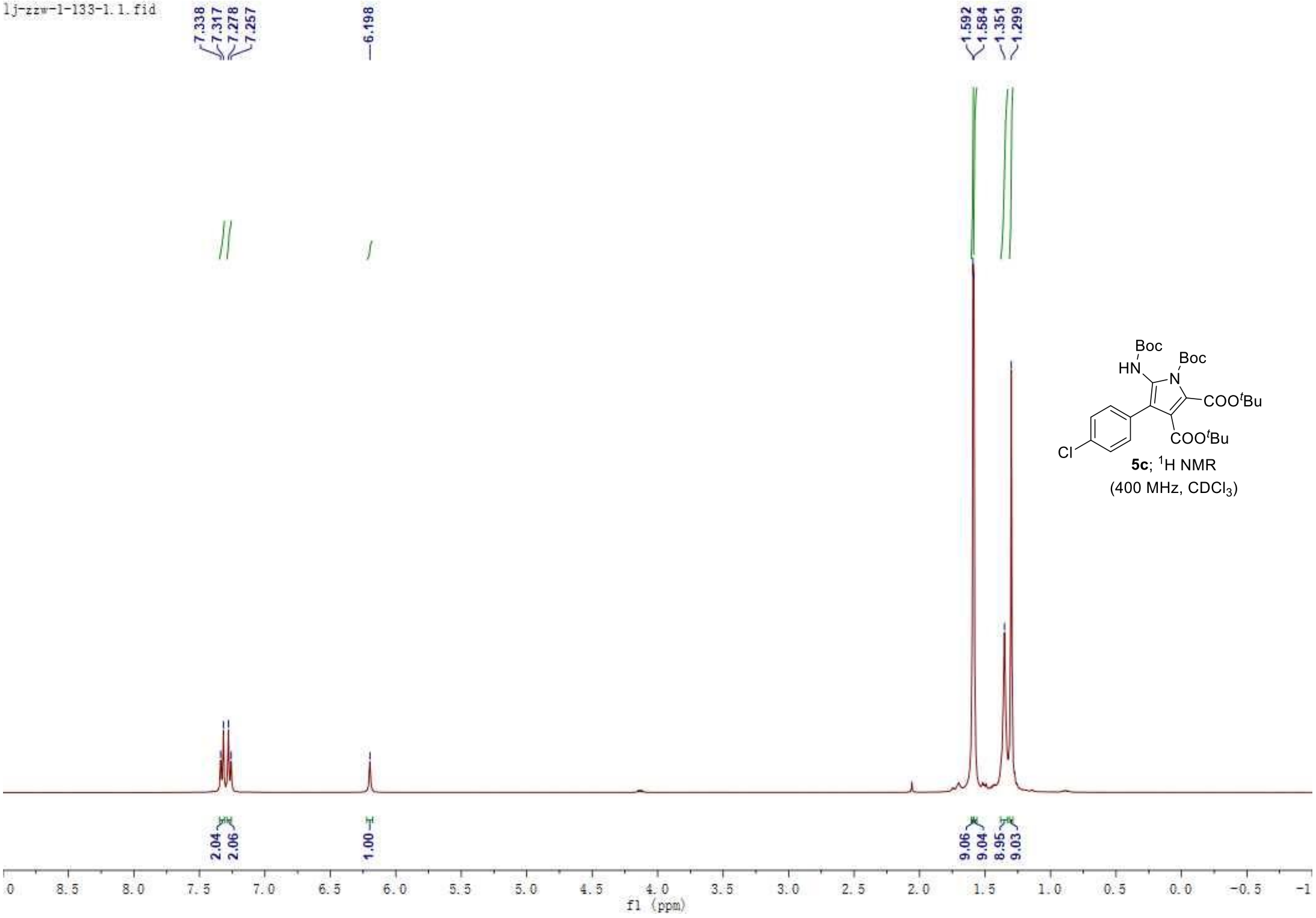
lj-zzw-1-134-1.2.fid




lj-zzw-1-157-1.2.fid
7.252
7.249
7.240
7.234
7.226
7.192
7.187
7.179
7.175
7.165
7.142
7.005
7.000
6.992
6.988
6.981
6.229
5.043
4.918
1.445
1.236
12.89
2.10
0.99
2.00
2.09
9.42
9.02
f1 (ppm)
Boc
HN
Boc
N
COOBn
COOBn
Cl
5b; 1H NMR
(400 MHz, CDCl3)

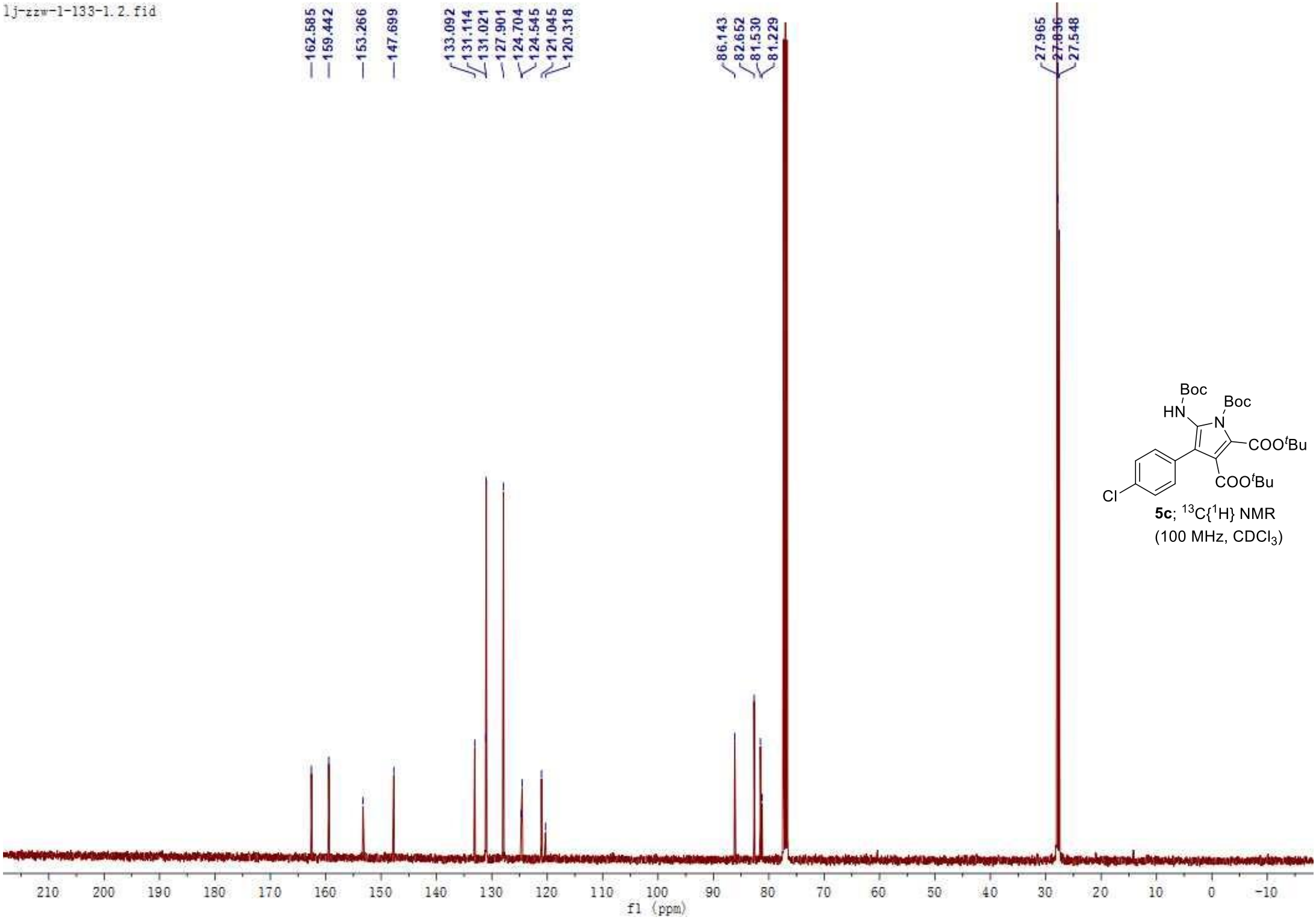


5b; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

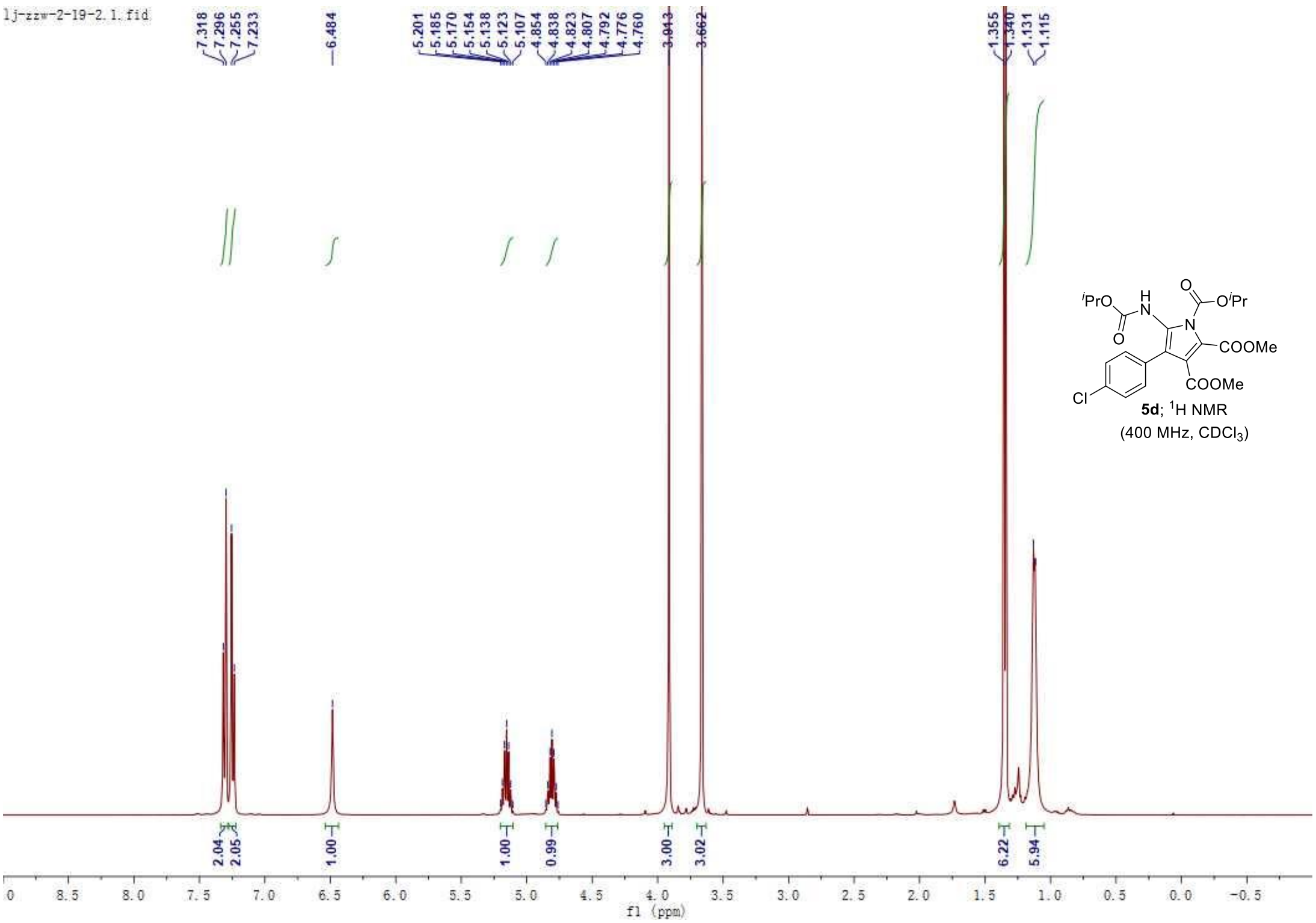


5c; ^{1}H NMR
(400 MHz, $CDCl_3$)

