Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Silver-Catalyzed Cyclization of Nitrones with 2-Azetine: A Radical Approach to 2,3-Disubstituted Quinolines

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Supporting Information

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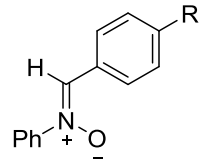
1. Substrate Preparation

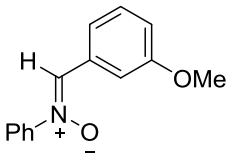
Nitrones[1] (listed below) and *N*-boc-2-azetine[2] were synthesized according to the reported procedures.

1.1 General procedure for the preparation of nitrones

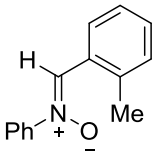
Nitroarene (1.0 equiv), aldehyde (1.1 equiv) and NH_4Cl (1.2 equiv) were dissolved in a 1:1 mixture of EtOH and water (2 mL/mmol of starting material) and cooled to 0 °C (ice bath). Then zinc powder (2.0 equiv) was added to the resulting mixture, and the reaction was allowed to warm to room temperature and stirred for 16 hours. The reaction mixture was filtered and washed with CH_2Cl_2. The filtrate was extracted with CH_2Cl_2 (4 × 50 mL) and the combined organic layer was washed with brine, dried over Na_2SO_4, concentrated under reduced pressure to give crude nitrones. Pure nitrones were obtained by recrystallization from ethyl acetate (cal. 65% yield).



1a: R = H **1e:** R = Br
1b: R = OMe **1f:** R = NO_2
1c: R = F **1g:** R = CF_3
1d: R = Cl



1h



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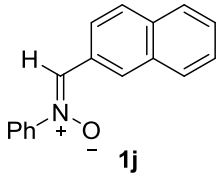

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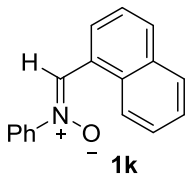
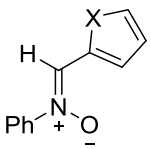
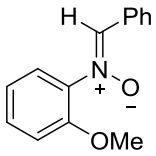


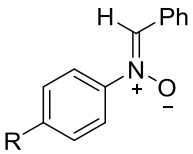
1k



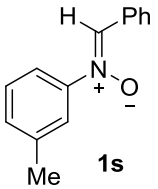
1l: X = O
1m: X = S



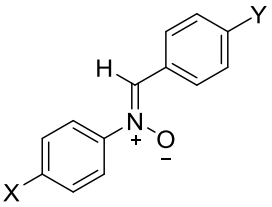
1n



1o: R = OMe **1q:** R = Br
1p: R = Cl **1r:** R = CO_2Et

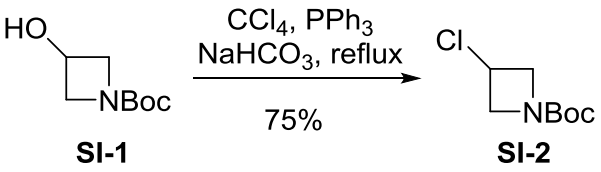


1s

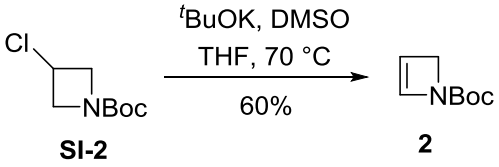


1t: X = Y = OMe
1u: X = OMe, Y = CF_3
1v: X = CO_2Et, Y = OMe
1w: X = CO_2Et, Y = CF_3

1.2 General procedure for the preparation of *N*-Boc-2-azetine



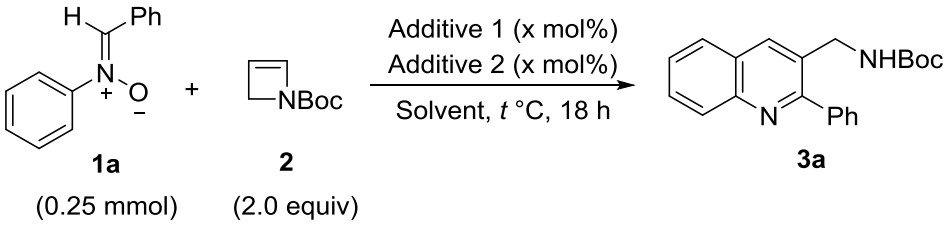
To a solution of azetidinol **SI-1** (8.00 g, 46.2 mmol) in CCl4 (50 mL) was added Ph_3P (13.3 g, 50.8 mmol, 1.1 equiv) and $NaHCO_3$ (30 mg). The reaction mixture was heated to reflux. After 17 h, the reaction mixture was cooled to rt, concentrated to dryness under reduced pressure, suspended in pet ether (50 mL) and filtered. The solid was resuspended in pet ether (50 mL) and filtered. The combined pet ether washings were concentrated to dryness under reduced pressure. Purification (Si-gel, pet ether/ ethyl acetate 1:0→4:1) gave chloride **SI-2** as a colorless oil (6.6 g, 75%).



To a solution of *t*-BuOK (440 mg, 3.92 mmol) in DMSO (5 mL) was added dropwise *N*-Boc-3-chloroazetidine **SI-2** (500 mg, 2.61 mmol) in THF (5 mL). The reaction mixture was then heated to 70°C for 17 h, then cooled to rt. Water (10 mL) was added and the reaction mixture extracted with n-Pentane (2 × 10 mL). The combined organic layers were concentrated to dryness under reduced pressure. Purification (Si-gel, pet ether/ ethyl acetate 1:0→10:1) gave azetine **2** as a colorless liquid (364 mg, 60%).

2. Screening Reaction Conditions

Table S1 summarizes in-depth condition tuning for the reaction of nitrone **1a** with *N*-Boc-2-azetine **2**.



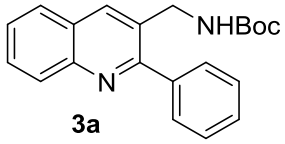
1a (0.25 mmol) **2** (2.0 equiv) **3a**

Table S1. Screening reaction conditions.[a]

Entry	Additive 1/x mol%	Additive 2/x mol%	Solvent	*t* [°C]	Yield of **3a**[b]
1	$[Cp^*RhCl_2]_2$/2.5	$AgSbF_6$/10	DCE	80	trace
2	$[Cp^*CoI_2]_2$/2.5	$AgSbF_6$ /10	DCE	80	trace
3	$[Rh(COD)BF_4]_2$/2.5	BINAP/5	DCE	80	NR
4	$[Cp^*RuCl_2]_2$/2.5	$AgSbF_6$/10	DCE	80	trace
5	$AgSbF_6$/10	--	DCE	80	36
6	AgOAc/10	--	DCE	80	NR
7	$AgBF_4$/10	--	DCE	80	46
8	AgOTf/10	--	DCE	80	58
9	Ag_2CO_3	--	DCE	80	NR
10	AgOTf/10	PPh_3/20	DCE	80	NR
11	AgOTf/10	$K_2S_2O_8$/100	DCE	80	50
12	AgOTf/5	--	DCE	80	23
13	AgOTf/100	--	DCE	80	30
14	AgOTf/10	--	DCE	40	74
15	AgOTf/10	--	DCE	25	48
16	AgOTf/10	--	THF	40	71
17	**AgOTf/10**	**--**	**toluene**	**40**	**85; 81**[c]
18	AgOTf/10	--	DCM	40	58
19	AgOTf/10	--	DMF	40	NR
20[d]	AgOTf/10	--	toluene	100	70[d]

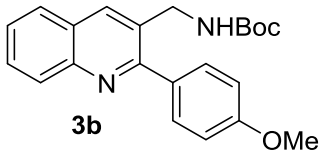
[a]Reaction conditions: **1a** (0.25 mmol), **2** (0.5 mmol), 2.0 mL of solvent reacted for 18 h unless otherwise stated. [b]Yield of **3a** was determined by HPLC analysis using naphthalene as an internal standard. [c]Isolated yield. [d]**1a** (0.5 mmol), **2** (0.25 mmol).

3. Characterization of Products



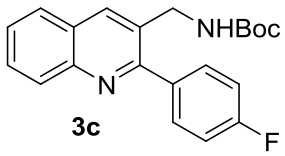
3a

3a, 81% yield, white solid, mp 112–114 °C, R_f = 0.5 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.57–7.52 (m, 3H), 7.51–7.43 (m, 3H), 4.87 (s, 1H),4.44 (d, *J* = 6.2 Hz, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 147.1, 140.1, 135.3, 130.5, 129.6, 129.4, 128.72, 128.7, 128.6, 127.5, 127.4, 126.8, 79.9, 42.5, 28.5; HRMS (ESI, m/z) calcd for $C_{21}H_{23}N_2O_2$ $[M + H]^+$ 335.1754, found 335.1762.



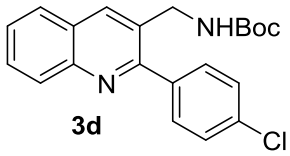
3b

3b, 80% yield, white solid, mp 104–106 °C, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, acetone-d_6) δ 8.28 (s, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.57 (s, 1H), 4.48 (d, *J* = 5.9 Hz, 2H), 3.88 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, acetone-d_6) δ 160.8, 159.6, 156.8, 147.9, 135.3, 133.6, 132.3, 131.3, 129.92, 129.90, 128.2, 128.1, 127.1, 114.3, 79.1, 55.6, 42.9, 28.6; HRMS (ESI, m/z) calcd for $C_{22}H_{25}N_2O_3$ $[M + H]^+$ 365.1860, found 365.1862.



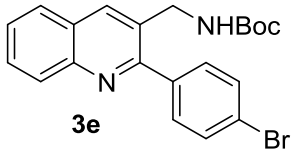
3c

3c, 74% yield, white solid, mp 115–118 °C, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.49–7.41 (m, 1H), 7.33–7.26 (m, 2H), 7.14 (m, 1H), 4.90 (s, 1H), 4.43 (d, *J* = 6.1 Hz, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (d, *J* = 247.3 Hz), 158.1, 155.9, 147.1, 142.2, 135.6, 130.3 (d, *J* = 8.3 Hz), 129.9, 129.4, 127.6, 127.5, 127.1, 124.6 (d, *J* = 3.1 Hz), 116.1(d, *J* = 22.6 Hz), 80.1, 42.4, 28.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -112.4; HRMS (ESI, m/z) calcd for $C_{21}H_{22}FN_2O_2$ $[M + H]^+$ 353.1660, found 353.1662.



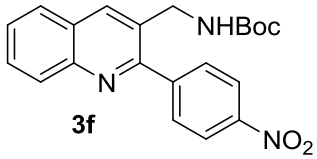
3d

3d, 73% yield, white solid, mp 120–123 °C, R_f = 0.3 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.41 (q, *J* = 8.5 Hz, 4H), 4.78 (s, 1H), 4.36 (d, *J* = 6.1 Hz, 2H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 155.9, 147.1, 138.5, 135.6, 134.9, 130.3, 129.9, 129.4, 128.9, 127.5, 127.49, 127.1, 80.1, 42.5, 28.5; HRMS (ESI, m/z) calcd for $C_{21}H_{22}ClN_2O_2$ $[M + H]^+$ 369.1364, found 369.1383.



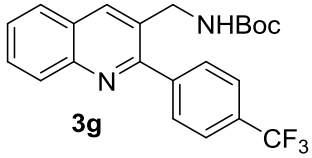
3e

3e, 78% yield, yellow solid, mp 120–123 °C, R_f = 0.35 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.79 (t, *J* = 5.8 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.61–7.50 (m, 3H), 7.43–7.34 (m, 2H), 5.08 (s, 1H), 4.38 (d, *J* = 6.4 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 155.8, 146.9, 138.8, 135.5, 131.7, 130.5, 130.2, 129.8, 129.2, 127.5, 127.4, 126.9, 123.0, 79.9, 42.3, 28.4, 28.3; HRMS (ESI, m/z) calcd for $C_{21}H_{22}BrN_2O_2$ $[M + H]^+$ 413.0859, found 413.0882.



3f

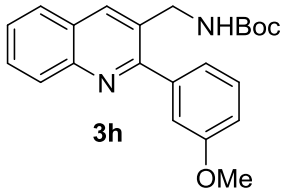
3f, 70% yield, white solid, mp 131–133 °C R_f = 0.2 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.5 Hz, 2H), 8.25 (s, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.91–7.86 (m, 1H), 7.80–7.73 (m, 3H), 7.60 (t, *J* = 7.5 Hz, 1H), 4.86 (s, 1H), 4.44 (d, *J* = 6.1 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 155.7, 147.9, 136.0, 130.3, 130.1, 129.5, 127.7, 127.6, 123.9, 80.3, 42.4, 28.5; HRMS (ESI, m/z) calcd for $C_{21}H_{22}N_3O_4$ $[M + H]^+$ 380.1605, found 380.1609.



3g

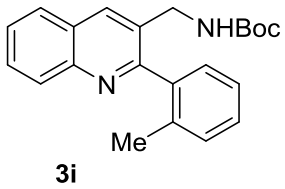
3g, 71% yield, white solid, mp 125–128 °C R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.78–7.72 (m, 3H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 4.83 (s, 1H), 4.44 (d, *J* = 6.0 Hz, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 158.0, 155.9, 147.2, 137.5, 135.5, 133.3, 129.8, 129.5, 128.6 (q, *J* = 270 Hz),

128.0 (q, *J* = 32 Hz), 126.9, 126.7, 126.6, 126.5, 125.0 (q, *J* = 3.8 Hz), 79.9, 42.6, 28.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.6; HRMS (ESI, m/z) calcd for $C_{22}H_{22}F_3N_2O_2$ $[M + H]^+$ 403.1628, found 403.1648.



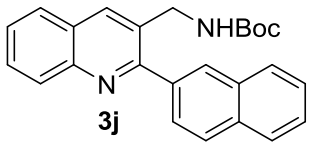
3h

3h, 81% yield, white solid, mp 115–118 °C, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.13–7.03 (m, 2H), 6.99 (dd, *J* = 8.3, 2.5 Hz, 1H), 4.86 (s, 1H), 4.44 (d, *J* = 6.2 Hz, 2H), 3.85 (s, 3H), 1.44 (s, 9H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 147.1, 141.4, 135.5, 130.5, 129.8, 129.7, 129.4, 127.5, 126.8, 121.0, 114.7, 114.1, 79.9, 55.5, 42.5, 28.5; HRMS (ESI, m/z) calcd for $C_{22}H_{25}N_2O_3$ $[M + H]^+$ 365.1860, found 365.1881.



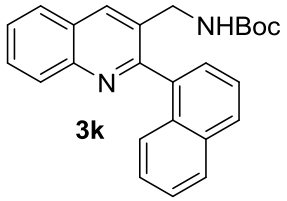
3i

3i, 75% yield, colourless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.71 (t, *J* = 6.8 Hz, 1H), 7.56 (t, *J* = 6.4 Hz, 1H), 7.37–7.24 (m, 4H), 4.89–4.77 (m, 1H), 4.20 (s, 2H), 2.10 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 139.4, 135.7, 135.0, 130.9, 130.7, 129.5, 129.3, 128.6, 128.2, 127.6, 127.5, 126.8, 126.2, 79.8, 42.20, 28.5, 19.7; HRMS (ESI, m/z) calcd for $C_{22}H_{25}N_2O_2$ $[M + H]^+$ 349.1911, found 349.1915.



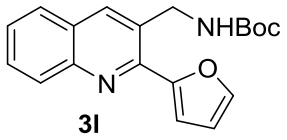
3j

3j, 65% yield, colourless oil, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 8.01 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.91–7.83 (m, 3H), 7.74–7.65 (m, 2H), 7.59–7.52 (m, 3H), 4.85 (s, 1H), 4.50 (d, *J* = 6.1 Hz, 2H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 155.9, 147.2, 137.5, 135.5, 133.3, 130.7, 129.7, 129.7, 128.55, 128.51, 128.2, 127.9, 127.6, 127.5, 126.9, 126.7, 126.6, 126.5, 80.0, 42.6, 28.5; HRMS (ESI, m/z) calcd for $C_{25}H_{25}N_2O_2$ $[M + H]^+$ 385.1911, found 385.1921.



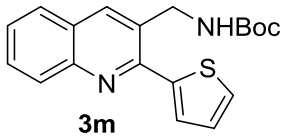
3k

3k, 68% yield, colourless oil, R_f = 0.3 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.94 (dd, *J* = 11.1, 8.2 Hz, 3H), 7.74 (t, *J* = 7.7 Hz, 1H), 7.60 (td, *J* = 8.1, 7.6, 5.8 Hz, 2H), 7.53–7.46 (m, 2H), 7.39–7.32 (m, 2H), 4.62 (s, 1H), 4.17 (d, *J* = 6.4 Hz, 2H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 155.8, 147.2, 137.4, 135.2, 133.9, 131.9, 131.7, 129.7, 129.5, 129.0, 128.6, 127.7, 127.0, 126.8, 126.4, 126.3, 125.6, 125.3, 79.8, 42.2, 28.4; HRMS (ESI, m/z) calcd for $C_{25}H_{25}N_2O_2$ $[M + H]^+$ 385.1911, found 385.1928.



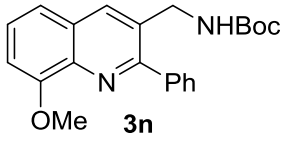
3l

3l, 71% yield, white solid, mp 98–100 °C, R_f = 0.5 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.42 (t, *J* = 6.9 Hz, 3H), 7.38–7.20 (m, 6H), 7.14 (s, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 154.3, 147.9, 147.2, 143.9, 137.3, 129.9, 129.2, 129.0, 127.6, 127.2, 126.8, 112.5, 112.3, 79.9, 43.1, 28.6; HRMS (ESI, m/z) calcd for $C_{19}H_{21}N_2O_3$ $[M + H]^+$ 325.1547, found 325.1560.



3m

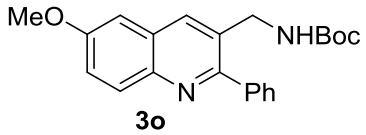
3m, 70% yield, white solid, mp 98–100 °C, R_f = 0.5 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 12.6 Hz, 2H), 7.49 (s, 1H), 7.26 (s, 1H), 6.63–6.61 (m, 1H), 5.27 (s, 1H), 4.73 (d, *J* = 6.4 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 147.9, 147.2, 143.9, 137.3, 129.9, 129.8, 129.0, 127.6, 126.8, 112.5, 112.3, 79.9, 43.1, 28.6; HRMS (ESI, m/z) calcd for $C_{19}H_{21}N_2O_2S$ $[M + H]^+$ 341.1318, found 341.1496.



3n

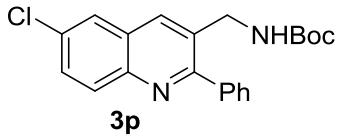
3n, 82% yield, colourless oil, R_f = 0.4 (petroleum ether/ethyl acetate =4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.56 (d, *J* = 6.6 Hz, 2H), 7.51–7.31 (m, 5H), 7.04 (d, *J* = 7.5 Hz, 1H), 4.80 (s, 1H), 4.45 (d, *J* = 6.2 Hz, 2H), 4.05 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 156.0, 155.6, 140.3, 139.1, 135.3, 129.2, 128.6,

126.9, 119.4, 107.9, 79.9, 56.2, 42.6, 28.5; HRMS (ESI, m/z) calcd for $C_{22}H_{25}N_2O_3$ $[M + H]^+$ 365.1860, found 365.1874.



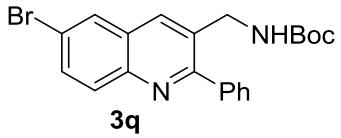
3o

3o, 83% yield, colourless oil, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 8.02 (d, *J* = 9.2 Hz, 1H), 7.54–7.42 (m, 5H), 7.35 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.09 (t, *J* = 2.4 Hz, 1H), 4.87 (s, 1H), 4.42 (d, *J* = 6.2 Hz, 2H), 3.93 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ157.9, 156.9, 143.1, 140.0, 134.2, 130.7, 128.7, 128.6, 128.3, 122.3, 104.8, 79.8, 55.6, 42.4, 28.4; HRMS (ESI, m/z) calcd for $C_{22}H_{25}N_2O_3$ $[M + H]^+$ 365.1860, found 365.1872.



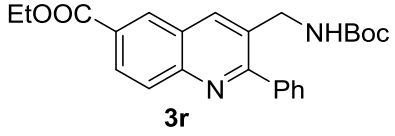
3p

3p, 72% yield, white solid, mp 100–102,R_f = 0.3 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 8.06 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 2.3 Hz, 1H), 7.63 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.54–7.45 (m, 5H), 4.85 (s, 1H), 4.44 (d, *J* = 6.3 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 155.9, 145.5, 139.7, 134.3, 132.5, 131.7, 131.1, 130.6, 128.9, 128.8, 128.7, 128.1, 126.2, 80.1, 42.5, 28.5; HRMS (ESI, m/z) calcd for $C_{21}H_{22}ClN_2O_2$ $[M + H]^+$ 369.1364, found 369.1373.



3q

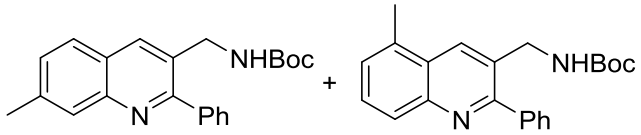
3q, 71% yield, white solid, mp 111–114, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.99 (d, *J* = 8.7 Hz, 2H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.55–7.45 (m, 5H), 4.85 (s, 1H), 4.44 (d, *J* = 6.2 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ159.9, 156.0, 145.7, 139.7, 134.2, 133.1, 131.7, 131.2, 129.5, 128.9, 128.8, 128.7, 128.6, 120.7, 80.1, 42.5, 28.5; HRMS (ESI, m/z) calcd for $C_{21}H_{22}BrN_2O_2$ $[M + H]^+$ 413.0859, found 413.0858.



3r

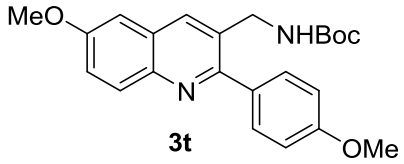
3r, 55% yield, white solid, mp 106–108, R_f = 0.3 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.30 (d, *J* = 7.7 Hz, 2H), 8.17 (d, *J* = 8.8 Hz, 1H), 7.59–7.48 (m, 5H), 4.84 (s, 1H), 4.47 (d, *J* = 7.1 Hz, 4H), 1.46 (s, 9H), 1.34–1.23 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 161.6, 155.9, 148.9, 139.7,

136.3, 130.6, 130.2, 129.6, 129.2, 128.9, 128.8, 128.7, 128.0, 126.6, 80.4, 61.5, 42.4, 28.5, 14.5; HRMS (ESI, m/z) calcd for $C_{24}H_{27}N_2O_4$ $[M + H]^+$ 407.1965, found 407.1971.



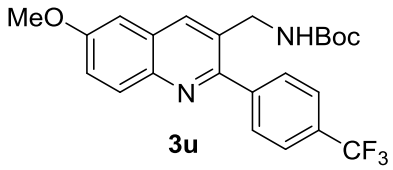
3s **3s'**

3s and **3s'**, 66% yield, **3s**:**3s'** = 2:1, white solid, mp 100–102 °C, R_f = 0.3 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 0.69H), 8.15 (s, 0.33H), 7.99 (d, *J* = 8.5 Hz, 0.71H), 7.92 (s, 0.32H), 7.73 (d, *J* = 8.3 Hz, 0.34H), 7.60–7.45 (m, 5.66H), 7.38 (t, *J* = 5.6 Hz, 1.03H), 4.84 (s, 0.96H), 4.45 (dd, *J* = 15.3, 6.2 Hz, 2H), 2.72 (s, 2H), 2.56 (s, 1H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 159. 0, 156.0, 147.4, 140.3, 140.2, 140.0, 135.2, 134.3, 132.0, 129.9, 129.4, 129.1, 128.79, 128.75, 128.71, 128.68, 128.61, 128.56, 128.4, 127.7, 127.2, 126.8, 79.89, 42.7, 28.5, 22.1, 18.8; HRMS (ESI, m/z) calcd for $C_{22}H_{25}N_2O_2$ $[M + H]^+$ 349.1911, found 349.1925.



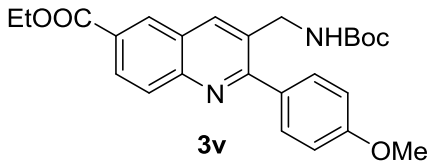
3t

3t, 80% yield, colorless oil, R_f = 0.4 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 7.48–7.42 (m, 2H), 7.32 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.05 (d, *J* = 2.8 Hz, 1H), 7.01–6.93 (m, 2H), 4.94 (s, 1H), 4.42 (d, *J* = 6.1 Hz, 2H), 3.91 (s, 3H), 3.83 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 157.9, 156.7, 143.2, 134.2, 132.6, 130.7, 130.2, 128.2, 122.3, 114.1, 104.9, 79.8, 55.6, 55.5, 42.6, 28.5; HRMS (ESI, m/z) calcd for $C_{23}H_{27}N_2O_4$ $[M + H]^+$ 395.1965, found 395.1986.



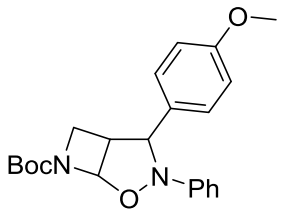
3u

3u, 70% yield, colorless oil, R_f = 0.25 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 8.00 (d, *J* = 9.2 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.37 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.10 (d, *J* = 2.8 Hz, 1H), 4.86 (s, 1H), 4.42 (d, *J* = 6.1 Hz, 2H), 3.95 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 155.9, 155.4, 143.8, 143.3, 134.6, 130.9 (q, *J* = 270 Hz), 130.4, 129.4, 128.7, 125.7, 125.62 (q, *J* = 3.8 Hz), 122.9, 104.9, 80.1, 55.7, 42.4, 28.5; HRMS (ESI, m/z) calcd for $C_{23}H_{24}F_3N_2O_3$ $[M + H]^+$ 433.1734, found 433.1756.



3v

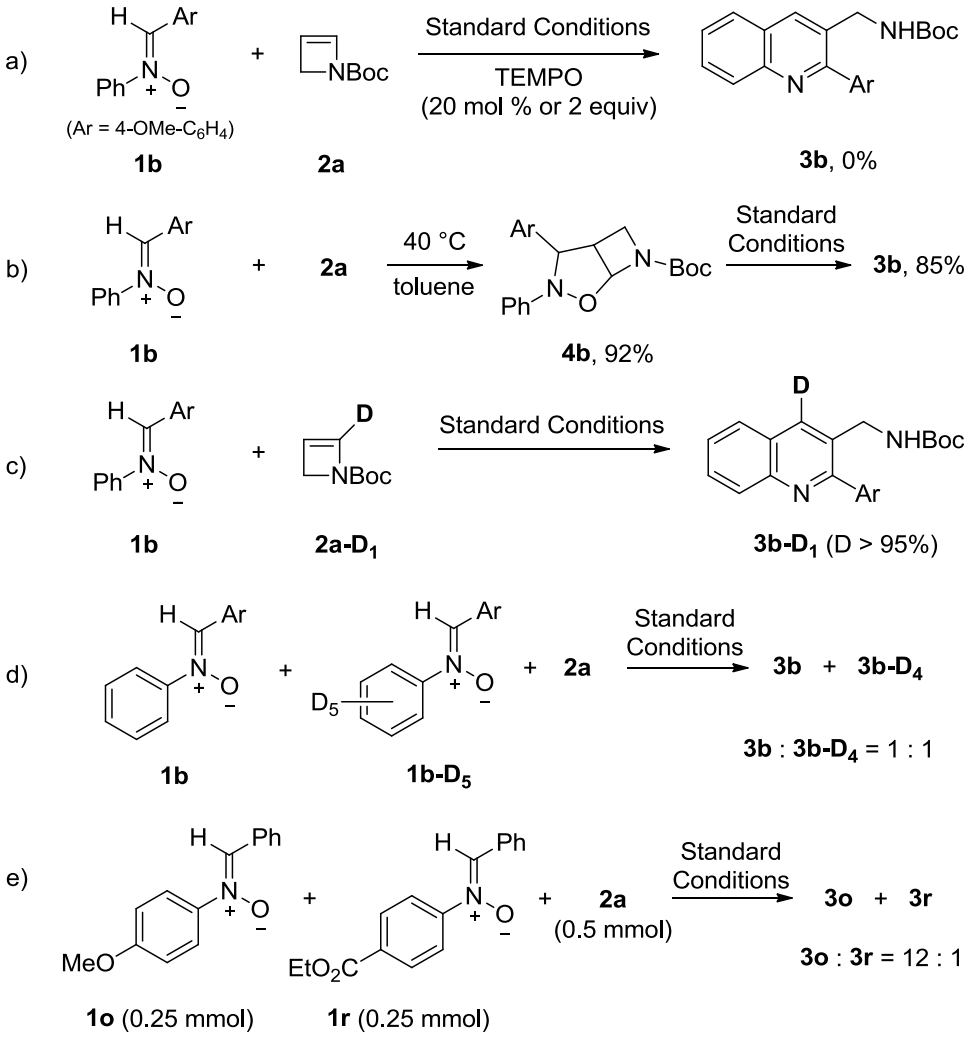
3v, 62% yield, white solid, mp 160–163 °C, R_f = 0.2 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 1.8 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.02 (d, *J* = 8.3 Hz, 2H), 4.92 (s, 1H), 4.47 (dq, *J* = 14.3, 7.1, 6.5 Hz, 4H), 3.87 (s, 3H), 1.46 (t, *J* = 4.7 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 160.2, 148.8, 136.2, 131.9, 131.5, 130.4, 130.1, 129.4, 128.9, 128.24, 126.3, 114.1, 79.9, 61.3, 55.4, 42.4, 28.4, 14.4; HRMS (ESI, m/z) calcd for $C_{25}H_{29}N_2O_5$ $[M + H]^+$ 437.2071, found 437.2074.



4b

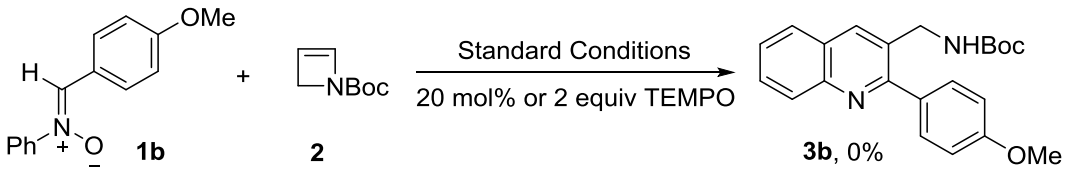
4b, 92% yield, white solid, mp 80–83 °C, R_f = 0.6 (petroleum ether/ethyl acetate = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16–7.12 (m, 2H), 7.08 (dd, *J* = 8.7, 7.1 Hz, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.78–6.70 (m, 3H), 5.93 (d, *J* = 25.9 Hz, 1H), 4.95 (s, 1H), 3.74 (dd, *J* = 8.2, 7.3 Hz, 1H), 3.65 (s, 3H), 3.47–3.42 (m, 1H), 3.34 (s, 1H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 153.7, 150.3, 132.2, 128.5, 127.9, 121.1, 114.0, 92.9, 80.4, 69.3, 55.3, 49.3, 28.5; HRMS (ESI, m/z) calcd for $C_{22}H_{27}N_2O_4$ $[M + H]^+$ 383.1965, found 383.1977.

