Syntheses and Antibacterial Activity of *N*-acylated Ciprofloxacin Derivatives Based on the Trimethyl Lock

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Supporting Information

I. General.

All reactions were carried out under argon by using standard techniques. All solvents and reagents were obtained from commercial sources and used without further purification unless otherwise stated. NMR spectra were recorded on a Varian Inova 500 MHz spectrometer or Varian 600 MHz spectrometer at ambient temperature. Silica gel column chromatography was performed using Sorbent Technologies silica gel 60 (32-63 μm). Reverse Phase C18 Silica Gel was a generous gift from Eli Lilly and Co. Analytical high-performance liquid chromatography (HPLC) was performed on a Waters 1525 Binary HPLC Pump instrument with a Waters 2487 Detector set at 254 nm, using a Phenomenex C18 BDS reverse phase column (4.6×250 mm). Mobile phases used were 10 mM ammonium acetate in HPLC grade water (A) and HPLC grade acetonitrile (B). A gradient was formed from 5%–100% of B in 10 min, then 100% of B in 5 min, and then 100%–5% of B in 5 min at a flow rate of 1 mL/min (total run time of 20 min). Lactone **4** was prepared according to a published procedure.[1]

II. Experimental Procedures and Compound Characterization Data

3-(5-Bromo-2,4-dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)-3-methylbutanoic acid, 5H. This compound was prepared by a modified literature procedure.[1] To a solution of lactone **4** (6.6 g, 30 mmol) dissolved in 200 mL of AcOH was added dropwise a solution of bromine (3.4 mL, 66 mmol) in 30 mL of AcOH and the reaction mixture was stirred at room temperature for 24 h. The reaction was concentrated under reduced pressure and the residue was partitioned between water (200 mL) and ether (200 mL). The aqueous layer was extracted with ether (3×50 mL). The ethereal solution was then extracted with sat. $NaHCO_3$ (5×150 mL), and the combined aqueous layers were acidified with conc. HCl to pH=2. The aqueous solution was extracted with ether (3 ×100 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated to give acid **5H** (7.5 g, 80%) as a yellow oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.05 (s, 2H), 2.19 (s, 3H), 2.17 (s, 3H), 1.46 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 184.6, 182.4, 177.8, 152.5, 144.0, 139.6, 136.2, 47.1, 38.6, 28.7, 16.7, 14.6.

Methyl 3-(5-bromo-2,4-dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)-3-methyl butanoate, 5Me. To a solution of bromo acid **5H** (4.88 g, 15.5 mmol) in 50 mL of MeOH cooled to 0 ºC was added $SOCl_2$ (2.25 mL, 31.0 mmol). The solution was heated to reflux for 1 h. After removal of the solvent, the tan oily residue was purified by chromatography on a silica gel column (hexanes:EtOAc=10:1 to 6:1) to give ester **5Me** (3.92 g, 77%) as a yellow oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.57 (s, 3H), 2.98 (s, 2H), 2.17 (s, 3H), 2.12 (s, 3H), 1.43 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 185.2, 182.3, 173.1, 152.6, 141.3, 140.3, 139.6, 51.5, 47.4, 38.8, 28.8, 14.6, 13.6; HRMS (EI) calcd. for $C_{14}H_{17}O_4{}^{79}Br$ $(M)^{\cdot+}$: 328.0310, found 328.0288.

Methyl 3-(5-azido-2,4-dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)-3-methyl butanoate, 6. To a solution of ester **5Me** (2.87 g, 8.72 mmol) dissolved in 30 mL of methanol was added sodium azide (1.7 g, 26.2 mmol) in three portions followed by 10 mL of water and the mixture was stirred at room temperature for 16 h. The organic solvent was removed under vacuum and the residue was taken into water (50 mL) and extracted with CH_2Cl_2 (50 mL×3). The combined organic layer was washed with brine, dried over Na_2SO_4 and filtered. After removal of the solvent under vacuum, the residue was purified by chromatography on a silica gel column (hexanes:EtOAc=10:1 to 8:1) to give azide **6** (2.31 g, 91%) as an orange oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.61 (s, 3H), 2.99 (s, 2H), 2.14 (s, 3H), 1.89 (s, 3H), 1.43 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.2, 184.7, 173.7, 151.0, 142.5, 140.3, 126.3, 51.8, 47.3, 38.5, 28.7, 14.7, 10.9; HRMS (EI) calcd. for $C_{14}H_{17}NO_4$ $(M\text{-}N_2)^{\cdot+}$: 263.1158, found 263.1151.

Methyl 3-(5-amino-2,4-dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)-3-methyl butanoate, 7Me. To a stirred solution of azide **6** (2.43 g, 8.35 mmol) in 50 mL of CH_2Cl_2 was added triphenylphosphine (2.19 g, 8.35 mmol) in three portions. The deep purple solution was stirred at room temperature for 1 h. After removal of the solvent under vacuum, the purple residue was taken into a mixture of acetic acid (30 mL), THF (30 mL) and water (10 mL). The mixture was heated to reflux for 4 h and all solvent was removed under vacuum. The residue was partitioned between EtOAc (100 mL) and H_2O (100 mL). The organic layer was washed sequentially with sat. $NaHCO_3$ (100 mL), brine (100 mL), dried over Na_2SO_4 and filtered. After removal of the solvent under vacuum, the residue was purified by chromatography on a silica gel column (hexanes:EtOAc=4:1 to 2:1) to give ester **7Me** (1.46 g, 66%) as a red solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.61 (s, 2H),

3.58 (s, 3H), 2.96 (s, 2H), 2.19 (s, 3H), 1.82 (s, 3H), 1.43 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 185.9, 185.7, 173.1, 146.7, 145.0, 142.7, 109.2, 51.6, 47.5, 38.7, 29.6, 15.1, 9.1; HRMS (ESI) calcd. for $C_{14}H_{19}NNaO_4$ $(M+Na)^+$: 288.1206, found 288.1218.

3-(5-Amino-2,4-dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)-3-methylbutanoic acid, 7H. To a solution of methyl ester **7Me** (1.30 g, 4.9 mmol) in 20 mL of MeOH/H_2O 4:1 was added LiOH (360 mg, 15 mmol) and the mixture was stirred at room temperature for 16 h. After removal of the MeOH under reduced pressure, the solution was diluted with 20 mL of water and acidified with 3 M HCl to pH=2. The precipitate was collected with filtration and dried under vacuum to give the acid **7H** (1.12 g, 91%) as a deep purple powder: ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.98 (br. s., 1H), 6.34 (s, 2H), 2.82 (s, 2H), 2.07 (s, 3H), 1.70 (s, 3H), 1.36 (s, 6H), ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.2, 184.0, 173.2, 146.7, 146.6, 141.0, 105.3, 47.2, 37.6, 28.9, 14.6, 9.1; HRMS (ESI) calcd. for $C_{13}H_{18}O_4$ $(M+H)^+$: 252.1230, found 252.1260.

3-(2,4-Dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)-3-methylbutanoic acid, 8H. This compound was prepared by a modified literature procedure.[2] To a solution of lactone **4** (600 mg, 2.73 mmol) dissolved in a mixture of acetonitrile (18 mL), acetone (4 mL), and water (18 mL) was added *N*-bromosuccinimide (728 mg, 4.09 mmol) in three portions and the mixture was stirred at room temperature for 30 min. After removal of the organic solvents under vacuum, the residue was extracted with ether (50 mL). The ethereal solution was then extracted with sat. $NaHCO_3$ (3×20 mL), and the combined aqueous layers were acidified with conc. HCl to pH=2. The aqueous solution was extracted with ether (2×20 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated to give acid **8H** (508 mg, 79%) as a yellow oil: ^{1}H NMR (600

MHz, $CDCl_3$) δ 6.47 (q, J = 1.5 Hz, 1H), 3.06 (s, 2H), 2.18 (s, 3H), 2.00 (d, J = 1.5 Hz, 3H), 1.45 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.9, 188.4, 177.8, 151.1, 144.0, 140.6, 135.1, 47.5, 38.4, 29.4, 15.7, 14.8.

Methyl 3-(2,4-dimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)-3-methylbutanoate, 8Me. To a solution of acid **8H** (610 mg, 2.58 mmol) in 20 mL of MeOH was added conc. H_2SO_4 (3 drops) and the reaction was heated to reflux for 3 h. After concentrating under vacuum, the residue was dissolved in EtOAc (50 mL) and washed with brine. The organic layer was dried over Na_2SO_4, filtered and evaporated. The residue was purified by chromatography on a silica gel column (hexanes:EtOAc=10:1 to 6:1) to give methyl ester **8Me** (613 mg, 95%) as a yellow oil: ^1H NMR (600 MHz, $CDCl_3$) δ 6.48 (q, J = 1.5 Hz, 1H), 3.57 (s, 3H), 3.00 (s, 2H), 2.16 (s, 3H), 1.98 (d, J = 1.5 Hz, 3H), 1.42 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.8, 188.3, 173.3, 151.6, 143.8, 140.1, 135.1, 51.5, 47.6, 38.5, 29.2, 15.7, 14.7.

General procedure for synthesis of *N*-acyl ciprofloxacin derivatives: To a solution of the acid (1 mmol) in 20 mL of CH_2Cl_2 were added EDC (192 mg, 1 mmol) and HOBt (135 mg, 1 mmol). The mixture was stirred for 15 min before ciprofloxacin (82 mg, 0.25 mmol) was added. The mixture was stirred at room temperature for 16 h. The mixture was diluted with 20 mL of CH_2Cl_2 and washed sequentially with sat. NH_4Cl (20 mL), brine (20 mL), dried over Na_2SO_4 and filtered. After removal of the solvent under vacuum, the residue was purified by chromatography to afford the *N*-acyl ciprofloxacin derivatives.

***N*-acyl ciprofloxacin derivative, 5-Cip.** The product was purified by chromatography on a reverse-phase silica gel column (CH_3CN:H_2O=2:3 to 3:2) to give a

yellow solid in 44% yield: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.03 (d, *J* = 12.6 Hz, 1H), 7.38 (d, *J* = 7.0 Hz, 1H), 3.75-3.80 (m, 2H), 3.71-3.75 (m, 2H), 3.53-3.59 (m, 1H), 3.38-3.43 (m, 2H), 3.25-3.31 (m, 2H), 3.08 (s, 2H), 2.20 (s, 3H), 2.16 (s, 3H), 1.50 (s, 6H), 1.39-1.44 (m, 2H), 1.20-1.24 (m, 2H); HRMS (ESI) calcd. for $C_{30}H_{32}{}^{79}BrFN_3O_6$ $(M+H)^+$: 628.1453, found 628.1456.

***N*-acyl ciprofloxacin derivative, 7-Cip.** The product was purified by chromatography on a silica gel column (5-10% MeOH in $CHCl_3$) to give a red solid in 71% yield: ^{1}H NMR (500 MHz, DMSO-d_6) *d* 8.67 (s, 1H), 7.93 (d, *J* = 13.2 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 6.22 (s, 2H), 3.79-3.83 (m, 1H), 3.68-3.73 (m, 2H), 3.58-3.63 (m, 2H), 3.33-3.37 (m, 2H), 3.23-3.28 (m, 2H), 3.03 (s, 2H), 2.05 (s, 3H), 1.70 (s, 3H), 1.38 (s, 6H), 1.29-1.34 (m, 2H), 1.17-1.21 (m, 2H); HRMS (ESI) calcd for $C_{30}H_{34}FN_4O_6$ $(M+H)^+$: 565.2457, found 565.2434.

***N*-acyl ciprofloxacin derivative, 8-Cip.** The product was purified by chromatography on a reverse-phase silica gel column (CH_3CN:H_2O=2:3 to 3:2) to give a yellow solid in 51% yield: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.05 (d, *J* = 12.6 Hz, 1H), 7.36 (d, *J* = 7.0 Hz, 1H), 6.45 (q, *J* = 1.5 Hz, 1H), 3.76-3.80 (m, 2H), 3.72-3.76 (m, 2H), 3.52-3.58 (m, 1H), 3.35-3.40 (m, 2H), 3.22-3.27 (m, 2H), 3.12 (s, 2H), 2.20 (s, 3H), 2.00 (d, *J* = 1.5 Hz, 3H), 1.48 (s, 6H), 1.39-1.44 (m, 2H), 1.19-1.25 (m, 2H); HRMS (ESI) calcd for $C_{30}H_{33}FN_3O_6$ $(M+H)^+$: 550.2348, found 550.2368.

***N*-Acyl ciprofloxacin derivative, 9.** To a suspension of ciprofloxacin (993 mg, 3.0 mmol) in 30 mL of THF were added 6.3 mL of 1 M NaOH solution and Boc_2O (690 mg, 3.16 mmol). The mixture was stirred at room temperature for 16 h. After removal of the organic solvent, the residue was taken into sat. NH_4Cl solution (100 mL) and

extracted with EtOAc (100 mL×3). The combined organic layers were washed with brine, dried over Na_2SO_4 and filtered. The solvent was removed to give the product in quantitative yield as a white solid, the spectra of which were identical to this known compound[3]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.02 (d, J = 13.0 Hz, 1H), 7.37 (d, J = 7.2 Hz, 1H), 3.63-3.74 (m, 4H), 3.55 (m, 1H), 3.21-3.37 (m, 4H), 1.51 (s, 9H), 1.41 (m, 2H), 1.17-1.26 (m, 2H); HRMS (ESI) calcd. for $C_{22}H_{26}FN_3NaO_5$ $(M+Na)^+$: 454.1754, found 454.1733.

***N*-Acyl ciprofloxacin derivative, 10.** To a solution of 3,3-dimethylbutyric acid (127 μL, 1 mmol) in 10 mL of CH_2Cl_2 were added EDC (192 mg, 1 mmol) and HOBt (135 mg, 1 mmol). The mixture was stirred at room temperature for 15 min before *O*-benzyl ciprofloxacin[4] (105 mg, 0.25 mmol) and Et_3N (139 μL, 1 mmol) were added followed by DMAP (2 mg). The mixture was stirred at room temperature for 16 h and diluted with 20 mL of CH_2Cl_2. The solution was washed sequentially with sat. $NaHCO_3$ (20 mL), brine (20 mL), dried over Na_2SO_4 and filtered. After removal of the solvent under vacuum, the residue was purified by chromatography on a silica gel column (5% MeOH in CH_2Cl_2) to afford the benzylated precursor **10Bn** as a waxy solid (104 mg, 80%): ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.99 (d, J = 13.2 Hz, 1H), 7.32-7.52 (m, 5H), 7.24 (d, J = 7.0 Hz, 1H), 5.37 (s, 2H), 3.82-3.93 (m, 2H), 3.70-3.78 (m, 2H), 3.36-3.45 (m, 1H), 3.15-3.30 (m, 4H), 2.32 (s, 2H), 1.19-1.34 (m, 2H), 1.10-1.12 (m, 11H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.1, 173.1, 170.7, 165.6, 154.3, 152.6, 148.5, 144.2, 144.1, 138.1, 136.6, 128.7, 128.2, 128.1, 123.6, 123.5, 113.6, 113.5, 110.3, 105.3, 105.3, 66.5, 50.7, 50.7, 49.8, 49.8, 46.7, 44.9, 41.3, 34.7, 31.7, 30.3, 8.3; HRMS (ESI) calcd. for $C_{30}H_{35}FN_3O_4$ $(M+H)^+$: 520.2606, found 520.2587. To a solution of **10Bn** (90

mg, 0.17 mmol) in 8 mL of MeOH was added 10% Pd/C (10 mg) under argon. The flask was flushed with H_2 gas and left to stir under a hydrogen atmosphere (balloon) for 4 h. After purging with argon, the mixture was filtered and concentrated under vacuum to give **10** (72 mg, 99%) as an off-white solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.96 (d, *J* = 12.9 Hz, 1H), 7.36 (d, *J* = 7.0 Hz, 1H), 3.84-3.95 (m, 2H), 3.72-3.81 (m, 2H), 3.52-3.61 (m, 1H), 3.26-3.41 (m, 4H), 2.33 (s, 2H), 1.34-1.46 (m, 2H), 1.17-1.24 (m, 2H), 1.09 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.2, 177.2, 170.8, 167.0, 154.6, 152.9, 147.7,145.6, 145.6, 139.2, 120.3, 120.3, 112.7, 112.6, 108.3, 105.2, 105.2, 77.4, 77.2, 77.0, 50.4, 50.4, 49.7, 49.7, 46.6, 44.9, 41.1, 35.5, 31.7, 30.2, 8.4; HRMS (ESI) calcd. for $C_{23}H_{29}FN_3O_4$ $(M+H)^+$: 430.2137, found 430.2130.

