Supporting Information

Synthesis of 4-(trichloromethyl)pyrido[2',1':3,4]pyrazino [2,1-b]quinazolinones through a Cyclized Dearomatization and Trichlomethylation Cascade Strategy

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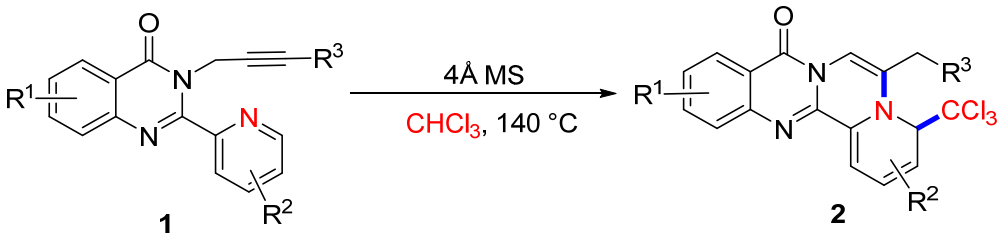
Contents

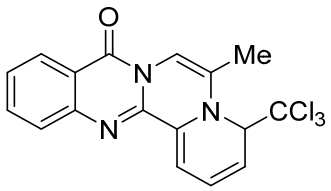
1. General experimental information

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at ambient temperature using 400, 500 or 600 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. High resolution mass spectra were acquired on an LTQ FT spectrometer, and were obtained by peak matching. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Chromatography was performed using with 300-400 mesh silica gel (SiO_2). Unless otherwise noted, all reagents and solvents were obtained from commercial sources and, where appropriate, purified prior to use.

2. Synthesis of compounds 2



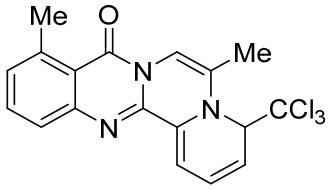
General procedure A: A 25 mL reaction flask was charged with compounds **1** (0.20 mmol) and 4Å MS (500 mg). $CHCl_3$ (2 mL) was then added via syringe and the reaction vessel was sealed with a Teflon cap. The reaction mixture was stirred vigorously at 140 °C in an oil bath for 12-48 h until **1** was consumed completely (monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (1/10 to 1/6, ethyl acetate/petroleum ether) to afford compounds **2.**



2a

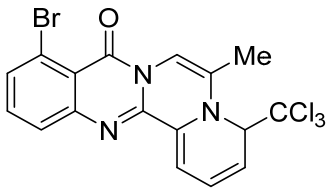
6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-

one (2a). **1a** (0.052 g, 0.20 mmol) ran for 16 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2a**. A yellow solid, 0.048 g, 63% yield; Mp: 184−185 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.0 Hz, 1H), 7.75-7.69 (m, 2H), 7.47-7.43 (m, 1H), 7.13 (s, 1H), 6.90 (d, J = 6.4 Hz, 1H), 6.75 (dd , J = 9.2, 6.4 Hz, 1H), 5.94 (dd , J = 8.8, 6.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 147.3, 144.2, 134.5, 132.5, 128.4, 128.3, 127.6, 127.0, 126.8, 119.9, 113.9, 106.1, 103.6, 102.5, 66.6, 16.7; HRMS (ESI) *m/z* calcd for $C_{17}H_{13}Cl_3N_3O$ $[M + H]^+$: 380.0119, found 380.0111.



2b

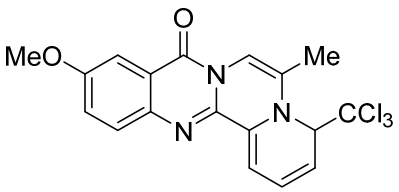
6,10-dimethyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2b). **1b** (0.055 g, 0.20 mmol) ran for 18 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2b**. A yellow solid, 0.045 g, 57% yield; Mp: 188−189 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.55 (m, 2H), 7.22 (d, J = 6.4 Hz, 1H), 7.13 (s, 1H), 6.94 (d, J = 6.0 Hz, 1H), 6.76 (dd , J = 8.8, 6.4 Hz, 1H), 5.94 (dd , J = 8.4, 6.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 2.89 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.7, 148.5, 144.0, 141.5, 133.7, 132.3, 129.5, 128.4, 128.1, 125.6, 118.4, 113.9, 106.0, 103.7, 102.4, 66.6, 23.2, 16.8; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}Cl_3N_3O$ $[M + H]^+$: 394.0275, found 394.0275.



2c

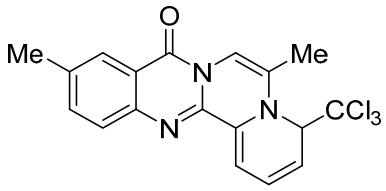
10-bromo-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2c). **1c** (0.068 g, 0.20 mmol) ran for 18 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether

= 1/10) afforded **2c**. A yellow solid, 0.046 g, 50% yield; Mp: 182−183 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.0 Hz, 2H), 7.49-7.45 (m, 1H), 7.12 (s, 1H), 6.91 (d, J = 6.0 Hz, 1H), 6.75 (dd , J = 8.8, 6.4 Hz, 1H), 5.95 (dd , J = 8.4, 6.8 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 149.3, 144.6, 134.1, 133.3, 131.9, 128.8, 128.3, 127.5, 121.8, 117.9, 114.4, 106.6, 103.5, 102.4, 66.5, 16.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}BrCl_3N_3O$ $[M + H]^+$: 457.9224, found 457.9206.



2d

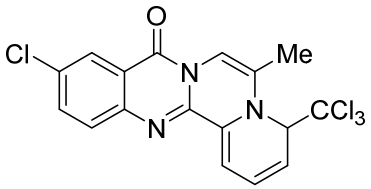
11-methoxy-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2d). **1d** (0.058 g, 0.20 mmol) ran for 12 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2d**. A yellow solid, 0.041 g, 50% yield; Mp: 180−181 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (m, 2H), 7.35 (dd, J = 9.2, 2.8 Hz, 1H), 7.14 (s, 1H), 6.85 (d, J = 5.6 Hz, 1H), 6.74 (dd , J = 9.2, 6.4 Hz, 1H), 5.92 (dd , J = 8.4, 6.4 Hz, 1H), 5.21 (d, J = 6.4 Hz, 1H), 3.93 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 157.3, 142.2, 132.8, 129.3, 128.4, 128.3, 125.1, 120.8, 113.4, 106.1, 105.2, 103.8, 102.6, 66.6, 55.9, 16.7; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}Cl_3N_3O_2$ $[M + H]^+$: 410.0224, found 410.0211.



2e

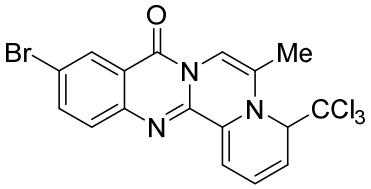
6,11-dimethyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2e). **1e** (0.055 g, 0.20 mmol) ran for 12 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2e**. A yellow solid, 0.050 g, 64% yield; Mp: 186−187 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.14 (s, 1H),

6.88 (d, J = 6.0 Hz, 1H), 6.75 (dd , J = 9.2, 6.4 Hz, 1H), 5.93 (dd , J = 8.8, 6.8 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 2.49 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 145.4, 143.4, 137.1, 136.0, 132.7, 128.4, 128.1, 127.5, 126.3, 119.7, 113.6, 105.5, 103.7, 102.6, 66.6, 21.4, 16.7; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}Cl_3N_3O$ $[M + H]^+$: 394.0275, found 394.0275.



2f

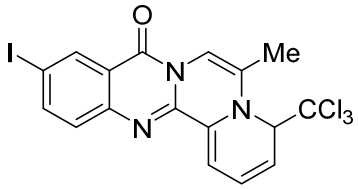
11-chloro-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2f). **1f** (0.059 g, 0.20 mmol) ran for 14 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2f**. A yellow solid, 0.050 g, 60% yield; Mp: 201−202 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.69-7.64 (m, 2H), 7.10 (s, 1H), 6.92 (d, J = 6.0 Hz, 1H), 6.76 (dd , J = 9.2, 6.4 Hz, 1H), 5.96 (dd , J = 8.8, 6.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 145.7, 144.4, 134.9, 132.6, 132.2, 129.2, 128.9, 128.4, 126.3, 120.8, 114.3, 106.5, 103.5, 102.4, 66.6, 16.7; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}Cl_4N_3O$ $[M + H]^+$: 413.9729, found 413.9716.



2g

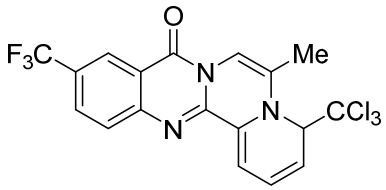
11-bromo-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2g). **1g** (0.068 g, 0.20 mmol) ran for 17 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2g**. A yellow solid, 0.055 g, 60% yield; Mp: 196−197 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 2.0 Hz, 1H), 7.80-7.77 (m, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.09 (s, 1H), 6.89 (d, J = 6.0 Hz, 1H), 6.75 (dd , J = 8.8, 6.0 Hz, 1H), 5.96 (dd , J = 8.8, 6.4 Hz, 1H), 5.21 (d, J = 6.0 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

156.3, 146.2, 144.5, 137.6, 132.3, 129.4, 129.3, 128.9, 128.4, 121.2, 120.2, 114.2, 106.4, 103.5, 102.4, 66.6, 16.7; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}BrCl_3N_3O$ $[M + H]^+$: 457.9224, found 457.9212.



2h

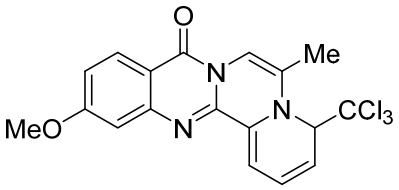
11-iodo-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2h). **1h** (0.077 g, 0.20 mmol) ran for 14 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2h**. A yellow solid, 0.056 g, 55% yield; Mp: 191−192 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.96-7.94 (m, 1H), 7.41 (d, J = 8.8 Hz, 1H), 7.08 (s, 1H), 6.87 (d, J = 6.0 Hz, 1H), 6.74 (dd , J = 9.2, 6.4 Hz, 1H), 5.95 (dd , J = 8.8, 6.4 Hz, 1H), 5.21 (d, J = 6.0 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 146.7, 144.7, 143.1, 135.7, 132.4, 129.4, 128.7, 128.4, 121.5, 114.2, 106.3, 103.6, 102.4, 91.0, 66.6, 16.7; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}Cl_3IN_3O$ $[M + H]^+$: 505.9085, found 505.9069.



2i

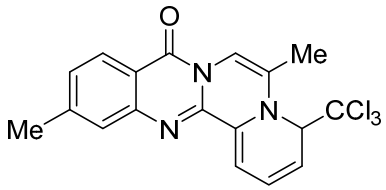
6-methyl-4-(trichloromethyl)-11-(trifluoromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2i). **1i** (0.066 g, 0.20 mmol) ran for 20.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2i**. A yellow solid, 0.041 g, 46% yield; Mp: 189−190 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.78 (d, J = 8.8 Hz, 1H), /7.11 (s, 1H), 6.93 (d, J = 6.0 Hz, 1H), 6.77 (dd , J = 8.8, 6.4 Hz, 1H), 5.98 (dd , J = 8.8, 6.8 Hz, 1H), 5.23 (d, J = 6.4 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 149.6, 145.9, 132.2, 130.4 (q, J = 2.9 Hz), 129.2 (q, J = 27.0 Hz), 128.6, 128.3 (q, J = 8.8 Hz), 128.2, 125.0 (d, J = 4.4 Hz), 122.3 (q, J = 270.5 Hz), 119.7, 114.6,

107.0, 103.5, 102.3, 66.5, 16.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4; HRMS (ESI) *m/z* calcd for $C_{18}H_{12}Cl_3F_3N_3O$ $[M + H]^+$: 447.9993, found 447.9986.



2j

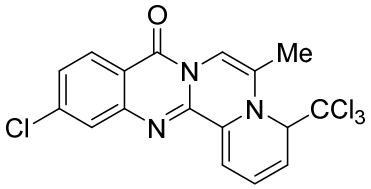
12-methoxy-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2j). **1j** (0.058 g, 0.20 mmol) ran for 21.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2j**. A yellow solid, 0.044 g, 54% yield; Mp: 174−175 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.8 Hz, 1H), 7.21 (s, 1H), 7.13 (s, 1H), 7.05 (s, 1H), 7.04-6.98 (m, 1H), 6.76 (dd , J = 8.8, 6.4 Hz, 1H), 5.95 (dd , J = 8.4, 6.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 3.92 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 156.8, 149.0, 144.9, 132.1, 128.6, 128.4, 128.2, 117.6, 114.1, 113.3, 107.4, 106.4, 103.6, 102.5, 66.6, 55.8, 16.7; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}Cl_3N_3O_2$ $[M + H]^+$: 410.0224, found 410.0211.



2k

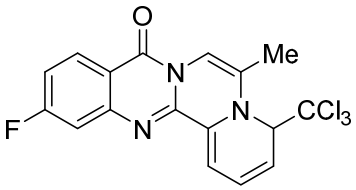
6,12-dimethyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2k). **1k** (0.055 g, 0.20 mmol) ran for 20.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2k**. A yellow solid, 0.049 g, 62% yield; Mp: 185−186 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 1H), 7.52 (s, 1H), 7.29-7.26 (m, 1H), 7.13 (s, 1H), 6.91 (d, J = 6.0 Hz, 1H), 6.76 (dd , J = 8.8, 6.0 Hz, 1H), 5.94 (dd , J = 8.8, 6.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 2.49 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 147.4, 145.6, 144.3, 132.6, 128.5, 128.4, 128.1, 127.3, 126.8, 117.5, 113.8, 105.8, 103.7, 102.6, 66.6, 21.9, 16.7; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}Cl_3N_3O$ $[M + H]^+$: 394.0275,

found 394.0266.



2l

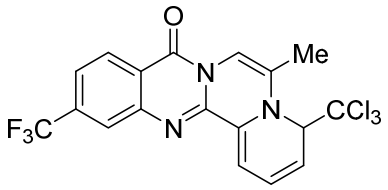
12-chloro-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2l). **1l** (0.059 g, 0.20 mmol) ran for 20.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2l**. A black solid, 0.051 g, 62% yield; Mp: 220−221 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.4 Hz, 1H), 7.70 (s, 1H), 7.40 (dd , J = 8.8, 1.6 Hz, 1H), 7.09 (s, 1H), 6.90 (d, J = 6.0 Hz, 1H), 6.76 (dd , J = 9.2, 6.4 Hz, 1H), 5.96 (dd , J = 8.4, 6.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 148.3, 145.3, 140.7, 132.3, 128.7, 128.4, 128.3, 127.3, 127.0, 118.3, 114.3, 106.5, 103.6, 102.3, 66.5, 16.7; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}Cl_4N_3O$ $[M + H]^+$: 413.9729, found 413.9720.



2m

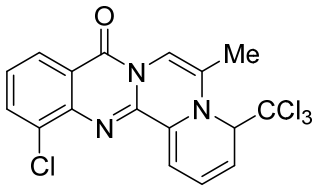
12-fluoro-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2m). **1m** (0.056 g, 0.20 mmol) ran for 21.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2m**. A yellow solid, 0.040 g, 50% yield; Mp: 173−174 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, J = 8.8, 6.4 Hz, 1H), 7.37 (d, J = 9.6 Hz, 1H), 7.19-7.14 (m, 1H), 7.11 (s, 1H), 6.93 (d, J = 6.0 Hz, 1H), 6.76 (dd , J = 9.2, 6.4 Hz, 1H), 5.96 (dd , J = 8.4, 6.8 Hz, 1H), 5.23 (d, J = 6.4 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.4, 165.8, 156.8, 149.5 (d, J = 13.5 Hz), 145.4, 132.2, 129.8 (d, J = 10.5 Hz), 128.6 (d, J = 36.0 Hz), 116.7, 115.8 (d, J = 24.0 Hz), 114.3, 112.7 (d, J = 21.0

Hz), 106.6, 103.6, 102.3, 66.6, 16.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}Cl_3FN_3O$ $[M + H]^+$: 398.0024, found 398.0021.



2n

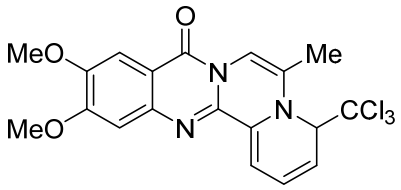
6-methyl-4-(trichloromethyl)-12-(trifluoromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2n). **1n** (0.066 g, 0.20 mmol) ran for 20.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2n**. A yellow solid, 0.055 g, 62% yield; Mp: 210−211 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 8.8 Hz, 1H), 7.97 (s, 1H), 7.63 (d , J = 8.4 Hz, 1H), 7.10 (s, 1H), 6.92 (d, J = 6.0 Hz, 1H), 6.76 (dd , J = 8.8, 6.4 Hz, 1H), 5.97 (dd , J = 8.8, 6.4 Hz, 1H), 5.22 (d, J = 6.4 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 147.4, 145.4, 136.3 (q, J = 32.9 Hz), 132.1, 129.2, 128.3 (q, J = 8.8 Hz), 127.4 (q, J = 271.2 Hz), 125.2 (q, J = 4.4 Hz), 122.5 (q, J = 2.9 Hz), 122.1, 122.0, 114.6, 106.7, 103.5, 102.3, 66.5, 16.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3; HRMS (ESI) *m/z* calcd for $C_{18}H_{12}Cl_3F_3N_3O$ $[M + H]^+$: 447.9993, found 447.9984.



2o

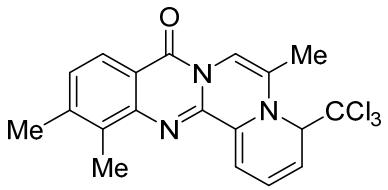
13-chloro-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2o). **1o** (0.059 g, 0.20 mmol) ran for 20.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2o**. A yellow solid, 0.044 g, 53% yield; Mp: 202−203 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.36-7.32 (m, 1H), 7.08 (s, 1H), 7.04 (d, J = 6.0 Hz, 1H), 6.77 (dd , J = 8.8, 6.4 Hz, 1H), 5.95 (dd , J = 8.8, 6.4 Hz, 1H), 5.23 (d, J = 6.0 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 144.6, 144.2, 134.6, 132.4, 132.1, 128.9, 128.5, 126.5, 125.8, 121.5, 114.0,

106.7, 103.6, 102.4, 66.6, 16.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}Cl_4N_3O$ $[M + H]^+$: 413.9729, found 413.9714.



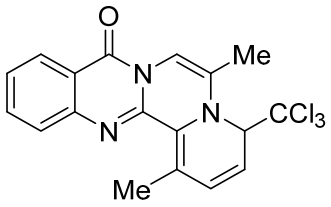
2p

11,12-dimethoxy-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2p). **1p** (0.064 g, 0.20 mmol) ran for 21 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2p**. A yellow solid, 0.054 g, 62% yield; Mp: 190−191 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.19 (s, 1H), 7.16 (s, 1H), 6.89 (d, J = 6.0 Hz, 1H), 6.76 (dd , J = 9.2, 6.8 Hz, 1H), 5.93 (dd , J = 8.8, 6.8 Hz, 1H), 5.23 (d, J = 6.0 Hz, 1H), 4.01 (s, 6H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.6, 155.3, 149.4, 143.5, 143.1, 132.5, 128.4, 128.3, 113.6, 113.4, 107.7, 105.8, 105.4, 103.7, 102.7, 66.6, 56.4, 56.3, 16.7; HRMS (ESI) *m/z* calcd for $C_{19}H_{17}Cl_3N_3O_3$ $[M + H]^+$: 440.0330, found 440.0333.



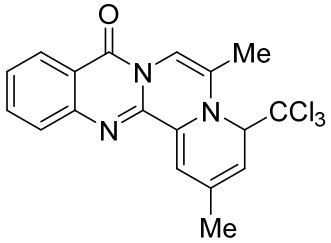
2q

6,12,13-trimethyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2q). **1q** (0.058 g, 0.20 mmol) ran for 20.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2q**. A yellow solid, 0.050 g, 61% yield; Mp: 221−222 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.12 (s, 1H), 6.95 (d, J = 6.0 Hz, 1H), 6.76 (dd , J = 9.2, 6.4 Hz, 1H), 5.92 (dd , J = 8.4, 6.4 Hz, 1H), 5.23 (d, J = 6.4 Hz, 1H), 2.58 (s, 3H), 2.43 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 145.6, 143.5, 142.7, 134.0, 133.1, 128.9, 128.5, 127.8, 123.8, 117.9, 113.2, 105.2, 103.9, 102.7, 66.7, 21.0, 16.7, 13.1; HRMS (ESI) *m/z* calcd for $C_{19}H_{17}Cl_3N_3O$ $[M + H]^+$: 408.0432, found 408.0417.



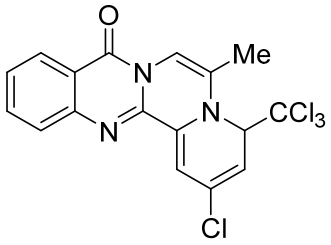
2r

1,6-dimethyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2r). **1r** (0.055 g, 0.20 mmol) ran for 40 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2r**. A yellow solid, 0.030 g, 38% yield; Mp: 235−236 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 7.5 Hz, 1H), 7.75-7.70 (m, 2H), 7.48-7.45 (m, 1H), 7.07 (s, 1H), 6.50 (d, J = 9.0 Hz, 1H), 6.04 (dd , J = 8.5, 6.5 Hz, 1H), 5.05 (d , J = 6.5 Hz, 1H), 2.48 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 146.9, 144.4, 134.3, 134.1, 130.3, 127.6, 126.9, 126.8, 126.1, 120.1, 119.7, 116.5, 102.6, 102.0, 65.9, 20.2, 16.8; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}Cl_3N_3O$ $[M + H]^+$: 394.0275, found 394.0275.



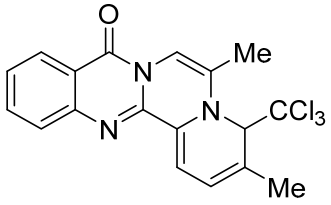
2s

2,6-dimethyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2s). **1s** (0.055 g, 0.20 mmol) ran for 15.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2s**. A yellow solid, 0.041 g, 52% yield; Mp: 170−171 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.0 Hz, 1H), 7.75-7.70 (m, 2H), 7.47-7.43 (m, 1H), 7.10 (s, 1H), 6.79 (s, 1H), 5.67 (d, J = 6.0 Hz, 1H), 5.14 (d , J = 6.4 Hz, 1H), 2.25 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 147.4, 144.3, 137.6, 134.4, 132.0, 128.4, 127.6, 127.0, 126.7, 120.0, 110.0, 109.0, 104.3, 102.0, 67.2, 20.6, 16.7; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}Cl_3N_3O$ $[M + H]^+$: 394.0275, found 394.0265.



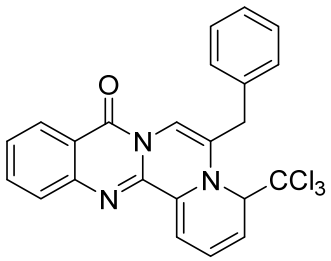
2t

2-chloro-6-methyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2t). **1t** (0.059 g, 0.20 mmol) ran for 22.5 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2t**. A yellow solid, 0.040 g, 48% yield; Mp: 215−216 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 6.4 Hz, 1H), 7.77 (s, 1H), 7.76 (s, 1H), 7.50-7.48 (m, 1H), 7.18 (s, 1H), 6.93 (s, 1H), 5.92 (d, J = 4.8 Hz, 1H), 5.25 (d , J = 5.2 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 146.9, 143.0, 134.8, 134.7, 133.9, 127.6, 127.5, 127.3, 127.1, 119.9, 109.3, 106.9, 103.2, 103.1, 68.1, 16.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}Cl_4N_3O$ $[M + H]^+$: 413.9729, found 413.9717.



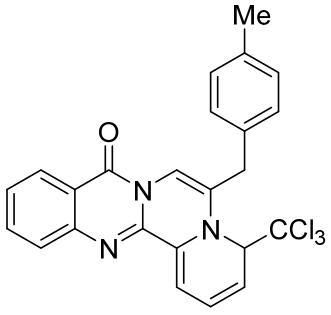
2u

3,6-dimethyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2u). **1u** (0.055 g, 0.20 mmol) ran for 22 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/6) afforded **2u**. A yellow solid, 0.020 g, 25% yield; Mp: 197−198 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 7.6 Hz, 1H), 7.82-7.73 (m, 2H), 7.48-7.44 (m, 1H), 7.04 (s, 1H), 6.76 (s, 1H), 6.70 (d, J = 6.4 Hz, 1H), 4.29 (d, J = 6.4 Hz, 1H), 2.18 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 146.6, 142.3, 134.6, 131.5, 127.5, 127.0, 126.9, 124.9, 123.7, 119.5, 111.3, 105.3, 100.2, 97.9, 60.3, 21.6, 17.0; HRMS (ESI) *m/z* calcd for $C_{18}H_{15}Cl_3N_3O$ $[M + H]^+$: 394.0275, found 394.0265.



2v

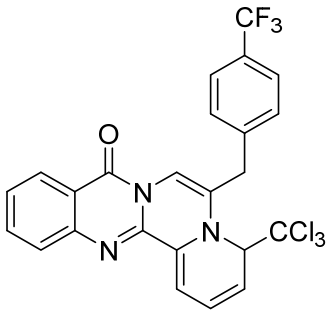
6-benzyl-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2v). **1v** (0.067 g, 0.20 mmol) ran for 48 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2v**. A black solid, 0.028 g, 31% yield; Mp: 272−273 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.0 Hz, 1H), 7.80-7.74 (m, 2H), 7.50-7.46 (m, 1H), 7.35-7.32 (m, 2H), 7.29 (d, J = 7.2 Hz, 2H), 7.23 (d, J = 7.2 Hz, 2H), 6.97 (d, J = 6.0 Hz, 1H), 6.60 (dd , J = 8.8, 6.0 Hz, 1H), 5.55 (dd, J = 9.2, 7.2 Hz, 1H), 5.07 (d , J = 6.4 Hz, 1H), 4.13 (d , J = 17.2 Hz, 1H), 3.95 (d , J = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 147.0, 144.5, 135.2, 134.7, 131.9, 130.8, 129.1, 128.1, 127.9, 127.5, 127.4, 127.1, 127.0, 119.9, 114.5, 106.9, 104.3, 103.6, 66.7, 35.8; HRMS (ESI) *m/z* calcd for $C_{23}H_{17}Cl_3N_3O$ $[M + H]^+$: 456.0432, found 456.0425.



2w

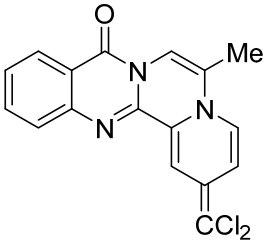
6-(4-methylbenzyl)-4-(trichloromethyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2w). **1w** (0.070 g, 0.20 mmol) ran for 48 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2w**. A yellow solid, 0.019 g, 20% yield; Mp: 180−181 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.0 Hz, 1H), 7.76 (d , J = 4.0 Hz, 2H), 7.49-7.45 (m, 1H), 7.23 (s, 1H), 7.14-7.08 (m, 4H), 6.94 (d, J = 6.0 Hz, 1H), 6.60 (dd , J = 9.2, 6.4

Hz, 1H), 5.57 (dd, J = 9.2, 6.8 Hz, 1H), 5.10 (d , J = 6.4 Hz, 1H), 4.08 (d , J = 17.2 Hz, 1H), 3.90 (d , J = 16.8 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 147.3, 144.4, 137.0, 134.6, 132.4, 132.1, 132.0, 131.0, 129.7, 127.9, 127.6, 127.1, 126.9, 120.1, 114.4, 106.5, 104.2, 103.7, 66.7, 35.4, 21.1; HRMS (ESI) *m/z* calcd for $C_{24}H_{19}Cl_3N_3O$ $[M + H]^+$: 470.0588, found 470.0574.



2x

4-(trichloromethyl)-6-(4-(trifluoromethyl)benzyl)pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (2x). **1x** (0.081 g, 0.20 mmol) ran for 48 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2x**. A yellow solid, 0.035 g, 33% yield; Mp: 205−206 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.0 Hz, 1H), 7.77 (d , J = 3.2 Hz, 2H), 7.61 (d , J = 8.0 Hz, 2H), 7.50-7.46 (m, 1H), 7.36 (d , J = 8.0 Hz, 2H), 7.27 (s, 1H), 6.97 (d, J = 6.0 Hz, 1H), 6.63 (dd , J = 9.2, 6.4 Hz, 1H), 5.59 (dd, J = 8.8, 6.4 Hz, 1H), 4.96 (d , J = 6.4 Hz, 1H), 4.22 (d , J = 17.2 Hz, 1H), 3.98 (d , J = 17.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 147.2, 144.2, 139.4, 134.8, 132.0, 130.3 (q, J = 32.1 Hz), 129.7, 128.4, 128.2, 128.0 (q, J = 270.6 Hz), 127.6, 127.1, 126.0 (q, J = 3.6 Hz), 122.9 (q, J = 34.3 Hz), 119.9, 114.4, 106.9, 104.8, 103.5, 66.7, 35.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5; HRMS (ESI) *m/z* calcd for $C_{24}H_{16}Cl_3F_3N_3O$ $[M + H]^+$: 524.0306, found 524.0290.

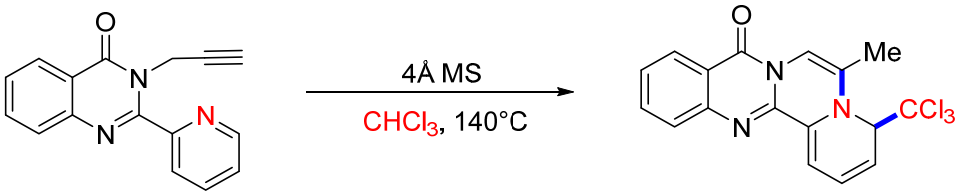


2aa

2-(dichloromethylene)-6-methylpyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-

9(2H)-one (2aa). **1a** (0.052 g, 0.20 mmol) with $CHBrCl_2$ (2 mL) ran for 16 h. Purification using medium pressure chromatography (eluents with a mixed ethyl acetate/petroleum ether = 1/10) afforded **2aa**. A yellow solid, 0.010 g, 15% yield; Mp: 227−228 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (d, J = 9.6 Hz, 1H), 7.79-7.74 (m, 2H), 7.72 (s, 1H), 7.60 (d, J = 4.2 Hz, 1H), 7.44-7.41 (m, 1H), 7.17 (s, 1H), 7.03 (d, J = 4.2 Hz, 1H), 2.64 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.9, 148.4, 141.1, 134.8, 127.2, 127.1, 126.3, 125.9, 125.4, 124.0, 122.4, 119.9, 118.0, 117.0, 112.0, 107.1, 19.0; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}Cl_2N_3O$ $[M + H]^+$: 344.0352, found 344.0341.

3. Gram scalable preparation of 2a

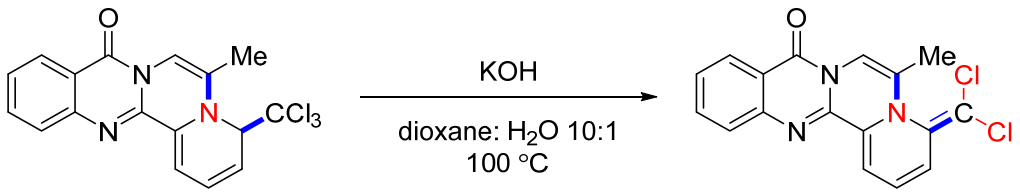


1a
1.0 g, 3.83 mmol

2a
58% yield, 0.773 g

A 100 mL reaction flask was charged with **1a** (1.0 g, 3.83 mmol) and 4Å MS (9.6 g). $CHCl_3$ (40 mL) was then added via syringe and the reaction vessel was sealed with a Teflon cap. The reaction mixture was heated at 140 °C in an oil bath for 16 h until **1a** was consumed completely (monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (1/10 to 1/6, ethyl acetate/petroleum ether) to afford 4-(trichloromethyl)pyrido[2',1':3,4] pyrazino [2,1-b]quinazolinones **2a** (0.773 g, 58% yield).

4. Synthesis of compounds 3a-5a



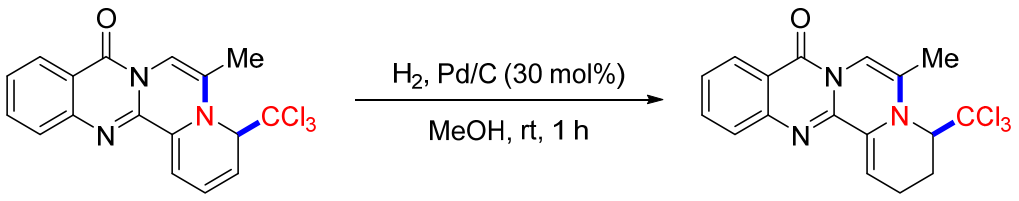
2a

3a, 50% yield

A 25 mL reaction flask was charged with **2a** (0.076 g, 0.2 mmol) and KOH (0.112 g,

10 equiv.). 1,4-dioxane (2 mL) and H_2O (0.2 mL) were then added via syringe and the reaction vessel was sealed with a Teflon cap. The reaction mixture was heated at 100 °C in an oil bath for 3 h until **2a** was consumed completely (monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (1/10, ethyl acetate/petroleum ether) to afford 4-(dichloromethylene)-6-methylpyrido[2',1':3,4] pyrazino[2,1-b]quinazolin-9(4H)-one **3a**.

4-(dichloromethylene)-6-methylpyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(4H)-one (3a). A reddish brown solid, 0.034 g, 50% yield; Mp: 261−262 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 7.5 Hz, 1H), 7.77-7.74 (m, 1H), 7.71 (d , J = 8.0 Hz, 1H), 7.49-7.46 (m, 1H), 7.17 (s, 1H), 7.02 (d, J = 6.5 Hz, 1H), 6.74 (d, J = 9.5 Hz, 1H), 6.52 (dd, J = 10.0, 6.5 Hz, 1H), 2.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 147.3, 143.9, 134.7, 134.6, 132.5, 127.7, 127.5, 127.1, 127.0, 125.5, 122.4, 120.1, 108.4, 105.3, 103.5, 16.8; HRMS (ESI) *m/z* calcd for $C_{17}H_{12}Cl_2N_3O$ $[M + H]^+$: 344.0352, found 344.0366.

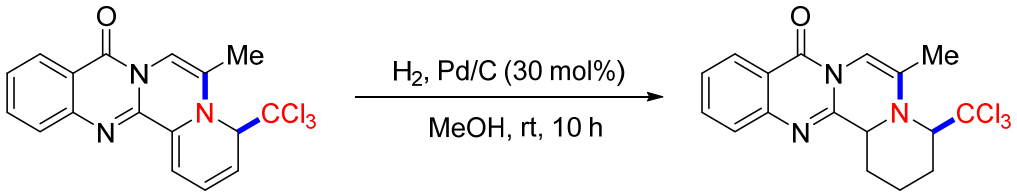


2a **4a,** 34% yield

A Schlenk flask was charged with **2a** (0.076 g, 0.20 mmol), MeOH (2.0 mL) and Pd/C (30%, 0.023 g). Then, the reaction mixture was performed in the presence of hydrogen (A balloon filled with hydrogen). The reaction mixture was stirred at room temperature for 1 h until **2a** was consumed completely (monitored by TLC). After completion, the mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (1/5, ethyl acetate/petroleum ether) to afford 6-methyl-4-(trichloromethyl)-3,4-dihydropyrido [2',1':3,4]pyrazino[2,1-b]quinazolin-9(2H)-one **4a**.

6-methyl-4-(trichloromethyl)-3,4-dihydropyrido[2',1':3,4]pyrazino[2,1-

b]quinazolin-9(2H)-one (4a). A yellow solid, 0.026 g, 34% yield; Mp: 173−174 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 1H), 7.70 (d , J = 4.0 Hz, 2H), 7.44-7.40 (m, 1H), 6.80 (s, 1H), 6.53 (s, 1H), 4.61 (d, J = 5.0 Hz, 1H), 2.90-2.85 (m, 1H), 2.77-2.68 (m, 1H), 2.50-2.44 (m, 1H), 2.17 (s, 3H), 2.08-2.00 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 147.2, 145.1, 134.2, 130.8, 129.2, 127.4, 126.9, 126.6, 120.1, 108.3, 102.4, 98.3, 64.6, 21.7, 19.3, 17.5; HRMS (ESI) *m/z* calcd for $C_{17}H_{15}Cl_3N_3O$ [M + H]$^+$: 382.0275, found 382.0294.

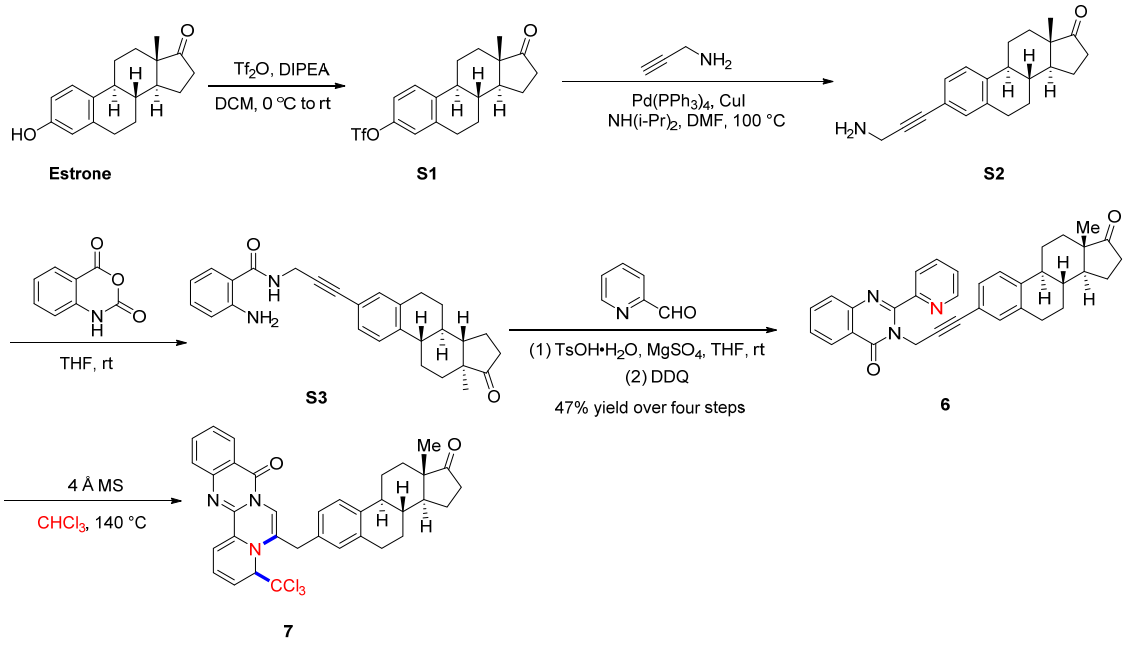


2a **5a,** 40% yield

A Schlenk flask was charged with **2a** (0.076 g, 0.20 mmol), MeOH (2.0 mL) and Pd/C (30%, 0.023 g). Then, the reaction mixture was performed in the presence of hydrogen (A balloon filled with hydrogen). The reaction mixture was stirred at room temperature for 10 h until **2a** was consumed completely (monitored by TLC). After completion, the mixture was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (1/4, ethyl acetate/petroleum ether) to afford 6-methyl-4-(trichloromethyl)-1,3,4,14b-tetrahydro pyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(2H)-one **5a**.

6-methyl-4-(trichloromethyl)-1,3,4,14b-tetrahydropyrido[2',1':3,4]pyrazino[2,1-b]quinazolin-9(2H)-one(5a). A yellow solid, 0.031 g, 40% yield; Mp: 128−129 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, J = 8.0 Hz, 1H), 7.70-7.67 (m, 2H), 7.45-7.42 (m, 1H), 6.96 (s, 1H), 4.48-4.45 (m, 1H), 3.91-3.87 (m, 1H), 2.62-2.55 (m, 1H), 2.52-2.47 (m, 1H), 2.36 (t, J = 5.0 Hz, 1H), 2.16 (s, 3H), 2.07-1.98 (m, 2H), 1.62-1.52 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 148.7, 147.7, 136.7, 133.5, 127.5, 127.0, 126.3, 120.4, 106.8, 104.2, 65.5, 58.3, 25.9, 21.8, 18.3, 16.2; HRMS (ESI) *m/z* calcd for $C_{17}H_{17}Cl_3N_3O$ [M + H]$^+$: 384.0432, found 384.0423.

5. Synthesis of compounds 6 and 7



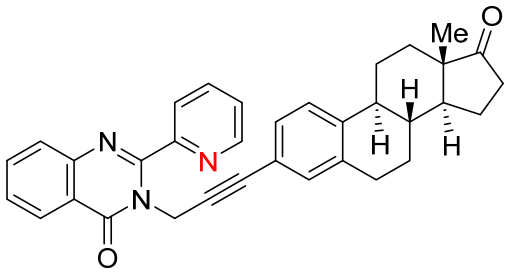
Procedure: estrone (1.0 equiv.) and DIPEA (1.1 equiv.) was sequentially dissolved in dry DCM. The resulting mixture was stirred at 25 °C for 0.5 h, following by dropwise addition of Tf_2O (1.1 equiv.) at 0 °C. After that, the mixture was warmed to room temperature, and stirred overnight. When the reaction was completed, 10% HCl was added to the solution to quench the reaction, and then the mixture was extracted with DCM. The organic layer was washed with saturated $NaHCO_3$ and saturated brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (1/10, ethyl acetate/petroleum ether) to afford compound **S1**.

A mixture of **S1** (1.0 equiv.), prop-2-yn-1-amine (1.5 equiv.), diisopropylamine (3.0 equiv.), and $Pd(PPh_3)_4$ (0.1 equiv.), CuI (0.1 equiv.) was dissolved in DMF and stirred at 100 °C for 8 h under nitrogen. The reaction mixture was diluted with water and extracted with EtOAc, the combined organic layers were washed with brine for three time, dried by Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (1/10, methanol/dichloromethane) to afford compound **S2**.

A mixture of isatoic anhydride (1.0 equiv.) and **S2** (1.5 equiv.) was dissolved in THF and stirred at room temperature for 12 h until isatoic anhydride was consumed

completely (monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (1/20, ethyl acetate/dichloromethane) to afford compound **S3**.

A mixture of **S3** (1.0 equiv.), 2-pyridinecarboxaldehyde (1.0 equiv.), $MgSO_4$ (3.0 equiv.) and $TsOH·H_2O$ (0.3 equiv.) was dissolved in THF and stirred at room temperature for 4 h under nitrogen until **S3** was consumed completely (monitored by TLC). Then DDQ (1.2 equiv.) was added. The resulting reaction mixture was stirred at room temperature for an additional 15 min (monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (1/2, ethyl acetate/ petroleum ether) to afford compound **6** with 47% yield.

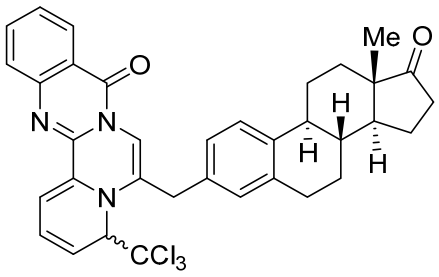


6

3-(3-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (6). A yellow solid, 0.27 g, 47% yield; Mp: 131-132 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, J = 4.0 Hz, 1H), 8.38 (d, J = 7.5 Hz, 1H), 7.94-7.89 (m, 2H), 7.79-7.75 (m, 2H), 7.55-7.52 (m, 1H), 7.48-7.45 (m, 1H), 7.13 (d, J = 8.5 Hz, 1H), 6.92 (d, J = 7.0 Hz, 2H), 5.53 (s, 2H), 2.80-2.78 (m, 2H), 2.51-2.45 (m, 1H), 2.35-2.33 (m, 1H), 2.24-2.22 (m, 1H), 2.16-2.08 (m, 1H), 2.02-1.92 (m, 2H), 1.63-1.48 (m, 3H), 1.46-1.33 (m, 2H), 1.26 (t, J = 7.0 Hz, 2H), 0.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 220.6, 161.5, 153.6, 152.8, 148.7, 146.9, 140.4, 137.2, 136.4, 134.5, 132.2, 128.9, 127.6, 127.5, 127.2, 125.1, 124.9, 124.6, 121.0, 119.4, 83.4, 83.1, 50.4, 47.8, 44.3, 37.8, 35.7, 34.2, 31.4, 28.9, 26.2, 25.4, 21.5, 13.7; HRMS (ESI) *m/z* calcd for $C_{34}H_{31}N_3NaO_2$ $[M + H]^+$: 536.2308, found 536.2303.

A 25 mL reaction flask was charged with **6** (0.2 mmol) and 4Å MS (500 mg). $CHCl_3$

(2 mL) was then added via syringe and the reaction vessel was sealed with a Teflon cap. The reaction mixture was stirred vigorously at 140 °C in an oil bath for 48 h until **6** was consumed completely (monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (1/10 to 1/6, ethyl acetate/petroleum ether) to afford compound **7** with 30% yield (0.038 g).

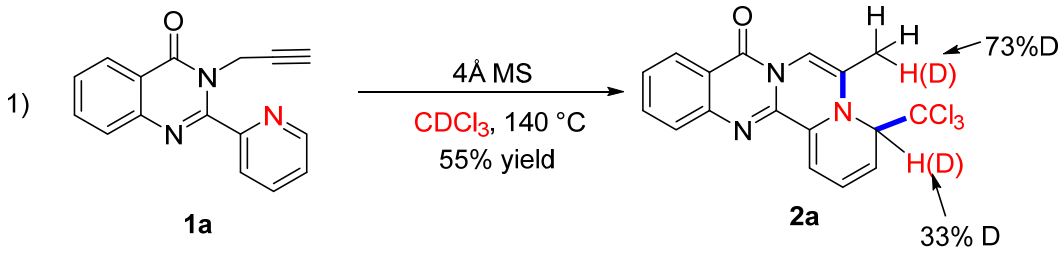


7 (*dr* = 2.8:1)

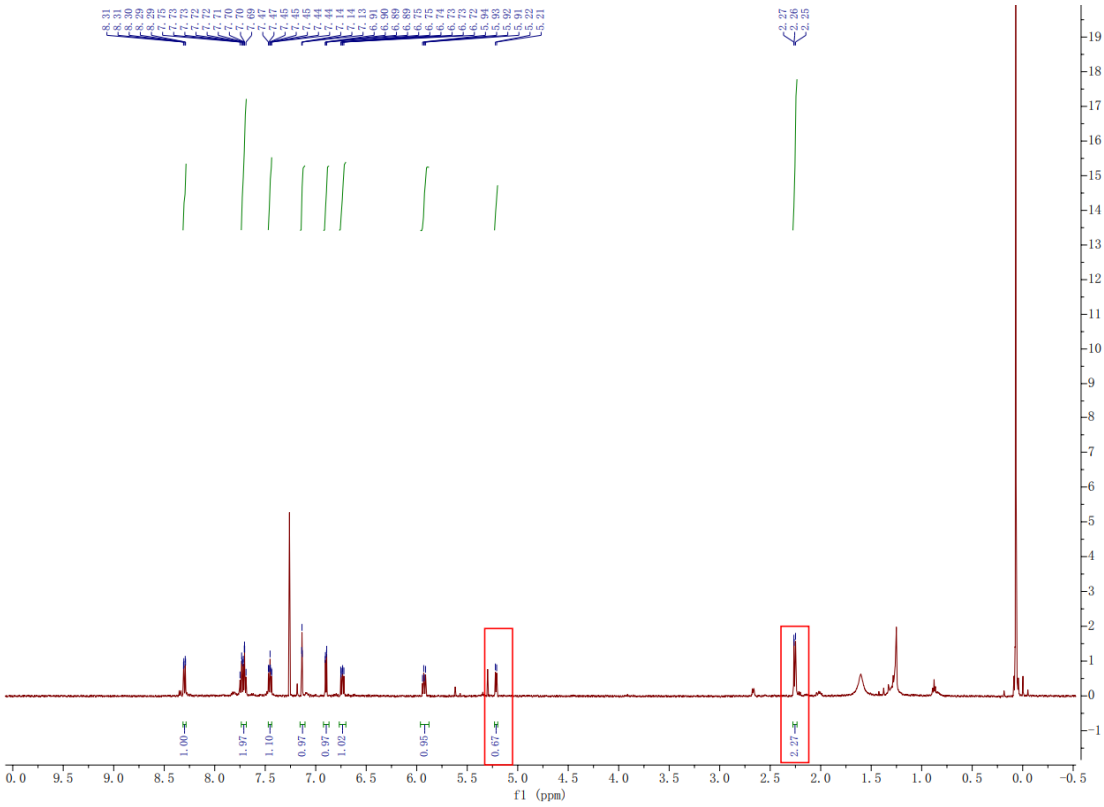
(R)-6-(((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)methyl)-4-(trichloromethyl)pyrido[2',1':3,4] pyrazino[2,1-b]quinazolin-9(4H)-one (7). A yellow solid, 0.038 g, 30% yield; Mp: 282−283 ℃; *Major isomer*: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31-8.29 (m, 1H), 7.79-7.73 (m, 2H), 7.49-7.45 (m, 1H), 7.25-7.20 (m, 2H), 7.04-6.98 (m, 2H), 6.96-6.93 (m, 1H), 6.64-6.58 (m, 1H), 5.64-5.60 (m, 1H), 5.13-5.11 (m, 1H), 4.04 (d, *J* = 20.4 Hz, 1H), 3.88 (d, *J* = 20.4 Hz, 1H), 2.88-2.83 (m, 2H), 2.54-2.39 (m, 4H), 2.18-2.13 (m, 1H), 2.09-2.02 (m, 3H), 1.67-1.61 (m, 2H), 1.55-1.50 (m, 3H), 0.92 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 220.9, 157.5, 147.1, 144.4, 138.9, 137.2, 134.7, 132.4, 131.0, 129.6, 128.4, 127.9, 127.5, 127.1, 127.0, 126.0, 125.6, 125.3, 119.9, 114.6, 104.2, 103.7, 101.0, 99.9, 66.7, 50.5, 48.0, 38.0, 35.8, 35.1, 31.5, 26.4, 25.7, 21.6, 13.8; *Minor isomer:* ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28-8.27 (m, 1H), 7.74-7.63 (m, 2H), 7.49-7.45 (m, 1H), 7.25-7.20 (m, 2H), 7.15-7.08 (m, 2H), 6.93-6.90 (m, 1H), 6.70-6.68 (m, 1H), 5.61-5.56 (m, 1H), 5.08-5.06 (m, 1H), 3.82 (d, *J* = 19.8 Hz, 1H), 3.74 (d, *J* = 19.8 Hz, 1H), 2.88-2.83 (m, 2H), 2.31-2.29 (m, 4H), 2.13-2.11 (m, 1H), 2.01-1.99 (m, 3H), 1.60-1.59 (m, 2H), 1.48-1.47 (m, 3H), 0.91 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 220.8, 157.5, 147.1, 144.4, 138.9, 137.1, 132.7, 132.1, 131.0, 128.6, 128.4, 127.8, 127.7, 127.5, 127.1, 126.0, 125.5, 125.3, 119.9, 114.6, 104.2, 103.7, 100.8, 99.9, 66.7, 50.5, 48.0, 38.0, 35.7,

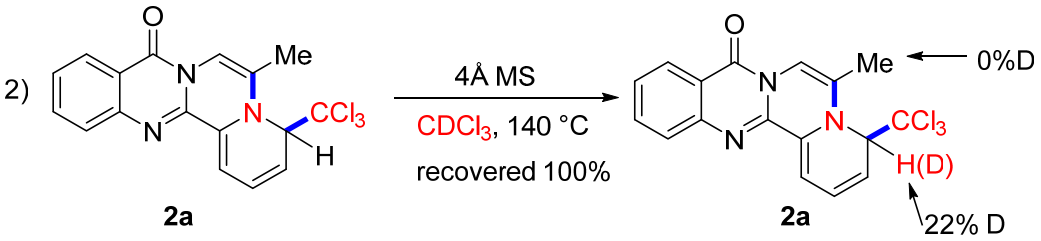
35.1, 31.5, 26.4, 25.7, 21.6, 13.8; HRMS (ESI) *m/z* calcd for $C_{35}H_{33}Cl_3N_3O_2$ $[M + H]^+$: 632.1633, found 632.1606.

6. Mechanistic studies

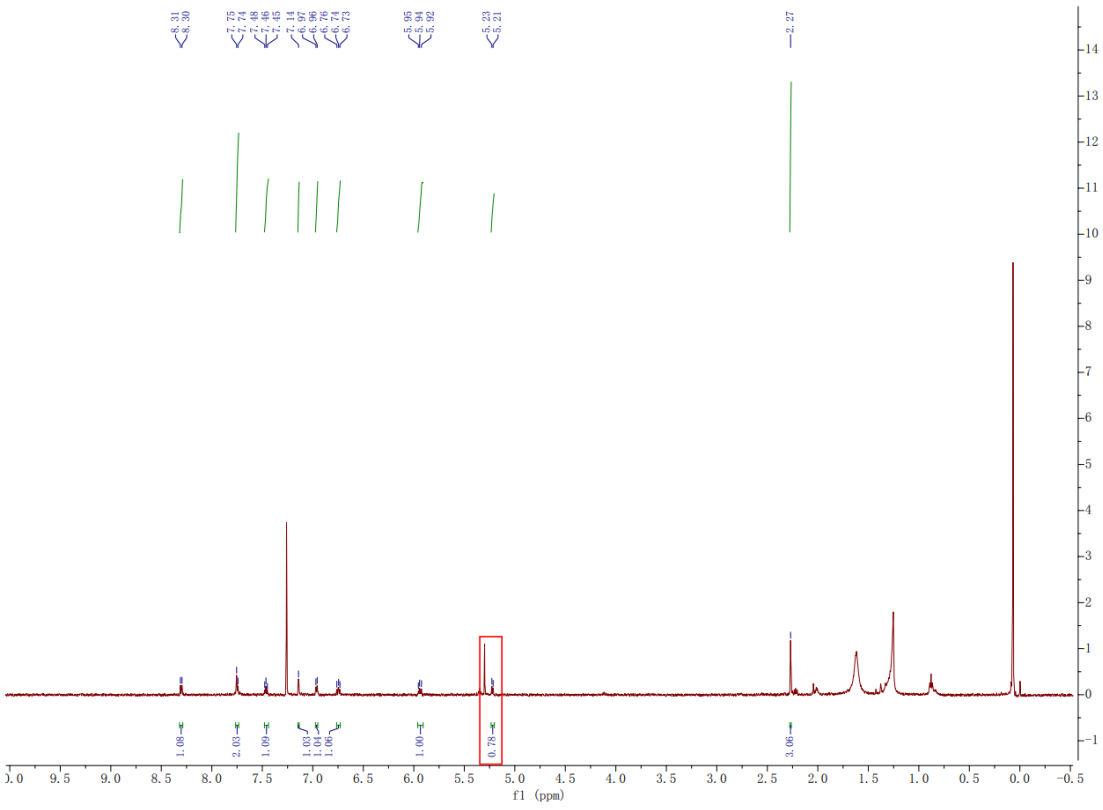


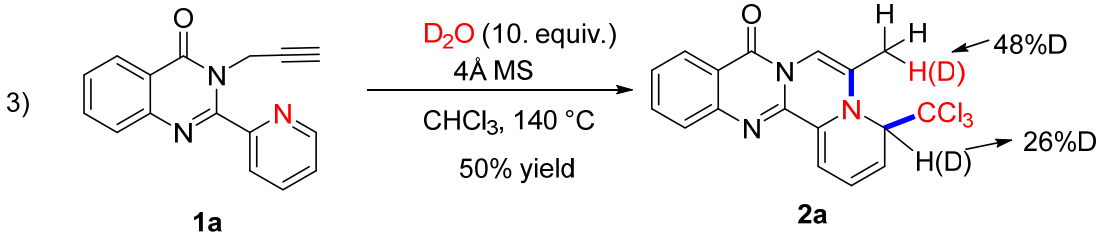
In a 25 mL reaction flask was charged with **1a** (0.20 mmol) and 4Å MS (500 mg). $CDCl_3$ (2 mL) was then added via syringe and the reaction vessel was sealed with a Teflon cap. The reaction mixture was stirred vigorously at 140 °C in an oil bath for 16 h until **1a** was consumed completely (monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (1/6, ethyl acetate/petroleum ether) to afford compound **D-2a.**





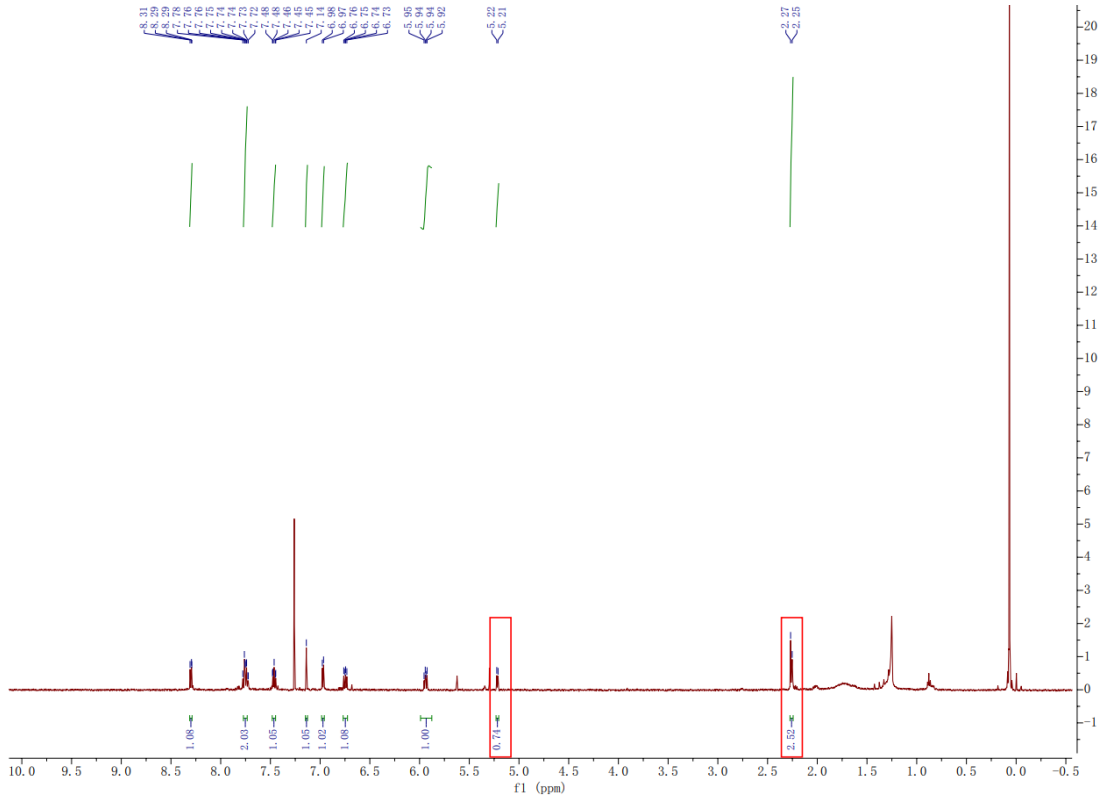
In a 25 mL reaction flask was charged with **2a** (0.20 mmol) and 4Å MS (500 mg). $CDCl_3$ (2 mL) was then added via syringe and the reaction vessel was sealed with a Teflon cap. The reaction mixture was stirred vigorously at 140 °C in an oil bath for 16 h and monitored by ^1H NMR.



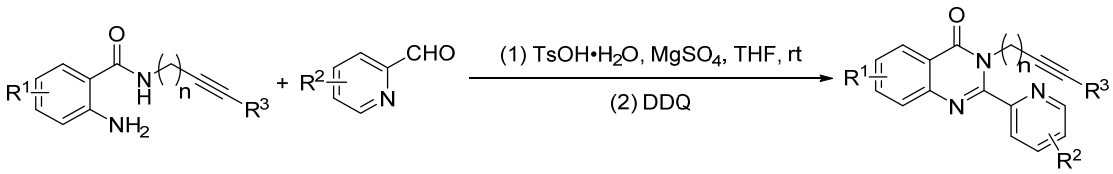


In a 25 mL reaction flask was charged with **1a** (0.20 mmol) and 4Å MS (500 mg) under. D_2O (0.036 mL, 10 equiv.) and $CHCl_3$ (2 mL) was then added via syringe and the reaction vessel was sealed with a Teflon cap. The reaction mixture was stirred vigorously at 140 °C in an oil bath for 16 h until **1a** was consumed completely

(monitored by TLC). At this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (1/6, ethyl acetate/petroleum ether) to afford compound **D-2a.**



7. Synthesis of compounds 1

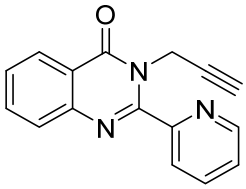


S4 **S5** **1**

Alkynyl anilines derivatives **S4** was prepared according to literature method.[1] pyridine aldehyde **S5** was purchased from Energy.

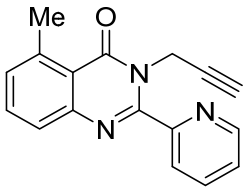
To a stirred mixture of N-alkynyl anilines **S4** (1 mmol, 1.0 equiv.), pyridine aldehyde **S5** (1 mmol, 1.0 equiv.) and anhydrous magnesium sulfate (0.36 g, 3.0 equiv.) in THF (5 mL, 0.2 M) was added p-toluene sulfonic acid (0.057 g, 0.3 equiv.) at 25 °C under nitrogen. The resulting mixture was stirred at 25 °C for 4-12 h. After completion indicated by TLC, 2,3-dicyano-5,6-dichlorobenzoquinone (DDQ, 0.272 g, 1.2 equiv.) was added. The resulting reaction mixture was stirred at room temperature for an

additional 15 min (monitored by TLC). The reaction was concentrated under reduced pressure. The crude product was purified by flash column chromatography (1/6 to 1/1, ethyl acetate/petroleum ether) to afford **1a-1z** and **6**.



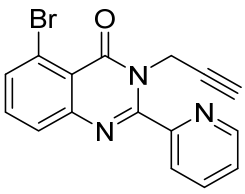
1a

3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1a). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1a**. A off-white solid, 0.188 g, 72% yield; Mp: 158-159 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.74 (d, J = 4.4 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.10-8.06 (m, 1H), 7.95 (d , J = 8.0 Hz, 1H), 7.91 (d , J = 7.6 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.66-7.62 (m, 2H), 5.11 (d , J = 2.0 Hz, 2H), 3.09 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.6, 152.6, 152.5, 148.5, 146.5, 137.8, 135.1, 128.0, 127.6, 126.5, 125.3, 125.1, 120.3, 78.7, 74.4, 33.7; HRMS (ESI) *m/z* calcd for $C_{16}H_{12}N_3O$ $[M + H]^+$: 262.0975, found 262.0996.



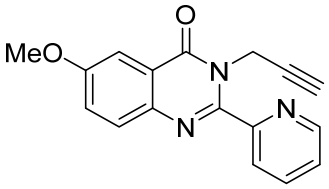
1b

5-methyl-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1b). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1b**. A white solid, 0.132 g, 48% yield; Mp: 182−183 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.4 Hz, 1H), 7.94-7.89 (m, 2H), 7.63-7.57 (m, 2H), 7.47-7.44 (m, 1H), 7.29 (d , J = 6.0 Hz, 1H), 5.11 (d, J = 2.0 Hz, 2H), 2.93 (s, 3H), 2.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 153.3, 152.3, 148.7, 148.4, 141.5, 137.4, 133.7, 130.2, 125.9, 124.9, 124.7, 119.5, 78.6, 71.3, 33.6, 23.1; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O$ $[M + H]^+$: 276.1131, found 276.1146.



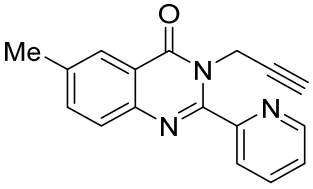
1c

5-bromo-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1c). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1c**. A white solid, 0.081 g, 24% yield; Mp: 190−191 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.4 Hz, 1H), 7.94-7.91 (m, 2H), 7.78 (d, J = 8.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.51-7.47 (m, 1H), 5.27 (d, J = 1.6 Hz, 2H), 2.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 152.8, 152.7, 149.1, 148.6, 137.4, 134.2, 134.0, 127.7, 124.9, 121.7, 119.0, 78.1, 71.7, 33.9; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}BrN_3O$ $[M + H]^+$: 340.0080, found 340.0099.



1d

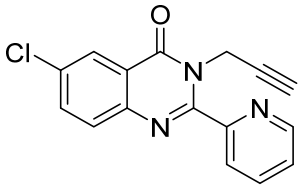
6-methoxy-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1d). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1d**. A pale yellow solid, 0.131 g, 45% yield; Mp: 190-191 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.4 Hz, 1H), 7.95-7.90 (m, 2H), 7.73-7.68 (m, 2H), 7.47-7.44 (m, 1H), 7.39-7.36 (m, 1H), 5.32 (d, J = 2.4 Hz, 2H), 3.95 (s, 3H), 2.03 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 159.0, 153.4, 150.3, 148.6, 141.6, 137.4, 129.3, 125.0, 124.9, 124.6, 121.8, 106.5, 78.4, 71.6, 55.9, 33.9; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O_2$ $[M + H]^+$: 292.1081, found 292.1108.



1e

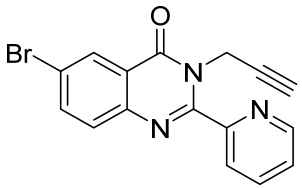
6-methyl-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1e).

Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1e**. A off-white solid, 0.212 g, 77% yield; Mp: 166-167 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.4 Hz, 1H), 8.15 (s, 1H), 7.95-7.90 (m, 2H), 7.67 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.47-7.44 (m, 1H), 5.29 (d, J = 2.0 Hz, 2H), 2.52 (s, 3H), 2.02 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 153.4, 151.7, 148.6, 144.9, 138.0, 137.4, 136.1, 127.5, 126.6, 125.0, 124.7, 120.7, 78.4, 71.5, 33.8, 21.4; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O$ $[M + H]^+$: 276.1131, found 276.1154.



1f

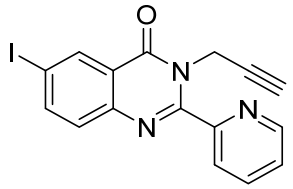
6-chloro-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1f). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1f**. A off-white solid, 0.233 g, 79% yield; Mp: 167-168 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.4 Hz, 1H), 8.31 (s, 1H), 7.94 (d, J = 4.4 Hz, 2H), 7.70 (s, 2H), 7.49-7.46 (m, 1H), 5.30 (d, J = 2.4 Hz, 2H), 2.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 153.0, 152.6, 148.7, 145.4, 137.5, 135.0, 133.4, 129.4, 126.5, 125.1, 124.9, 121.9, 78.0, 71.9, 34.0; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}ClN_3O$ $[M + H]^+$: 296.0585, found 296.0602.



