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Supporting Information

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Iodo-Annulations of *N*-benzyl-propiolamide leading to azaspiro[5.5]undecatrienones/benzo[*c*]azepinones

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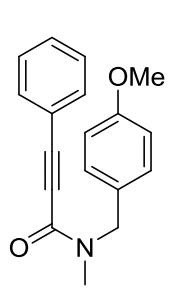

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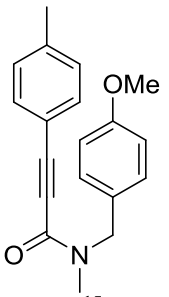

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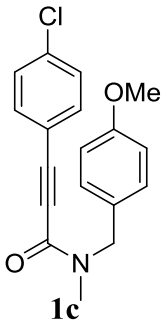

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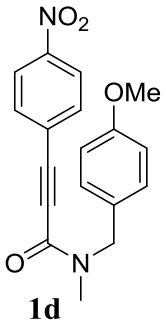

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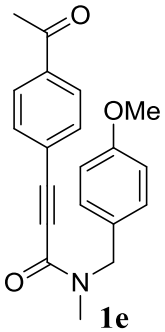

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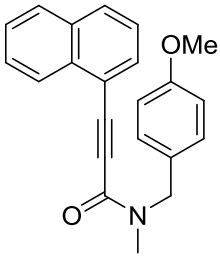

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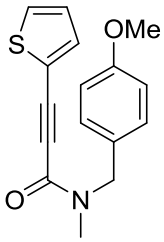

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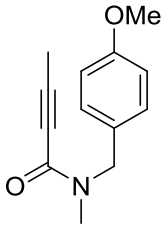

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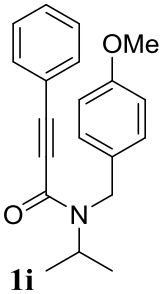

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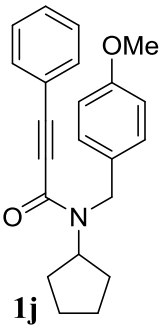

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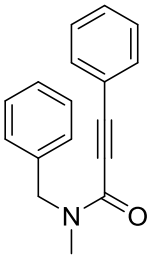

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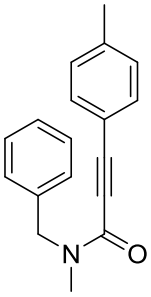

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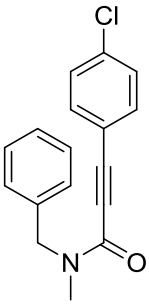

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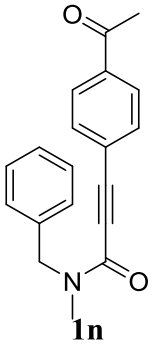

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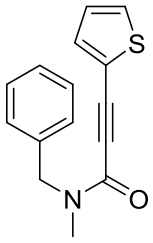

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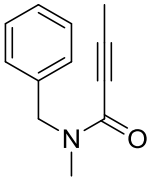

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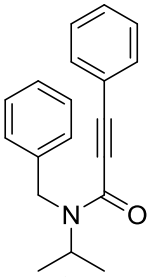

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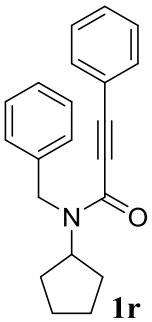

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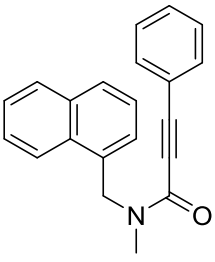

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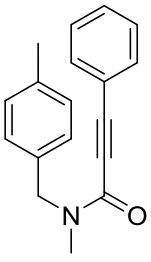
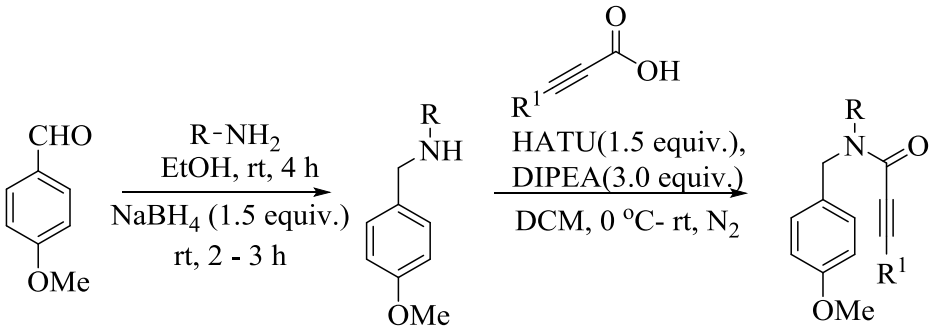


1t

2. General procedure and characterization data of starting material 1:



1

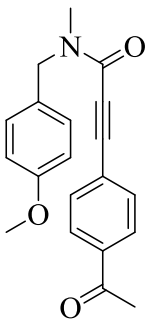
A. General procedure for the Synthesis of *N*-Alkylpropiolamides:

Step 1: To a stirred solution of Benzaldehyde (10.0 mmol) in ethanol (20 mL), was added alkyl amine (11 mmol**)** and allowed to stir at room temperature for 4 h. $NaBH_4$ (15 mmol) was added at 0 ºC and stirred for 2-3 h. Upon completion, the solvent was evaporated. The resulting residue was quenched by adding 10% KOH solution (15 mL) and extracted with EtOAc (25 mL x 3) and washed with water (20 mL x 2), dried over Na_2SO_4 and concentrated under reduced pressure to afford the corresponding secondary amine, which was used to the next reaction without further purification.

Step 2: To a stirred solution of acid (1.2 equiv., 3.6 mmol) in DCM under nitrogen conditions at 0°C was added HATU (1.5 equiv., 4.5 mmol). After 30 min, *N*- substituted benzylamine (1 equiv., 3 mmol) was added, followed by the addition of DIPEA (3 equiv., 9 mmol) drop by drop over a period of 5 min at 0 °C. The reaction mixture was allowed to stir for 2 h at room temperature. The reaction was quenched with water. The organic layer was extracted with DCM (30 mL × 3) and dried over Na_2SO_4, and DCM was removed under reduced pressure to get crude. The crude was purified by column chromatography on silica gel (100−200) using petroleum ether and EtOAc as an eluent to obtain *N*- Substituted Propiolamides **1**.

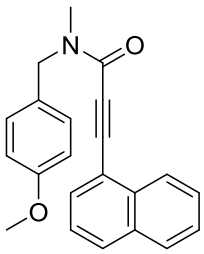
B. Spectral data for substrates:

3-(4-Acetylphenyl)-*N*-(4-methoxybenzyl)-*N*-methylpropiolamide (1e):



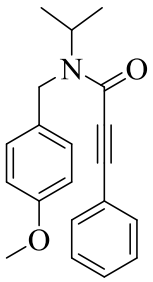
Yellow Liquid, 548 mg, 57% yield, R_f= 0.5 (Ethyl Acetate : Hexane = 3 : 7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 8.3, 5.5 Hz, 2H), 7.64 (t, J = 8.2 Hz, 2H), 7.26 (d, J = 7.8 Hz, 2H), 6.92 (dd, J = 12.1, 8.7 Hz, 2H), 4.81 (s, 1H), 4.63 (s, 1H), 3.84, 3.83 (s, 3H), 3.19, 2.94 (s, 3H), 2.64, 2.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 162.6, 162.5, 159.5, 159.3, 154.3, 154.1, 137.6, 132.6, 132.5, 129.7, 128.8, 128.8, 128.3, 128.2, 127.8, 125.3, 125.1, 114.3, 114.1, 114.1, 89.3, 88.9, 84.2, 84.1, 55.4, 55.3, 54.5, 49.4, 35.7, 31.8, 29.7, 26.7; HRMS (ESI): *m/z* calcd for $C_{20}H_{20}NO_3$ $(M+H)^+$ 322.1443, Found 322.1441.

***N*-(4-Methoxybenzyl)-*N*-methyl-3-(naphthalen-1-yl)propiolamide (1f):**



Brown liquid, 611 mg, 62% yield, R_f= 0.5 (Ethyl Acetate : Hexane = 2:8); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 50.8, 7.6 Hz, 1H), 7.86 – 7.68 (m, 3H), 7.55 – 7.29 (m, 4H), 7.19 (d, J = 6.7 Hz, 1H), 6.83 (t, J = 9.0 Hz, 2H), 4.83 (s, 1H), 4.57 (s, 1H), 3.73 (s, 3H), 3.19, 2.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 159.2, 154.8, 154.8, 133.4, 133.1, 133.1, 132.1, 132.2, 130.7, 129.8, 128.7, 128.5, 128.5, 128.2, 127.5, 126.8, 125.8, 125.8, 125.2, 118.2, 118.1, 114.3, 114.1, 89.1, 88.6, 86.4, 55.6, 54.5, 49.4, 35.8, 31.9; HRMS (ESI): *m/z* calcd for $C_{22}H_{20}NO_2$ $(M+H)^+$ 330.1494, Found 330.1490.

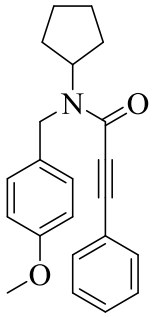
***N*-Isopropyl-*N*-(4-methoxybenzyl)-3-phenylpropiolamide (1i):**



Yellow liquid, 598 mg, 65% yield, R_f = 0.5 (Ethyl Acetate : Hexane = 2 : 8); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.48 (m, 1H), 7.38 – 7.27 (m, 3H), 7.25 – 7.20 (m, 2H), 7.18 – 7.15 (m, 1H), 6.84 – 6.74 (m, 2H), 4.77 – 4.49 (m, 3H), 3.74, 3.73 (s, 3H), 1.15, 1.14 (s, 3H), 1.06, 1.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 158.6, 155.2, 155.0, 132.4, 132.4, 130.8, 130.4, 129.9, 129.9, 128.7, 128.5, 128.5, 128.2, 120.8, 120.6, 14.0,113.8, 90.6, 89.4, 82.7,

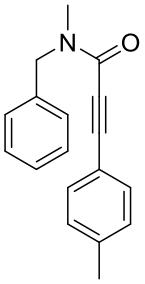
81.9, 55.3, 55.3, 51.1, 48.7, 46.6, 43.3, 21.6, 20.3; HRMS (ESI): *m/z* calcd for $C_{20}H_{22}NO_2$ $(M+H)^+$ 308.1645, Found 308.1641.

***N*-Cyclopentyl-*N*-(4-methoxybenzyl)-3-phenylpropiolamide (1j):**



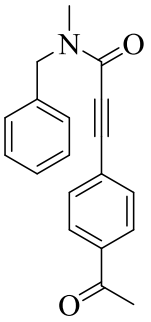
White solid, 629 mg, 63% yield; mp 53-55 ^oC; R_f= 0.5 (Ethyl Acetate : Hexane = 2:8); ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.47 (m, 1H), 7.38 – 7.26 (m, 3H), 7.24 – 7.19 (m, 1H), 7.19 – 7.09 (m, 2H), 6.84 – 6.75 (m, 2H), 4.83 – 4.49 (m, 3H), 3.73, 3.72 (s, 3H), 1.87 – 1.77 (m, 1H), 1.76 – 1.68 (m, 1H), 1.65 – 1.55 (m, 2H), 1.53 – 1.40 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 158.6, 155.6, 155.3, 132.4, 132.4, 130.5, 130.4, 129.9, 129.9, 128.6, 128.4, 128.1, 127.7, 120.8, 120.6, 114.1, 113.9, 90.6, 89.4, 82.7, 82.1, 60.8, 56.6, 55.3, 55.3, 49.7, 44.4, 30.1, 29.1, 23.8, 23.7; HRMS (ESI): *m/z* calcd for $C_{22}H_{14}NO_2$ $(M+H)^+$ 334.1801, Found 334.1798.

***N*-benzyl-*N*-methyl-3-(p-tolyl)propiolamide (1l):**



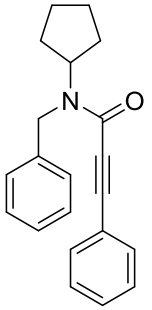
White Solid, 470 mg, 63% yield; mp 66-68 ^oC; R_f = 0.5 (Ethyl Acetate : Hexane = 2 : 8); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.21 (m, 7H), 7.11 – 7.05 (m, 2H), 4.78 (s, 1H), 4.59 (s, 1H), 3.11, 2.86 (s,3H), 2.30, 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1, 154.9, 140.6, 140.6, 136.4, 136.3, 132.4, 132.4, 129.3, 128.9, 128.7, 128.2, 127.9, 127.7, 127.6, 117.5, 117.4, 91.3, 90.7, 81.3, 81.2, 55.0, 49.9, 35.9, 31.9, 21.7; HRMS (ESI): *m/z* calcd for $C_{18}H_{17}NO$ $(M+H)^+$ 264.1388, Found 264.1399.

3-(4-Acetylphenyl)-*N*-benzyl-*N*-methylpropiolamide (1n):



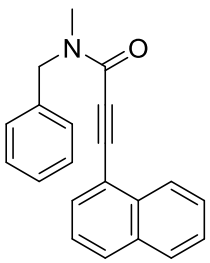
White solid, 584 mg, 67% yield; mp 72-74 ^{o}C; R_f = 0.5 (Ethyl Acetate : Hexane = 3 : 7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, J = 10.4, 8.5 Hz, 2H), 7.62 (dd, J = 19.7, 8.3 Hz, 2H), 7.43 – 7.26 (m, 5H), 4.86 (s, 1H), 4.68 (s, 1H), 3.20, 2.95 (s, 3H), 2.61, 2.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 154.4, 154.3, 137.6, 136.1, 135.9, 132.6, 132.5, 128.9, 128.8, 128.3, 128.3, 128.2, 128.1, 127.8, 127.4, 125.2, 125.1, 89.4, 88.9, 84.0, 84.0, 55.0, 49.9, 35.9, 32.1, 26.7; HRMS (ESI): *m/z* calcd for $C_{19}H_{17}NO_2$ $(M+H)^+$ 292.1338, Found 292.1354.

***N*-Benzyl-*N*-cyclopentyl-3-phenylpropiolamide (1r):**



White Solid, 554 mg, 61% yield; mp 70-72 ^{o}C; R_f = 0.5 (Ethyl Acetate : Hexane = 2 : 8); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.46 (m, 1H), 7.38 – 7.26 (m, 3H), 7.22 – 7.11 (m, 6H), 4.85 – 4.56 (m, 3H), 1.91 – 1.68 (m, 2H), 1.60 – 1.35 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 155.3, 138.4, 138.3, 132.4, 130.0, 129.9, 128.7, 128.6, 128.5, 128.4, 127.3, 126.9, 126.7, 126.4, 120.8, 120.5, 89.5, 82.7, 82.0, 60.8, 56.4, 49.9, 44.9, 30.1, 29.2, 23.8, 23.7; HRMS (ESI): *m/z* calcd for $C_{21}H_{21}NO$ $(M+H)^+$ 304.1701, Found 304.1710.

***N*-Benzyl-*N*-methyl-3-(naphthalen-1-yl)propiolamide (1s):**



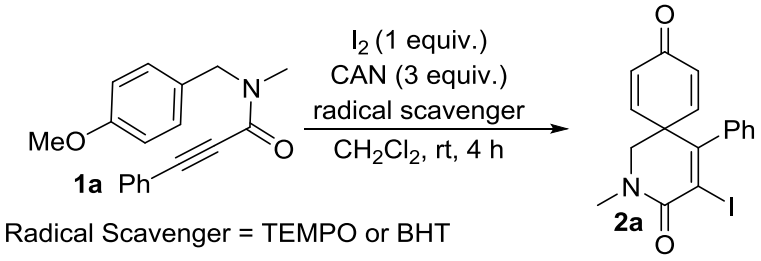
White Solid, 583 mg, 65% yield; mp 83-85 ^{o}C; R_f = 0.5 (Ethyl Acetate : Hexane = 3 : 7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 8.09 (m, 1H), 7.96 – 7.84 (m, 2H), 7.63 – 7.35 (m, 8H), 7.31 (d, J = 7.6 Hz, 1H), 5.38 (s, 1H), 5.18 (s, 1H), 3.15, 3.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 154.6, 133.9, 133.9, 132.5, 132.4, 131.7, 131.64, 131.4, 131.3, 130.1, 129.1, 128.8, 128.7, 128.7, 128.6, 128.5, 127.4, 126.8, 126.7, 126.1, 126.1, 125.5, 125.4, 125.2, 123.9, 122.6, 120.6, 120.4, 90.8, 90.6, 81.7, 52.7, 47.9, 35.6, 32.3. HRMS (ESI): *m/z* calcd for $C_{21}H_{17}NO$ $(M+H)^+$ 300.1388, Found 300.1399.

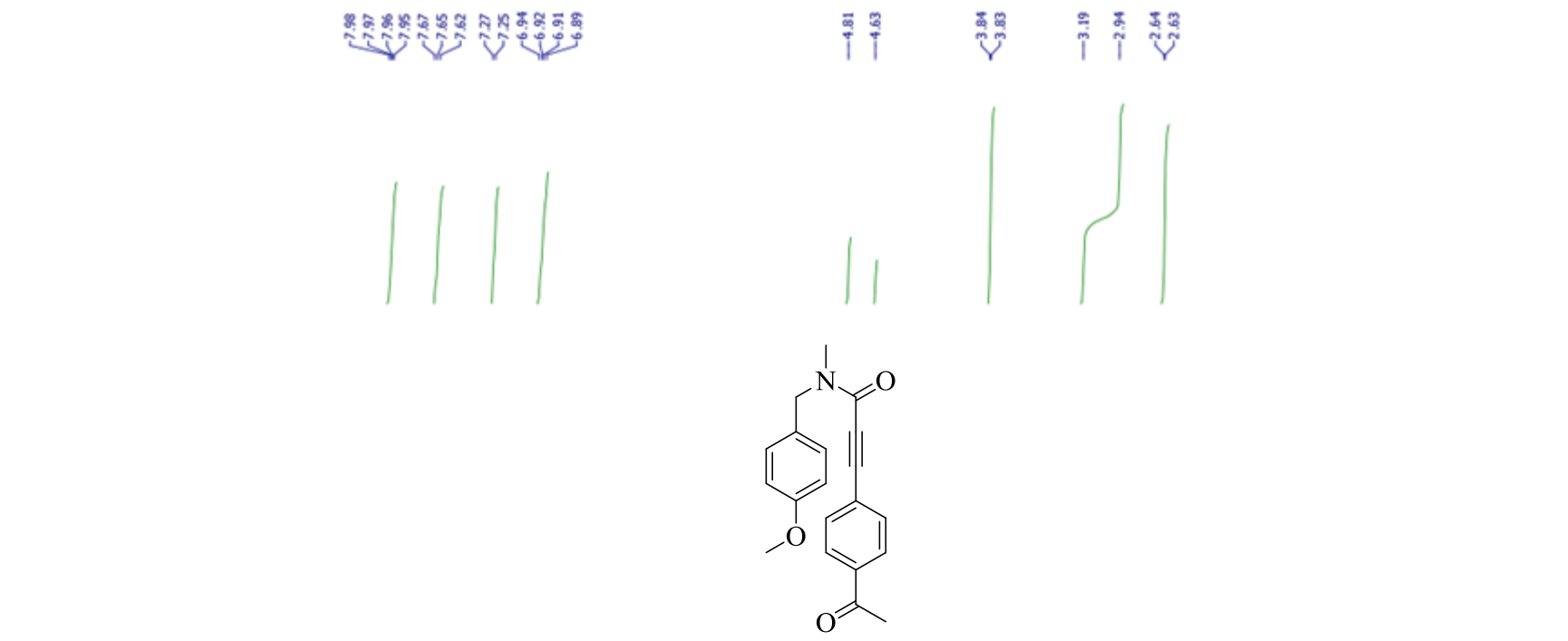
3. Control Experiment

Radical trapping reaction with 2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl (TEMPO) and Butylated hydroxytoluene (BHT):

General procedure for synthesis of azaspiro[5.5]- undecatrienones (2):

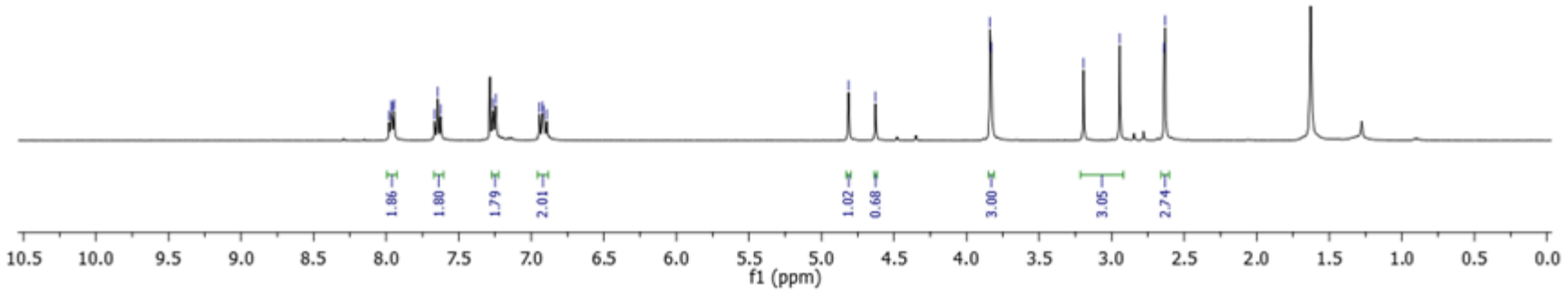
To a stirred solution of *N*-Alkylpropiolamide **1** (100 mg, 0.3 mmol) in CH_2Cl_2 in a reaction vial, were added I_2 (83 mg, 0.3 mmol), CAN (542 mg, 0.9 mmol) and radical scavenger {(2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl (TEMPO) or Butylated hydroxytoluene (BHT)} (0.6 mmol) and the mixture was stirred at rt for 4 h., After completion of the reaction (the progress of the reaction was monitored by TLC), solvent was evaporated under vacuo and the resulting crude was purified by column chromatography to afford the desired 4-Iodo-2-methyl-5-phenyl-2-azaspiro [5.5]undeca-4,7,10-triene-3,9-dione **2a**.

