Supporting Information

Practical synthesis of quinolone drugs *via* novel TsCl-mediated domino reaction sequence

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General Experimental

^{1}H and ^{13}C NMR were recorded on a Bruker 400 spectrometer. ^{1}H NMR data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (Hz), relative intensity. ^{13}C NMR data are reported as follows: chemical shift in ppm (δ). LC/MS analyses were performed on a Shimadzu-2020 LC-MS instrument using the following conditions: Shim-pack VP-ODS C18 column (reverse phase, 150 x 4.6 mm); a linear gradient from 10% water and 90% acetonitrile to 75% acetonitrile and 25% water over 6.0 min; flow rate of 0.5 mL/min; UV photodiode array detection from 200 to 400 nm. High-resolution mass spectra (HRMS) were recorded on Thermo Scientific Exactive Plus System. UV-VIS spectrophotometer TU-1950. The products were purified by Biotage Isolera™ Spektra Systems and hexane/EtOAc solvent systems. All reagents and solvents were obtained from commercial sources and used without further purification.

General procedures for compound 4

A solution of chromone-3-carboxaldehyde (0.2 mmol), amine (0.22 mmol), sulfochloride (0.2 mmol) and ^{t}BuOLi (0.4 mmol) was stirred in toluene (2.0 mL) under 100 °C for 8 h with a sealed system. The reaction mixture was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (15.0 mL), washed with brine. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product.

Transformation from 4a to 4x

A solution of **4a** (0.2 mmol) and 1 mol/L of HCl (2.0 equiv.) was stirred in MeCN (5.0 mL) under 80 ^{o}C for 6 h in a sealed system. The reaction mixture was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (15.0 mL), washed with brine three times. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford **4x** with the yield 87%.

General procedures for compounds 5, 8, 11, 12, and 13

4 (0.5 mmol) was treated with NH_2SO_3H (4.0 equiv.) and $NaClO_2$ (5.0 equiv.) in DCM (5.0 mL) under room temperature for 4 h. The reaction mixture was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (30.0 mL), washed with brine. The organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography using a gradient of MeOH/DCM (0-10%). For gram scale synthesis of Oxilinic acid: **4e** (5.0 mmol) was treated with NH_2SO_3H (4.0 equiv.) and $NaClO_2$ (5.0 equiv.) under same reaction condition, providing Oxilinic acid with the yield of 80%.

General procedures for compounds 6, 7, 9, and 10

A solution of F-substituted quinolone (2.0 mmol) and secondary amine (2.5 equiv.) in DMSO was treated with microwave 120 ^oC for 30 min. When the reaction was completed, the mixture was cooled to room temperature and washed with MeOH (3x10 mL). The final compound was purified by recrystallization in MeOH/H_2O (v:v = 1:1).

General procedures for compound 14

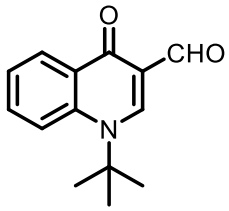
9a, 5-amino-2,4-di-*tert*-butylphenol (1.1 equiv.) and Et_3N (3.0 equiv.) were added into the solvent of DCM at room temperature. Then condensation reagent of TBTU (1.2 equiv.) was added during 10 min. The mixture was stirred at room temperature for 12 h, which was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (30.0 mL), washed with brine. The organic layer was dried over Na_2SO_4 and concentrated. The final compound was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) (**14**, 93%). For gram scale synthesis: **9a** (4.0 mmol), 5-amino-2,4-di-*tert*-butylphenol (1.1 equiv.) and Et_3N (3.0 equiv.) TBTU (1.2 equiv.) were treated with the standard condition, affording the desired product 87%.

General procedures for compound 15

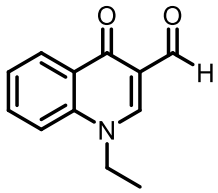
A solution of chromone-3-carboxaldehyde (0.2 mmol), *tert*-butylamine (0.22 mmol) and *p*-toluenesulfonyl chloride (0.2 mmol) was stirred in toluene (2.0 mL) under room temperature for 12 h. The reaction mixture was monitored by TLC. When the reaction was completed, the mixture was extracted with EtOAc (15.0 mL), washed with brine. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified

by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product.

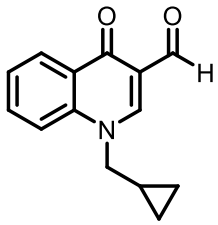
NMR Characterization Data and Figures of Products



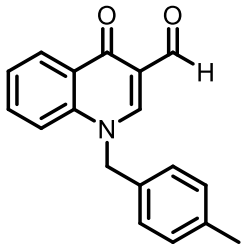
1-(tert-butyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde **4a**, 86%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 8.66 (s, 1H), 8.56 (d, *J* = 7.9 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 1H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 1.84 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.66, 175.52, 142.13, 138.40, 130.65, 129.94, 126.95, 124.28, 119.37, 115.09, 62.73, 29.83. HRMS (ESI) m/z calcd for $C_{14}H_{15}NO_2^+$ $(M+H)^+$ 230.1176, found 230.1177.



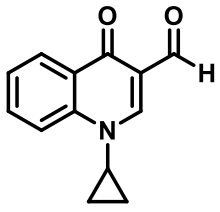
1-ethyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde **4b,** 81%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ10.36 (s, 1H), 8.48 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.27 (s, 1H), 7.72 – 7.65 (m, 1H), 7.49 – 7.42 (m, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.51 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ189.49, 176.95, 145.50, 139.13, 133.27, 129.69, 127.64, 125.71, 117.26, 116.15, 49.20, 14.56. HRMS (ESI) m/z calcd for $C_{12}H_{12}NO_2^+$ $(M+H)^+$ 202.0863, found 202.0865.



1-(cyclopropylmethyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde **4c,** 89%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 8.46 (d, *J* = 7.9 Hz, 1H), 8.36 (s, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.49 – 7.40 (m, 2H), 4.86 – 4.73 (m, 1H), 2.62 (dd, *J* = 9.6, 6.3 Hz, 2H), 2.49 – 2.35 (m, 2H), 1.98 – 1.89 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.49, 176.88, 141.92, 139.42, 133.02, 129.34, 127.39, 125.80, 116.62, 55.91, 29.83, 14.60. HRMS (ESI) m/z calcd for $C_{14}H_{14}NO_2^+$ $(M+H)^+$ 228.1019, found 228. 1022.

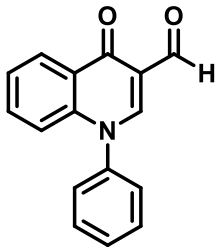


1-*(4-methylbenzyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde* **4d**, 77%, light yellow solid, (EA/Hex = 25%, R_f = 0.20), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.47 (d, *J* = 1.1 Hz, 1H), 8.54 (d, *J* = 8.0 Hz, 1H), 8.43 (s, 1H), 7.65 – 7.56 (m, 1H), 7.44 (dd, *J* = 16.5, 8.3 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.8 Hz, 2H), 5.38 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.53, 177.08, 146.63, 139.69, 138.81, 133.23, 130.67, 129.63, 127.39, 126.23, 125.79, 117.22, 57.65, 21.14. HRMS (ESI) m/z calcd for $C_{18}H_{16}NO_2^+$ $(M+H)^+$ 278.1176, found 278.1177.

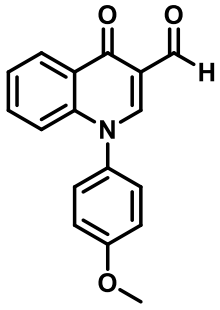


1-cyclopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde **4e**, 85%, light yellow solid, (EA/Hex = 25%, R_f = 0.20), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.33 (d, J = 1.1 Hz, 1H), 8.42 (d, J = 8.0 Hz, 1H), 8.37 (s, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.69 (dd, J = 8.4, 7.2 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 3.50 – 3.40 (m, 1H), 1.29 (d, J = 6.8 Hz, 2H), 1.12 – 1.03 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.40, 177.02, 145.58, 141.05, 133.08,

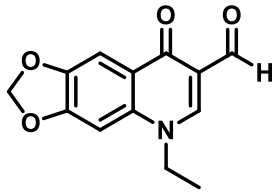
128.93, 127.13 , 125.82, 117.08, 117.01, 34.81, 8.16. HRMS (ESI) m/z calcd for $C_{14}H_{14}NO_2^+$ $(M+H)^+$ 214.0863, found 214.0865.



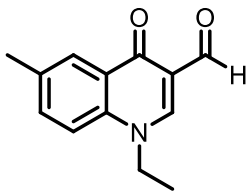
4-oxo-1-phenyl-1,4-dihydroquinoline-3-carbaldehyde **4f**, 80%, light yellow solid, (EA/Hex = 25%, R_f = 0.20), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51 (d, J = 1.1 Hz, 1H), 8.58 (d, J = 8.0 Hz, 1H), 8.37 (d, J = 1.1 Hz, 1H), 7.65 (d, J = 5.4 Hz, 3H), 7.60 (dd, J = 8.4, 7.2 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.06 (d, J = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.62, 177.04, 145.91, 141.11, 140.41, 133.00, 130.55, 130.31, 128.80, 127.22, 126.99, 125.91, 118.36, 117.20. HRMS (ESI) m/z calcd for $C_{16}H_{12}NO_2^+$ $(M+H)^+$ 250.0863, found 250.0863.



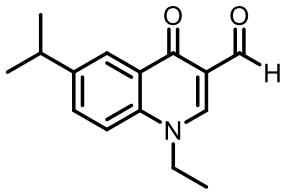
1-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde **4g**, 73%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.50 (s, 1H), 8.56 (d, *J* = 8.0 Hz, 1H), 8.36 (s, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 6.1 Hz, 2H), 7.14 – 7.09 (m, 2H), 7.07 (d, *J* = 8.5 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.66, 177.09, 160.65, 146.31, 141.52, 133.02, 132.96, 128.81, 128.36, 126.92, 125.84, 118.46, 117.12, 115.50, 55.77. HRMS (ESI) m/z calcd for $C_{17}H_{14}NO_3^+$ $(M+H)^+$ 280.0969, found 280.0967.



5-ethyl-8-oxo-5,8-dihydro-[1,3]dioxolo[4,5-g]quinoline-7-carbaldehyde **4h**, 80%, light yellow solid, (EA/Hex = 30%, R_f = 0.15), ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.16 (s, 1H), 8.50 (s, 1H), 7.59 (s, 1H), 7.49 (s, 1H), 6.24 (s, 2H), 4.40 (q, *J* = 7.0 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 189.02, 174.84, 153.03, 146.80, 145.93, 136.63, 125.08, 116.27, 103.14, 97.95, 49.29, 14.96. HRMS (ESI) m/z calcd for $C_{13}H_{12}NO_2^+$ $(M+H)^+$ 246.0761, found 246.0761.

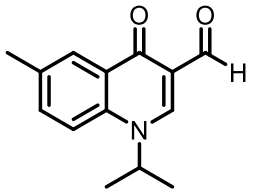


1-ethyl-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde **4i**, 85%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 8.26 (d, *J* = 0.8 Hz, 1H), 8.23 (s, 1H), 7.49 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.35 (d, *J* = 8.7 Hz, 1H), 4.21 (q, *J* = 7.3 Hz, 2H), 2.43 (s, 3H), 1.49 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.58, 176.95, 144.99, 137.08, 136.00, 134.50, 129.53, 127.12, 117.05, 116.08, 49.17, 20.99, 14.59. HRMS (ESI) m/z calcd for $C_{13}H_{14}NO_2^+$ $(M+H)^+$ 216.1019, found 216.1019.

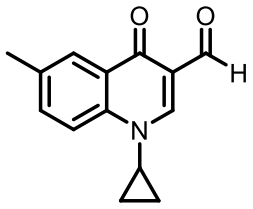


1-ethyl-6-isopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4j**, 73%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 8.32 (d, *J* = 2.0 Hz, 1H), 8.24 (s, 1H), 7.55 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.39 (d, *J* = 8.7 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 3.01 (dt, *J* = 13.8, 6.9 Hz, 1H),

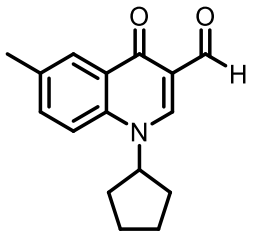
1.49 (t, *J* = 7.3 Hz, 3H), 1.25 (d, *J* = 6.9 Hz, 7H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.65, 177.09, 146.85, 144.99, 137.32, 132.16, 129.63, 124.55, 117.01, 116.25, 49.18, 33.79, 23.85, 14.62. HRMS (ESI) m/z calcd for $C_{15}H_{18}NO_2^+$ $(M+H)^+$ 244.1332, found 244.1333.



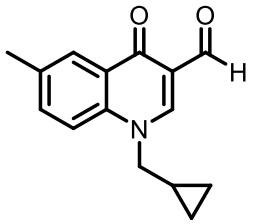
1-isopropyl-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4k**, 90%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 8.39 (s, 1H), 8.30 (s, 1H), 7.52 – 7.43 (m, 2H), 7.20 (s, 1H), 4.85 (dt, *J* = 13.3, 6.6 Hz, 1H), 2.43 (s, 3H), 1.55 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.56, 176.69, 140.51, 137.70, 135.82, 134.41, 129.65, 127.26, 117.01, 115.47, 51.51, 22.14, 20.86. HRMS (ESI) m/z calcd for $C_{14}H_{16}NO_2^+$ $(M+H)^+$ 230.1176, found 230.1177.



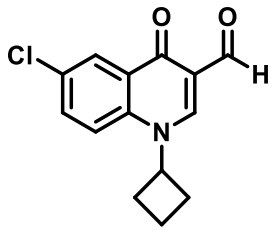
1-cyclopropyl-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4l**, 84%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (d, *J* = 1.4 Hz, 1H), 8.33 (s, 1H), 8.21 (s, 1H), 7.80 (d, *J* = 8.6 Hz, 1H), 7.49 (d, *J* = 8.6 Hz, 1H), 3.47 – 3.39 (m, 1H), 2.43 (s, 3H), 1.27 (d, *J* = 6.7 Hz, 2H), 1.20 (d, *J* = 11.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.49, 177.01, 145.06, 139.03, 136.08, 134.31, 128.78, 126.64, 116.92, 34.78, 20.98, 8.05. HRMS (ESI) m/z calcd for $C_{14}H_{14}NO_2^+$ $(M+H)^+$ 228.1019, found 228.1019.



1-cyclopentyl-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4m**, 77%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.35 (s, 1H), 8.27 (s, 1H), 7.55 – 7.45 (m, 2H), 4.88 (ddd, *J* = 13.2, 7.2, 5.6 Hz, 1H), 2.43 (s, 3H), 2.25 (td, *J* = 8.4, 7.5, 3.9 Hz, 2H), 1.98 – 1.83 (m, 5H), 1.83 – 1.74 (m, 2H), 1.66 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.49, 176.69, 140.94, 138.28, 135.82, 134.22, 129.62, 127.02, 116.29, 61.85, 33.67, 32.31, 23.73, 23.60, 20.87. HRMS (ESI) m/z calcd for $C_{16}H_{18}NO_2^+$ $(M+H)^+$ 256.1332, found 256.1333.

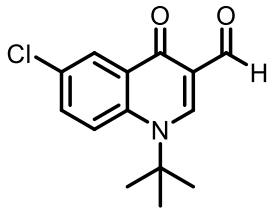


1-(cyclopropylmethyl)-6-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4n**, 85%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (s, 1H), 8.26 (d, *J* = 13.6 Hz, 2H), 7.45 (dd, *J* = 19.8, 8.7 Hz, 2H), 3.97 (d, *J* = 7.0 Hz, 2H), 2.42 (s, 3H), 1.37 – 1.21 (m, 1H), 0.69 (dd, *J* = 10.0, 2.9 Hz, 2H), 0.39 (t, *J* = 5.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.49, 176.92, 144.79, 137.72, 135.97, 134.37, 129.39, 126.95, 116.88, 116.19, 58.18, 20.94, 10.04, 4.66. HRMS (ESI) m/z calcd for $C_{15}H_{16}NO_2^+$ $(M+H)^+$ 242.1176, found 242.1177.

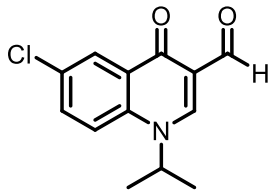


6-chloro-1-cyclobutyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4o**, 79%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (s, 1H),

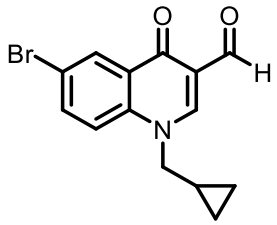
8.44 – 8.31 (m, 2H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.63 (dd, *J* = 9.0, 2.4 Hz, 1H), 3.49 – 3.37 (m, 1H), 1.30 (t, *J* = 6.6 Hz, 2H), 1.20 (d, *J* = 12.1 Hz, 2H), 1.09 (d, *J* = 3.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.05, 175.83, 145.68, 139.47, 133.30, 132.37, 130.06, 126.60, 118.73, 117.25, 34.94, 8.21. HRMS (ESI) m/z calcd for $C_{14}H_{13}NO_2^+$ $(M+H)^+$ 262.0629 found 262.0629.



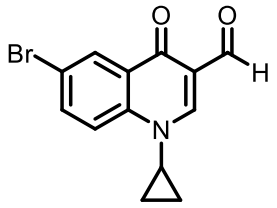
1-(tert-butyl)-6-chloro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4p**, 87%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (d, *J* = 1.8 Hz, 1H), 8.63 (s, 1H), 8.49 (s, 1H), 7.92 – 7.82 (m, 1H), 7.57 (ddd, *J* = 9.3, 2.8, 1.8 Hz, 1H), 1.82 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.28, 175.28, 143.18, 137.78, 132.33, 131.80, 127.29, 121.93, 116.23, 63.99, 30.81. HRMS (ESI) m/z calcd for $C_{14}H_{15}NO_2^+$ $(M+H)^+$ 264.0786, found 264.0786.



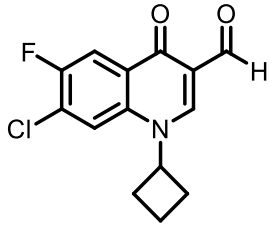
6-chloro-1-isopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4q**, 89%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.42 (d, *J* = 1.6 Hz, 1H), 8.50 (dd, *J* = 18.8, 2.0 Hz, 2H), 7.69 (ddd, *J* = 9.1, 2.5, 1.6 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 1H), 4.90 (dt, *J* = 13.2, 6.6 Hz, 1H), 1.64 (dd, *J* = 6.6, 1.5 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.16, 175.56, 141.07, 133.37, 131.89, 131.33, 127.16, 117.34, 52.01, 22.13. HRMS (ESI) m/z calcd for $C_{13}H_{13}ClNO_2^+$ $(M+H)^+$ 250.0629, found 250.0629.



6-bromo-1-(cyclopropylmethyl)-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4r**, 82%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (d, *J* = 2.9 Hz, 1H), 8.58 (t, *J* = 2.5 Hz, 1H), 8.32 (d, *J* = 2.8 Hz, 1H), 7.75 (dt, *J* = 9.0, 2.6 Hz, 1H), 7.42 (dd, *J* = 9.0, 2.7 Hz, 1H), 3.97 (dd, *J* = 6.9, 2.5 Hz, 2H), 1.28 (dd, *J* = 7.4, 4.5 Hz, 1H), 0.80 – 0.66 (m, 2H), 0.41 (d, *J* = 1.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.07, 175.63, 145.36, 138.58, 136.06, 130.94, 130.18, 119.84, 118.07, 117.44, 58.37, 9.95, 4.75. HRMS (ESI) m/z calcd for $C_{14}H_{13}BrNO_2^+$ $(M+H)^+$ 306.0124, found 306.0125.

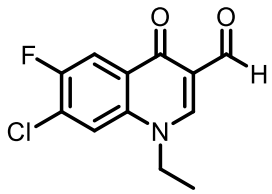


6-bromo-1-cyclopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4s**, 85%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (s, 1H), 8.52 (d, J = 2.1 Hz, 1H), 8.35 (s, 1H), 7.87 – 7.71 (m, 2H), 3.51 – 3.34 (m, 1H), 1.30 (q, J = 6.8 Hz, 2H), 1.09 (q, J = 6.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.96, 175.64, 145.66, 139.88, 136.03, 130.29, 129.76, 120.03, 118.88, 117.39, 34.87, 8.19. HRMS (ESI) m/z calcd for $C_{13}H_{11}BrNO_2^+$ $(M+H)^+$ 291.9968, found 291.9969.

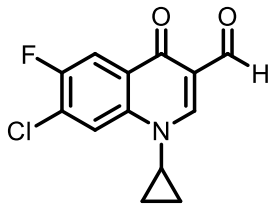


7-chloro-1-cyclobutyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4aa**, 78%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.41 (d,

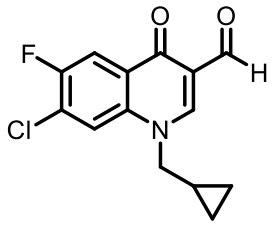
J = 1.6 Hz, 1H), 8.43 (d, *J* = 1.6 Hz, 1H), 8.27 (d, *J* = 8.8 Hz, 1H), 7.61 (dd, *J* = 5.7, 1.6 Hz, 1H), 4.81 (td, *J* = 8.4, 7.5, 2.1 Hz, 1H), 2.82 – 2.63 (m, 2H), 2.51 (ddd, *J* = 11.3, 7.0, 2.1 Hz, 2H), 2.14 – 1.97 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.98, 175.35, 157.08, 154.57, 142.20, 135.97, 129.68, 127.55, 119.21, 116.29, 113.87, 56.11, 29.76, 14.53. HRMS (ESI) m/z calcd for $C_{14}H_{12}ClFNO_2^+$ $(M+H)^+$ 280.0535, found 280.0535.



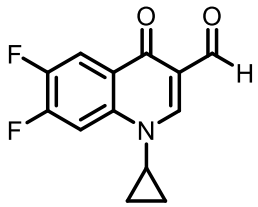
7-chloro-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4ab**, 77%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31 (s, 1H), 8.25 (s, 1H), 8.19 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 5.6 Hz, 1H), 4.20 (q, *J* = 7.3 Hz, 2H), 1.52 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.93, 175.40, 157.00, 154.49, 145.68, 135.79, 129.90, 118.69, 117.00, 114.08, 49.54, 14.48. HRMS (ESI) m/z calcd for $C_{12}H_{10}ClFNO_2^+$ $(M+H)^+$ 254.0379, found 254.0380.



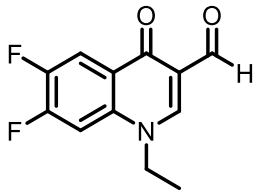
7-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4ac**, 81%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.42 (s, 1H), 8.21 (d, *J* = 8.7 Hz, 1H), 8.06 (d, *J* = 5.8 Hz, 1H), 3.50 (dt, *J* = 7.0, 3.8 Hz, 1H), 1.41 (d, *J* = 6.8 Hz, 2H), 1.18 (d, *J* = 2.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.87, 175.49, 157.23, 154.73, 145.87, 137.66, 129.14, 127.70, 119.60, 116.74, 113.62, 35.08, 8.29. HRMS (ESI) m/z calcd for $C_{13}H_{10}ClFNO_2^+$ $(M+H)^+$ 266.0379, found 266.0381.



7-chloro-1-(cyclopropylmethyl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4ad**, 85%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.41 (s, 1H), 8.42 (s, 1H), 8.28 (d, *J* = 8.8 Hz, 1H), 7.71 (d, *J* = 5.6 Hz, 1H), 4.05 (d, *J* = 7.0 Hz, 2H), 1.48 – 1.31 (m, 1H), 0.85 (d, *J* = 8.1 Hz, 2H), 0.52 (d, *J* = 5.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.94, 175.45, 157.02, 154.52, 145.41, 136.39, 129.82, 127.77, 118.84, 116.77, 113.71, 58.65, 9.83, 4.87. HRMS (ESI) m/z calcd for $C_{14}H_{12}ClFNO_2^+$ $(M+H)^+$ 280.0535, found 280.0537.

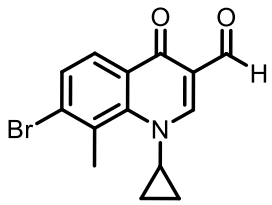


1-cyclopropyl-6,7-difluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4ae**, 79%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.43 (s, 1H), 8.27 (dd, *J* = 9.7, 9.0 Hz, 1H), 7.80 (dd, *J* = 11.2, 6.4 Hz, 1H), 3.53 – 3.44 (m, 1H), 1.40 (q, *J* = 6.7 Hz, 2H), 1.18 (q, *J* = 6.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.96, 175.38, 154.97, 150.13, 147.75, 145.94, 138.06, 126.11, 116.80, 115.08, 106.37, 35.12, 8.24. HRMS (ESI) m/z calcd for $C_{13}H_{10}ClFNO_2^+$ $(M+H)^+$ 250.0674, found 250.0675.

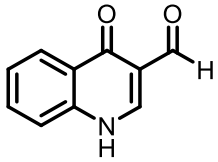


1-ethyl-6,7-difluoro-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4af**, 76%, light yellow solid, (EA/Hex = 25%, R_f = 0.25) ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.14 (s,

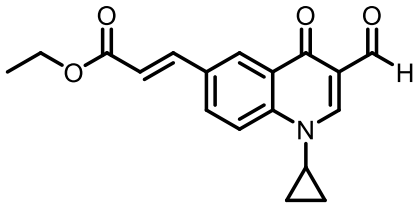
1H), 8.64 (s, 1H), 8.19 – 8.04 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 188.24, 174.48, 148.16, 137.02, 126.74, 116.53, 114.06, 113.88, 108.23, 108.01, 49.32, 14.92. HRMS (ESI) m/z calcd for $C_{12}H_{10}F_2NO_2^+$ $(M+H)^+$ 280.0674, found 280.0675.



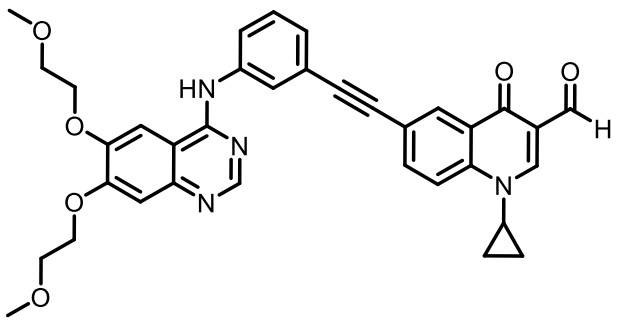
7-bromo-1-cyclopropyl-8-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4ag**, 80%, light yellow solid, (EA/Hex = 25%, R_f = 0.25) ^{1}H NMR (400 MHz, DMSO- *d*$_6$) δ 10.09 (s, 1H), 8.51 (s, 1H), 7.99 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 8.5 Hz, 1H), 4.26 (dt, *J* = 10.7, 3.5 Hz, 1H), 2.29 (s, 3H), 1.16 (d, *J* = 5.8 Hz, 2H), 0.86 (d, *J* = 1.5 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 188.29, 175.65, 151.95, 146.59, 130.29, 129.71, 128.99, 125.28, 117.17, 41.04, 22.90, 21.26, 10.86. HRMS (ESI) m/z calcd for $C_{14}H_{13}BrNO_2^+$ $(M+H)^+$ 306.0124, found 306.0125.



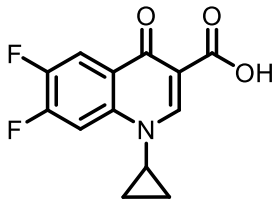
4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4ah**, 75%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 12.71 (s, 1H), 10.20 (s, 1H), 8.49 (s, 1H), 8.22 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.76 (dd, *J* = 7.1, 1.3 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.52 – 7.43 (m, 1H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 189.18, 176.69, 143.67, 139.84, 133.55, 128.20, 125.87, 119.87, 116.77. HRMS (ESI) m/z calcd for $C_{10}H_8NO_2^+$ $(M+H)^+$ 174.0550, found 174.0551.



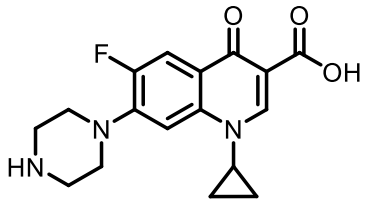
ethyl (E)-3-(1-cyclopropyl-3-formyl-4-oxo-1,4-dihydroquinolin-6-yl)acrylate, **4ai**, 73%, light yellow solid, (EA/Hex = 30%, R_f = 0.2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.33 (s, 1H), 8.54 (d, *J* = 1.8 Hz, 1H), 8.36 (s, 1H), 7.93 (d, *J* = 8.8 Hz, 1H), 7.81 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.72 (d, *J* = 16.0 Hz, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 3.77 (s, 3H), 3.45 (qd, *J* = 7.6, 3.9 Hz, 1H), 1.31 (q, *J* = 6.7 Hz, 2H), 1.10 (q, *J* = 6.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.11, 176.61, 166.96, 145.67, 142.74, 141.90, 132.02, 129.12, 126.95, 119.73, 117.79, 117.57, 51.87, 34.92, 8.23. HRMS (ESI) m/z calcd for $C_{18}H_{18}NO_4^+$ $(M+H)^+$ 312.1230, found 312.1231.



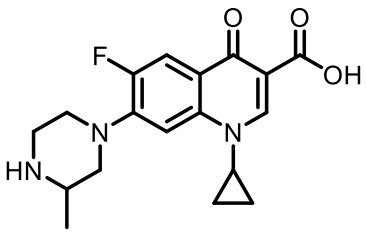
6-((3-((6,7-bis(2-methoxyethoxy)quinazolin-4-yl)amino)phenyl)ethynyl)-1-cyclopropyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde, **4aj**, 76%, white solid, (EA/Hex = 60%, R_f = 0.25), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.37 (s, 1H), 8.61 (s, 1H), 8.27 (d, *J* = 19.4 Hz, 3H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.81 (d, *J* = 8.7 Hz, 1H), 7.70 – 7.60 (m, 2H), 7.48 (s, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 7.18 – 7.11 (m, 2H), 4.20 (dd, *J* = 19.0, 14.5 Hz, 4H), 3.79 – 3.71 (m, 4H), 3.37 (d, *J* = 3.5 Hz, 7H), 1.21 (dd, *J* = 10.0, 4.9 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.45, 176.39, 156.48, 154.51, 153.47, 149.07, 147.41, 145.95, 140.32, 139.39, 135.58, 130.06, 129.09, 128.55, 126.73, 124.41, 122.93, 122.26, 120.82, 117.32, 109.56, 108.61, 102.67, 90.84, 87.82, 70.84, 69.02, 68.34, 59.24, 35.05, 29.68, 8.05. HRMS (ESI) m/z calcd for $C_{35}H_{33}N_4O_6^+$ $(M+H)^+$ 605.2395, found 605.2396.



1-cyclopropyl-6,7-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, **5**, 91%, light yellow solid, (MeOH/DCM=10%, R_f = 0.2), ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 14.74 (s, 1H), 8.77 (s, 1H), 8.39 (dd, *J* = 12.0, 6.8 Hz, 1H), 8.34 – 8.20 (m, 1H), 3.86 – 3.76 (m, 1H), 1.33 (d, *J* = 5.7 Hz, 2H), 1.25 – 1.21 (m, 2H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 177.15, 165.89, 150.06, 139.30, 123.13, 113.87, 108.86, 107.91, 37.10, 8.04. HRMS (ESI) m/z calcd for $C_{13}H_{10}F_2NO_3^+$ $(M+H)^+$ 266.0623, found 266.0625.

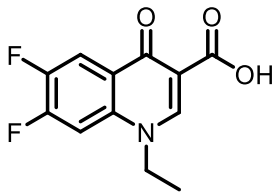


1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid, **6**, 91%, light yellow solid, (MeOH/DCM=15%, R_f = 0.15), ^{1}H NMR (400 MHz, D_2O) δ 8.29 (s, 1H), 7.23 (d, *J* = 7.1 Hz, 1H), 7.02 (d, *J* = 12.9 Hz, 1H), 3.47 (s, 5H), 3.38 (s, 4H), 1.28 (d, *J* = 6.5 Hz, 2H), 1.00 (s, 2H). ^{13}C NMR (101 MHz, D_2O) δ 175.28 (s), 168.41, 154.31, 151.81, 147.84, 144.50, 138.62, 118.20, 110.39, 106.25, 105.24, 46.18, 46.13, 43.09, 36.02, 7.40. HRMS (ESI) m/z calcd for $C_{17}H_{19}FN_3O_3^+$ $(M+H)^+$ 332.1405, found 332.1408.

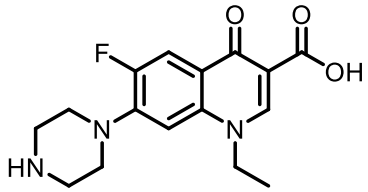


1-cyclopropyl-6-fluoro-7-(3-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, **7**, 87%, light yellow solid, (MeOH/DCM=15%, R_f = 0.15), ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.64 (s, 1H), 7.87 (d, *J* = 13.4 Hz, 1H), 7.53 (d, *J* = 7.3 Hz,

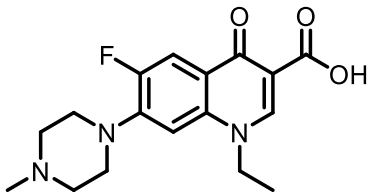
1H), 3.84 (s, 1H), 3.60 (d, *J* = 9.9 Hz, 2H), 3.35 (s, 1H), 3.13 – 2.93 (m, 4H), 2.66 (t, *J* = 11.0 Hz, 1H), 1.32 (d, *J* = 5.6 Hz, 2H), 1.18 (s, 2H), 1.11 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 176.75, 166.40, 154.64, 152.16, 148.39, 145.66, 139.67, 118.95, 111.53, 107.15, 56.21, 50.48, 49.47, 44.91, 36.33, 18.86, 8.01. HRMS (ESI) m/z calcd for $C_{18}H_{21}FN_3O_3^+$ $(M+H)^+$ 346.1561, found 346.1560.