1g

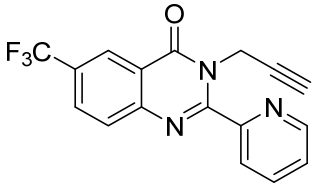
6-bromo-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1g). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1g**. A white solid, 0.159 g, 47% yield; Mp: 165-166 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.8 Hz, 1H), 8.49 (s, 1H), 7.94 (d, J = 4.8 Hz, 2H), 7.87 (dd, J = 8.8, 2.0 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.49-7.48 (m, 1H), 5.30 (d, J = 2.4 Hz, 2H), 2.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 153.0, 152.8, 148.7, 145.8, 137.8,

137.5, 129.7, 129.5, 125.1, 124.9, 122.3, 121.2, 78.0, 71.9, 34.0; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}BrN_3O$ $[M + H]^+$: 340.0080, found 340.0096.



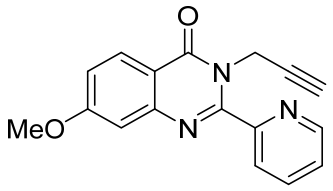
1h

6-iodo-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1h). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1h**. A grey solid, 0.205 g, 53% yield; Mp: 166-167 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73-8.70 (m, 2H), 8.06-8.04 (m, 1H), 7.94 (d, J = 5.6 Hz, 2H), 7.50-7.46 (m, 2H), 5.31 (d, J = 2.4 Hz, 2H), 2.03 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 153.0, 152.9, 148.7, 146.3, 143.4, 137.4, 136.0, 129.5, 125.1, 124.9, 122.5, 92.2, 78.1, 71.8, 34.0; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}IN_3O$ $[M + H]^+$: 387.9941, found 387.9976.



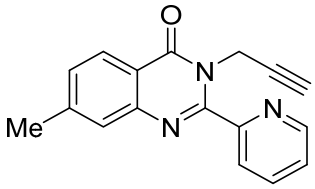
1i

3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)-6-(trifluoromethyl)quinazolin-4(3H)-one (1i). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1i**. A yellow solid, 0.171 g, 52% yield; Mp: 125-126 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 4.4 Hz, 1H), 8.64 (s, 1H), 7.98-7.92 (m, 3H), 7.86 (d, J = 8.8 Hz, 1H), 7.50-7.48 (m, 1H), 5.33 (d, J = 1.6 Hz, 2H), 2.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 154.3, 152.8, 149.0, 148.7, 137.5, 130.8 (q, J = 3.0 Hz), 129.9 (q, J = 33.6 Hz), 128.7, 127.6 (q, J = 270.5 Hz), 125.2 (q, J = 2.9 Hz), 125.1, 120.8, 77.8, 72.0, 34.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4; HRMS (ESI) *m/z* calcd for $C_{17}H_{11}F_3N_3O$ $[M + H]^+$: 330.0849, found 330.0872.



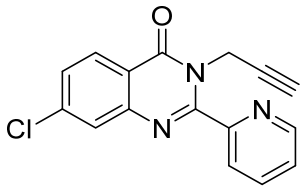
1j

7-methoxy-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1j). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1j**. A grey solid, 0.099 g, 34% yield; Mp: 138-139 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.8 Hz, 1H), 8.26 (d, J = 8.8 Hz, 1H), 7.92 (d, J = 4.0 Hz, 2H), 7.46 (d, J = 4.4 Hz, 1H), 7.14 (d, J = 2.0 Hz, 2H), 5.25 (d, J = 2.0 Hz, 2H), 3.90 (s, 3H), 2.02 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 161.0, 153.3, 153.2, 149.1, 148.7, 137.4, 128.7, 124.9, 124.7, 117.7, 114.4, 108.3, 78.4, 71.5, 55.7, 33.6; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O_2$ $[M + H]^+$: 292.1081, found 292.1102.



1k

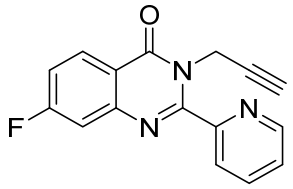
7-methyl-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1k). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1k**. A off-white solid, 0.094 g, 34% yield; Mp: 155-156 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.8 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.93-7.89 (m, 2H), 7.55 (s, 1H), 7.47-7.44 (m, 1H), 7.36 (d, J = 8.0 Hz, 1H), 5.28 (d, J = 2.4 Hz, 2H), 2.51 (s, 3H), 2.02 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 153.4, 152.5, 148.6, 147.0, 145.7, 137.4, 129.2, 127.4, 127.0, 125.0, 124.7, 118.5, 78.5, 71.5, 33.7, 21.9; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O$ $[M + H]^+$: 276.1131, found 276.1156.



1l

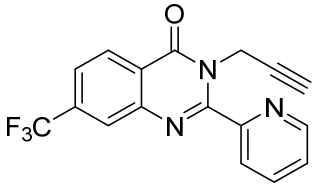
7-chloro-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1l). Purification

by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1l**. A off-white solid, 0.068 g, 23% yield; Mp: 180-181 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.4 Hz, 1H), 8.30 (d, J = 8.8 Hz, 1H), 7.94 (d, J = 4.0 Hz, 2H), 7.75 (s, 1H), 7.50-7.47 (m, 2H), 5.30 (d, J = 2.0 Hz, 2H), 2.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 153.6, 153.0, 148.7, 147.9, 140.8, 137.5, 128.6, 128.2, 127.3, 125.1, 125.0, 119.4, 78.1, 71.8, 33.9; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}ClN_3O$ $[M + H]^+$: 296.0585, found 296.0599.



1m

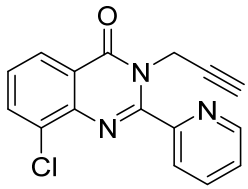
7-fluoro-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1m). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1m**. A off-white solid, 0.084 g, 30% yield; Mp: 177-178 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 4.8 Hz, 1H), 8.40 (dd, J = 8.8, 6.0 Hz, 1H), 7.95-7.92 (m, 2H), 7.50-7.47 (m, 1H), 7.42 (dd, J = 9.6, 2.0 Hz, 1H), 7.28-7.23 (m, 1H), 5.30 (d, J = 2.4 Hz, 2H), 2.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 165.3, 160.8, 153.7, 153.0, 149.1 (d, J = 13.2 Hz), 148.7, 137.5, 130.0 (d, J = 10.2 Hz), 125.1 (d, J = 10.2 Hz), 117.7, 116.5 (d, J = 24.1 Hz), 113.0 (d, J = 21.9 Hz), 78.1, 71.8, 33.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.7; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}FN_3O$ $[M + H]^+$: 280.0881, found 280.0904.



1n

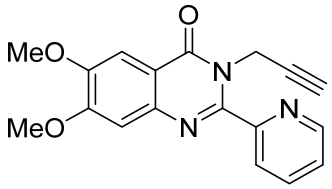
3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)-7-(trifluoromethyl)quinazolin-4(3H)-one (1n). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1n**. A white solid, 0.138 g, 42% yield; Mp: 138-139 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, J = 4.8 Hz, 1H), 8.49 (d, J = 8.0 Hz, 1H), 8.05 (s, 1H), 7.98-7.93 (m,

2H), 7.75 (d, J = 8.4 Hz, 1H), 7.51-7.48 (m, 1H), 5.35 (d, J = 2.4 Hz, 2H), 2.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 153.7, 152.8, 148.7, 146.9, 137.5, 136.7 (q, J = 32.1 Hz), 128.3, 125.4 (q, J = 3.6 Hz), 125.2, 125.1, 124.7 (q, J = 272.0 Hz), 123.6 (q, J = 2.9 Hz), 123.2, 77.9, 72.0, 34.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3; HRMS (ESI) *m/z* calcd for $C_{17}H_{11}F_3N_3O$ $[M + H]^+$: 330.0849, found 330.0869.



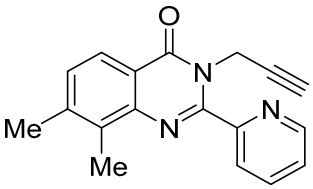
1o

7-chloro-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1o). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1o**. A off-white solid, 0.089 g, 30% yield; Mp: 229-230 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 4.4 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 7.6 Hz, 1H), 7.96-7.72 (m, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.49-7.43 (m, 2H), 5.43 (d, J = 2.0 Hz, 2H), 2.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 153.1, 152.7, 148.3, 143.7, 137.5, 134.9, 132.2, 127.6, 126.0, 125.8, 125.0, 122.5, 78.2, 71.7, 34.0; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}ClN_3O$ $[M + H]^+$: 296.0585, found 296.0610.



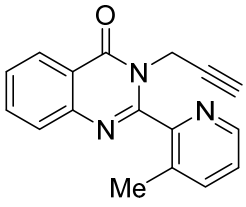
1p

6,7-dimethoxy-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1p). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1p**. A off-white solid, 0.080 g, 25% yield; Mp: 216-217 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 3.2 Hz, 1H), 7.92 (s, 2H), 7.68 (s, 1H), 7.47-7.45 (m, 1H), 7.17 (s, 1H), 5.29 (s, 2H), 4.02 (s, 3H), 3.99 (s, 3H), 2.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 155.1, 153.3, 151.4, 149.7, 148.7, 143.1, 137.4, 124.9, 124.6, 114.4, 108.1, 106.0, 78.5, 71.5, 56.4, 56.3, 33.8; HRMS (ESI) *m/z* calcd for $C_{18}H_{16}N_3O_3$ $[M + H]^+$: 322.1186, found 322.1214.



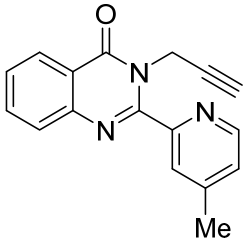
1q

7,8-dimethyl-3-(prop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1q). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1q**. A off-white solid, 0.147 g, 51% yield; Mp: 130-131 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.4 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.93-7.90 (m, 1H), 7.47-7.43 (m, 1H), 7.35 (d, J = 8.0 Hz, 1H), 5.39 (d, J = 1.6 Hz, 2H), 2.57 (s, 3H), 2.45 (s, 3H), 1.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 153.9, 150.7, 148.2, 145.2, 143.6, 137.2, 134.3, 129.5, 125.4, 124.5, 124.0, 118.9, 78.8, 71.3, 33.5, 20.9, 13.0; HRMS (ESI) *m/z* calcd for $C_{18}H_{16}N_3O$ $[M + H]^+$: 290.1288, found 290.1311.



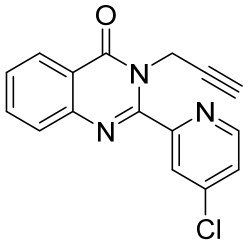
1r

2-(3-methylpyridin-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (1r). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1r**. A white solid, 0.061 g, 22% yield; Mp: 186-187 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 4.0 Hz, 1H), 8.39 (d, J = 7.6 Hz, 1H), 7.81-7.77 (m, 1H), 7.74-7.71 (m, 2H), 7.57-7.53 (m, 1H), 7.39 (dd, J = 7.6, 4.8 Hz, 1H), 4.91 (s, 2H), 2.43 (s, 3H), 2.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 152.2, 151.8, 147.0, 146.7, 139.3, 134.6, 133.3, 127.6, 127.1, 124.7, 121.1, 77.6, 71.5, 33.4, 18.7; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O$ $[M + H]^+$: 276.1131, found 276.1150.



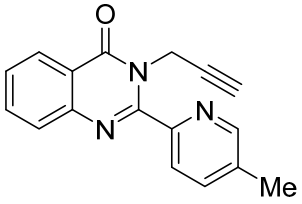
1s

2-(4-methylpyridin-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (1s). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1s**. A off-white solid, 0.149 g, 54% yield; Mp: 160-161 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 4.8 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 7.81-7.77 (m, 3H), 7.56-7.52 (m, 1H), 7.29 (d, J = 4.4 Hz, 1H), 5.28 (d, J = 2.0 Hz, 2H), 2.49 (s, 3H), 2.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 153.0, 152.8, 148.9, 148.5, 147.0, 134.6, 127.7, 127.6, 127.1, 125.8, 125.7, 121.0, 78.4, 71.5, 33.9, 21.2; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O$ $[M + H]^+$: 276.1131, found 276.1157.



1t

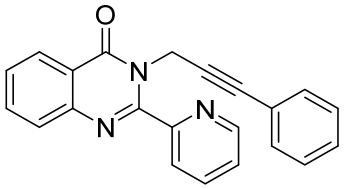
2-(4-chloropyridin-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (1t). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1t**. A white solid, 0.100 g, 34% yield; Mp: 190-191 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 5.2 Hz, 1H), 8.37 (d, J = 7.6 Hz, 1H), 8.00 (s, 1H), 7.82-7.75 (m, 2H), 7.57-7.54 (m, 1H), 7.48 (d, J = 4.0 Hz, 1H), 5.34 (s, 2H), 2.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 154.5, 151.3, 149.4, 146.7, 145.4, 134.7, 127.9, 127.7, 127.2, 125.6, 125.1, 121.0, 78.2, 71.9, 33.6; HRMS (ESI) *m/z* calcd for $C_{16}H_{11}ClN_3O$ $[M + H]^+$: 296.0585, found 296.0605.



1u

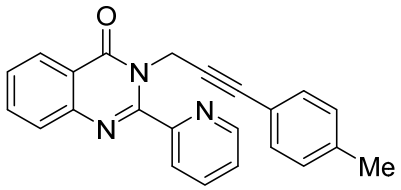
2-(5-methylpyridin-2-yl)-3-(prop-2-yn-1-yl)quinazolin-4(3H)-one (1u). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1u**. A yellow solid, 0.160 g, 58% yield; Mp: 156-157 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.36 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.79-7.71 (m, 3H), 7.54-7.50 (d, J = 4.4 Hz, 1H), 5.30 (d, J = 2.0 Hz, 2H), 2.45 (s, 3H), 2.03 (s, 1H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 161.6, 152.6, 150.6, 149.0, 147.0, 137.8, 134.9, 134.5, 127.7, 127.5, 127.1, 124.6, 120.9, 78.5, 71.5, 33.8, 18.5; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O$ [M + H]$^+$: 276.1131, found 276.1147.



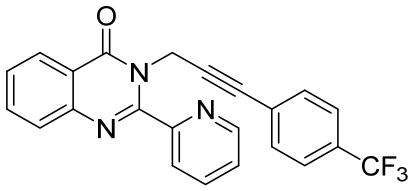
1v

3-(3-phenylprop-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1v). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **2v**. A yellow solid, 0.179 g, 53% yield; Mp: 105-106 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 4.4 Hz, 1H), 8.40 (d, J = 8.0 Hz, 1H), 7.96-7.90 (m, 2H), 7.81-7.76 (m, 2H), 7.57-7.53 (m, 1H), 7.49-7.46 (m, 1H), 7.25-7.19 (m, 3H), 7.15 (d, J = 6.8 Hz, 2H), 5.57 (s, 2H), 1.59 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 153.6, 152.8, 148.7, 147.0, 137.3, 134.5, 131.7, 128.4, 128.1, 127.7, 127.6, 127.2, 124.9, 124.7, 122.2, 121.0, 83.9, 83.3, 34.1; HRMS (ESI) *m/z* calcd for $C_{22}H_{15}N_3NaO$ [M + Na]$^+$: 360.1107, found 360.1122.



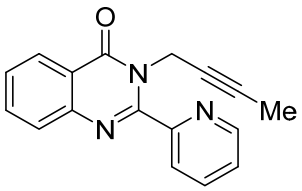
1w

2-(pyridin-2-yl)-3-(3-(p-tolyl)prop-2-yn-1-yl)quinazolin-4(3H)-one (1w). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1w**. A yellow solid, 0.176 g, 50% yield; Mp: 145-146 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 4.8 Hz, 1H), 8.39 (d, J = 8.0 Hz, 1H), 7.94-7.89 (m, 2H), 7.78-7.75 (m, 2H),7.56-7.52 (m, 1H), 7.48-7.45 (m, 1H), 7.04-7.00 (m, 4H), 5.55 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 153.7, 152.8, 148.7, 147.0, 138.6, 137.2, 134.5, 131.6, 128.9, 127.7, 127.5, 127.2, 124.9, 124.6, 121.0, 119.1, 83.9, 83.1, 34.1, 21.4; HRMS (ESI) *m/z* calcd for $C_{23}H_{18}N_3O$ [M + H]$^+$: 352.1444, found 352.1461.



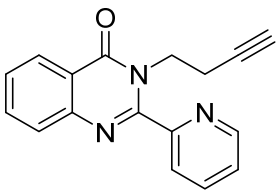
1x

2-(pyridin-2-yl)-3-(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)quinazolin-4(3H)-one (1x). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1x**. A yellow solid, 0.137 g, 32% yield; Mp: 164-165 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 4.4 Hz, 1H), 8.40 (d, J = 7.6 Hz, 1H), 7.98-7.91 (m, 2H), 7.80-7.77 (m, 2H), 7.58-7.54 (m, 1H), 7.48 (d, J = 8.0 Hz, 3H), 7.27 (d, J = 7.6 Hz, 2H), 5.61 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 153.5, 152.5, 149.5 (q, J = 255.2 Hz), 148.7, 137.4 (q, J = 25.5 Hz), 137.3, 134.7, 131.9, 130.6 (q, J = 32.8 Hz), 127.7, 127.6, 127.2, 126.0, 125.1 (q, J = 3.6 Hz), 124.8, 122.4, 120.9, 86.5, 81.9, 34.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.9; HRMS (ESI) *m/z* calcd for $C_{23}H_{14}F_3N_3NaO$ $[M + Na]^+$: 428.0981, found 428.0997.



1y

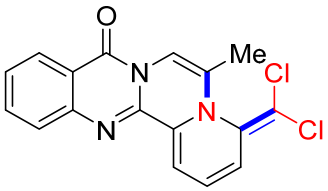
3-(but-2-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1y). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1y**. A grey solid, 0.154 g, 56% yield; Mp: 160-161 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 4.4 Hz, 1H), 8.37 (d, J = 7.6 Hz, 1H), 7.94-7.89 (m, 2H), 7.80-7.74 (m, 2H),7.55-7.49 (m, 1H), 7.47-7.44 (m, 1H), 5.18 (d, J = 2.0 Hz, 2H), 1.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 153.5, 152.9, 148.7, 147.0, 137.2, 134.4, 127.6, 127.4, 127.1, 124.7, 124.6, 121.1, 79.6, 73.6, 34.2; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O$ $[M + H]^+$: 276.1131, found 276.1145.



1z

3-(but-3-yn-1-yl)-2-(pyridin-2-yl)quinazolin-4(3H)-one (1z). Purification by flash column chromatography (2/1, ethyl acetate/petroleum ether) to afford **1z**. A off-white solid, 0.248 g, 90% yield; Mp: 138-139 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 4.4 Hz, 1H), 8.34 (d, J = 8.4 Hz, 1H), 7.93-7.90 (m, 2H), 7.79-7.73 (m, 2H), 7.54-7.50 (m, 1H), 7.46-7.45 (m, 1H), 4.37 (t, J = 7.2 Hz, 2H), 2.80-2.77 (m, 2H), 1.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 153.7, 153.5, 148.6, 146.9, 137.4, 134.4, 127.5, 127.4, 126.8, 125.1, 124.7, 120.9, 80.6, 70.2, 44.3, 18.4; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}N_3O$ $[M + H]^+$: 276.1131, found 276.1128.

8. X-ray structures for compound 3a



3a

X-ray of **3a**

Figure S1: ORTEP diagram of **3a** at 50% ellipsoid probability

The preparation of crystal of **3a**: compound **3a** (30 mg) was dissolved in DCM (5 mL) at room temperature. n-Hexane (1.0 mL) was dropped carefully to the mixture. Then, the flask was capped with thin film. Finally, a needle crystal was obtained for 4 days.

Table S1. Crystal data and structure refinement details for compound **3a**.

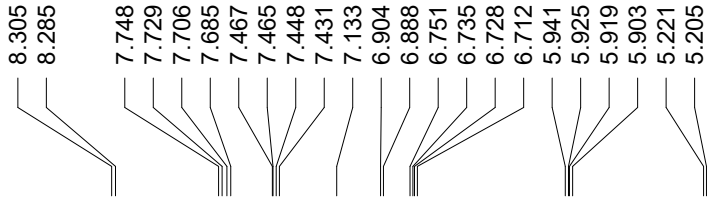
Empirical formula	$C_{17}H_{11}Cl_2N_3O$
Formula weight (*M*)	344.19
Crystal system	Monoclinic
Space group	P 1 21/c 1

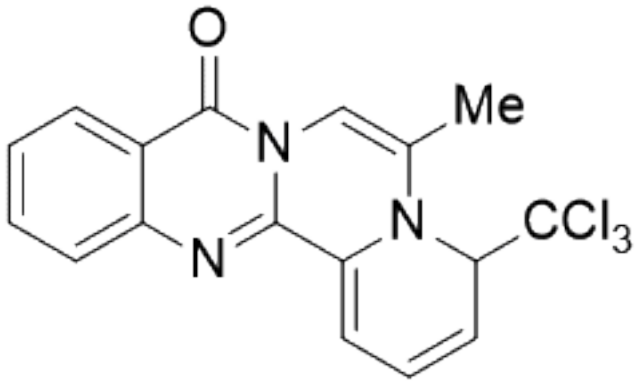
a/Å	14.9897 (4)
b/Å	4.88490 (10)
c/Å	21.3648 (5)
α/°	90
β/°	107.901 (3)
γ/°	90
V/ Å^3	1488.66 (7)
Z	4
Dc (Mg cm^{-3})	1.536
F (000)	704
2θ range for data collection (°)	3.098 to 77.464
Reflections collected	9563
Independent reflections	2880 [R(int) = 0.0376]
Goodness-of-fit on F^2	1.061
Final R indices [I>2sigma(I)]	R_1 = 0.0365, ωR_2 = 0.0964
R indices (all data)	R_1 = 0.0464, ωR_2 = 0.1003

9. References

[1] Kong, X.-F.; Zhan, F.; He, G.-X.; Pan, C.-X.; Gu, C.-X.; Lu, K.; Mo, D.-L.; Su, G.-F. *J. Org. Chem.* **2018**, *83*, 2006.

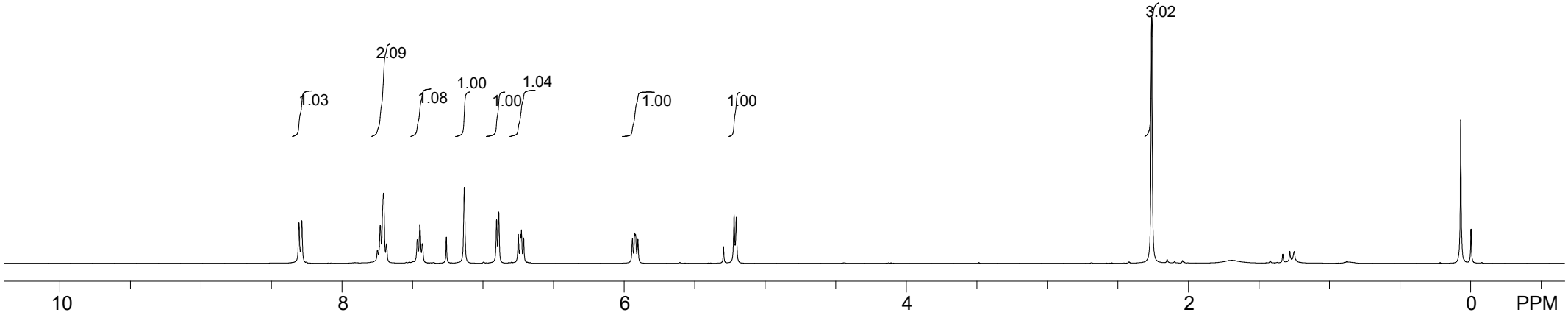
10. NMR spectra for compounds 2, 3a, 4a, 5a, 6, 7 and 1

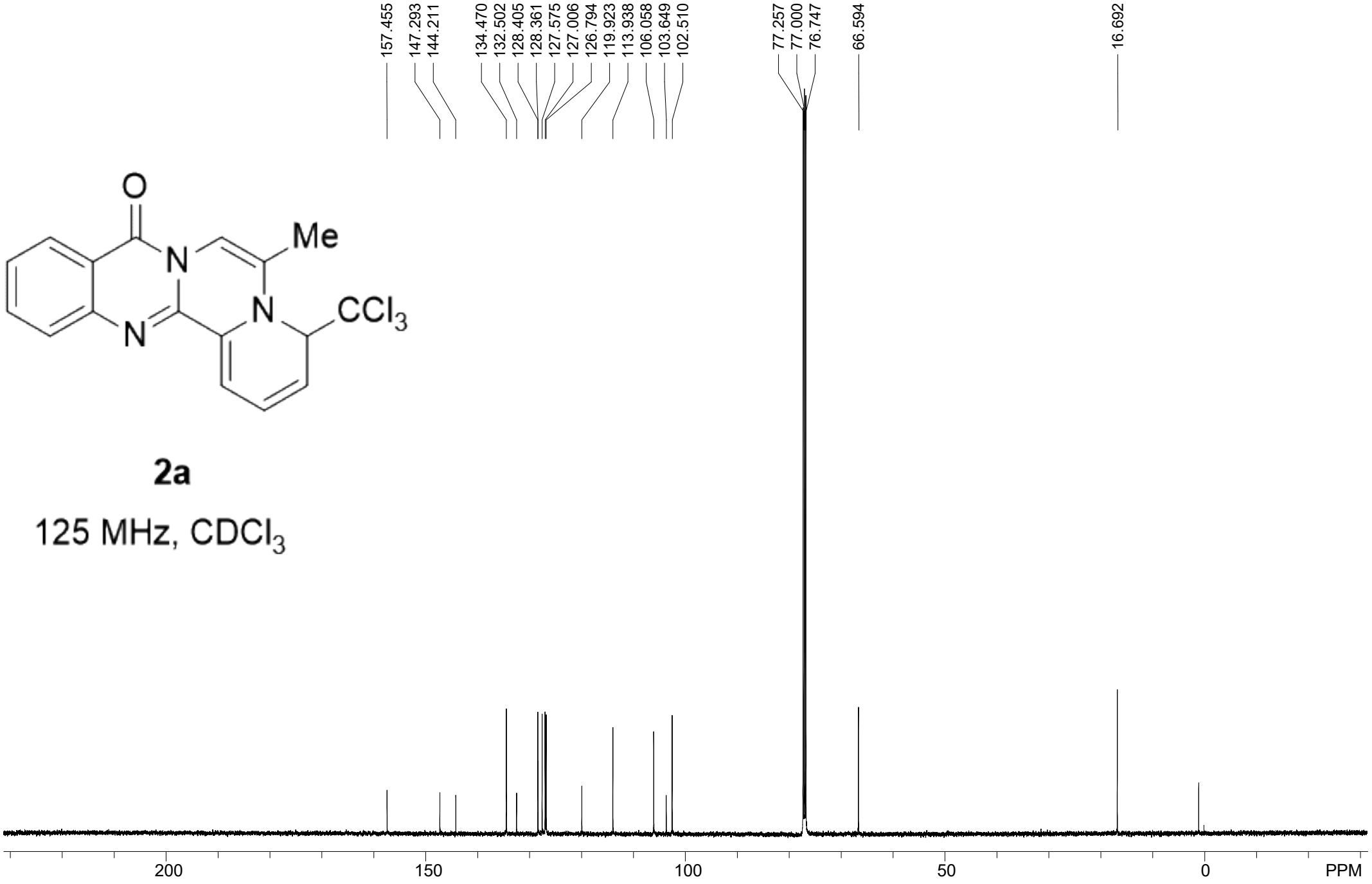




2a

400 MHz, $CDCl_3$

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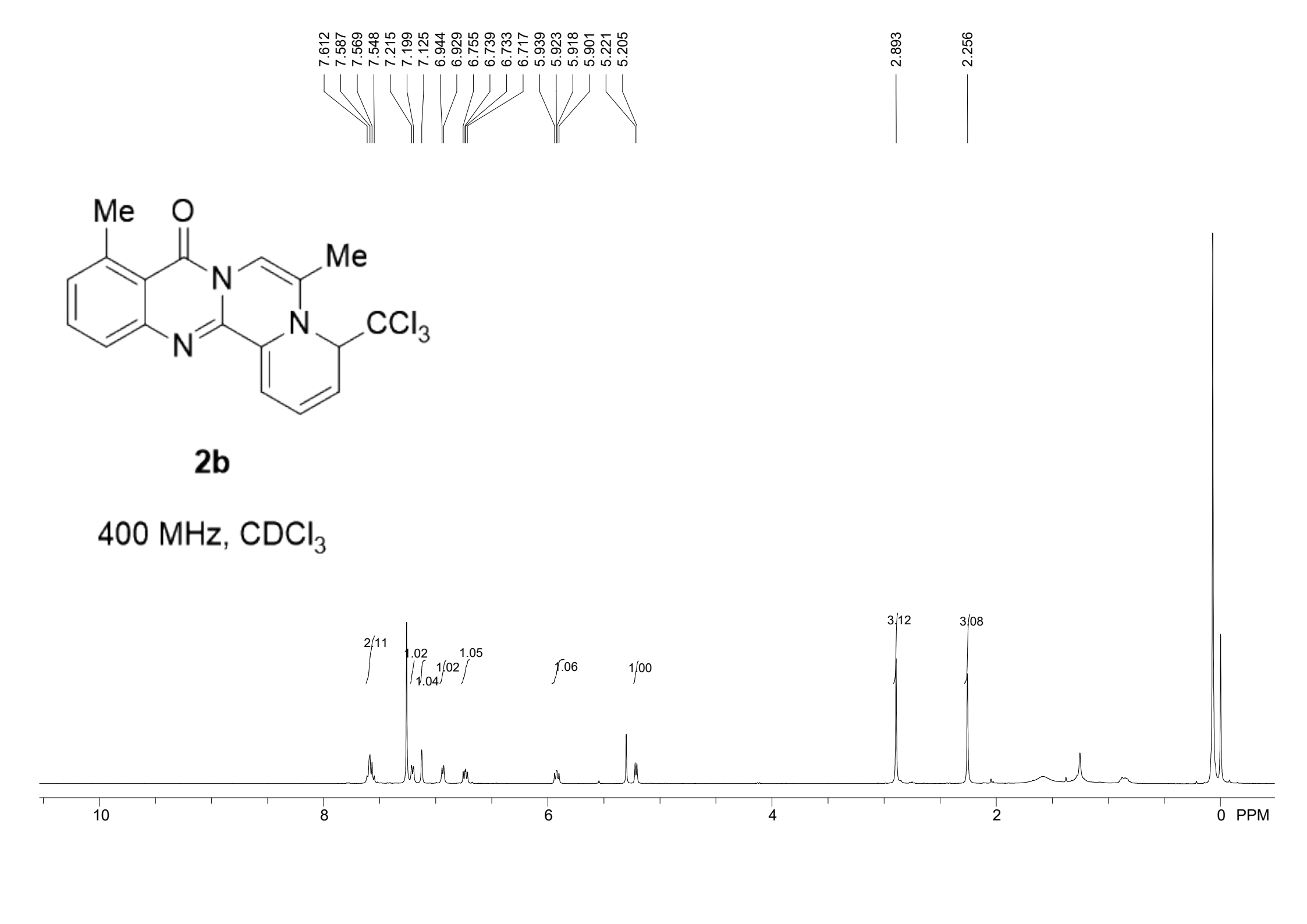
147.293
144.211
134.470
132.502
128.405
128.361
127.575
127.006
126.794
119.923
113.938
106.058
103.649
102.510
77.257
77.000
76.747
66.594
16.692
O
N
Me
N
N
CCl3
2a
125 MHz, CDCl3
200
150
100
50
0
PPM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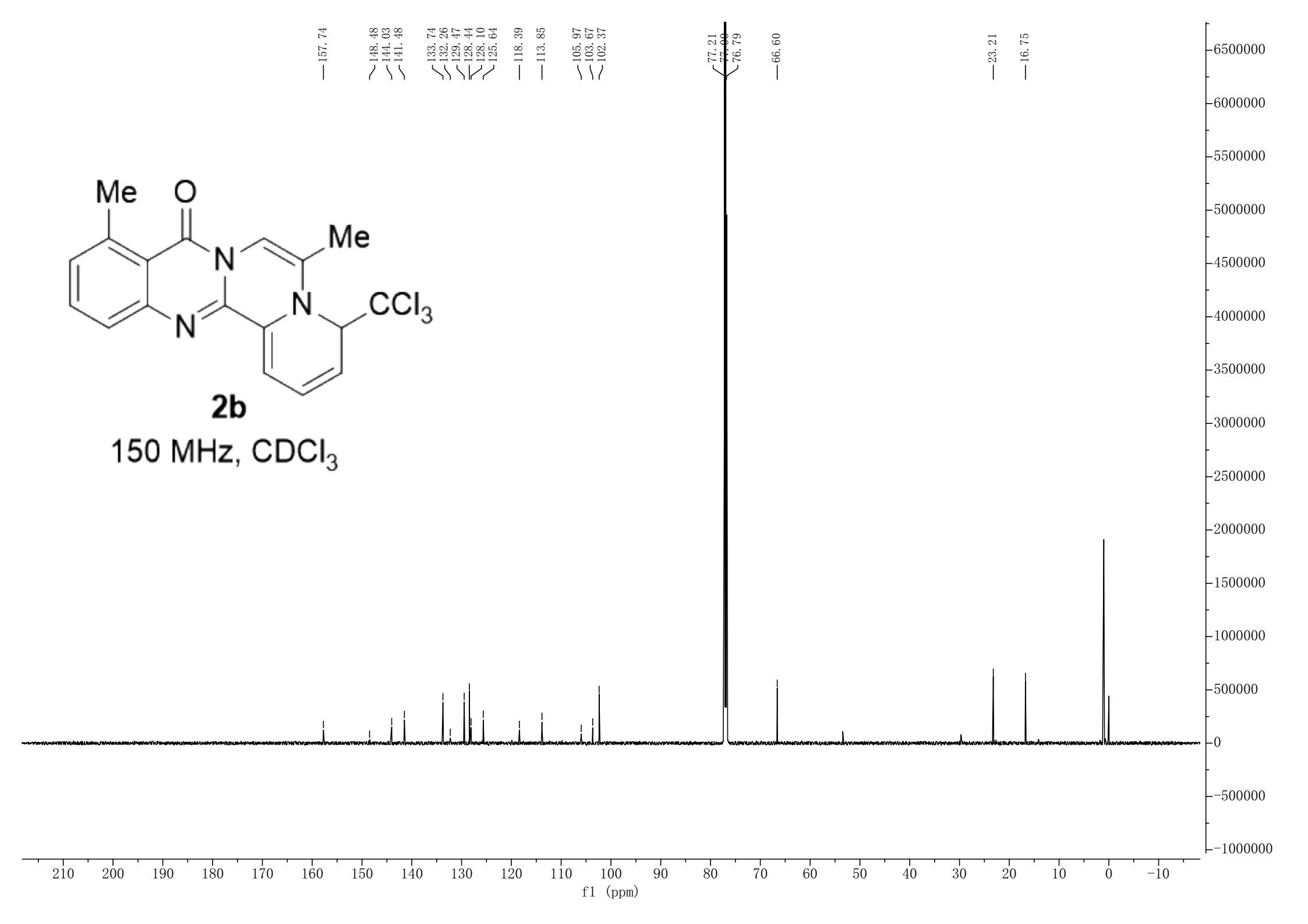
7.587
7.569
7.548
7.215
7.199
7.125
6.944
6.929
6.755
6.739
6.733
6.717
5.939
5.923
5.918
5.901
5.221
5.205
2.893
2.256
Me
O
Me
N
N
N
CCl3
2b
400 MHz, CDCl3
2.11
1.02
1.04
1.02
1.05
1.06
1.00
3.12
3.08
10
8
6
4
2
0
PPM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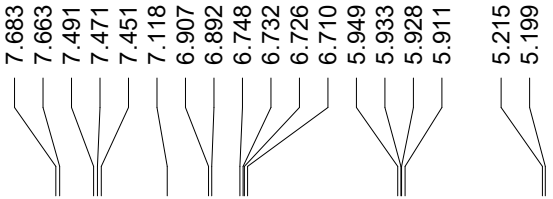
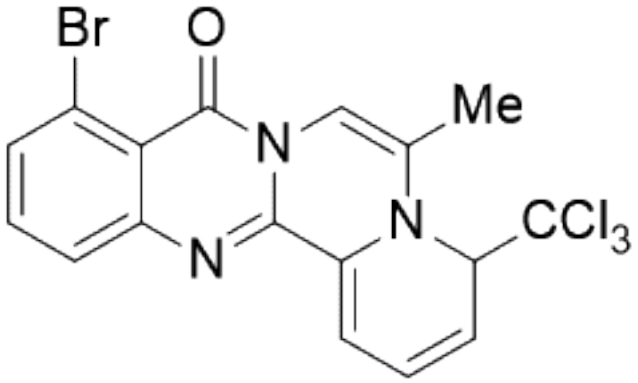
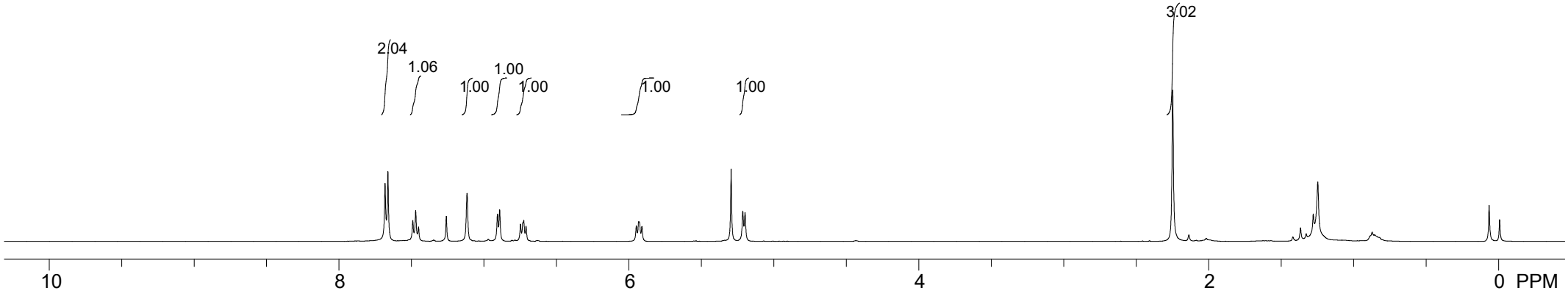
144.03
141.48
133.74
132.26
129.47
128.44
128.10
125.64
118.39
113.85
105.97
103.67
102.37
77.21
77.00
76.79
66.60
23.21
16.75
Me
O
Me
N
N
N
CCl3
2b
150 MHz, CDCl3
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
-1000000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

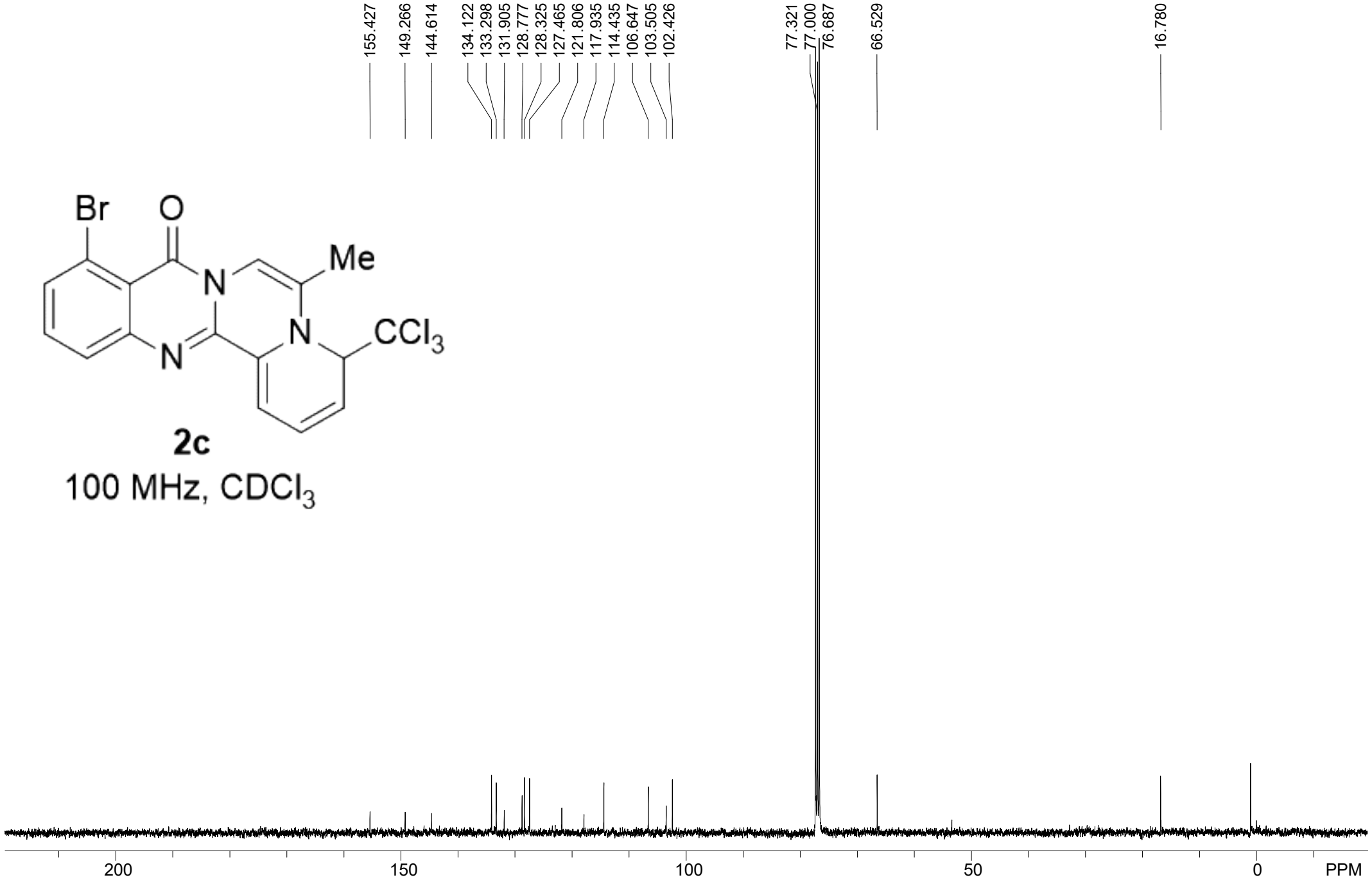




2c

400 MHz, $CDCl_3$

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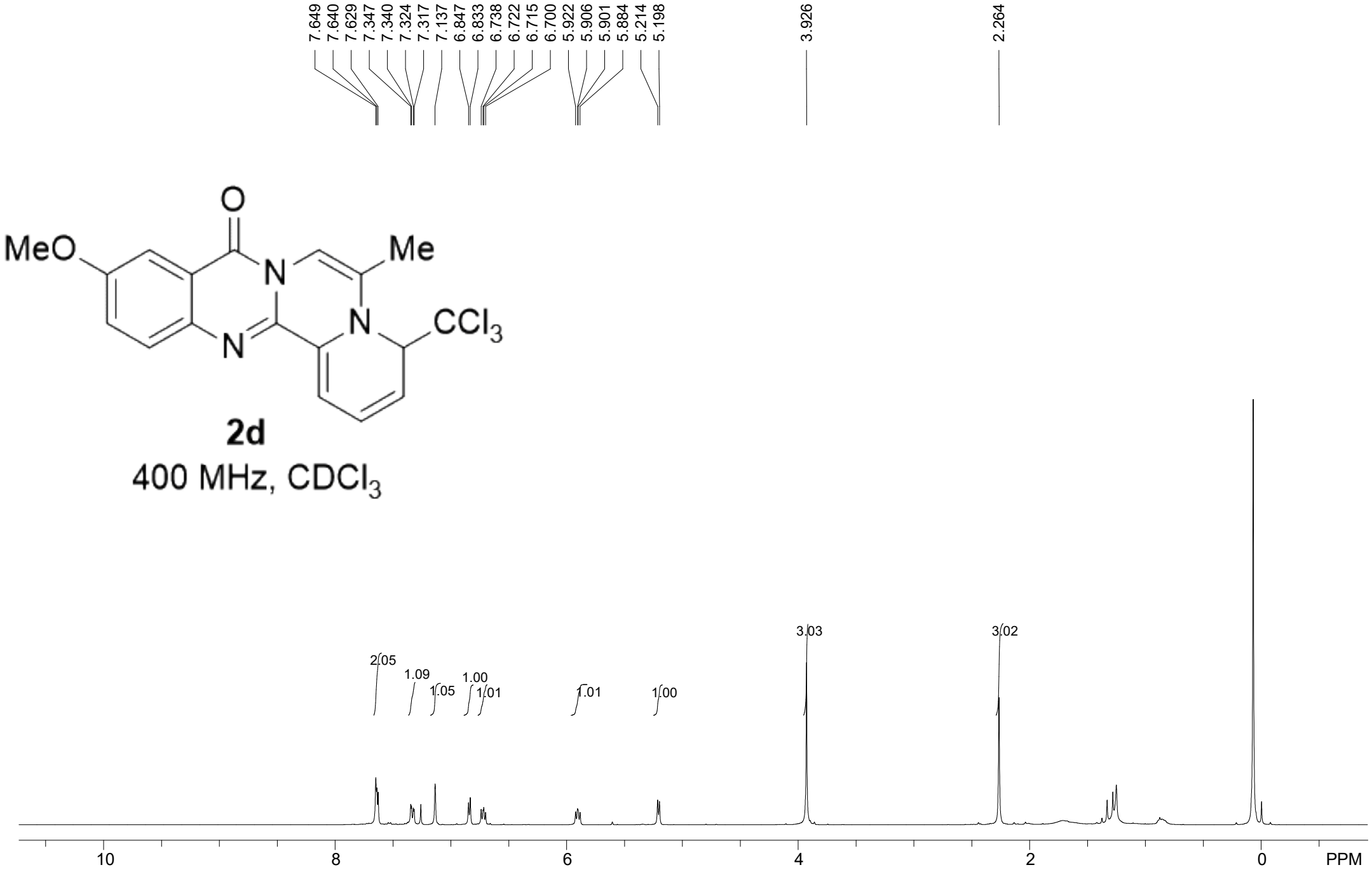
149.266
144.614
134.122
133.298
131.905
128.777
128.325
127.465
121.806
117.935
114.435
106.647
103.505
102.426
77.321
77.000
76.687
66.529
16.780
Br
O
N
Me
N
CCl3
N
2c
100 MHz, CDCl3
200
150
100
50
0
PPM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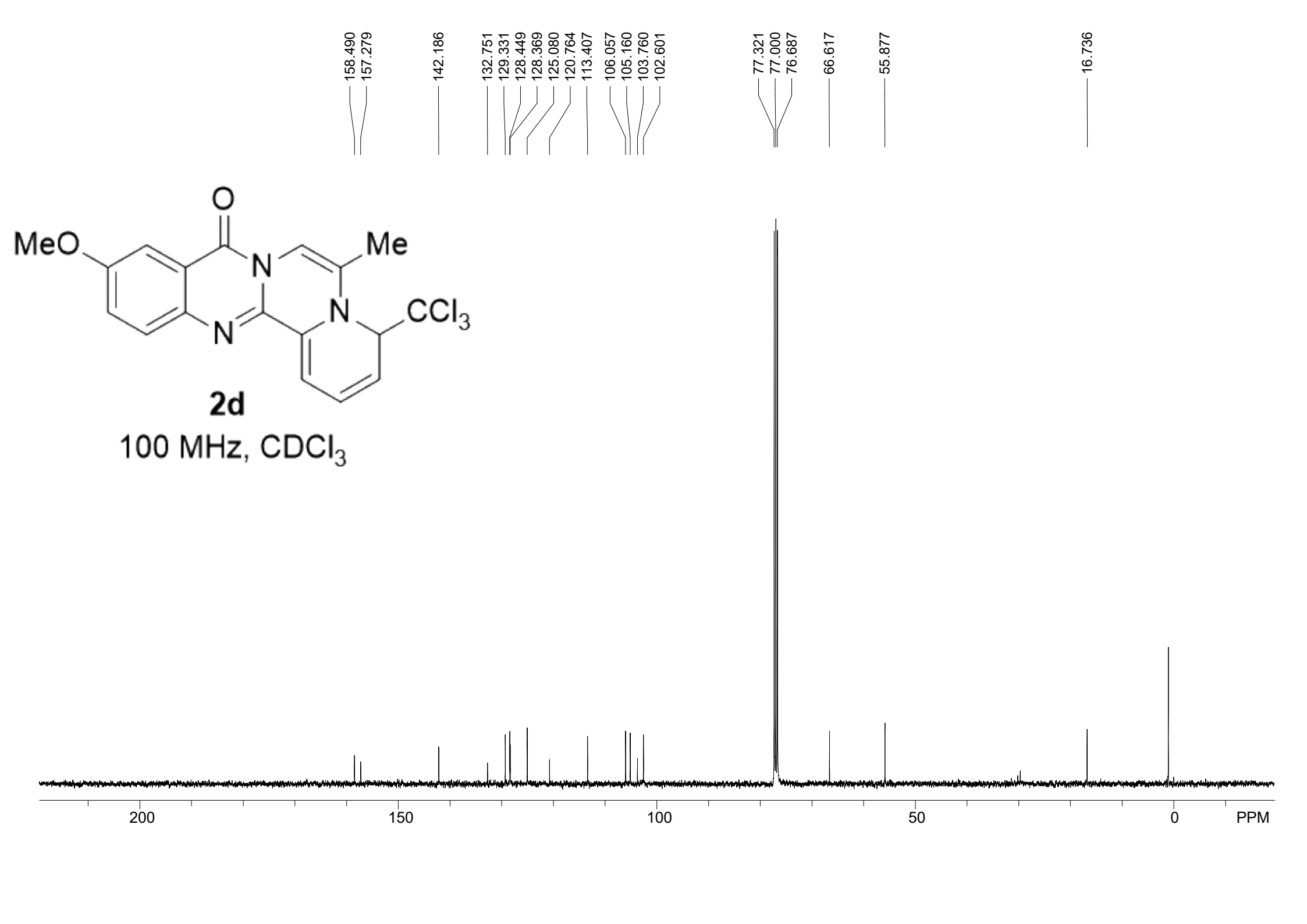
7.640
7.629
7.347
7.340
7.324
7.317
7.137
6.847
6.833
6.738
6.722
6.715
6.700
5.922
5.906
5.901
5.884
5.214
5.198
3.926
2.264
MeO
O
N
Me
N
N
CCl3
2d
400 MHz, CDCl3
2.05
1.09
1.05
1.00
1.01
1.01
1.00
3.03
3.02
10
8
6
4
2
0
PPM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132.751
129.331
128.449
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125.080
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113.407
106.057
105.160
103.760
102.601
77.321
77.000
76.687
66.617
55.877
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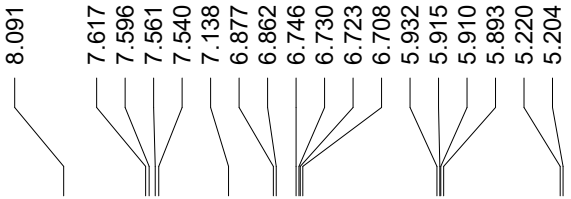
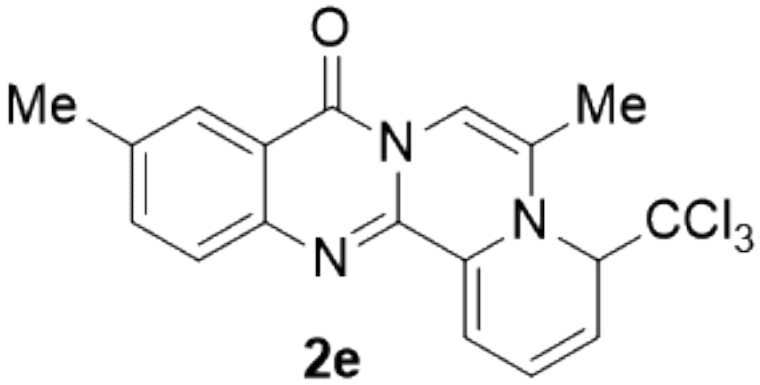
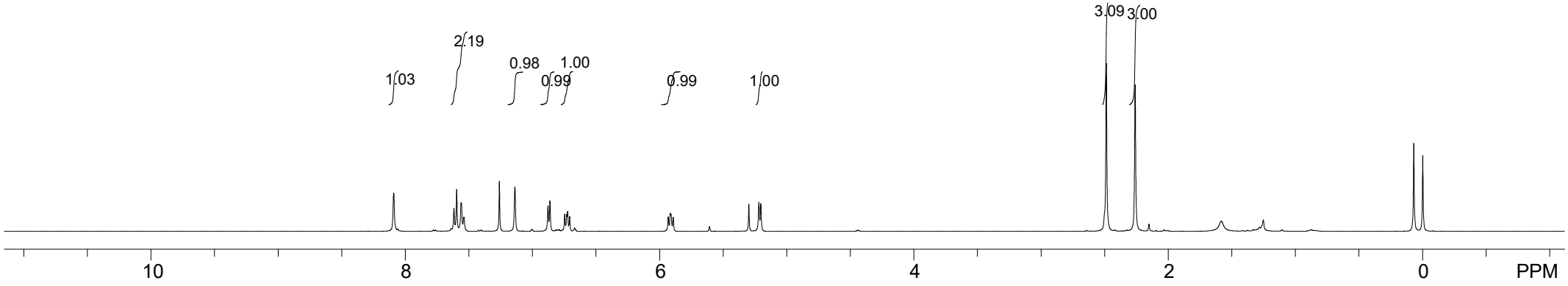
Me
N
N
N
CCl3
2d
100 MHz, CDCl3
200
150
100
50
0
PPM

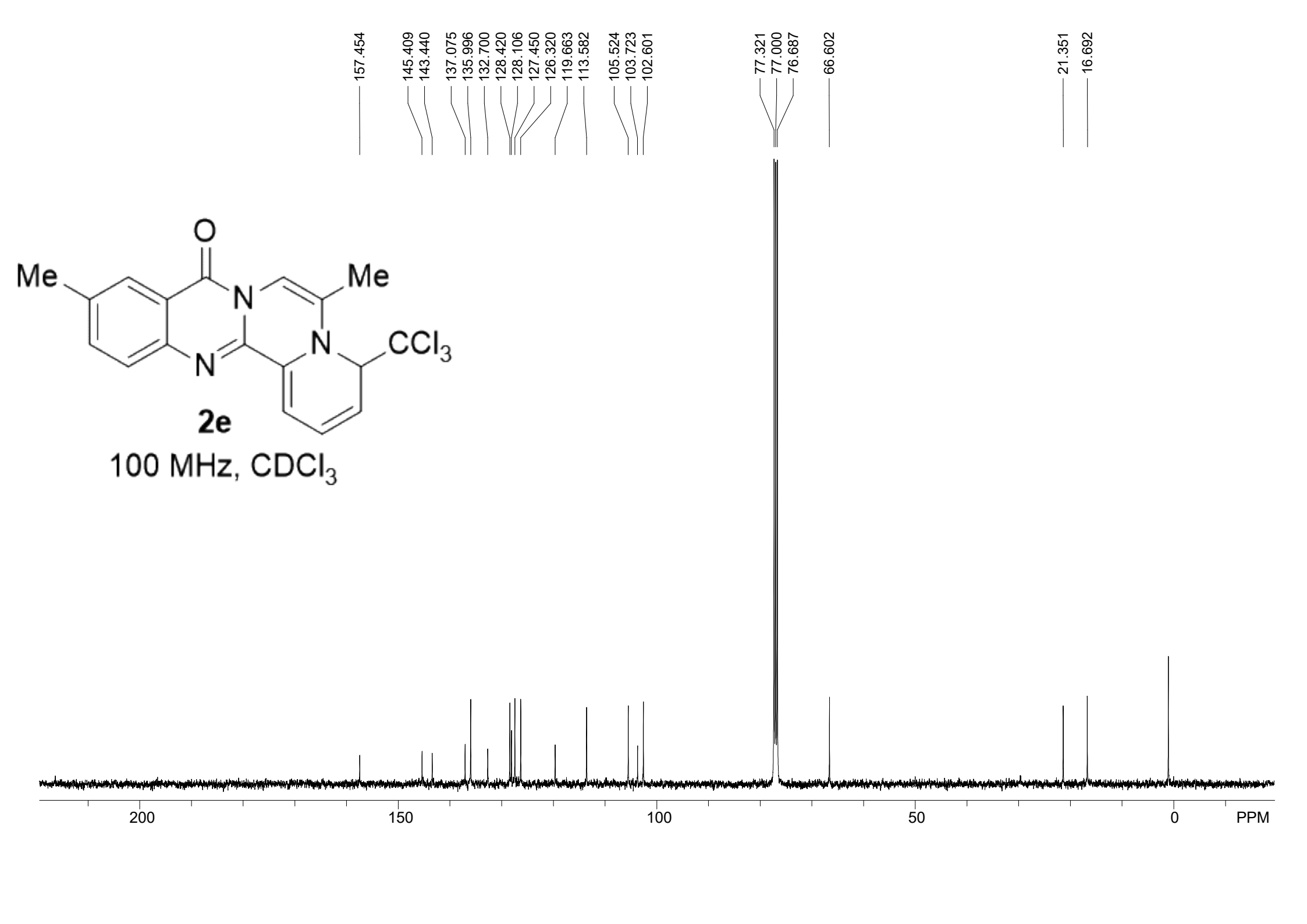




2e

400 MHz, $CDCl_3$

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128.106
127.450
126.320
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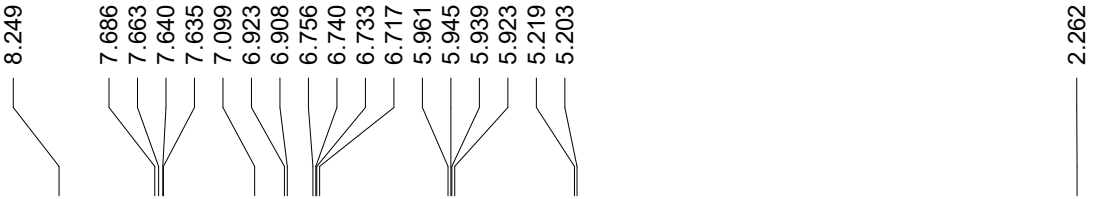
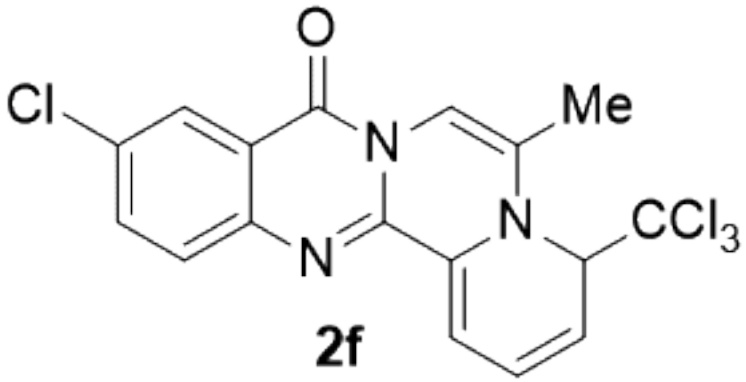
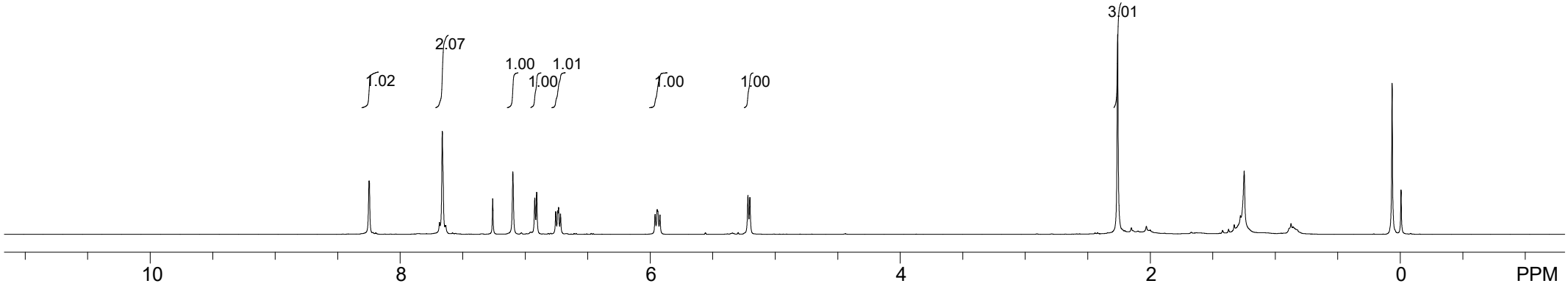
103.723
102.601
77.321
77.000
76.687
66.602
21.351
16.692
O
Me
Me
N
N
N
CCl3
2e
100 MHz, CDCl3
200
150
100
50
0
PPM

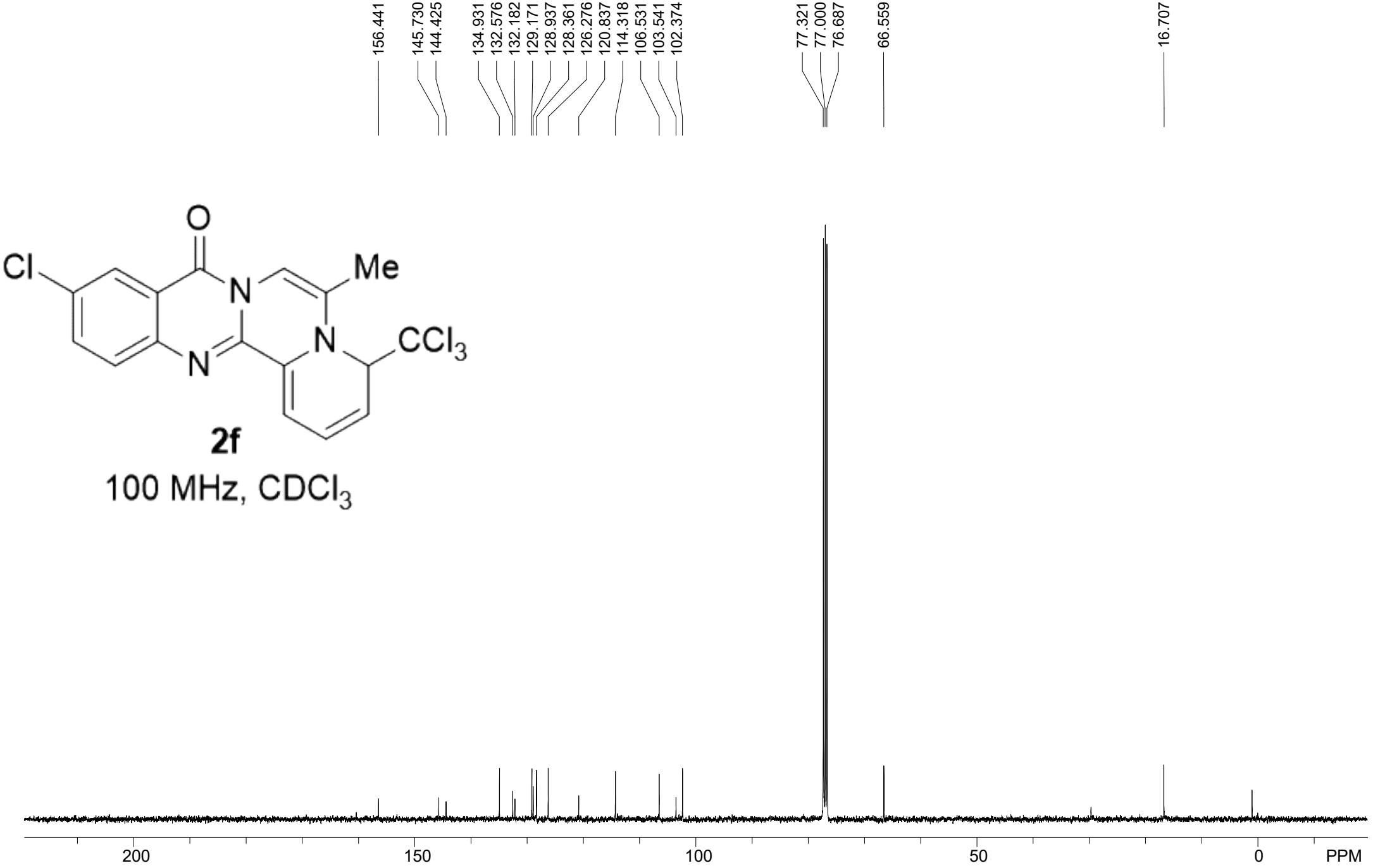




2f

400 MHz, $CDCl_3$

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132.182
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128.937
128.361
126.276
120.837
114.318
106.531
103.541
102.374
77.321
77.000
76.687
66.559
16.707
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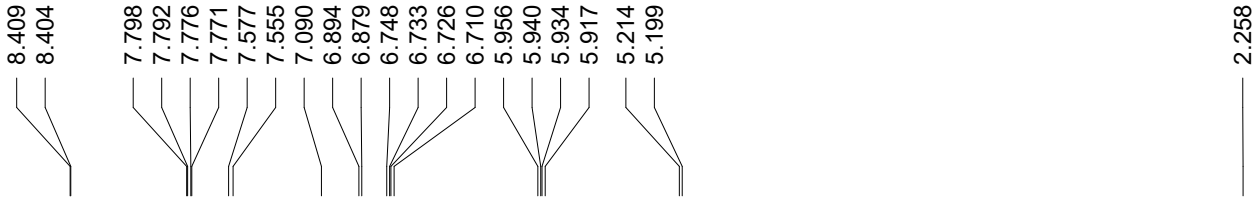
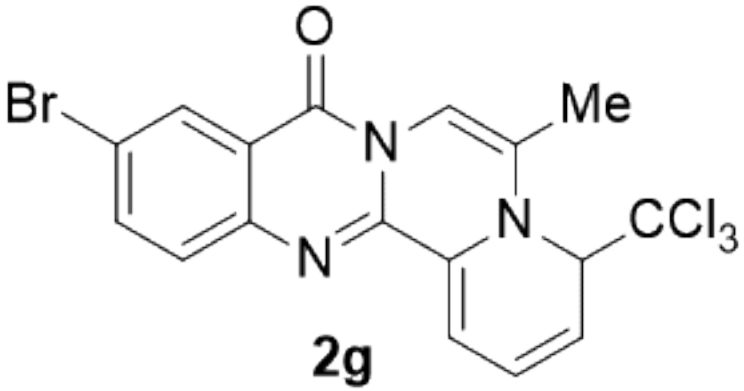
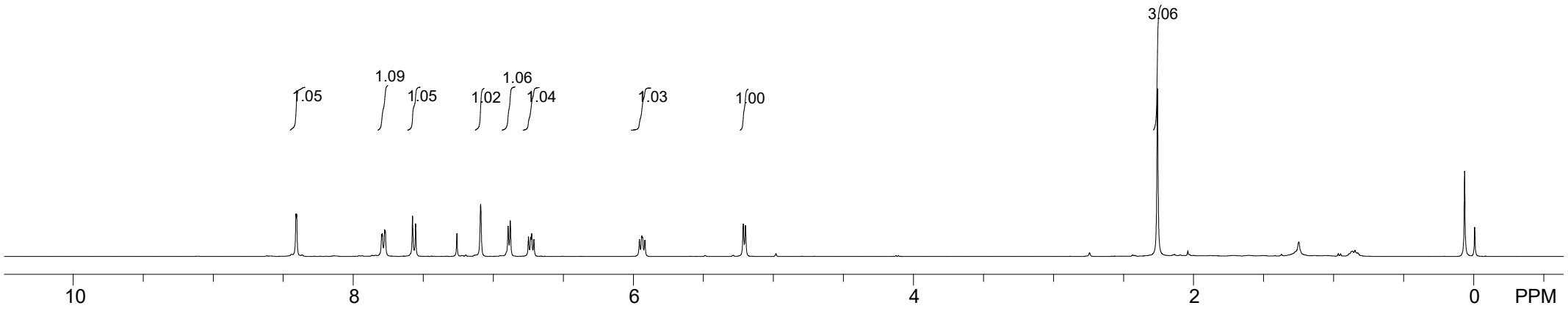
Cl
N
Me
N
N
CCl3
2f
100 MHz, CDCl3
200
150
100
50
0
PPM