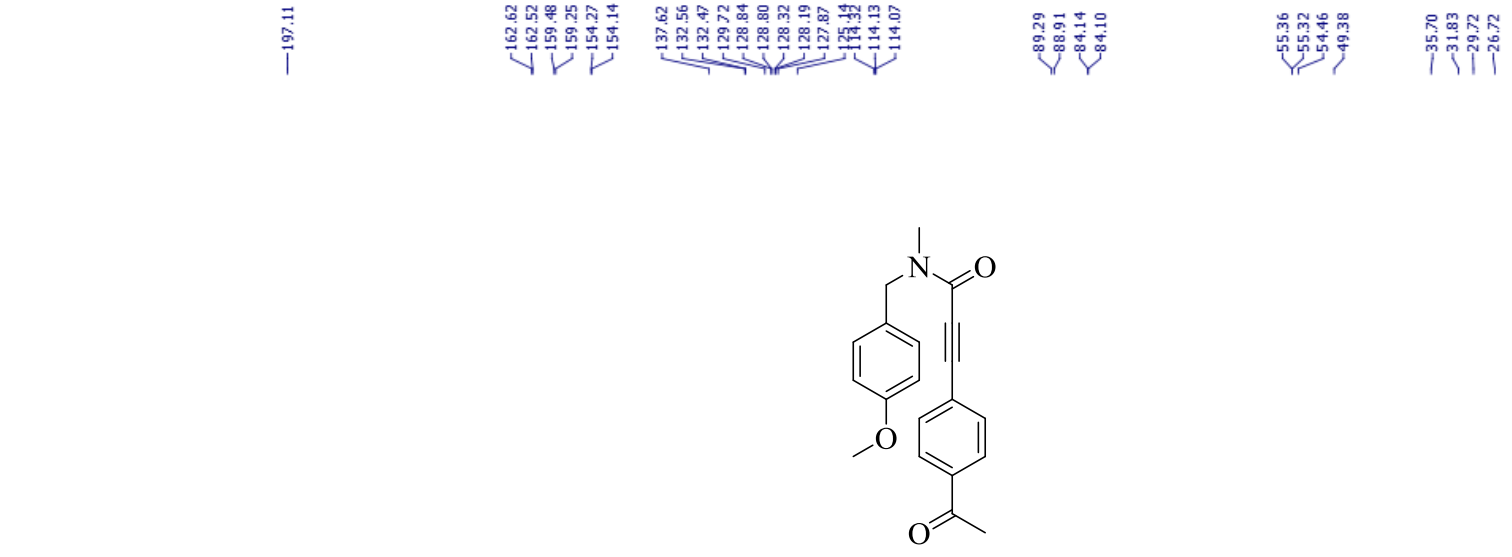




1e

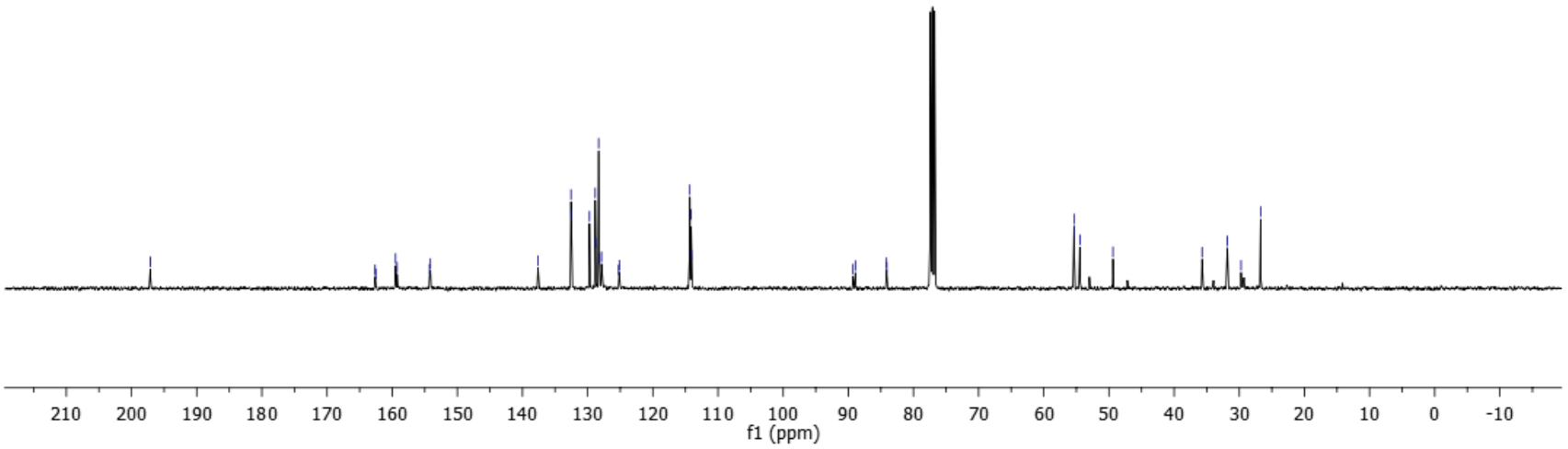
^{1}H NMR, 400 MHz, $CDCl_3$

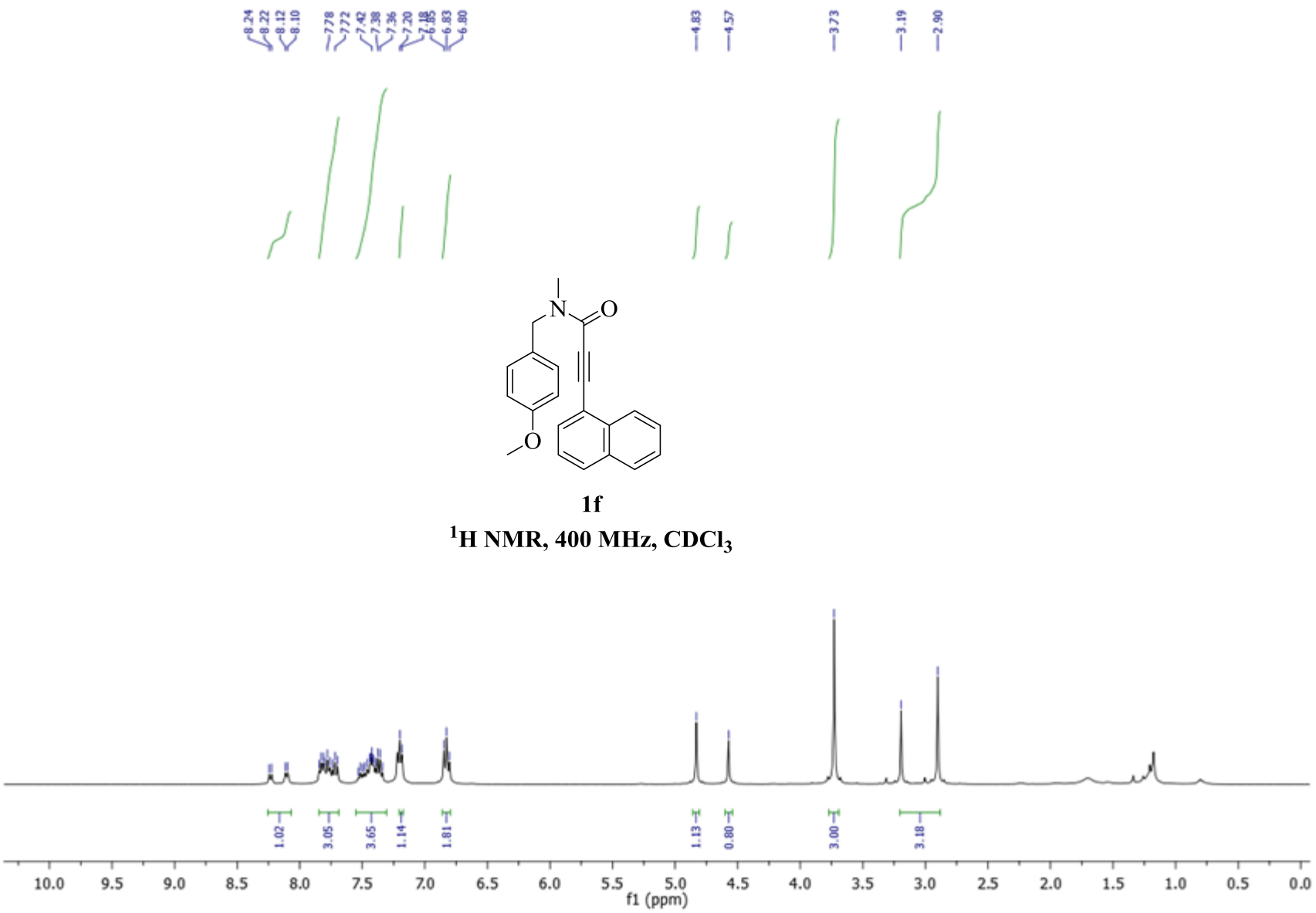




1e

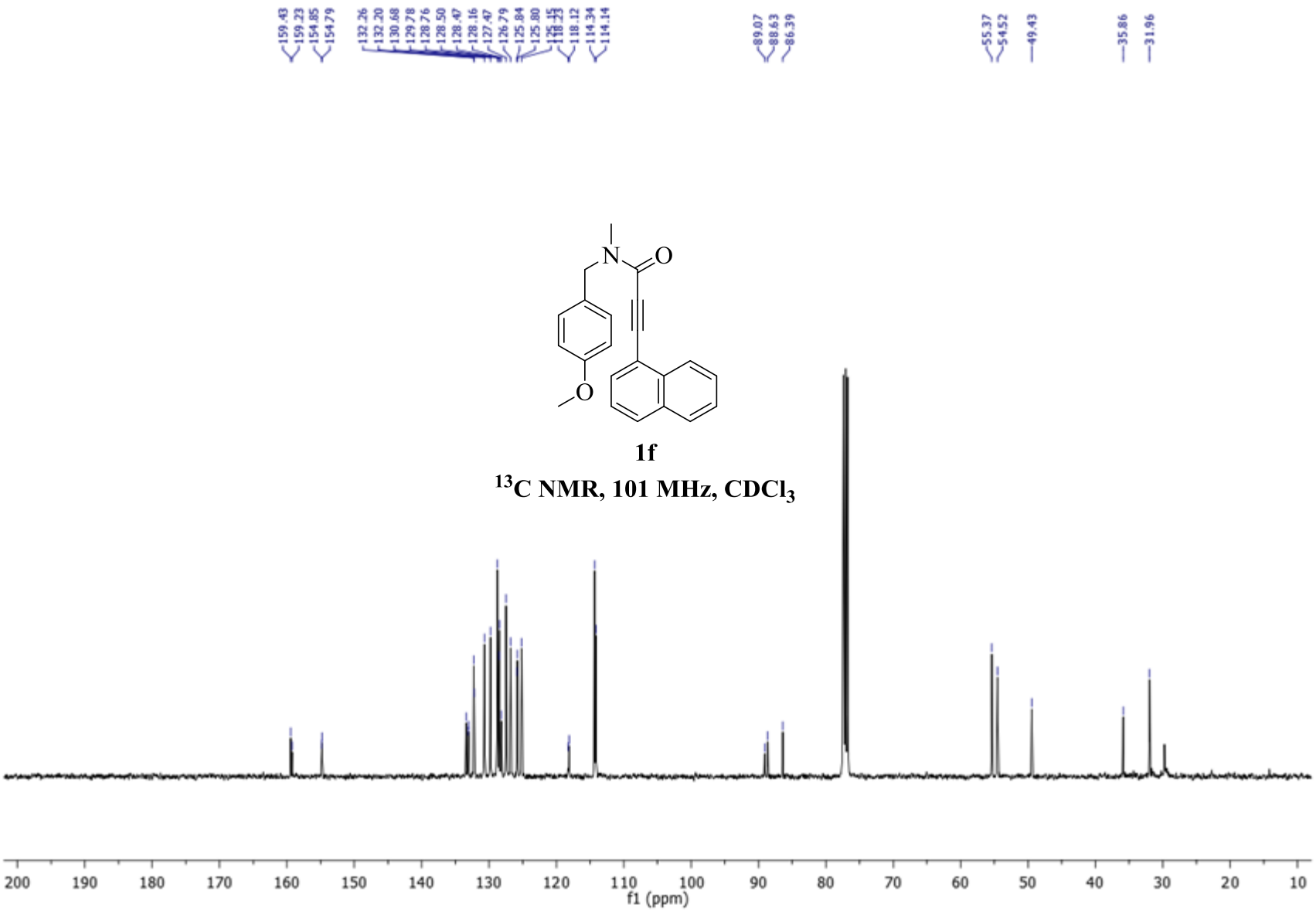
^{13}C NMR, 101 MHz, $CDCl_3$





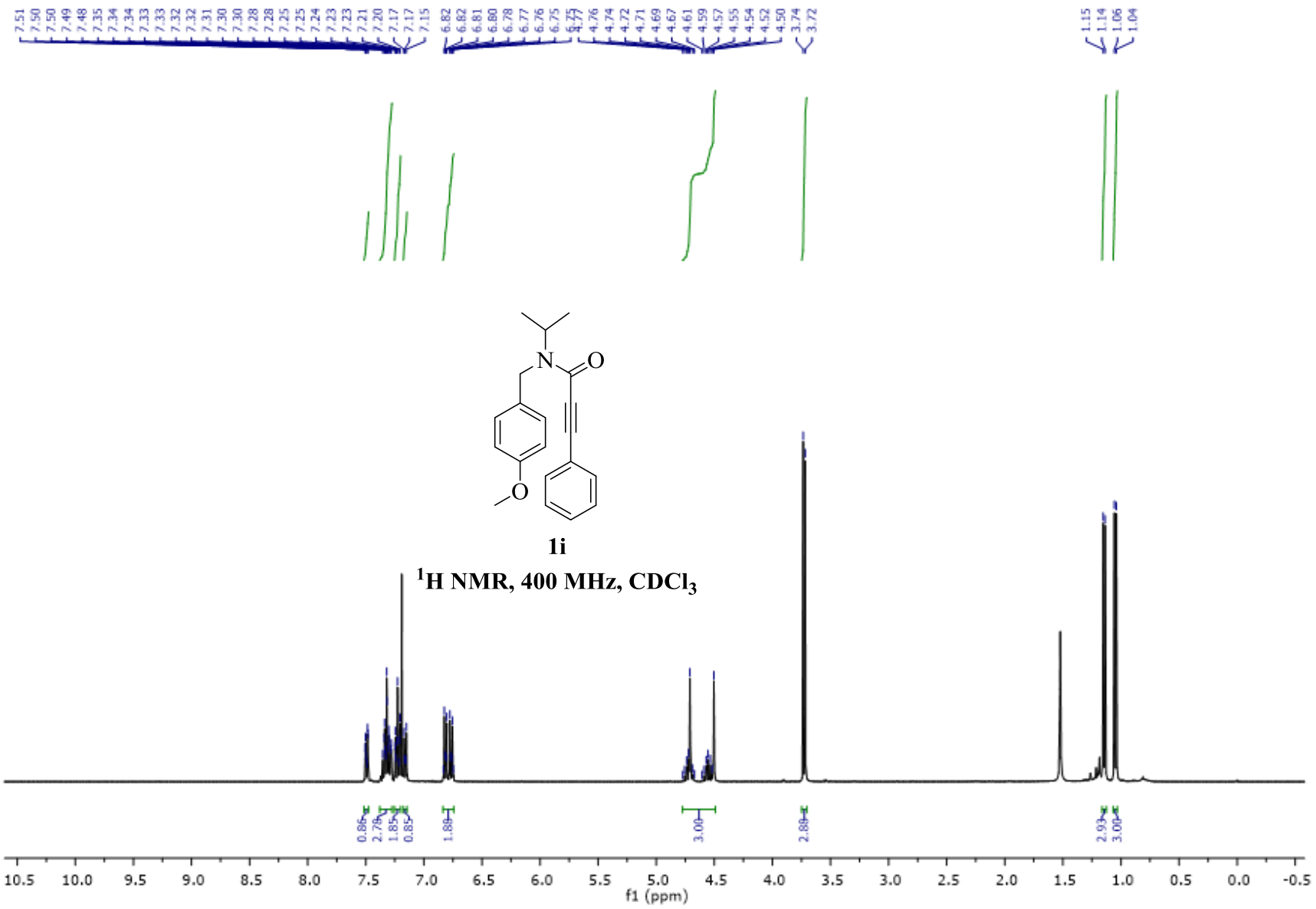
1f

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



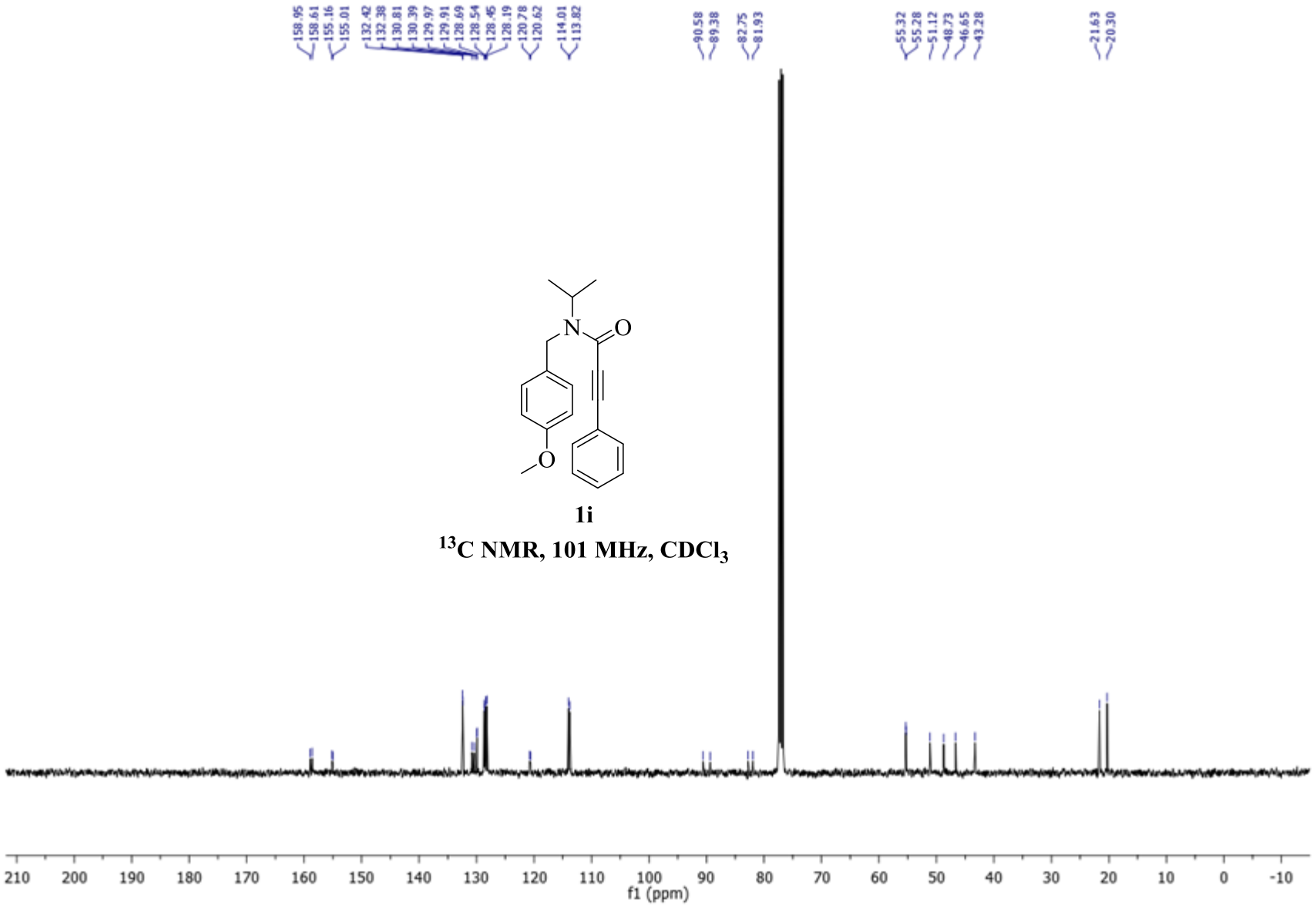
1f

^{13}C NMR, 101 MHz, $CDCl_3$



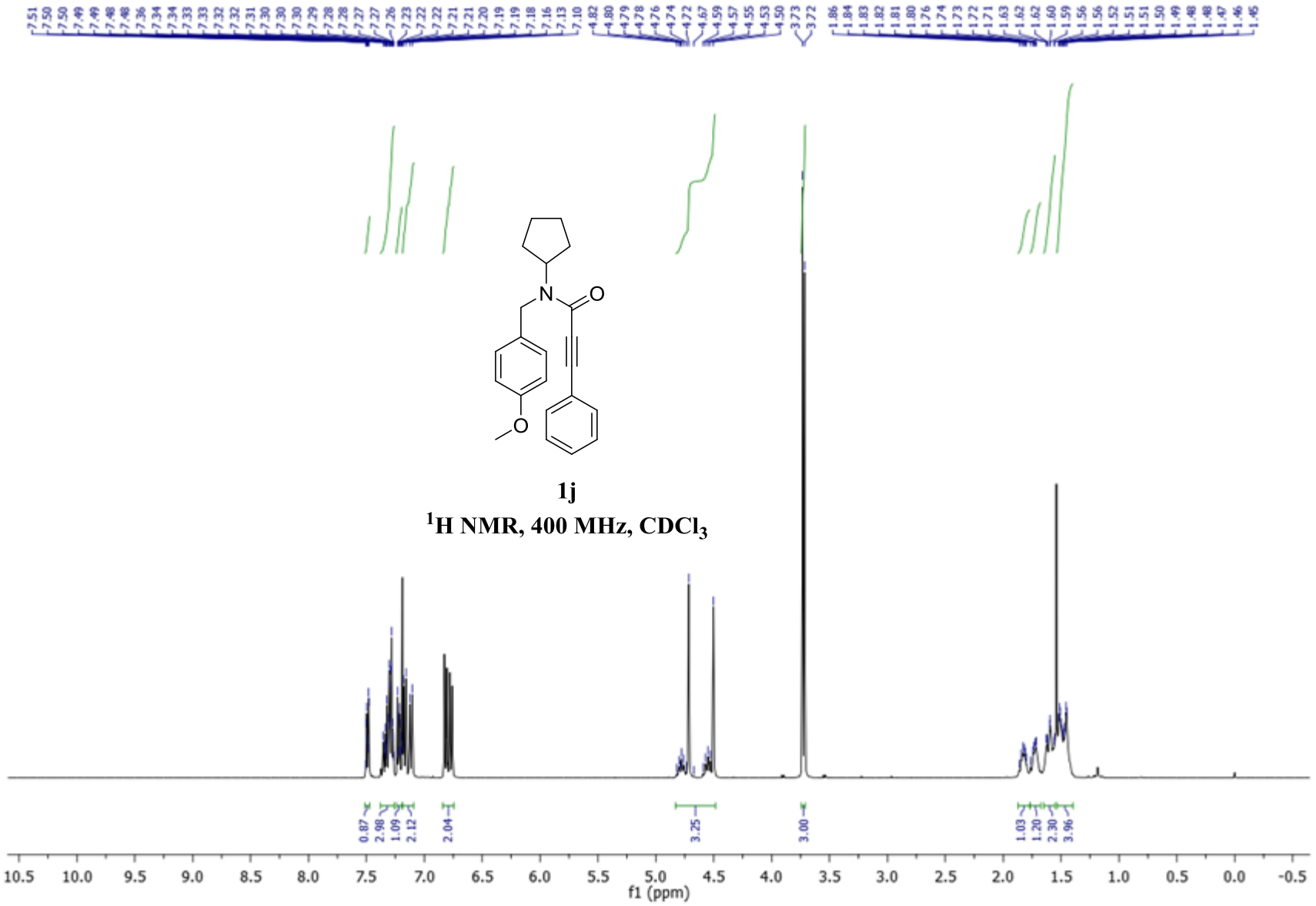
1i

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



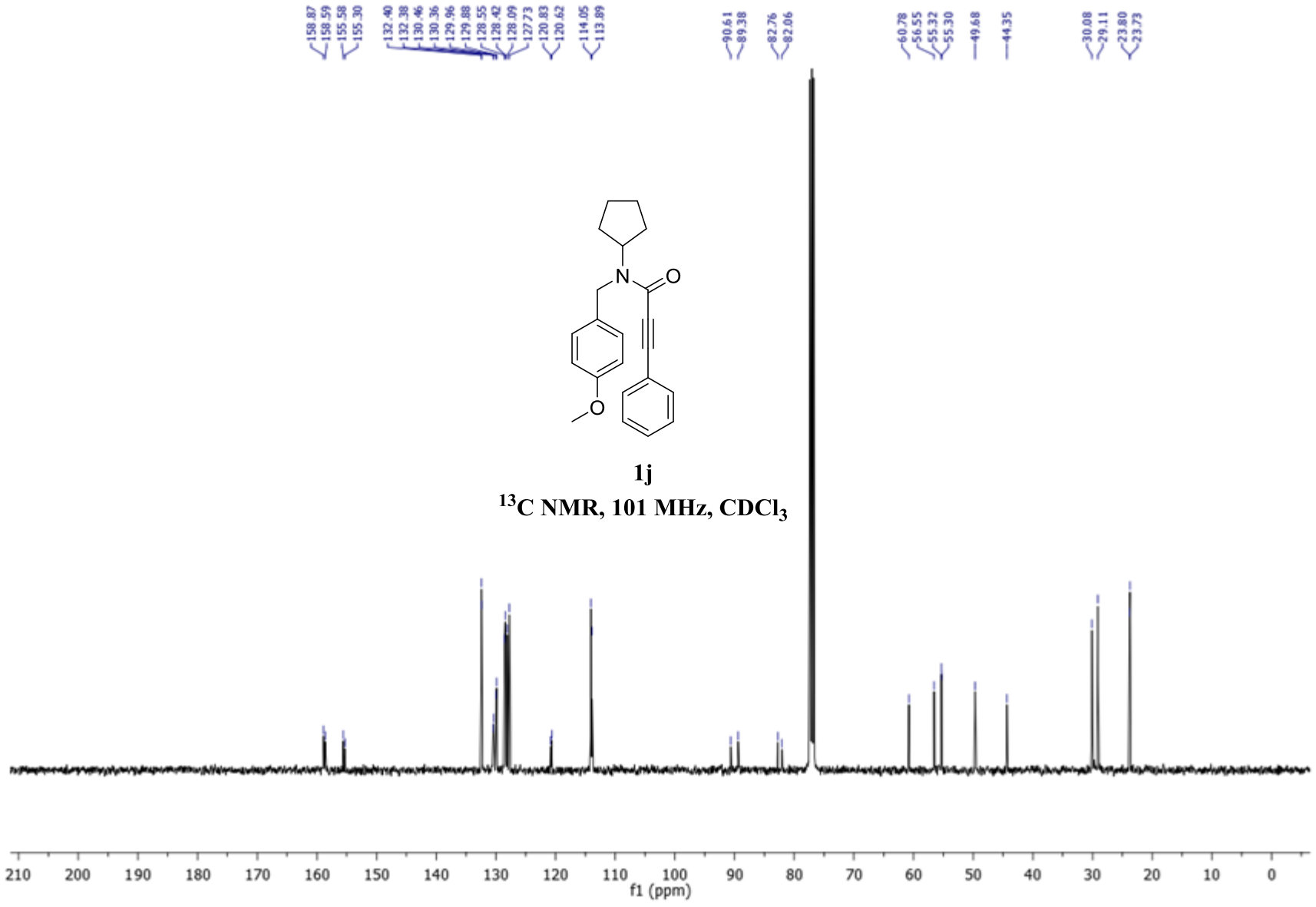
1i

^{13}C NMR, 101 MHz, $CDCl_3$



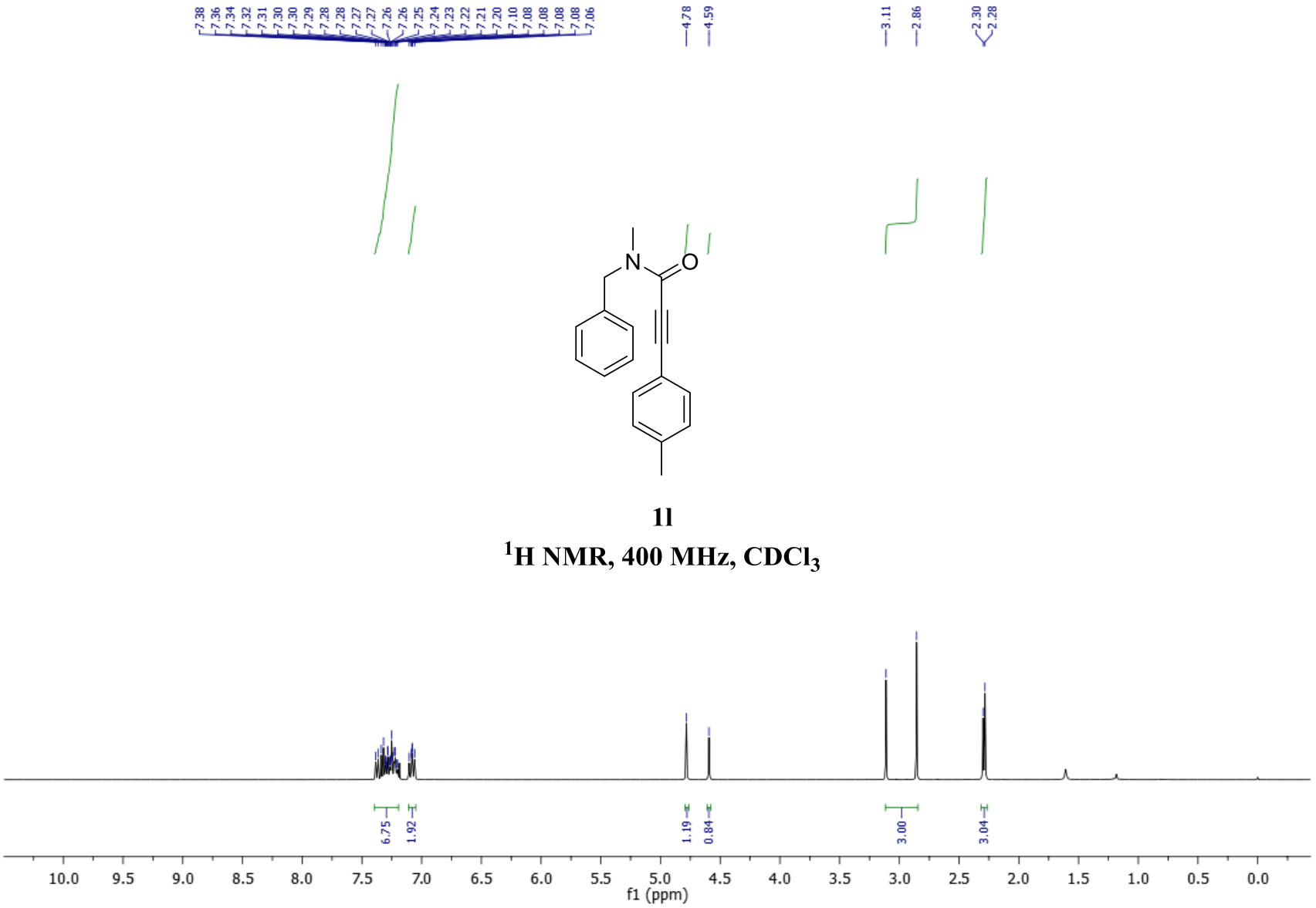
1j

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