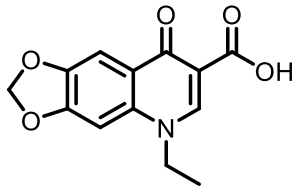
1-ethyl-6,7-difluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, **8**, 89%, light yellow solid, (MeOH/DCM=10%, R_f = 0.2), ^{1}H NMR (400 MHz, $CDCl_3$), ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 14.87 (s, 1H), 9.09 (s, 1H), 8.39 – 8.25 (m, 2H), 4.58 (q, *J* = 6.9 Hz, 2H), 1.39 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 176.91, 166.06, 150.29, 137.36, 123.77, 113.96, 108.45, 108.22, 50.04, 14.98. HRMS (ESI) m/z calcd for $C_{12}H_{10}FNO_3^+$ $(M+H)^+$ 254.0623, found 254.0625.



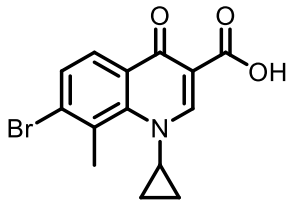
1-ethyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid, **9**, 92%, light yellow solid, (MeOH/DCM=15%, R_f = 0.15), ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.93 (s, 1H), 7.84 (d, *J* = 13.5 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 4.58 (q, *J* = 7.0 Hz, 2H), 3.33 – 3.12 (m, 4H), 2.98 – 2.80 (m, 4H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 175.54, 166.61, 154.58 152.10, 148.82, 146.53, 137.66, 119.43, 111.62, 107.48, 105.93, 51.29, 49.47, 45.87, 14.79. HRMS (ESI) m/z calcd for $C_{16}H_{19}FN_3O_3^+$ $(M+H)^+$ 320.1405, found 320.1408.



1-ethyl-6-fluoro-7-(4-methylpiperazin-1-yl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, **10**, 90%, light yellow solid, (MeOH/DCM=15%, R_f = 0.15), ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.95 (s, 1H), 7.90 (d, *J* = 13.4 Hz, 1H), 7.17 (d, *J* = 7.2 Hz, 1H), 4.59 (q, *J* = 6.9 Hz, 2H), 3.33 (d, *J* = 4.2 Hz, 4H), 2.53 (s, 4H), 2.26 (s, 3H), 1.42 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 176.62, 166.61, 148.98, 145.89, 137.67, 119.65, 111.73, 107.51, 106.28, 54.76, 49.76, 49.51, 46.16, 14.84. HRMS (ESI) m/z calcd for $C_{17}H_{21}FN_3O_3^+$ $(M+H)^+$ 334.1561, found 334.1564.

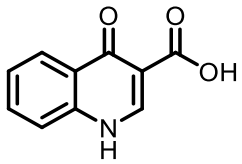


5-ethyl-8-oxo-5,8-dihydro-[1,3]dioxolo[4,5-g]quinoline-7-carboxylic acid, **11**, 88%, light yellow solid, (MeOH/DCM=10%, R_f = 0.2), ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 15.70 (s, 1H), 8.90 (s, 1H), 7.62 (d, *J* = 11.1 Hz, 2H), 6.30 (s, 2H), 4.54 (d, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$) δ 176.46, 166.79, 154.20, 147.57, 137.42, 103.74, 102.33, 97.71, 50.04, 15.09. HRMS (ESI) m/z calcd for $C_{13}H_{12}NO_5^+$ $(M+H)^+$ 262.0710, found 262.0715.

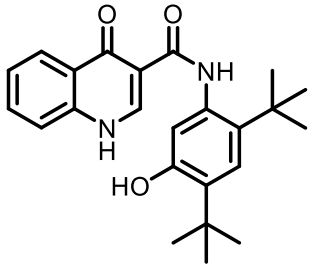


7-bromo-1-cyclopropyl-8-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid, **12**, 91%, light yellow solid, (MeOH/DCM=10%, R_f = 0.2), ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 14.68 (s, 1H), 8.87 (s, 1H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 4.48 – 4.31 (m, 1H), 2.92 (s, 3H), 1.22 (d, *J* = 6.3 Hz, 2H), 0.93 (s, 2H). ^{13}C NMR (101 MHz,

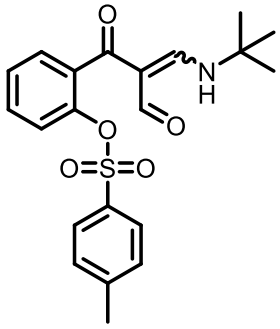
DMSO-d_6) δ 178.16, 165.79, 153.50, 143.18, 133.92, 131.06, 125.11, 108.50, 55.40, 41.95, 23.12, 11.01. HRMS (ESI) m/z calcd for $C_{14}H_{13}BrNO_3^+$ $(M+H)^+$ 322.0073, found 322.0073.



4-oxo-1,4-dihydroquinoline-3-carboxylic acid, **13**, 92%, light yellow solid, (MeOH/DCM=10%, R_f = 0.2), ^{1}H NMR (400 MHz, DMSO-d_6) δ 15.37 (s, 1H), 13.51 (s, 1H), 8.90 (s, 1H), 8.40 – 8.22 (m, 1H), 8.01 – 7.75 (m, 2H), 7.61 (dd, *J* = 11.1, 3.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.81, 166.87, 145.64, 139.92, 134.42, 126.69, 125.52, 124.86, 120.14, 108.03. HRMS (ESI) m/z calcd for $C_{10}H_8NO_3^+$$(M+H)^+$ 190.0499, found 190.0498.

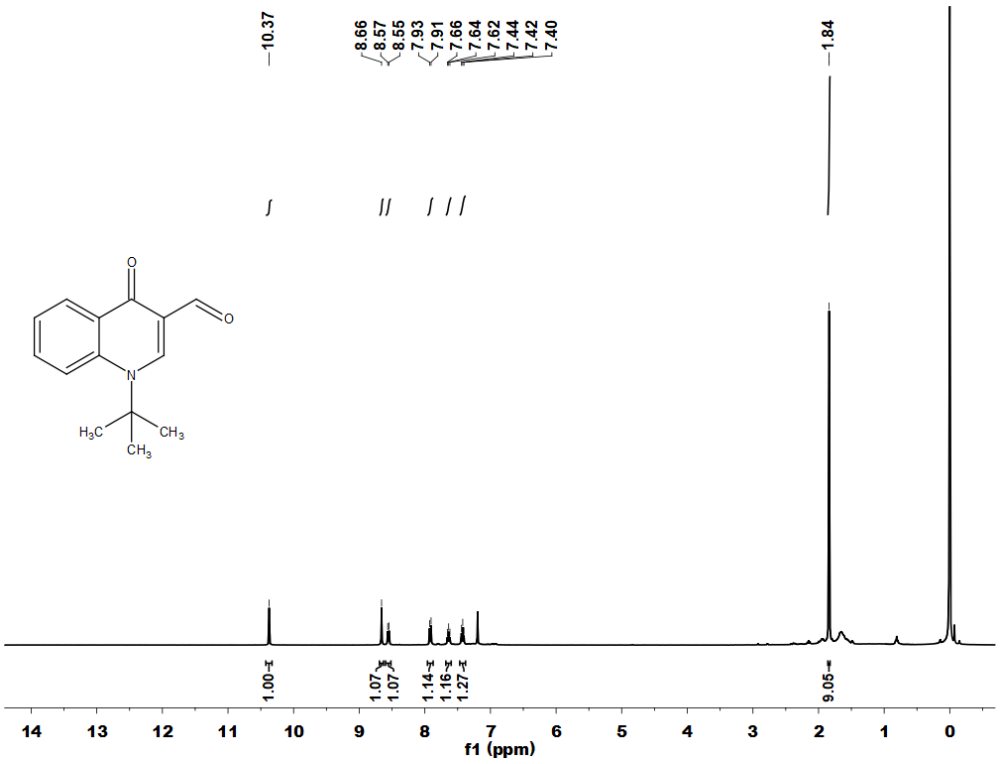


N-(2,4-di-tert-butyl-5-hydroxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxamide, **14**, 93%, light yellow solid, (EA/Hex = 25%, R_f = 0.25), ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.89 (s, 1H), 11.82 (s, 1H), 9.21 (s, 1H), 8.87 (s, 1H), 8.33 (d, *J* = 8.1 Hz, 1H), 7.78 (dd, *J* = 19.3, 7.7 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 26.1 Hz, 2H), 1.37 (d, *J* = 6.7 Hz, 18H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 176.87, 163.29, 153.75, 144.64, 139.63, 134.00, 133.40, 132.75, 131.97, 126.46, 125.62, 124.23, 119.60, 116.42, 111.35, 34.80, 34.44, 31.03, 29.88. HRMS (ESI) m/z calcd for $C_{24}H_{29}N_2O_3^+$ $(M+H)^+$ 393.2173, found 393.2174.

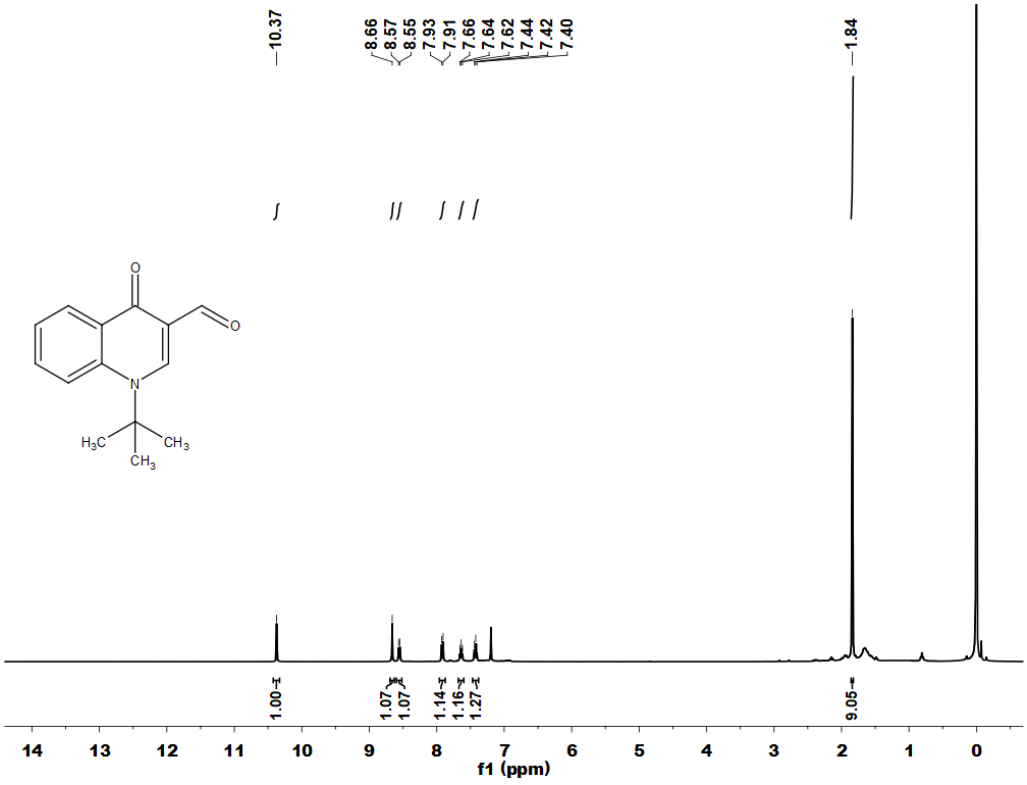


2-(3-(tert-butylamino)-2-formylacryloyl)phenyl 4-methylbenzenesulfonate, **15**, 97%, light yellow solid, (EA/Hex = 20%, R_f = 0.2), ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.40 (s, 1H), 9.31 (s, 0.6H), 9.04 (s, 0.4H), 8.13 (d, *J* = 14.7 Hz, 0.4H), 7.97 (s, 0.6H), 7.64 (t, *J* = 8.6 Hz, 2H), 7.41 (dd, *J* = 14.0, 6.0 Hz, 1H), 7.34 – 7.29 (m, 1H), 7.24 (dd, *J* = 12.5, 6.9 Hz, 4H), 2.43 (s, 3H), 1.46 (s, 4H), 1.40 (s, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.78, 190.84, 189.46, 188.43, 156.09, 145.95, 145.53, 133.76, 132.46, 131.09, 129.74, 128.51, 127.13, 123.27, 110.18, 54.85, 29.52, 21.74. HRMS (ESI) m/z calcd for $C_{21}H_{24}NO_5S^+$ $(M+H)^+$ 402.1370, found 402.1370.