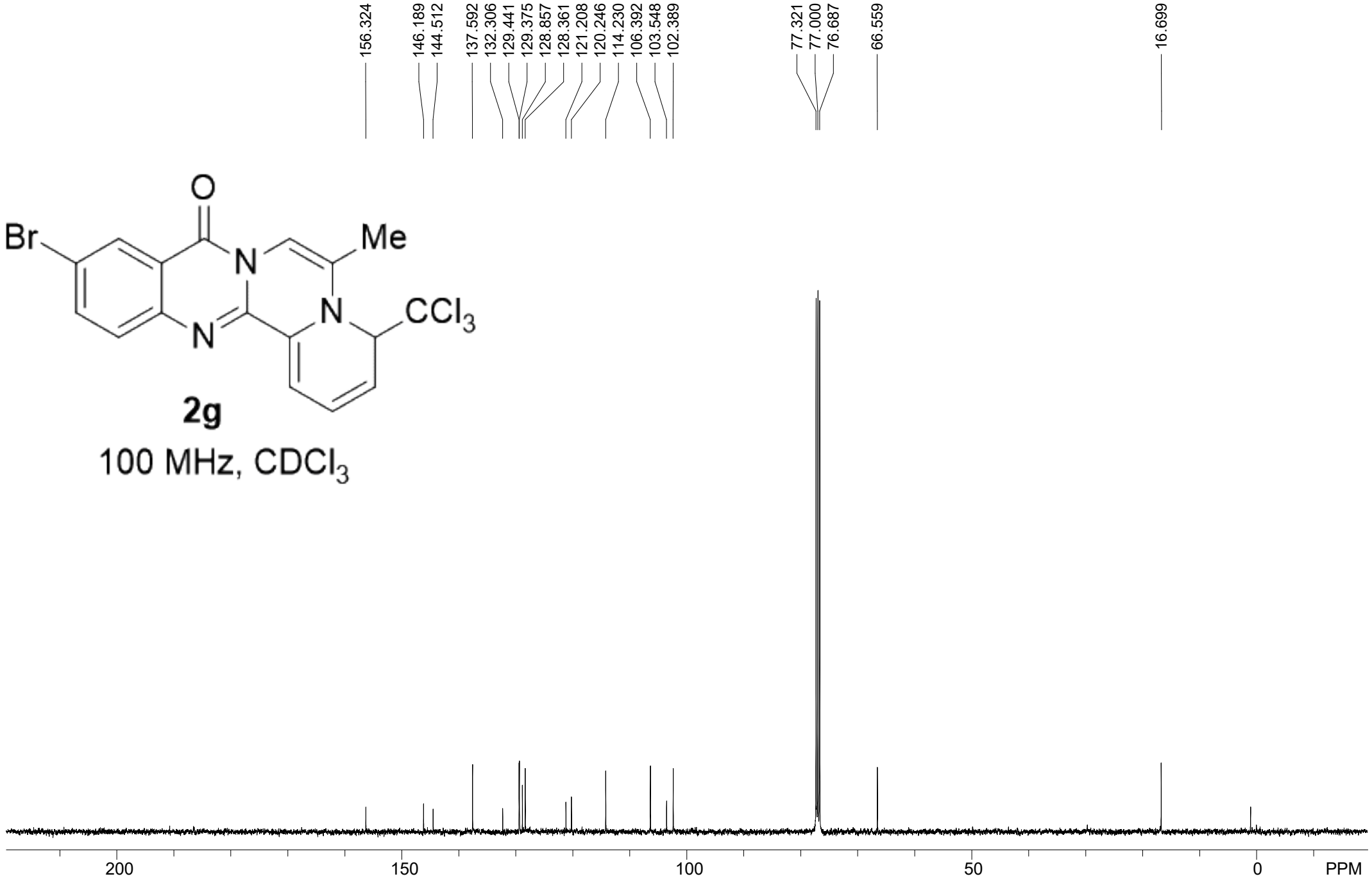




2g

400 MHz, $CDCl_3$

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132.306
129.441
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128.857
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121.208
120.246
114.230
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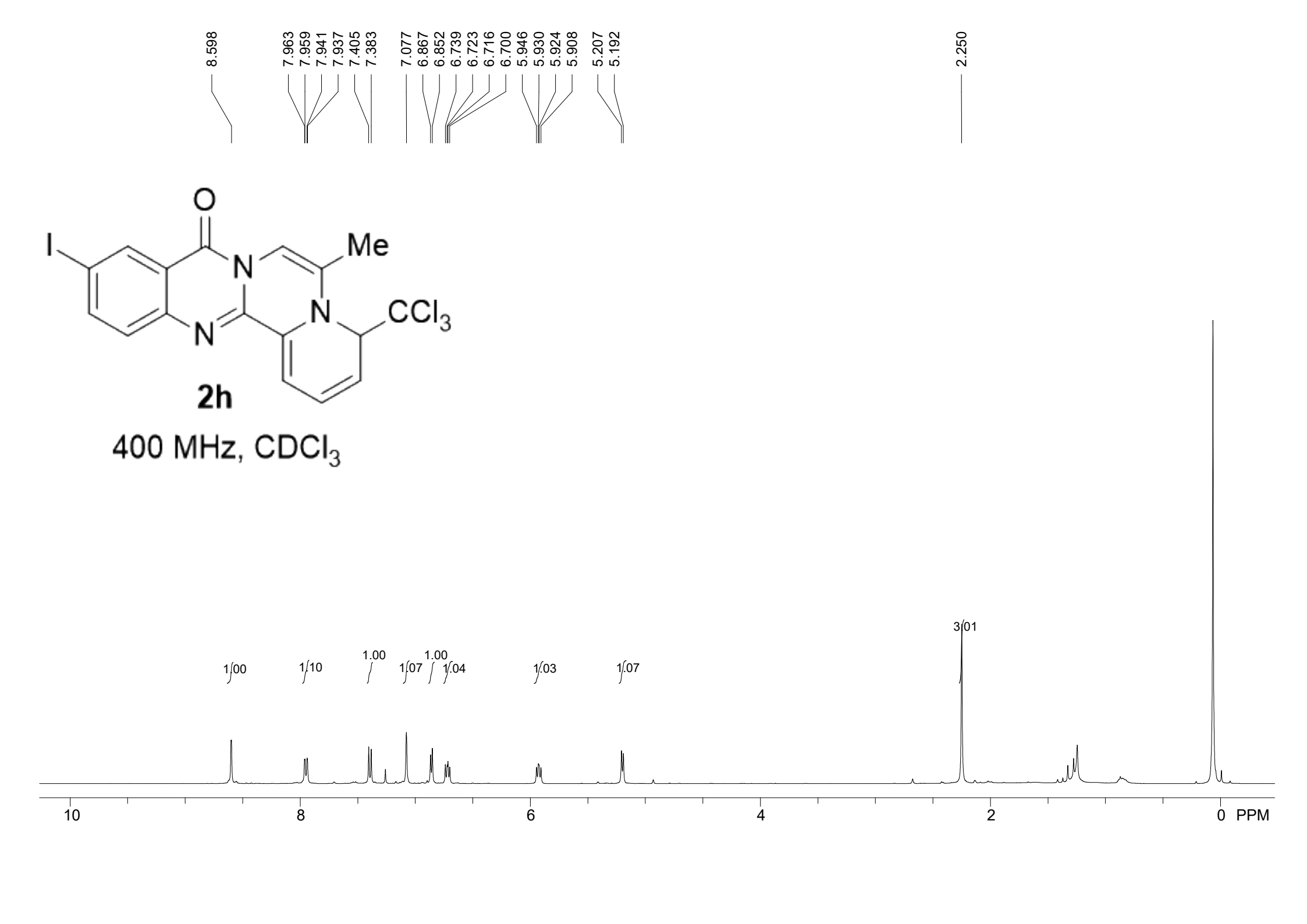
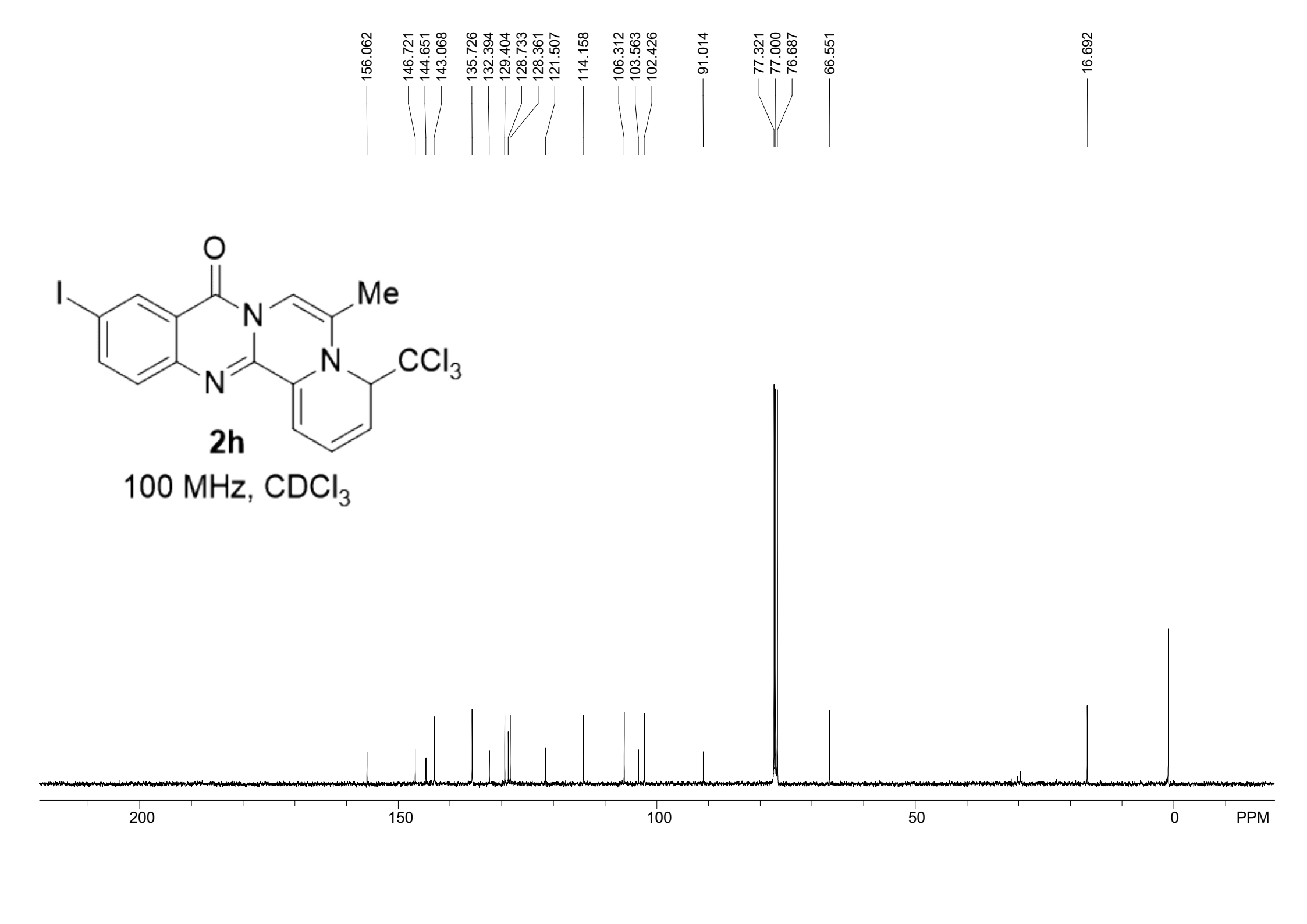
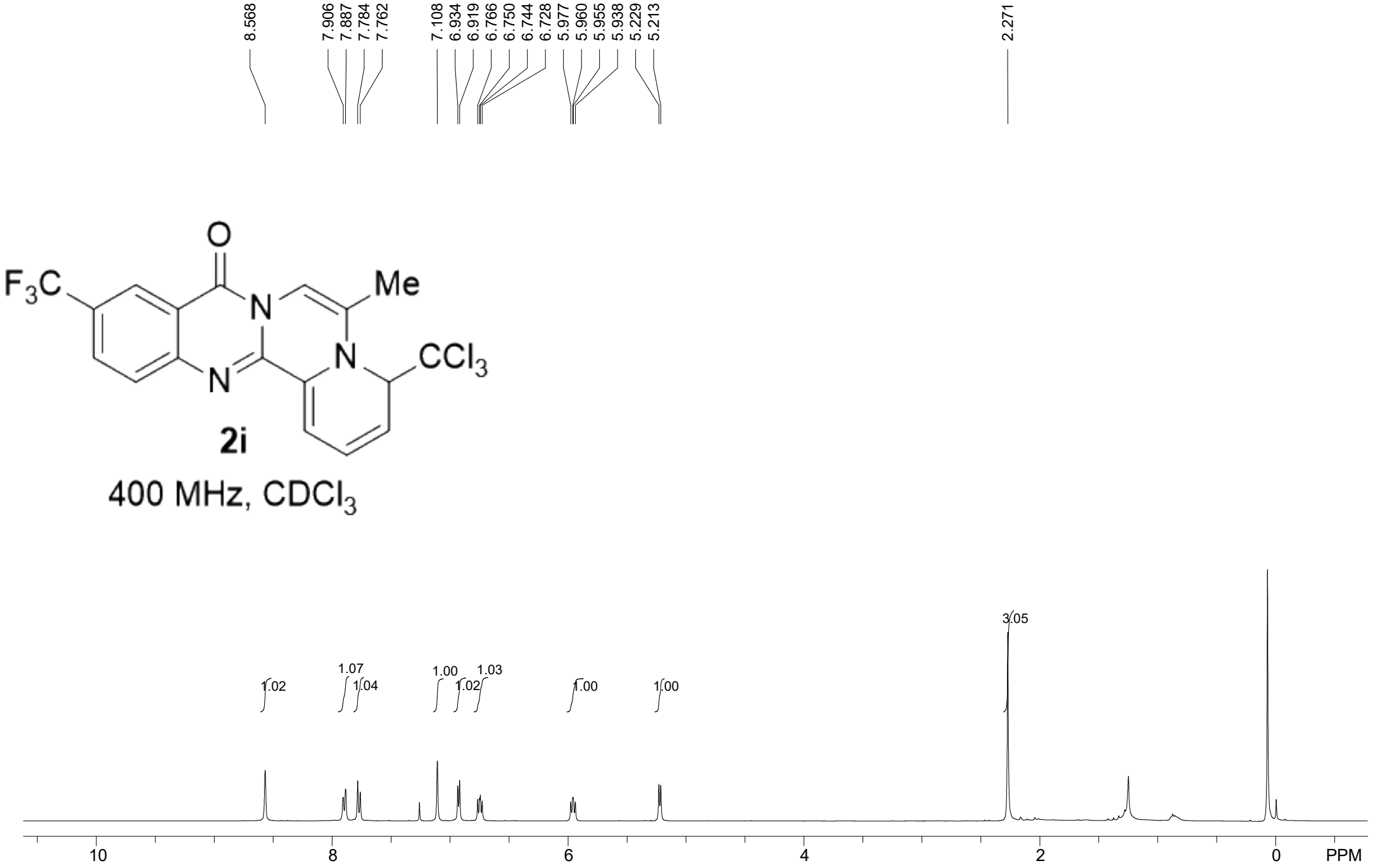
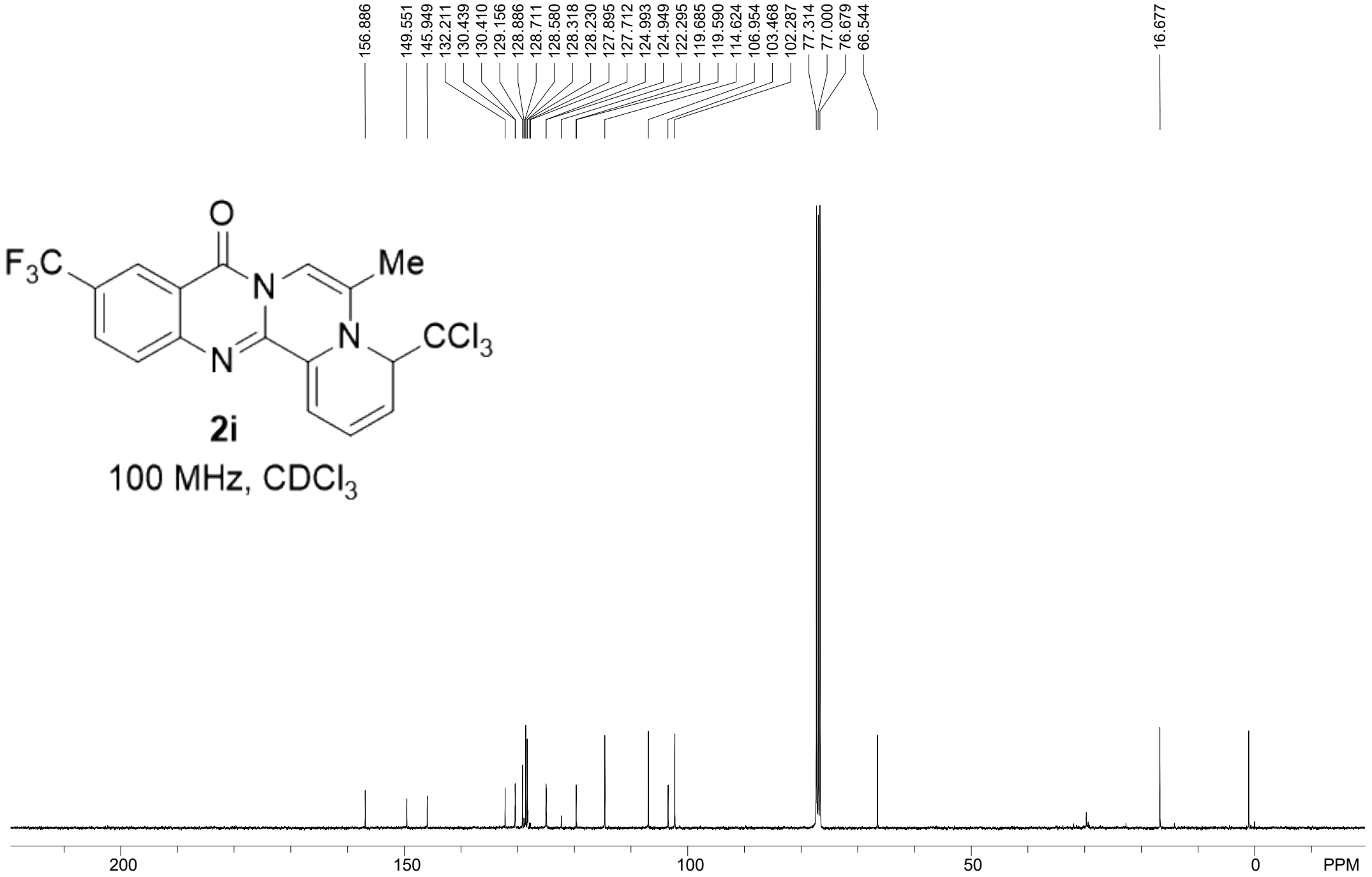
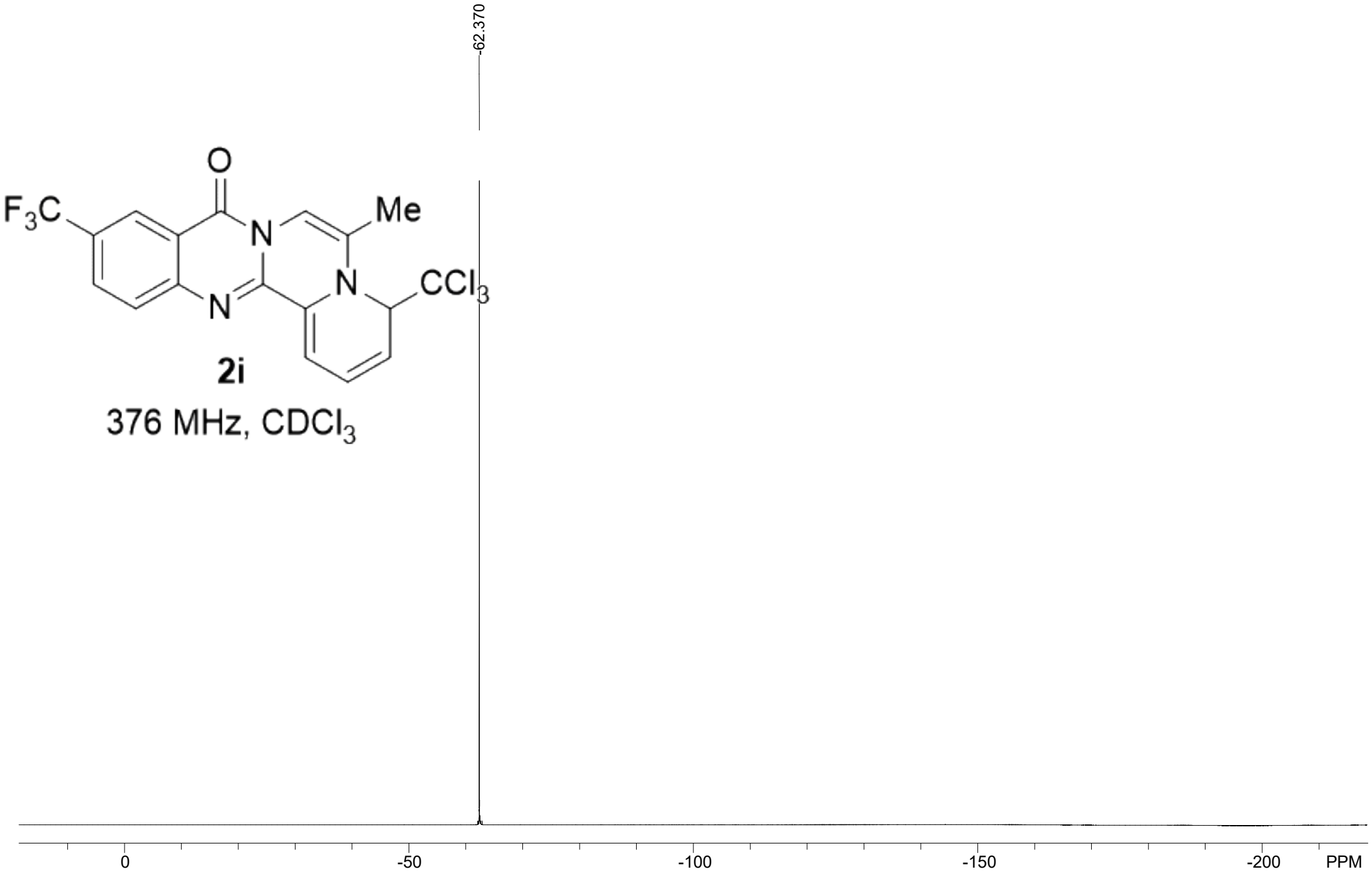
103.548
102.389
77.321
77.000
76.687
66.559
16.699
O
Br
Me
N
N
N
CCl3
2g
100 MHz, CDCl3
200
150
100
50
0
PPM

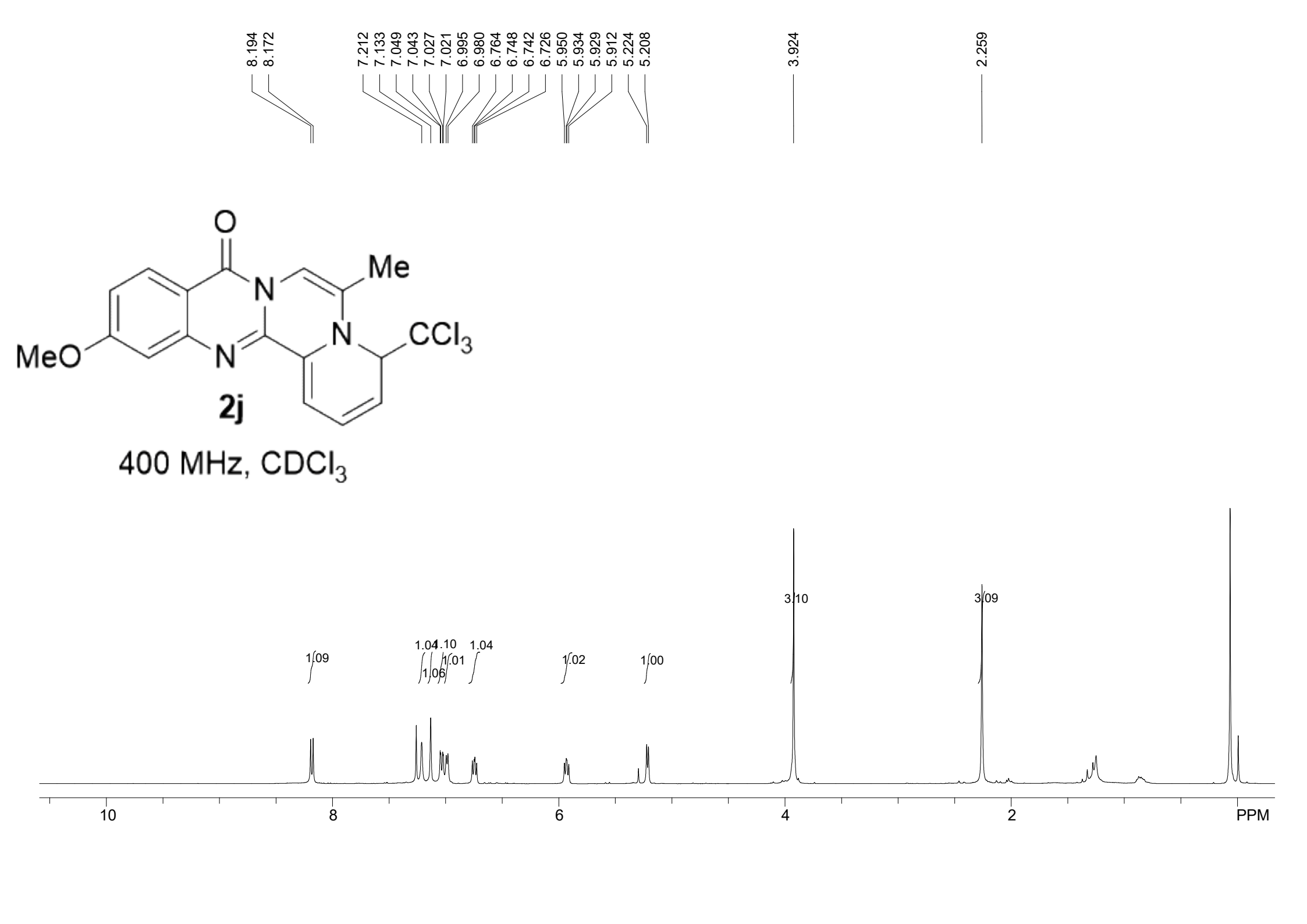

8.598
7.963
7.959
7.941
7.937
7.405
7.383
7.077
6.867
6.852
6.739
6.723
6.716
6.700
5.946
5.930
5.924
5.908
5.207
5.192
2.250
O
I
Me
N
N
N
CCl3
2h
400 MHz, CDCl3
1.00
1.10
1.00
1.07
1.00
1.04
1.03
1.07
3.01
10
8
6
4
2
0
PPM

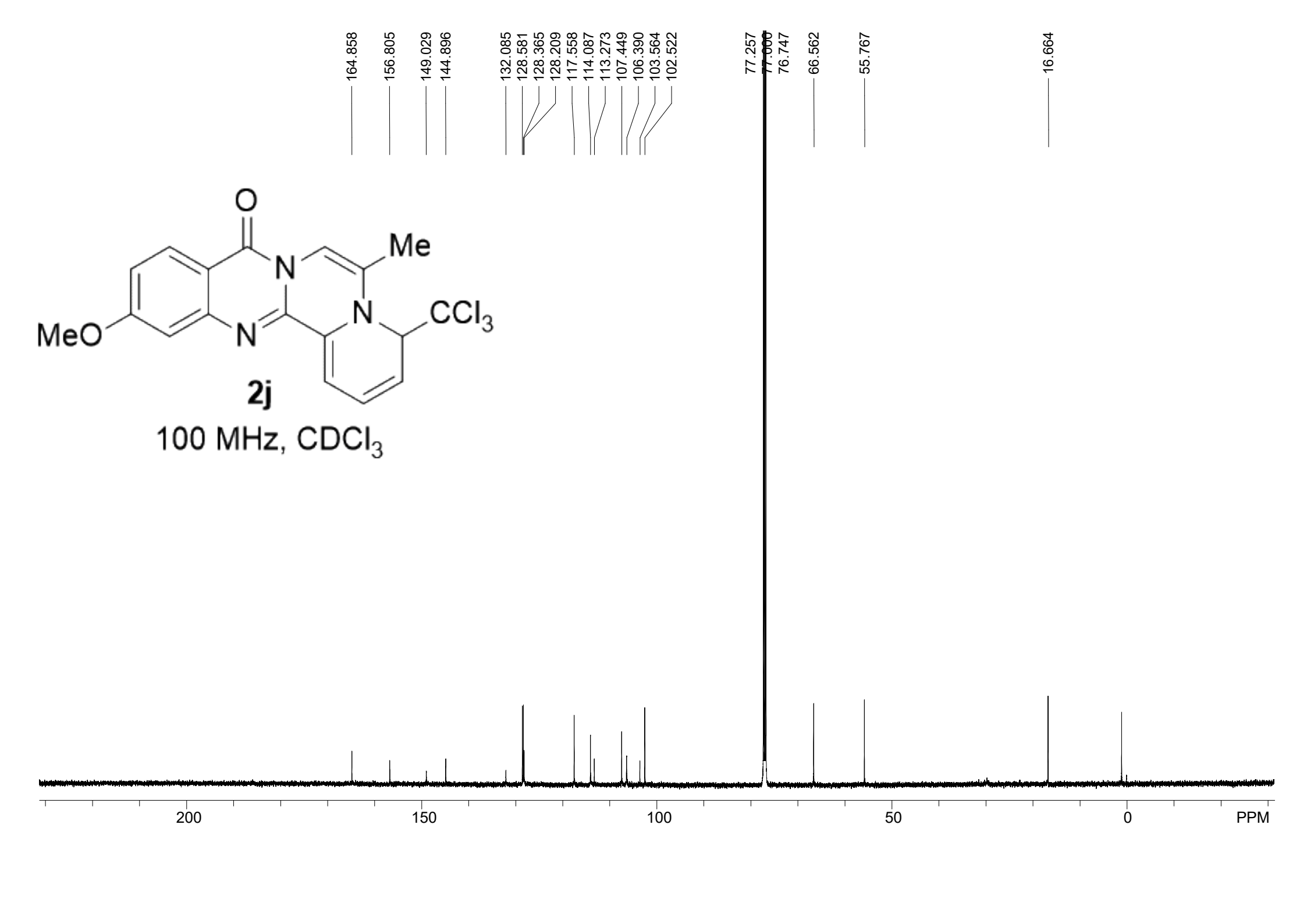

156.062
146.721
144.651
143.068
135.726
132.394
129.404
128.733
128.361
121.507
114.158
106.312
103.563
102.426
91.014
77.321
77.000
76.687
66.551
16.692
O
I
Me
N
N
N
CCl3
2h
100 MHz, CDCl3
200
150
100
50
0
PPM

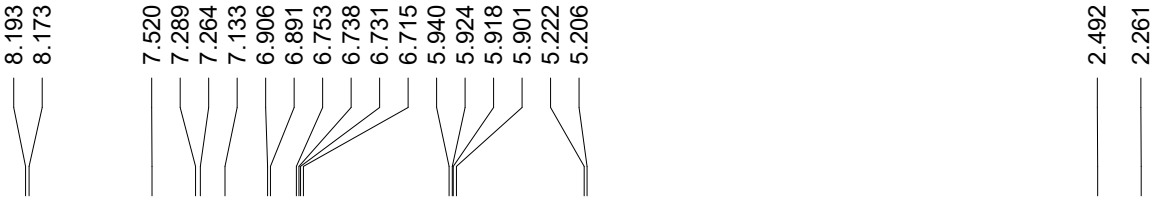

8.568
7.906
7.887
7.784
7.762
7.108
6.934
6.919
6.766
6.750
6.744
6.728
5.977
5.960
5.955
5.938
5.229
5.213
2.271
O
F3C
Me
N
N
N
CCl3
2i
400 MHz, CDCl3
1.02
1.07
1.04
1.00
1.02
1.03
1.00
1.00
3.05
10
8
6
4
2
0
PPM

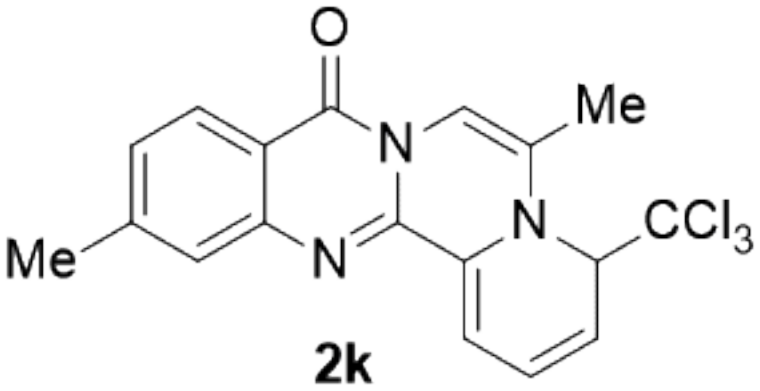

156.886
149.551
145.949
132.211
130.439
130.410
129.156
128.886
128.711
128.580
128.318
128.230
127.895
127.712
124.993
124.949
122.295
119.685
119.590
114.624
106.954
103.468
102.287
77.314
77.000
76.679
66.544
16.677
O
F3C
Me
N
N
N
CCl3
2i
100 MHz, CDCl3
200
150
100
50
0
PPM


-62.370
O
F3C
Me
N
N
N
CCl3
2i
376 MHz, CDCl3
0
-50
-100
-150
-200
PPM


8.194
8.172
7.212
7.133
7.049
7.043
7.027
7.021
6.995
6.980
6.764
6.748
6.742
6.726
5.950
5.934
5.929
5.912
5.224
5.208
3.924
2.259
O
Me
N
N
CCl3
MeO
N
2j
400 MHz, CDCl3
1.09
1.04
1.06
1.10
1.01
1.04
1.02
1.00
3.10
3.09
10
8
6
4
2
PPM

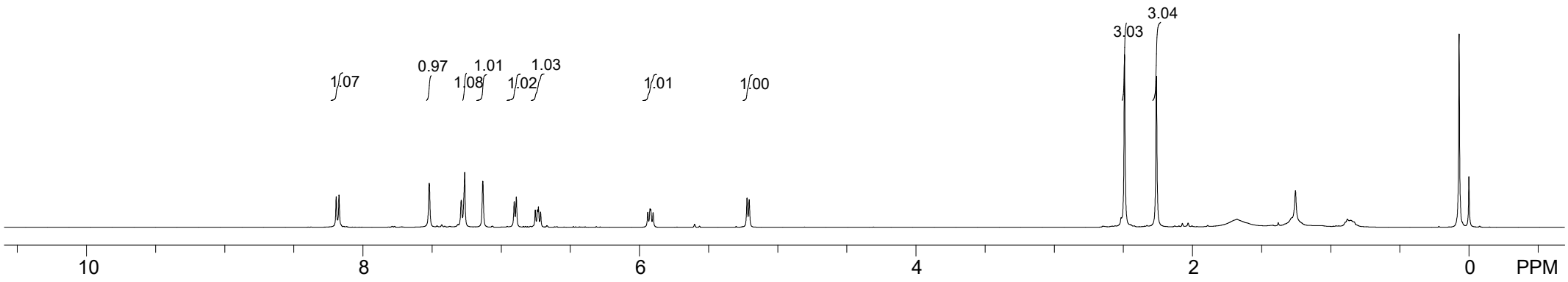

164.858
156.805
149.029
144.896
132.085
128.581
128.365
128.209
117.558
114.087
113.273
107.449
106.390
103.564
102.522
77.257
77.000
76.747
66.562
55.767
16.664
O
Me
N
N
CCl3
MeO
N
2j
100 MHz, CDCl3
200
150
100
50
0
PPM

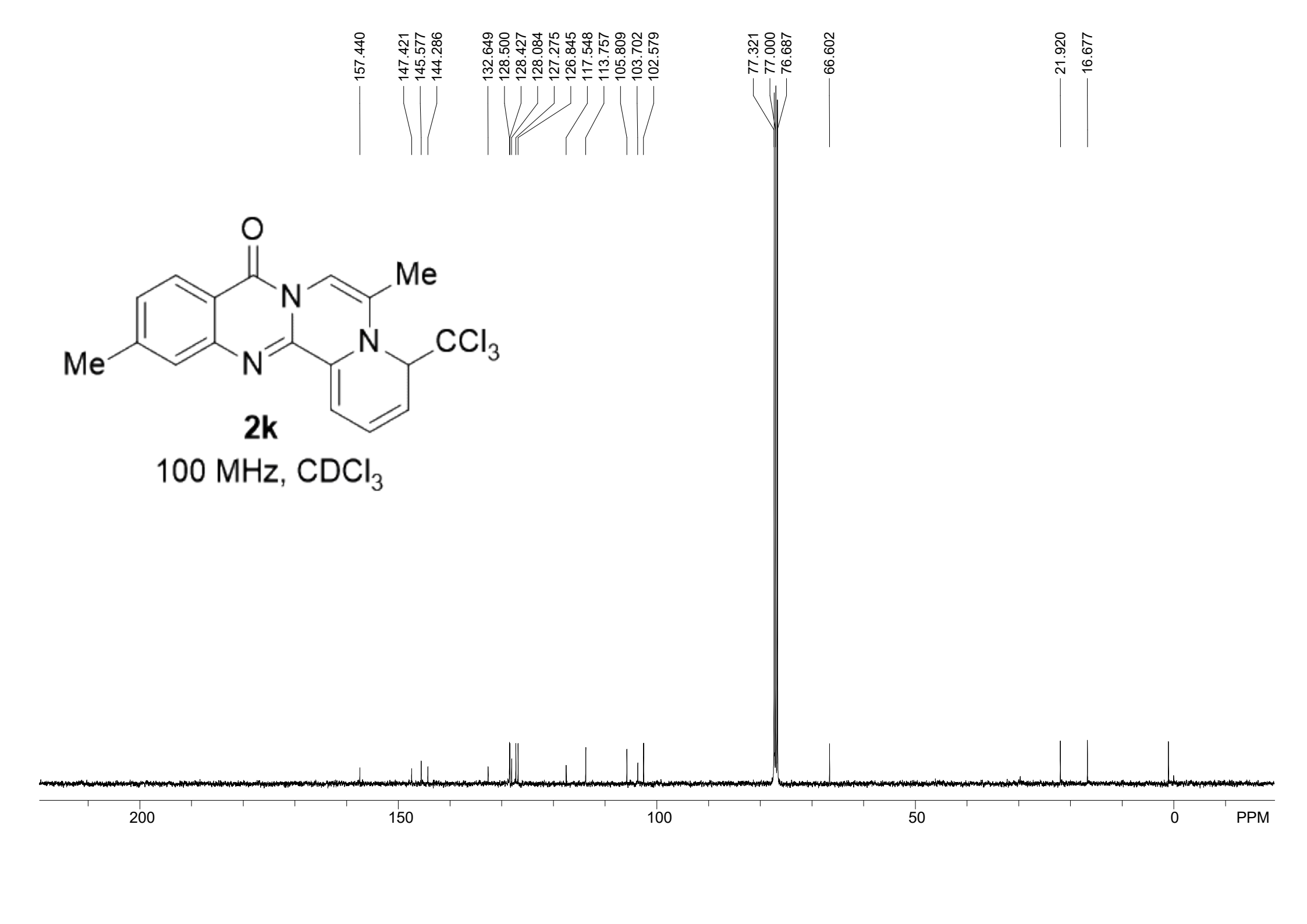


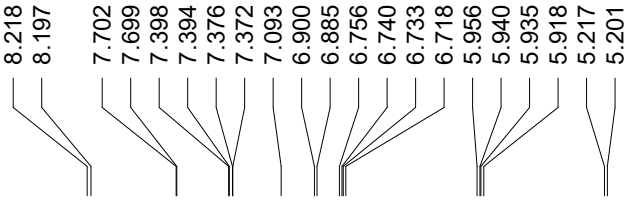


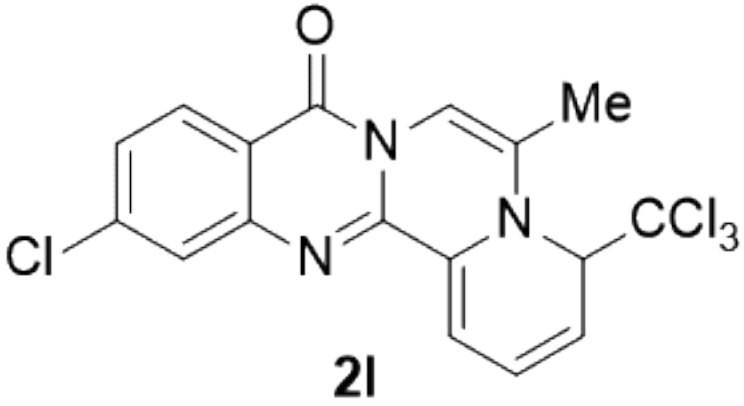
2k

400 MHz, $CDCl_3$



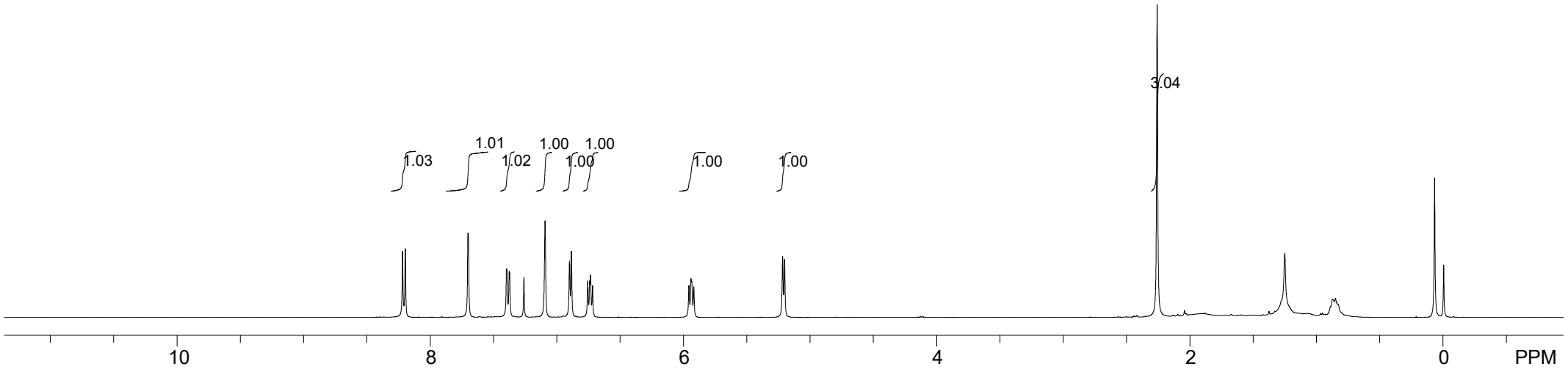

157.440
147.421
145.577
144.286
132.649
128.500
128.427
128.084
127.275
126.845
117.548
113.757
105.809
103.702
102.579
77.321
77.000
76.687
66.602
21.920
16.677
O
N
Me
N
N
CCl3
Me
2k
100 MHz, CDCl3
200
150
100
50
0
PPM

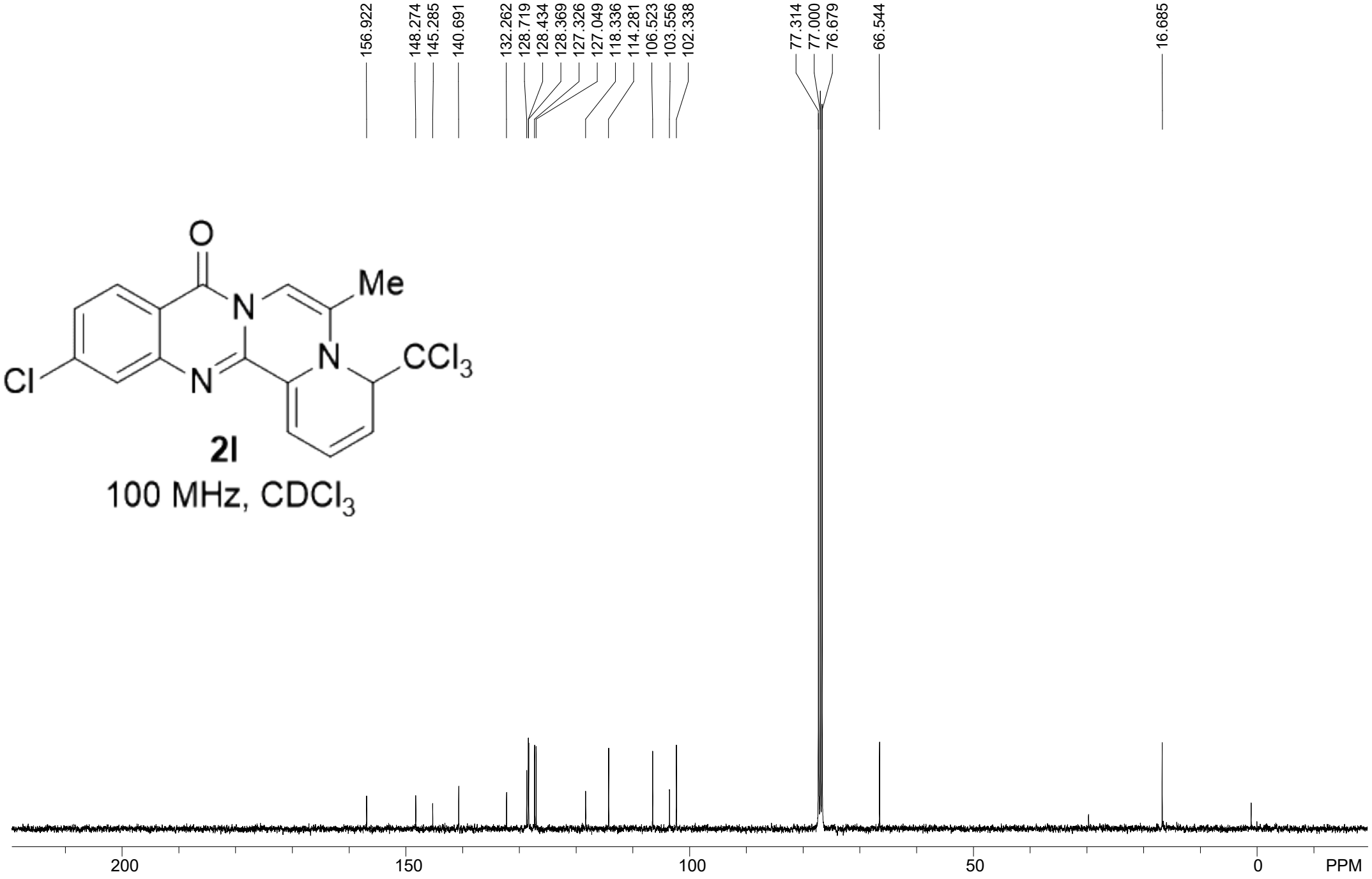


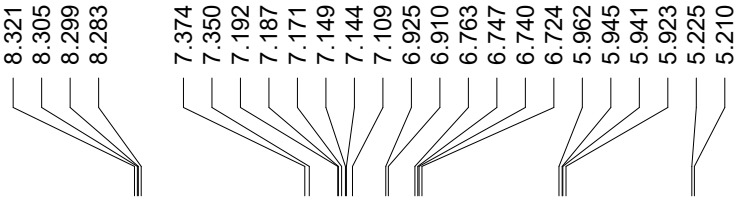


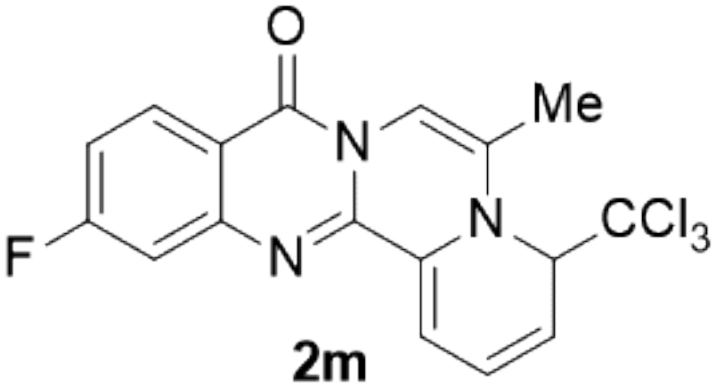
2l

400 MHz, $CDCl_3$



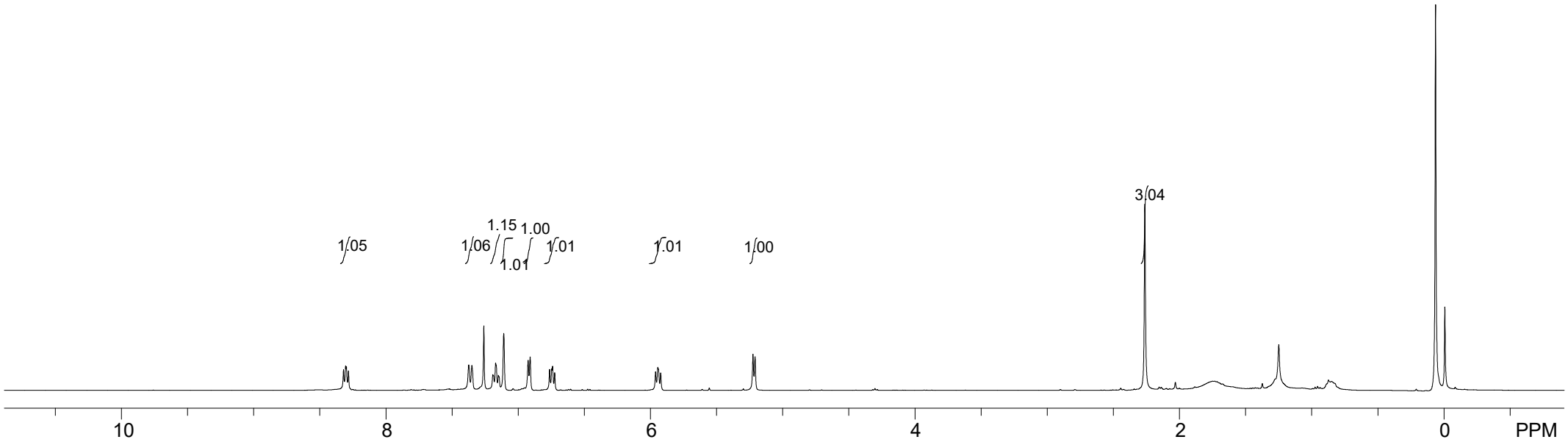

156.922
148.274
145.285
140.691
132.262
128.719
128.434
128.369
127.326
127.049
118.336
114.281
106.523
103.556
102.338
77.314
77.000
76.679
66.544
16.685
O
N
Me
N
CCl3
Cl
N
2l
100 MHz, CDCl3
200
150
100
50
0
PPM

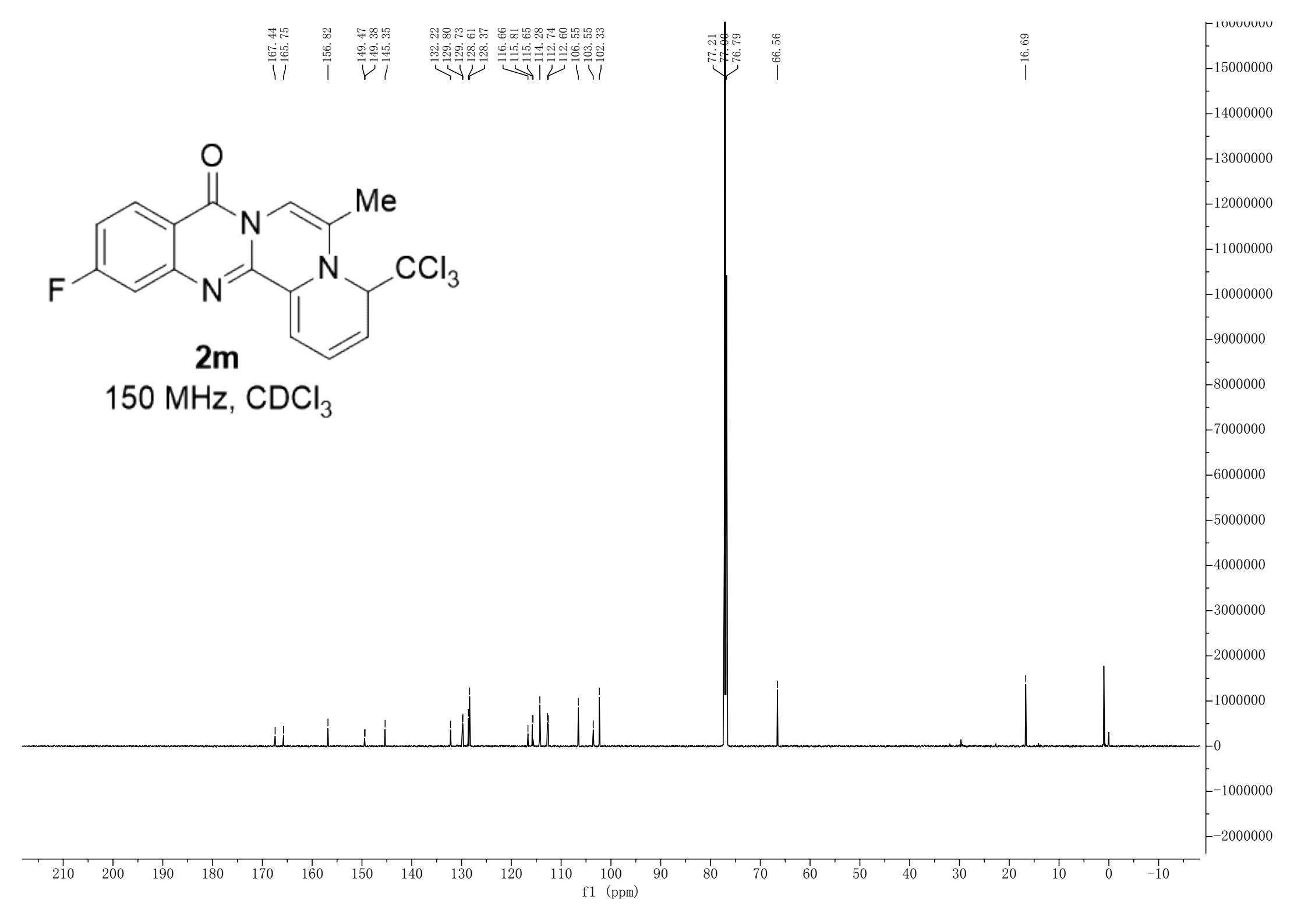


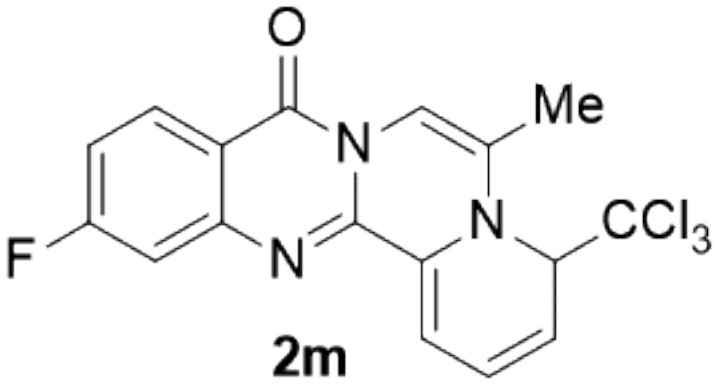


2m

400 MHz, $CDCl_3$

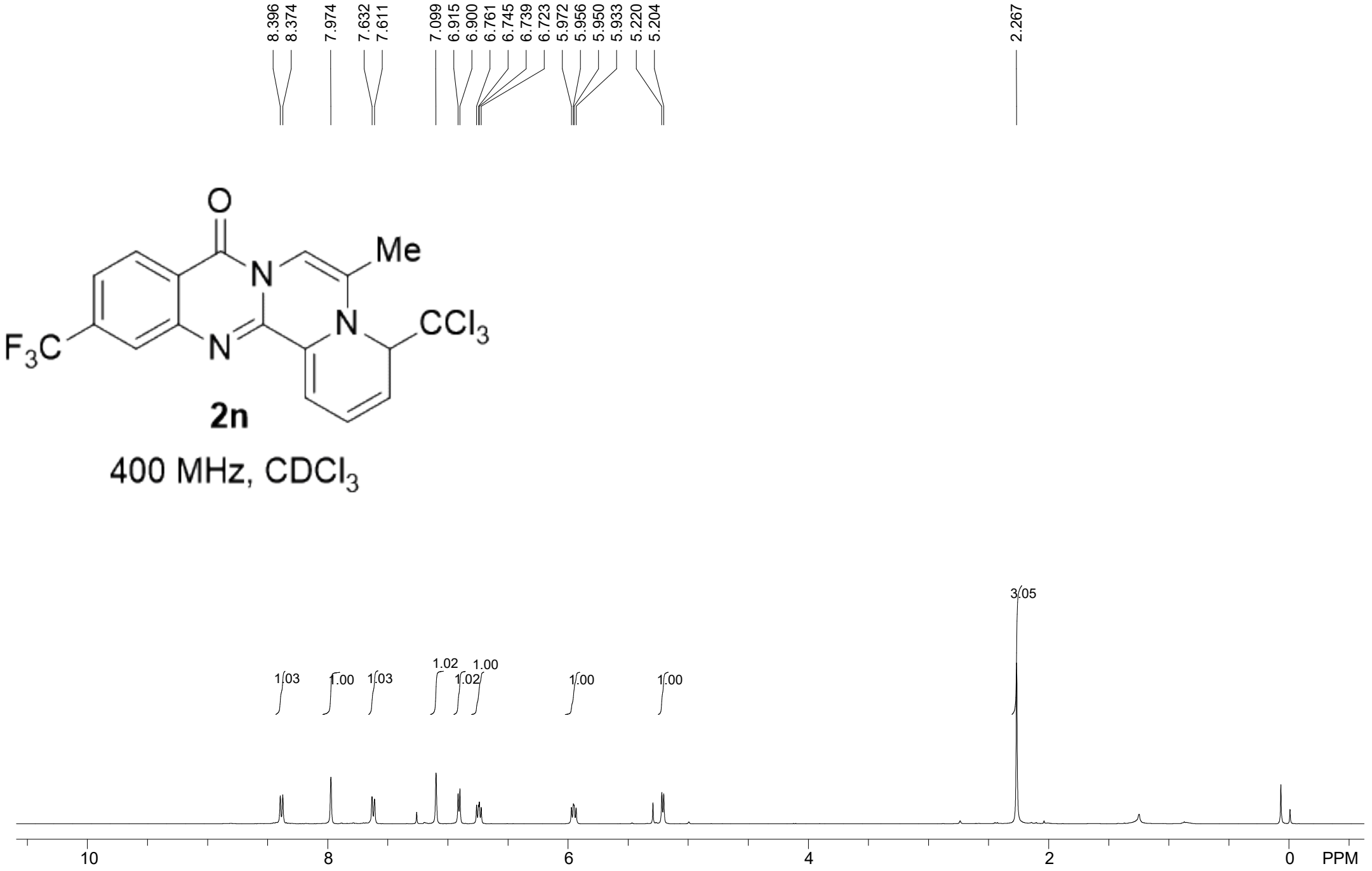


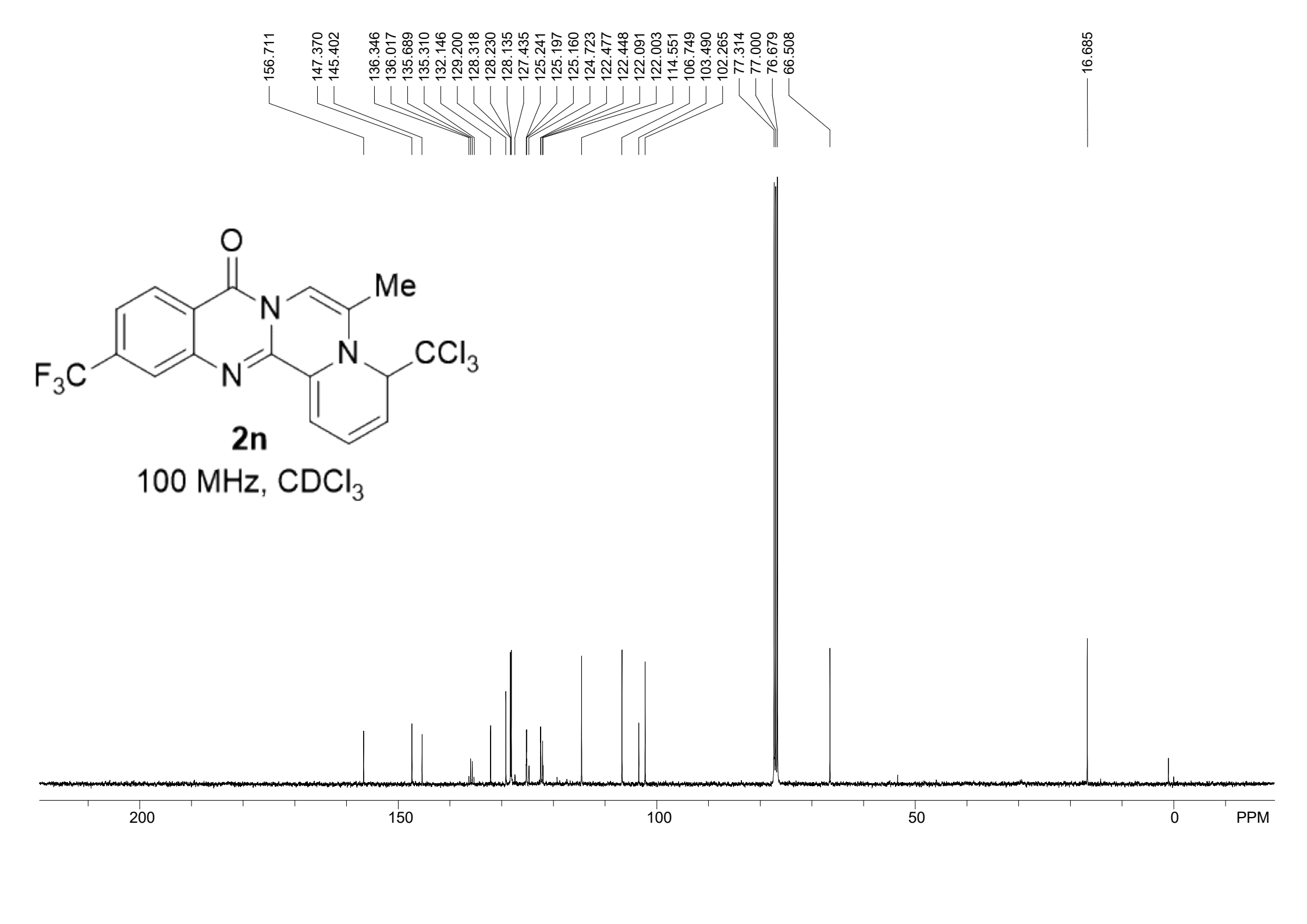

167.44
165.75
156.82
149.47
149.38
145.35
132.22
129.80
129.73
128.61
128.37
116.66
115.81
115.65
114.28
112.74
112.60
106.55
103.55
102.33
77.21
77.00
76.79
66.56
16.69
O
N
Me
N
CCl3
F
N
2m
150 MHz, CDCl3
f1 (ppm)

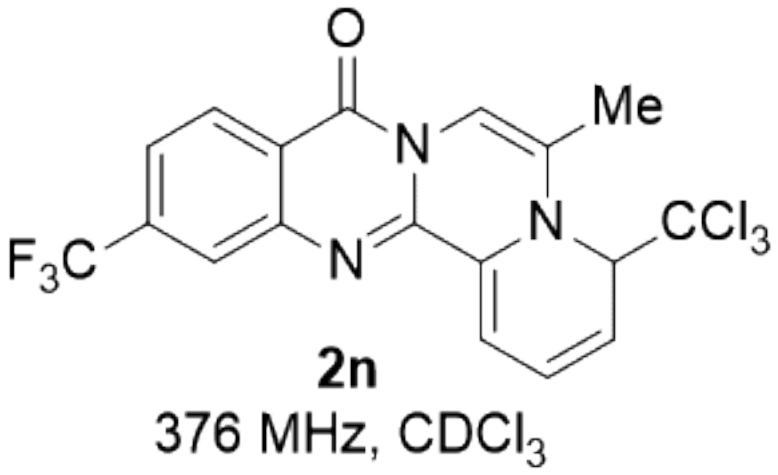


2m

376 MHz, $CDCl_3$

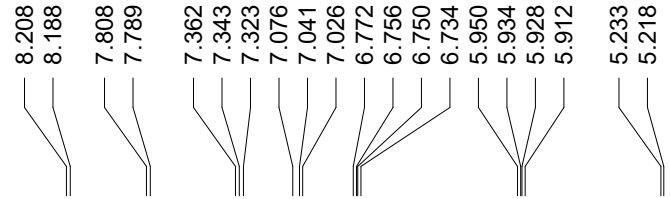

8.396
8.374
7.974
7.632
7.611
7.099
6.915
6.900
6.761
6.745
6.739
6.723
5.972
5.956
5.950
5.933
5.220
5.204
2.267
O
Me
N
N
N
CCl3
F3C
2n
400 MHz, CDCl3
3.05
1.03
1.00
1.03
1.02
1.02
1.00
1.00
1.00
10
8
6
4
2
0
PPM

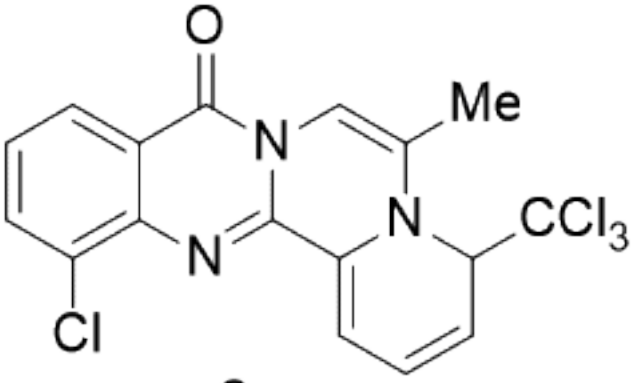

156.711
147.370
145.402
136.346
136.017
135.689
135.310
132.146
129.200
128.318
128.230
128.135
127.435
125.241
125.197
125.160
124.723
122.477
122.448
122.091
122.003
114.551
106.749
103.490
102.265
77.314
77.000
76.679
66.508
16.685
O
N
Me
N
CCl3
F3C
N
2n
100 MHz, CDCl3
200
150
100
50
0
PPM



