DMAP-Promoted Oxidative Functionalization of α-Amino Ketones via Oxygen Delivery from Water/Alcohols

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1. General methods

Column chromatography was carried out on silica gel (200~300mesh) purchased from Shanghai Xian-Ding Biotechnology CO., Ltd. Unless noted, all commercially available reagents were used without further purification. Solvents were dried using standard methods. ^{1}H and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ or d^6-DMSO on a Bruker Ascend^{TM} 400 or 600 spectrometer. ^{1}H NMR spectra was recorded with tetramethylsilane (δ = 0.00 ppm) or solvent residual peak ($CDCl_3$: 7.26 ppm; d^6-DMSO: 2.50 ppm) as internal reference; ^{13}C NMR spectra was recorded with $CDCl_3$ (77.00 ppm) or d^6-DMSO (39.52 ppm) as internal reference. Multiplicities are given as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), q (quartet), or m (multiplet). High-resolution mass spectra were obtained by using the ultrahigh performance liquid chromatograph-coupled with agilent 6545 iFunnel accurate mass quadrupole time-of-flight mass spectrometer. The melting points of compounds were measured by MPA100 Optimelt point apparatus with USB port and MeltView software.

2. Synthesis and characterization of substrates

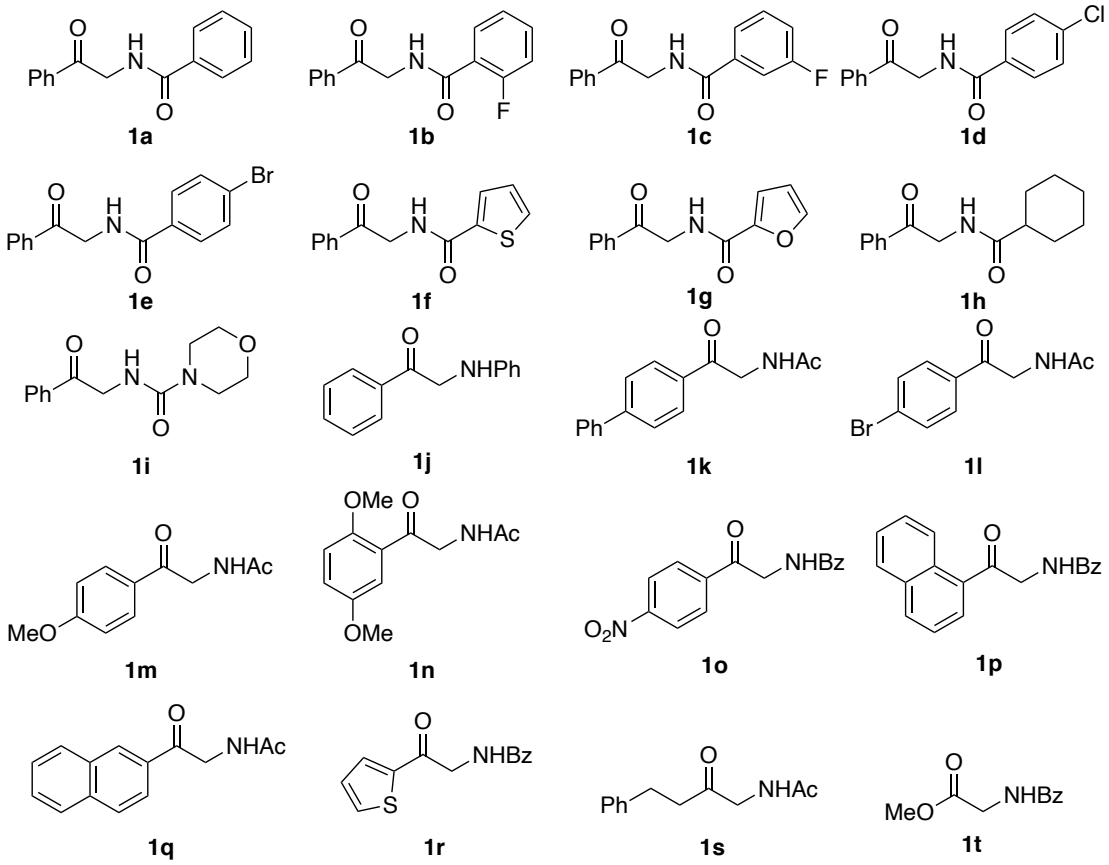
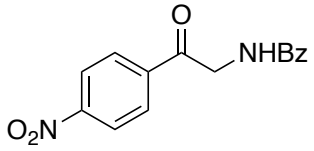


Figure **S1**. α-Amino carbonyl compounds used as substrates

Unless otherwise specified, α-amino ketones are known compounds and were synthesized according to the related literature.[1]

1o-q and **1r** were synthesized according to the similar procedure with **1a**.[1]



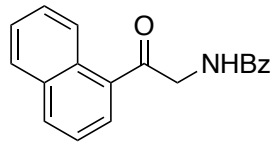
N-(2-(4-nitrophenyl)-2-oxoethyl)benzamide (**1o**): 2 mmol scale was conducted to afford the product **1o** (313.7 mg, 55%) as a white solid.

Rf = 0.21 (petroleum ether: EtOAc = 3:2)

m. p. 157-158 ℃

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 8.8 Hz, 2H), 8.21 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 6.9 Hz, 2H), 7.57 – 7.54 (m, 1H), 7.50 – 7.48 (m, 2H), 7.18 (bs, 1H), 5.02 (d, *J* = 4.4 Hz, 2H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 193.11, 167.46, 150.97, 138.73, 133.54, 132.03, 129.13, 128.74, 127.12, 124.23, 47.36.

HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{13}N_2O_4$ 285.0875; found 285.0859.



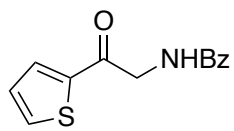
N-(2-(naphthalen-1-yl)-2-oxoethyl)benzamide (**1p**): 2 mmol scale was conducted to afford the product **1p** (290.2 mg, 50%) as a white solid.

Rf = 0.36 (petroleum ether: EtOAc = 3:2)

m. p. 140-142 ℃

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.85 (d, *J* = 8.7 Hz, 1H), 8.10 (d, *J* = 7.5 Hz,2H), 7.94 – 7.91 (m, 3H), 7.67 – 7.64 (m, 1H), 7.60 – 7.54 (m, 3H), 7.51 – 7.49 (m, 2H), 7.38 (bs, 1H), 5.03 (dd, *J* = 4.4, 1.6 Hz, 2H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 197.41, 167.39, 134.42, 134.05, 133.98, 131.89, 131.78, 130.37, 128.76, 128.66, 127.14, 126.79, 125.56, 124.45, 48.59.

HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{19}H_{16}NO_2$ 290.1181; found 290.1165.



N-(2-oxo-2-(thiophen-2-yl)ethyl)benzamide (**1r**): 2 mmol scale was conducted to afford the product **1r** (306.5 mg, 63%) as a white solid.

Rf = 0.25 (petroleum ether: EtOAc = 3:2)

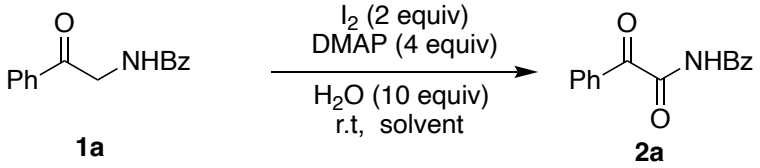
m. p. 145-147 ℃ (146-147 ℃)[2]

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.88 – 7.86 (m, 3H), 7.75 (d, *J* = 4.9 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.21 (dd, *J* = 4.9, 3.8 Hz, 1H), 7.17 (bs, 1H), 4.91 (d, *J* = 4.3 Hz, 2H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 187.26, 167.36, 140.84, 134.76, 133.81, 132.58, 131.81, 128.65, 128.54, 127.12, 46.89.

HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_{12}NO_2S$ 246.0589; found 246.0573.

3. Reaction optimization

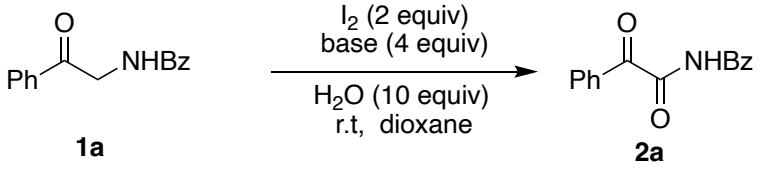
Table **S1**. Screening of solvents [a]



entry	solvent	time (h)	yield (%)[b]
1	CH_2Cl_2	1	69
2	$CHCl_3$	1	68
3	PhMe	12	90
4	EtOAc	8	75
5	THF	8	81
6	dioxane	4	95

[a] Reaction conditions: **1a** (0.2 mmol), I_2 (2 equiv), DMAP (4 equiv), H_2O (10 equiv), solvent (2 mL), air, room temperature. [b] Isolated yield.

Table **S2**. Screening of bases[a]

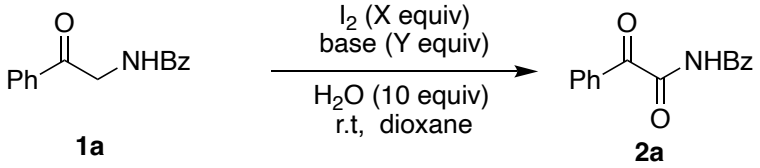


entry	base	time (h)	yield (%)[b]
1	DBU	3	trace
2	Et_3N	5	7
3	pyridine	18	12 (80)
4	4-methoxypyridine	15	41
5	2,6-dimethoxypyridine	18	trace (95)

6	DMAP	4	95
7	K_3PO_4	18	0 (92)
8	CsF	18	0 (80)

[a] Reaction conditions: **1a** (0.2 mmol), I_2 (2 equiv), base (4 equiv), H_2O (10 equiv), dioxane (2 mL), air, room temperature. [b] Isolated yield. Recovery rate of **1a** is given in parentheses.

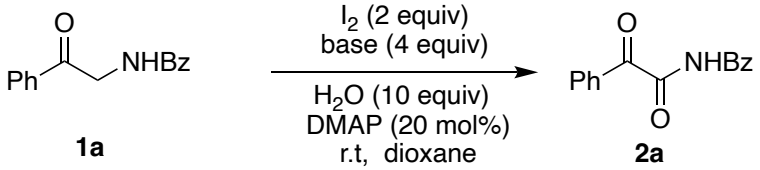
Table **S3**. Screening of amount of I_2 or DMAP[a]



entry	X	Y	time (h)	yield (%)[b]
1	2	2	36	27 (58)
2	2	3	36	73 (21)
3	2	4	4	95
4	1	4	36	47 (52)
5	0	4	36	0
6	2	0	36	0

[a] Reaction conditions: **1a** (0.2 mmol), I_2 (X equiv), base (Y equiv), H_2O (10 equiv), dioxane (2 mL), air, room temperature. [b] Isolated yield. Recovery rate of **1a** is given in parentheses.

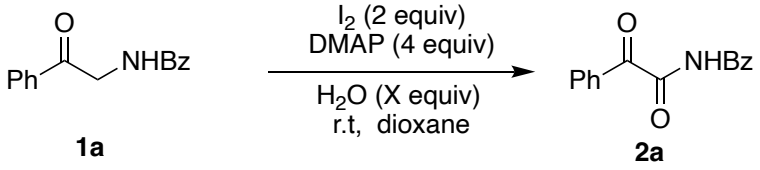
Table **S4**. Screening of inorganic bases in the presence of a catalytic amount of DMAP[a]



entry	inorganic base	time (h)	yield (%)[b]
1	K_3PO_4	8	90
2	CsF	8	40 (57)
3	K_2CO_3	2	57 (5)
4	Na_2CO_3	9	83

[a] Reaction conditions: **1a** (0.2 mmol), I_2 (2 equiv), base (4 equiv), H_2O (10 equiv), dioxane (2 mL), air, room temperature. [b] Isolated yield. Recovery rate of **1a** is given in parentheses.

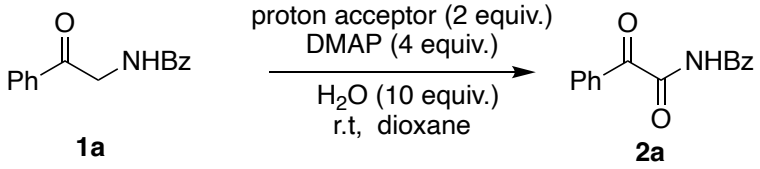
Table **S5**. Screening of amount of H_2O[a]



entry	X	time (h)	yield (%)[b]
1	1.2	12	90
2	10	4	95 (57)
3	139 (dioxane: H_2O = 4:1)	0.5	78 (5)

[a] Reaction conditions: **1a** (0.2 mmol), I_2 (2 equiv), DMAP (4 equiv), H_2O (X equiv), dioxane (2 mL), air, room temperature. [b] Isolated yield. Recovery rate of **1a** is given in parentheses.

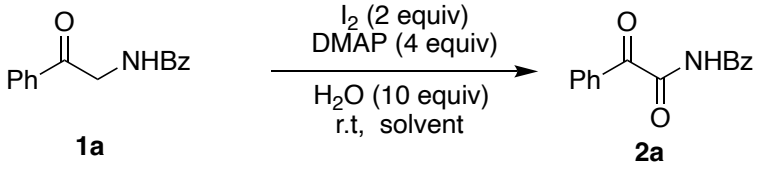
Table **S6**. Screening proton acceptors[a]



entry	proton acceptor	time (h)	yield (%)[b]
1	I_2	4	95
2	NCS	4	79
3	NBS	5	82
4	NIS	4	90

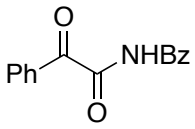
[a] Reaction conditions: **1a** (0.2 mmol), proton acceptor (2 equiv.), DMAP (4 equiv.), H_2O (10 equiv.), dioxane (2 mL), air, room temperature. [b] Isolated yield.

4. General procedure for C-H oxidation of α-amino ketones to α-ketoamides



General procedure: To a tube was charged with I_2 (2 equiv, 0.4 mmol, 101.5 mg), DMAP (4 equiv, 0.8 mmol, 97.8 mg), H_2O (10 equiv, 2 mmol, 36 μL) and dioxane (2 mL), then the reaction mixture was stirred for 5 min at room temperature. Add α-Amino ketone **1** (0.2 mmol) to the suspension system and continue stirring at room temperature until the starting material disappeared (monitored by TLC). After completion of the reaction, the crude reaction mixture was quenched by 10% aq. $Na_2S_2O_3$ (4 mL) solution (w/w) and extracted with CH_2Cl_2 (2*4 mL). The combined organic extracts were

washed with 0.05 N HCl solution (5 mL) and brine (5 mL), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to afford the desired product **2**.

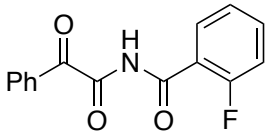


N-(2-oxo-2-phenylacetyl)benzamide (**2a**): The general procedure was performed using *N*-(2-oxo-2-phenylethyl)benzamide **1a** (0.2 mmol, 47.8 mg) for 4 h, Purification by chromatography (petroleum ether: EtOAc = 2:1) afforded compound **2a** (48.2 mg, 95%) as a white solid.

Rf = 0.26 (petroleum ether: EtOAc = 2:1)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.76 (bs, 1H), 8.15 (d, *J* = 7.7 Hz, 2H), 7.92 – 7.91 (m, 2H), 7.68 – 7.63 (m, 2H), 7.55 – 7.51 (m, 4H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 186.51, 165.15, 134.75, 133.99, 132.31, 131.08, 130.22, 129.15, 128.93, 128.04. The spectral characteristics are in agreement with spectral data previously reported. [3]

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{15}H_{11}NNaO_3$ 276.0637; found 276.0630.



2-fluoro-*N*-(2-oxo-2-phenylacetyl)benzamide (**2b**): The general procedure was performed using 2-fluoro-*N*-(2-oxo-2-phenylethyl)benzamide **1b** (0.2 mmol, 51.4 mg) for 5 h, Purification by chromatography (petroleum ether: EtOAc = 3:1) afforded compound **2b** (52.3 mg, 96%) as a white solid.

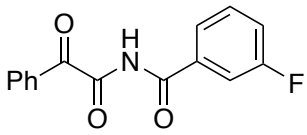
Rf = 0.52 (petroleum ether: EtOAc = 2:1)

M.p. 90-93 ℃

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (s, 1H), 7.91 – 7.89 (m, 2H), 7.77 – 7.73 (m, 2H), 7.72 – 7.66 (m, 1H), 7.63 (t, *J* = 7.7 Hz, 2H), 7.41 – 7.33 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 188.11, 170.35, 165.55, 160.31 (d, *J* = 253.8 Hz), 135.63 (d, *J* = 9.0 Hz), 135.07, 132.60, 131.18, 129.75, 129.46, 125.27 (d, *J* = 3.6 Hz), 121.05 (d, *J* = 12.3

Hz), 117.09 (d, J = 21.5 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ -112.16.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{15}H_{10}FNNaO_3$ 294.0542; found 294.0548.



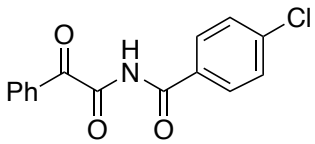
3-fluoro-*N*-(2-oxo-2-phenylacetyl)benzamide (**2c**): The general procedure was performed using 3-fluoro-*N*-(2-oxo-2-phenylethyl)benzamide **1c** (0.2 mmol, 51.4 mg) for 8 h, Purification by chromatography (petroleum ether: EtOAc = 3:1 ~ 3:2) afforded compound **2c** (49.8 mg, 92%) as a white solid.

Rf = 0.49 (petroleum ether: EtOAc = 3:2)

M.p. 142 – 143 ℃

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.53 (s, 1H), 7.92 – 7.85 (m, 4H), 7.73 (t, J = 7.4 Hz, 1H), 7.64 – 7.54 (m, 4H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 187.99, 171.46, 166.61 (d, J = 2.7 Hz), 162.38 (d, J = 245.2 Hz), 134.92, 133.17 (d, J = 7.3 Hz), 132.76, 131.55 (d, J = 8.0 Hz), 129.69, 129.46, 125.57 (d, J = 2.9 Hz), 121.43 (d, J = 21.3 Hz), 116.11 (d, J = 23.5 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ -111.80.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{15}H_{10}FNNaO_3$ 294.0542; found 294.0536.

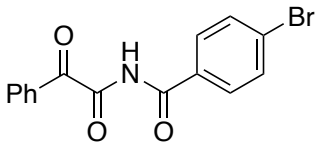


4-chloro-*N*-(2-oxo-2-phenylacetyl)benzamide (**2d**): The general procedure was performed using 4-chloro-*N*-(2-oxo-2-phenylethyl)benzamide **1d** (0.2 mmol, 54.6 mg) for 8 h, Purification by chromatography (petroleum ether: EtOAc = 4:1) afforded compound **2d** (50.2 mg, 87%) as a white solid.

Rf = 0.33 (petroleum ether: EtOAc = 4:1)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.80 (s, 1H), 8.15 (d, J = 6.9 Hz, 2H), 7.87 – 7.84 (m, 2H), 7.69 – 7.66 (m, 1H), 7.55 – 7.53 (m, 2H), 7.51 – 7.49 (m, 2H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 186.30, 164.26, 140.63, 134.91, 132.19, 130.34, 129.54, 129.51, 129.47, 128.97.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{15}H_{10}ClNNaO_3$ 310.0247; found 310.0260.



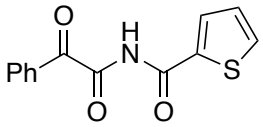
4-bromo-*N*-(2-oxo-2-phenylacetyl)benzamide (**2e**): The general procedure was performed using 4-bromo-*N*-(2-oxo-2-phenylethyl)benzamide **1e** (0.2 mmol, 63.4 mg) for 8 h, Purification by chromatography (petroleum ether: EtOAc = 4:1) afforded compound **2e** (58.7 mg, 89%) as a light yellow solid.

Rf = 0.35 (petroleum ether: EtOAc = 4:1)

M.p. 201 – 202 ℃

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.77 (bs, 1H), 8.16 (d, *J* = 7.8 Hz, 2H), 7.78 (d, *J* = 8.6 Hz, 2H), 7.69 – 7.66 (m, 3H),7.54 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 186.27, 164.40, 134.93, 132.50, 132.18, 130.37, 130.04, 129.52, 129.25, 128.97.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{15}H_{10}BrNNaO_3$ 353.9742; found 353.9717.



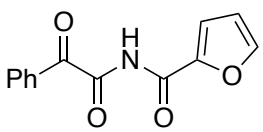
N-(2-oxo-2-phenylacetyl)thiophene-2-carboxamide (**2f**): The general procedure was performed using *N*-(2-oxo-2-phenylethyl)thiophene-2-carboxamide **1f** (0.2 mmol, 49.0 mg) for 3 h, Purification by chromatography (petroleum ether: EtOAc = 1:1) afforded compound **2f** (46.9 mg, 91%) as a white solid.

Rf = 0.51 (petroleum ether: EtOAc = 1:1)

M.p. 167 – 169 ℃

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.82 (bs, 1H), 8.12 (d, *J* = 7.8 Hz, 2H), 7.83 (d, *J* = 3.9 Hz, 1H), 7.71 (d, *J* = 5.0 Hz, 1H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 4.4 Hz, 1H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 186.43, 159.42, 135.67, 134.79, 134.76, 132.27, 131.83, 131.15, 130.12, 128.96, 128.54.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{13}H_9NNaO_3S$ 282.0201; found 282.0205.



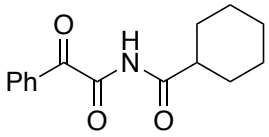
N-(2-oxo-2-phenylacetyl)furan-2-carboxamide (**2g**): The general procedure was performed using *N*-(2-oxo-2-phenylethyl)furan -2-carboxamide **1g** (0.2 mmol, 45.8 mg) for 3 h, Purification by chromatography (petroleum ether: EtOAc = 1:1) afforded compound **2g** (48.2 mg, 99%) as a white solid.

Rf = 0.35 (petroleum ether: EtOAc = 1:1)

M.p. 162 – 163 ℃

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.69 (bs, 1H), 8.16 (d, *J* = 7.9 Hz, 2H), 7.68 – 7.65 (m, 1H), 7.62 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.54 – 7.51 (m, 2H), 7.37 (dd, *J* = 3.6, 0.8 Hz, 1H), 6.63 (dd, *J* = 3.6, 1.7 Hz, 1H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 186.24, 155.03, 146.27, 145.32, 134.82, 132.23, 130.34, 128.91, 119.18, 113.51.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{13}H_9NNaO_4$ 266.0429; found 266.0443.



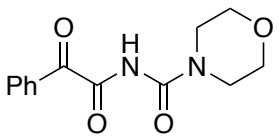
N-(2-oxo-2-phenylacetyl)cyclohexanecarboxamide (**2h**): The general procedure was performed using *N*-(2-oxo-2-phenylethyl)cyclohexanecarboxamide **1h** (0.2 mmol, 49.0 mg) for 4 h, Purification by chromatography (petroleum ether: EtOAc = 4:1) afforded compound **2h** (43.8 mg, 85%) as a white solid.

Rf = 0.30 (petroleum ether: EtOAc = 4:1)

M.p. 129 – 130 ℃

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.09 (s, 1H), 8.17 (d, *J* = 7.8 Hz, 2H), 7.67 – 7.65 (m, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 2.80 (s, 1H), 1.96 – 1.94 (m, 2H), 1.84 – 1.81 (m, 2H), 1.72 – 1.69 (m, 1H), 1.51 – 1.44 (m, 2H), 1.38 – 1.31 (m, 2H), 1.28 – 1.20 (m, 1H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 186.24, 176.06, 134.87, 132.29, 130.67, 128.83, 44.95, 28.66, 25.60, 25.37.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{15}H_{17}NNaO_3$ 282.1106; found 282.1099.



N-(2-oxo-2-phenylacetyl)morpholine-4-carboxamide (**2i**): The general procedure was

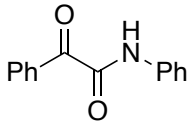
performed using *N*-(2-oxo-2-phenylethyl)morpholine-4-carboxamide **1i** (0.2 mmol, 49.6 mg) for 12 h, Purification by chromatography (petroleum ether: EtOAc = 1:4) afforded compound **2i** (32.1 mg, 61%) as a white solid.

Rf = 0.48 (petroleum ether: EtOAc = 1:4)

M.p. 125-126 ℃ (135.5-132 ℃)[4]

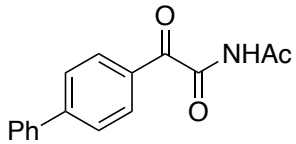
^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.31 (bs, 1H), 8.06 (s, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 3.70 (t, *J* = 4.9 Hz, 4H), 3.51 (t, *J* = 4.9 Hz, 4H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 186.65, 151.36, 134.48, 132.58, 130.00, 128.83, 66.30, 44.91.

HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_{15}N_2O_4$ 263.1032; found 263.1019.



2-oxo-*N*,2-diphenylacetamide (**2j**): The general procedure was performed using 1-phenyl-2-(phenylamino)ethan-1-one **1j** (0.2 mmol, 42.2 mg) for 12 h, Purification by chromatography (petroleum ether: EtOAc = 10:1) afforded compound **2j** (42.6 mg, 95%) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.96 (bs, 1H), 8.42 (d, *J* = 7.8 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.66 (t, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.39, 158.82, 136.59, 134.64, 133.05, 131.46, 129.22, 128.56, 125.30, 119.90. The spectral characteristics are in agreement with spectral data previously reported.[5]



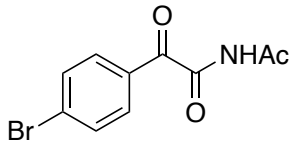
2-([1,1'-biphenyl]-4-yl)-*N*-acetyl-2-oxoacetamide (**2k**): The general procedure was performed using *N*-(2-([1,1'-biphenyl]-4-yl)-2-oxoethyl)acetamide **1k** (0.2 mmol, 50.6 mg) for 8 h, Purification by chromatography (petroleum ether: EtOAc = 2:1) afforded compound **2k** (46.1 mg, 86%) as a white solid.

Rf = 0.38 (petroleum ether: EtOAc = 2:1)

M.p. 141 – 144 ℃

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.28 (bs, 1H), 8.39 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.5 Hz, 2H), 7.66 – 7.64 (m, 2H), 7.51 – 7.48 (m, 2H), 7.45 – 7.42 (m, 1H), 2.56 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 185.00, 171.07, 147.83, 139.38, 131.85, 130.89, 129.07, 128.75, 127.40, 127.37, 25.19.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{16}H_{13}NNaO_3$ 290.0793; found 290.0777.



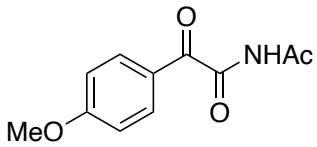
N-acetyl-2-(4-bromophenyl)-2-oxoacetamide (**2l**): The general procedure was performed using *N*-(2-(4-bromophenyl)-2-oxoethyl)acetamide **1l** (0.2 mmol, 51.0 mg) for 4 h, Purification by chromatography (petroleum ether: EtOAc = 2:1) afforded compound **2l** (42.5 mg, 78%) as a light yellow solid.

Rf = 0.33 (petroleum ether: EtOAc = 2:1)

M.p. 109-110 ℃

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.29 (bs, 1H), 8.16 (d, *J* = 6.9 Hz, 2H), 7.67 – 7.65 (m, 2H), 2.52 (s, 3H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 184.64, 170.97, 132.50, 132.23, 131.01, 130.92, 25.09.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{10}H_8BrNNaO_3$ 291.9585; found 291.9592.



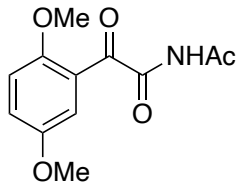
N-acetyl-2-(4-methoxyphenyl)-2-oxoacetamide (**2m**): The general procedure was performed using *N*-(2-(4-methoxyphenyl)-2-oxoethyl)acetamide **1m** (0.2 mmol, 41.4 mg) for 18 h, Purification by chromatography (petroleum ether: EtOAc = 3:2) afforded compound **2m** (38.0 mg, 86%) as a white solid.

Rf = 0.37 (petroleum ether: EtOAc = 3:2)

M.p. 132-133 ℃

^{1}H NMR (600 MHz, DMSO-d_6) δ 11.73 (s, 1H), 7.77 (d, J = 8.8 Hz, 2H), 7.10 (d, J = 8.9 Hz, 2H), 3.86 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 187.22, 171.56, 164.49, 131.76, 125.61, 114.99, 56.20, 23.75.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{11}H_{11}NNaO_4$ 244.0586; found 244.0582.



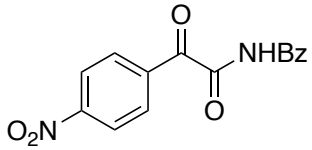
N-acetyl-2-(2,5-dimethoxyphenyl)-2-oxoacetamide (**2n**): The general procedure was performed using *N*-(2-(2,5-dimethoxyphenyl)-2-oxoethyl)acetamide **1n** (0.2 mmol, 47.4 mg) for 14 h, Purification by chromatography (petroleum ether: EtOAc = 1:2) afforded compound **2n** (40.5 mg, 81%) as a white solid.

Rf = 0.30 (petroleum ether: EtOAc = 1:2)

M.p. 136 – 137 ℃

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.51 (s, 1H), 7.32 (d, J = 3.2 Hz, 1H), 7.27 (dd, J = 9.0, 3.2 Hz, 1H), 7.17 (d, J = 9.1 Hz, 1H), 3.78 (s, 3H), 3.73 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.93, 171.63, 170.25, 154.90, 154.04, 123.53, 122.82, 115.68, 112.23, 57.26, 56.11, 23.25.

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{12}H_{13}NNaO_5$ 274.0691; found 274.0701.



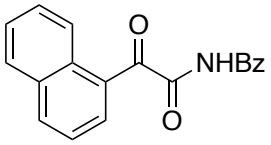
N-(2-(4-nitrophenyl)-2-oxoacetyl)benzamide (**2o**): The general procedure was performed using *N*-(2-(4-nitrophenyl)-2-oxoethyl)benzamide **1o** (0.2 mmol, 56.8 mg) for 0.5 h, Purification by chromatography (petroleum ether: EtOAc = 3:2) afforded compound **2o** (14.9 mg, 25%) as a yellow solid.

Rf = 0.40 (petroleum ether: EtOAc = 3:2)

^{1}H NMR (600 MHz, DMSO-d_6) δ 12.67 (s, 1H), 8.41 (d, J = 8.8 Hz, 2H), 8.17 (d, J = 8.8 Hz, 2H), 8.04 – 8.02 (m, 2H), 7.73 – 7.70 (m, 1H), 7.58 – 7.55 (m, 2H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 186.35, 170.92, 168.28, 151.00, 137.35, 134.71, 130.69, 130.47, 129.39, 129.33, 124.87. The spectral characteristics are in agreement with

spectral data previously reported.[3]

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{15}H_{10}N_2NaO_5$ 321.0487; found 321.0482.

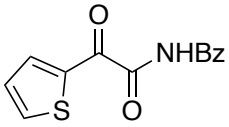


N-(2-(naphthalen-1-yl)-2-oxoacetyl)benzamide (**2p**): The general procedure was performed using *N*-(2-(naphthalen-1-yl)-2-oxoethyl)benzamide **1p** (0.2 mmol, 57.8 mg) for 5 h, Purification by chromatography (petroleum ether: EtOAc = 2:1) afforded compound **2p** (32.0 mg, 53%) as a white solid.

Rf = 0.31 (petroleum ether: EtOAc = 2:1)

^{1}H NMR (600 MHz, DMSO-d_6) δ 12.44 (s, 1H), 9.11 (d, J = 8.6 Hz, 1H), 8.29 (d, J = 8.2 Hz, 1H), 8.10 (d, J = 8.1 Hz, 1H), 8.02 – 8.00 (m, 3H), 7.78 (t, J = 7.7 Hz, 1H), 7.70 – 7.66 (m, 3H), 7.54 (t, J = 7.7 Hz, 2H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 190.16, 170.97, 167.72, 135.57, 134.41, 134.13, 133.73, 130.93, 130.82, 129.46, 129.37, 129.27, 129.25, 127.96, 127.43, 125.64, 125.44. The spectral characteristics are in agreement with spectral data previously reported.[3]

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{19}H_{13}NNaO_3$ 326.0793; found 326.0783



N-(2-oxo-2-(thiophen-2-yl)acetyl)benzamide (**2r**): The general procedure was performed using *N*-(2-oxo-2-(thiophen-2-yl)ethyl)benzamide **1r** (0.2 mmol, 49.0 mg) for 8 h, Purification by chromatography (petroleum ether: EtOAc = 2:1) afforded compound **2r** (32.0 mg, 53%) as a yellow solid.

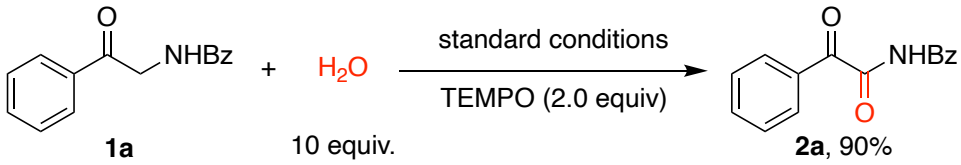
Rf = 0.45 (petroleum ether: EtOAc = 2:1)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 10.37 (s, 1H), 8.51 (d, J = 3.5 Hz, 1H), 7.94 – 7.92 (m, 3H), 7.66 – 7.63 (m, 1H), 7.54 (t, J = 7.8 Hz, 2H), 7.26 – 7.24 (m, 1H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ 176.98, 164.44, 139.69, 139.20, 136.16, 133.66, 132.35, 129.10, 128.93, 127.89. The spectral characteristics are in agreement with spectral data previously reported.[3]

HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{13}H_9NNaO_3S$ 282.0201; found 282.0180.

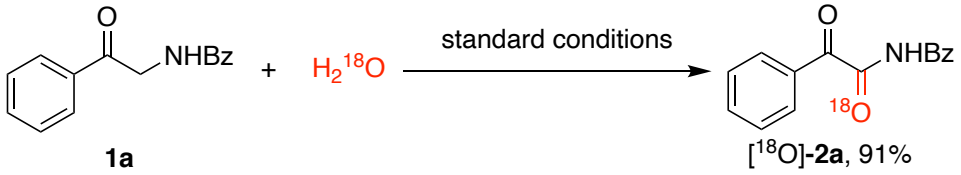
5. Mechanistic studies

(a) Free radical capture experiment

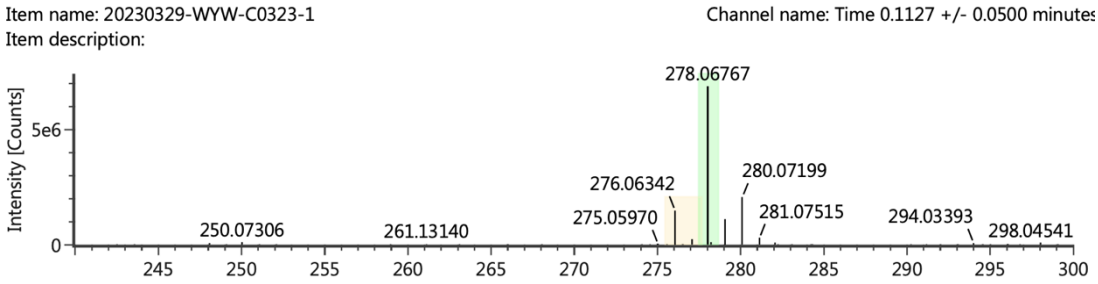


The reaction was operated according to the general procedure with 2.0 equiv of TEMPO (0.4 mmol). No Tempo-bound adduct was determined by HRMS and the product **2a** was isolated by chromatography in 90% yield (45.3 mg).

(b) ^{18}O Labeling experiment

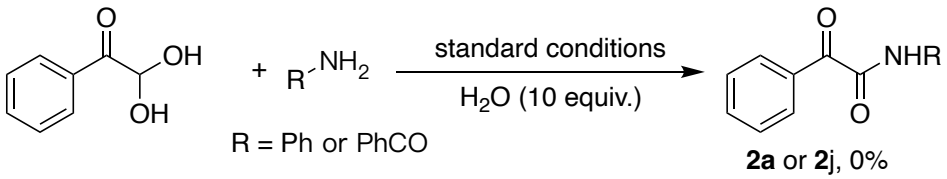


The reaction was operated according to the general procedure with $H_2{}^{18}O$ instead of $H_2{}^{16}O$. The product **2a** was isolated by chromatography and determined by the HRMS. The peak of [^{18}O]-**2a** was detected [HRMS (ESI) Calcd for $(C_{15}H_{11}NNaO_2{}^{18}O)^+$: 278.0679; Found 278.0677.



High-resolution mass spectrometry (HRMS) analysis showed that the corresponding product was composed of two species of [^{16}O]-**2a** (minor) and [^{18}O]-**2a** (major) because the reaction of by-product HI with air provided a trace of water for the generation of a hydroxyl anion under the alkaline conditions. Furthermore, when the reaction was carried out under an Ar atmosphere, **2a** was still obtained without loss of yield, suggesting that molecular oxygen from air did not serve as the oxygen source in present transformation.

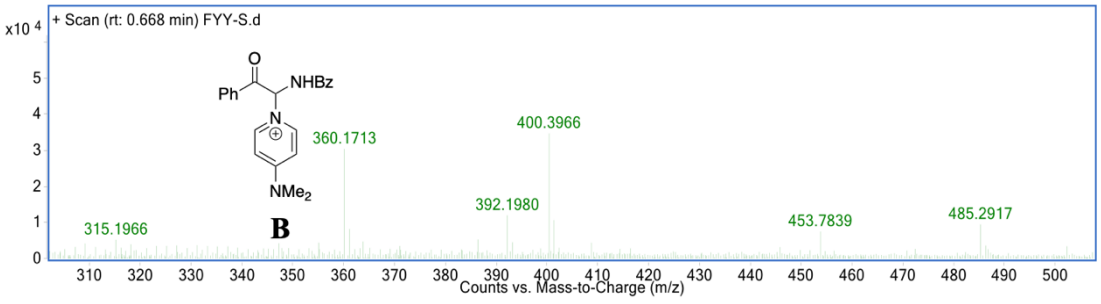
(c) Verification of α-ketoimine intermediate



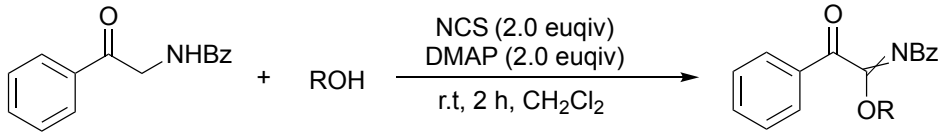
To a tube was charged with phenylglyoxal monohydrate (0.2 mmol, 30.4 mg), aniline (1 equiv., 0.2 mmol, 36.5μL) or benzamide (1 equiv., 0.2 mmol, 24.2 mg) and dioxane (2 mL), then the reaction mixture was stirred for 1 h at room temperature. Add I_2 (2 equiv., 0.4 mmol, 101.5 mg), DMAP (4 equiv., 0.8 mmol, 97.8 mg), and H_2O (10 equiv., 2 mmol, 36 μL) to the system, and continue stirring for 12 h at room temperature. The reaction mixture was detected by TLC and no product **2a** or **2j** was obtained.

(d) The intermediate captur experiment

To a tube was charged with I_2 (2 equiv., 0.4 mmol, 101.5 mg), DMAP (4 equiv., 0.8 mmol, 97.8 mg), and H_2O (10 equiv., 2 mmol, 36 μL) and dioxane (2 mL), then the reaction mixture was stirred for 5 min at room temperature. Add α-Amino ketone **1a** (0.2 mmol) to the suspension system and continue stirring at room temperature for 10 minutes. To the crude reaction mixture was added H_2O (2 mL). The aqueous solution was determined by the HMRS. The peak of intermediate **B** was detected [HRMS (ESI) Calcd for $(C_{22}H_{22}N_3O_2)^+$: 360.1707, Found: 360.1713].

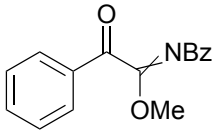


6. The reaction of 1a with alcohols



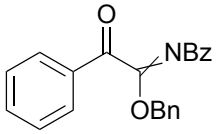
To a tube was charged with NCS (2 equiv, 0.4 mmol, 53.4 mg), DMAP (2 equiv, 0.4 mmol, 48.8 mg), alcohol (2 equiv, 0.4 mmol) and CH_2Cl_2 (2 mL), then the reaction mixture was stirred for 5 min at room temperature. Add α-Amino ketone **1a** (0.2 mmol,

47.8 mg) to the suspension system and continue stirring for 2 h at room temperature. After completion of the reaction, the crude reaction mixture was purified by flash column chromatography on silica gel to afford the desired product **3**. ***Cautions: The products are sensitive to acid and moisture.***



Methyl *N*-benzoyl-2-oxo-2-phenylacetimidate (**3a**): The general procedure was performed using MeOH. Purification by flash chromatography (petroleum ether: EtOAc = 4:1) afforded compound **3a** (49.5 mg, 93%) as a colorless oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (d, *J* = 7.8 Hz, 2H), 7.91 (d, *J* = 7.8 Hz, 2H), 7.64 – 7.55 (m, 2H), 7.49 – 7.43 (m, 4H), 4.14 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 187.31, 176.65, 161.39, 134.62, 133.64, 133.32, 129.91, 129.78, 128.75, 128.38, 55.48.



Benzyl N-benzoyl-2-oxo-2-phenylacetimidate (**3b**): The general procedure was performed using BnOH. Purification by flash chromatography (petroleum ether: EtOAc = 4:1) afforded compound **3b** (56.2 mg, 82%) as a white solid.

^{1}H NMR (400 MHz, Chloroform-d) δ 7.98 – 7.95 (m, 2H), 7.92 – 7.89 (m, 2H), 7.63 – 7.54 (m, 2H), 7.51 – 7.49 (m, 2H), 7.47 – 7.40 (m, 7H), 5.57 (s, 2H); ^{13}C NMR (101 MHz, Chloroform-d) δ 187.09, 176.45, 160.43, 134.63, 134.57, 133.56, 133.30, 133.20, 132.99, 129.92, 129.78, 128.72, 128.71, 128.55, 128.33, 70.44. HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{22}H_{17}NNaO_3$ 366.1106; found 366.1105.

7. References

[1] Wang, Y.; Yang, M.; Lao, C.; Jiang, Z. Potassium-base-mediated autoxidative diastereoselective homocoupling of *n*-acyl-2-aminoacetophenones. *Org. Lett.* **2022,** *24*, 2625-2629.

[2] Moriya, T.; Takabe, S.; Maeda, S.; Matsumoto, K.; Takashima, K.; Mori, T.; Takeyama, S. Synthesis and hypolipidemic activities of 5-thienyl-4-oxazoleacetic acid-derivatives. *J. Med. Chem.* **1986,** *29*, 333-341.

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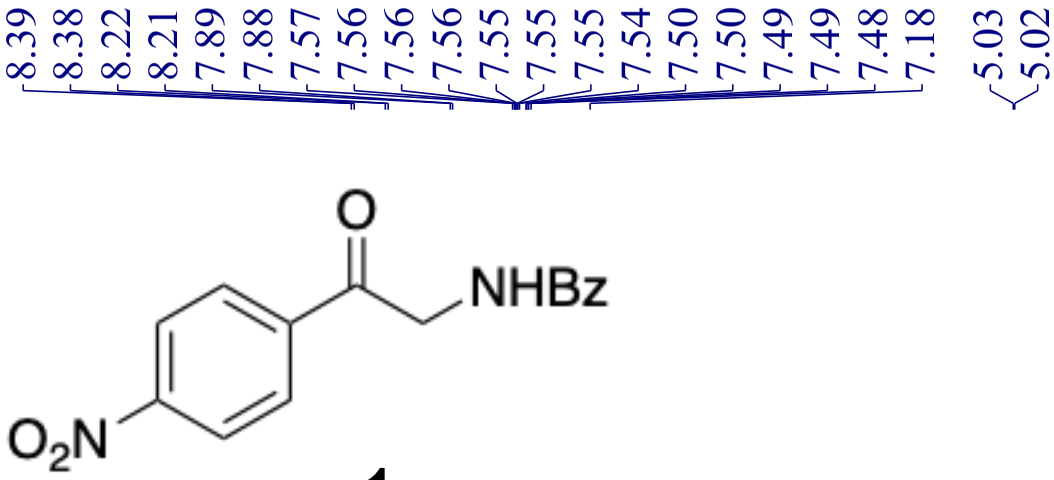
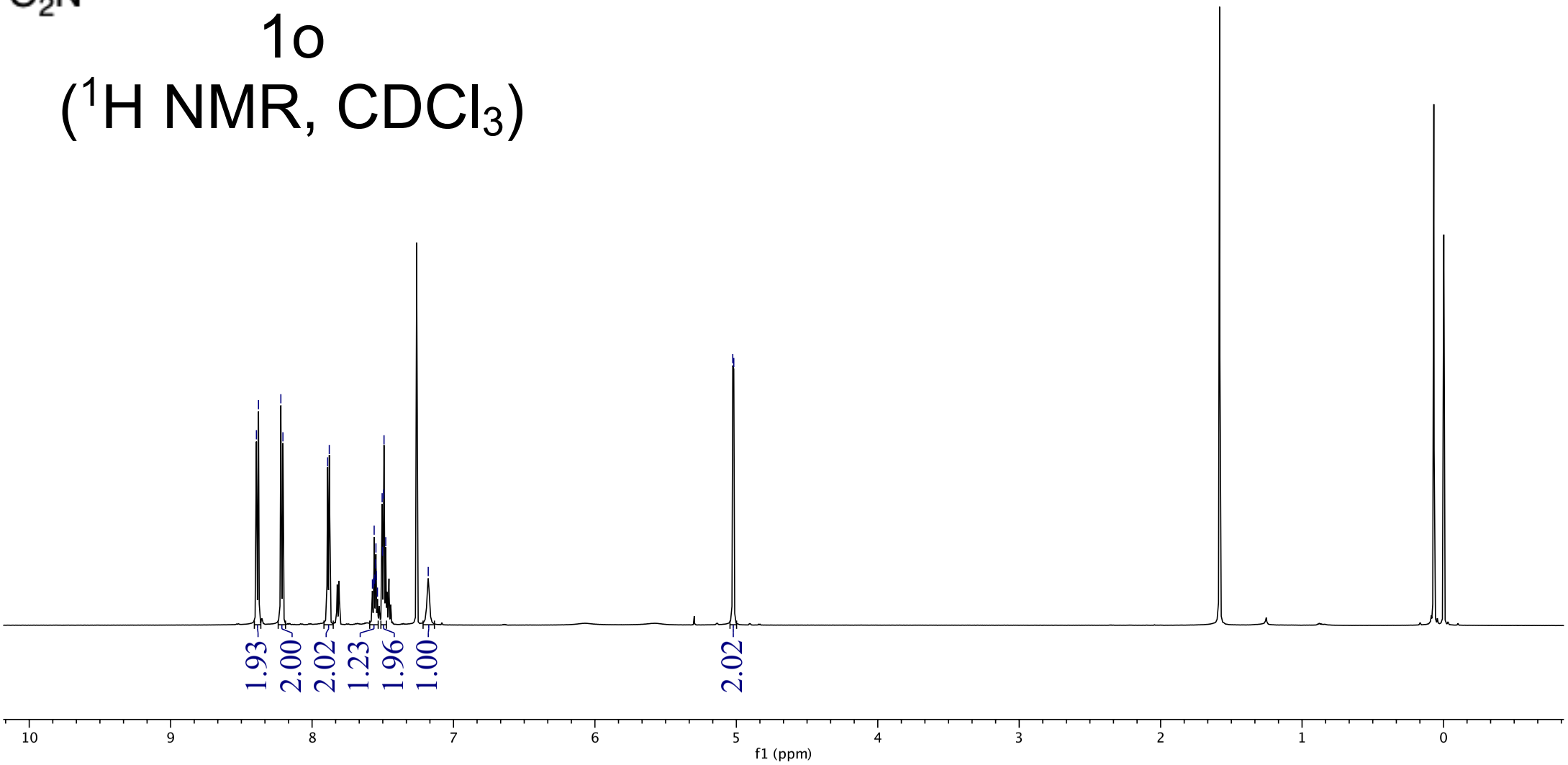
benzamidines hydrochloride: A facile access to α-ketoimides. *Org. Lett.* **2014,** *16*, 2888-2891.
[4] Ried, W.; Schopke, K. Nucleophilic reactions on chloro-*N*-(2-oxoacyl)formamidines. *Liebigs Ann. Chem.* **1988**, 141-148.
[5] Deshidi, R.; Devari, S.; Shah, B. A. Iodine-promoted oxidative amidation of terminal alkenes - synthesis of α-ketoamides, benzothiazoles, and quinazolines. *Eur. J. Org. Chem.* **2015,** *2015*, 1428-1432.