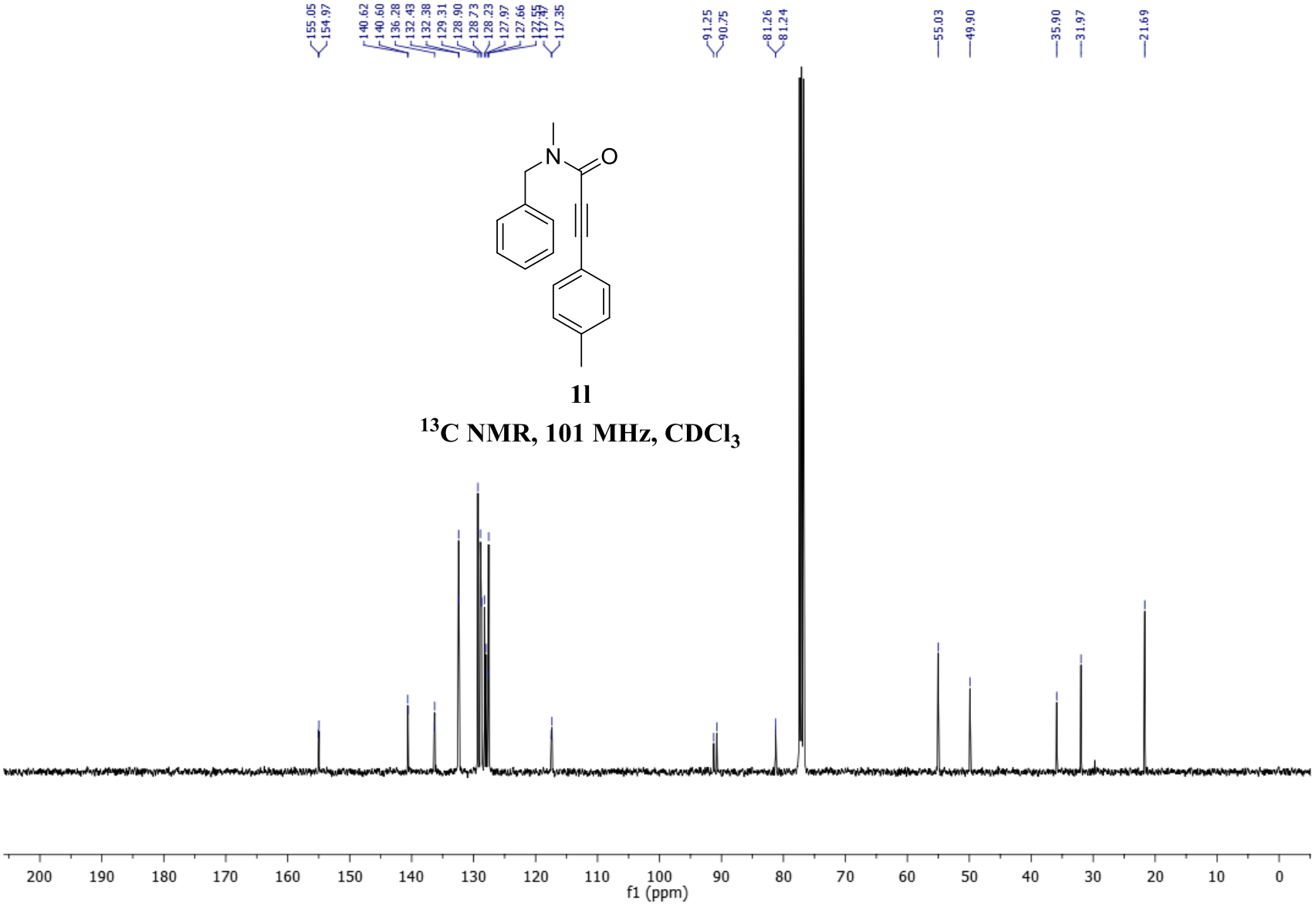
1j

^{13}C NMR, 101 MHz, $CDCl_3$



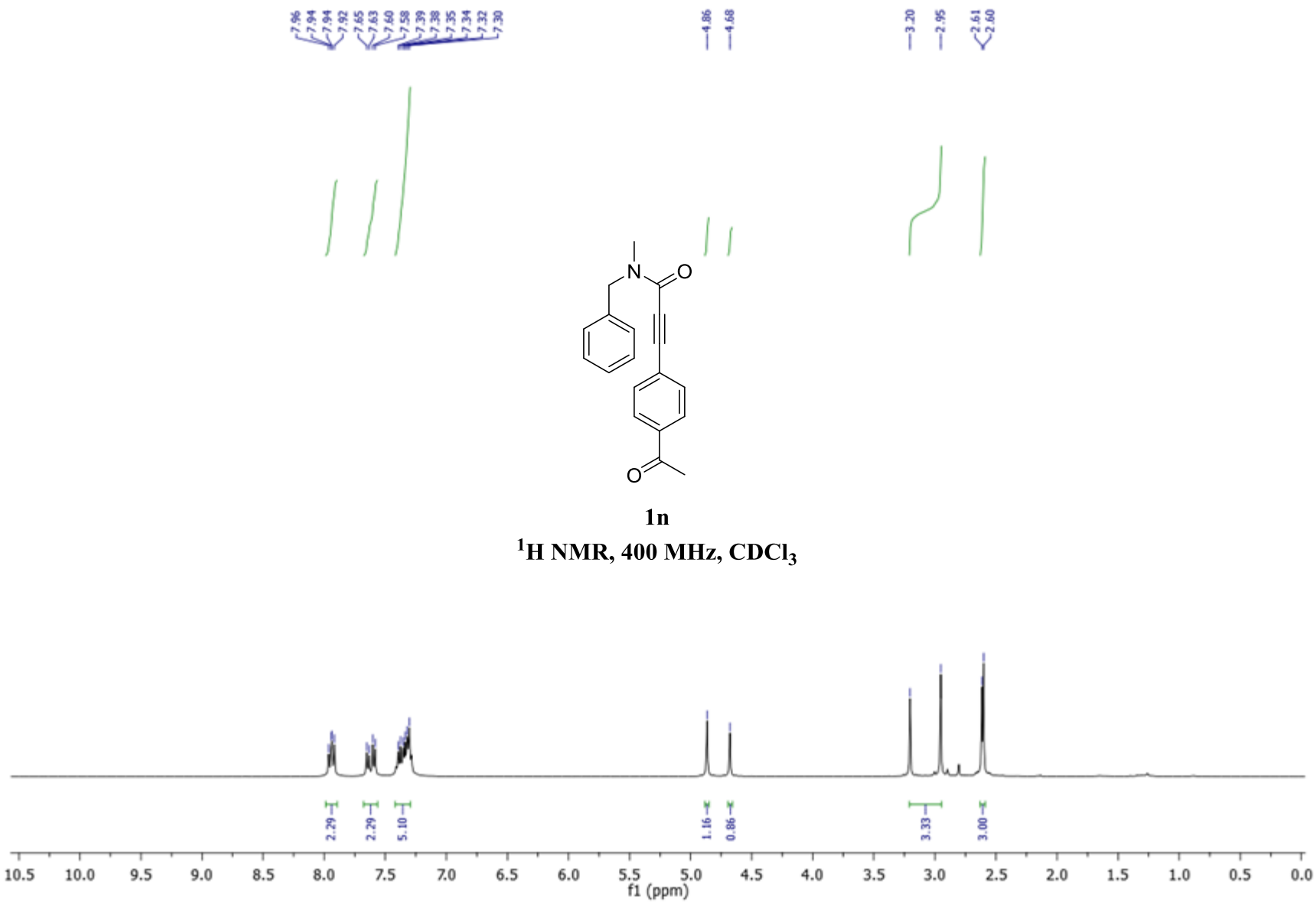
1l

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



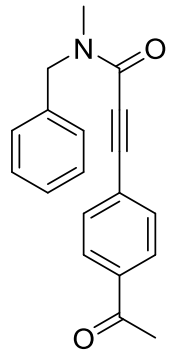
1l

^{13}C NMR, 101 MHz, $CDCl_3$



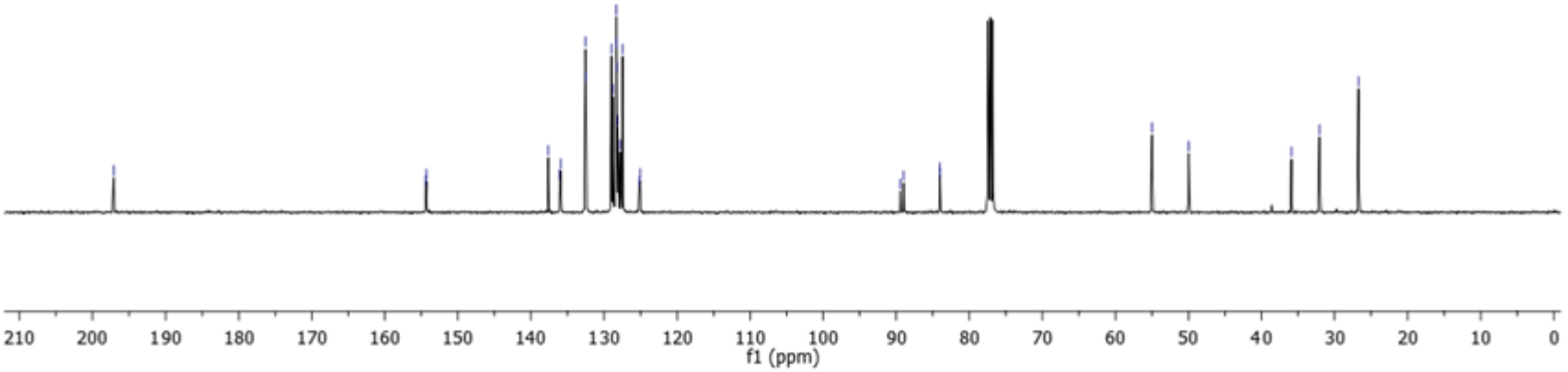
1n

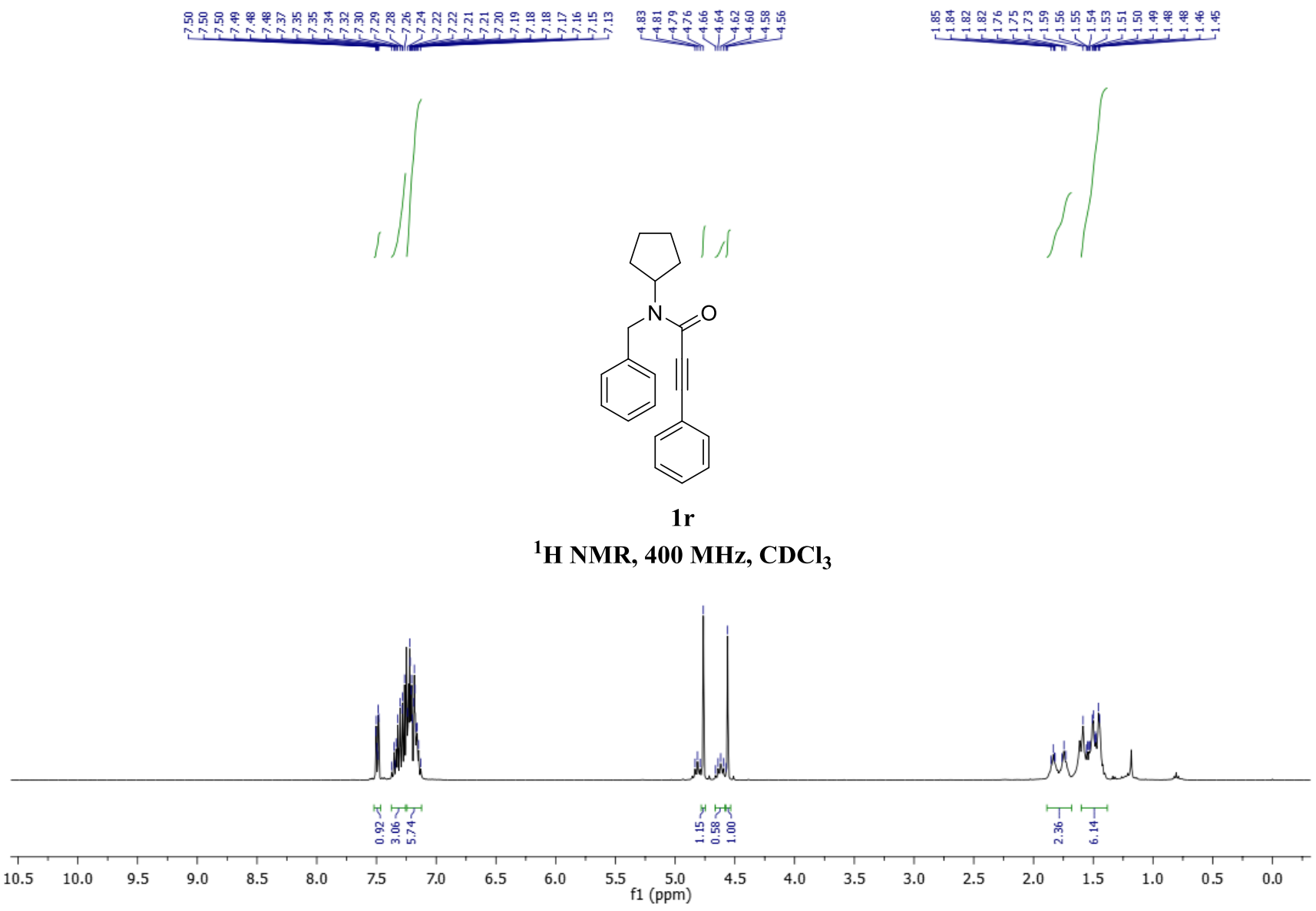
^{1}H NMR, 400 MHz, $CDCl_3$



1n

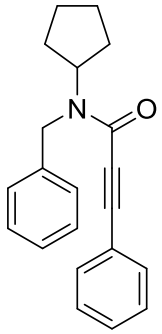
^{13}C NMR, 101 MHz, $CDCl_3$





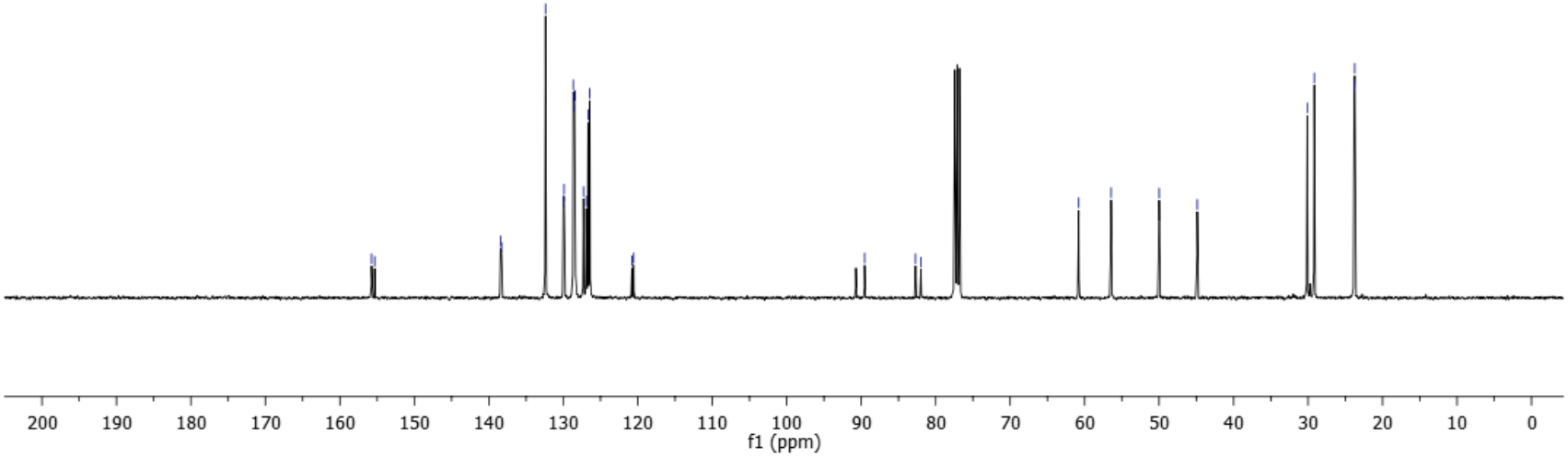
1r

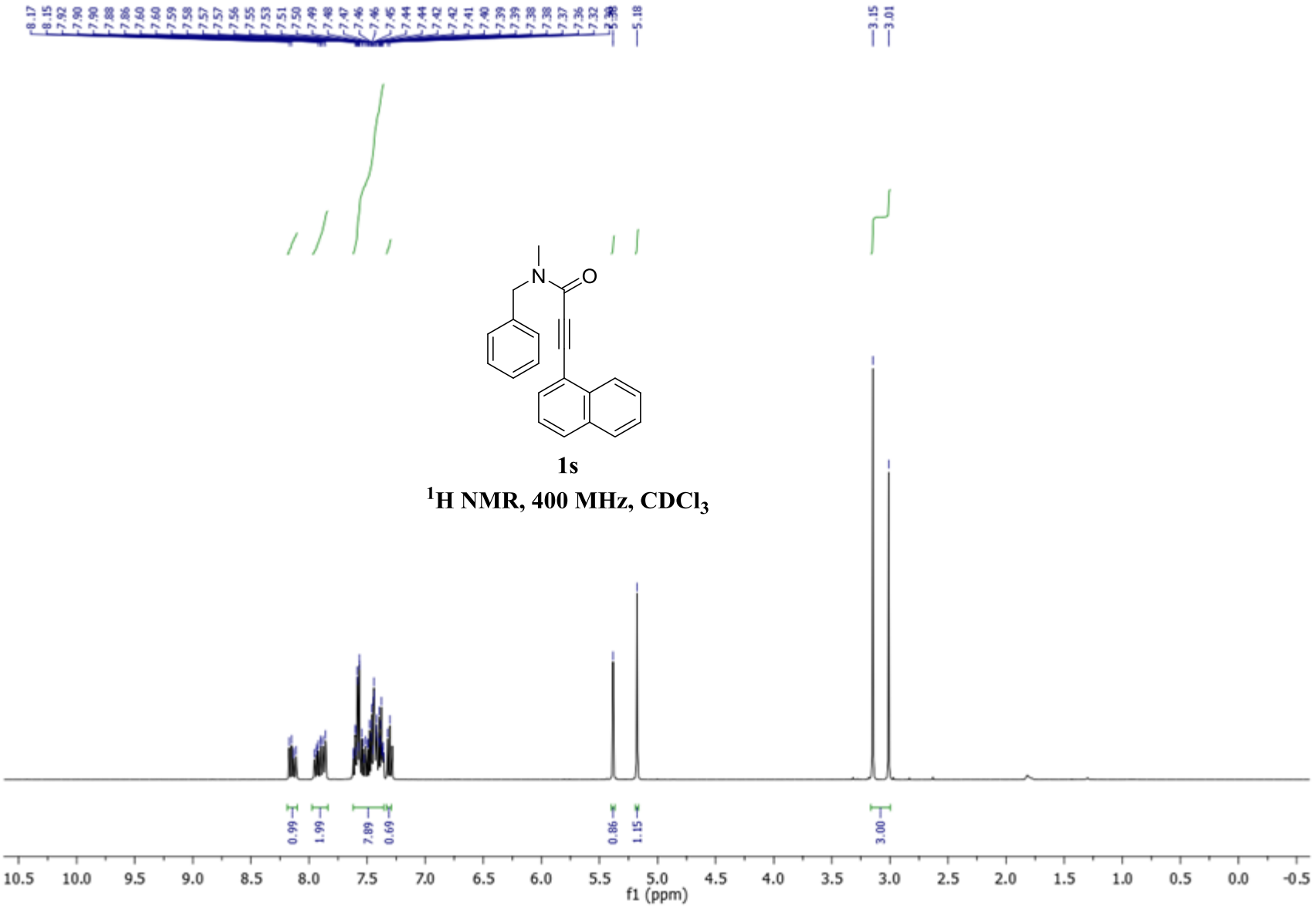
^{1}H NMR, 400 MHz, $CDCl_3$



1r

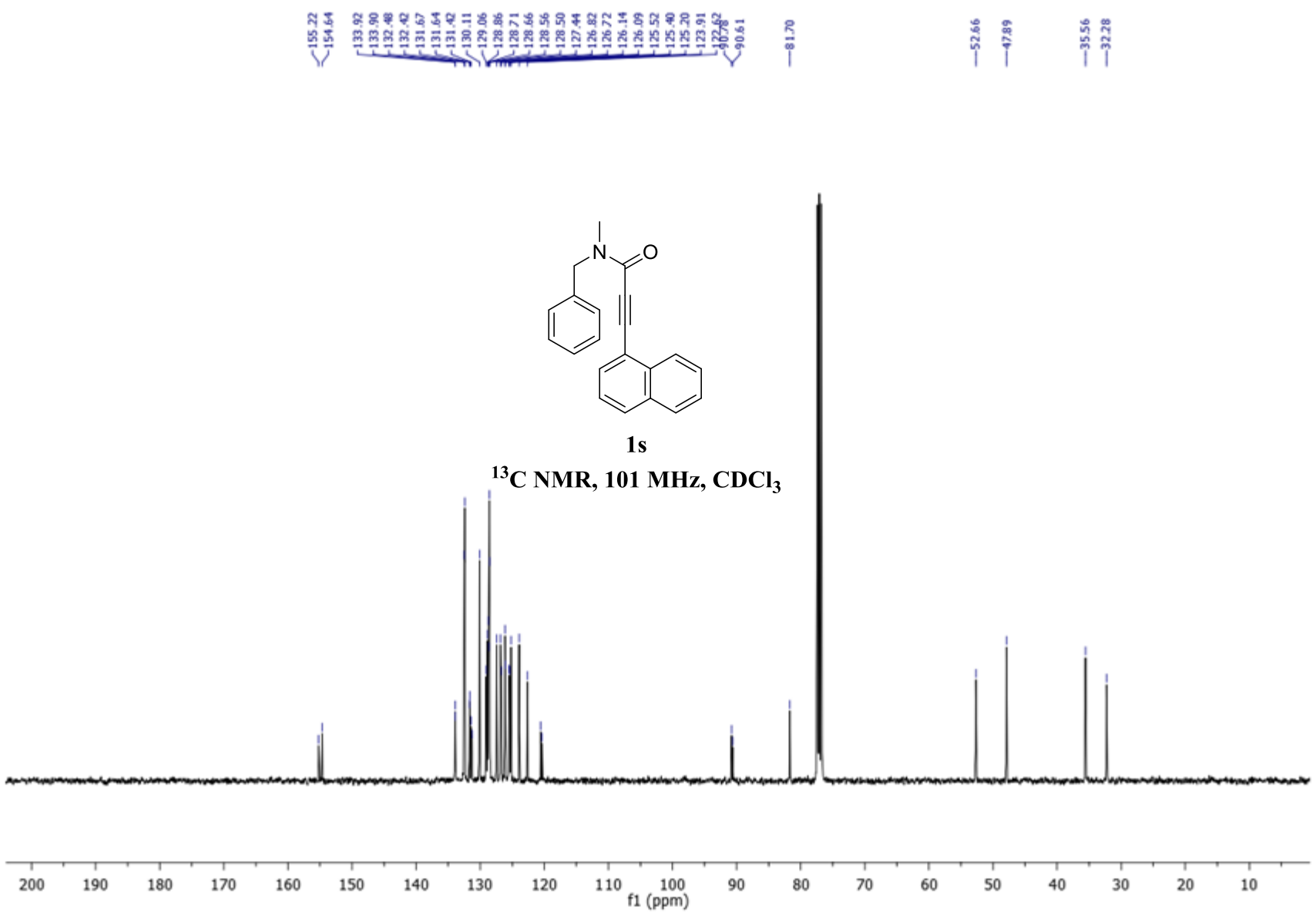
^{13}C NMR, 101 MHz, $CDCl_3$





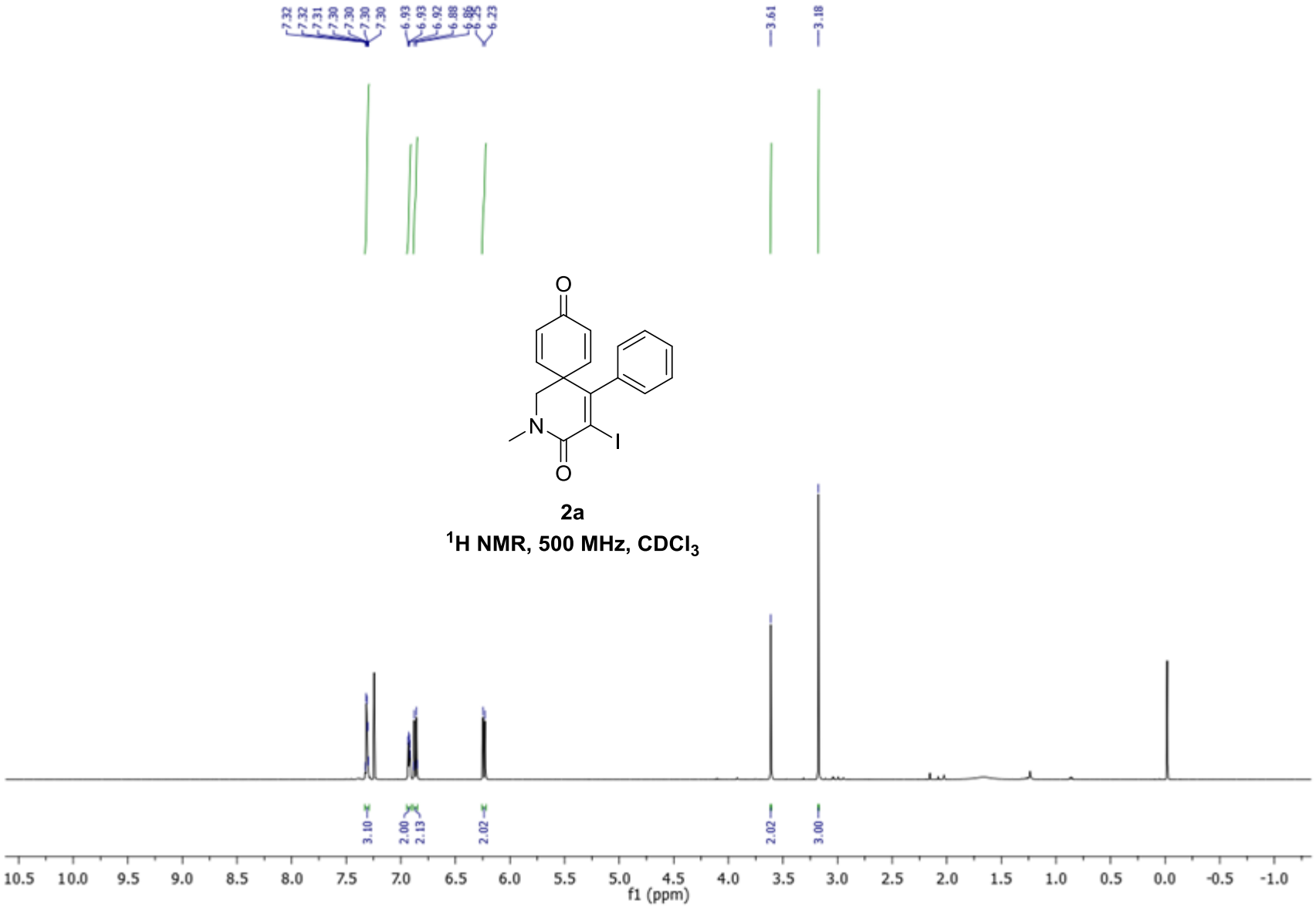
1s

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