2-Amino-3,5-dimethyl-6-(2-methyl-4-oxo-4-(4-phenylpiperazin-1-yl)butan-2-yl)cyclohexa-2,5-diene-1,4-dione, 7-PP. To a suspension of acid **7H** (110 mg, 0.44 mmol) in 8 mL of CH_2Cl_2 were added EDC (101 mg, 0.53 mmol) and HOBt (72 mg, 0.53 mmol). The mixture was stirred at room temperature for 15 min before phenylpiperazine (80 μL, 0.53 mmol) was added. The mixture was stirred at room temperature for 16 h and diluted with 20 mL of CH_2Cl_2. The solution was washed sequentially with water (20 mL), brine (20 mL), dried over Na_2SO_4 and filtered. After removal of the solvent under vacuum, the residue was purified by chromatography on a silica gel column (hexanes:EtOAc=4:1 to 1:1) to afford the product **7-PP** (153 mg, 88%) as a red oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21-7.33 (m, 2H), 6.82-6.95 (m, 3H), 4.56 (s, 2H), 3.65-3.70 (m, 2H), 3.60-3.65 (m, 2H), 3.14-3.19 (m, 2H), 3.05-3.10 (m, 2H), 3.04 (s, 2H), 2.17 (s, 3H), 1.78 (s, 3H), 1.44 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 186.3, 185.8, 170.5, 151.0, 148.4, 145.1, 140.4, 129.3, 120.5, 116.6, 109.1, 49.7, 49.6, 46.4, 45.7, 41.5, 38.3, 29.5, 15.1, 9.0; HRMS (ESI)

calcd for $C_{23}H_{30}N_3O_3$ $(M+H)^+$: 396.2282, found 396.2260.

3,5-Dimethyl-2-(2-methyl-4-oxo-4-(4-phenylpiperazin-1-yl)butan-2-yl)cyclohexa-2,5-diene-1,4-dione, 8-PP. To a solution of acid **8H** (200 mg, 0.85 mmol) in 10 mL of CH_2Cl_2 were added EDC (192 mg, 1 mmol) and HOBt (135 mg, 1 mmol). The mixture was stirred at room temperature for 15 min before phenylpiperazine (157 μL, 1 mmol) was added. The mixture was stirred at room temperature for 16 h and diluted with 20 mL of CH_2Cl_2. The solution was washed sequentially with water (20 mL), brine (20 mL), dried over Na_2SO_4 and filtered. After removal of the solvent under vacuum, the residue was purified by chromatography on a silica gel column (hexanes:EtOAc=4:1 to 2:1) to afford the product **8-PP** (221 mg, 68%) as an orange oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21-7.37 (m, 2H), 6.85-7.00 (m, 3H), 6.46 (q, *J* = 1.4 Hz, 1H), 3.69 (t, *J* = 5.0 Hz, 2H), 3.65 (t, *J* = 5.0 Hz, 2H), 3.20 (t, *J* = 5.0 Hz, 2H), 3.12 (t, *J* = 5.0 Hz, 2H), 3.10 (s, 2H), 2.19 (s, 3H), 2.00 (d, J = 1.40 Hz, 3H), 1.48 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1, 188.5, 170.6, 153.5, 151.1, 143.7, 137.9, 136.7, 135.1, 129.4, 120.6, 116.7, 49.8, 49.6, 47.1, 45.7, 41.6, 38.3, 29.3, 15.8, 14.6; HRMS (ESI) calcd for $C_{23}H_{28}N_2NaO_3$ $(M+Na)^+$: 403.1992, found 403.2007.

Methyl 2-((6-hydroxy-4,4,5,7-tetramethyl-2-oxochroman-8-yl)thio)acetate, 14. To a solution of amide **8-PP** (47 mg, 0.12 mmol) in a mixture of CH_3CN/PBS buffer 1:1 (4 mL) was added methyl thiolglycolate (12 μL, 0.13 mmol). The mixture was stirred at 37 °C and the reaction progress was monitored by HPLC. After 3 h, the organic solvent was removed under vacuum and the residue was partitioned between EtOAc (20 mL) and water (10 mL). The organic layer was washed with brine, dried over Na_2SO_4 and filtered. After removal of the solvent under vacuum, the residue was purified by chromatography

on a silica gel column (hexanes:EtOAc=4:1 to 2:1) to afford lactone **14** (30 mg, 77%) as an light yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.82 (s, 1H), 3.64 (s, 3H), 3.50 (s, 2H), 2.57 (s, 2H), 2.47 (s, 3H), 2.38 (s, 3H), 1.46 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 168.0, 149.3, 146.7, 129.5, 127.0, 123.9, 119.4, 52.5, 46.0, 36.8, 36.1, 27.8, 15.0, 14.4; HRMS (ESI) calcd for $C_{16}H_{20}NaO_5S$ $(M+Na)^+$: 347.0924, found 347.0944.

III. References

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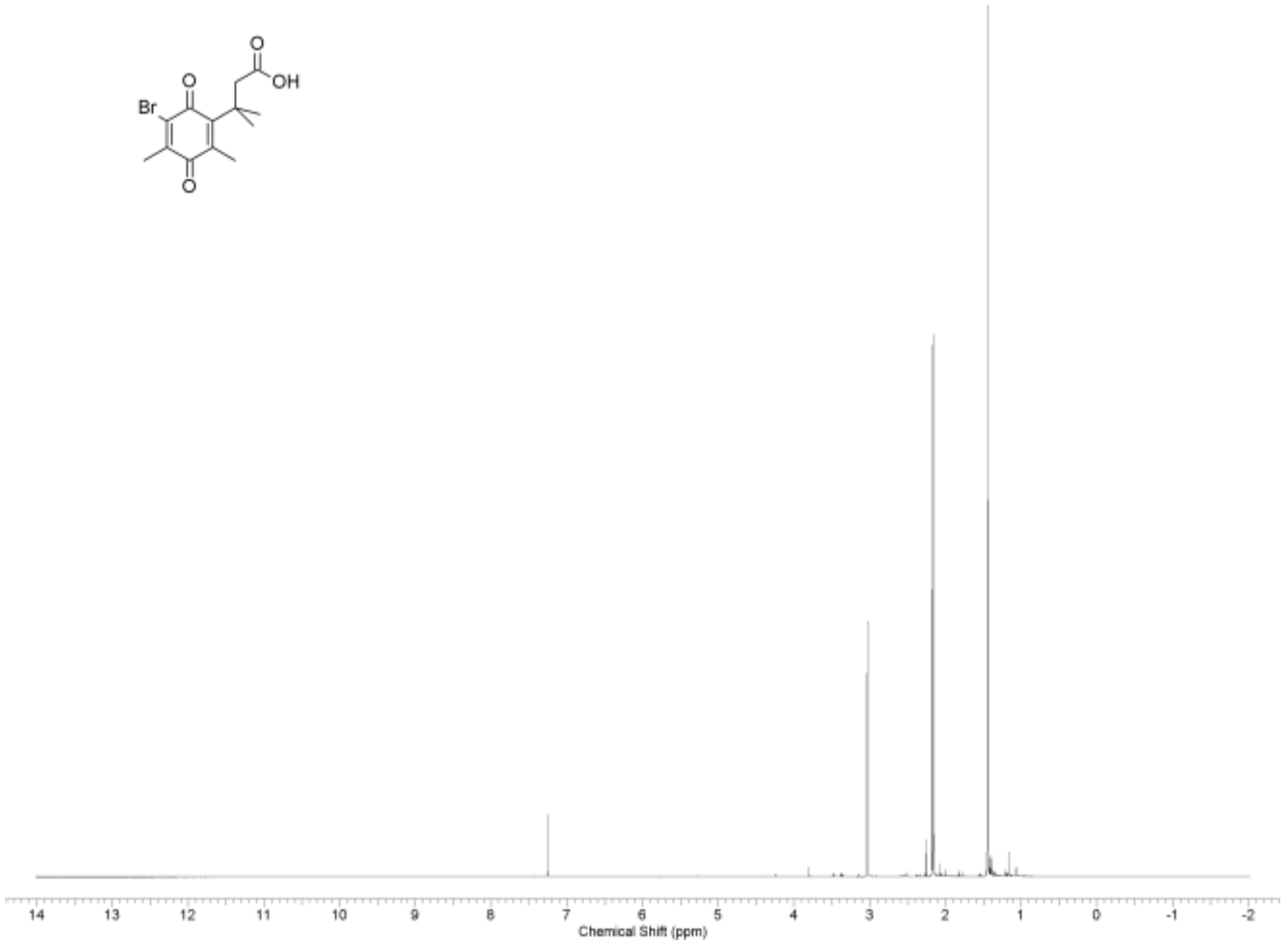
IV. Copies of ^{1}H NMR and ^{13}C NMR Spectra



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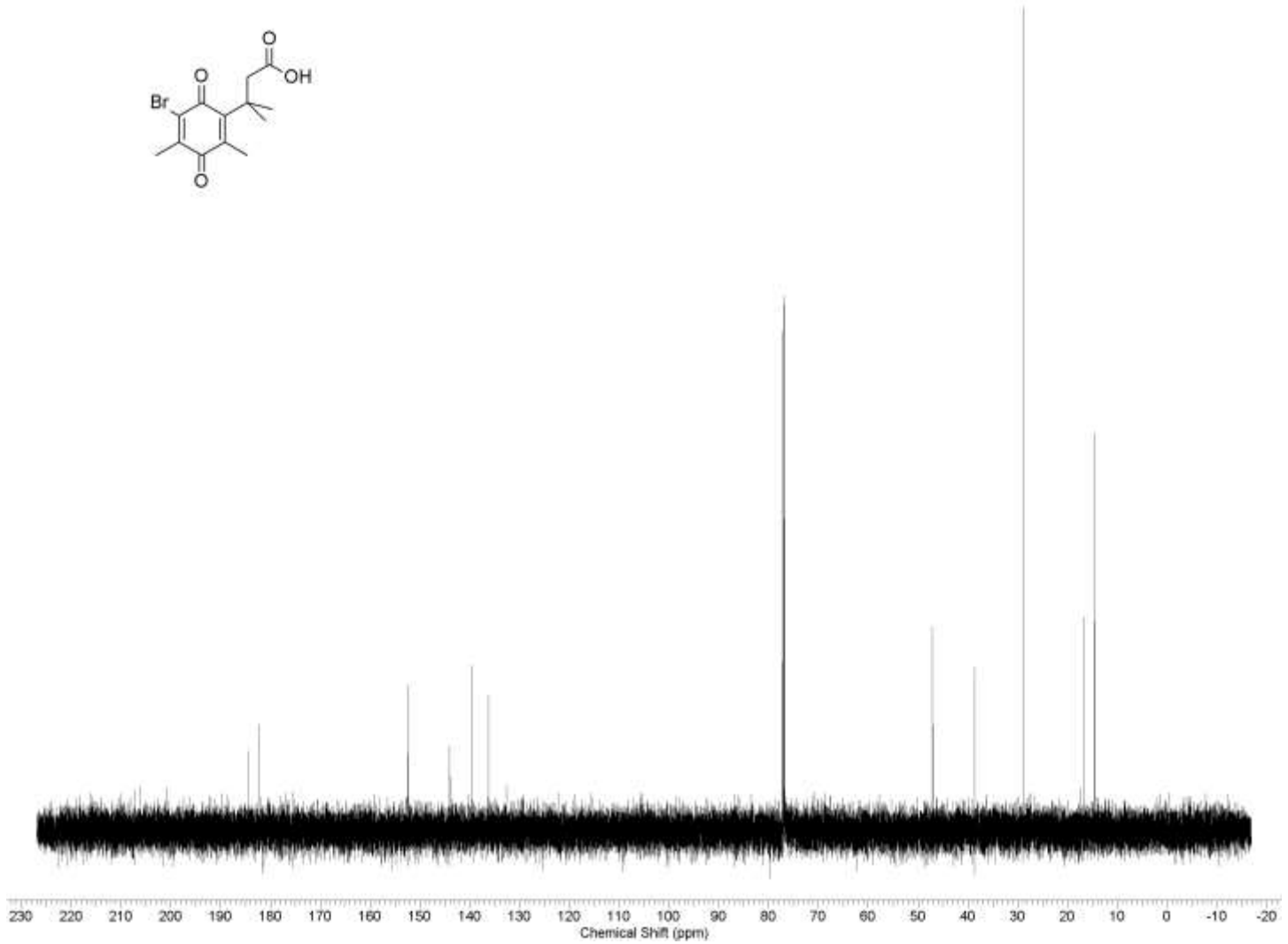

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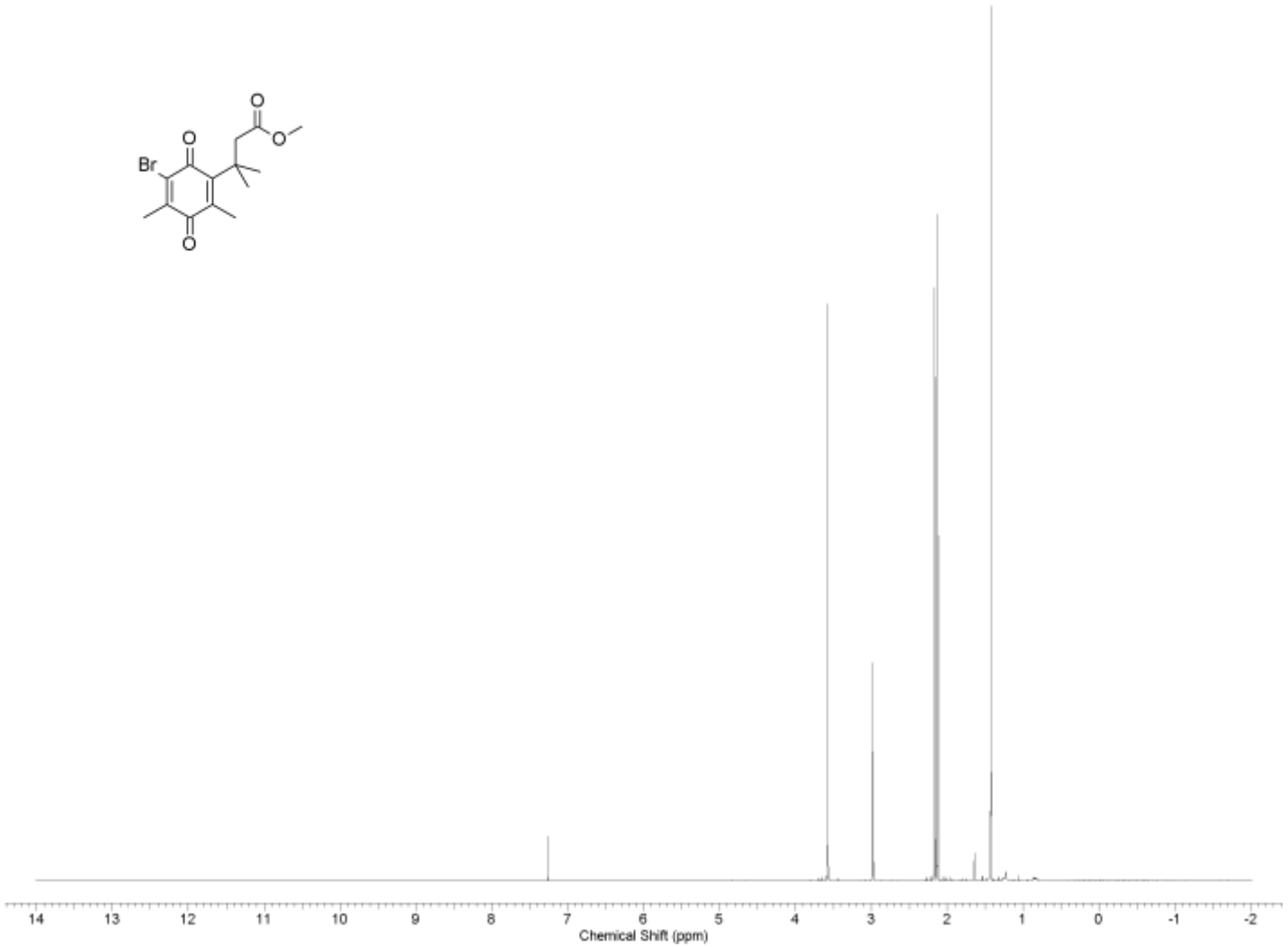