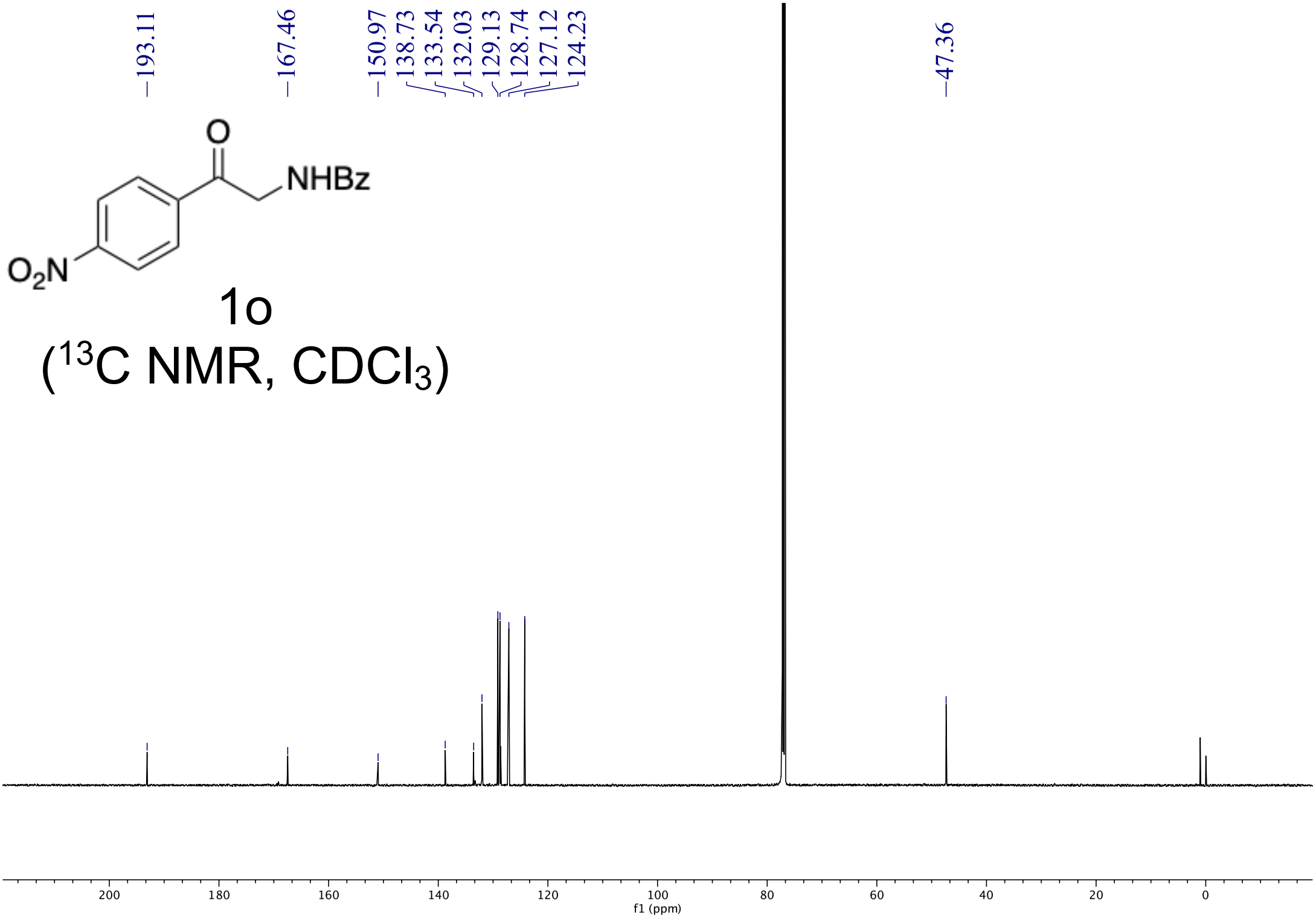
8. Copies of ^{1}H and ^{13}C NMR spectra



1o

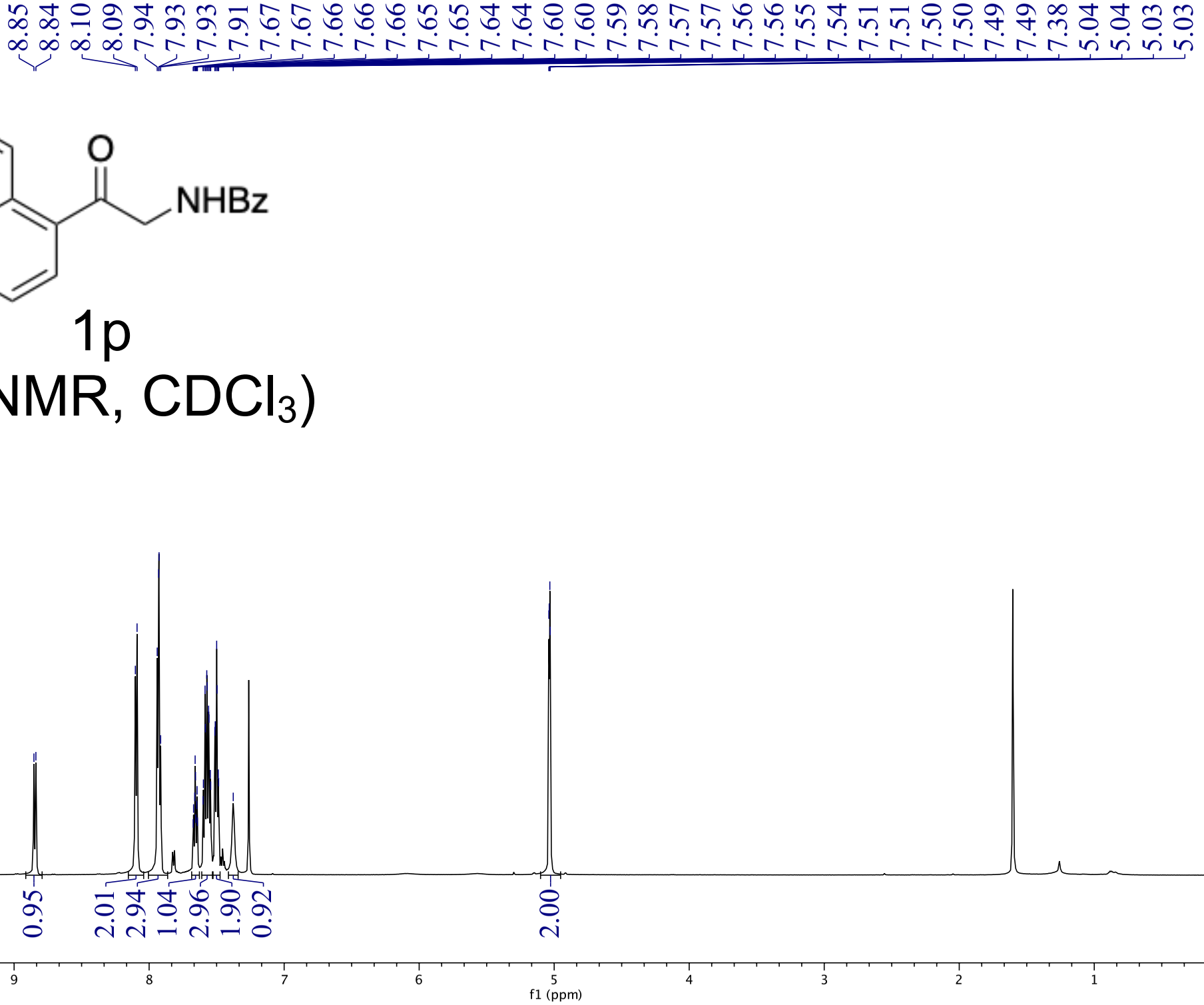
(^{1}H NMR, $CDCl_3$)





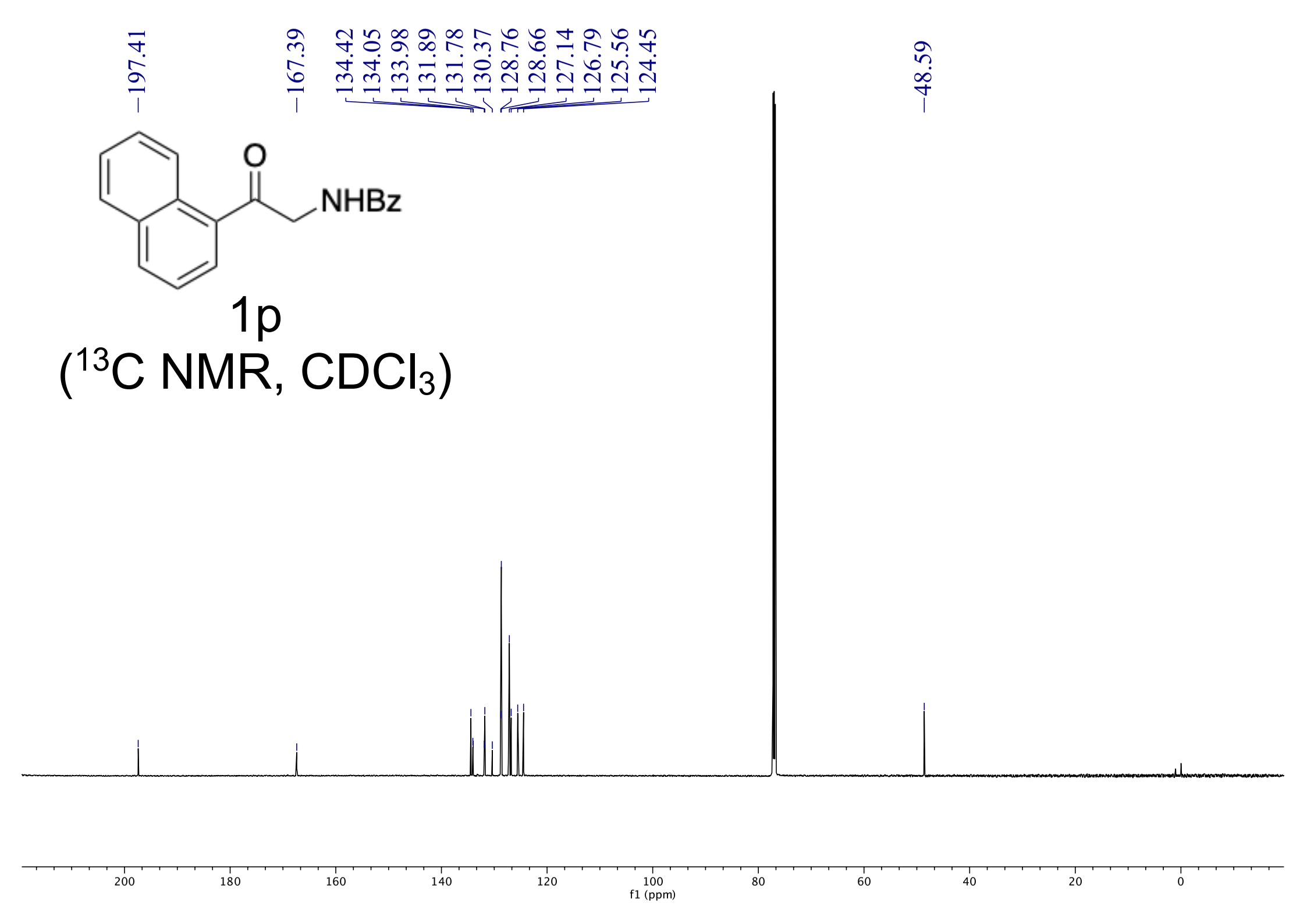
1o

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



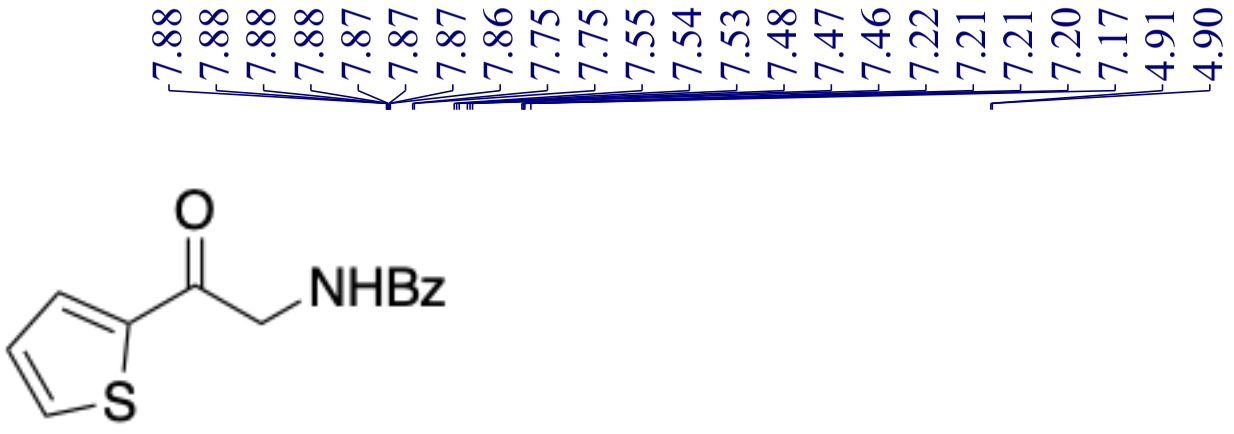
1p

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

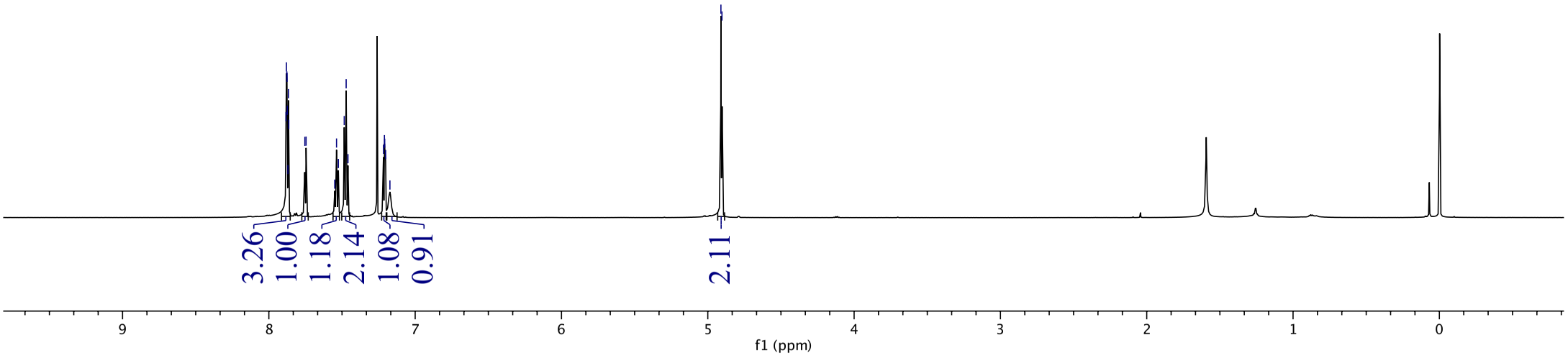


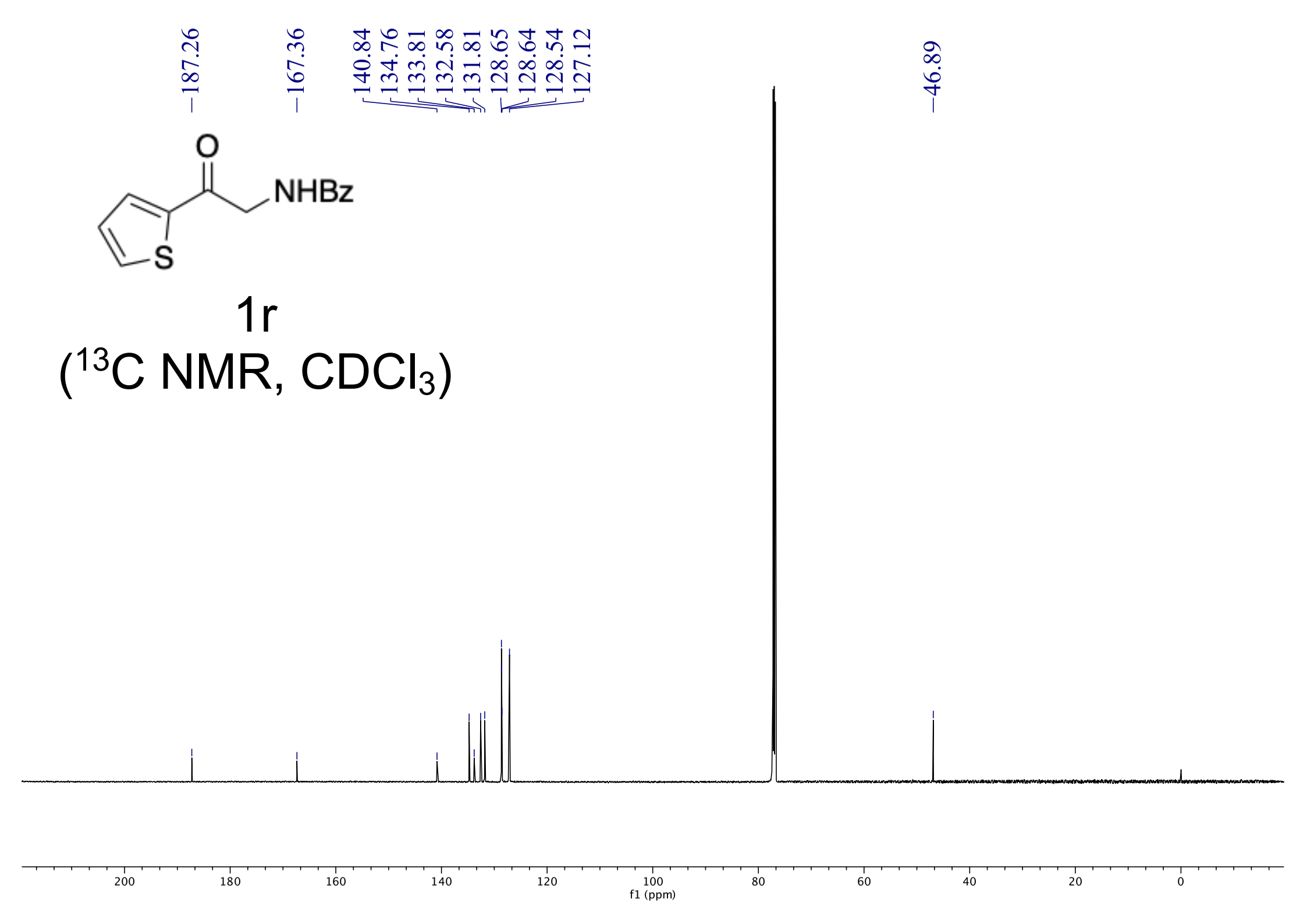
1p

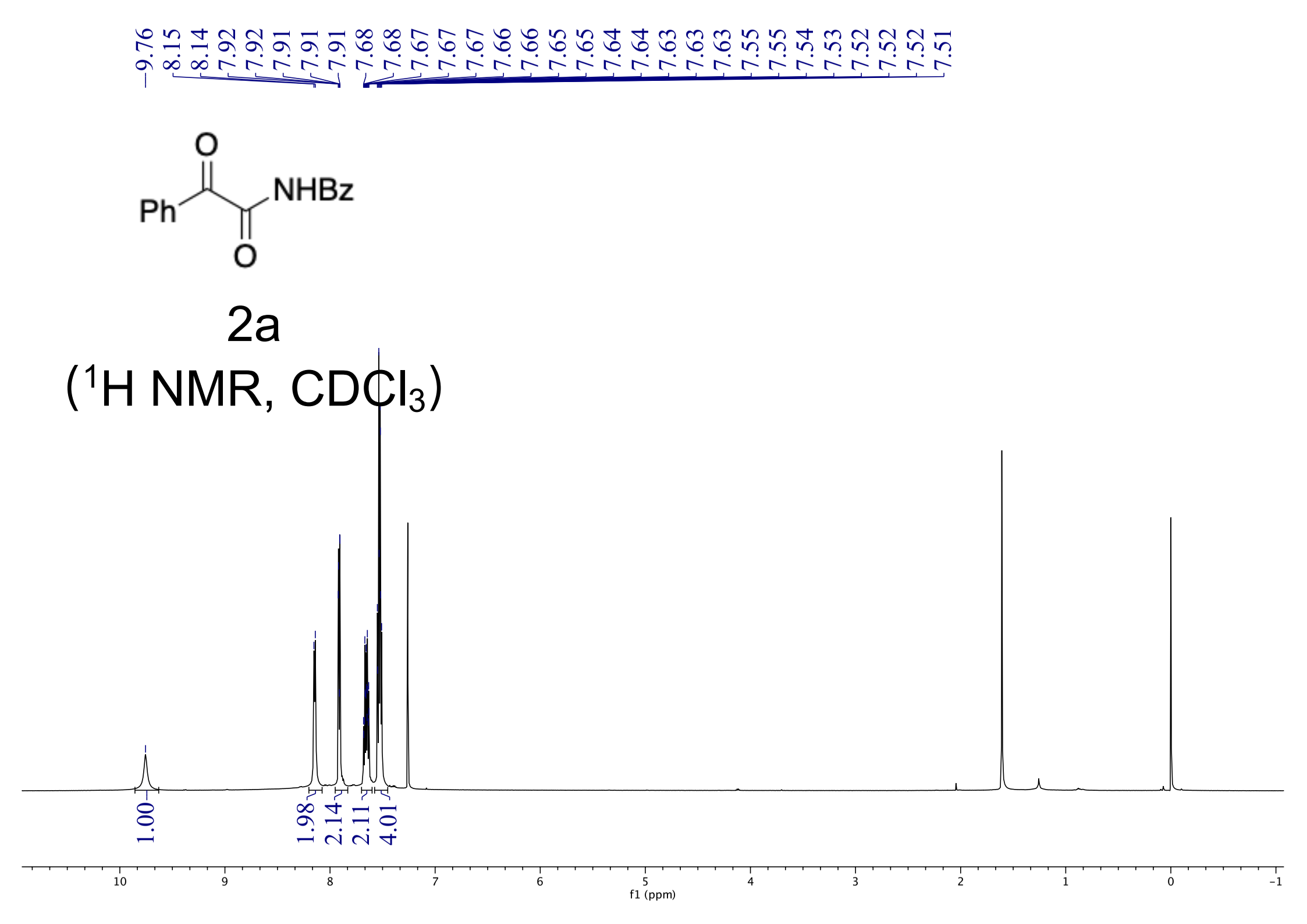
(^{13}C NMR, $CDCl_3$)

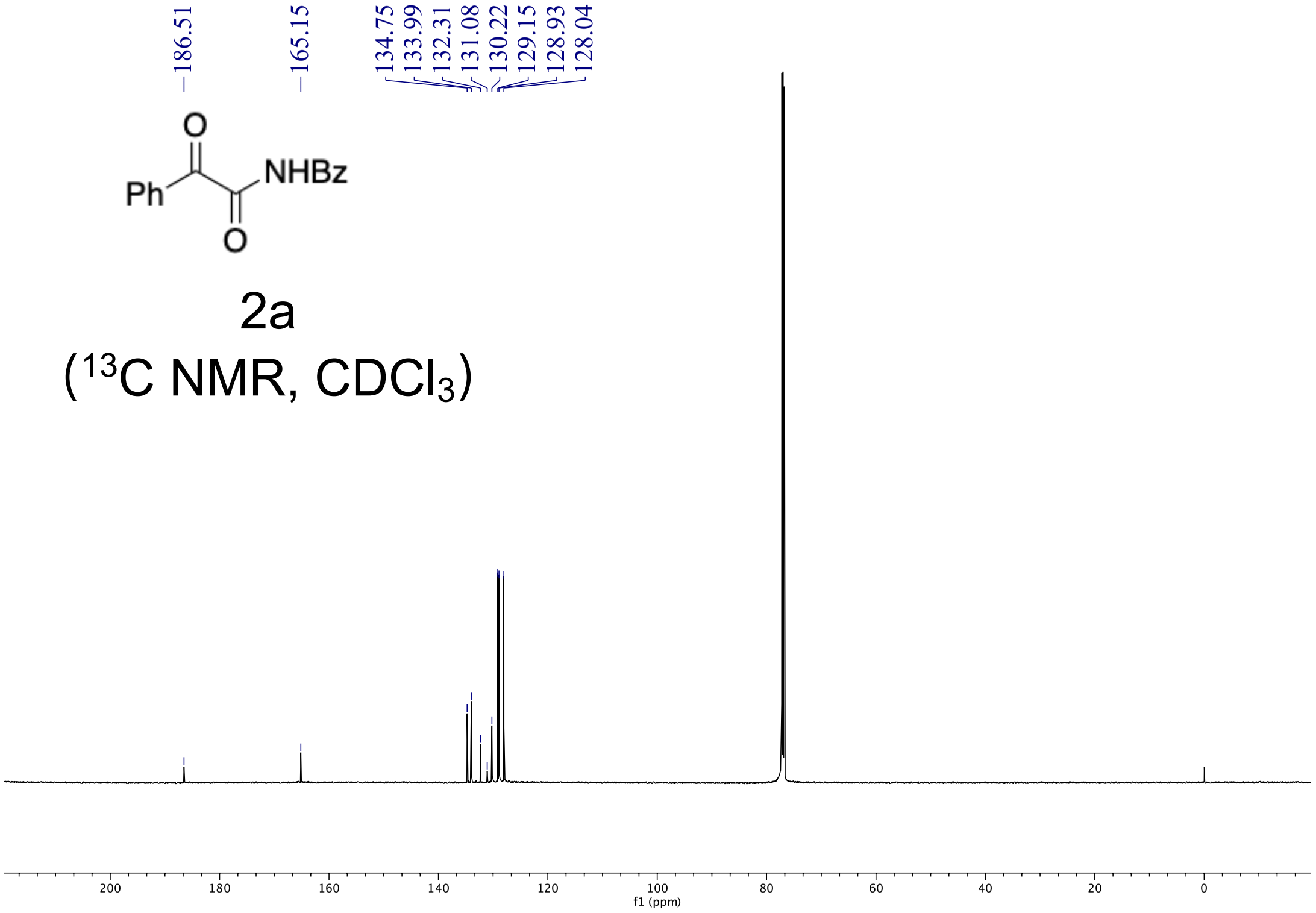


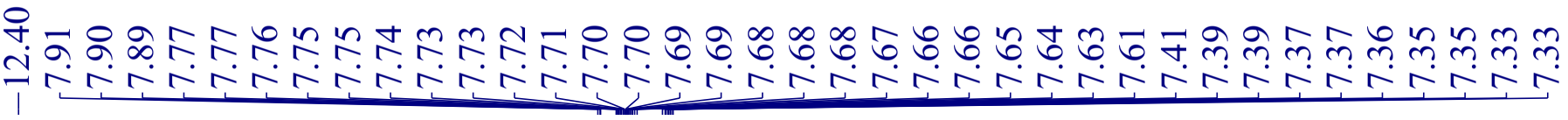
1r
(^{1}H NMR, $CDCl_3$)