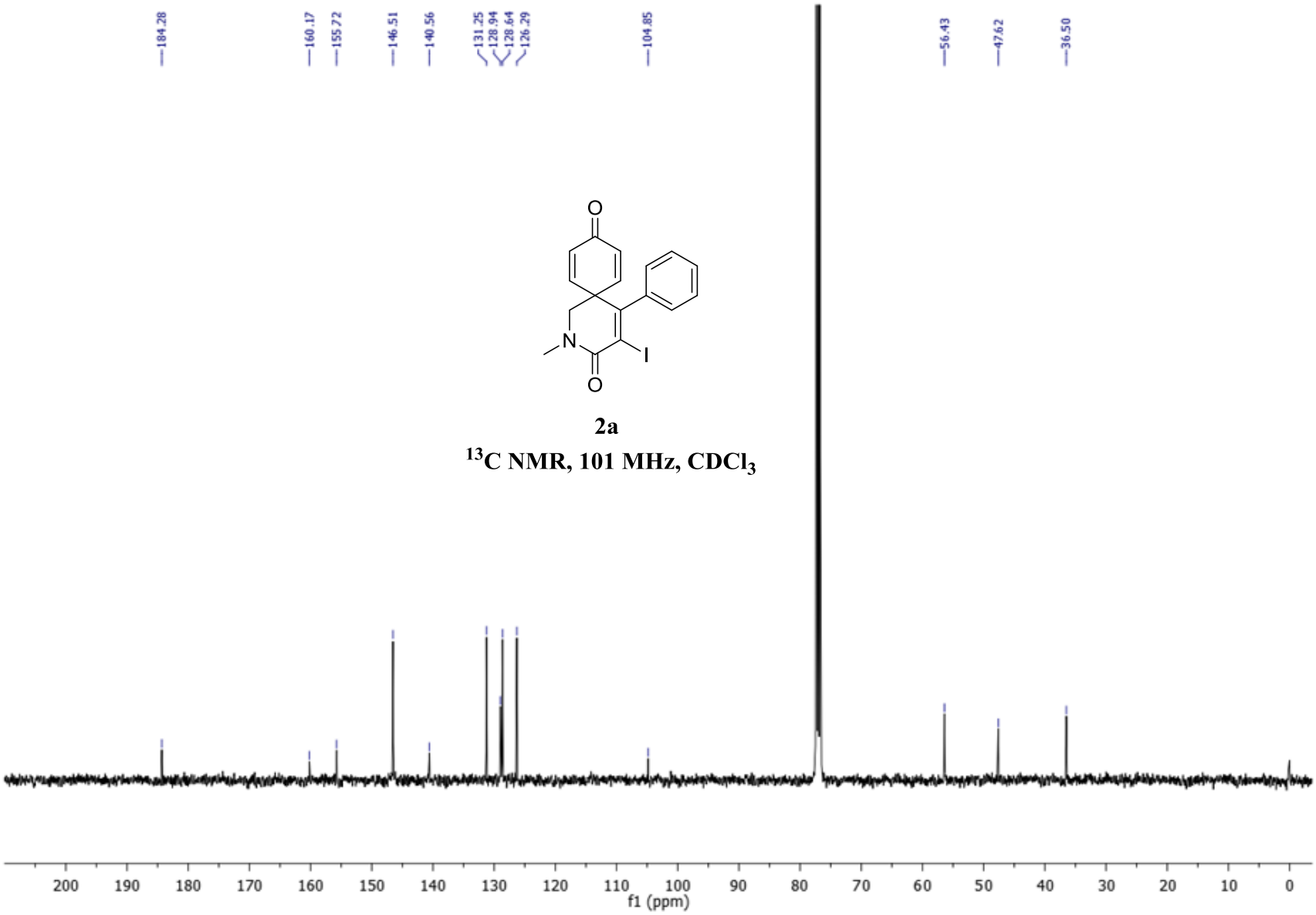
1s

^{13}C NMR, 101 MHz, $CDCl_3$



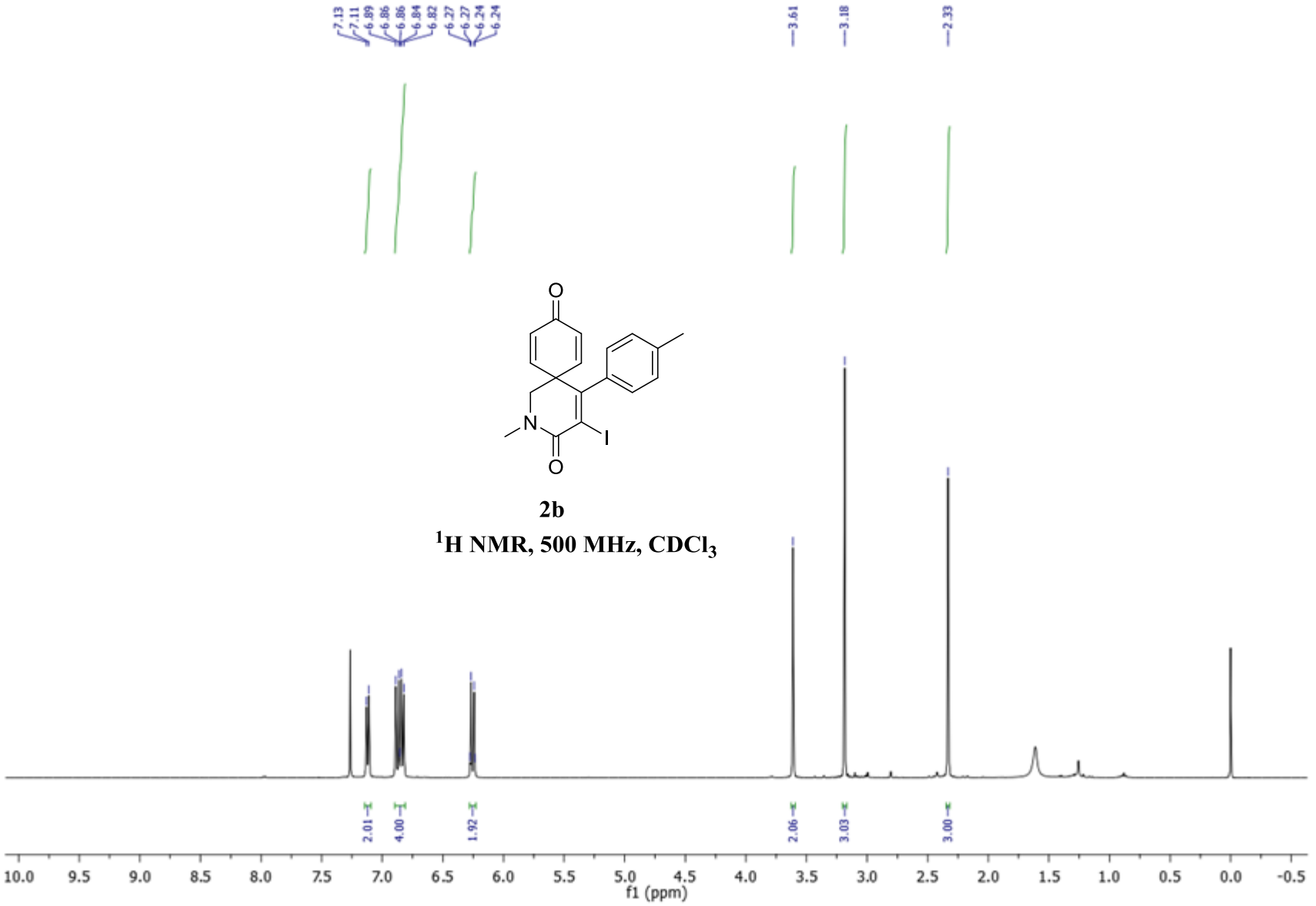
2a

^{1}H NMR, 500 MHz, $CDCl_3$



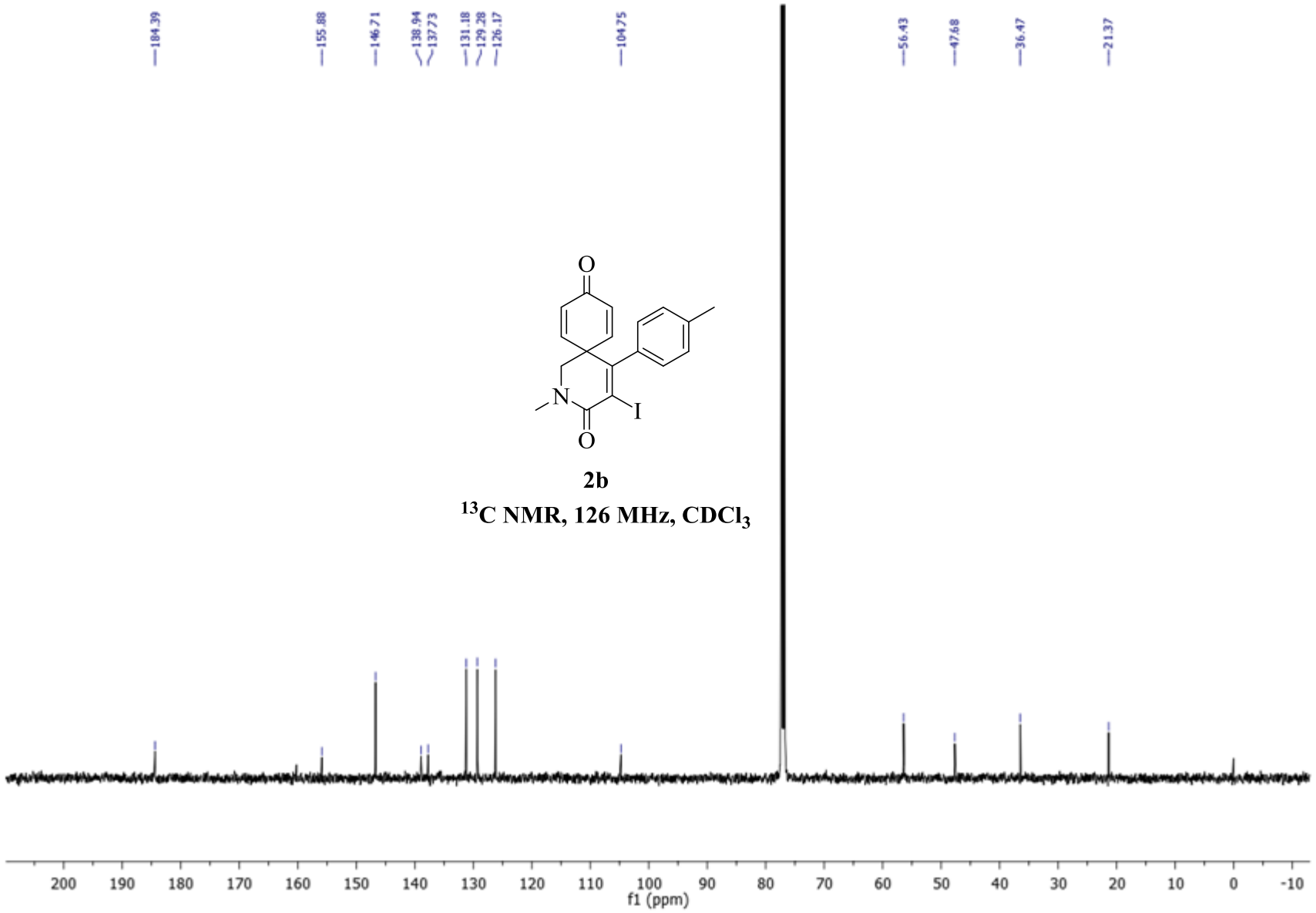
2a

^{13}C NMR, 101 MHz, $CDCl_3$



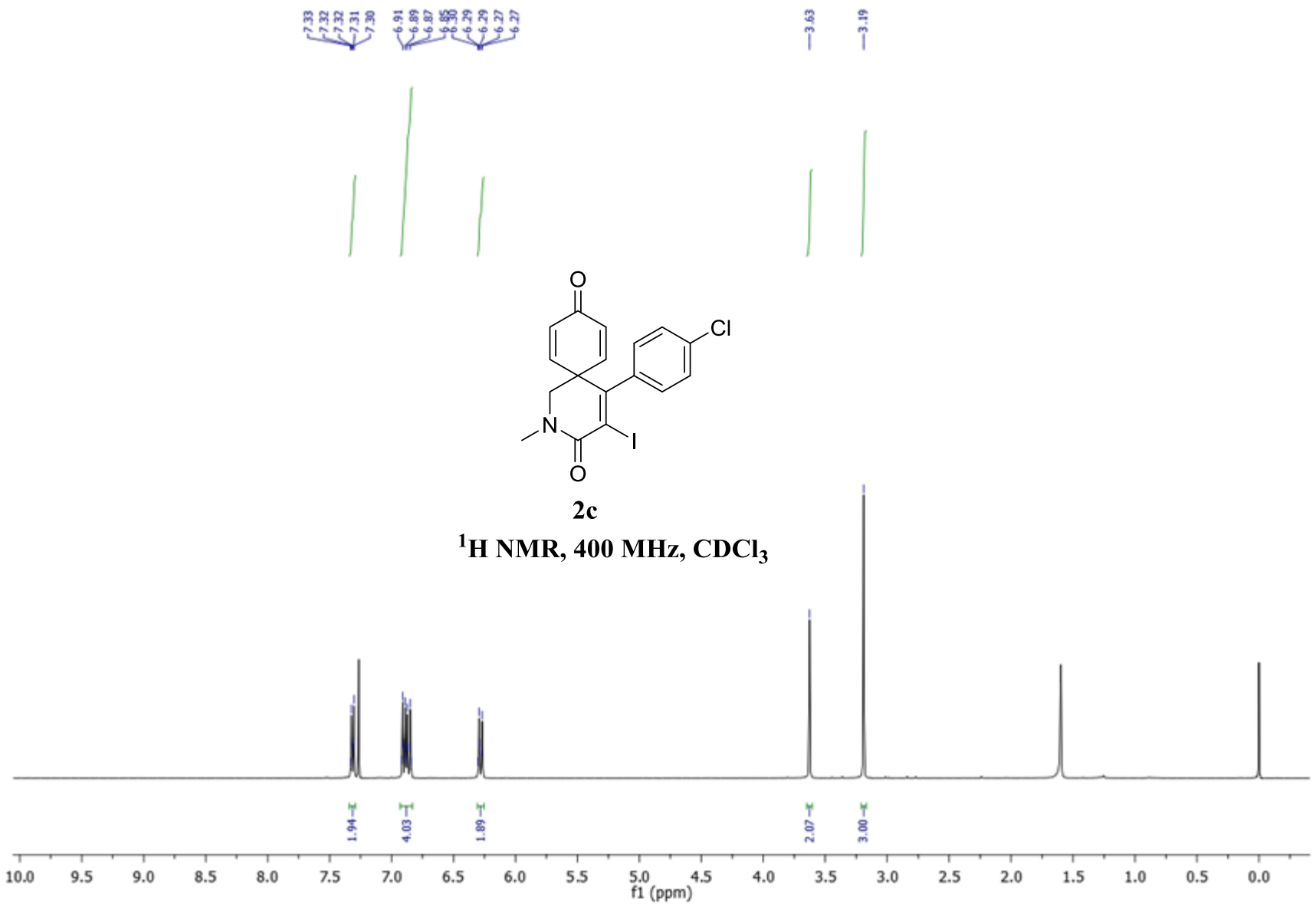
2b

^{1}H NMR, 500 MHz, $CDCl_3$



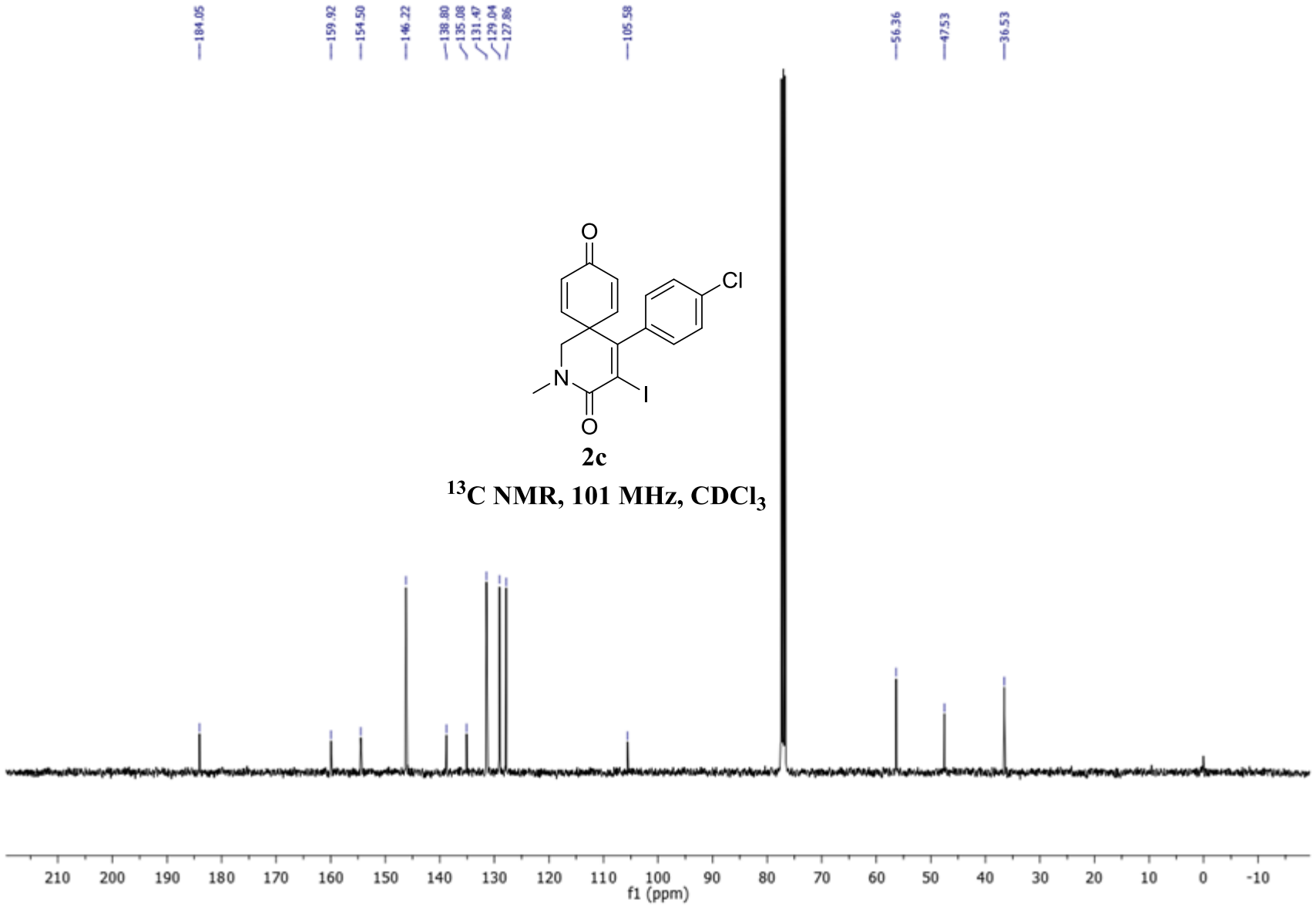
2b

^{13}C NMR, 126 MHz, $CDCl_3$



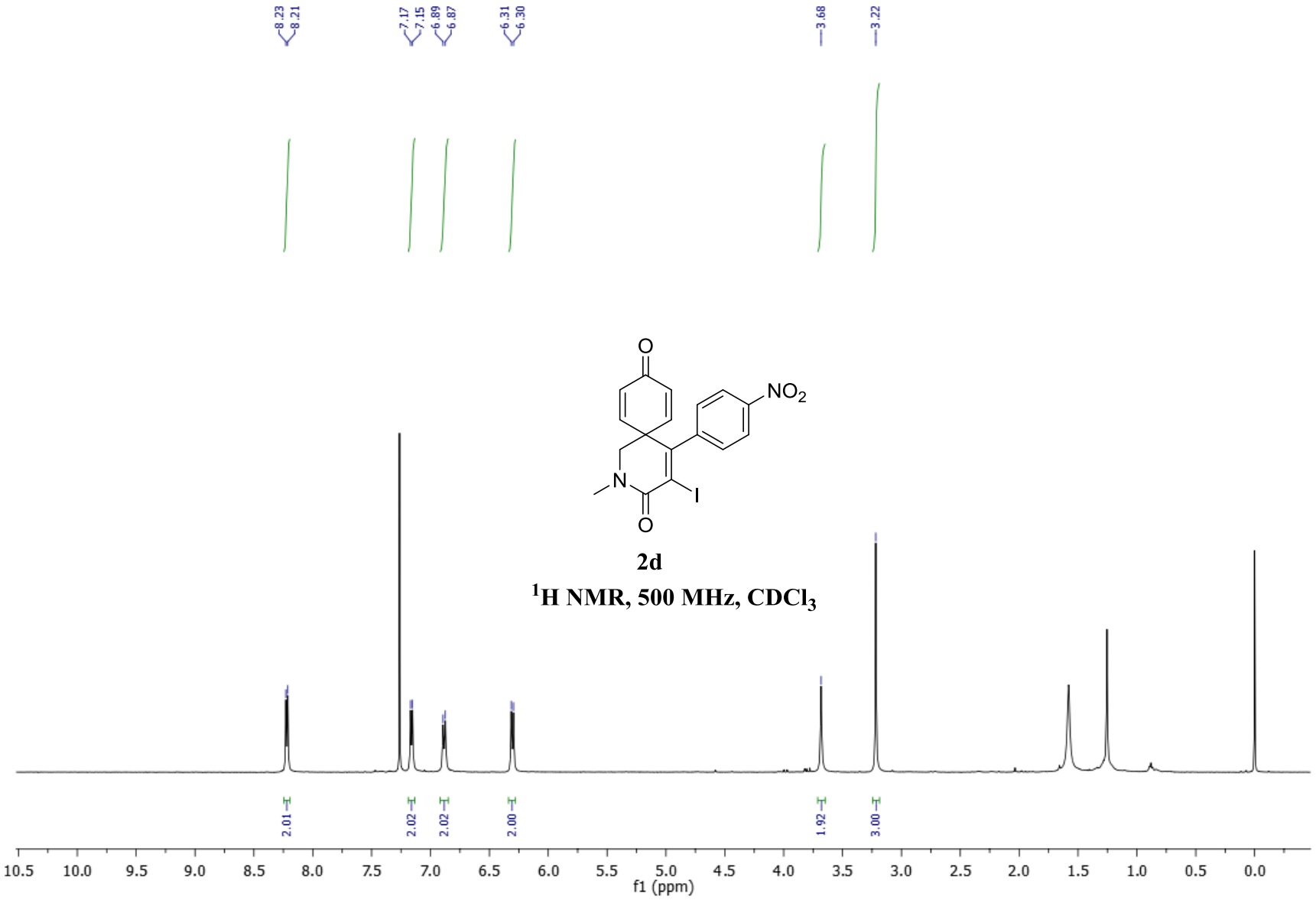
2c

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



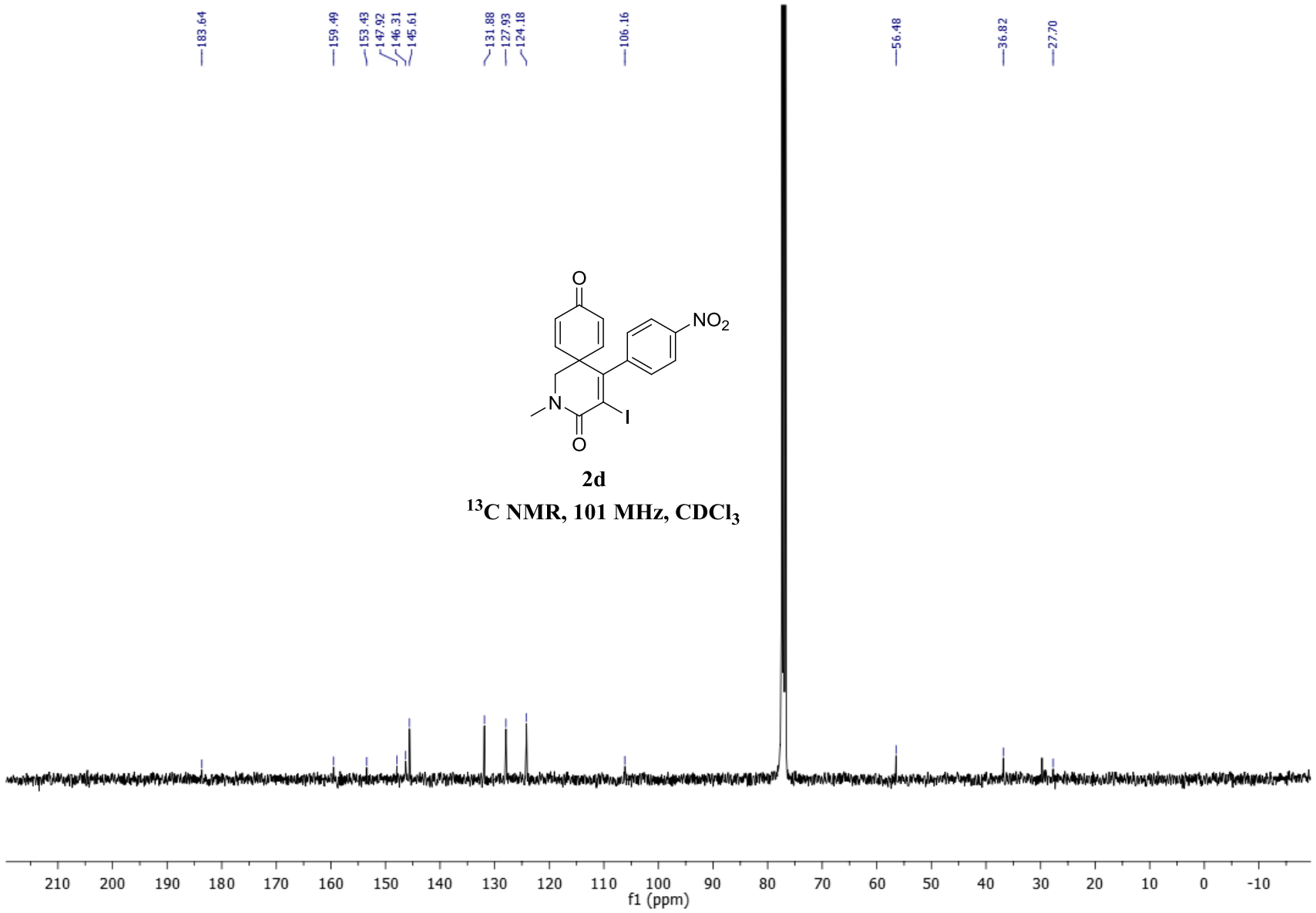
2c

^{13}C NMR, 101 MHz, $CDCl_3$



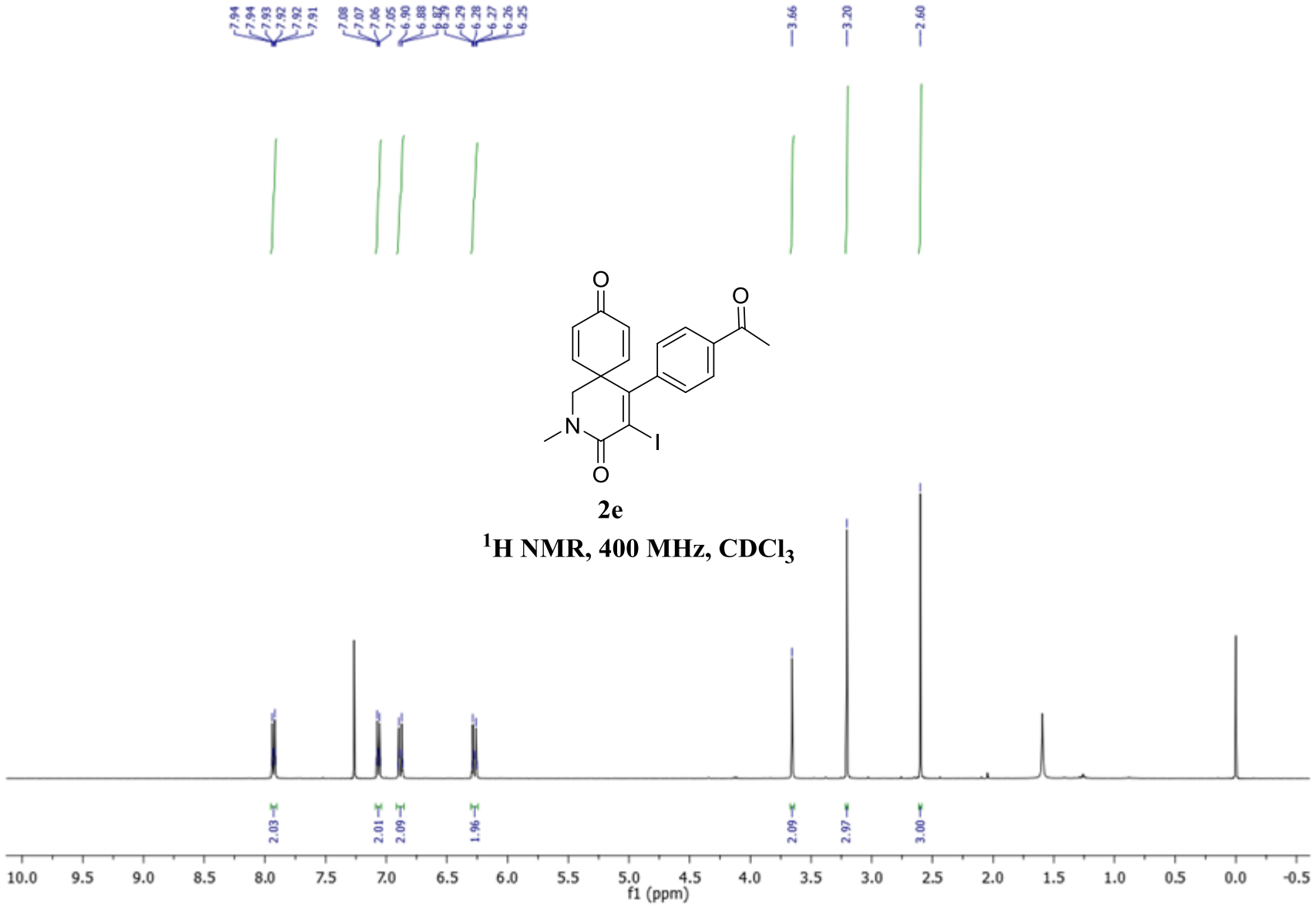
2d

^{1}H NMR, 500 MHz, $CDCl_3$



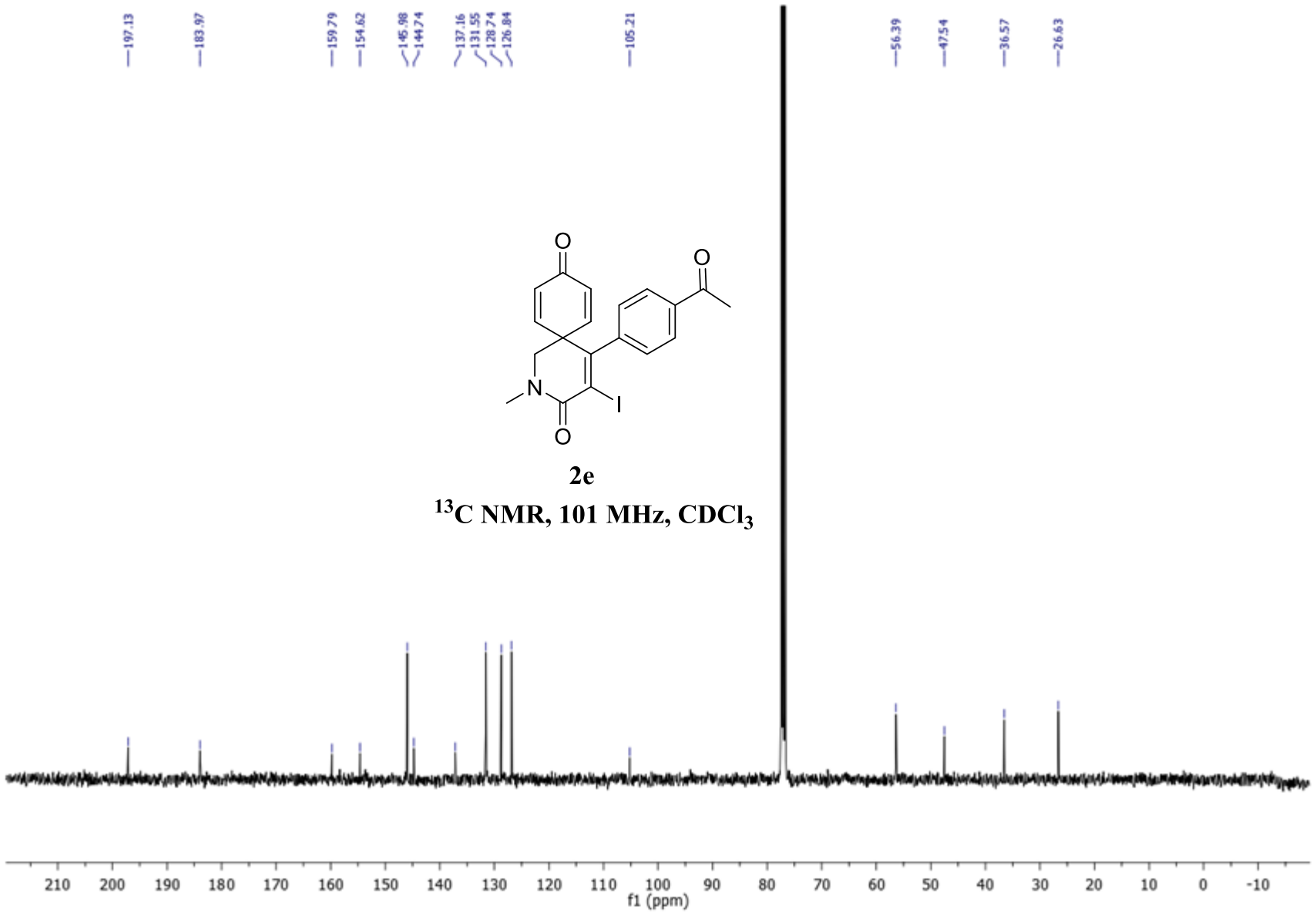
2d