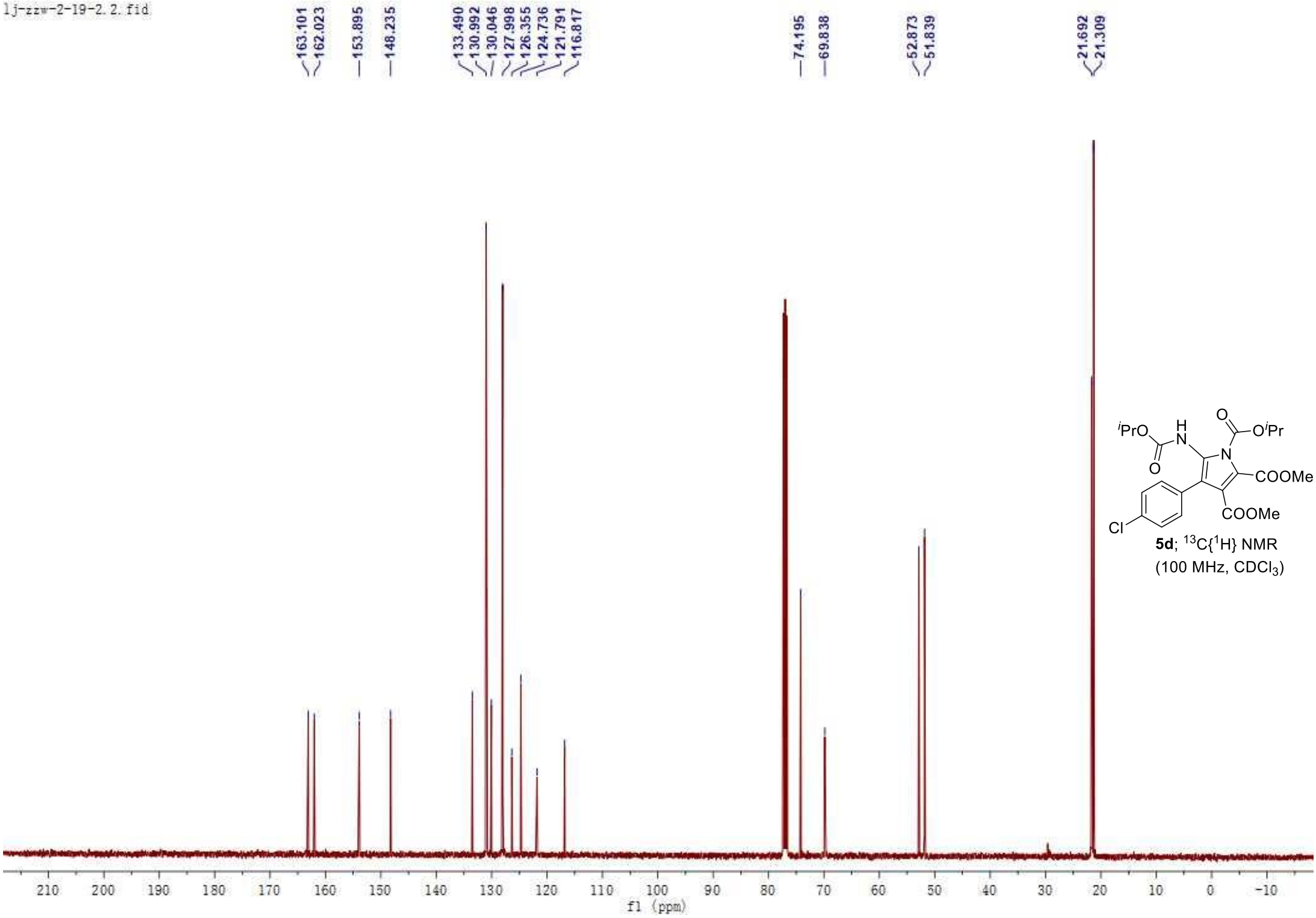
lj-zzw-1-133-1.2.fid



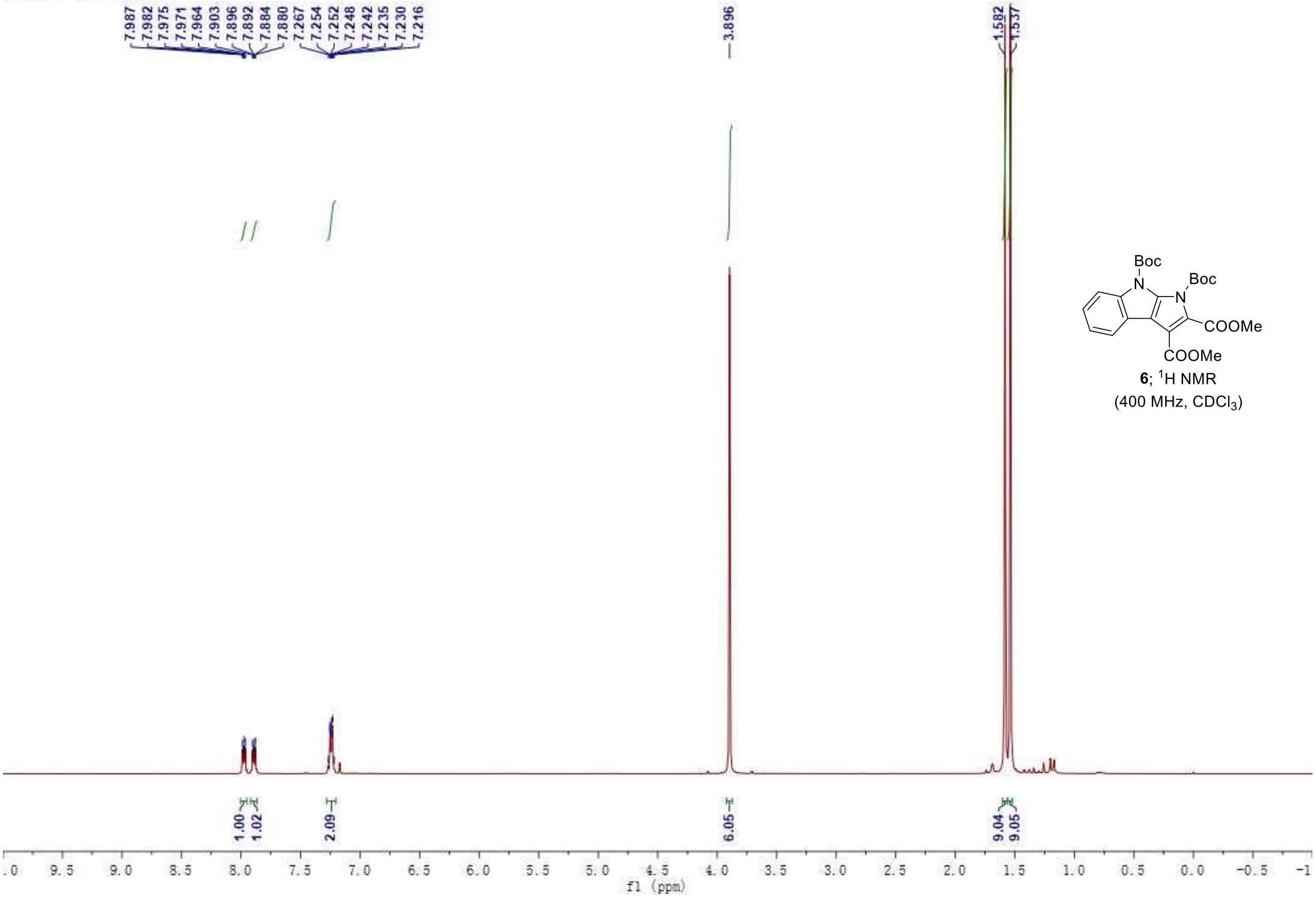
5c; $^{13}C\{^1H\}$ NMR
(100 MHz, $CDCl_3$)


lj-zzw-2-19-2.1.fid
7.318
7.296
7.255
7.233
6.484
5.201
5.185
5.170
5.154
5.138
5.123
5.107
4.854
4.838
4.823
4.807
4.792
4.776
4.760
3.043
3.662
1.355
1.340
1.131
1.115
2.04
2.05
1.00
1.00
0.99
3.00
3.02
6.22
5.94
f1 (ppm)
iPrO
H
N
O
O
O
OiPr
N
COOMe
COOMe
Cl
5d; 1H NMR
(400 MHz, CDCl3)