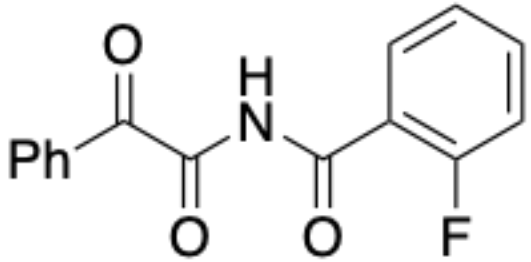



187.26
167.36
140.84
134.76
133.81
132.58
131.81
128.65
128.64
128.54
127.12
46.89
O
NHBz
S
1r
(^{13}C NMR, $CDCl_3$)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


9.76
8.15
8.14
7.92
7.92
7.91
7.91
7.91
7.68
7.68
7.67
7.67
7.67
7.66
7.66
7.65
7.65
7.64
7.64
7.63
7.63
7.63
7.55
7.55
7.54
7.53
7.52
7.52
7.52
7.51
O
NHBz
Ph
O
2a
(1H NMR, CDCl3)
1.00
1.98
2.14
2.11
4.01
10
9
8
7
6
5
4
3
2
1
0
−1
f1 (ppm)

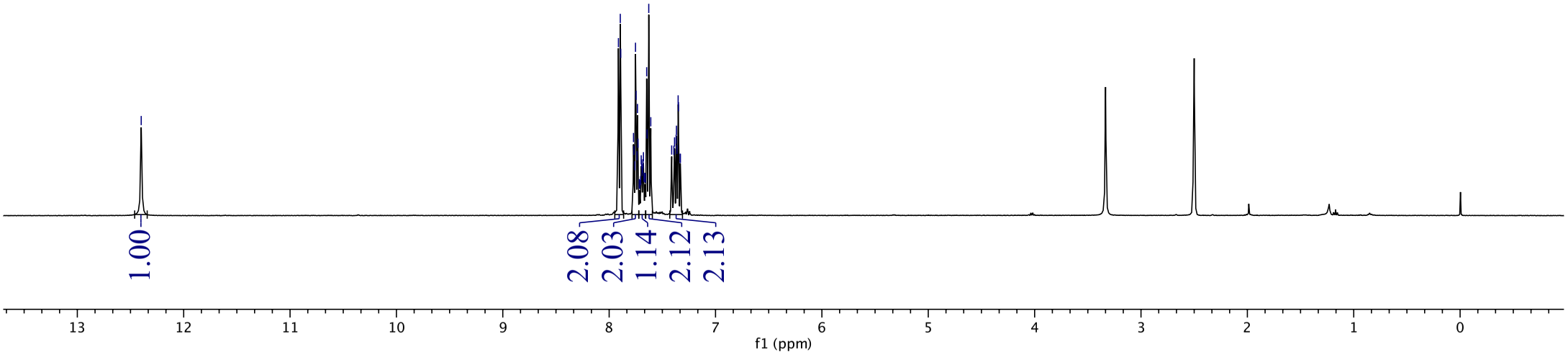

186.51
165.15
134.75
133.99
132.31
131.08
130.22
129.15
128.93
128.04
O
Ph
NHBz
O
2a
(^{13}C NMR, $CDCl_3$)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

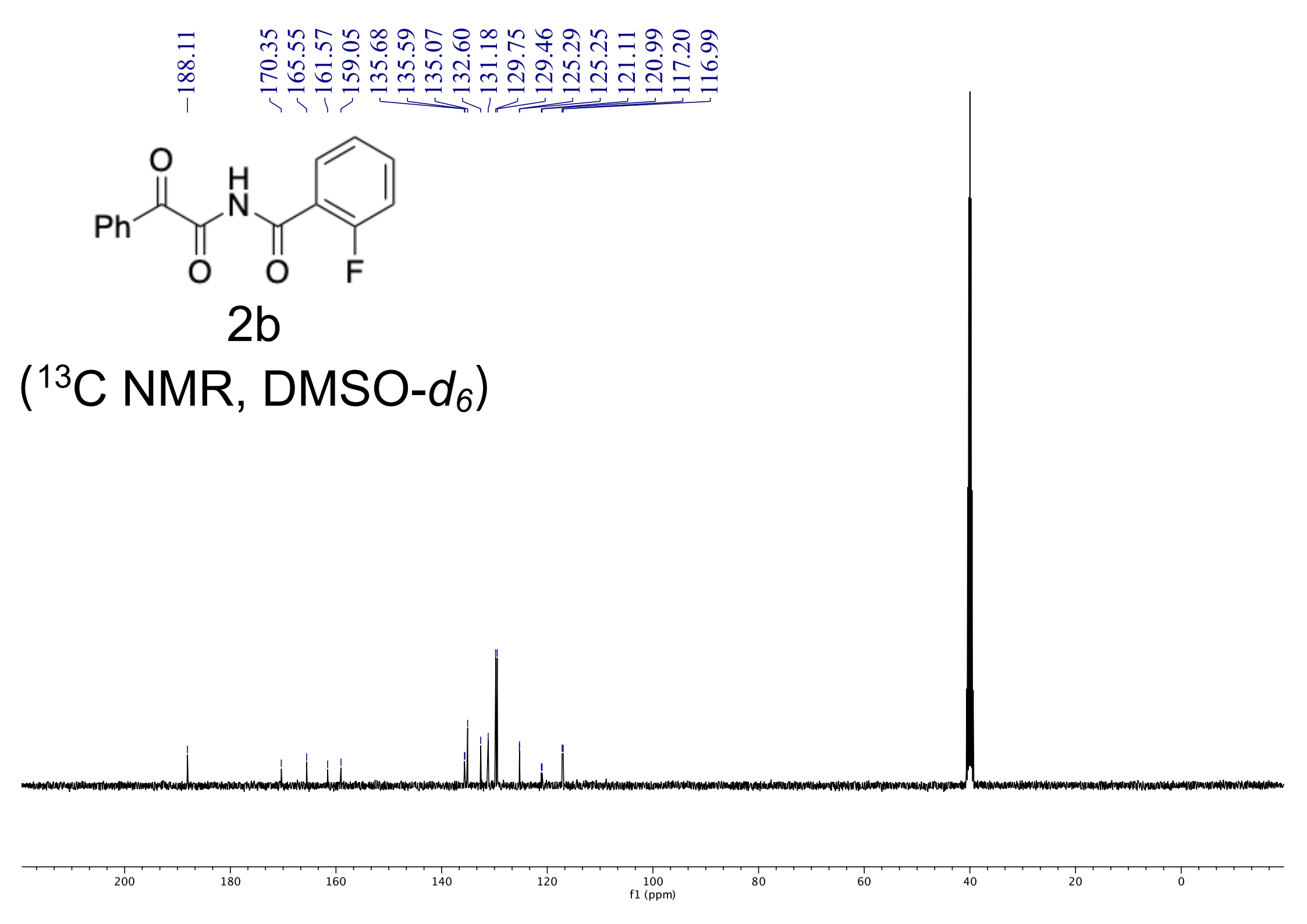




2b

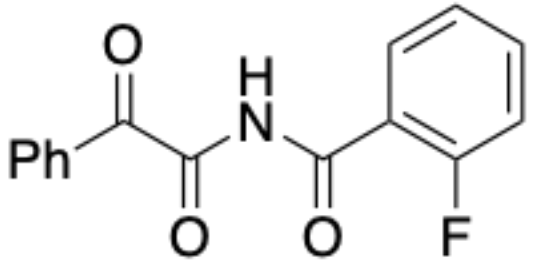
(¹H NMR, DMSO-d_6)





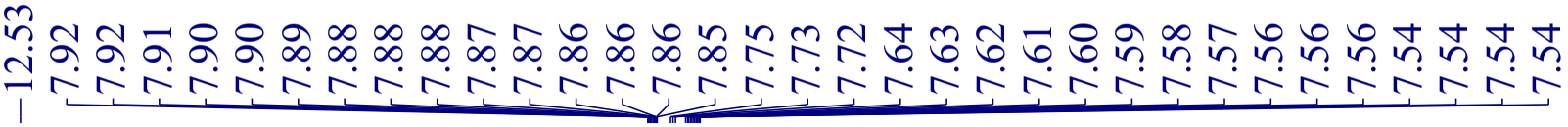
2b

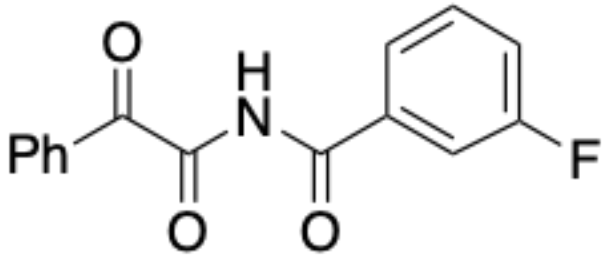
(^{13}C NMR, DMSO-d_6)



2b

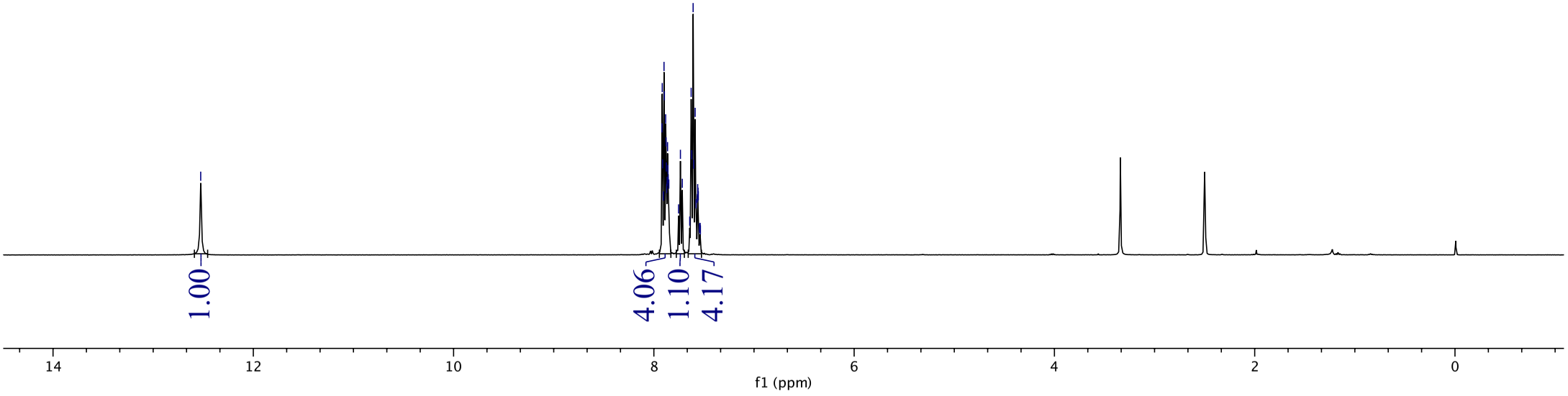
(^{19}F NMR, DMSO-d_6)

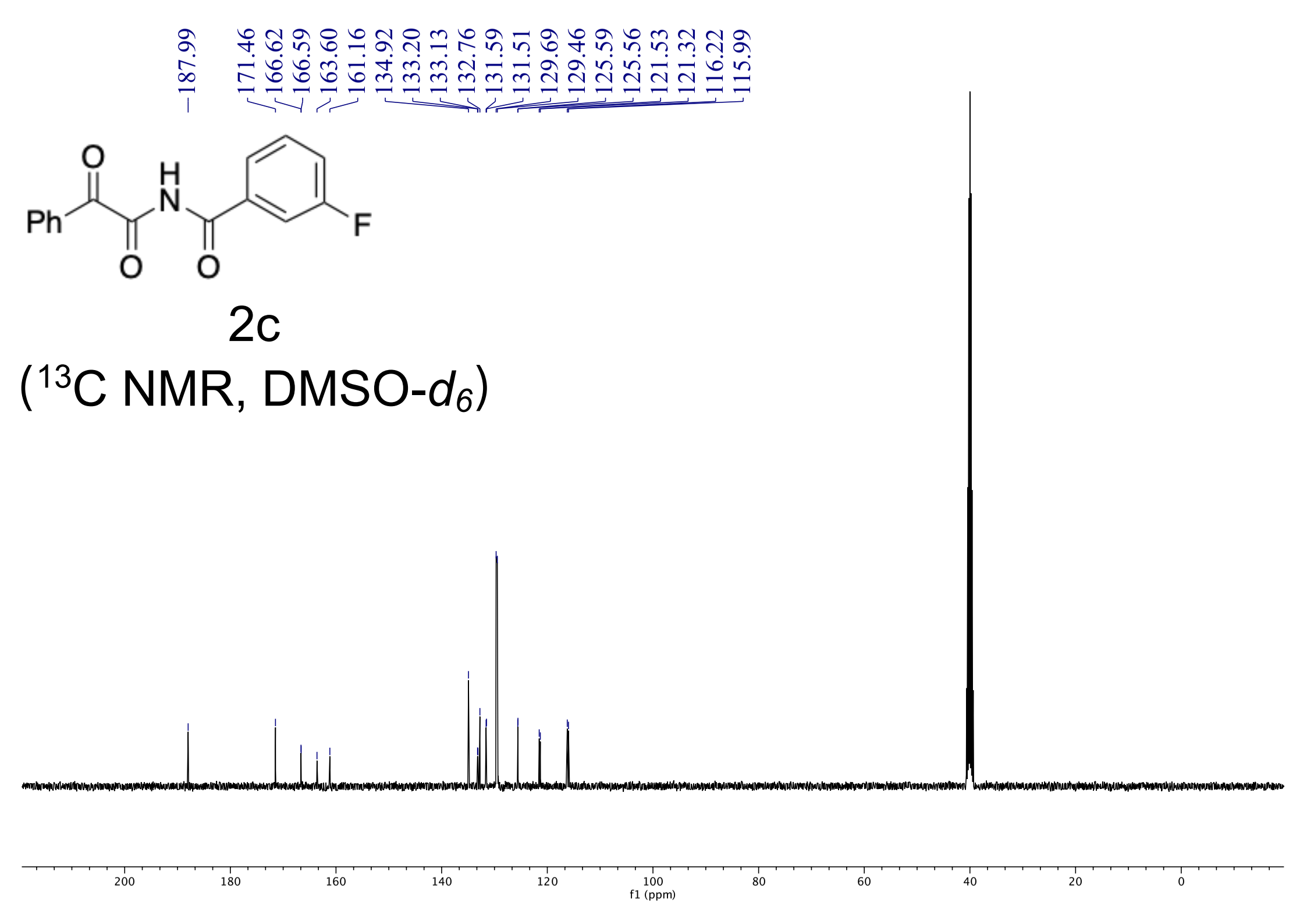




2c

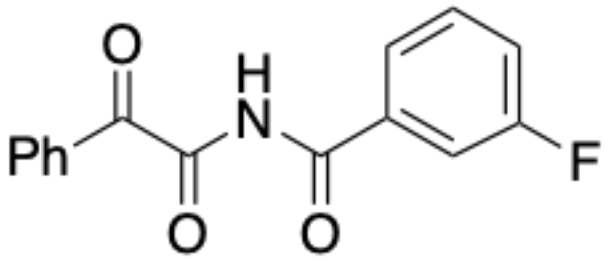
(¹H NMR, DMSO-d_6)





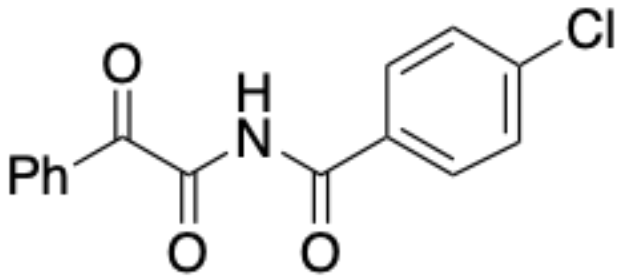
2c

(^{13}C NMR, DMSO-d_6)



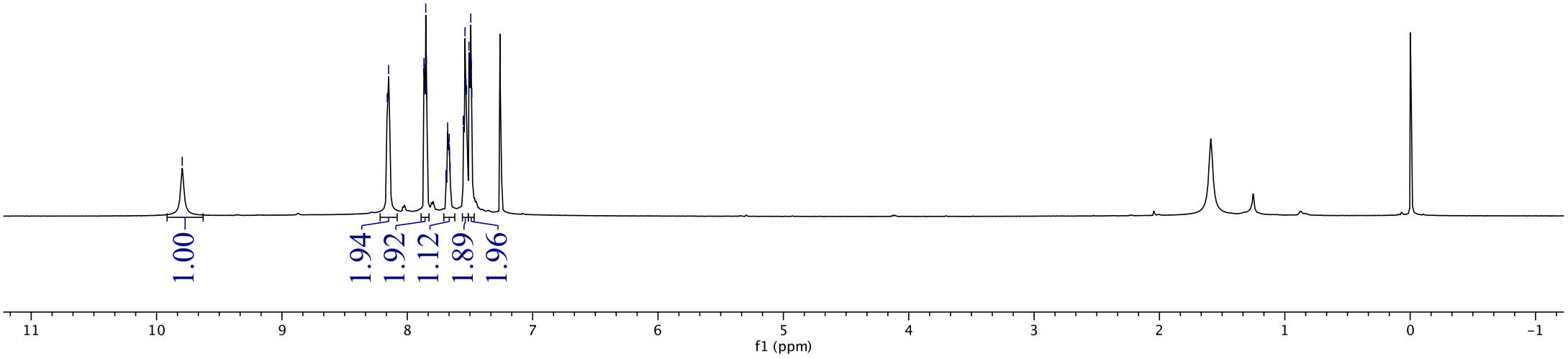
2c

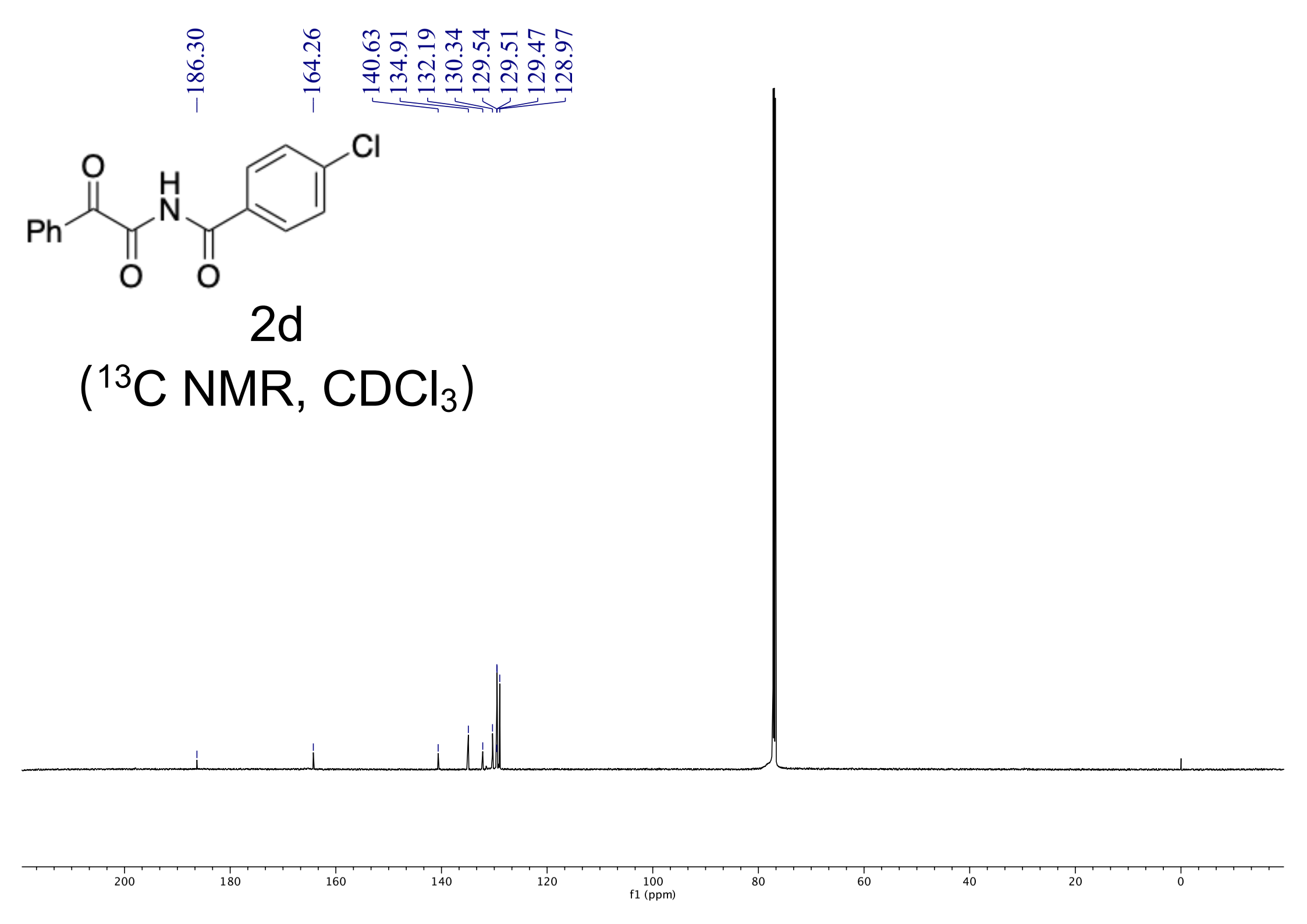
(^{19}F NMR, DMSO-d_6)