^{13}C NMR, 101 MHz, $CDCl_3$



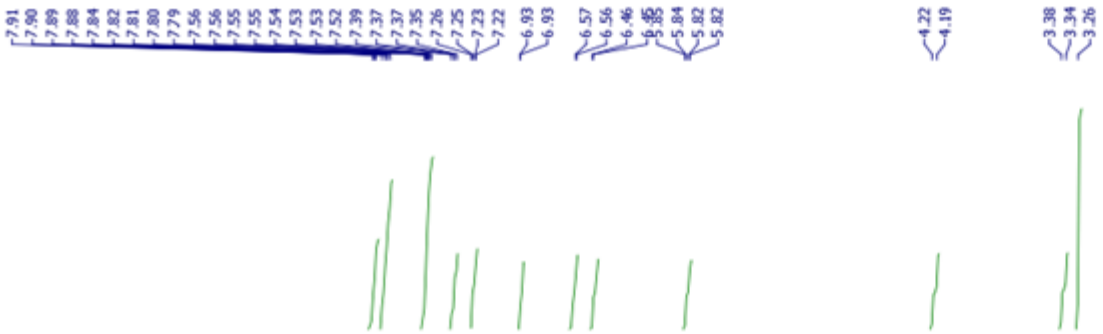
2e

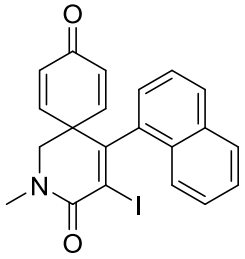
^{1}H NMR, 400 MHz, $CDCl_3$



2e

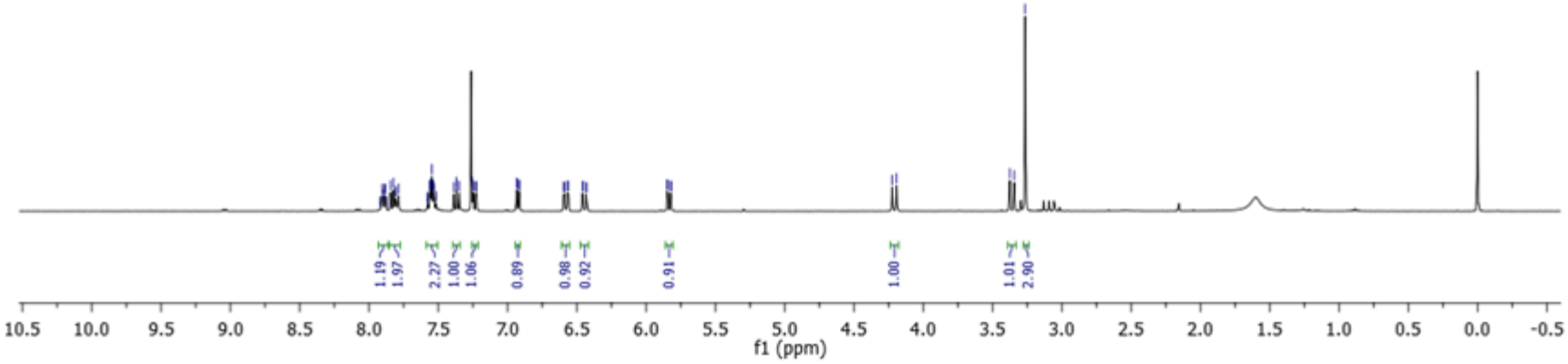
^{13}C NMR, 101 MHz, $CDCl_3$

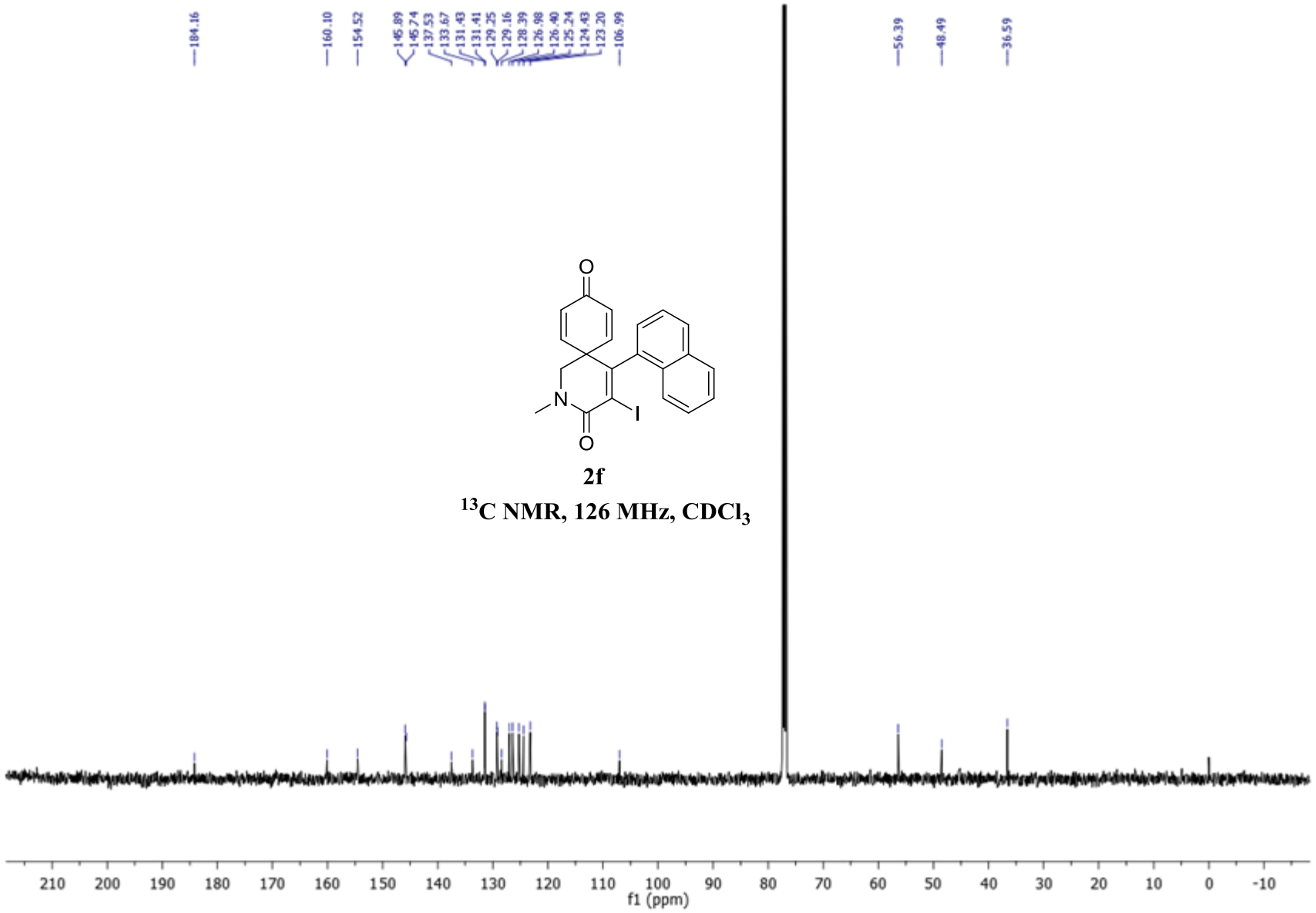




2f

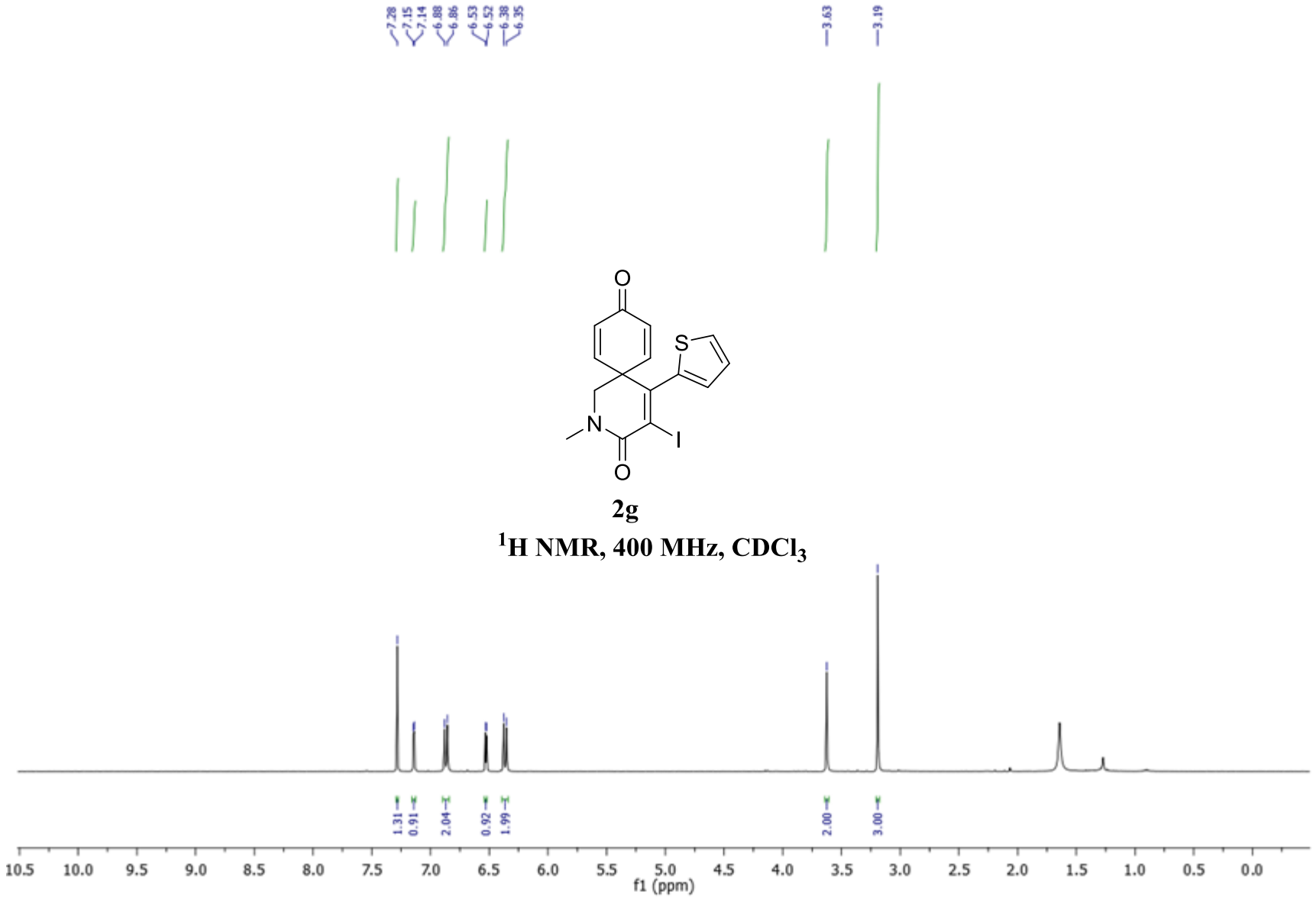
^{1}H NMR, 400 MHz, $CDCl_3$





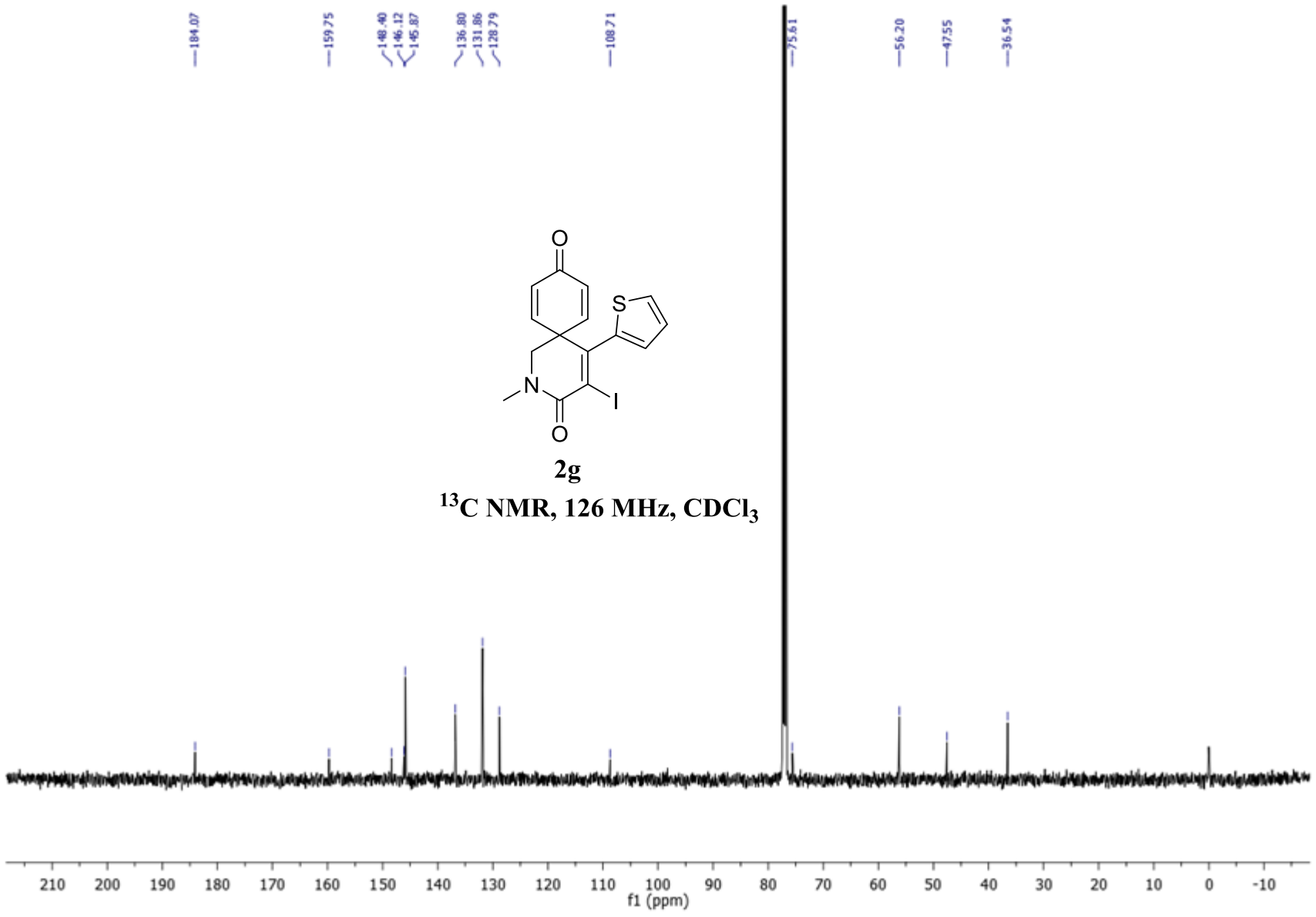
2f

^{13}C NMR, 126 MHz, $CDCl_3$



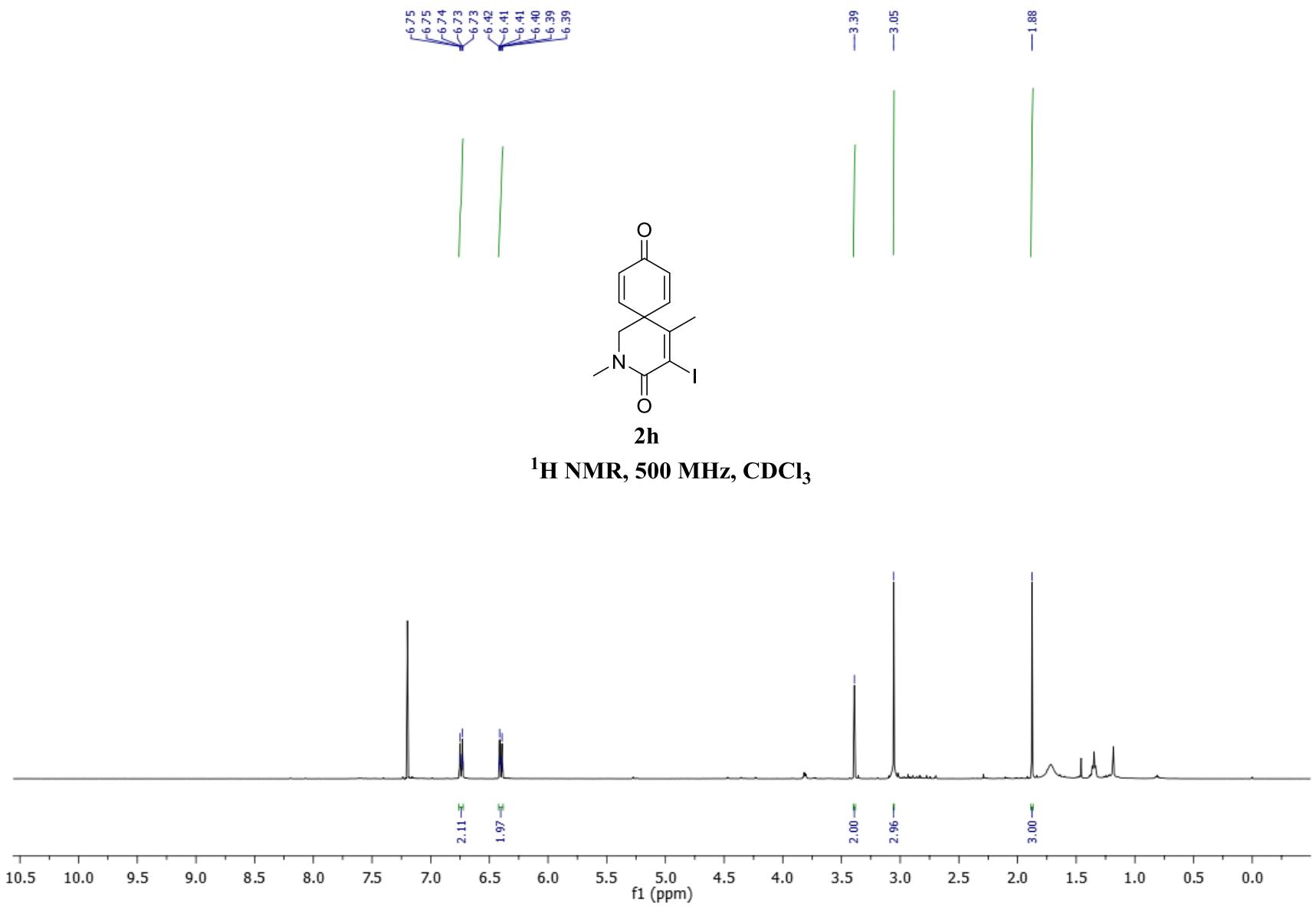
2g

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



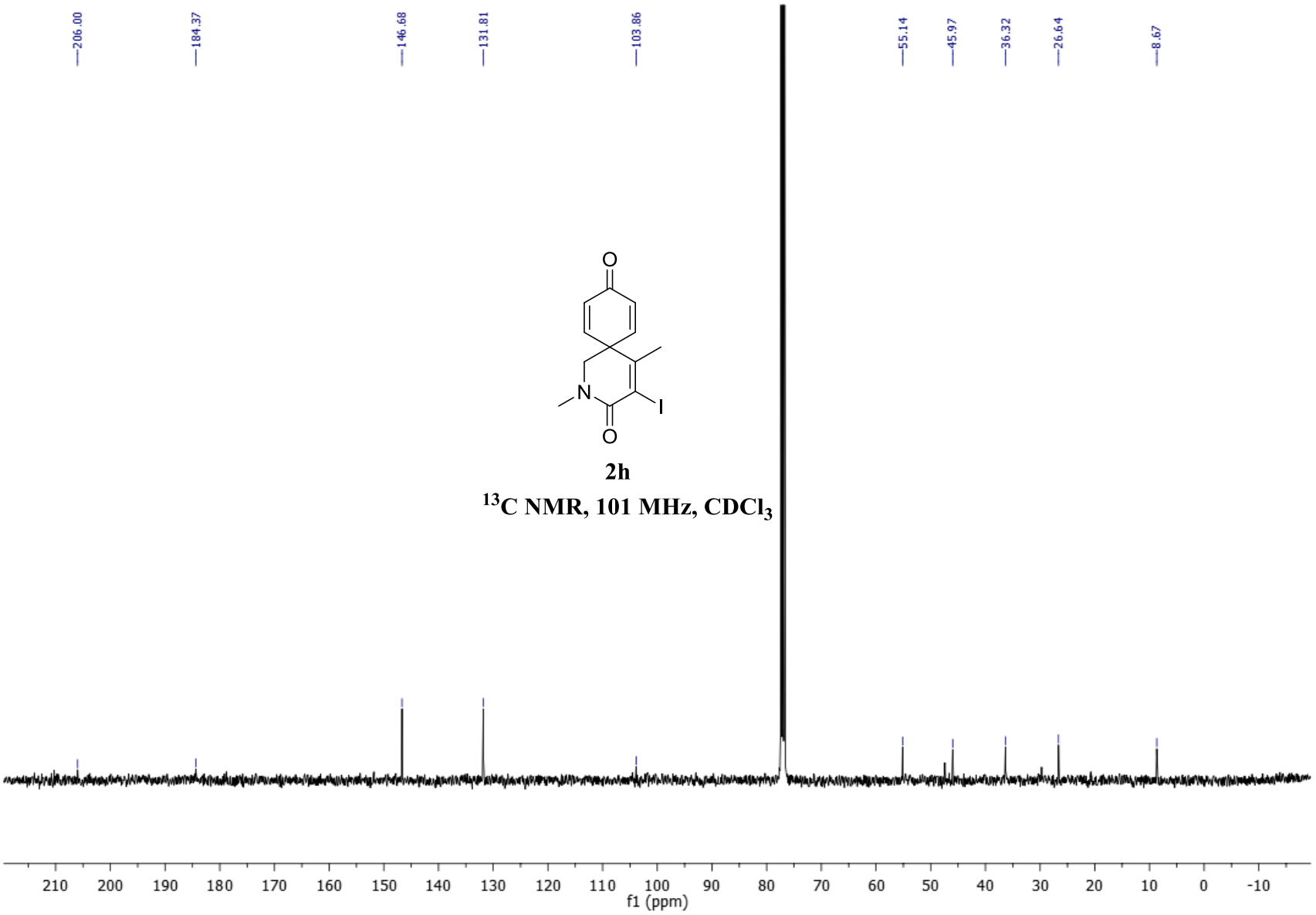
2g

^{13}C NMR, 126 MHz, $CDCl_3$



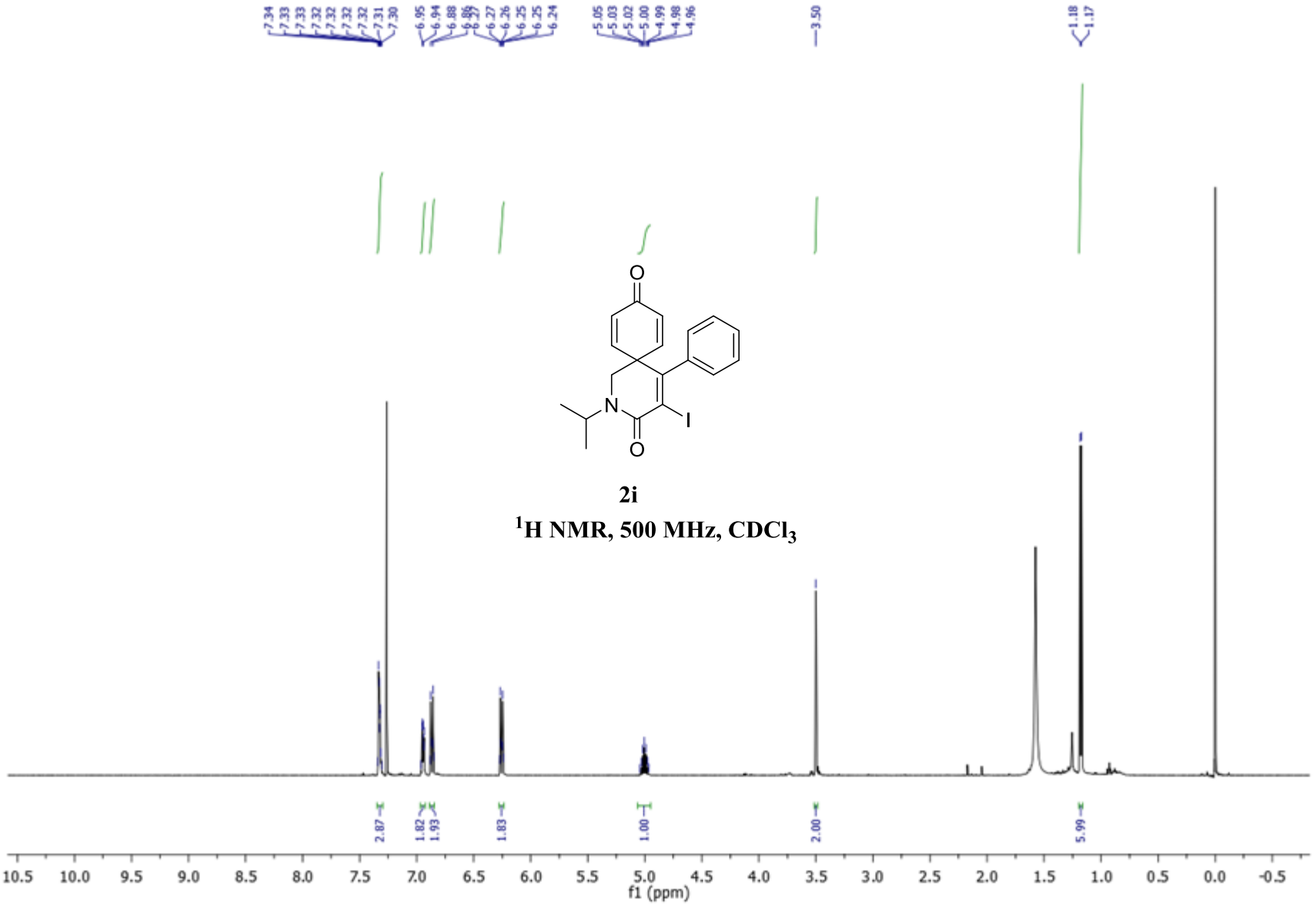
2h

^{1}H NMR, 500 MHz, $CDCl_3$



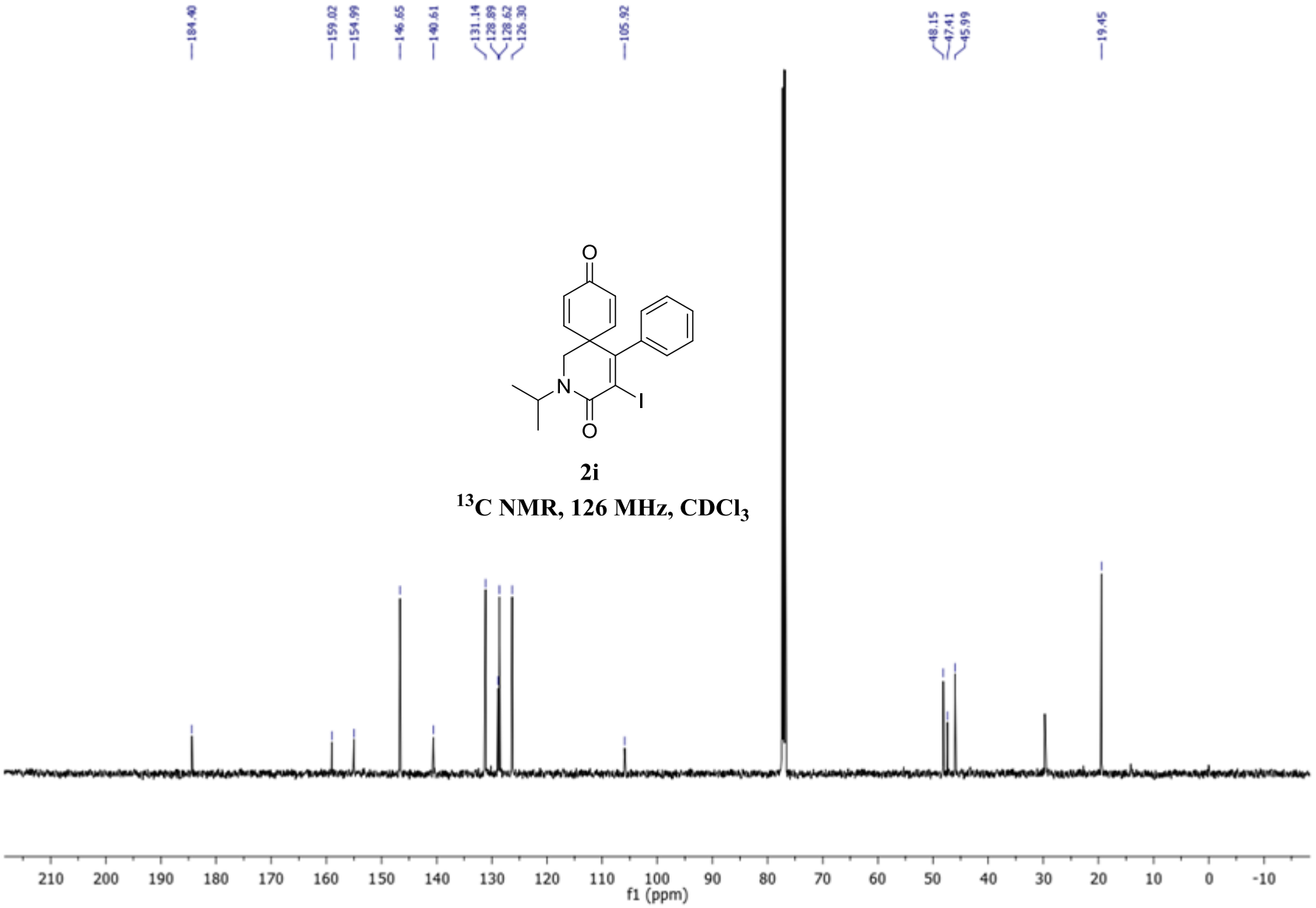