2n

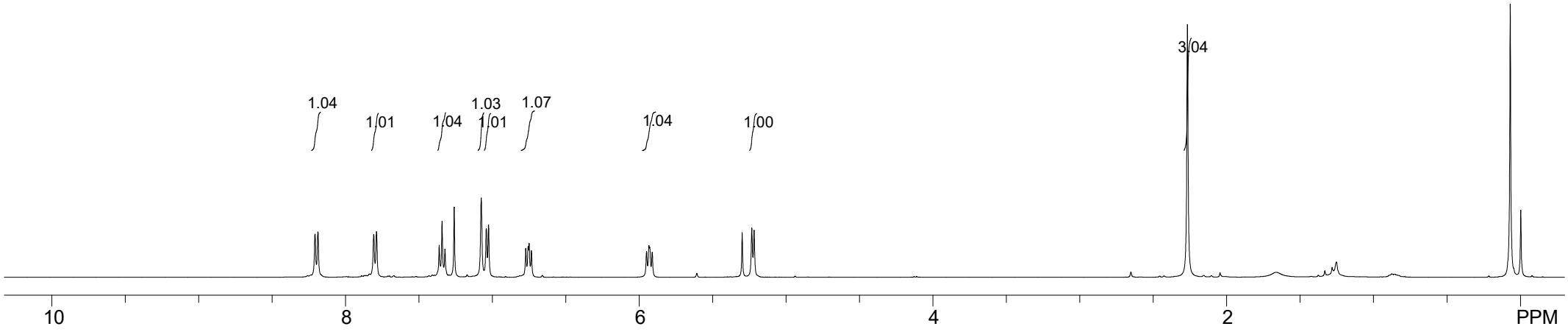
376 MHz, $CDCl_3$

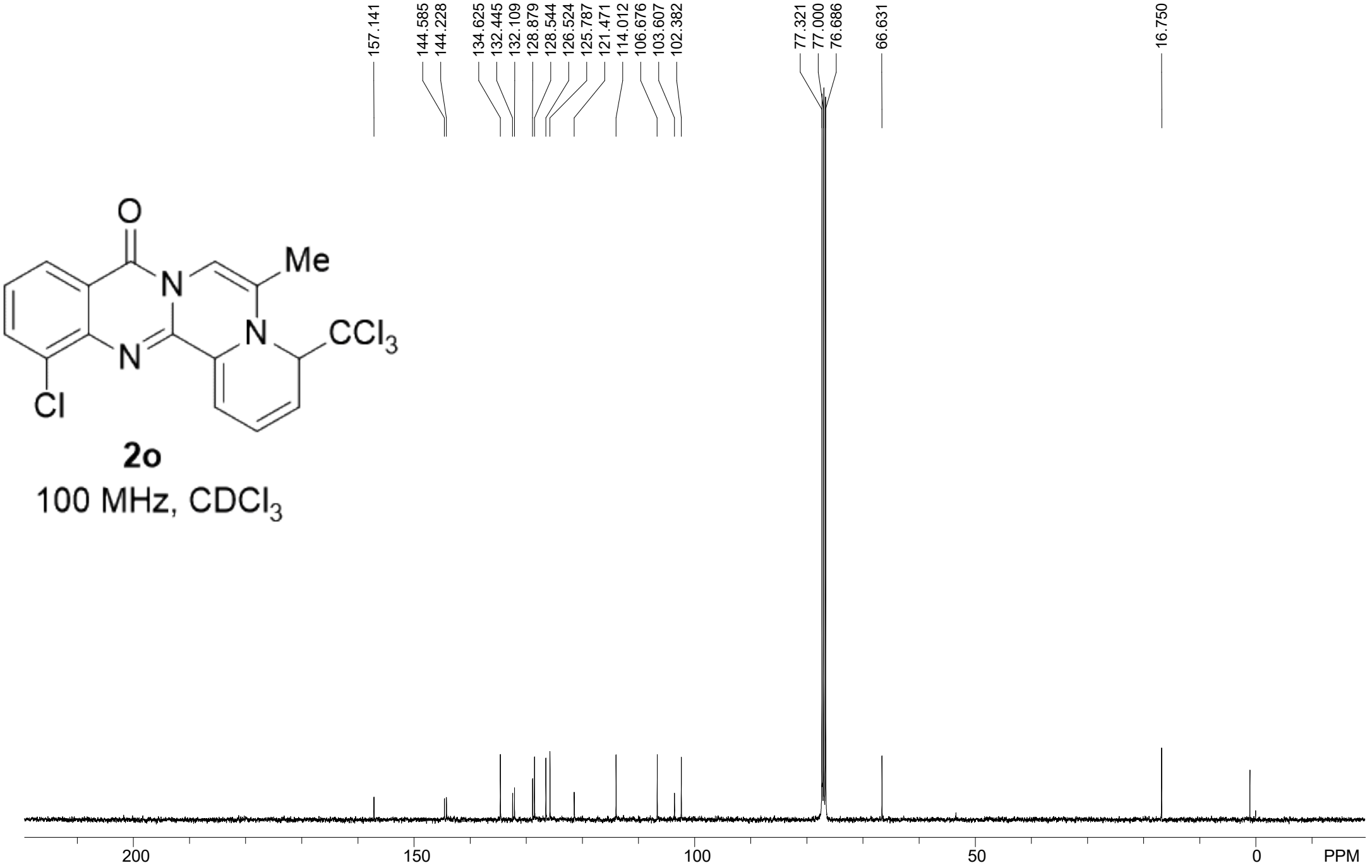


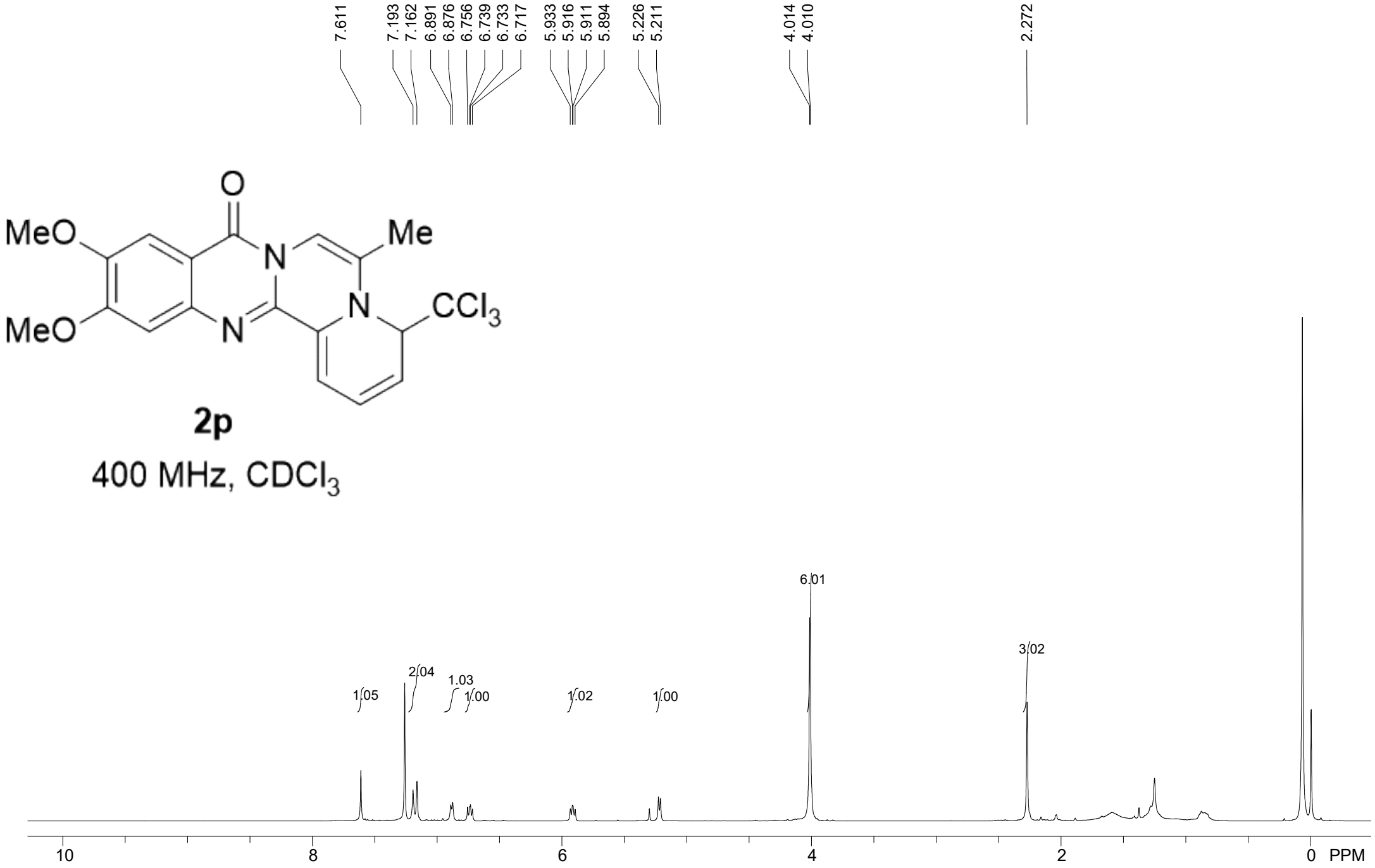


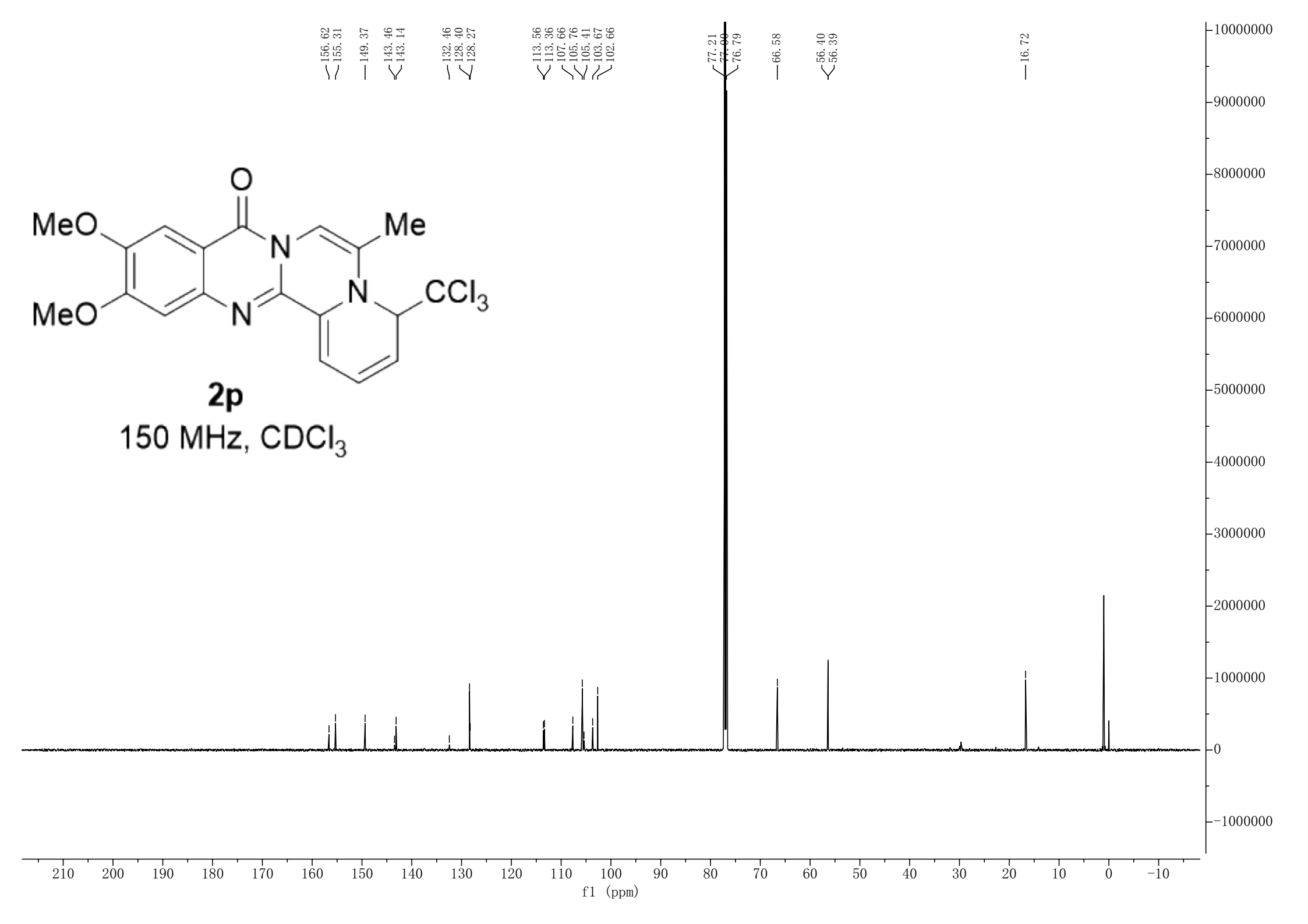
2o

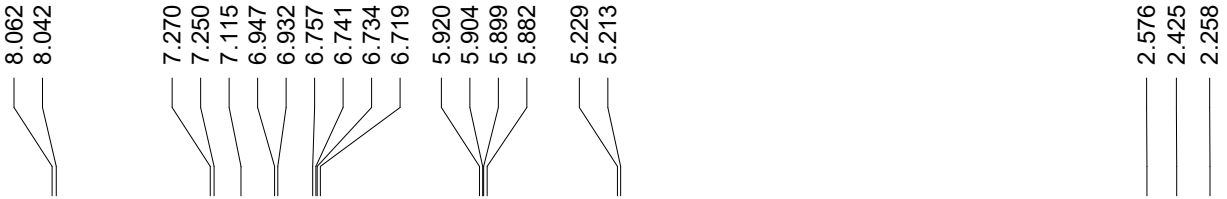
400 MHz, $CDCl_3$

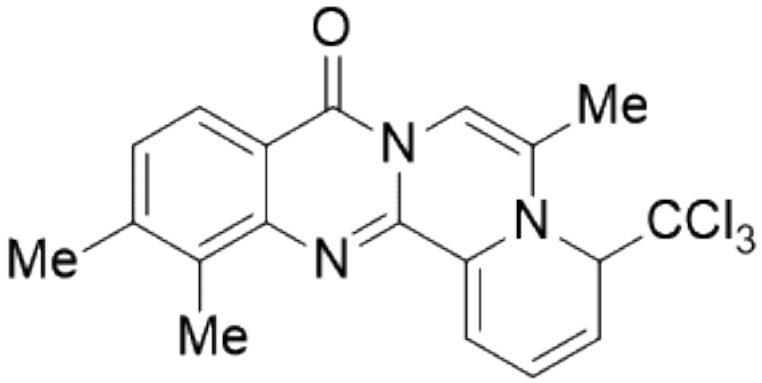



157.141
144.585
144.228
134.625
132.445
132.109
128.879
128.544
126.524
125.787
121.471
114.012
106.676
103.607
102.382
77.321
77.000
76.686
66.631
16.750
O
N
Me
N
CCl3
N
Cl
2o
100 MHz, CDCl3
200
150
100
50
0
PPM


7.611
7.193
7.162
6.891
6.876
6.756
6.739
6.733
6.717
5.933
5.916
5.911
5.894
5.226
5.211
4.014
4.010
2.272
O
MeO
MeO
N
N
N
Me
CCl3
2p
400 MHz, CDCl3
1.05
2.04
1.03
1.00
1.02
1.00
6.01
3.02
10
8
6
4
2
0
PPM

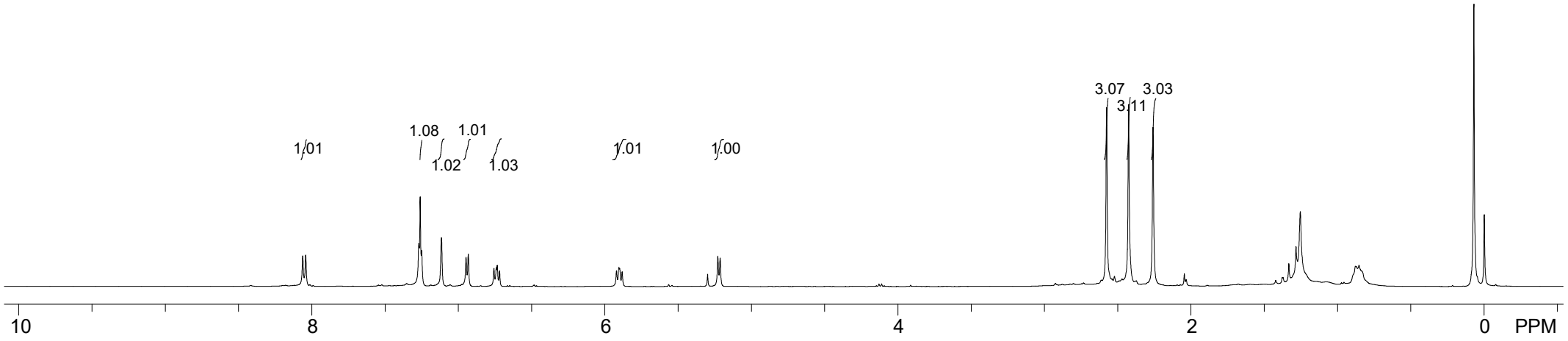

156.62
155.31
149.37
143.46
143.14
132.46
128.40
128.27
113.56
113.36
107.66
105.76
105.41
103.67
102.66
77.21
77.00
76.79
66.58
56.40
56.39
16.72
MeO
MeO
Me
CCl3
N
N
N
O
2p
150 MHz, CDCl3
f1 (ppm)

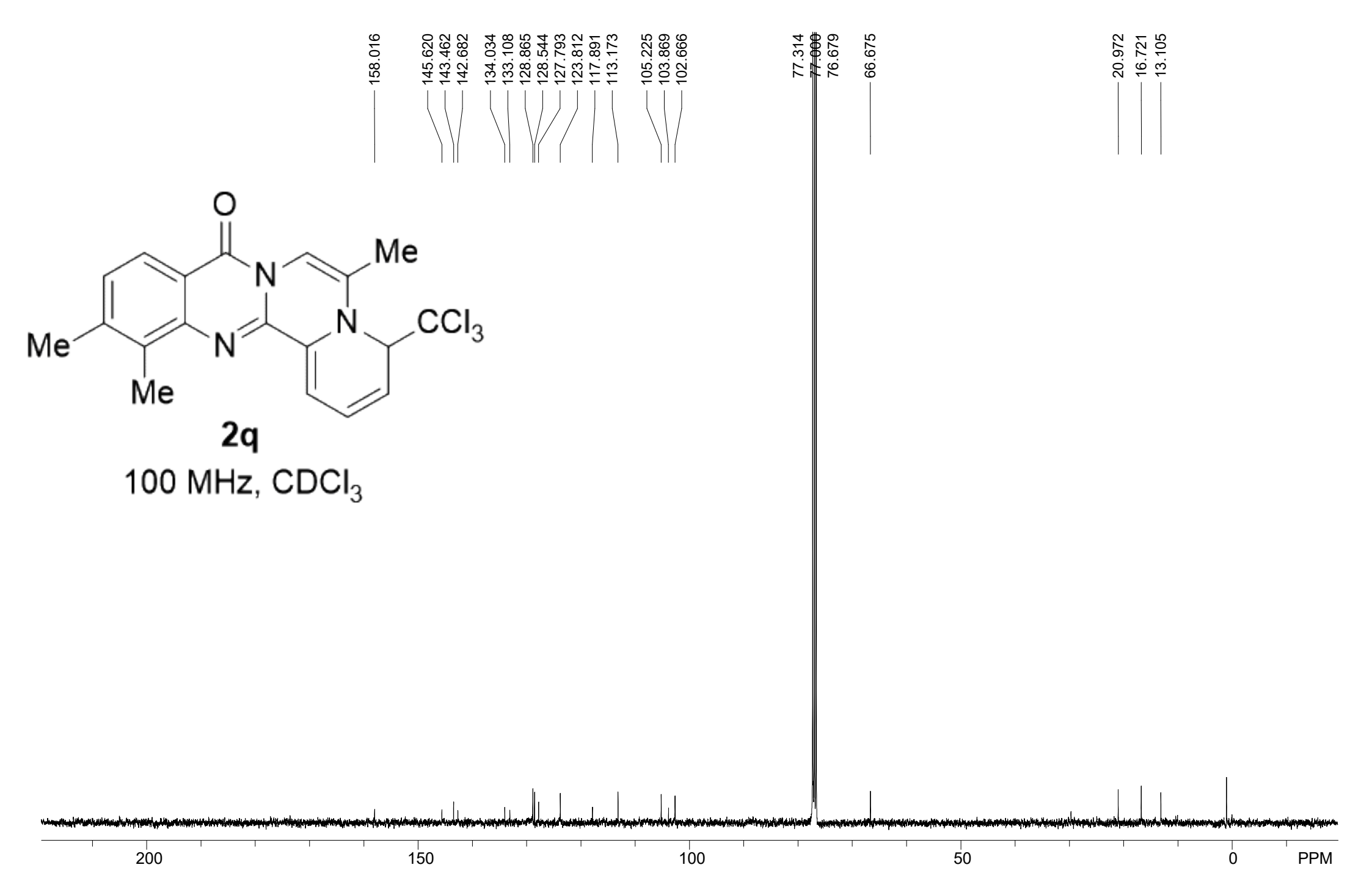


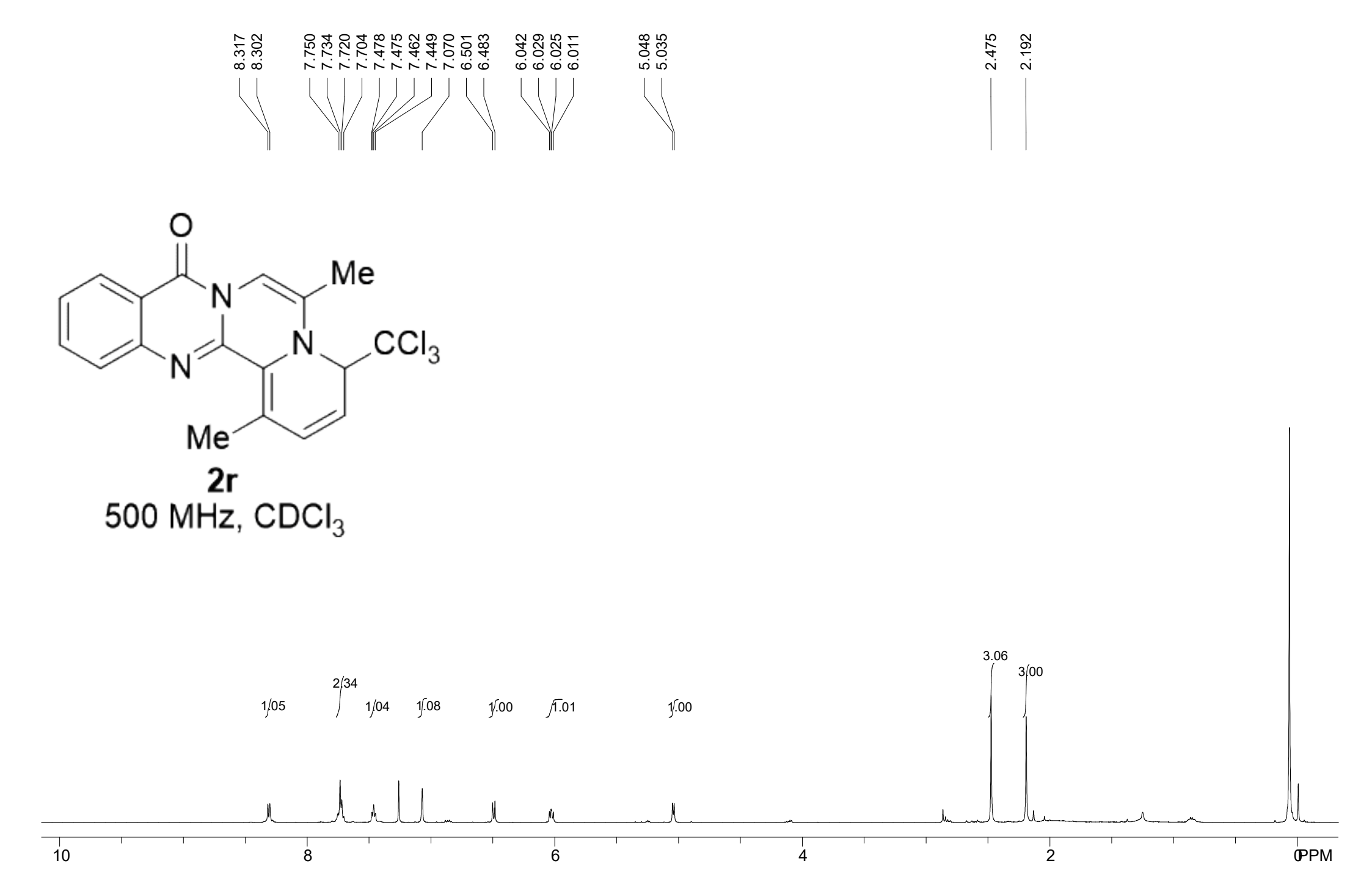


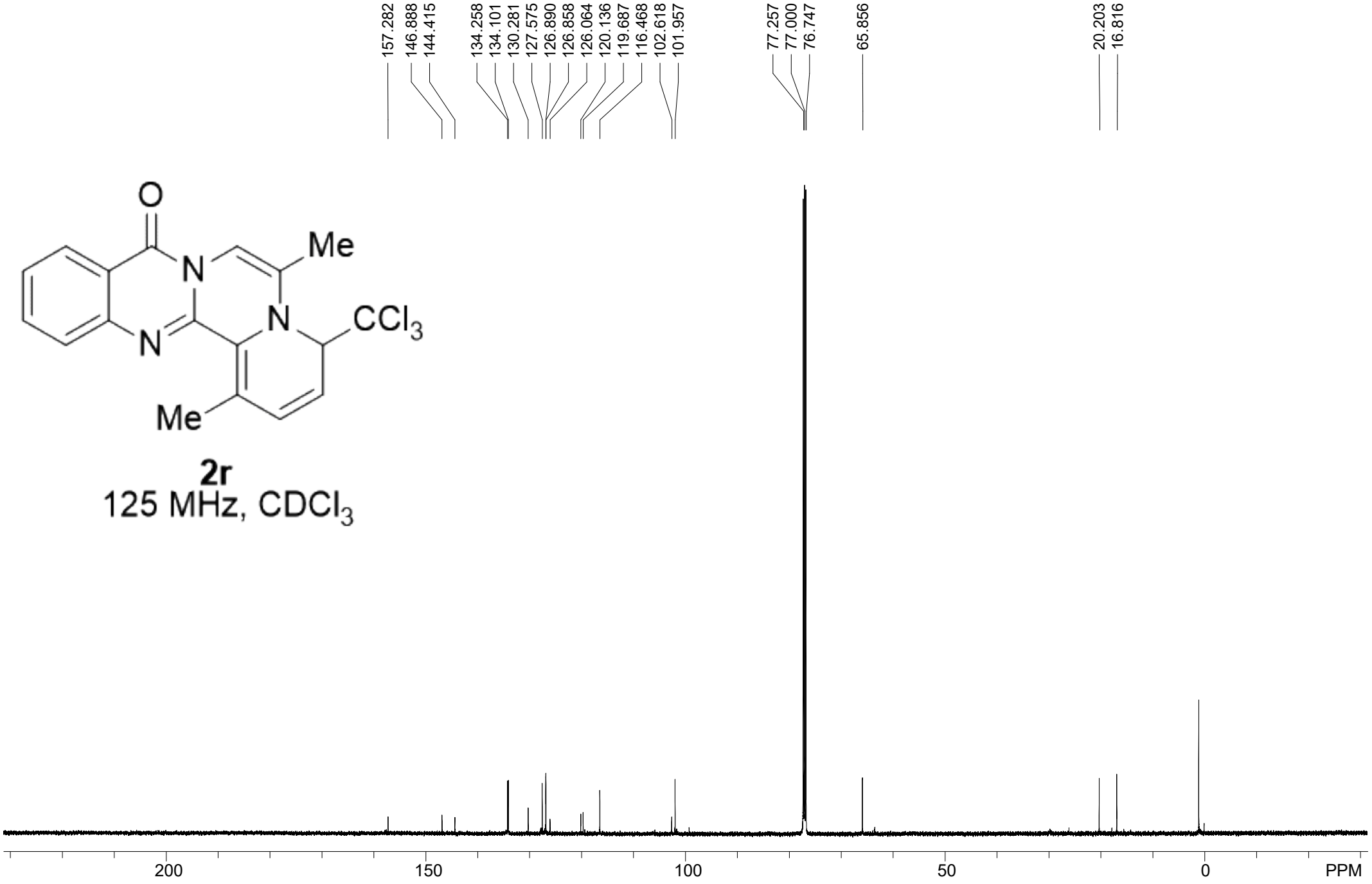
2q

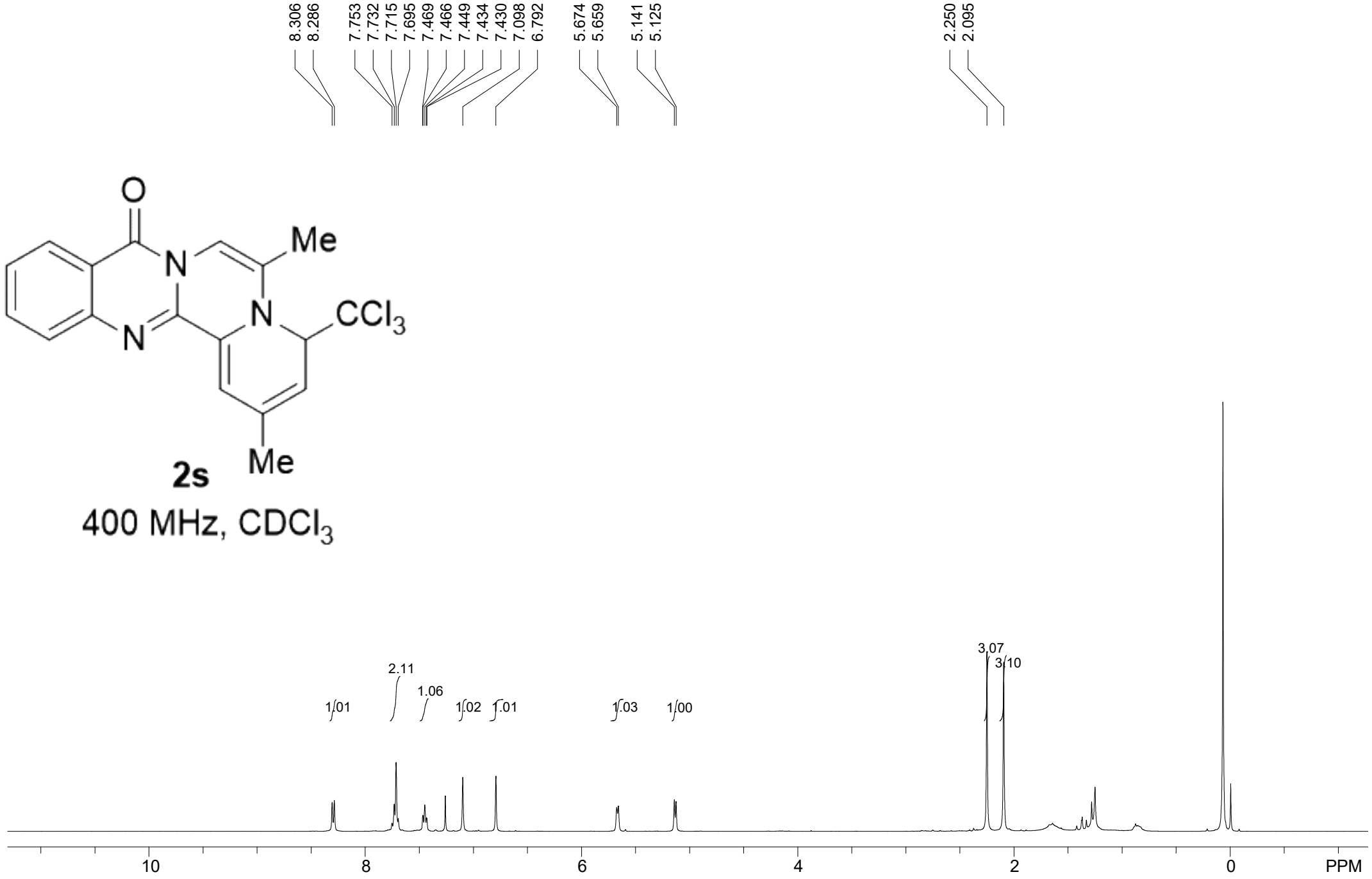
400 MHz, $CDCl_3$

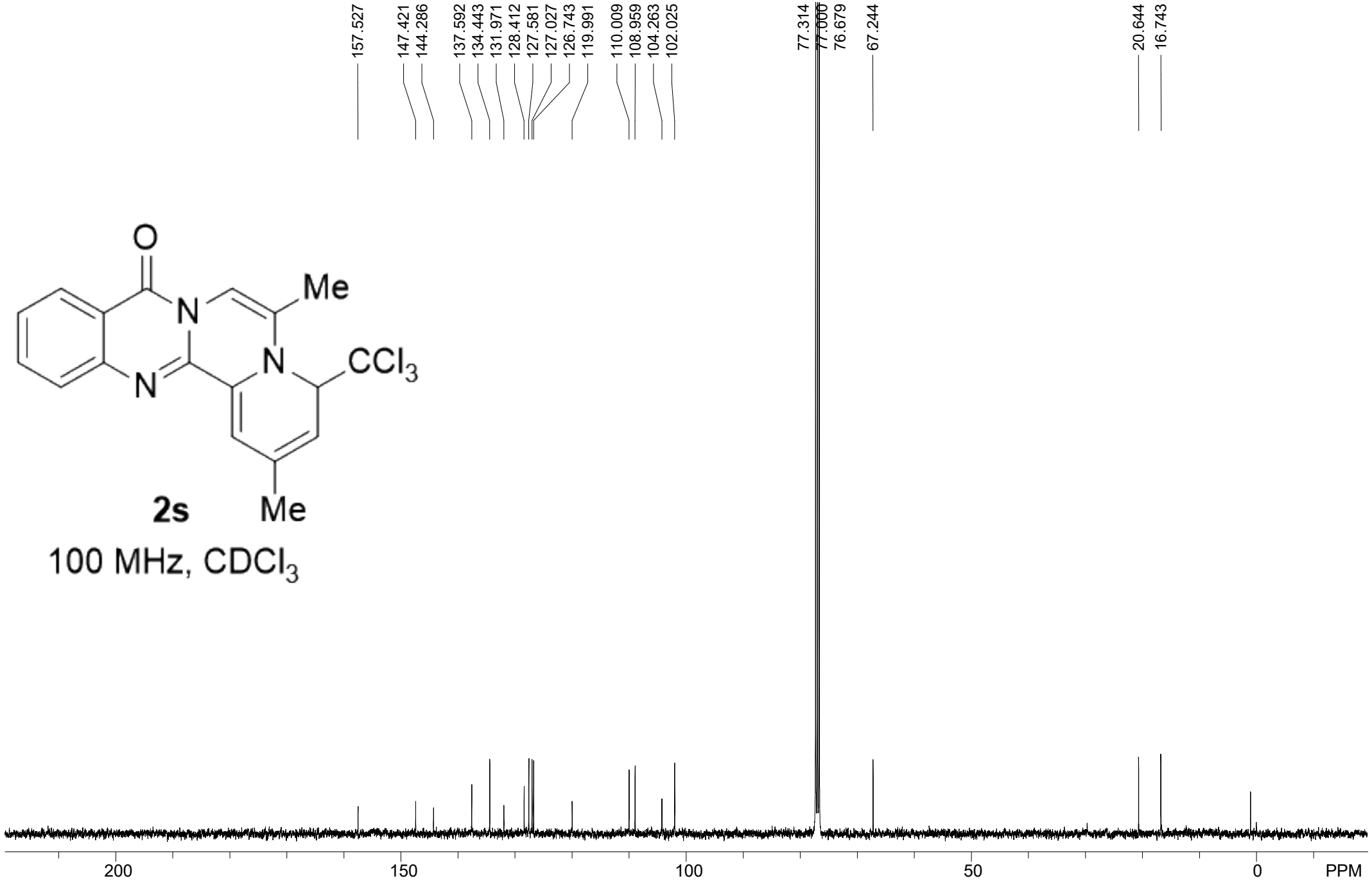


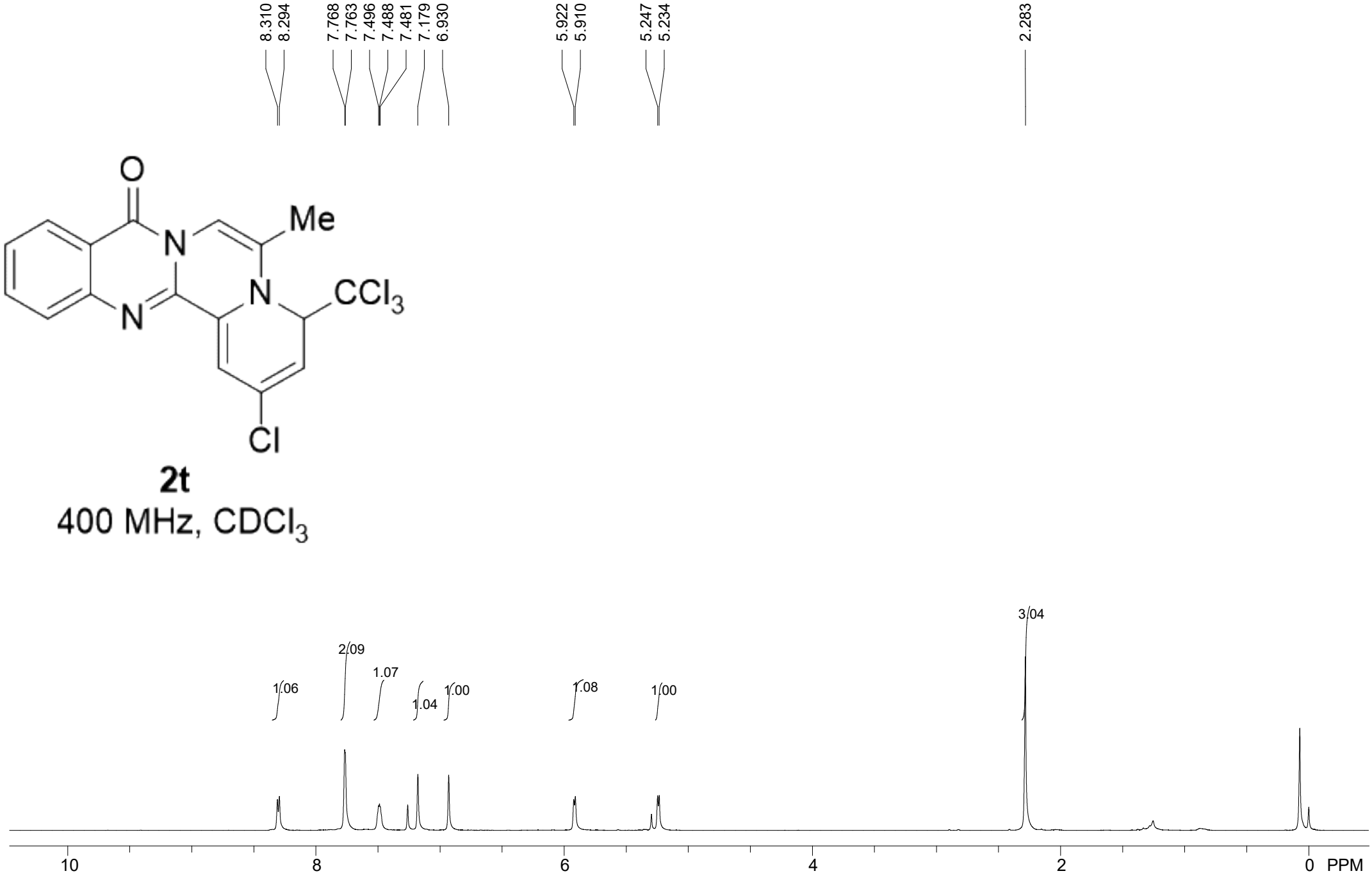

158.016
145.620
143.462
142.682
134.034
133.108
128.865
128.544
127.793
123.812
117.891
113.173
105.225
103.869
102.666
77.314
77.000
76.679
66.675
20.972
16.721
13.105
O
N
Me
N
N
CCl3
Me
Me
2q
100 MHz, CDCl3
200
150
100
50
0
PPM

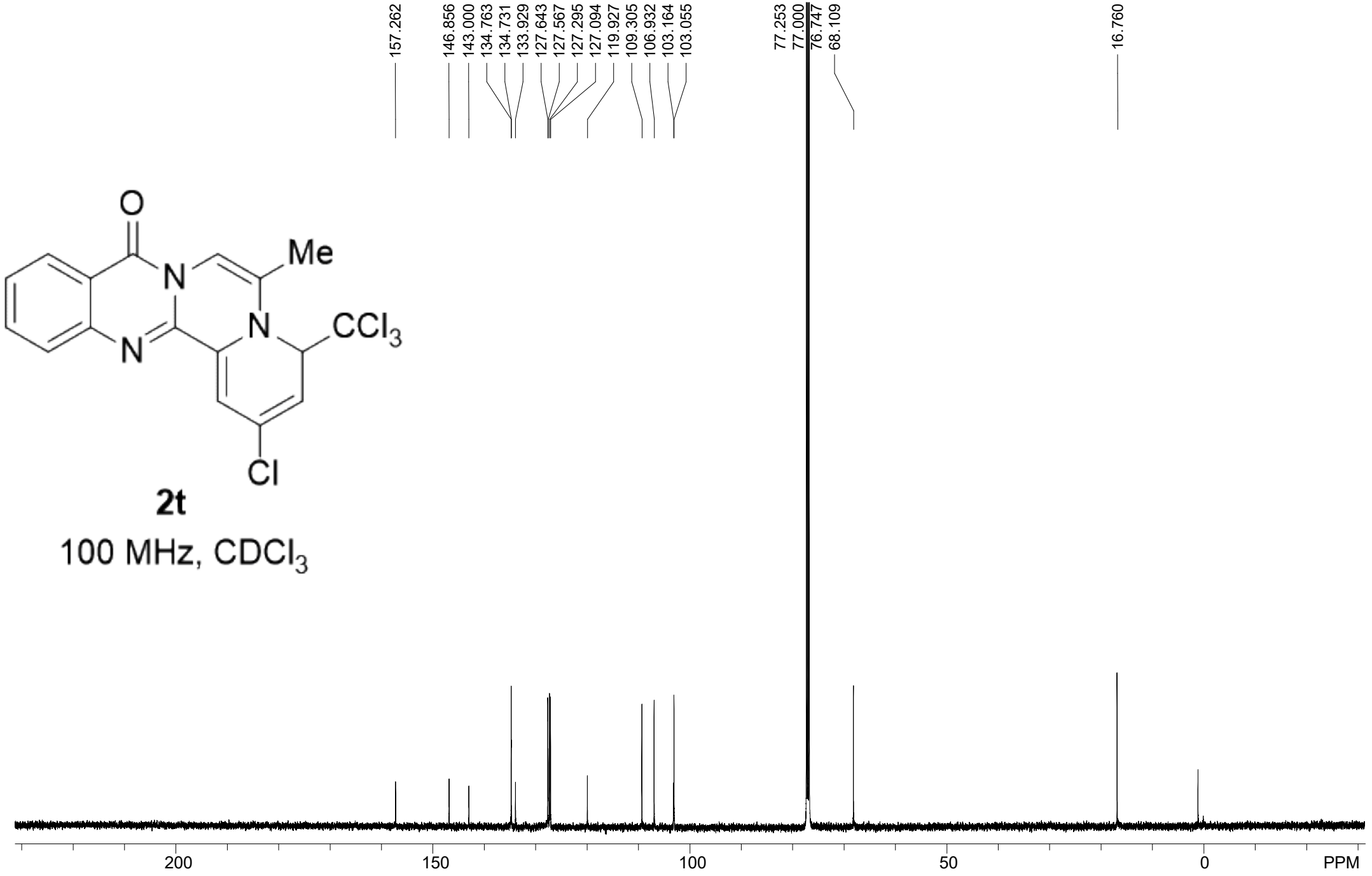

8.317
8.302
7.750
7.734
7.720
7.704
7.478
7.475
7.462
7.449
7.070
6.501
6.483
6.042
6.029
6.025
6.011
5.048
5.035
2.475
2.192
O
N
Me
N
N
CCl3
Me
2r
500 MHz, CDCl3
1.05
2.34
1.04
1.08
1.00
1.01
1.00
3.06
3.00
10
8
6
4
2
0
PPM

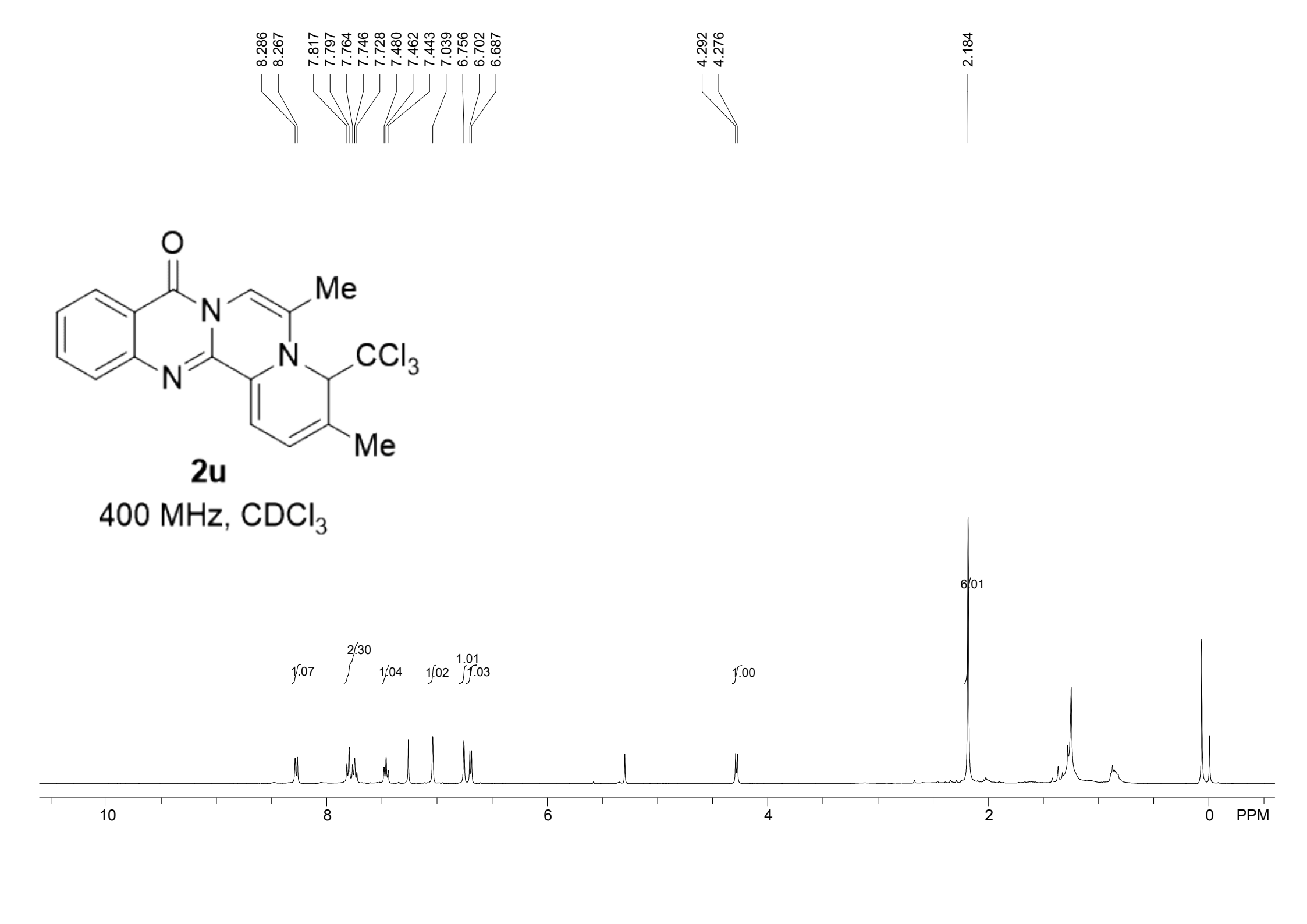

157.282
146.888
144.415
134.258
134.101
130.281
127.575
126.890
126.858
126.064
120.136
119.687
116.468
102.618
101.957
77.257
77.000
76.747
65.856
20.203
16.816
O
N
Me
N
N
CCl3
Me
2r
125 MHz, CDCl3
200
150
100
50
0
PPM

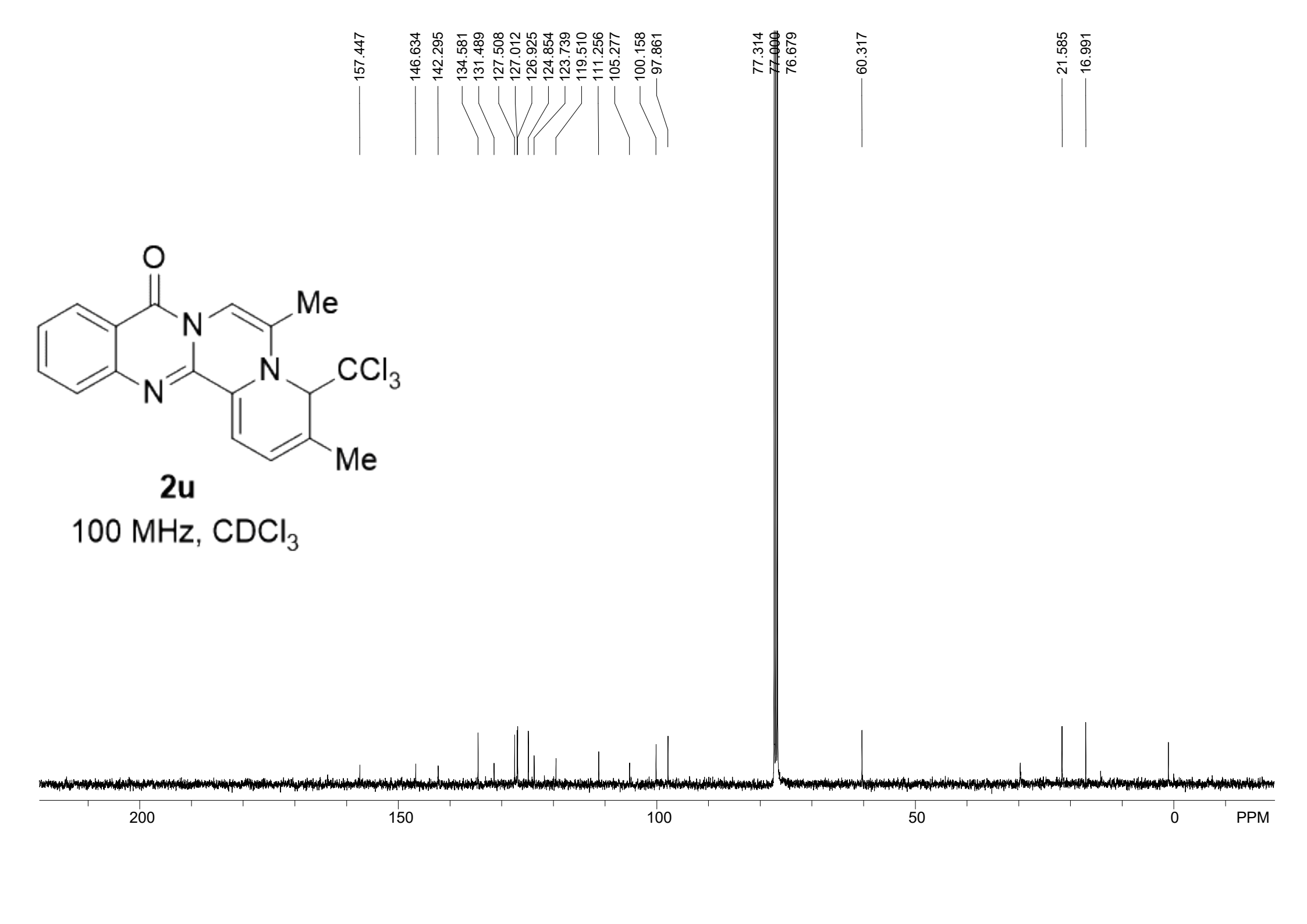

8.306
8.286
7.753
7.732
7.715
7.695
7.469
7.466
7.449
7.434
7.430
7.098
6.792
5.674
5.659
5.141
5.125
2.250
2.095
O
N
Me
N
N
CCl3
Me
2s
400 MHz, CDCl3
1.01
2.11
1.06
1.02
1.01
1.03
1.00
3.07
3.10
10
8
6
4
2
0
PPM

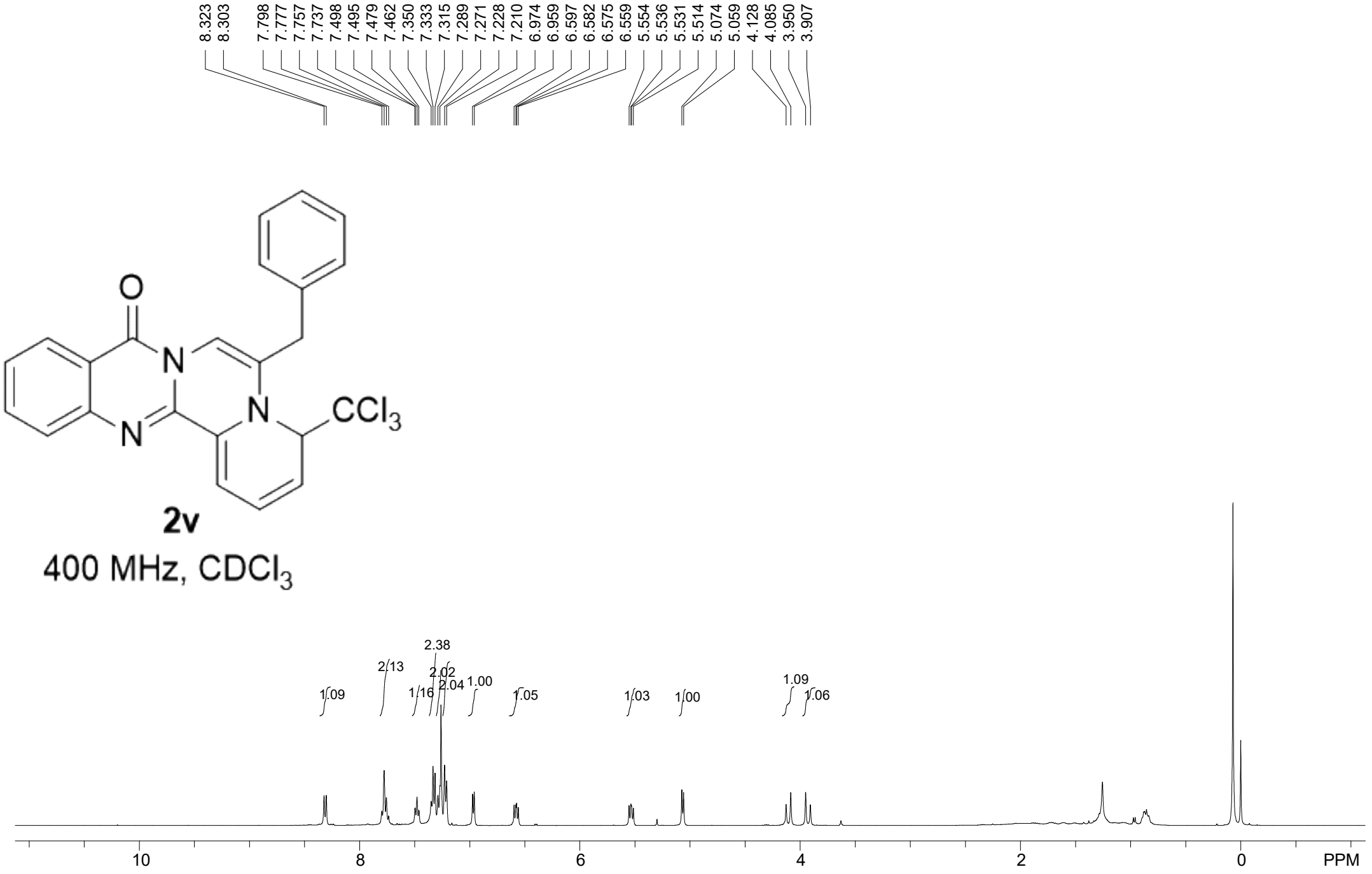

157.527
147.421
144.286
137.592
134.443
131.971
128.412
127.581
127.027
126.743
119.991
110.009
108.959
104.263
102.025
77.314
77.000
76.679
67.244
20.644
16.743
O
N
N
N
Me
CCl3
Me
2s
100 MHz, CDCl3
200
150
100
50
0
PPM

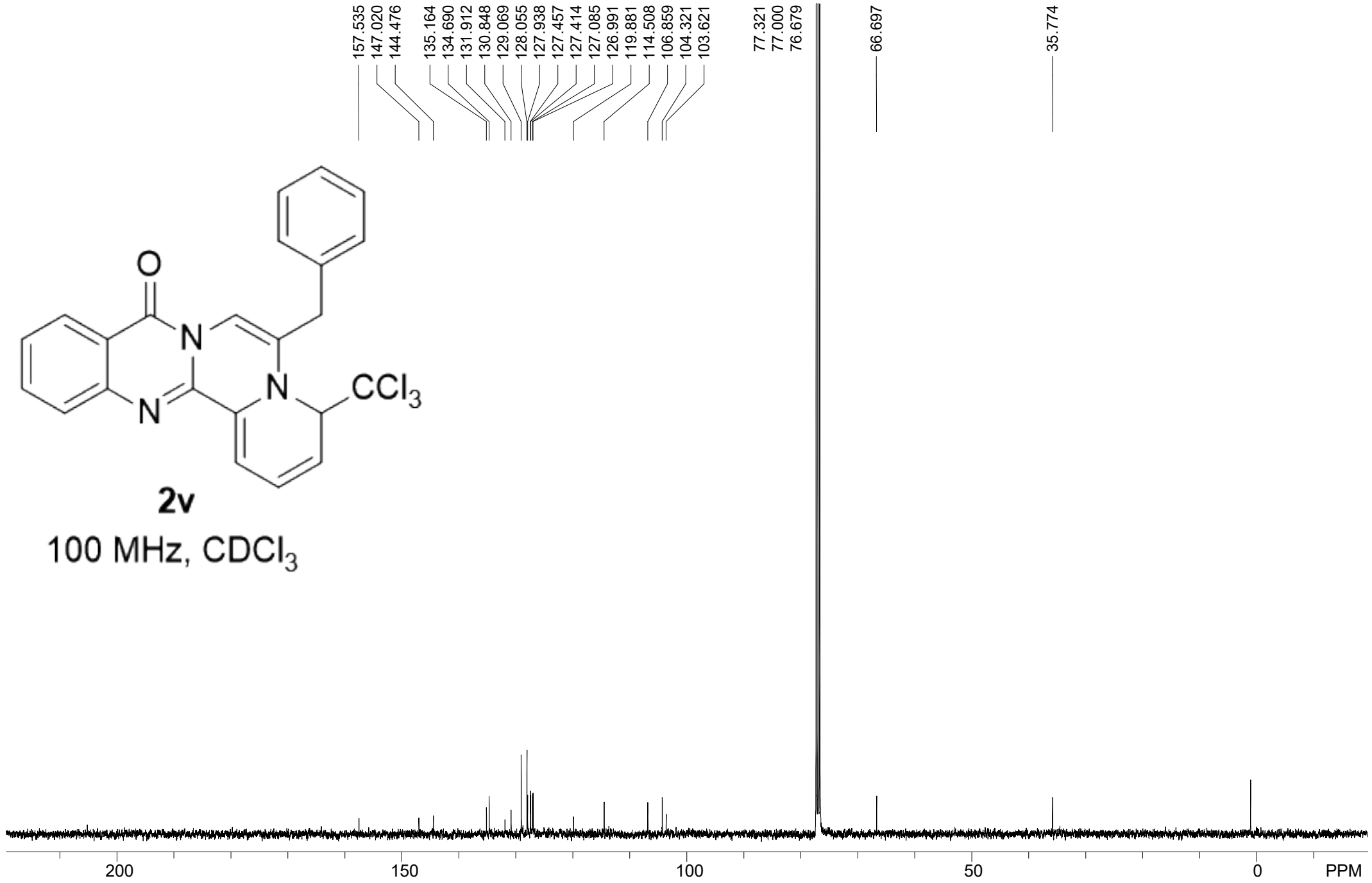

8.310
8.294
7.768
7.763
7.496
7.488
7.481
7.179
6.930
5.922
5.910
5.247
5.234
2.283
O
N
Me
N
N
CCl3
Cl
2t
400 MHz, CDCl3
3.04
2.09
1.07
1.06
1.04
1.00
1.08
1.00
10
8
6
4
2
0
PPM

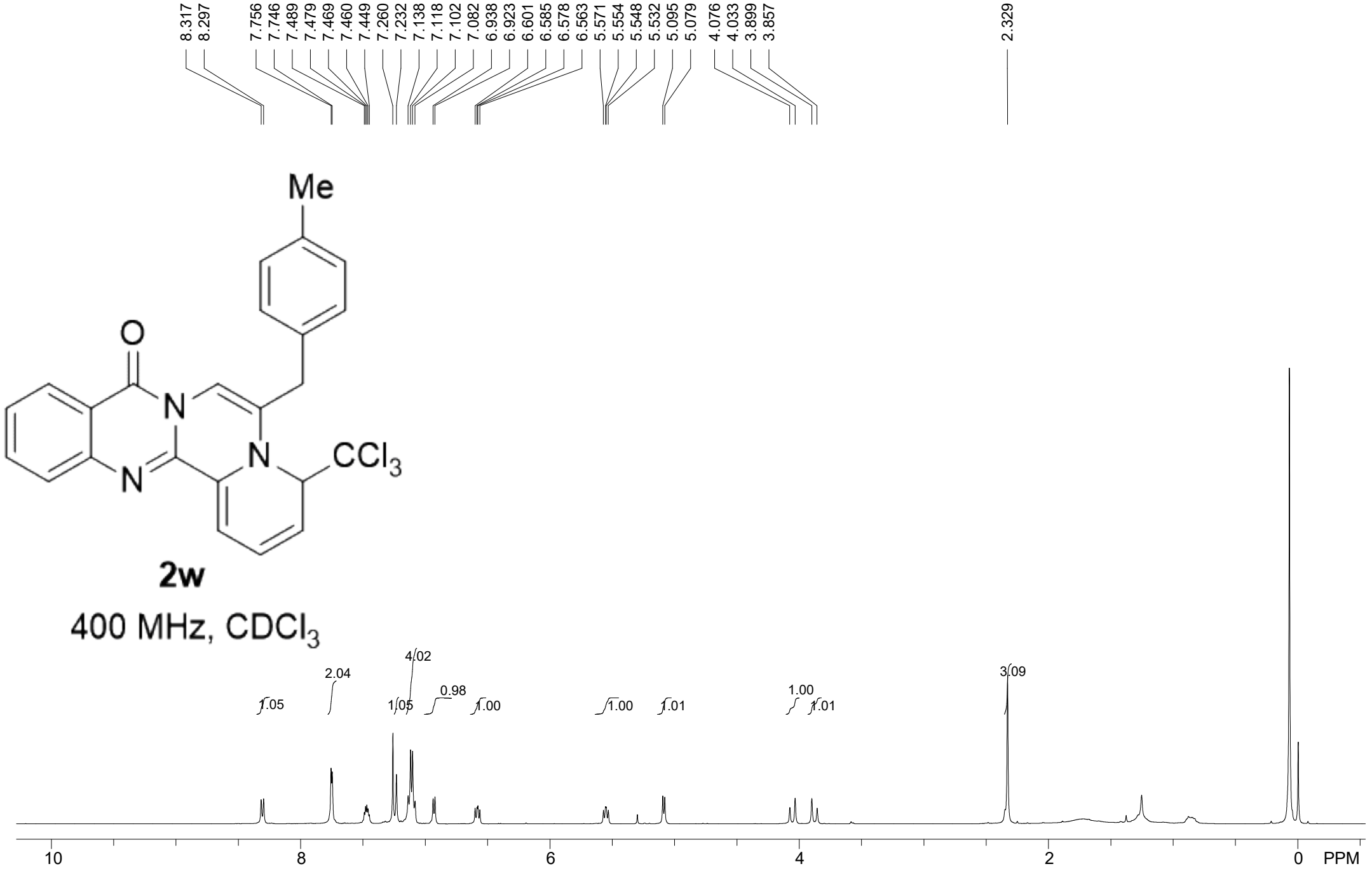

157.262
146.856
143.000
134.763
134.731
133.929
127.643
127.567
127.295
127.094
119.927
109.305
106.932
103.164
103.055
77.253
77.000
76.747
68.109
16.760
O
N
Me
N
N
CCl3
Cl
2t
100 MHz, CDCl3
200
150
100
50
0
PPM