4. Control Experiments



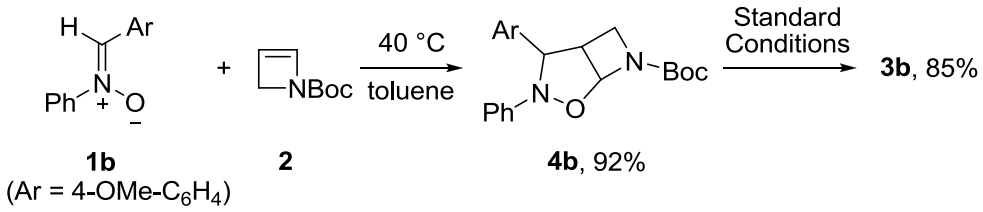
Scheme S1. Summary of control experiments

Scheme S1-1. The effect of radical inhibitor



This reaction was performed following the "General Procedure", only except that 20 mol% or 2.0 equiv TEMPO was added. The desired product **3b** was not observed, suggesting that a radical-mediated pathway might be involved.

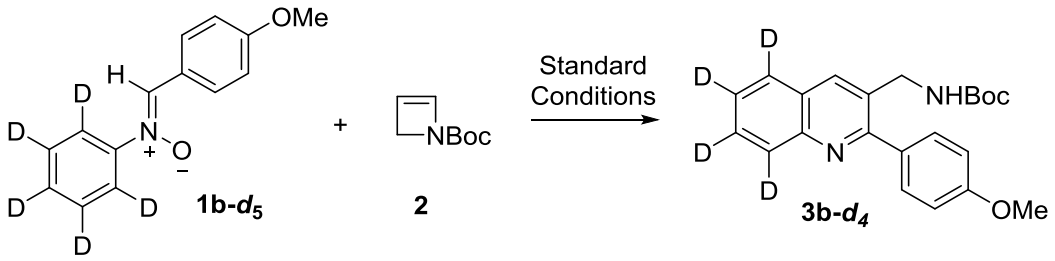
Scheme S1-2. Isolation of intermediate 4b and its further transformation to 3b



Nitrone **1b** (0.25 mmol) and 2.0 mL of solvent toluene was weighted and placed in a dried Schlenk tube, followed by the *N*-Boc-2-azetine **2** (0.5 mmol, 2 equiv). The reaction mixture was stirred at 40 °C for 10 h. After cooling to room temperature, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the intermediate **4b**. The product was isolated in 92% yield.

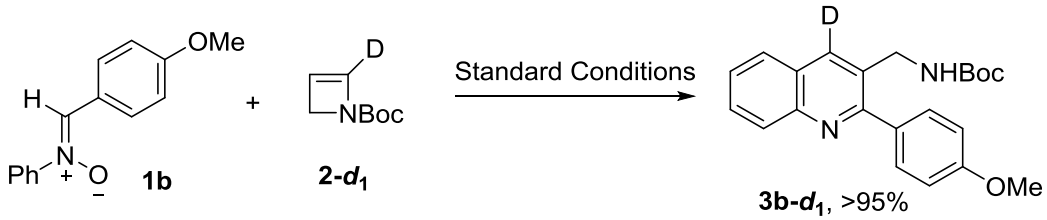
AgOTf (0.025 mmol, 6.4 mg, 10 mol%), intermediate **4b** (0.25 mmol) and 2.0 mL of solvent toluene were weighted in the glove box and placed in a dried Schlenk tube. The reaction mixture was stirred at 40 °C for 18 h. After cooling to room temperature, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the desired product **3b** in 85% yield.

Scheme S1-3. Reaction of 1b-d_5 with 2



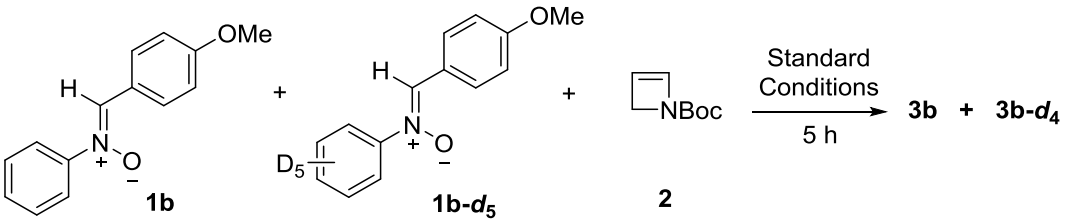
This reaction was performed following the "General Procedure", only except that **1b-d_5** was used as nitrone.

Scheme S1-4. Reaction of 1b with 2-d_1

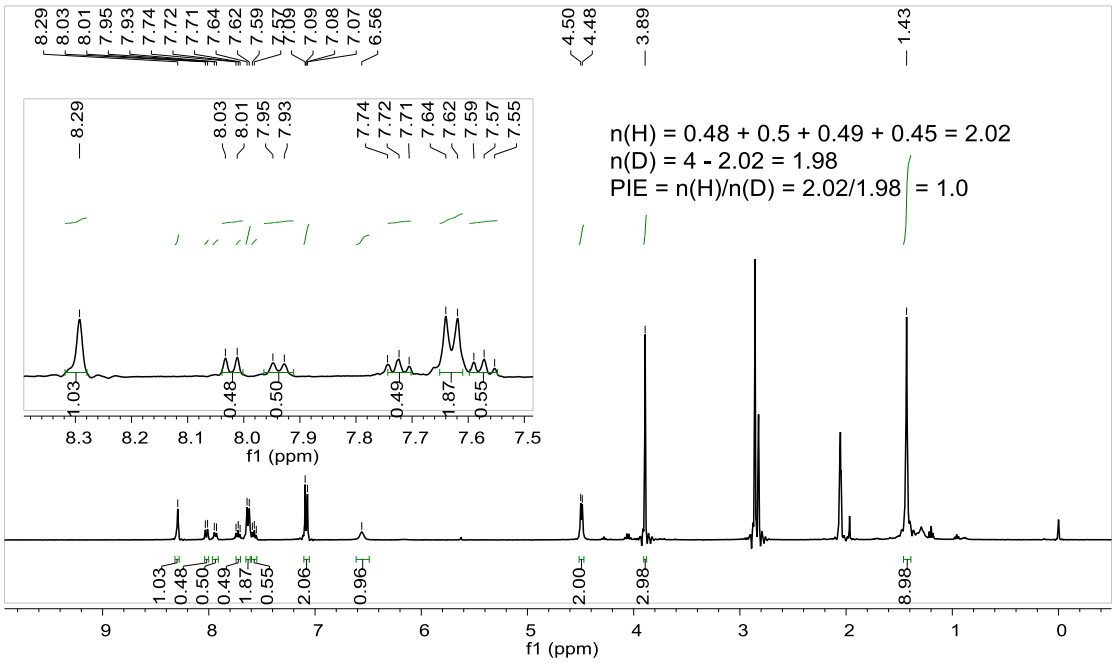


This reaction was performed following the "General Procedure", only except that **2-d_1** was used. Compared with the ^{1}H NMR spectra of **3b**, the deuterium atom was completely transferred into the product (>95% deuterium incorporation).

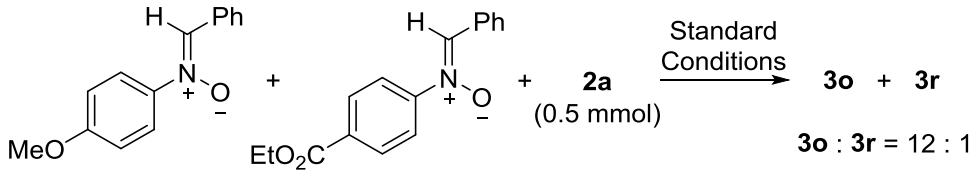
Scheme S1-5. Intermolecular competitive reactions



AgOTf (0.025 mmol, 6.4 mg, 10 mol%), nitrone **1b** (0.25 mmol), nitrone **1b-d_5** were weighted in the glove box and placed in a dried Schlenk tube. Then 2.0 mL of solvent toluene was added, followed by the *N*-Boc-2-azetine **2** (0.5 mmol, 2 equiv). The reaction mixture was stirred at 40 °C for 5 h. After cooling to room temperature, the solvent was evaporated and the crude product was directly purified by silica gel column chromatography to give the mixture of **3b** and **3b-d_4**. A PIE value of 1.0 was obtained on the basis of ^{1}H NMR analysis.



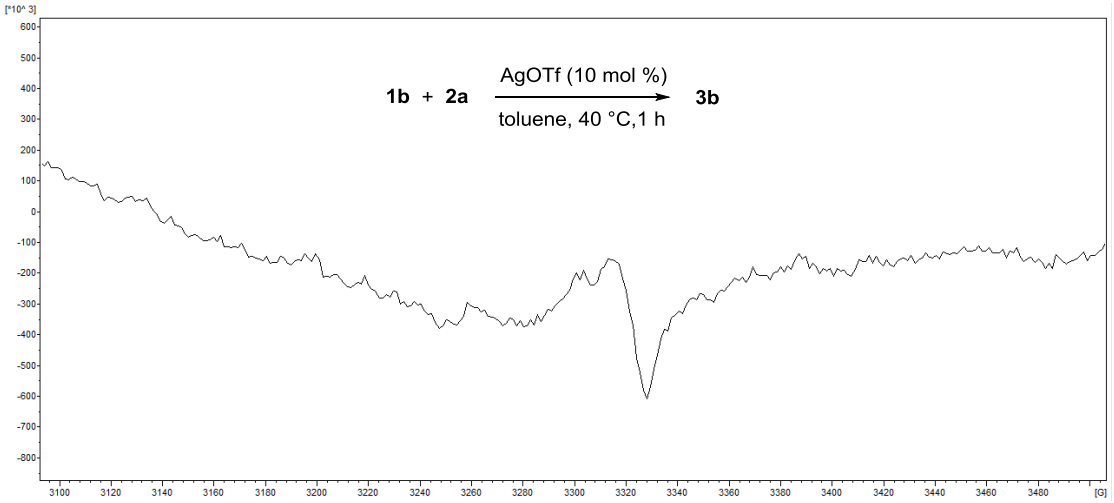
Scheme S1-5. Competition reaction between 1o and 1r

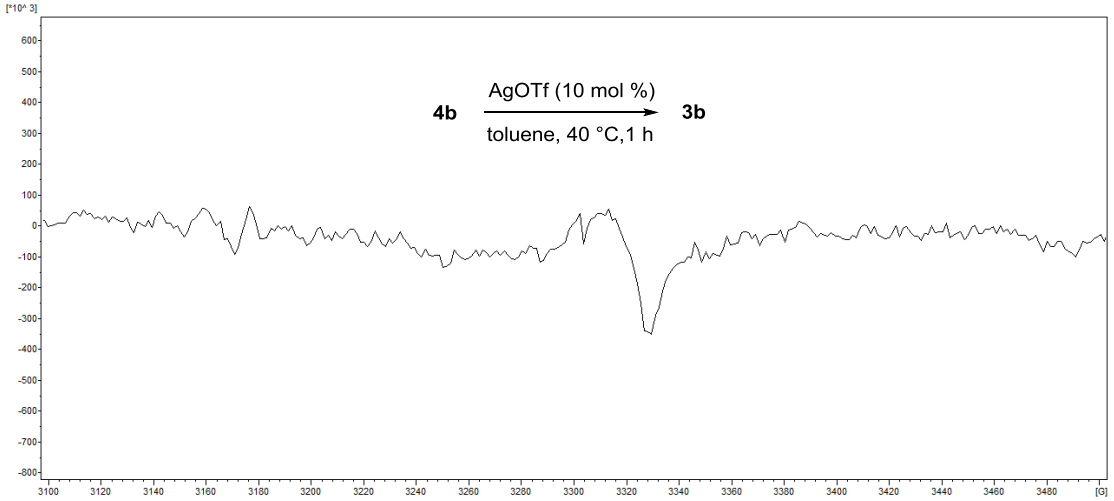


1o (0.25 mmol) **1r** (0.25 mmol)

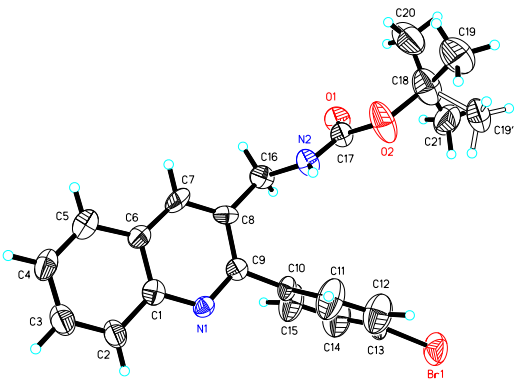
AgOTf (0.025 mmol, 6.4 mg, 10 mol%), nitrone **1o** (0.25 mmol), nitrone **1r** were weighted in the glove box and placed in a dried Schlenk tube. Then 2.0 mL of solvent toluene was added, followed by the *N*-Boc-2-azetine **2** (0.5 mmol, 2 equiv). The reaction mixture was stirred at 40 °C for 18 h. After cooling to room temperature, the solvent was evaporated and the crude product was directly purified by silica gel column chromatography to give the product **3o** and **3r** respectively. The isolated yield ratio of **3o**:**3r** was 12:1.

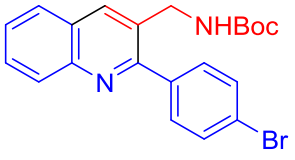
5. EPR spectra of Ag-catalyzed transformations





6. Crystal Structure of Products





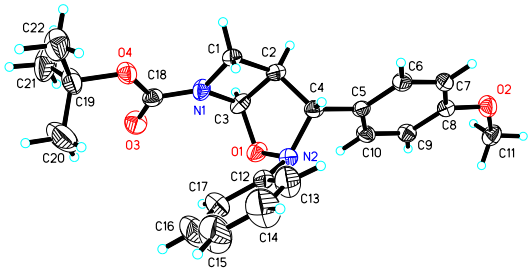
3e

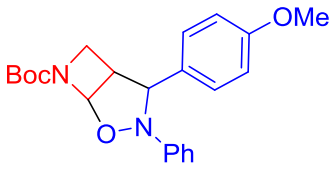
ORTEP drawing of **3e** (CCDC1526502) with thermal ellipsoids at the 50% probability

Table S1. Crystal data and structure refinement for cd16158m_a.

Identification code	cd16158m_a	
Empirical formula	C21 H21 Br N2 O2	
Formula weight	413.31	
Temperature	273(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 5.095(8) Å	α = 73.395(18)°.
	b = 12.261(19) Å	β = 81.56(2)°.
	c = 17.00(3) Å	γ = 78.69(2)°.
Volume	993(3) $Å^3$	
Z	2	
Density (calculated)	1.382 Mg/m^3	
Absorption coefficient	2.085 mm^{-1}	
F(000)	424	
Crystal size	0.160 x 0.080 x 0.040 mm^3	
Theta range for data collection	1.757 to 24.998°.	
Index ranges	-6<=h<=5, -13<=k<=14, -20<=l<=19	
Reflections collected	4250	
Independent reflections	3288 [R(int) = 0.1751]	
Completeness to theta = 25.242°	91.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.3425	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	3288 / 78 / 249
Goodness-of-fit on F^2	0.963
Final R indices [I>2sigma(I)]	R1 = 0.0911, wR2 = 0.2098
R indices (all data)	R1 = 0.2545, wR2 = 0.2887
Largest diff. peak and hole	0.494 and -0.436 e.Å^{-3}





4b

ORTEP drawing of **3e** (CCDC1526503) with thermal ellipsoids at the 50% probability

Table S2. Crystal data and structure refinement for cd16586.

Identification code	cd16586	
Empirical formula	C22 H26 N2 O4	
Formula weight	382.45	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 6.1408(17) Å	α = 87.399(7)°.
	b = 10.540(3) Å	β = 81.181(6)°.
	c = 16.567(5) Å	γ = 79.922(6)°.
Volume	1043.1(5) Å^3	
Z	2	
Density (calculated)	1.218 Mg/m^3	
Absorption coefficient	0.084 mm^{-1}	
F(000)	408	
Crystal size	0.200 x 0.140 x 0.080 mm^3	
Theta range for data collection	1.963 to 24.994°.	
Index ranges	-7<=h<=7, -12<=k<=9, -19<=l<=19	
Reflections collected	5786	
Independent reflections	3671 [R(int) = 0.0343]	
Completeness to theta = 25.242°	97.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.5750	
Refinement method	Full-matrix least-squares on F^2	

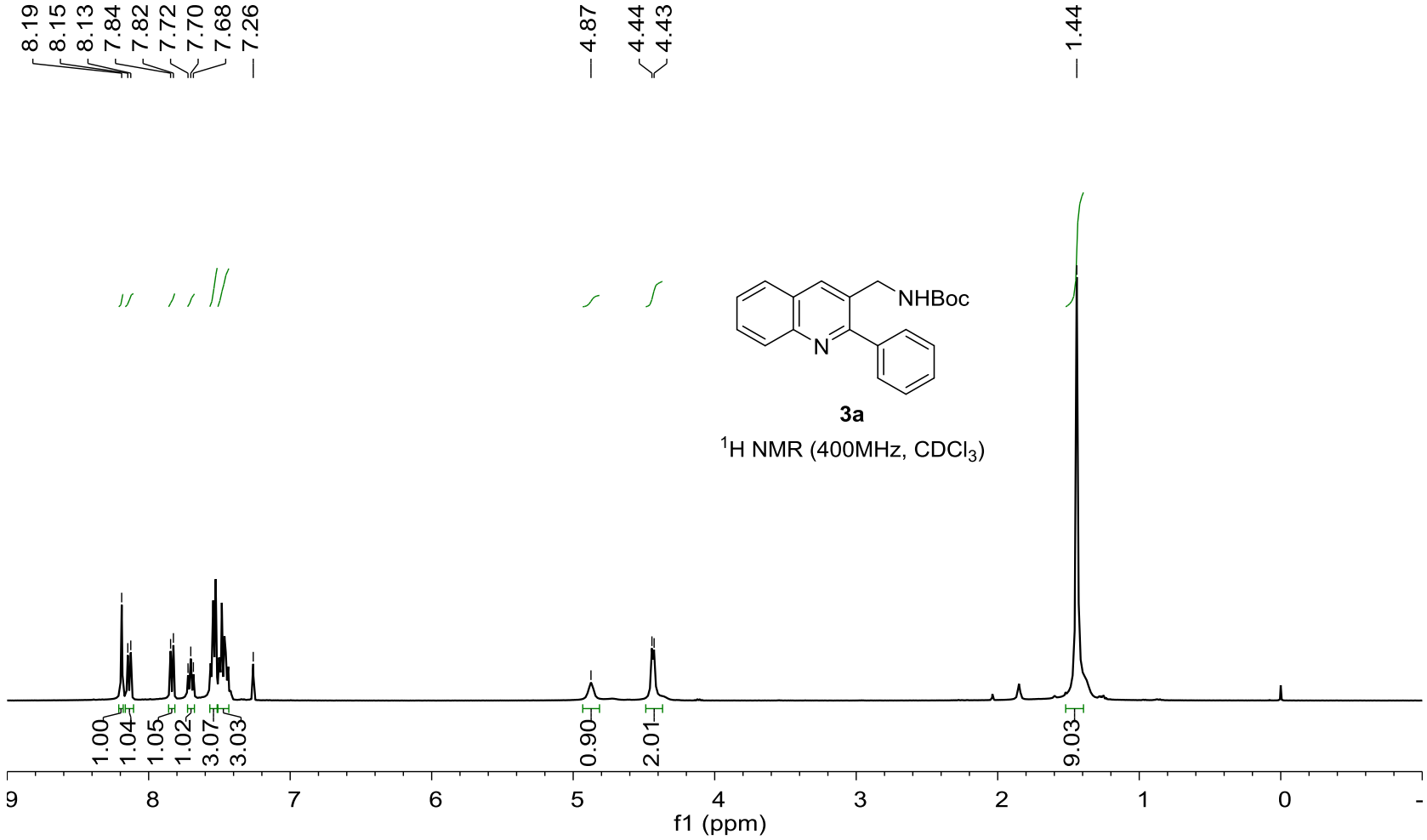
Data / restraints / parameters	3671 / 12 / 257
Goodness-of-fit on F^2	1.081
Final R indices [I>2sigma(I)]	R1 = 0.0721, wR2 = 0.1651
R indices (all data)	R1 = 0.1062, wR2 = 0.1818
Extinction coefficient	n/a
Largest diff. peak and hole	0.199 and -0.223 e.$Å^{-3}$