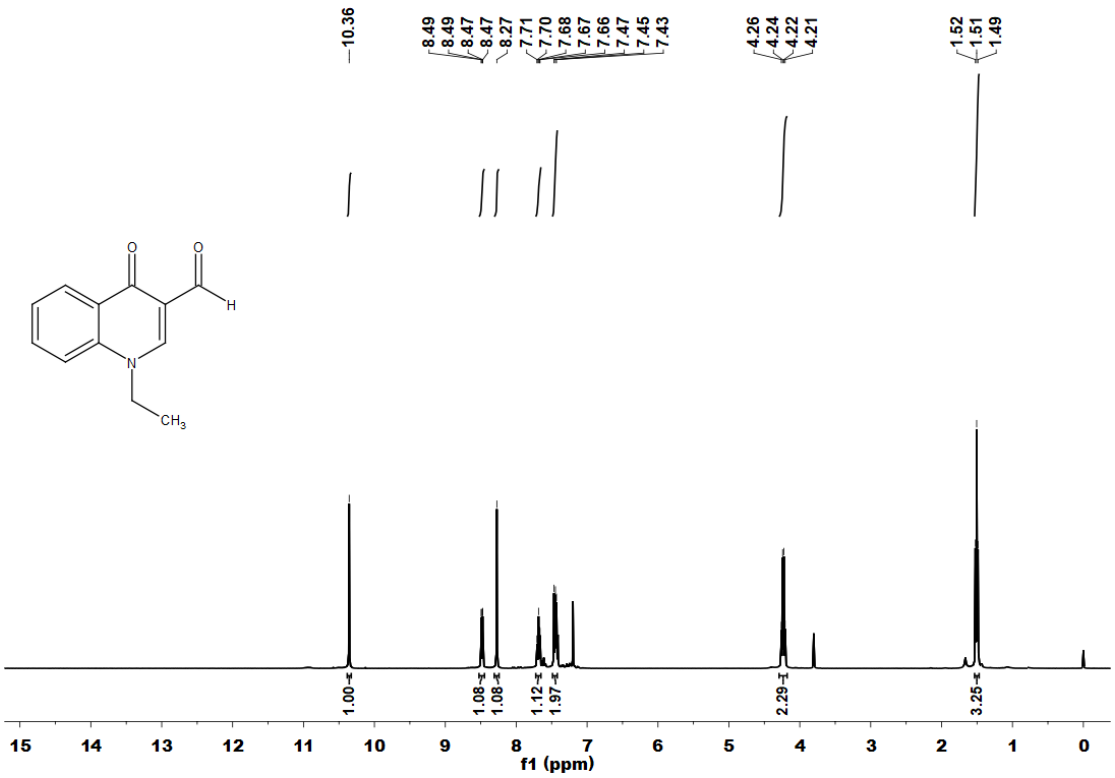
NMR Figures of Products



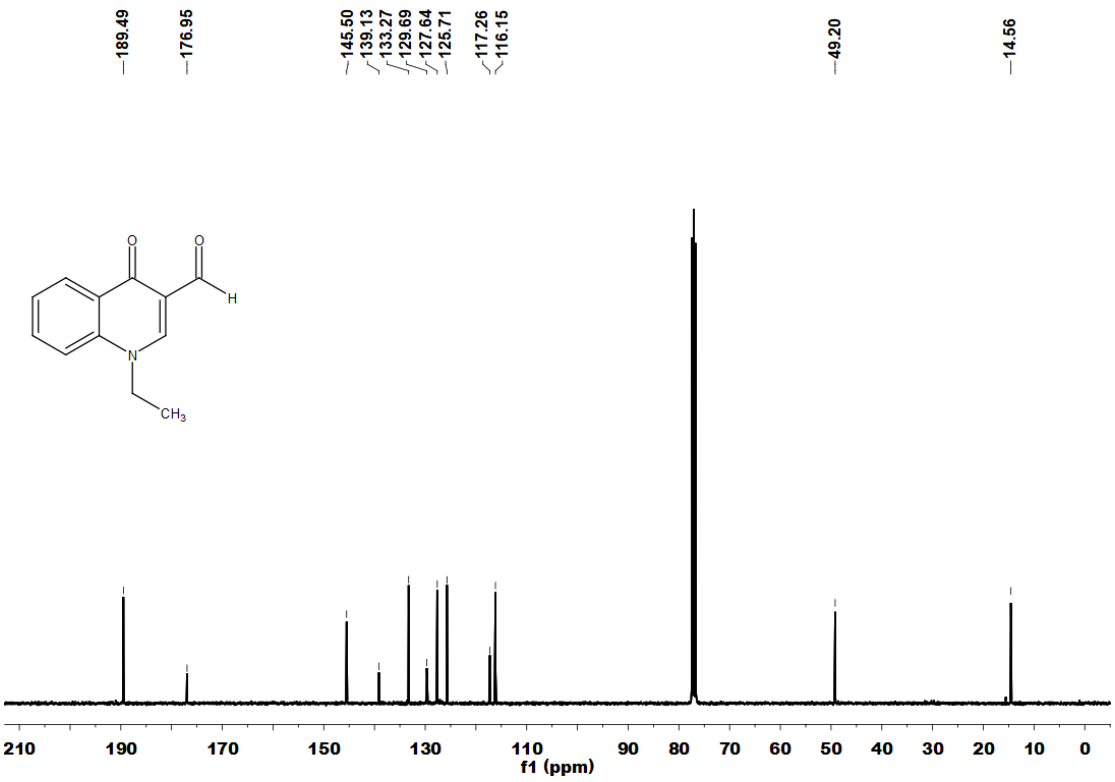
^{1}H NMR spectrum of **4a**



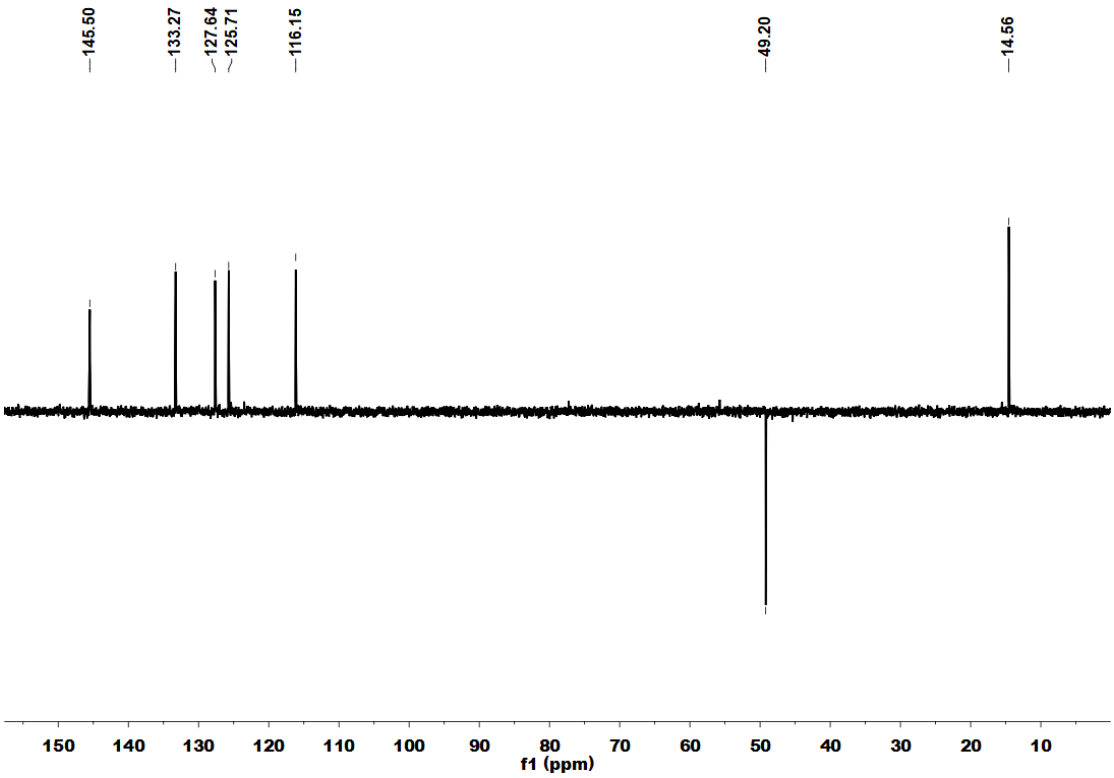
^{13}C NMR spectrum of **4a**



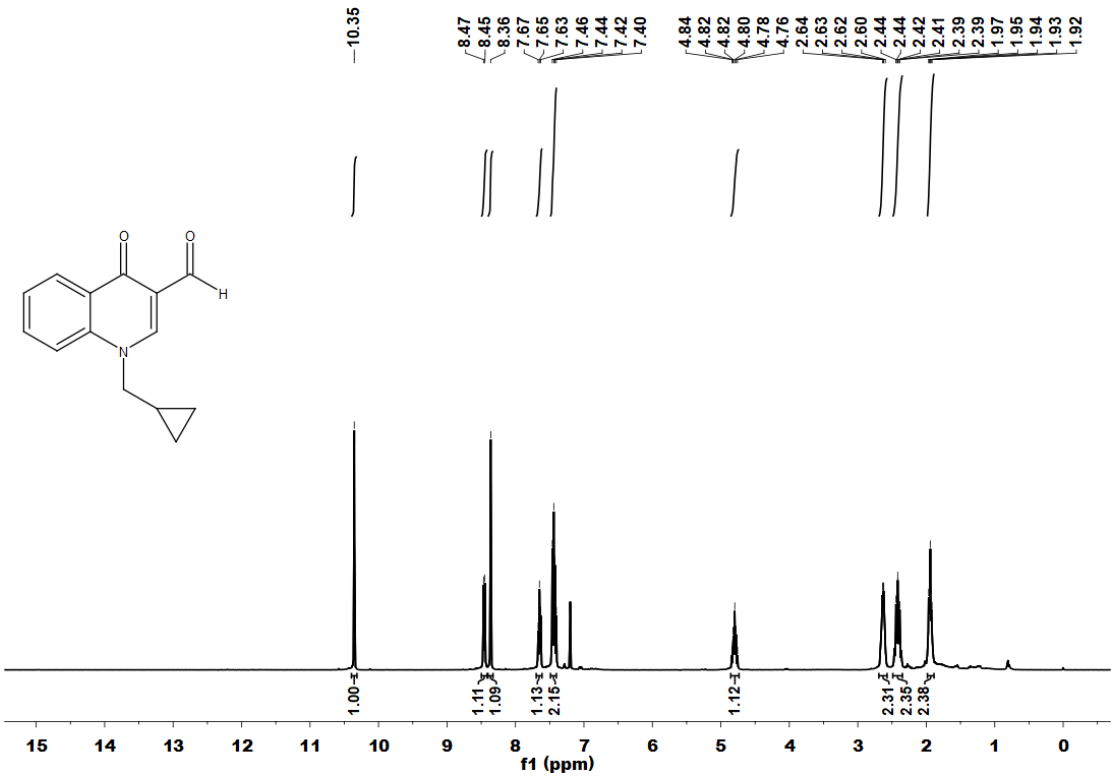
^{1}H NMR spectrum of **4b**



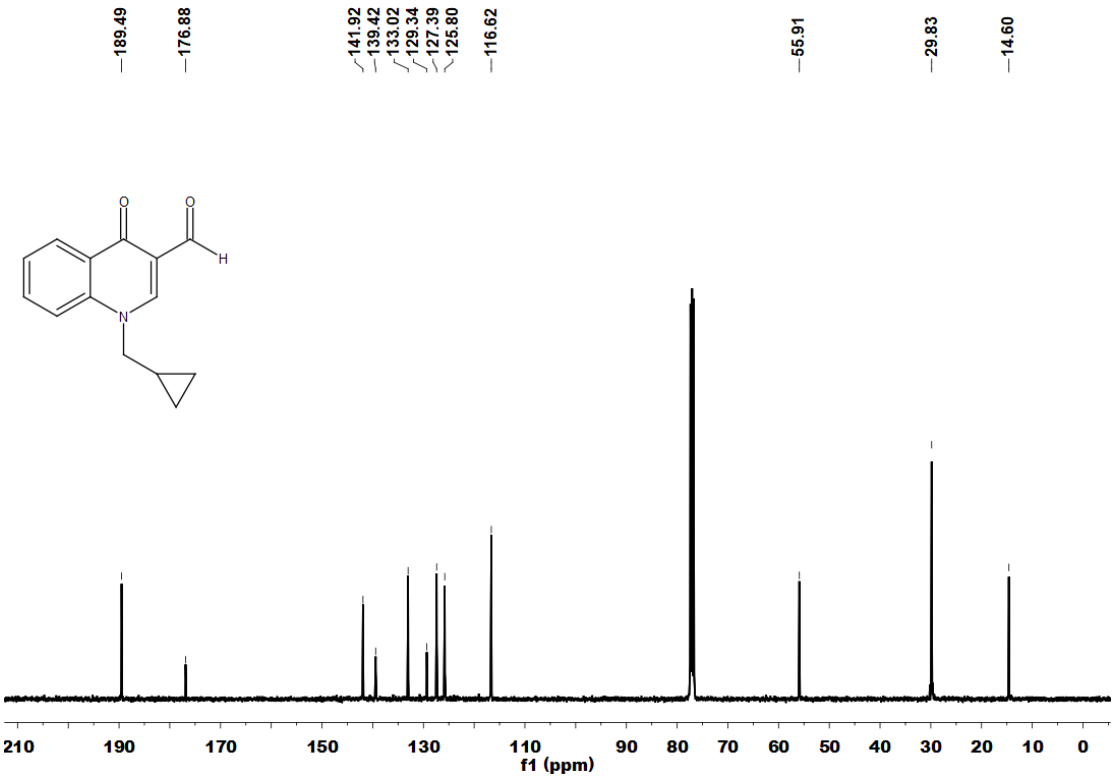
^{13}C NMR spectrum of **4b**



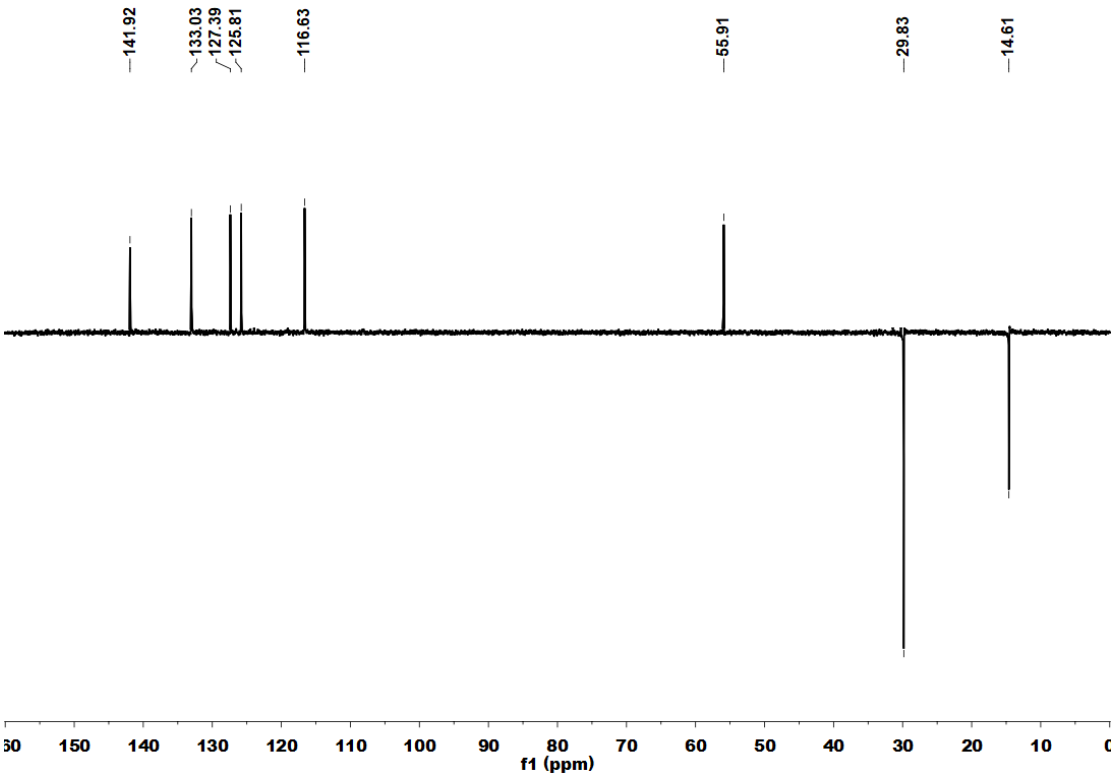
DEP 135^{o} spectrum of **4b**



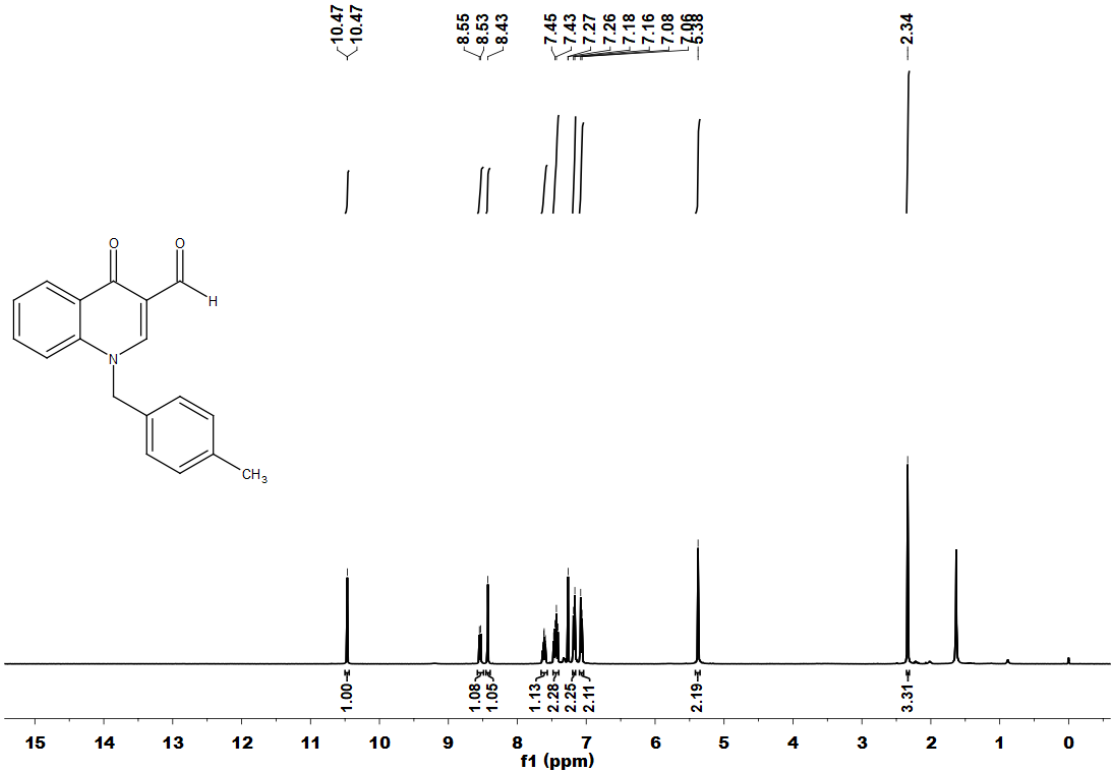
^{1}H NMR spectrum of **4c**



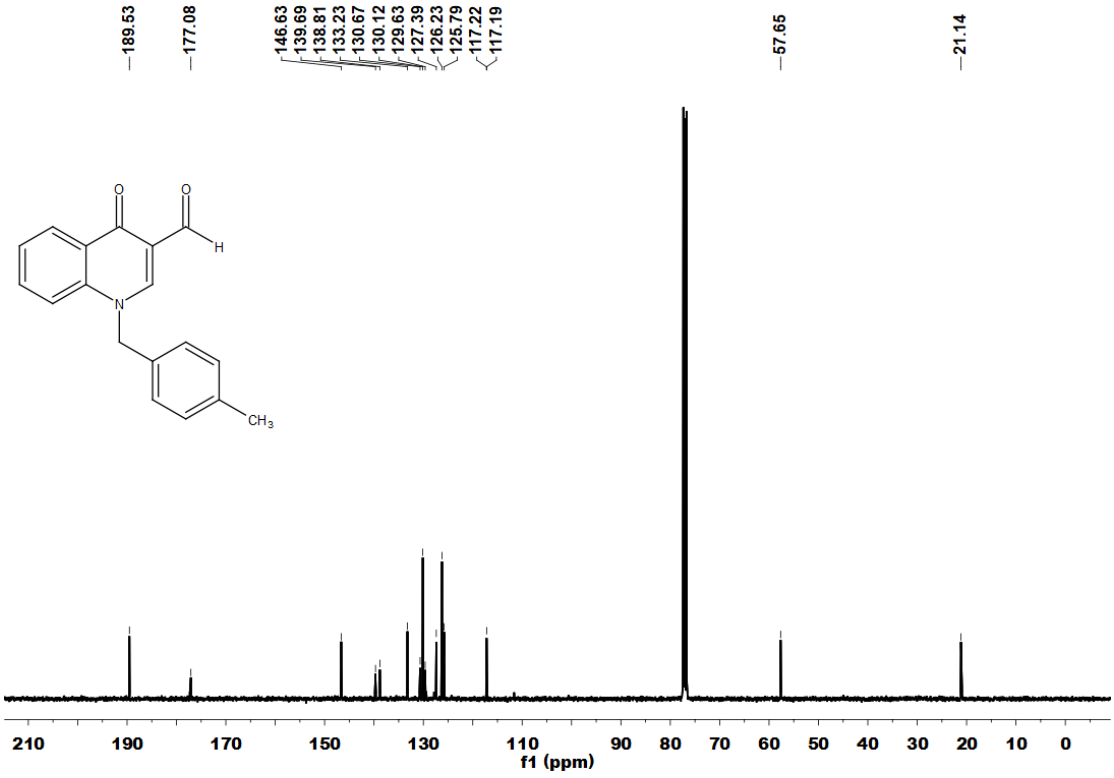
^{13}C NMR spectrum of **4c**



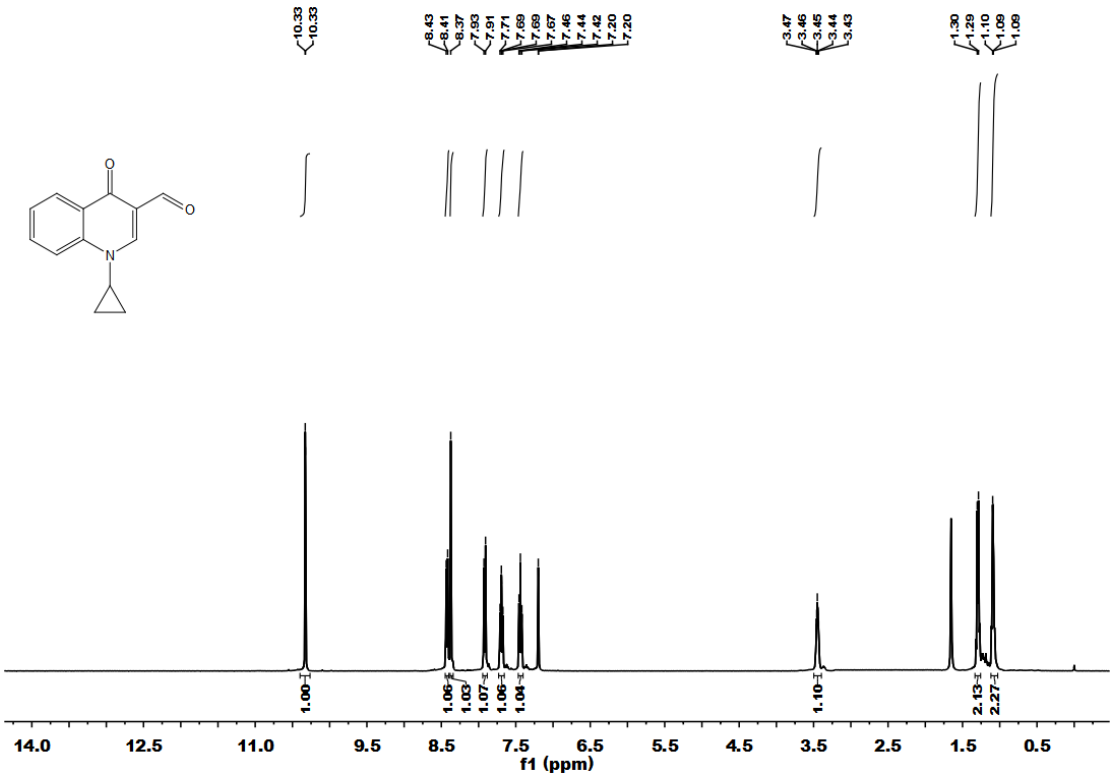
DEP 135^{o} spectrum of **4c**



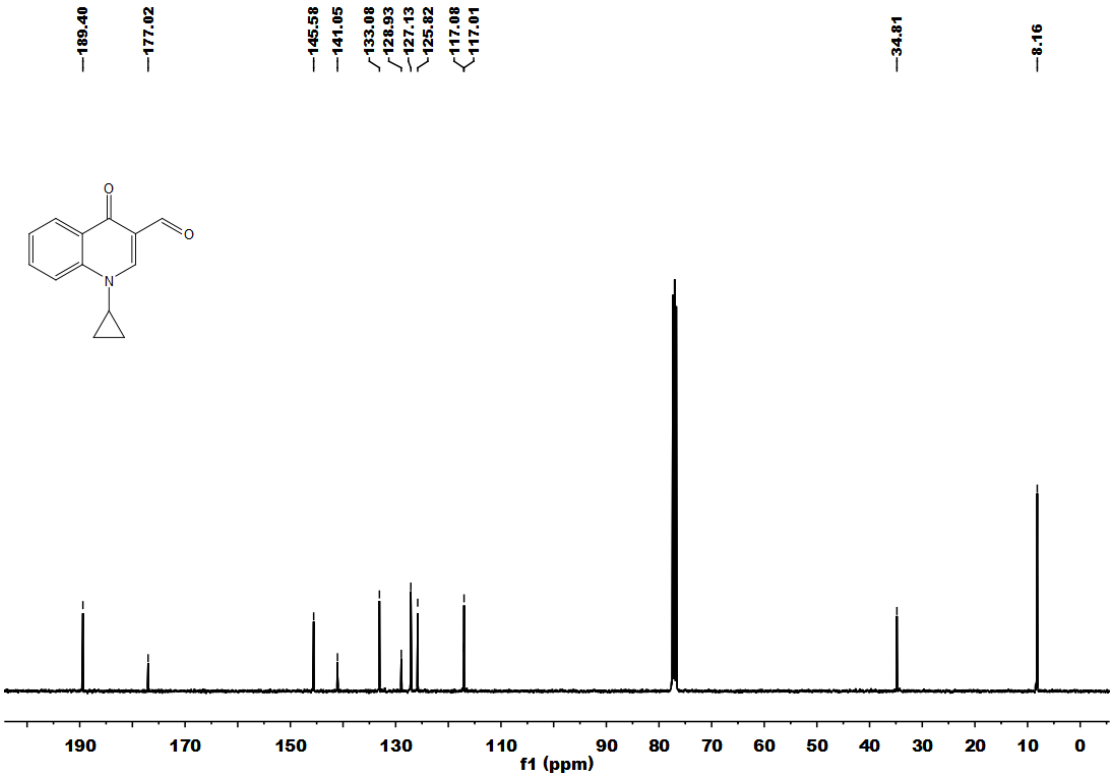
^{1}H NMR spectrum of **4d**



^{13}C NMR spectrum of **4d**



^{1}H NMR spectrum of **4e**



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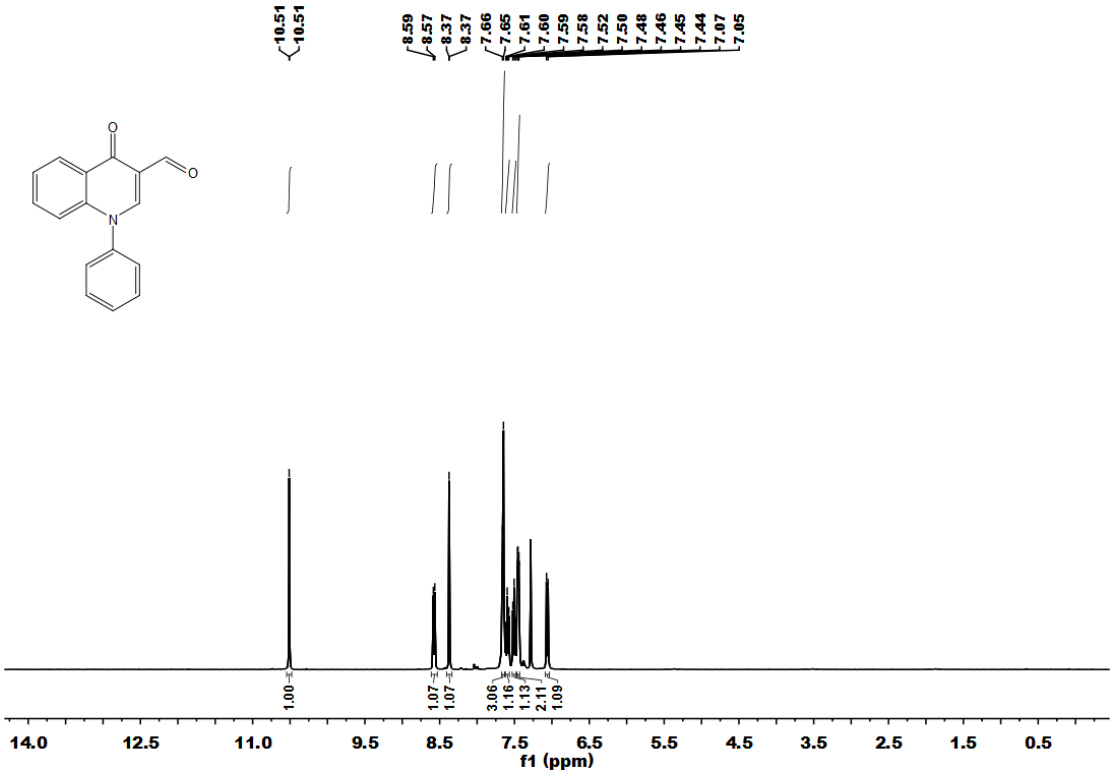
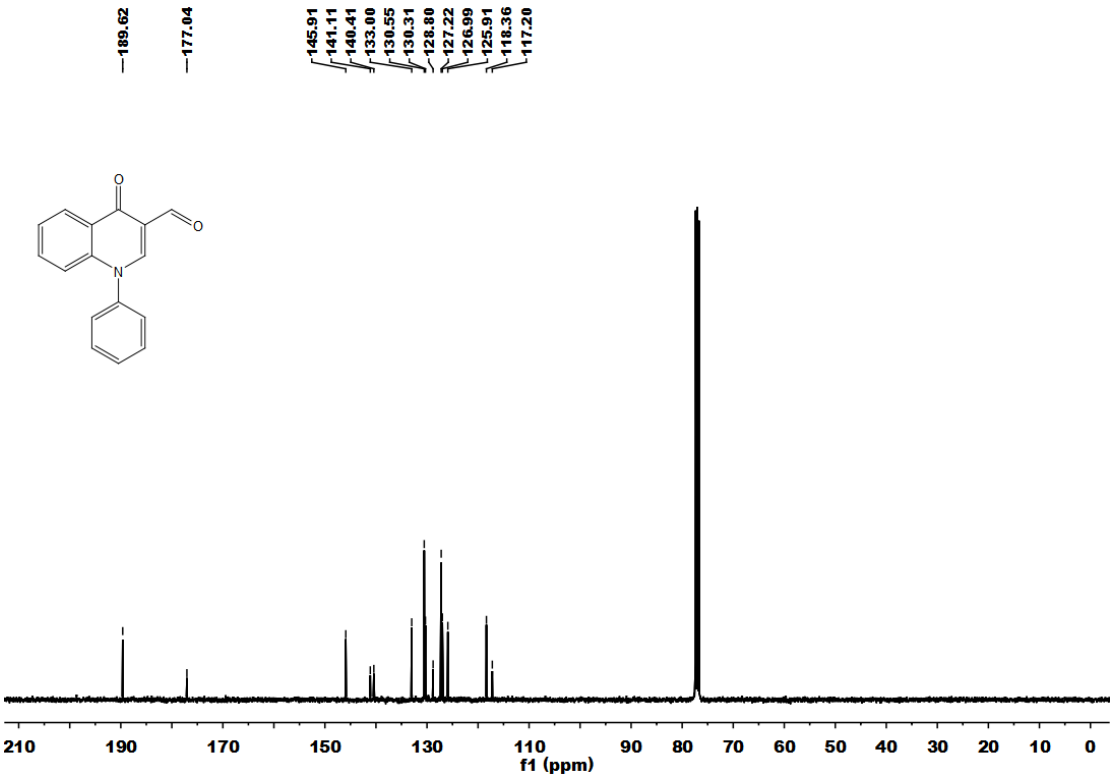
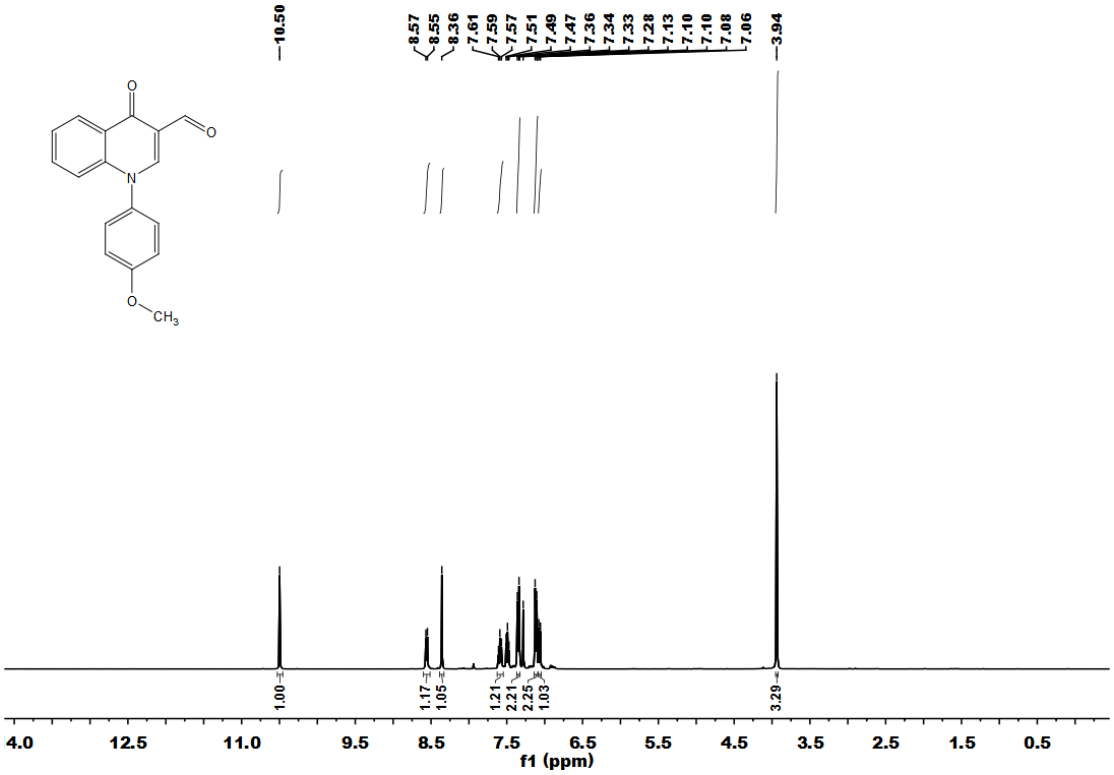