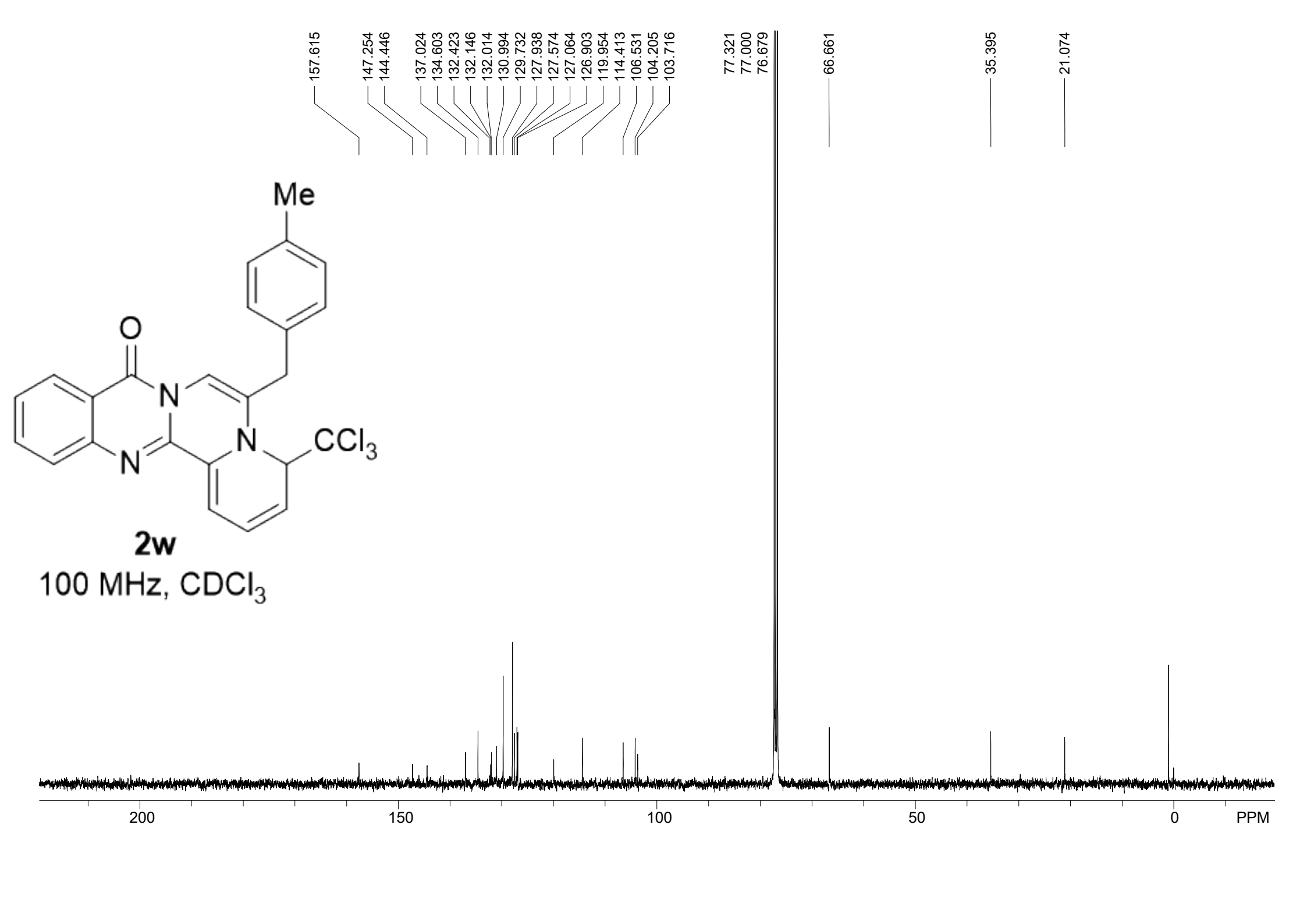

8.286
8.267
7.817
7.797
7.764
7.746
7.728
7.480
7.462
7.443
7.039
6.756
6.702
6.687
4.292
4.276
2.184
O
N
N
N
Me
CCl3
Me
2u
400 MHz, CDCl3
6.01
2.30
1.01
1.07
1.04
1.02
1.03
1.00
10
8
6
4
2
0
PPM

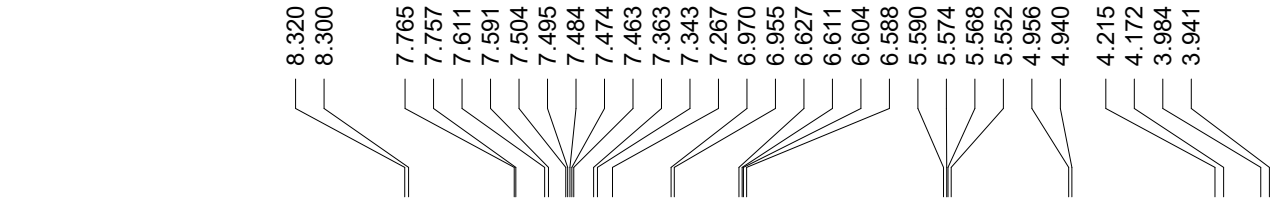

157.447
146.634
142.295
134.581
131.489
127.508
127.012
126.925
124.854
123.739
119.510
111.256
105.277
100.158
97.861
77.314
77.000
76.679
60.317
21.585
16.991
O
N
N
N
Me
CCl3
Me
2u
100 MHz, CDCl3
200
150
100
50
0
PPM

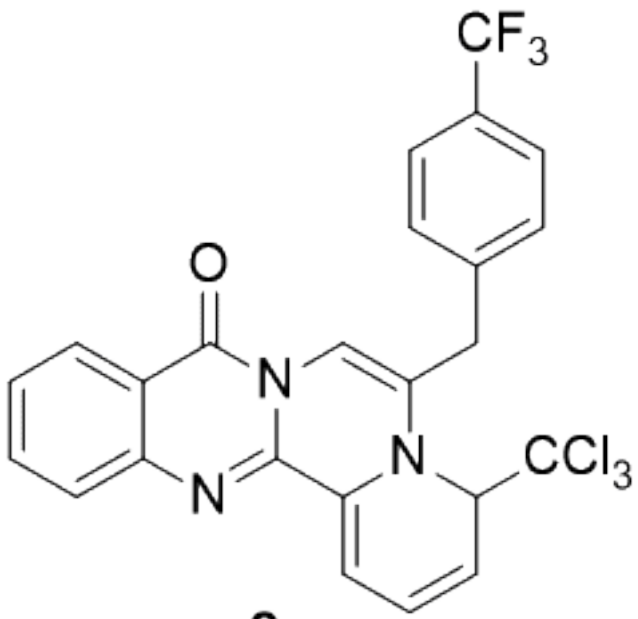

8.323
8.303
7.798
7.777
7.757
7.737
7.498
7.495
7.479
7.462
7.350
7.333
7.315
7.289
7.271
7.228
7.210
6.974
6.959
6.597
6.582
6.575
6.559
5.554
5.536
5.531
5.514
5.074
5.059
4.128
4.085
3.950
3.907
O
N
N
N
CCl3
2v
400 MHz, CDCl3
2.38
2.13
2.02
2.04
1.00
1.09
1.16
1.05
1.03
1.00
1.09
1.06
10
8
6
4
2
0
PPM


157.535
147.020
144.476
135.164
134.690
131.912
130.848
129.069
128.055
127.938
127.457
127.414
127.085
126.991
119.881
114.508
106.859
104.321
103.621
77.321
77.000
76.679
66.697
35.774
O
N
N
N
CCl3
2v
100 MHz, CDCl3
200
150
100
50
0
PPM


8.317
8.297
7.756
7.746
7.489
7.479
7.469
7.460
7.449
7.260
7.232
7.138
7.118
7.102
7.082
6.938
6.923
6.601
6.585
6.578
6.563
5.571
5.554
5.548
5.532
5.095
5.079
4.076
4.033
3.899
3.857
2.329
Me
O
N
N
N
CCl3
2w
400 MHz, CDCl3
1.05
2.04
1.05
4.02
0.98
1.00
1.00
1.01
1.00
1.01
3.09
10
8
6
4
2
0
PPM

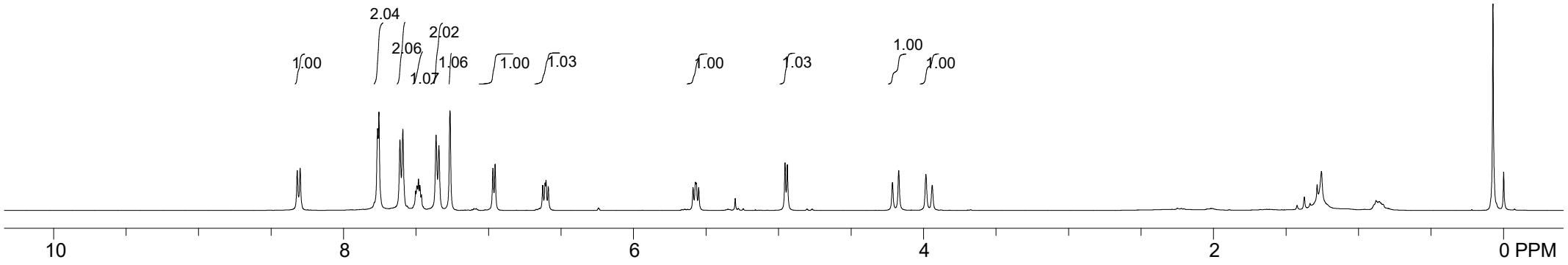

157.615
147.254
144.446
137.024
134.603
132.423
132.146
132.014
130.994
129.732
127.938
127.574
127.064
126.903
119.954
114.413
106.531
104.205
103.716
77.321
77.000
76.679
66.661
35.395
21.074
Me
O
N
N
N
CCl3
2w
100 MHz, CDCl3
200
150
100
50
0
PPM

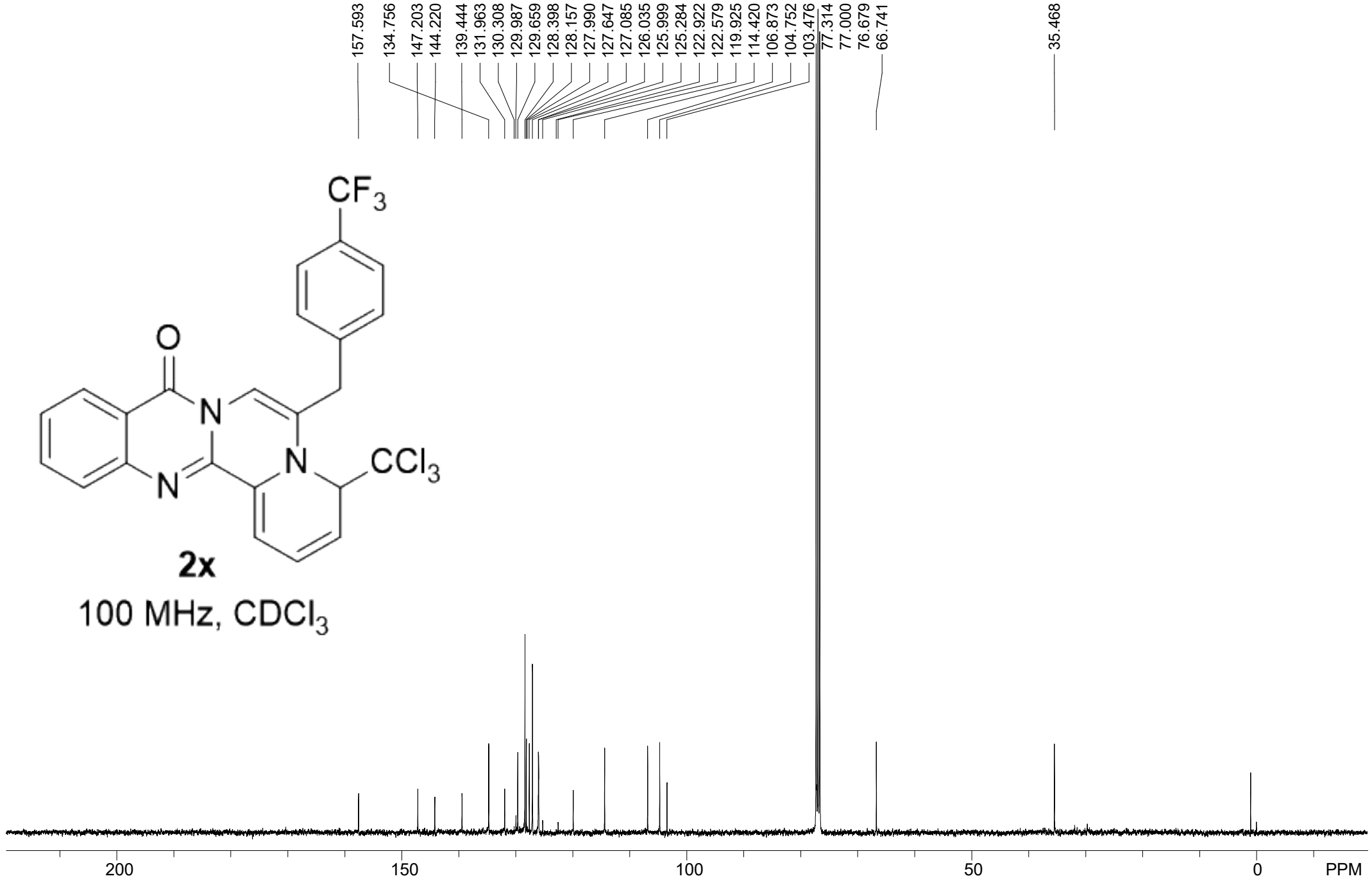


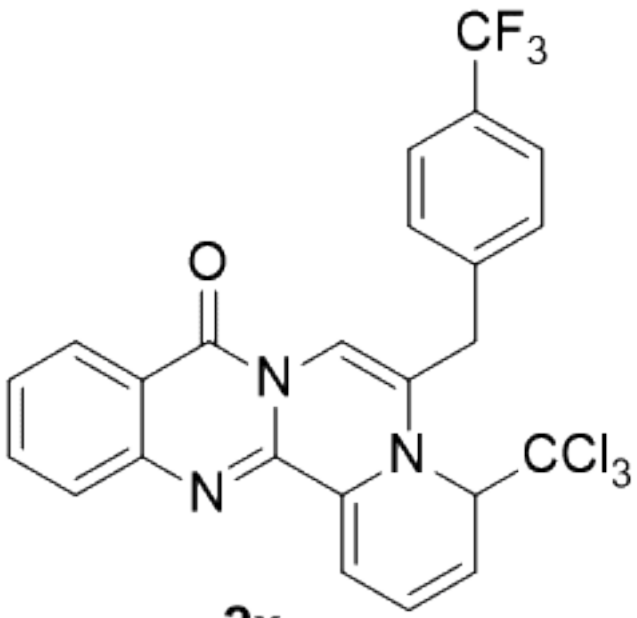


2x

400 MHz, $CDCl_3$

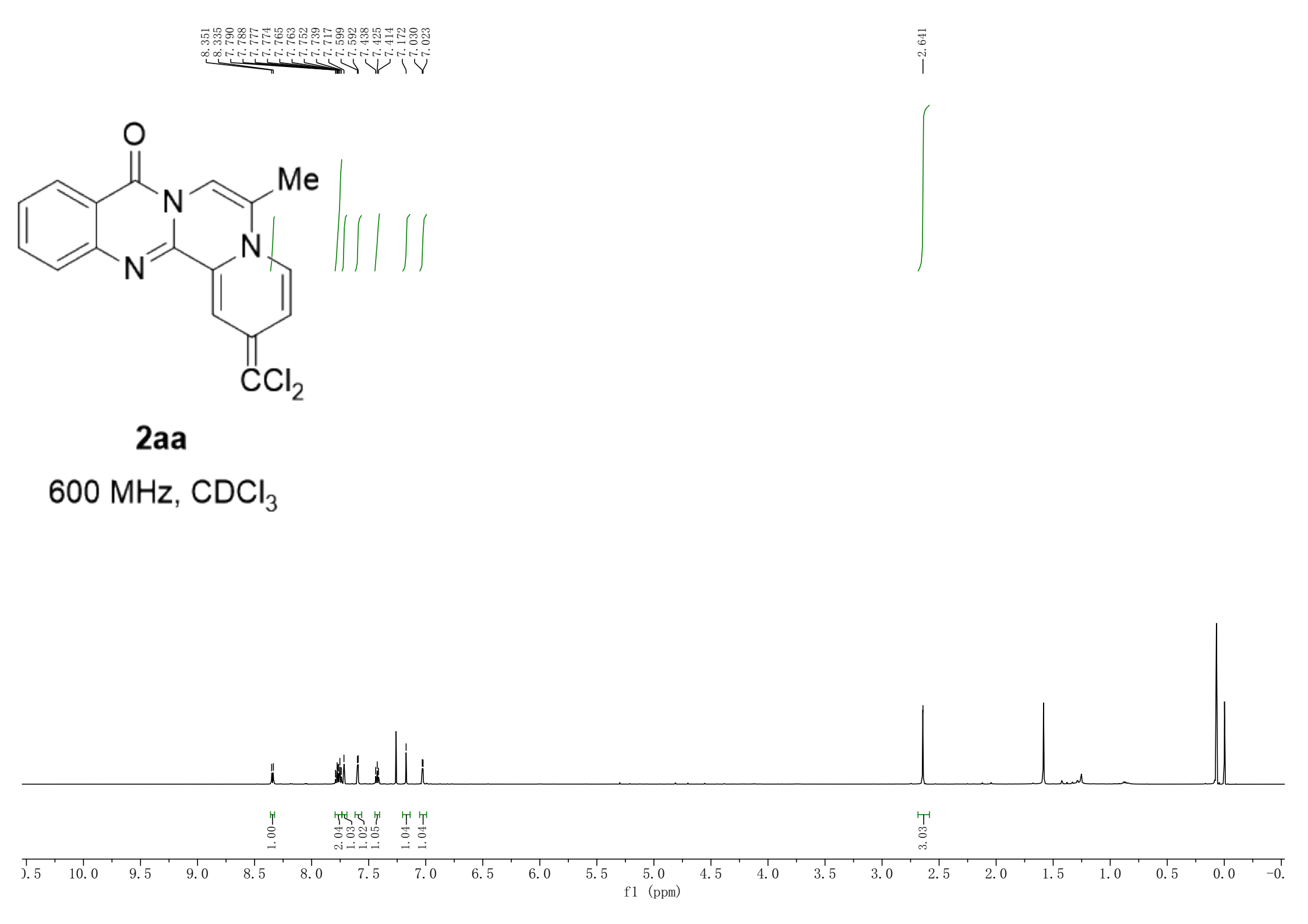


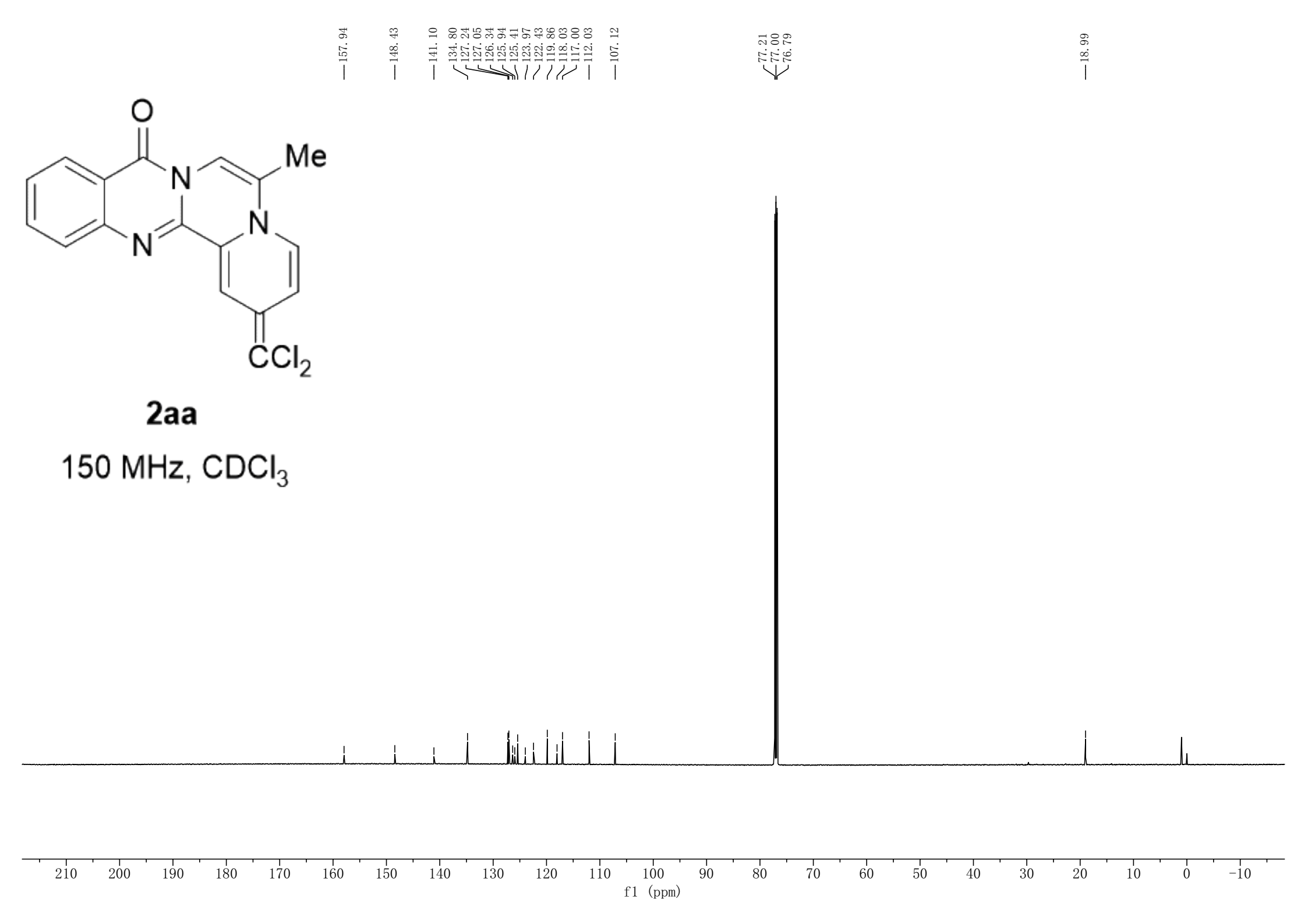

157.593
134.756
147.203
144.220
139.444
131.963
130.308
129.987
129.659
128.398
128.157
127.990
127.647
127.085
126.035
125.999
125.284
122.922
122.579
119.925
114.420
106.873
104.752
103.476
77.314
77.000
76.679
66.741
35.468
CF3
O
N
N
N
CCl3
2x
100 MHz, CDCl3
200
150
100
50
0
PPM

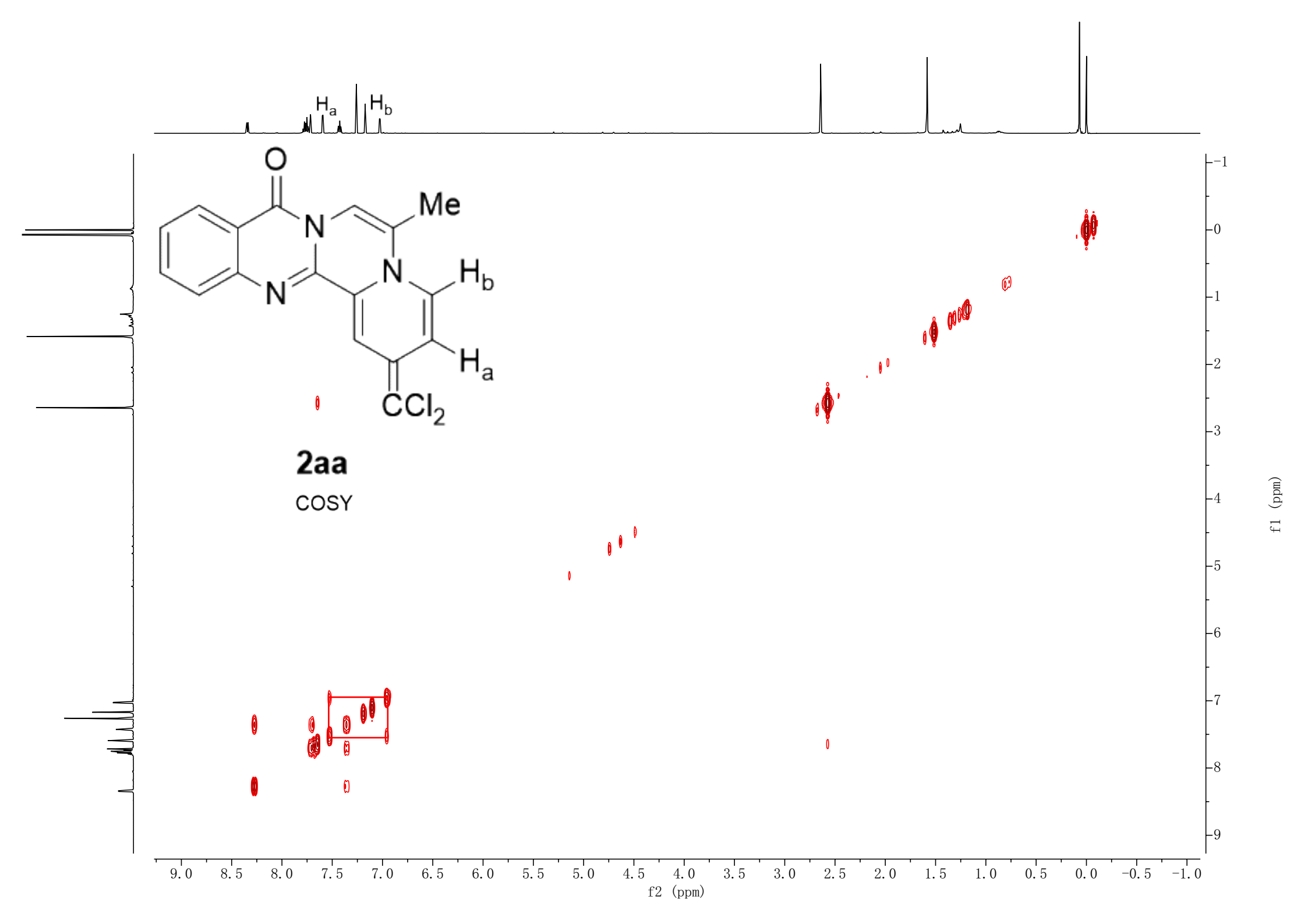


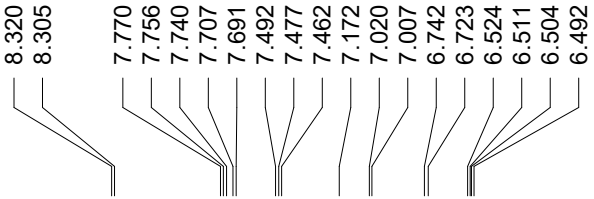
2x

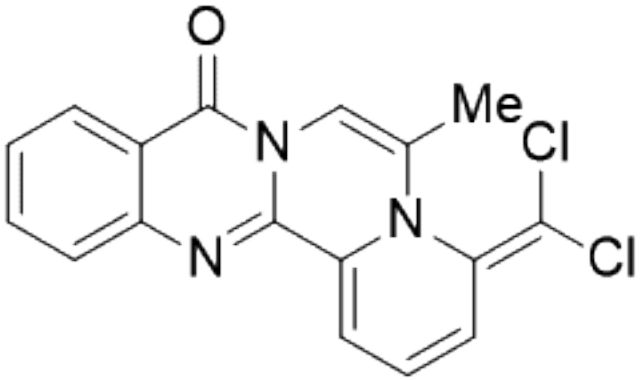
376 MHz, $CDCl_3$


8.351
8.335
7.790
7.788
7.777
7.774
7.765
7.763
7.752
7.739
7.717
7.599
7.592
7.438
7.425
7.414
7.172
7.030
7.023
2.641
O
N
Me
N
N
CCl2
2aa
600 MHz, CDCl3
1.00
2.04
1.03
1.02
1.05
1.04
1.04
3.03
f1 (ppm)


157.94
148.43
141.10
134.80
127.24
127.05
126.34
125.94
125.41
123.97
122.43
119.86
118.03
117.00
112.03
107.12
77.21
77.00
76.79
18.99
O
N
Me
N
N
CCl2
2aa
150 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

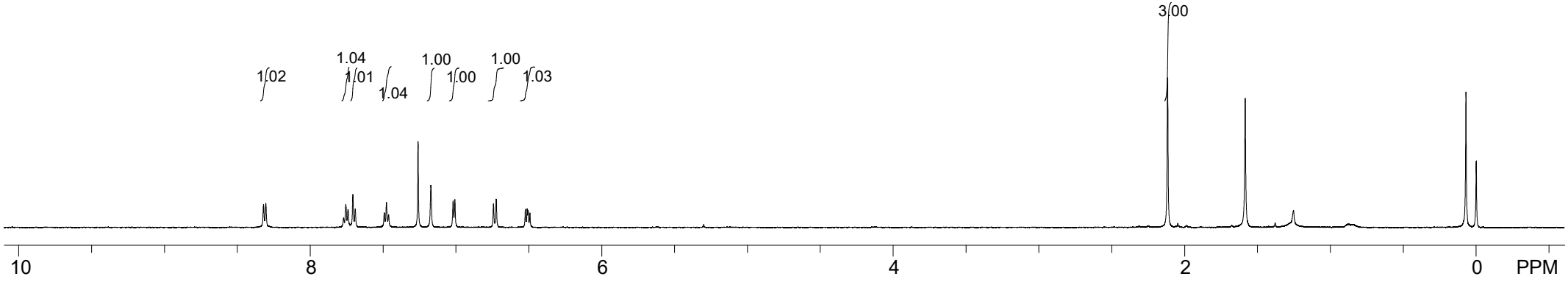

Ha
Hb
O
N
Me
N
Hb
Ha
CCl2
2aa
COSY
f2 (ppm)
f1 (ppm)

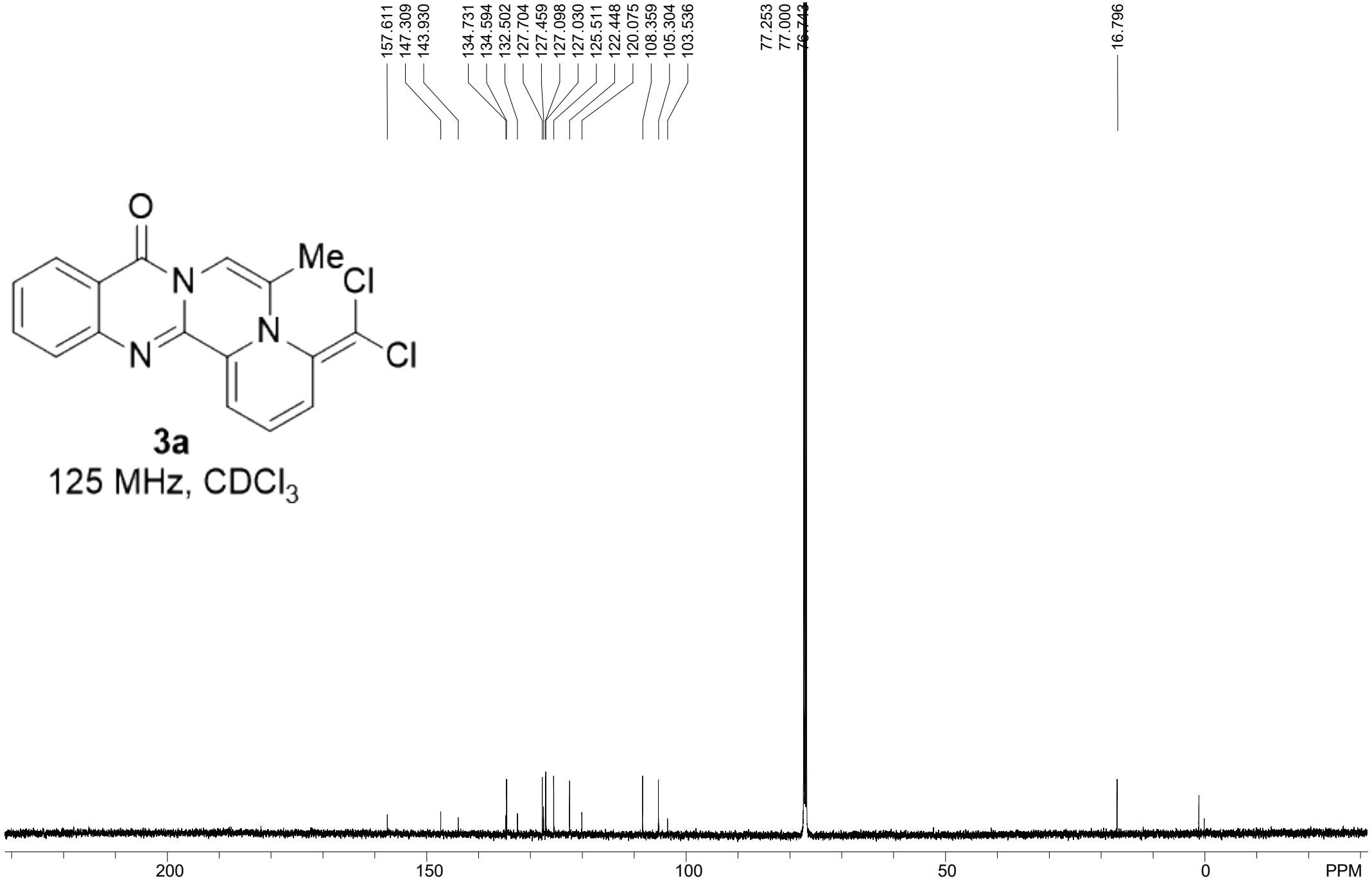


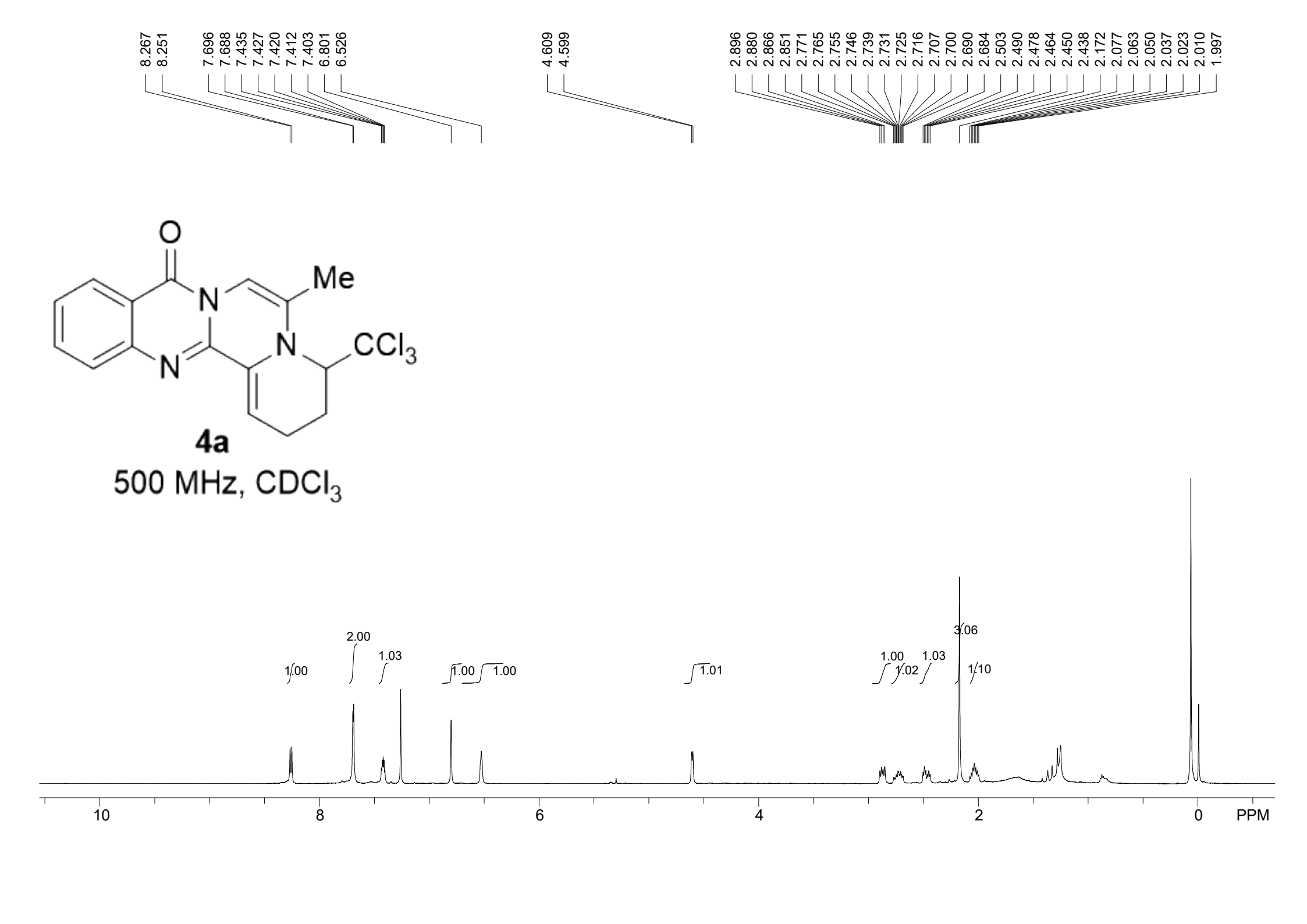


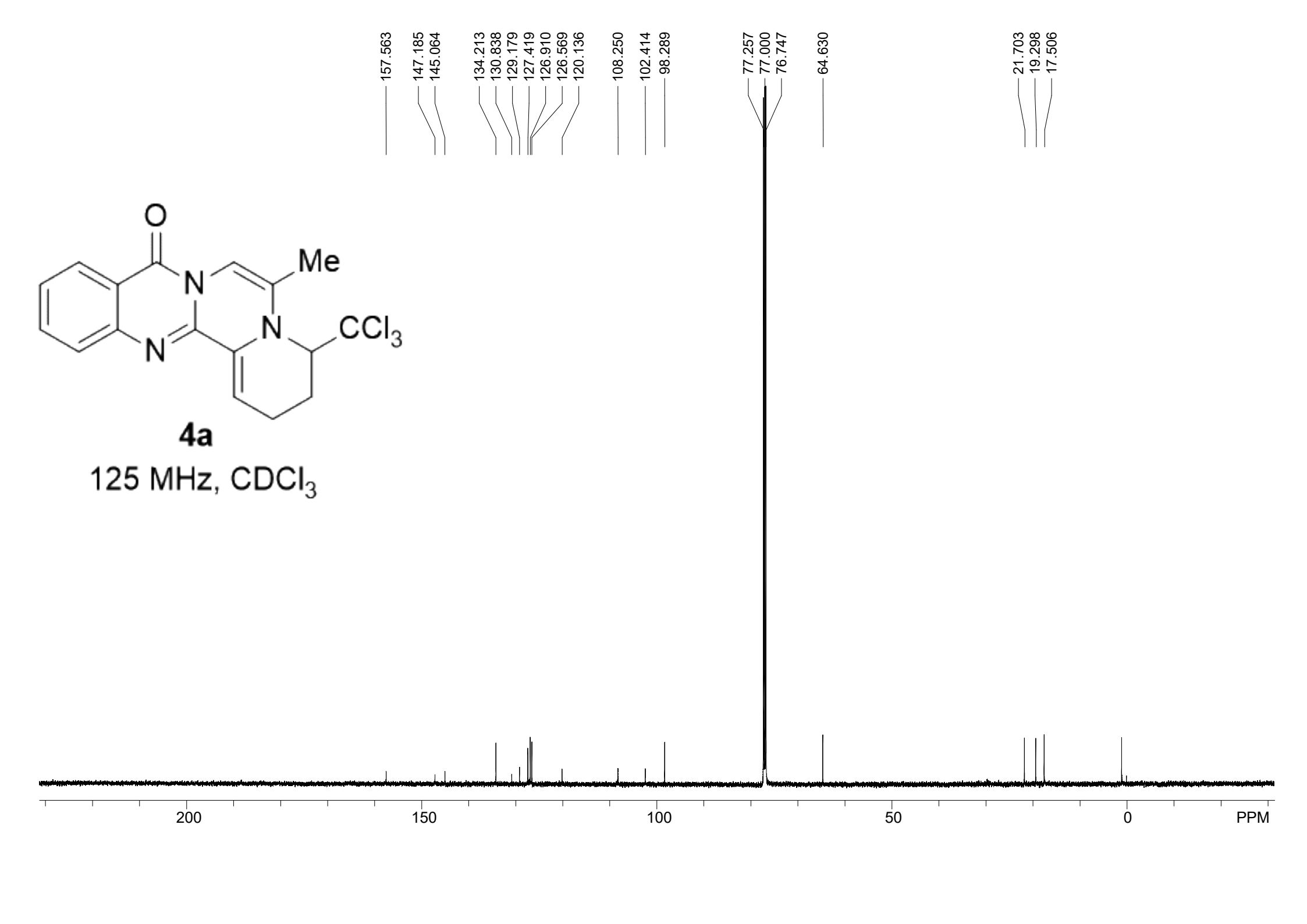
3a

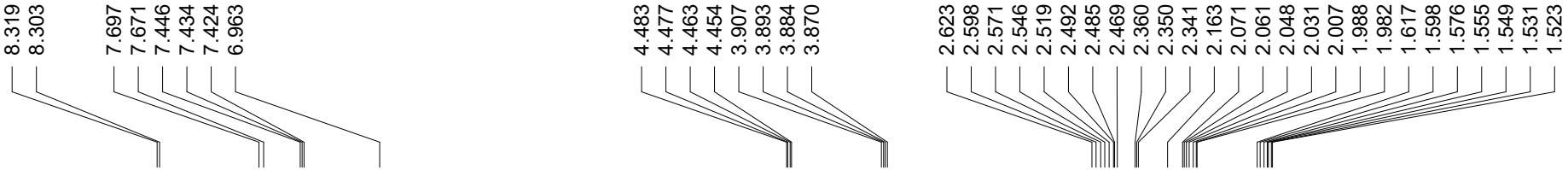
500 MHz, $CDCl_3$

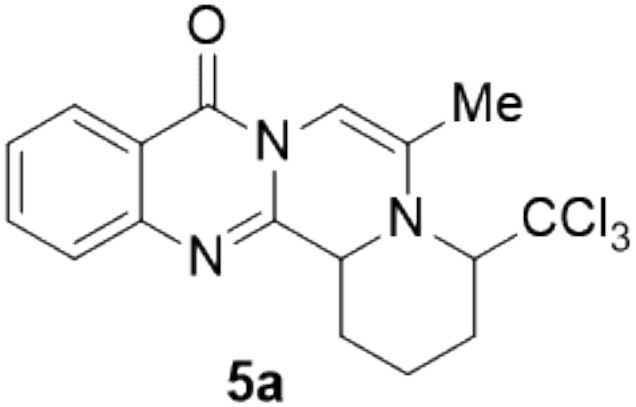



157.611
147.309
143.930
134.731
134.594
132.502
127.704
127.459
127.098
127.030
125.511
122.448
120.075
108.359
105.304
103.536
77.253
77.000
76.743
16.796
O
N
Me
Cl
N
N
Cl
3a
125 MHz, CDCl3
200
150
100
50
0
PPM


8.267
8.251
7.696
7.688
7.435
7.427
7.420
7.412
7.403
6.801
6.526
4.609
4.599
2.896
2.880
2.866
2.851
2.771
2.765
2.755
2.746
2.739
2.731
2.725
2.716
2.707
2.700
2.690
2.684
2.503
2.490
2.478
2.464
2.450
2.438
2.172
2.077
2.063
2.050
2.037
2.023
2.010
1.997
O
N
Me
N
N
CCl3
4a
500 MHz, CDCl3
1.00
2.00
1.03
1.00
1.00
1.01
1.00
1.02
1.03
3.06
1.10
10
8
6
4
2
0
PPM

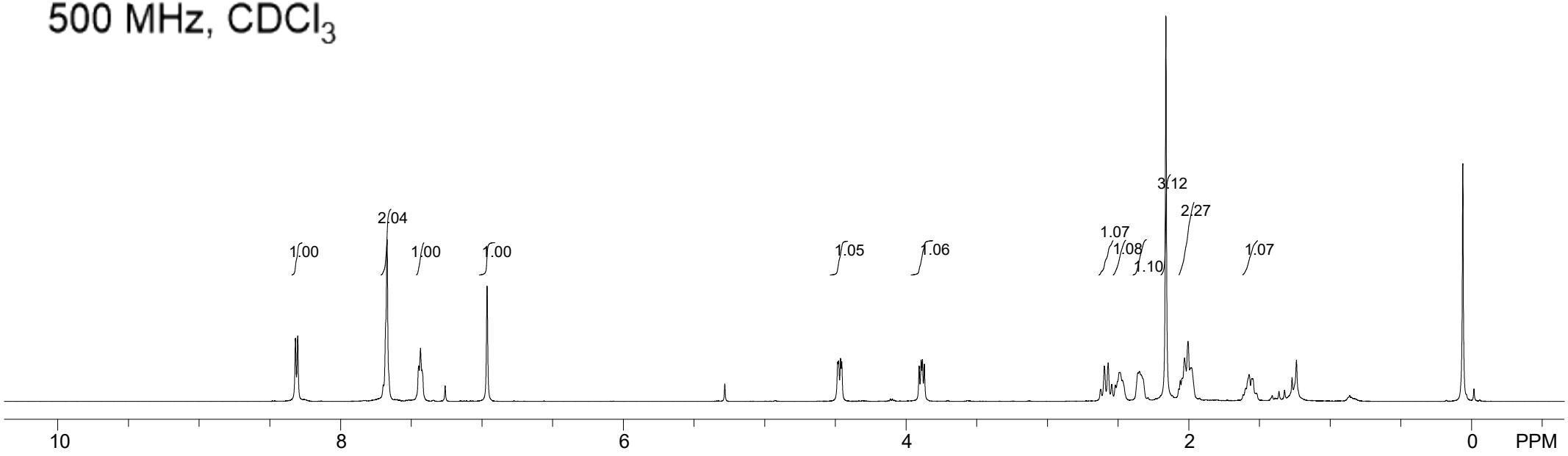

157.563
147.185
145.064
134.213
130.838
129.179
127.419
126.910
126.569
120.136
108.250
102.414
98.289
77.257
77.000
76.747
64.630
21.703
19.298
17.506
O
N
Me
N
N
CCl3
4a
125 MHz, CDCl3
200
150
100
50
0
PPM

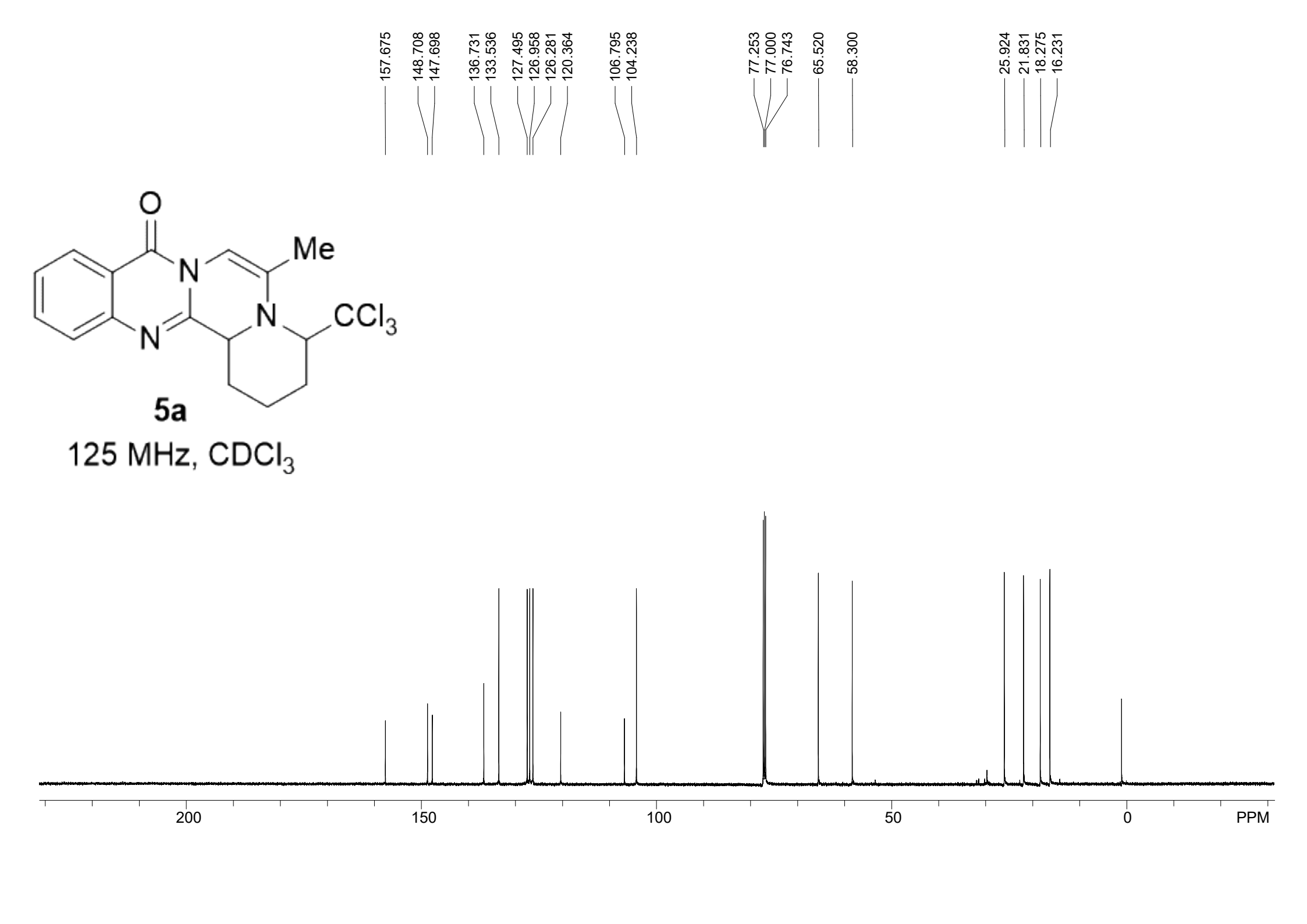


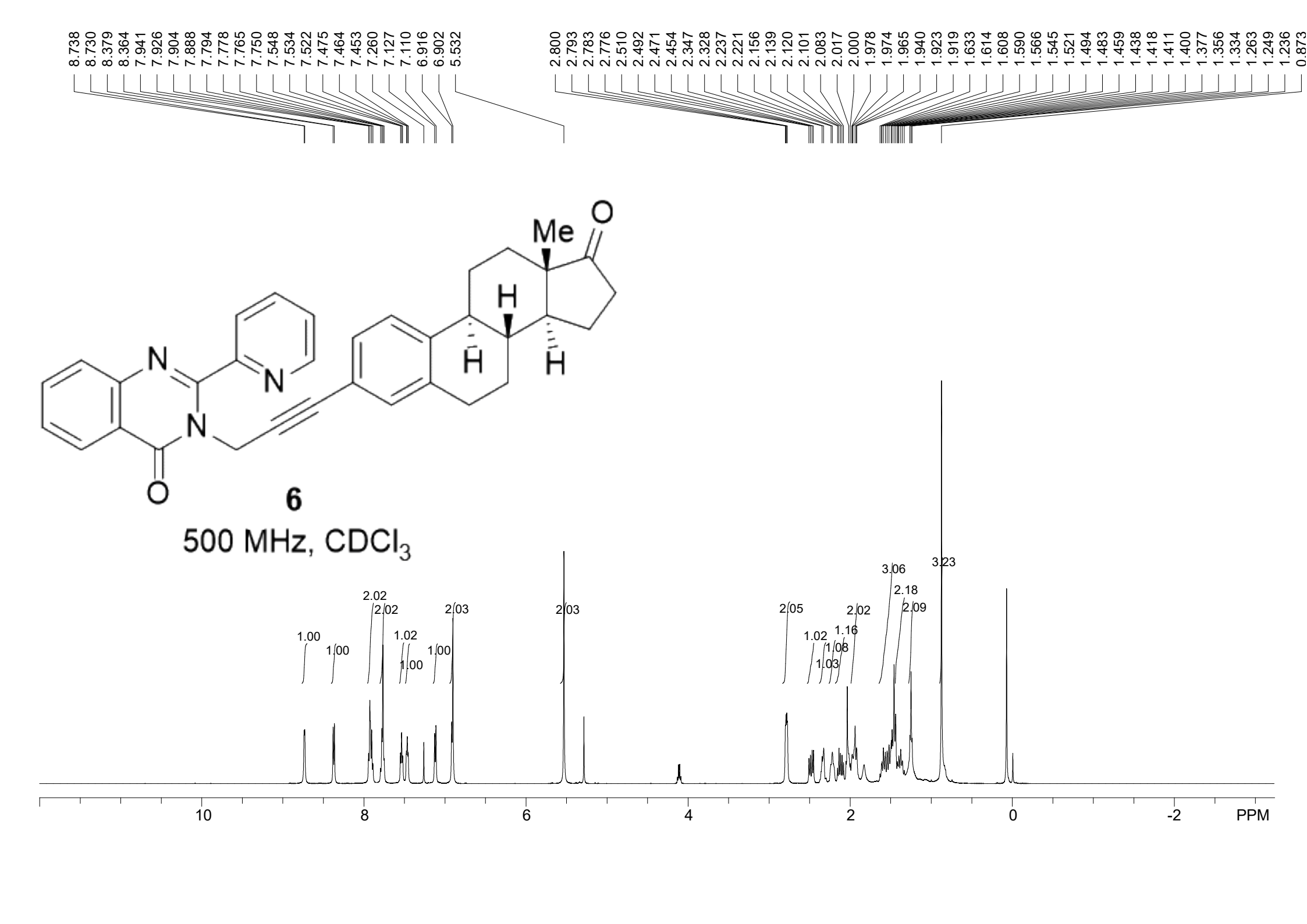


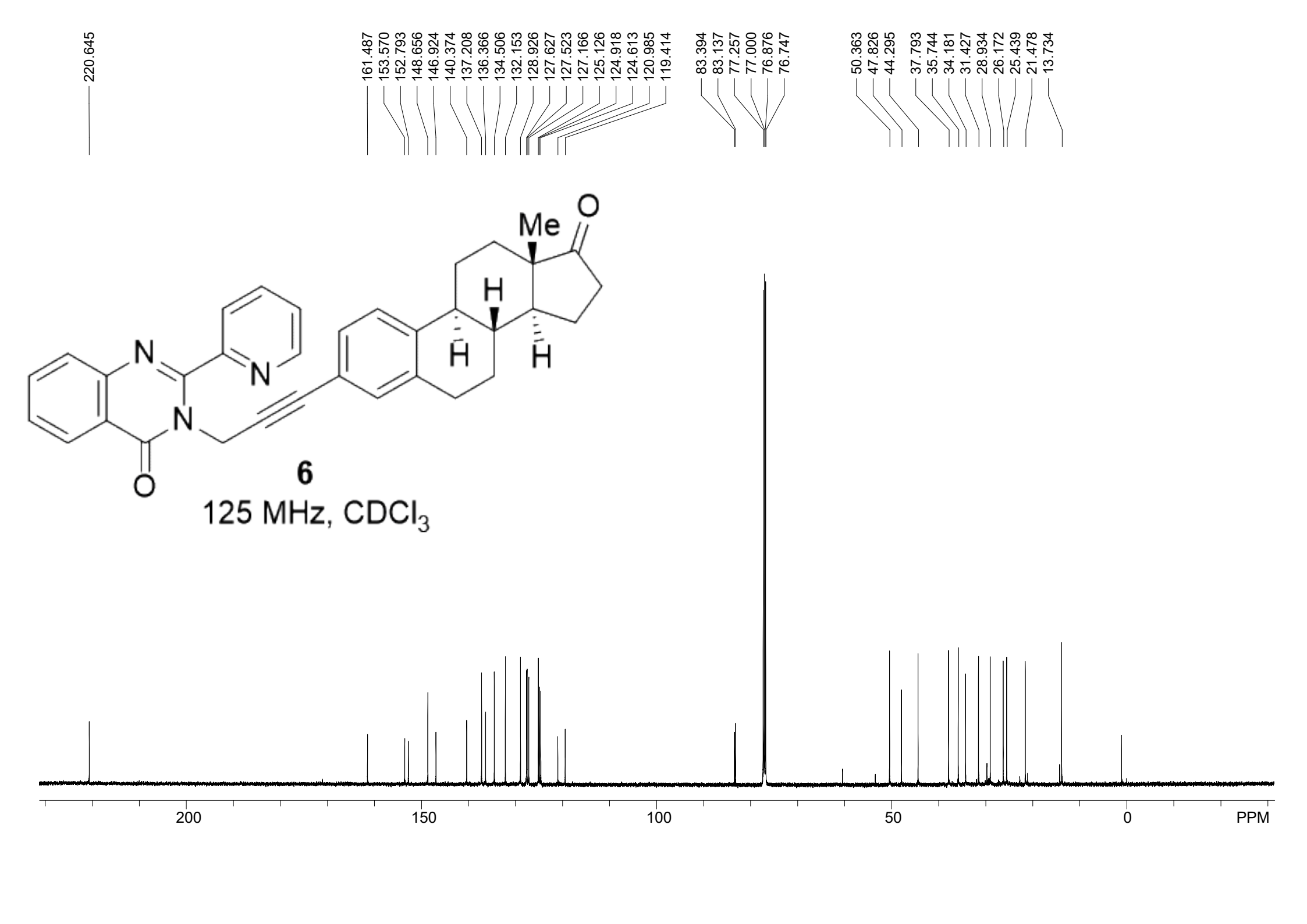
5a

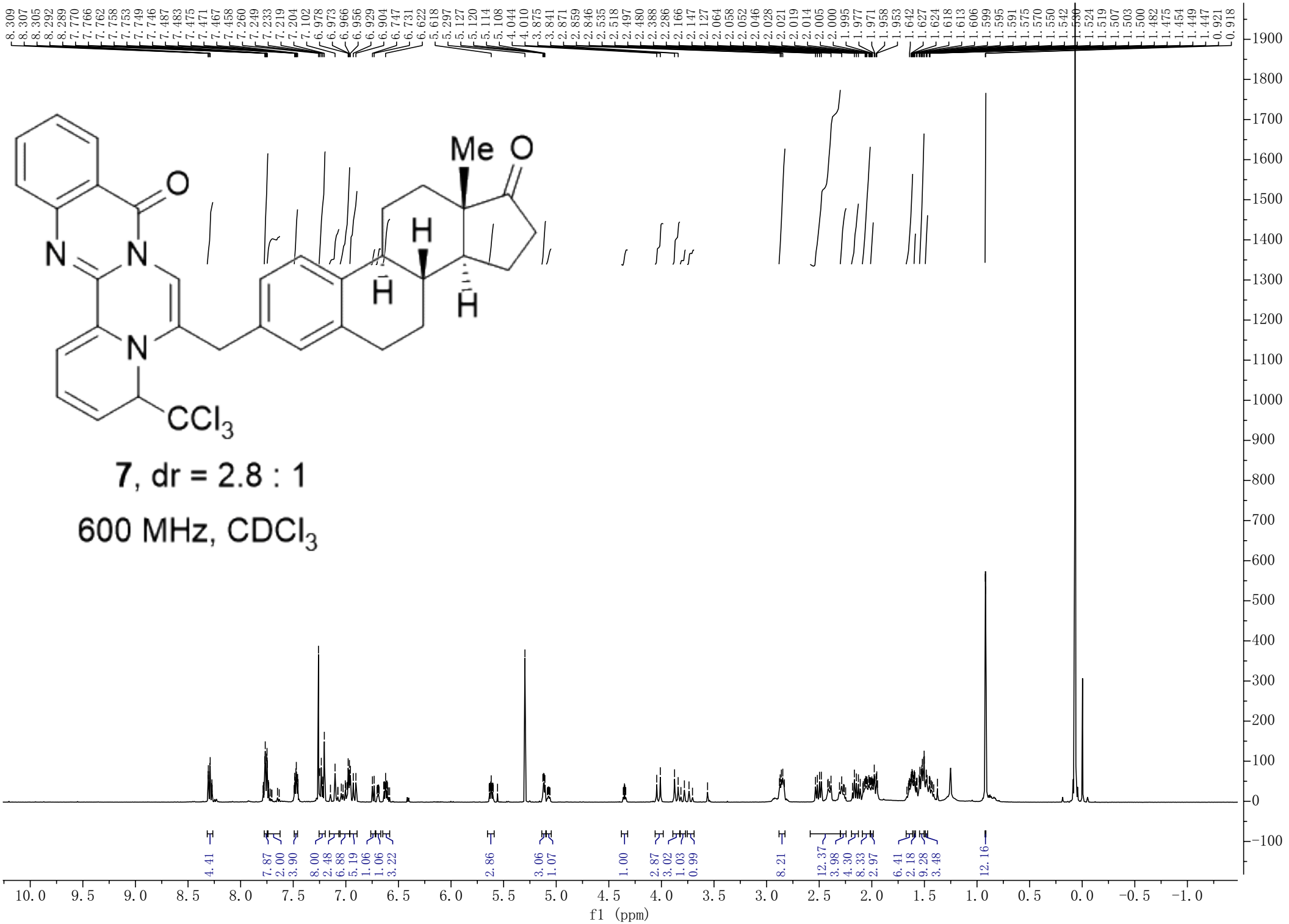
500 MHz, $CDCl_3$

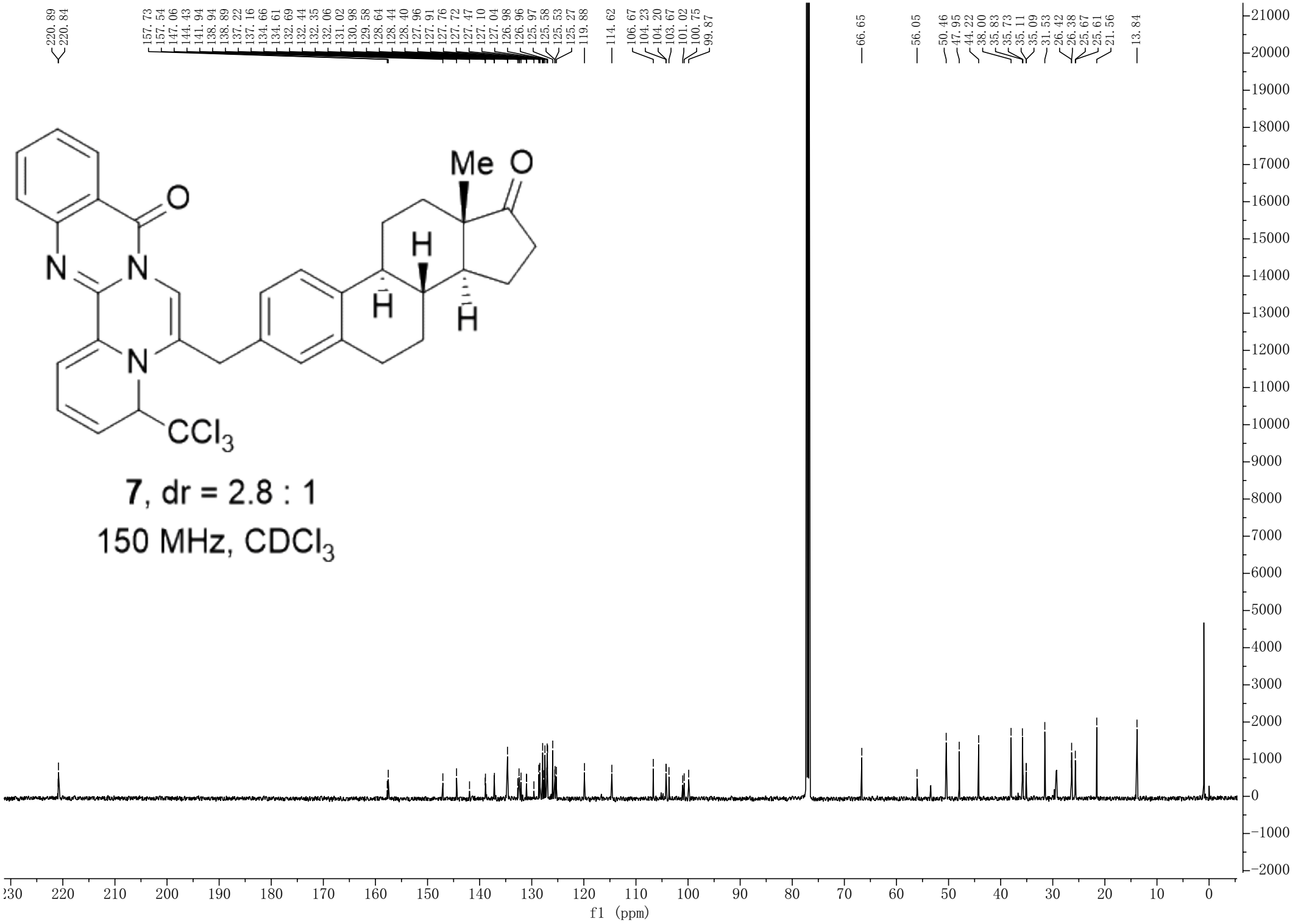


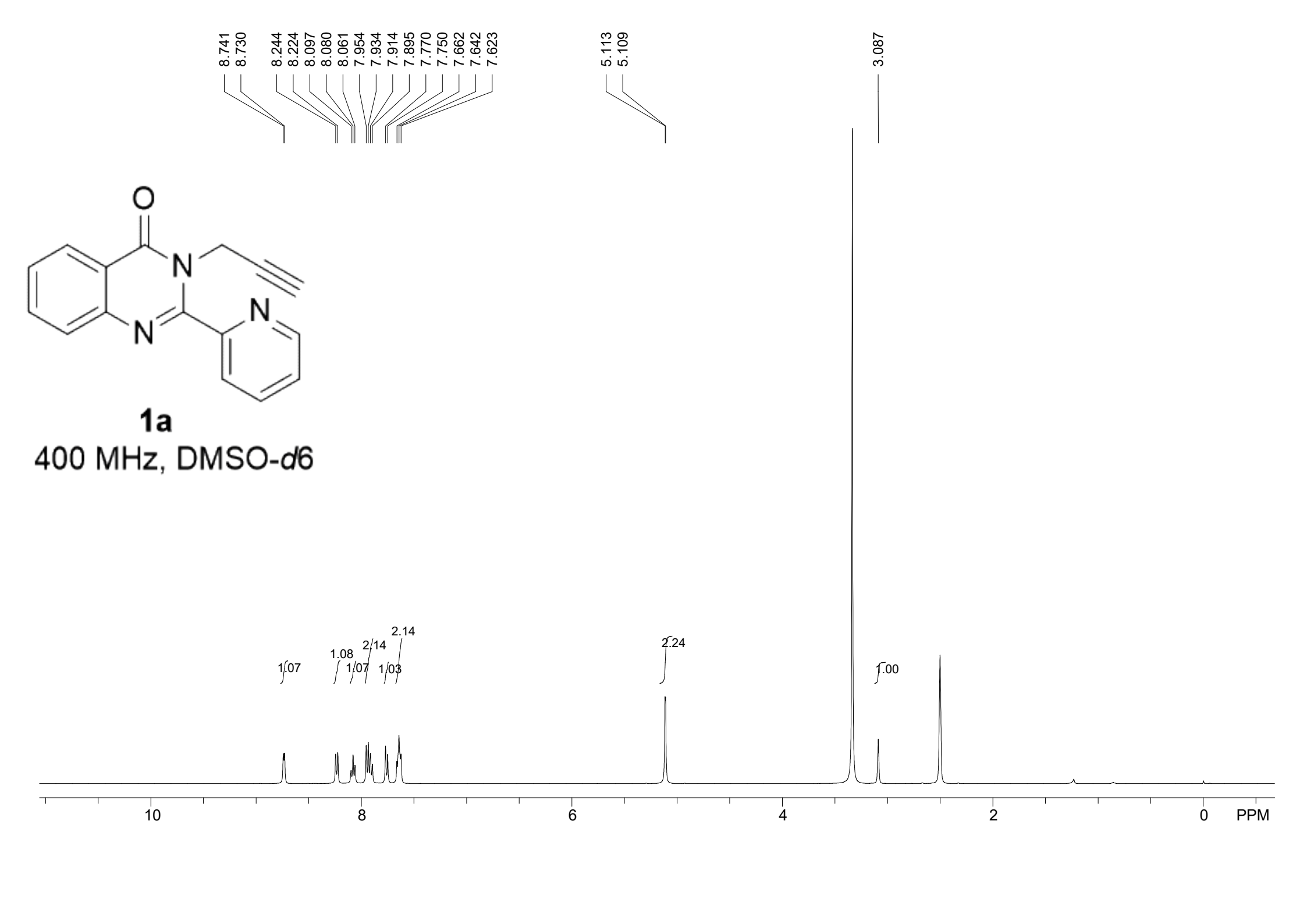

157.675
148.708
147.698
136.731
133.536
127.495
126.958
126.281
120.364
106.795
104.238
77.253
77.000
76.743
65.520
58.300
25.924
21.831
18.275
16.231
O
N
Me
N
N
CCl3
5a
125 MHz, CDCl3
200
150
100
50
0
PPM