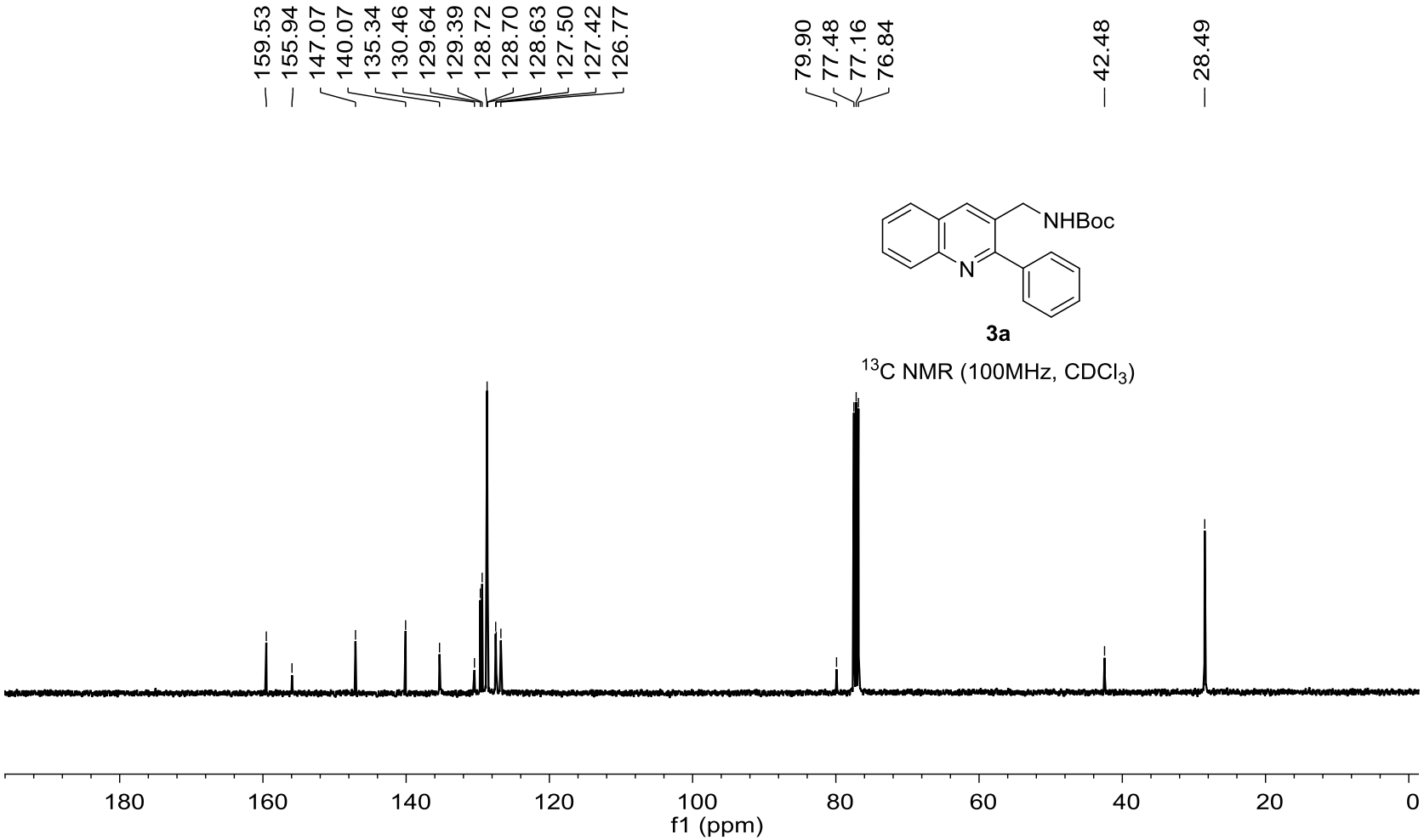
7. References

1. N. Duguet, A. M. Z. Slawin and A. D. Smith, *Org. Lett*. 2009, **11**, 3858.

2. D. M. Hodgson, C. I. Pearson and M. Kazmi, *Org. Lett.* 2014, **16**, 856.

8. Copies of NMR Spectra

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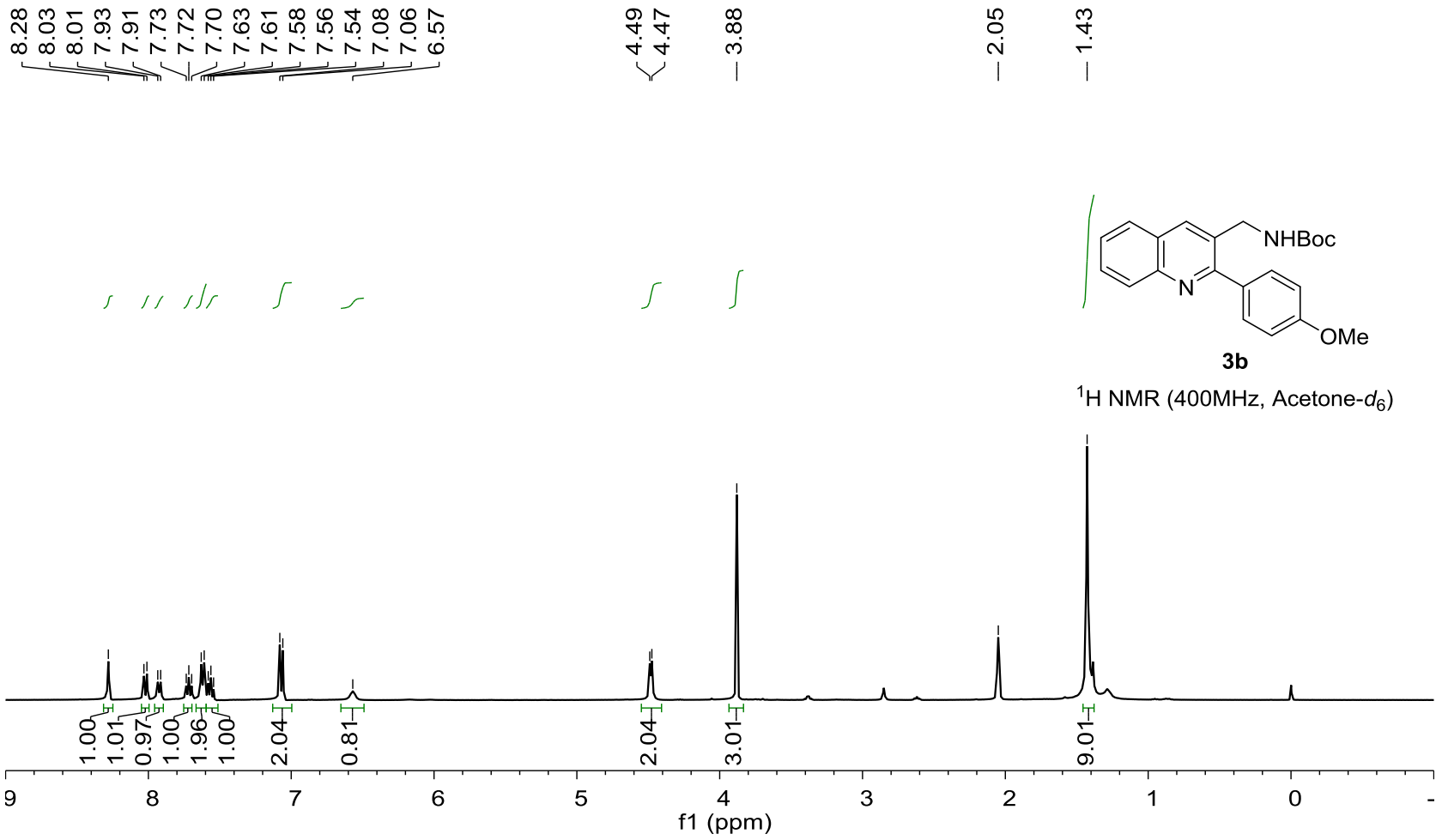
147.07
140.07
135.34
130.46
129.64
129.39
128.72
128.70
128.63
127.50
127.42
126.77
79.90
77.48
77.16
76.84
42.48
28.49
NHBoc
N
3a
13C NMR (100MHz, CDCl3)
180
160
140
120
100
80
60
40
20
0
f1 (ppm)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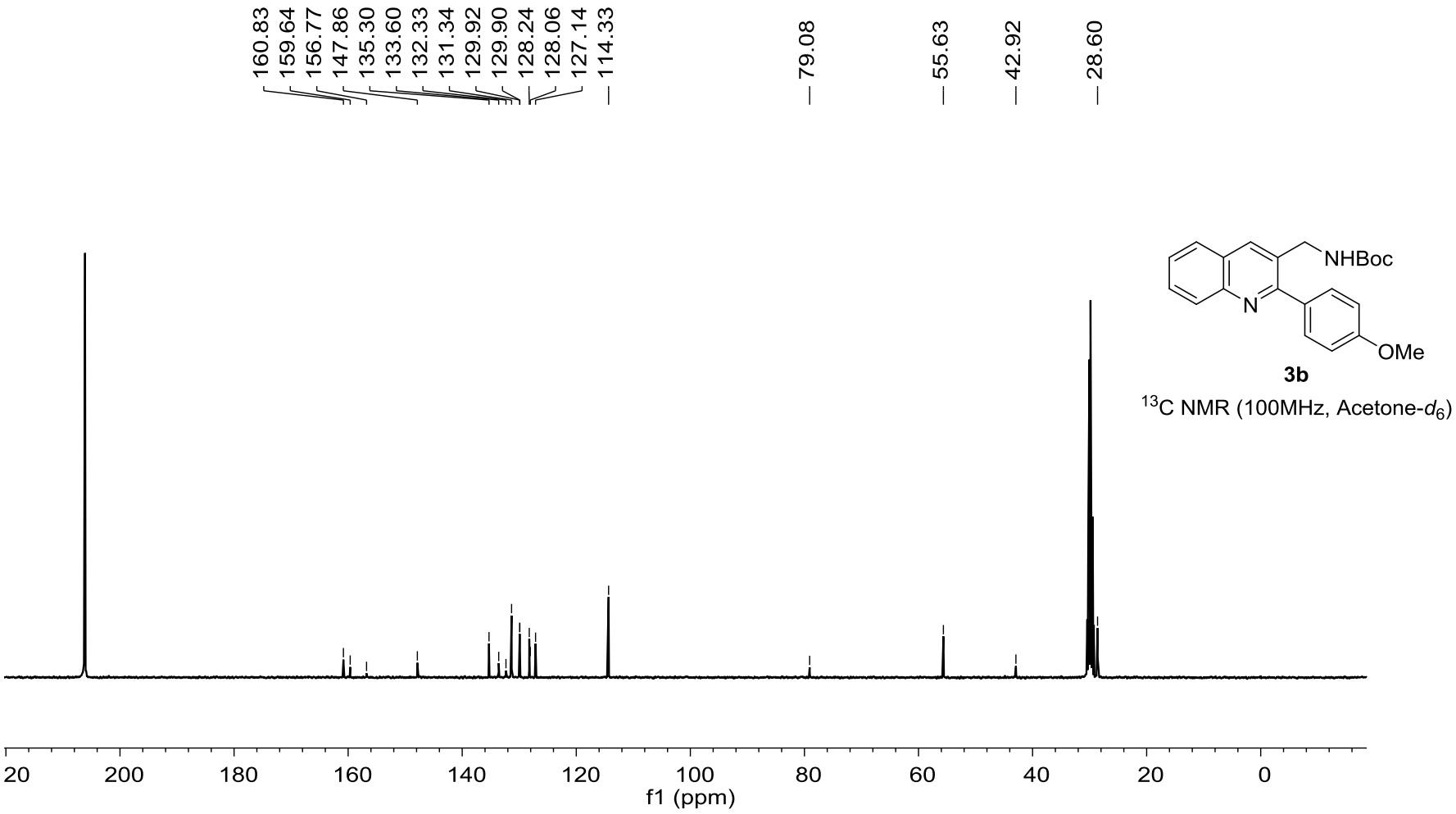
8.03
8.01
7.93
7.91
7.73
7.72
7.70
7.63
7.61
7.58
7.56
7.54
7.08
7.06
6.57
4.49
4.47
3.88
2.05
1.43
NHBoc
N
OMe
3b
1H NMR (400MHz, Acetone-d6)
1.00
1.01
0.97
1.00
1.96
1.00
2.04
0.81
2.04
3.01
9.01
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)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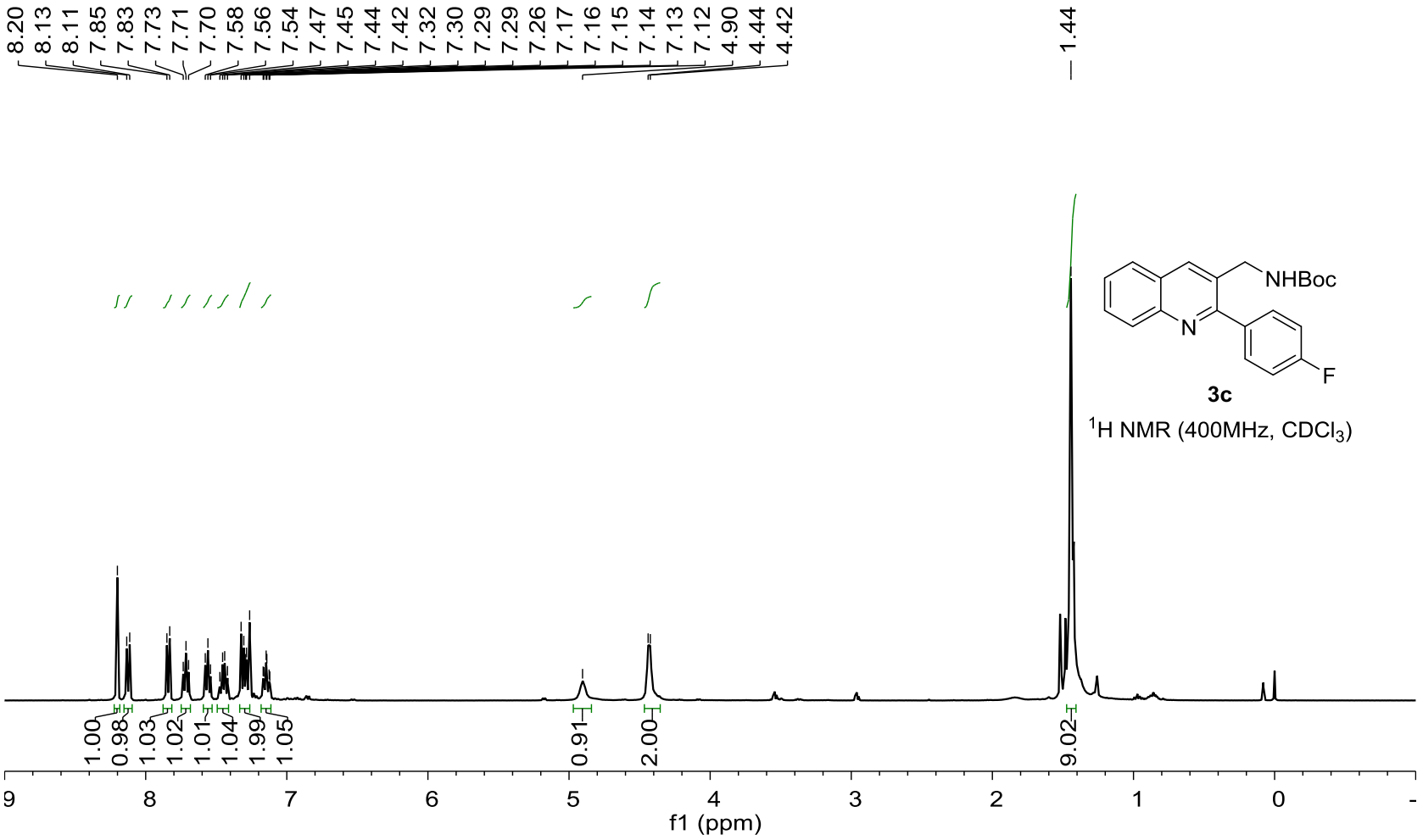
159.64
156.77
147.86
135.30
133.60
132.33
131.34
129.92
129.90
128.24
128.06
127.14
114.33
79.08
55.63
42.92
28.60
NHBoc
N
OMe
3b
^{13}C NMR (100MHz, Acetone-d_6)
20
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)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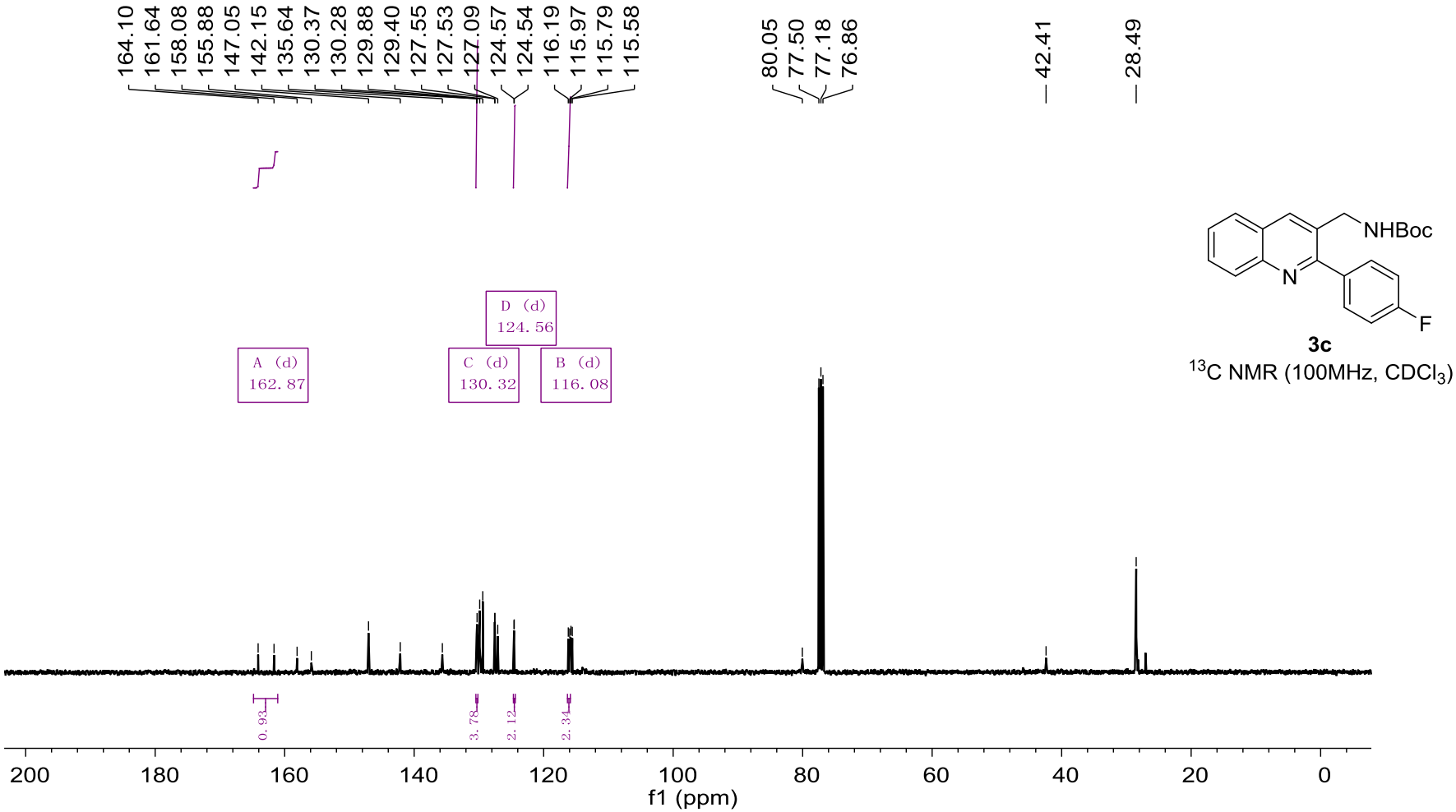
8.13
8.11
7.85
7.83
7.73
7.71
7.70
7.58
7.56
7.54
7.47
7.45
7.44
7.42
7.32
7.30
7.29
7.29
7.26
7.17
7.16
7.15
7.14
7.13
7.12
4.90
4.44
4.42
1.44
NHBoc
N
F
3c
1H NMR (400MHz, CDCl3)
1.00
0.98
1.03
1.02
1.01
1.04
1.99
1.05
0.91
2.00
9.02
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)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161.64
158.08
155.88
147.05
142.15
135.64
130.37
130.28
129.88
129.40
127.55
127.53
127.09
124.57
124.54
116.19
115.97
115.79
115.58
80.05
77.50
77.18
76.86
42.41
28.49
D (d)
124.56
A (d)
162.87
C (d)
130.32
B (d)
116.08
NHBoc
N
F
3c
13C NMR (100MHz, CDCl3)
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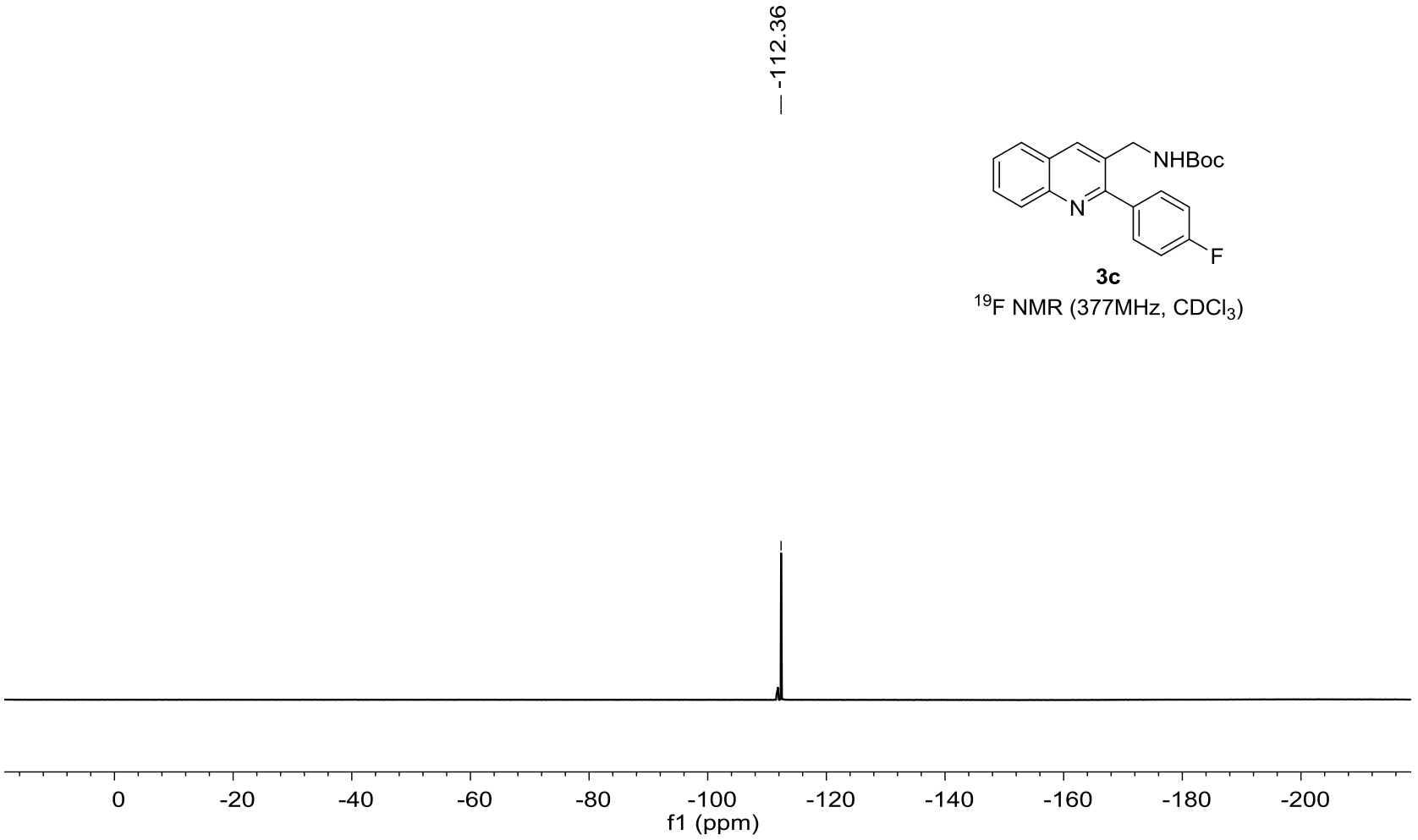
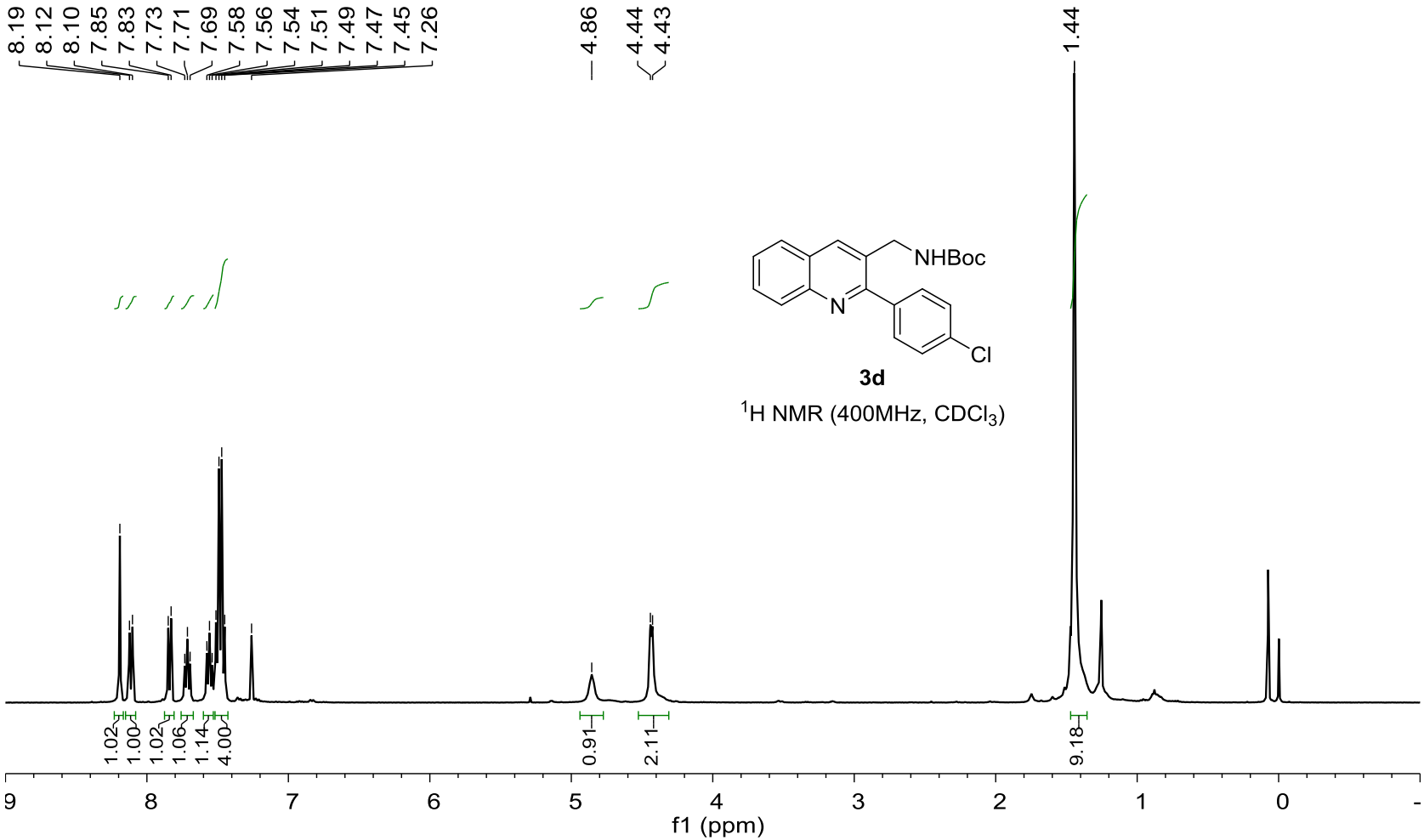
2.12
2.34
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