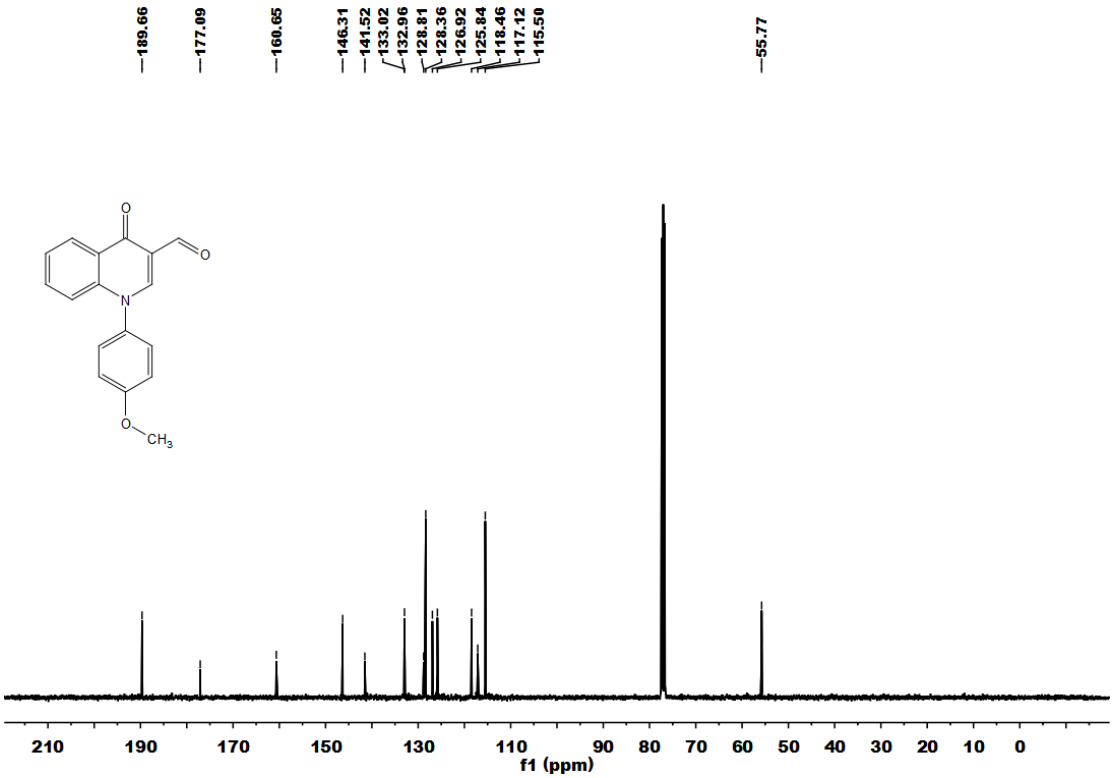
^{13}C NMR spectrum of **4f**



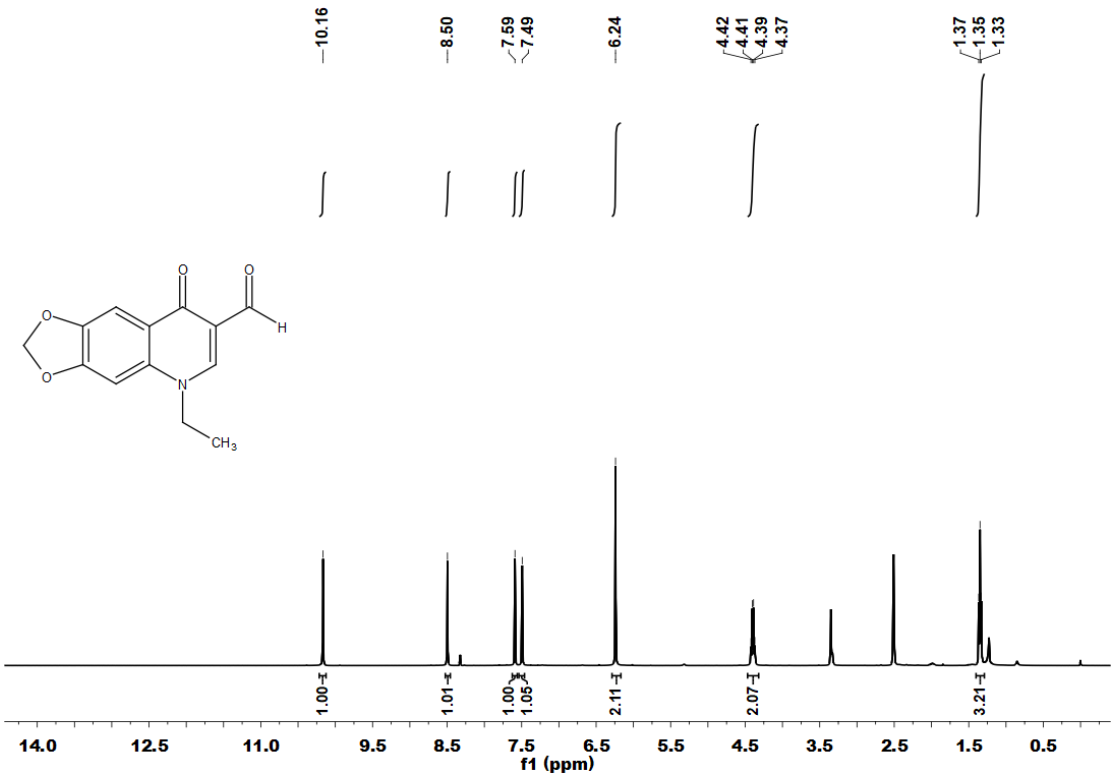
^{13}C NMR spectrum of **4f**



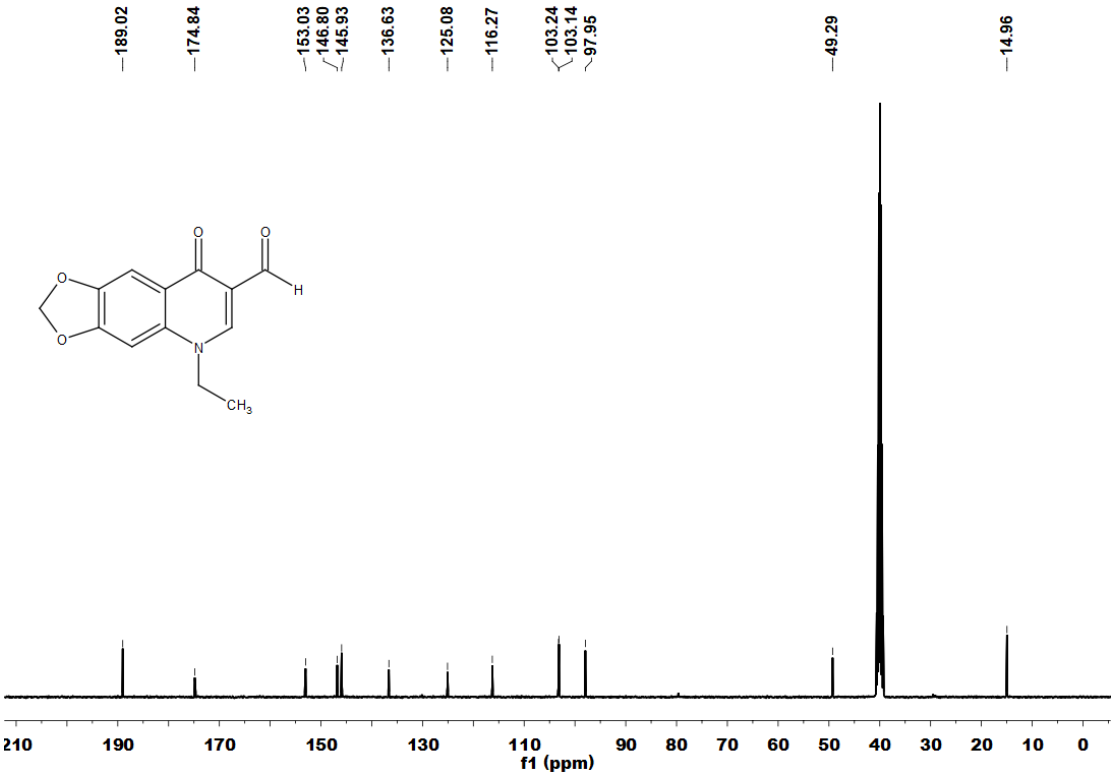
^{1}H NMR spectrum of **4g**



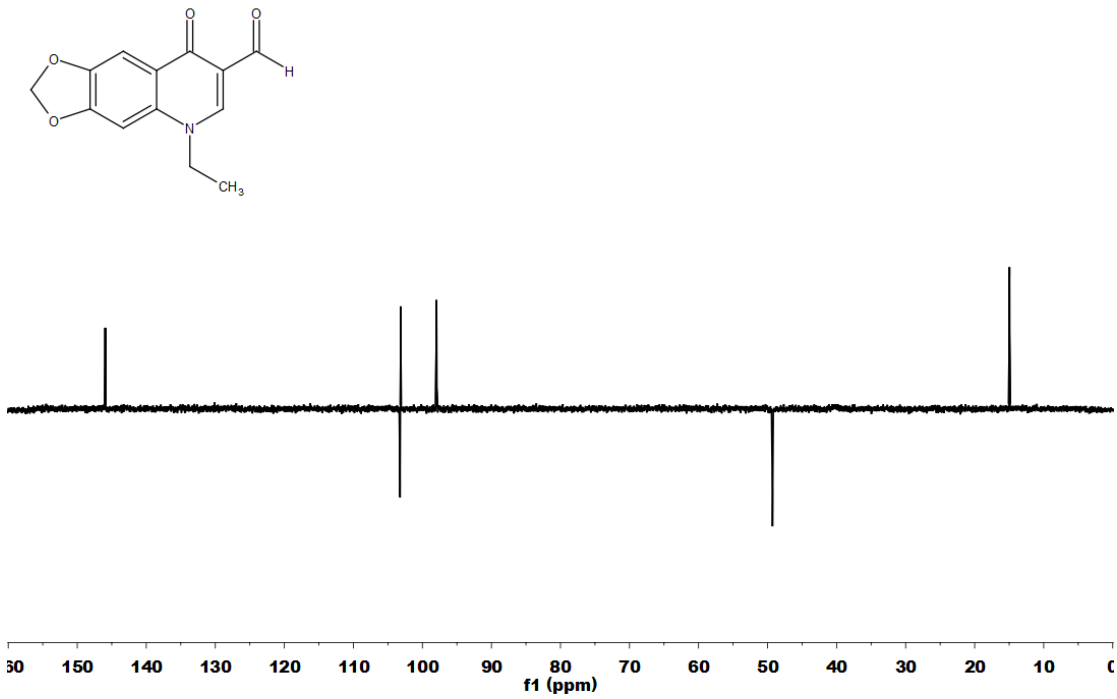
^{13}C NMR spectrum of **4g**



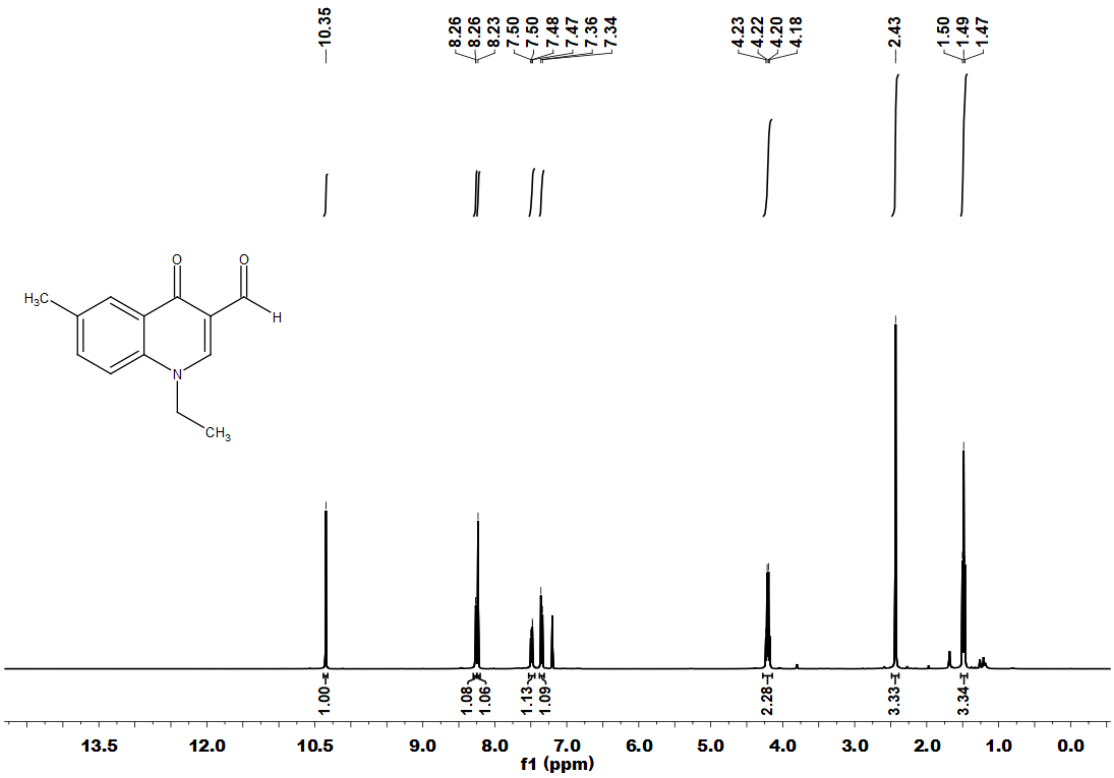
^{1}H NMR spectrum of **4h**



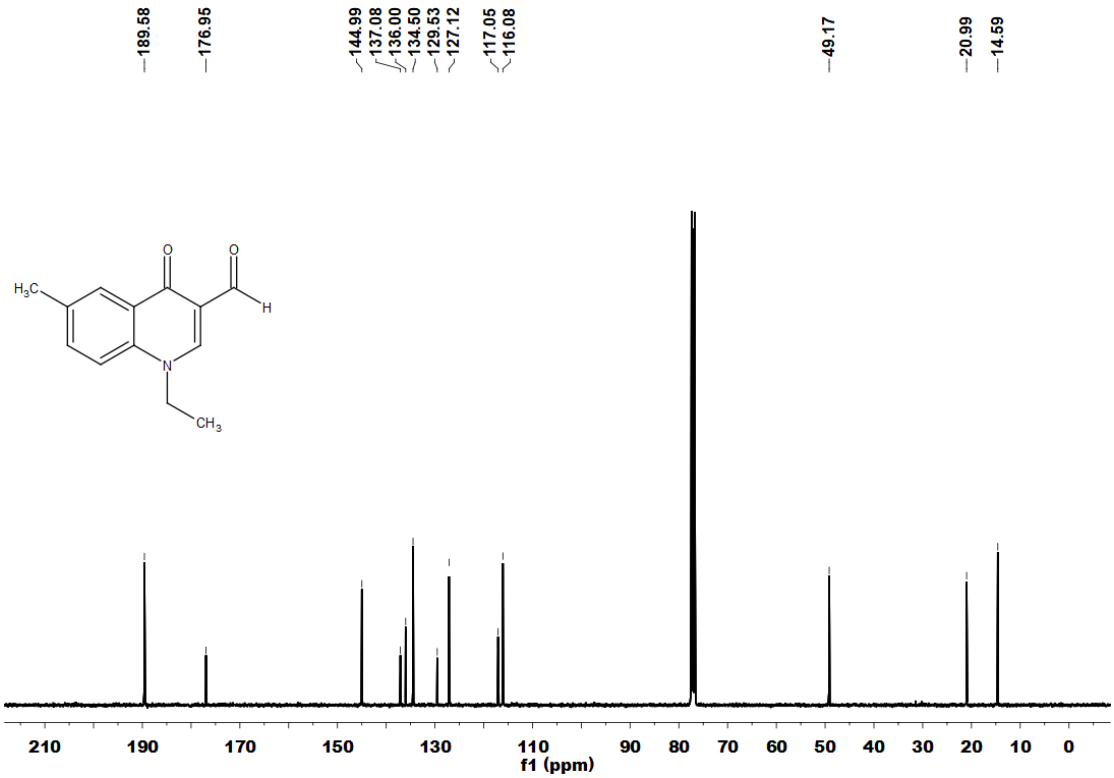
^{13}C NMR spectrum of **4h**



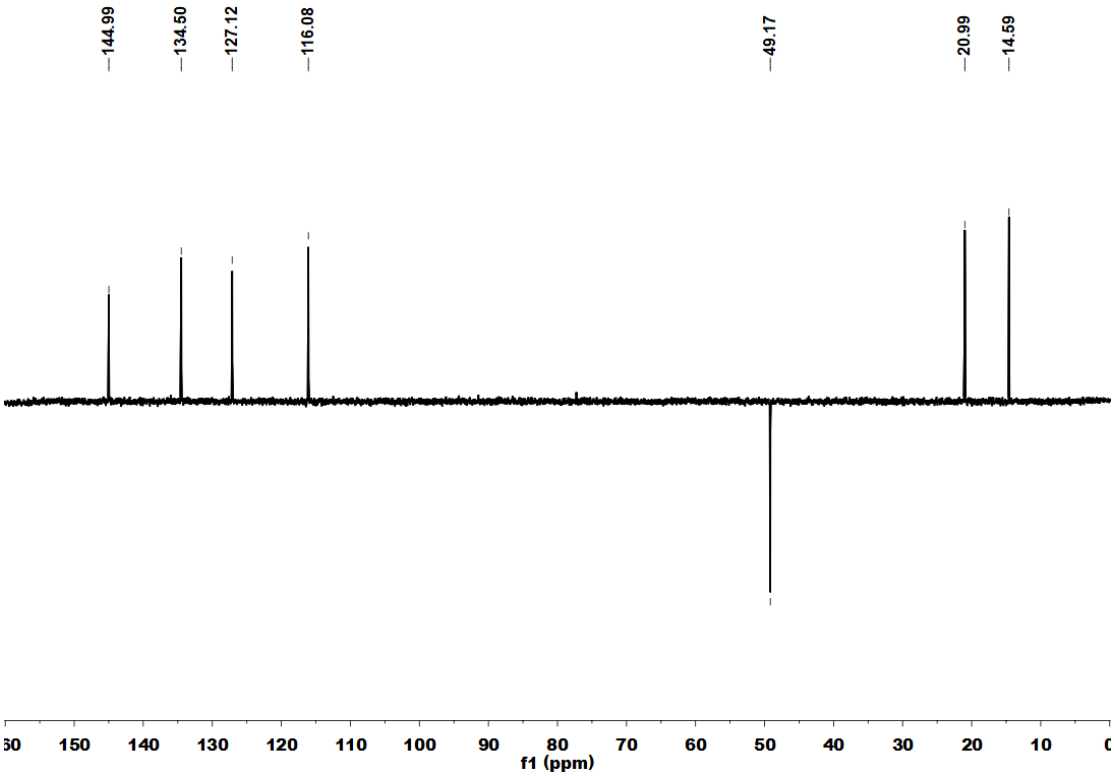
DEP 135^{o} spectrum of **4h**



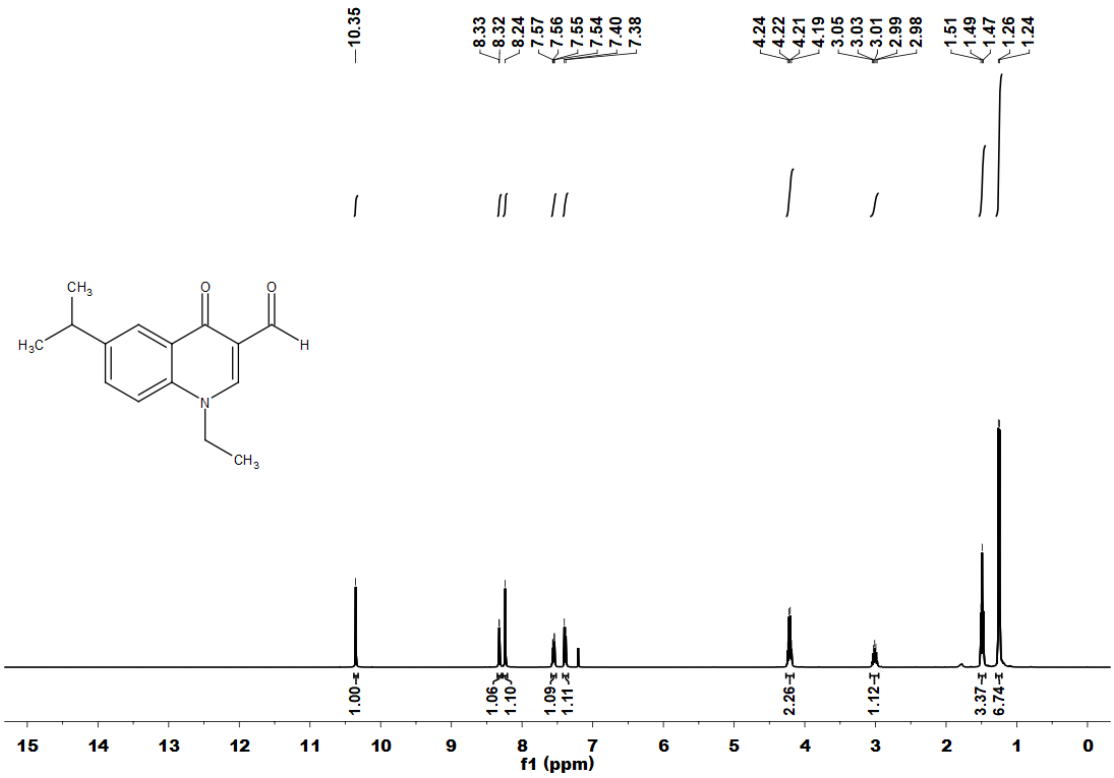
^{1}H NMR spectrum of **4i**



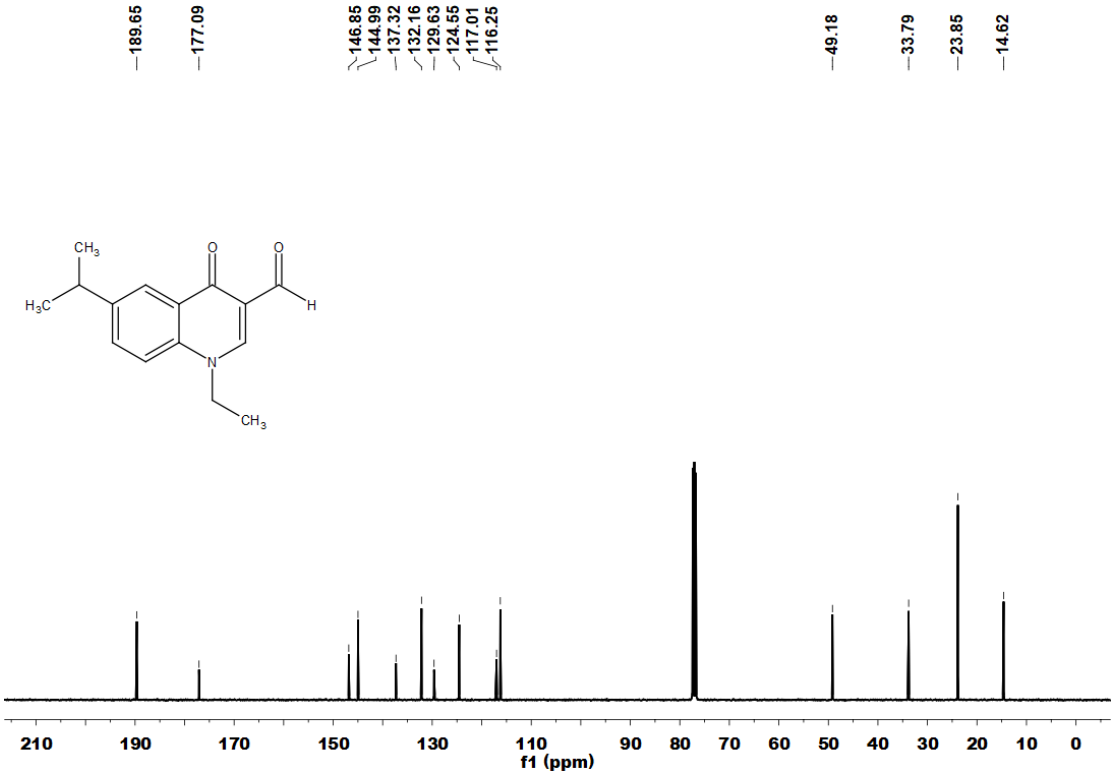
^{13}C NMR spectrum of **4i**



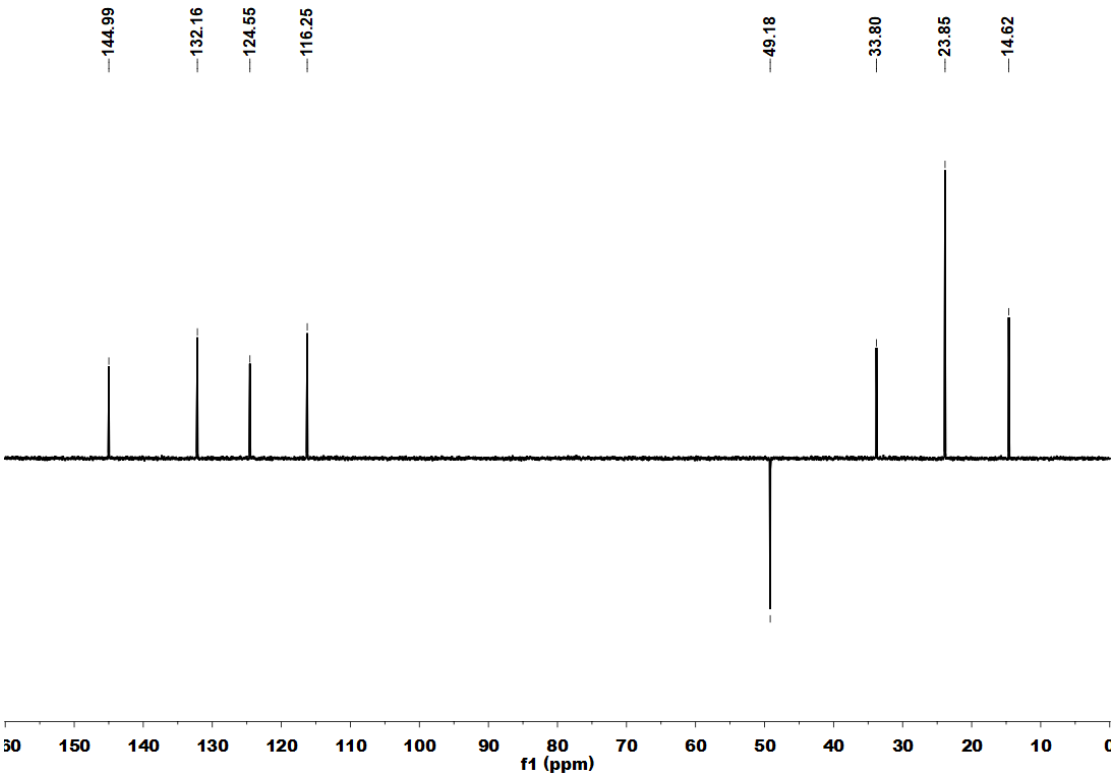
DEP135^{o} spectrum of **4i**



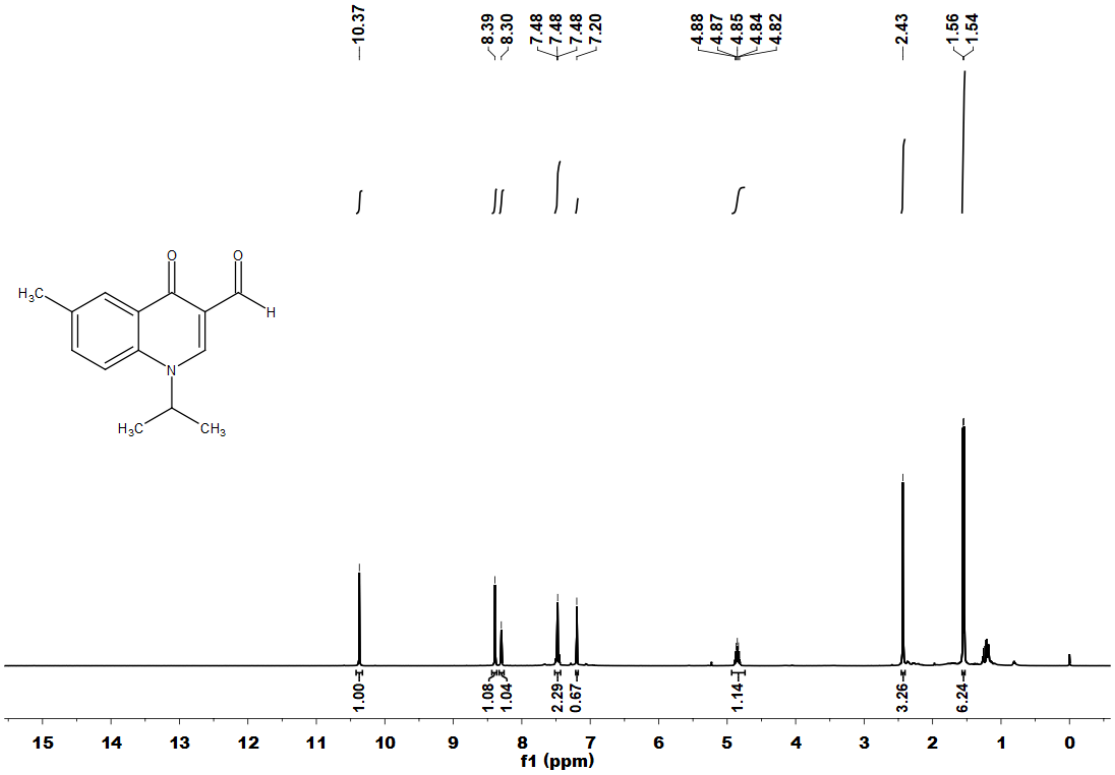
^{1}H NMR spectrum of **4j**



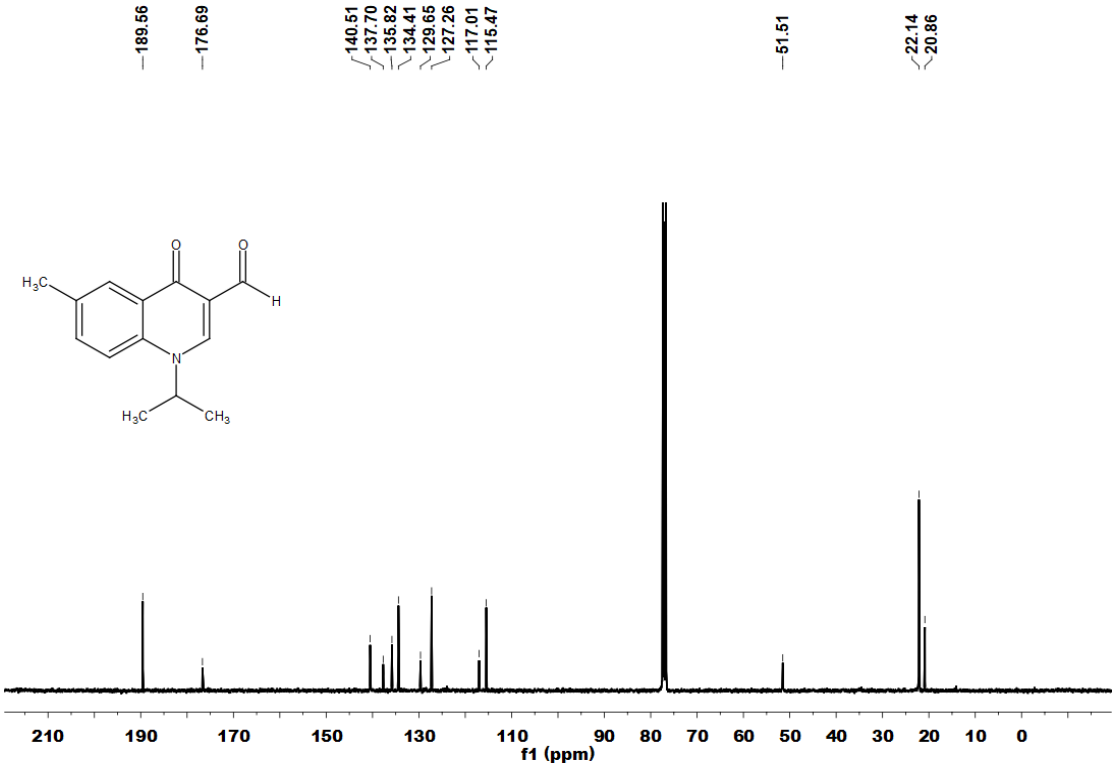
^{13}C NMR spectrum of **4j**



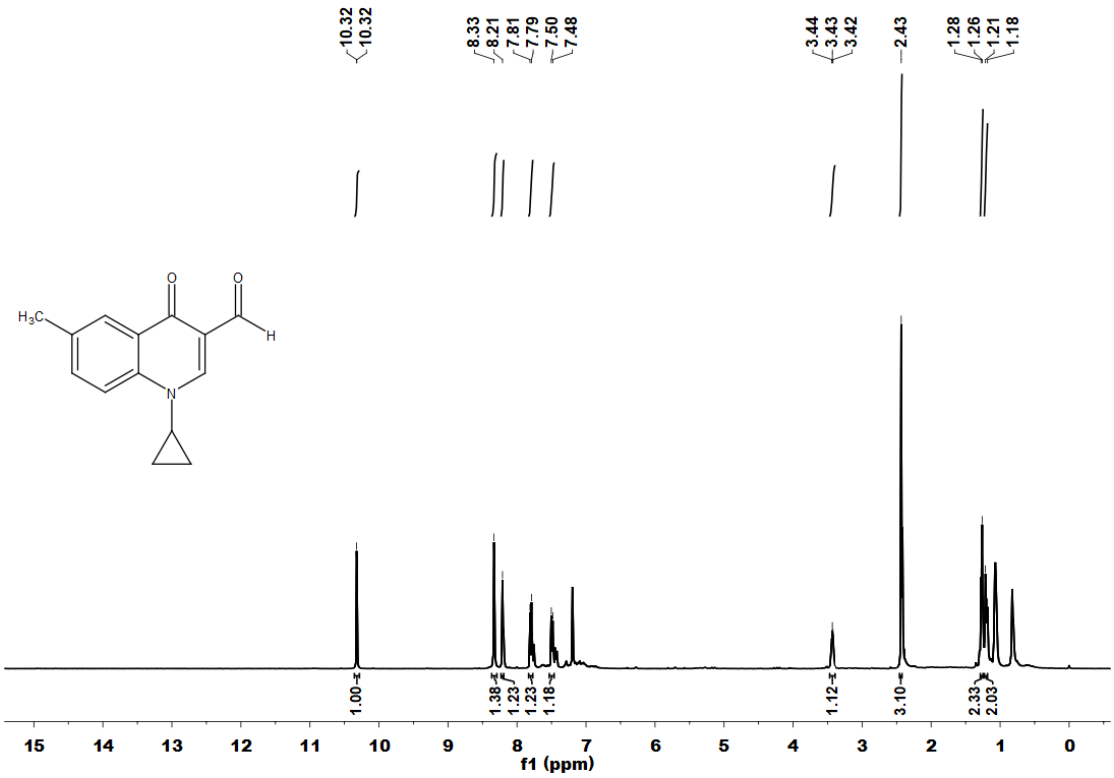
DEP 135^{o} spectrum of **4j**



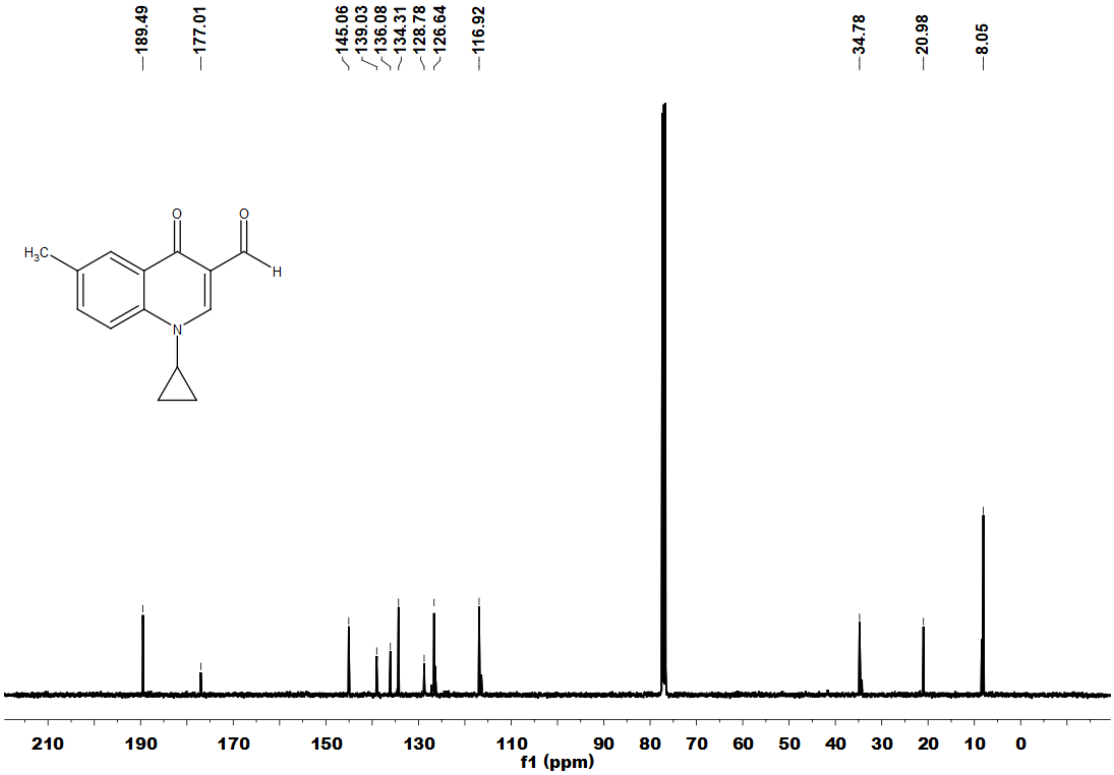
^{1}H NMR spectrum of **4k**