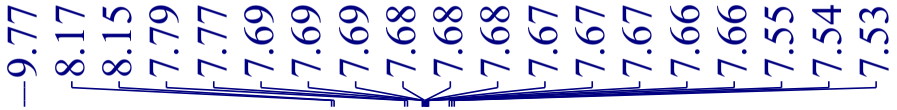


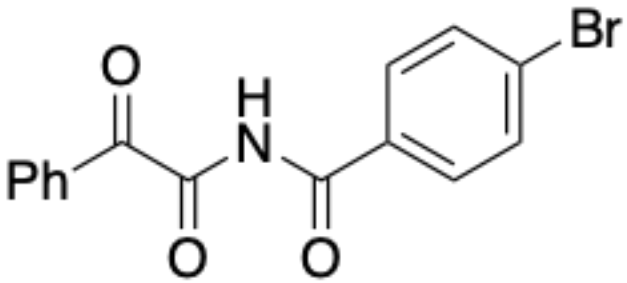
2d

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



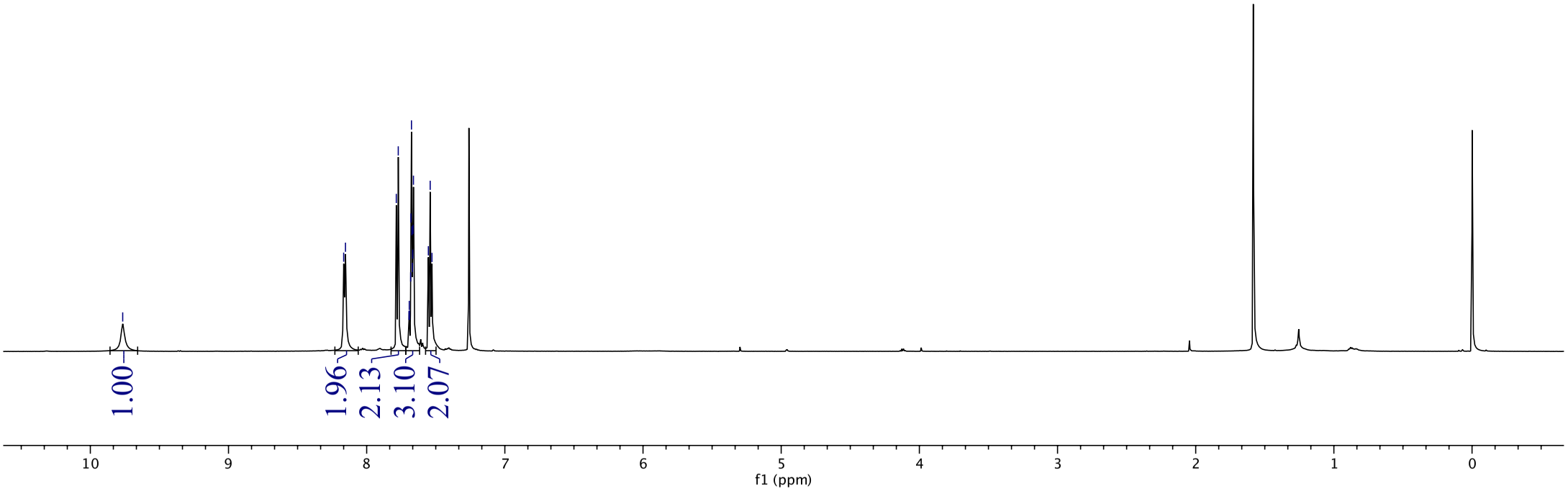

186.30
164.26
140.63
134.91
132.19
130.34
129.54
129.51
129.47
128.97
Cl
O
H
N
Ph
O
O
2d
(13C NMR, CDCl3)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

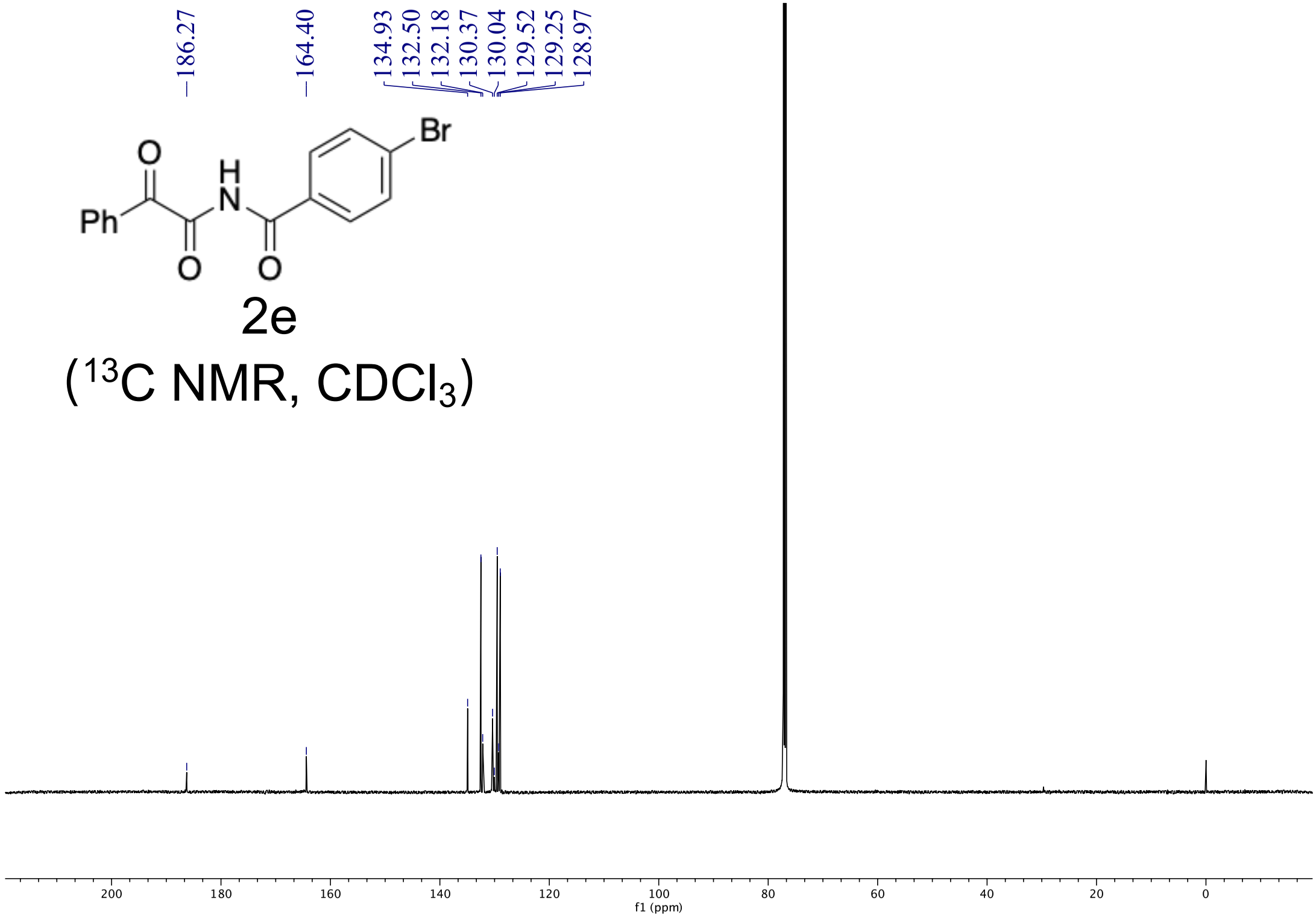




2e

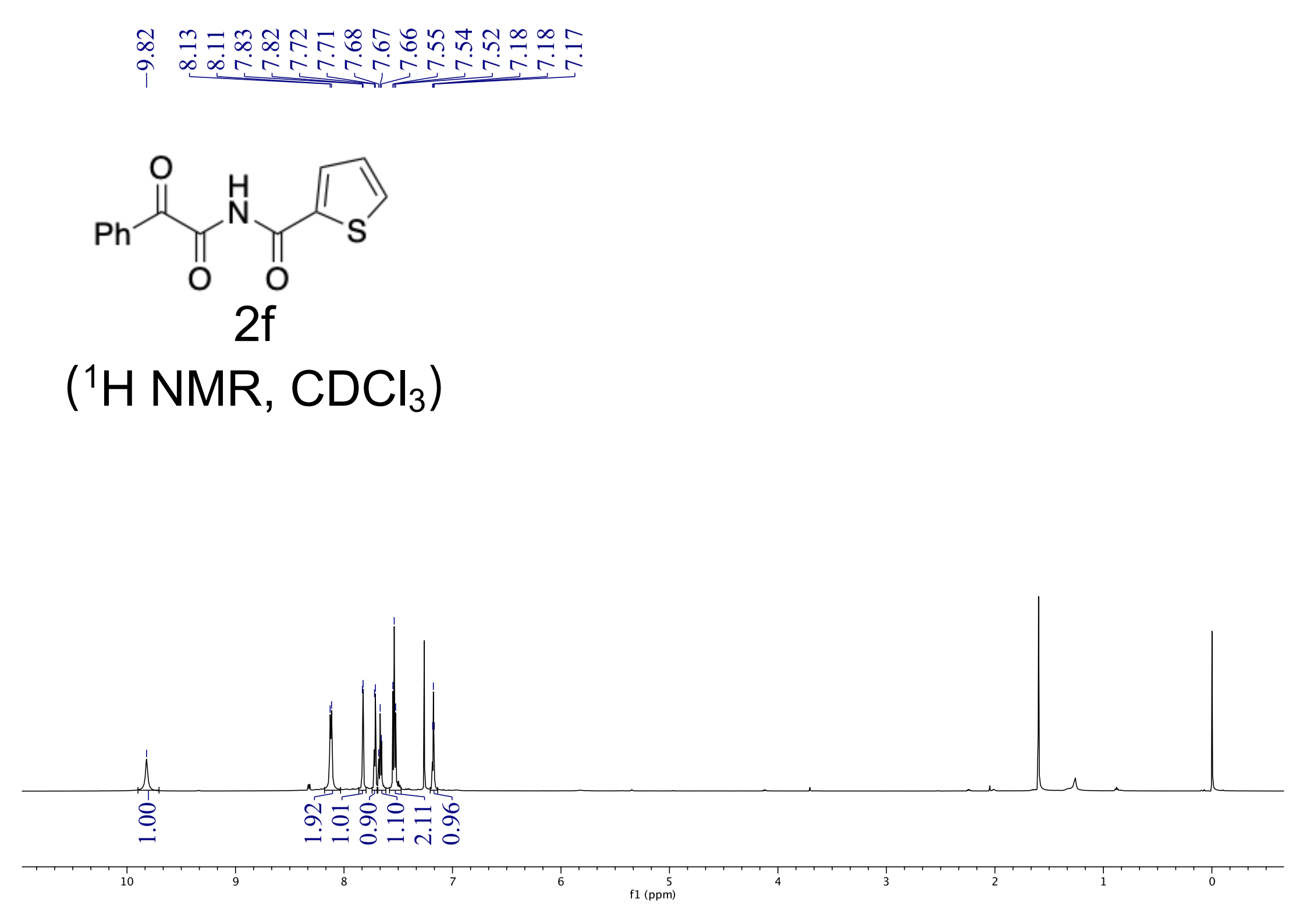
(^{1}H NMR, $CDCl_3$)





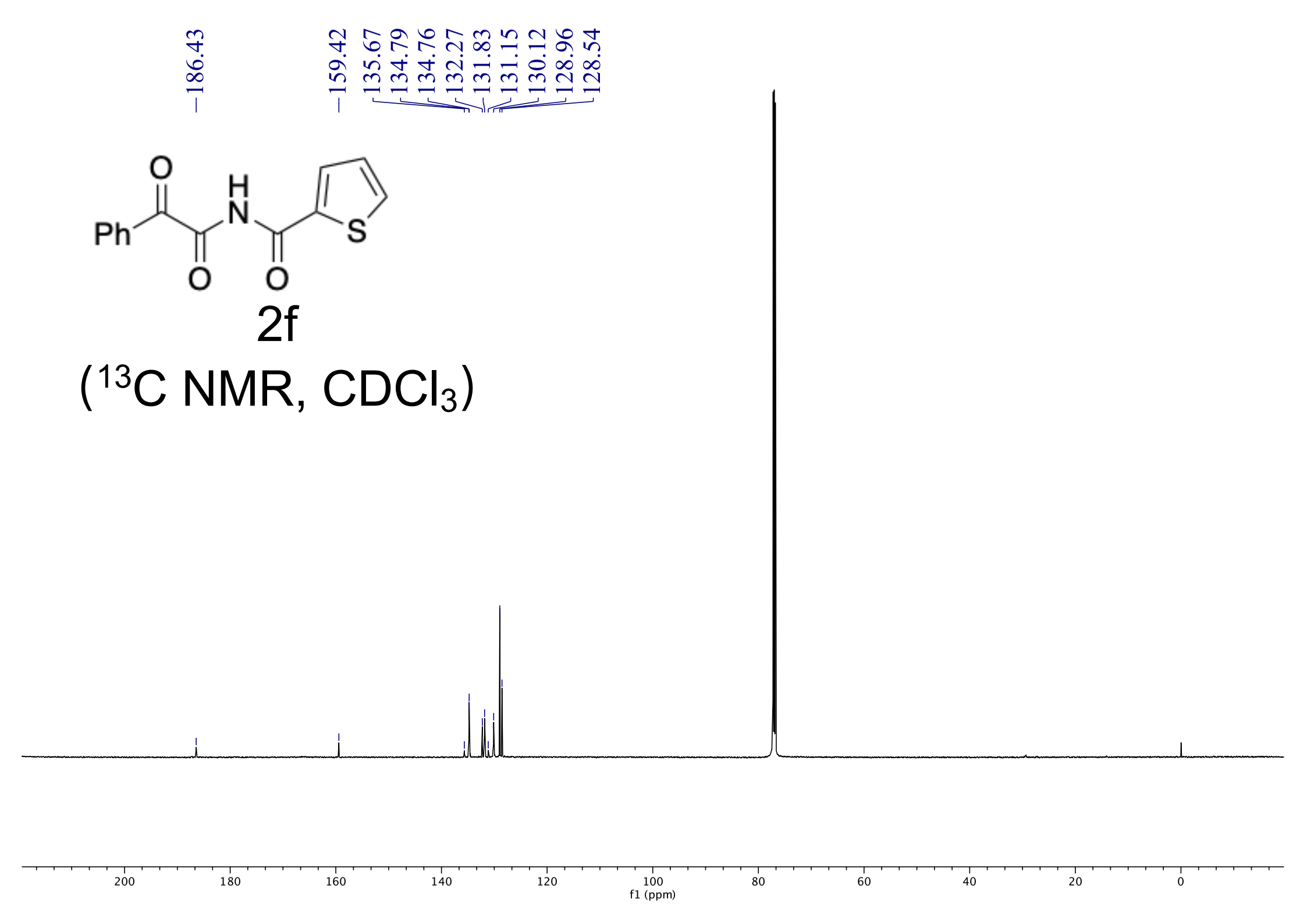
2e

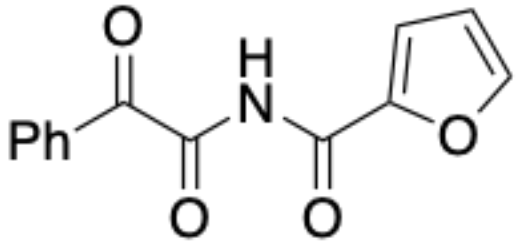
(^{13}C NMR, $CDCl_3$)



2f

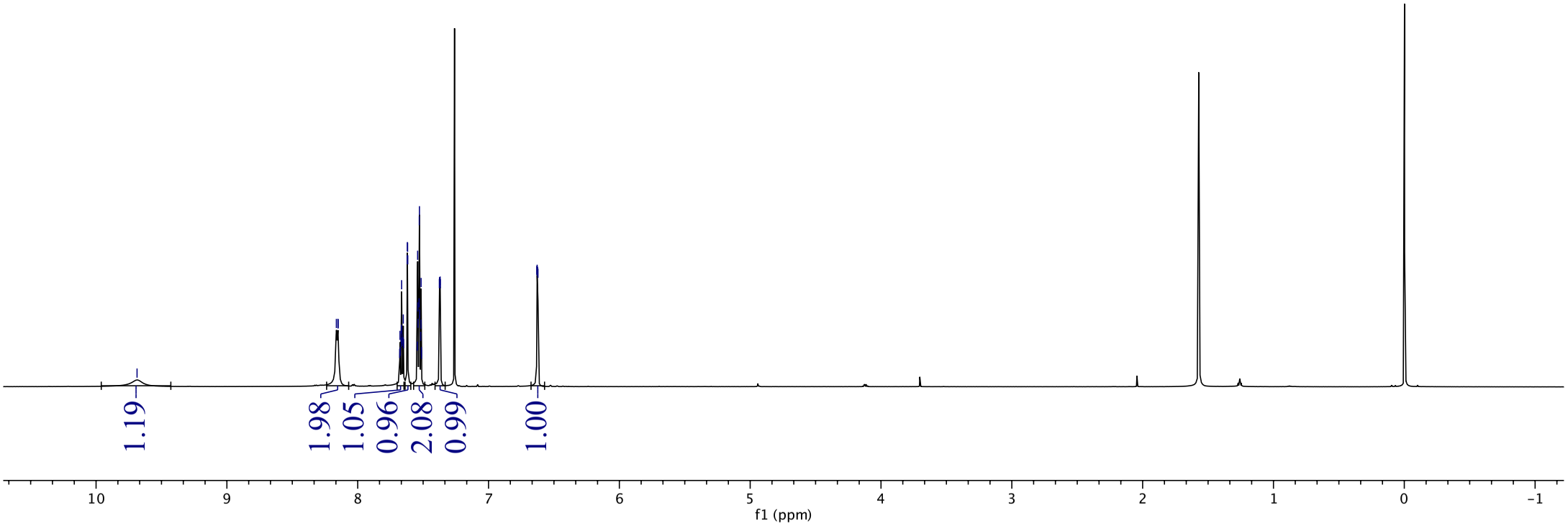
(^{1}H NMR, $CDCl_3$)

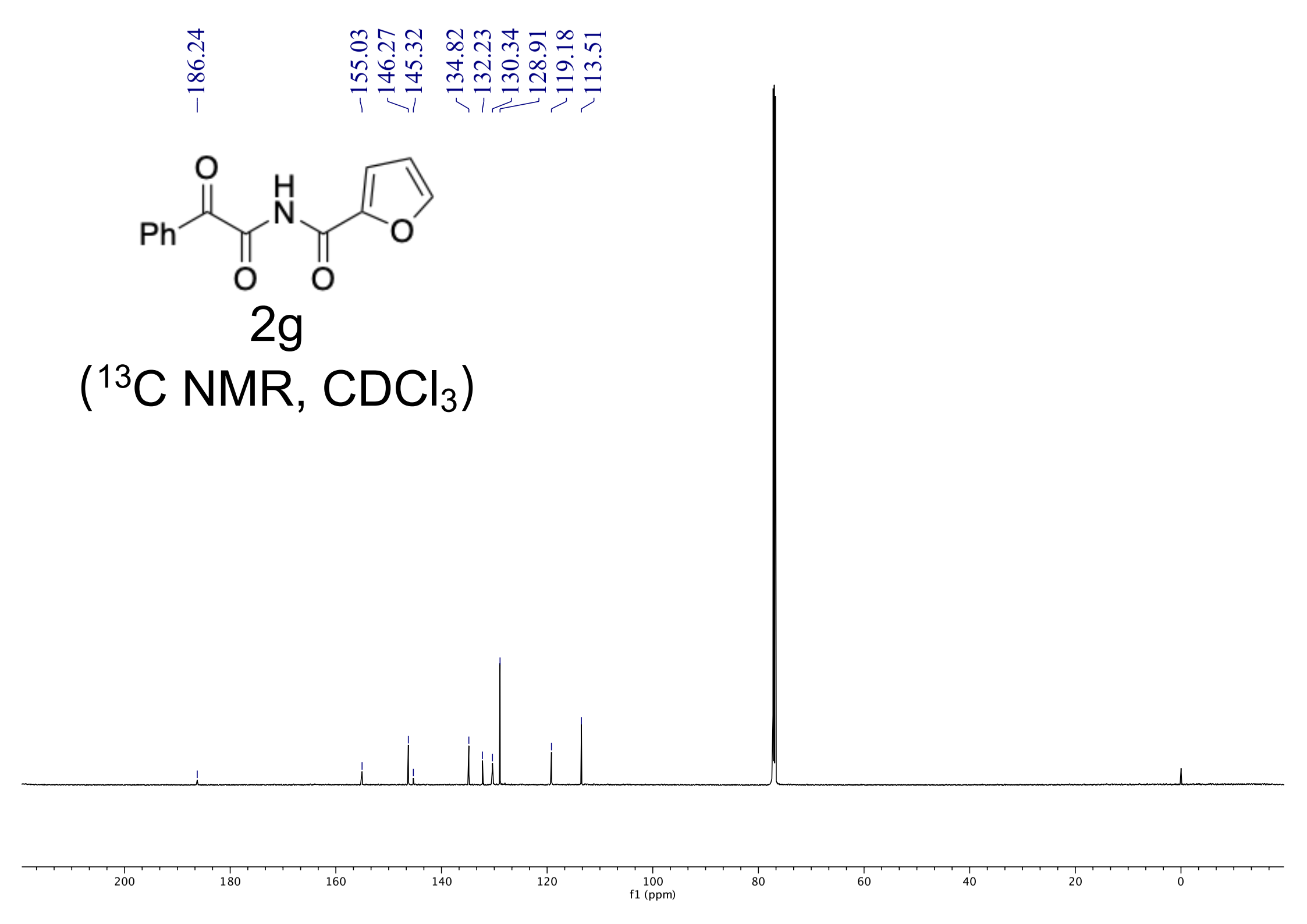

186.43
159.42
135.67
134.79
134.76
132.27
131.83
131.15
130.12
128.96
128.54
O
H
N
Ph
O
O
S
2f
(13C NMR, CDCl3)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