3c

^{19}F NMR (377MHz, $CDCl_3$)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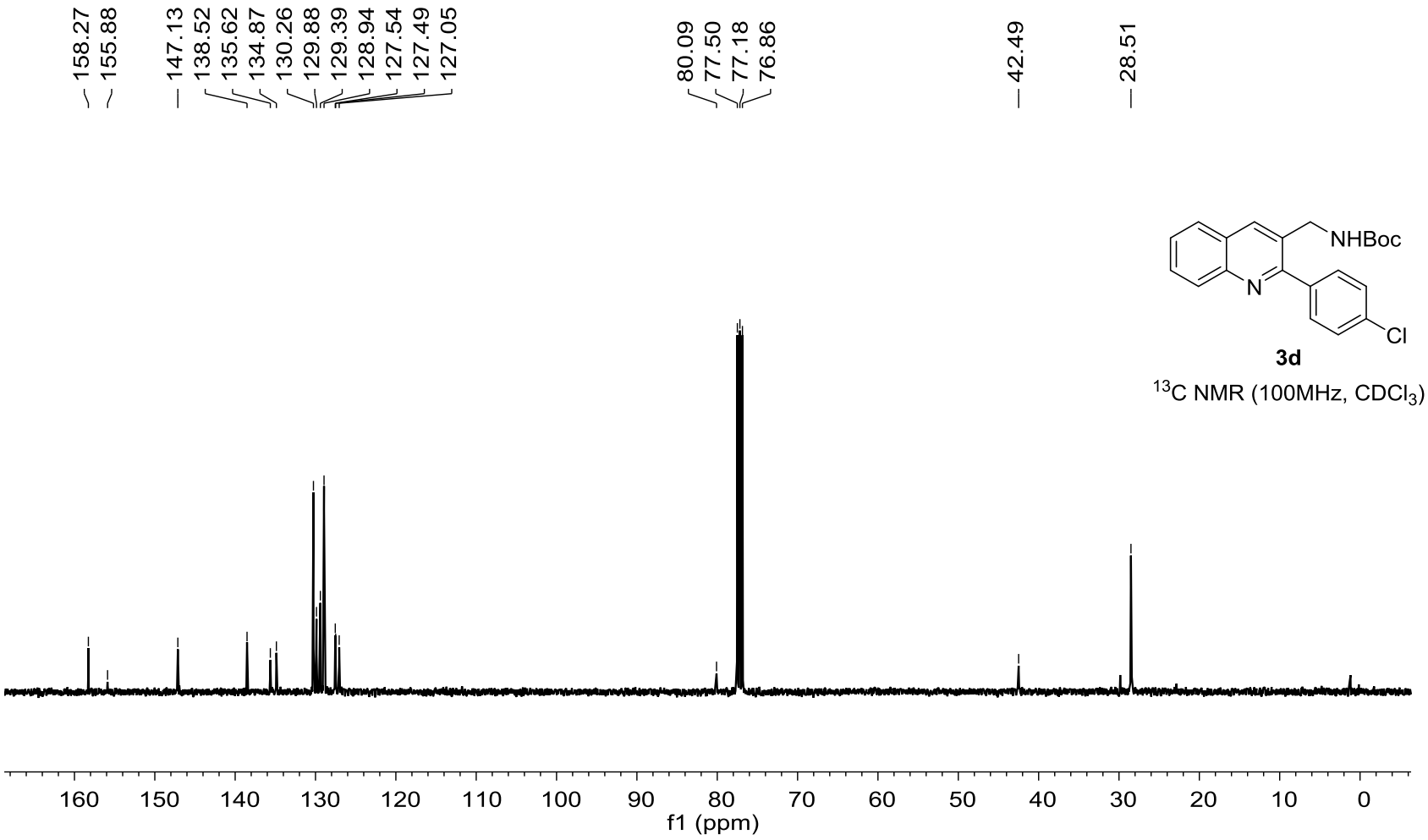
8.12
8.10
7.85
7.83
7.73
7.71
7.69
7.58
7.56
7.54
7.51
7.49
7.47
7.45
7.26
4.86
4.44
4.43
1.44
NHBoc
N
Cl
3d
1H NMR (400MHz, CDCl3)
1.02
1.00
1.02
1.06
1.14
4.00
0.91
2.11
9.18
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)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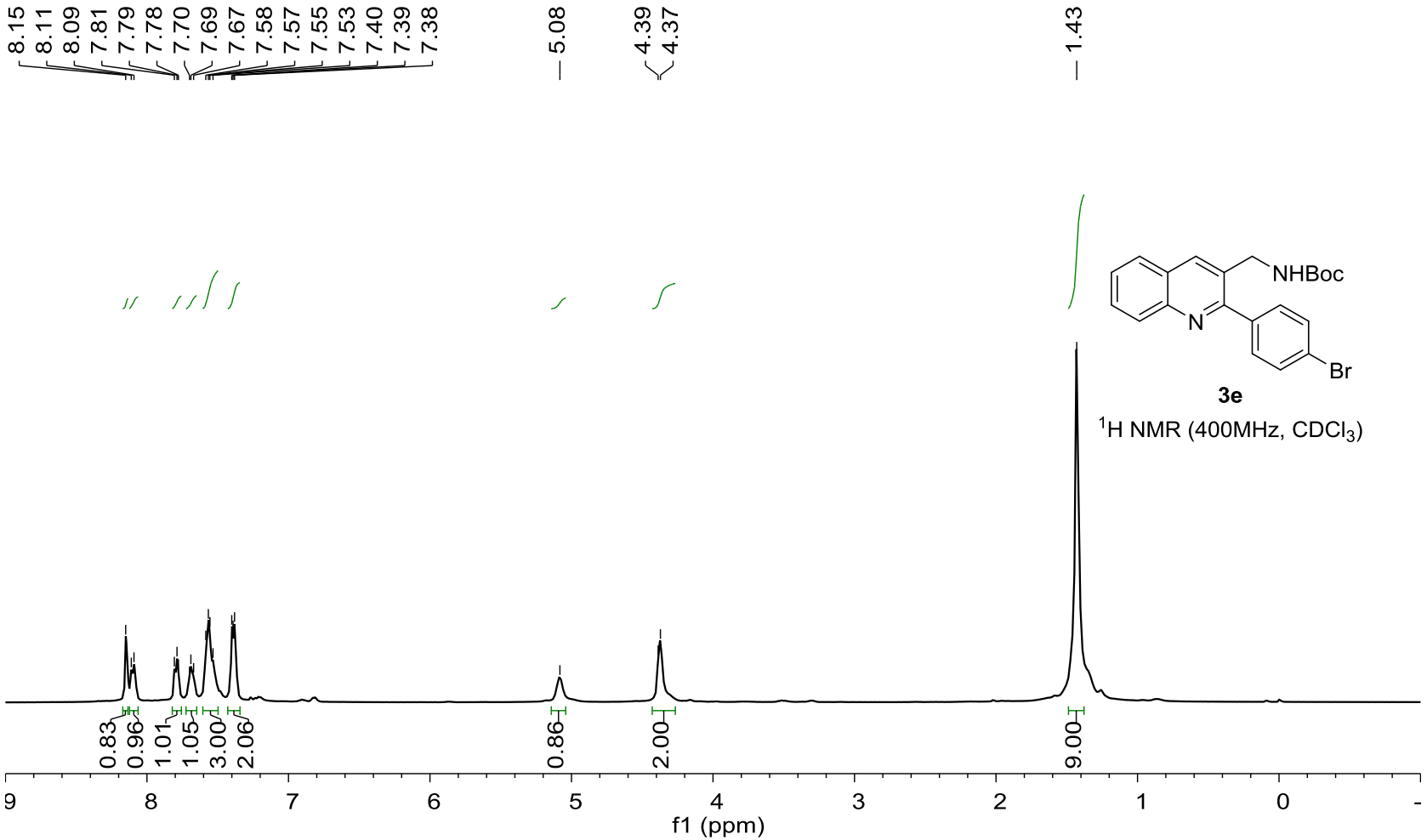
155.88
147.13
138.52
135.62
134.87
130.26
129.88
129.39
128.94
127.54
127.49
127.05
80.09
77.50
77.18
76.86
42.49
28.51
NHBoc
N
Cl
3d
13C NMR (100MHz, CDCl3)
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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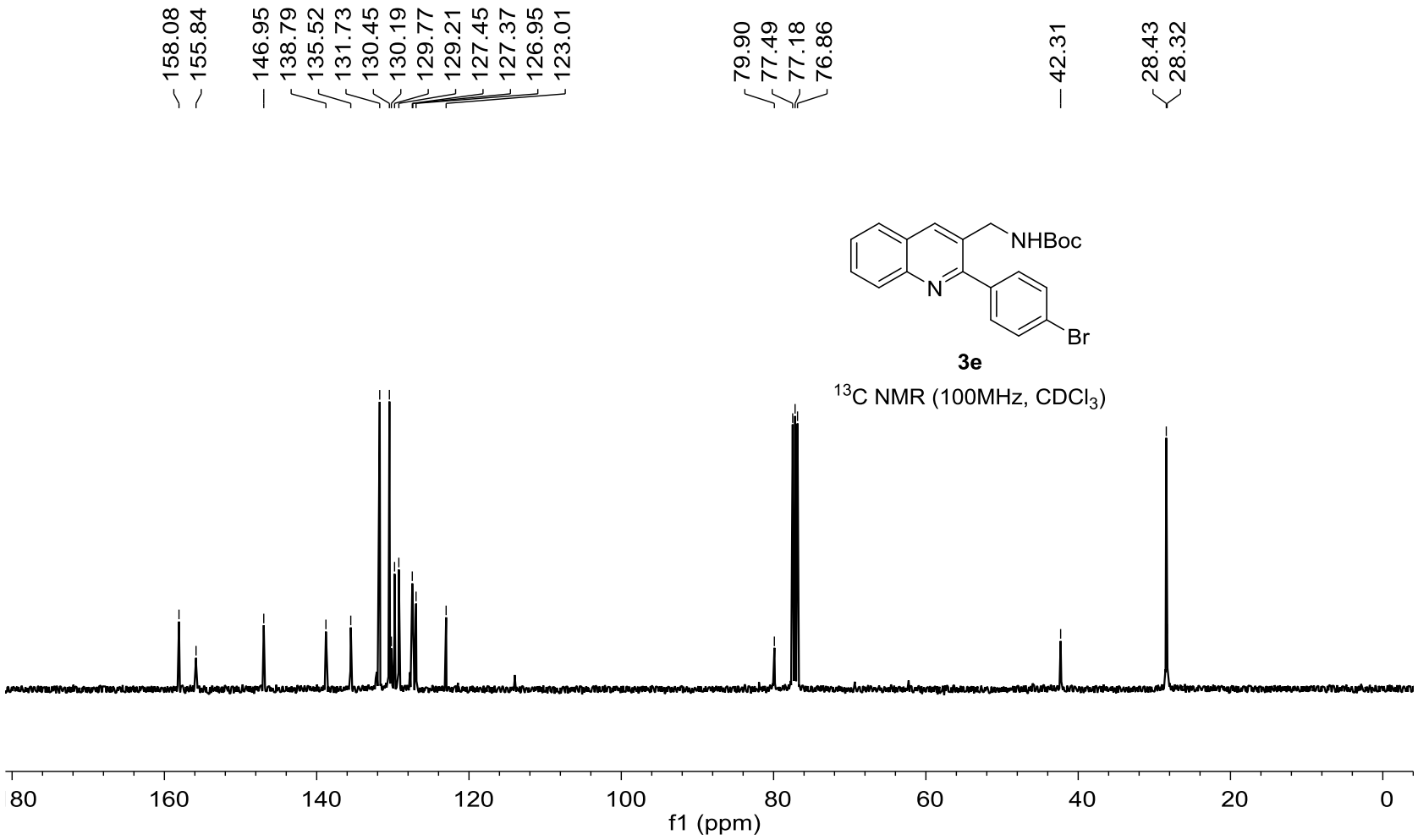
8.11
8.09
7.81
7.79
7.78
7.70
7.69
7.67
7.58
7.57
7.55
7.53
7.40
7.39
7.38
5.08
4.39
4.37
1.43
NHBoc
N
Br
3e
1H NMR (400MHz, CDCl3)
0.83
0.96
1.01
1.05
3.00
2.06
0.86
2.00
9.00
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)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155.84
146.95
138.79
135.52
131.73
130.45
130.19
129.77
129.21
127.45
127.37
126.95
123.01
79.90
77.49
77.18
76.86
42.31
28.43
28.32
NHBoc
N
Br
3e
13C NMR (100MHz, CDCl3)
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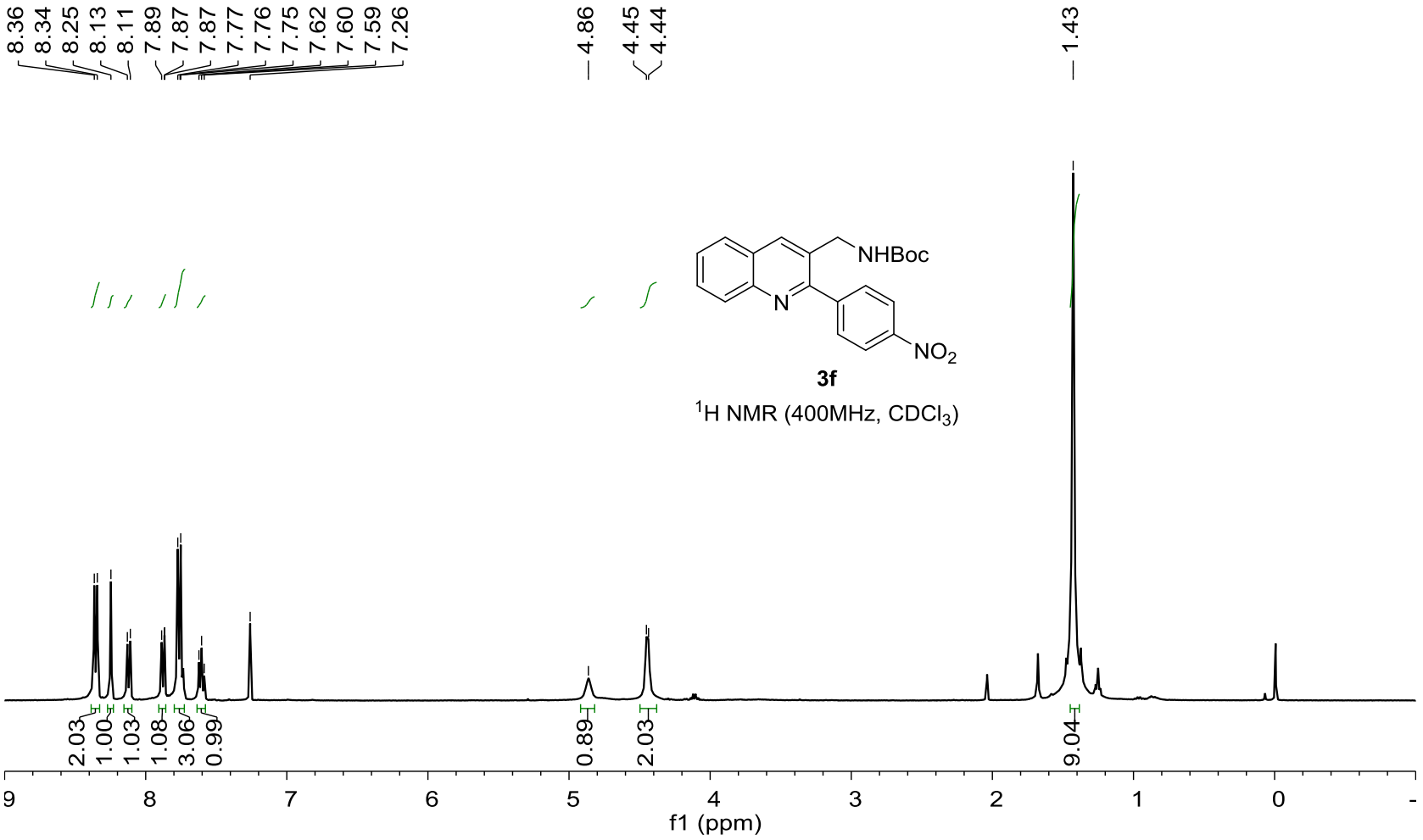
160
140
120
100
80
60
40
20
0
f1 (ppm)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8.13
8.11
7.89
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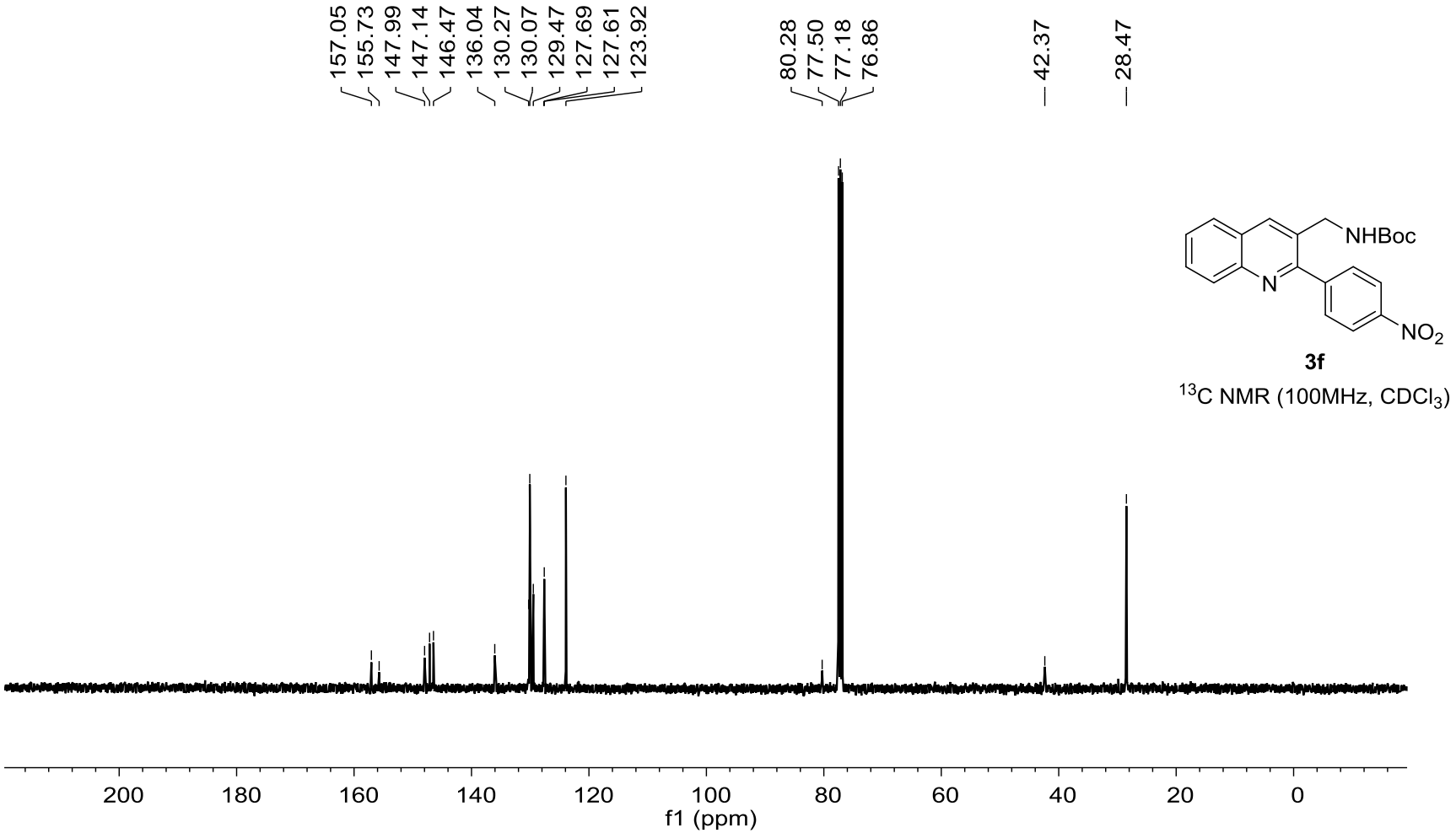
7.87
7.77
7.76
7.75
7.62
7.60
7.59
7.26
4.86
4.45
4.44
1.43
NHBoc
N
NO2
3f
1H NMR (400MHz, CDCl3)
2.03
1.00
1.03
1.08
3.06
0.99
0.89
2.03
9.04
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)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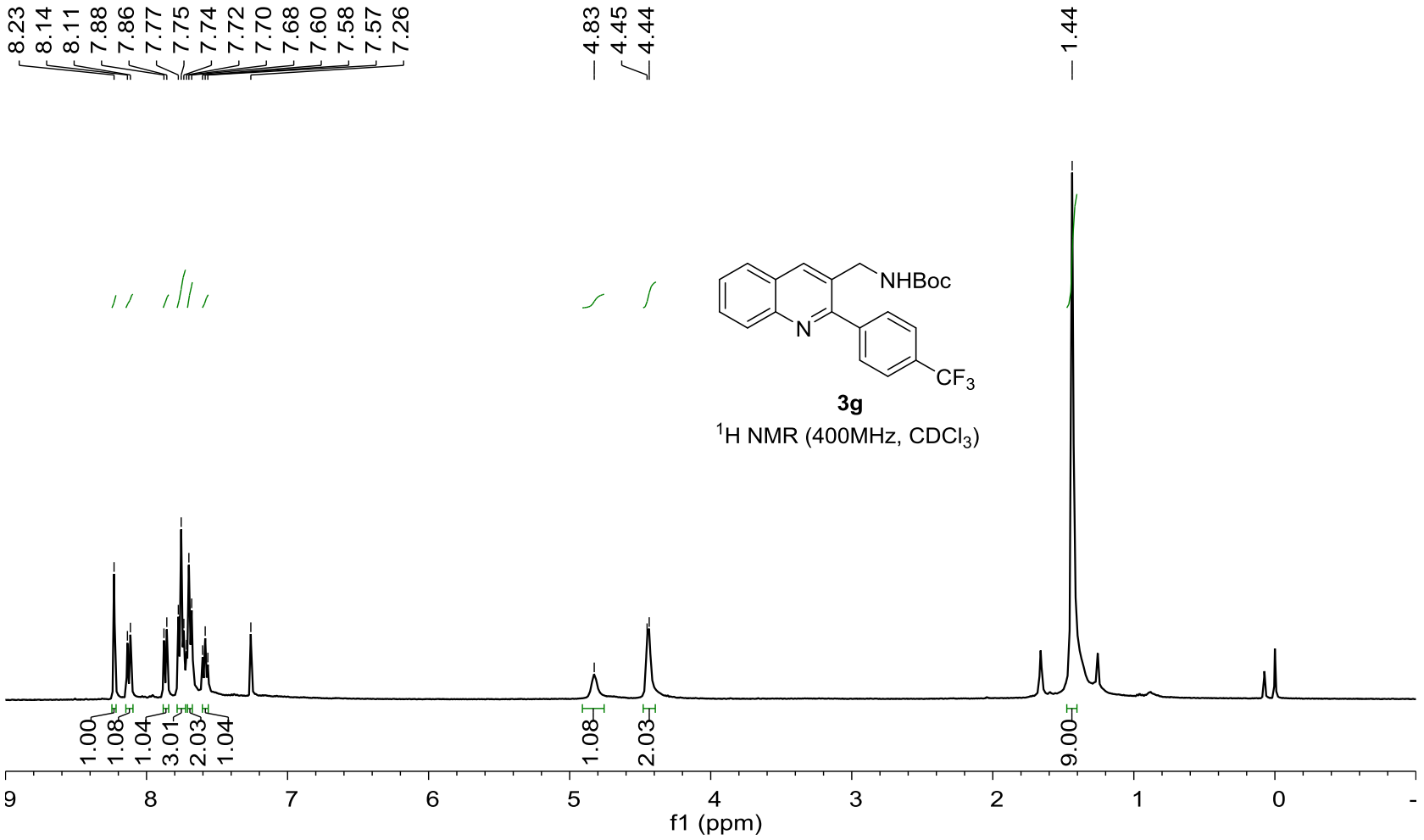
147.14
146.47
136.04
130.27
130.07
129.47
127.69
127.61
123.92
80.28
77.50
77.18
76.86
42.37
28.47
NHBoc
N
NO2
3f
13C NMR (100MHz, CDCl3)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)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8.14
8.11
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7.75
7.74
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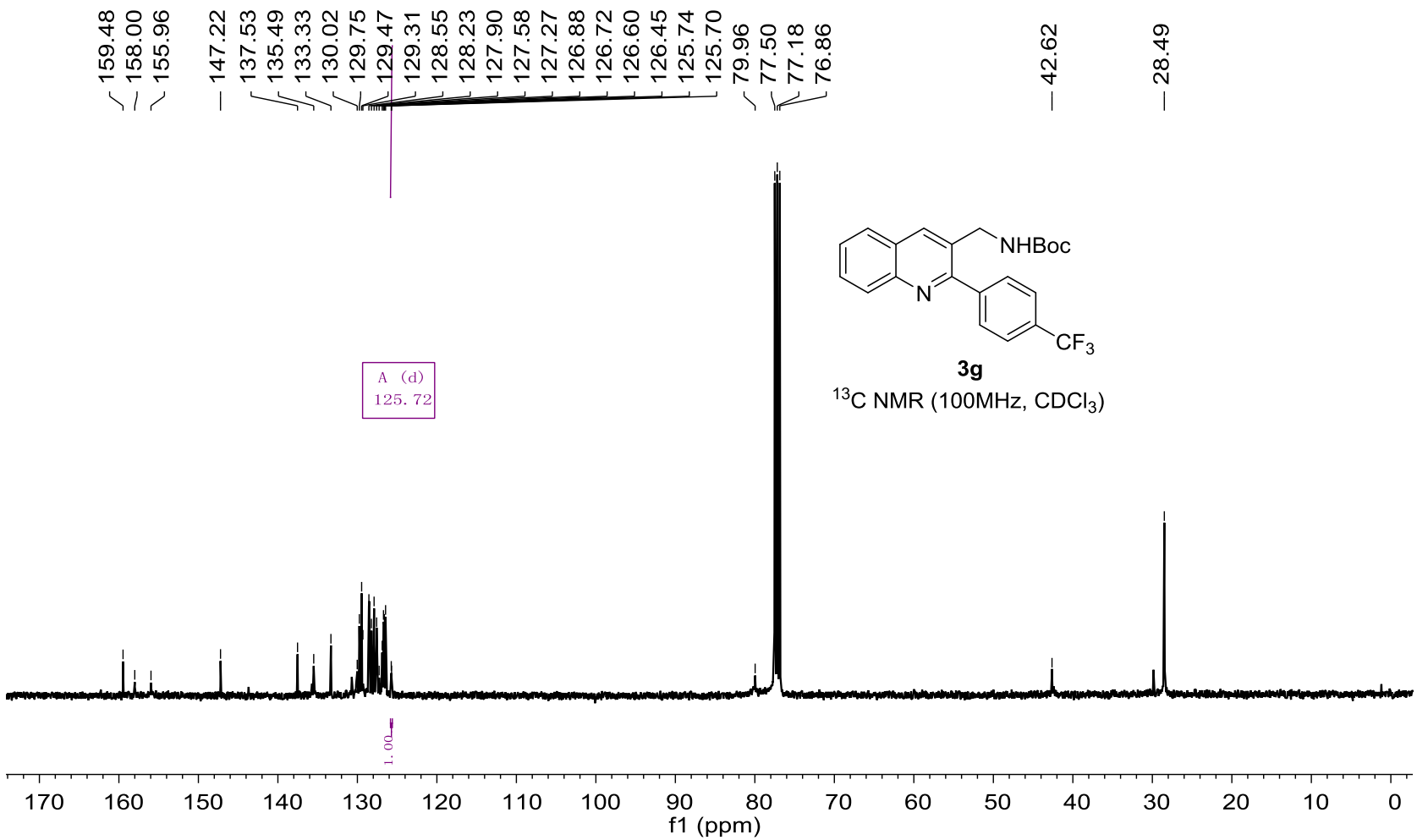
7.70
7.68
7.60
7.58
7.57
7.26
4.83
4.45
4.44
1.44
NHBoc
N
CF3
3g
1H NMR (400MHz, CDCl3)
1.00
1.08
1.04
3.01
2.03
1.04
1.08
2.03
9.00
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)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137.53
135.49
133.33
130.02
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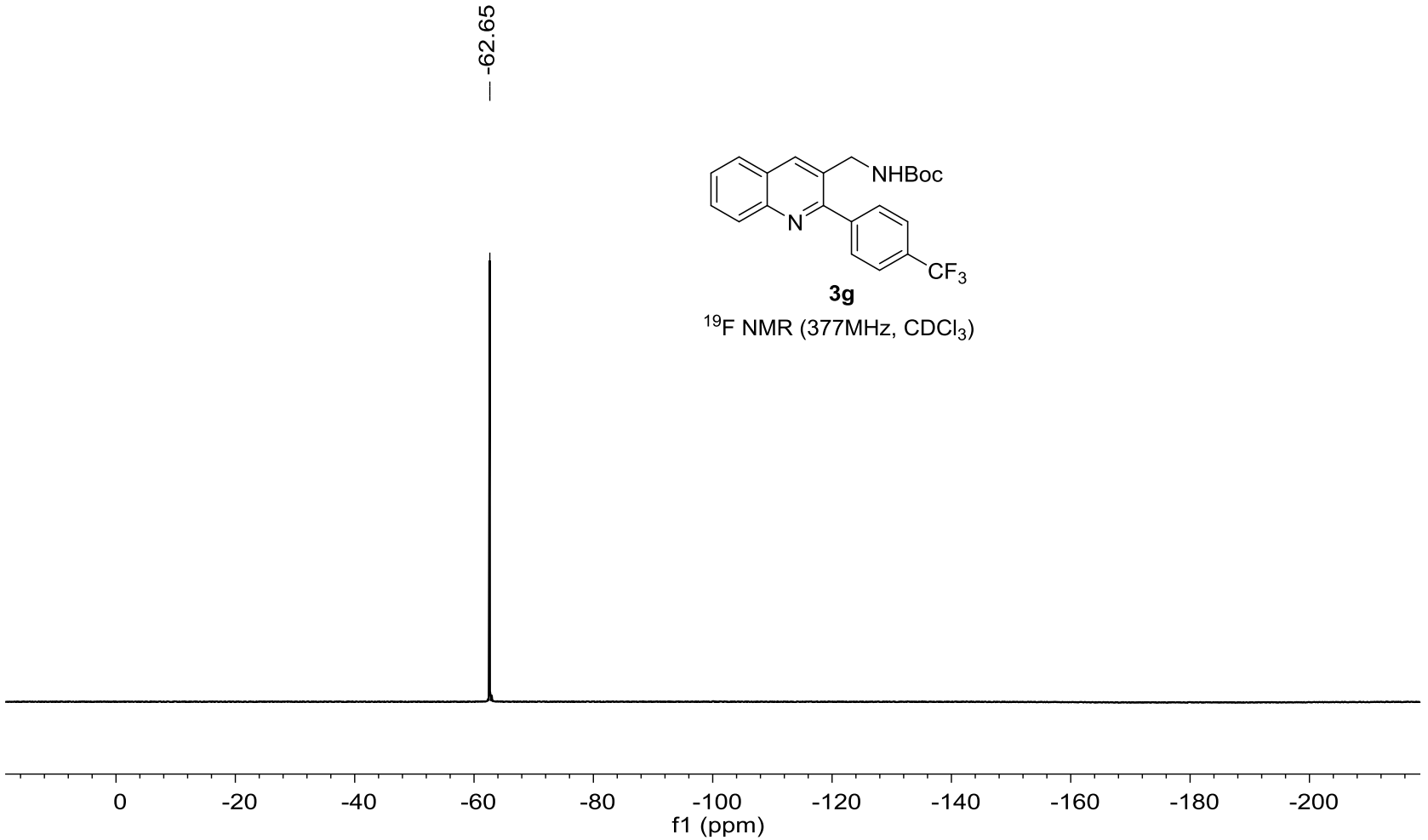
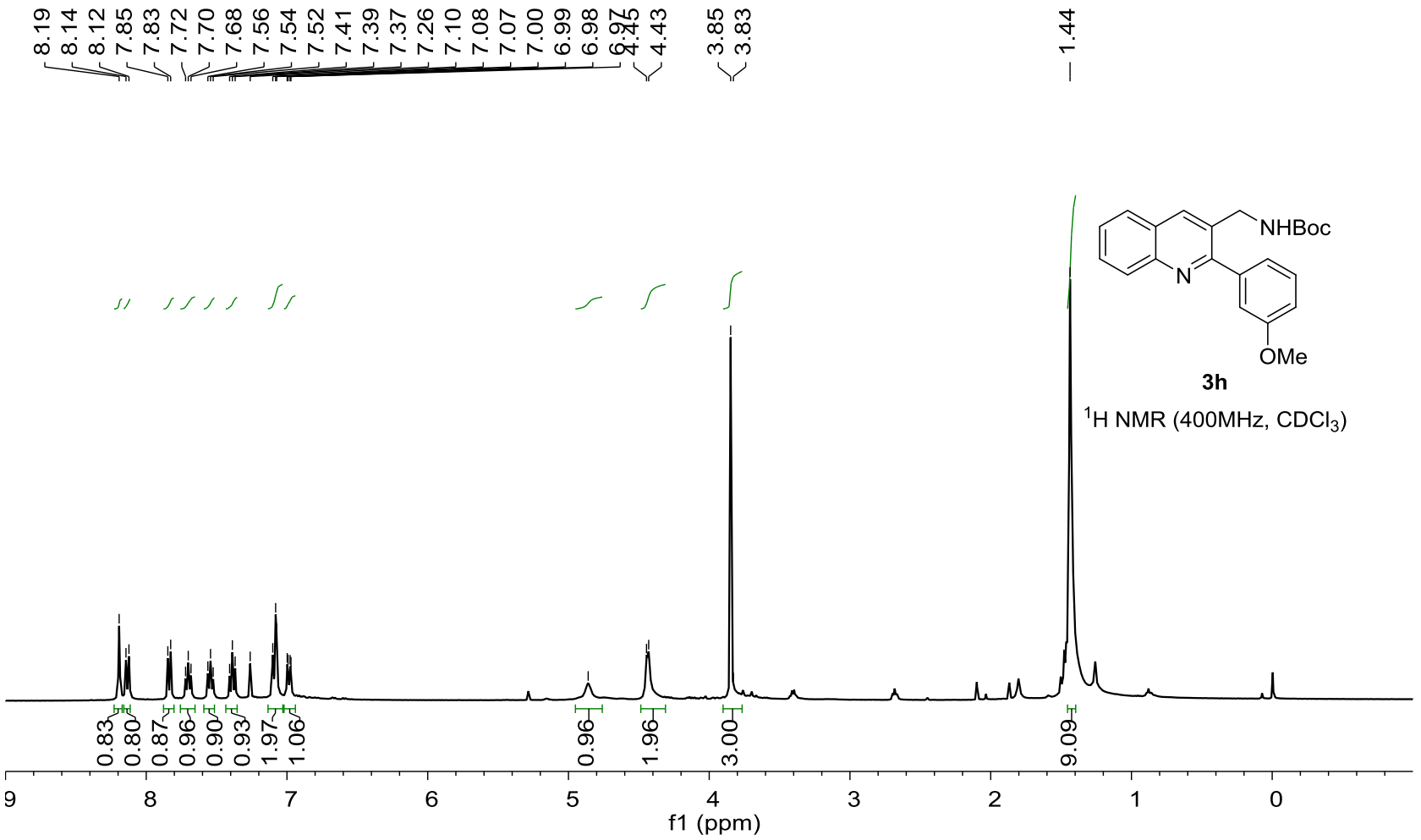
129.47
129.31
128.55
128.23
127.90
127.58
127.27
126.88
126.72
126.60
126.45
125.74
125.70
79.96
77.50
77.18
76.86
42.62
28.49
A (d)
125.72
NHBoc
N
CF3
3g
13C NMR (100MHz, CDCl3)
1.00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



3g

^{19}F NMR (377MHz, $CDCl_3$)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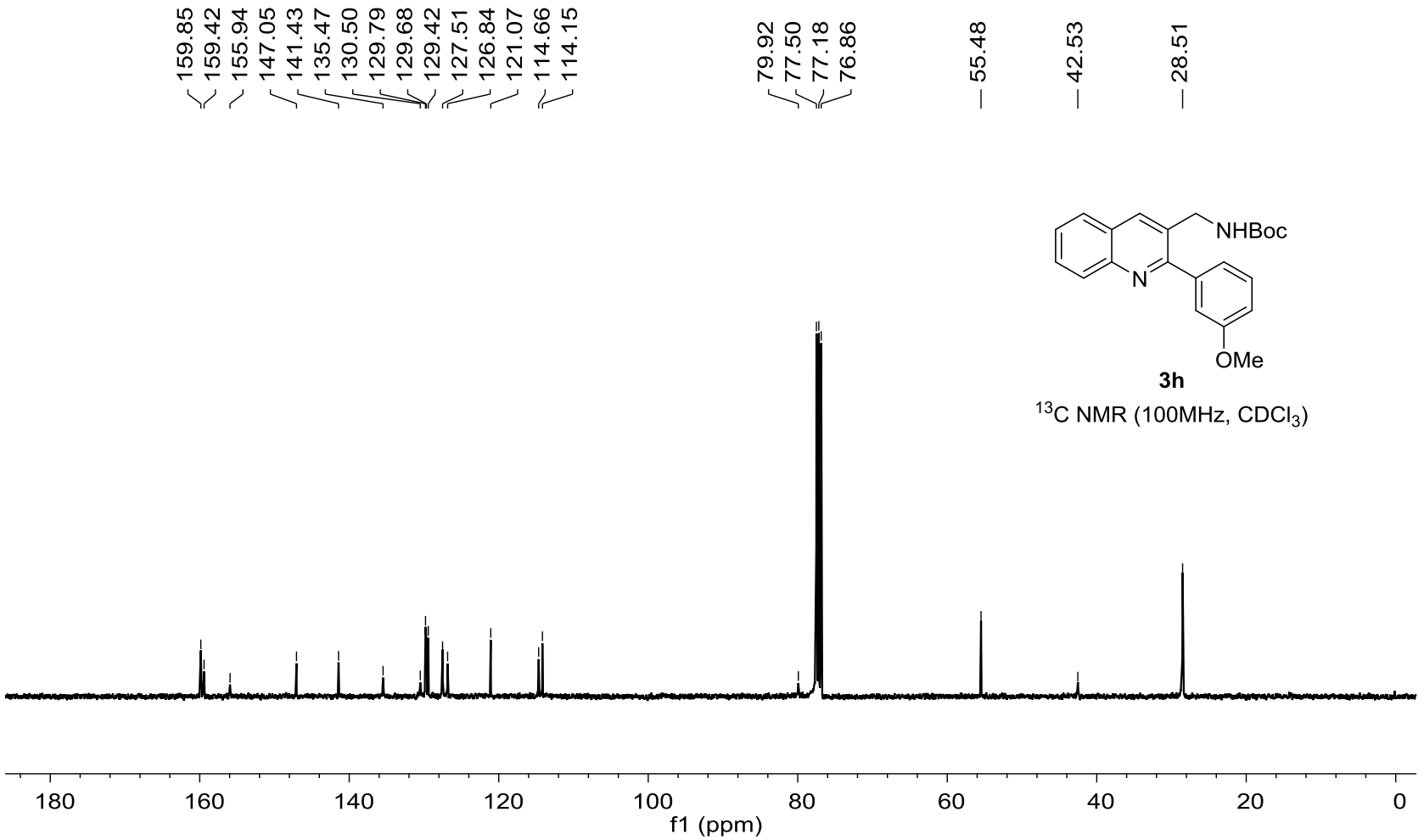
7.83
7.72
7.70
7.68
7.56
7.54
7.52
7.41
7.39
7.37
7.26
7.10
7.08
7.07
7.00
6.99
6.98
6.97
4.45
4.43
3.85
3.83
1.44
NHBoc
N
OMe
3h
1H NMR (400MHz, CDCl3)
0.83
0.80
0.87
0.96
0.90
0.93
1.97
1.06
0.96
1.96
3.00
9.09
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