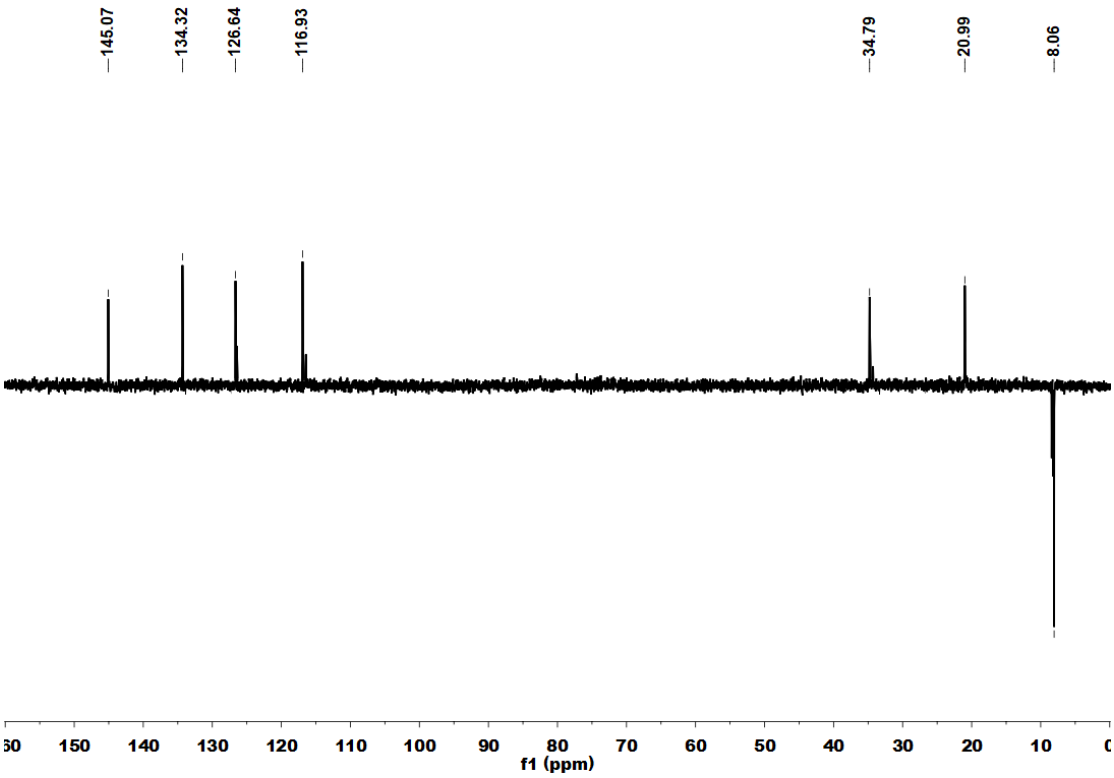
^{13}C NMR spectrum of **4k**



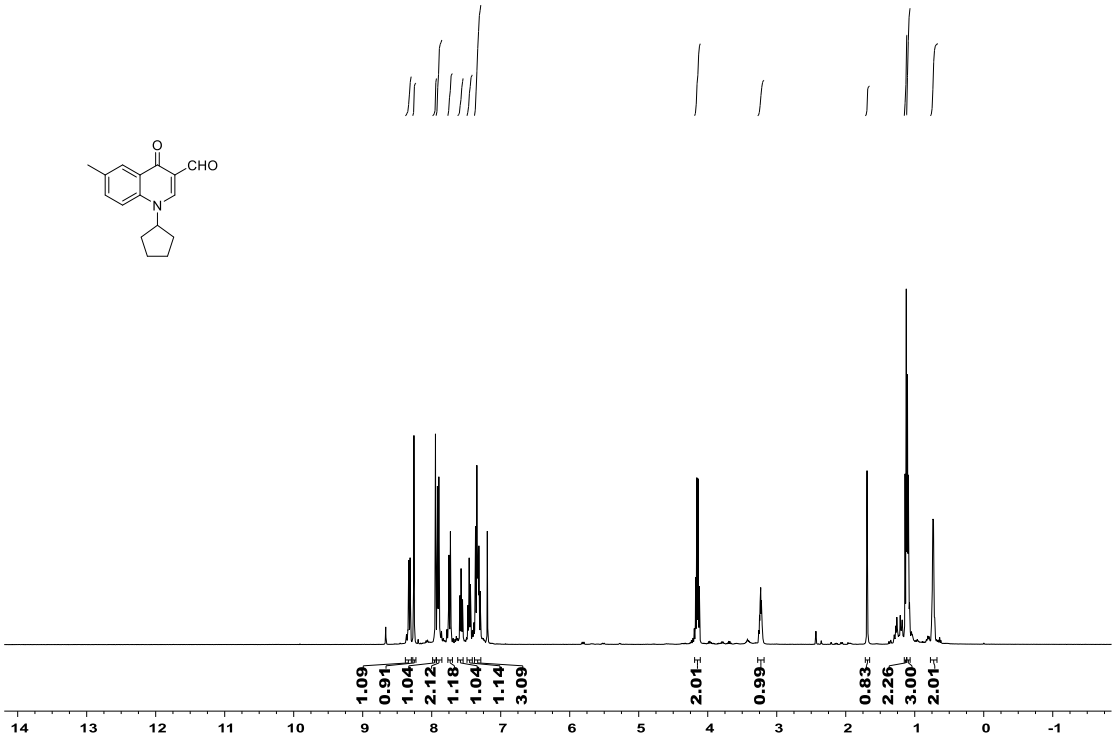
^{1}H NMR spectrum of **4l**



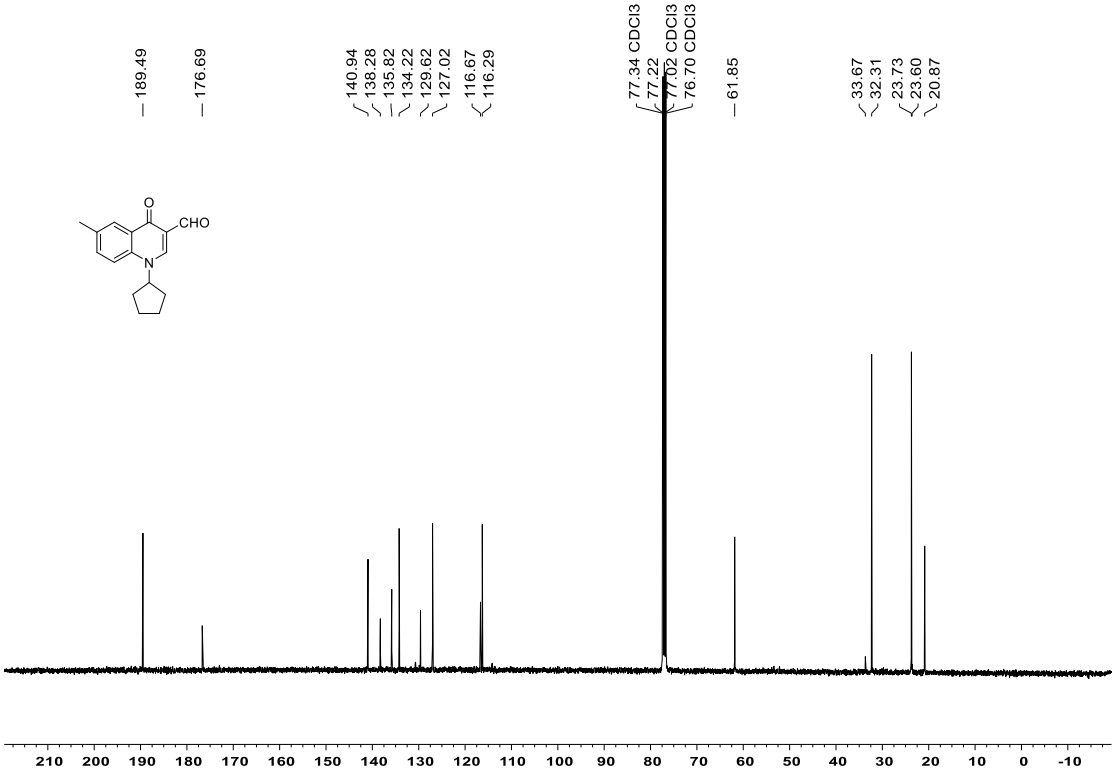
^{13}C NMR spectrum of **4l**



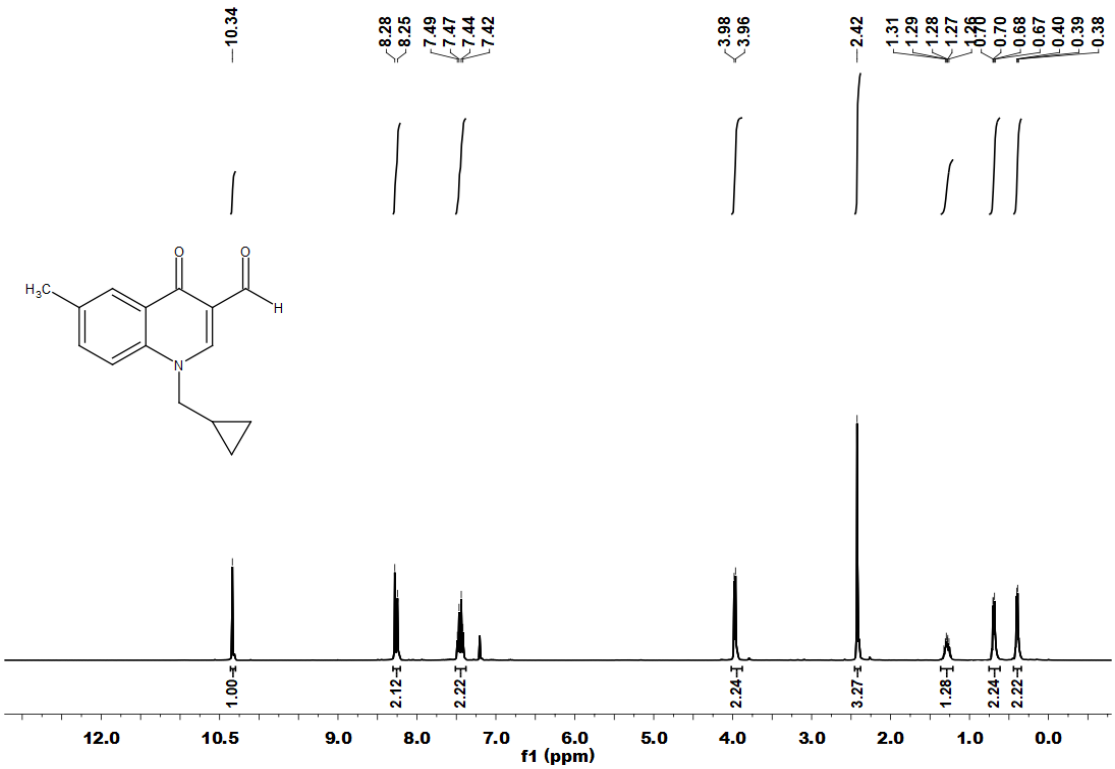
DEP 135^{o} spectrum of **4l**



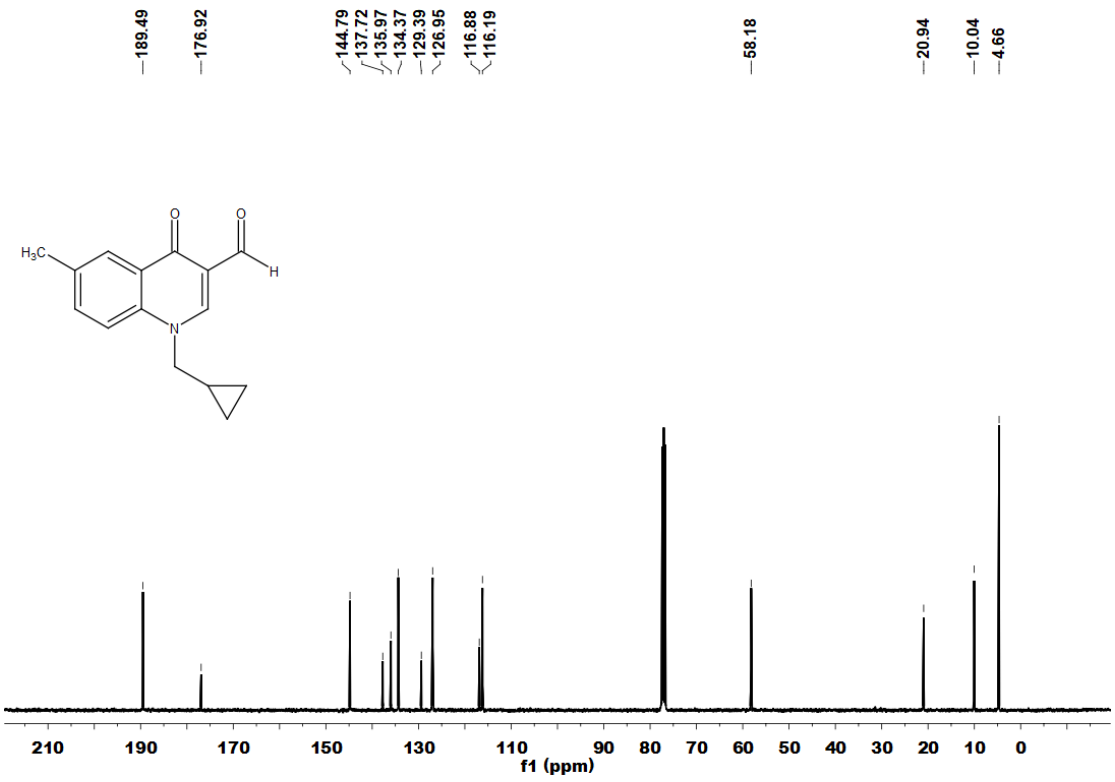
^{1}H NMR spectrum of **4m**



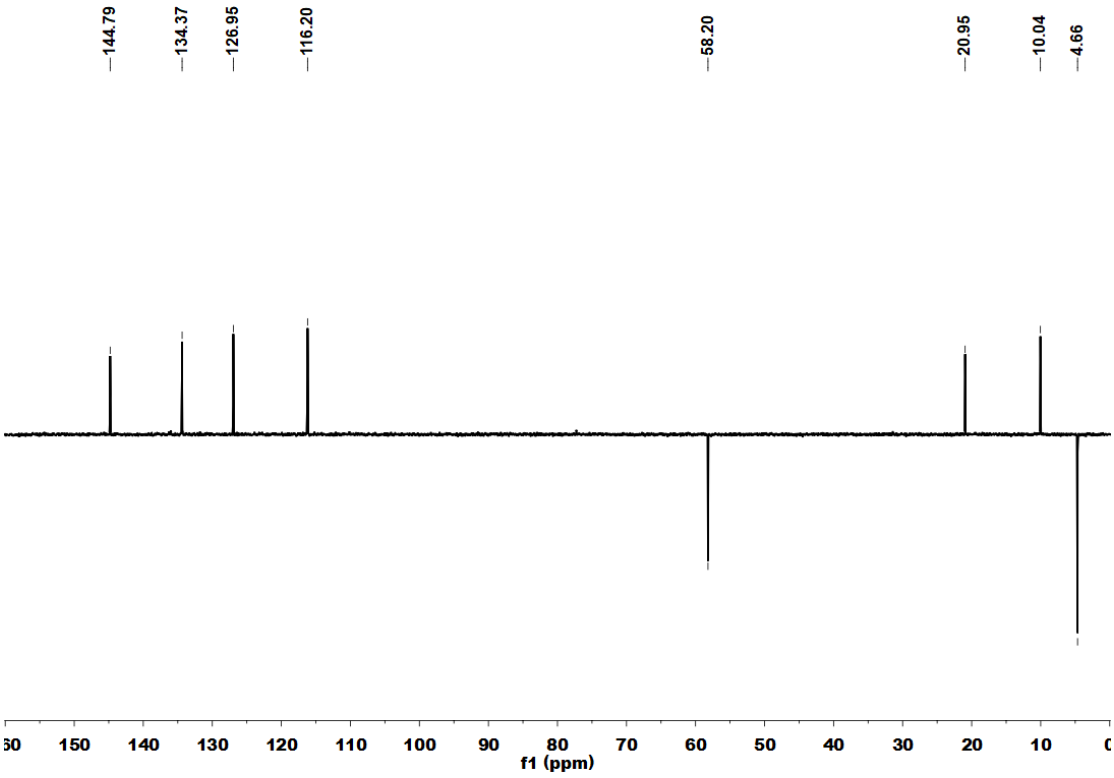
^{13}C NMR spectrum of **4m**



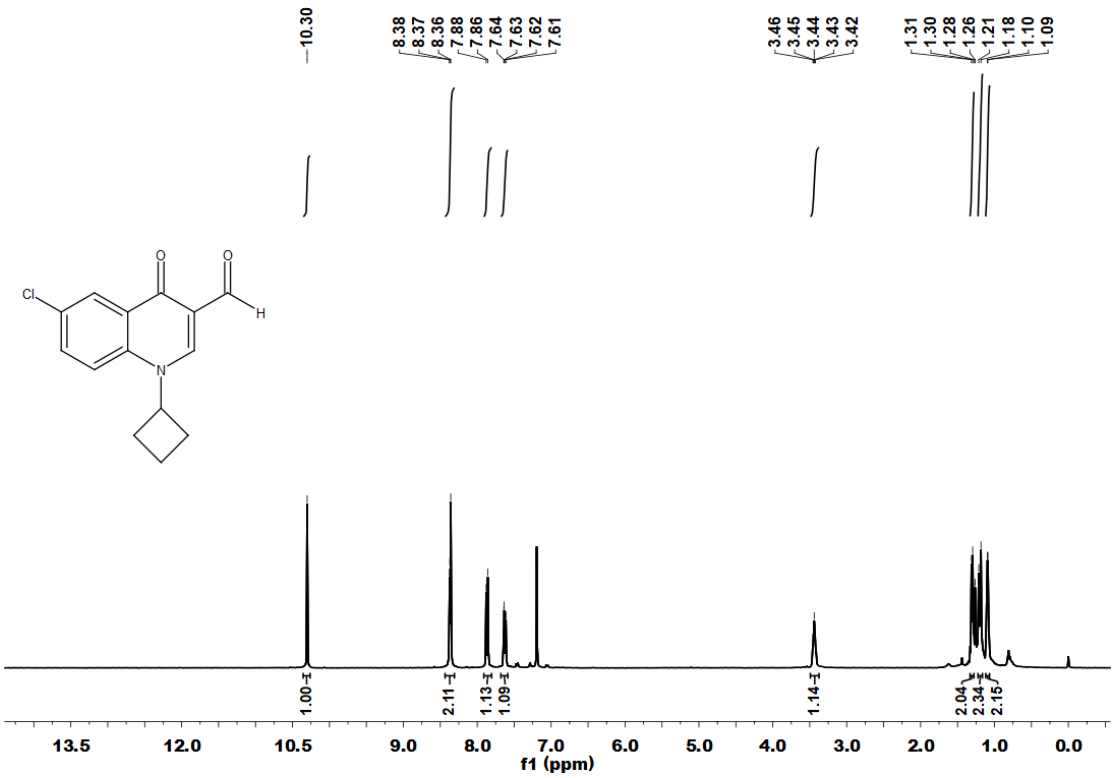
^{1}H NMR spectrum of **4n**



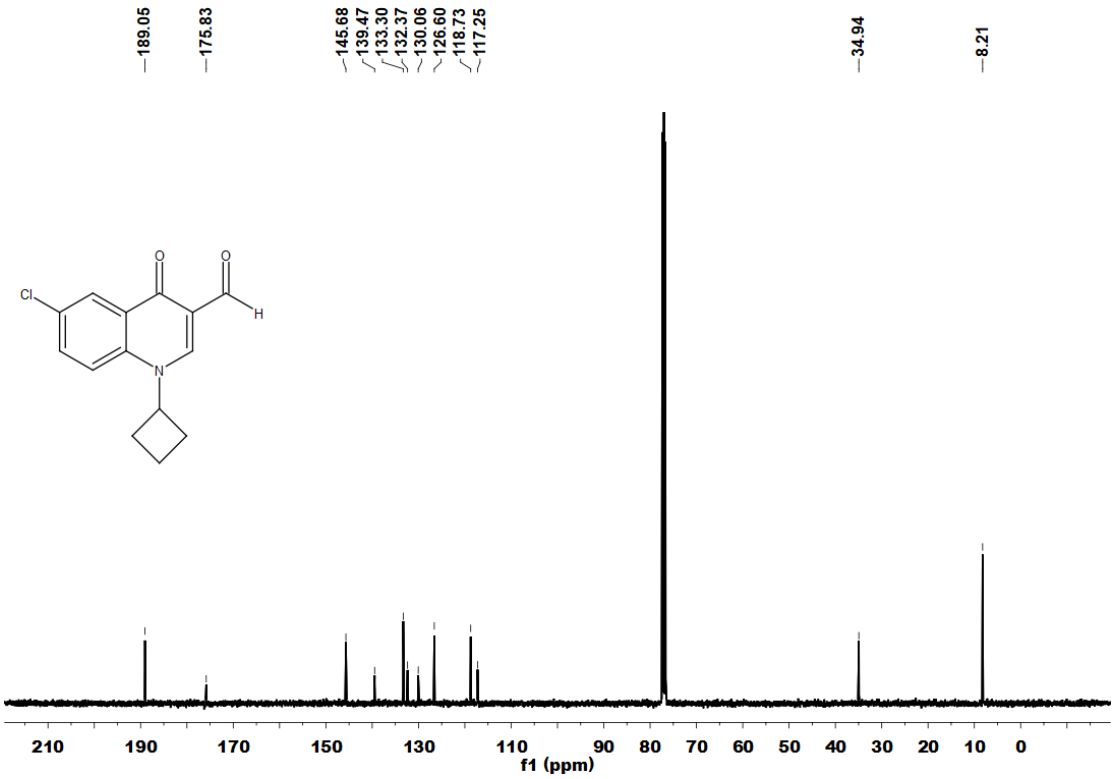
^{13}C NMR spectrum of **4n**



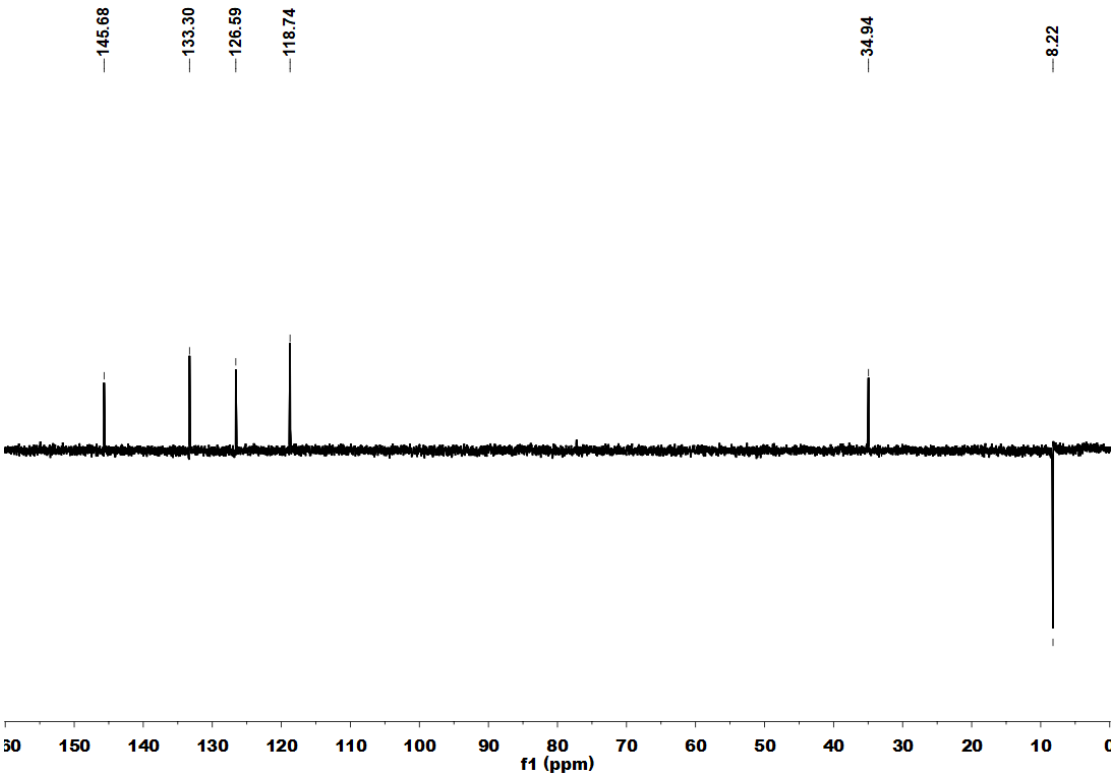
DEP 135^{o} spectrum of **4n**



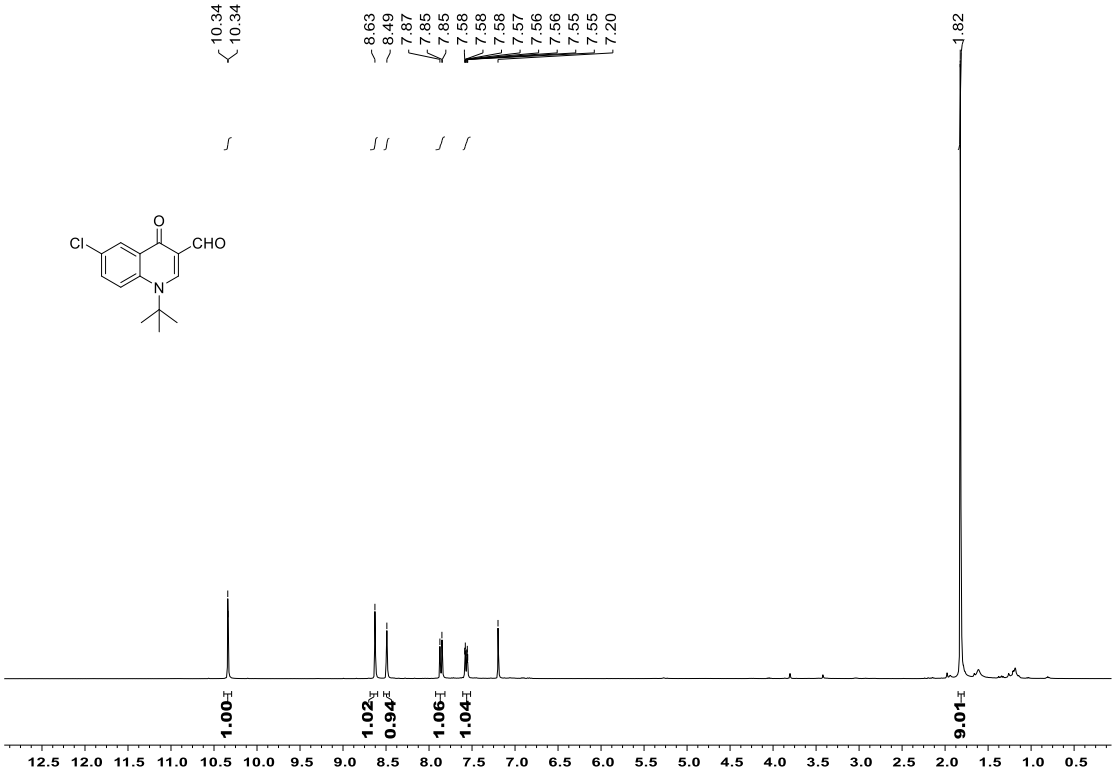
^{1}H NMR spectrum of **4o**



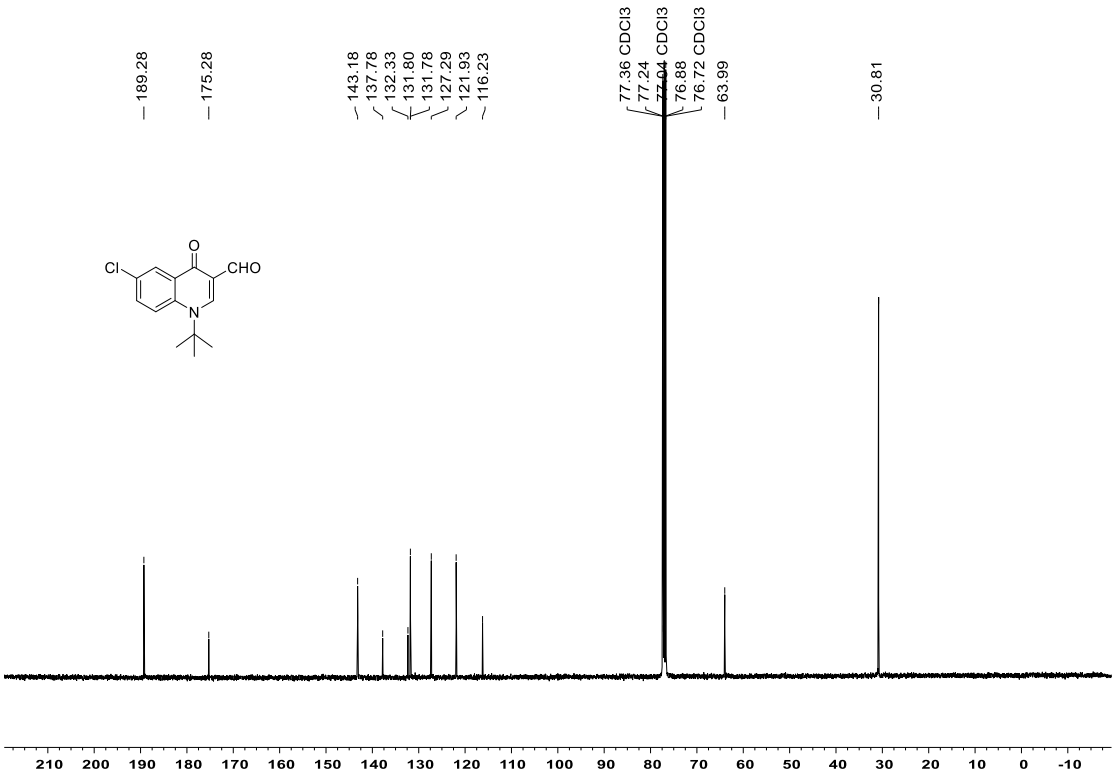
^{13}C NMR spectrum of **4o**



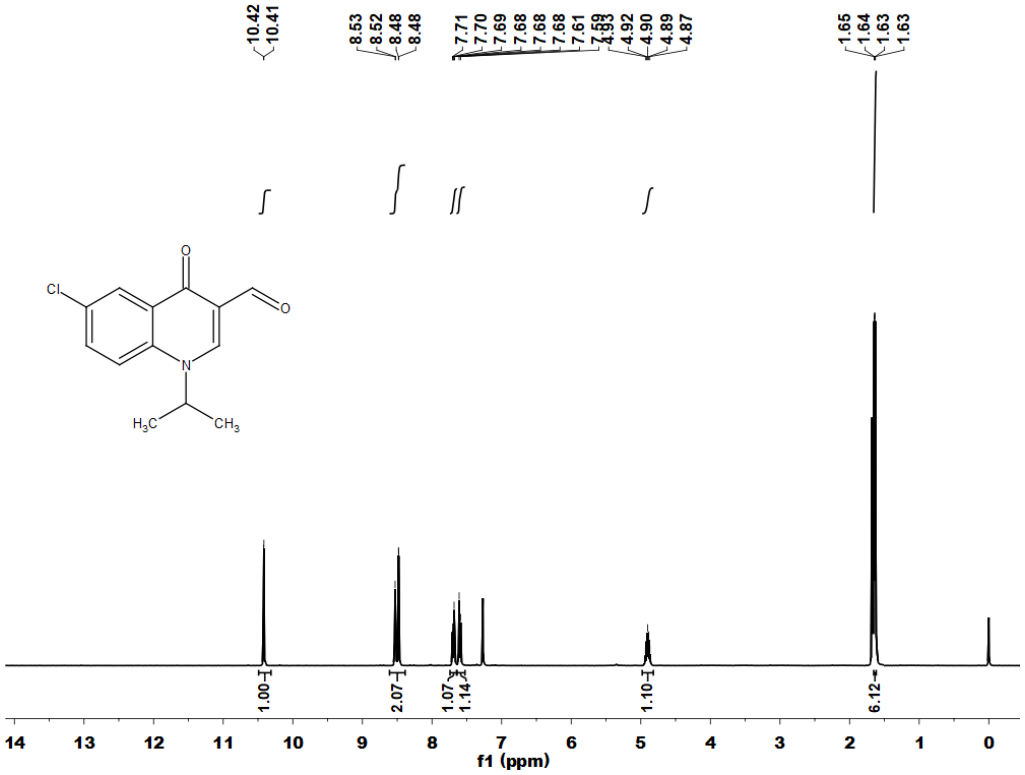
DEP 135^{o} spectrum of **4o**



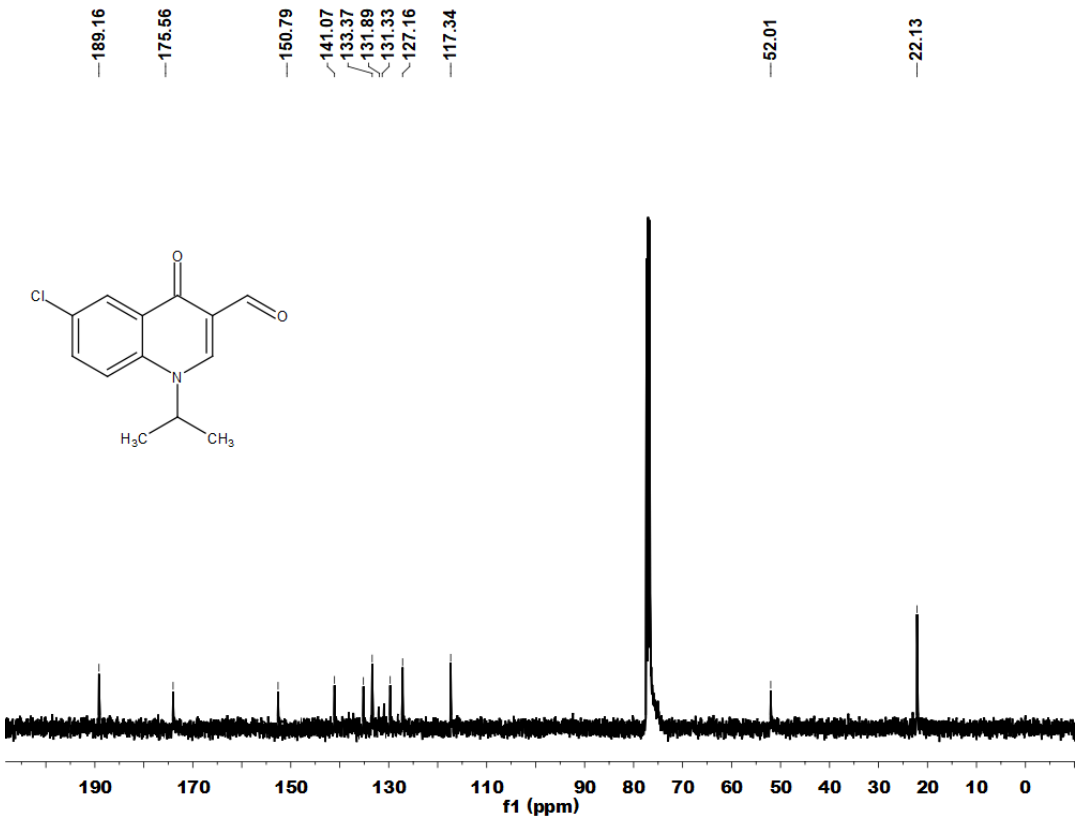
^{1}H NMR spectrum of **4p**



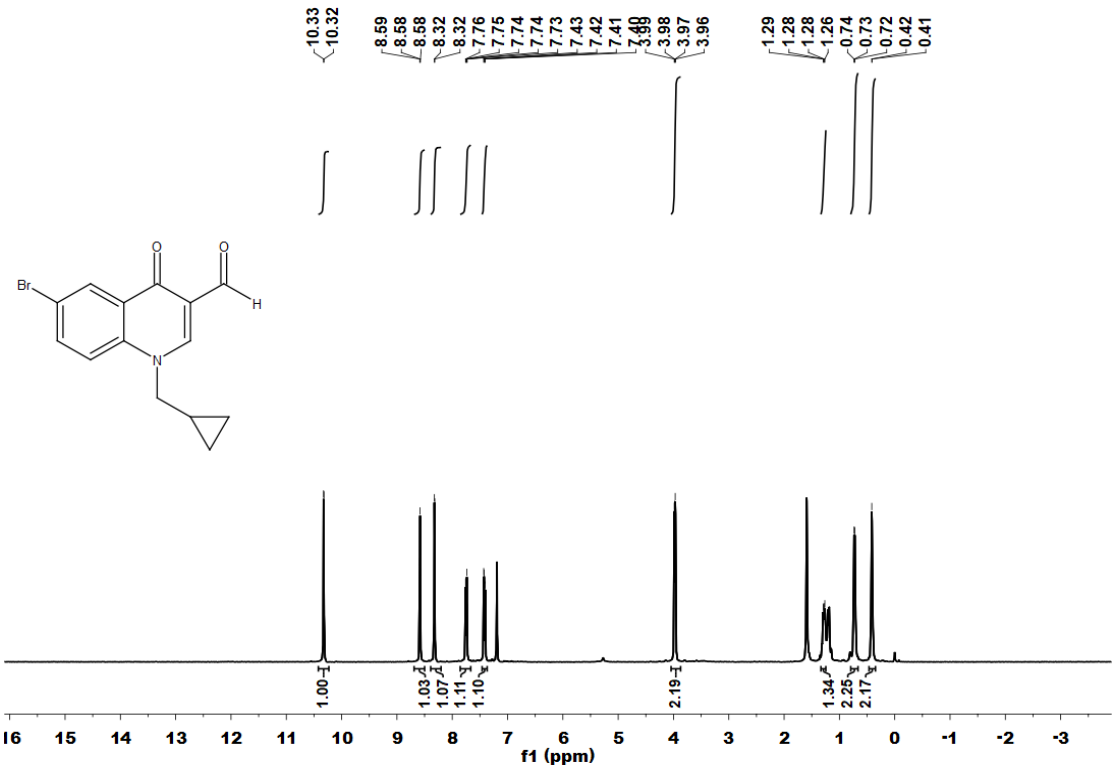