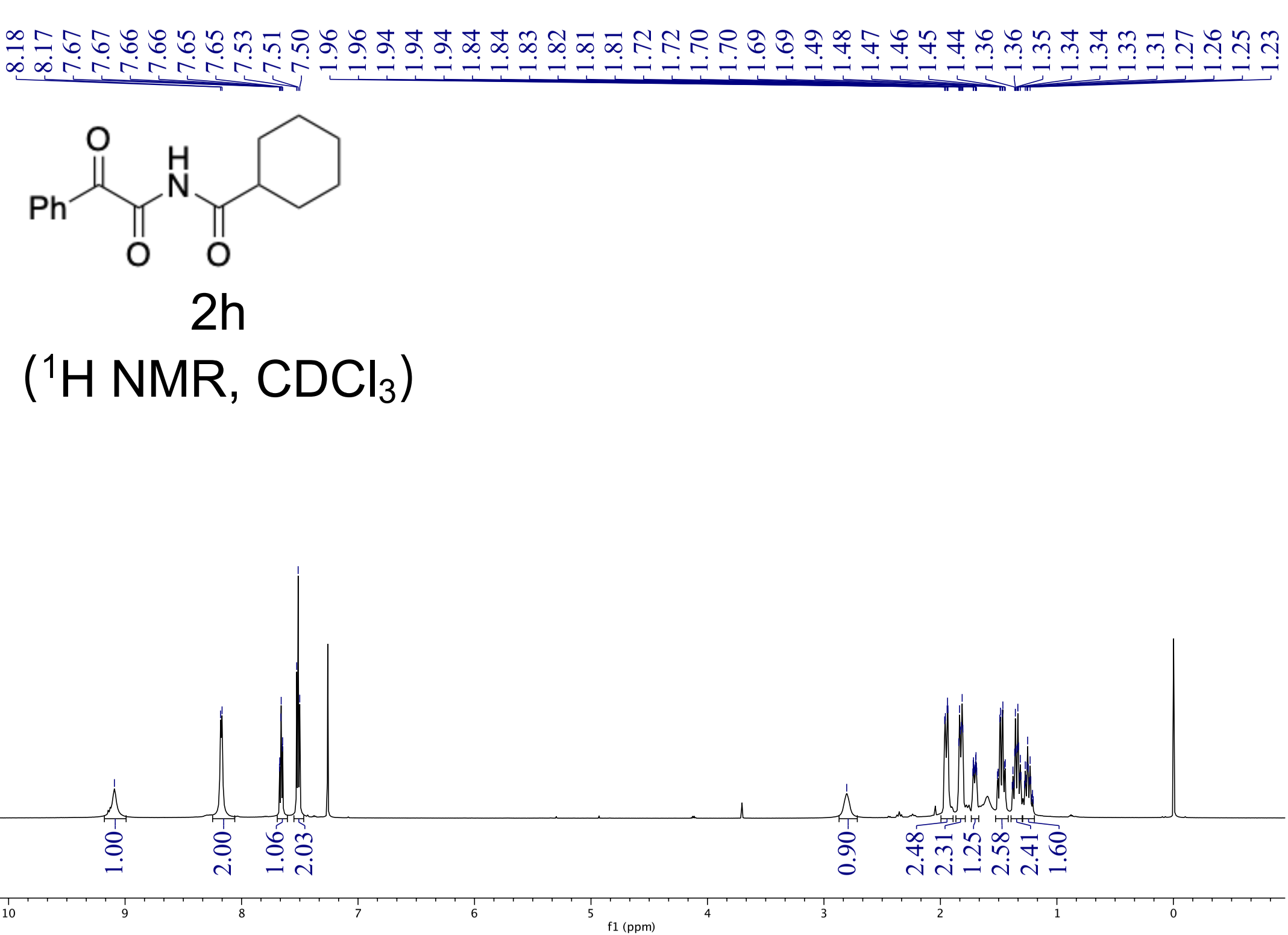


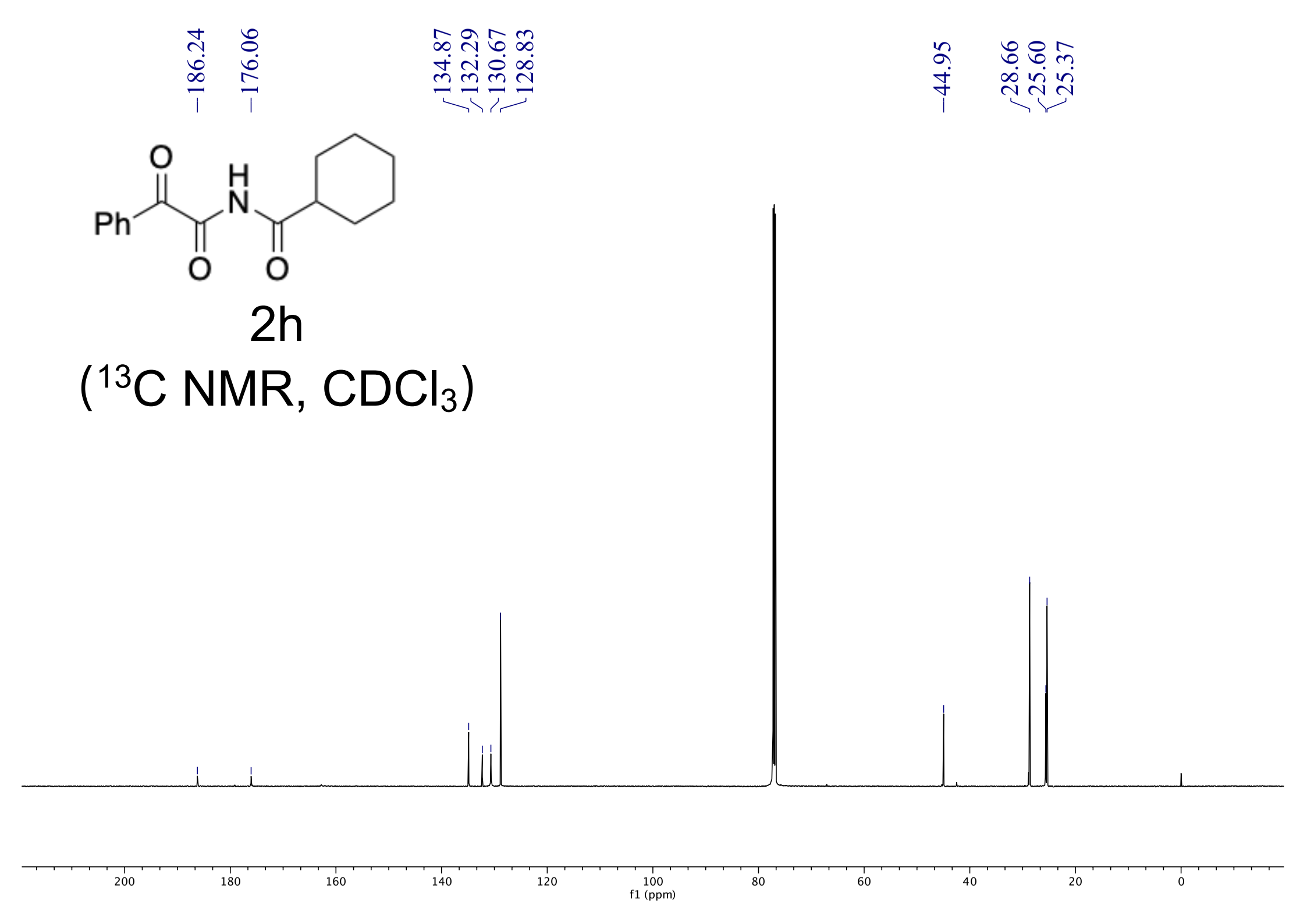
2g

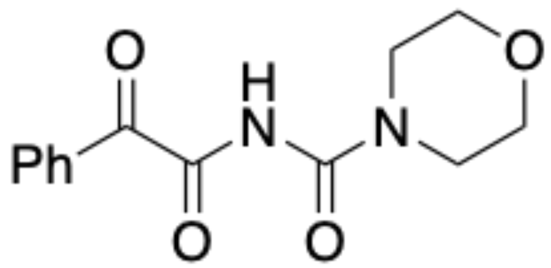
(^{1}H NMR, $CDCl_3$)




186.24
155.03
146.27
145.32
134.82
132.23
130.34
128.91
119.18
113.51
O
H
N
Ph
O
O
O
2g
(^{13}C NMR, $CDCl_3$)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

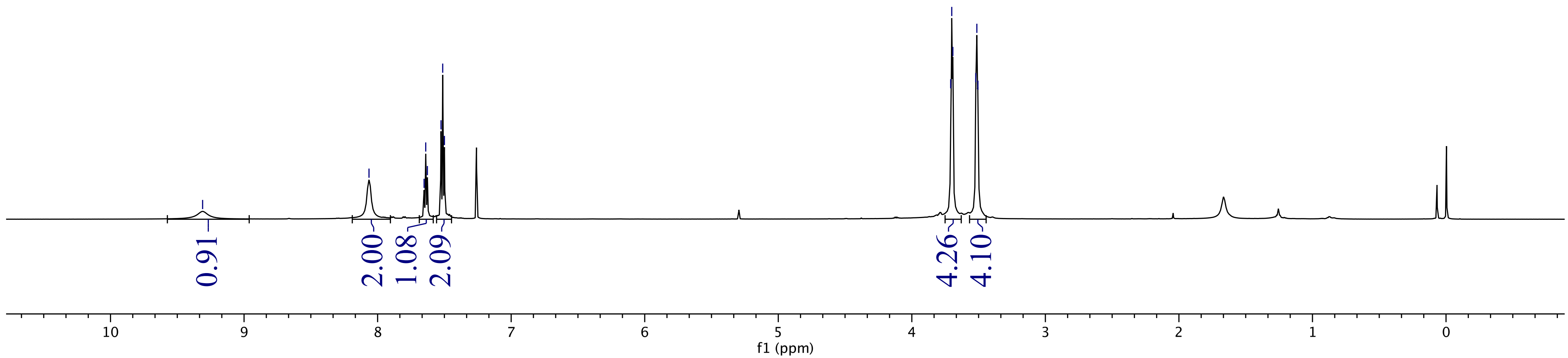

8.18
8.17
7.67
7.67
7.66
7.66
7.65
7.65
7.53
7.51
7.50
1.96
1.96
1.94
1.94
1.94
1.84
1.84
1.83
1.82
1.81
1.81
1.72
1.72
1.70
1.70
1.69
1.69
1.49
1.48
1.47
1.46
1.45
1.44
1.36
1.36
1.35
1.34
1.34
1.33
1.31
1.27
1.26
1.25
1.23
O
H
N
Ph
O
O
2h
(1H NMR, CDCl3)
1.00
2.00
1.06
2.03
0.90
2.48
2.31
1.25
2.58
2.41
1.60
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

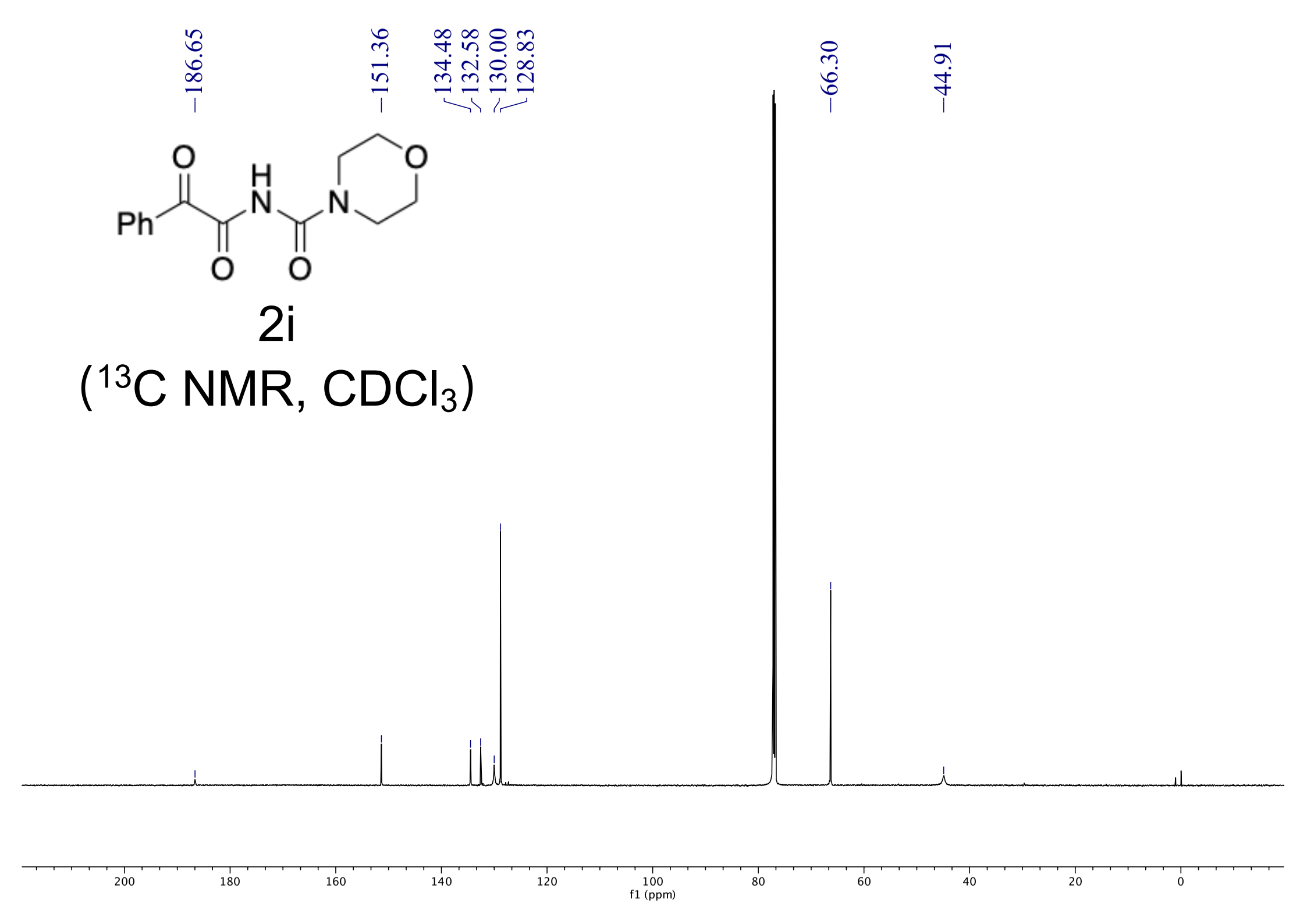

186.24
176.06
134.87
132.29
130.67
128.83
44.95
28.66
25.60
25.37
O
H
N
Ph
O
O
2h
(13C NMR, CDCl3)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



2i

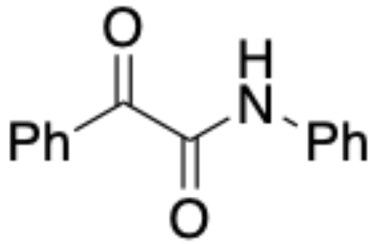
(^{1}H NMR, $CDCl_3$)





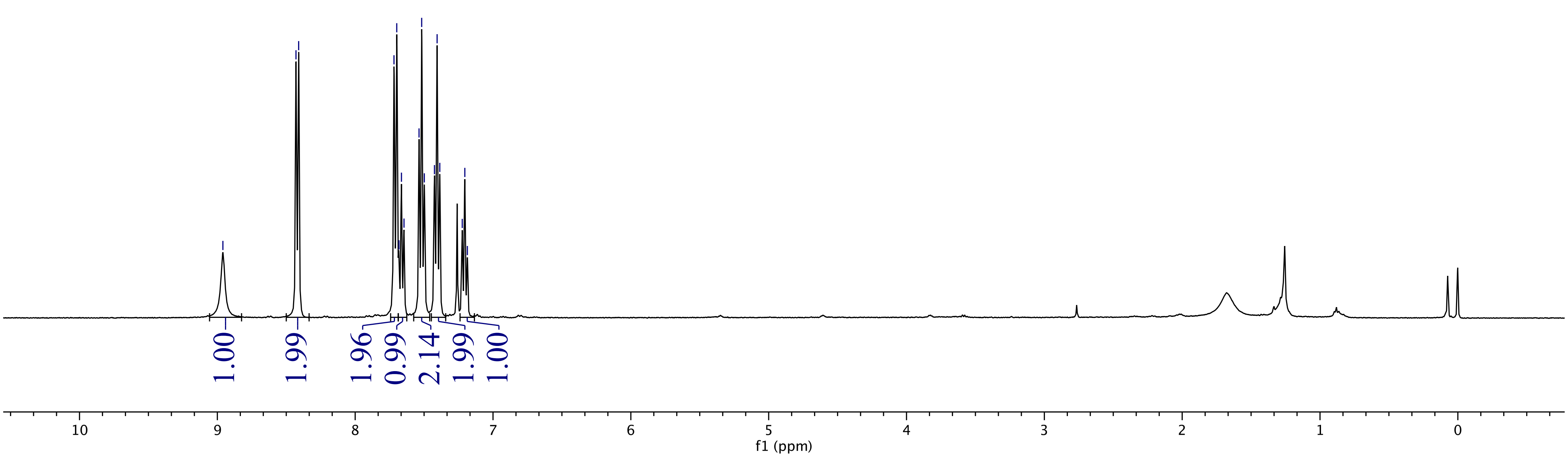
2i

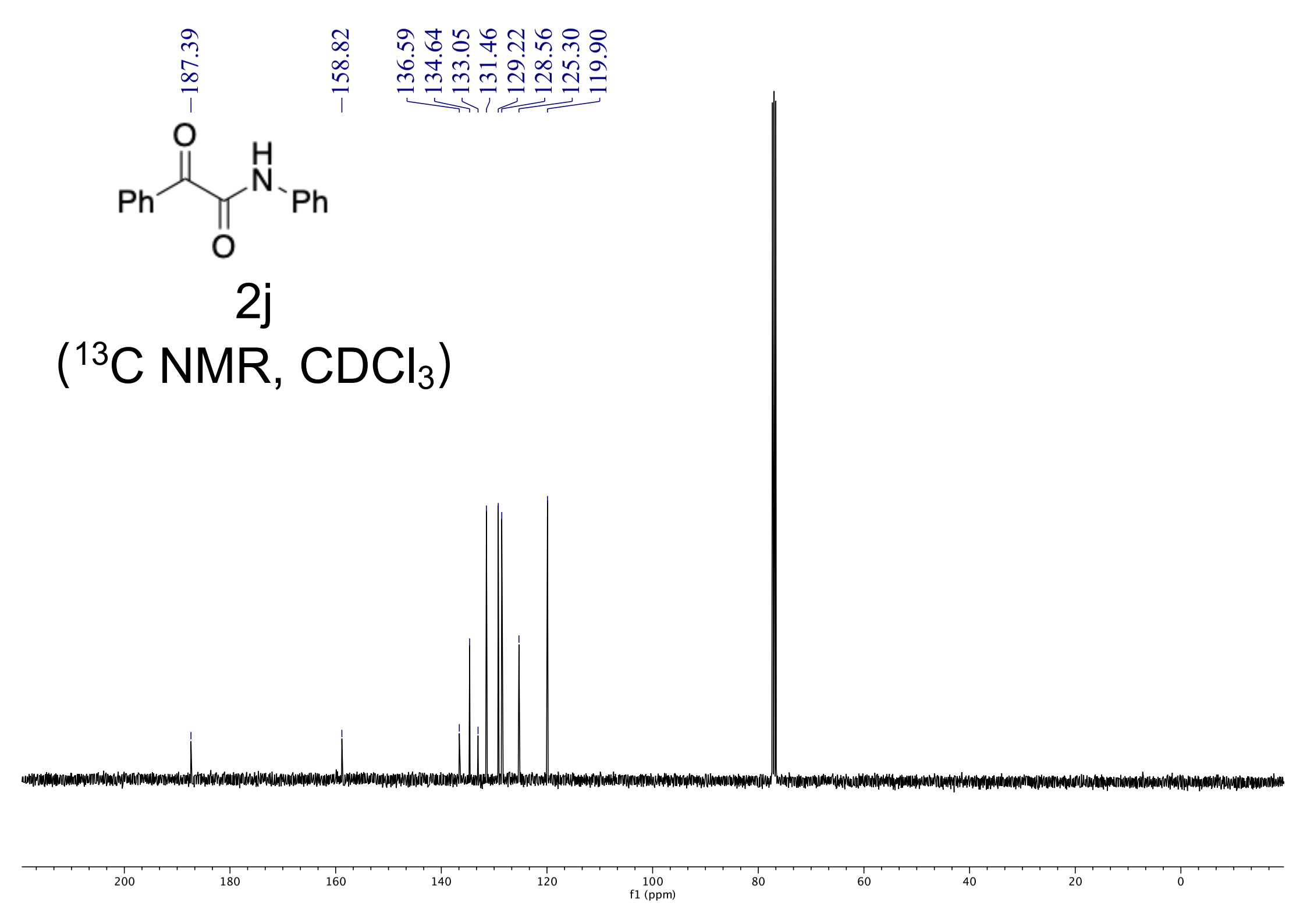
(^{13}C NMR, $CDCl_3$)

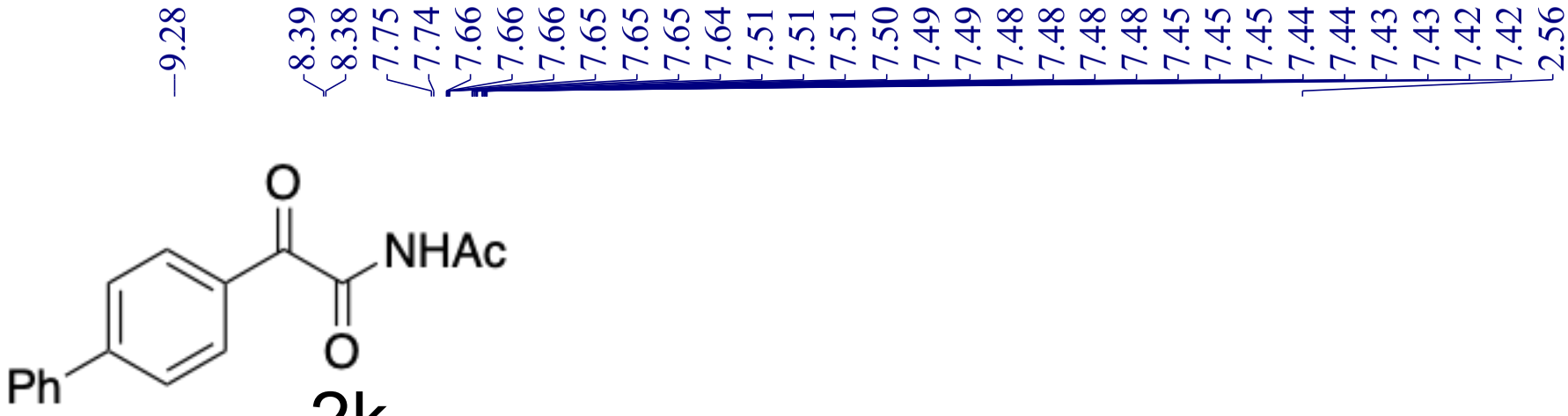


2j

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

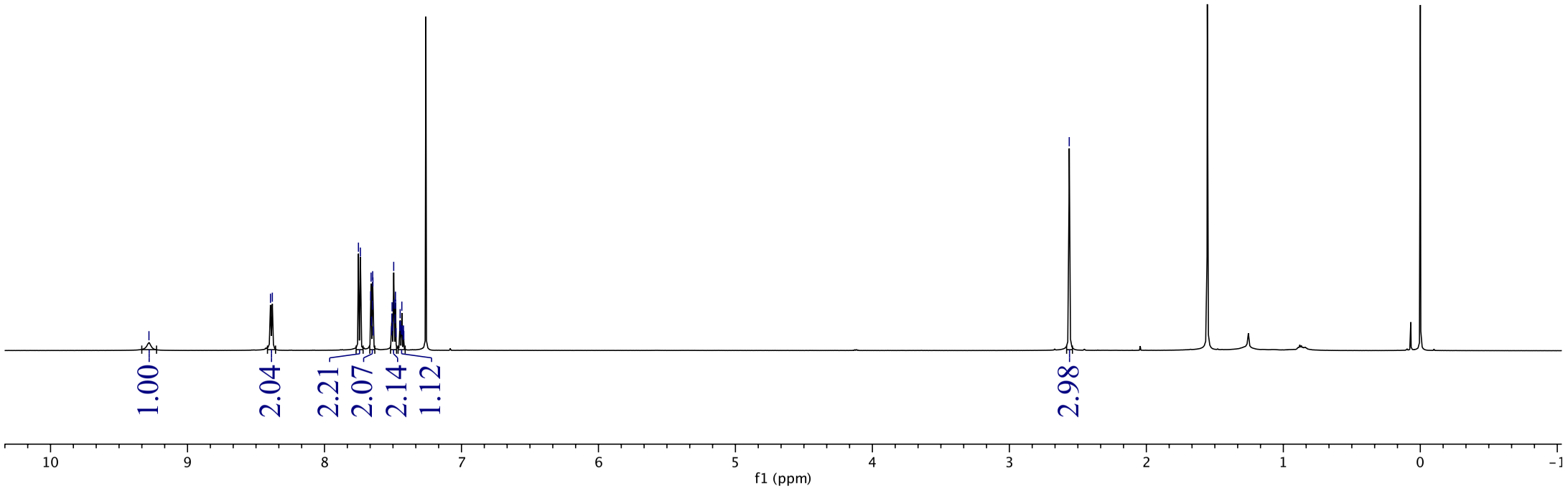


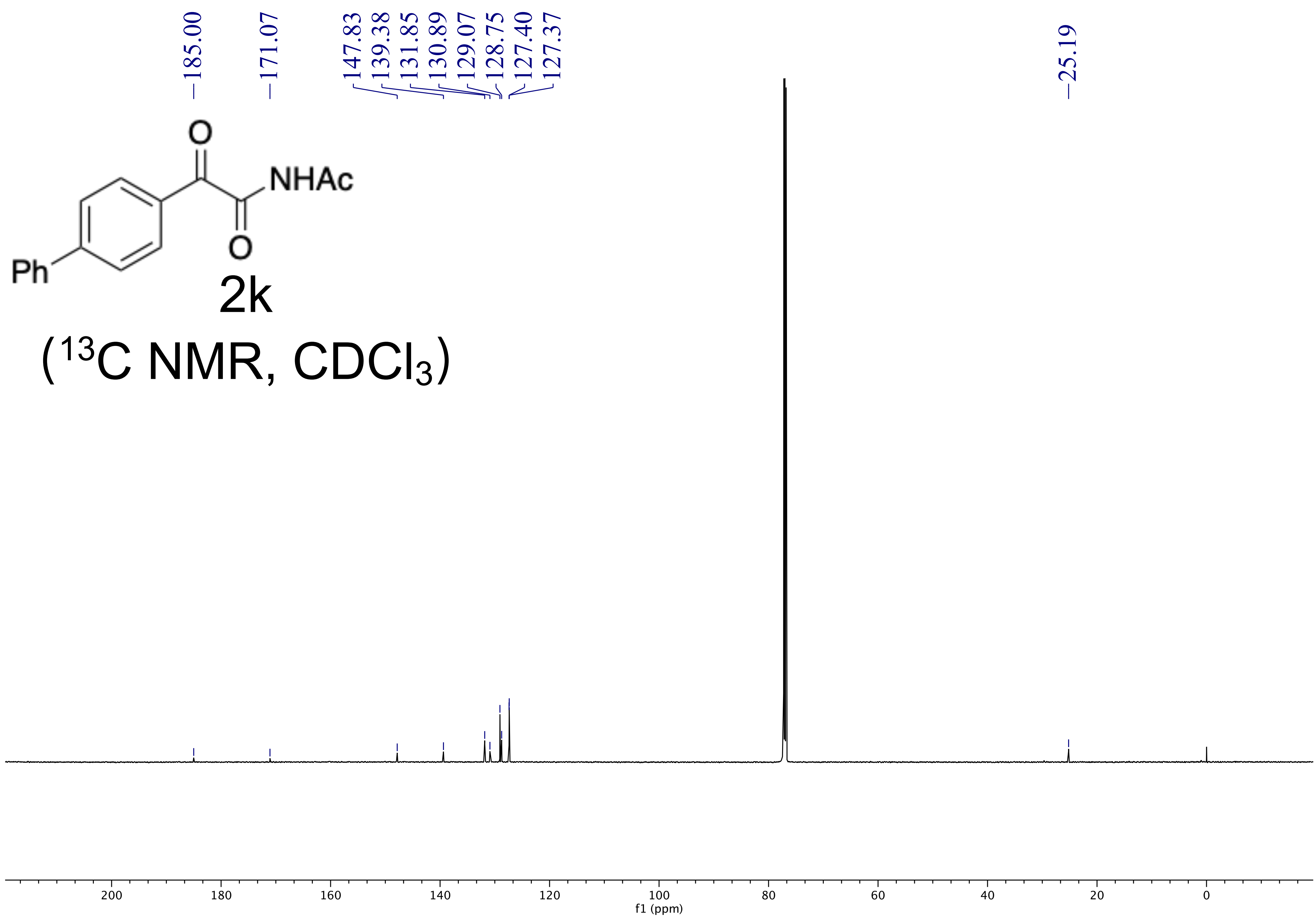

187.39
158.82
136.59
134.64
133.05
131.46
129.22
128.56
125.30
119.90
O
H
N
Ph
Ph
O
2j
(^{13}C NMR, $CDCl_3$)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