2h

^{13}C NMR, 101 MHz, $CDCl_3$



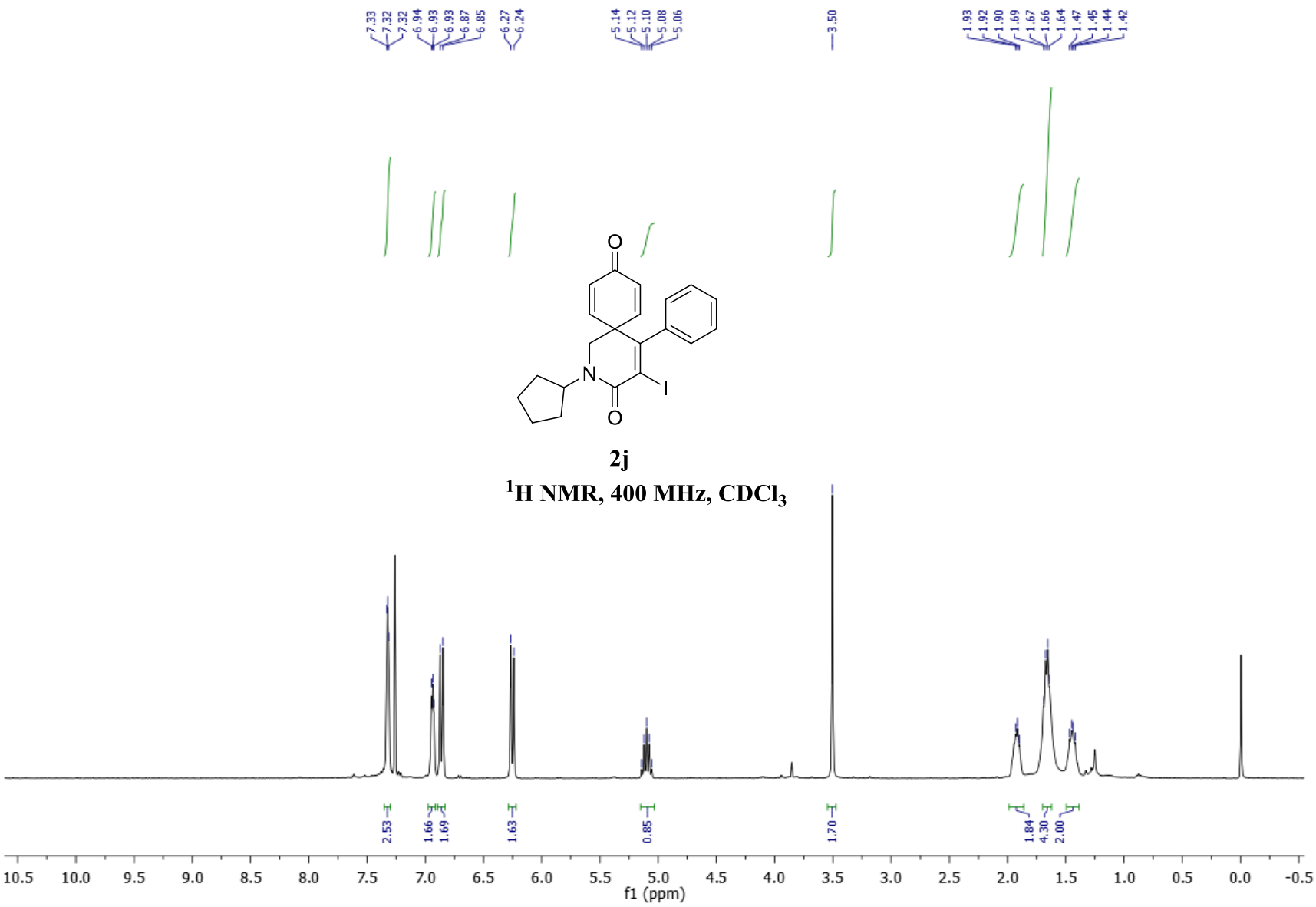
2i

^{1}H NMR, 500 MHz, $CDCl_3$



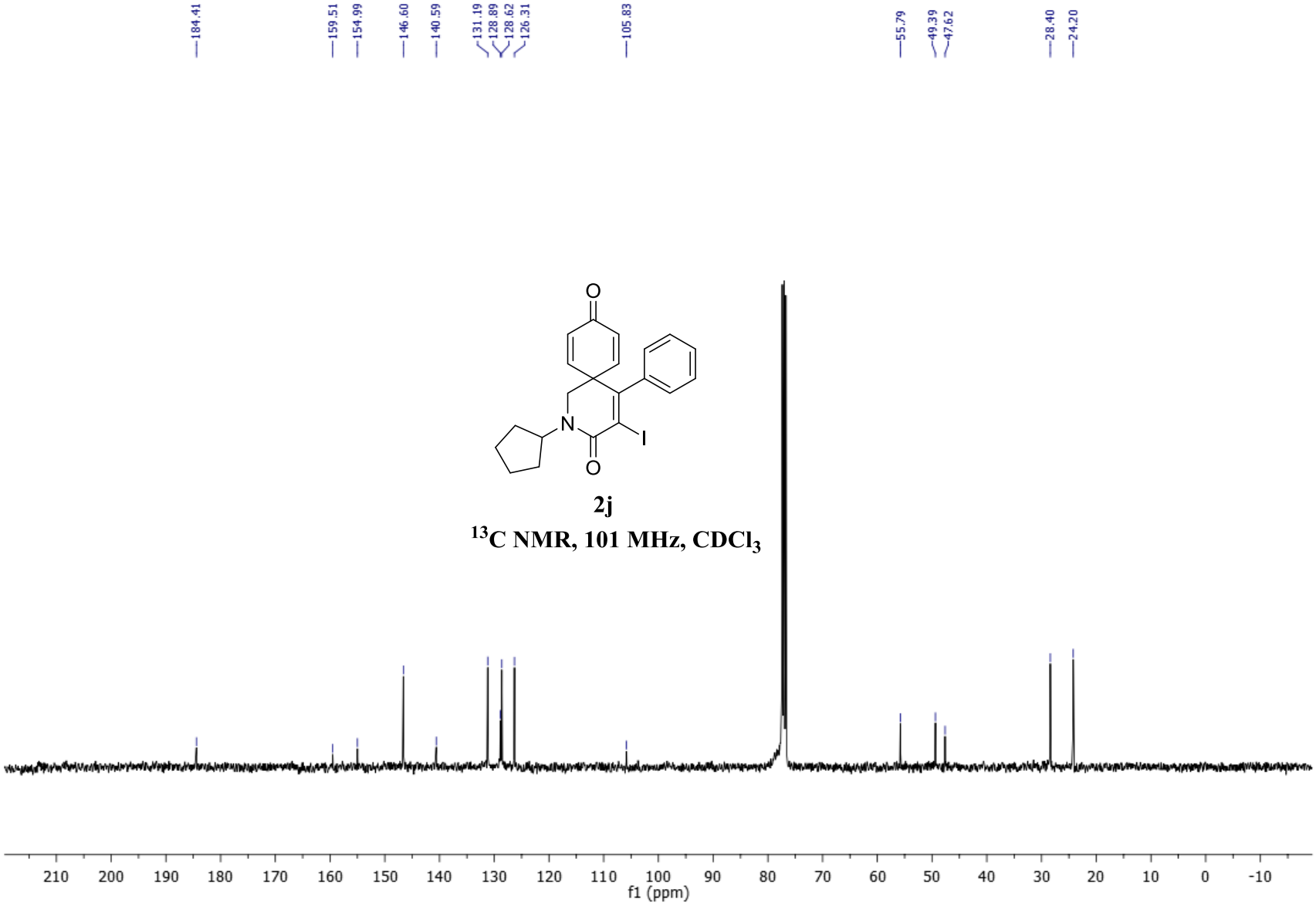
2i

^{13}C NMR, 126 MHz, $CDCl_3$



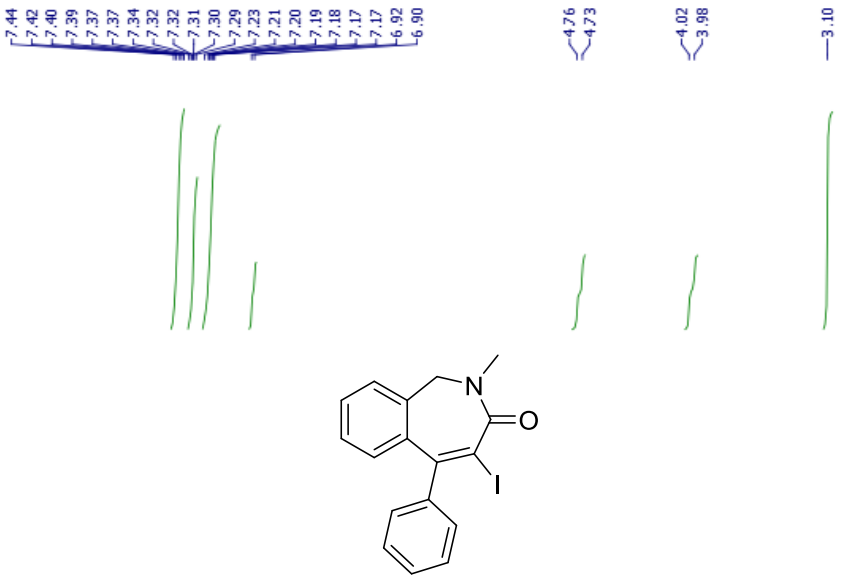
2j

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



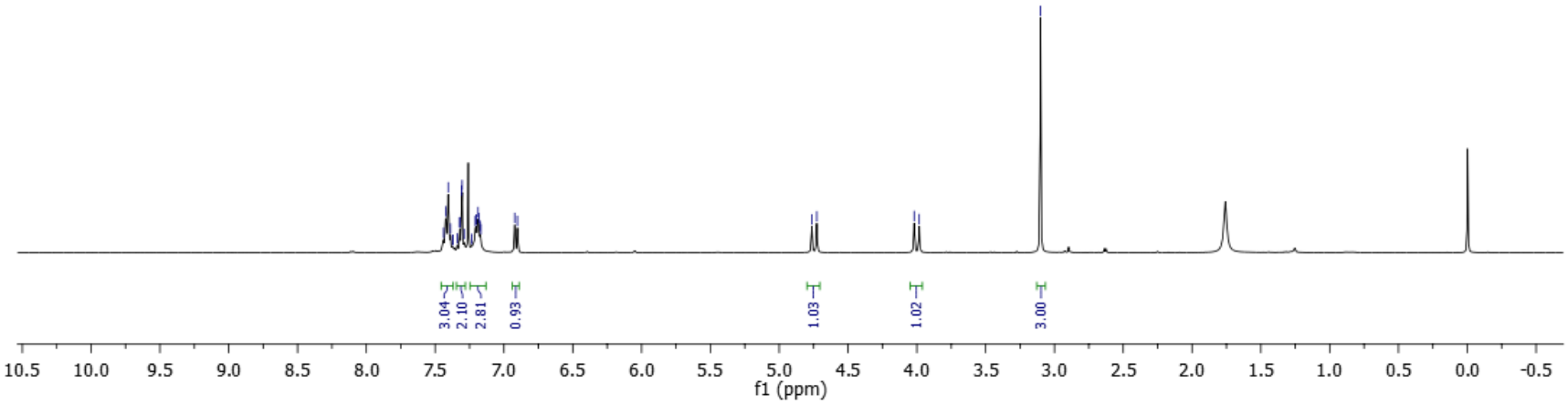
2j

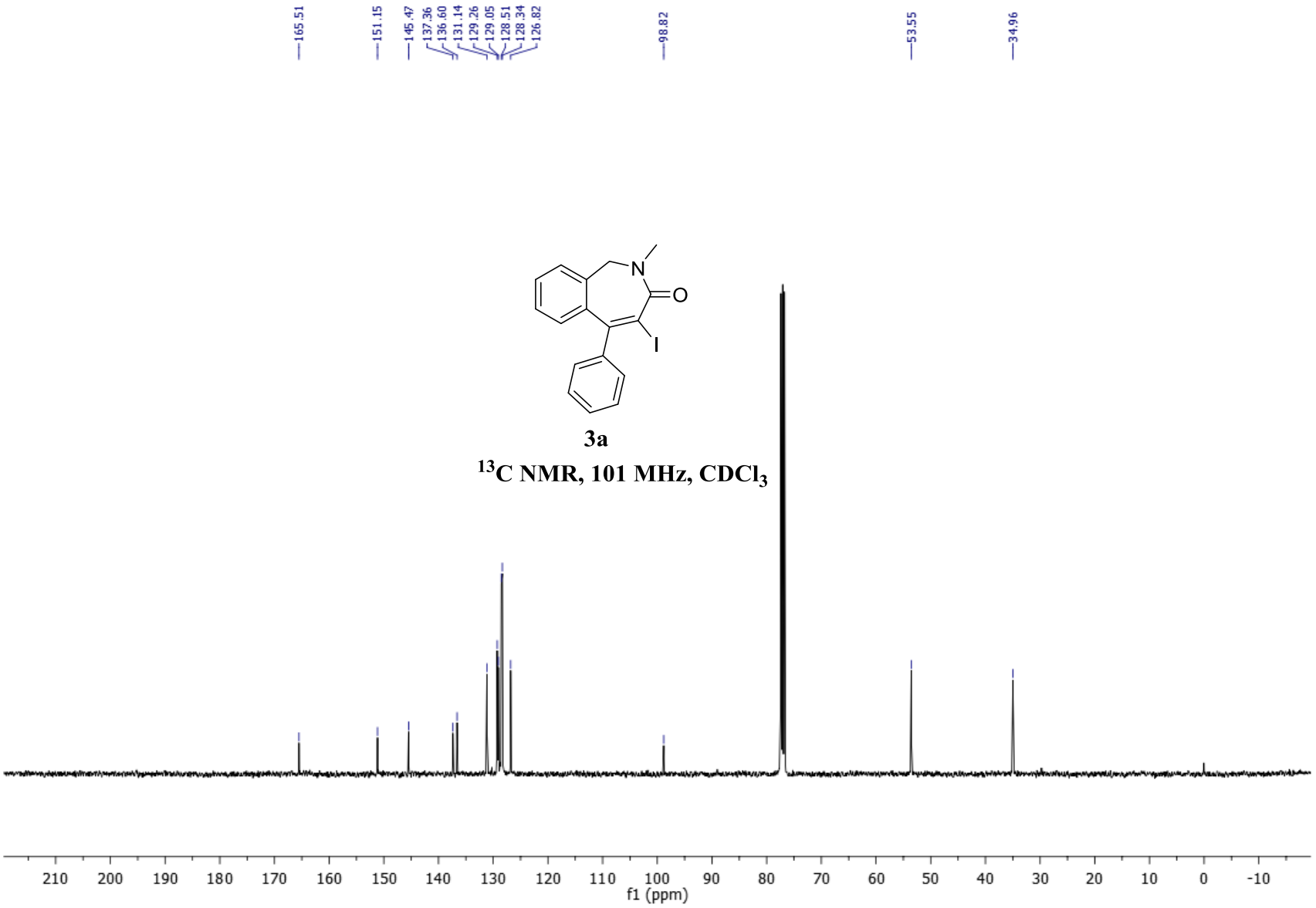
^{13}C NMR, 101 MHz, $CDCl_3$



3a

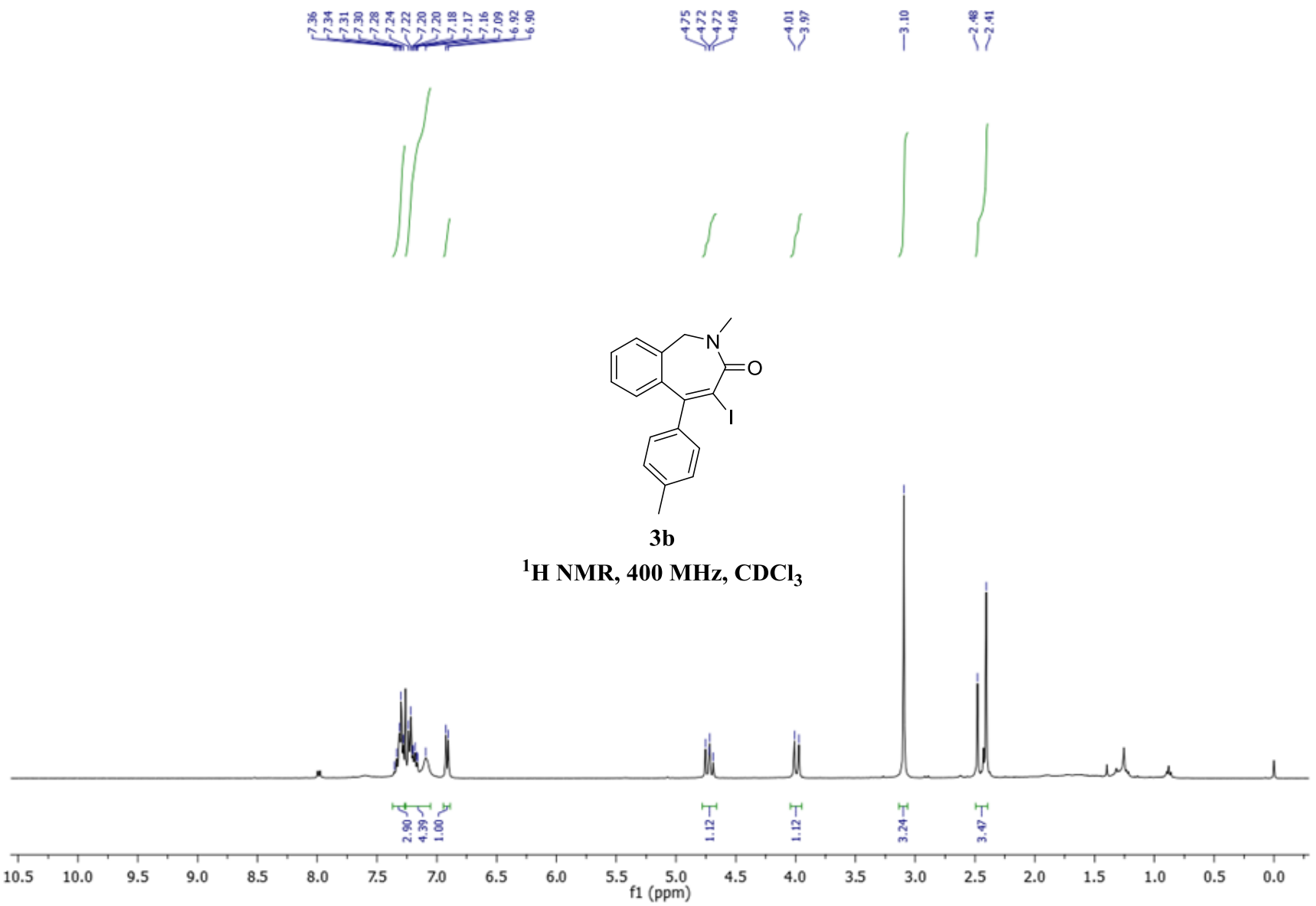
^{1}H NMR, 400 MHz, $CDCl_3$





3a

^{13}C NMR, 101 MHz, $CDCl_3$



3b

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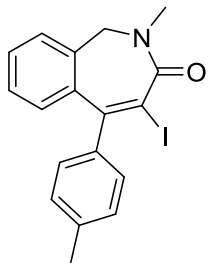
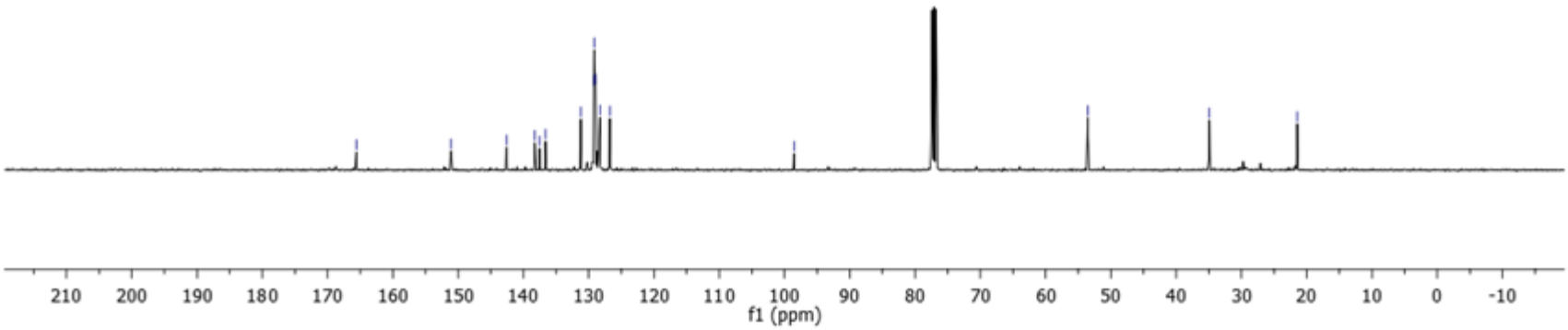
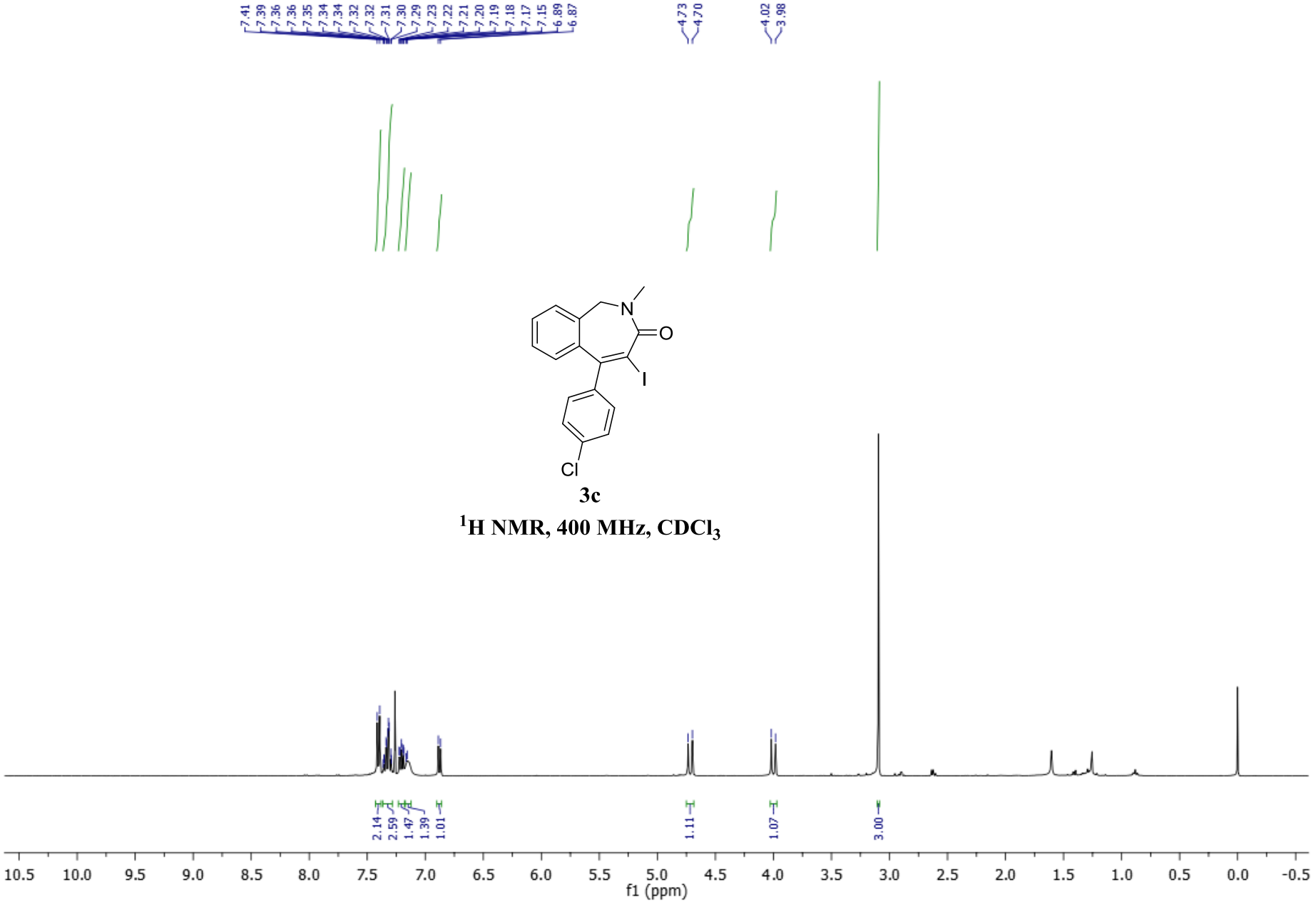