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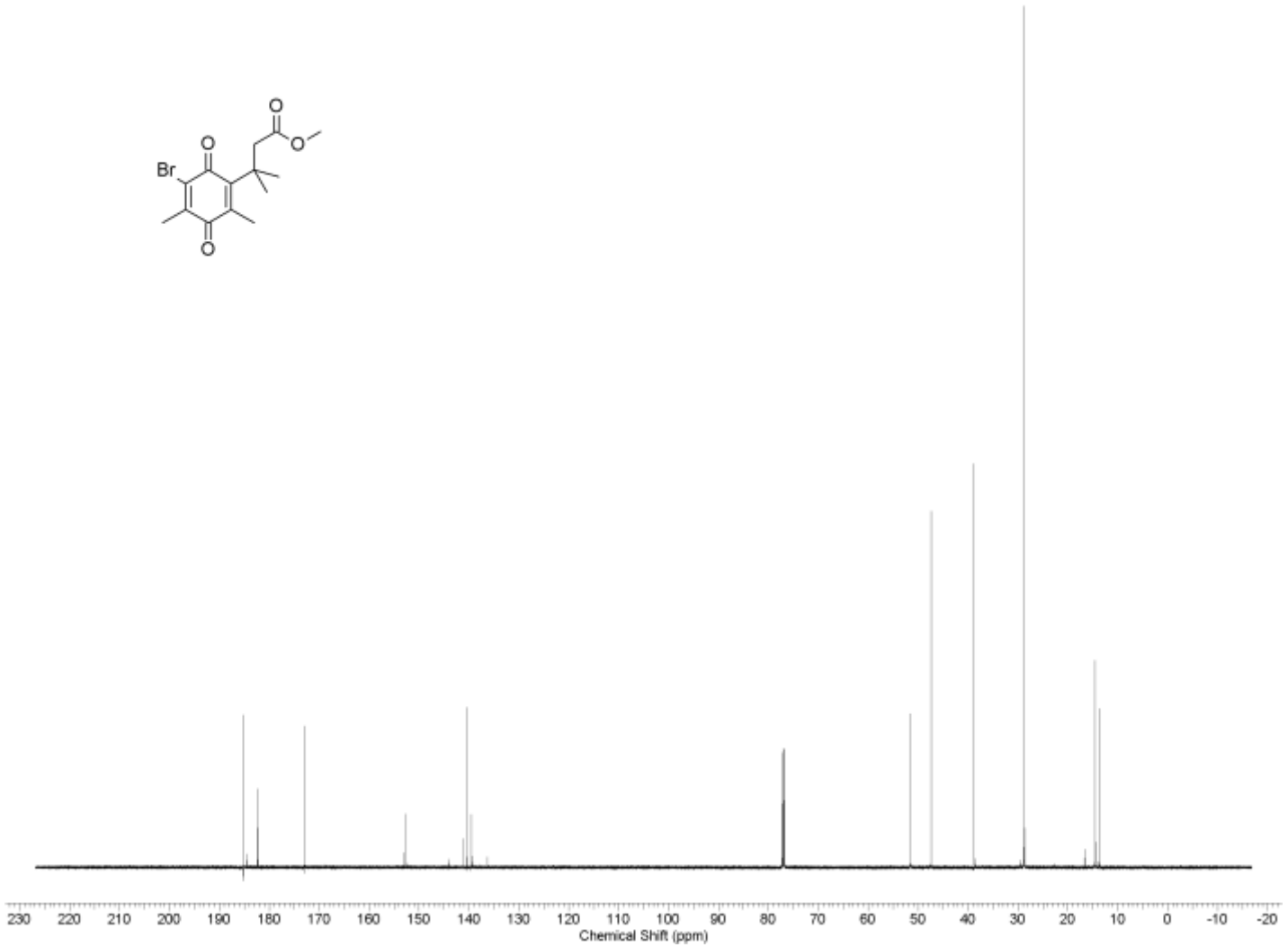
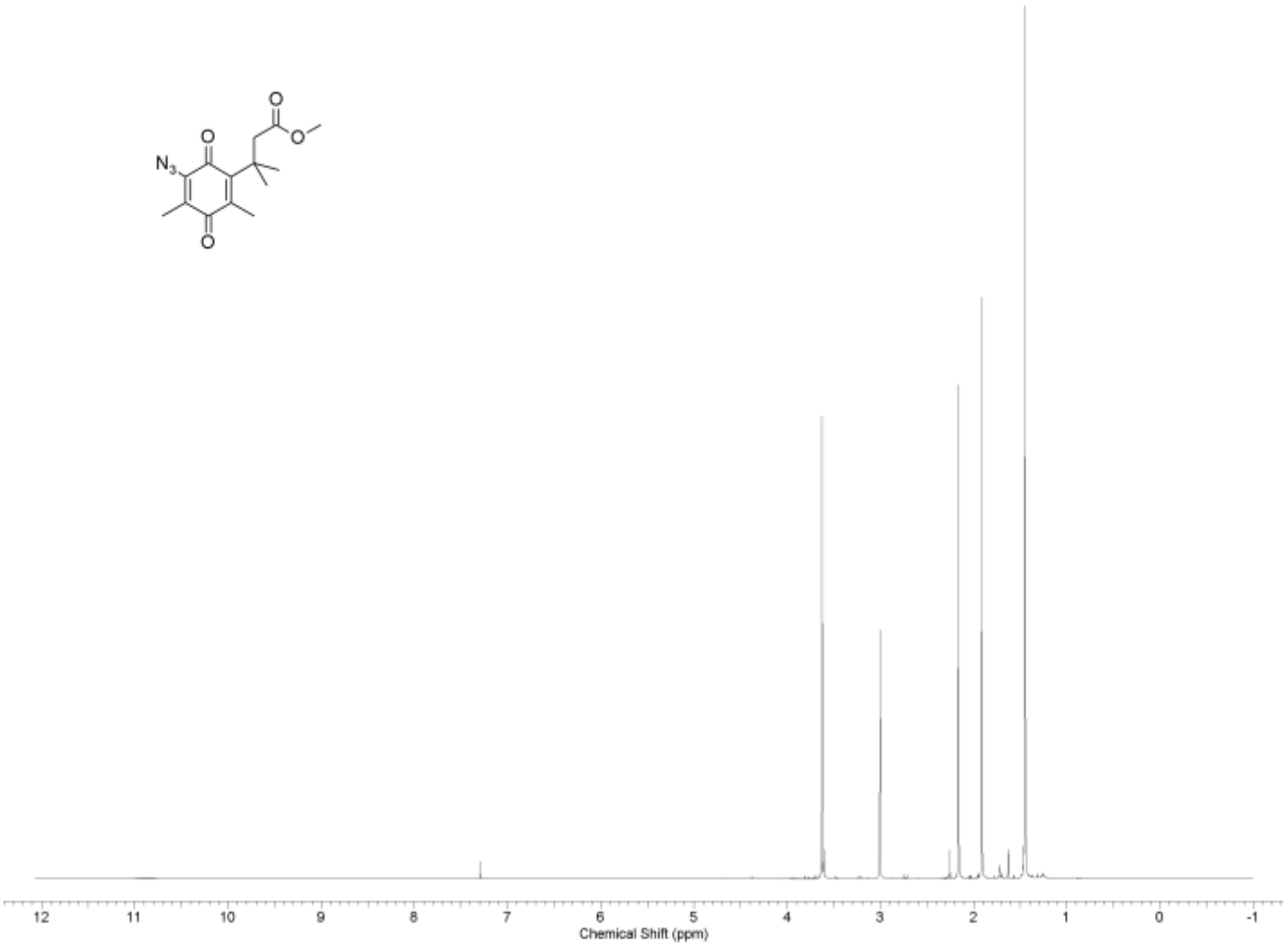
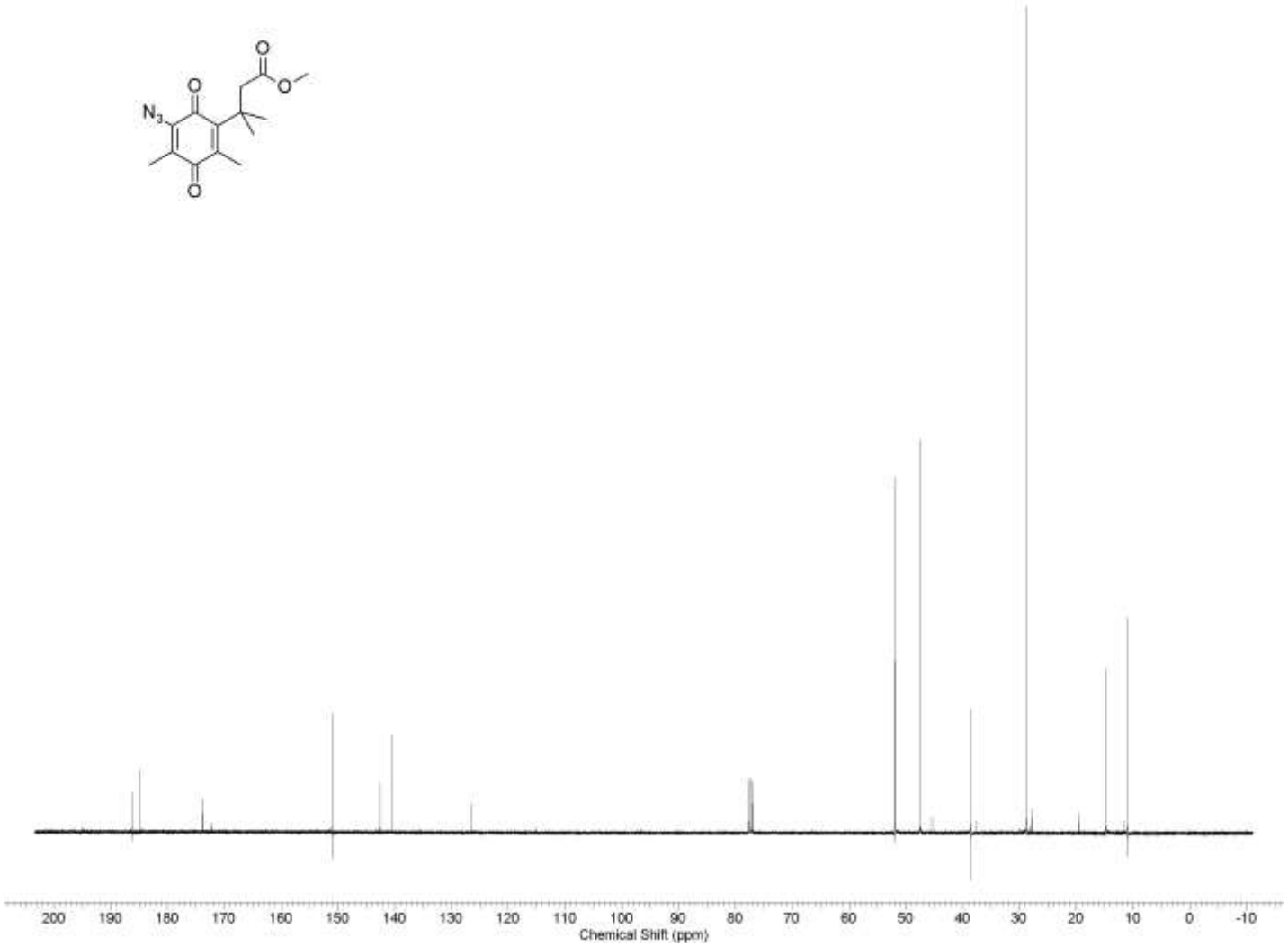


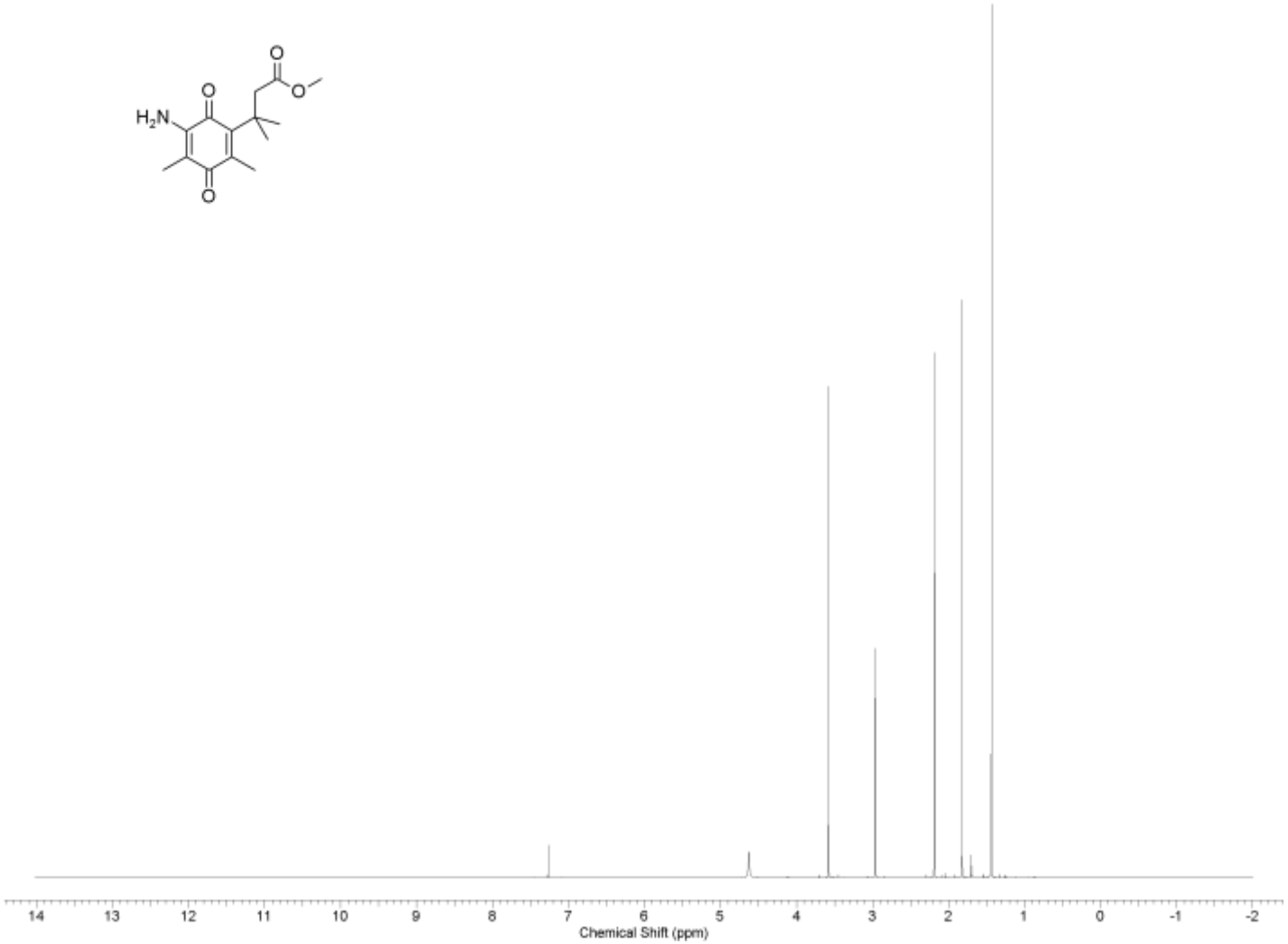
^{13}C NMR of **5Me** (150 MHz, $CDCl_3$)