159.85
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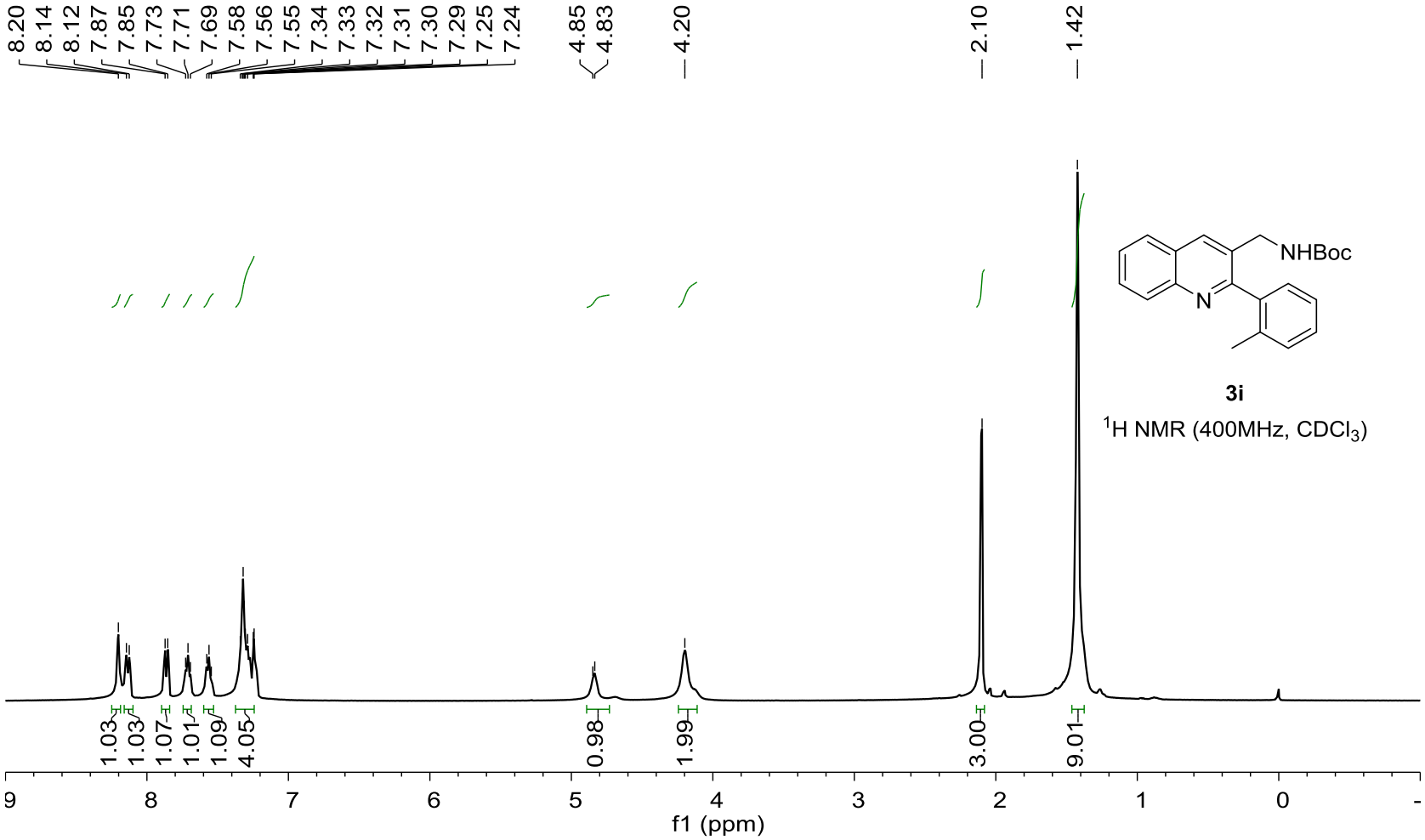
135.47
130.50
129.79
129.68
129.42
127.51
126.84
121.07
114.66
114.15
79.92
77.50
77.18
76.86
55.48
42.53
28.51
NHBoc
N
OMe
3h
13C NMR (100MHz, CDCl3)
180
160
140
120
100
80
60
40
20
0
f1 (ppm)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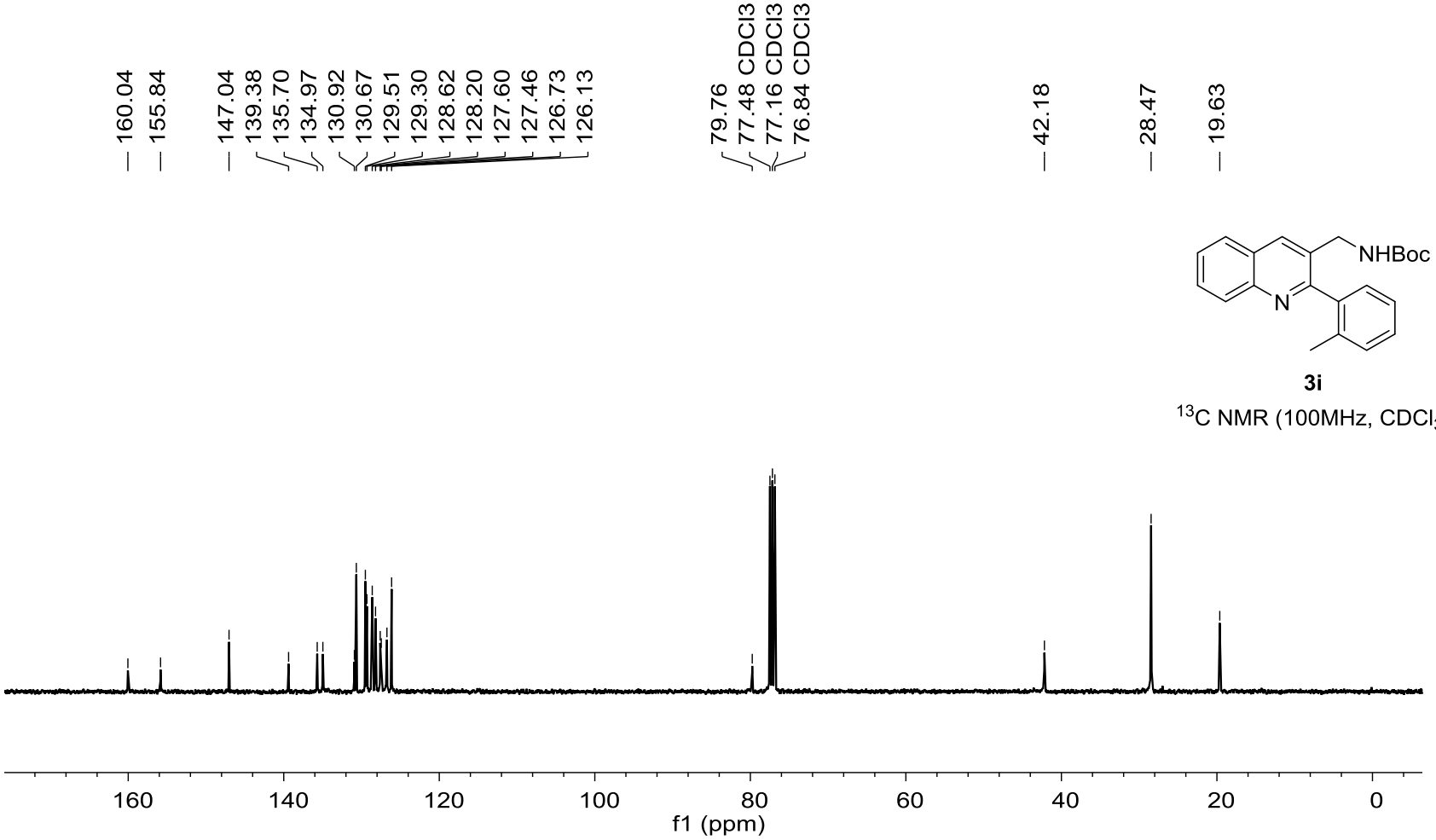
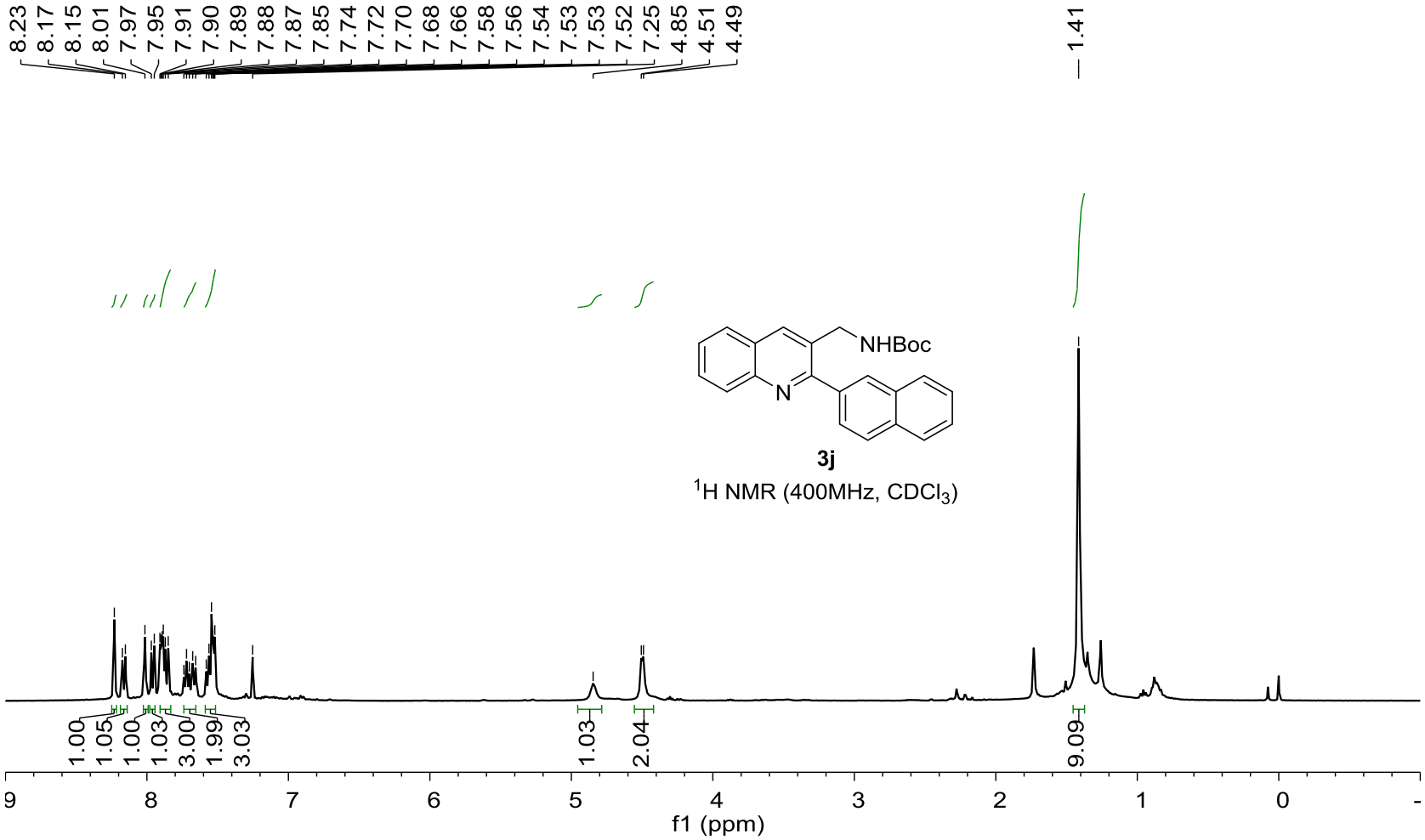
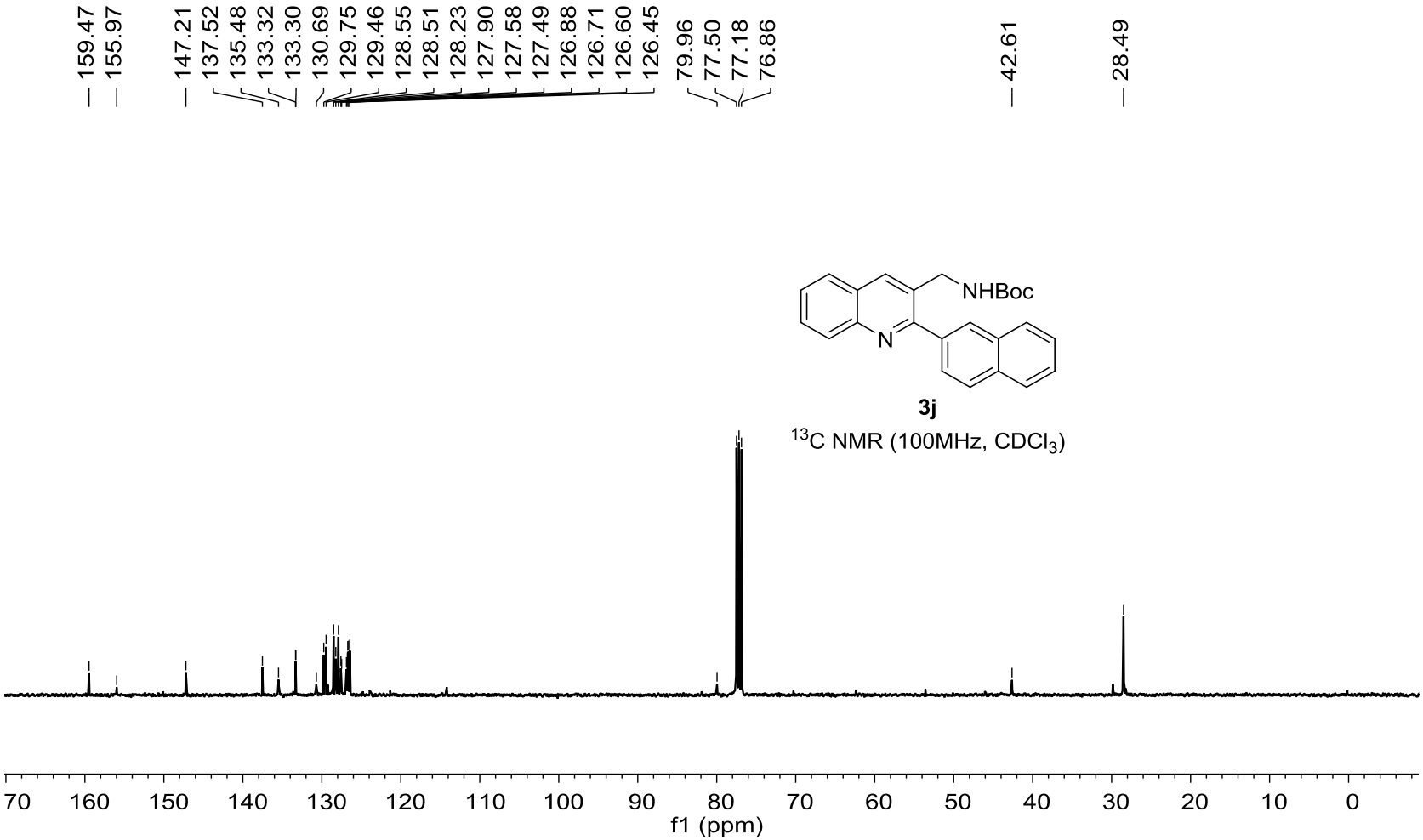
7.34
7.33
7.32
7.31
7.30
7.29
7.25
7.24
4.85
4.83
4.20
2.10
1.42
NHBoc
N
3i
1H NMR (400MHz, CDCl3)
1.03
1.03
1.07
1.01
1.09
4.05
0.98
1.99
3.00
9.01
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)

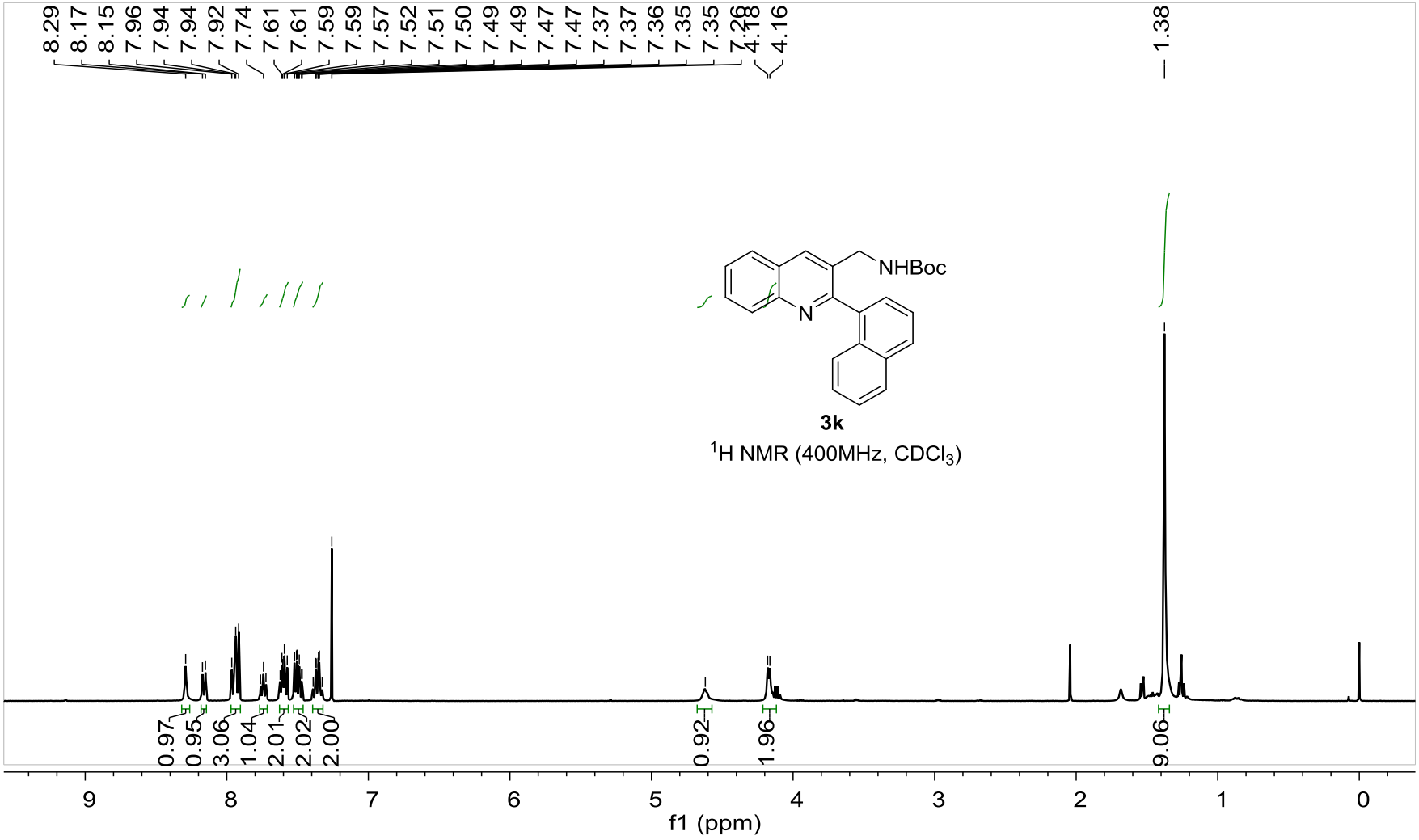


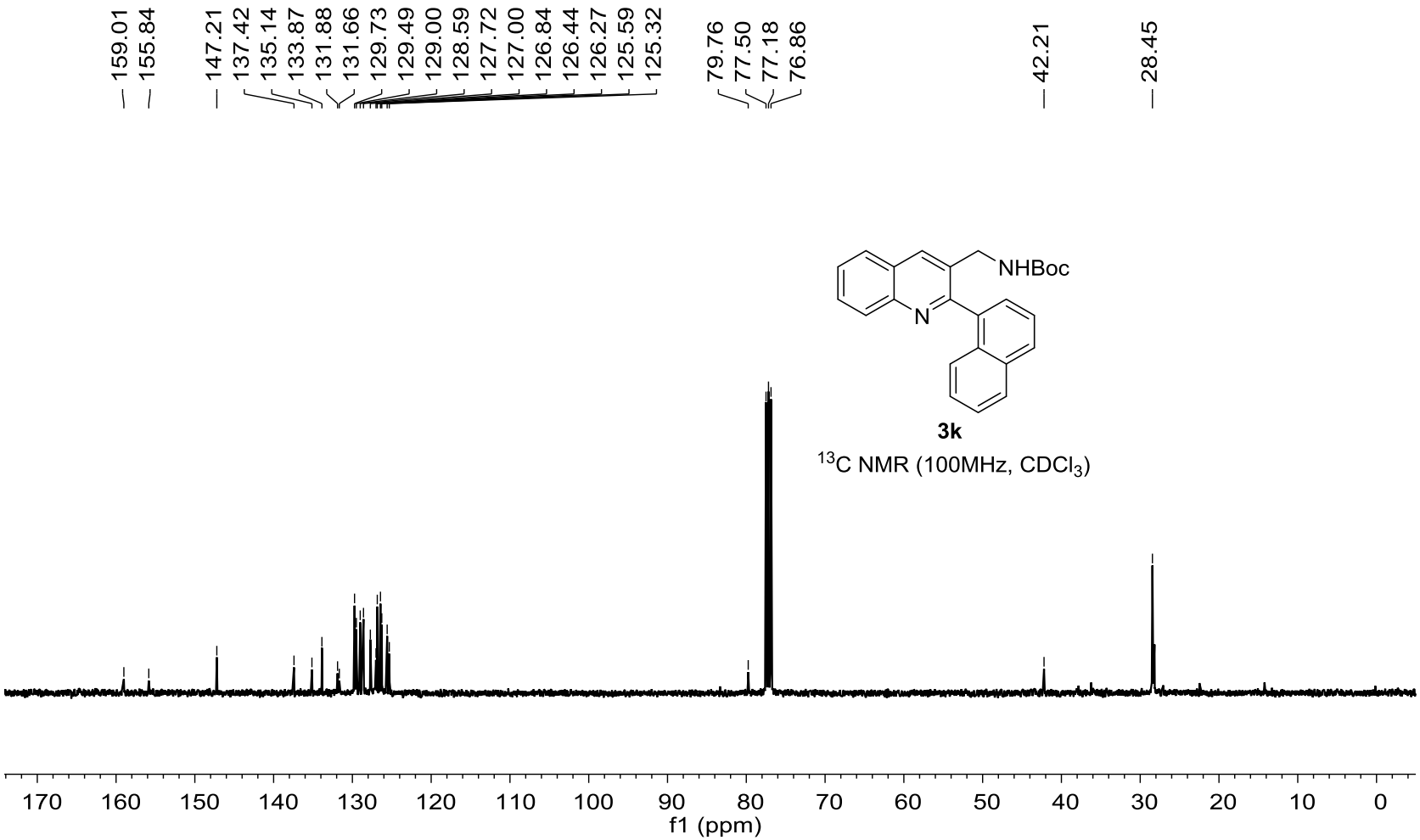
3i

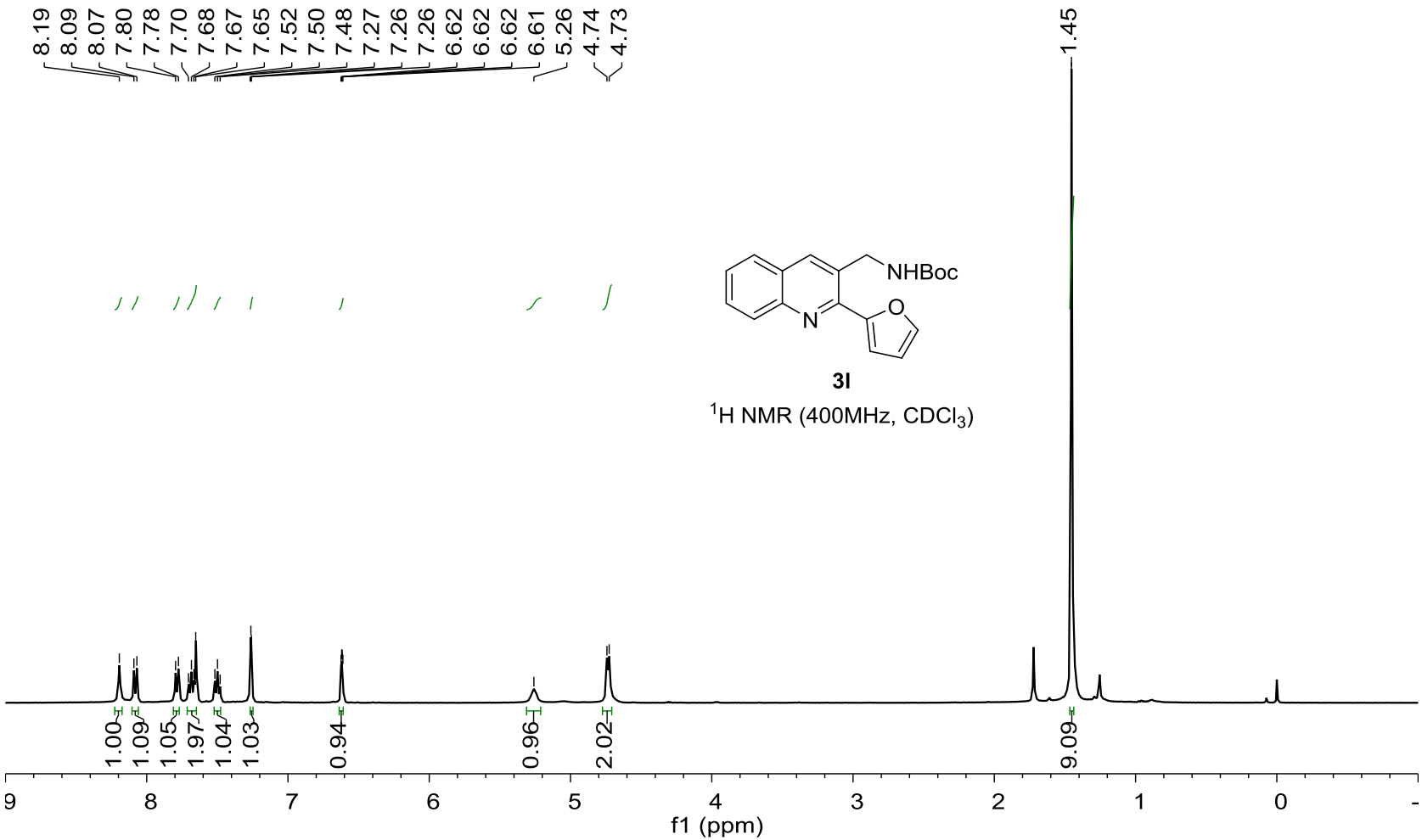
^{13}C NMR (100MHz, $CDCl_3$)

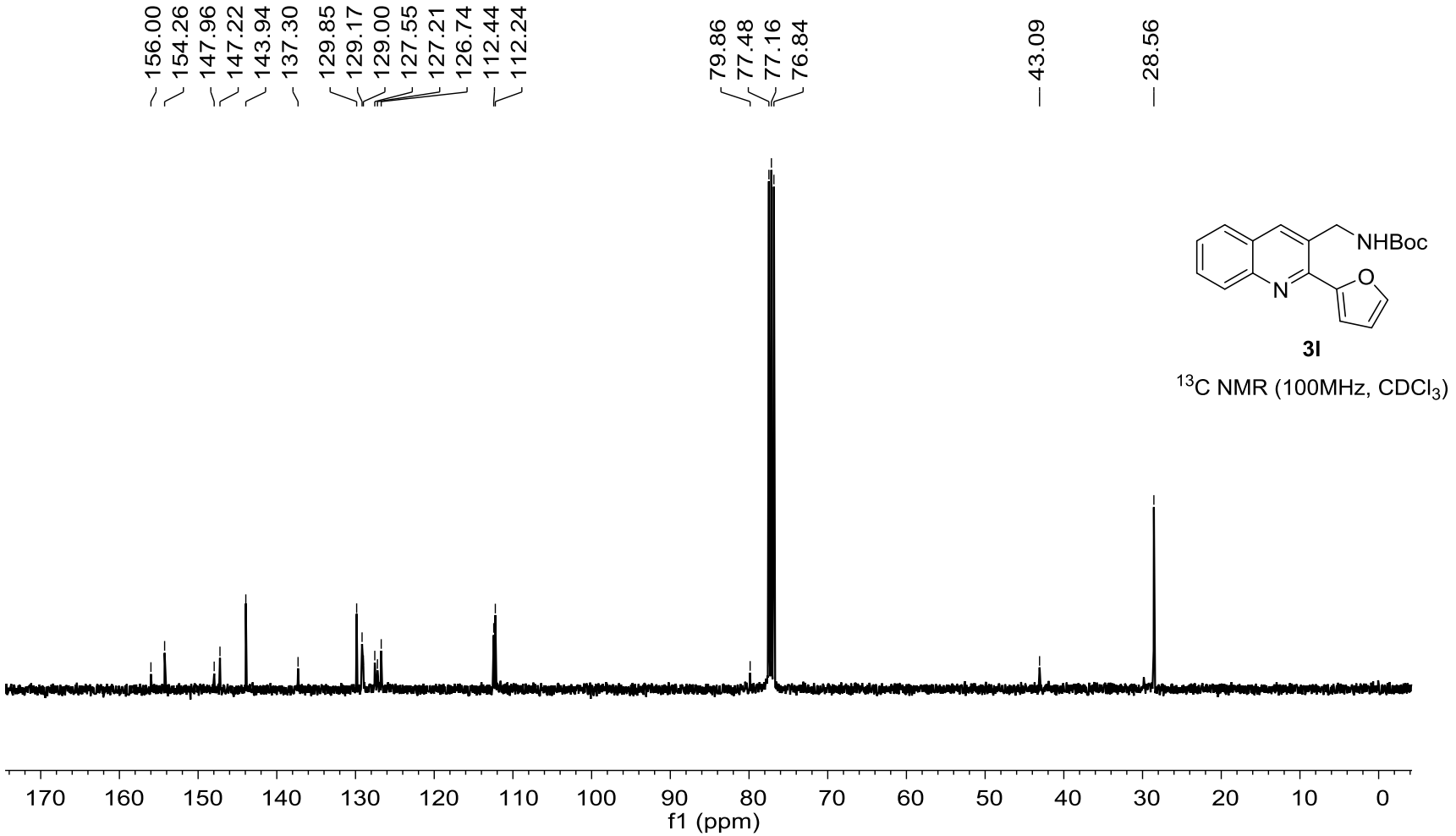

8.23
8.17
8.15
8.01
7.97
7.95
7.91
7.90
7.89
7.88
7.87
7.85
7.74
7.72
7.70
7.68
7.66
7.58
7.56
7.54
7.53
7.53
7.52
7.25
4.85
4.51
4.49
1.41
NHBoc
N
3j
1H NMR (400MHz, CDCl3)
1.00
1.05
1.00
1.03
3.00
1.99
3.03
1.03
2.04
9.09
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)


159.47
155.97
147.21
137.52
135.48
133.32
133.30
130.69
129.75
129.46
128.55
128.51
128.23
127.90
127.58
127.49
126.88
126.71
126.60
126.45
79.96
77.50
77.18
76.86
42.61
28.49
NHBoc
N
3j
13C NMR (100MHz, CDCl3)
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.29
8.17
8.15
7.96
7.94
7.94
7.92
7.74
7.61
7.61
7.59
7.59
7.57
7.52
7.51
7.50
7.49
7.49
7.47
7.47
7.37
7.37
7.36
7.35
7.35
7.26
4.18
4.16
1.38
NHBoc
N
3k
1H NMR (400MHz, CDCl3)
0.97
0.95
3.06
1.04
2.01
2.02
2.00
0.92
1.96
9.06
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

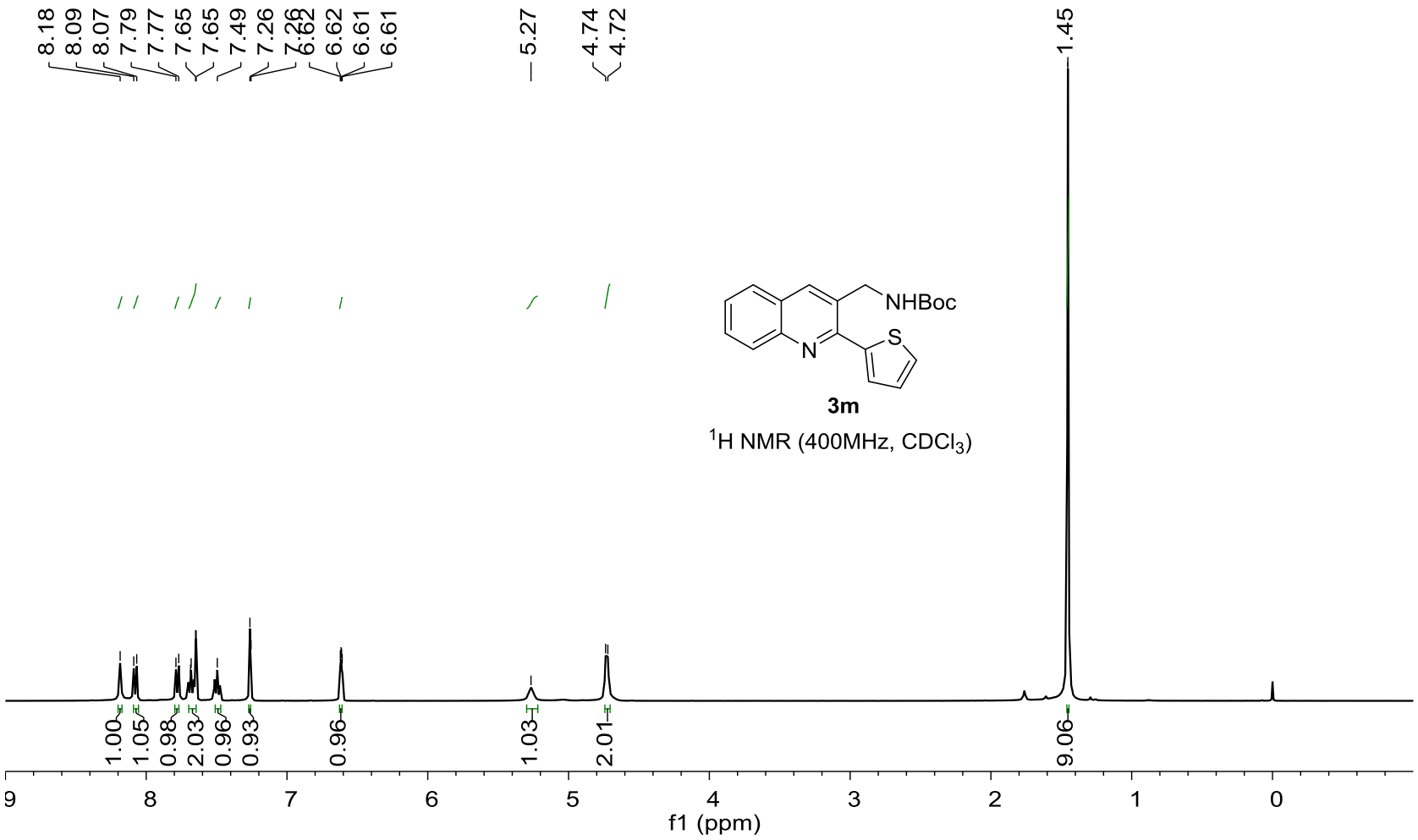

159.01
155.84
147.21
137.42
135.14
133.87
131.88
131.66
129.73
129.49
129.00
128.59
127.72
127.00
126.84
126.44
126.27
125.59
125.32
79.76
77.50
77.18
76.86
42.21
28.45
NHBoc
N
3k
13C NMR (100MHz, CDCl3)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

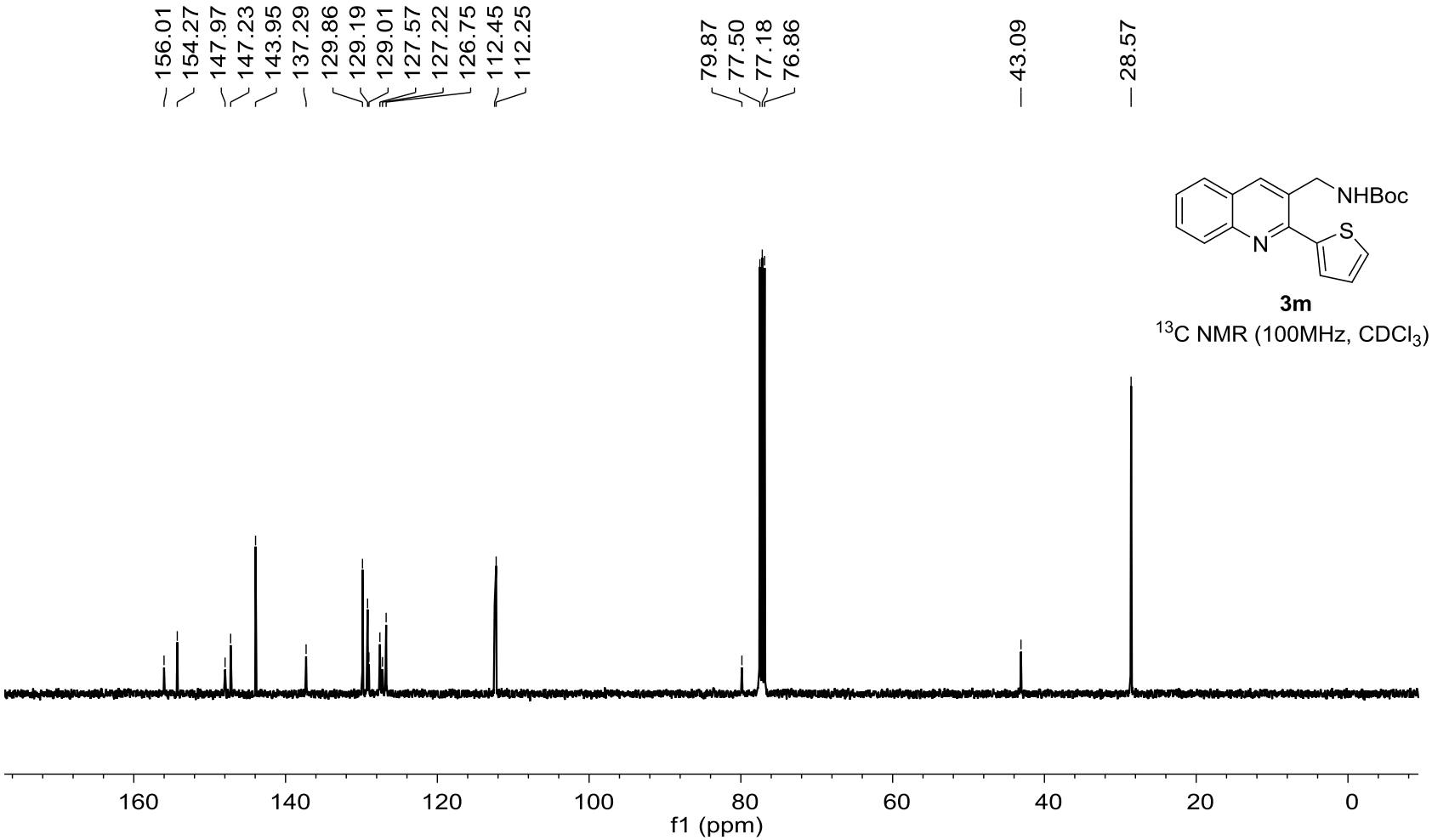

8.19
8.09
8.07
7.80
7.78
7.70
7.68
7.67
7.65
7.52
7.50
7.48
7.27
7.26
7.26
6.62
6.62
6.62
6.61
5.26
4.74
4.73
1.45
NHBoc
N
O
3l
1H NMR (400MHz, CDCl3)
1.00
1.09
1.05
1.97
1.04
1.03
0.94
0.96
2.02
9.09
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)