3b

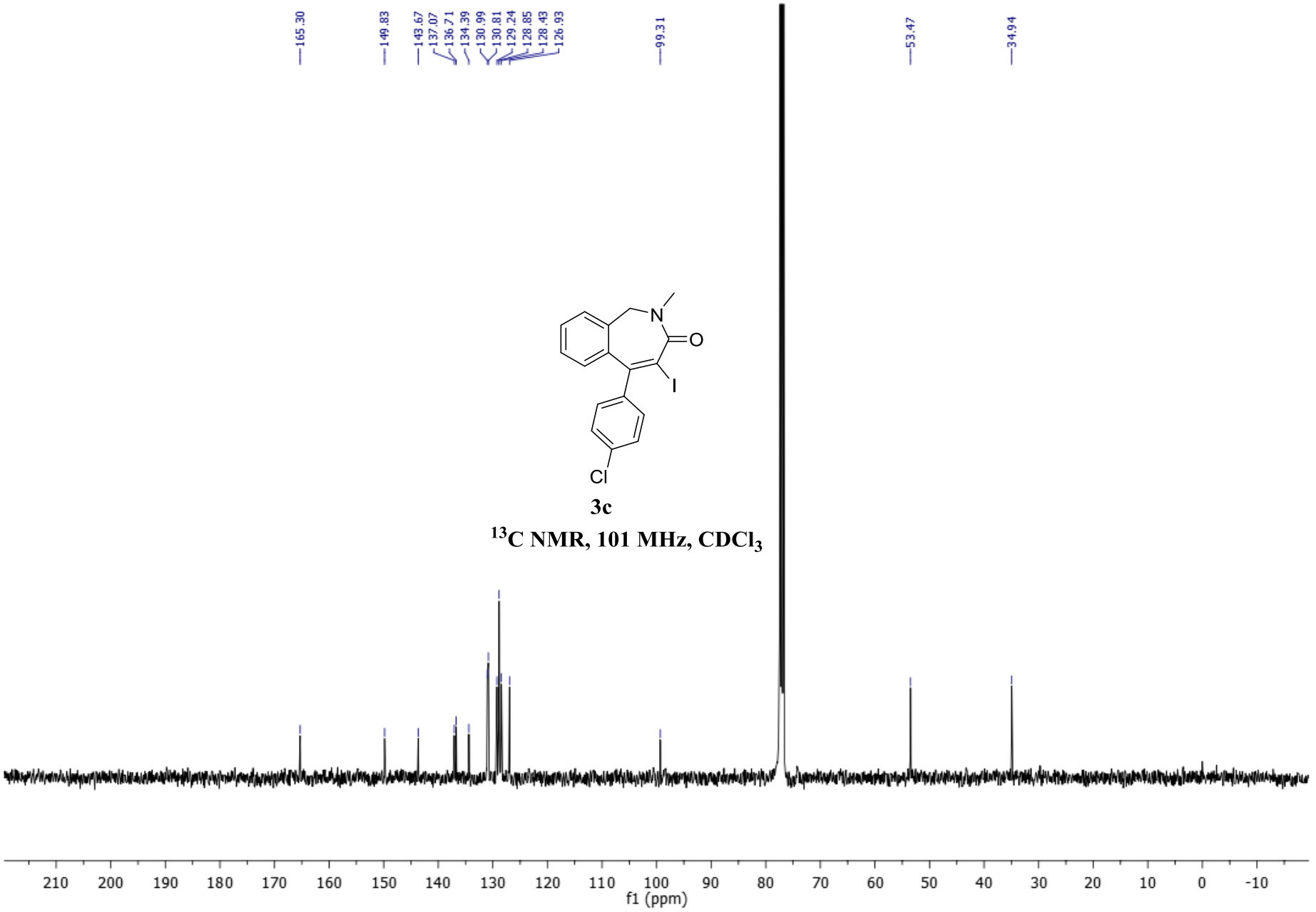
^{13}C NMR, 101 MHz, $CDCl_3$





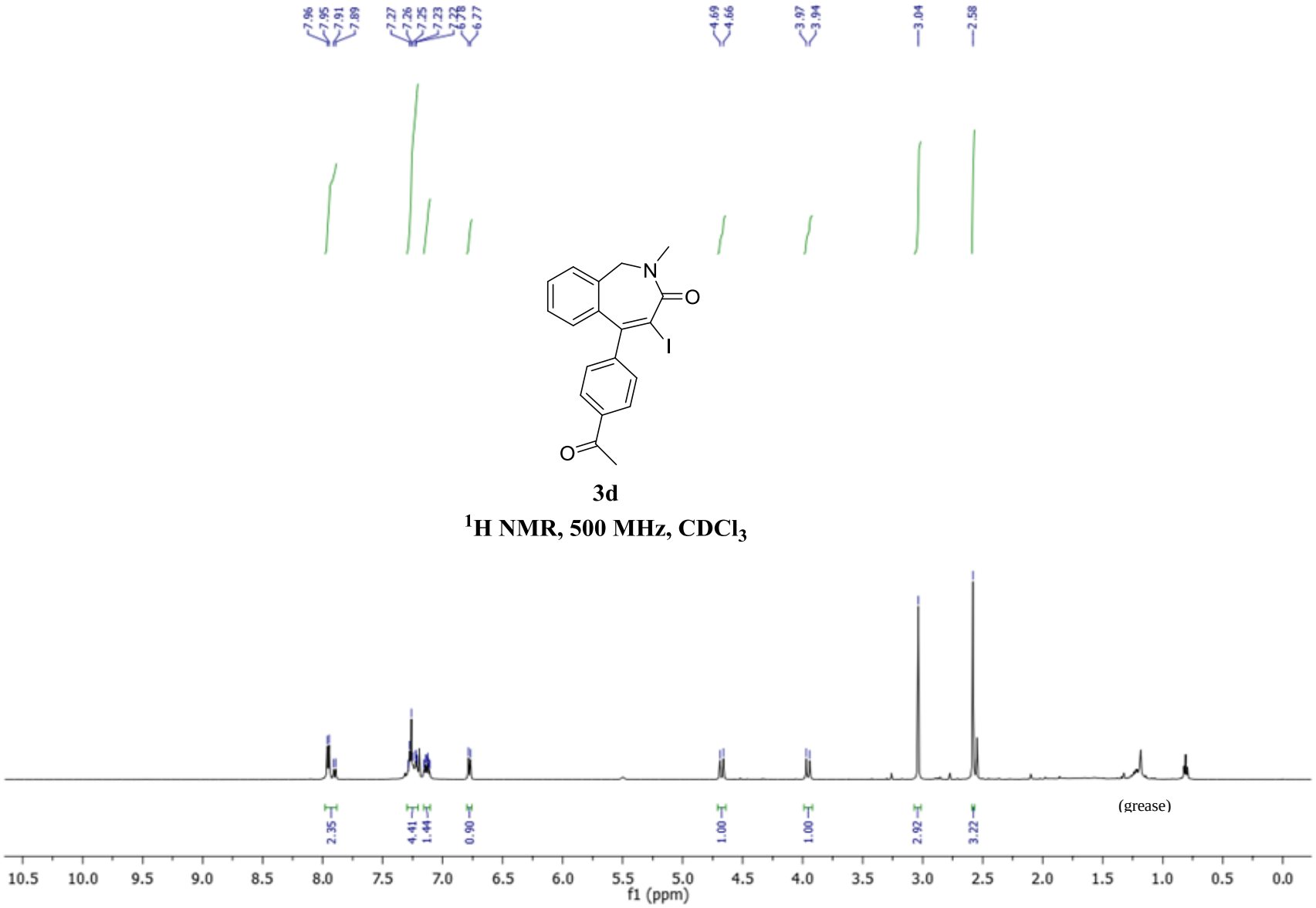
3c

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



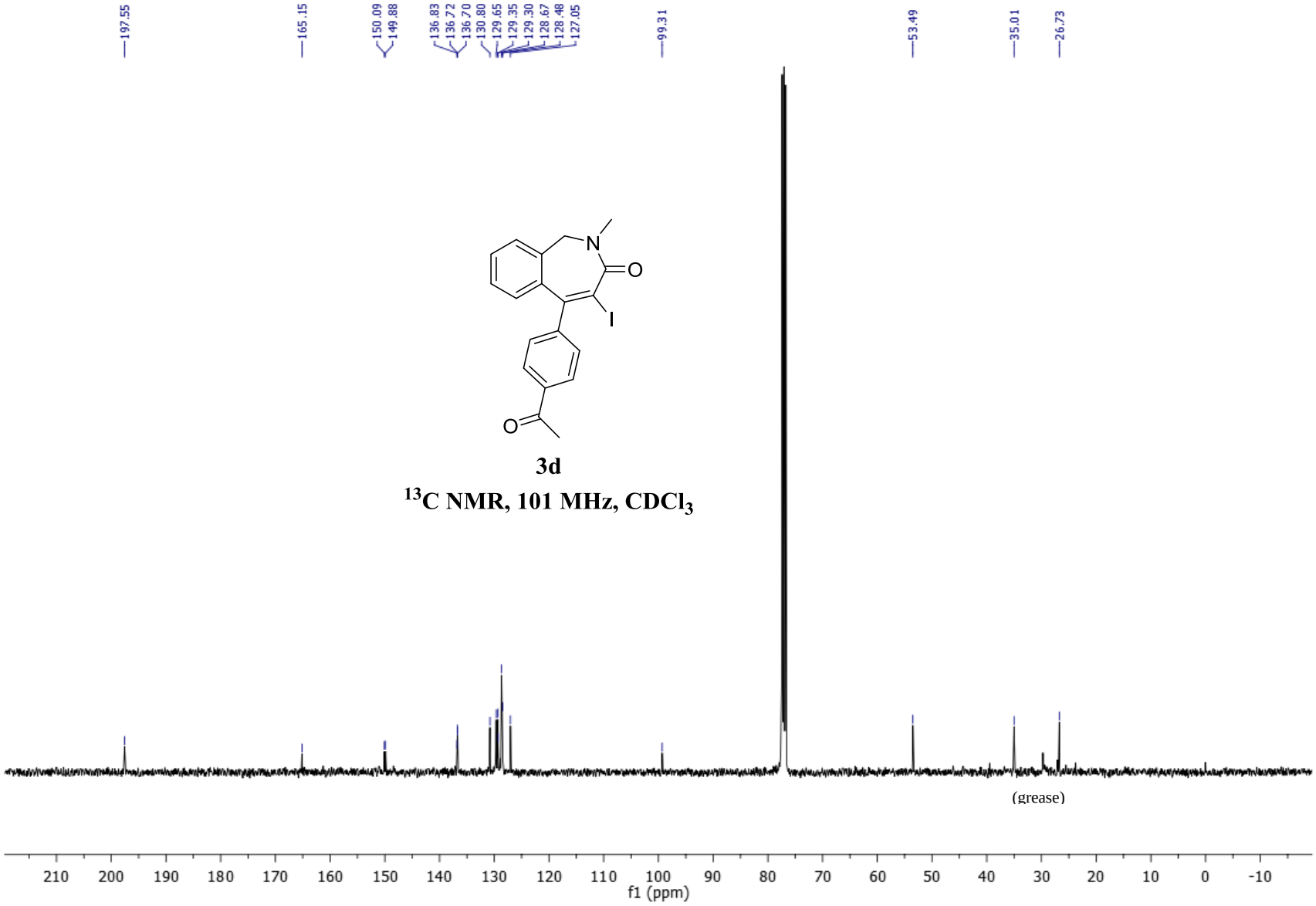
3c

^{13}C NMR, 101 MHz, $CDCl_3$



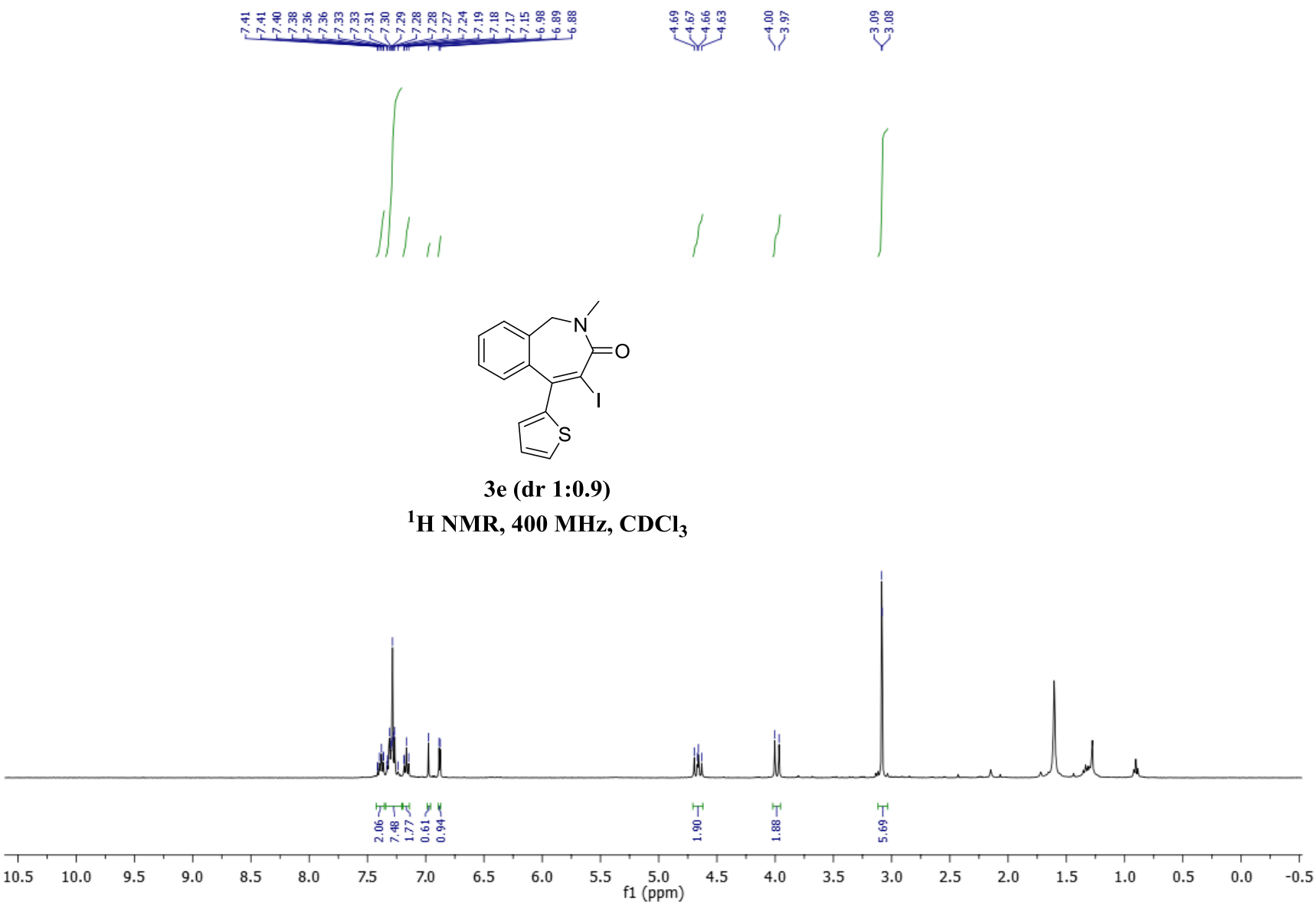
3d

^{1}H NMR, 500 MHz, $CDCl_3$



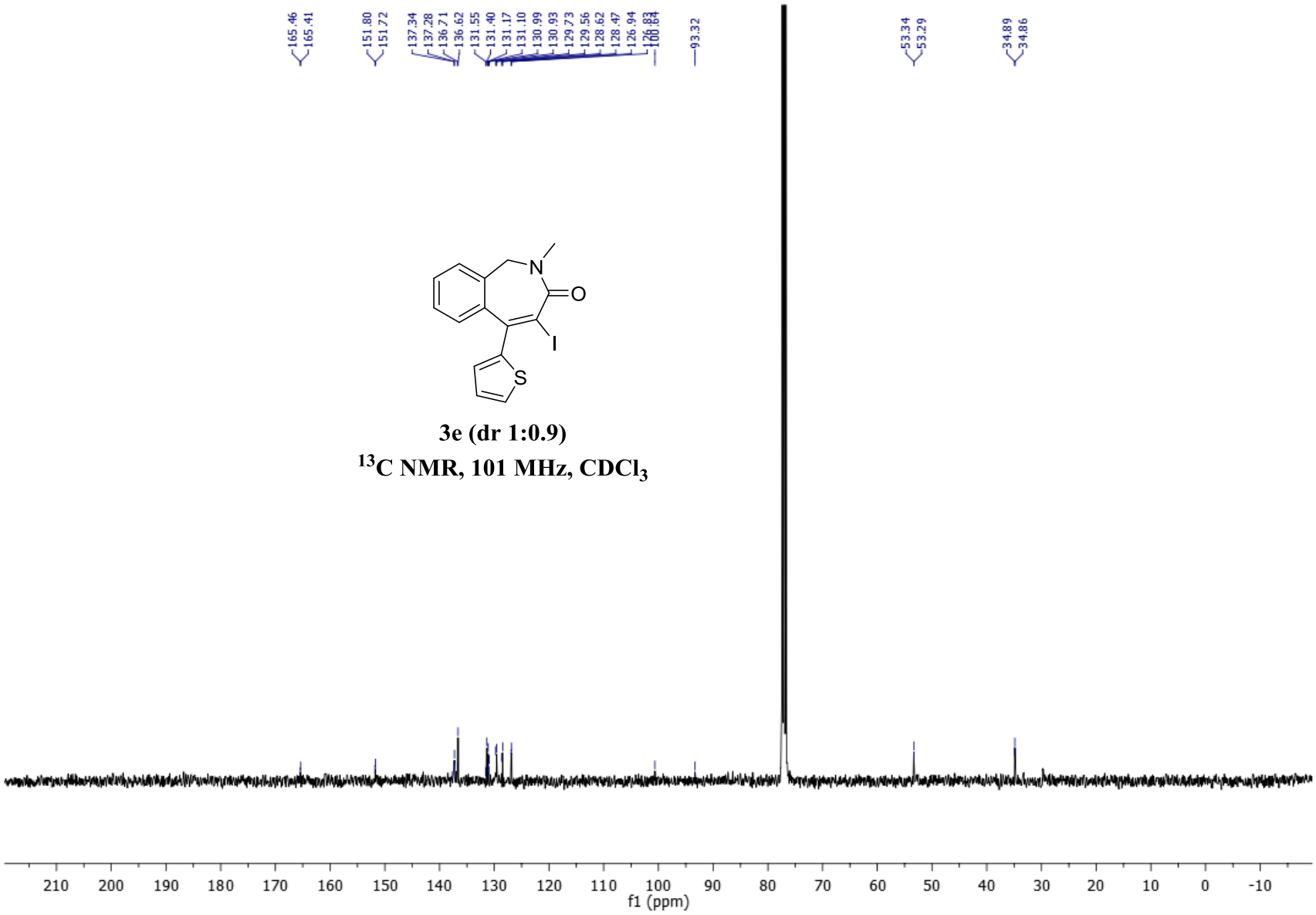
3d

^{13}C NMR, 101 MHz, $CDCl_3$



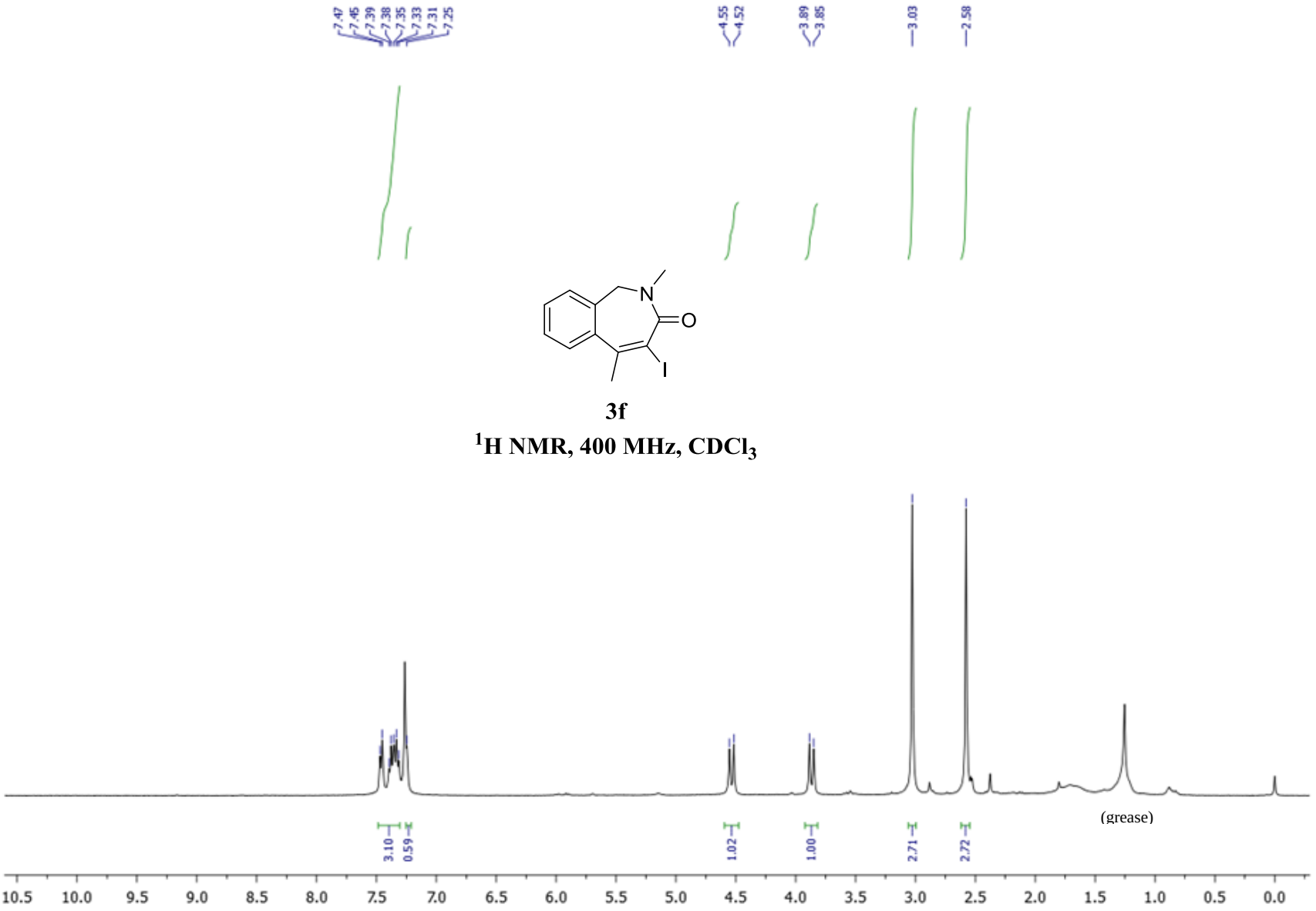
3e (dr 1:0.9)

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



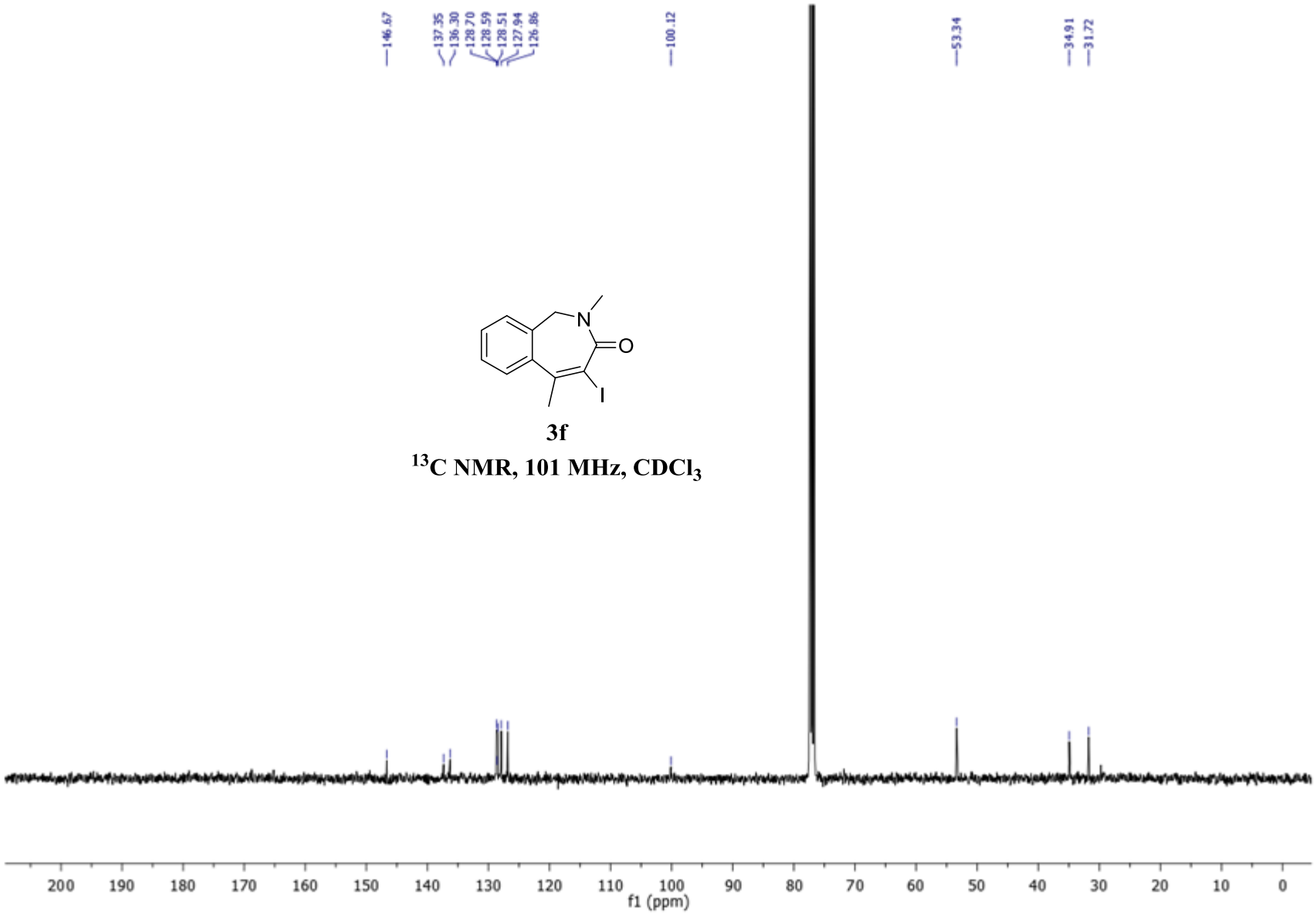
3e (dr 1:0.9)