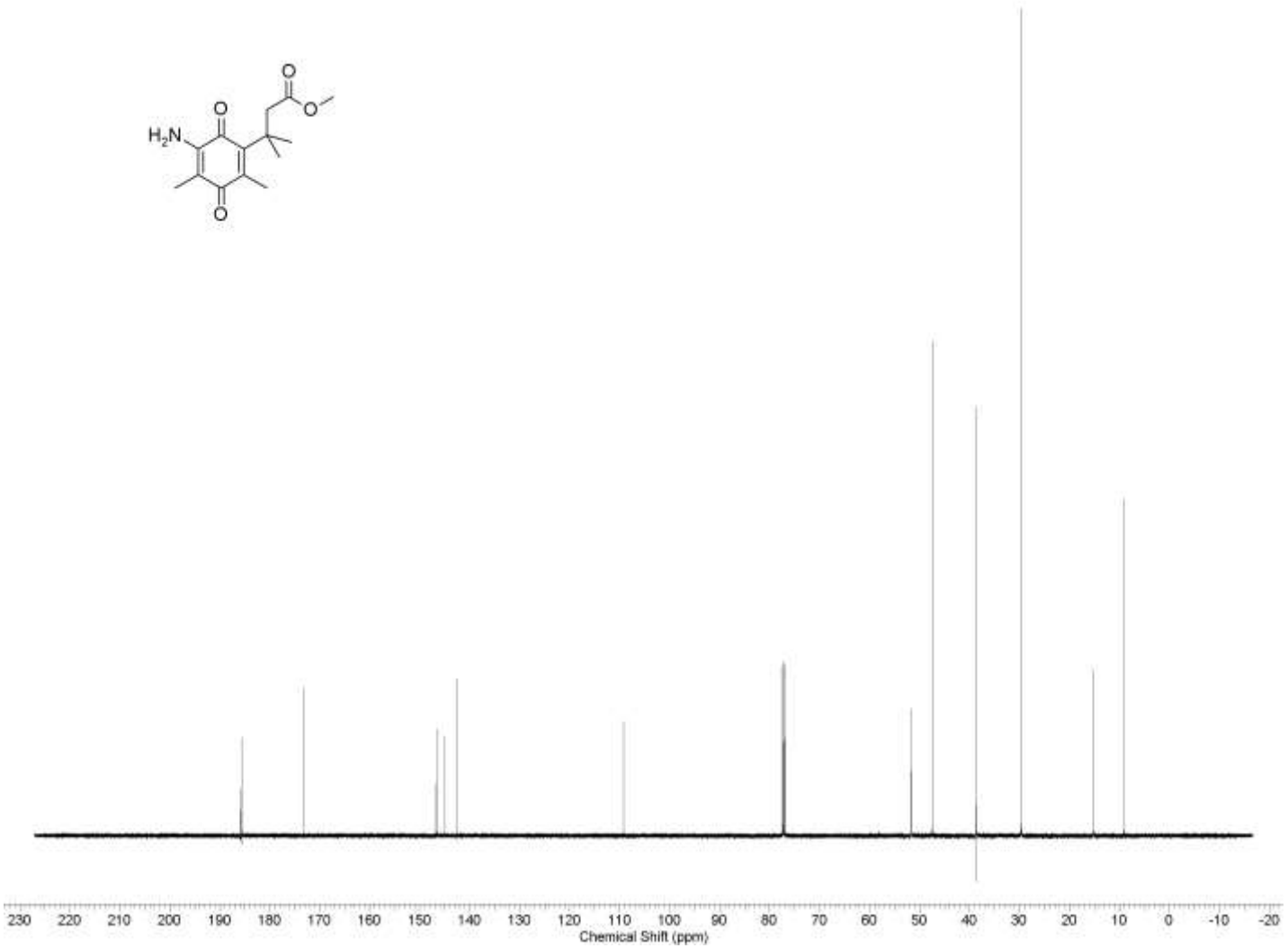
^{1}H NMR of **6** (500 MHz, $CDCl_3$)



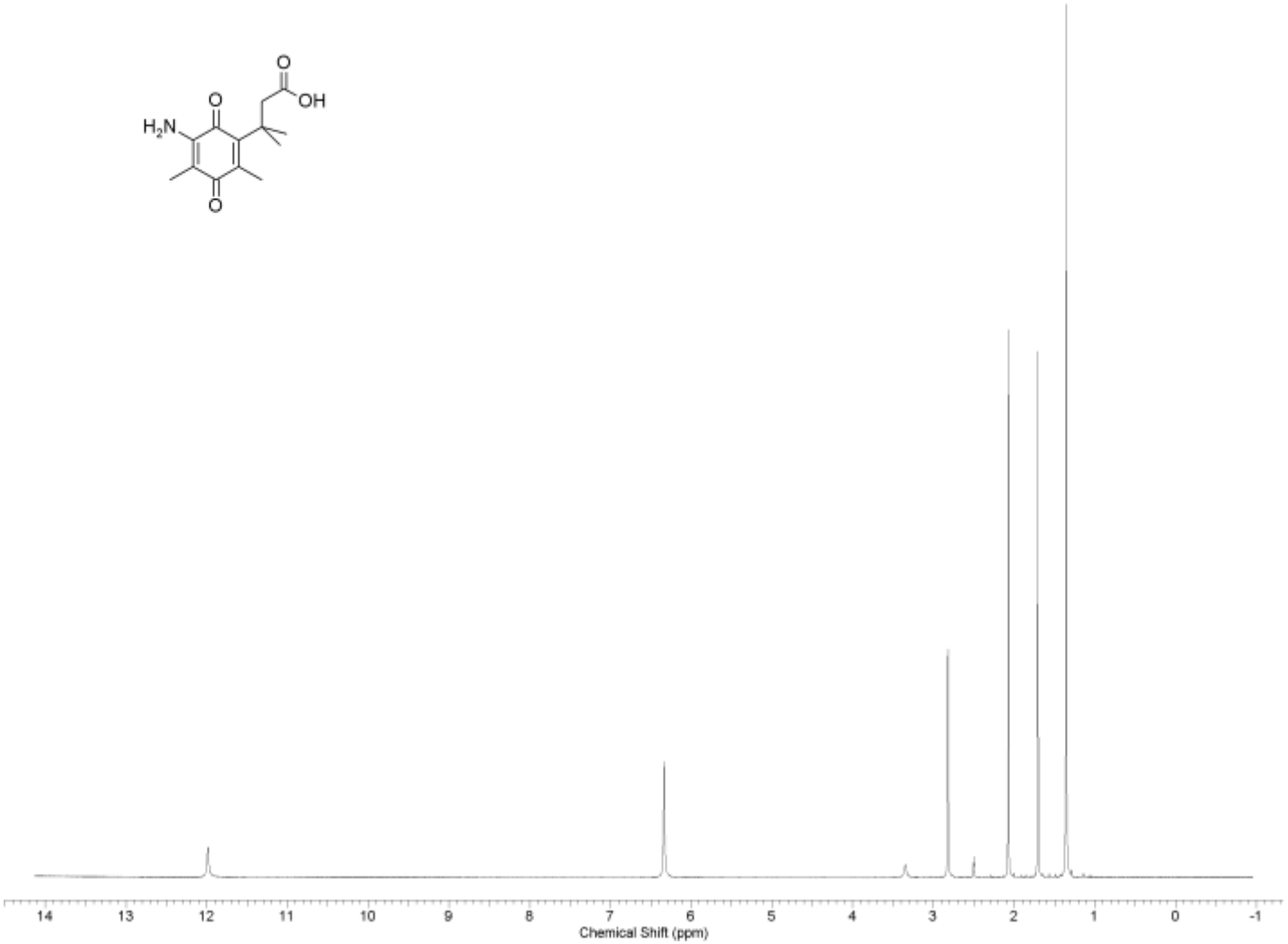
^{13}C NMR of **6** (125 MHz, $CDCl_3$)



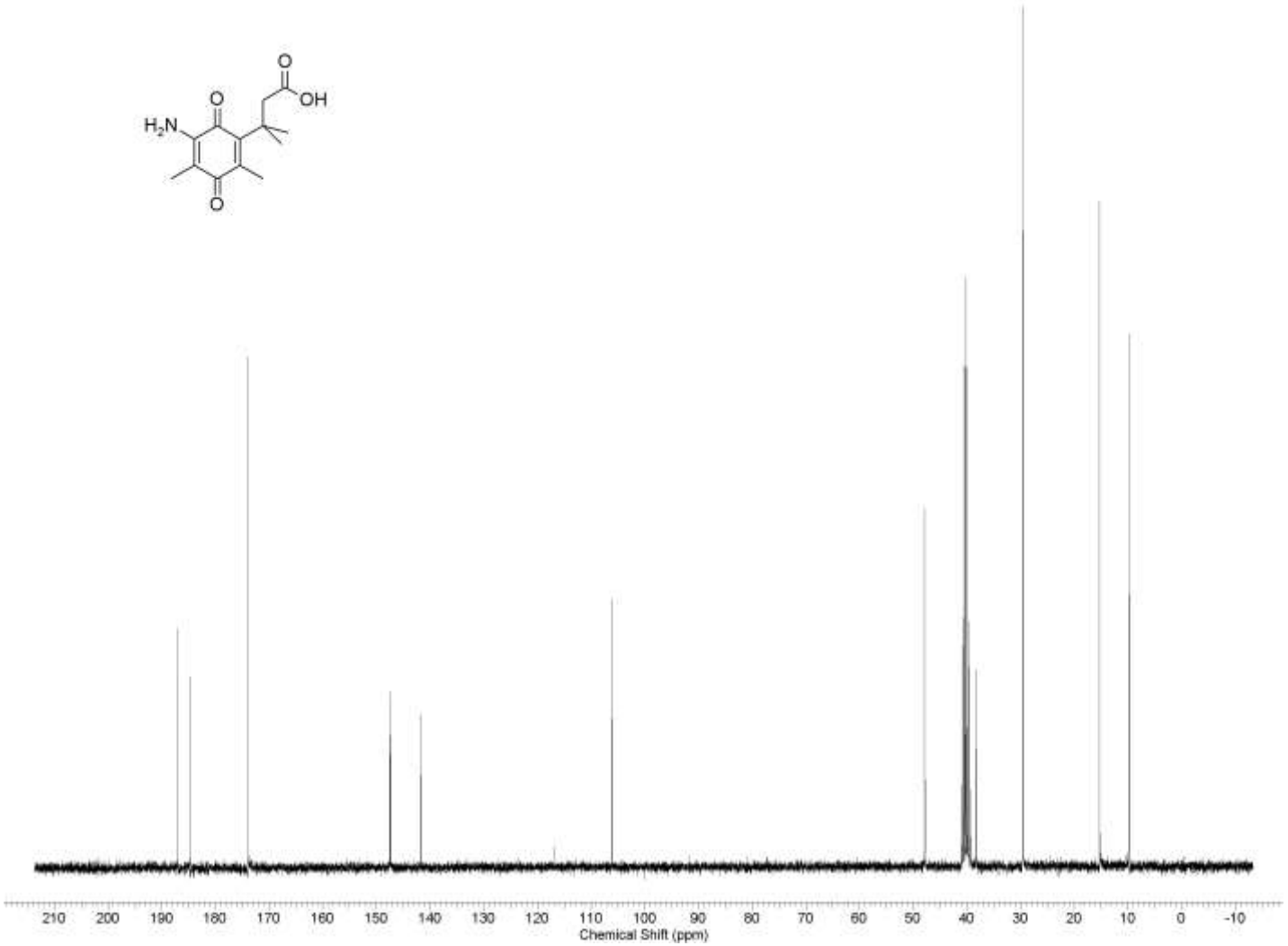
^{1}H NMR of **7Me** (600 MHz, $CDCl_3$)



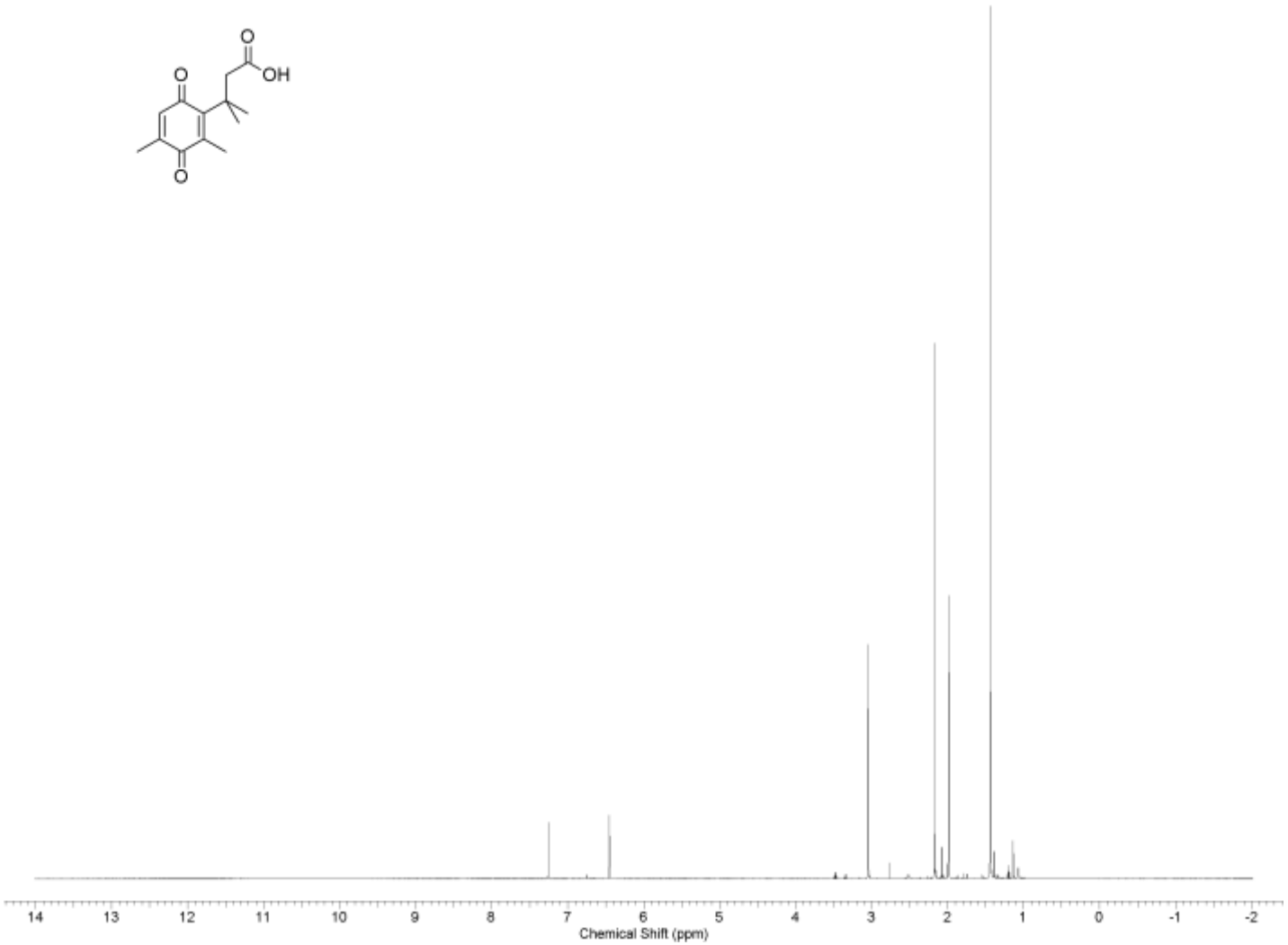
^{13}C NMR of **7Me** (150 MHz, $CDCl_3$)