3l

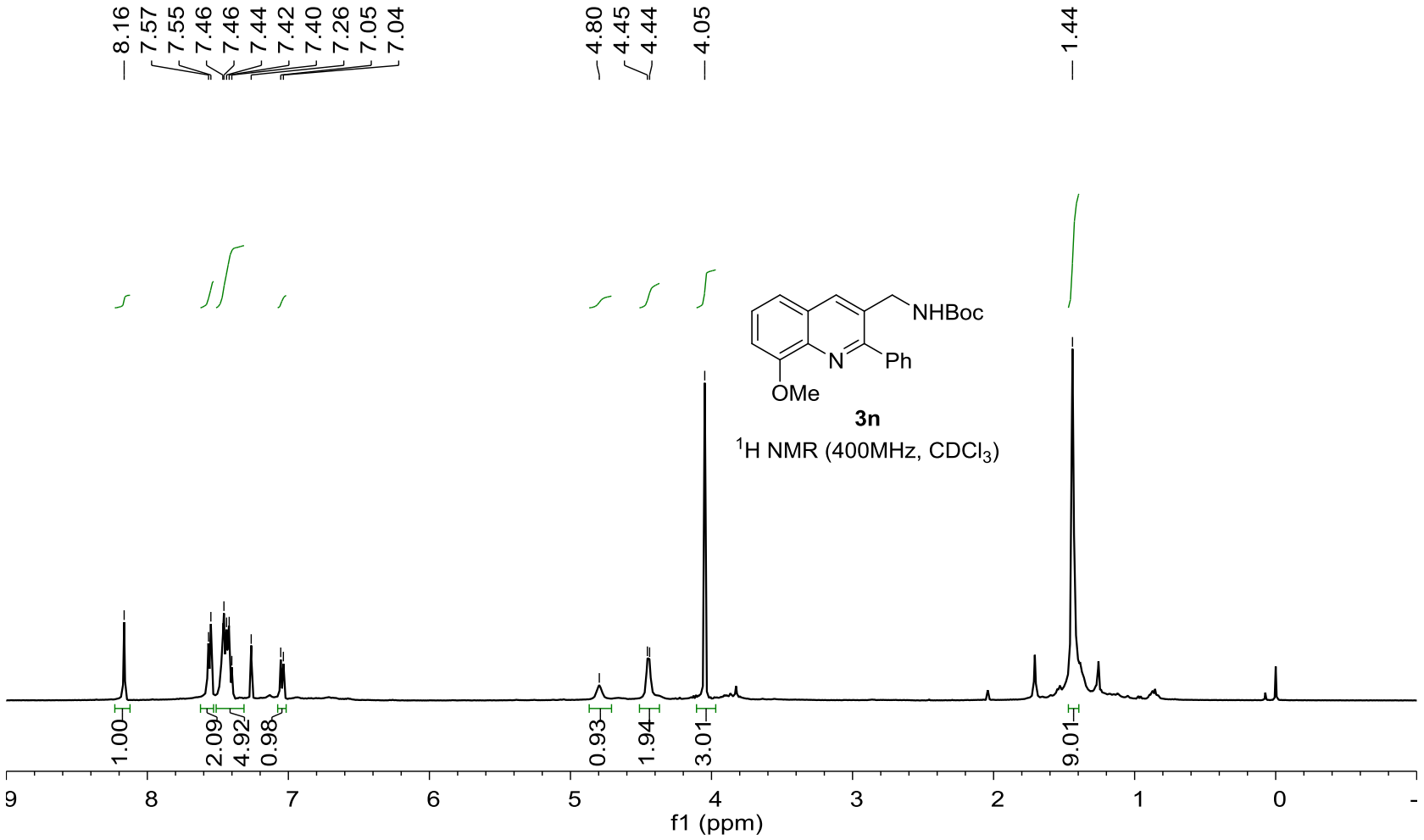
^{13}C NMR (100MHz, $CDCl_3$)

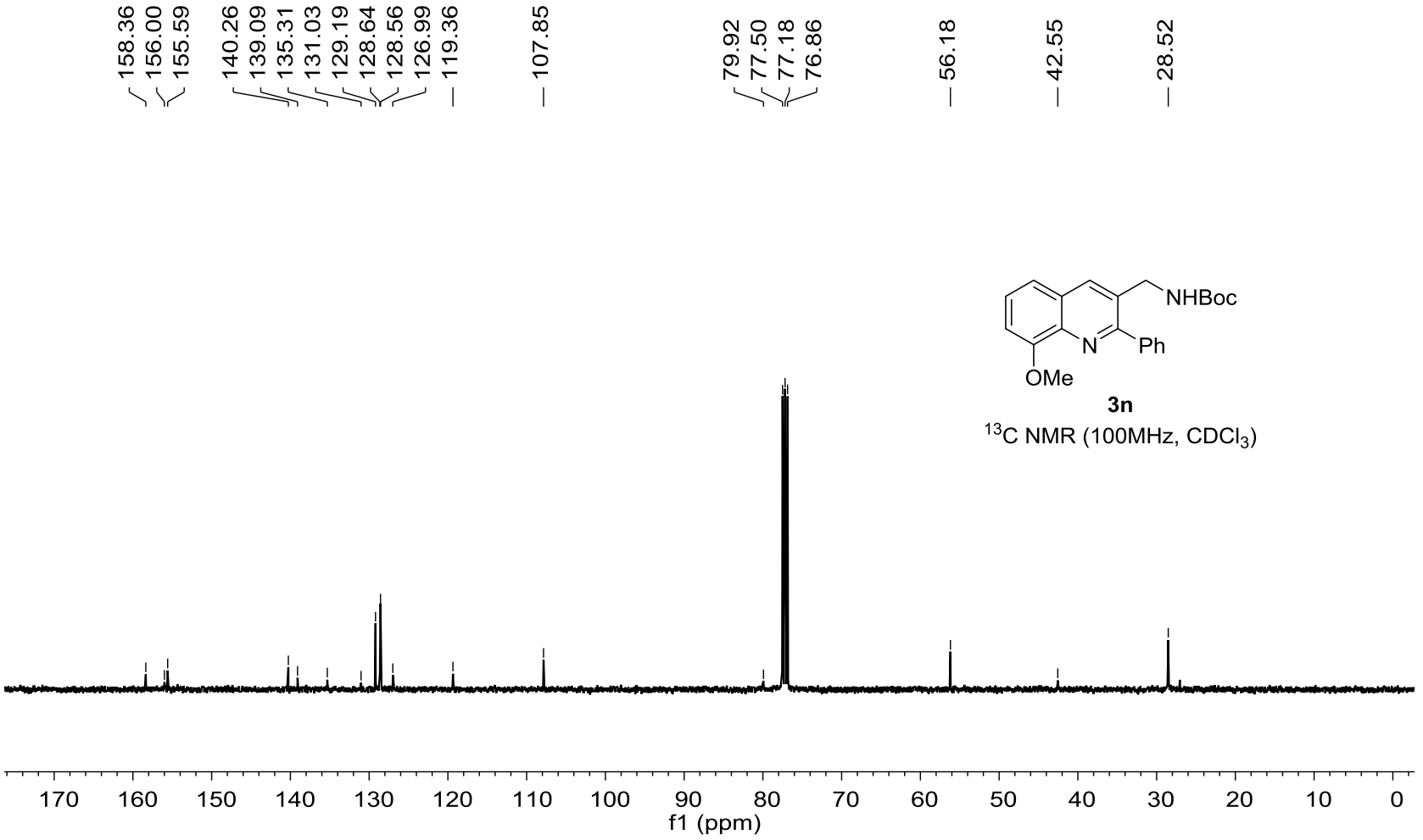

8.18
8.09
8.07
7.79
7.77
7.65
7.65
7.49
7.26
7.26
6.62
6.62
6.61
6.61
5.27
4.74
4.72
1.45
NHBoc
N
S
3m
1H NMR (400MHz, CDCl3)
1.00
1.05
0.98
2.03
0.96
0.93
0.96
1.03
2.01
9.06
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

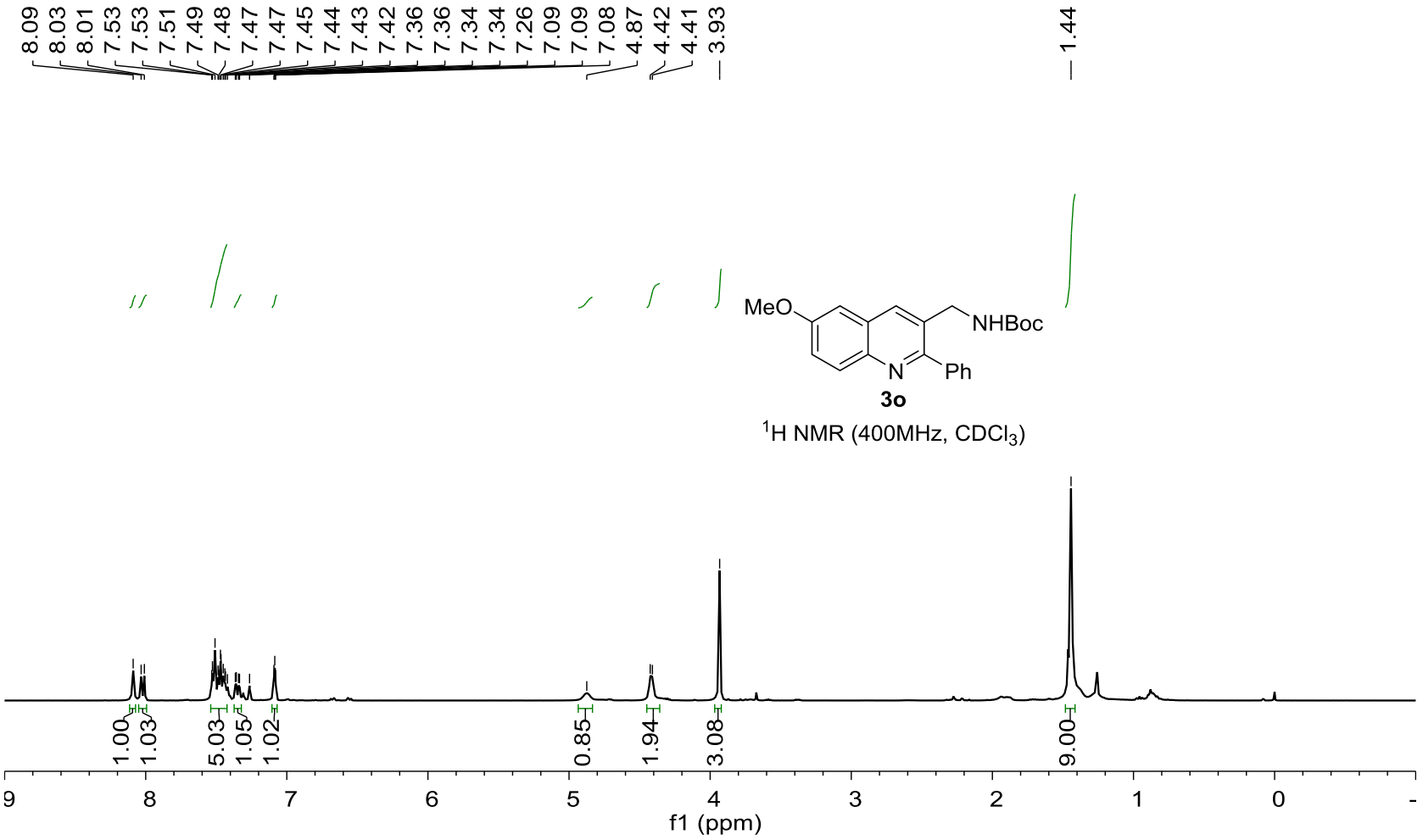


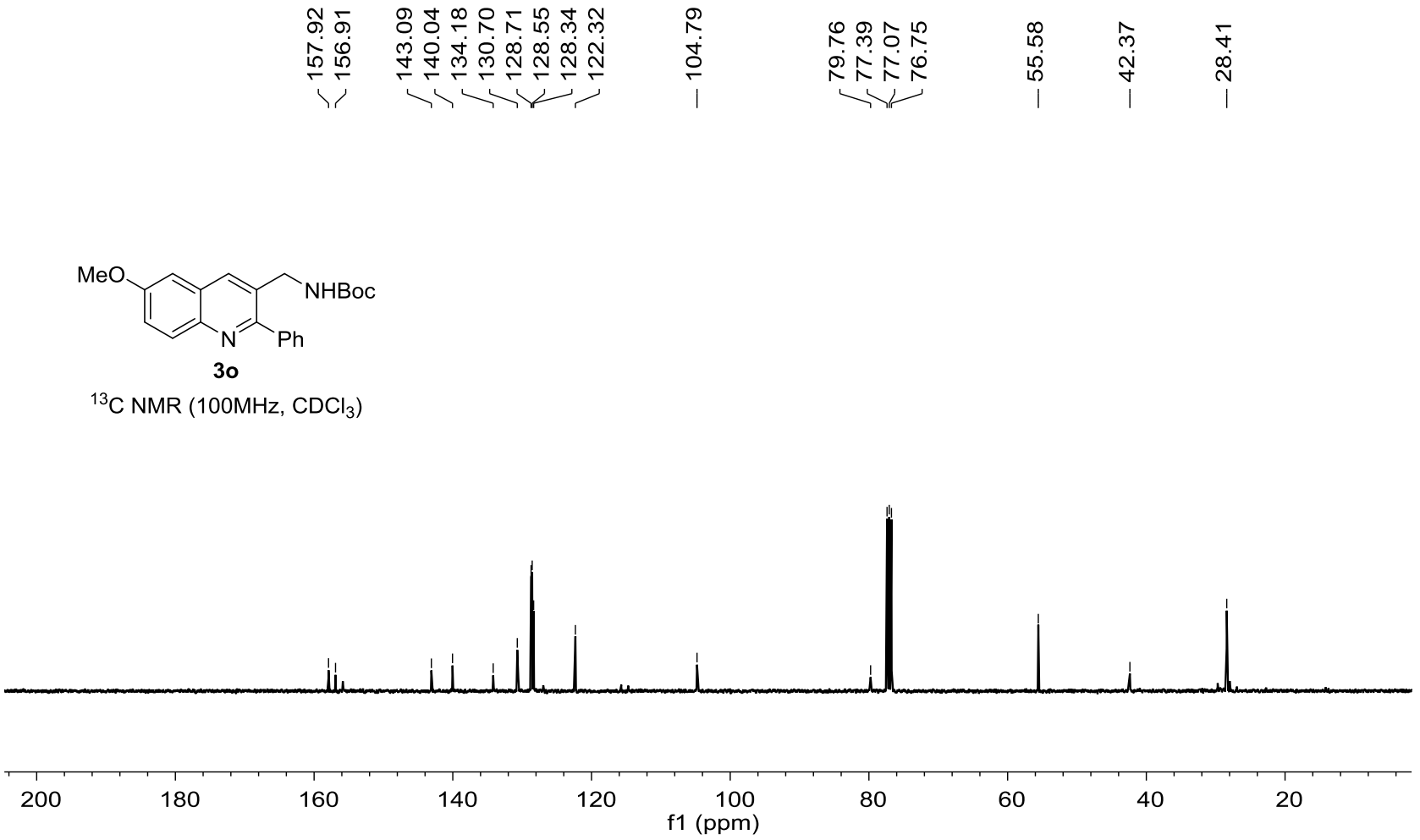
3m

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


8.16
7.57
7.55
7.46
7.46
7.44
7.42
7.40
7.26
7.05
7.04
4.80
4.45
4.44
4.05
1.44
NHBoc
N
Ph
OMe
3n
1H NMR (400MHz, CDCl3)
1.00
2.09
4.92
0.98
0.93
1.94
3.01
9.01
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)

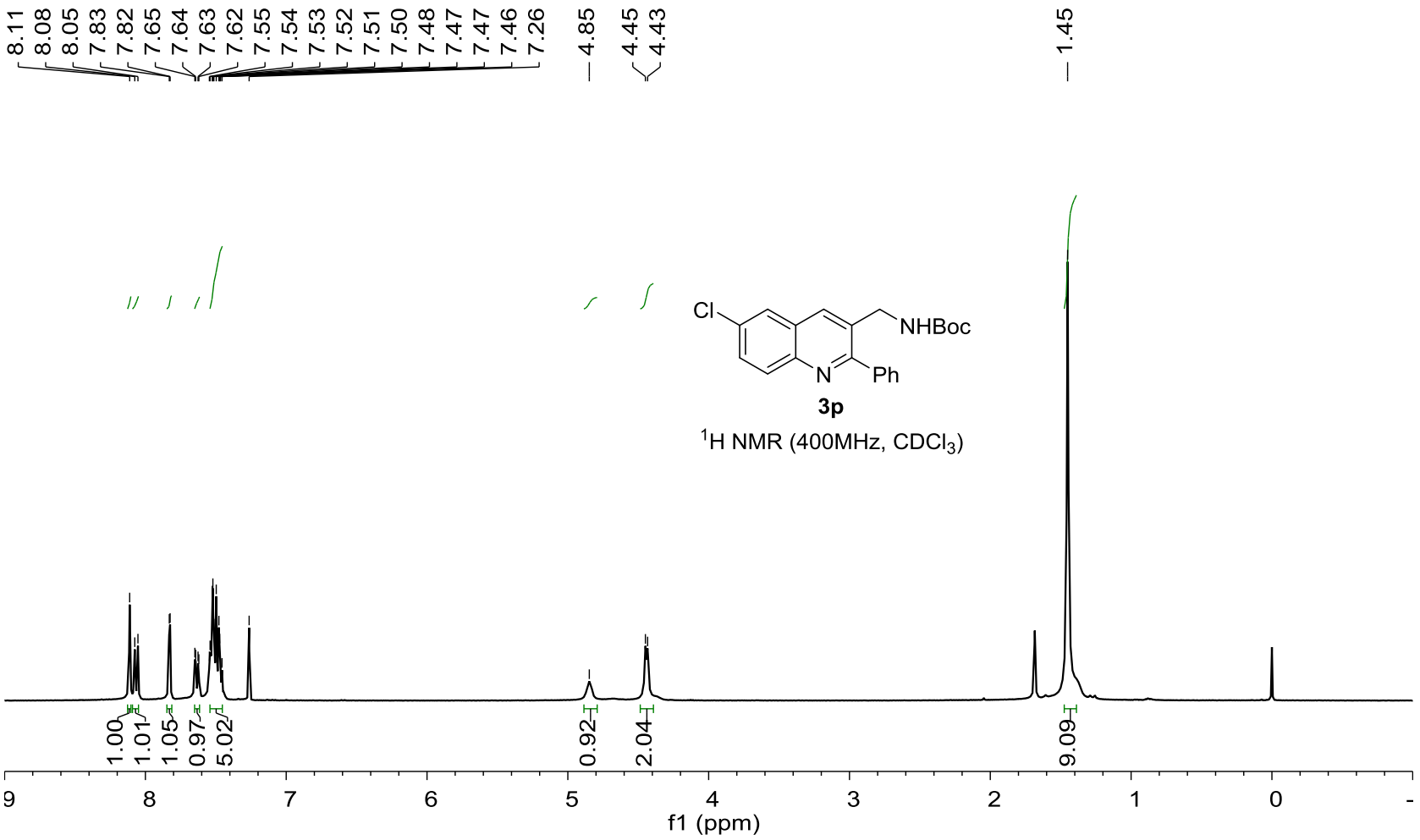

158.36
156.00
155.59
140.26
139.09
135.31
131.03
129.19
128.64
128.56
126.99
119.36
107.85
79.92
77.50
77.18
76.86
56.18
42.55
28.52
NHBoc
N
Ph
OMe
3n
13C NMR (100MHz, CDCl3)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

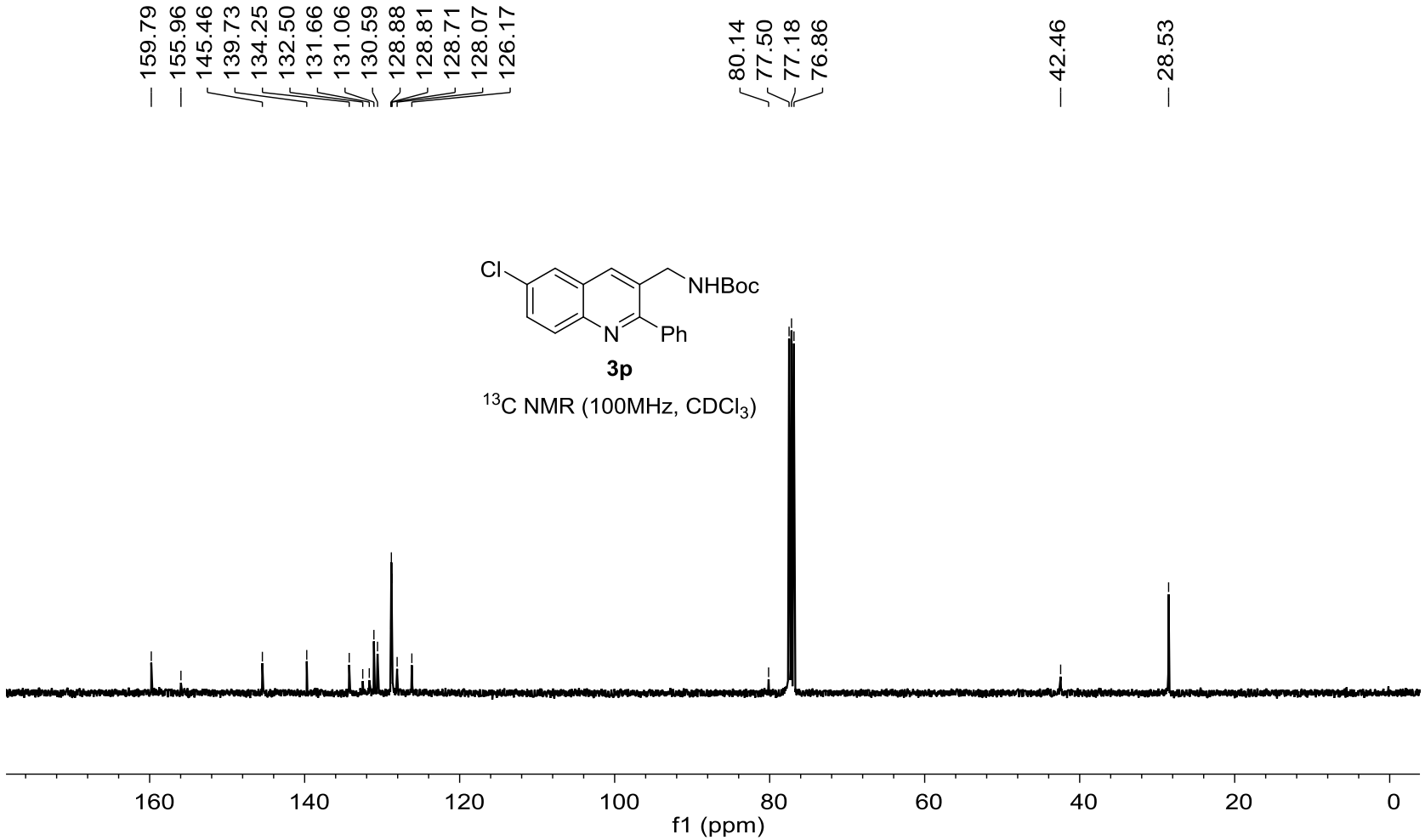

8.09
8.03
8.01
7.53
7.53
7.51
7.49
7.48
7.47
7.47
7.45
7.44
7.43
7.42
7.36
7.36
7.34
7.34
7.26
7.09
7.09
7.08
4.87
4.42
4.41
3.93
1.44
MeO
NHBoc
N
Ph
3o
1H NMR (400MHz, CDCl3)
1.00
1.03
5.03
1.05
1.02
0.85
1.94
3.08
9.00
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)