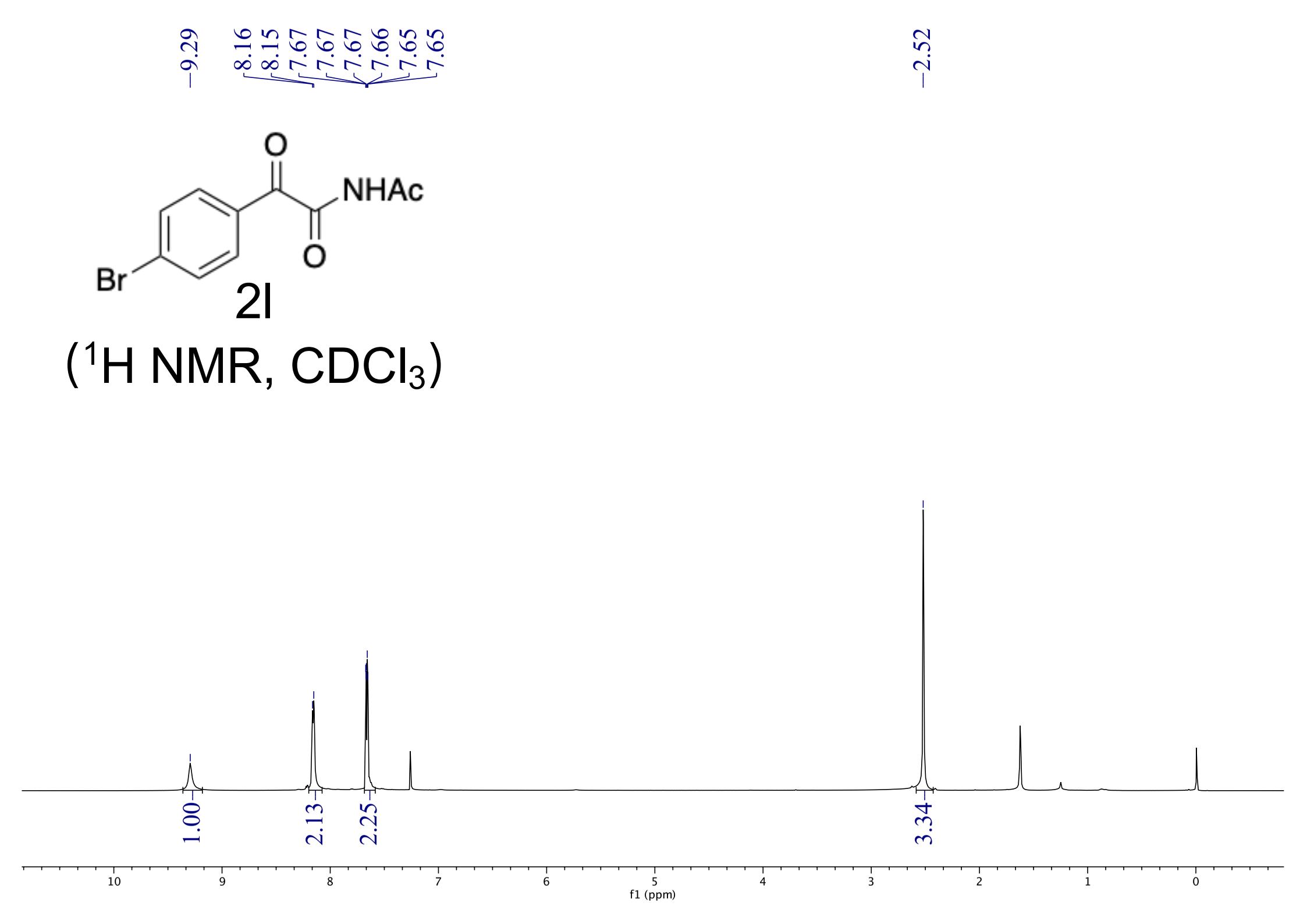
2k

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



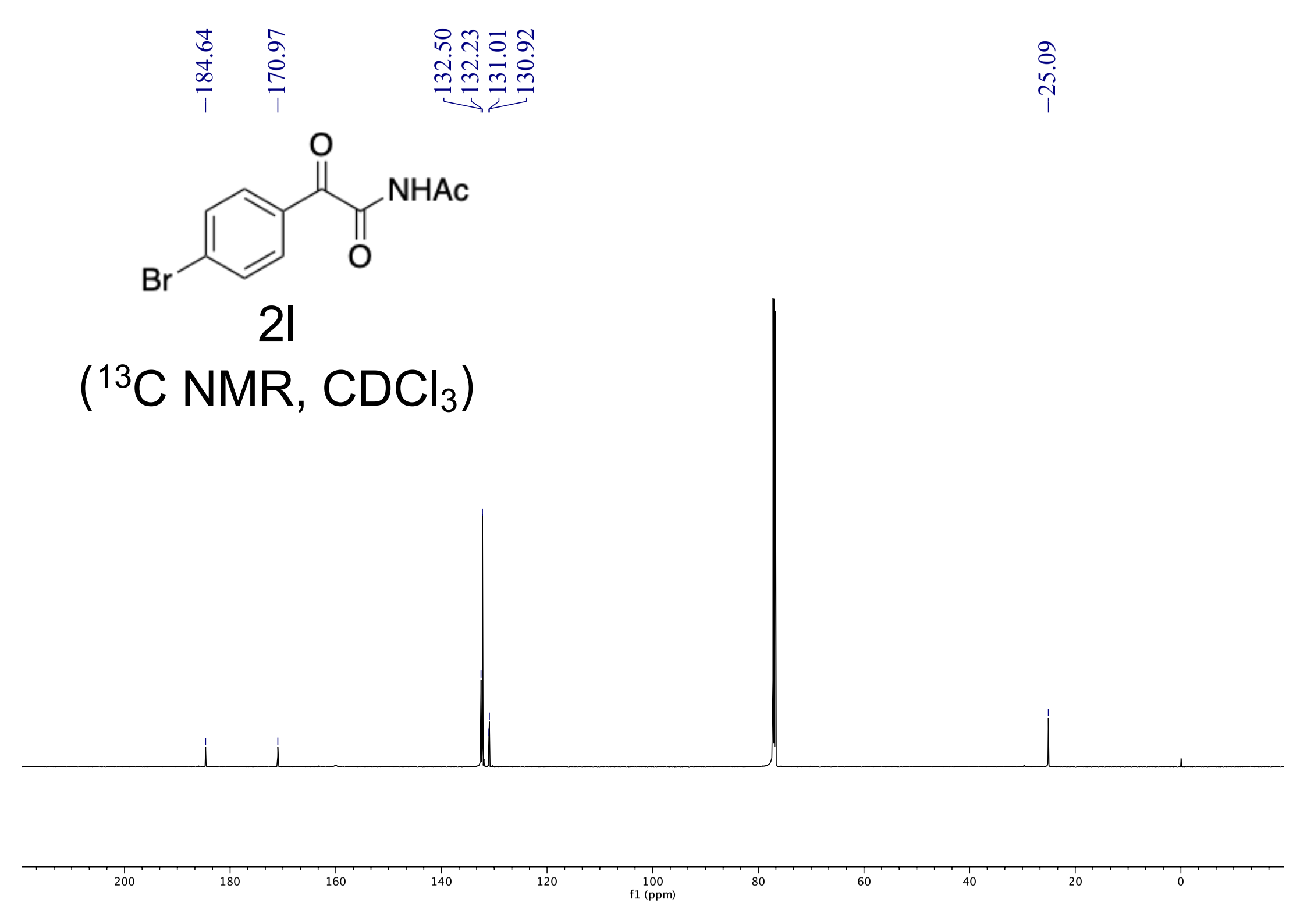


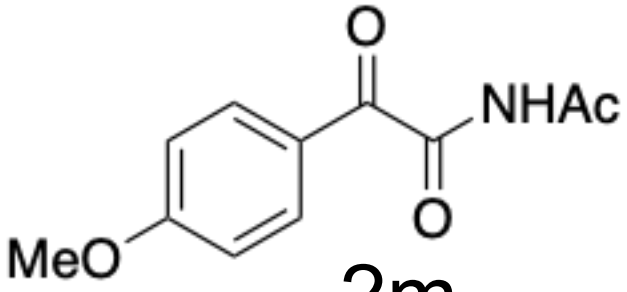
NHAc
Ph
2k
(13C NMR, CDCl3)
185.00
171.07
147.83
139.38
131.85
130.89
129.07
128.75
127.40
127.37
25.19
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



2l

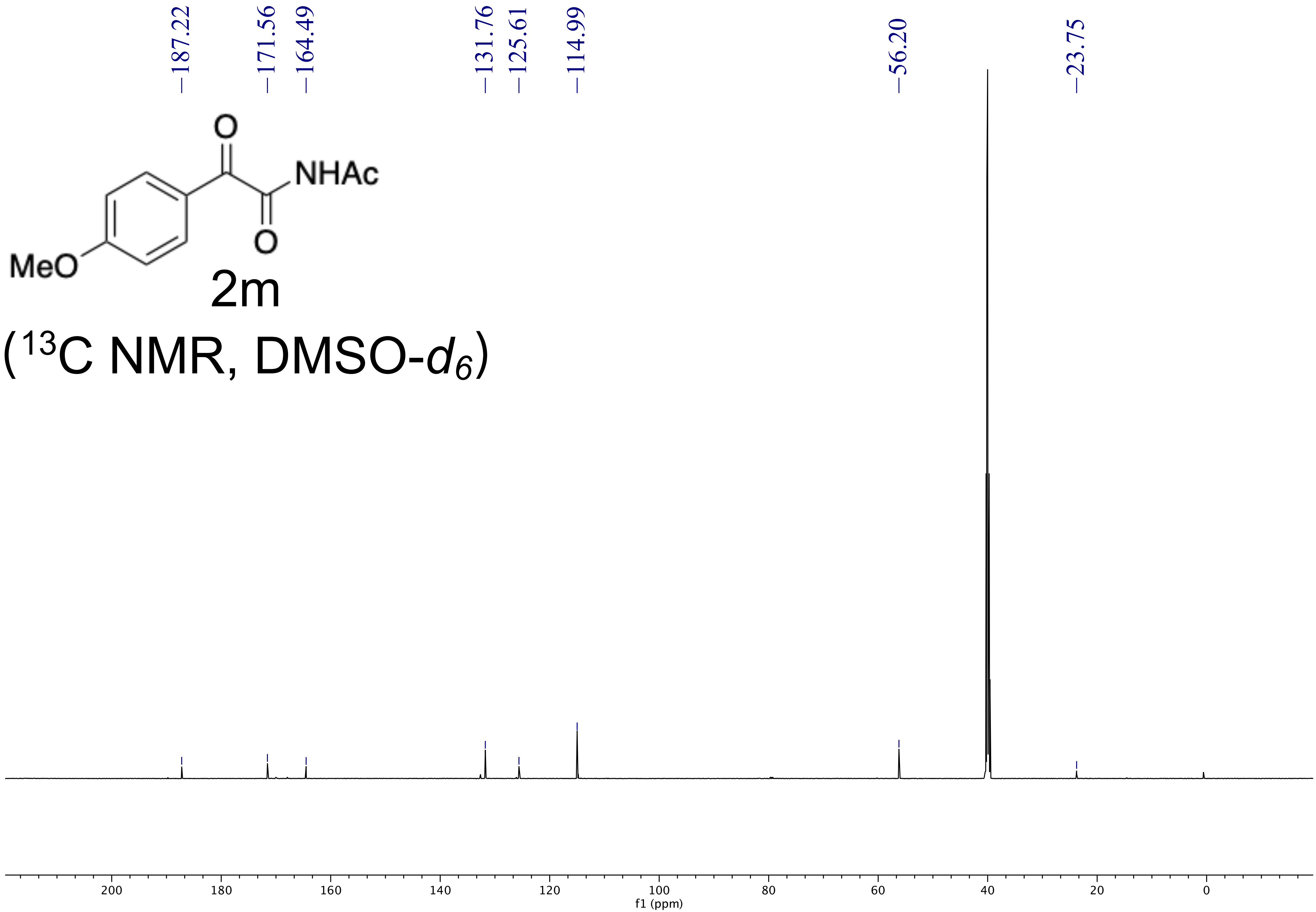
(^{1}H NMR, $CDCl_3$)


184.64
170.97
132.50
132.23
131.01
130.92
25.09
O
NHAc
O
Br
2l
(13C NMR, CDCl3)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

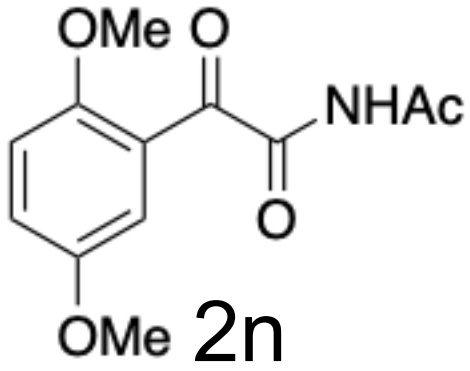


2m

(^{1}H NMR, DMSO-d_6)

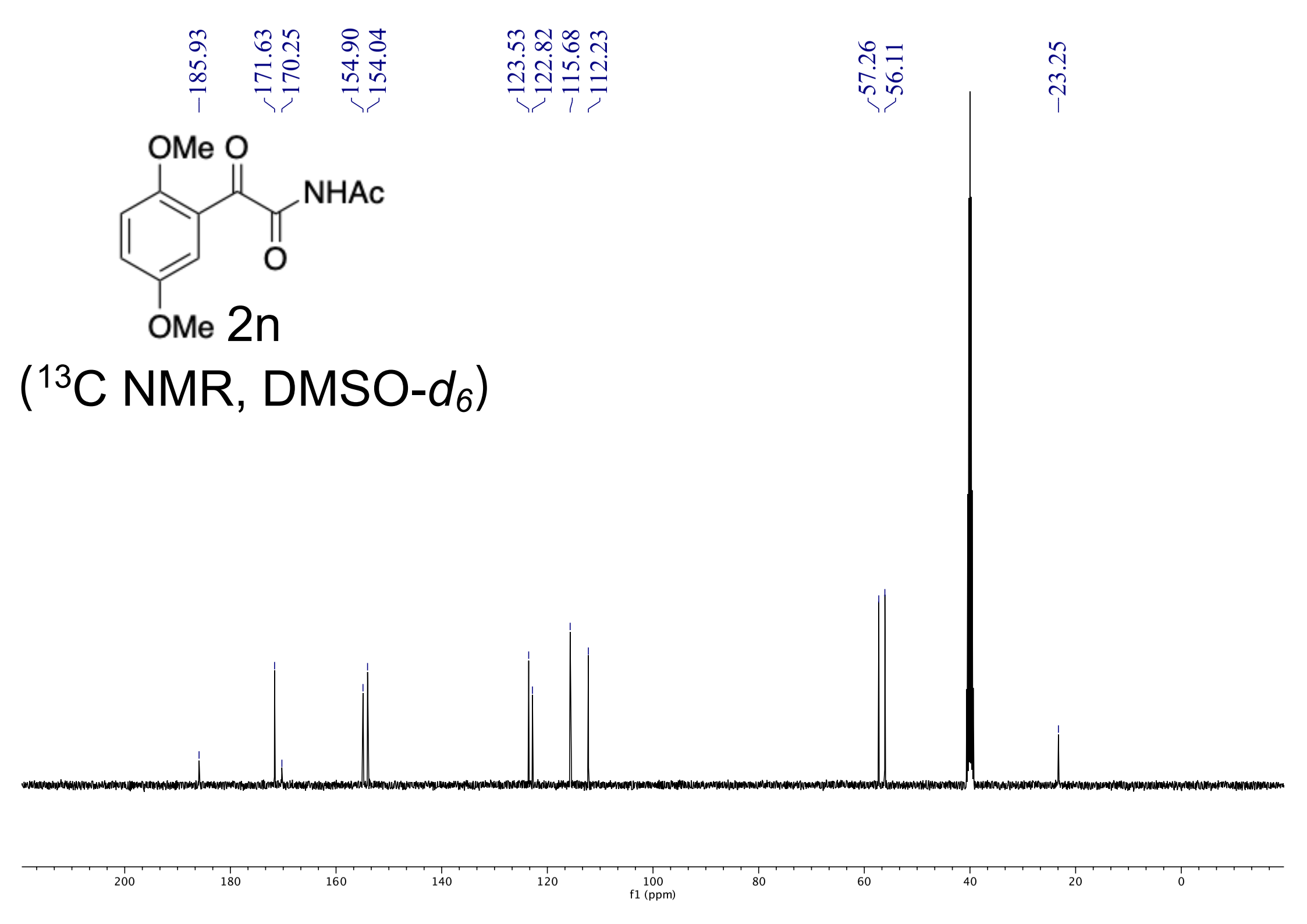


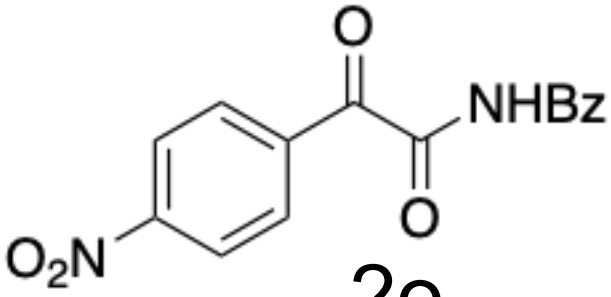
187.22
171.56
164.49
131.76
125.61
114.99
56.20
23.75
MeO
NHAc
O
O
2m
(13C NMR, DMSO-d6)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



2n

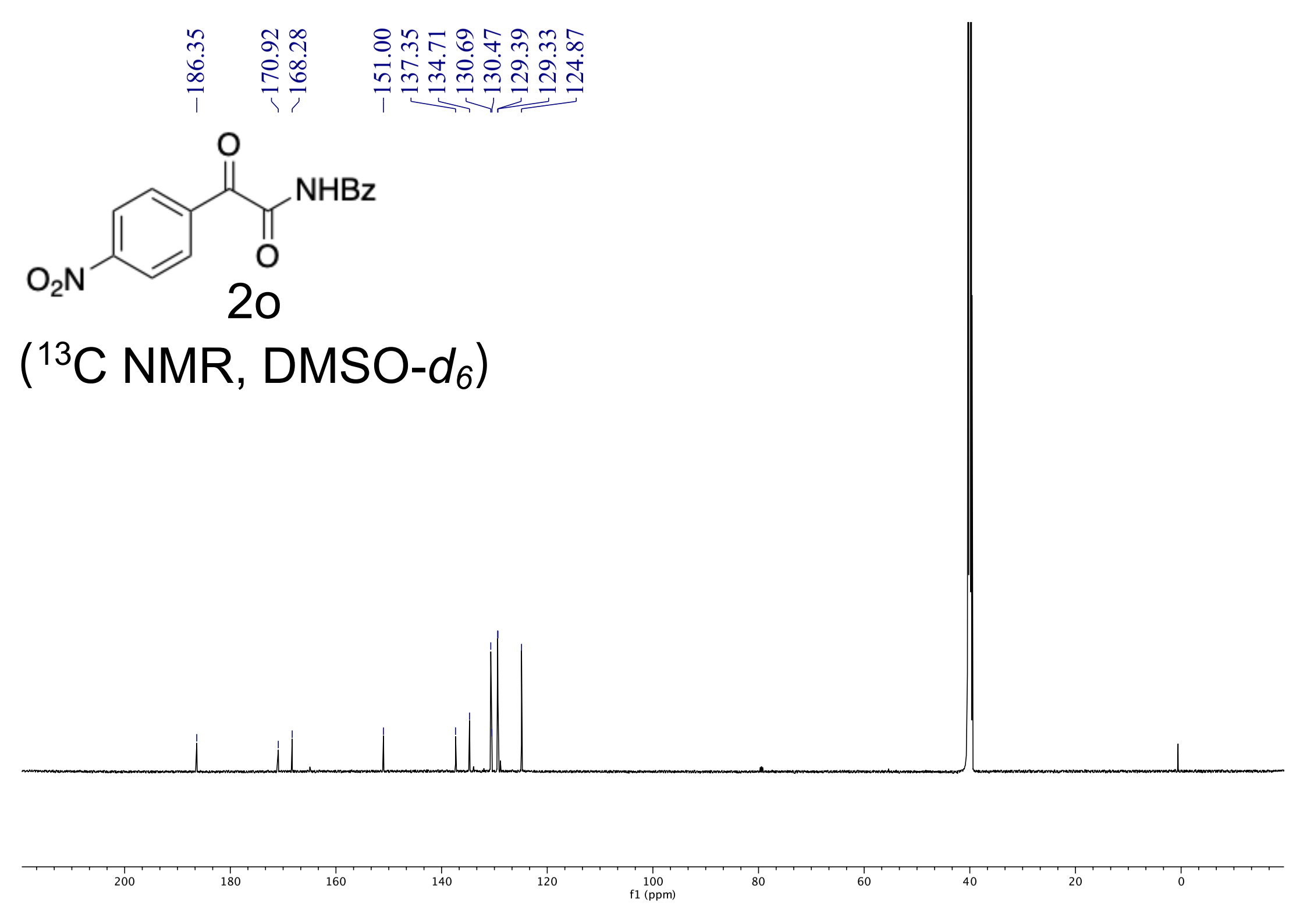
(^{1}H NMR, DMSO-d_6)


185.93
171.63
170.25
154.90
154.04
123.53
122.82
115.68
112.23
57.26
56.11
23.25
OMe
O
NHAc
O
OMe
2n
(13C NMR, DMSO-d6)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



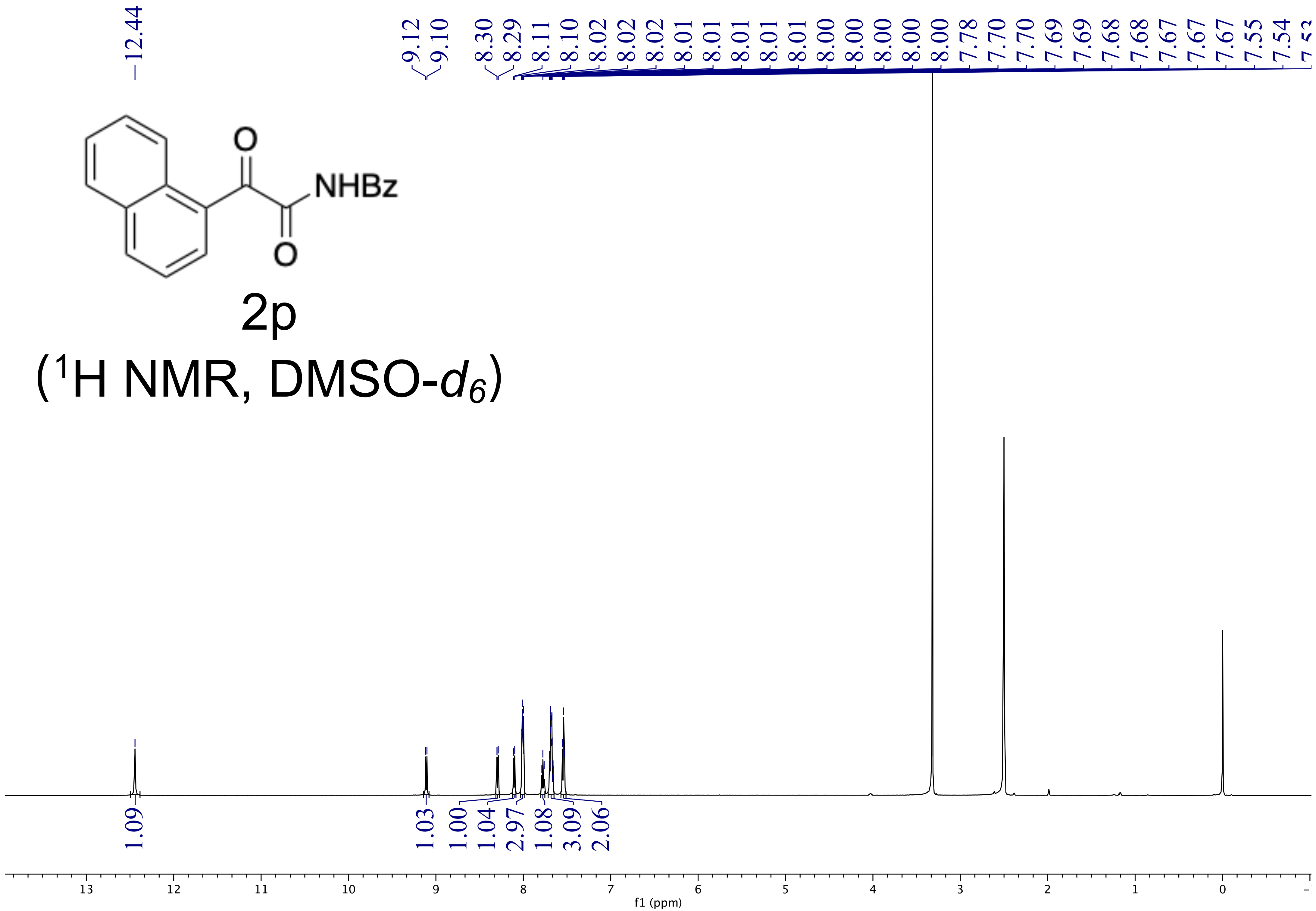
2o

(^{1}H NMR, DMSO-d_6)