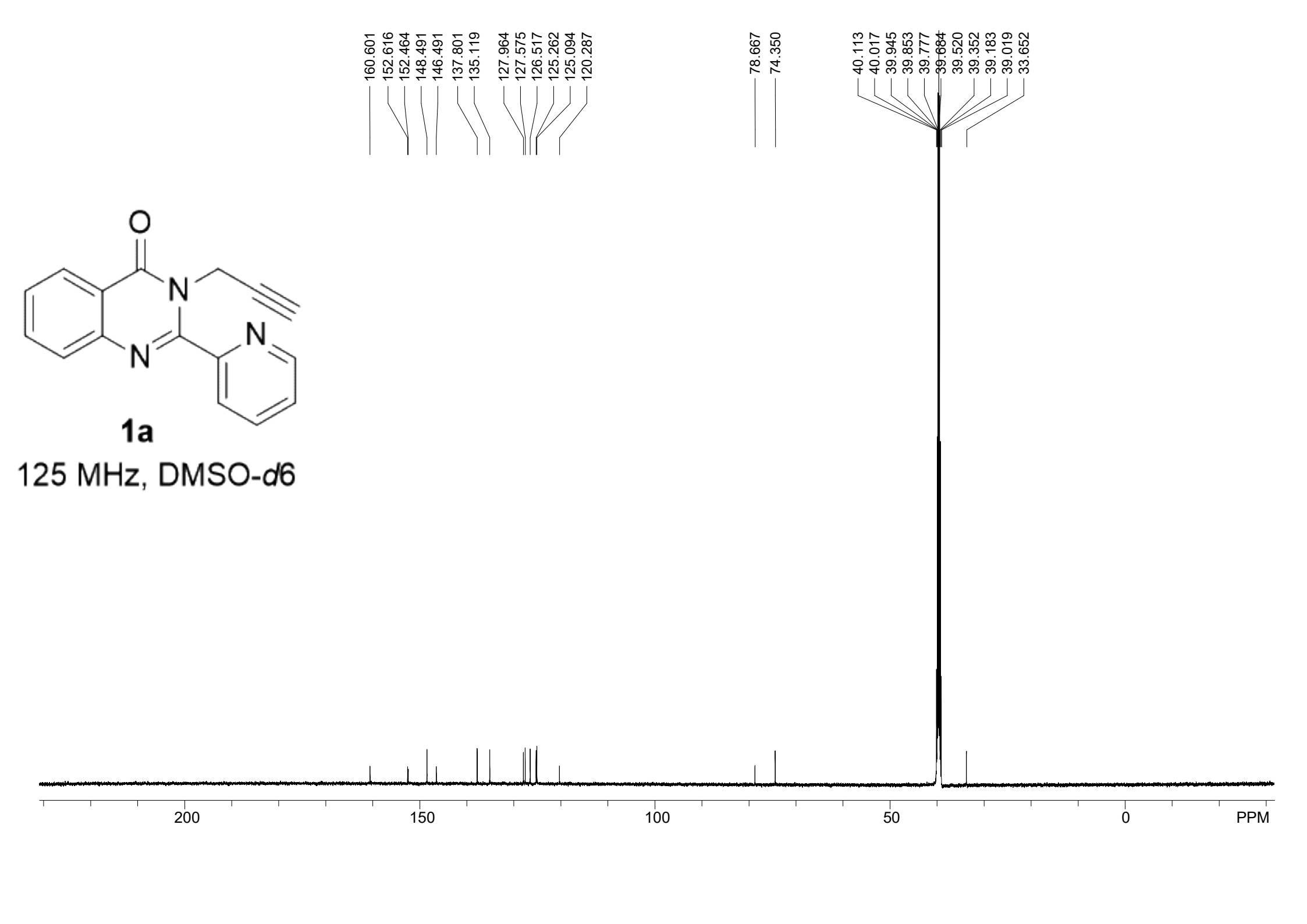

8.738
8.730
8.379
8.364
7.941
7.926
7.904
7.888
7.794
7.778
7.765
7.750
7.548
7.534
7.522
7.475
7.464
7.453
7.260
7.127
7.110
6.916
6.902
5.532
2.800
2.793
2.783
2.776
2.510
2.492
2.471
2.454
2.347
2.328
2.237
2.221
2.156
2.139
2.120
2.101
2.083
2.017
2.000
1.978
1.974
1.965
1.940
1.923
1.919
1.633
1.614
1.608
1.590
1.566
1.545
1.521
1.494
1.483
1.459
1.438
1.418
1.411
1.400
1.377
1.356
1.334
1.263
1.249
1.236
0.873
Me
O
H
H
H
N
N
N
O
6
500 MHz, CDCl3
1.00
1.00
2.02
2.02
1.02
1.00
1.00
2.03
2.03
2.05
1.02
1.03
1.08
1.16
2.02
3.06
2.18
2.09
3.23
10
8
6
4
2
0
-2
PPM

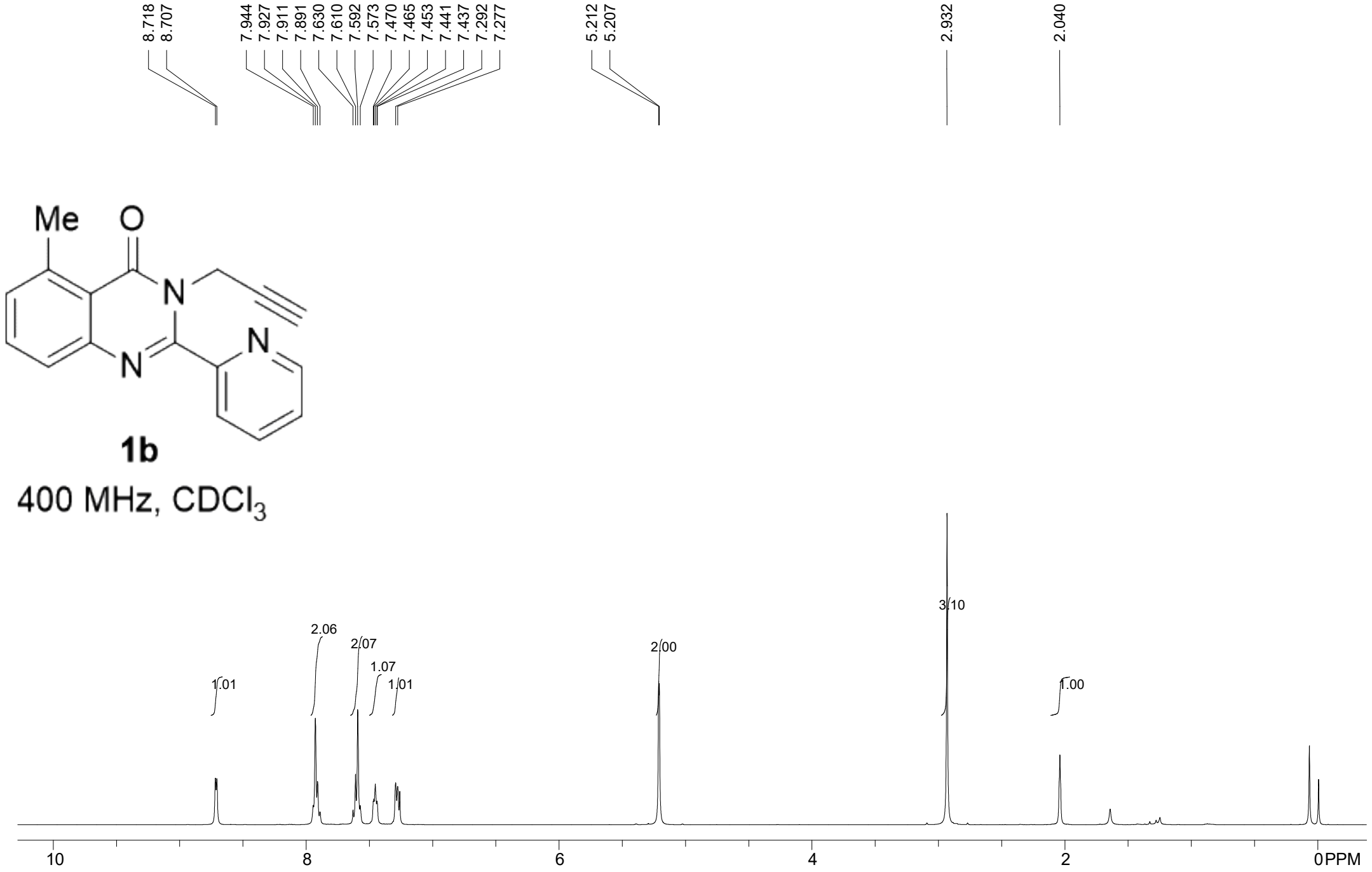

220.645
161.487
153.570
152.793
148.656
146.924
140.374
137.208
136.366
134.506
132.153
128.926
127.627
127.523
127.166
125.126
124.918
124.613
120.985
119.414
83.394
83.137
77.257
77.000
76.876
76.747
50.363
47.826
44.295
37.793
35.744
34.181
31.427
28.934
26.172
25.439
21.478
13.734
Me
O
H
H
H
N
N
N
O
6
125 MHz, CDCl3
200
150
100
50
0
PPM

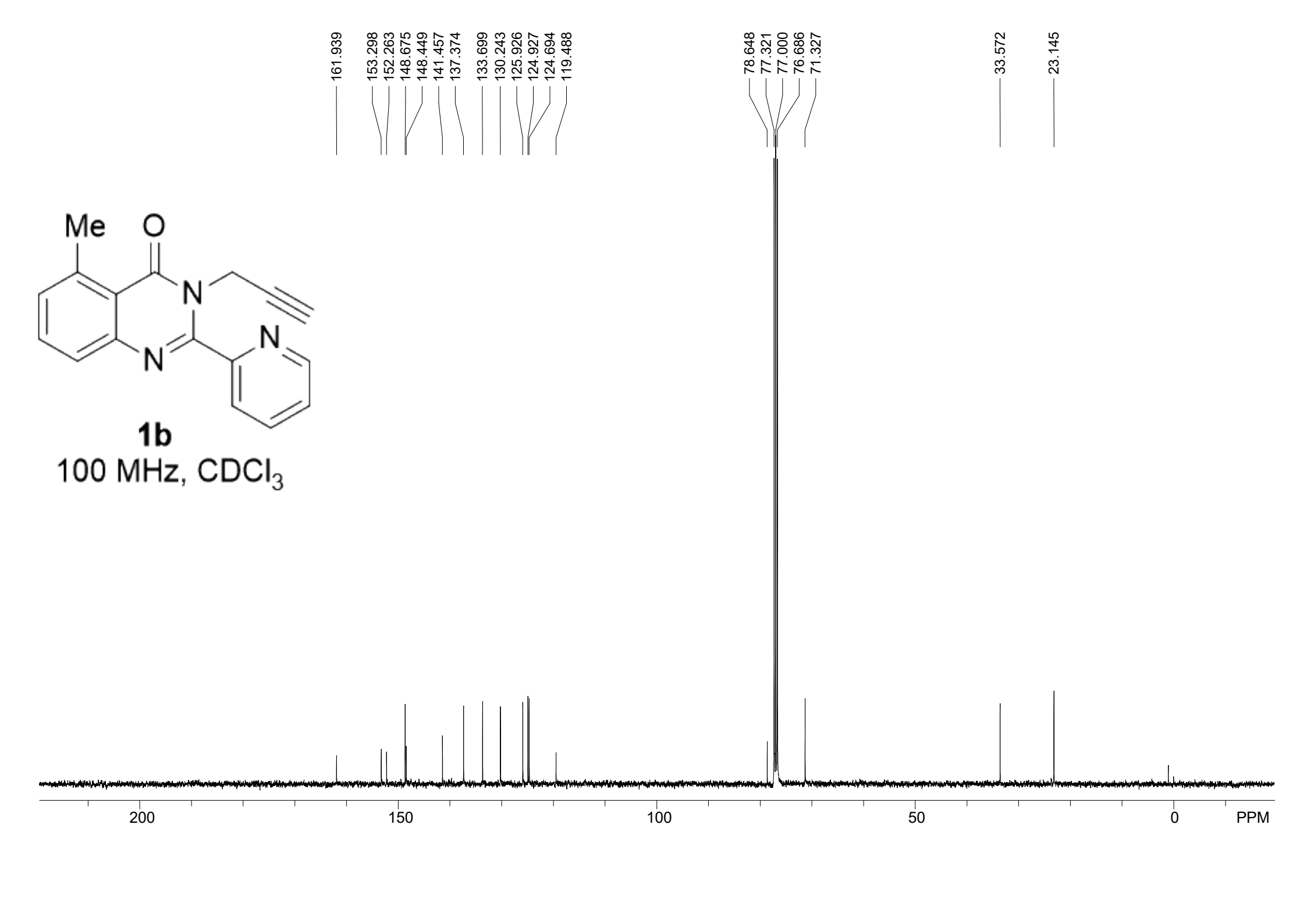

Me O
O
N
N
N
H
H
H
CCl3
7, dr = 2.8 : 1
600 MHz, CDCl3
f1 (ppm)

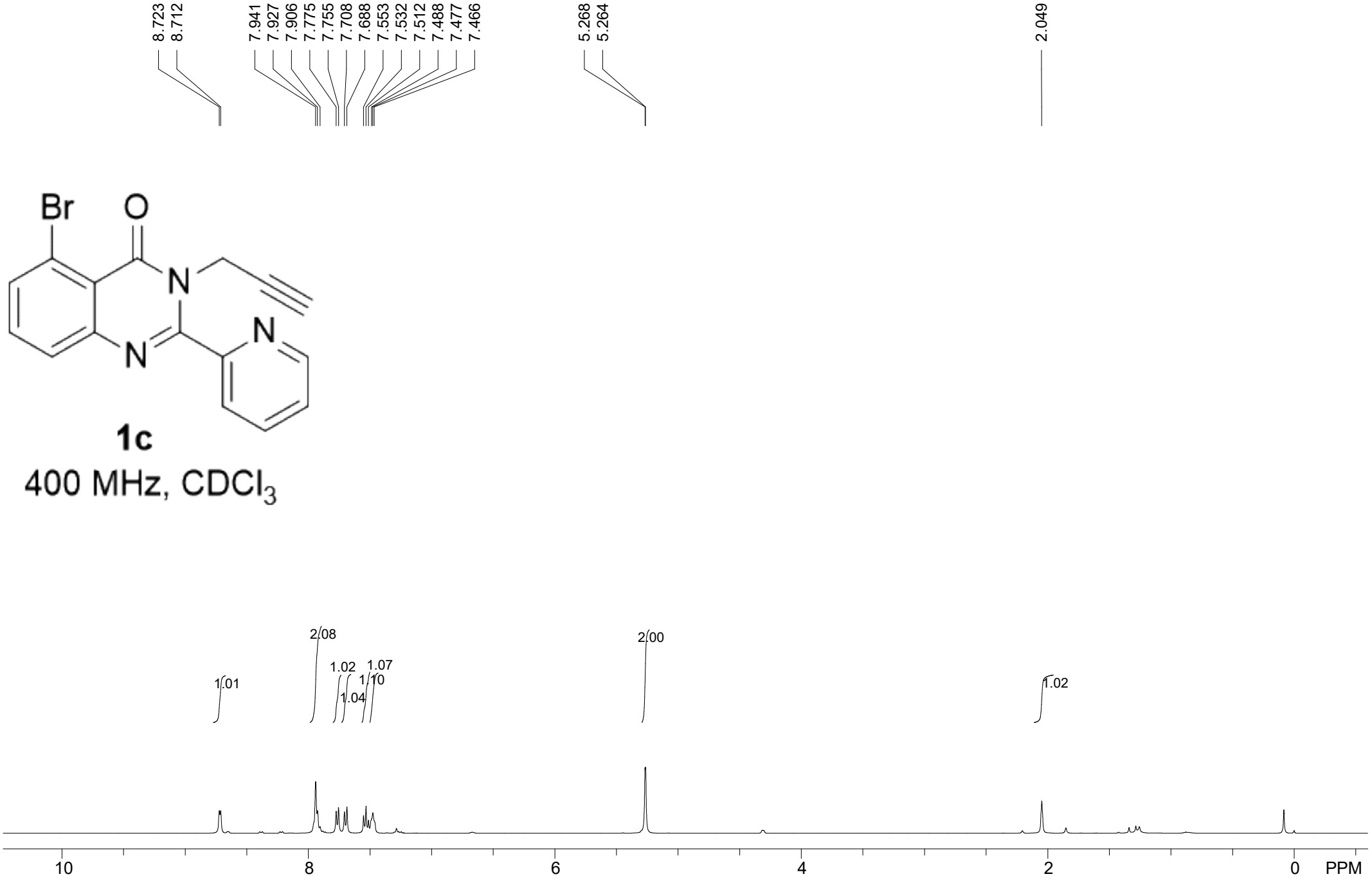

220.89
220.84
157.73
157.54
147.06
144.43
141.94
138.94
138.89
137.22
137.16
134.66
134.61
132.69
132.44
132.35
132.06
131.02
130.98
129.58
128.64
128.44
128.40
127.96
127.91
127.76
127.72
127.47
127.10
127.04
126.98
126.96
125.97
125.58
125.53
125.27
119.88
114.62
106.67
104.23
104.20
103.67
101.02
100.75
99.87
66.65
56.05
50.46
47.95
44.22
38.00
35.83
35.73
35.11
35.09
31.53
26.42
26.38
25.67
25.61
21.56
13.84
Me
O
O
N
N
N
H
H
H
CCl3
7, dr = 2.8 : 1
150 MHz, CDCl3
f1 (ppm)


8.741
8.730
8.244
8.224
8.097
8.080
8.061
7.954
7.934
7.914
7.895
7.770
7.750
7.662
7.642
7.623
5.113
5.109
3.087
O
N
N
N
1a
400 MHz, DMSO-d6
1.07
1.08
1.07
2.14
1.03
2.14
2.24
1.00
10
8
6
4
2
0
PPM

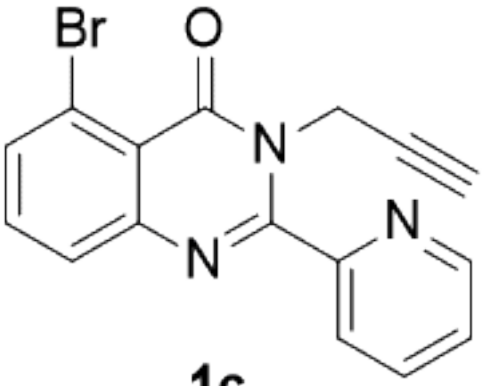

160.601
152.616
152.464
148.491
146.491
137.801
135.119
127.964
127.575
126.517
125.262
125.094
120.287
78.667
74.350
40.113
40.017
39.945
39.853
39.777
39.684
39.520
39.352
39.183
39.019
33.652
O
N
N
N
1a
125 MHz, DMSO-d6
200
150
100
50
0
PPM


8.718
8.707
7.944
7.927
7.911
7.891
7.630
7.610
7.592
7.573
7.470
7.465
7.453
7.441
7.437
7.292
7.277
5.212
5.207
2.932
2.040
Me
O
N
N
N
1b
400 MHz, CDCl3
1.01
2.06
2.07
1.07
1.01
2.00
3.10
1.00
10
8
6
4
2
0
PPM


161.939
153.298
152.263
148.675
148.449
141.457
137.374
133.699
130.243
125.926
124.927
124.694
119.488
78.648
77.321
77.000
76.686
71.327
33.572
23.145
Me
O
N
N
N
1b
100 MHz, CDCl3
200
150
100
50
0
PPM

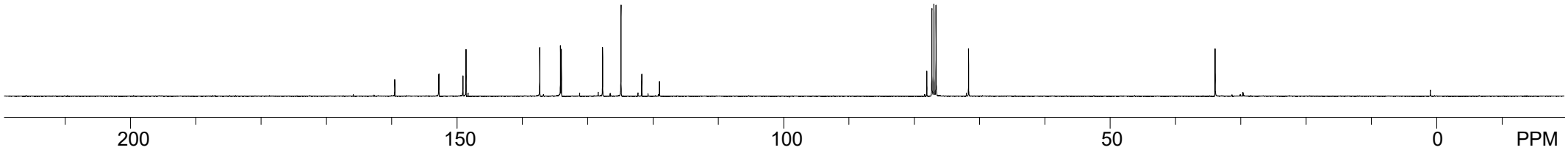

8.723
8.712
7.941
7.927
7.906
7.775
7.755
7.708
7.688
7.553
7.532
7.512
7.488
7.477
7.466
5.268
5.264
2.049
Br
O
N
N
N
1c
400 MHz, CDCl3
1.01
2.08
1.02
1.07
1.10
1.04
2.00
1.02
10
8
6
4
2
0
PPM

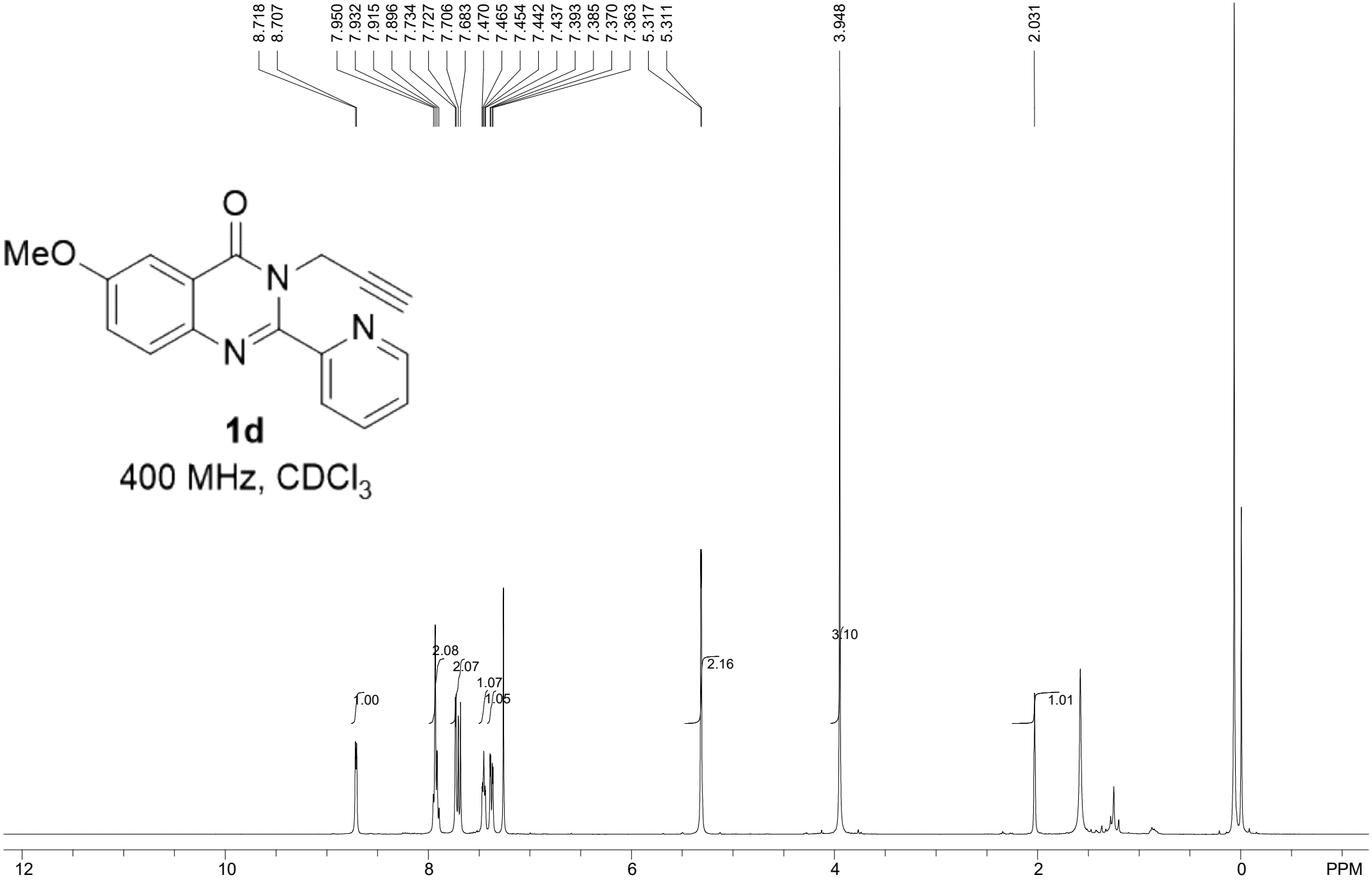
159.540
152.803
152.773
149.098
148.632
137.352
134.173
134.034
127.720
124.905
121.726
119.021
78.094
77.314
77.000
76.679
71.699
33.915

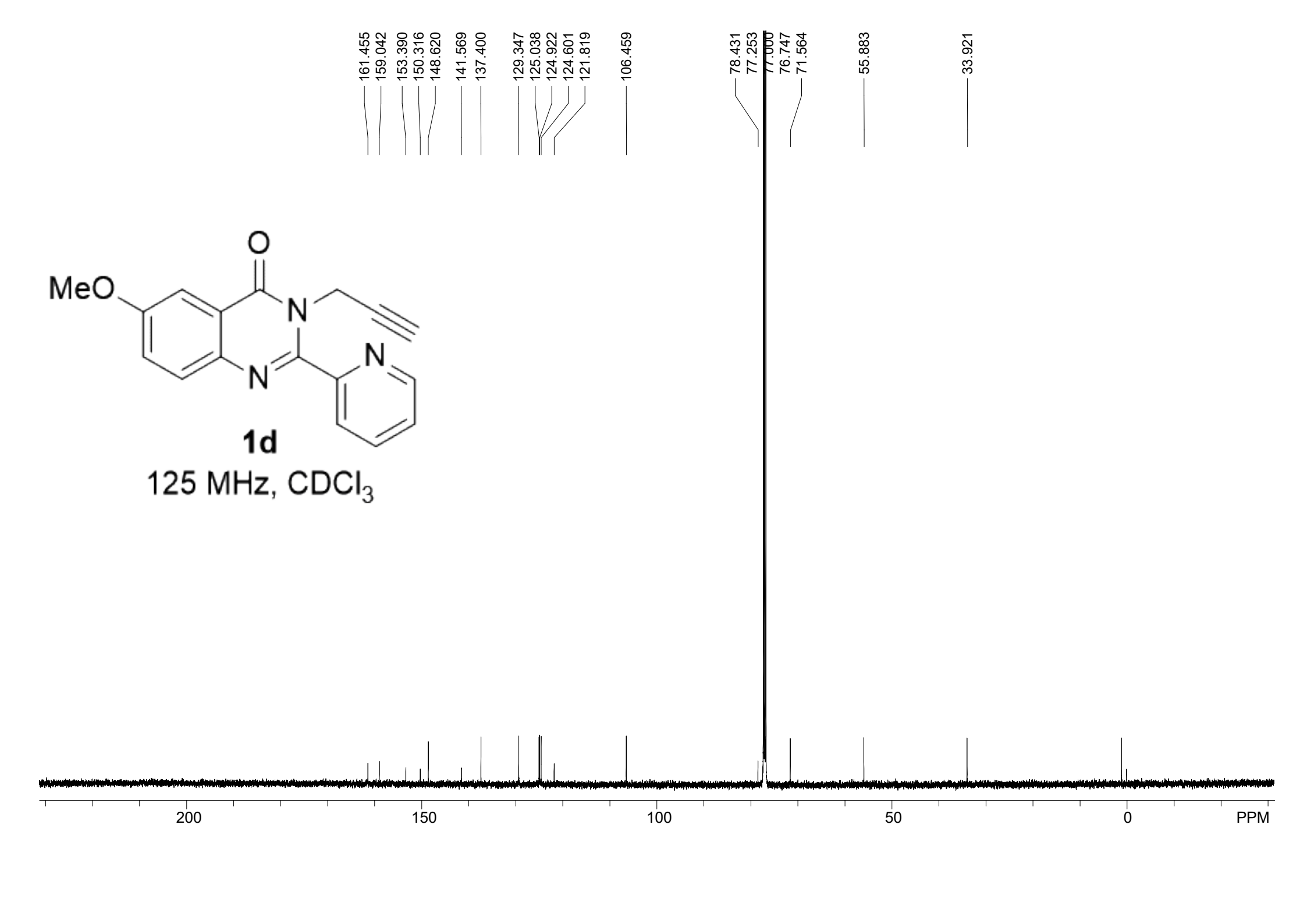


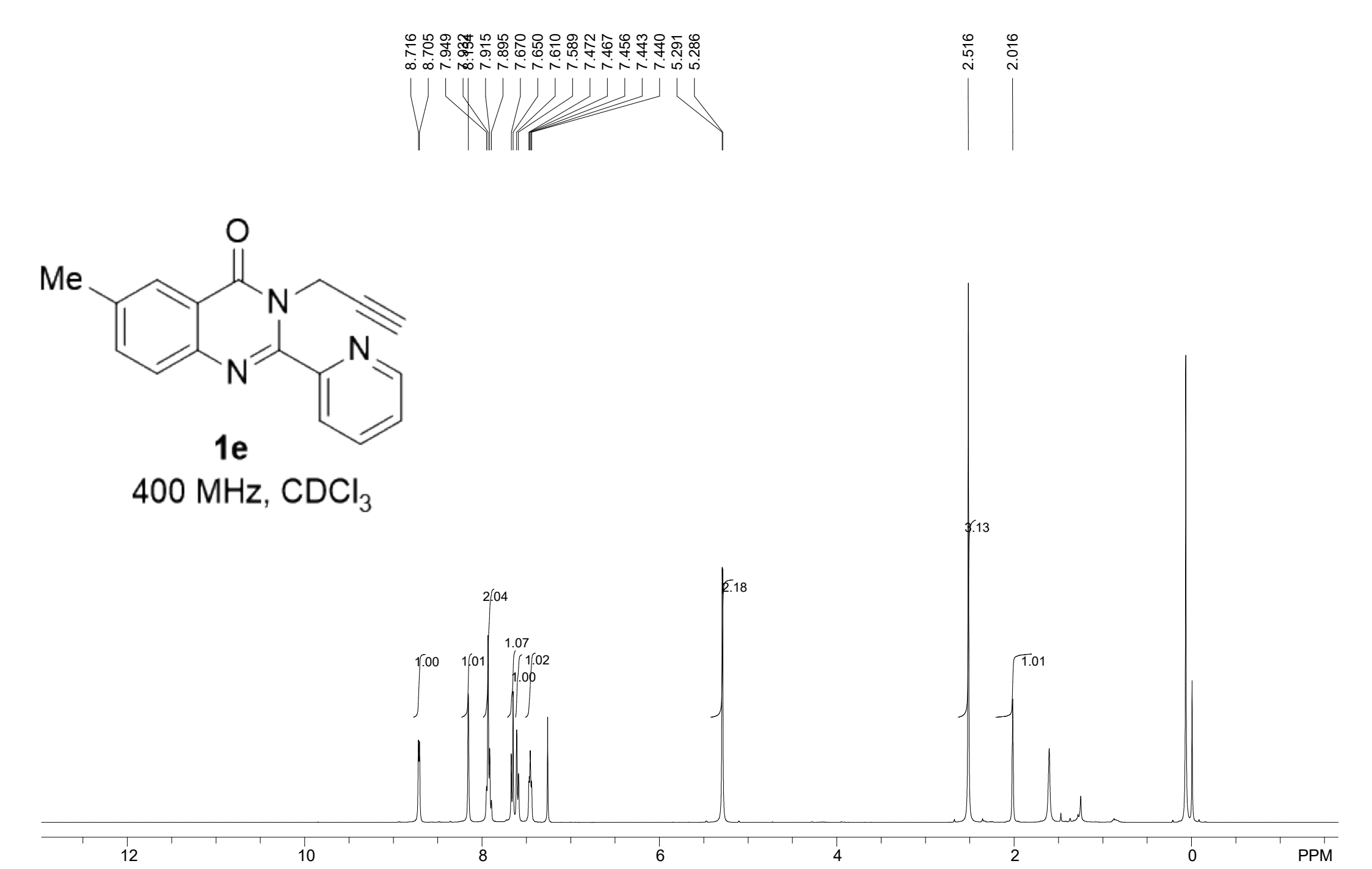
1c

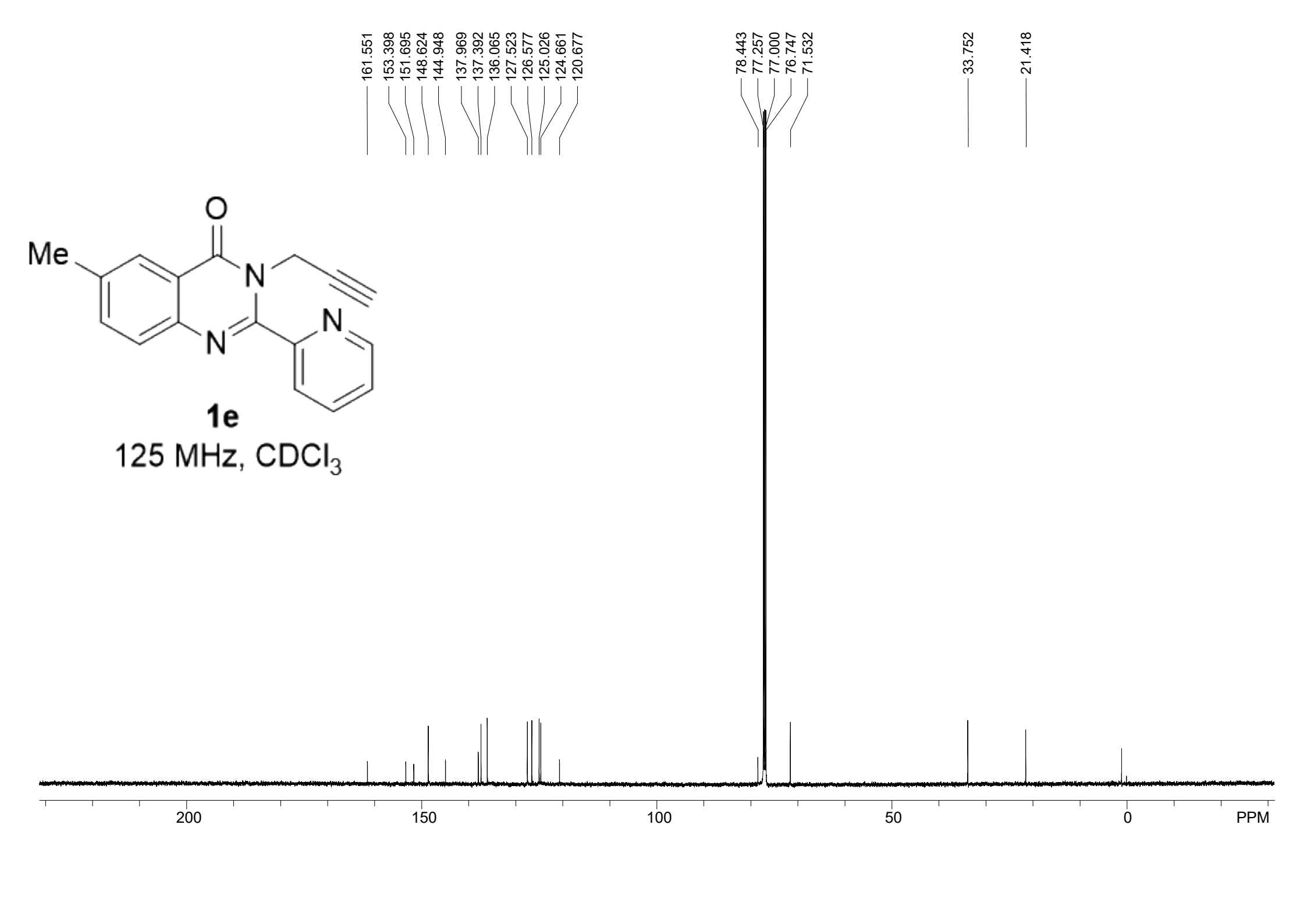
100 MHz, $CDCl_3$

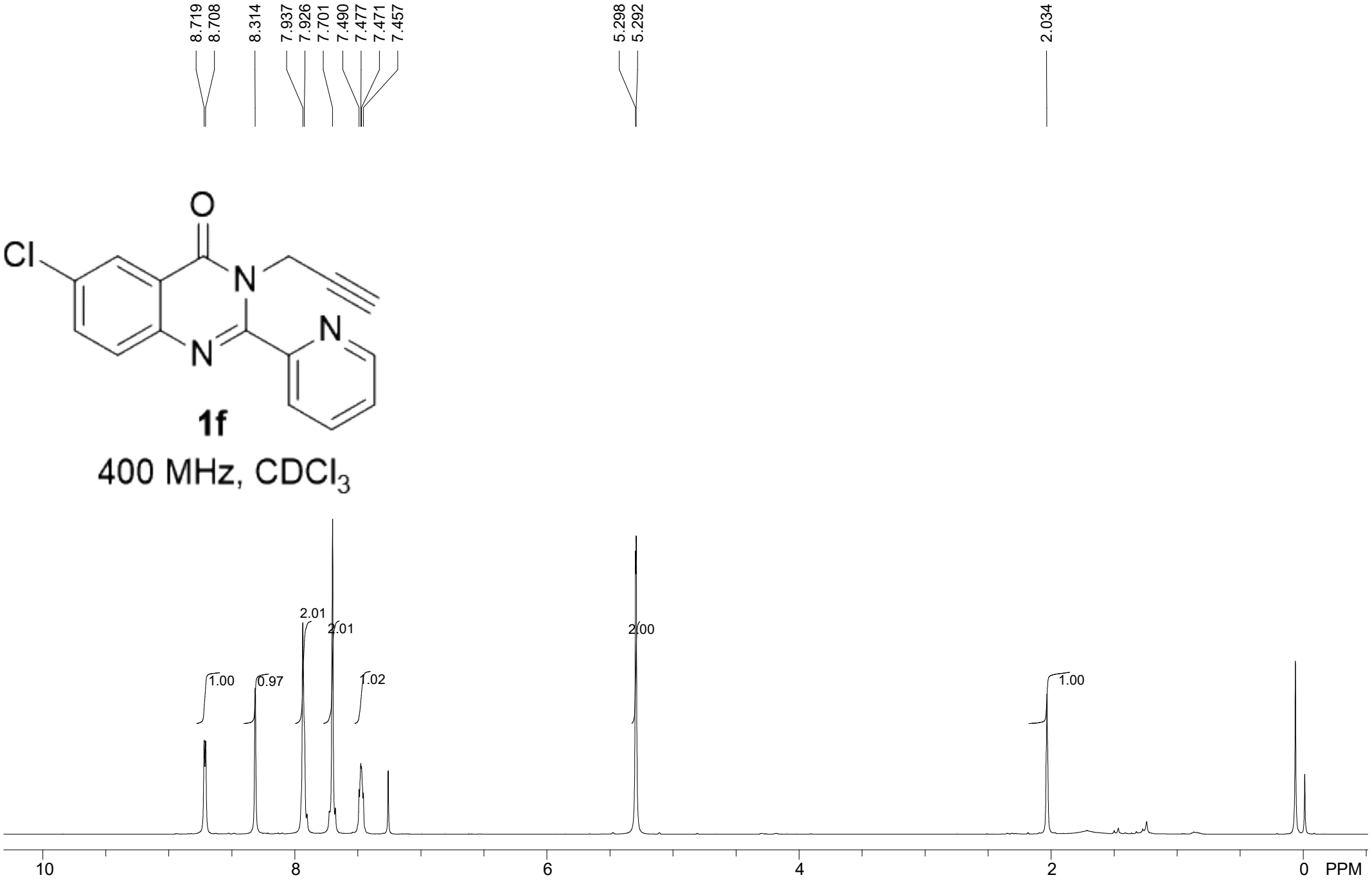


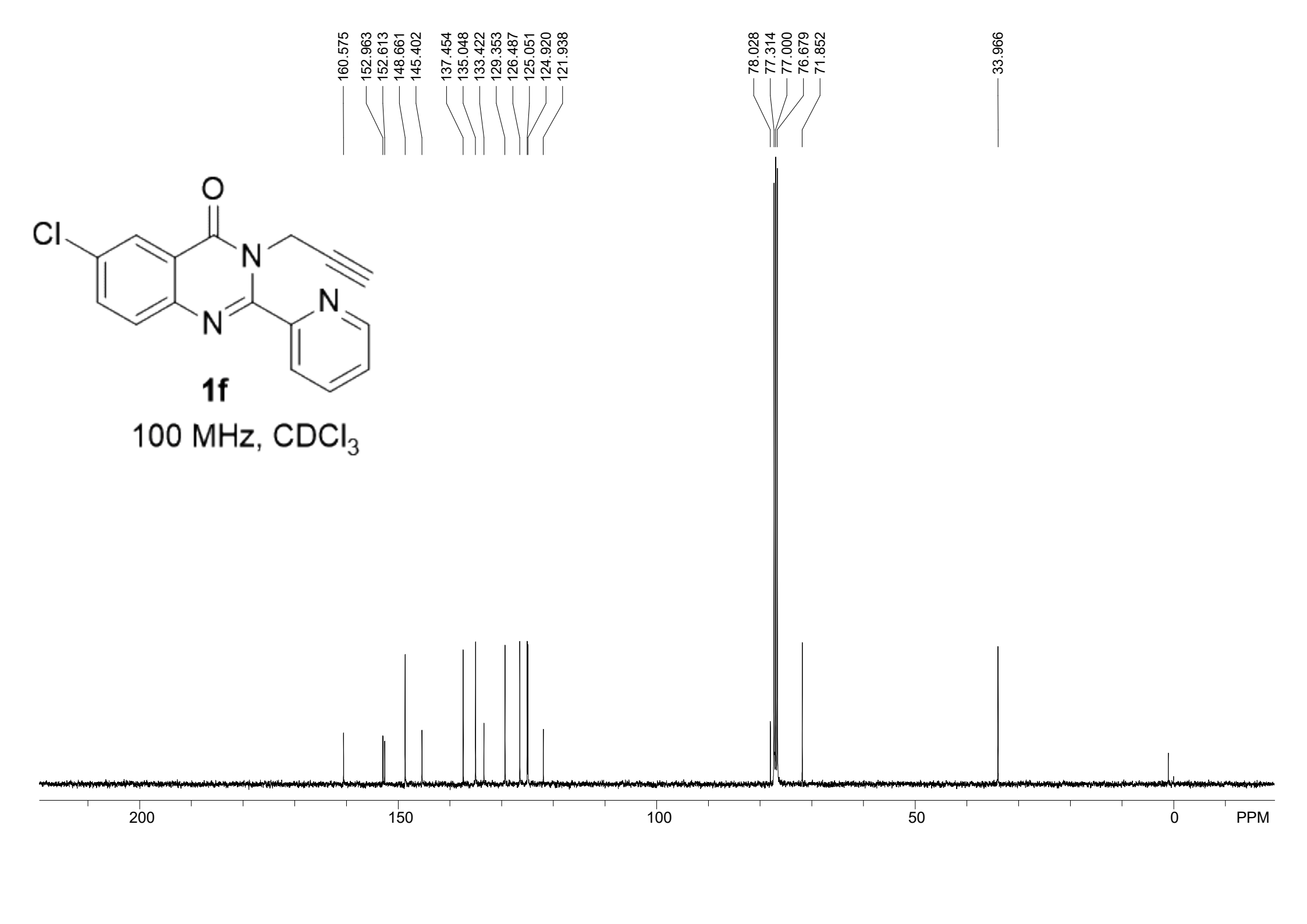

8.718
8.707
7.950
7.932
7.915
7.896
7.734
7.727
7.706
7.683
7.470
7.465
7.454
7.442
7.437
7.393
7.385
7.370
7.363
5.317
5.311
3.948
2.031
MeO
O
N
N
N
1d
400 MHz, CDCl3
1.00
2.08
2.07
1.07
1.05
2.16
3.10
1.01
12
10
8
6
4
2
0
PPM

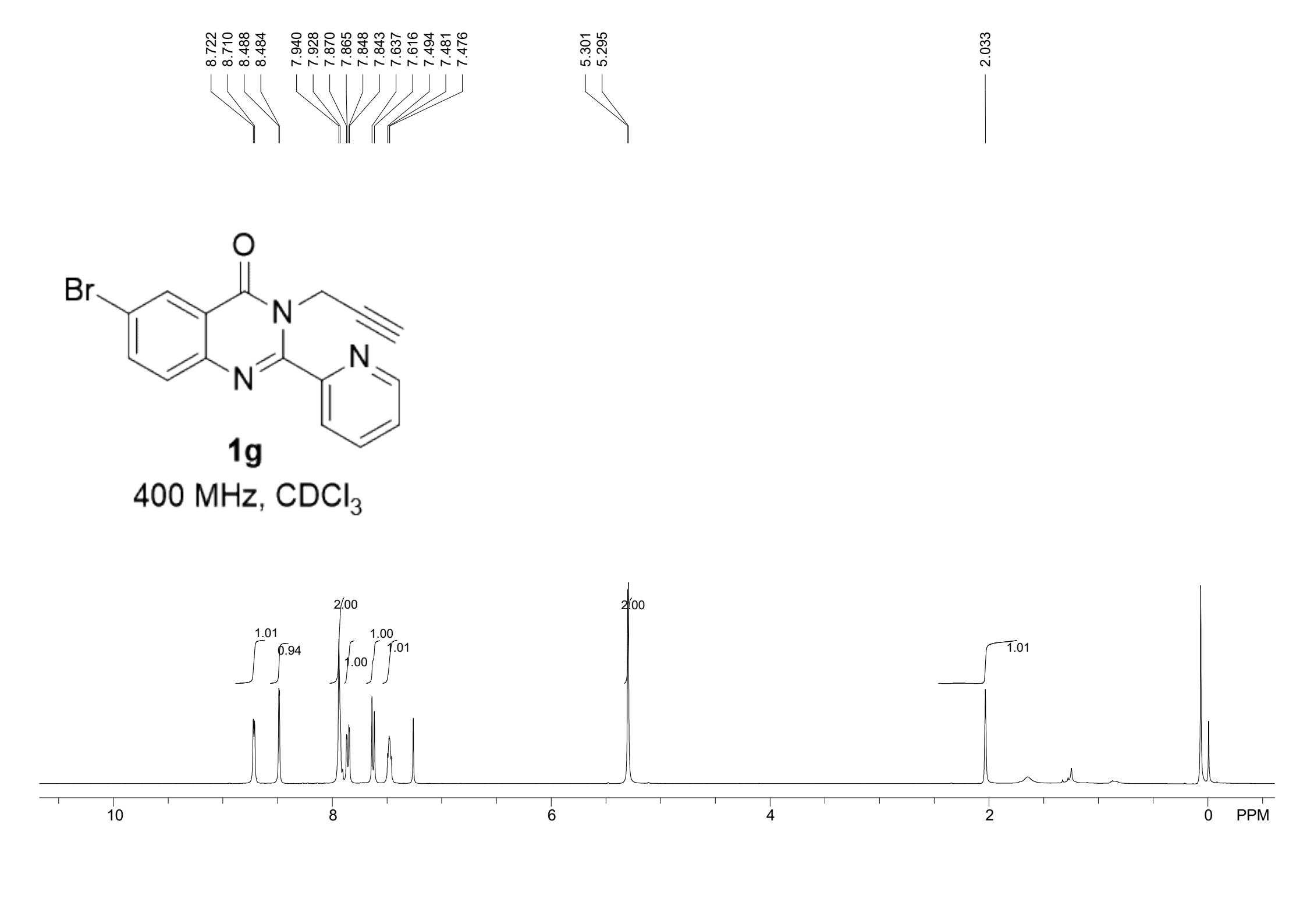

161.455
159.042
153.390
150.316
148.620
141.569
137.400
129.347
125.038
124.922
124.601
121.819
106.459
78.431
77.253
77.000
76.747
71.564
55.883
33.921
MeO
O
N
N
N
1d
125 MHz, CDCl3
200
150
100
50
0
PPM

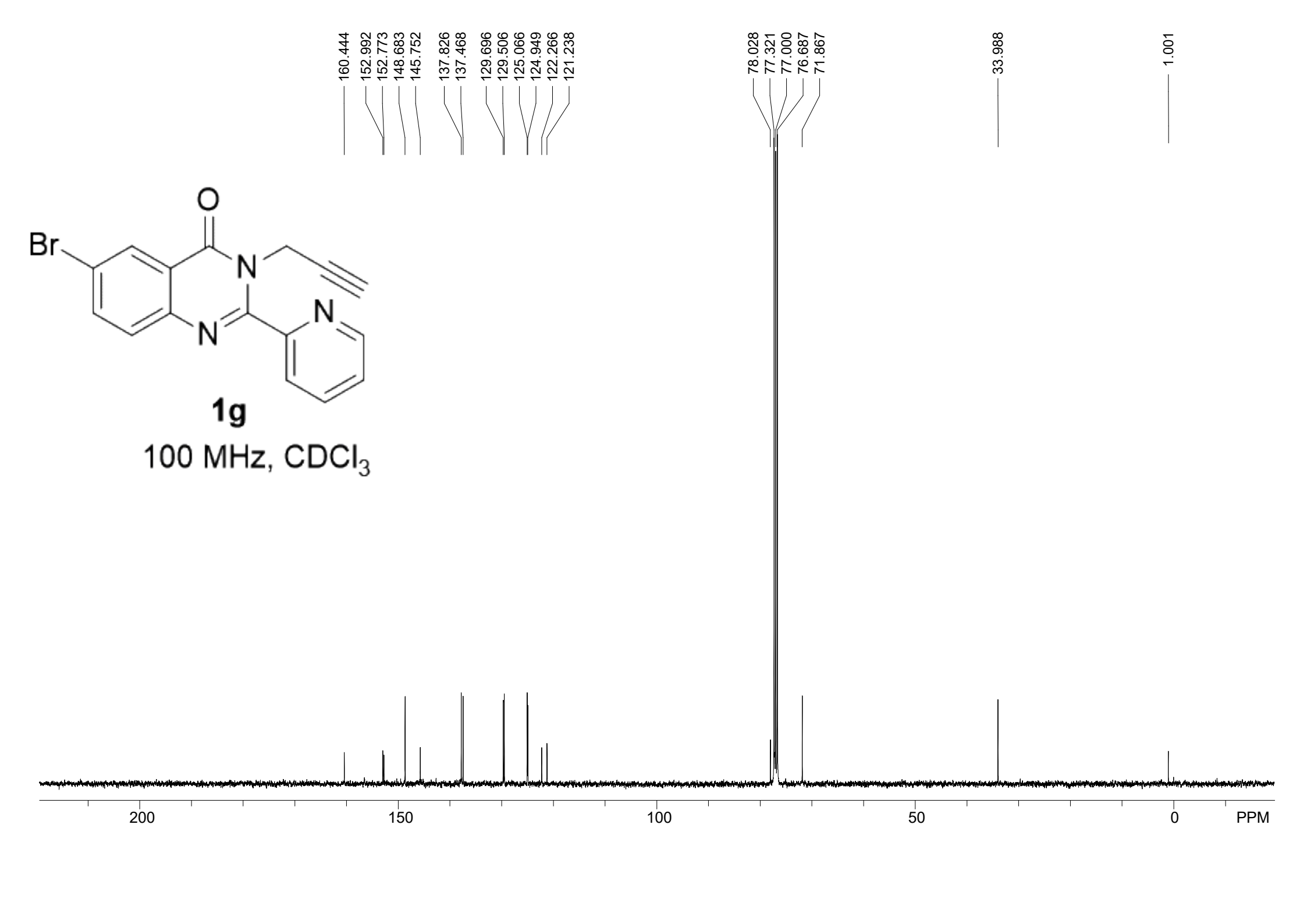

8.716
8.705
7.949
7.915
7.895
7.670
7.650
7.610
7.589
7.472
7.467
7.456
7.443
7.440
5.291
5.286
2.516
2.016
Me
O
N
N
N
1e
400 MHz, CDCl3
1.00
1.01
2.04
1.07
1.02
1.00
2.18
3.13
1.01
12
10
8
6
4
2
0
PPM

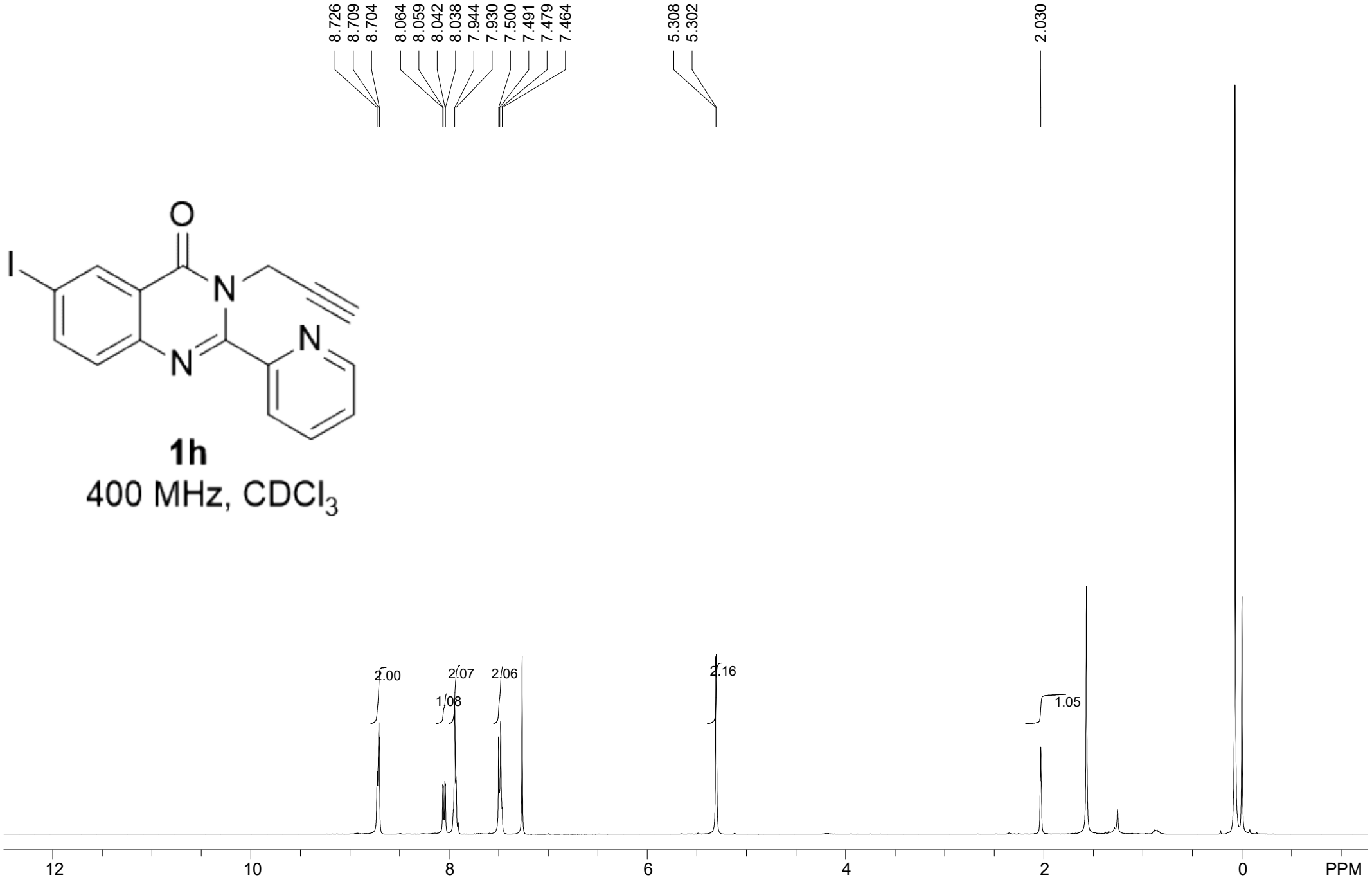

161.551
153.398
151.695
148.624
144.948
137.969
137.392
136.065
127.523
126.577
125.026
124.661
120.677
78.443
77.257
77.000
76.747
71.532
33.752
21.418
O
Me
N
N
N
1e
125 MHz, CDCl3
200
150
100
50
0
PPM

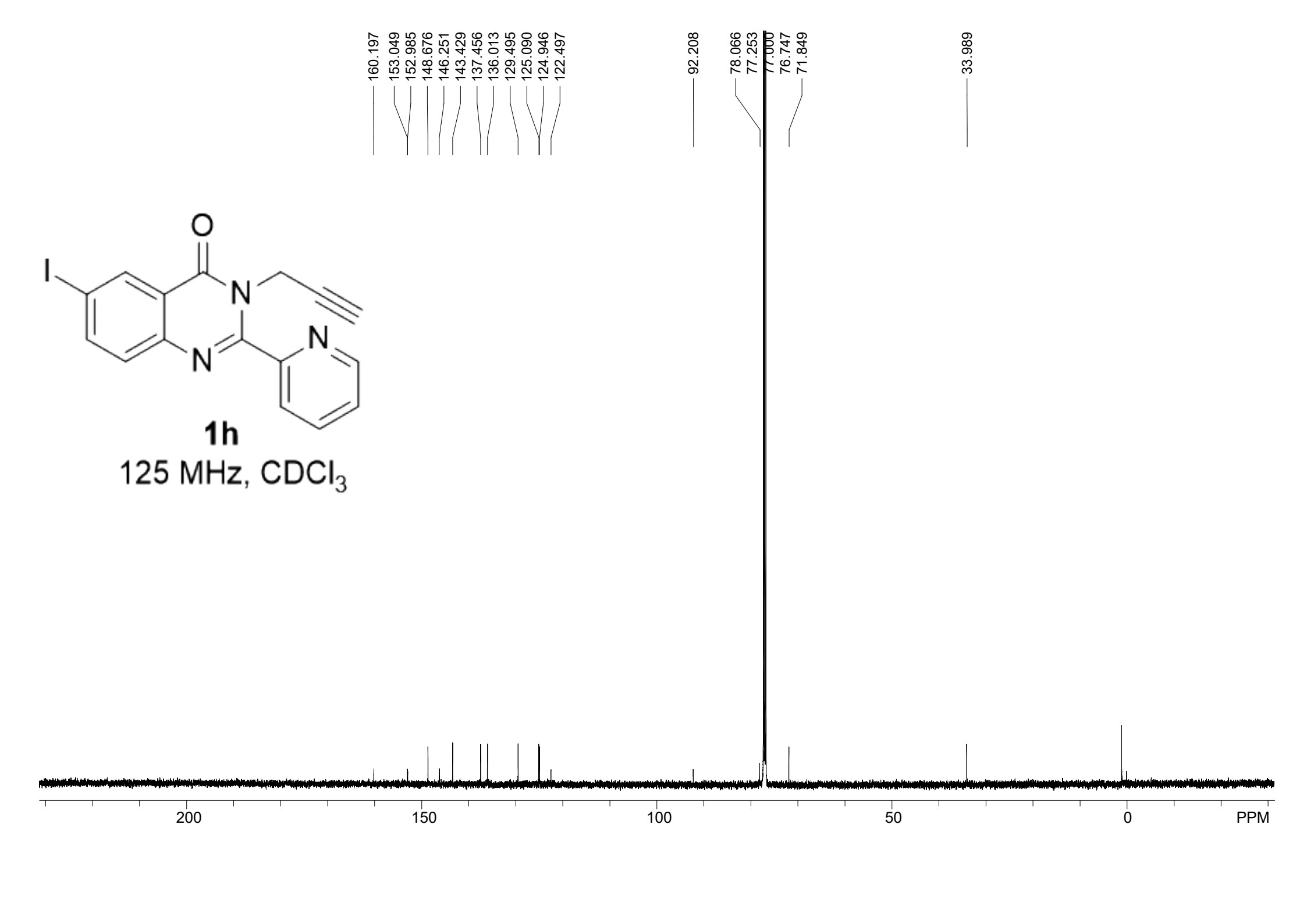

8.719
8.708
8.314
7.937
7.926
7.701
7.490
7.477
7.471
7.457
5.298
5.292
2.034
O
Cl
N
N
N
1f
400 MHz, CDCl3
2.01
2.01
2.00
1.00
0.97
1.02
1.00
10
8
6
4
2
0
PPM


160.575
152.963
152.613
148.661
145.402
137.454
135.048
133.422
129.353
126.487
125.051
124.920
121.938
78.028
77.314
77.000
76.679
71.852
33.966
Cl
O
N
N
N
1f
100 MHz, CDCl3
200
150
100
50
0
PPM

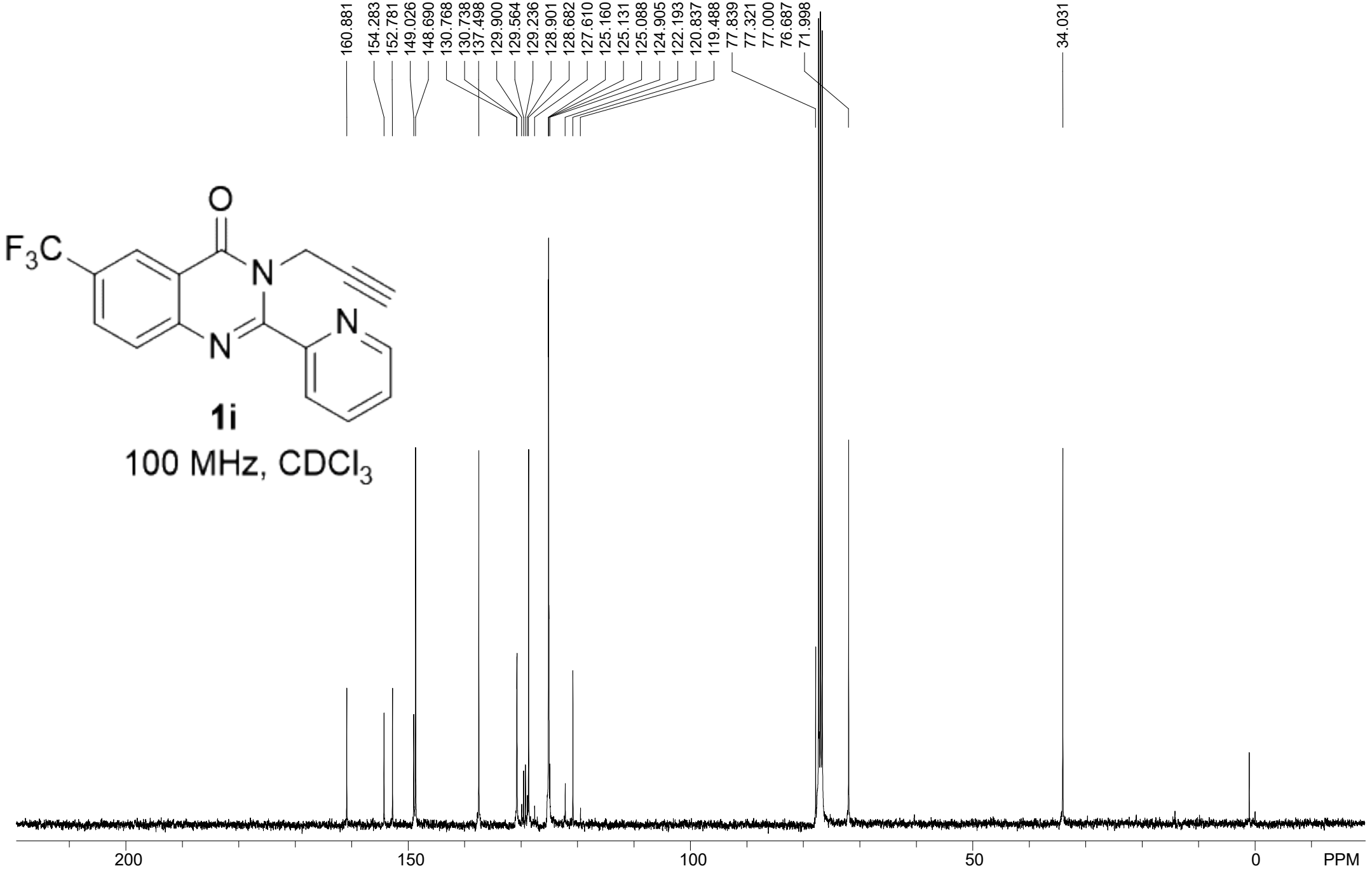

8.722
8.710
8.488
8.484
7.940
7.928
7.870
7.865
7.848
7.843
7.637
7.616
7.494
7.481
7.476
5.301
5.295
2.033
O
Br
N
N
N
1g
400 MHz, CDCl3
1.01
0.94
2.00
1.00
1.00
1.01
2.00
1.01
10
8
6
4
2
0
PPM

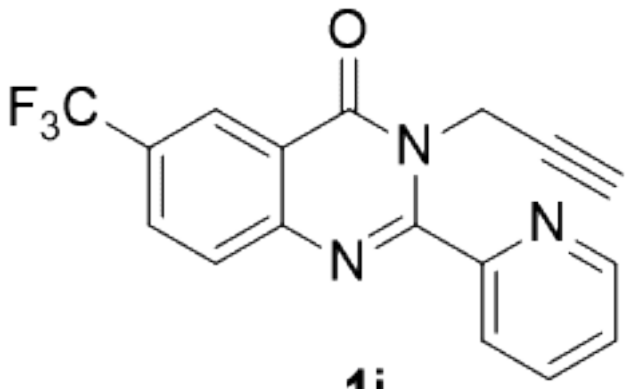

160.444
152.992
152.773
148.683
145.752
137.826
137.468
129.696
129.506
125.066
124.949
122.266
121.238
78.028
77.321
77.000
76.687
71.867
33.988
1.001
Br
O
N
N
N
1g
100 MHz, CDCl3
200
150
100
50
0
PPM


8.726
8.709
8.704
8.064
8.059
8.042
8.038
7.944
7.930
7.500
7.491
7.479
7.464
5.308
5.302
2.030
O
I
N
N
N
1h
400 MHz, CDCl3
2.00
1.08
2.07
2.06
2.16
1.05
12
10
8
6
4
2
0
PPM


160.197
153.049
152.985
148.676
146.251
143.429
137.456
136.013
129.495
125.090
124.946
122.497
92.208
78.066
77.253
77.000
76.747
71.849
33.989
O
I
N
N
N
1h
125 MHz, CDCl3
200
150
100
50
0
PPM


8.729
8.718
8.641
7.976
7.958
7.939
7.920
7.864
7.842
7.504
7.492
7.479
5.330
5.326
2.037
O
F3C
N
N
N
1i
400 MHz, CDCl3
3.06
2.00
1.01
1.01
1.05
1.00
1.00
10
8
6
4
2
0
PPM


160.881
154.283
152.781
149.026
148.690
130.768
130.738
137.498
129.900
129.564
129.236
128.901
128.682
127.610
125.160
125.131
125.088
124.905
122.193
120.837
119.488
77.839
77.321
77.000
76.687
71.998
34.031
O
F3C
N
N
N
1i
100 MHz, CDCl3
200
150
100
50
0
PPM