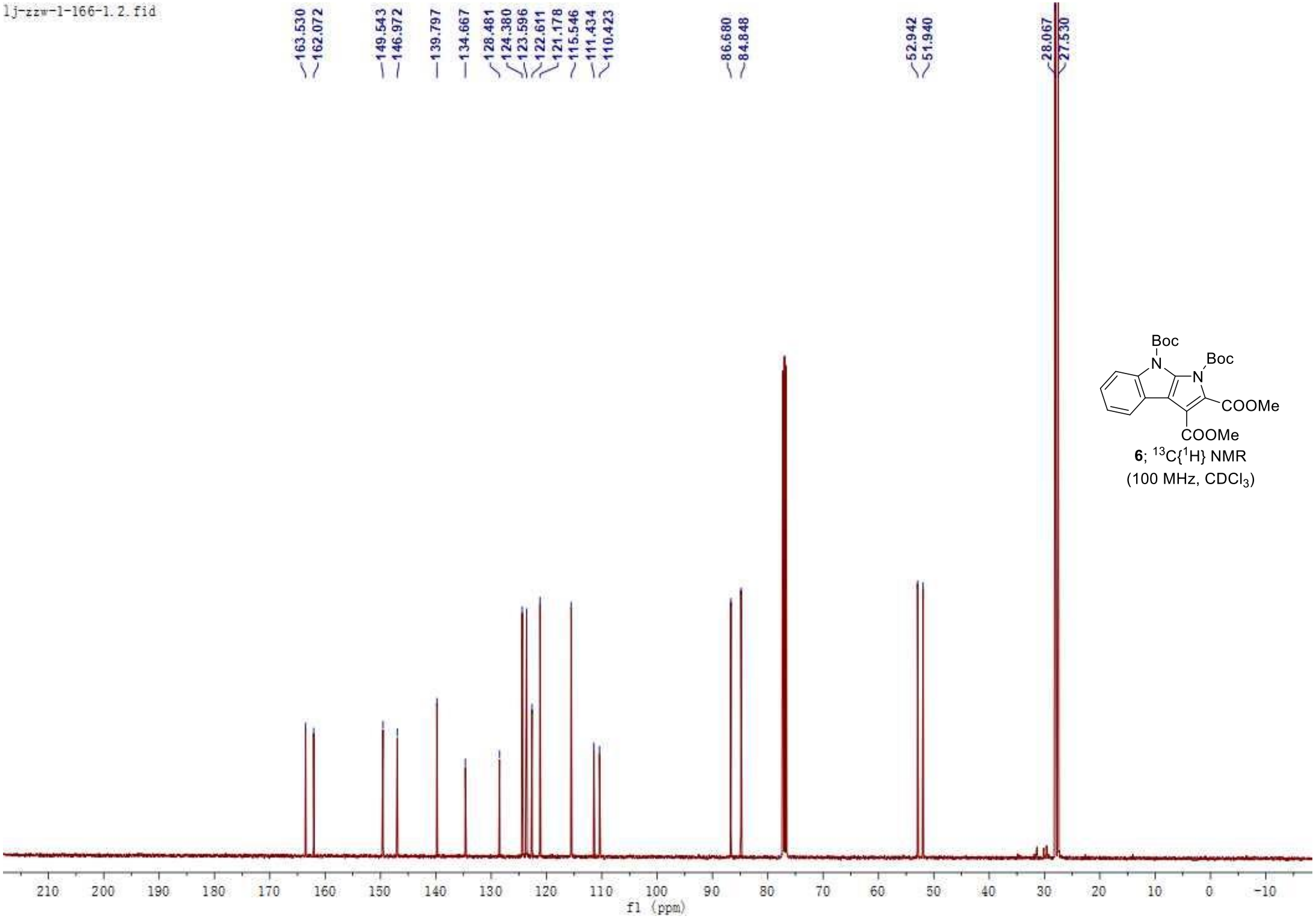
lj-zzw-2-19-2.2.fid



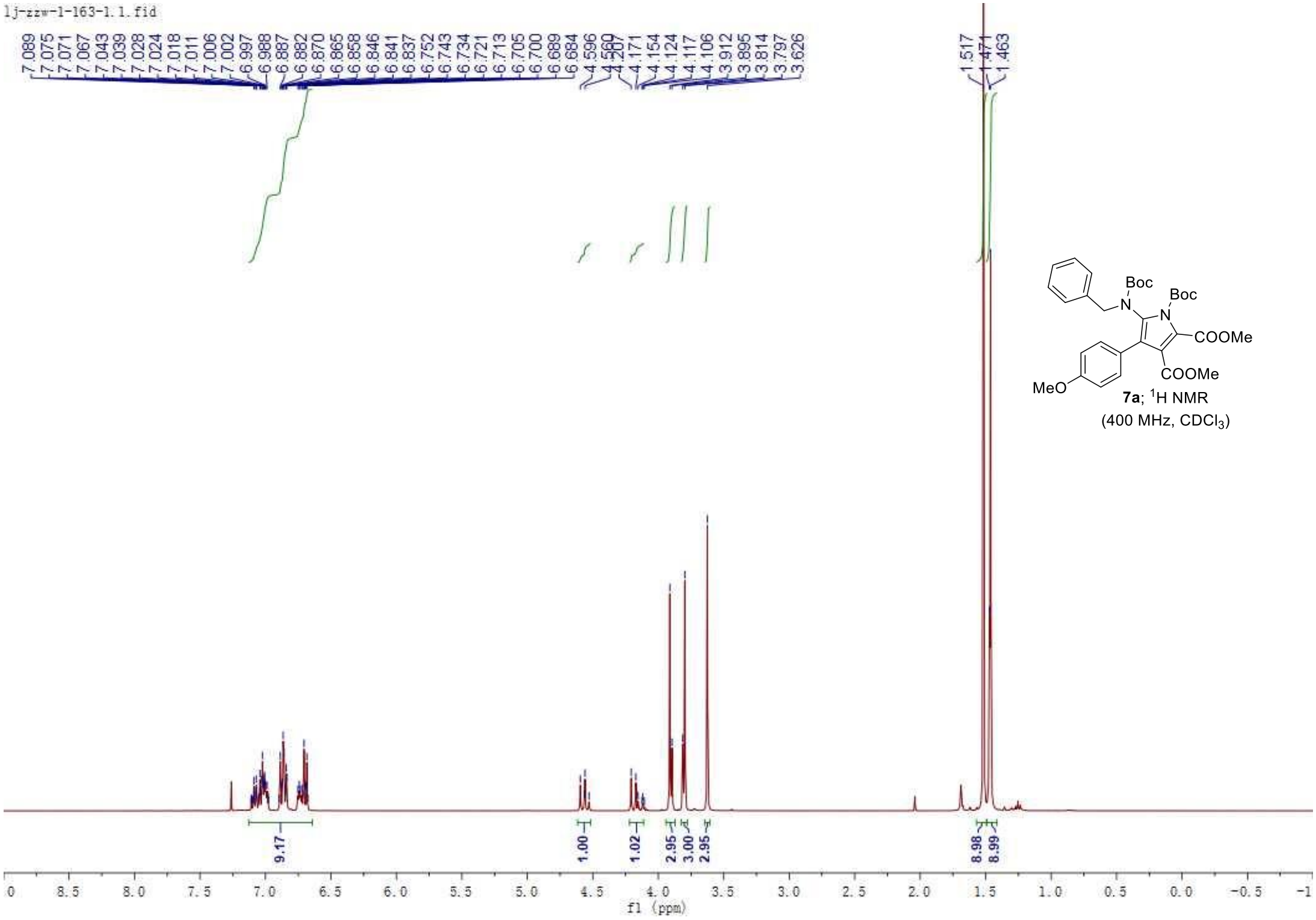
5d; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)



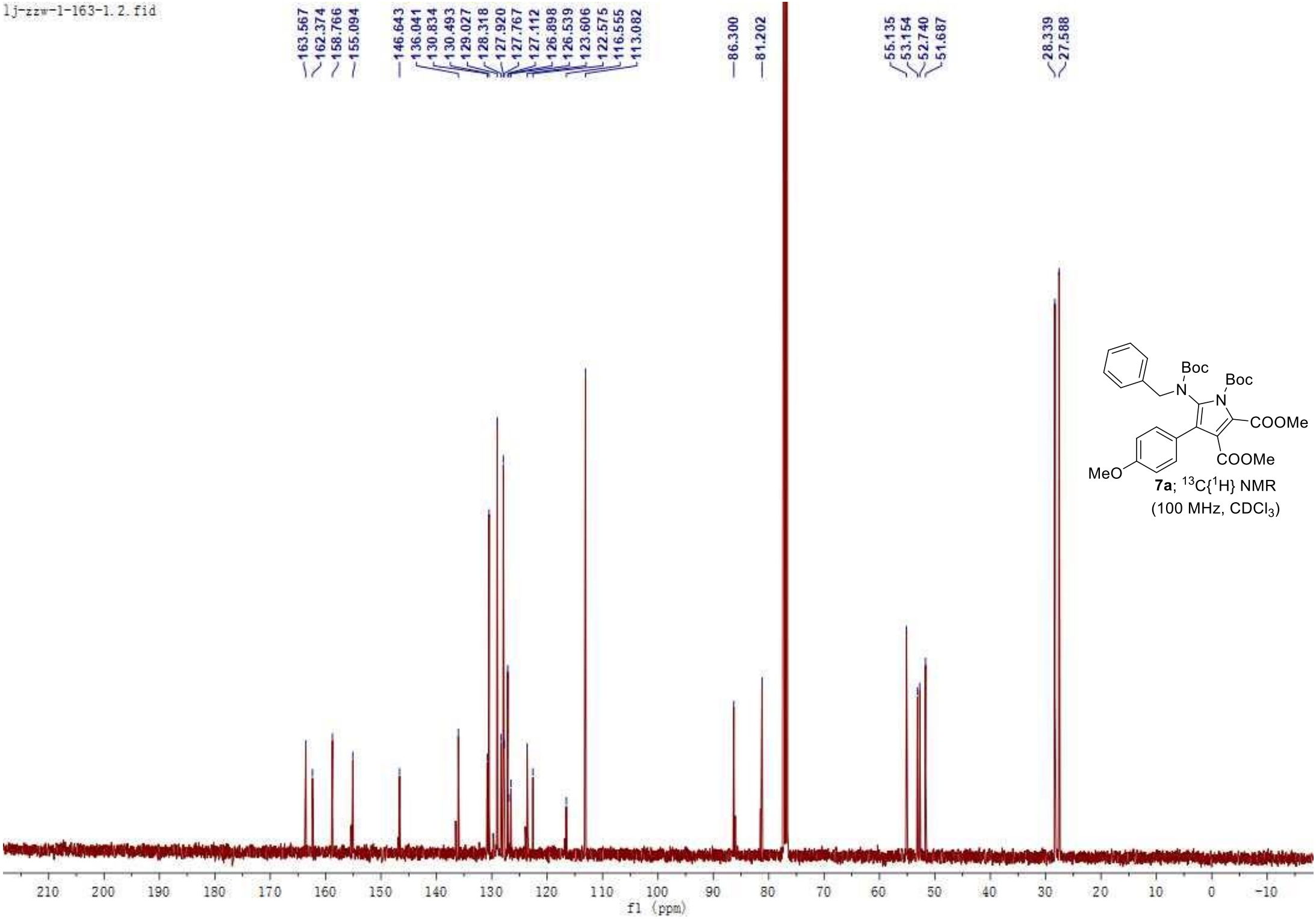
6; ^{1}H NMR
(400 MHz, $CDCl_3$)