^{13}C NMR spectrum of **4p**



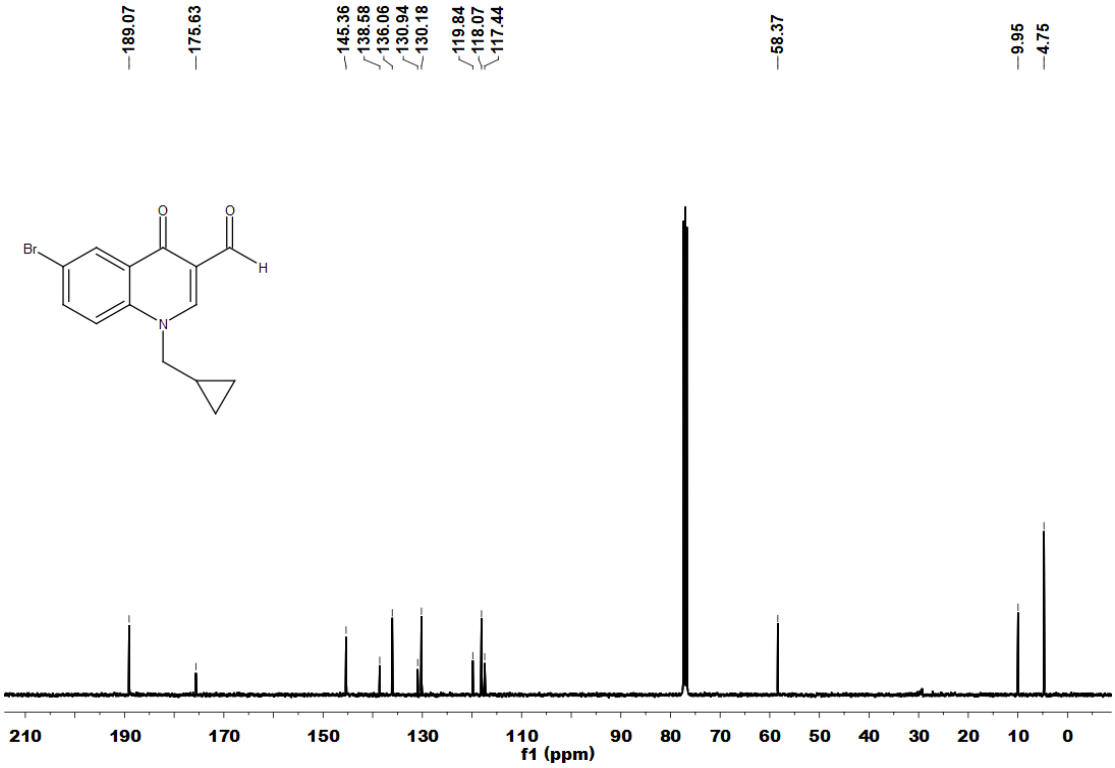
^{1}H NMR spectrum of **4q**



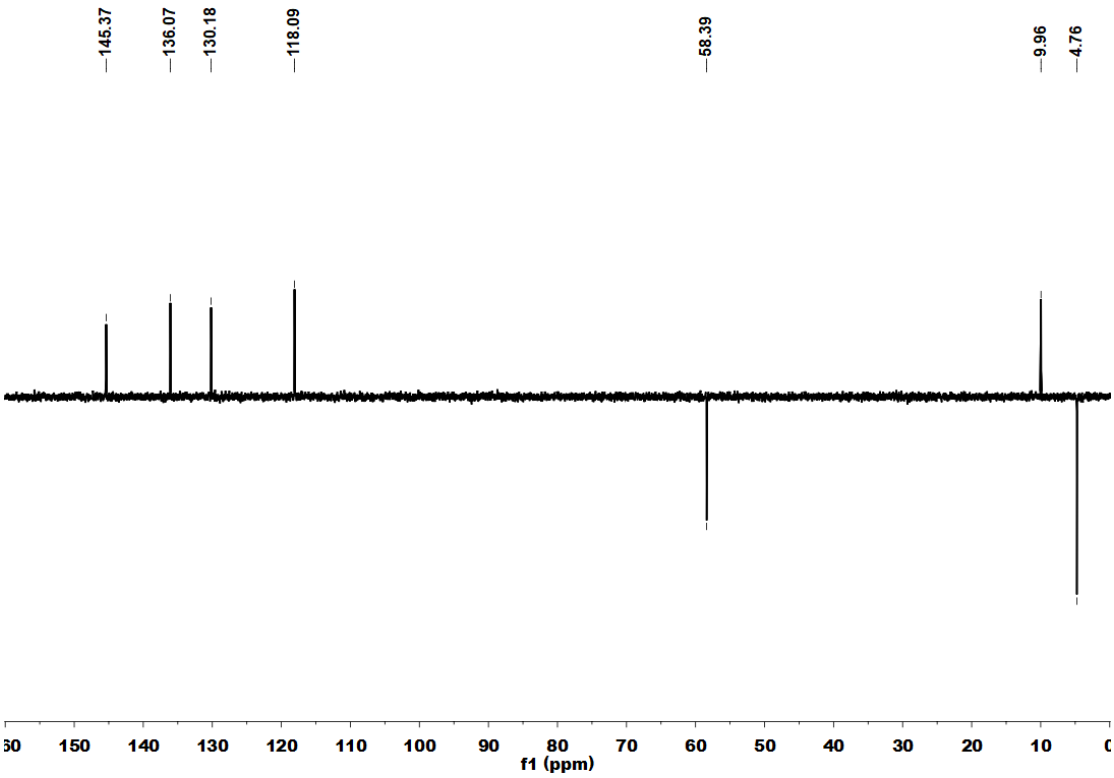
^{13}C NMR spectrum of **4q**



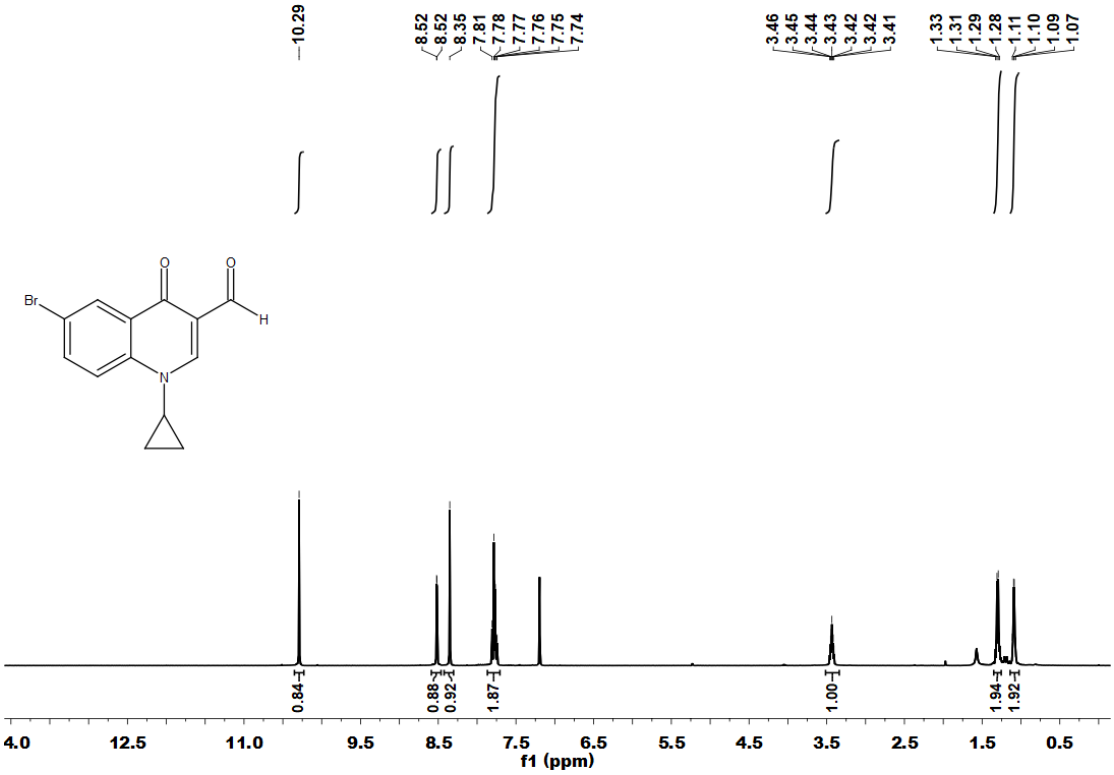
^{1}H NMR spectrum of **4r**



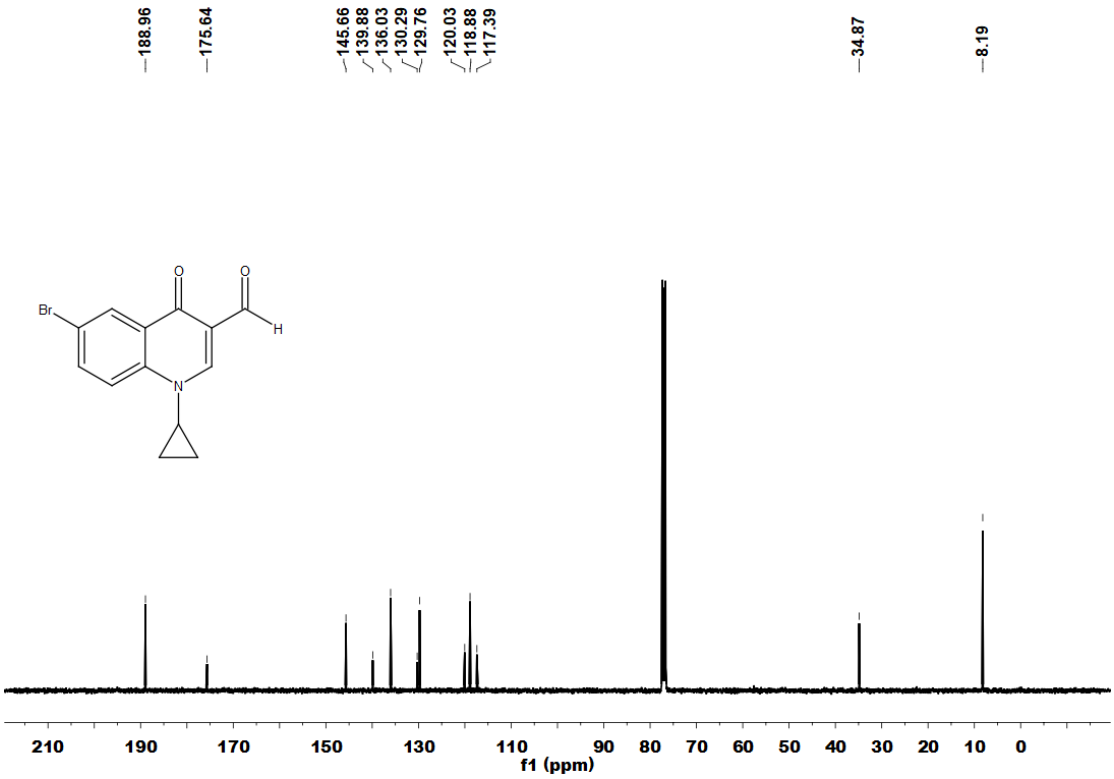
^{13}C NMR spectrum of **4r**



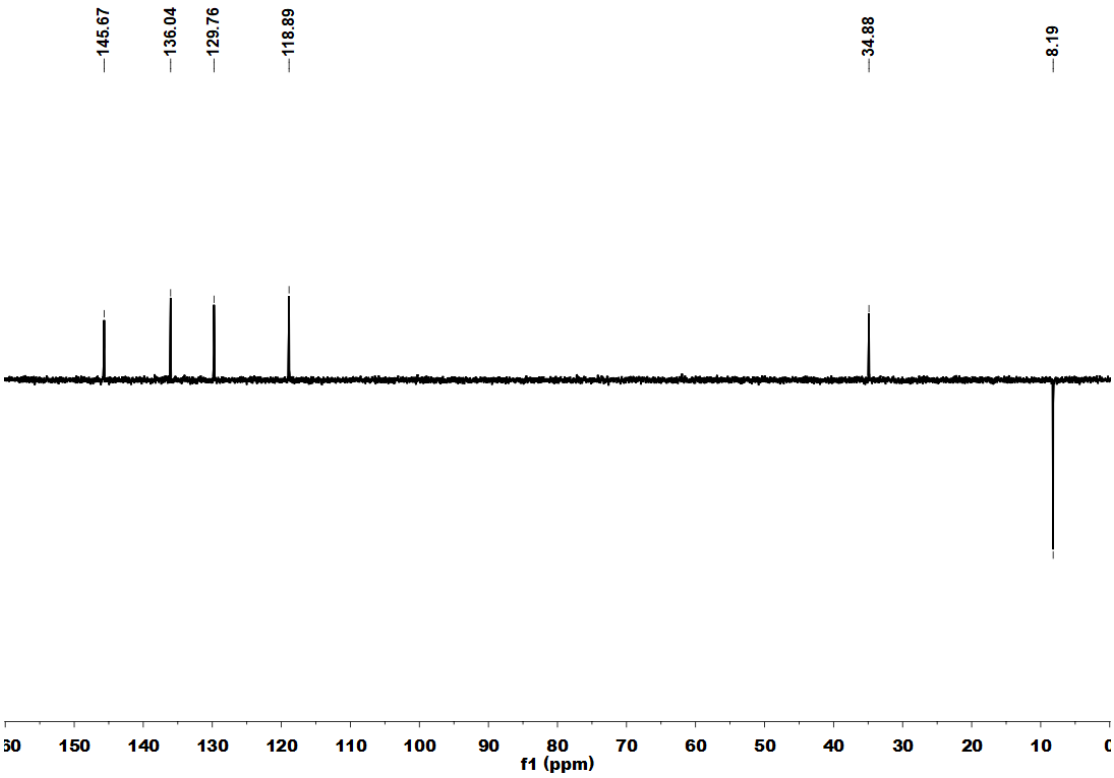
DEP 135^{o} spectrum of **4r**



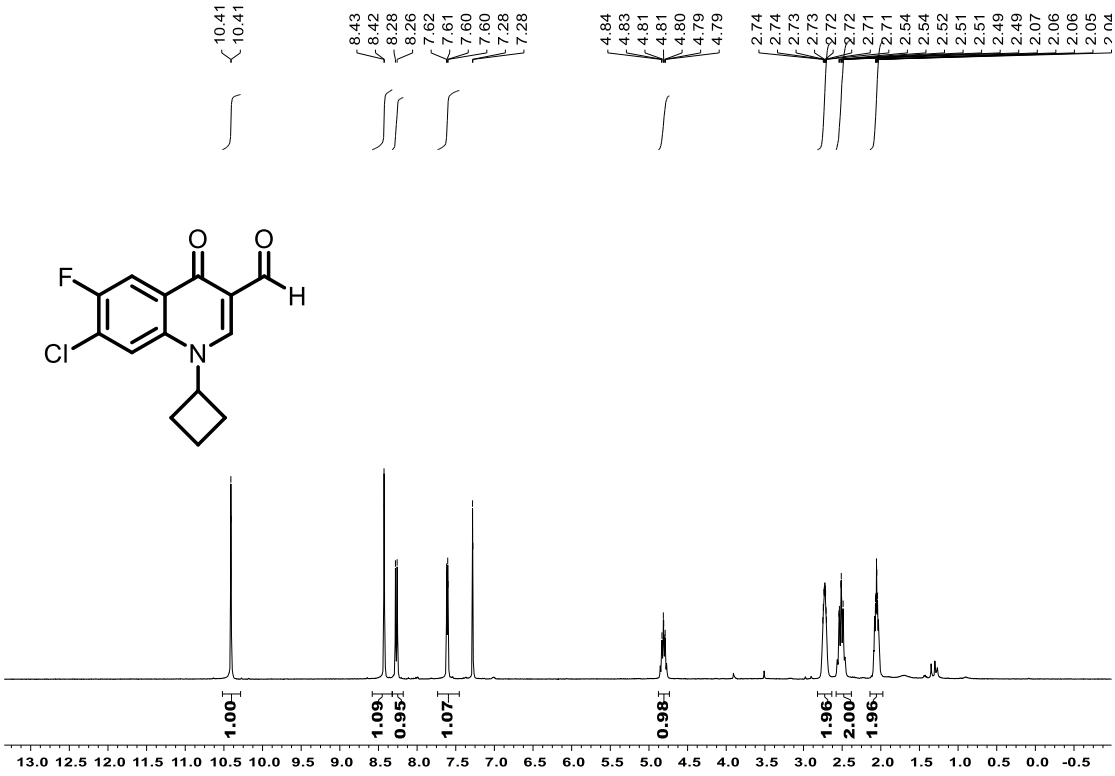
^{1}H NMR spectrum of **4s**



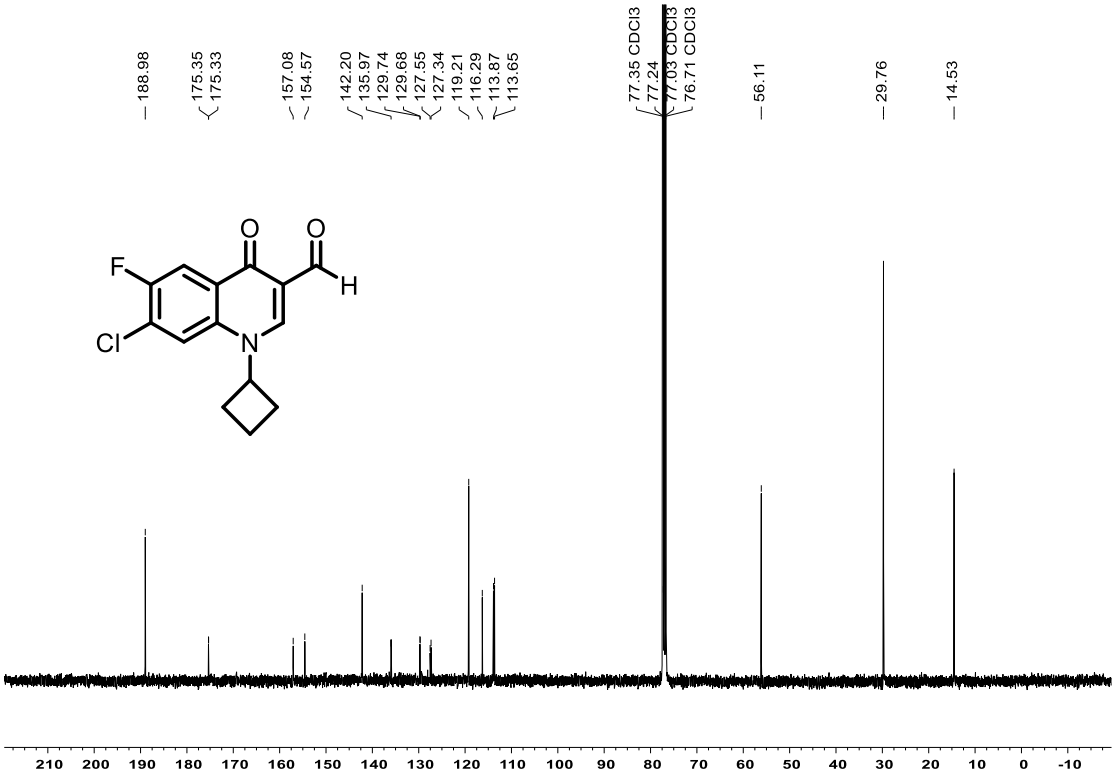
^{13}C NMR spectrum of **4s**



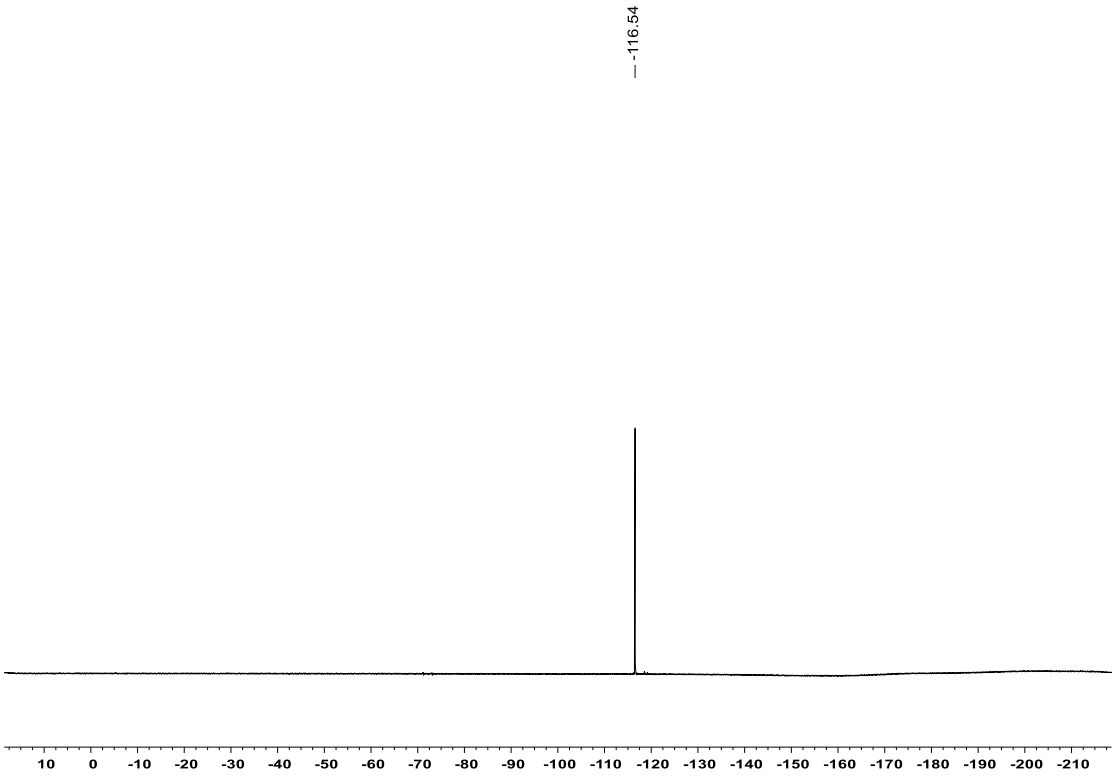
DEP 135^{o} spectrum of **4s**



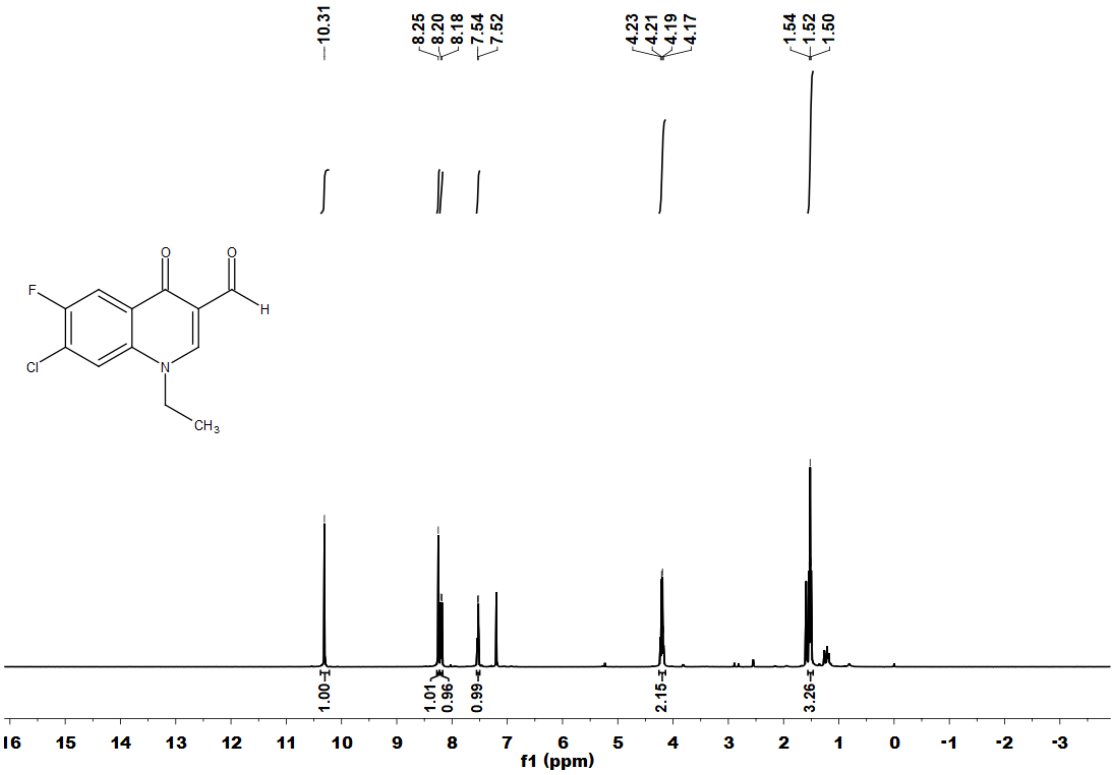
^{1}H NMR spectrum of **4aa**



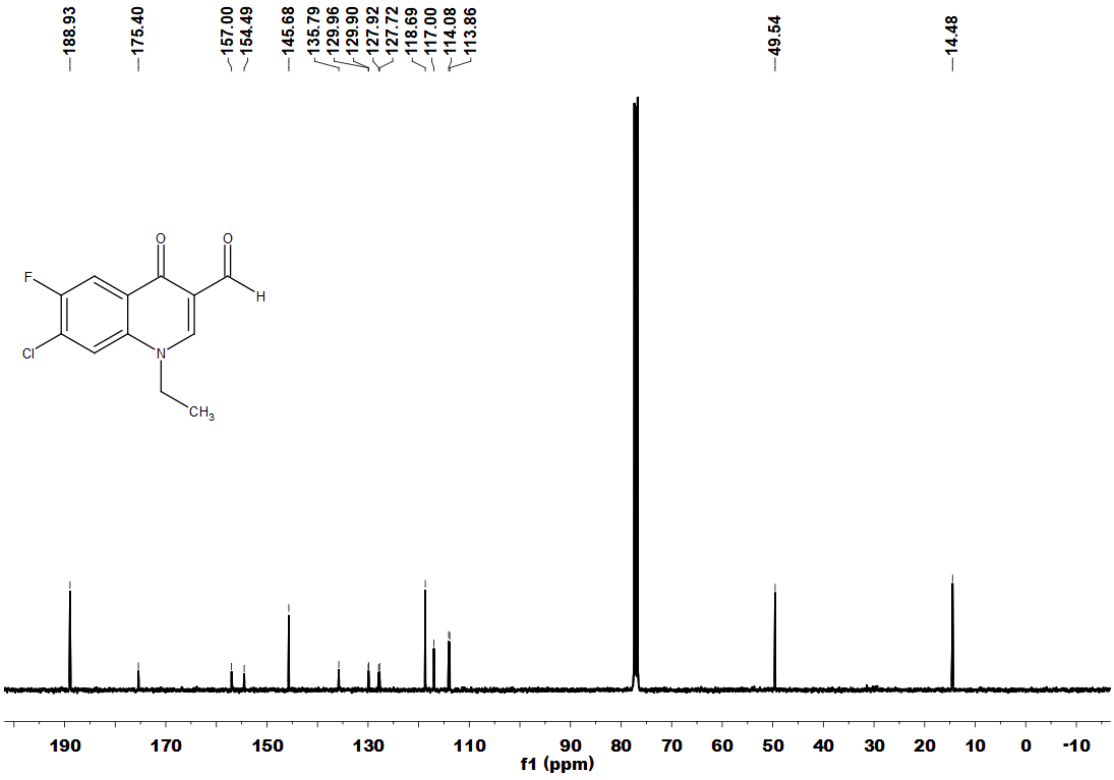
^{13}C NMR spectrum of **4aa**



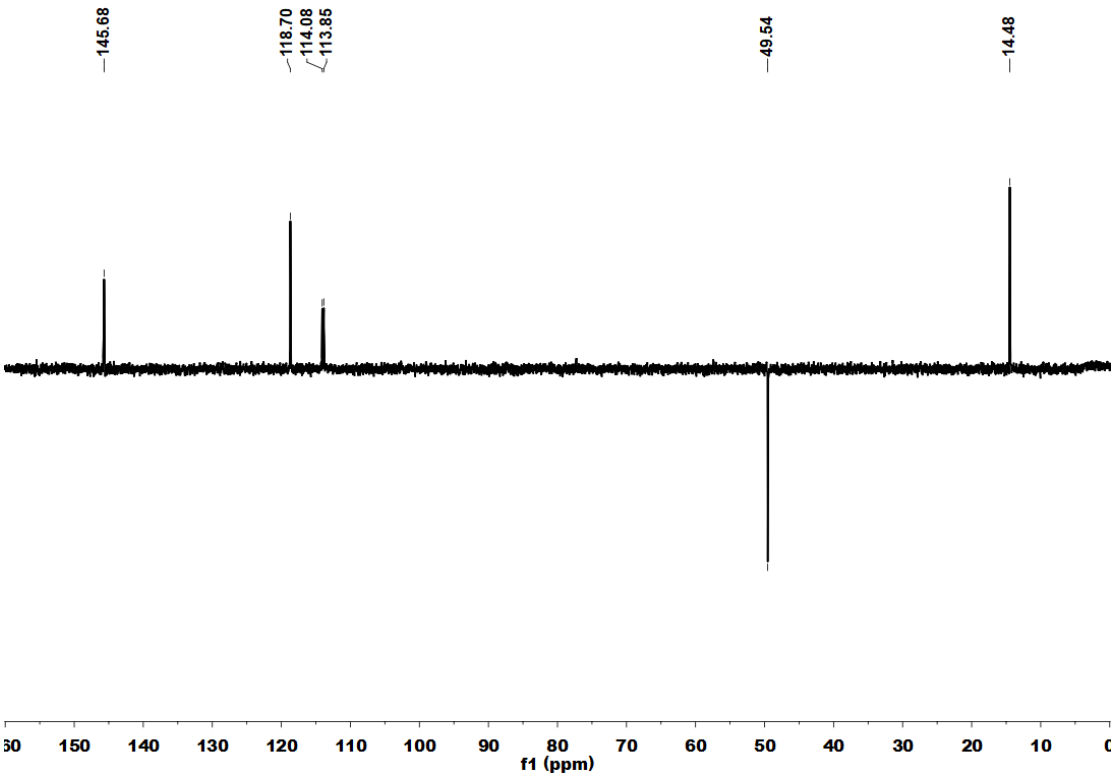
^{19}F NMR spectrum of **4aa**



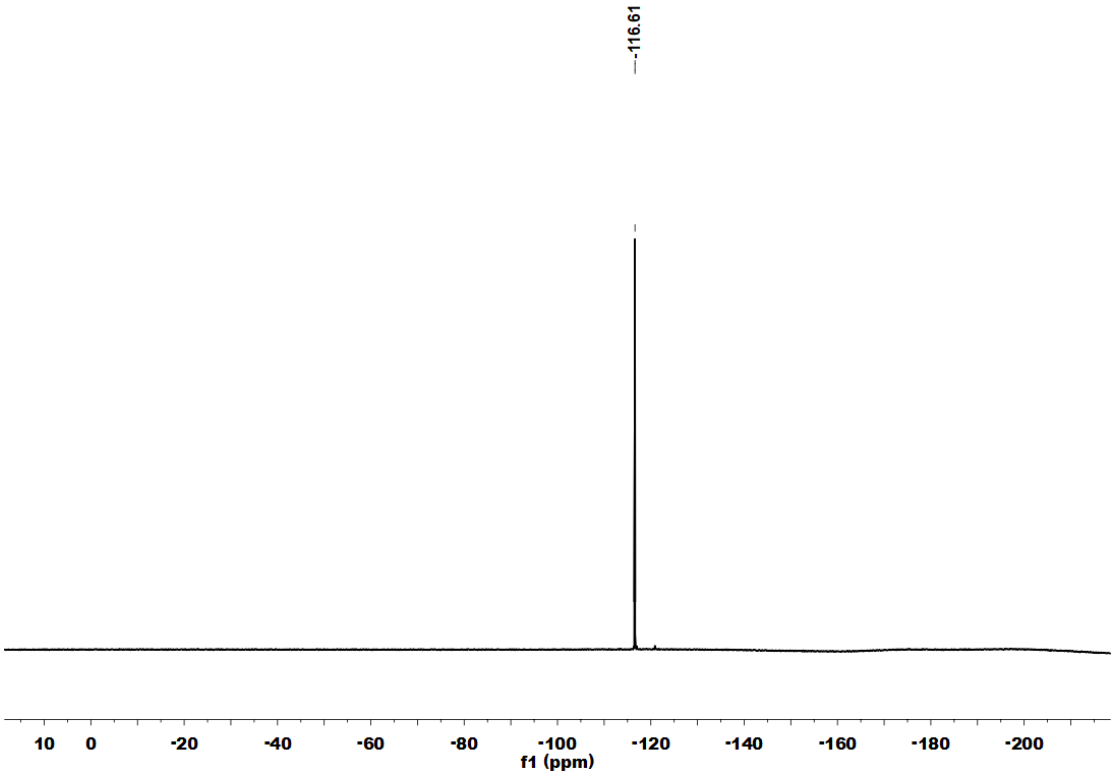
^{1}H NMR spectrum of **4ab**



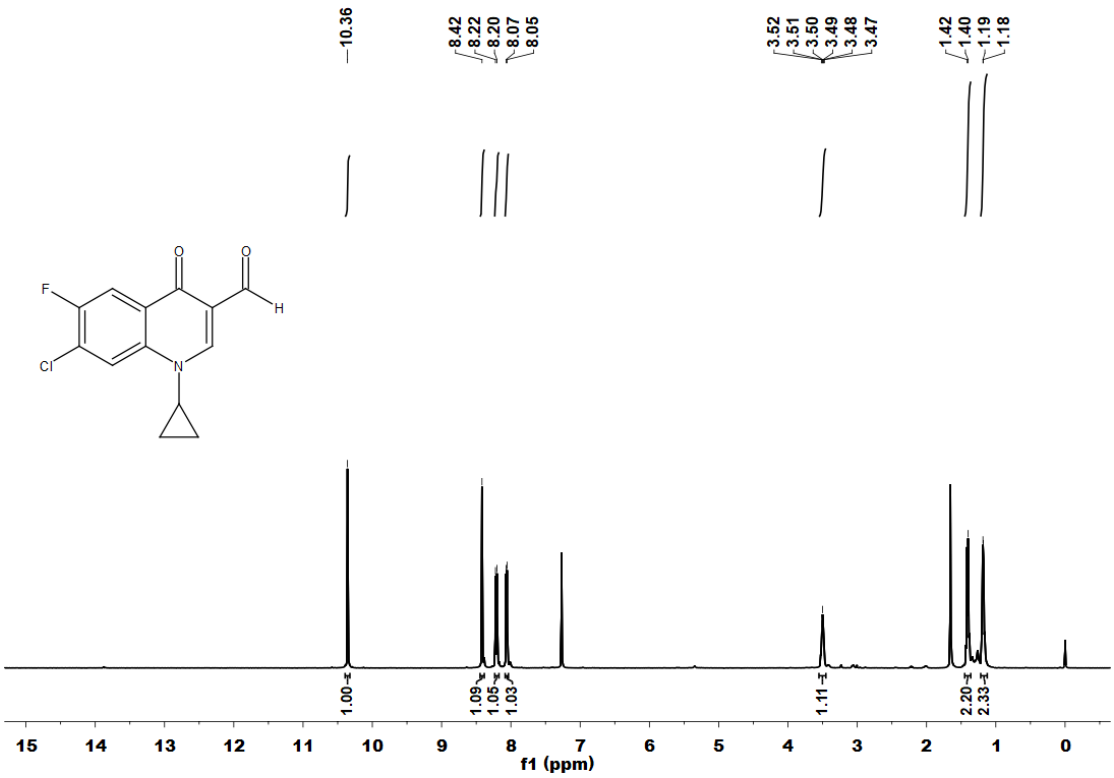
^{13}C NMR spectrum of **4ab**



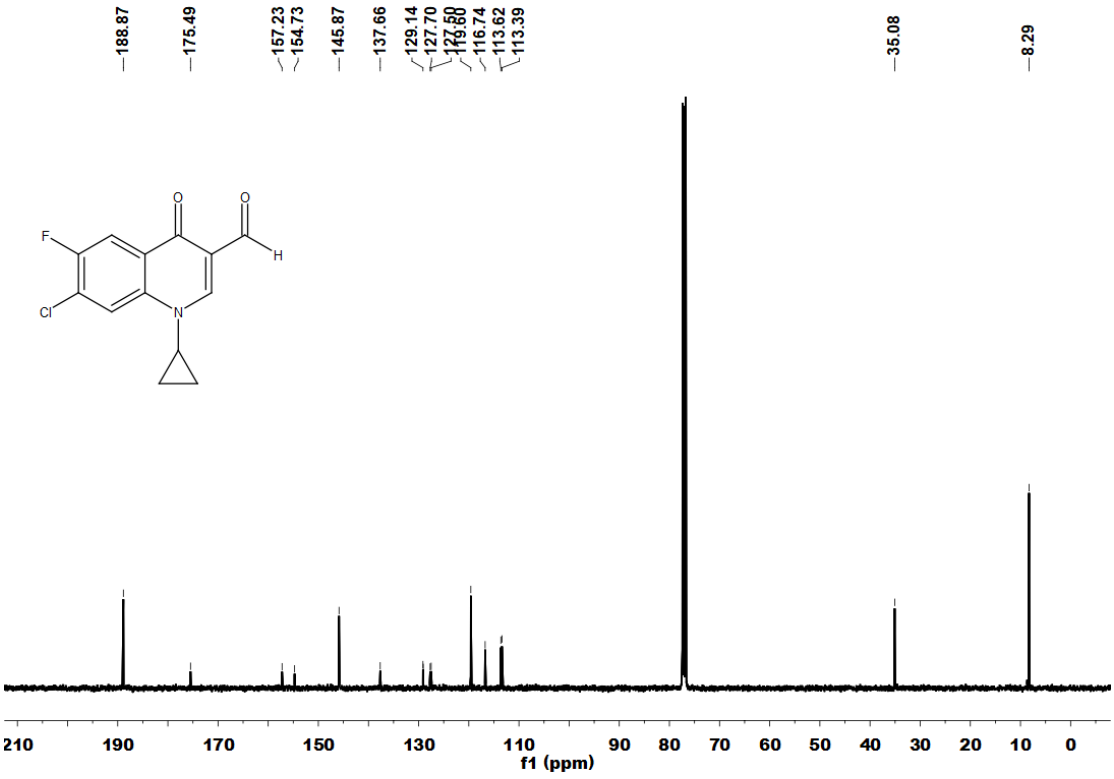