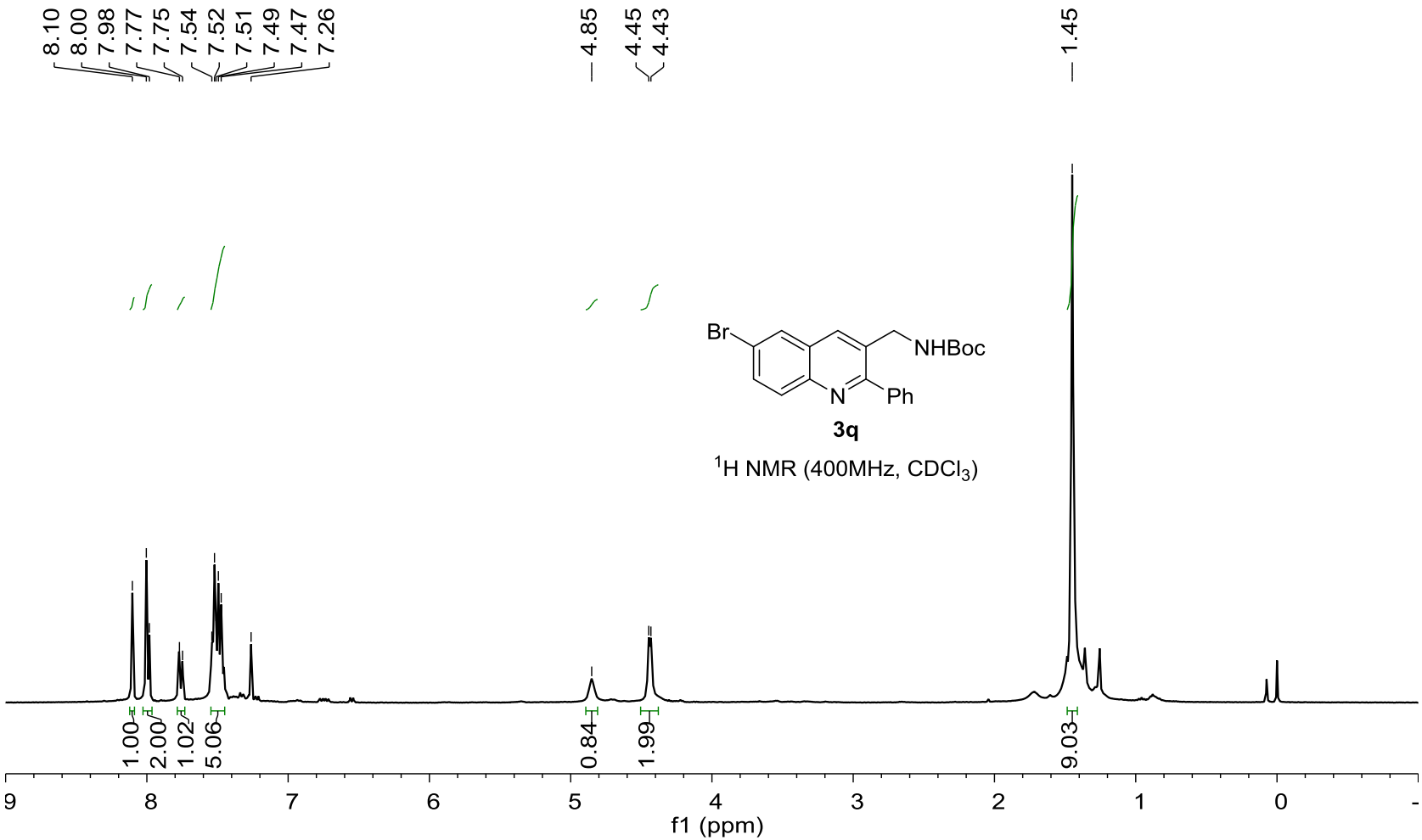


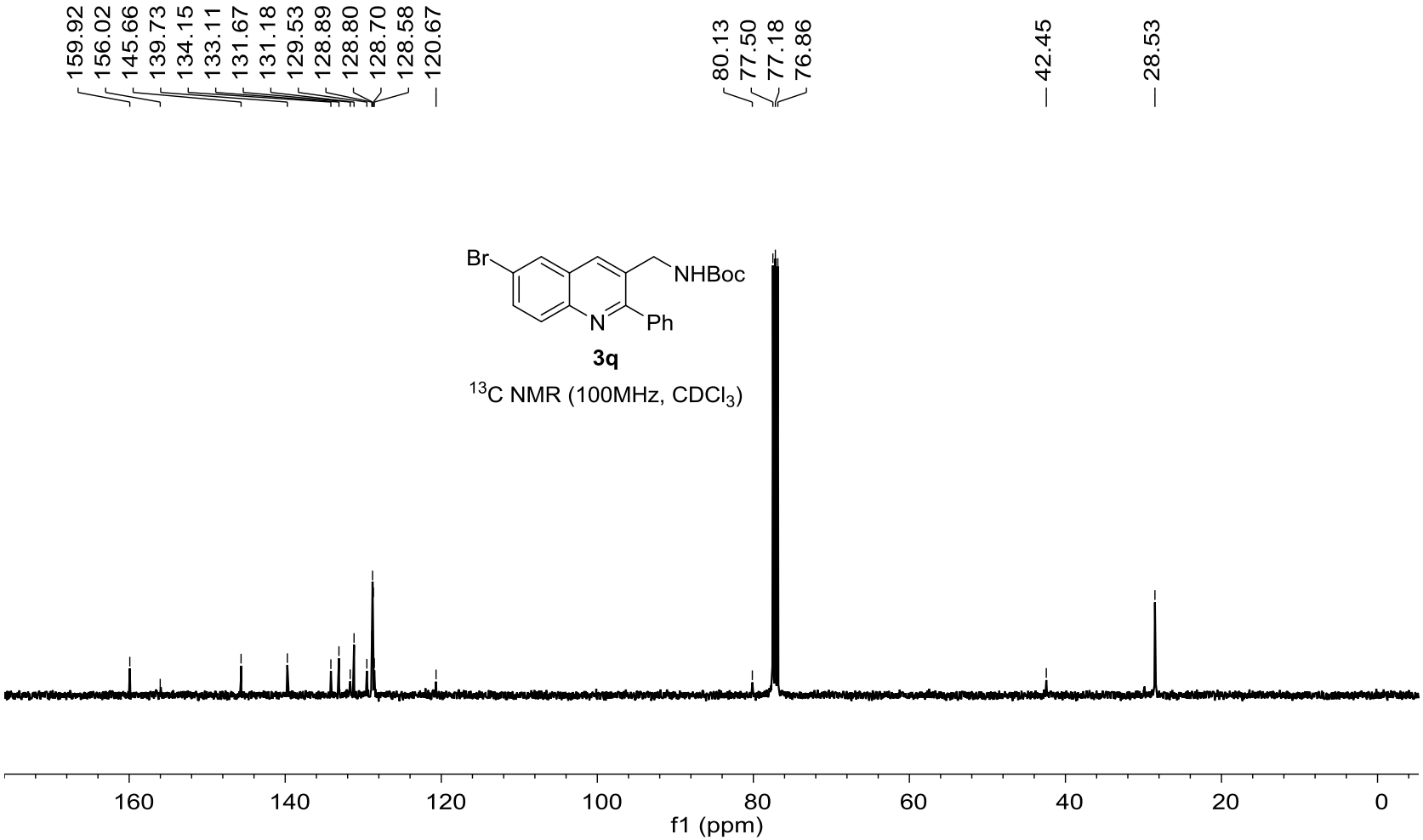
3o

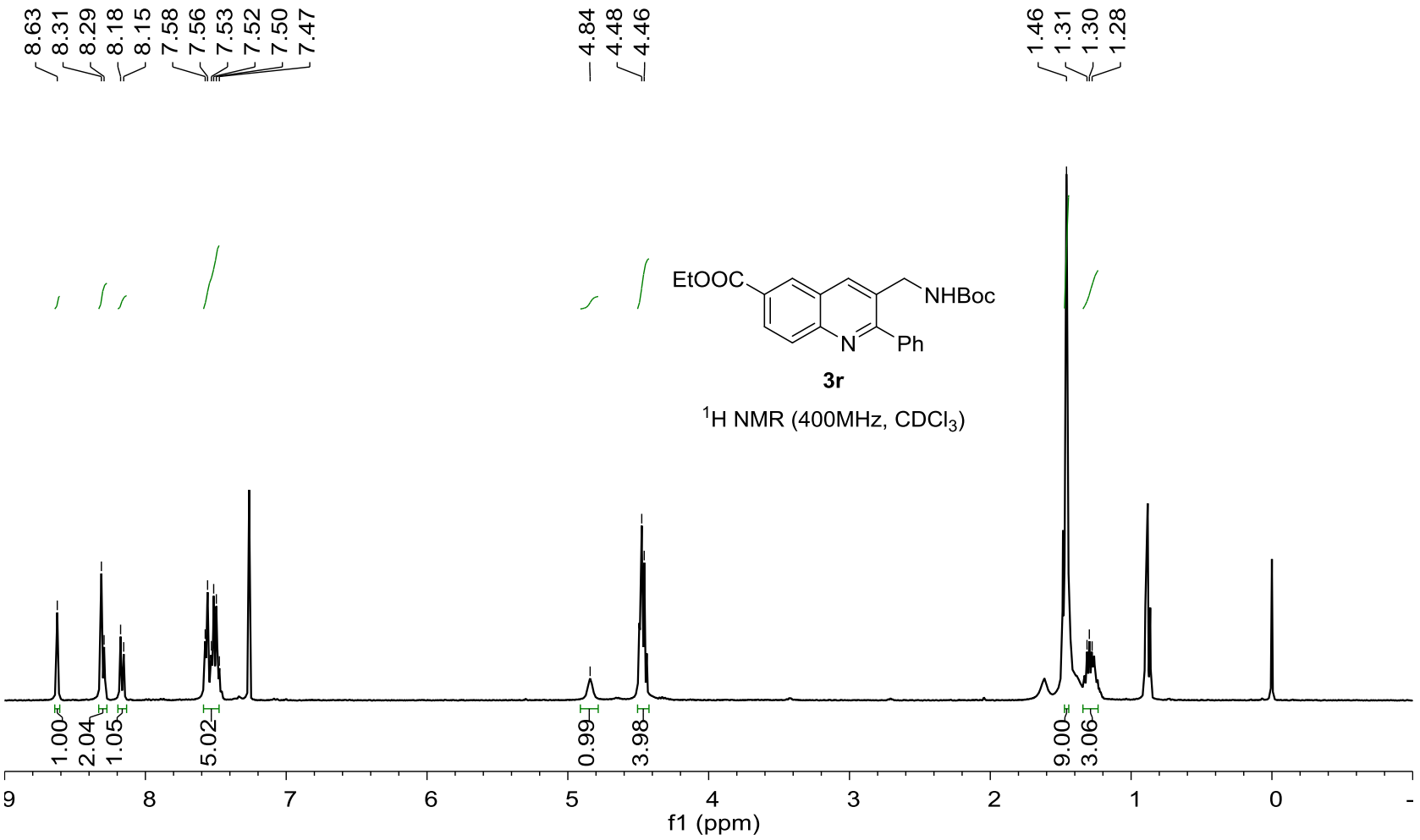
^{13}C NMR (100MHz, $CDCl_3$)

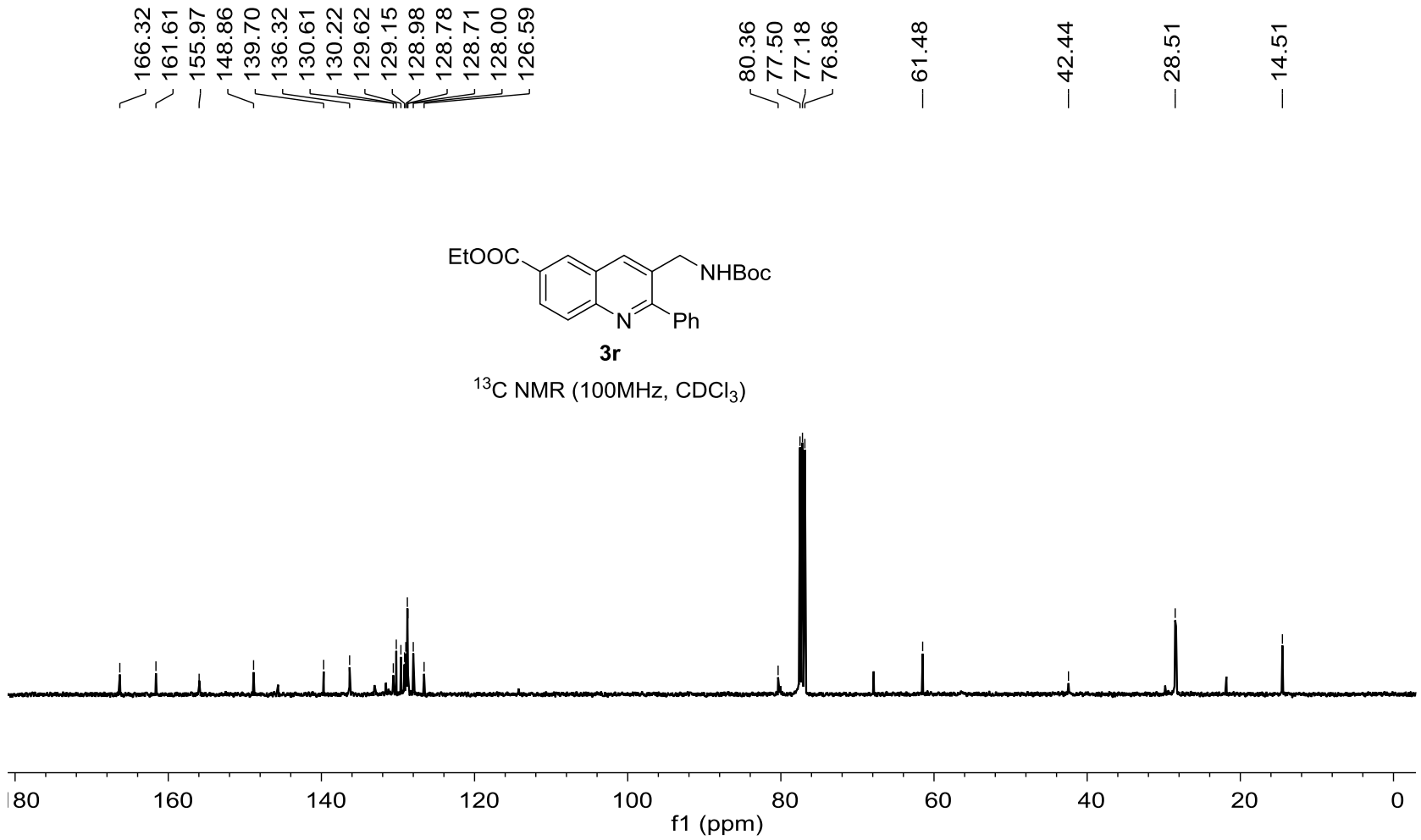

8.11
8.08
8.05
7.83
7.82
7.65
7.64
7.63
7.62
7.55
7.54
7.53
7.52
7.51
7.50
7.48
7.47
7.47
7.46
7.26
4.85
4.45
4.43
1.45
Cl
NHBoc
N
Ph
3p
1H NMR (400MHz, CDCl3)
1.00
1.01
1.05
0.97
5.02
0.92
2.04
9.09
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)

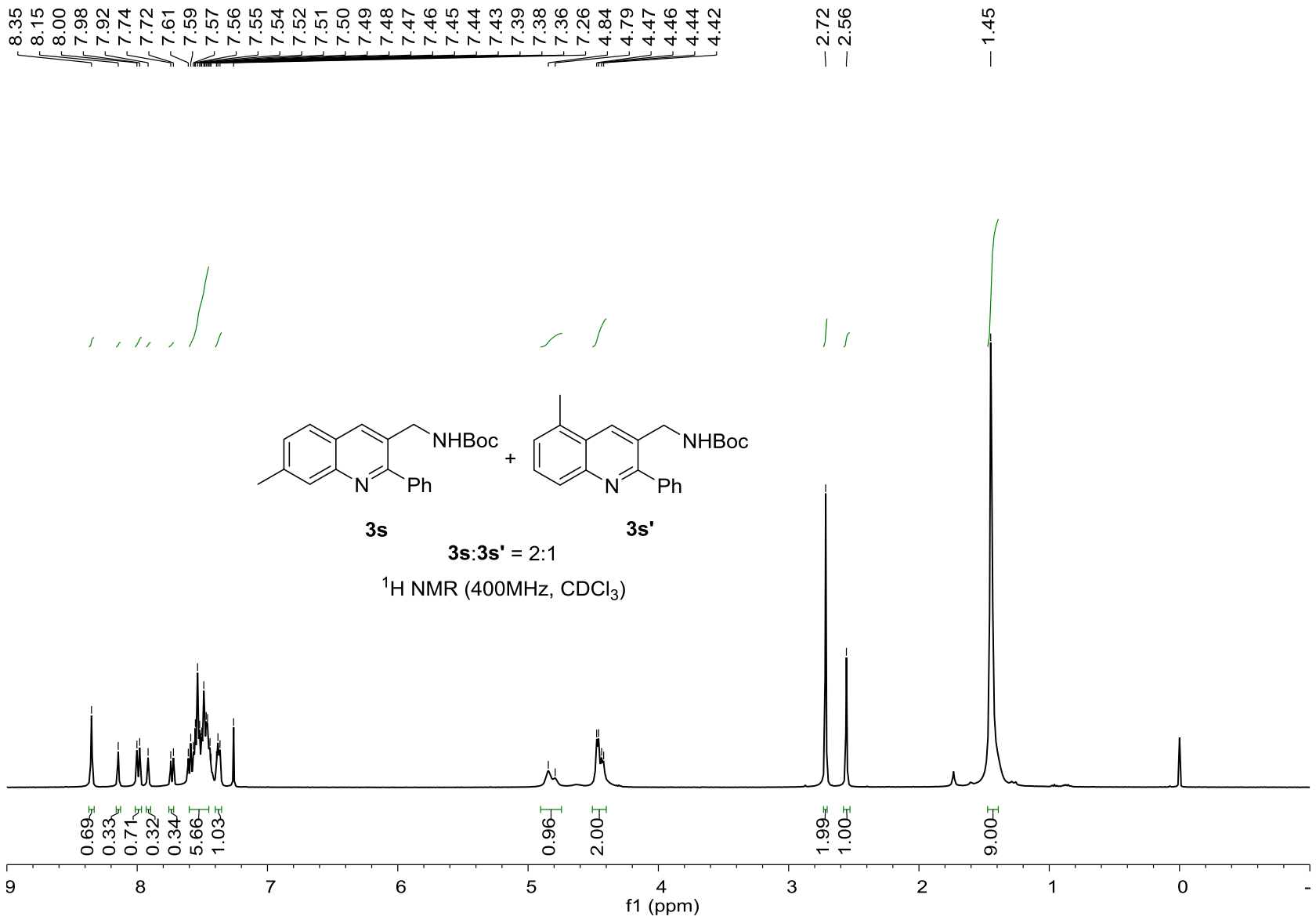

159.79
155.96
145.46
139.73
134.25
132.50
131.66
131.06
130.59
128.88
128.81
128.71
128.07
126.17
80.14
77.50
77.18
76.86
42.46
28.53
Cl
NHBoc
N
Ph
3p
13C NMR (100MHz, CDCl3)
160
140
120
100
80
60
40
20
0
f1 (ppm)

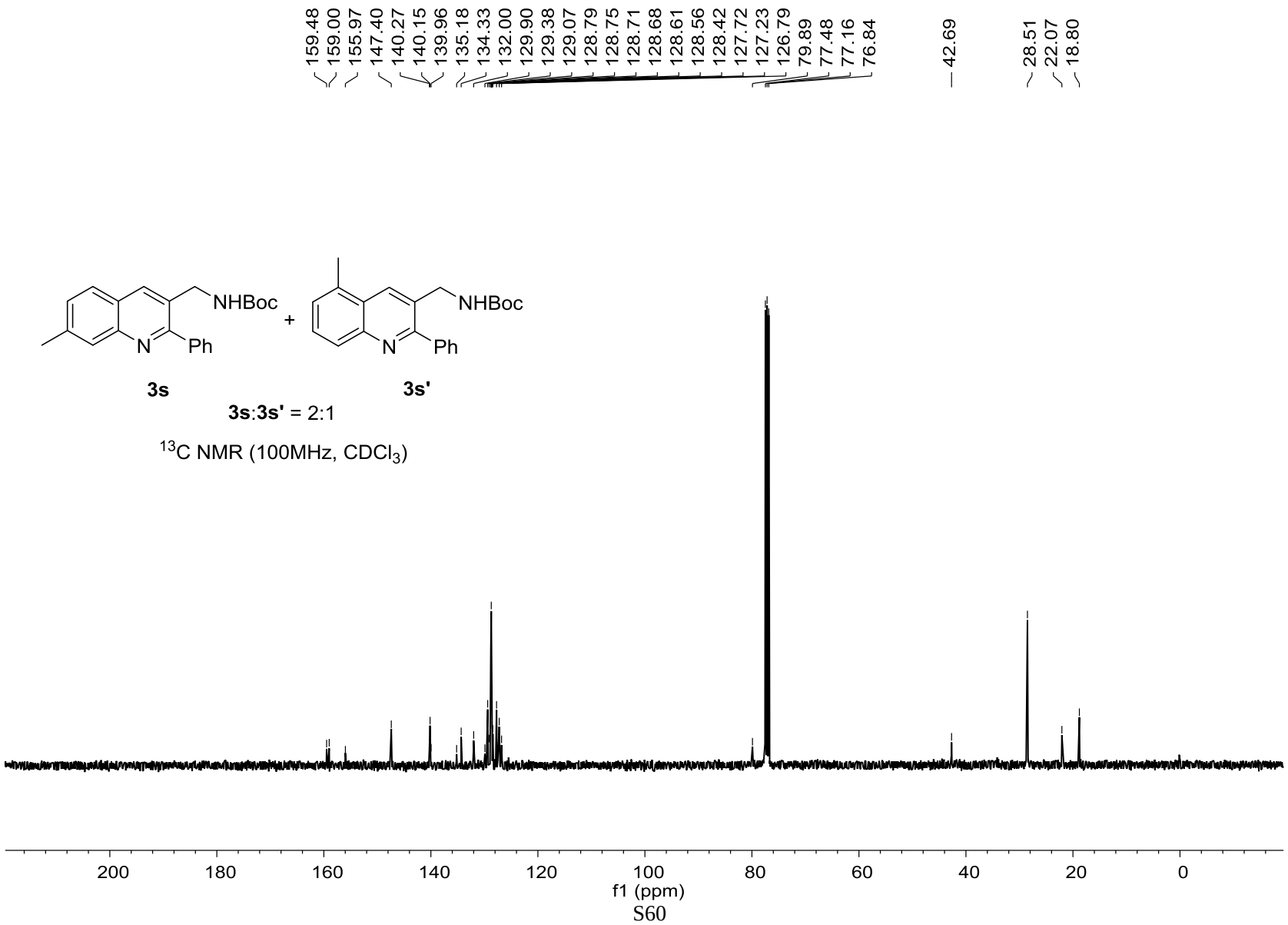

8.10
8.00
7.98
7.77
7.75
7.54
7.52
7.51
7.49
7.47
7.26
4.85
4.45
4.43
1.45
Br
NHBoc
N
Ph
3q
1H NMR (400MHz, CDCl3)
1.00
2.00
1.02
5.06
0.84
1.99
9.03
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)

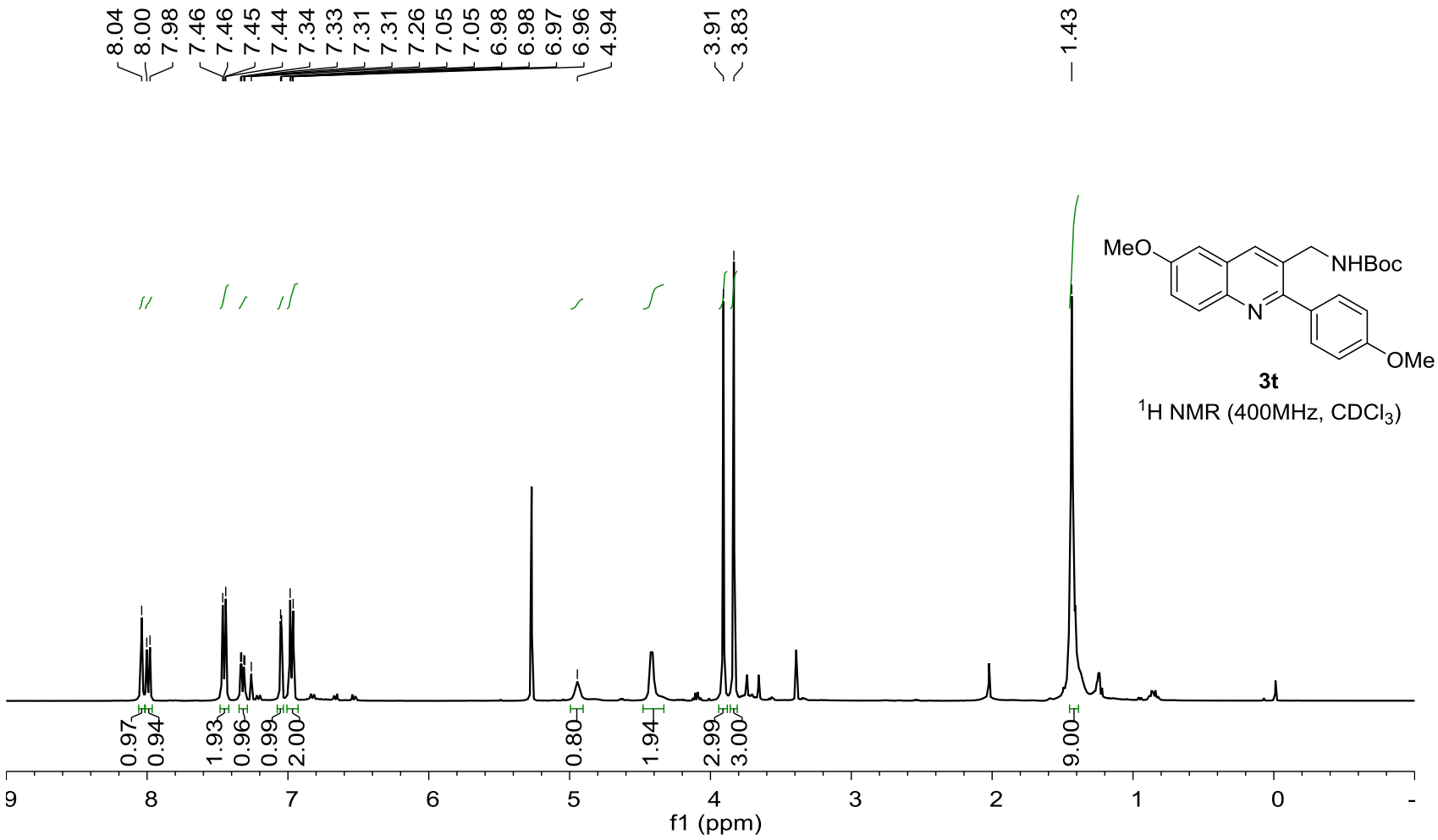

159.92
156.02
145.66
139.73
134.15
133.11
131.67
131.18
129.53
128.89
128.80
128.70
128.58
120.67
80.13
77.50
77.18
76.86
42.45
28.53
Br
NHBoc
N
Ph
3q
13C NMR (100MHz, CDCl3)
160
140
120
100
80
60
40
20
0
f1 (ppm)

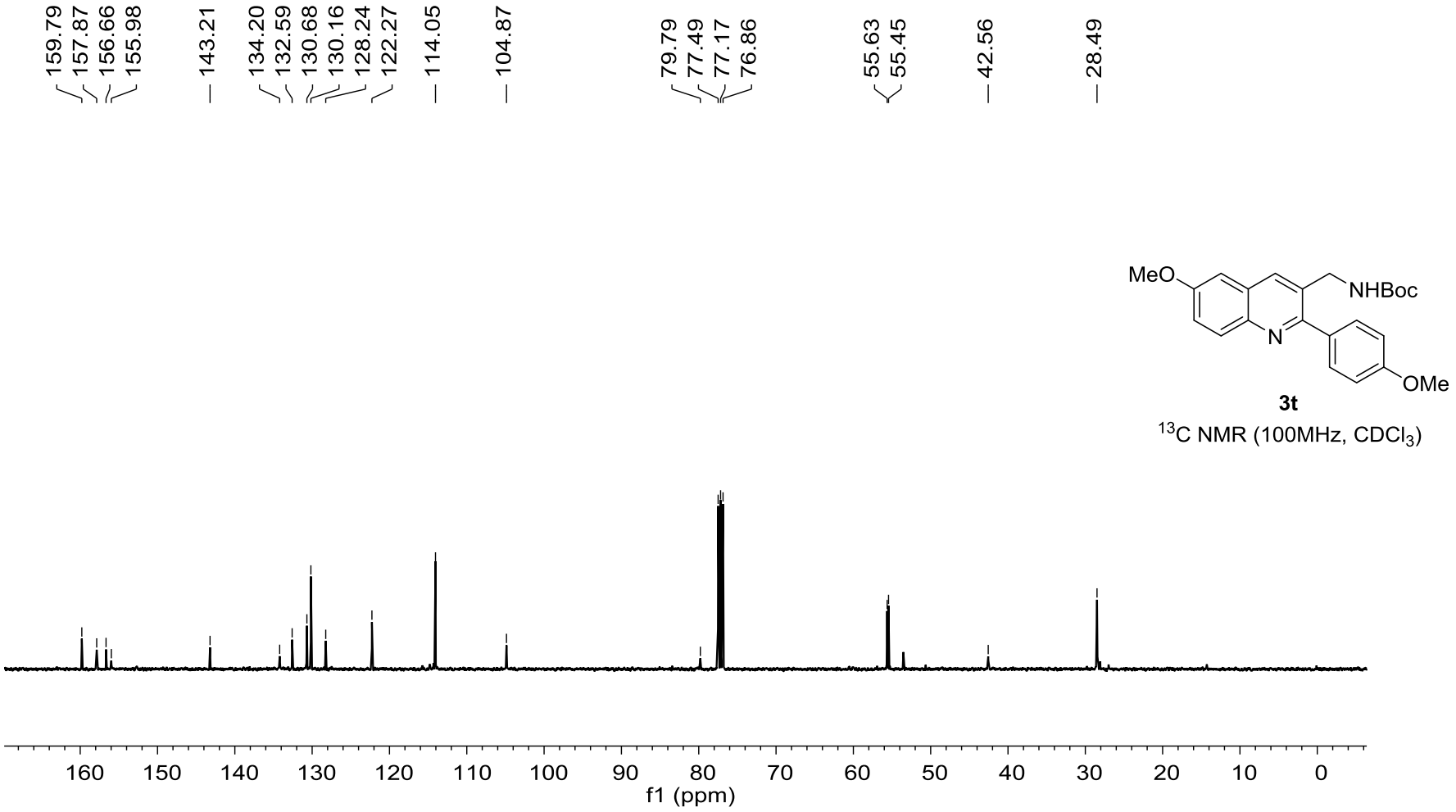

8.63
8.31
8.29
8.18
8.15
7.58
7.56
7.53
7.52
7.50
7.47
4.84
4.48
4.46
1.46
1.31
1.30
1.28
EtOOC
NHBoc
N
Ph
3r
1H NMR (400MHz, CDCl3)
1.00
2.04
1.05
5.02
0.99
3.98
9.00
3.06
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)


166.32
161.61
155.97
148.86
139.70
136.32
130.61
130.22
129.62
129.15
128.98
128.78
128.71
128.00
126.59
80.36
77.50
77.18
76.86
61.48
42.44
28.51
14.51
EtOOC
NHBoc
N
Ph
3r
13C NMR (100MHz, CDCl3)
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


8.35
8.15
8.00
7.98
7.92
7.74
7.72
7.61
7.59
7.57
7.56
7.55
7.54
7.52
7.51
7.50
7.49
7.48
7.47
7.46
7.45
7.44
7.43
7.39
7.38
7.36
7.26
4.84
4.79
4.47
4.46
4.44
4.42
2.72
2.56
1.45
NHBoc
N
Ph
+
NHBoc
N
Ph
3s
3s'
3s:3s' = 2:1
1H NMR (400MHz, CDCl3)
0.69
0.33
0.71
0.32
0.34
5.66
1.03
0.96
2.00
1.99
1.00
9.00
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)

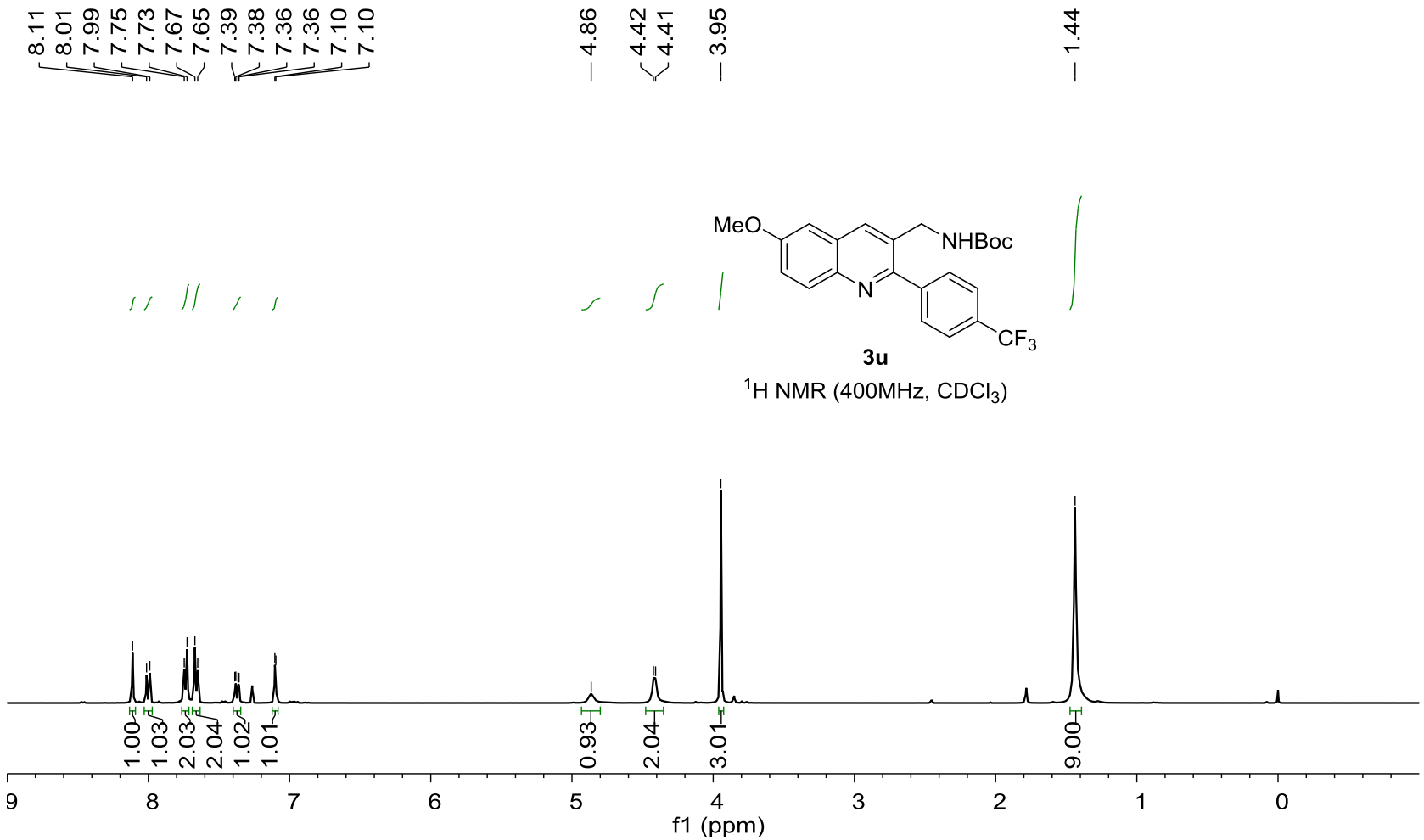

159.48
159.00
155.97
147.40
140.27
140.15
139.96
135.18
134.33
132.00
129.90
129.38
129.07
128.79
128.75
128.71
128.68
128.61
128.56
128.42
127.72
127.23
126.79
79.89
77.48
77.16
76.84
42.69
28.51
22.07
18.80
NHBoc
N
Ph
+
NHBoc
N
Ph
3s
3s'
3s:3s' = 2:1
13C NMR (100MHz, CDCl3)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


8.04
8.00
7.98
7.46
7.46
7.45
7.44
7.34
7.33
7.31
7.31
7.26
7.05
7.05
6.98
6.98
6.97
6.96
4.94
3.91
3.83
1.43
MeO
NHBoc
N
OMe
3t
1H NMR (400MHz, CDCl3)
0.97
0.94
1.93
0.96
0.99
2.00
0.80
1.94
2.99
3.00
9.00
f1 (ppm)