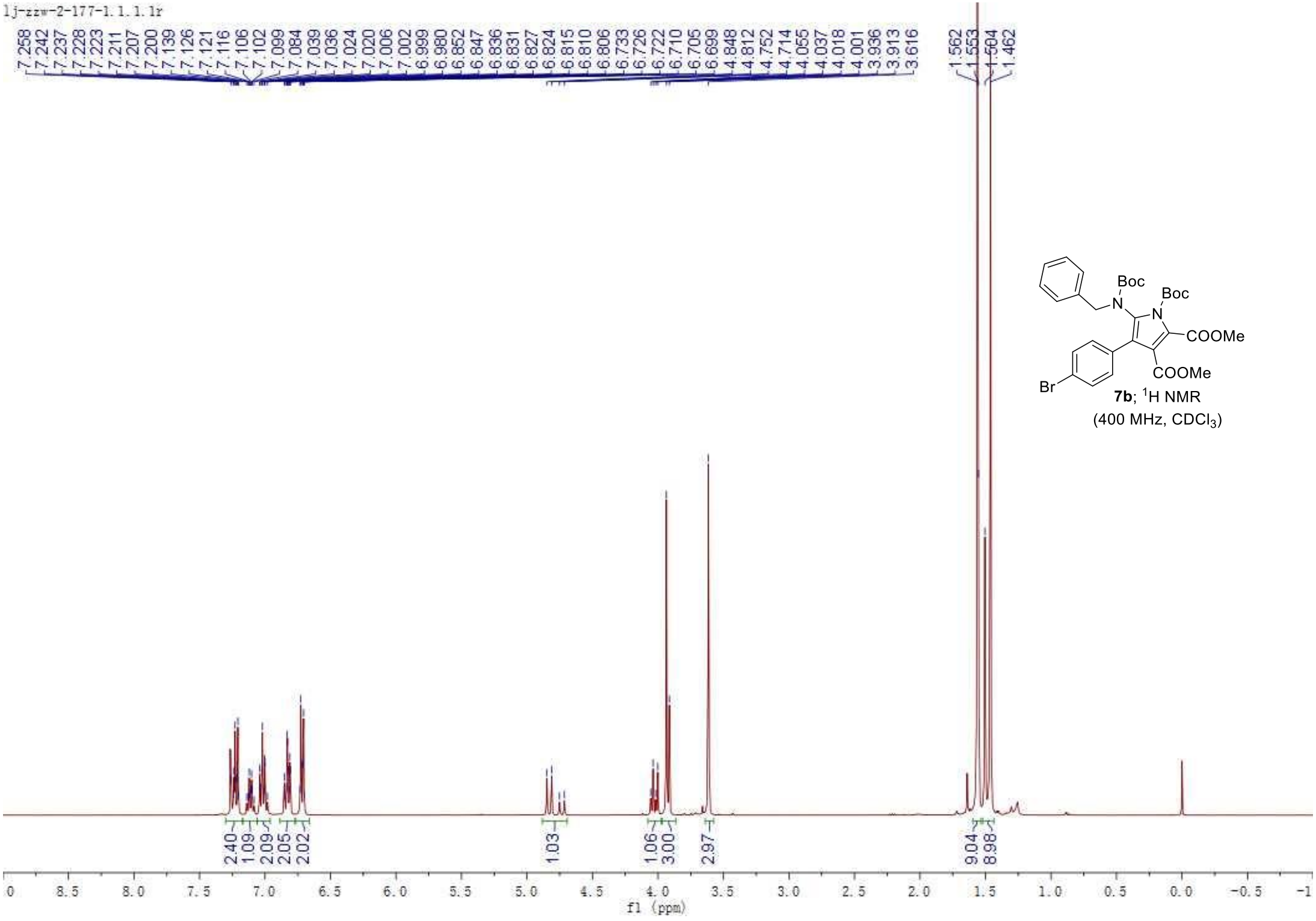
6; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

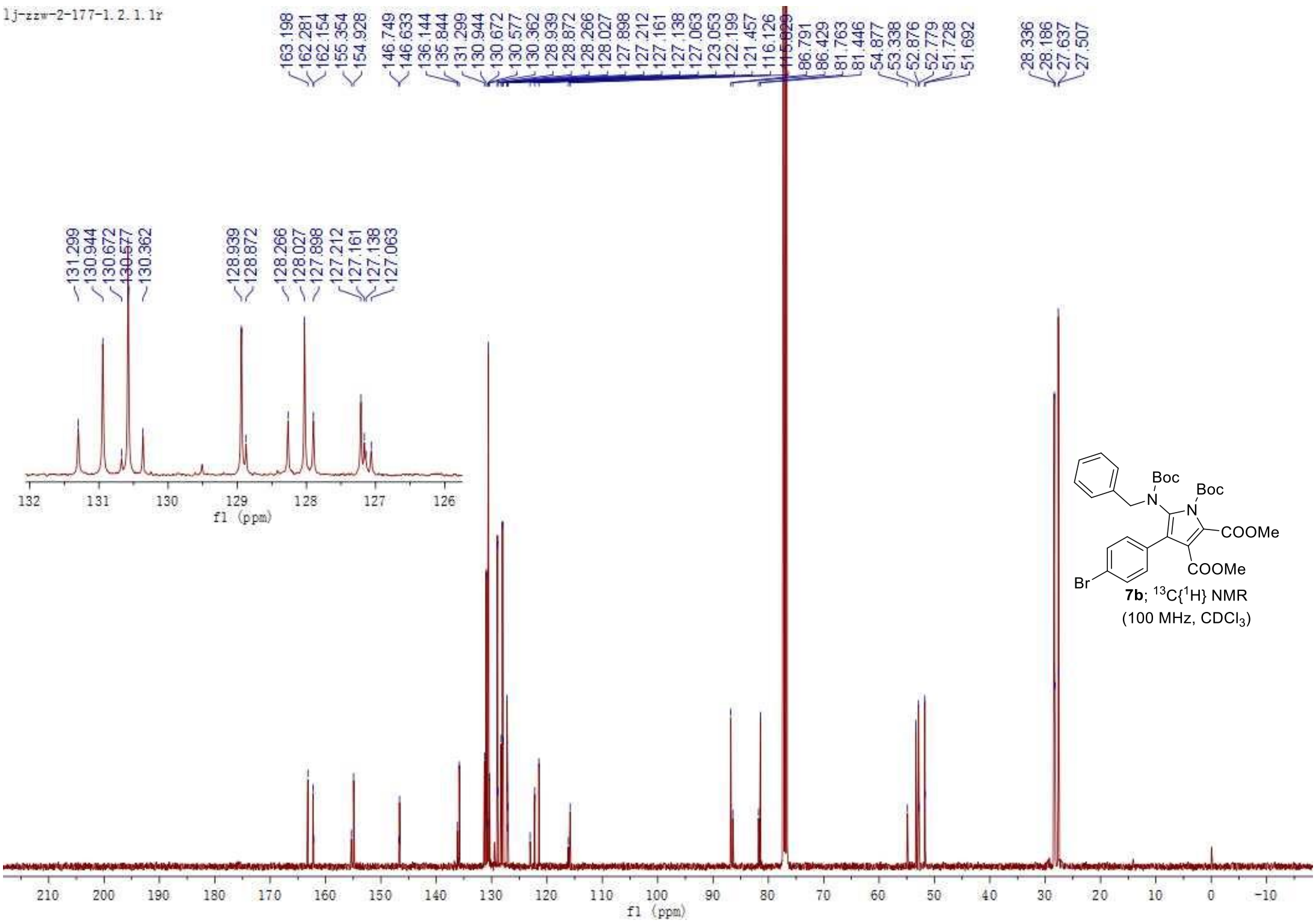

lj-zzw-1-163-1.1.fid
7.089
7.075
7.071
7.067
7.043
7.039
7.028
7.024
7.018
7.011
7.006
7.002
6.997
6.988
6.887
6.882
6.870
6.865
6.858
6.846
6.841
6.837
6.752
6.743
6.734
6.721
6.713
6.705
6.700
6.689
6.684
4.596
4.560
4.207
4.171
4.154
4.124
4.117
4.106
3.912
3.895
3.814
3.797
3.626
1.517
1.471
1.463
9.17
1.00
1.02
2.95
3.00
2.95
8.98
8.99
f1 (ppm)
Boc
Boc
N
N
COOMe
COOMe
MeO
7a; 1H NMR
(400 MHz, CDCl3)