DEP 135° spectrum of **4ab**



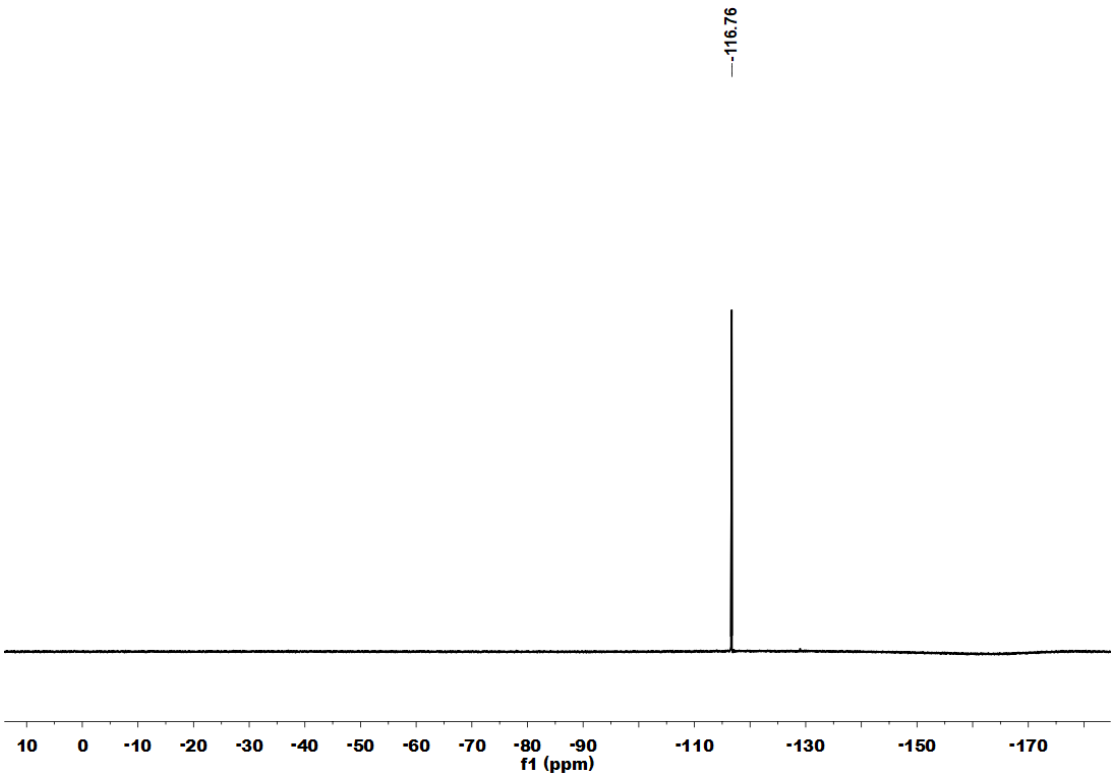
^{19}F NMR spectrum of **4ab**



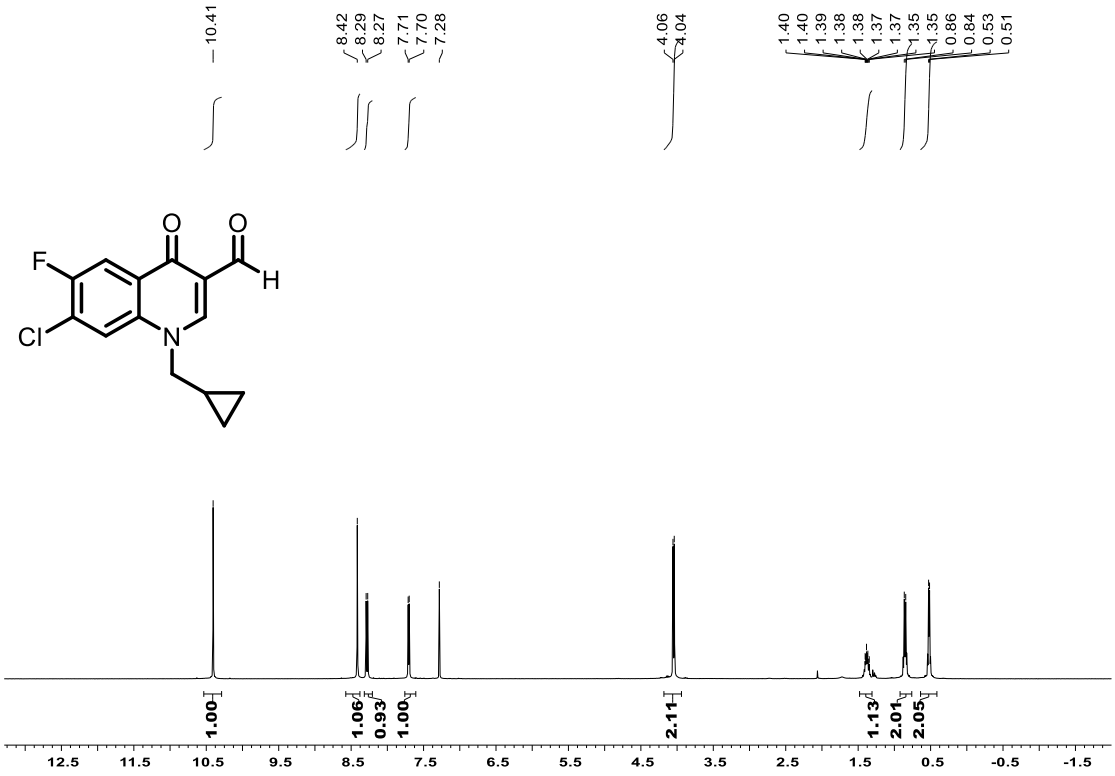
^{1}H NMR spectrum of **4ac**



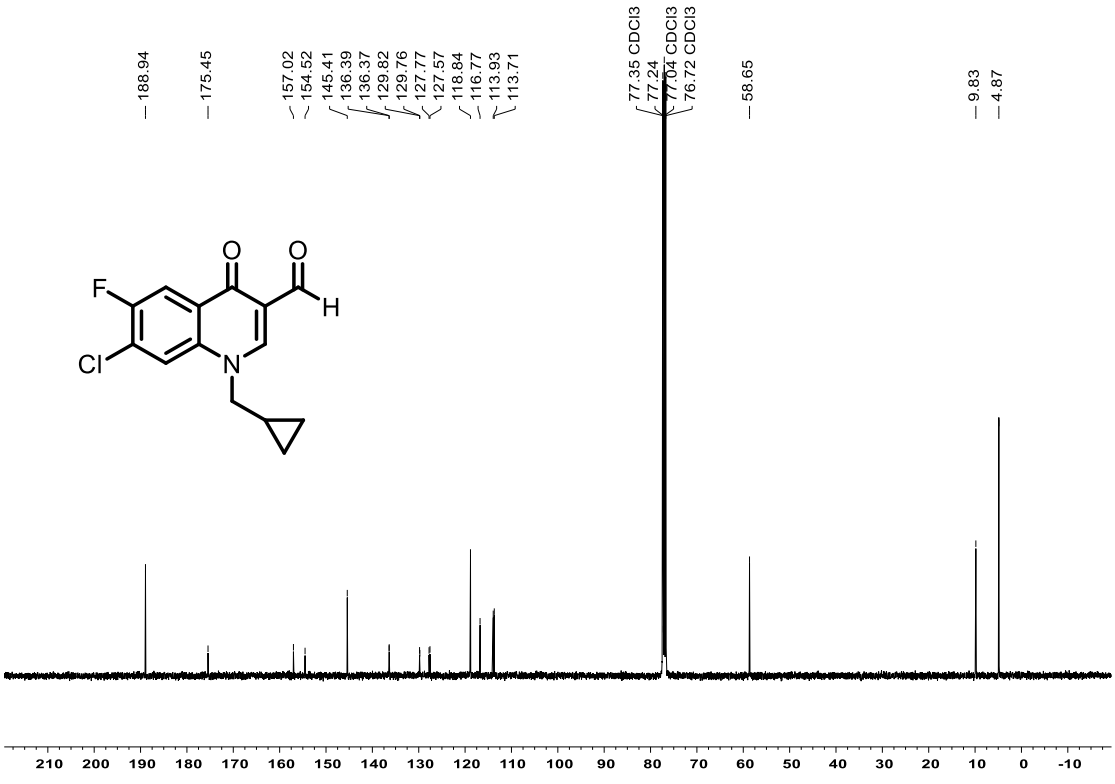
^{13}C NMR spectrum of **4ac**



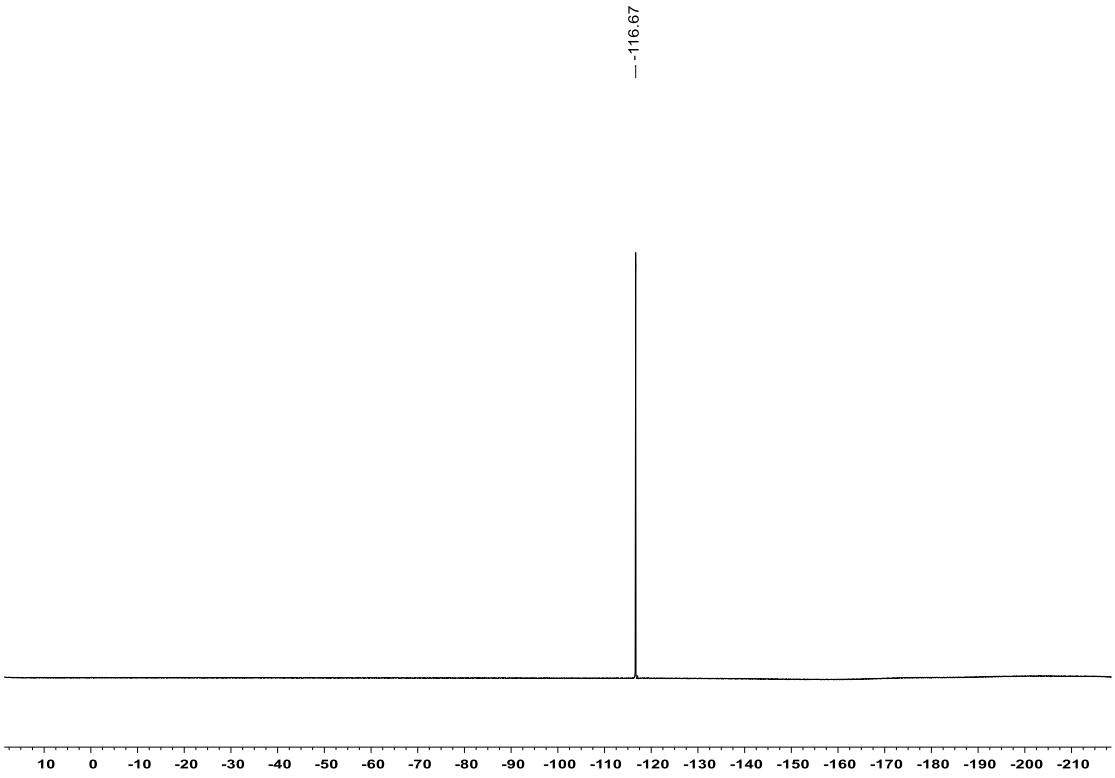
^{19}F NMR spectrum of **4ac**



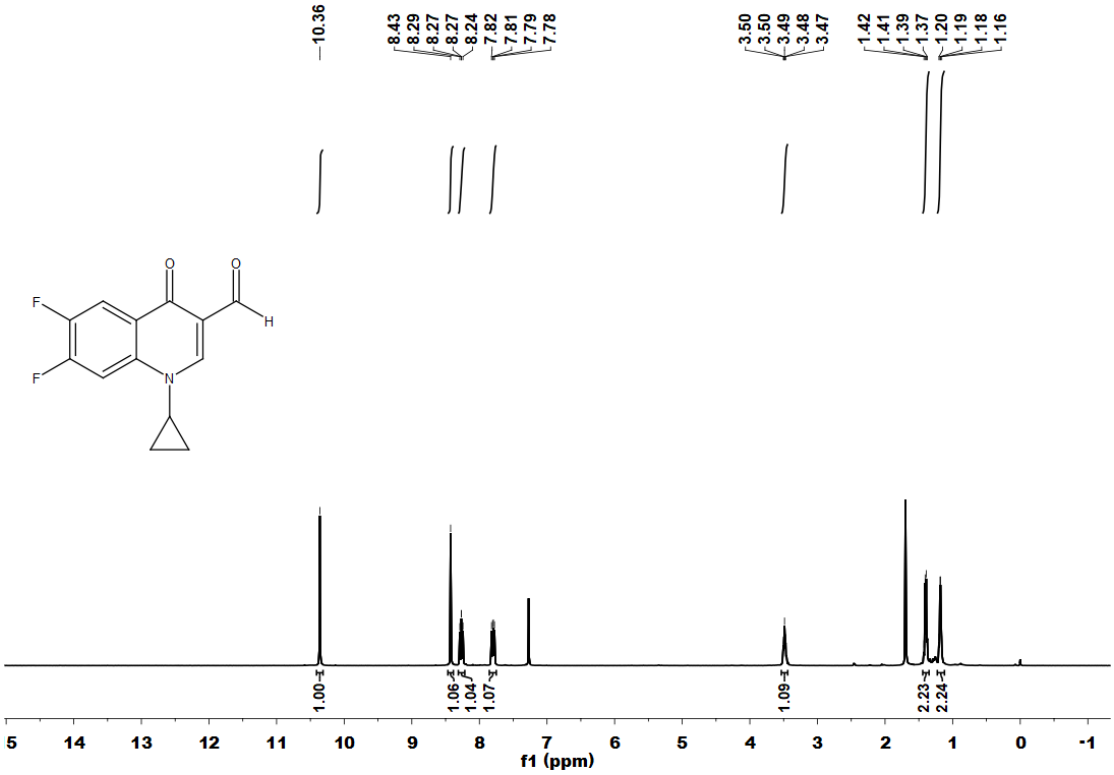
^{1}H NMR spectrum of **4ad**



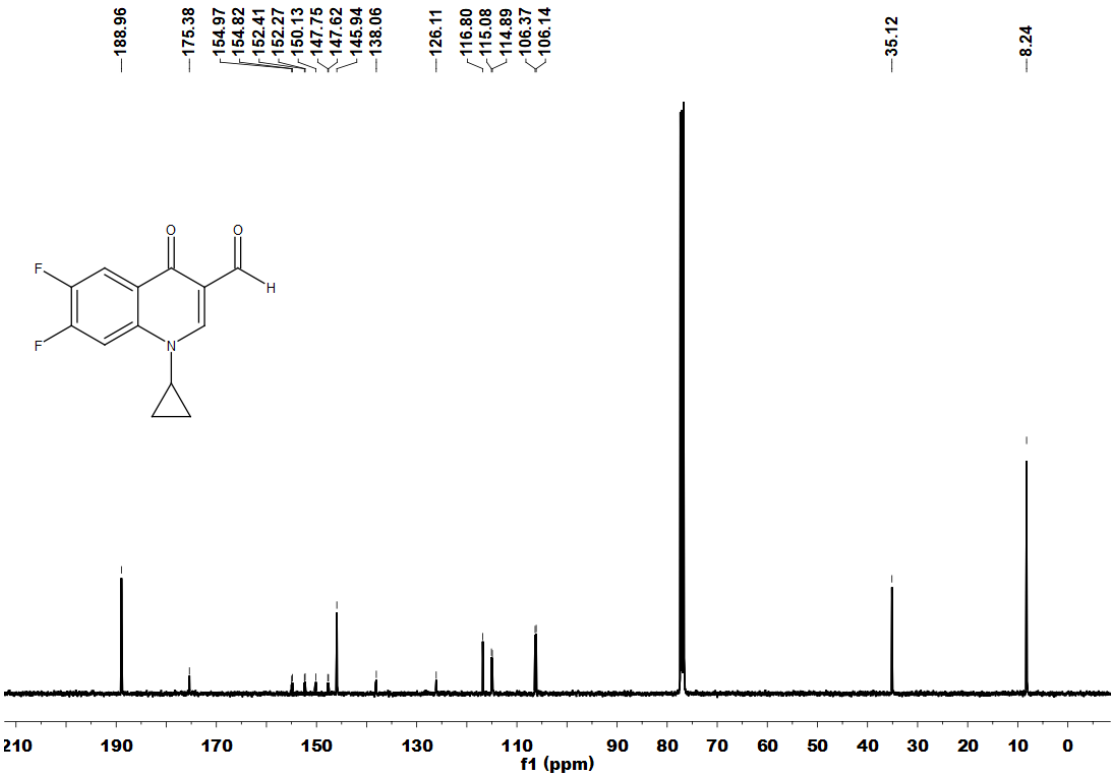
^{13}C NMR spectrum of **4ad**



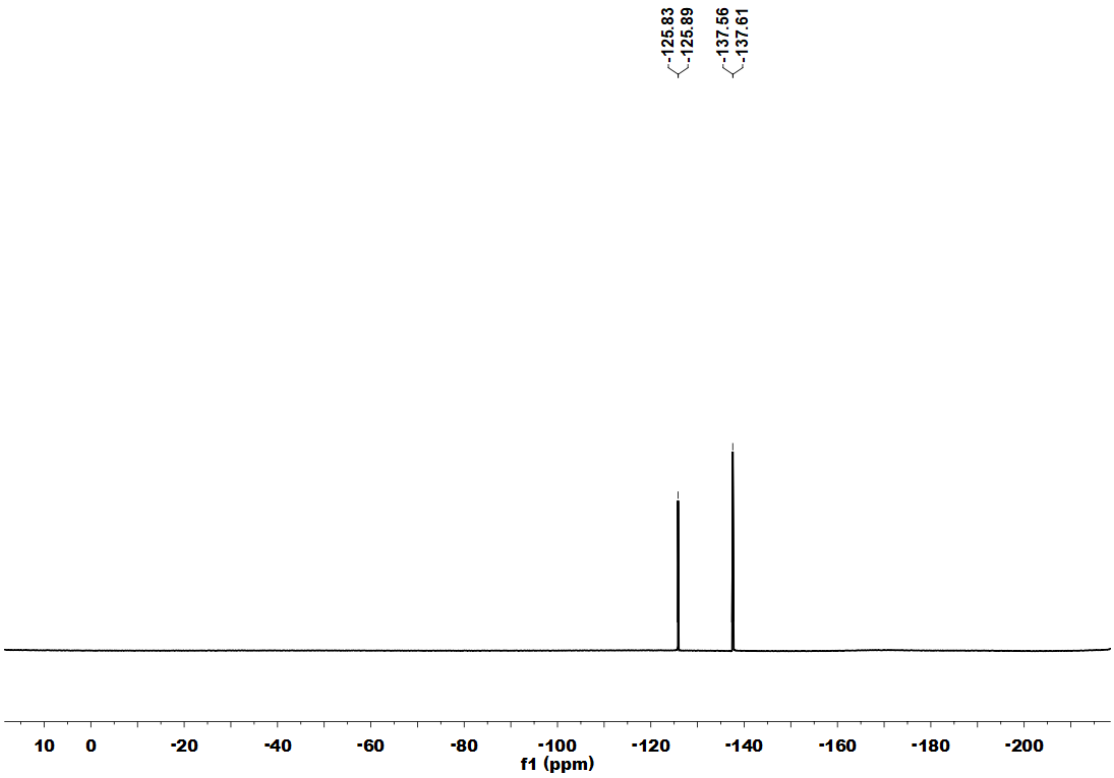
^{19}F NMR spectrum of **4ad**



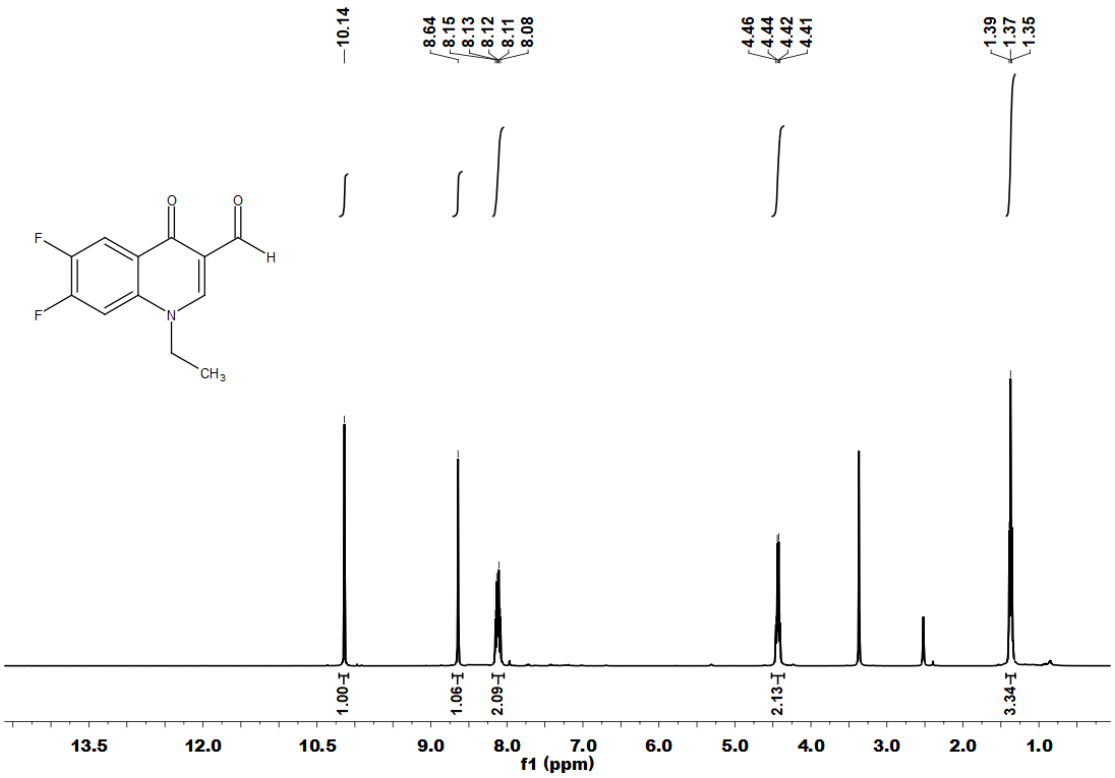
^{1}H NMR spectrum of **4ae**



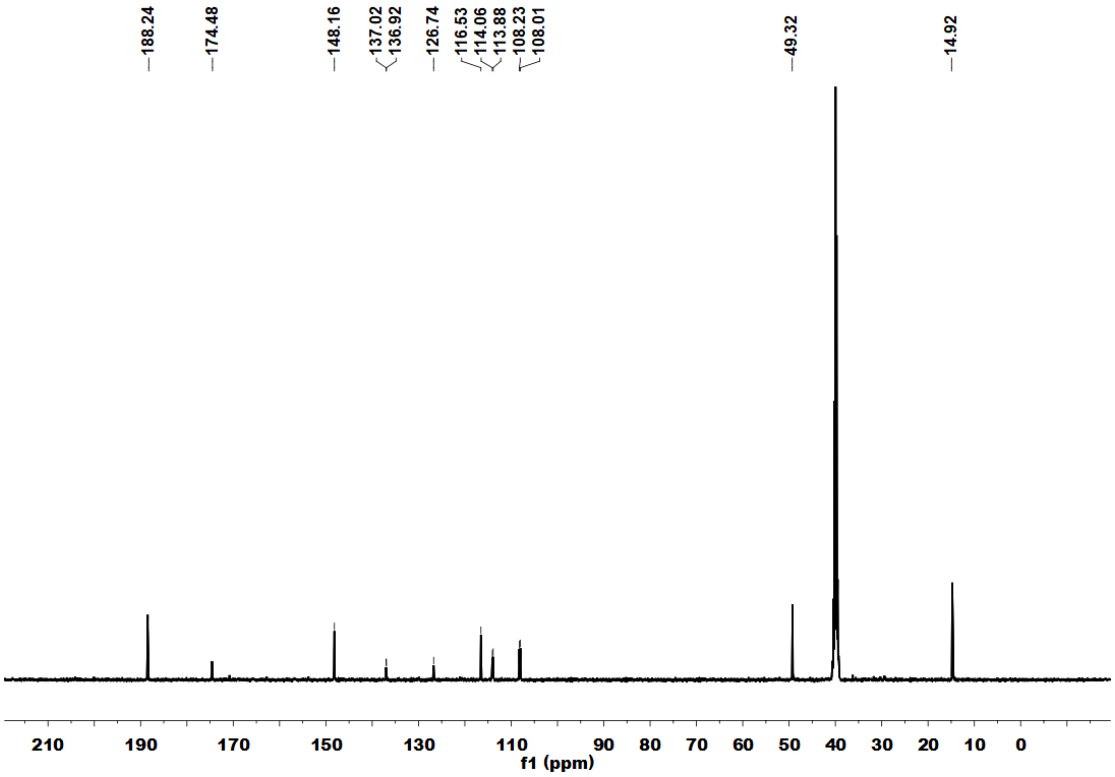
^{13}C NMR spectrum of **4ae**



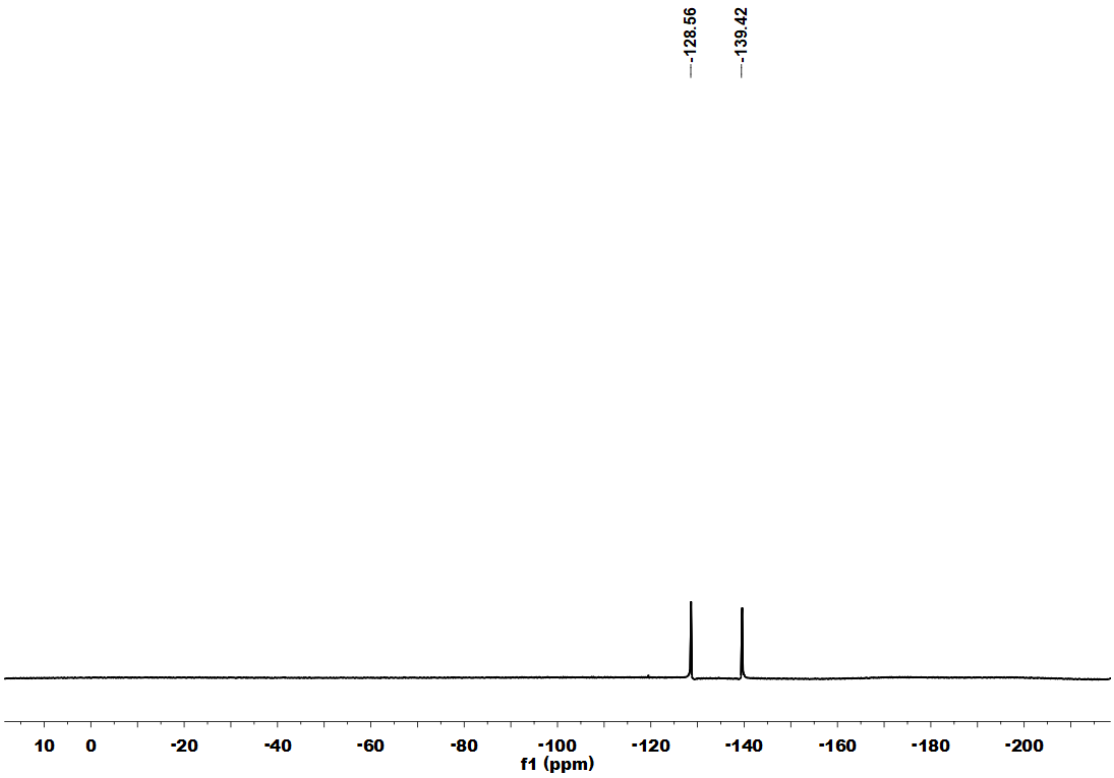
^{19}F NMR spectrum of **4ae**



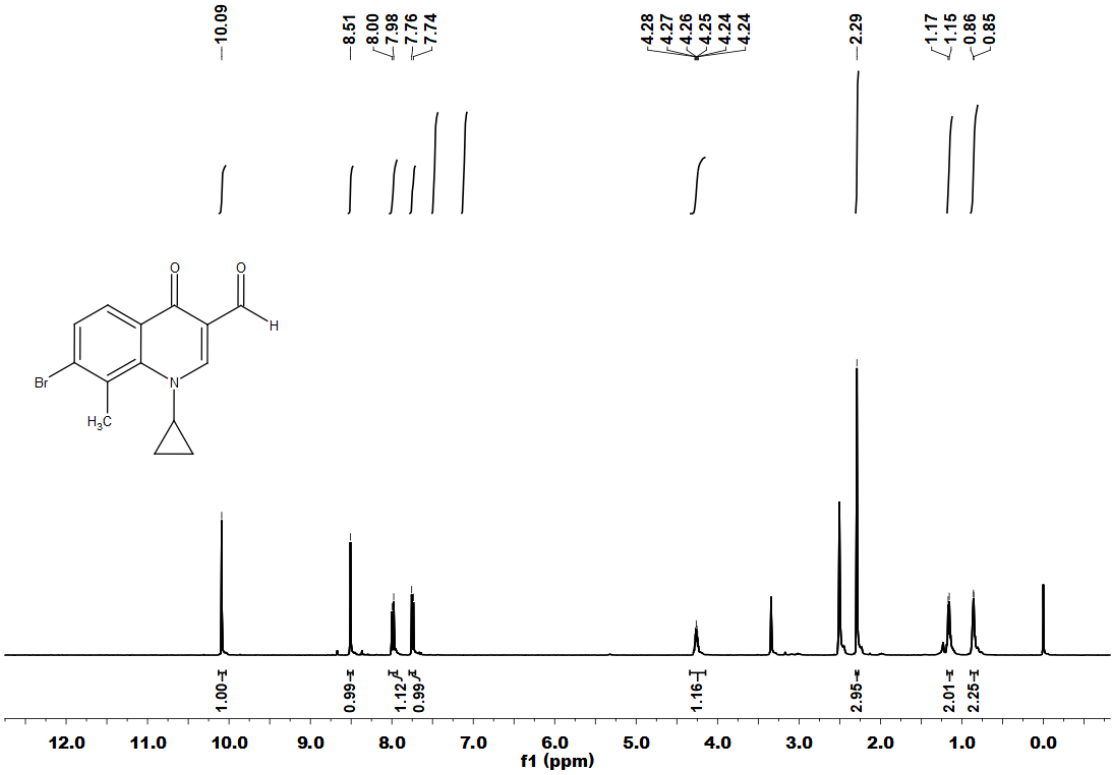
^{1}H NMR spectrum of **4af**



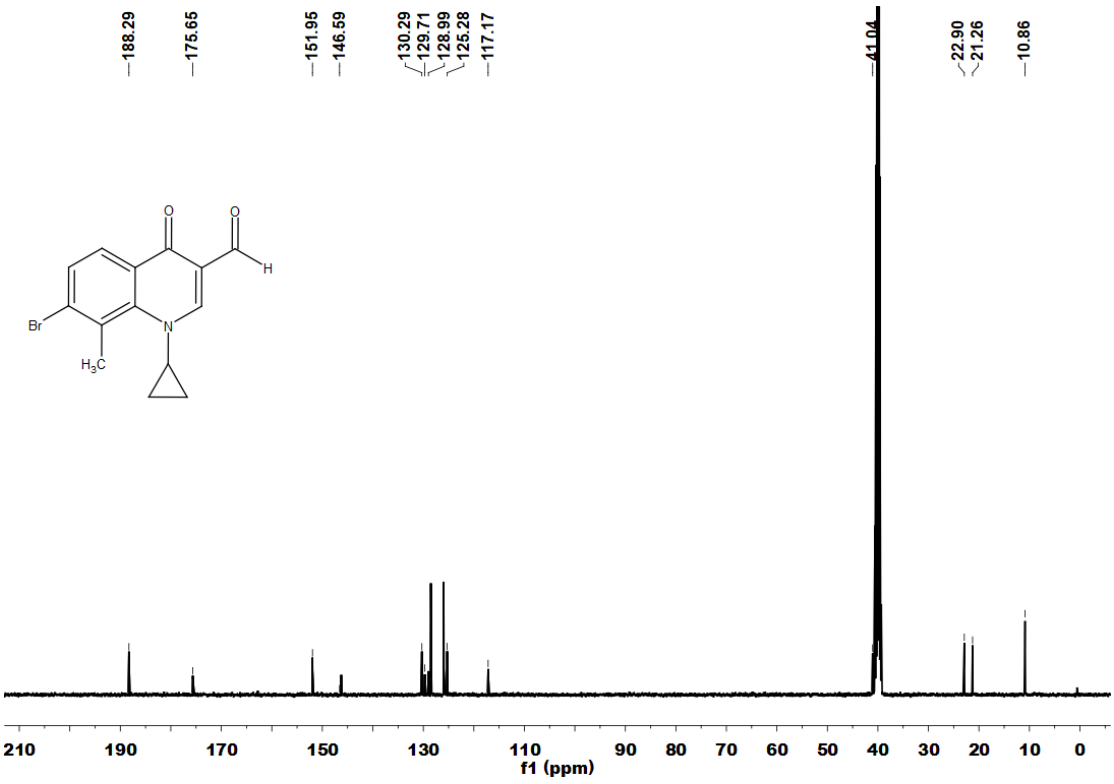
^{13}C NMR spectrum of **4af**



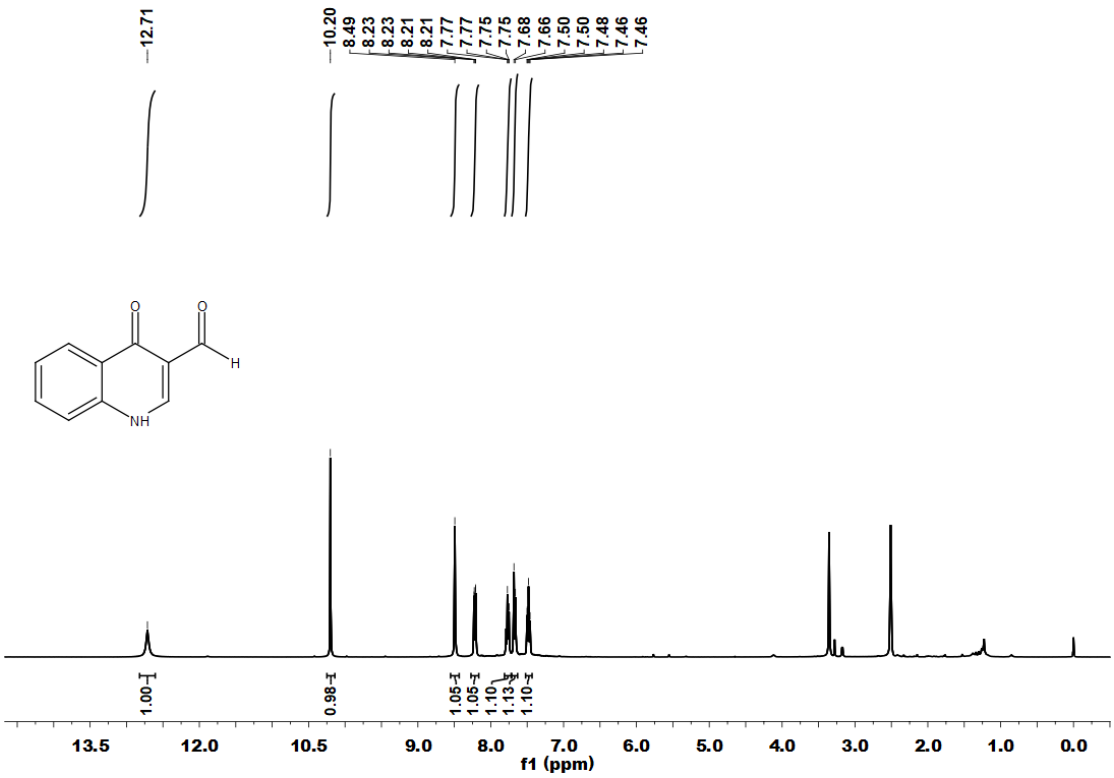
^{19}F NMR spectrum of **4af**