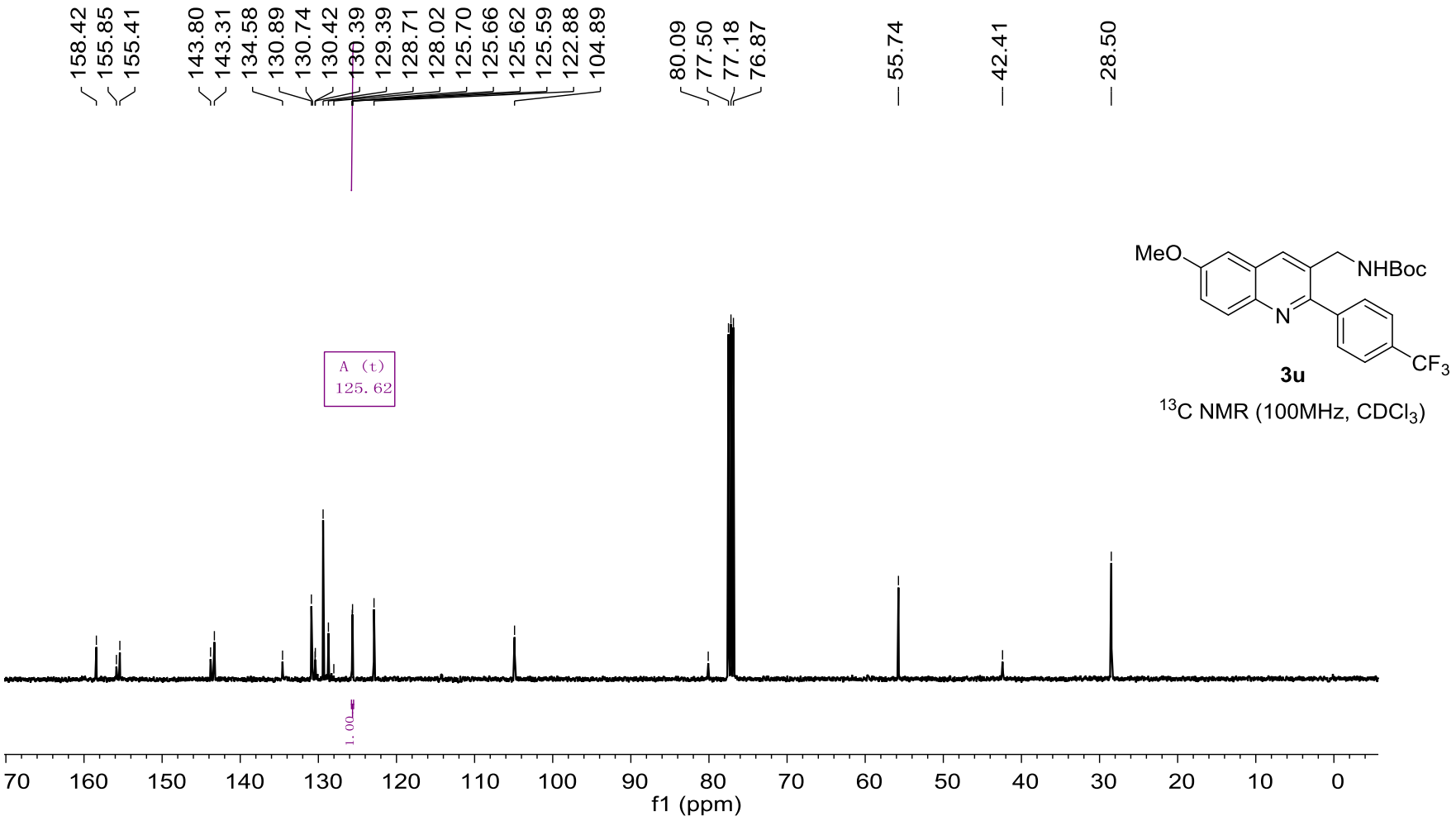
3t

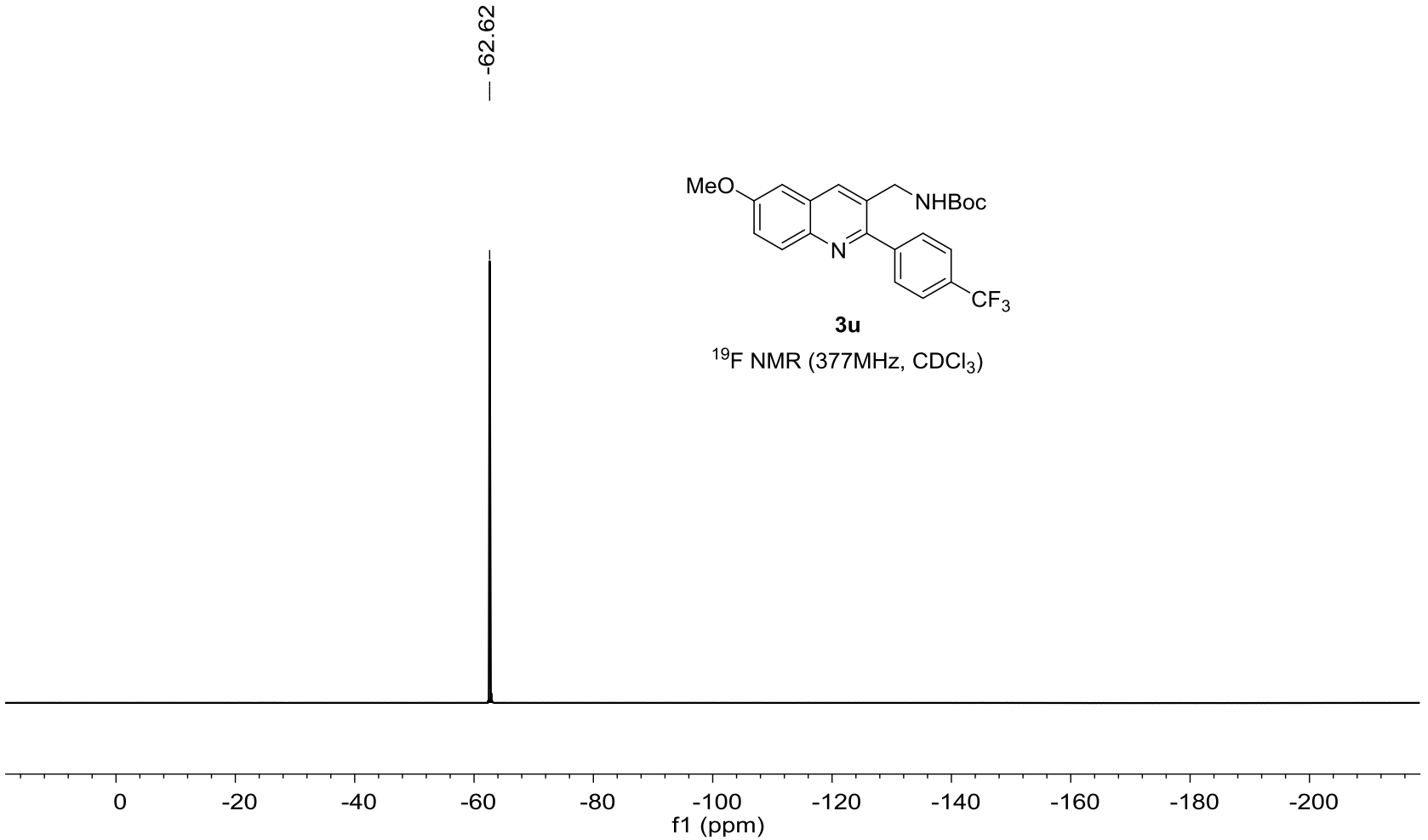
^{13}C NMR (100MHz, $CDCl_3$)



3u

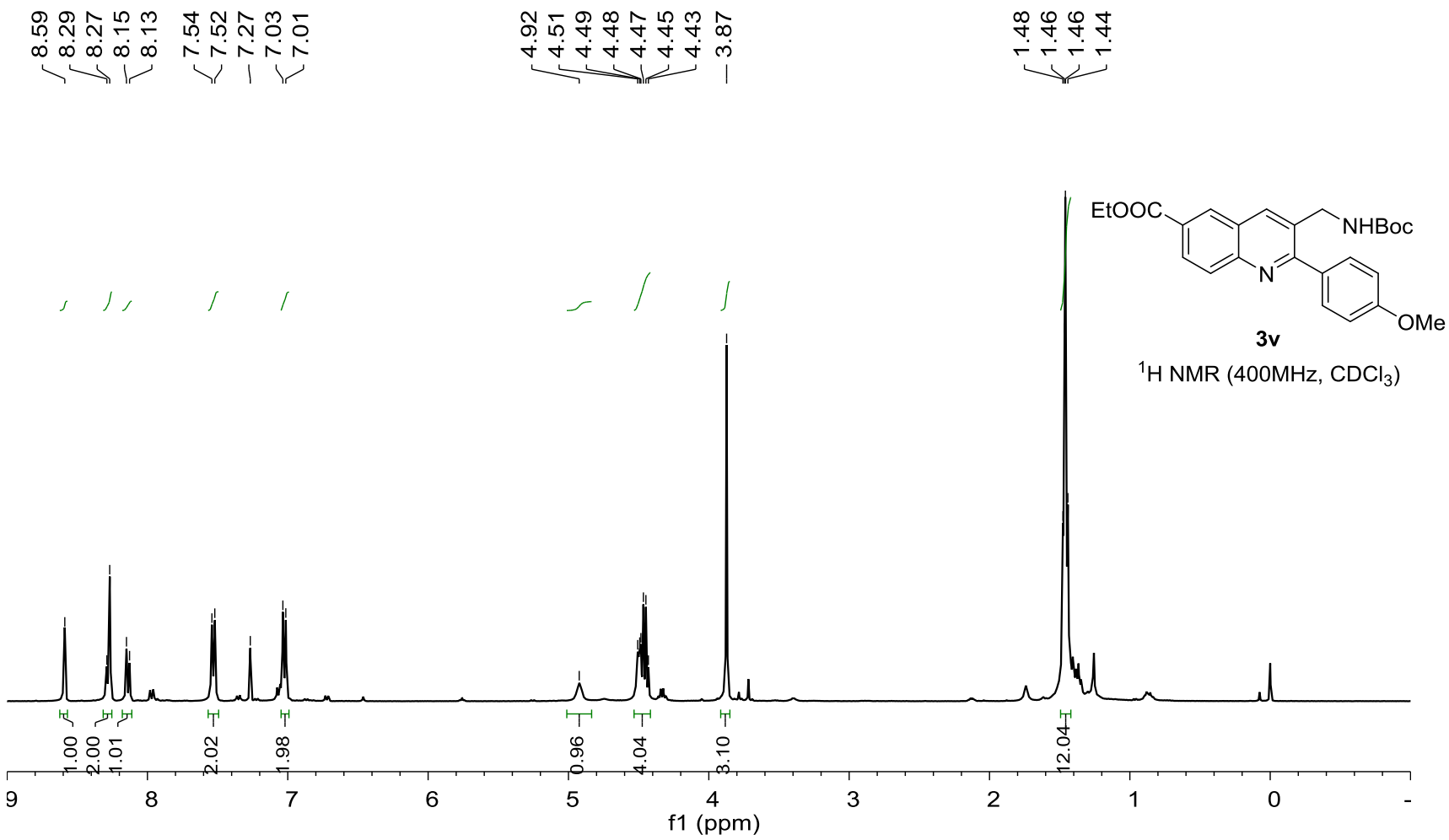
^{1}H NMR (400MHz, $CDCl_3$)

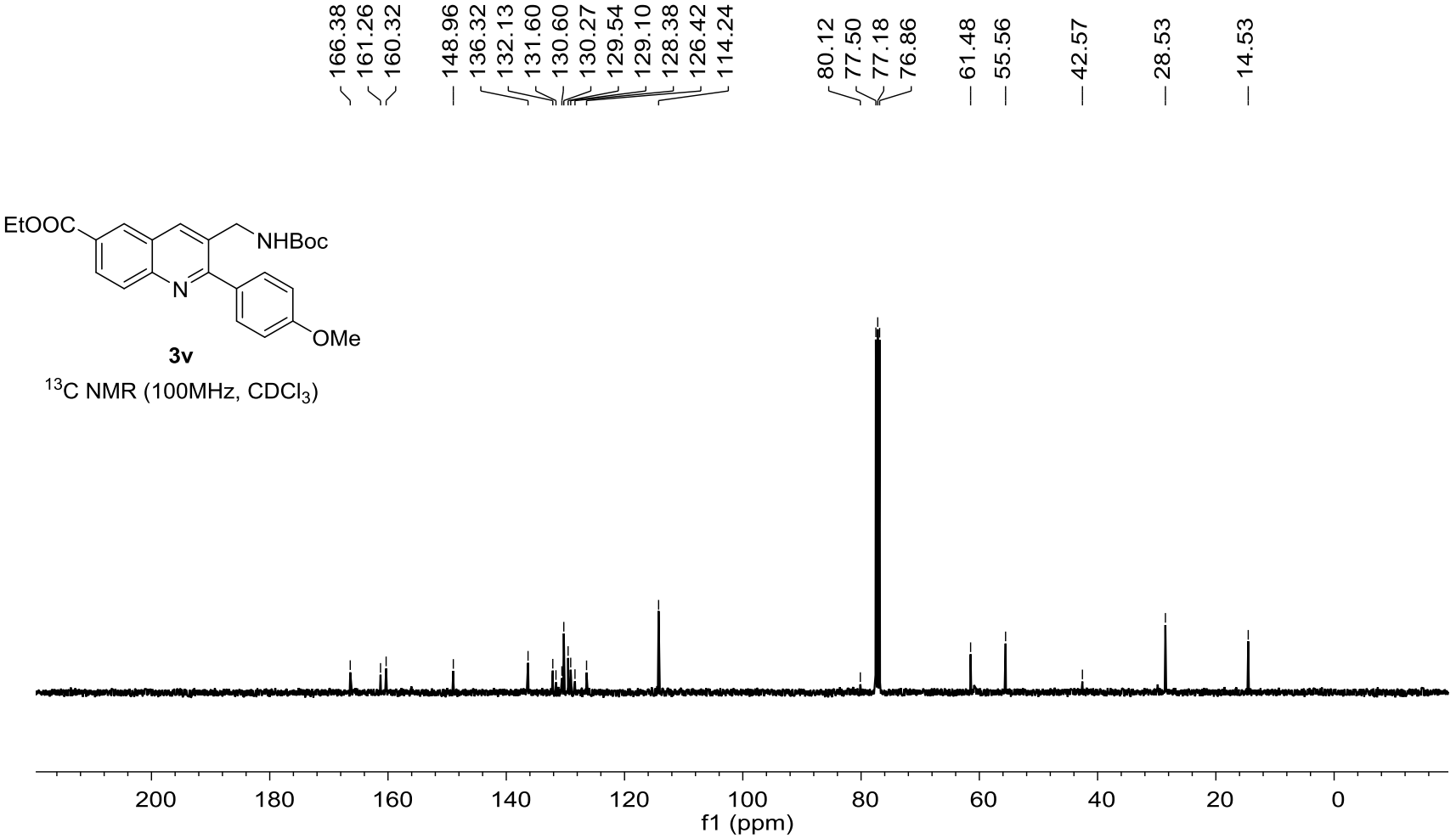

158.42
155.85
155.41
143.80
143.31
134.58
130.89
130.74
130.42
130.39
129.39
128.71
128.02
125.70
125.66
125.62
125.59
122.88
104.89
80.09
77.50
77.18
76.87
55.74
42.41
28.50
A (t)
125.62
1.00
MeO
NHBoc
N
CF3
3u
13C NMR (100MHz, CDCl3)
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

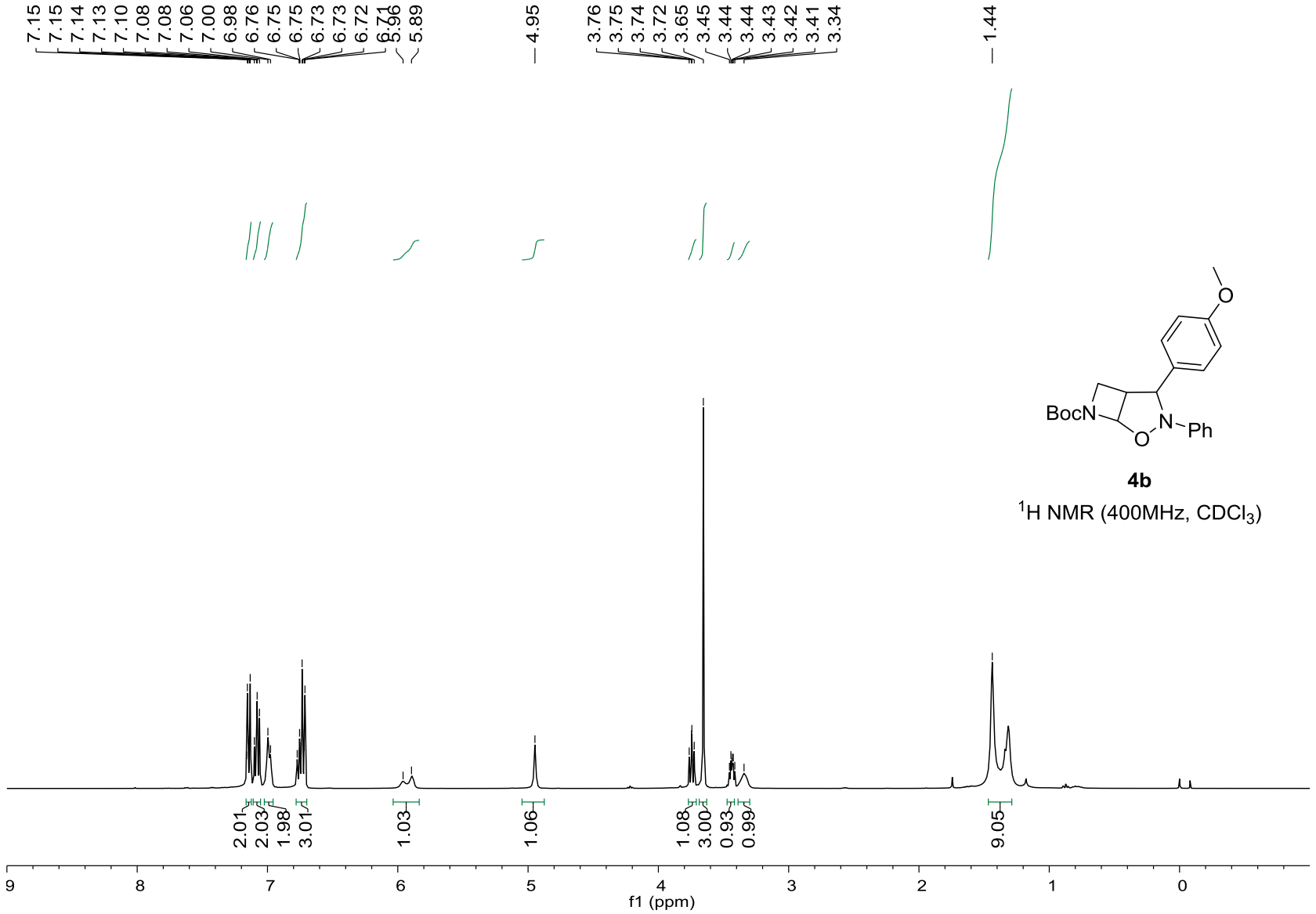


3u

^{19}F NMR (377MHz, $CDCl_3$)

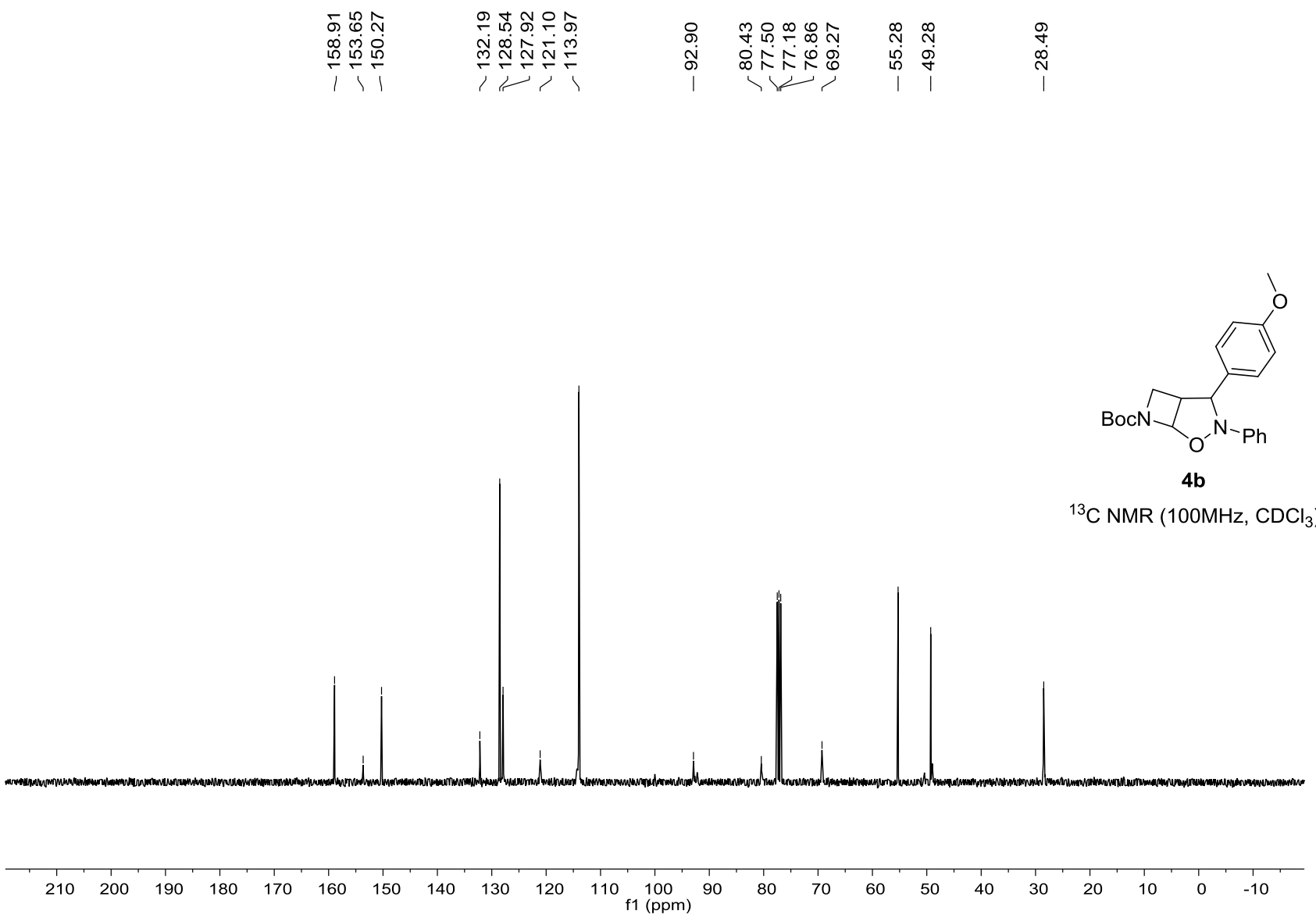

8.59
8.29
8.27
8.15
8.13
7.54
7.52
7.27
7.03
7.01
4.92
4.51
4.49
4.48
4.47
4.45
4.43
3.87
1.48
1.46
1.46
1.44
EtOOC
NHBoc
N
OMe
3v
1H NMR (400MHz, CDCl3)
1.00
2.00
1.01
2.02
1.98
0.96
4.04
3.10
12.04
9
8
7
6
5
4
3
2
1
0
-
f1 (ppm)

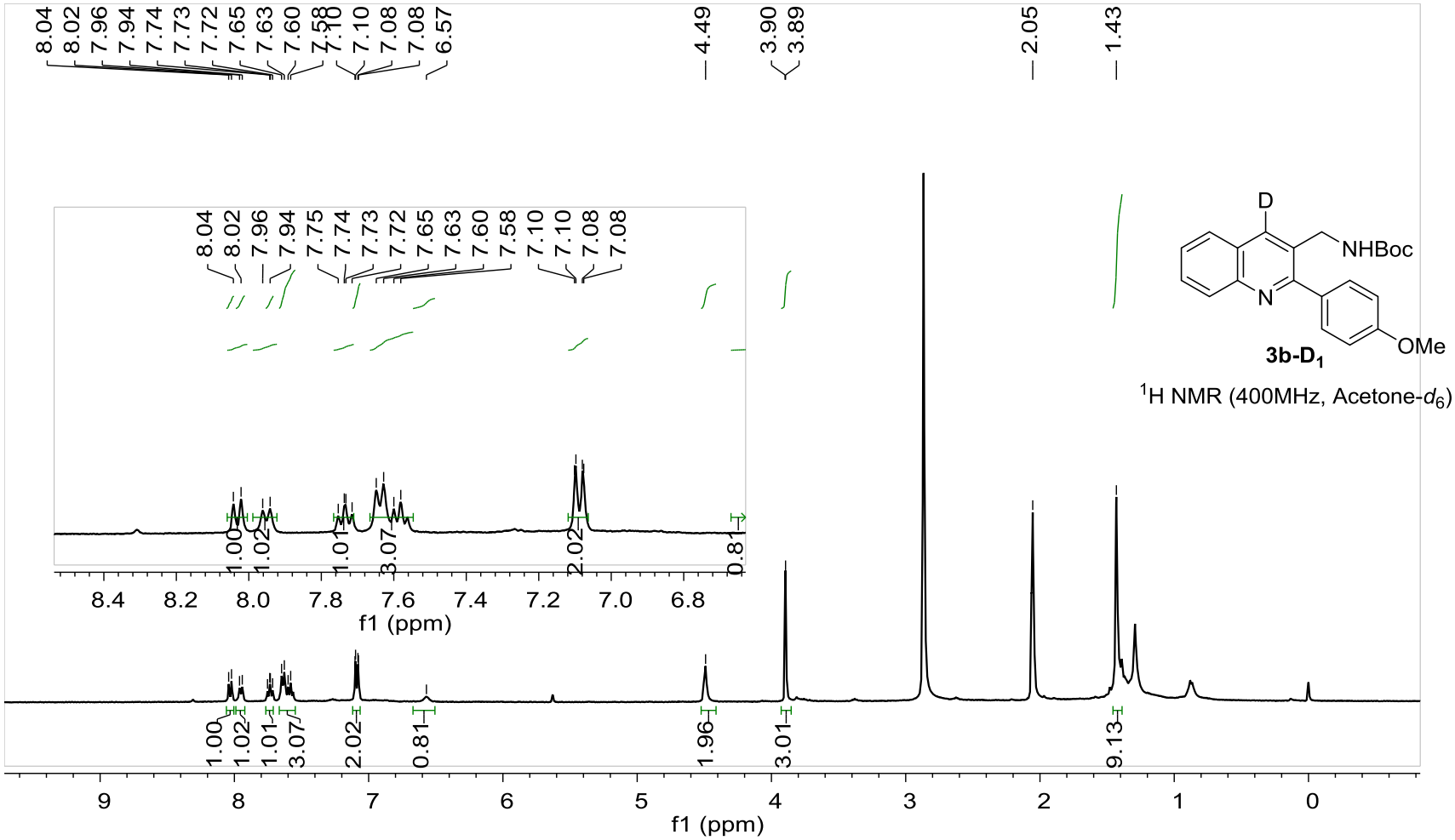

166.38
161.26
160.32
148.96
136.32
132.13
131.60
130.60
130.27
129.54
129.10
128.38
126.42
114.24
80.12
77.50
77.18
76.86
61.48
55.56
42.57
28.53
14.53
EtOOC
NHBoc
N
OMe
3v
13C NMR (100MHz, CDCl3)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

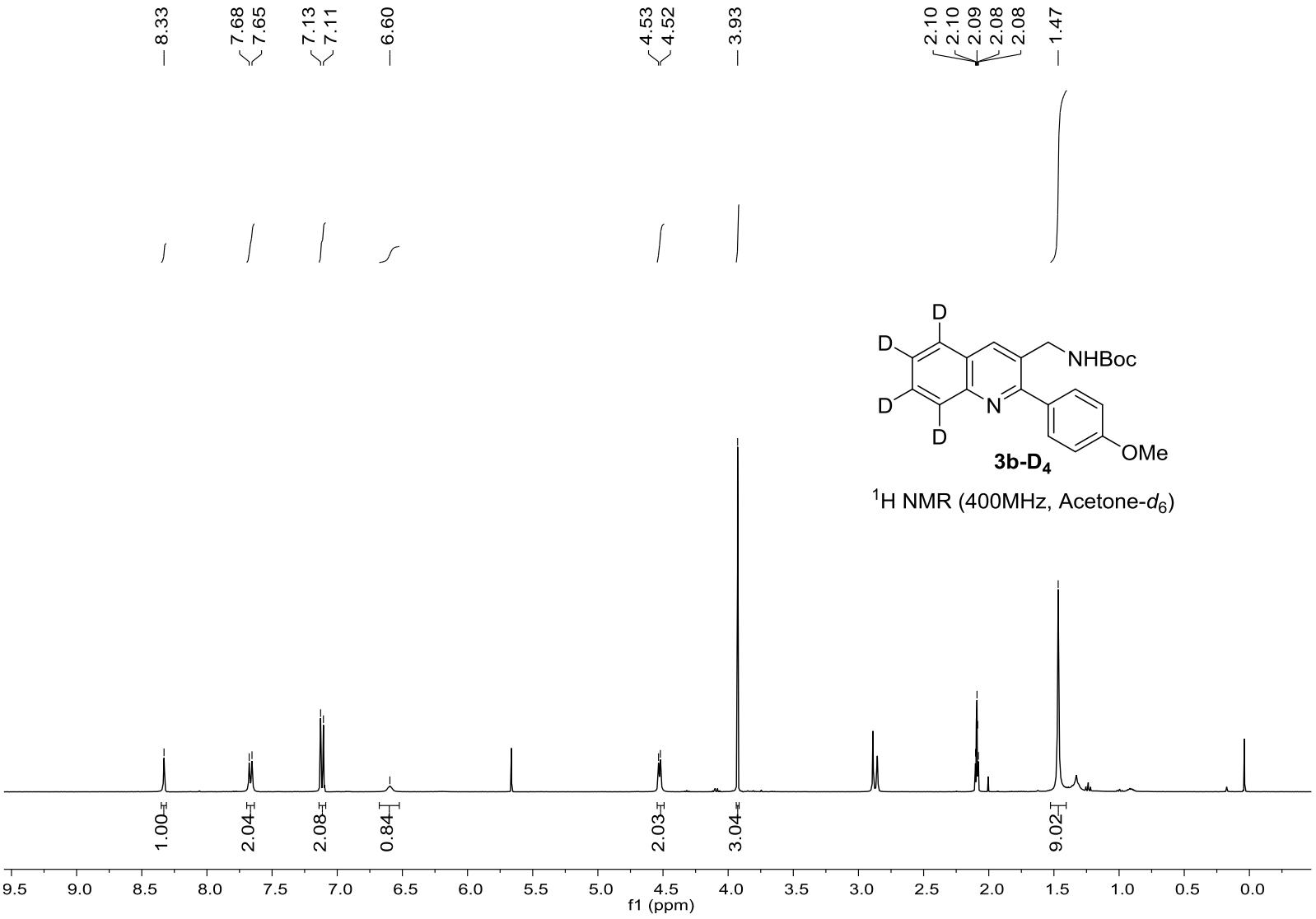


4b

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


158.91
153.65
150.27
132.19
128.54
127.92
121.10
113.97
92.90
80.43
77.50
77.18
76.86
69.27
55.28
49.28
28.49
BocN
O
N
Ph
O
4b
13C NMR (100MHz, 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)


8.04
8.02
7.96
7.94
7.74
7.73
7.72
7.65
7.63
7.60
7.58
7.10
7.08
7.08
6.57
4.49
3.90
3.89
2.05
1.43
1.00
1.02
1.01
3.07
2.02
0.81
1.96
3.01
9.13
f1 (ppm)
D
NHBoc
N
OMe
3b-D1
1H NMR (400MHz, Acetone-d6)


8.33
7.68
7.65
7.13
7.11
6.60
4.53
4.52
3.93
2.10
2.10
2.09
2.08
2.08
1.47
D
D
D
D
N
NHBoc
OMe
3b-D4
1H NMR (400MHz, Acetone-d6)
1.00
2.04
2.08
0.84
2.03
3.04
9.02
f1 (ppm)