lj-zzw-1-163-1.2.fid

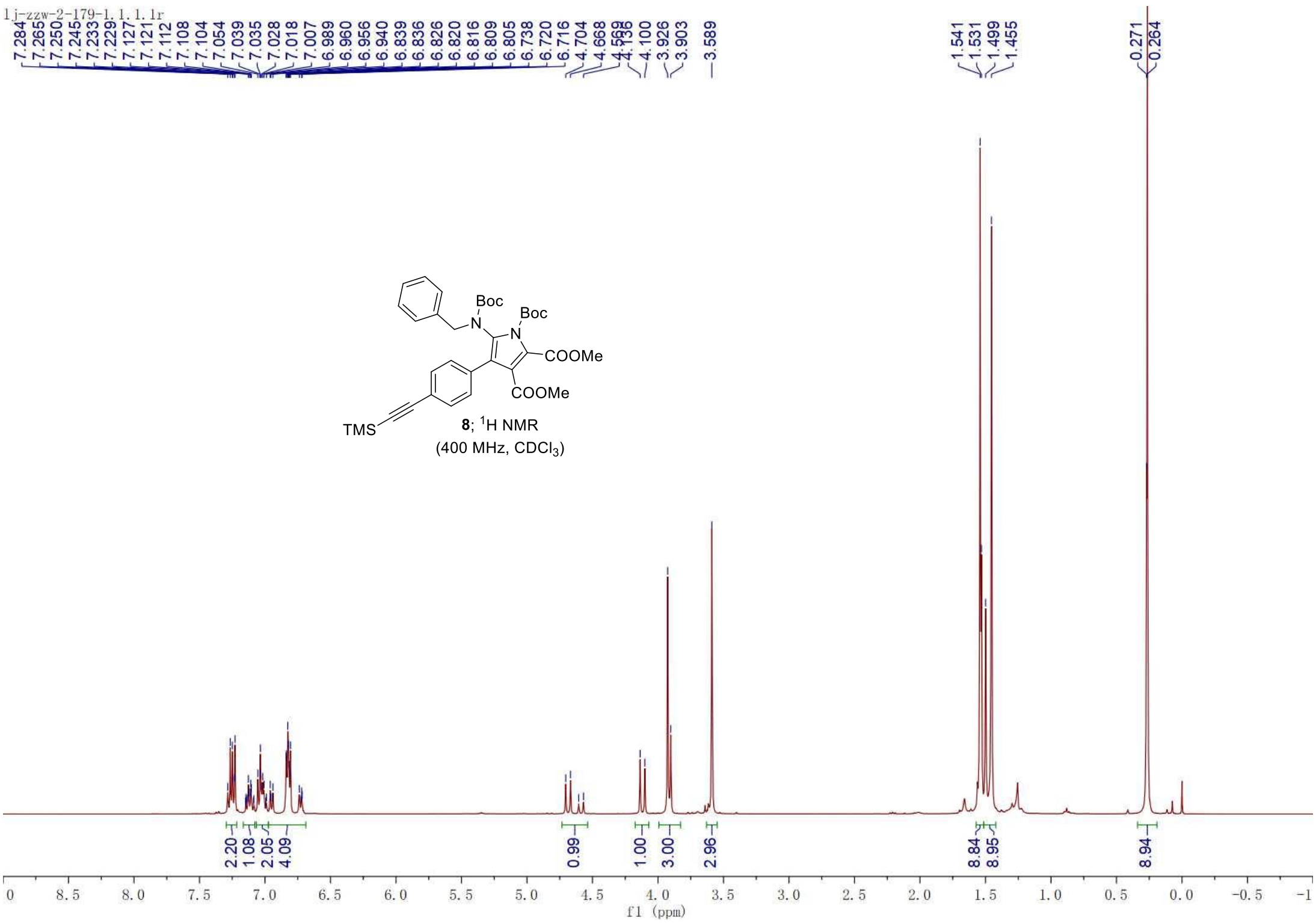


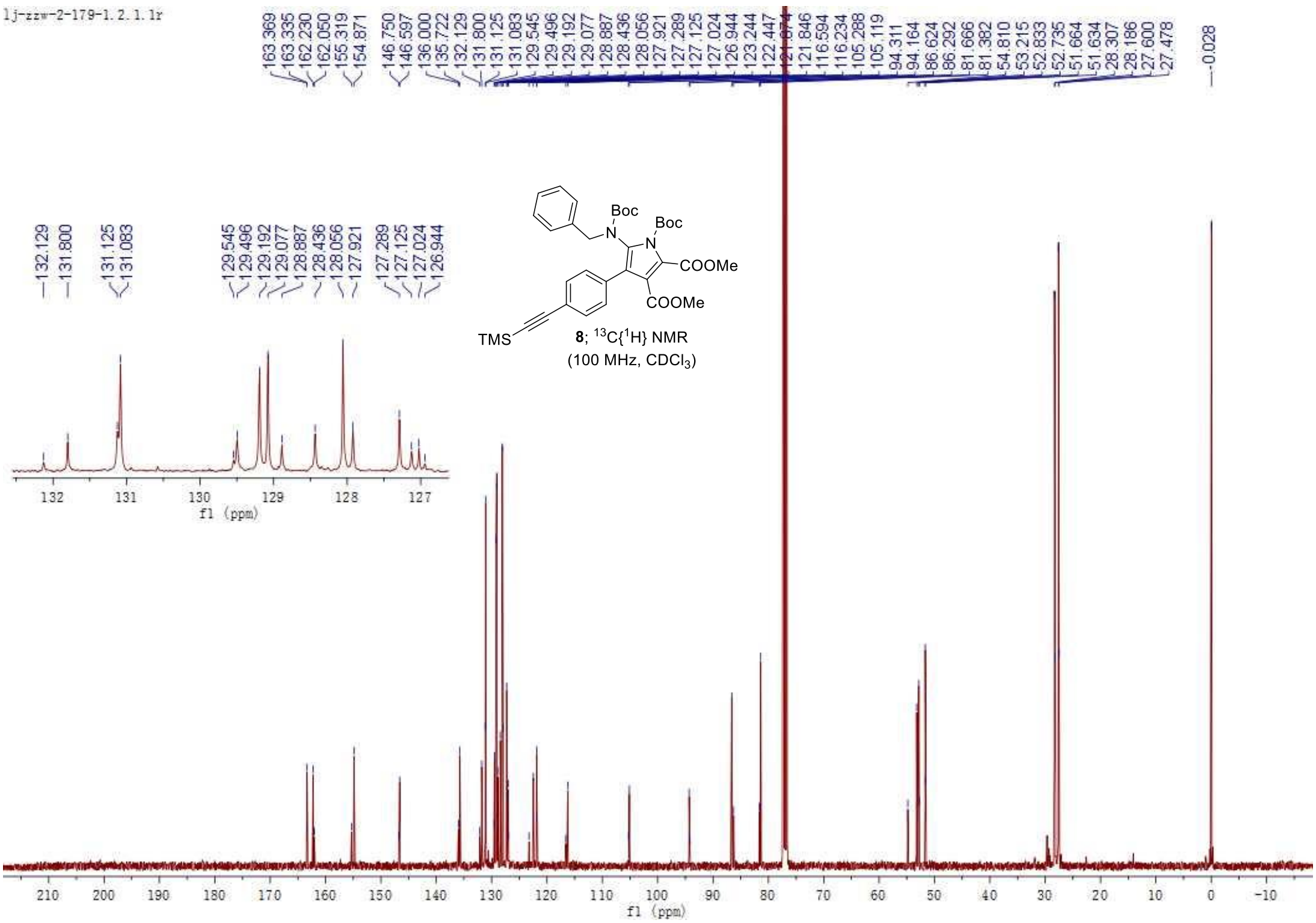
7a; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

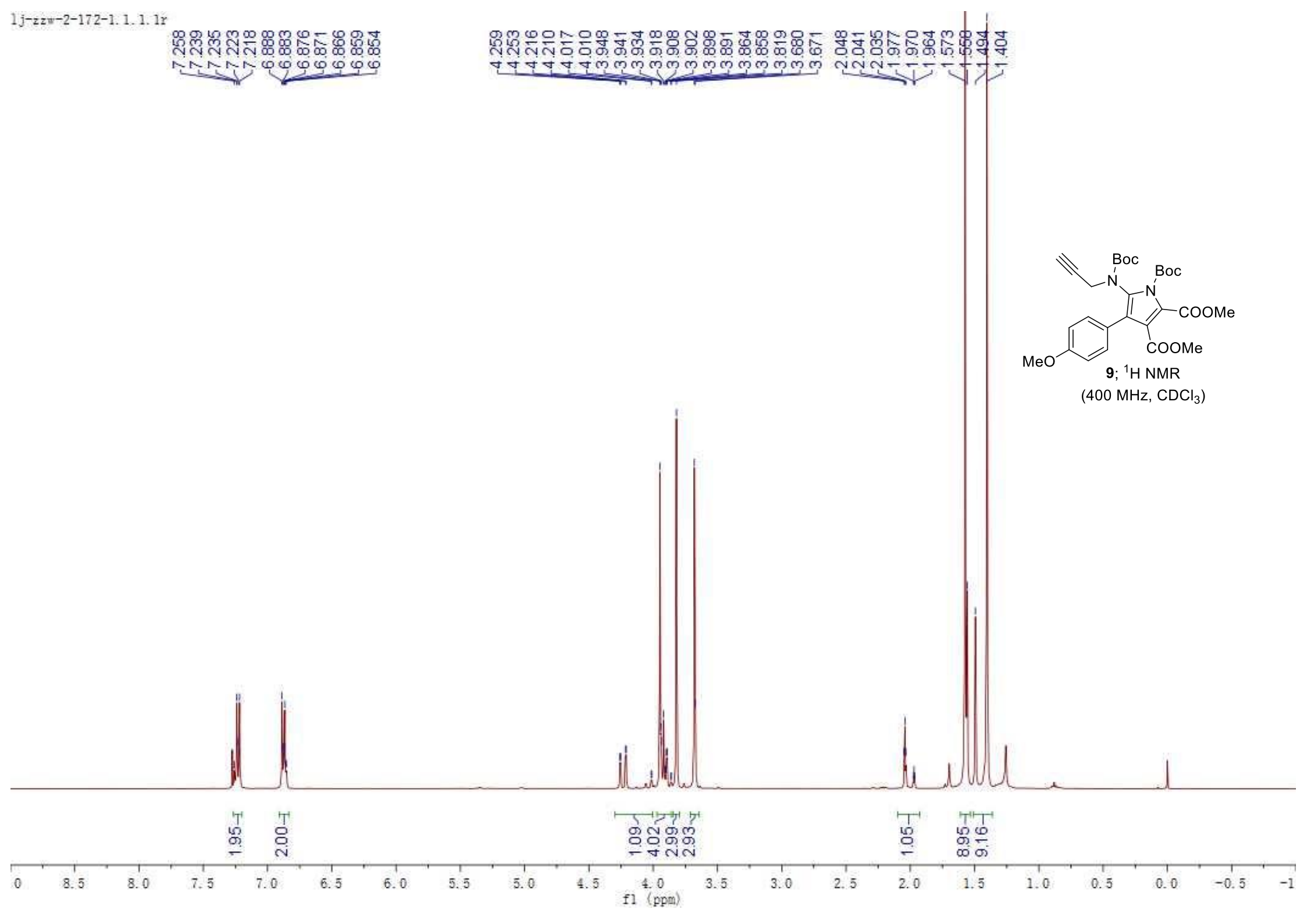

lj-zzw-2-177-1.1.1.1r
7.258
7.242
7.237
7.228
7.223
7.211
7.207
7.200
7.139
7.126
7.121
7.116
7.106
7.102
7.099
7.084
7.039
7.036
7.024
7.020
7.006
7.002
6.999
6.980
6.852
6.847
6.836
6.831
6.827
6.824
6.815
6.810
6.806
6.733
6.726
6.722
6.710
6.705
6.699
4.848
4.812
4.752
4.714
4.055
4.037
4.018
4.001
3.936
3.913
3.616
1.562
1.553
1.504
1.462
2.40
1.09
2.09
2.05
2.02
1.03
1.06
3.00
2.97
9.04
8.98
f1 (ppm)
Boc
Boc
N
N
COOMe
COOMe
Br
7b; 1H NMR
(400 MHz, CDCl3)



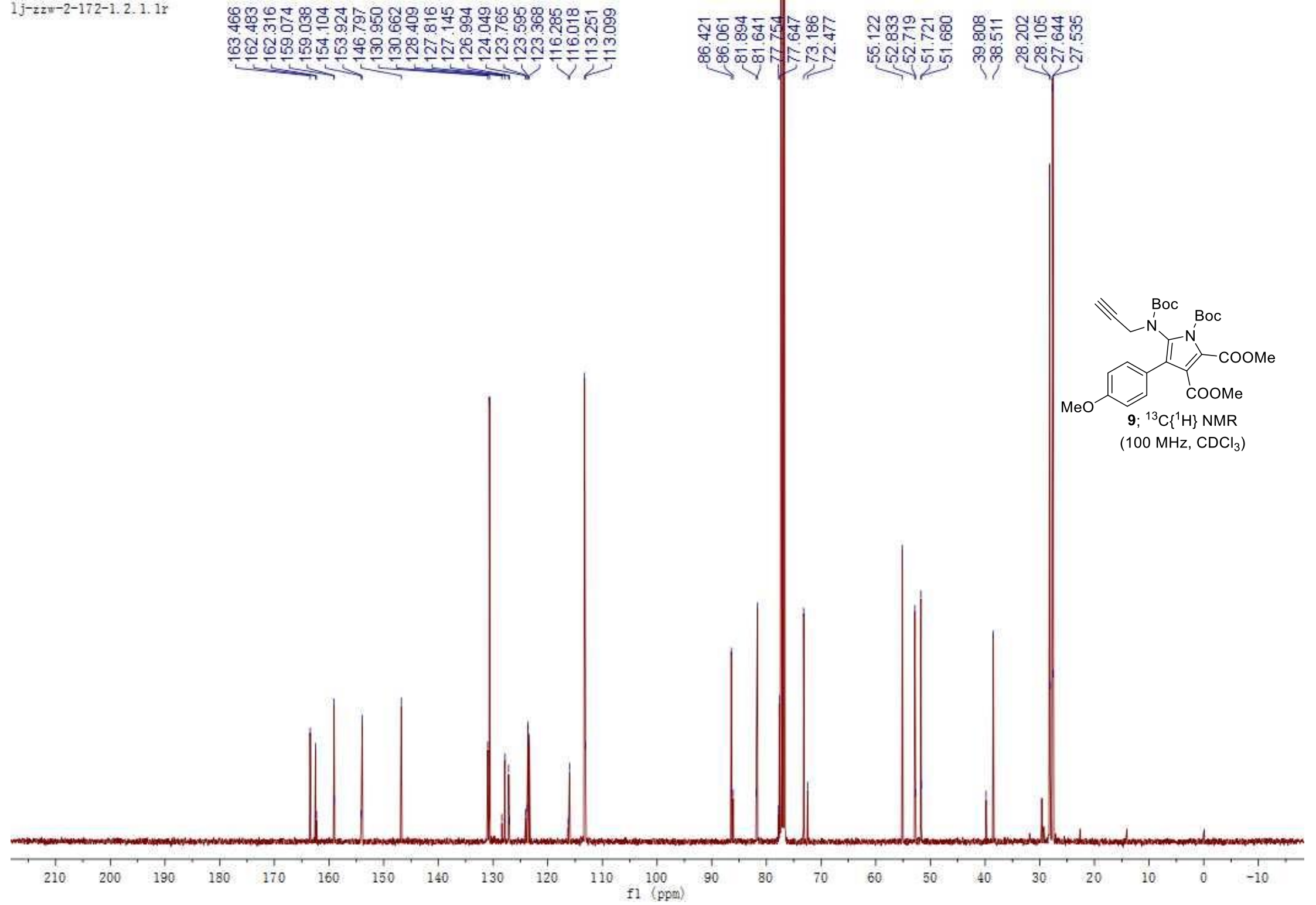
7b; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)