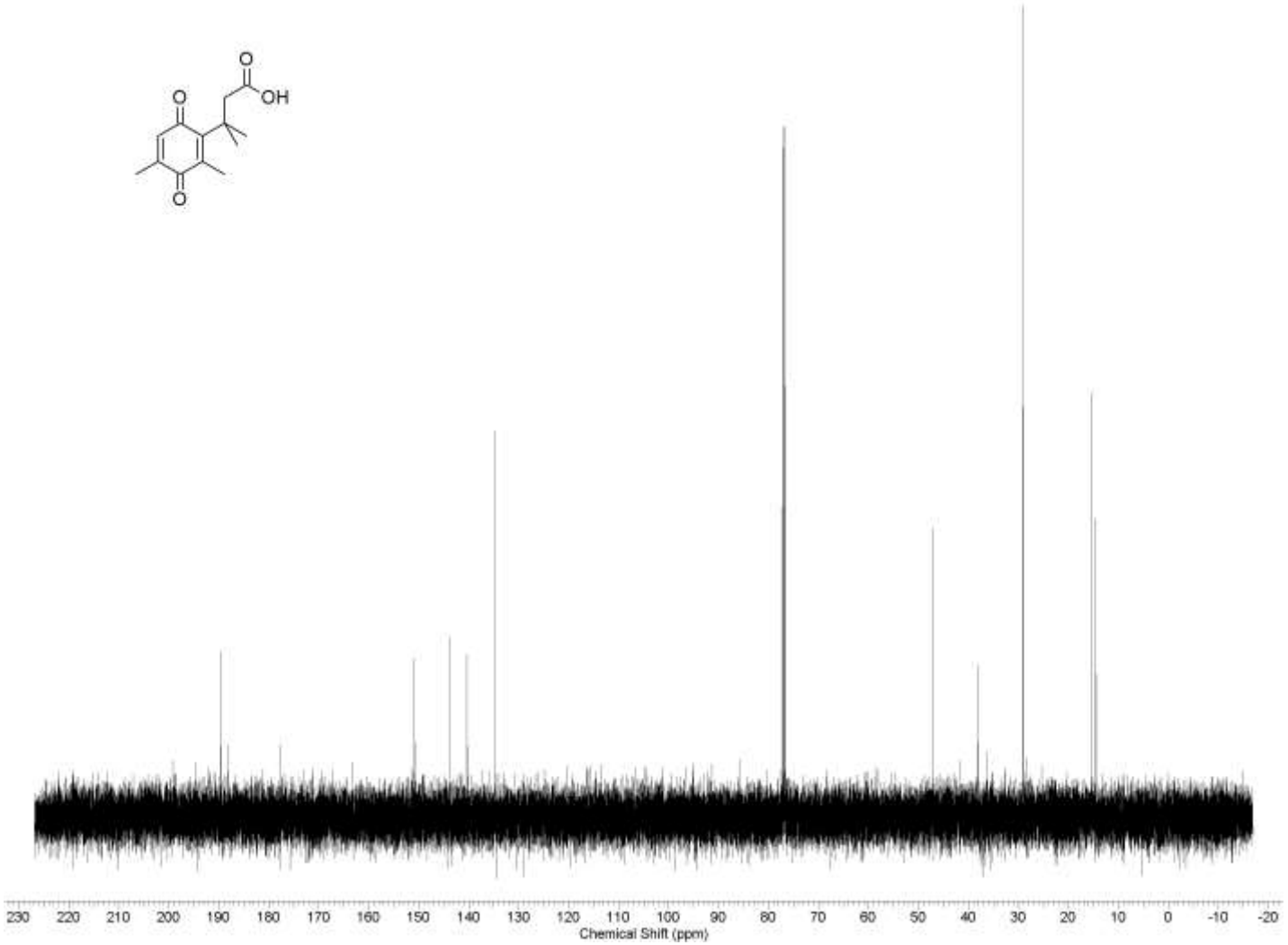
^{1}H NMR of **7H** (600 MHz, DMSO-d_6)



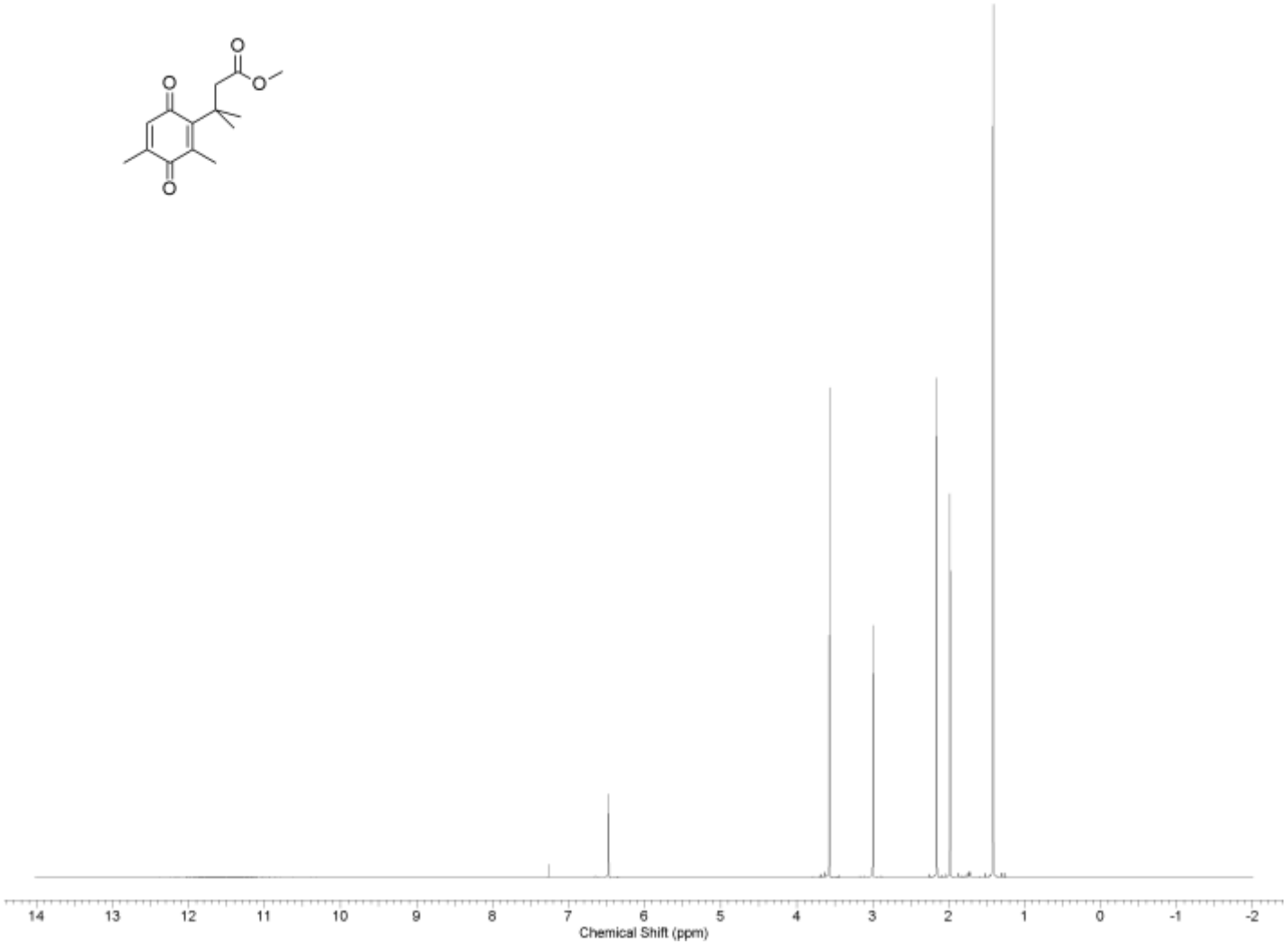
^{13}C NMR of **7H** (150 MHz, DMSO-d_6)



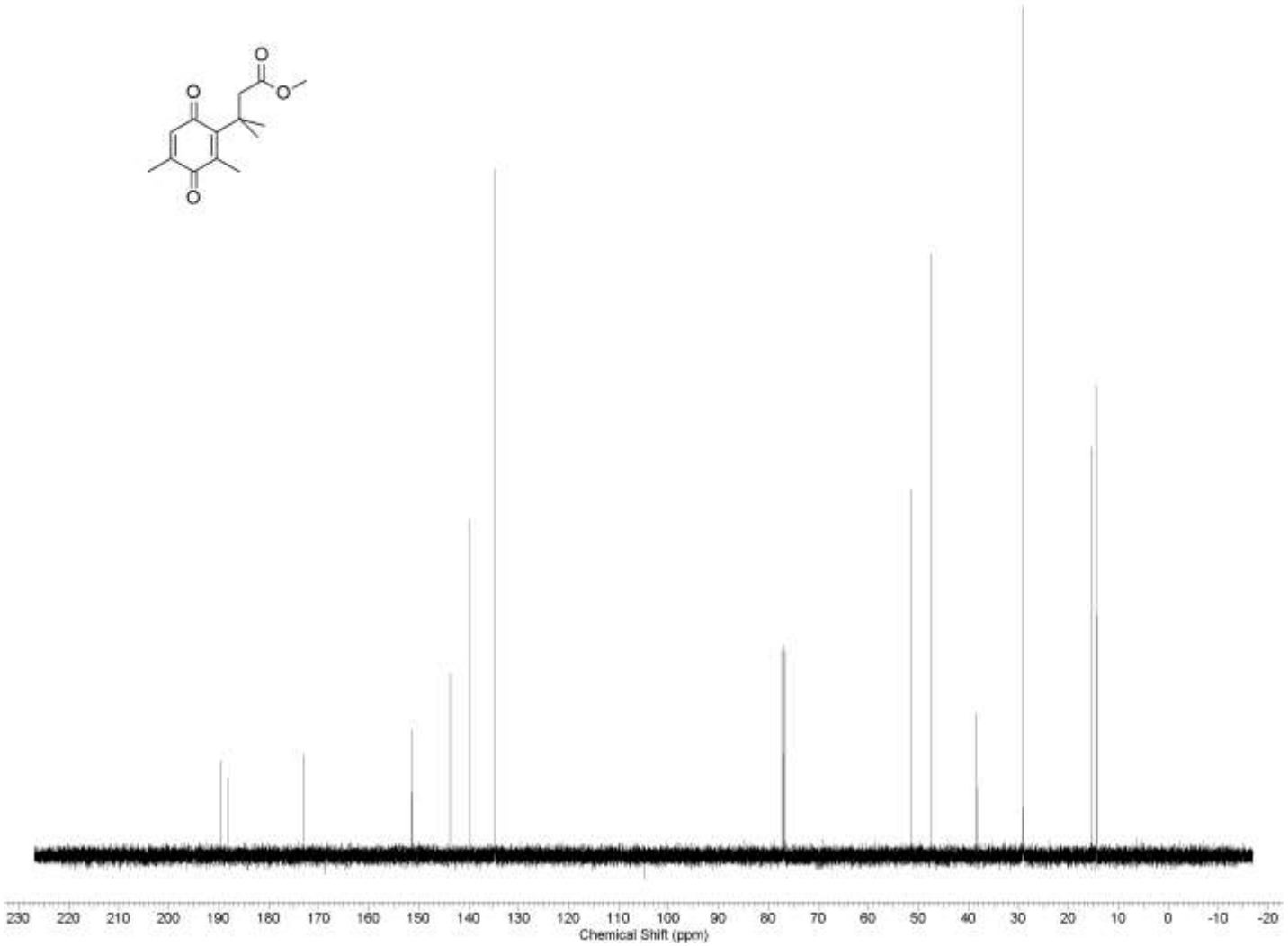
^{1}H NMR of **8H** (600 MHz, $CDCl_3$)



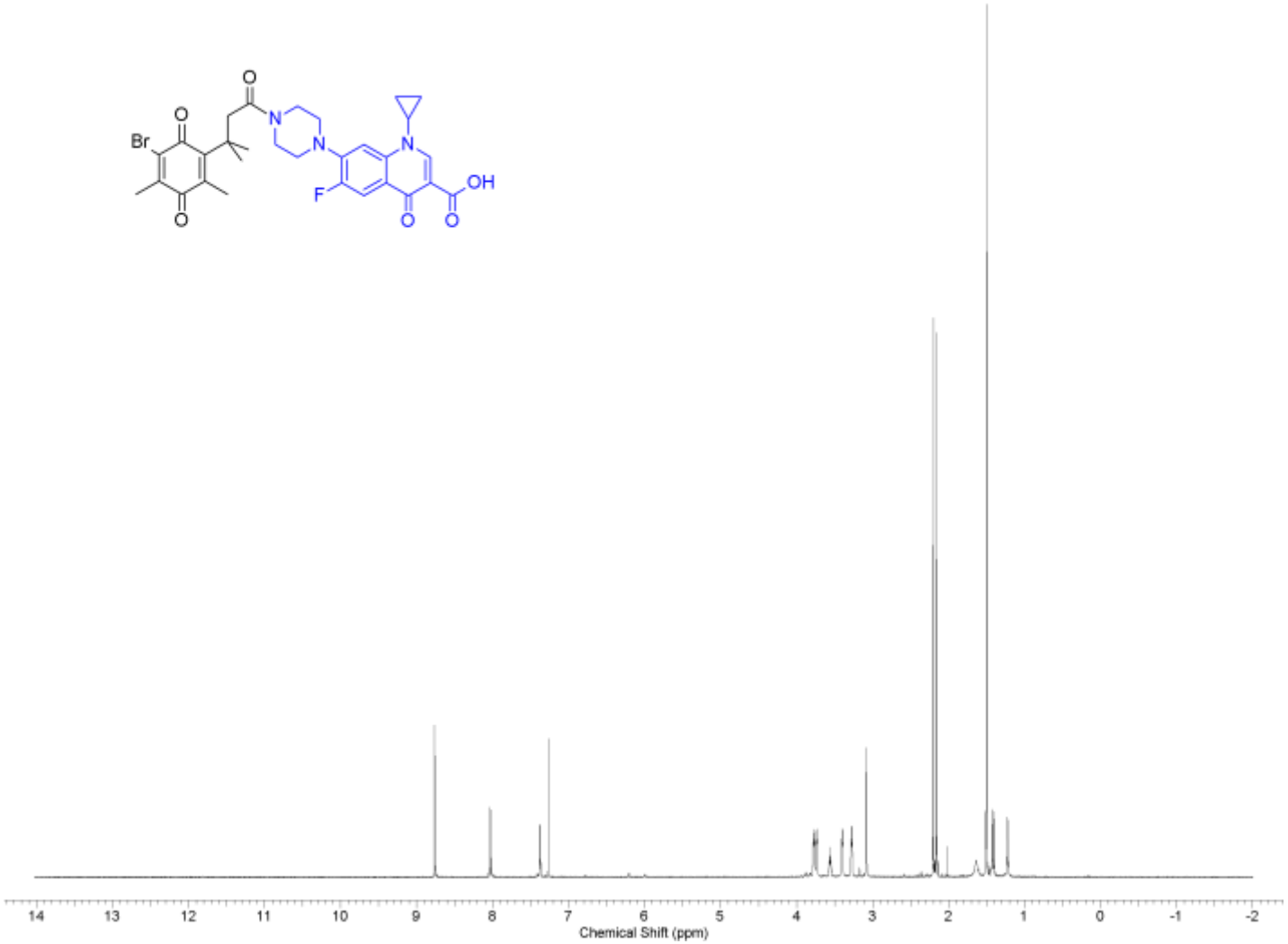
^{13}C NMR of **8H** (150 MHz, $CDCl_3$)



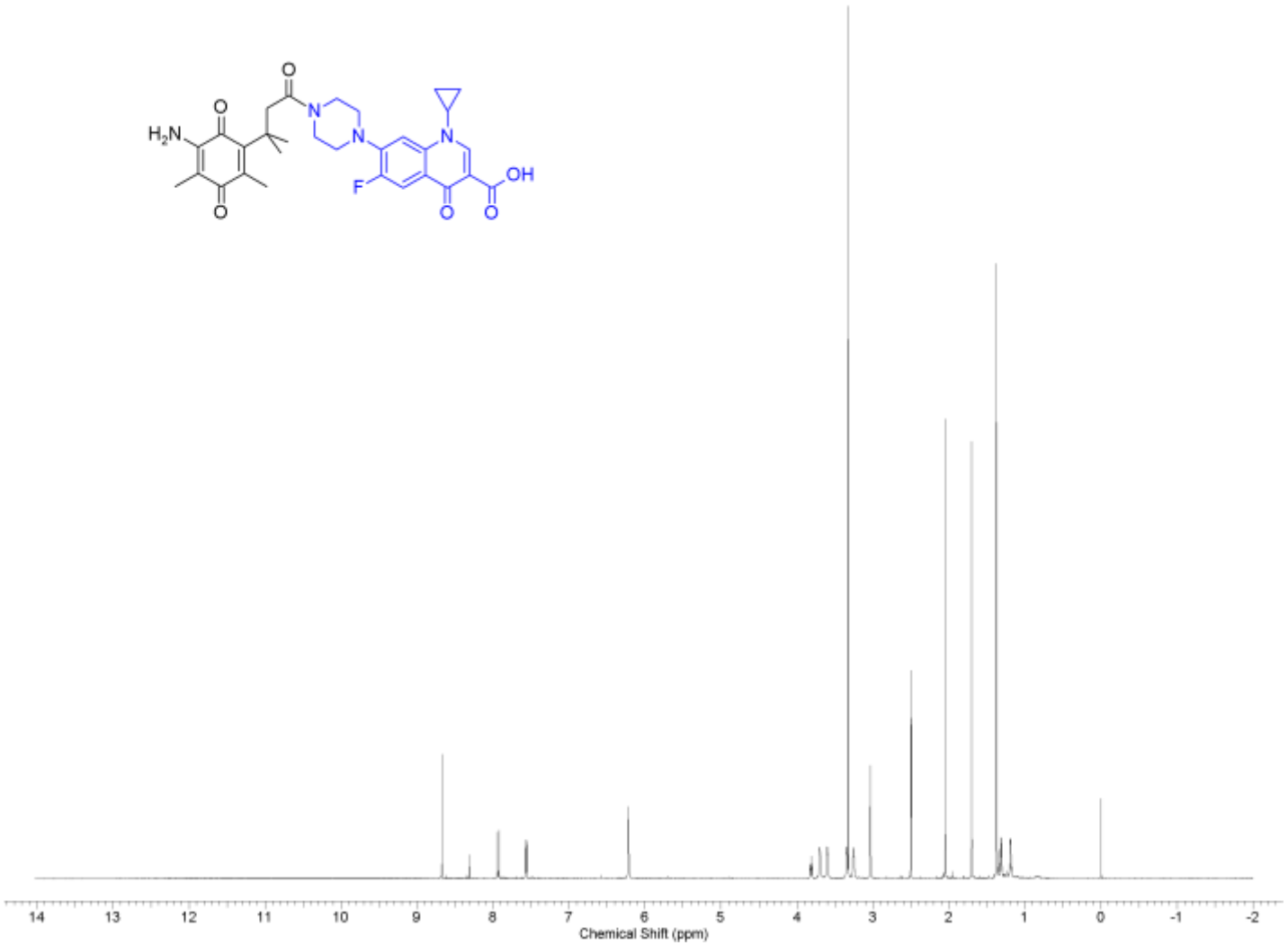
^{1}H NMR of **8Me** (600 MHz, $CDCl_3$)