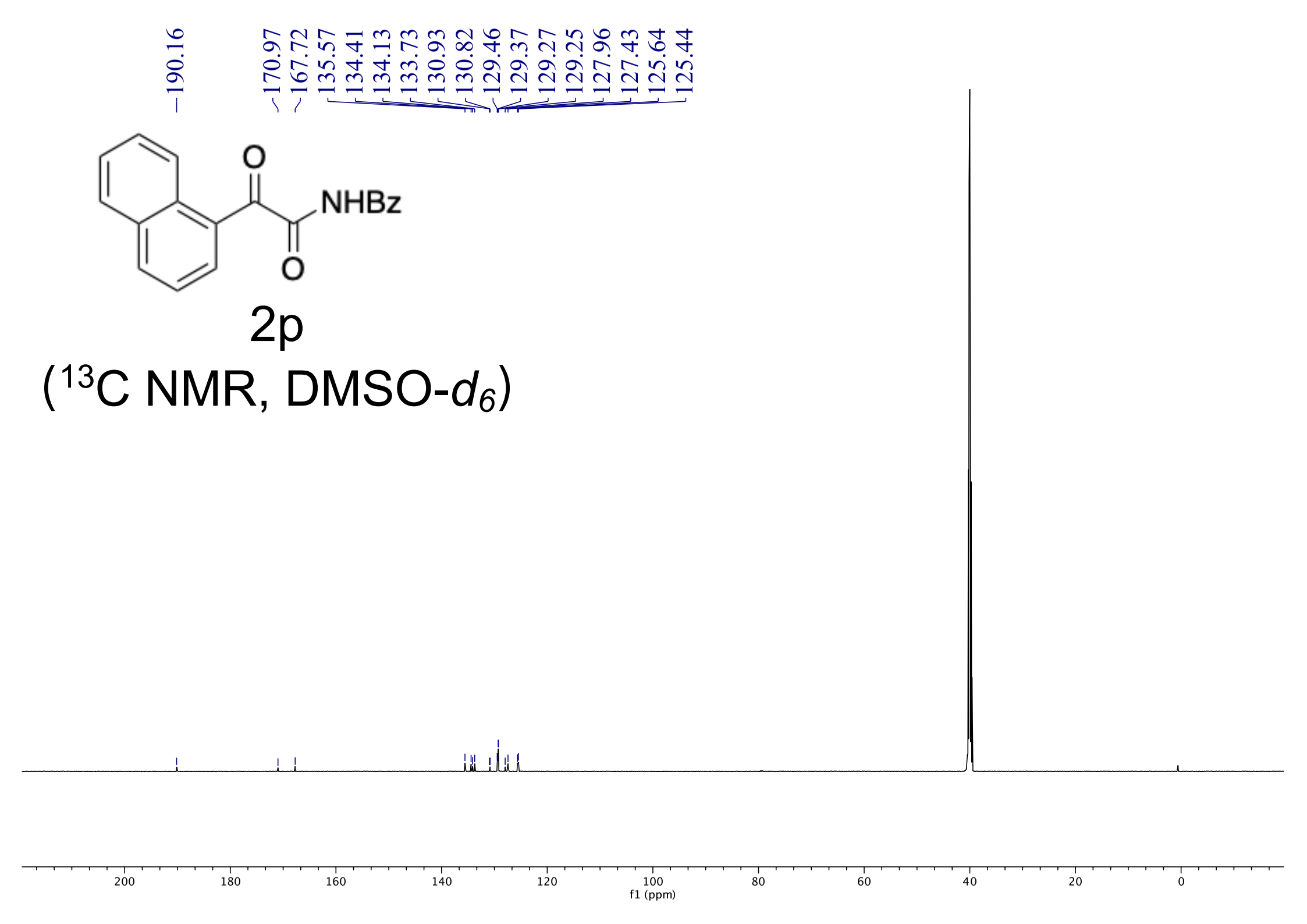


2o

(^{13}C NMR, DMSO-d_6)

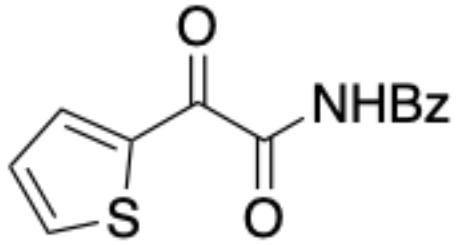


NHBz
2p
(1H NMR, DMSO-d6)
12.44
9.12
9.10
8.30
8.29
8.11
8.10
8.02
8.02
8.02
8.01
8.01
8.01
8.01
8.01
8.00
8.00
8.00
8.00
8.00
7.78
7.70
7.70
7.69
7.69
7.68
7.68
7.67
7.67
7.67
7.55
7.54
1.09
1.03
1.00
1.04
2.97
1.08
3.09
2.06
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)



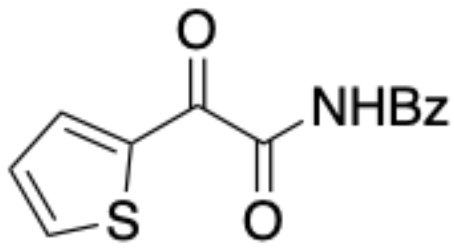
2p

(^{13}C NMR, DMSO-d_6)



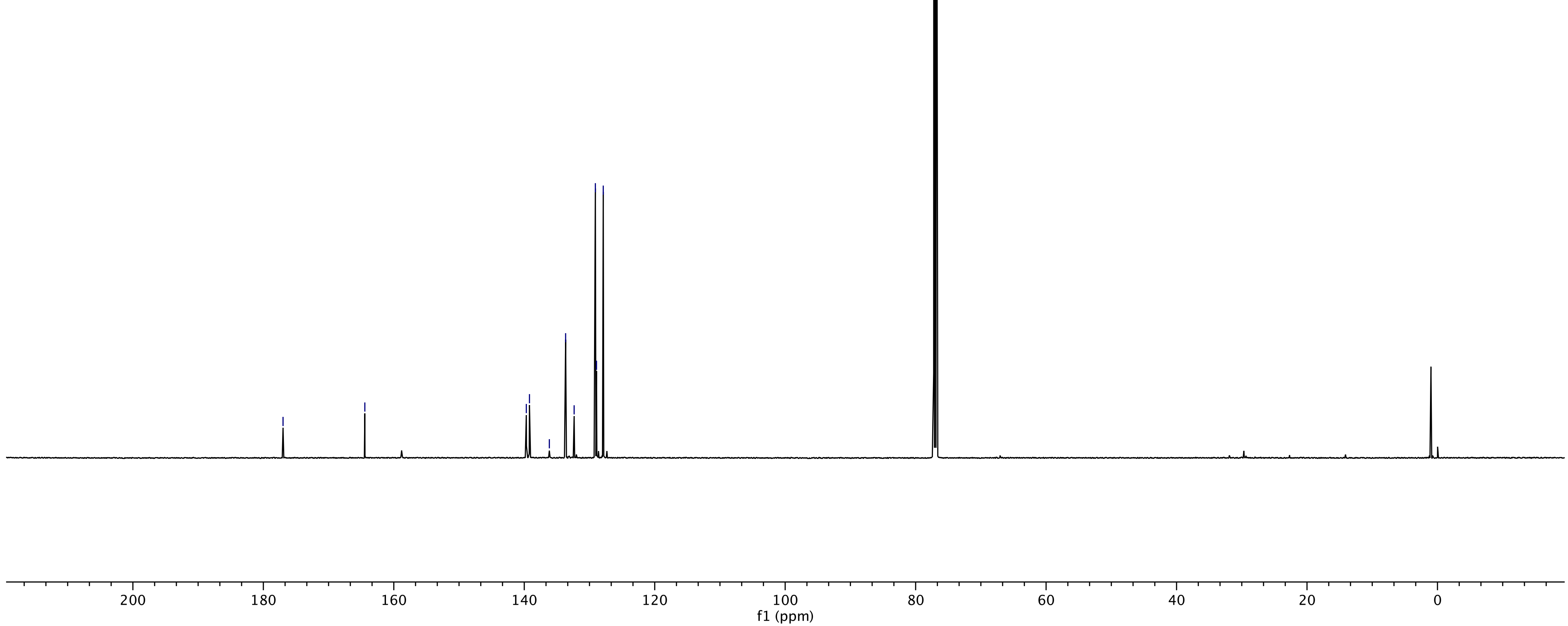
2r

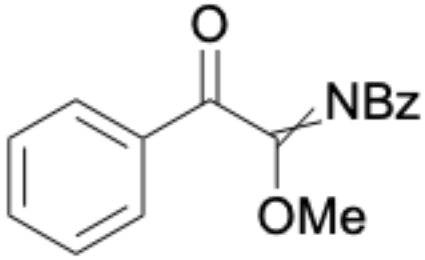
(^{1}H NMR, $CDCl_3$)



2r

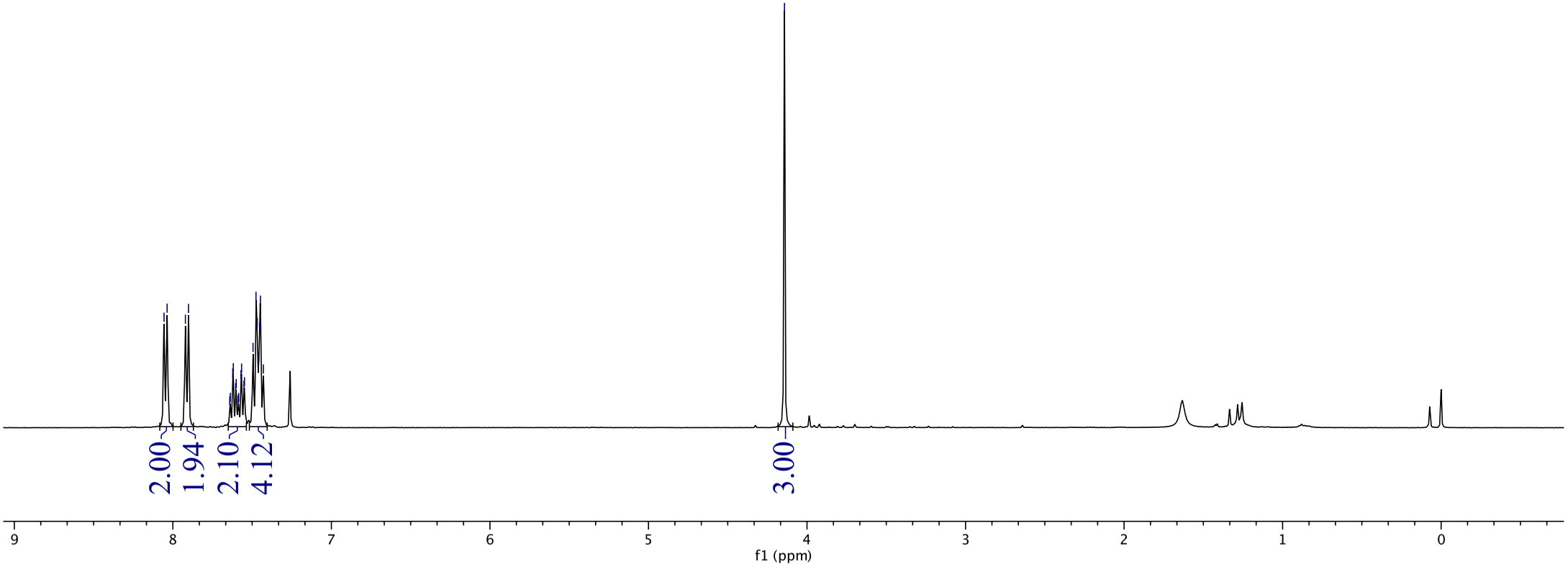
(^{13}C NMR, $CDCl_3$)

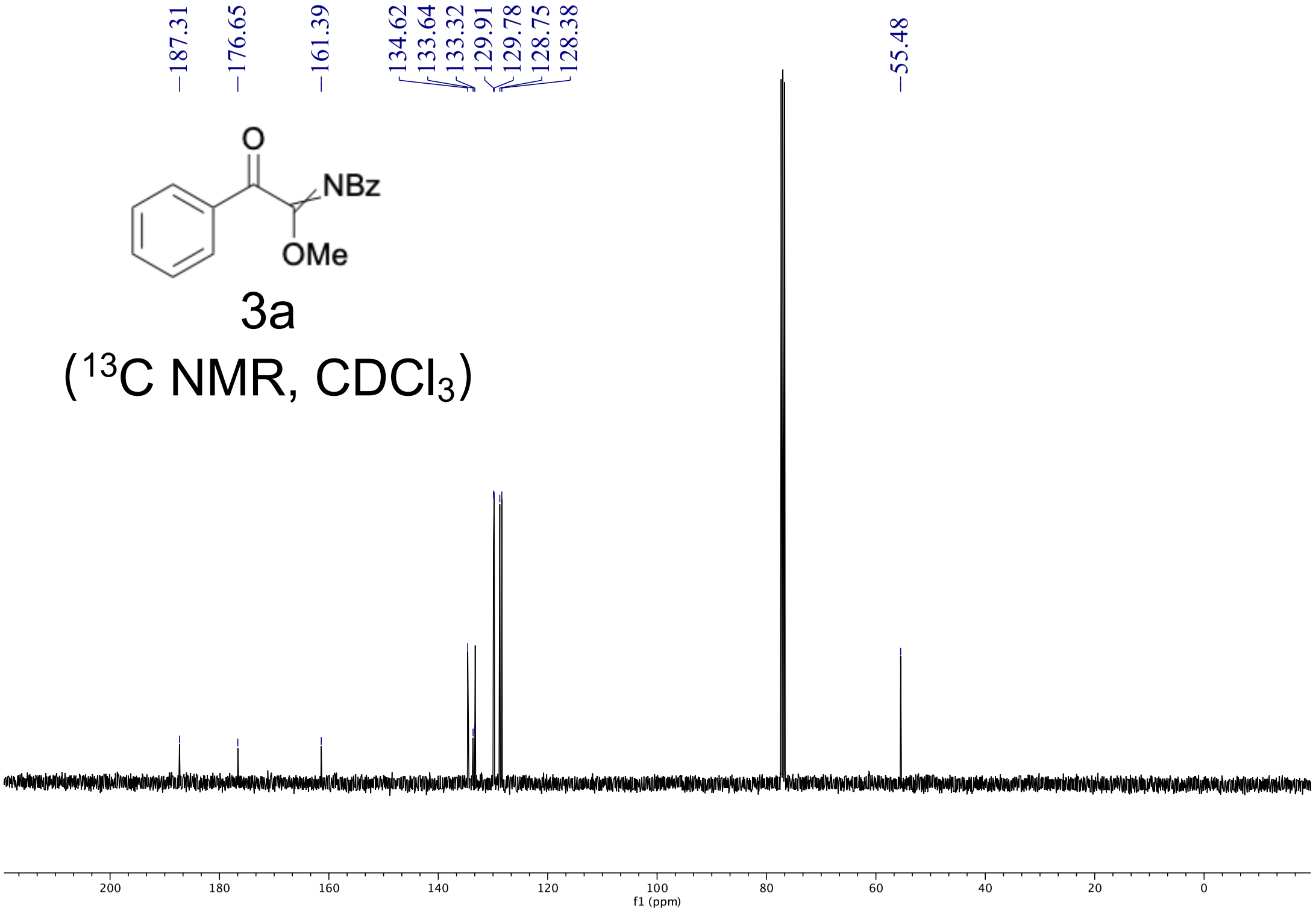


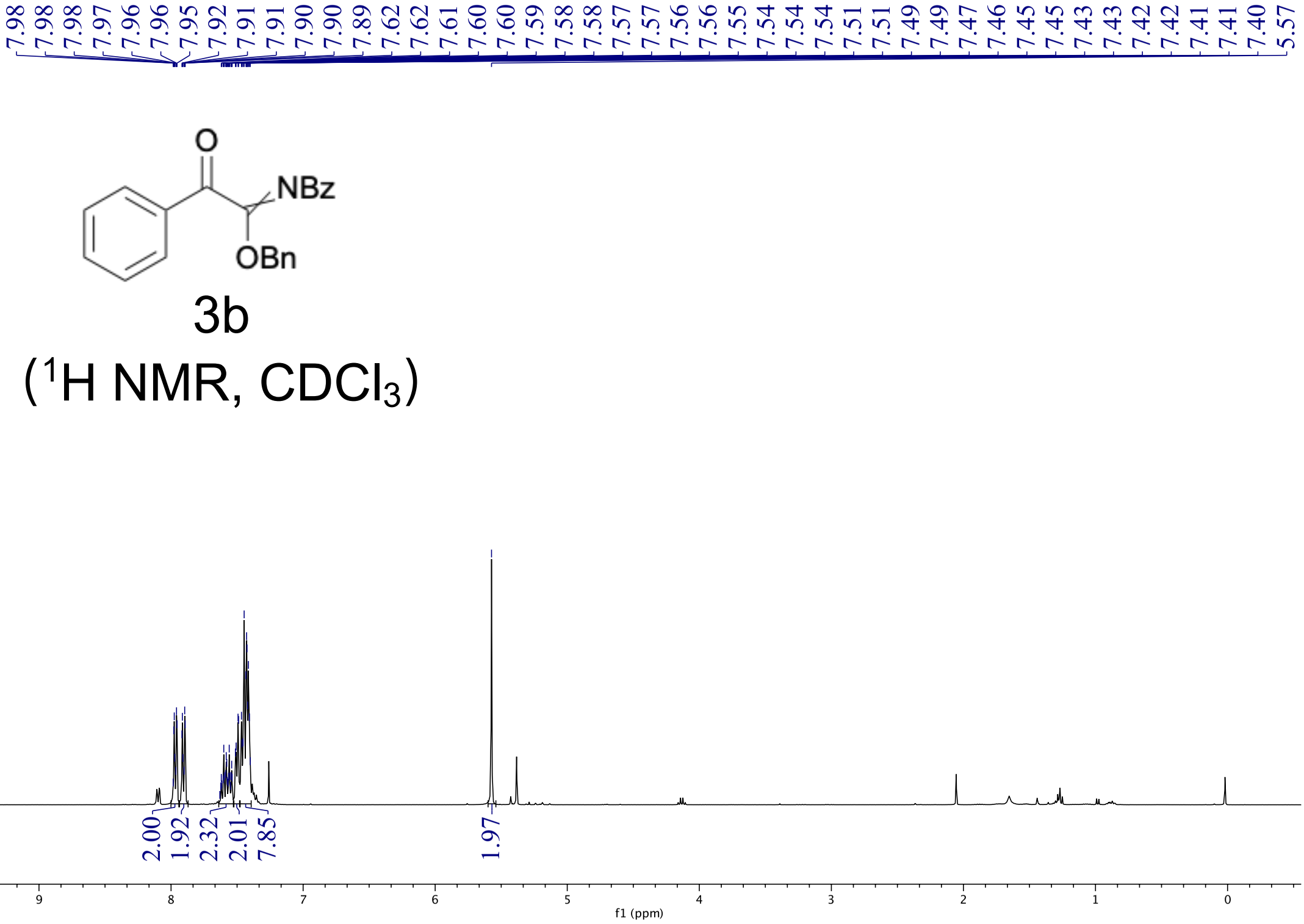


3a

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

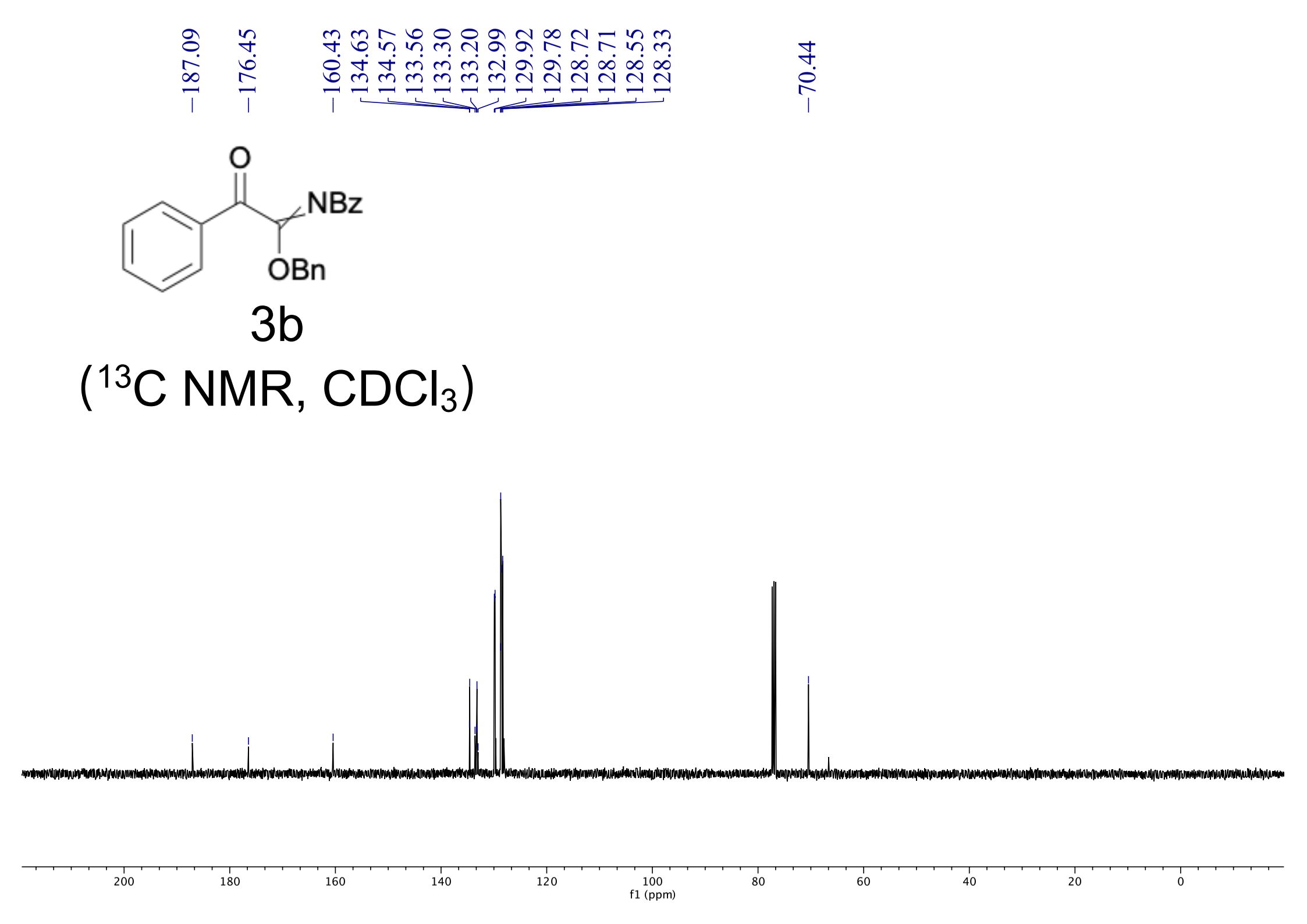



187.31
176.65
161.39
134.62
133.64
133.32
129.91
129.78
128.75
128.38
55.48
O
NBz
OMe
3a
(13C NMR, CDCl3)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



3b

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



3b

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