1j-zzw-2-179-1.1.1.1r
7.284
7.265
7.250
7.245
7.233
7.229
7.127
7.121
7.112
7.108
7.104
7.054
7.039
7.035
7.028
7.018
7.007
6.989
6.960
6.956
6.940
6.839
6.836
6.826
6.820
6.816
6.809
6.805
6.738
6.720
6.716
4.704
4.668
4.569
4.138
4.100
3.926
3.903
3.589
1.541
1.531
1.499
1.455
0.271
0.264
Boc
Boc
N
N
COOMe
COOMe
TMS
8; 1H NMR
(400 MHz, CDCl3)
2.20
1.08
2.05
4.09
0.99
1.00
3.00
2.96
8.84
8.95
8.94
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
-1
f1 (ppm)

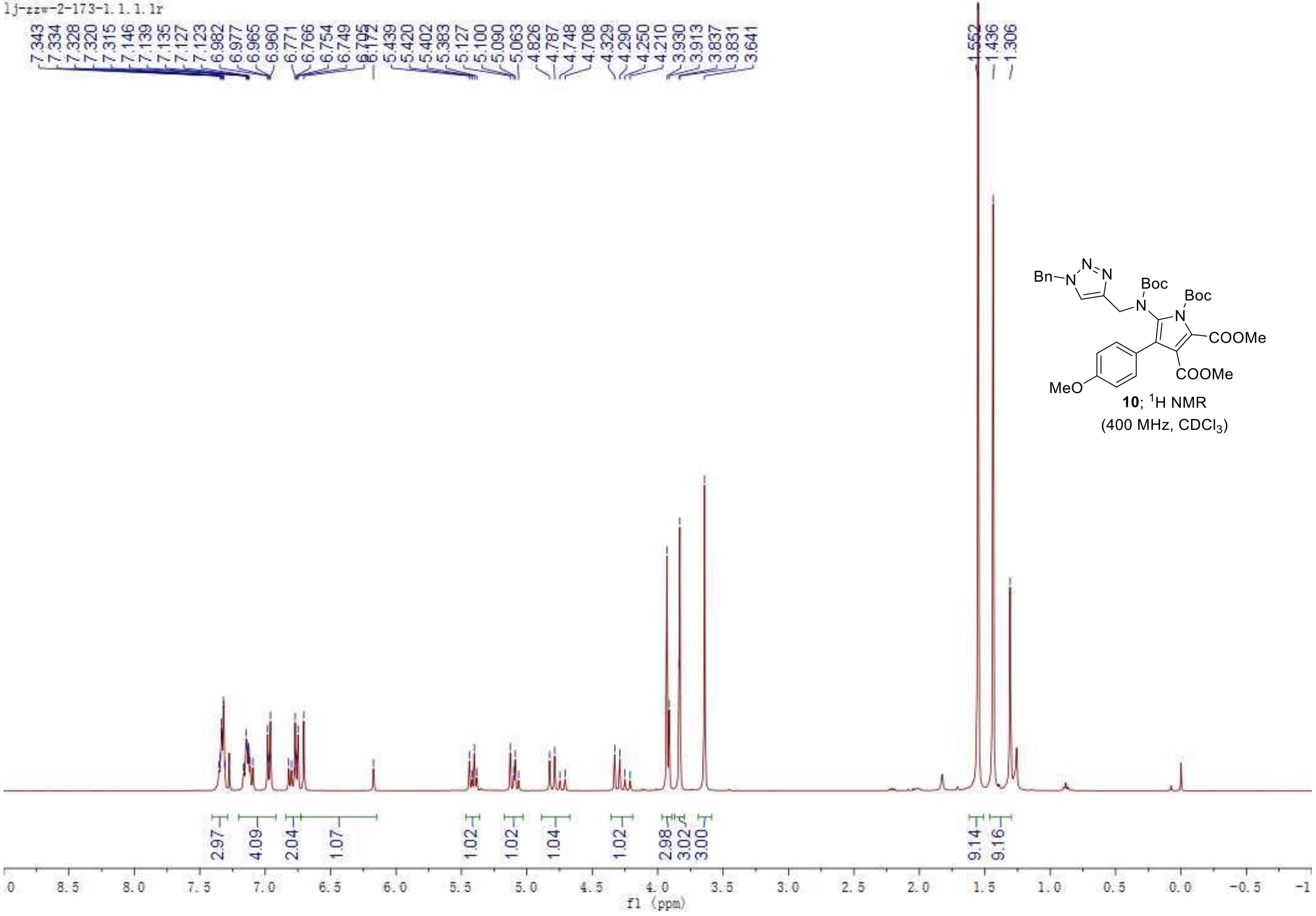

lj-zzw-2-179-1.2.1.1r
163.369
163.335
162.230
162.050
155.319
154.871
146.750
146.597
136.000
135.722
132.129
131.800
131.125
131.083
129.545
129.496
129.192
129.077
128.887
128.436
128.056
127.921
127.289
127.125
127.024
126.944
123.244
122.447
121.874
121.846
116.594
116.234
105.288
105.119
94.311
94.164
86.624
86.292
81.666
81.382
54.810
53.215
52.833
52.735
51.664
51.634
28.307
28.186
27.600
27.478
-0.028
Boc
Boc
N
N
COOMe
COOMe
TMS
8; 13C{1H} NMR
(100 MHz, CDCl3)
f1 (ppm)
f1 (ppm)



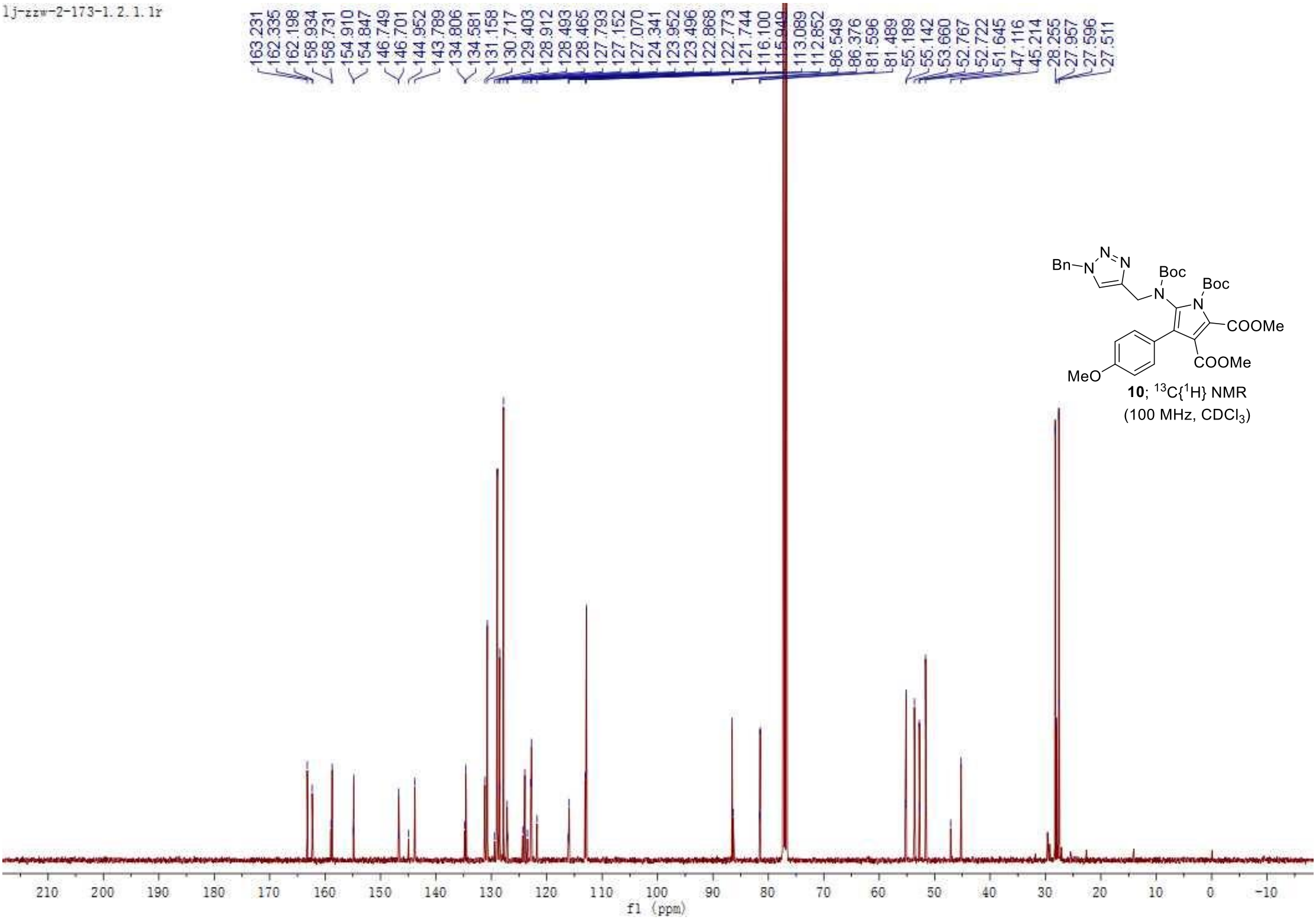
9; ^{1}H NMR
(400 MHz, $CDCl_3$)