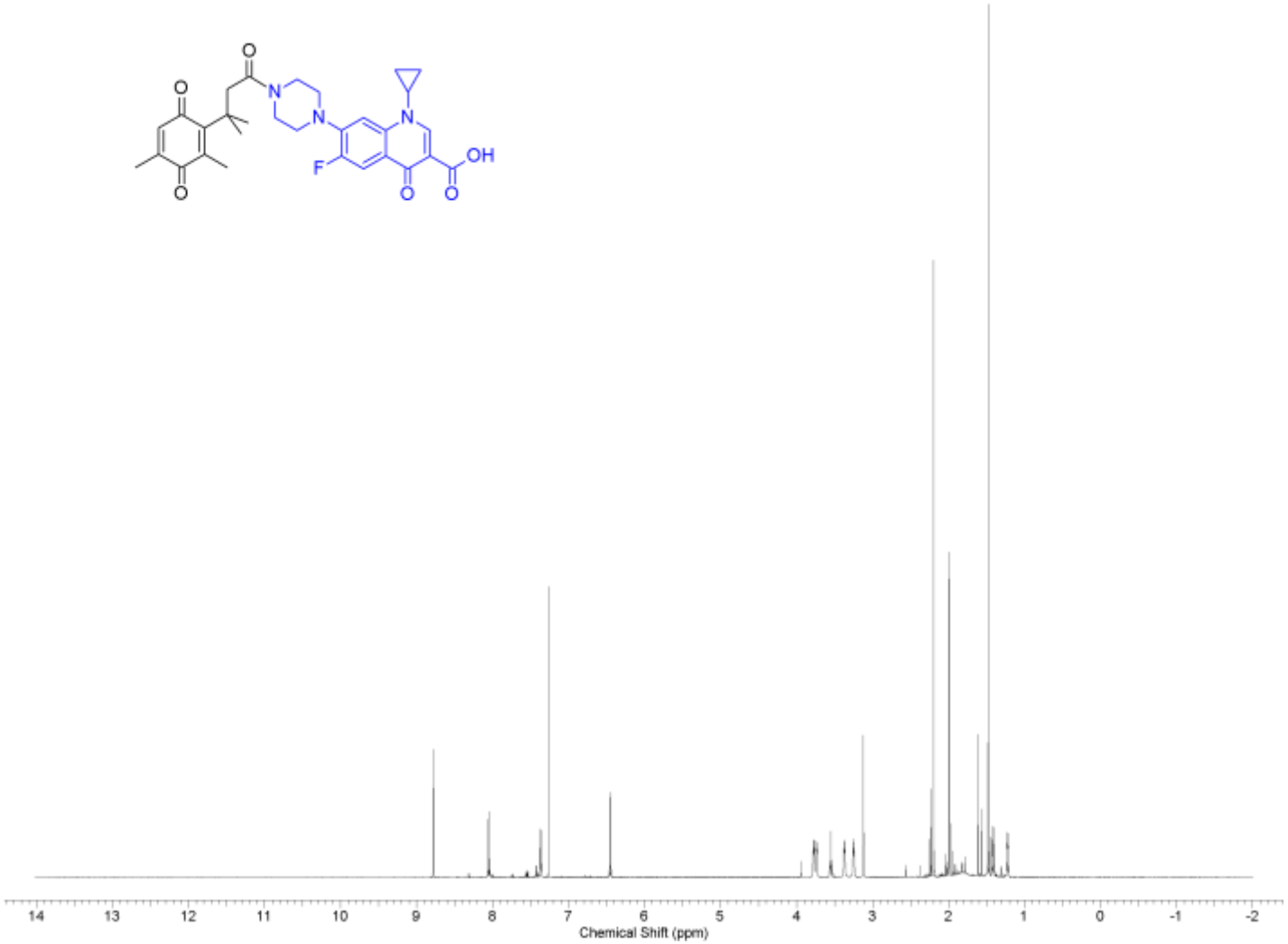
^{13}C NMR of **8Me** (150 MHz, $CDCl_3$)



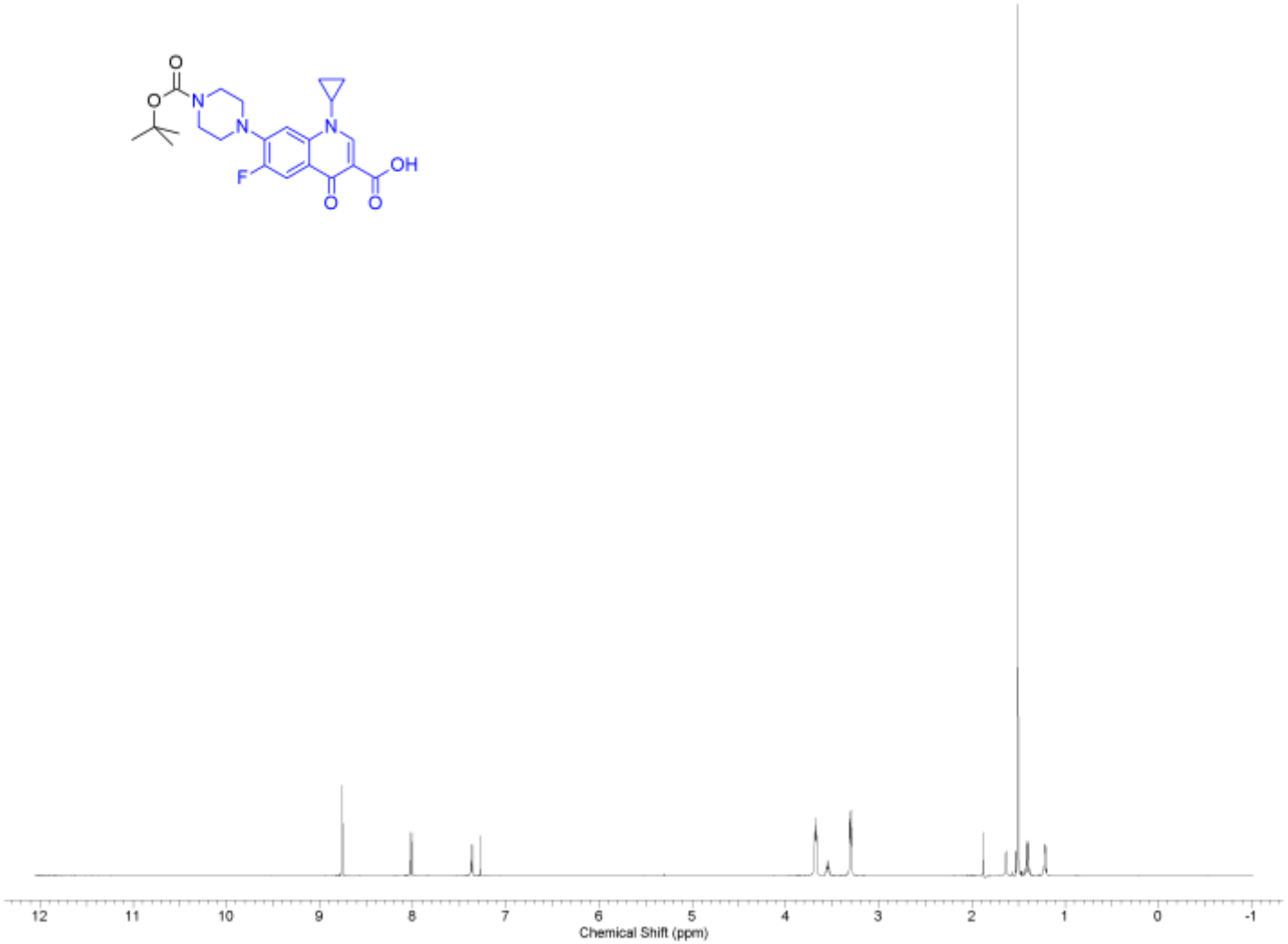
^{1}H NMR of **5-Cip** (600 MHz, $CDCl_3$)



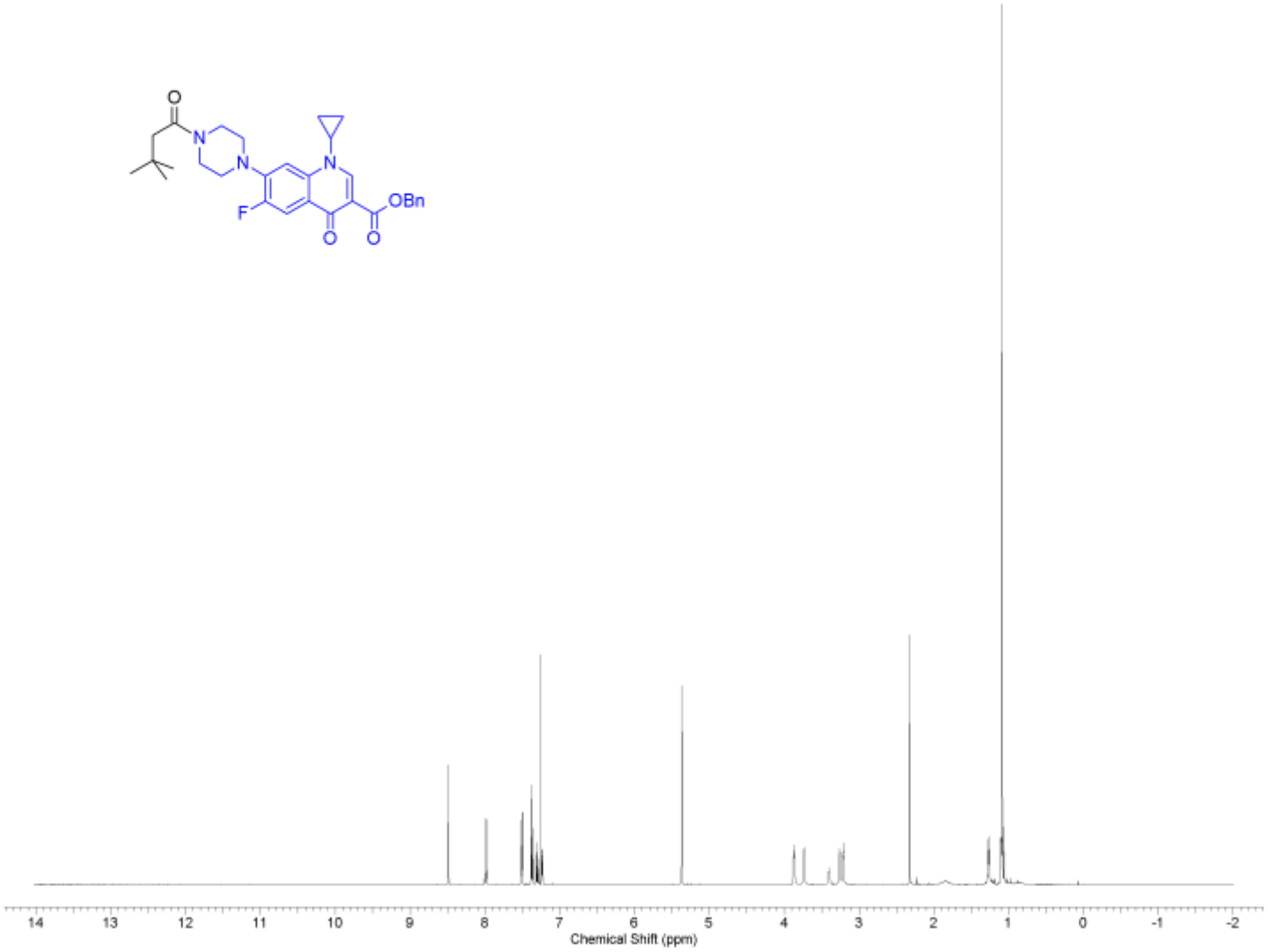
^{1}H NMR of **7-Cip** (600 MHz, $CDCl_3$)



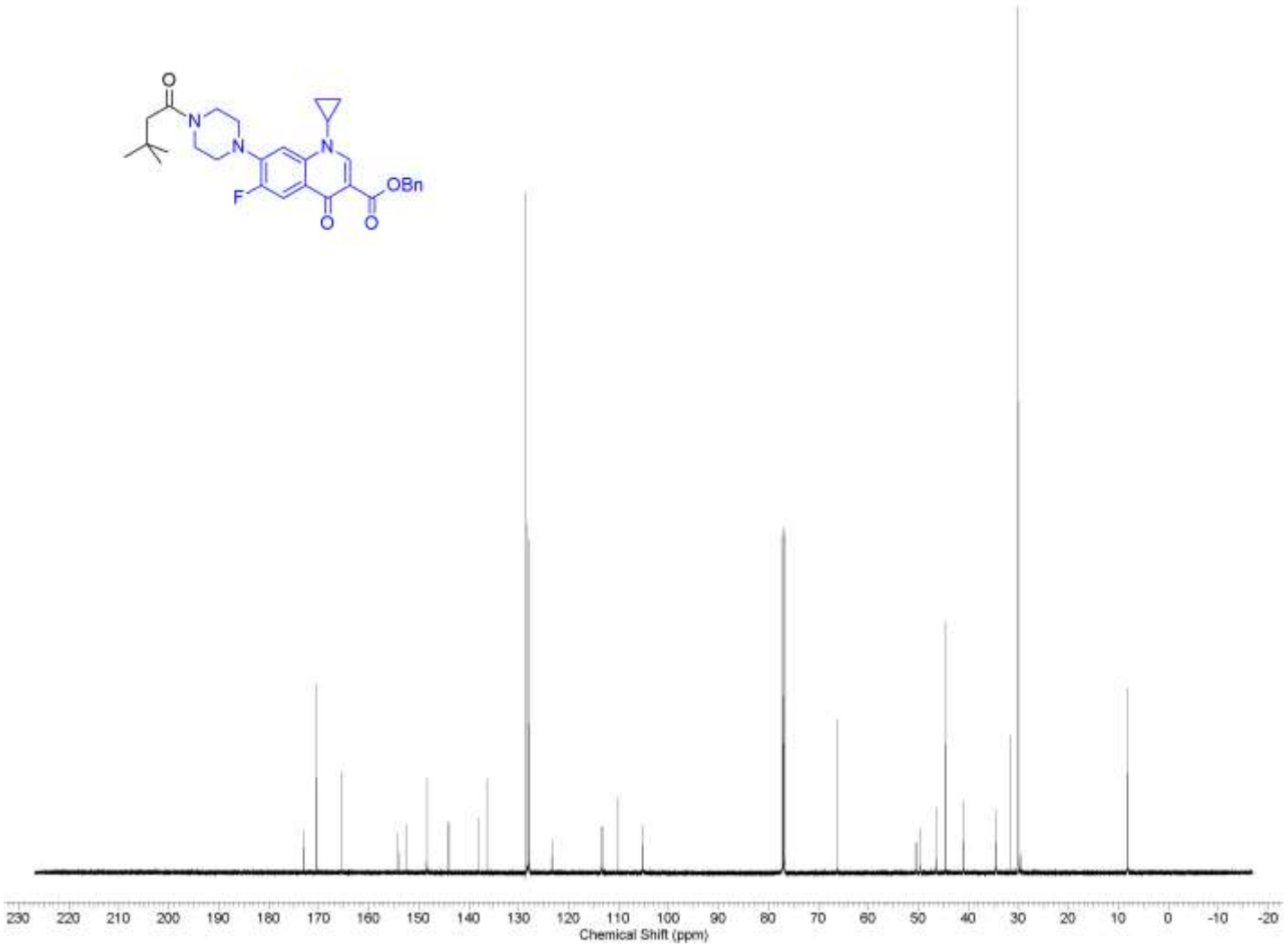
^{1}H NMR of **8-Cip** (600 MHz, $CDCl_3$)