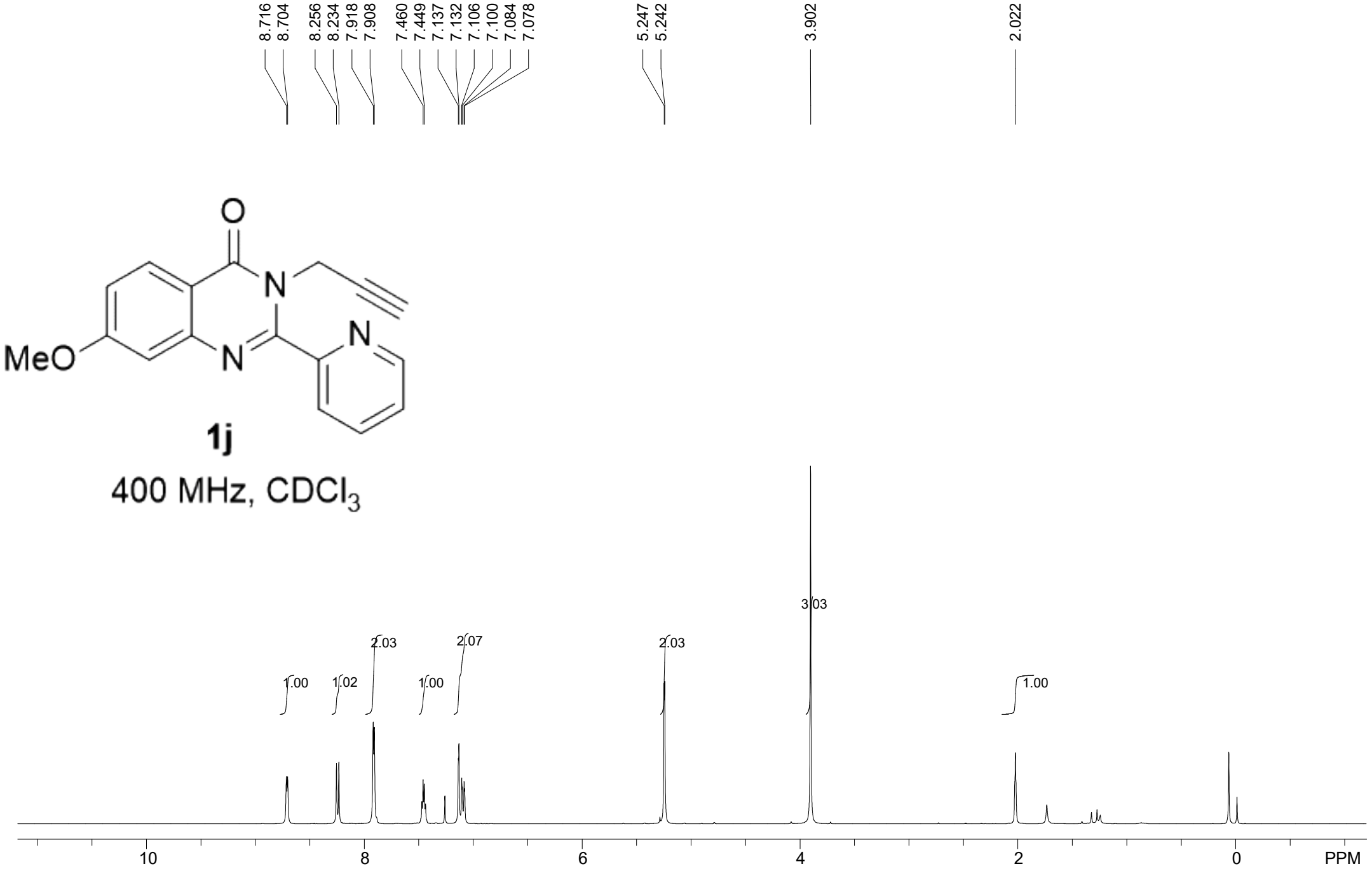


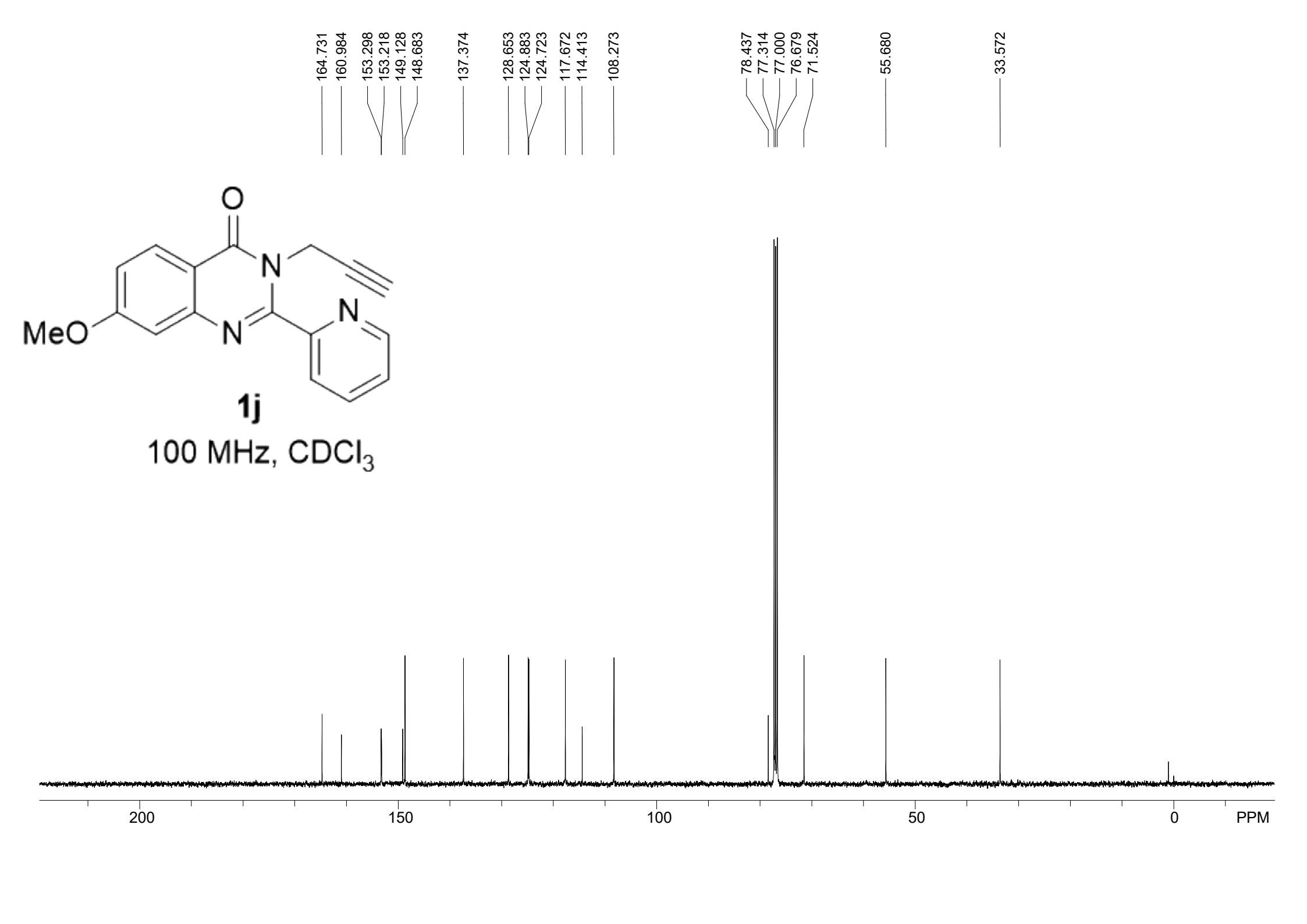
1i

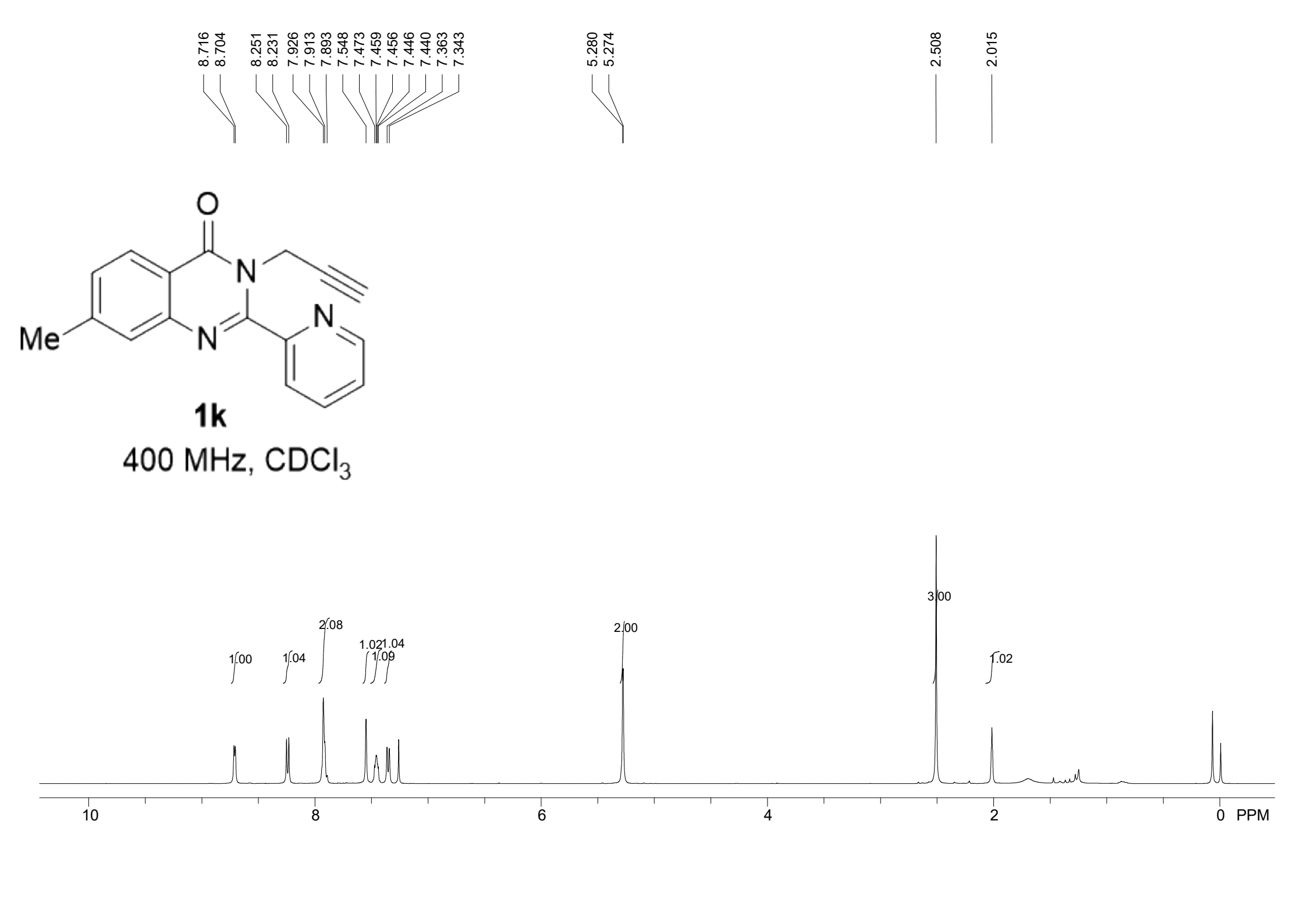
376 MHz, $CDCl_3$

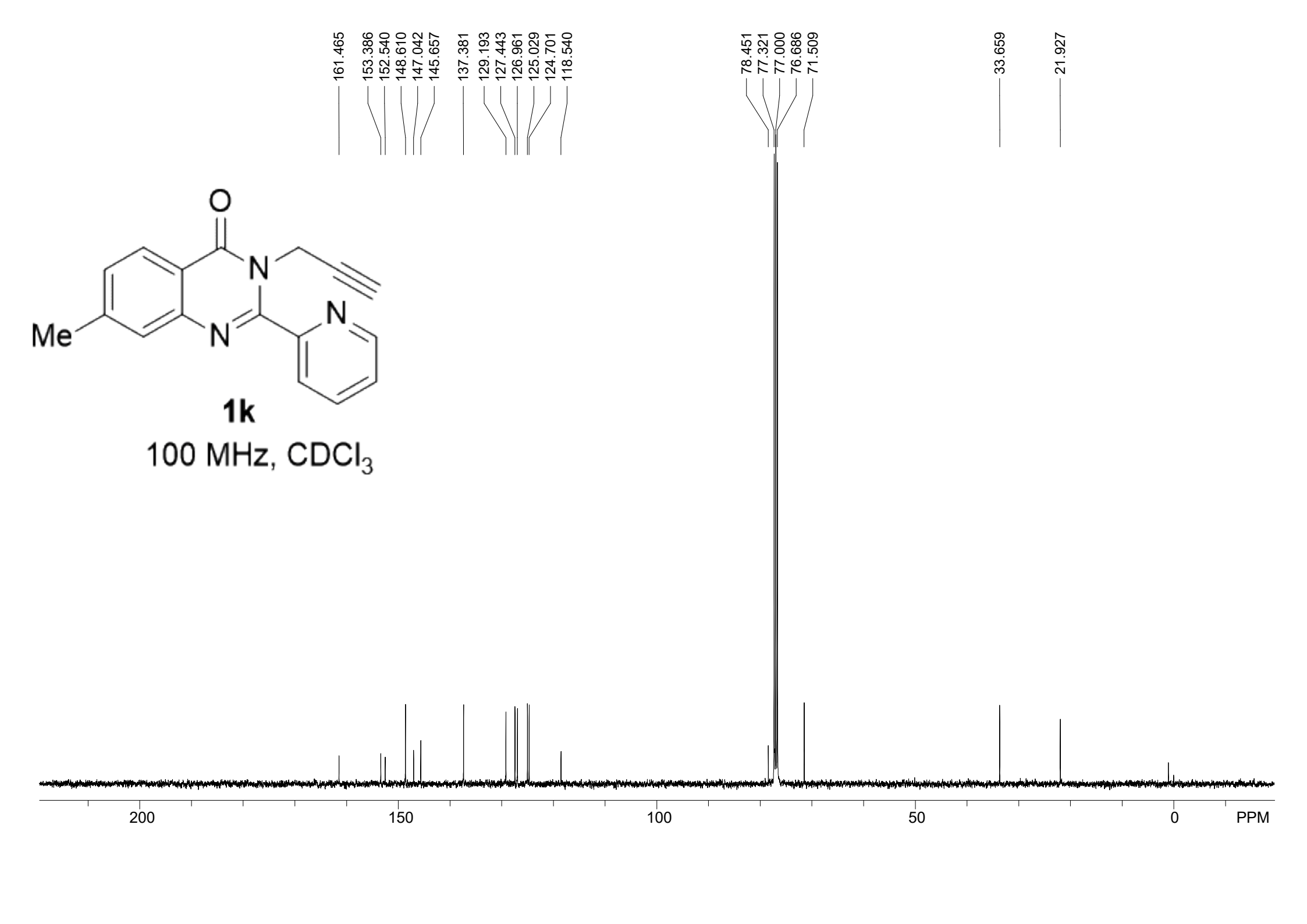
-62.402

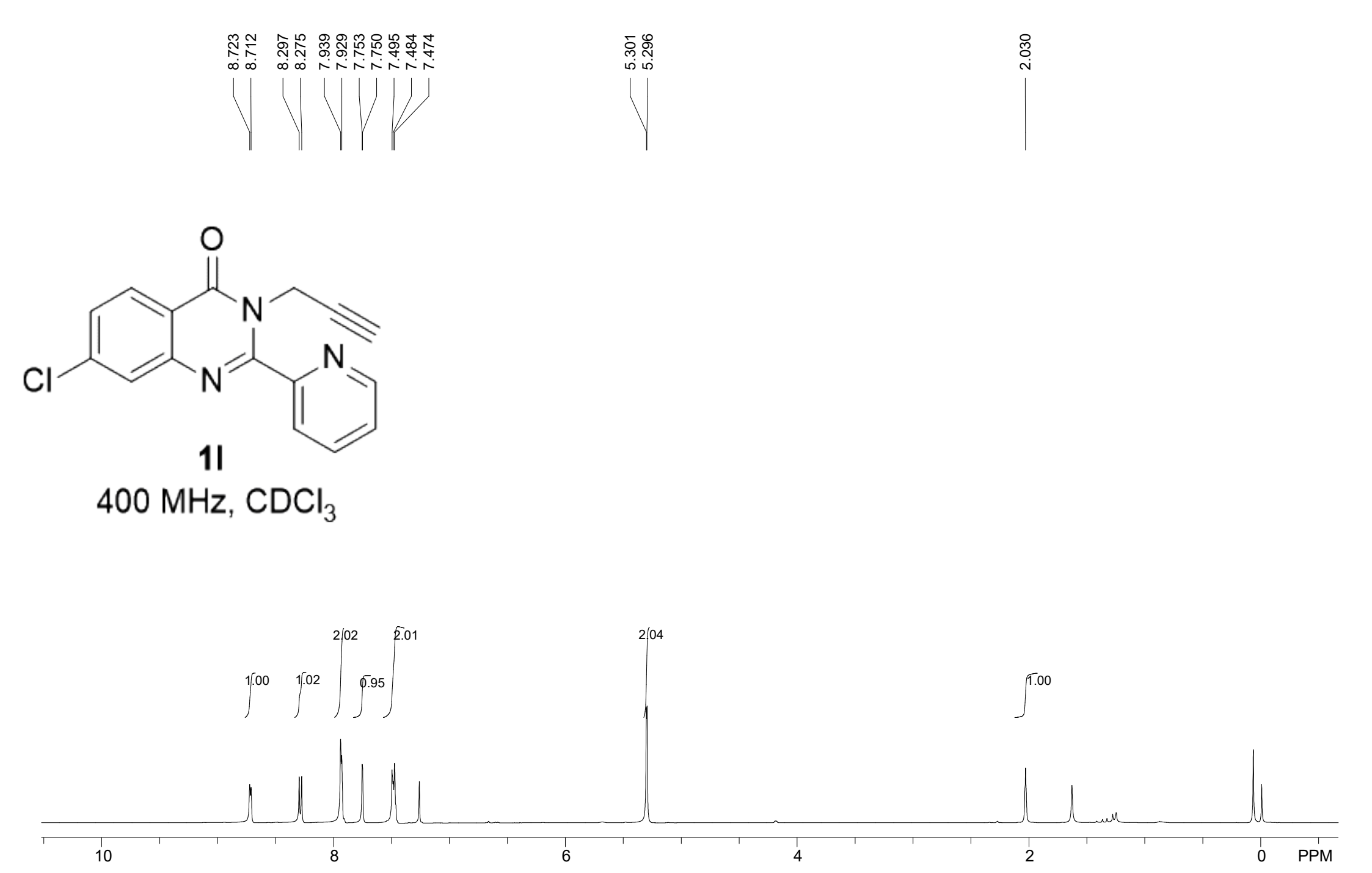
0 -50 -100 -150 -200 PPM

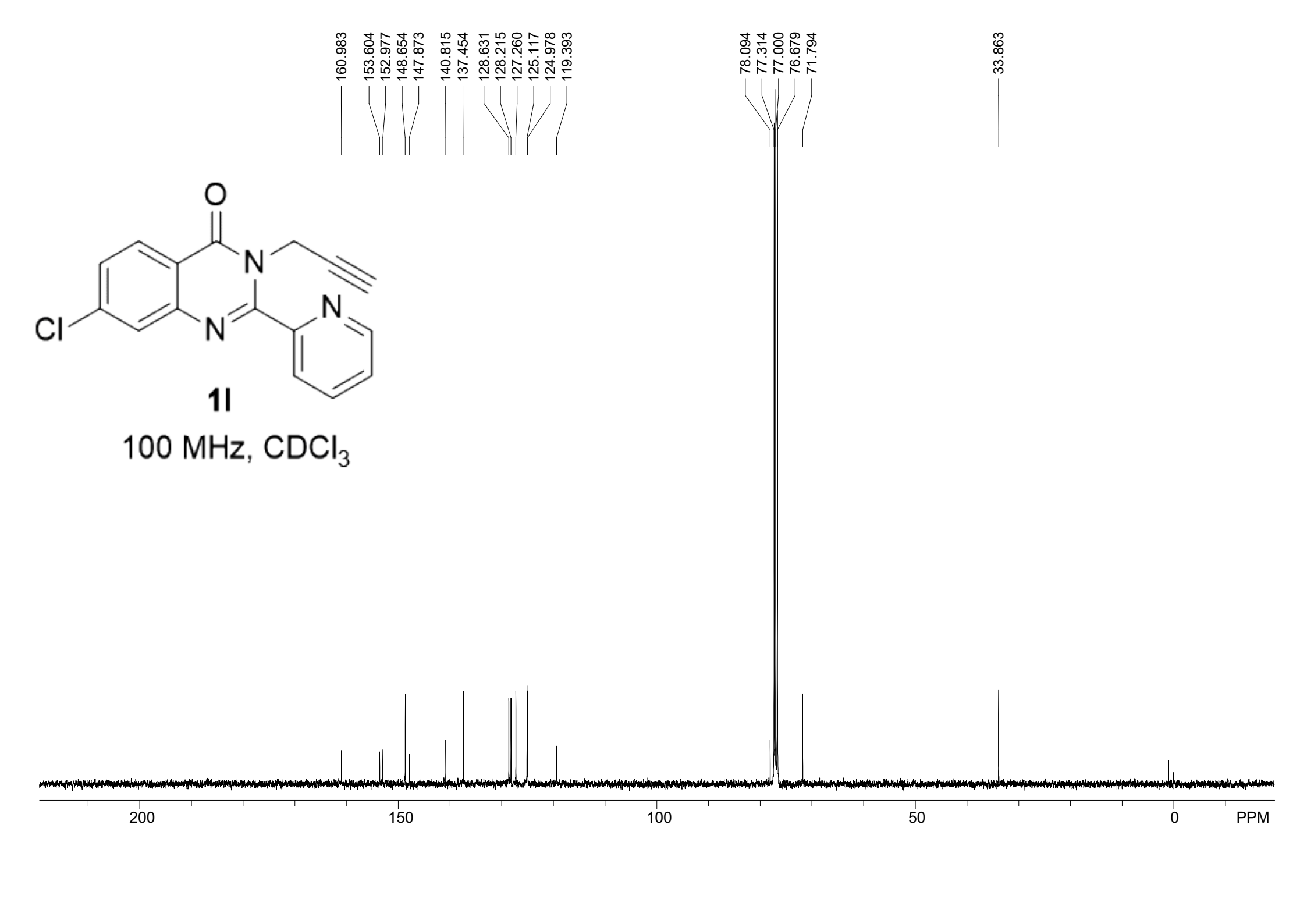

8.716
8.704
8.256
8.234
7.918
7.908
7.460
7.449
7.137
7.132
7.106
7.100
7.084
7.078
5.247
5.242
3.902
2.022
O
N
N
N
MeO
1j
400 MHz, CDCl3
1.00
1.02
2.03
1.00
2.07
2.03
3.03
1.00
10
8
6
4
2
0
PPM

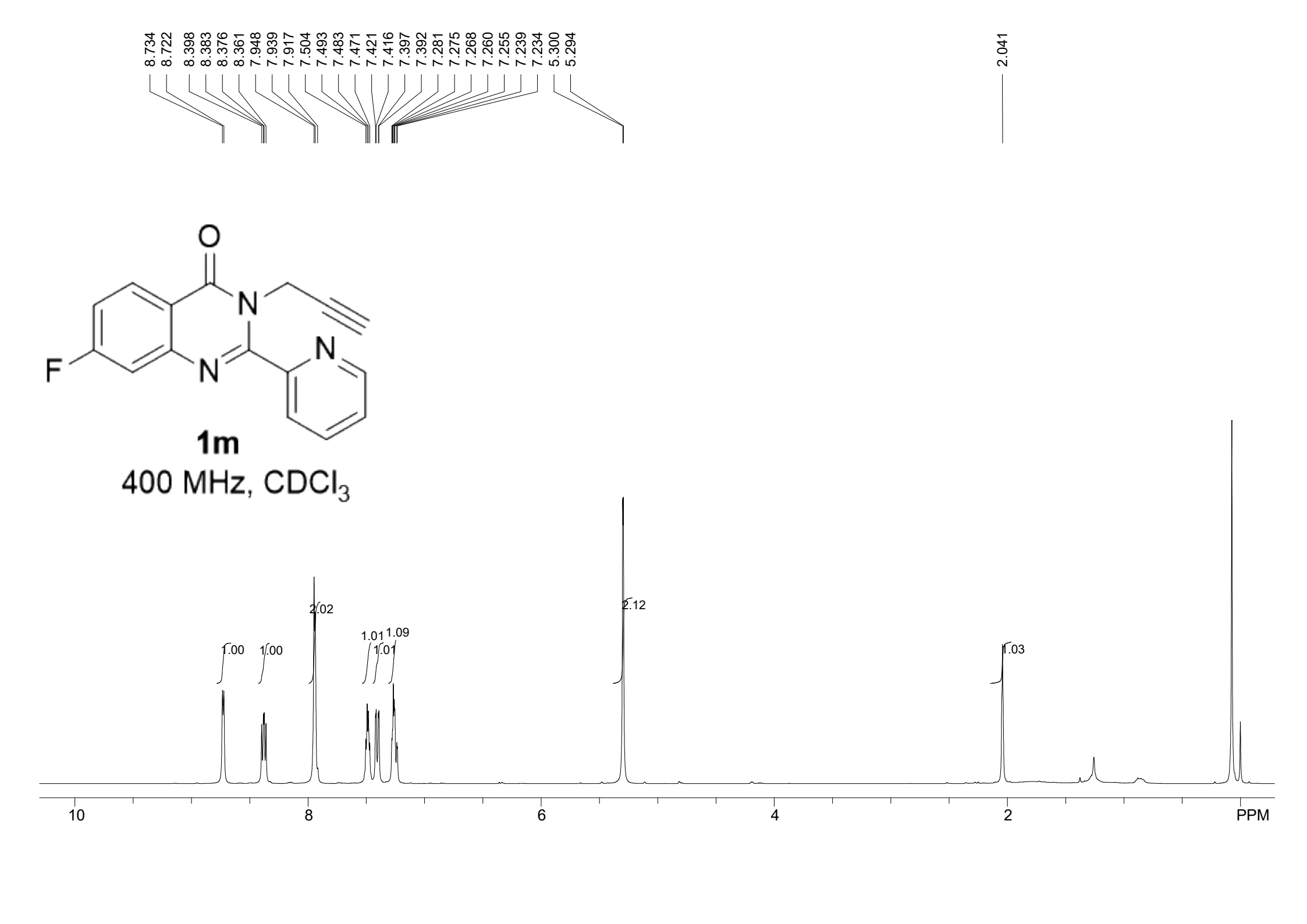

164.731
160.984
153.298
153.218
149.128
148.683
137.374
128.653
124.883
124.723
117.672
114.413
108.273
78.437
77.314
77.000
76.679
71.524
55.680
33.572
O
N
N
N
MeO
1j
100 MHz, CDCl3
200
150
100
50
0
PPM

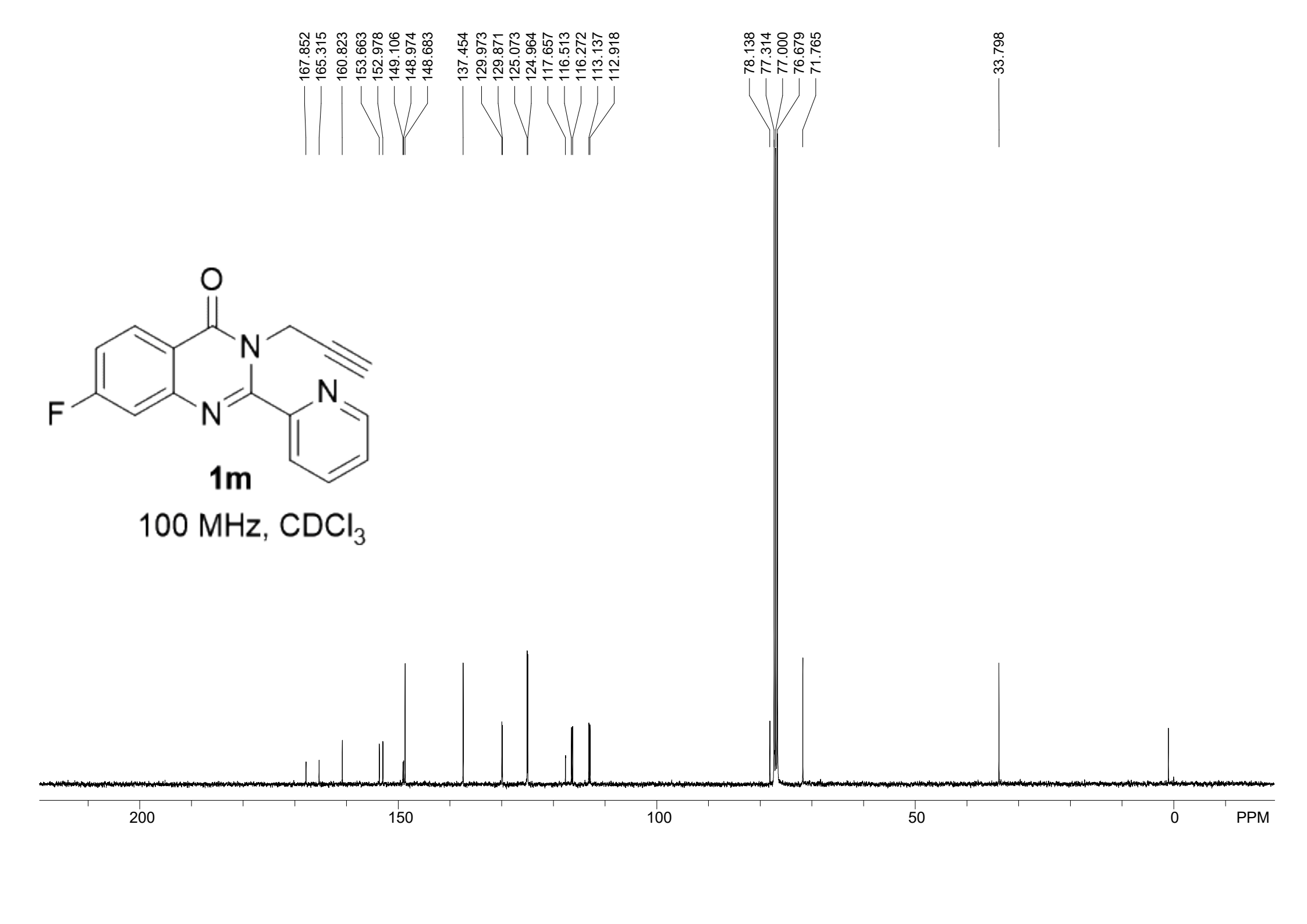

8.716
8.704
8.251
8.231
7.926
7.913
7.893
7.548
7.473
7.459
7.456
7.446
7.440
7.363
7.343
5.280
5.274
2.508
2.015
O
N
N
N
Me
1k
400 MHz, CDCl3
1.00
1.04
2.08
1.02
1.04
1.09
2.00
3.00
1.02
10
8
6
4
2
0
PPM

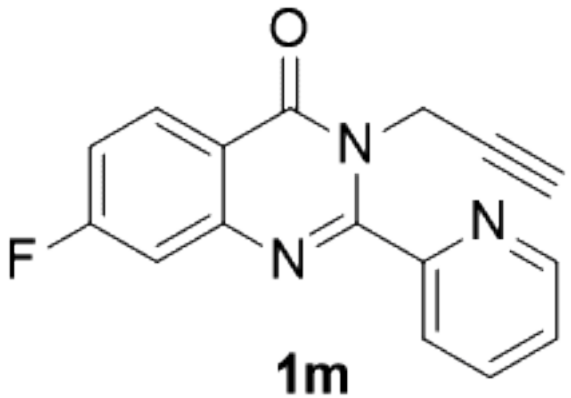

161.465
153.386
152.540
148.610
147.042
145.657
137.381
129.193
127.443
126.961
125.029
124.701
118.540
78.451
77.321
77.000
76.686
71.509
33.659
21.927
O
N
N
N
Me
1k
100 MHz, CDCl3
200
150
100
50
0
PPM


8.723
8.712
8.297
8.275
7.939
7.929
7.753
7.750
7.495
7.484
7.474
5.301
5.296
2.030
O
N
N
N
Cl
1I
400 MHz, CDCl3
1.00
1.02
2.02
0.95
2.01
2.04
1.00
10
8
6
4
2
0
PPM


160.983
153.604
152.977
148.654
147.873
140.815
137.454
128.631
128.215
127.260
125.117
124.978
119.393
78.094
77.314
77.000
76.679
71.794
33.863
O
N
N
N
Cl
1l
100 MHz, CDCl3
200
150
100
50
0
PPM


8.734
8.722
8.398
8.383
8.376
8.361
7.948
7.939
7.917
7.504
7.493
7.483
7.471
7.421
7.416
7.397
7.392
7.281
7.275
7.268
7.260
7.255
7.239
7.234
5.300
5.294
2.041
O
N
N
N
F
1m
400 MHz, CDCl3
1.00
1.00
2.02
1.01
1.01
1.09
2.12
1.03
10
8
6
4
2
PPM


167.852
165.315
160.823
153.663
152.978
149.106
148.974
148.683
137.454
129.973
129.871
125.073
124.964
117.657
116.513
116.272
113.137
112.918
78.138
77.314
77.000
76.679
71.765
33.798
O
N
N
N
F
1m
100 MHz, CDCl3
200
150
100
50
0
PPM

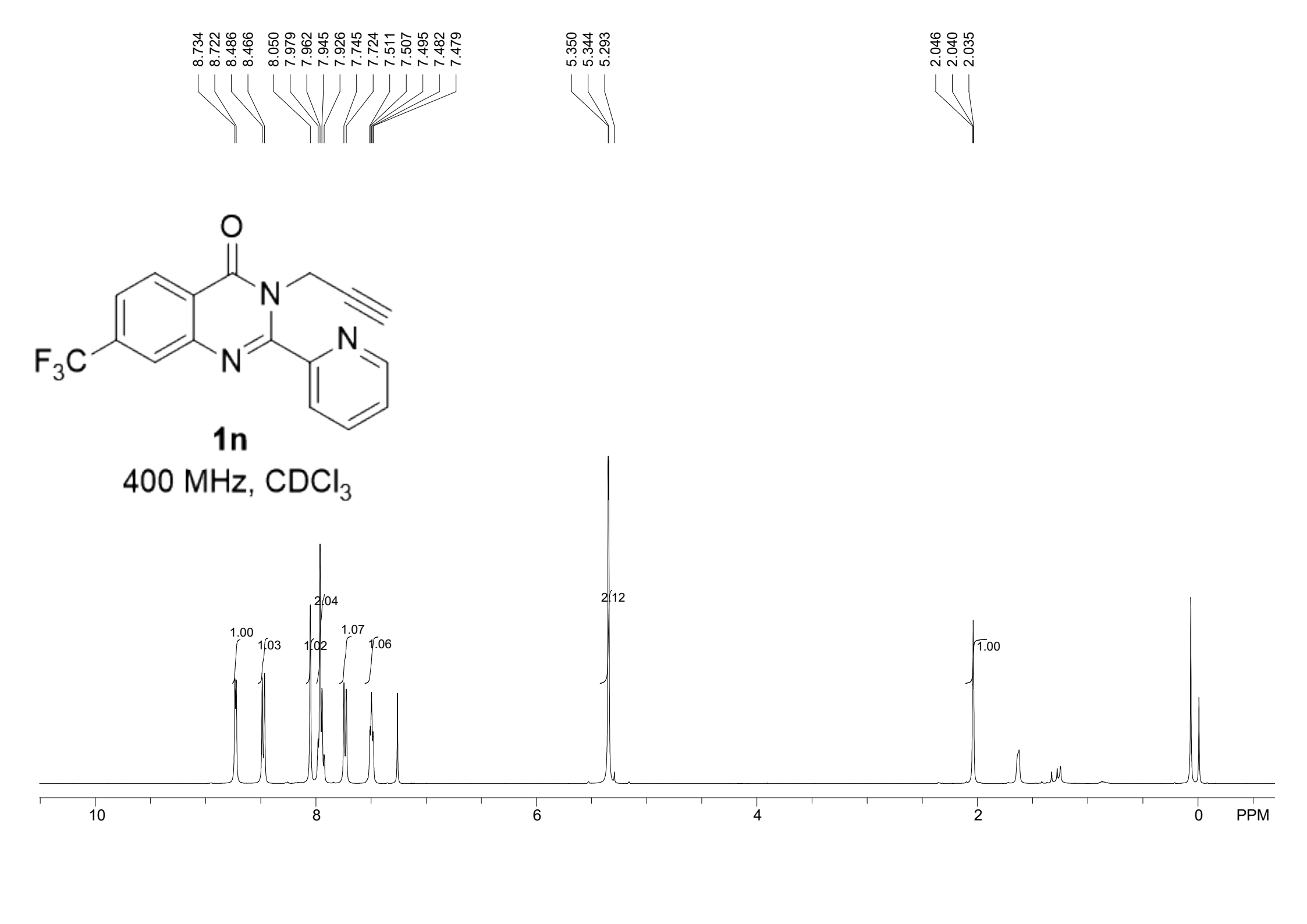


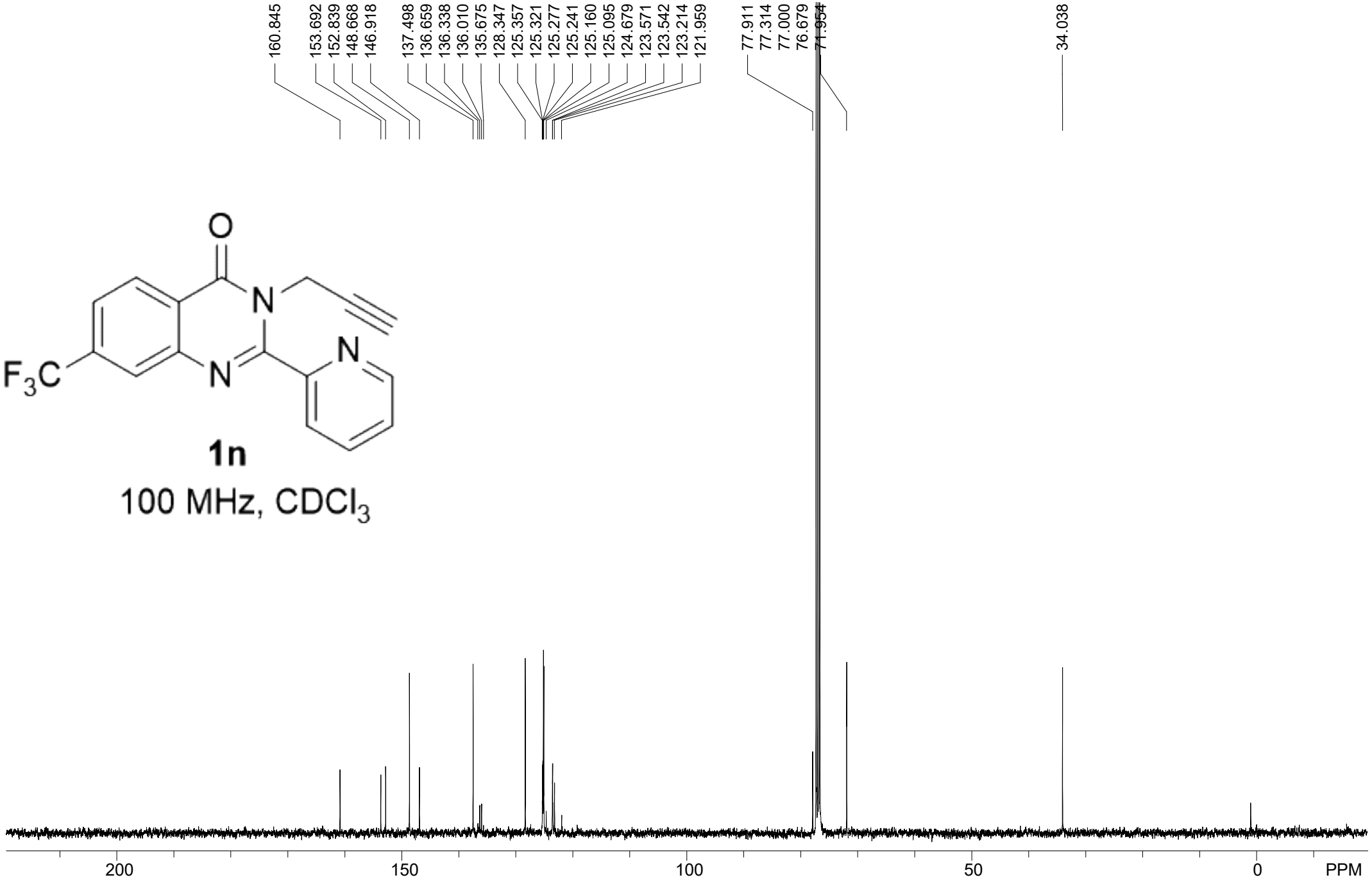
1m

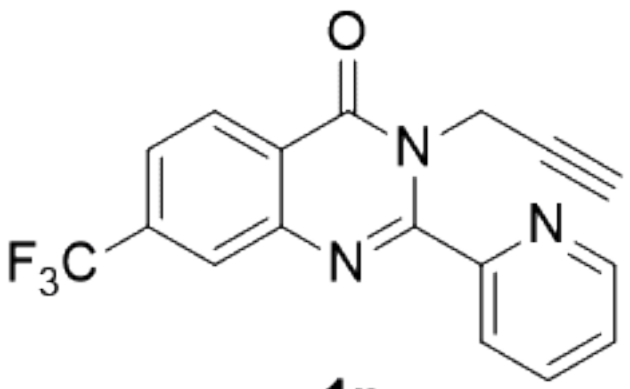
376 MHz, $CDCl_3$

-102.700

0 -50 -100 -150 -200 PPM


8.734
8.722
8.486
8.466
8.050
7.979
7.962
7.945
7.926
7.745
7.724
7.511
7.507
7.495
7.482
7.479
5.350
5.344
5.293
2.046
2.040
2.035
O
N
N
N
F3C
1n
400 MHz, CDCl3
1.00
1.03
1.02
2.04
1.07
1.06
2.12
1.00
10
8
6
4
2
0
PPM


160.845
153.692
152.839
148.668
146.918
137.498
136.659
136.338
136.010
135.675
128.347
125.357
125.321
125.277
125.241
125.160
125.095
124.679
123.571
123.542
123.214
121.959
77.911
77.314
77.000
76.679
71.954
34.038
O
N
N
N
F3C
1n
100 MHz, CDCl3
200
150
100
50
0
PPM

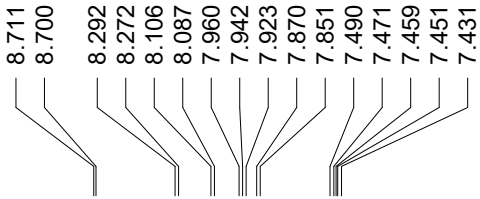


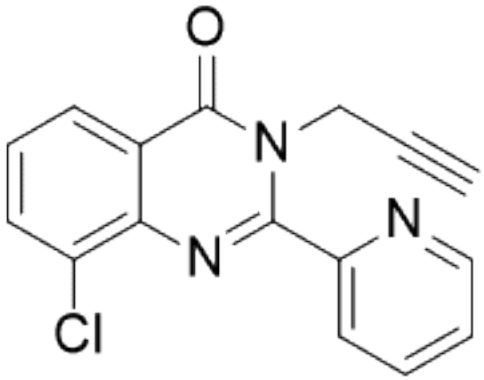
1n

376 MHz, $CDCl_3$

-63.264

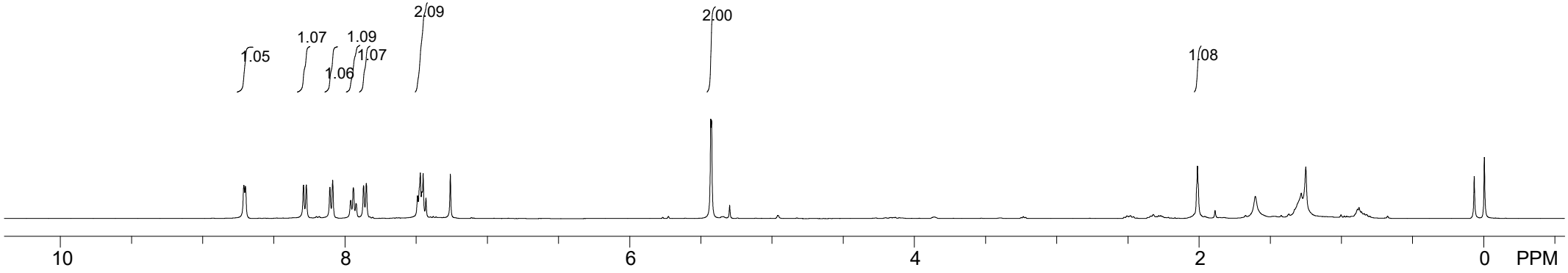
0 -50 -100 -150 -200 PPM

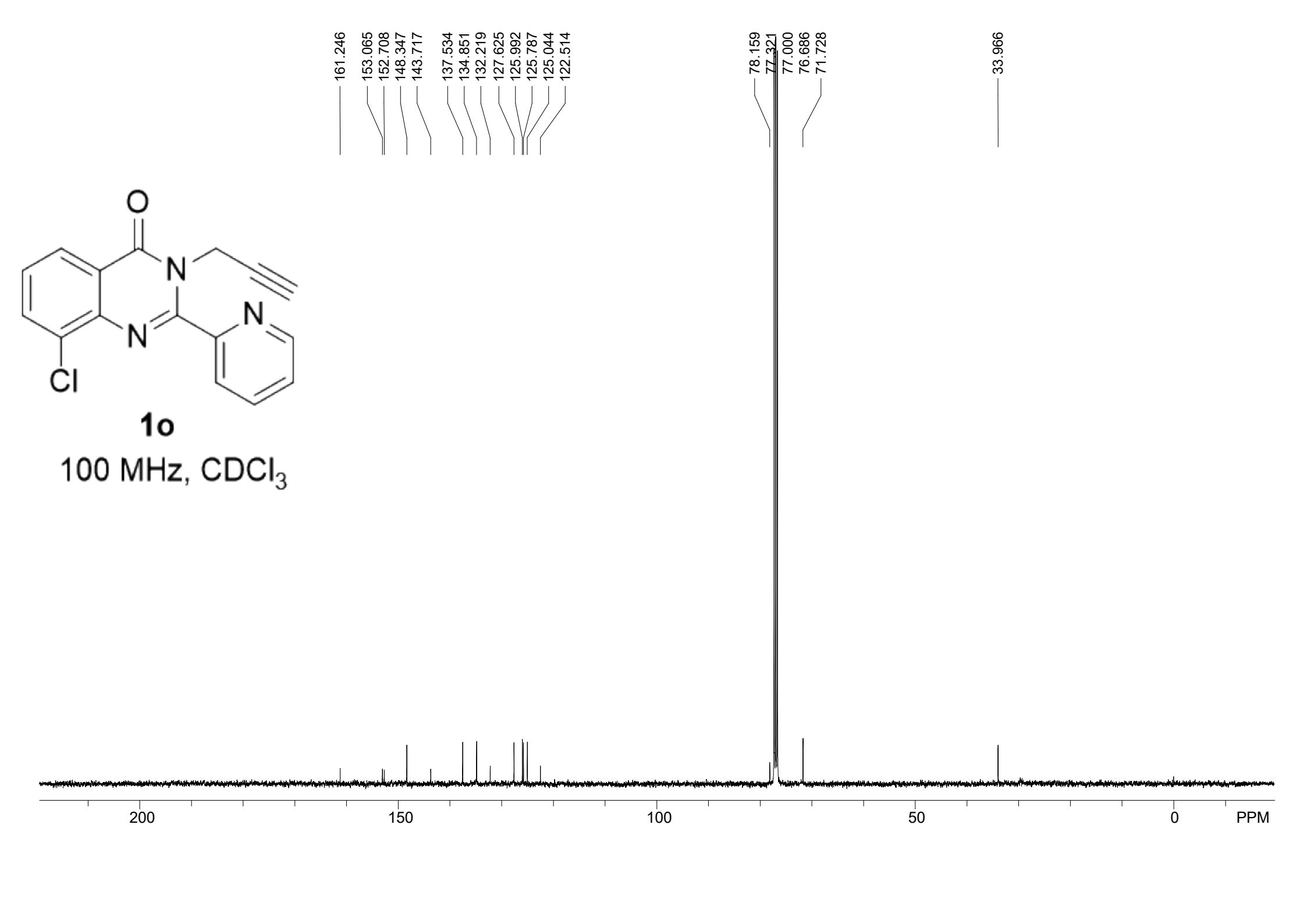


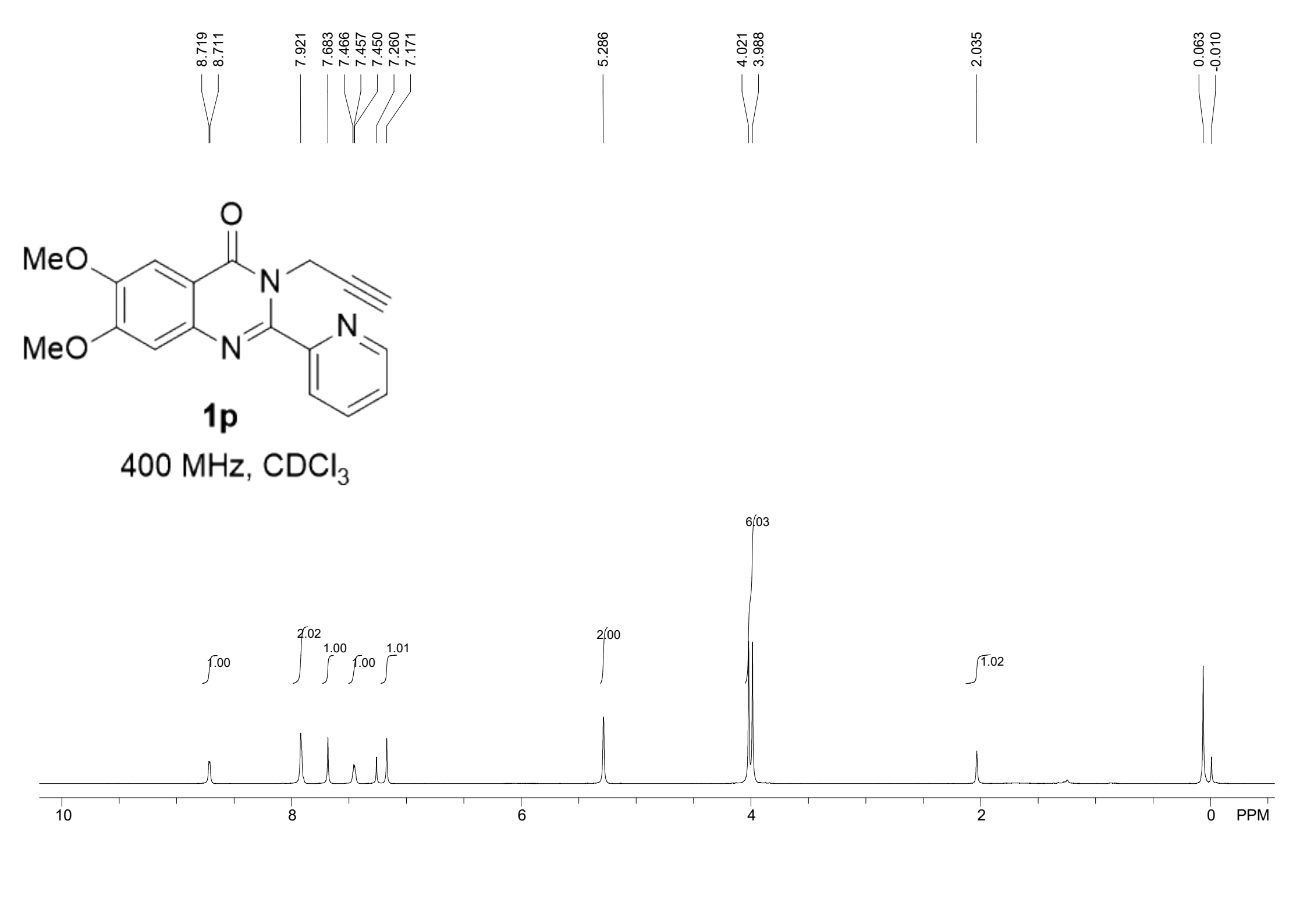


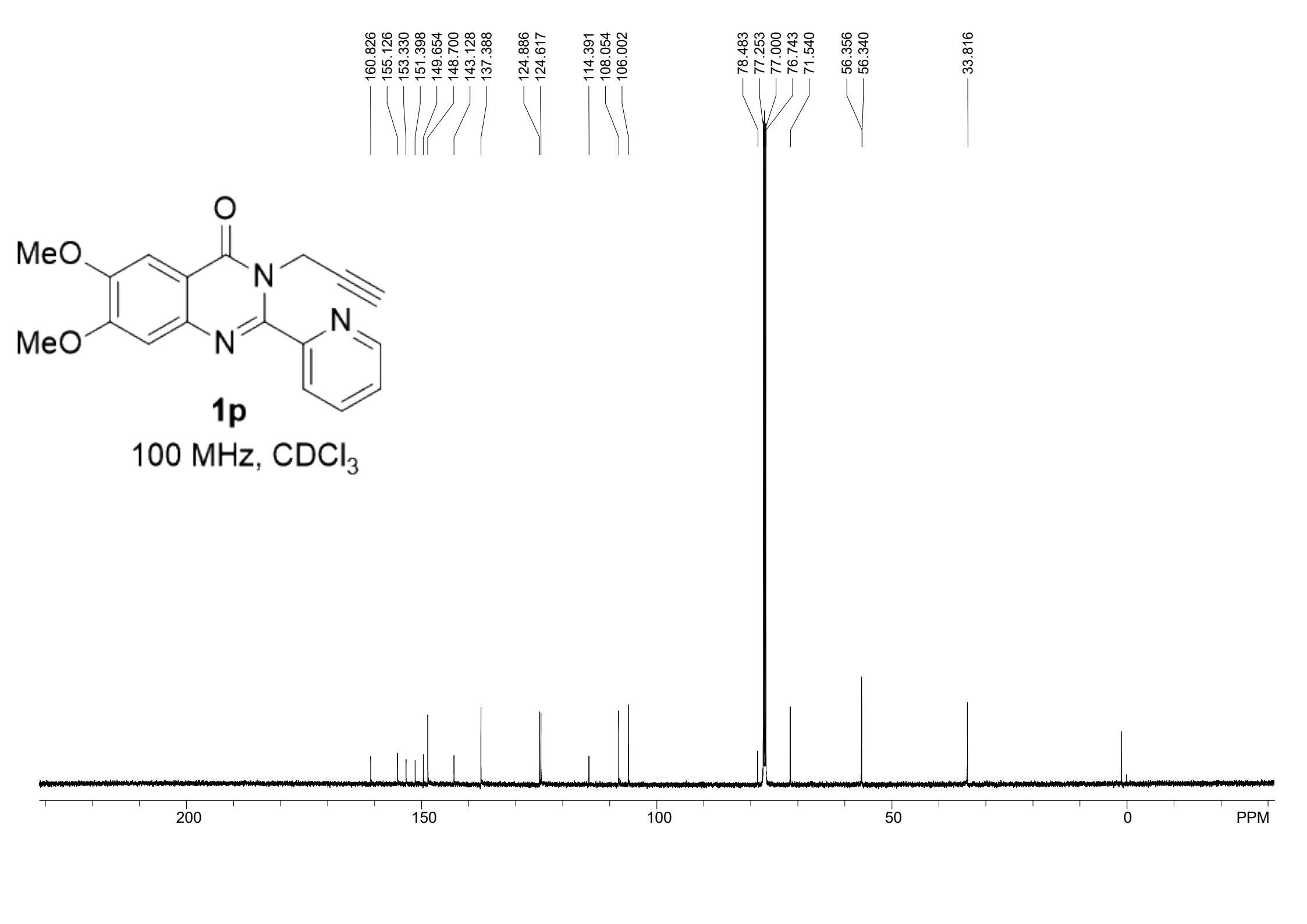
1o

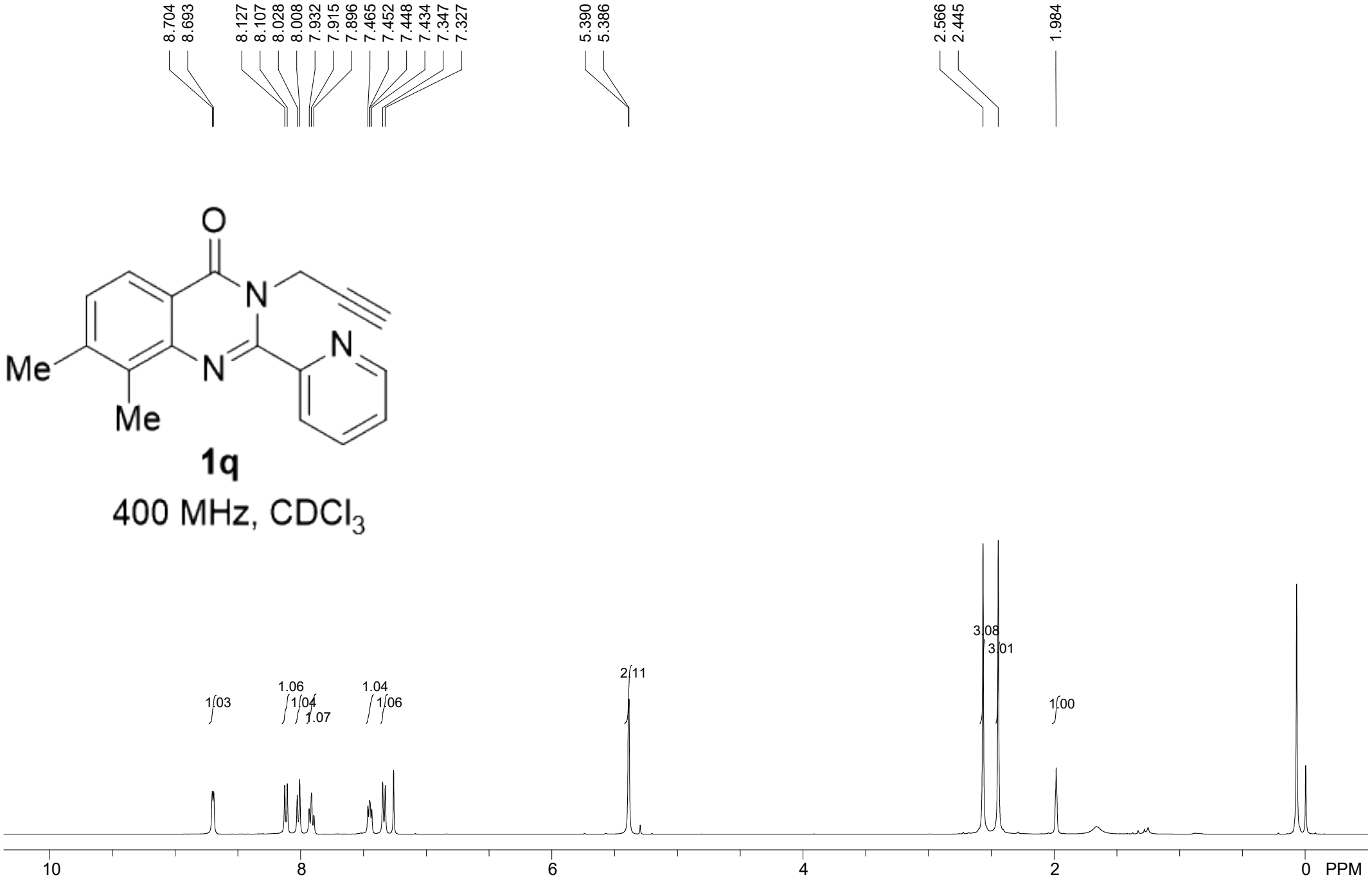
400 MHz, $CDCl_3$

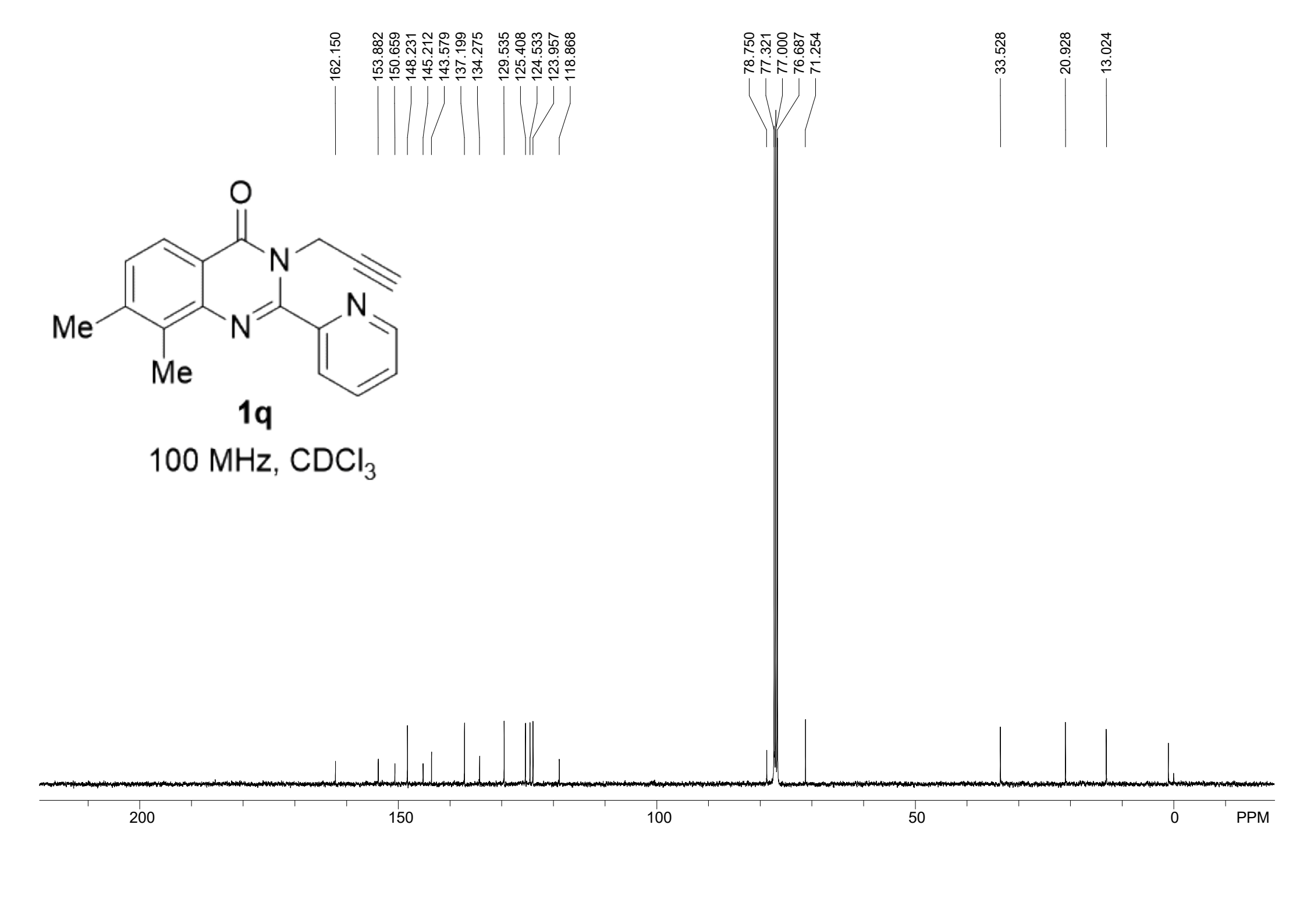



161.246
153.065
152.708
148.347
143.717
137.534
134.851
132.219
127.625
125.992
125.787
125.044
122.514
78.159
77.321
77.000
76.686
71.728
33.966
O
N
N
N
Cl
1o
100 MHz, CDCl3
200
150
100
50
0
PPM

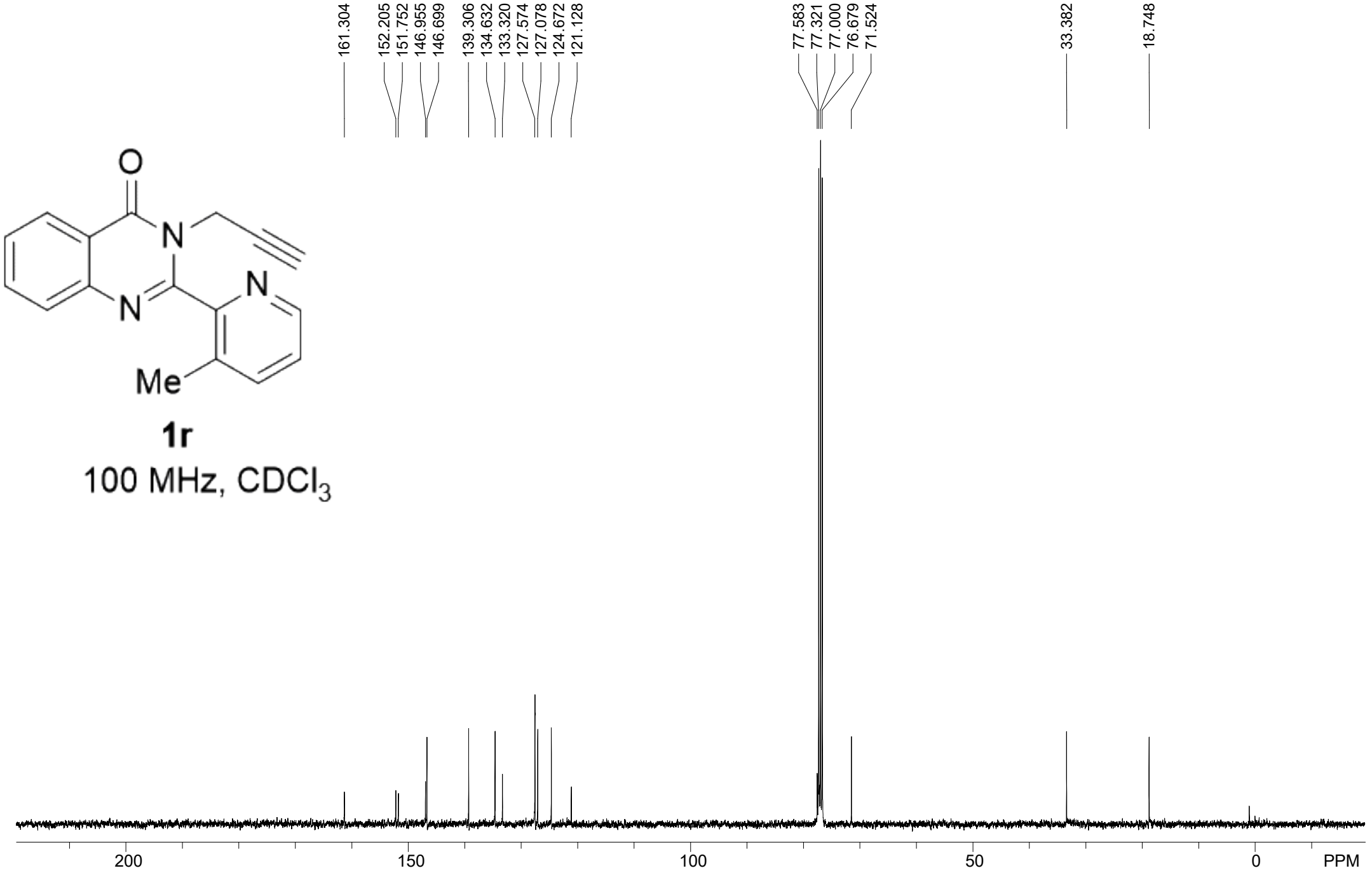

8.719
8.711
7.921
7.683
7.466
7.457
7.450
7.260
7.171
5.286
4.021
3.988
2.035
0.063
-0.010
MeO
MeO
O
N
N
N
1p
400 MHz, CDCl3
1.00
2.02
1.00
1.00
1.01
2.00
6.03
1.02
10
8
6
4
2
0
PPM