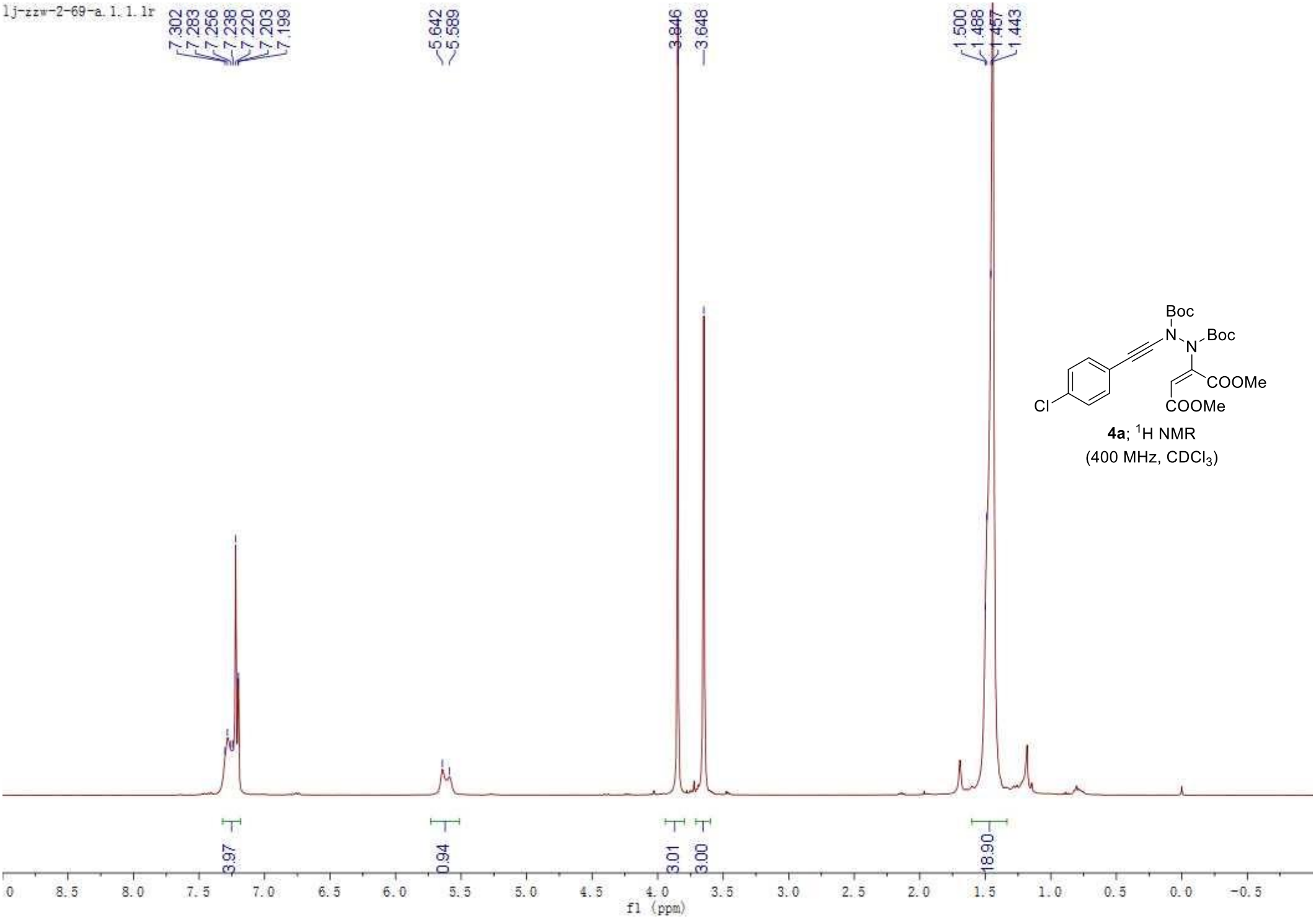
9; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)



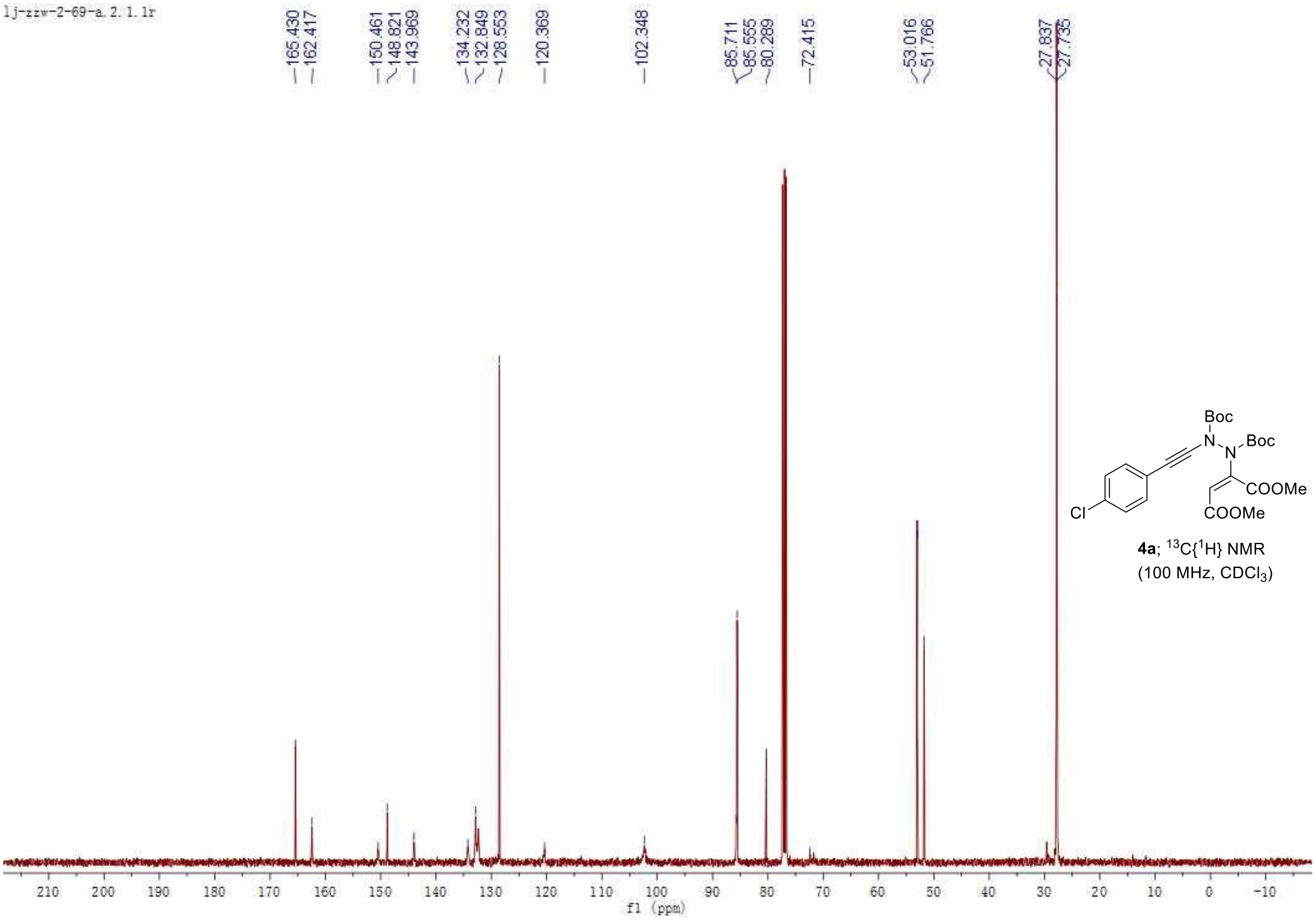
10; ^{1}H NMR
(400 MHz, $CDCl_3$)



10; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

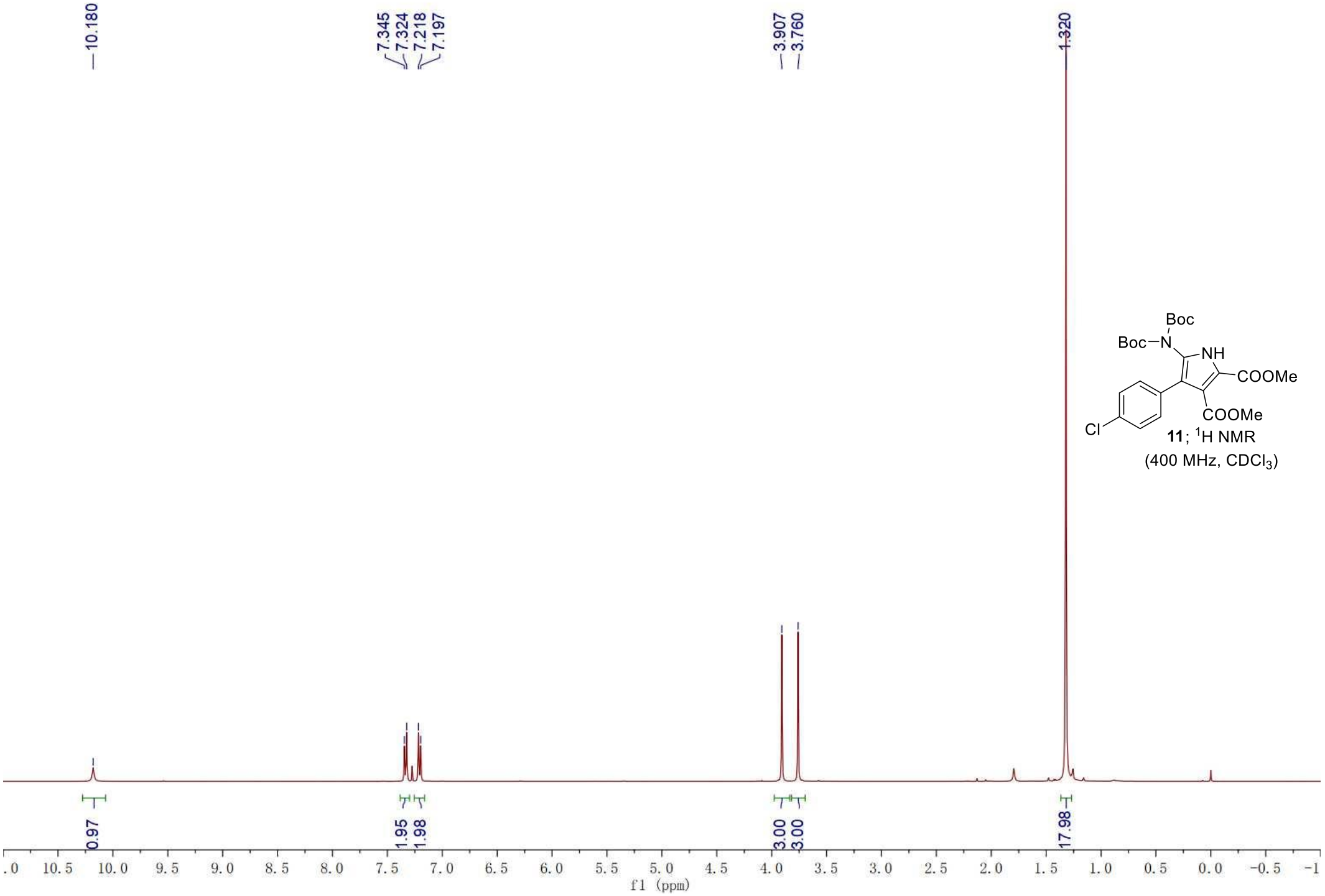


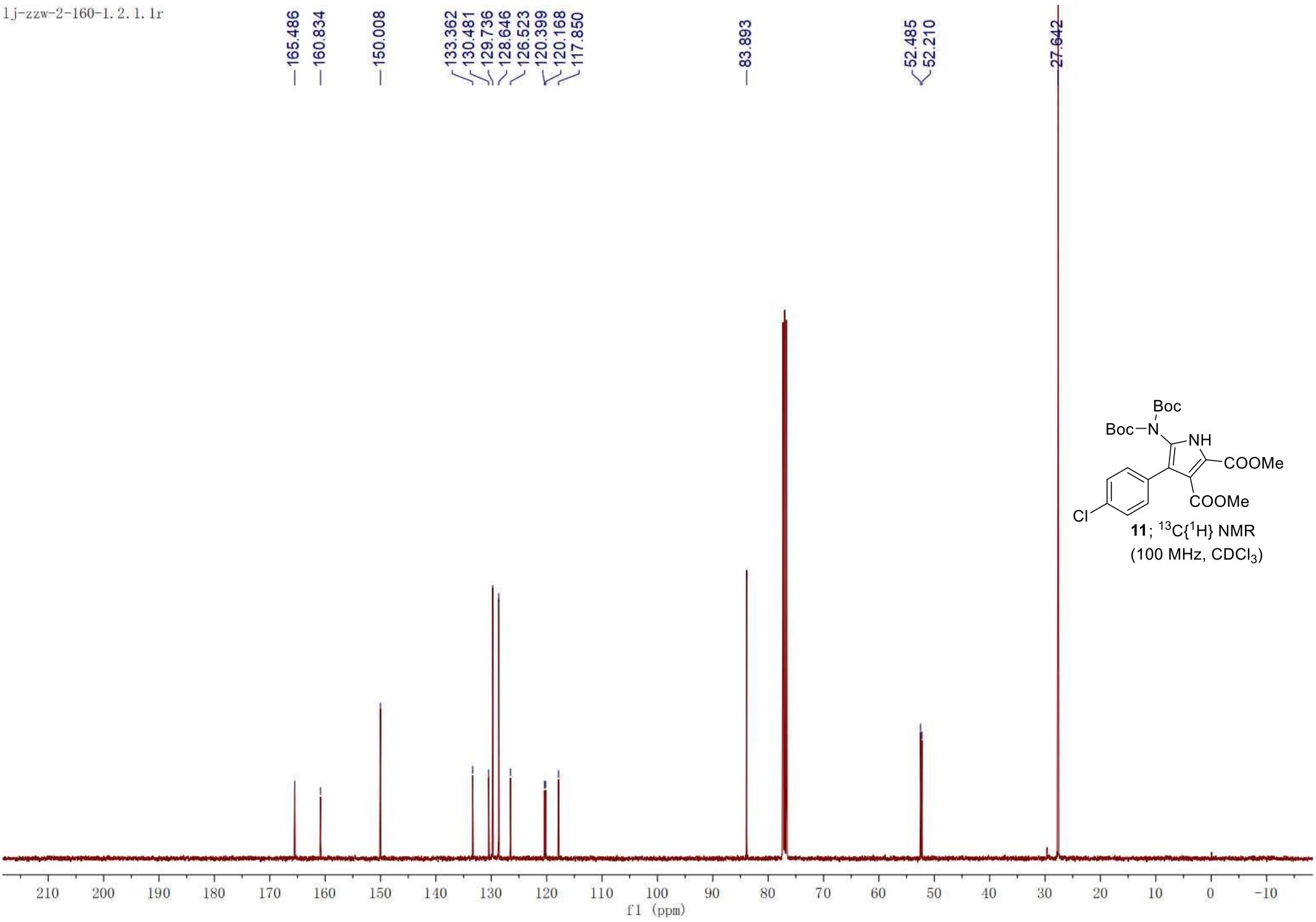
4a; ^{1}H NMR
(400 MHz, $CDCl_3$)

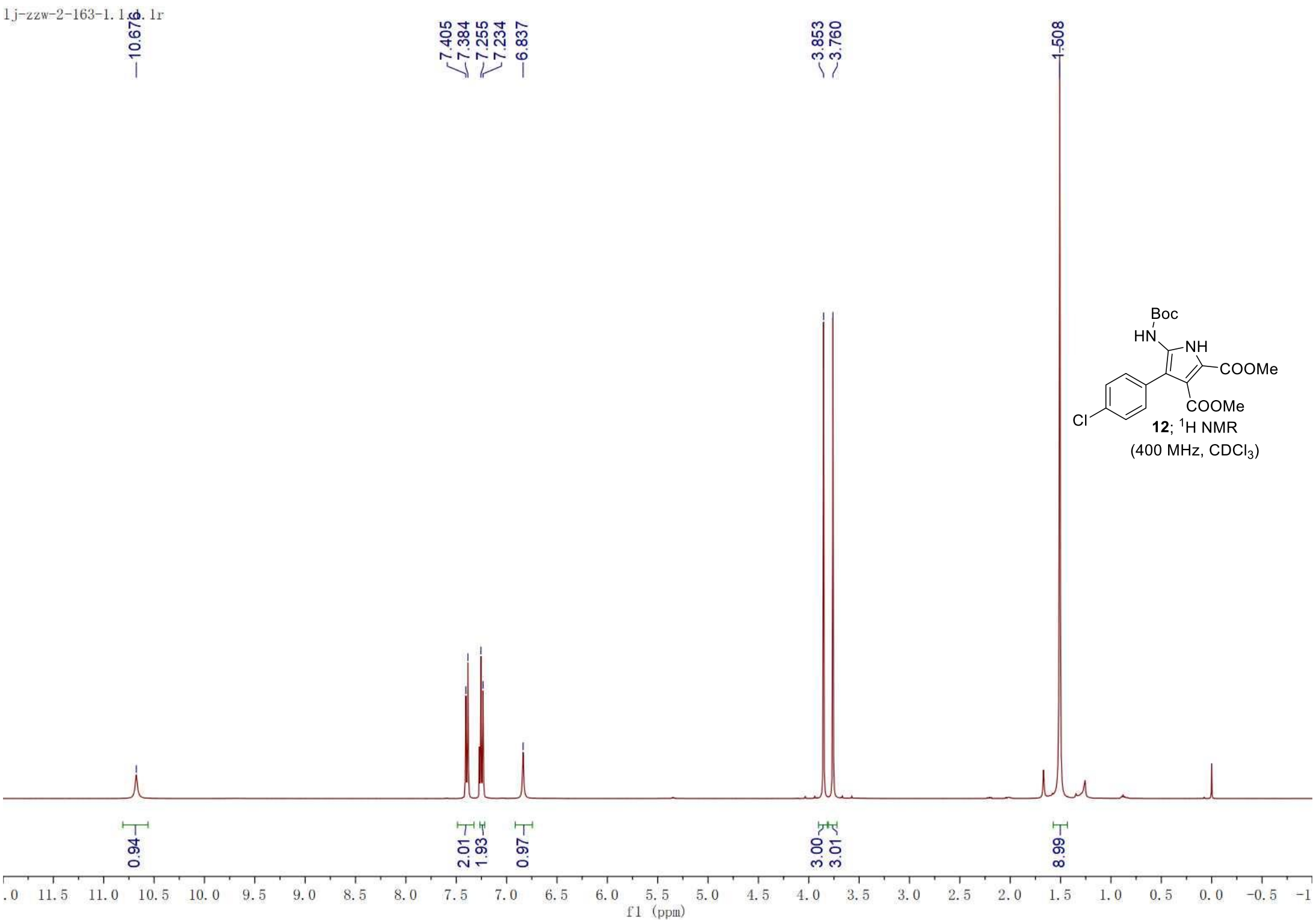


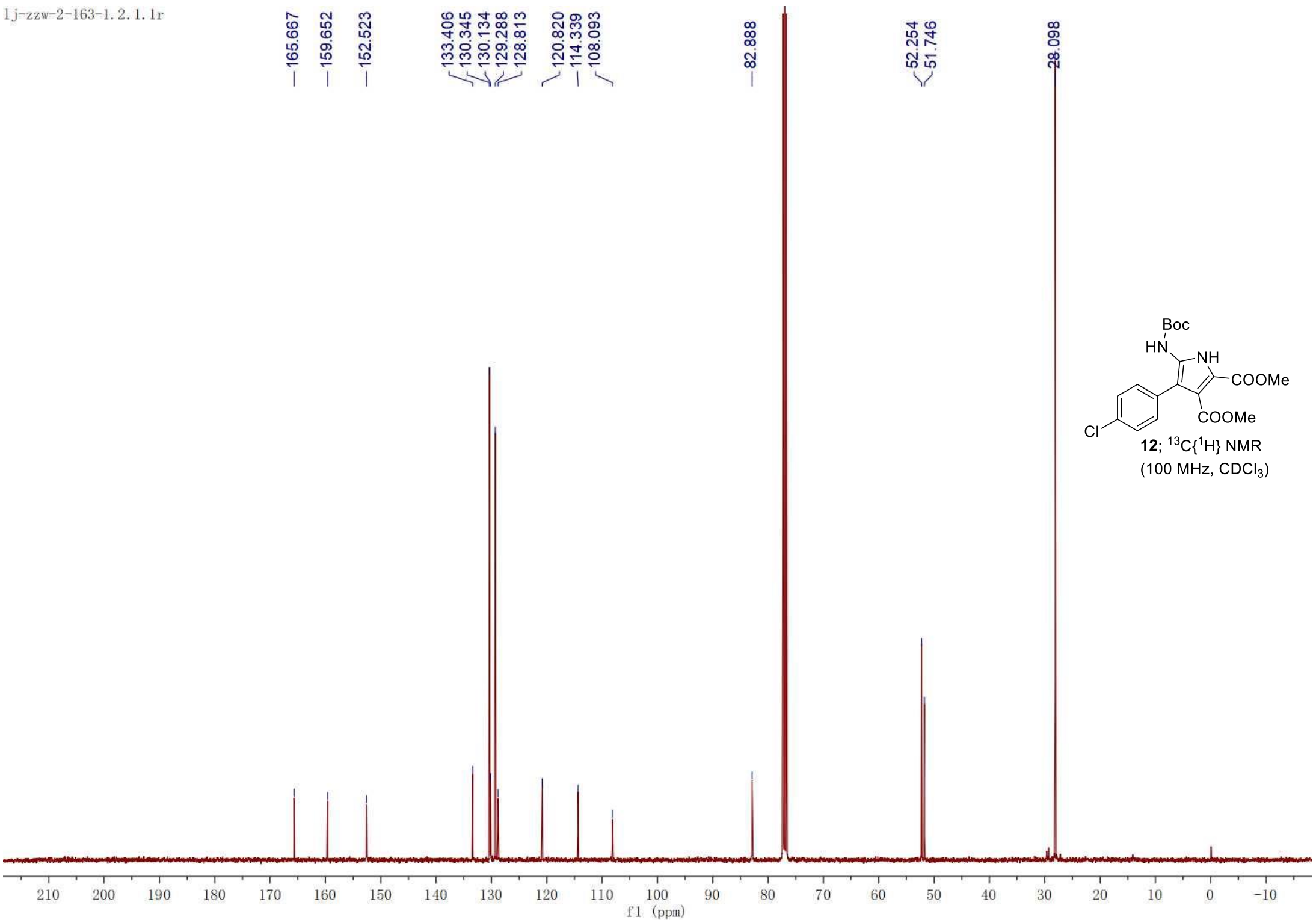
4a; $^{13}C\{^{1}H\}$ NMR
(100 MHz, $CDCl_3$)

1j-zzw-2-160-1.1.1.1r




1j-zzw-2-160-1.2.1.1r
165.486
160.834
150.008
133.362
130.481
129.736
128.646
126.523
120.399
120.168
117.850
83.893
52.485
52.210
27.642
Boc
Boc—N
NH
COOMe
COOMe
Cl
11; 13C{1H} NMR
(100 MHz, 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)


10.676
7.405
7.384
7.255
7.234
6.837
3.853
3.760
1.508
0.94
2.01
1.93
0.97
3.00
3.01
8.99
f1 (ppm)
Boc
HN
NH
COOMe
COOMe
Cl
12; 1H NMR
(400 MHz, CDCl3)


1j-zzw-2-163-1.2.1.1r
165.667
159.652
152.523
133.406
130.345
130.134
129.288
128.813
120.820
114.339
108.093
82.888
52.254
51.746
28.098
Boc
HN
NH
COOMe
COOMe
Cl
12; 13C{1H} NMR
(100 MHz, 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)