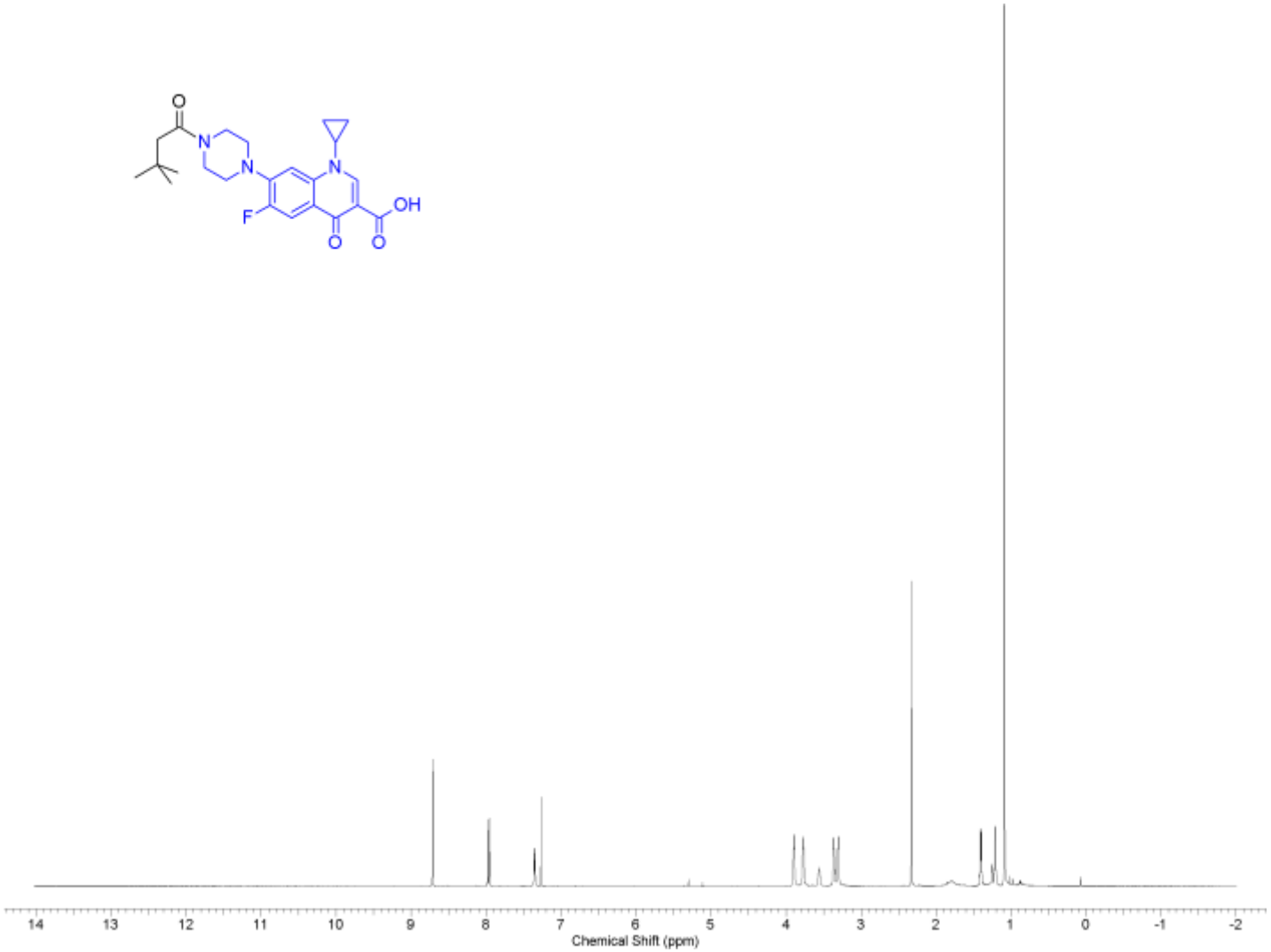
^{1}H NMR of **9** (500 MHz, $CDCl_3$)



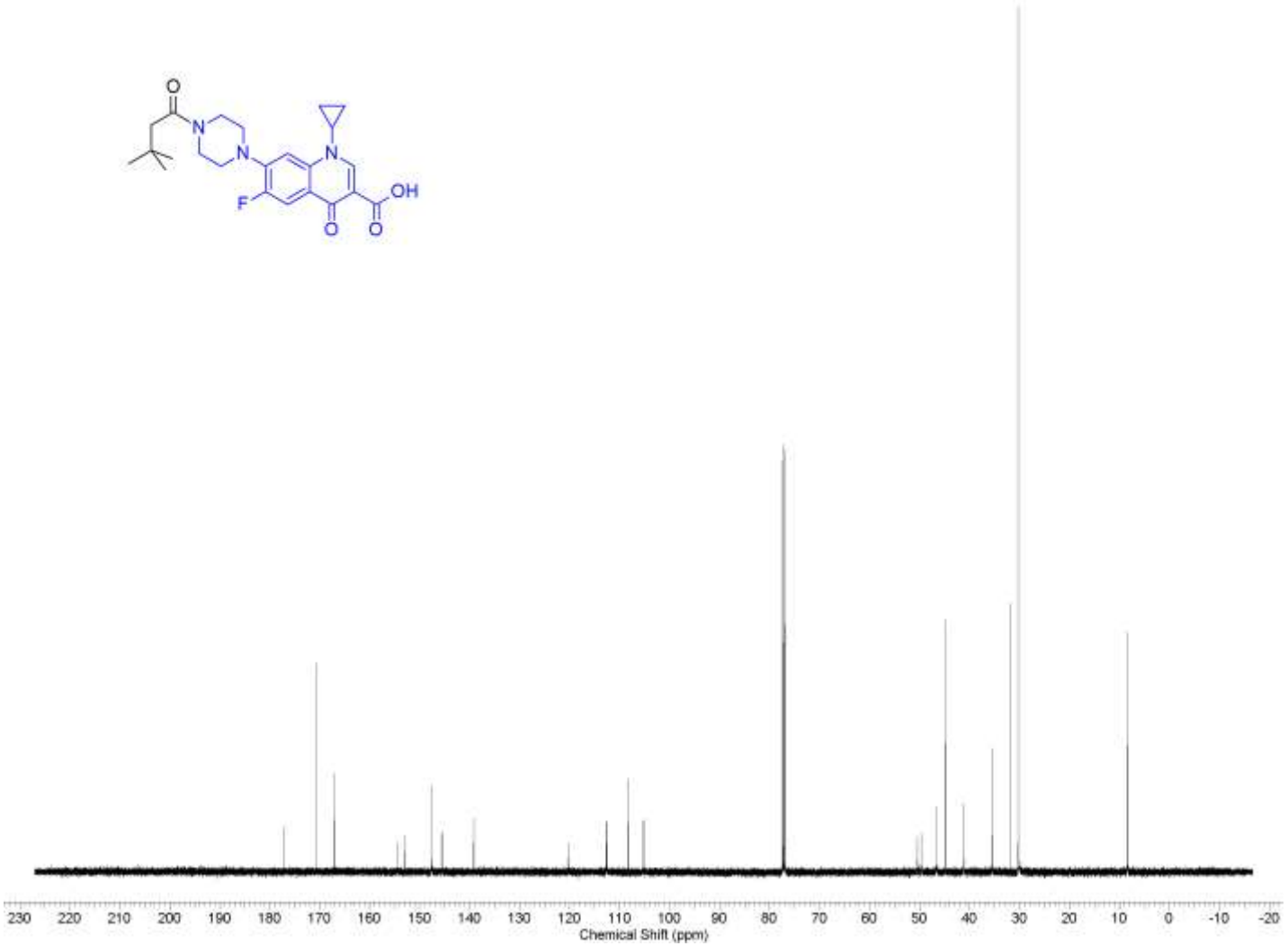
^{1}H NMR of **10Bn** (600 MHz, $CDCl_3$)



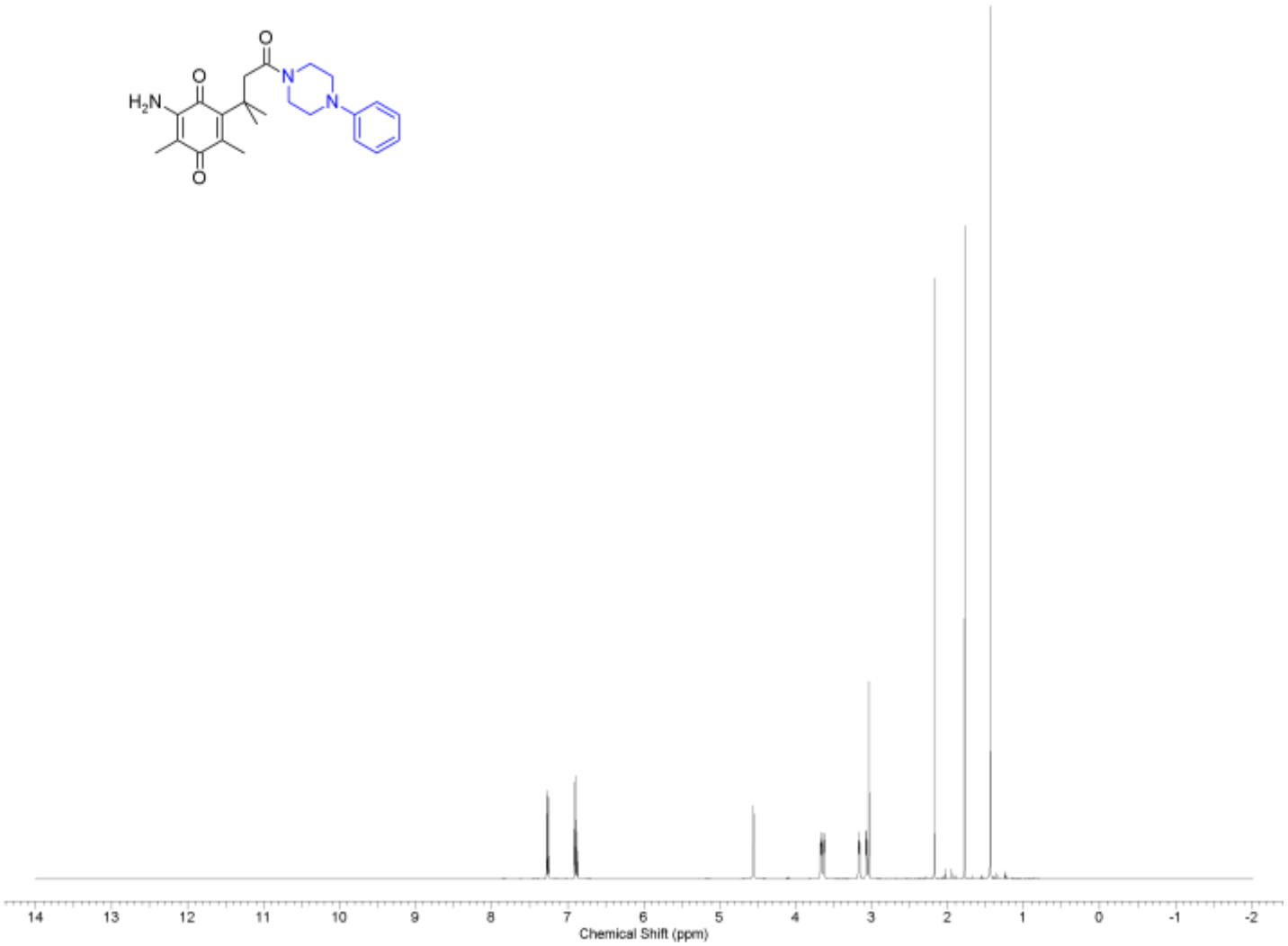
^{13}C NMR of **10Bn** (150 MHz, $CDCl_3$)



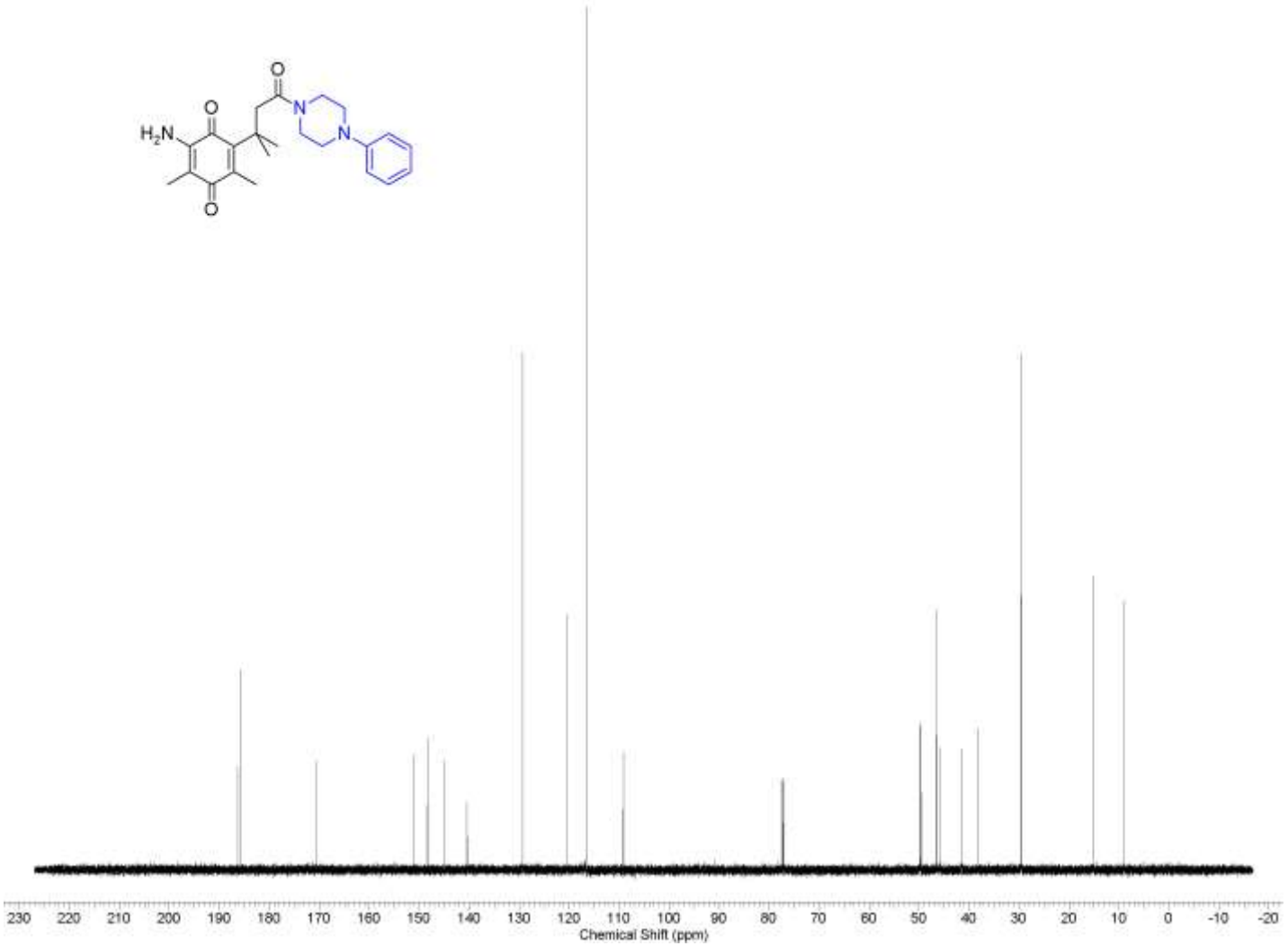
^{1}H NMR of **10** (600 MHz, $CDCl_3$)