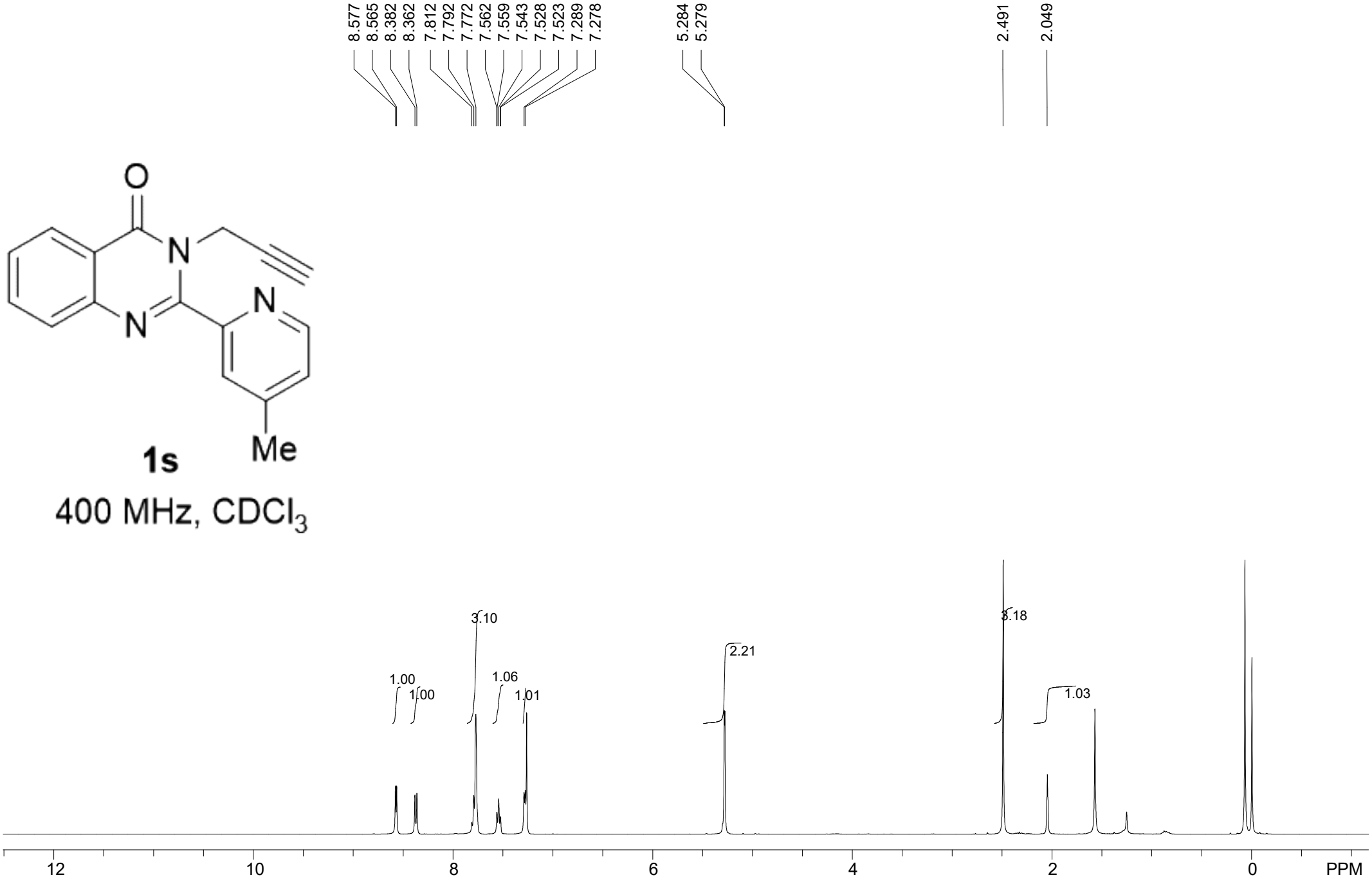

160.826
155.126
153.330
151.398
149.654
148.700
143.128
137.388
124.886
124.617
114.391
108.054
106.002
78.483
77.253
77.000
76.743
71.540
56.356
56.340
33.816
O
MeO
MeO
N
N
N
1p
100 MHz, CDCl3
200
150
100
50
0
PPM

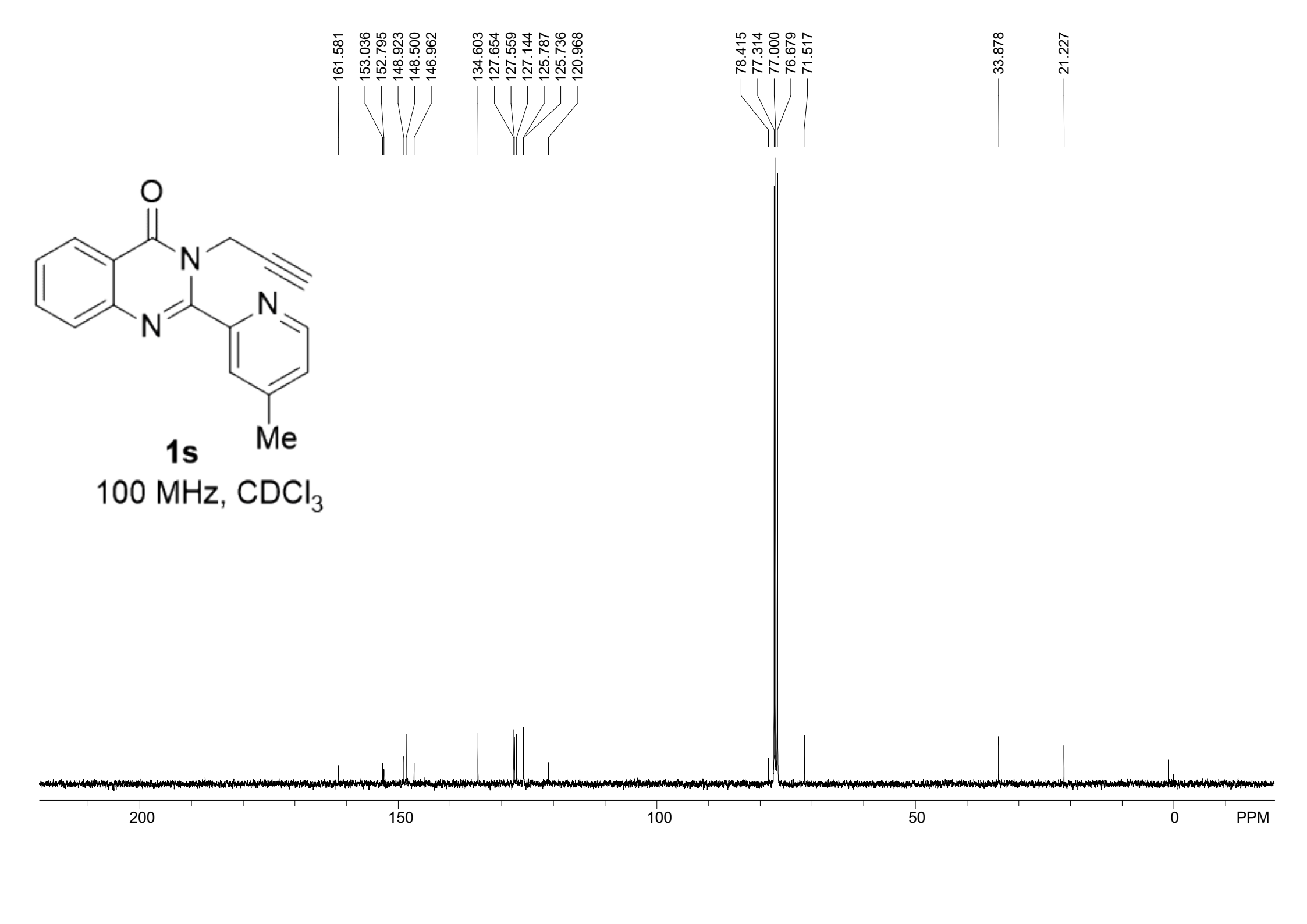

8.704
8.693
8.127
8.107
8.028
8.008
7.932
7.915
7.896
7.465
7.452
7.448
7.434
7.347
7.327
5.390
5.386
2.566
2.445
1.984
O
N
N
N
Me
Me
1q
400 MHz, CDCl3
1.03
1.06
1.04
1.07
1.04
1.06
2.11
3.08
3.01
1.00
10
8
6
4
2
0
PPM

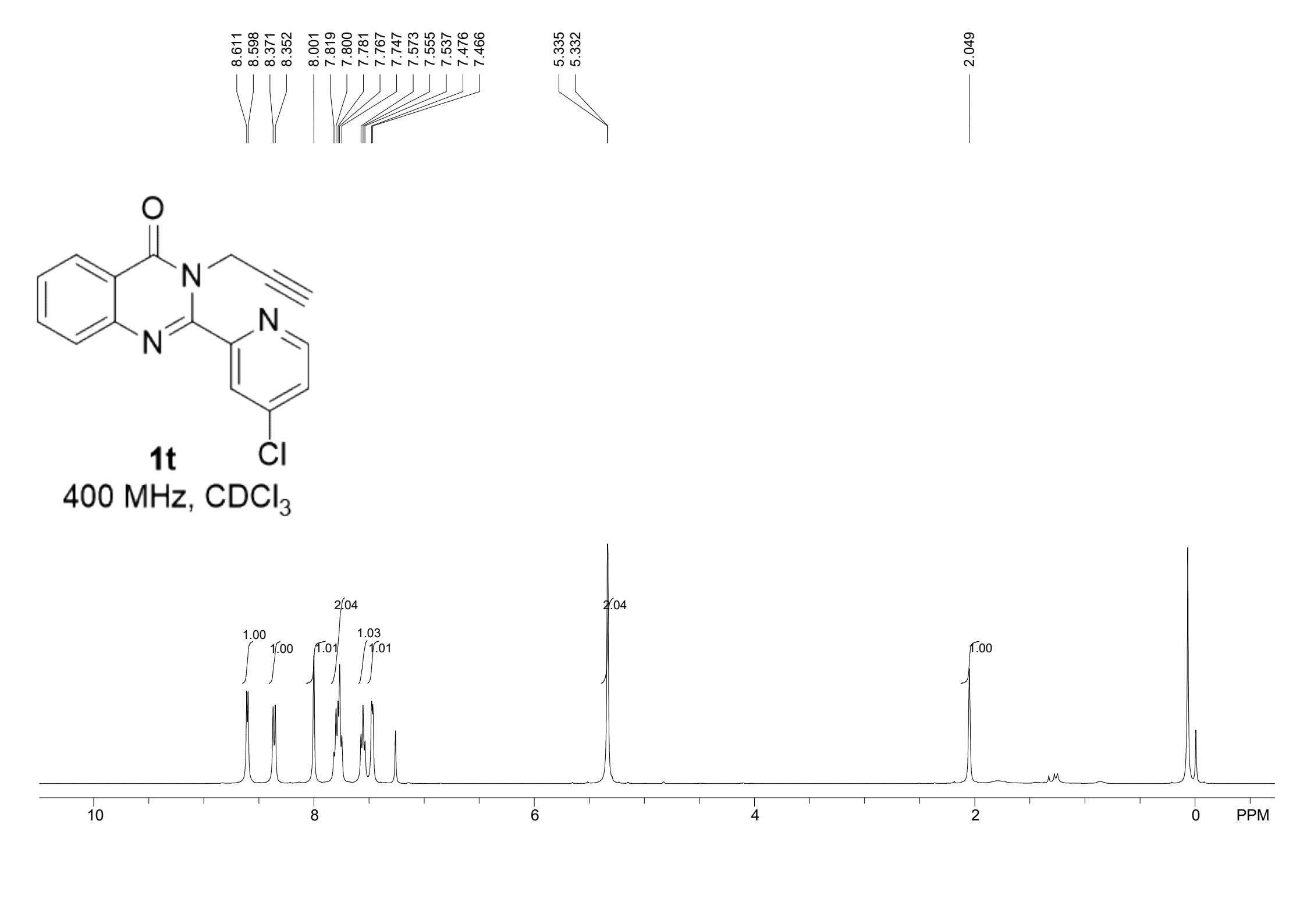

162.150
153.882
150.659
148.231
145.212
143.579
137.199
134.275
129.535
125.408
124.533
123.957
118.868
78.750
77.321
77.000
76.687
71.254
33.528
20.928
13.024
O
N
N
N
Me
Me
1q
100 MHz, CDCl3
200
150
100
50
0
PPM

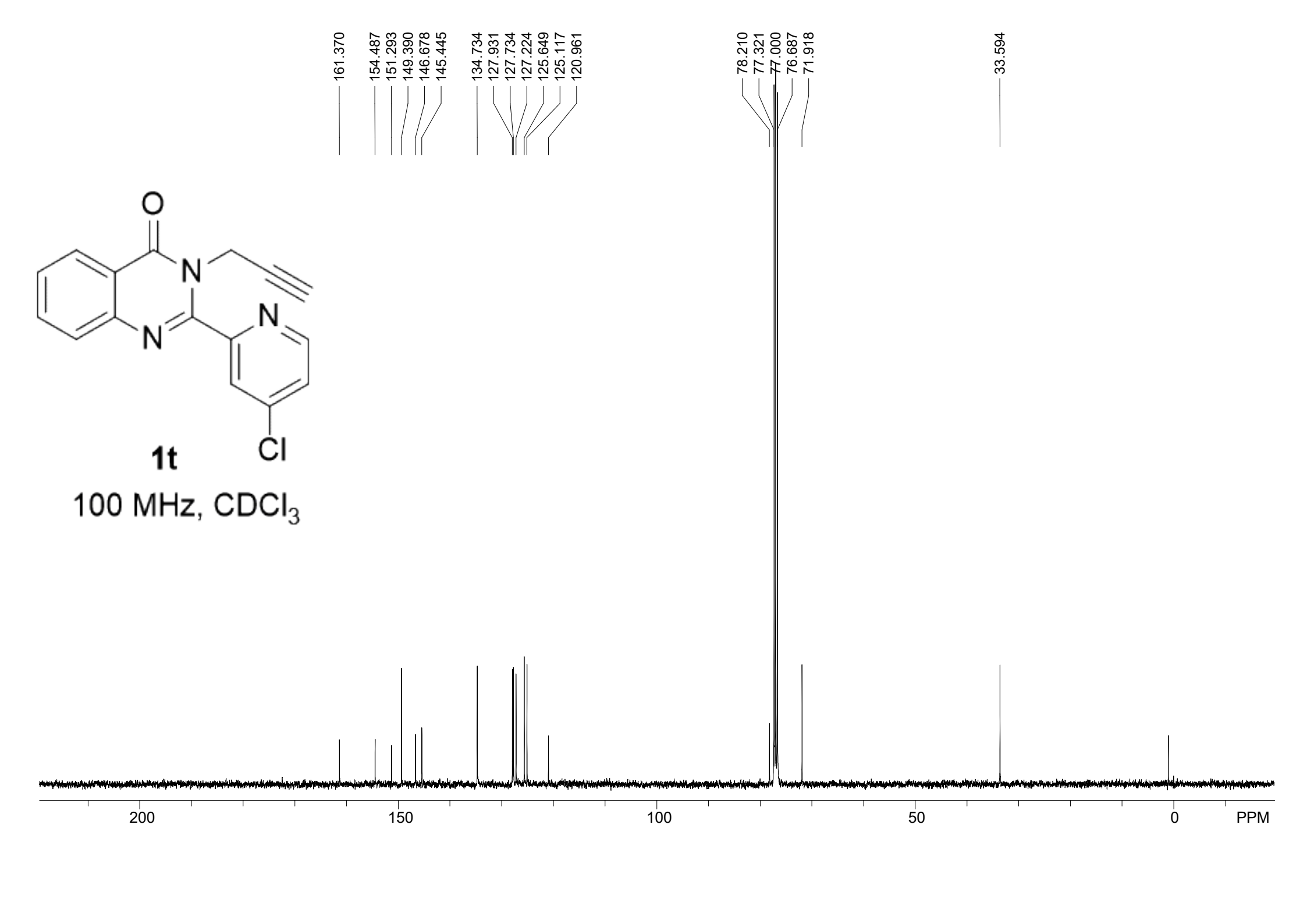

8.551
8.541
8.389
8.370
7.808
7.789
7.771
7.740
7.731
7.721
7.711
7.566
7.548
7.530
7.389
7.377
7.370
7.358
7.260
4.908
2.426
2.053
O
N
N
N
Me
1r
400 MHz, CDCl3
1.00
1.03
2.02
1.07
1.06
1.03
2.09
3.08
1.00
10
8
6
4
2
PPM

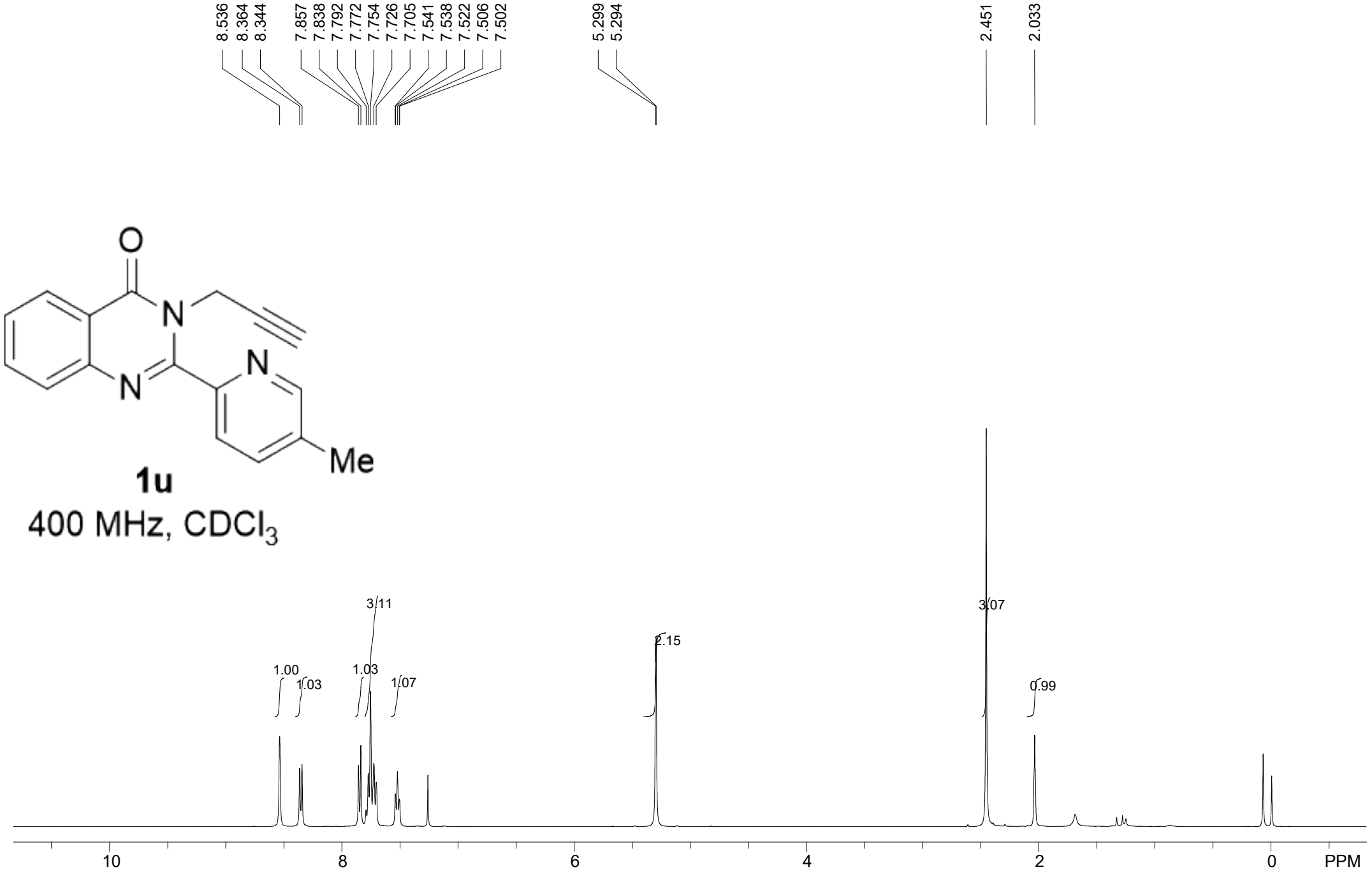

161.304
152.205
151.752
146.955
146.699
139.306
134.632
133.320
127.574
127.078
124.672
121.128
77.583
77.321
77.000
76.679
71.524
33.382
18.748
O
N
N
N
Me
1r
100 MHz, CDCl3
200
150
100
50
0
PPM

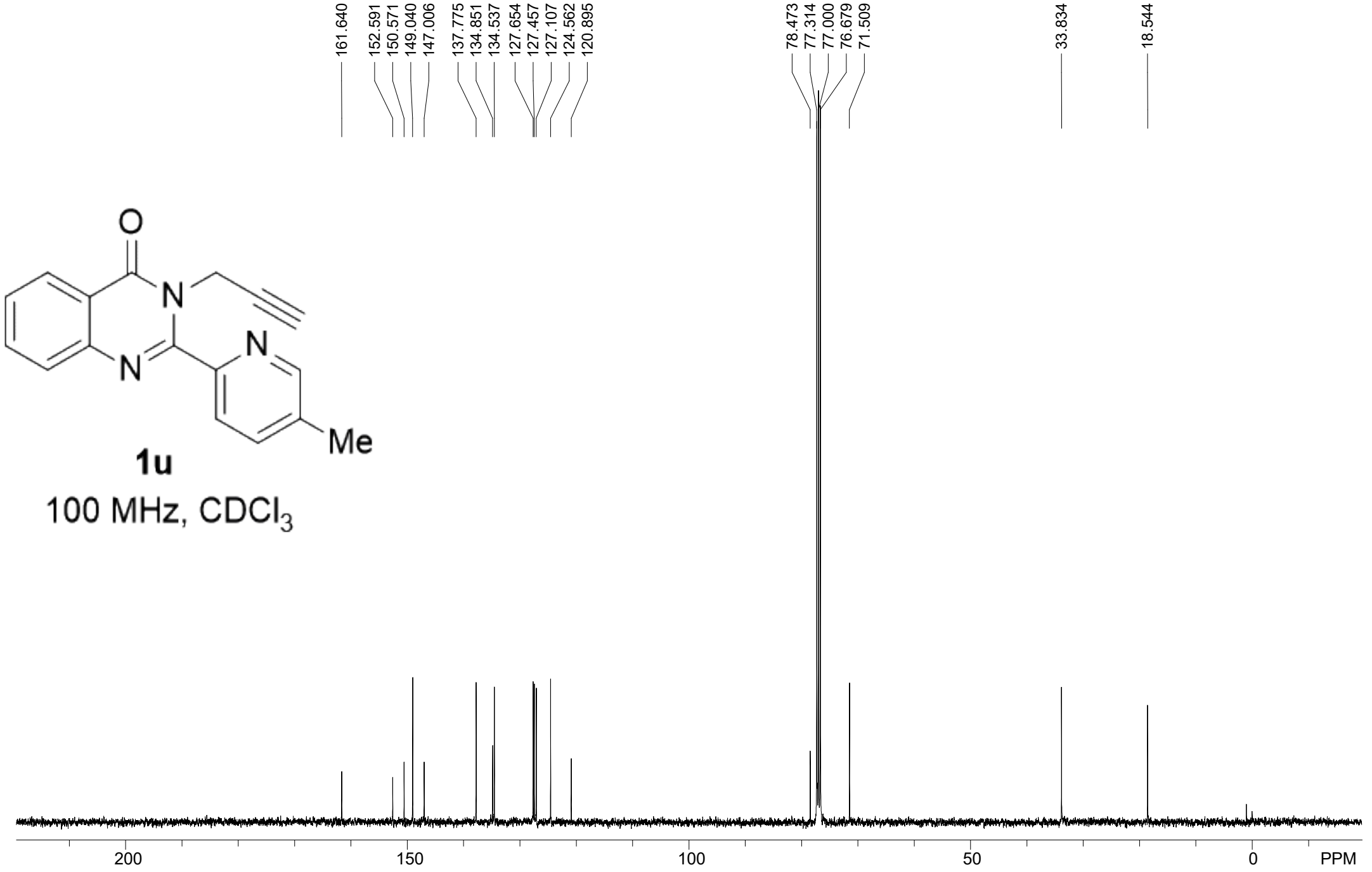

8.577
8.565
8.382
8.362
7.812
7.792
7.772
7.562
7.559
7.543
7.528
7.523
7.289
7.278
5.284
5.279
2.491
2.049
O
N
N
N
Me
1s
400 MHz, CDCl3
1.00
1.00
3.10
1.06
1.01
2.21
3.18
1.03
12
10
8
6
4
2
0
PPM

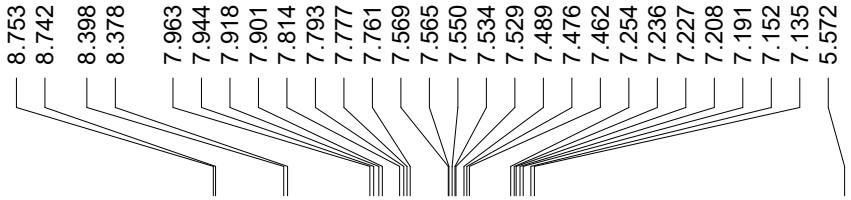

161.581
153.036
152.795
148.923
148.500
146.962
134.603
127.654
127.559
127.144
125.787
125.736
120.968
78.415
77.314
77.000
76.679
71.517
33.878
21.227
O
N
N
N
Me
1s
100 MHz, CDCl3
200
150
100
50
0
PPM

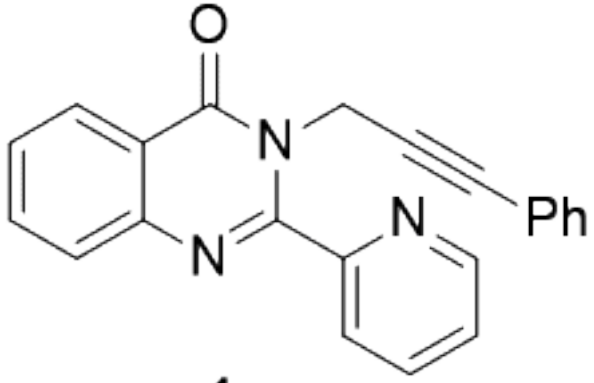

8.611
8.598
8.371
8.352
8.001
7.819
7.800
7.781
7.767
7.747
7.573
7.555
7.537
7.476
7.466
5.335
5.332
2.049
O
N
N
N
Cl
1t
400 MHz, CDCl3
1.00
1.00
1.01
2.04
1.03
1.01
2.04
1.00
10
8
6
4
2
0
PPM


161.370
154.487
151.293
149.390
146.678
145.445
134.734
127.931
127.734
127.224
125.649
125.117
120.961
78.210
77.321
77.000
76.687
71.918
33.594
O
N
N
N
Cl
1t
100 MHz, CDCl3
200
150
100
50
0
PPM


8.536
8.364
8.344
7.857
7.838
7.792
7.772
7.754
7.726
7.705
7.541
7.538
7.522
7.506
7.502
5.299
5.294
2.451
2.033
O
N
N
N
Me
1u
400 MHz, CDCl3
3.11
2.15
3.07
1.00
1.03
1.03
1.07
0.99
10
8
6
4
2
0
PPM

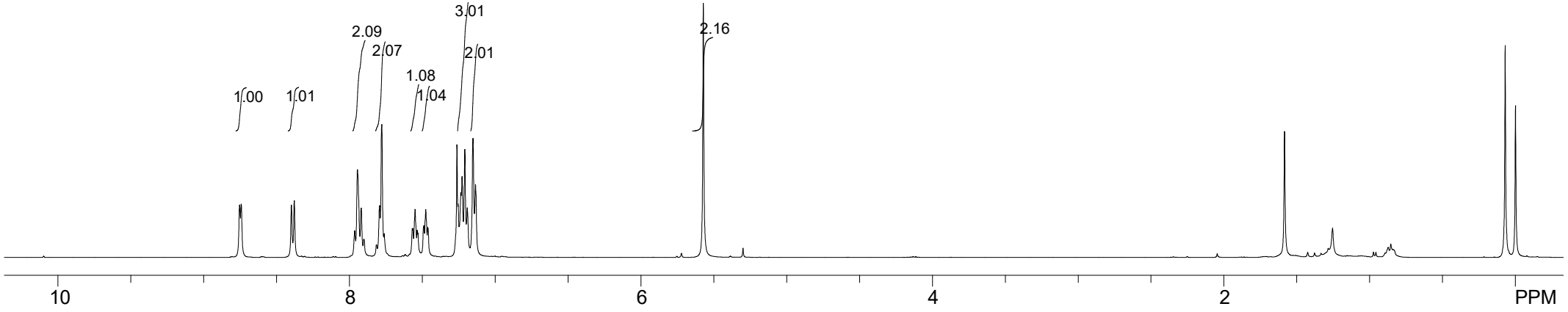

161.640
152.591
150.571
149.040
147.006
137.775
134.851
134.537
127.654
127.457
127.107
124.562
120.895
78.473
77.314
77.000
76.679
71.509
33.834
18.544
O
N
N
N
Me
1u
100 MHz, CDCl3
200
150
100
50
0
PPM

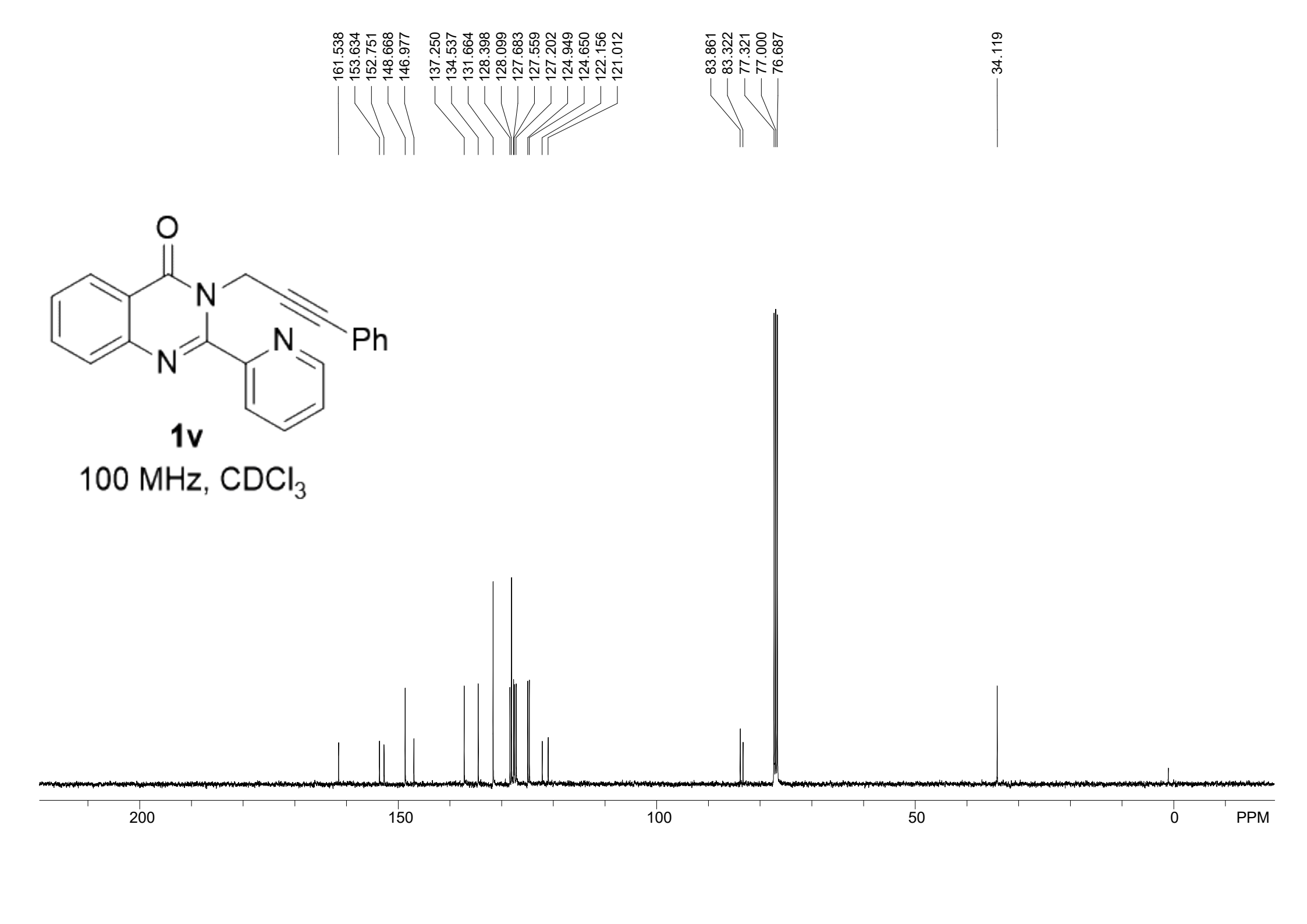


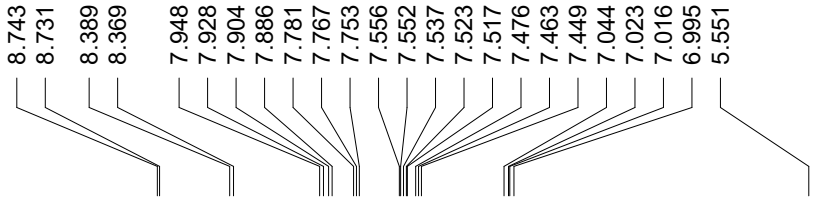


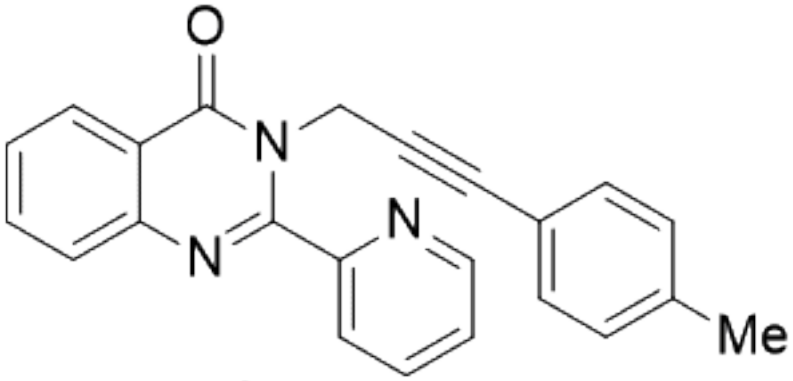
1v

400 MHz, $CDCl_3$



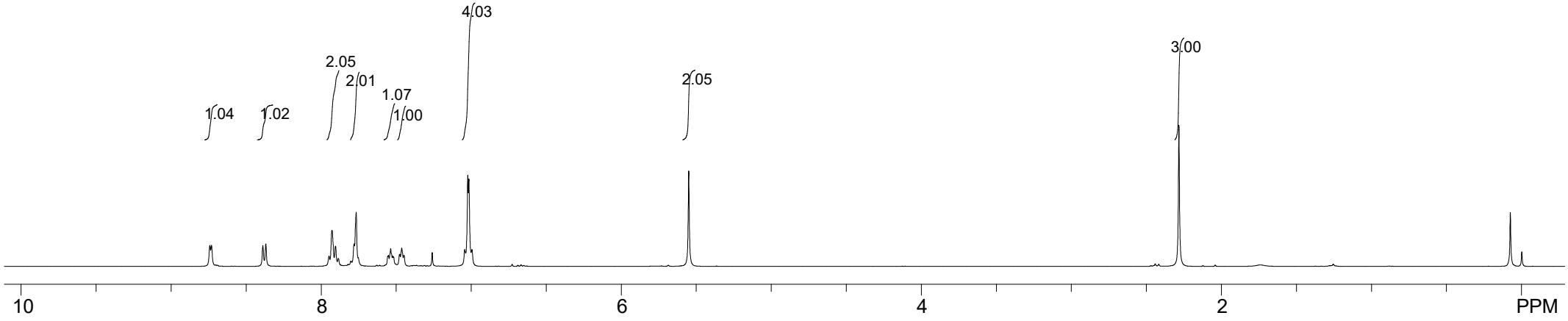

161.538
153.634
152.751
148.668
146.977
137.250
134.537
131.664
128.398
128.099
127.683
127.559
127.202
124.949
124.650
122.156
121.012
83.861
83.322
77.321
77.000
76.687
34.119
O
N
N
N
Ph
1v
100 MHz, CDCl3
200
150
100
50
0
PPM

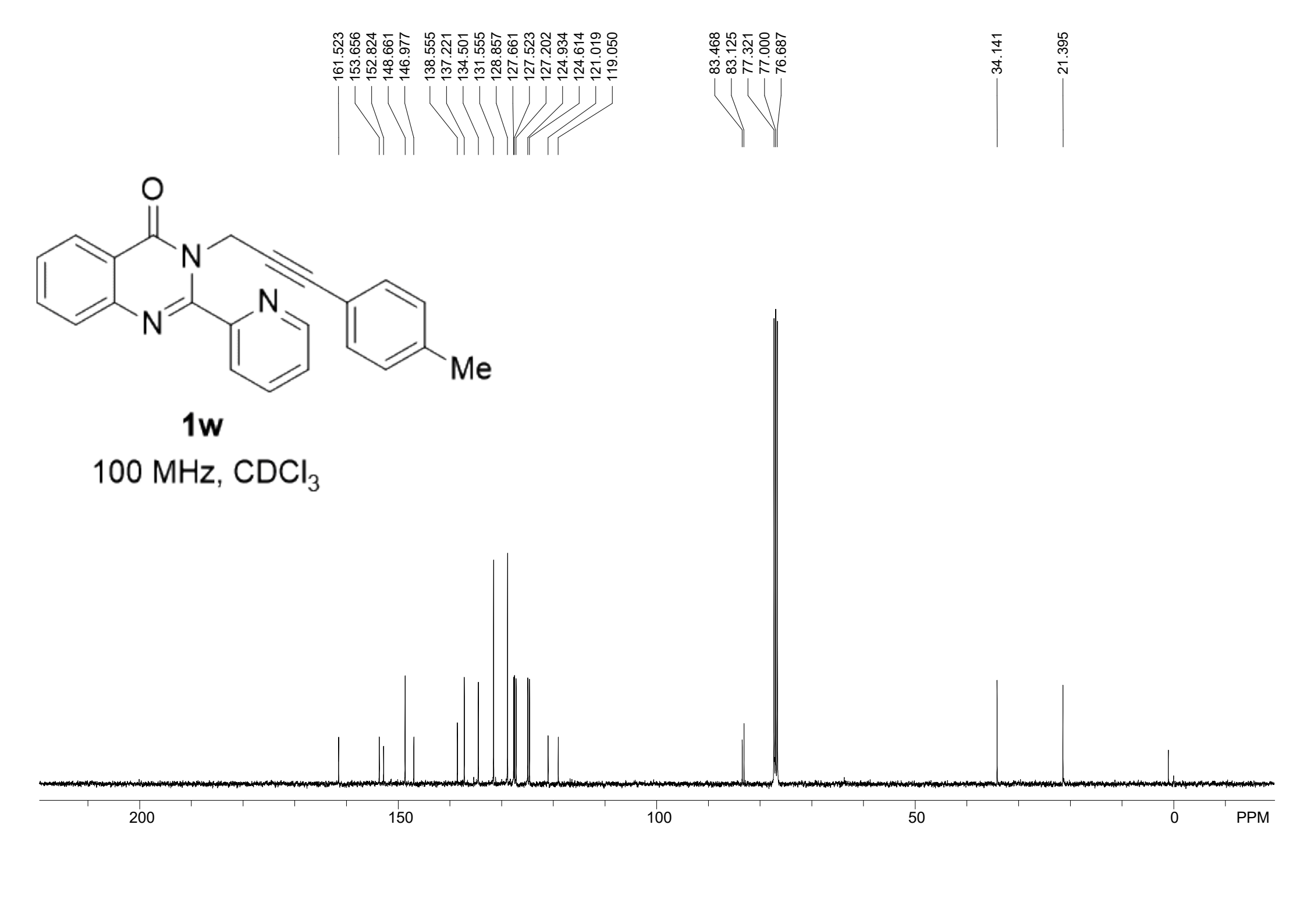


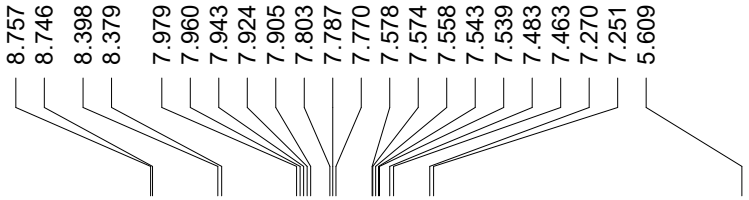


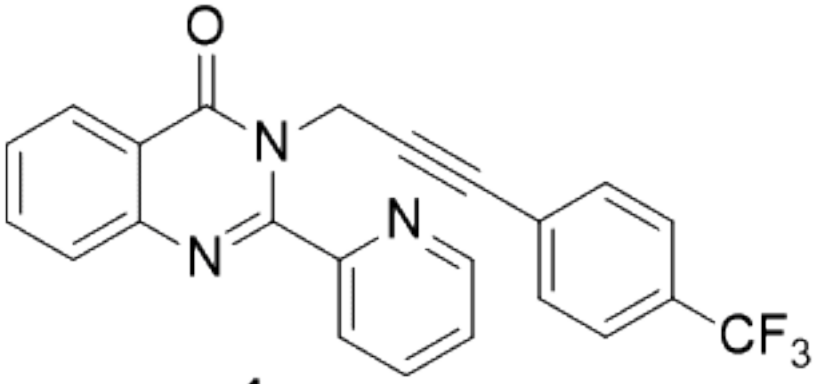
1w

400 MHz, $CDCl_3$



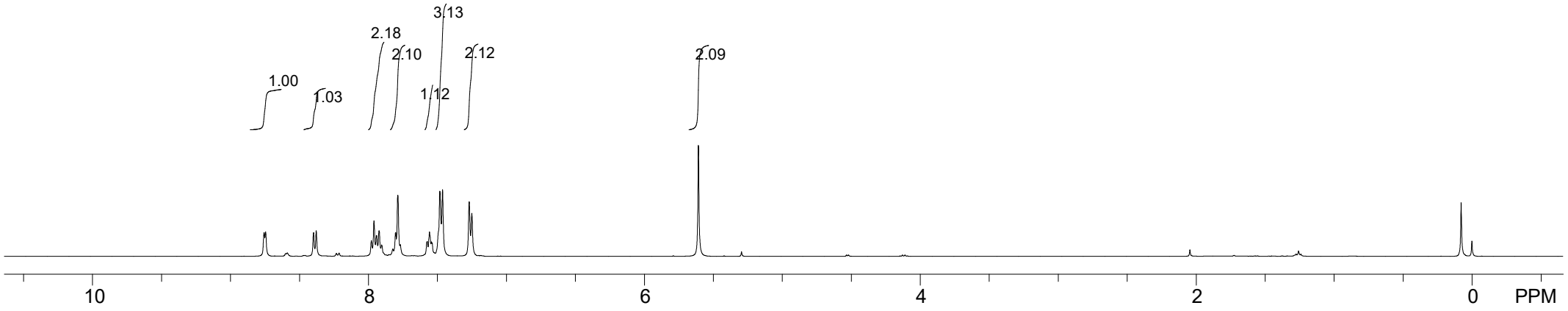

161.523
153.656
152.824
148.661
146.977
138.555
137.221
134.501
131.555
128.857
127.661
127.523
127.202
124.934
124.614
121.019
119.050
83.468
83.125
77.321
77.000
76.687
34.141
21.395
O
N
N
N
Me
1w
100 MHz, CDCl3
200
150
100
50
0
PPM

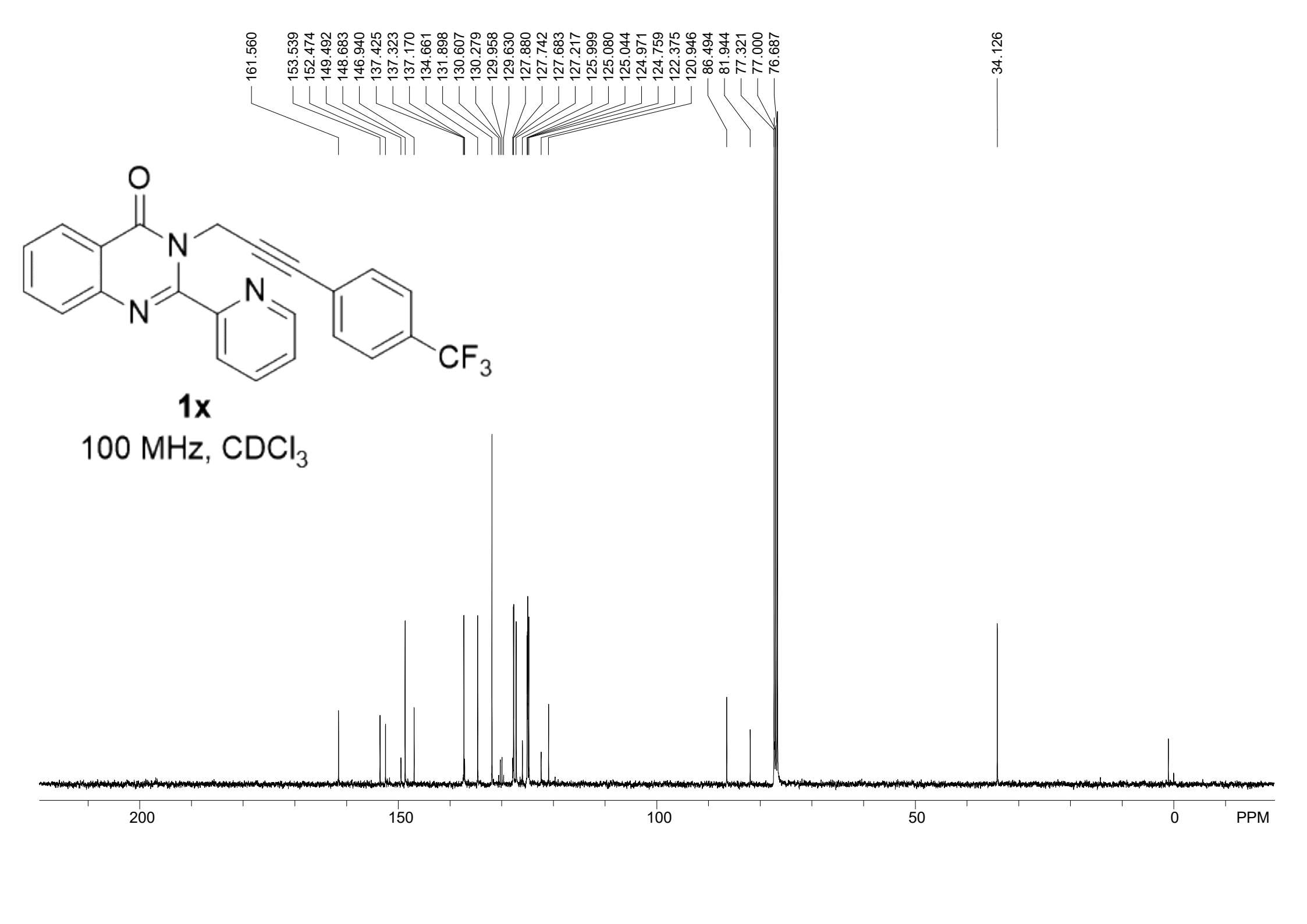


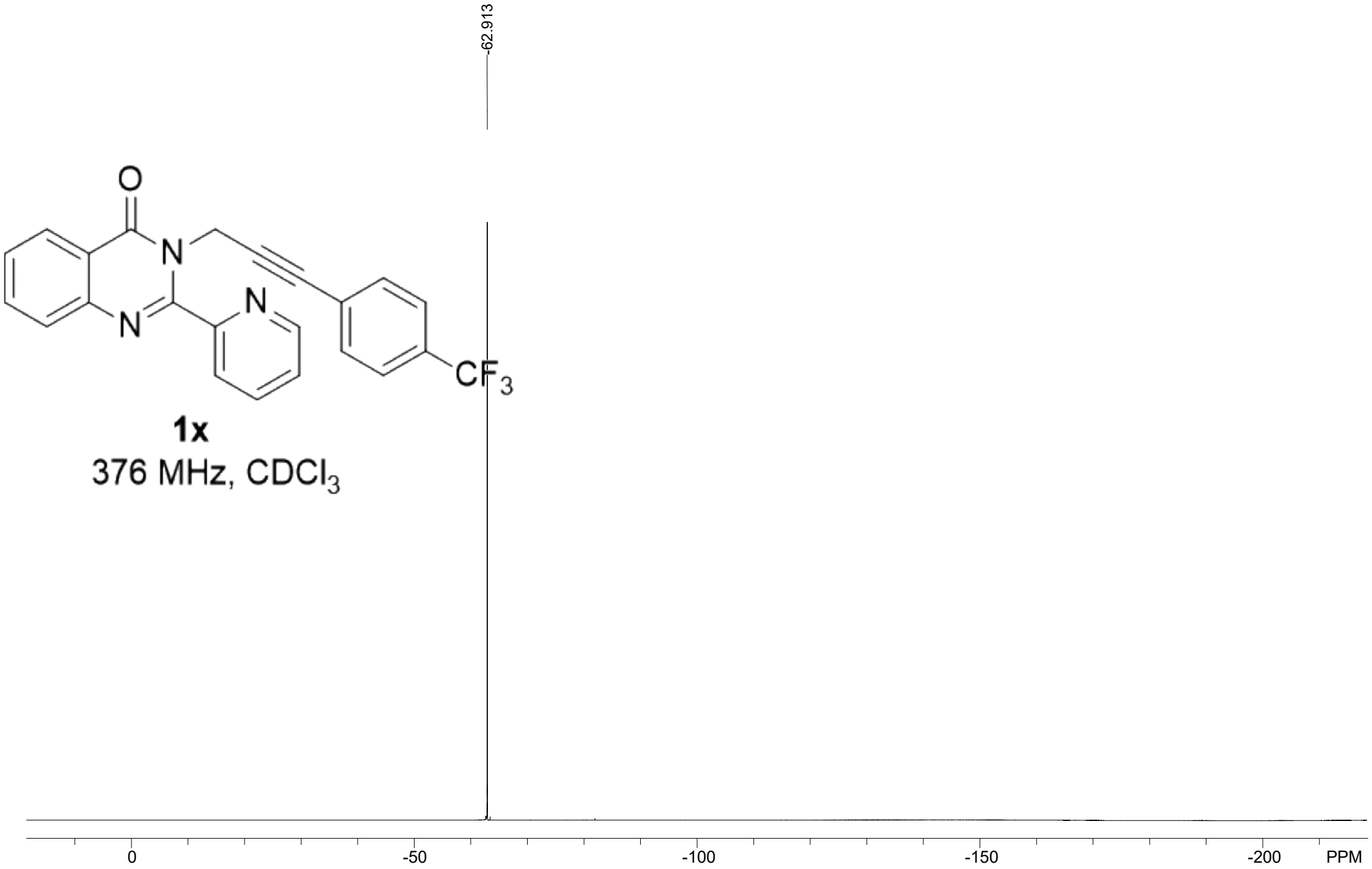


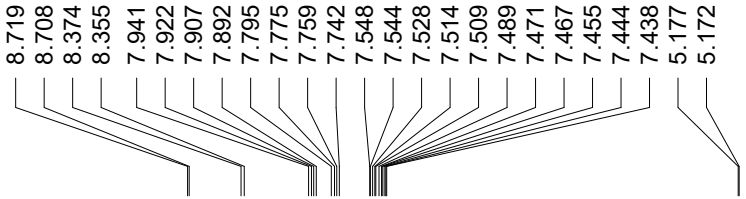
1x

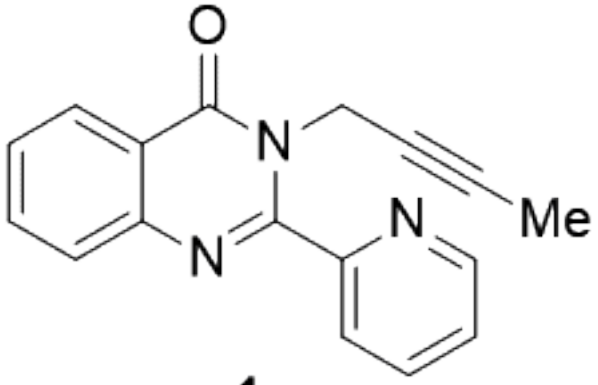
400 MHz, $CDCl_3$




161.560
153.539
152.474
149.492
148.683
146.940
137.425
137.323
137.170
134.661
131.898
130.607
130.279
129.958
129.630
127.880
127.742
127.683
127.217
125.999
125.080
125.044
124.971
124.759
122.375
120.946
86.494
81.944
77.321
77.000
76.687
34.126
O
N
N
N
CF3
1x
100 MHz, CDCl3
200
150
100
50
0
PPM

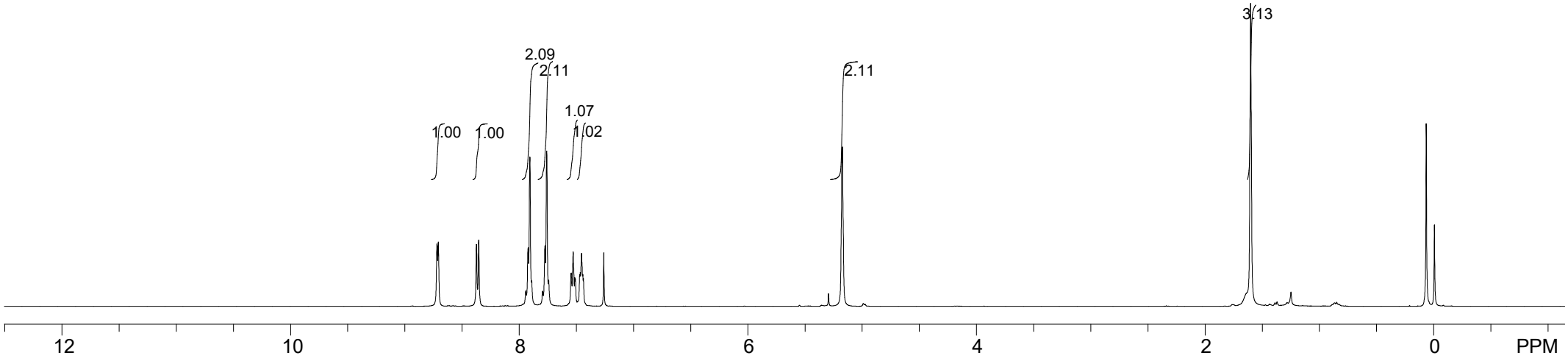

-62.913
O
N
N
N
CF3
1x
376 MHz, CDCl3
0
-50
-100
-150
-200
PPM

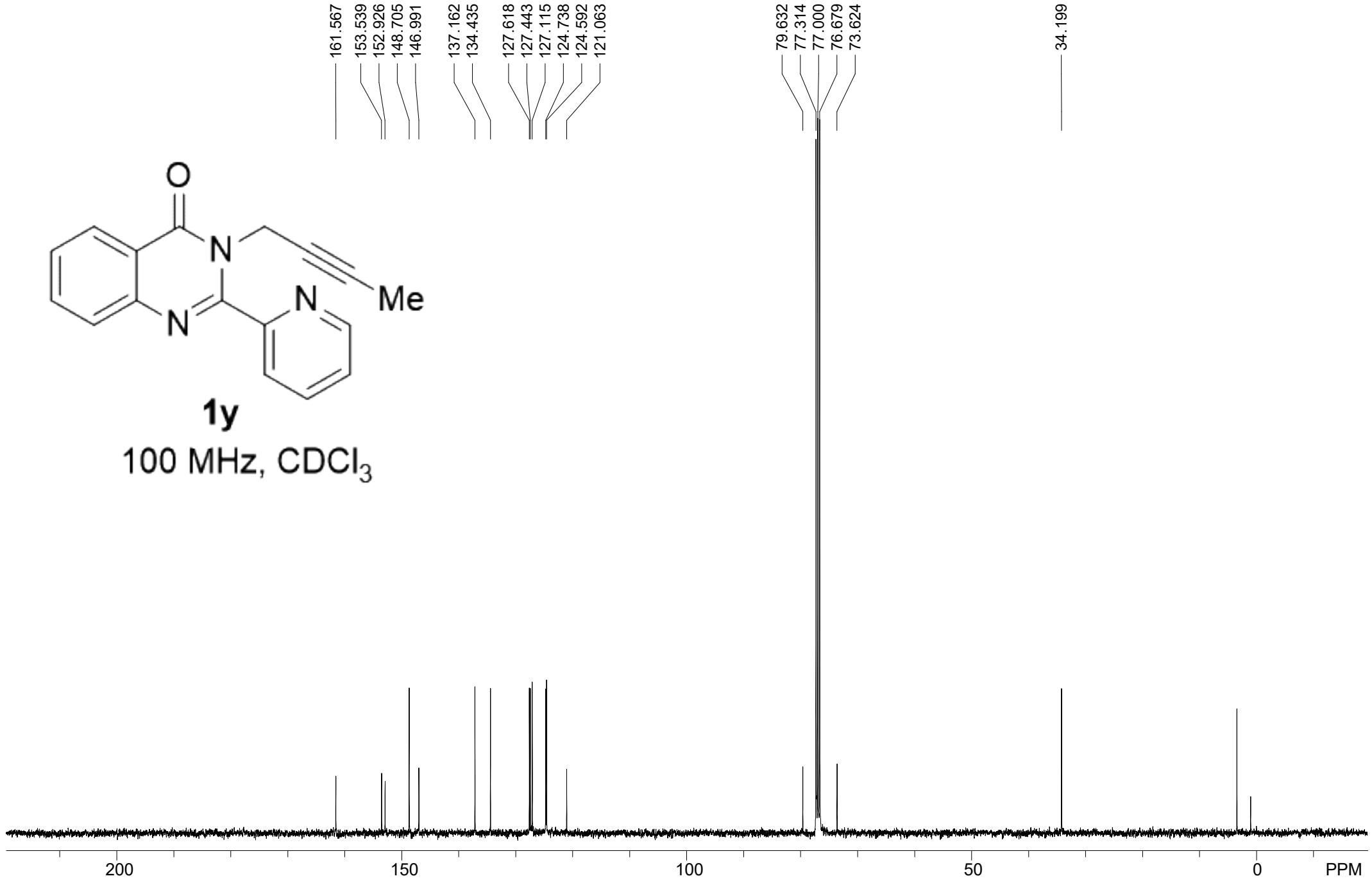


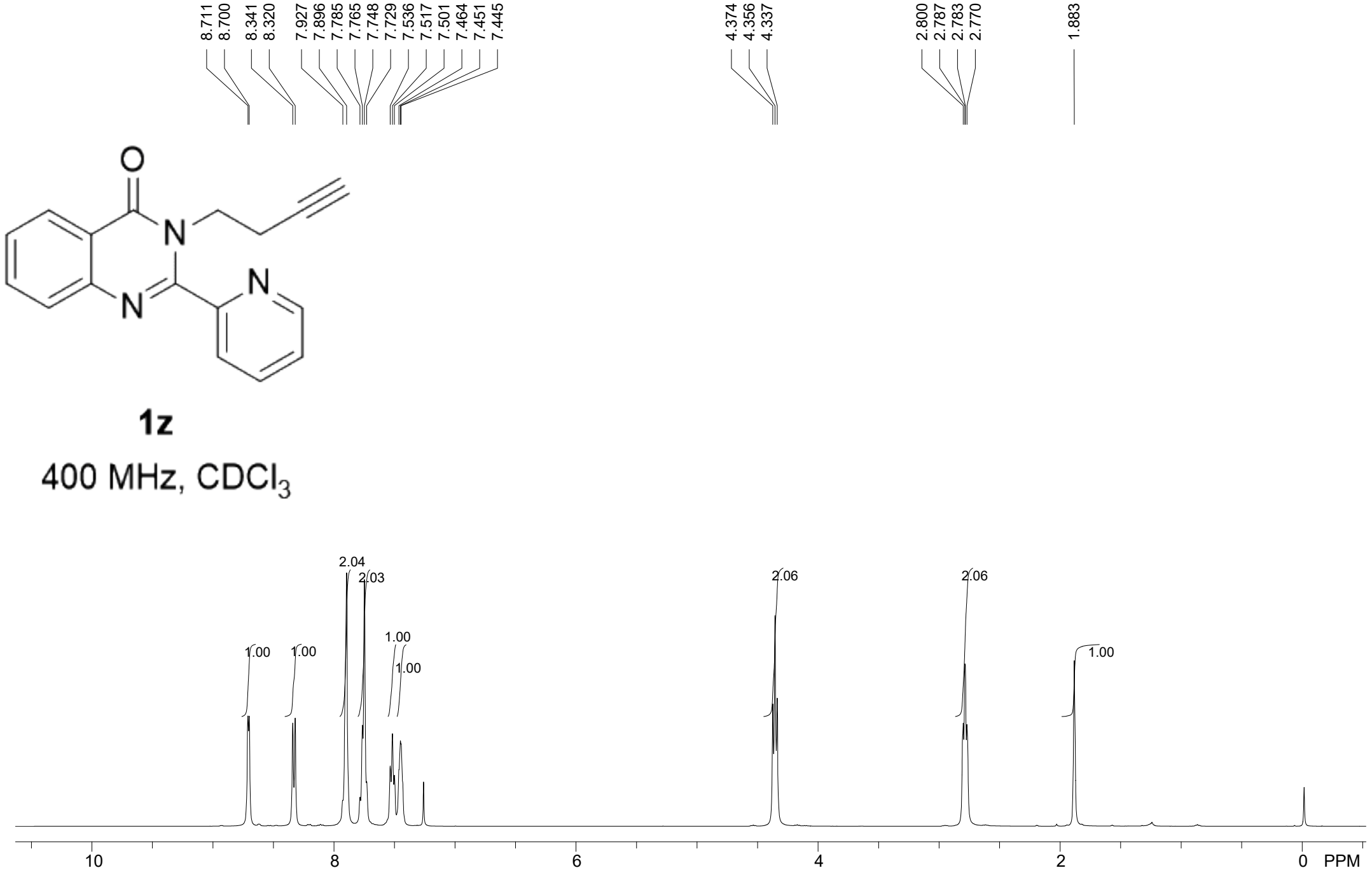


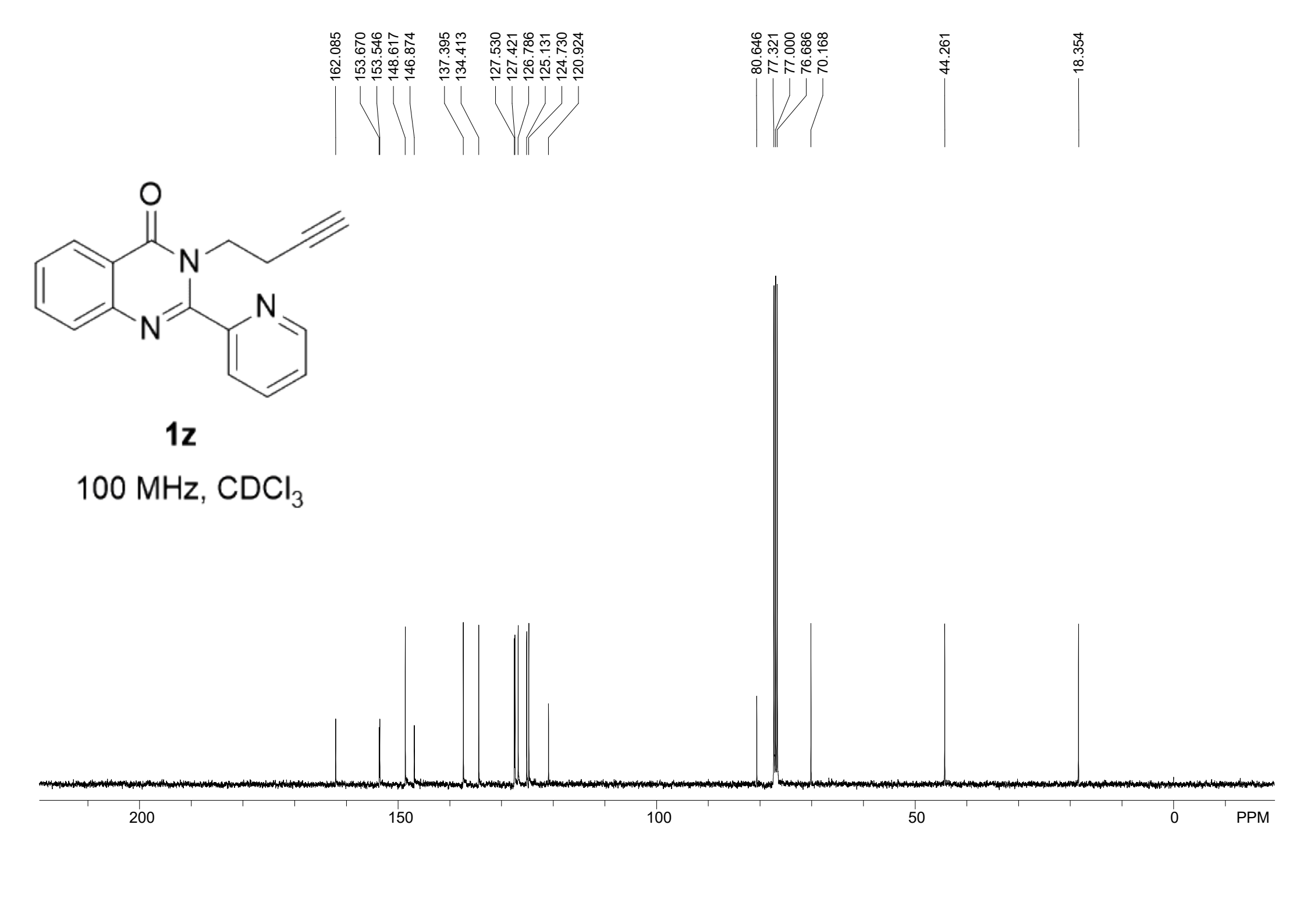
1y

400 MHz, $CDCl_3$




161.567
153.539
152.926
148.705
146.991
137.162
134.435
127.618
127.443
127.115
124.738
124.592
121.063
79.632
77.314
77.000
76.679
73.624
34.199
O
N
N
N
Me
1y
100 MHz, CDCl3
200
150
100
50
0
PPM


8.711
8.700
8.341
8.320
7.927
7.896
7.785
7.765
7.748
7.729
7.536
7.517
7.501
7.464
7.451
7.445
4.374
4.356
4.337
2.800
2.787
2.783
2.770
1.883
O
N
N
N
1z
400 MHz, CDCl3
1.00
1.00
2.04
2.03
1.00
1.00
2.06
2.06
1.00
10
8
6
4
2
0
PPM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80.646
77.321
77.000
76.686
70.168
44.261
18.354
O
N
N
N
1z
100 MHz, CDCl3
200
150
100
50
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PPM