^{13}C NMR, 101 MHz, $CDCl_3$



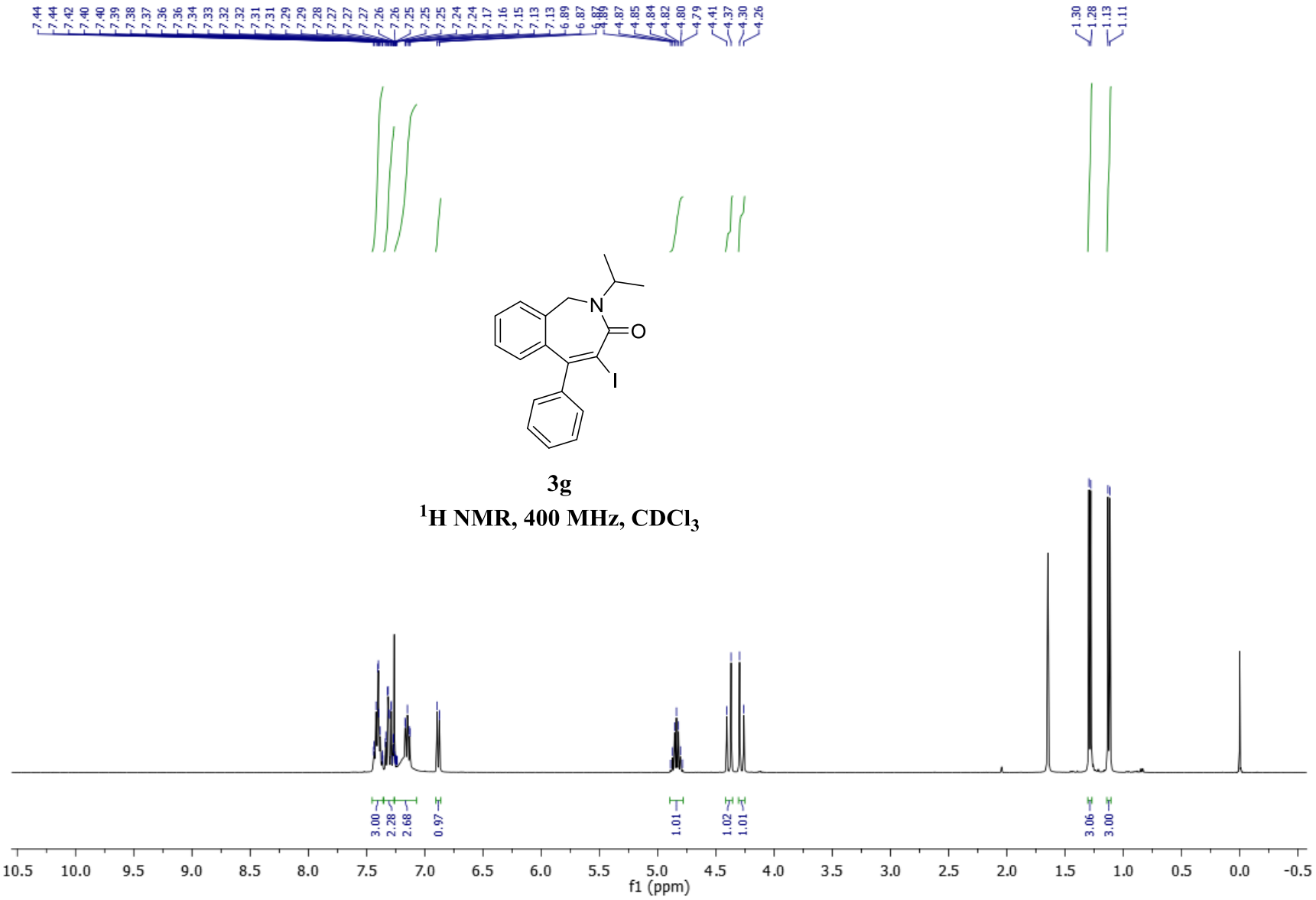
3f

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



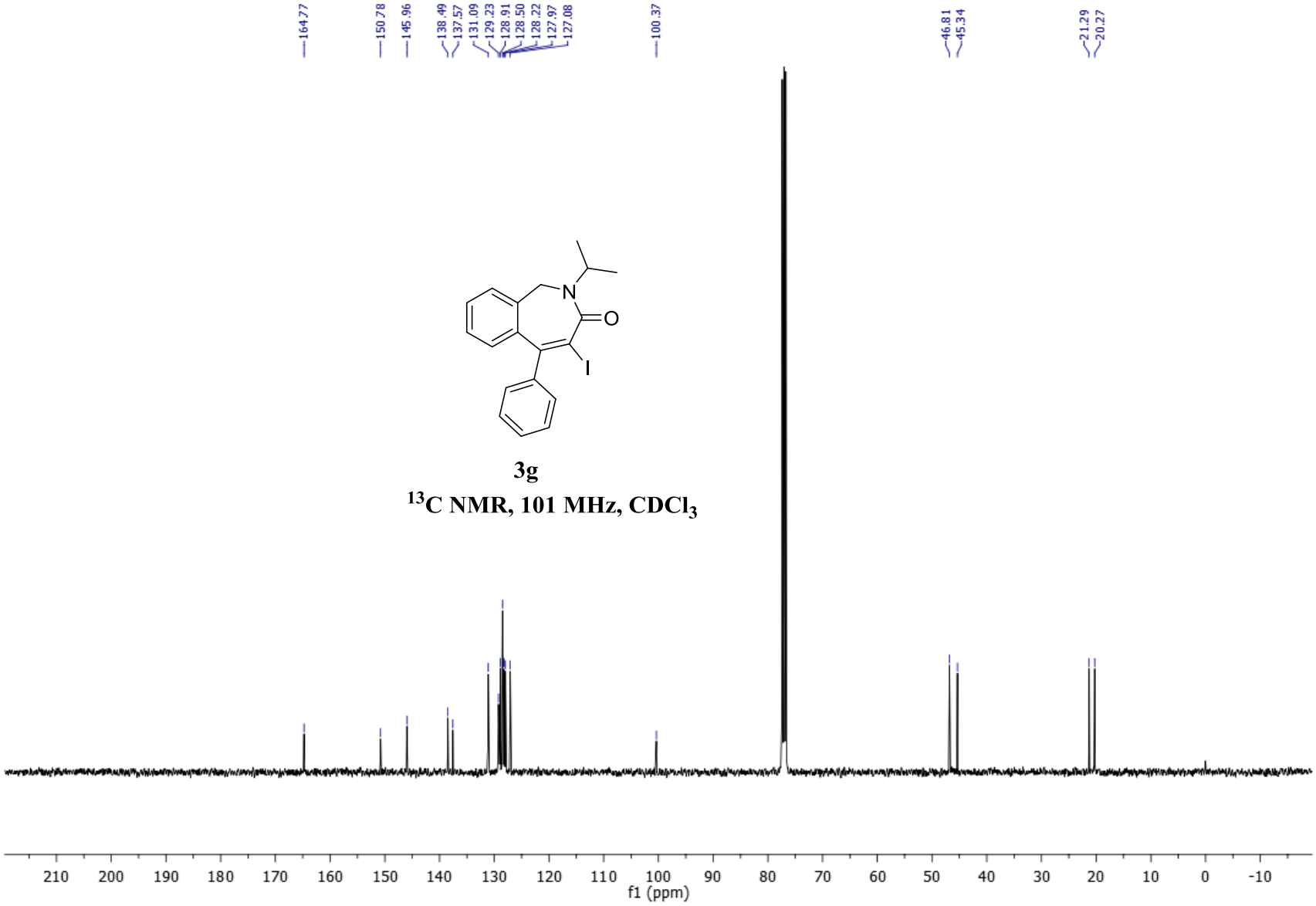
3f

^{13}C NMR, 101 MHz, $CDCl_3$



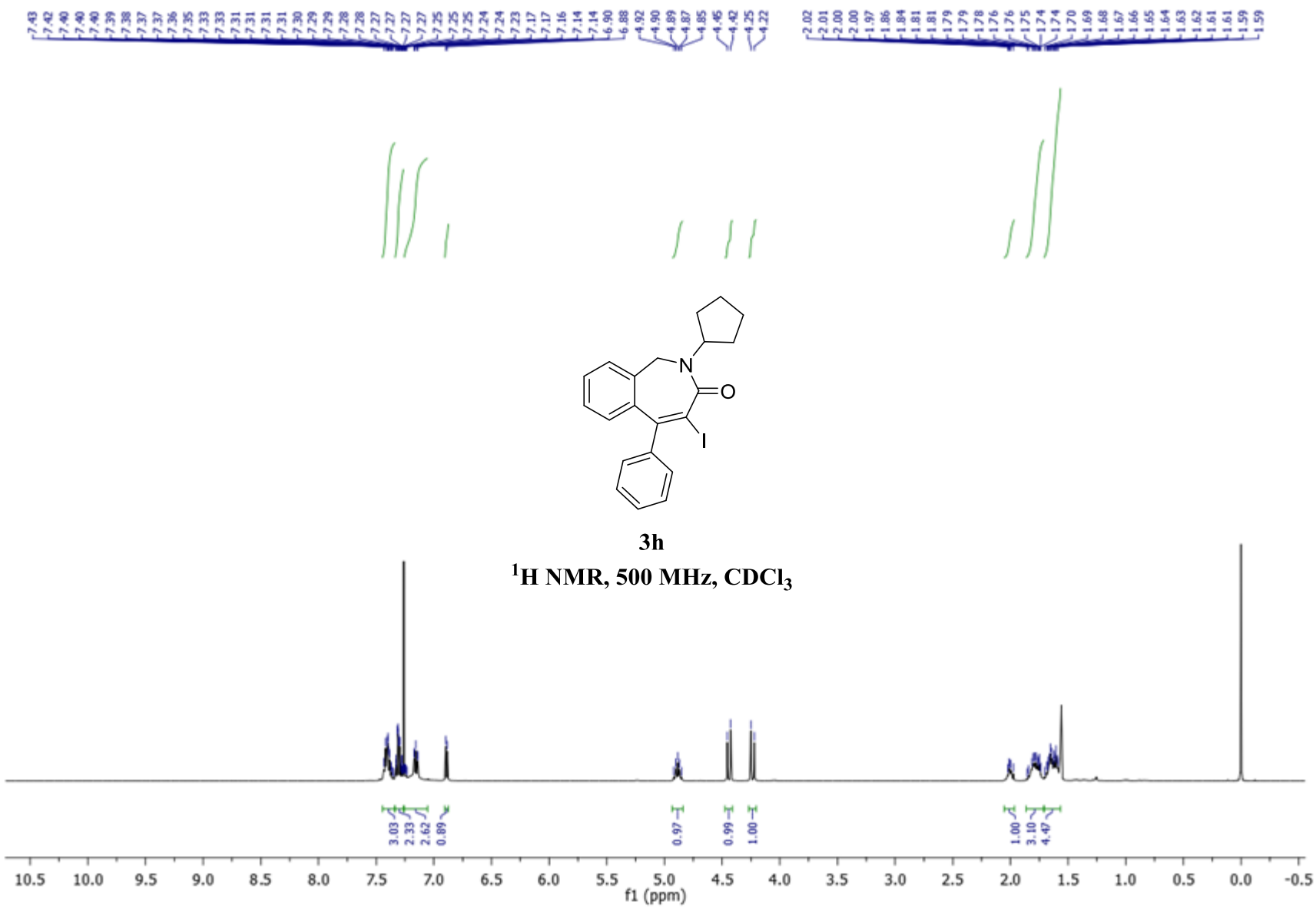
3g

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



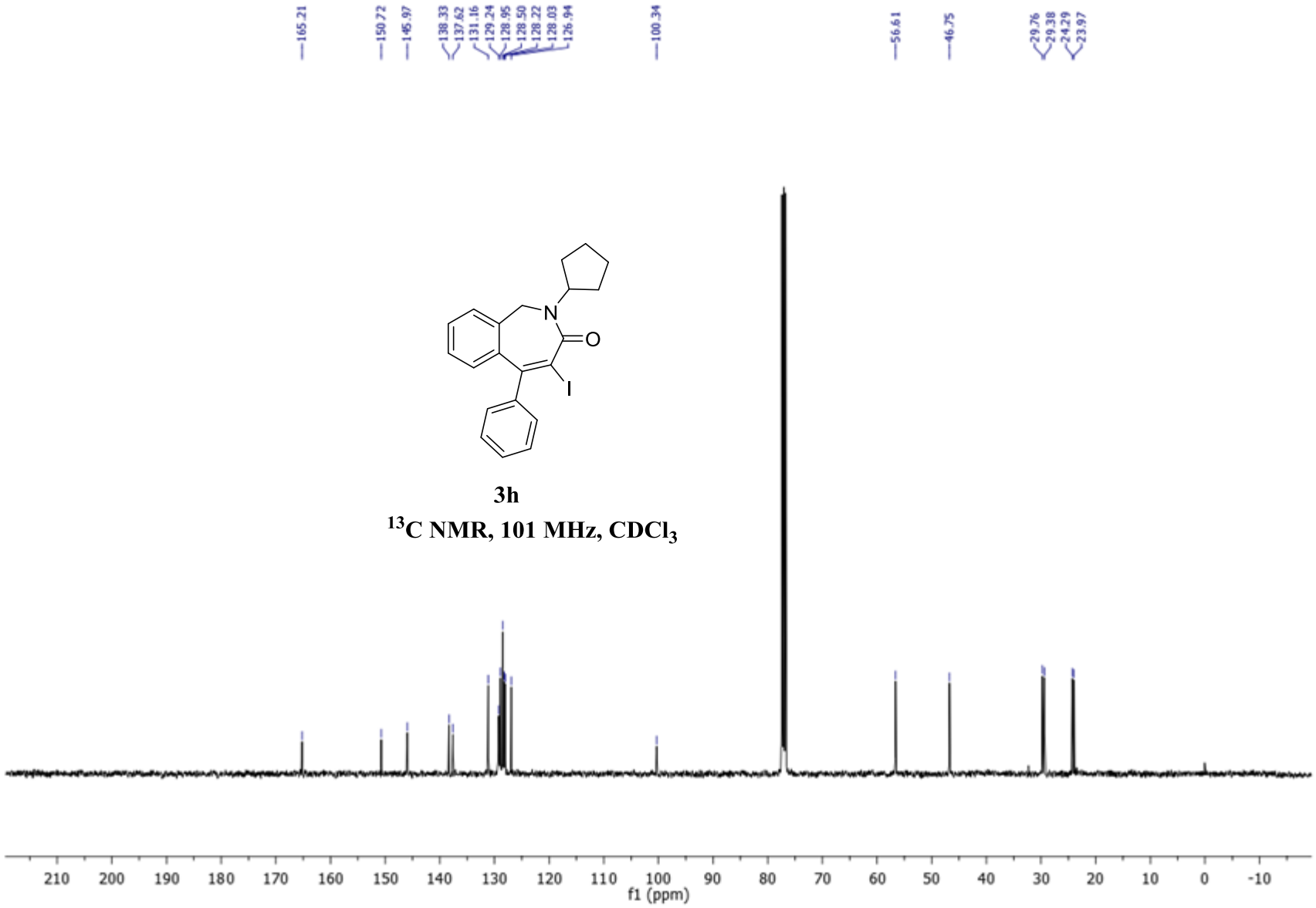
3g

^{13}C NMR, 101 MHz, $CDCl_3$



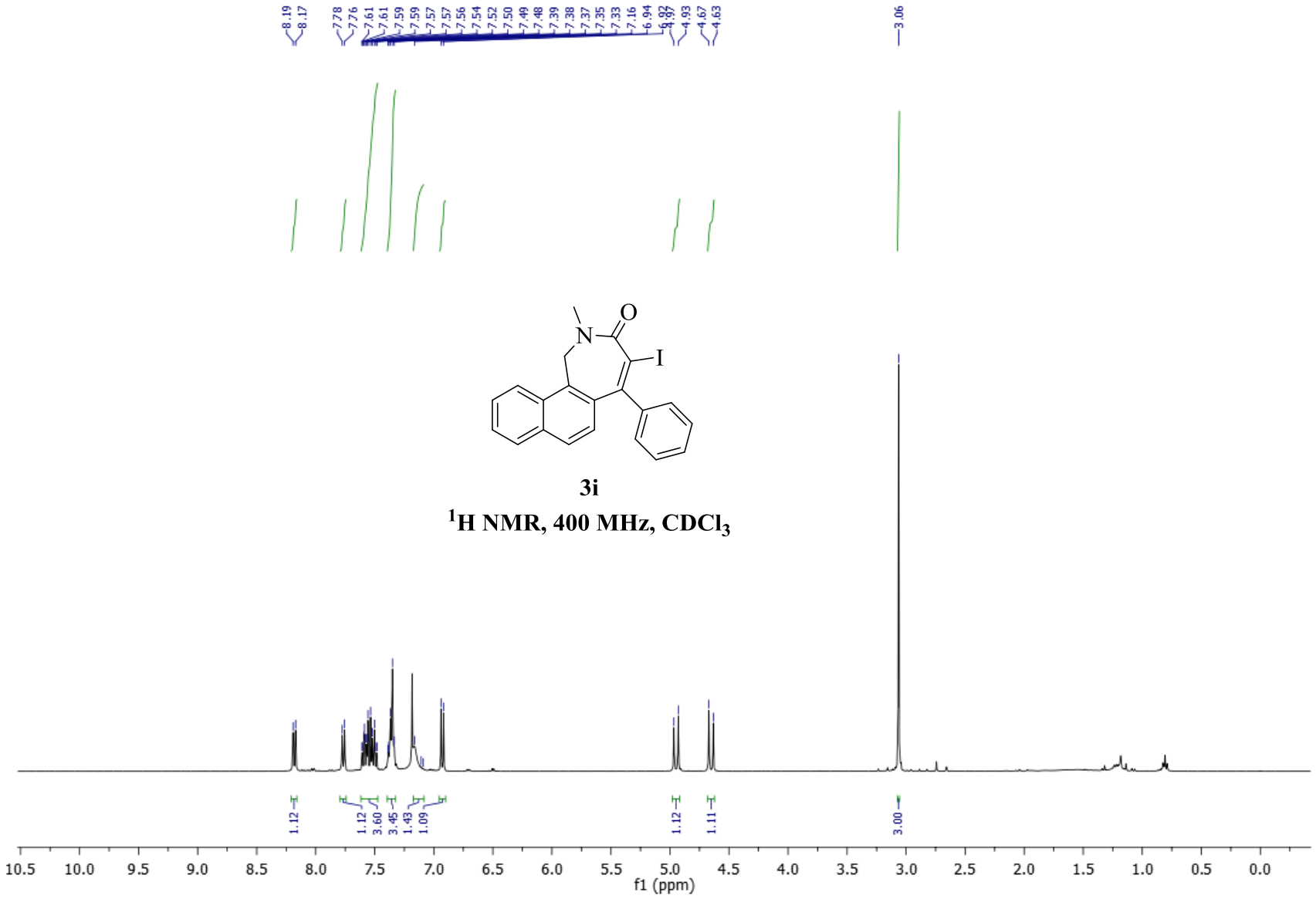
3h

^{1}H NMR, 500 MHz, $CDCl_3$



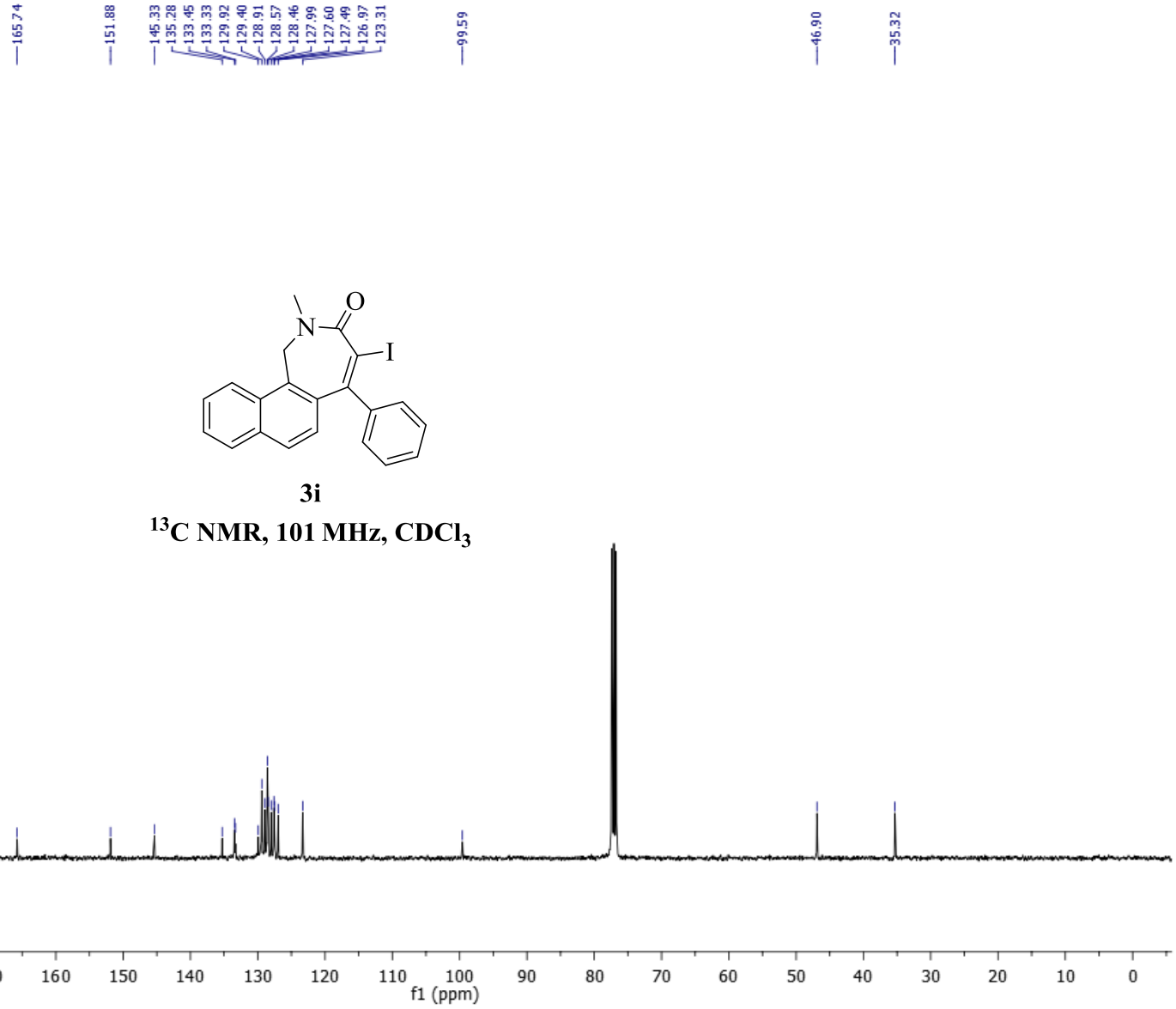
3h

^{13}C NMR, 101 MHz, $CDCl_3$



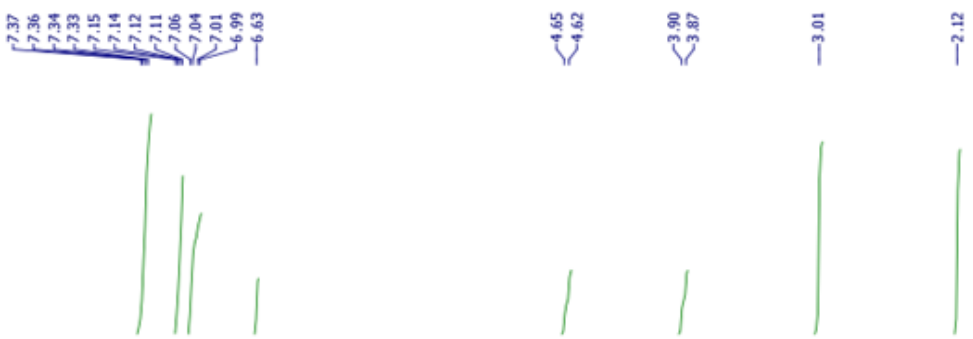
3i

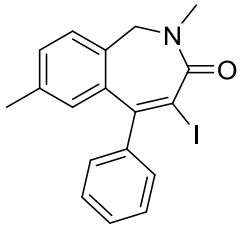
^{1}H NMR, 400 MHz, $CDCl_3$



3i

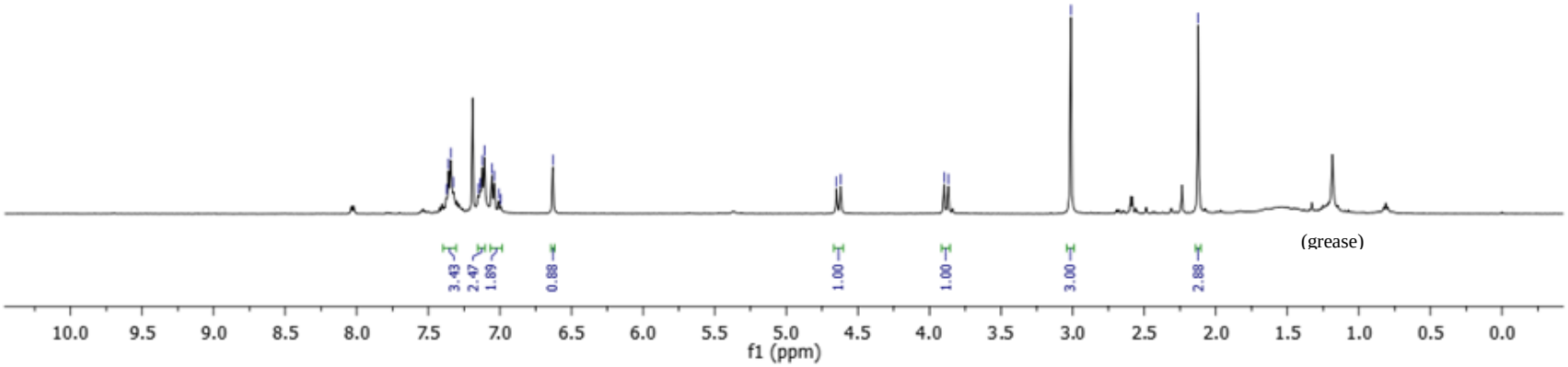
^{13}C NMR, 101 MHz, $CDCl_3$

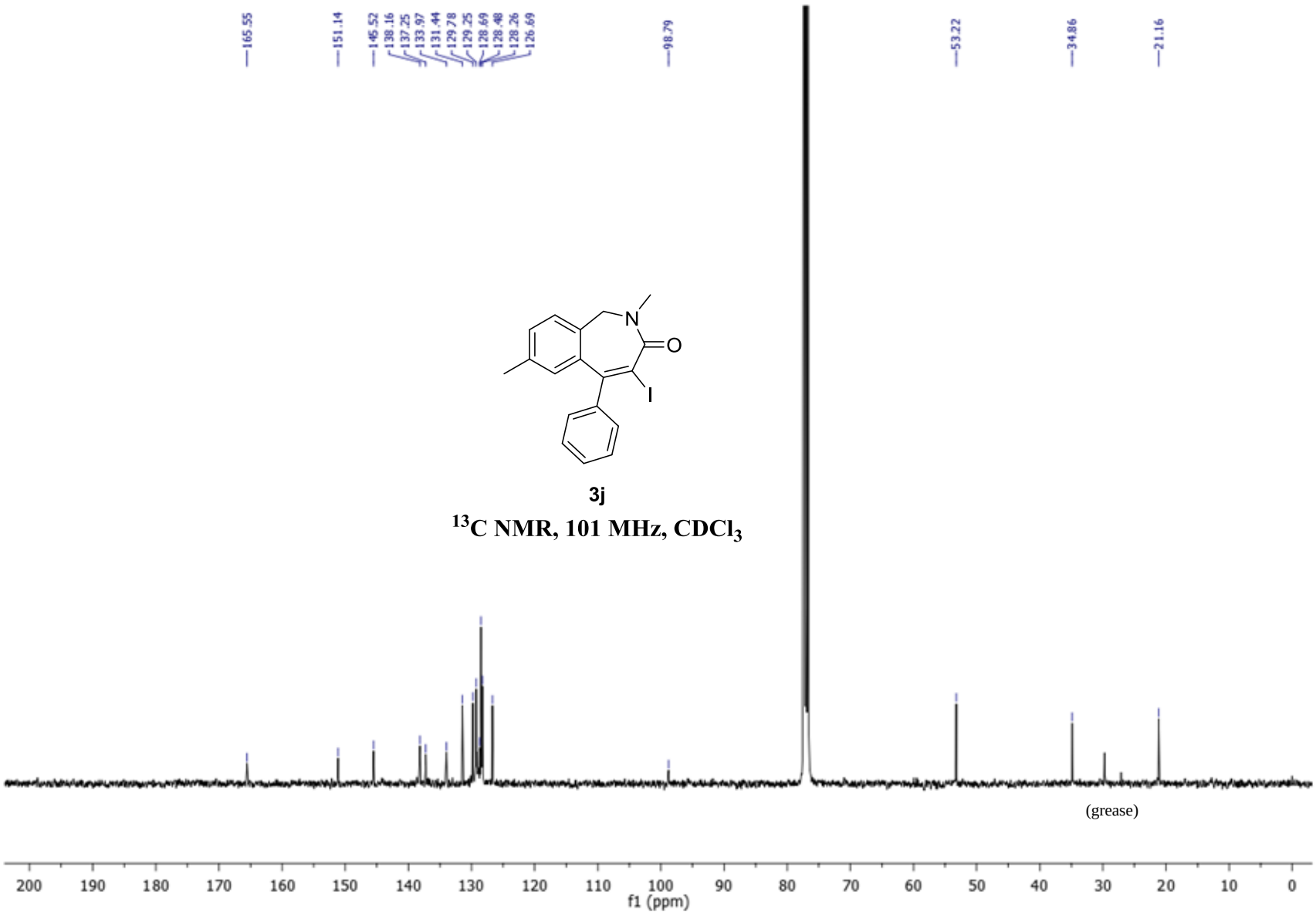




3j

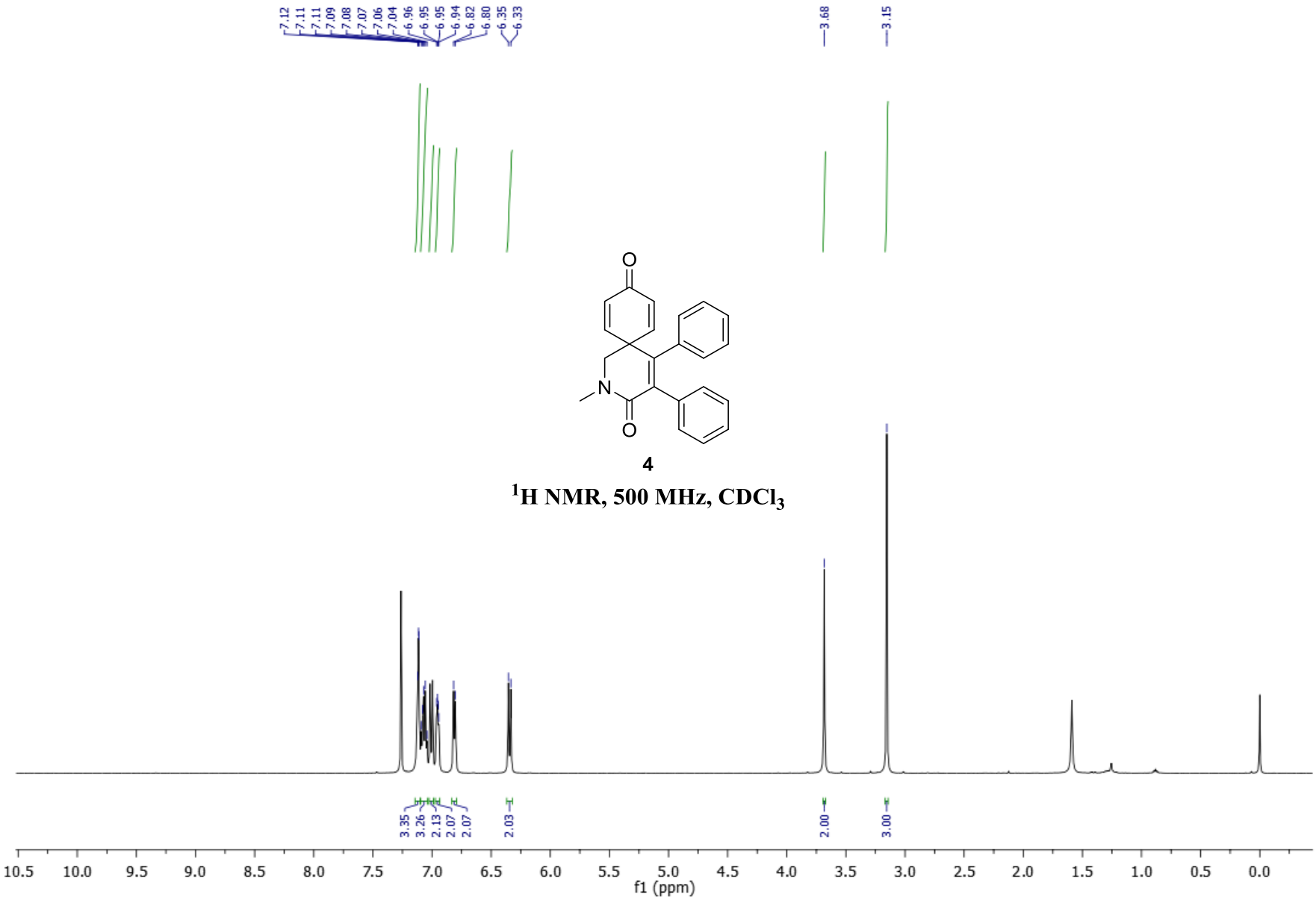
^{1}H NMR, 500 MHz, $CDCl_3$





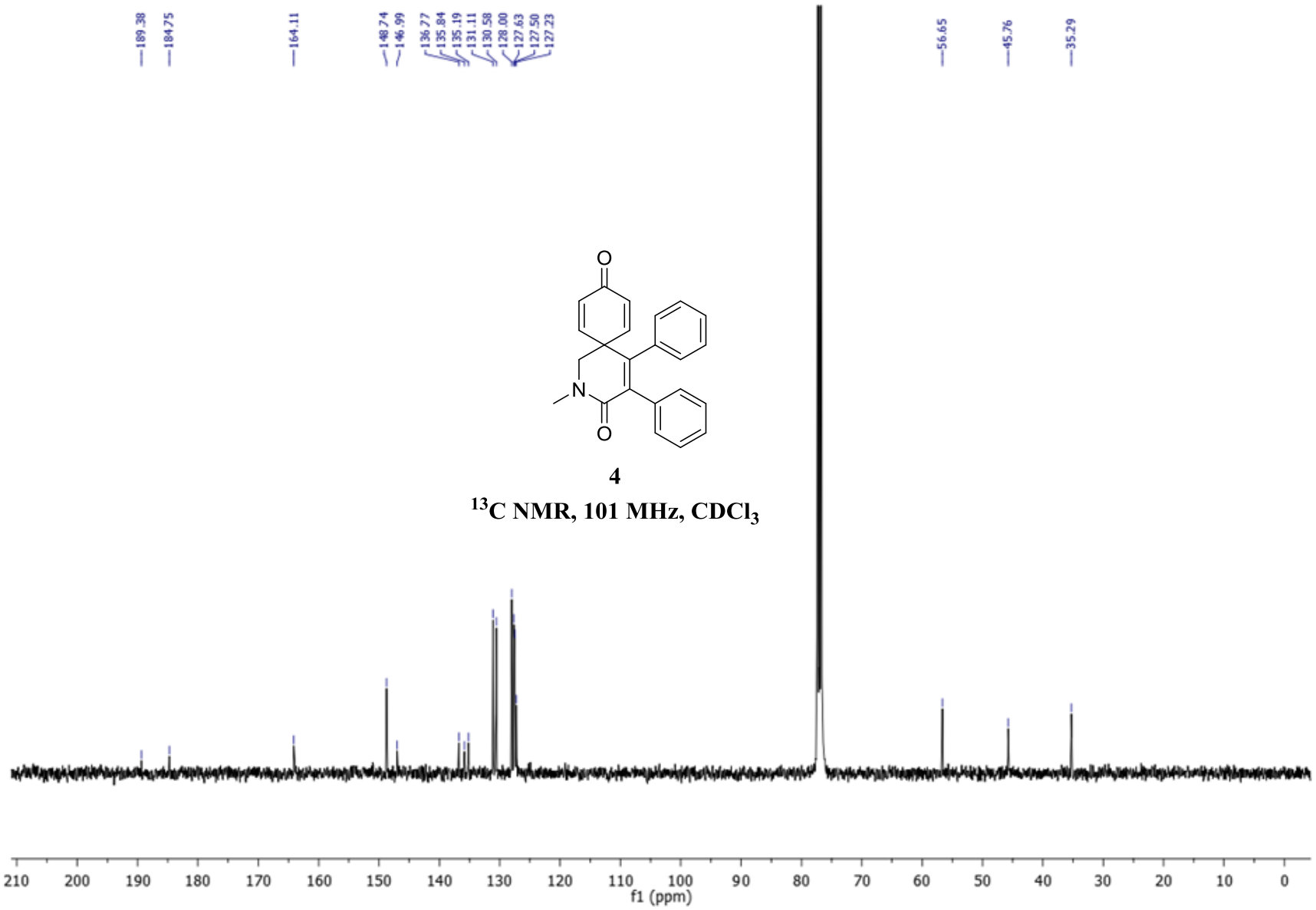
3j

^{13}C NMR, 101 MHz, $CDCl_3$



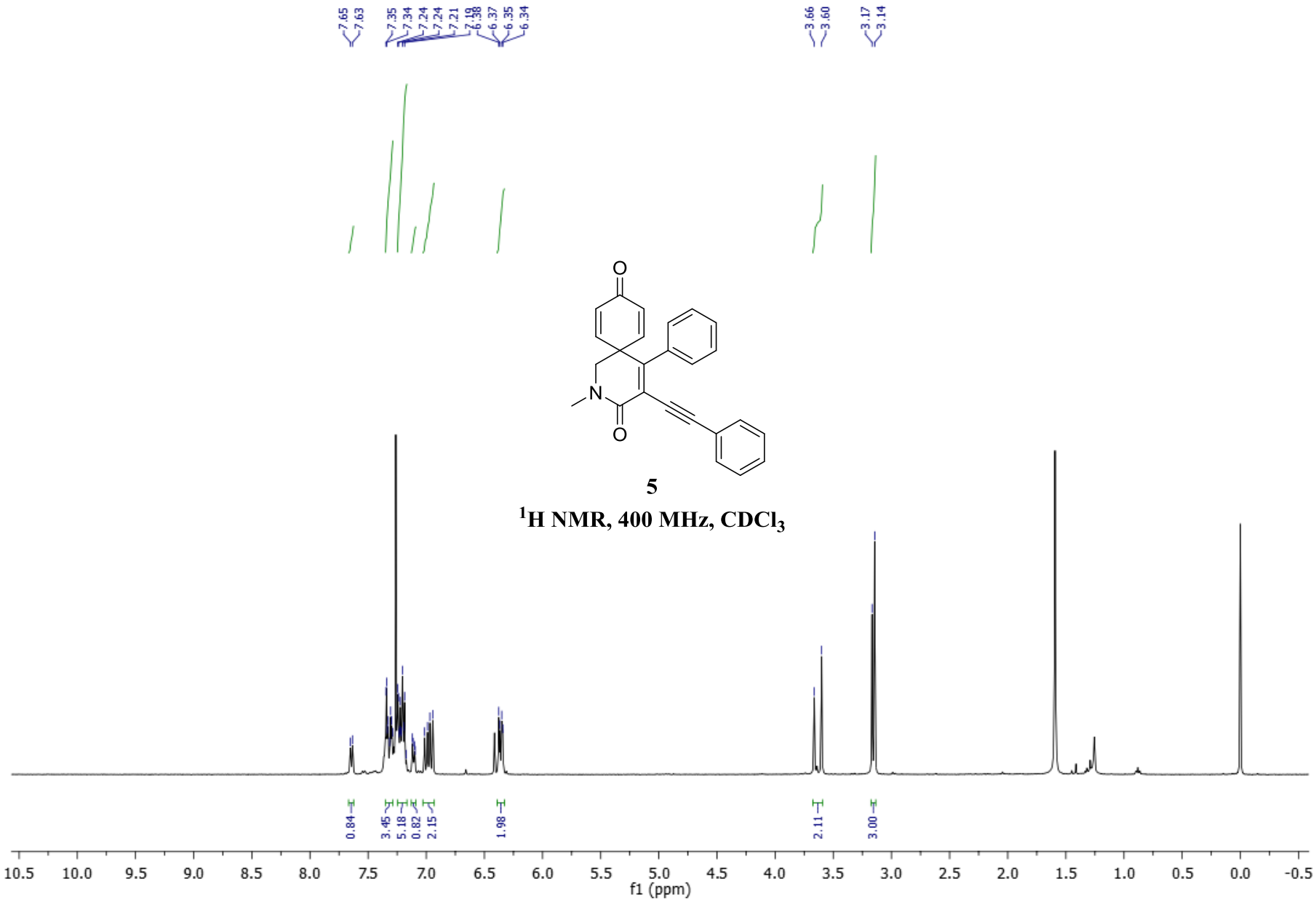
4

^{1}H NMR, 500 MHz, $CDCl_3$



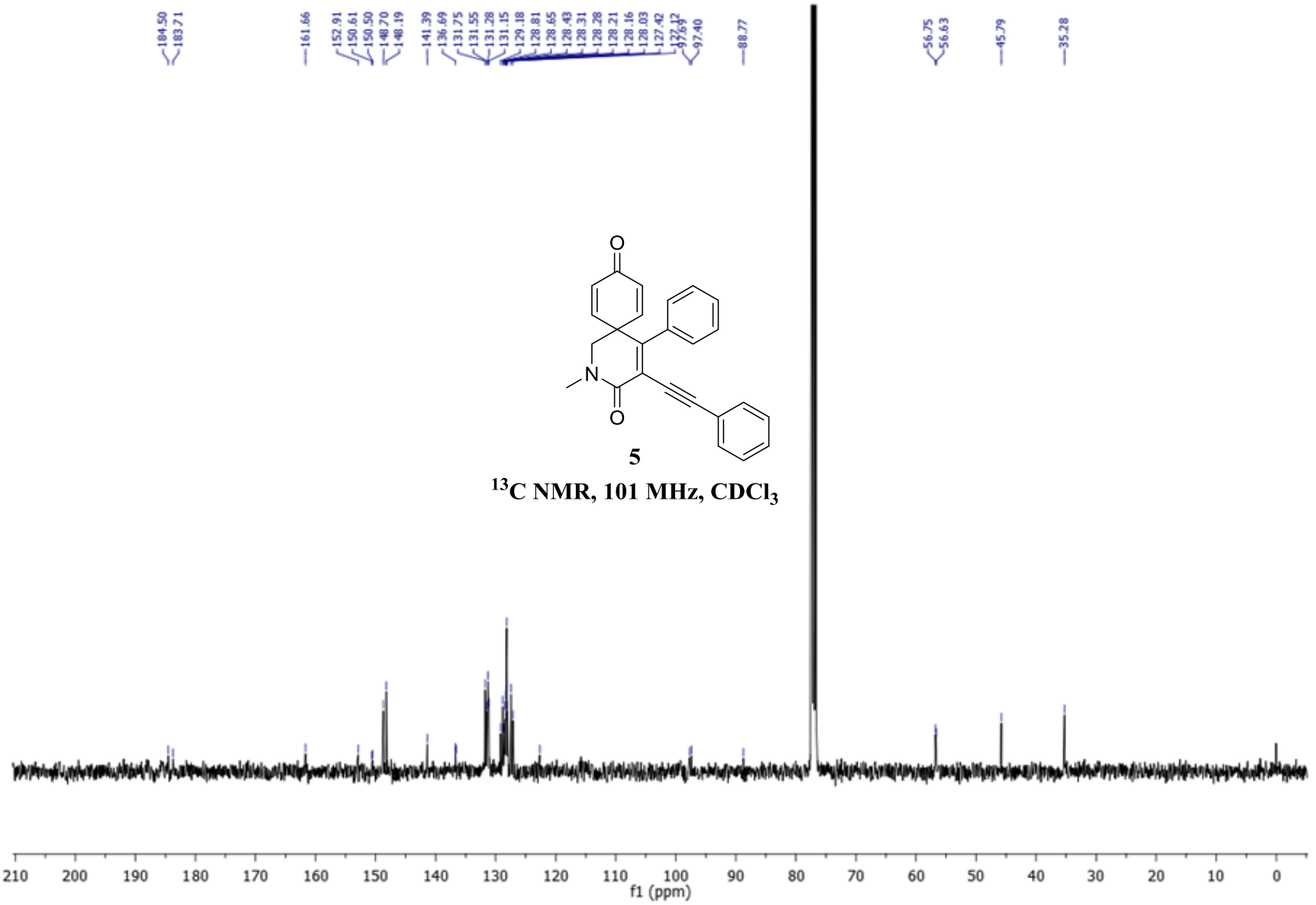
4

^{13}C NMR, 101 MHz, $CDCl_3$



5

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



5

^{13}C NMR, 101 MHz, $CDCl_3$