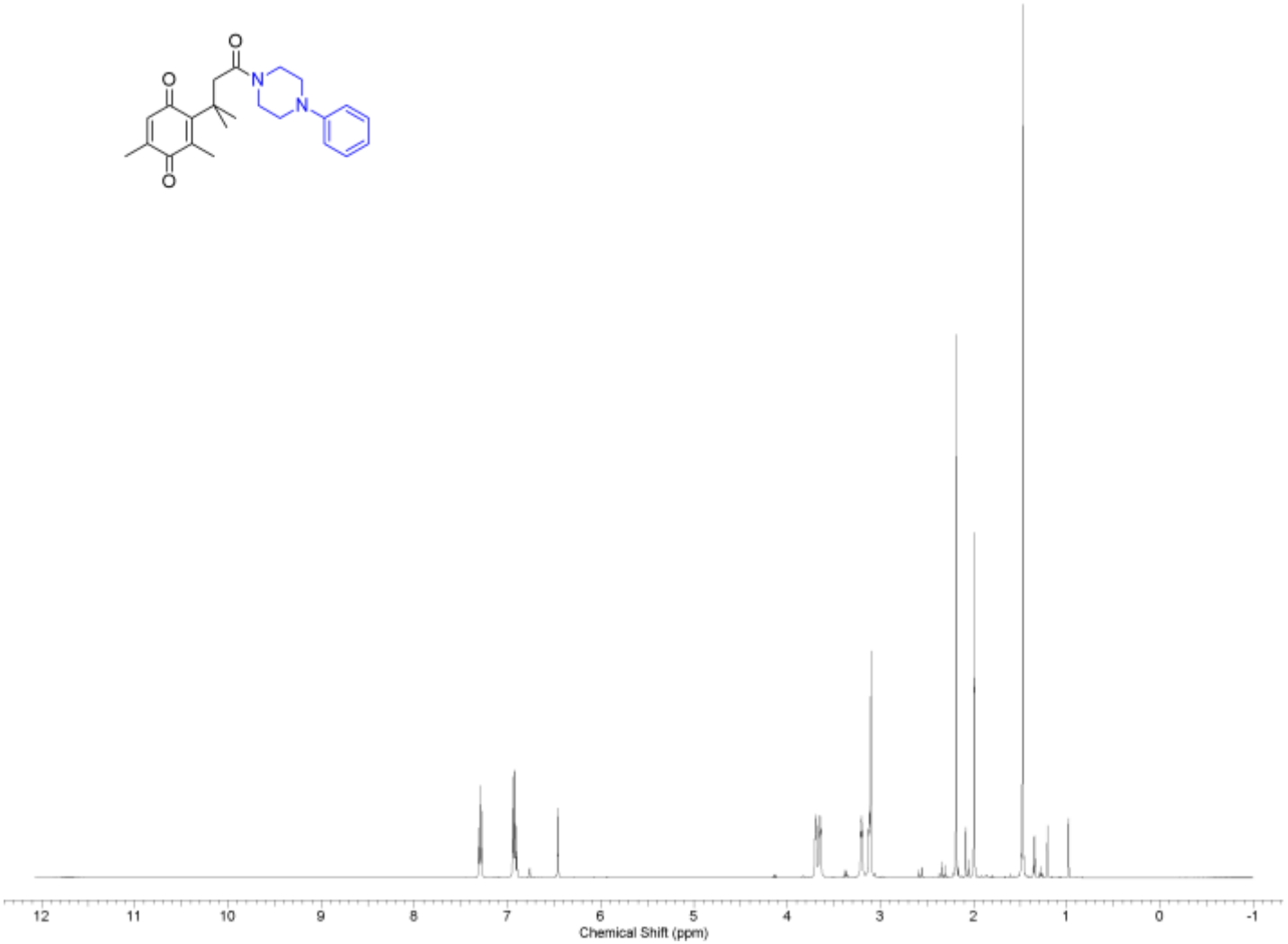
^{13}C NMR of **10** (150 MHz, $CDCl_3$)



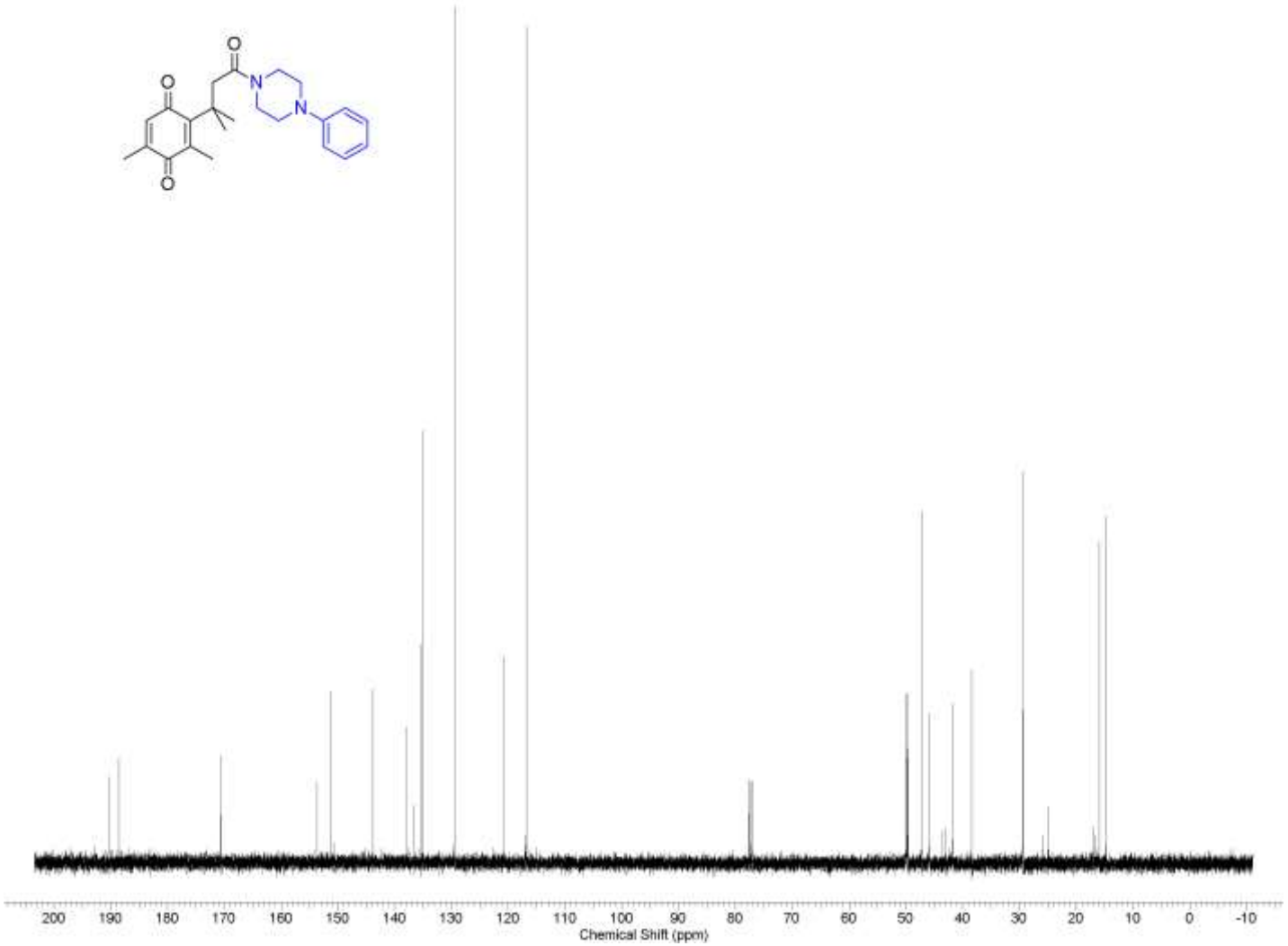
^{1}H NMR of **7-PP** (600 MHz, $CDCl_3$)



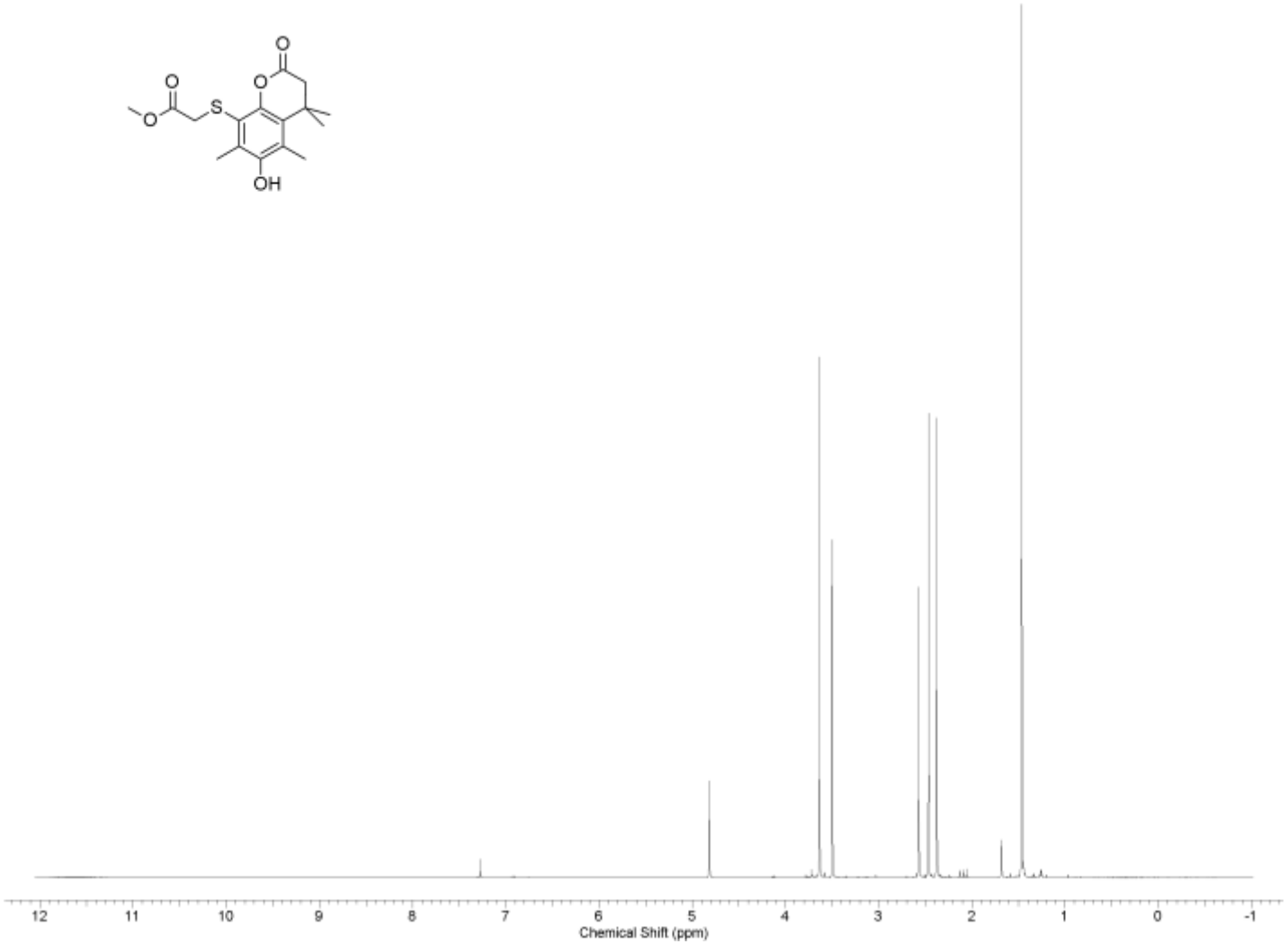
^{13}C NMR of **7-PP** (150 MHz, $CDCl_3$)



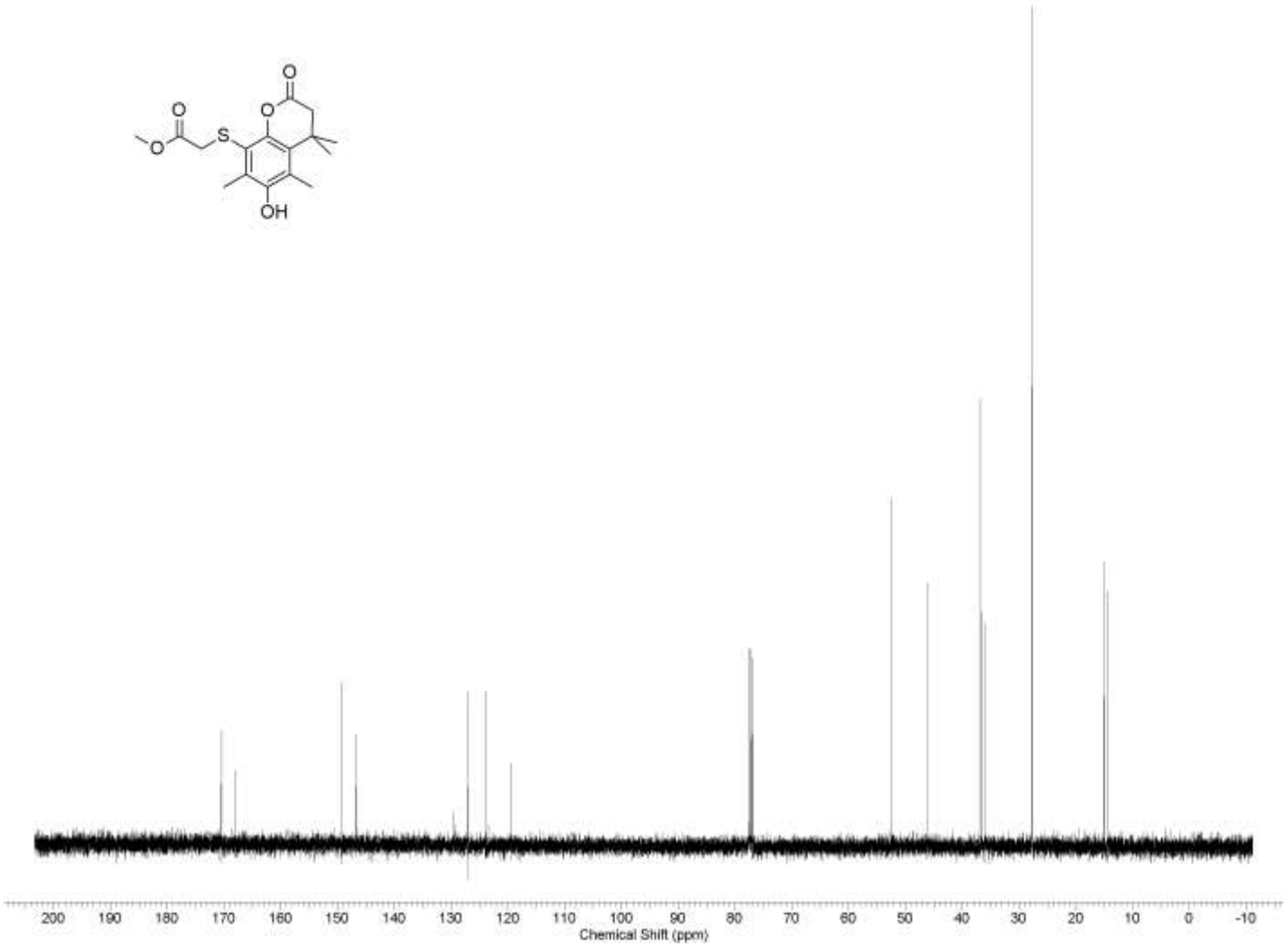
^{1}H NMR of **8-PP** (500 MHz, $CDCl_3$)



^{13}C NMR of **8-PP** (125 MHz, $CDCl_3$)



^{1}H NMR of **14** (500 MHz, $CDCl_3$)



^{13}C NMR of **14** (125 MHz, $CDCl_3$)