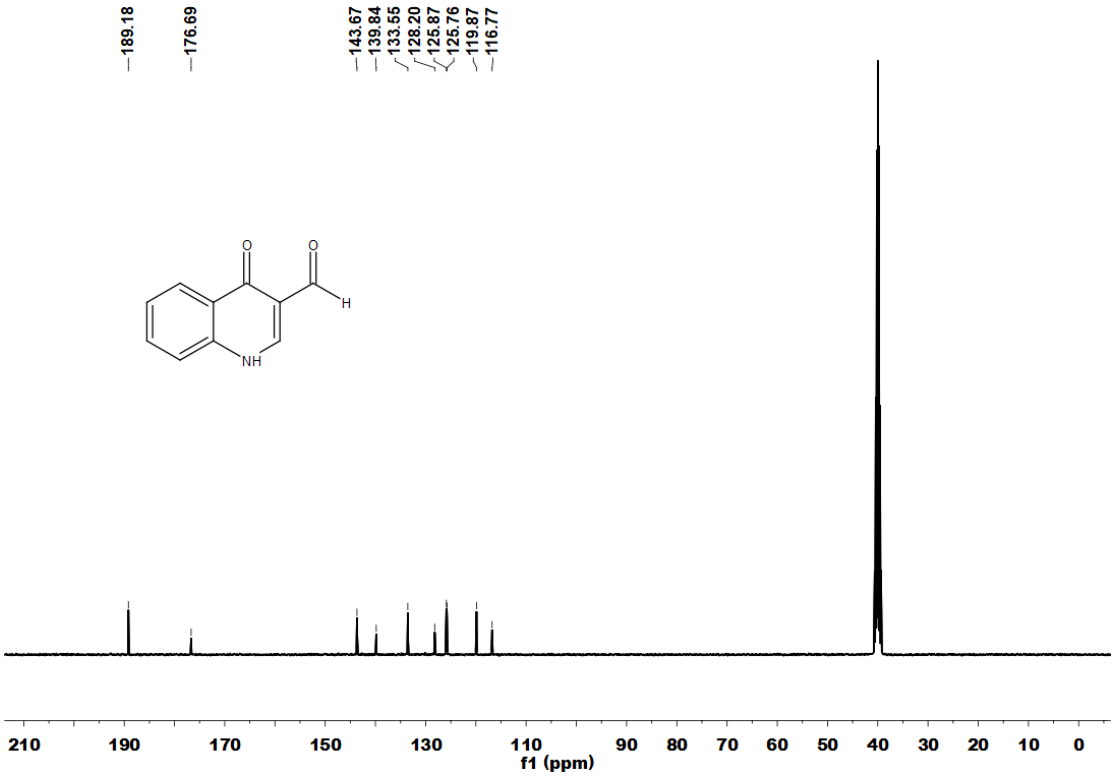
^{1}H NMR spectrum of **4ag**



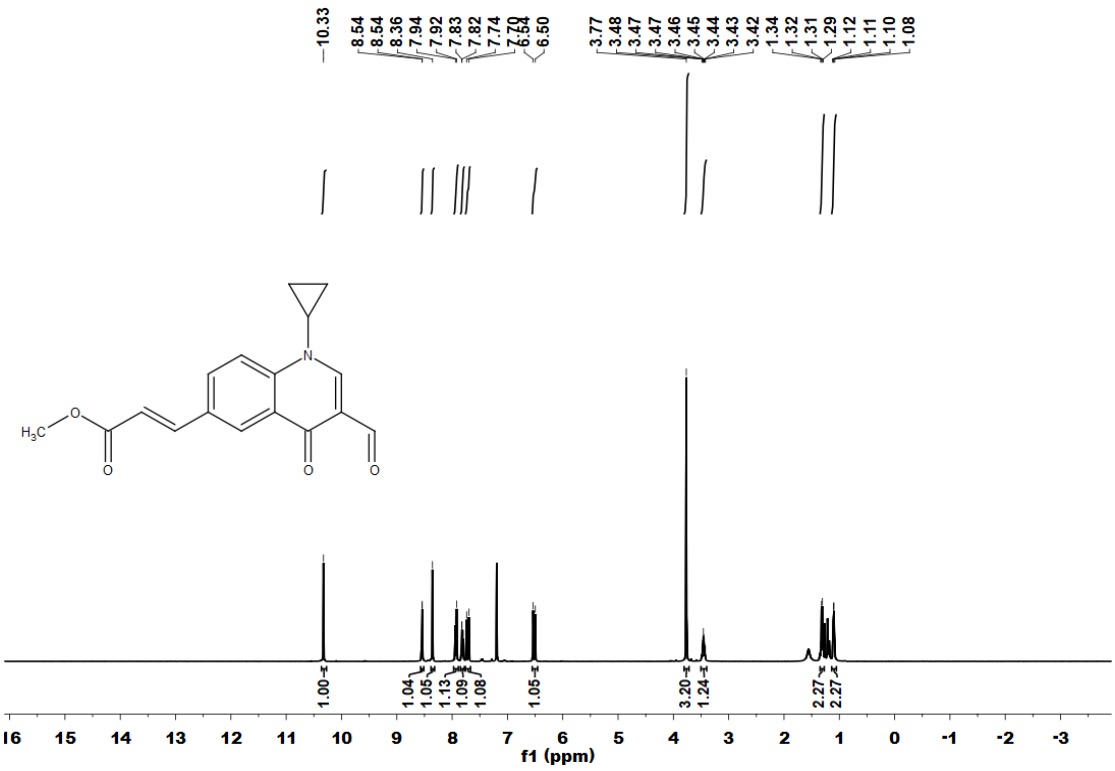
^{13}C NMR spectrum of **4ag**



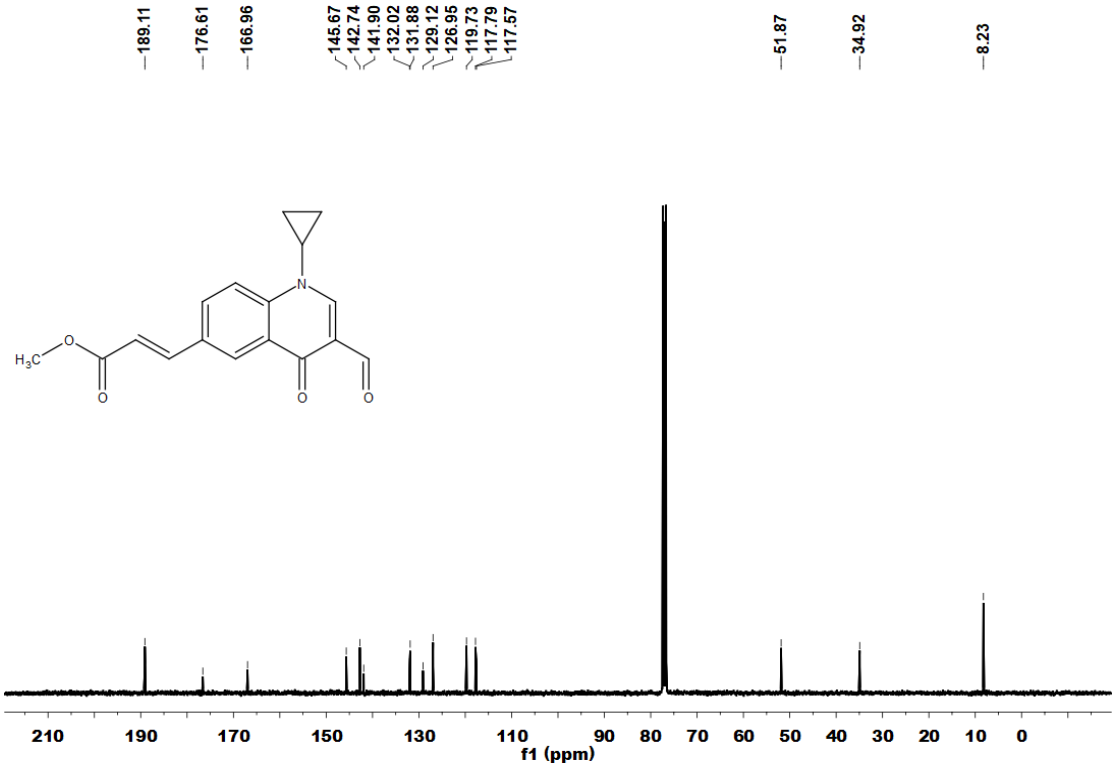
^{1}H NMR spectrum of **4ah**



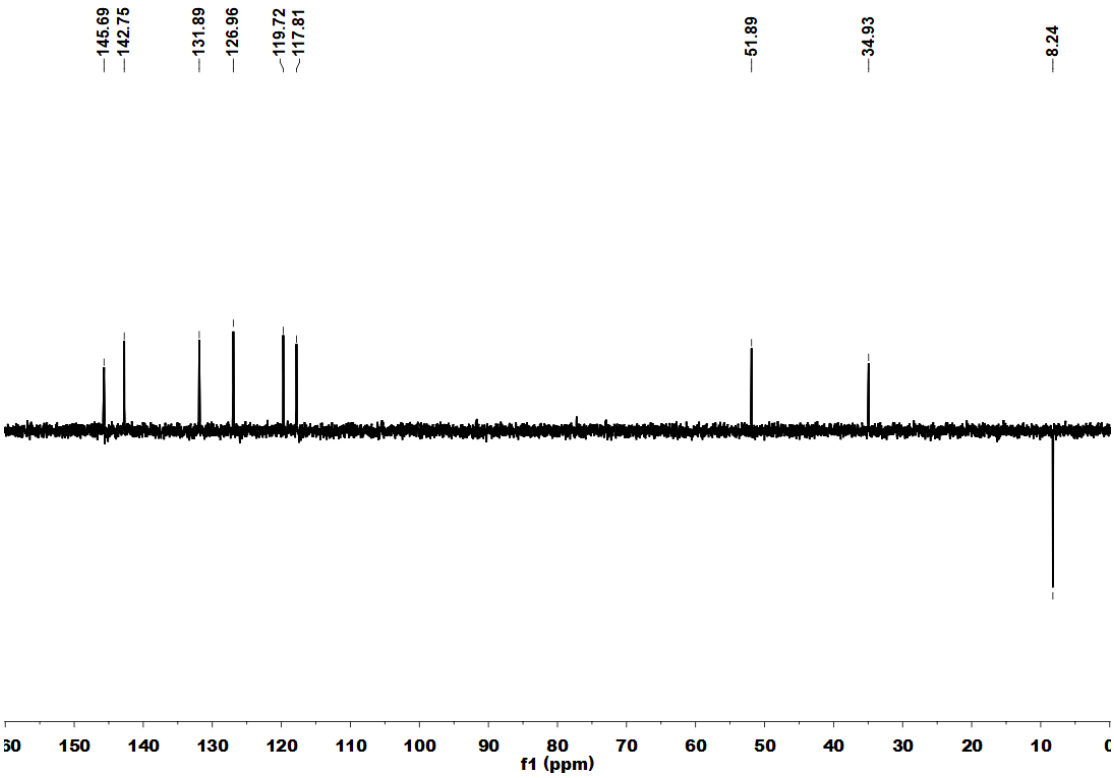
^{13}C NMR spectrum of **4ah**



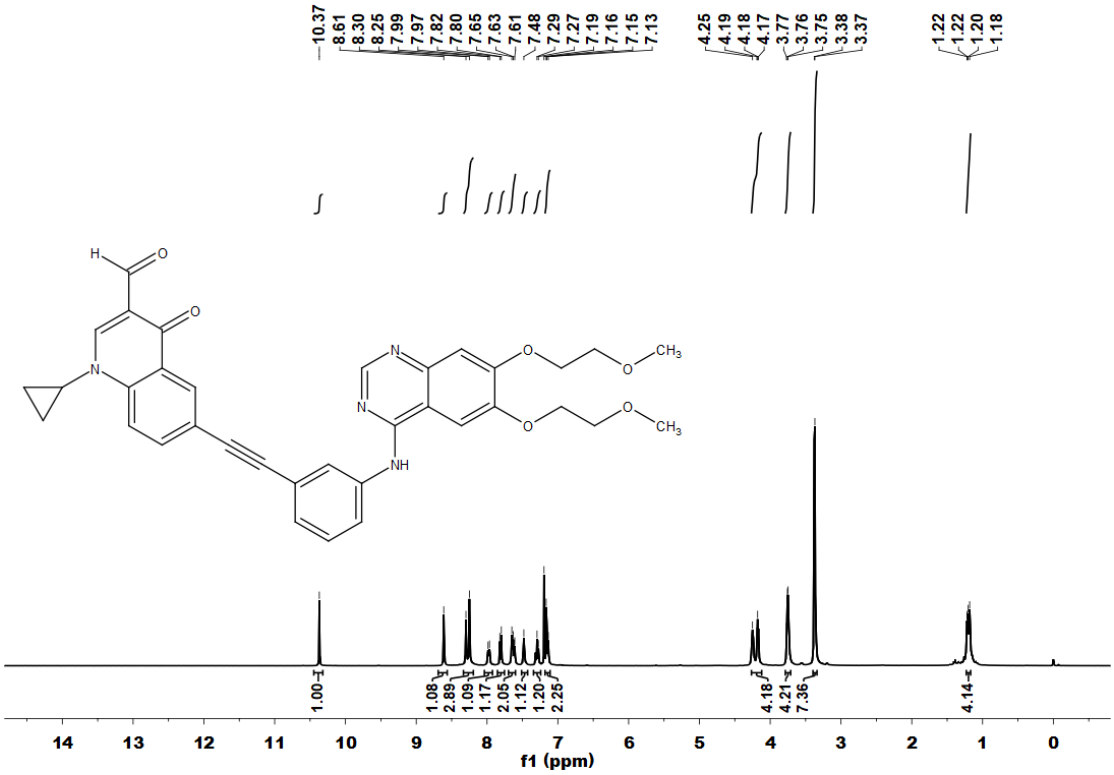
^{1}H NMR spectrum of **4ai**



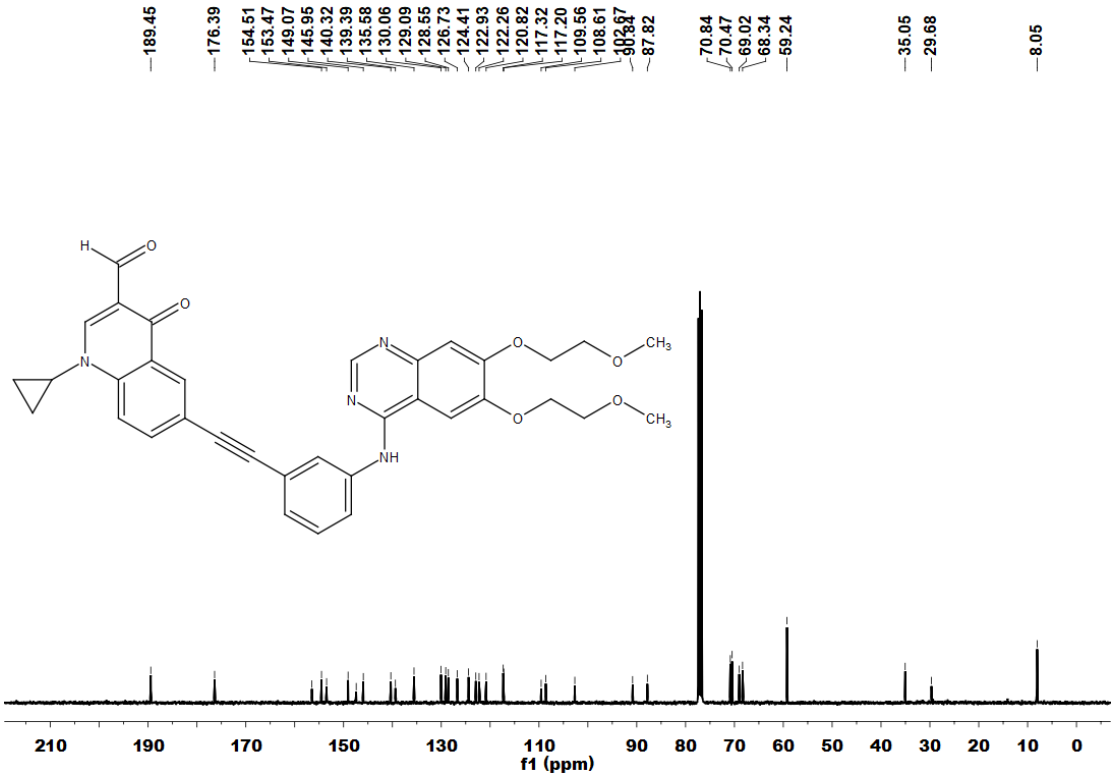
^{13}C NMR spectrum of **4ai**



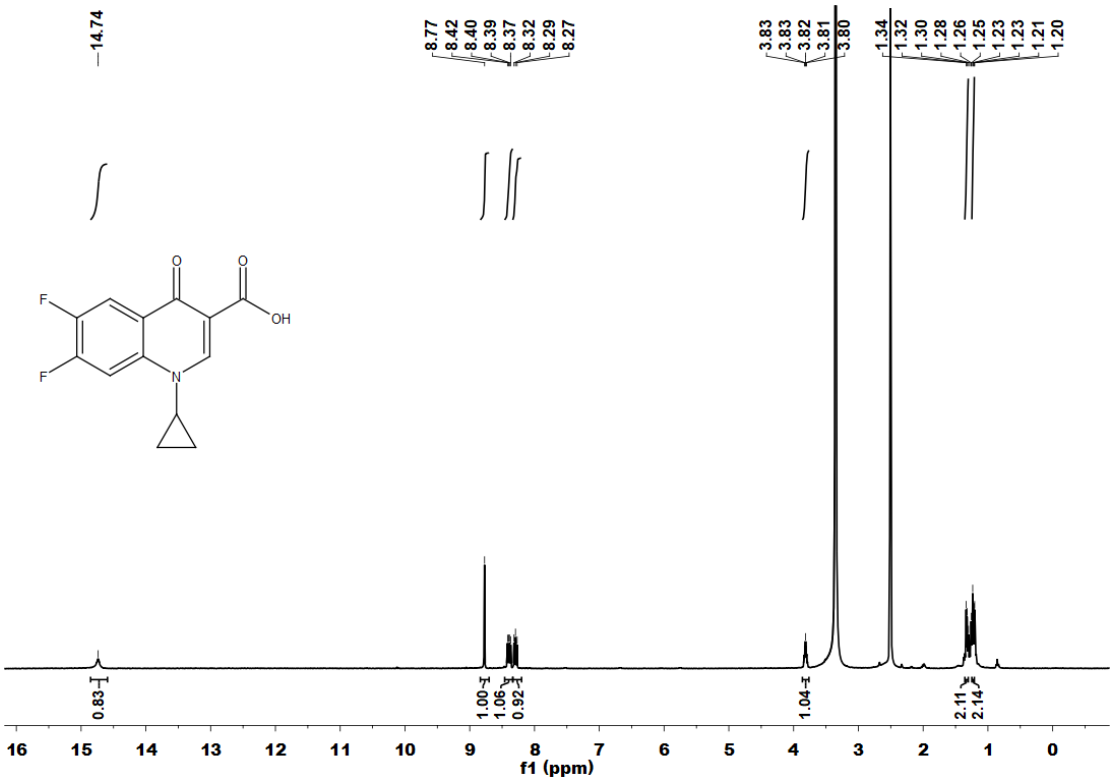
DEP 135^{o} spectrum of **4ai**



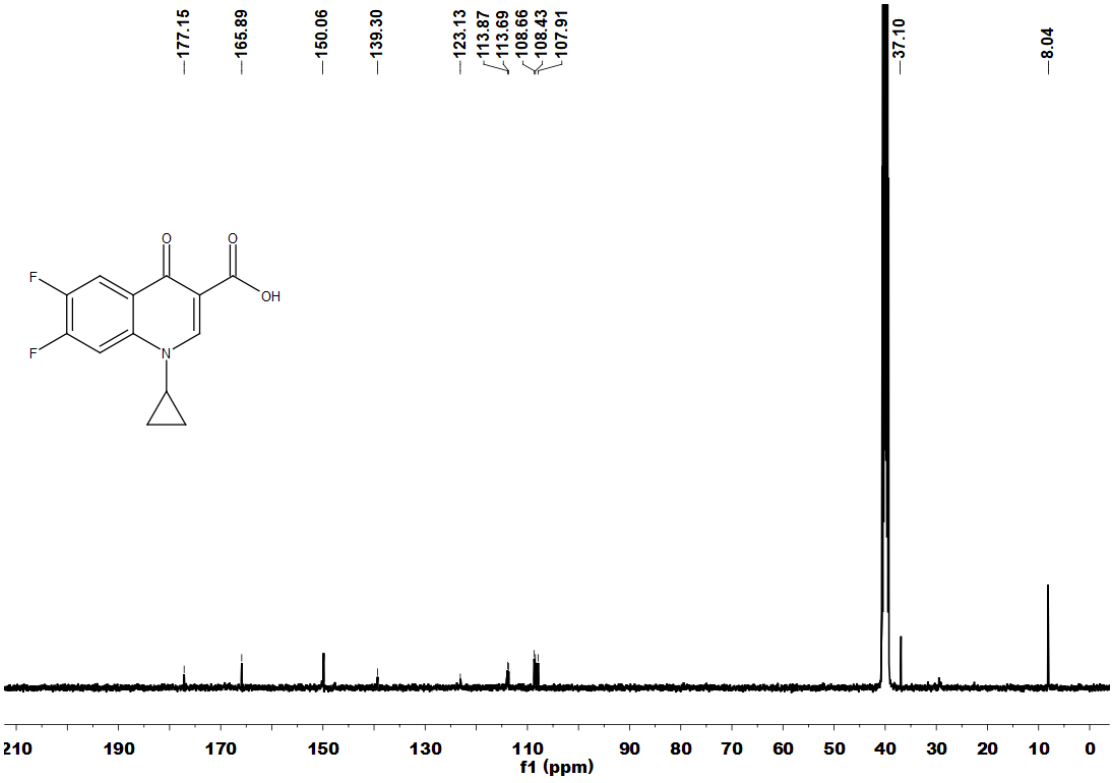
^{1}H NMR spectrum of **4aj**



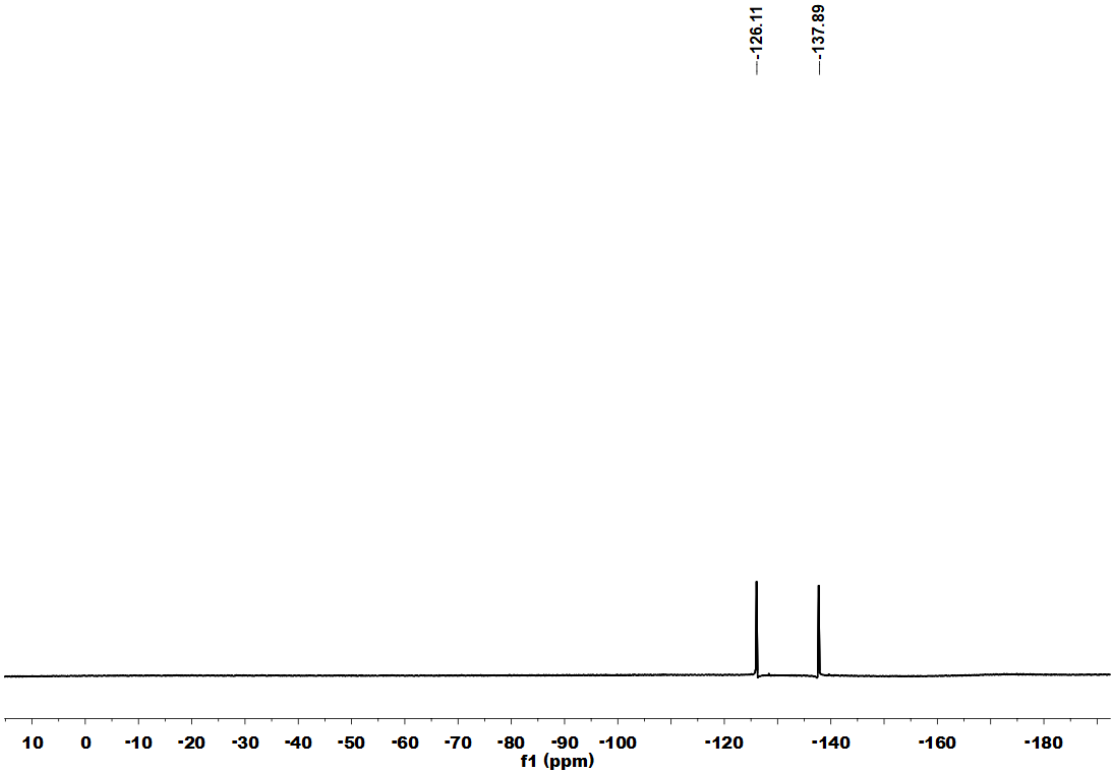
^{13}C NMR spectrum of **4aj**



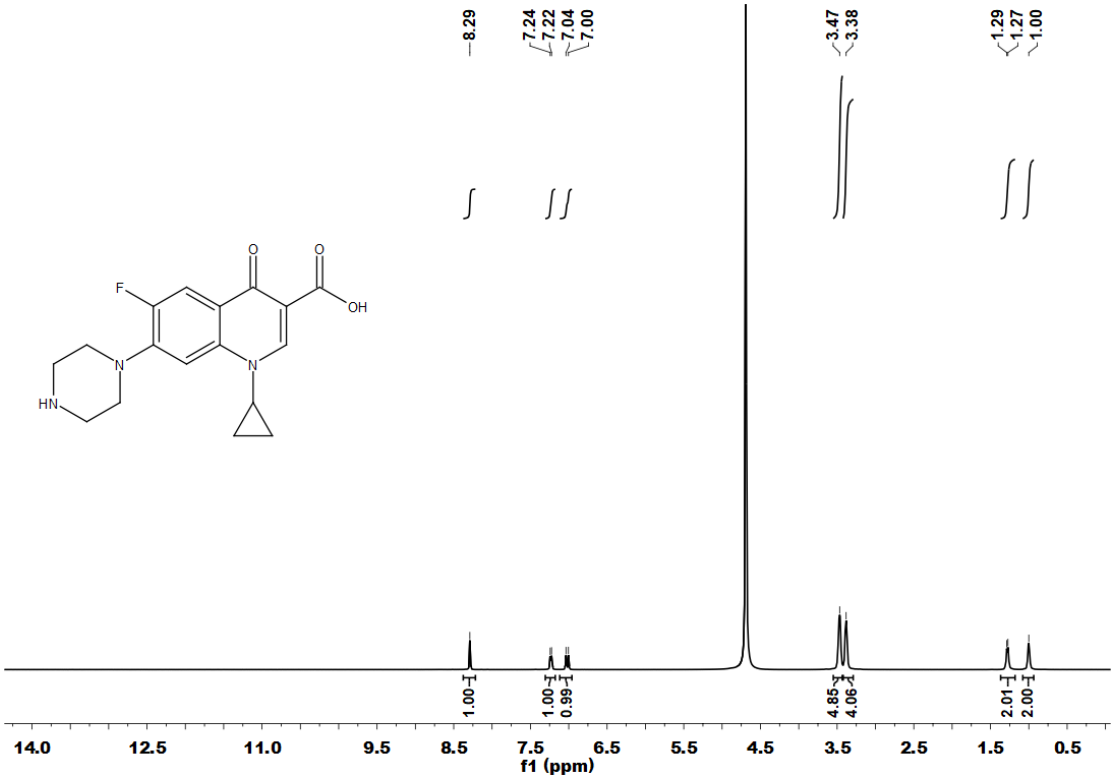
^{1}H NMR spectrum of **5**



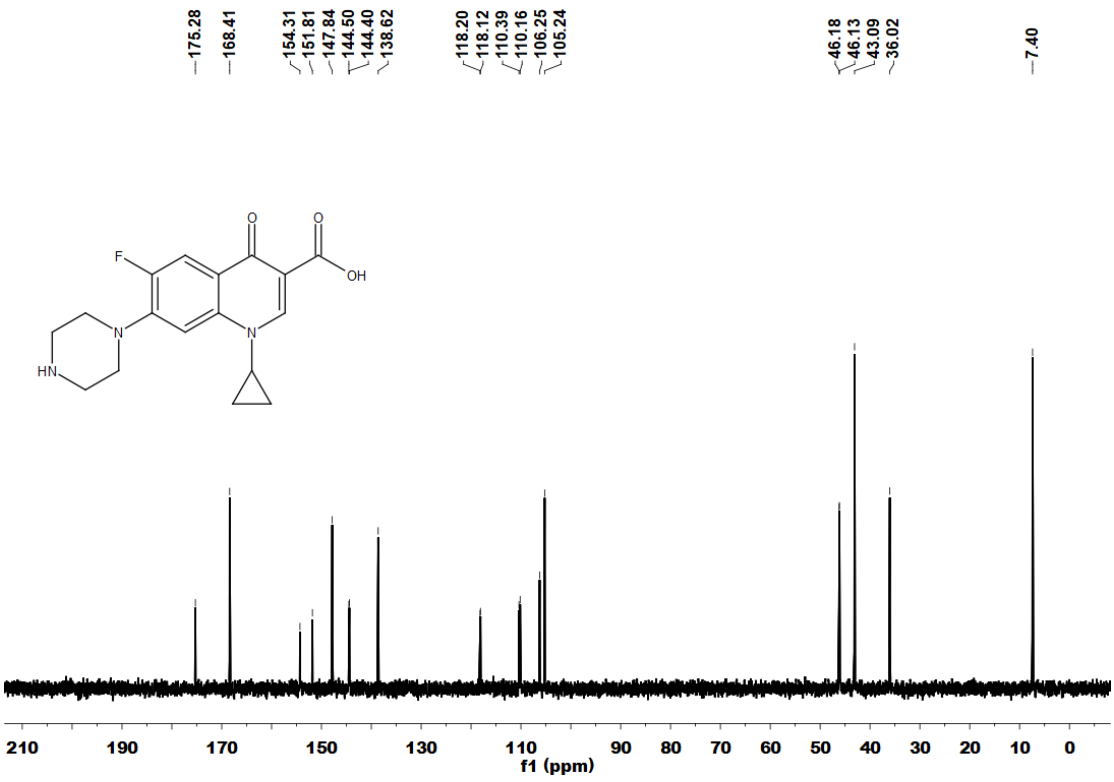
^{13}C NMR spectrum of **5**



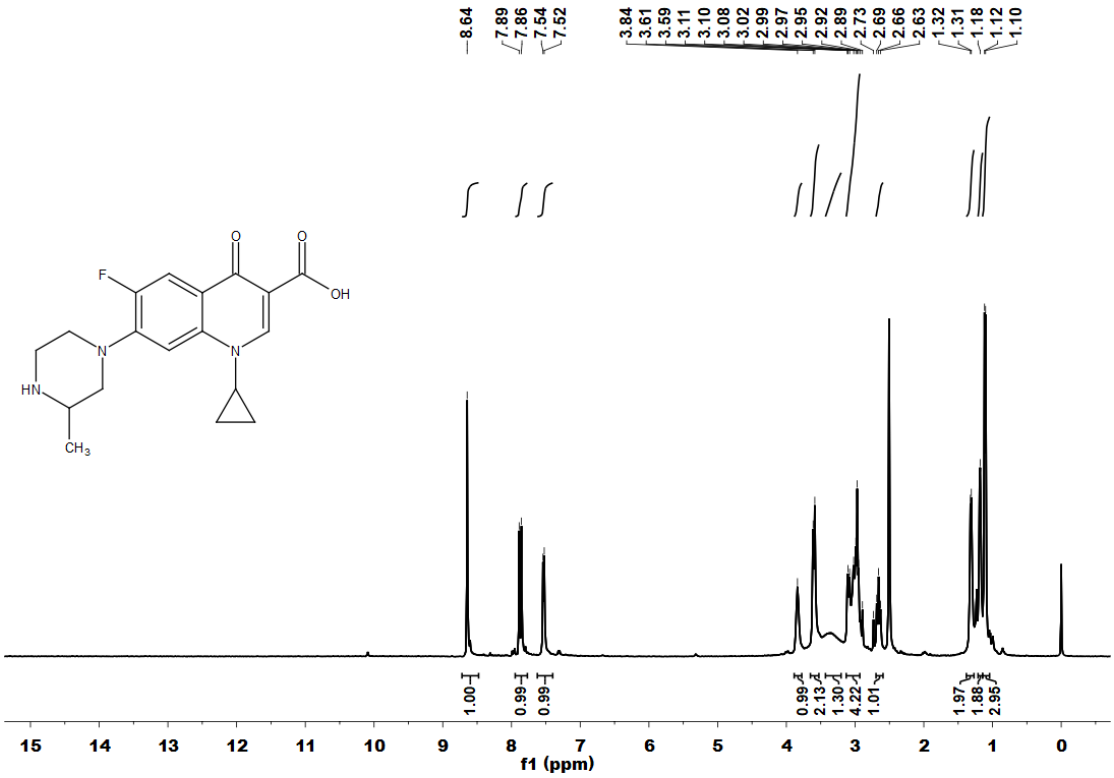
^{19}F NMR spectrum of **5**



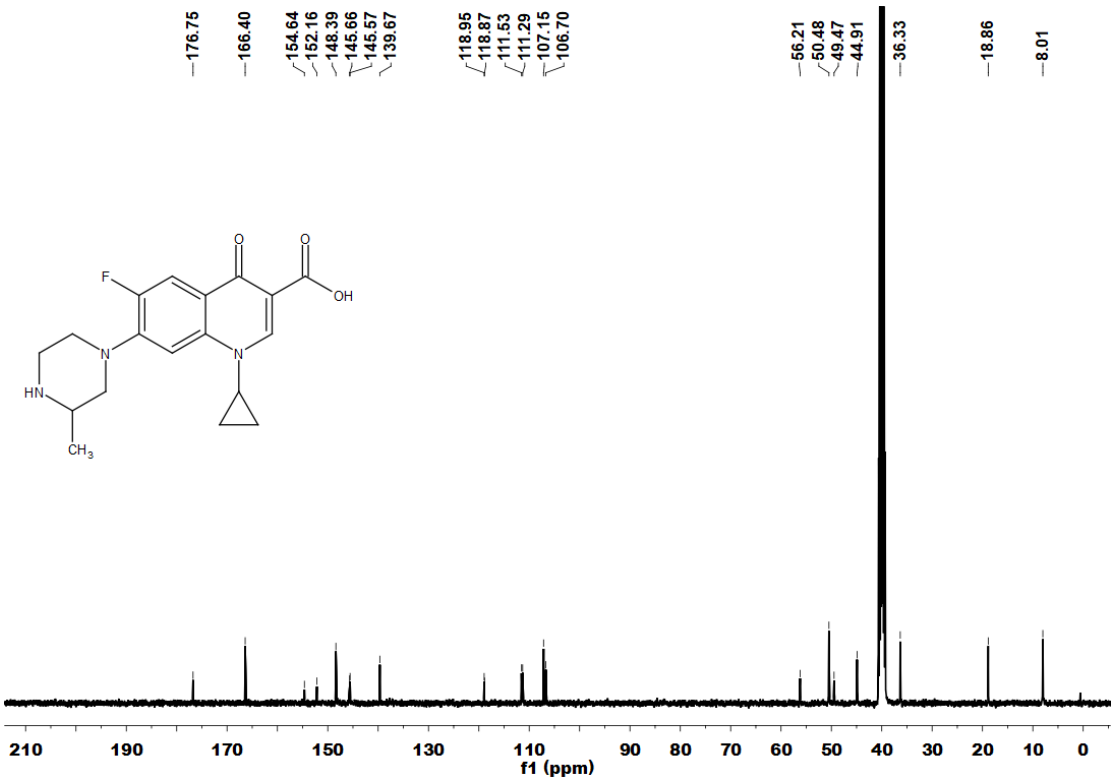
^{1}H NMR spectrum of **6**



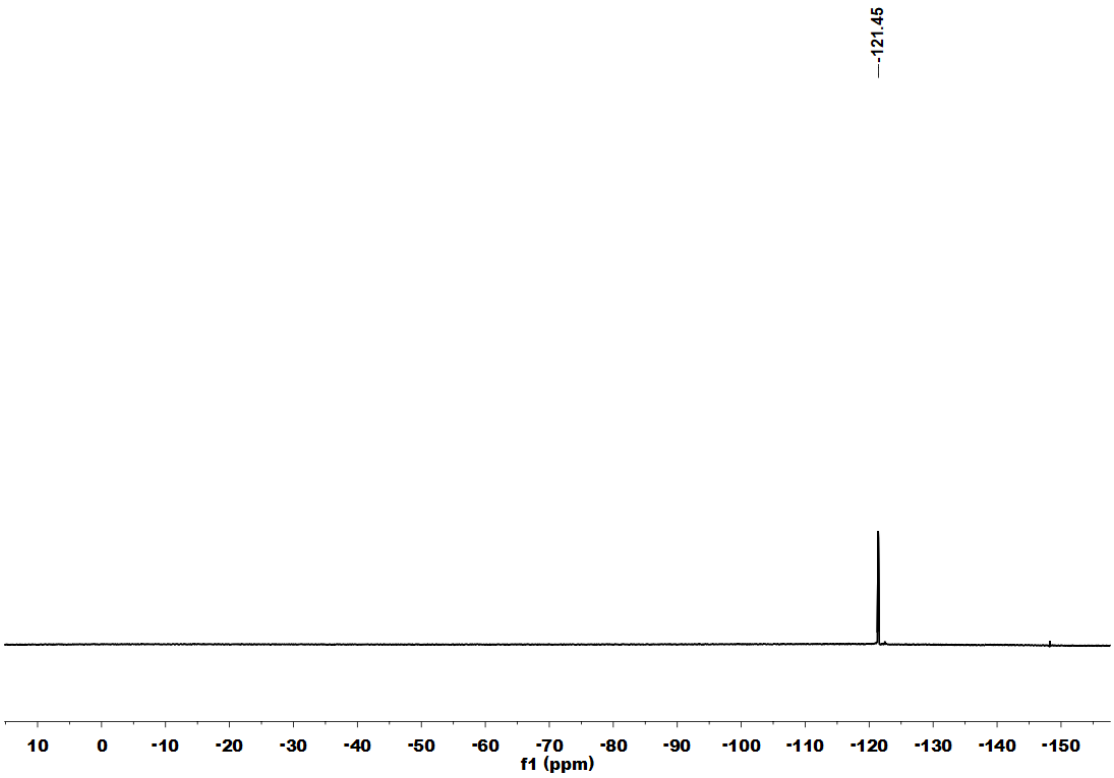
^{13}C NMR spectrum of **6**



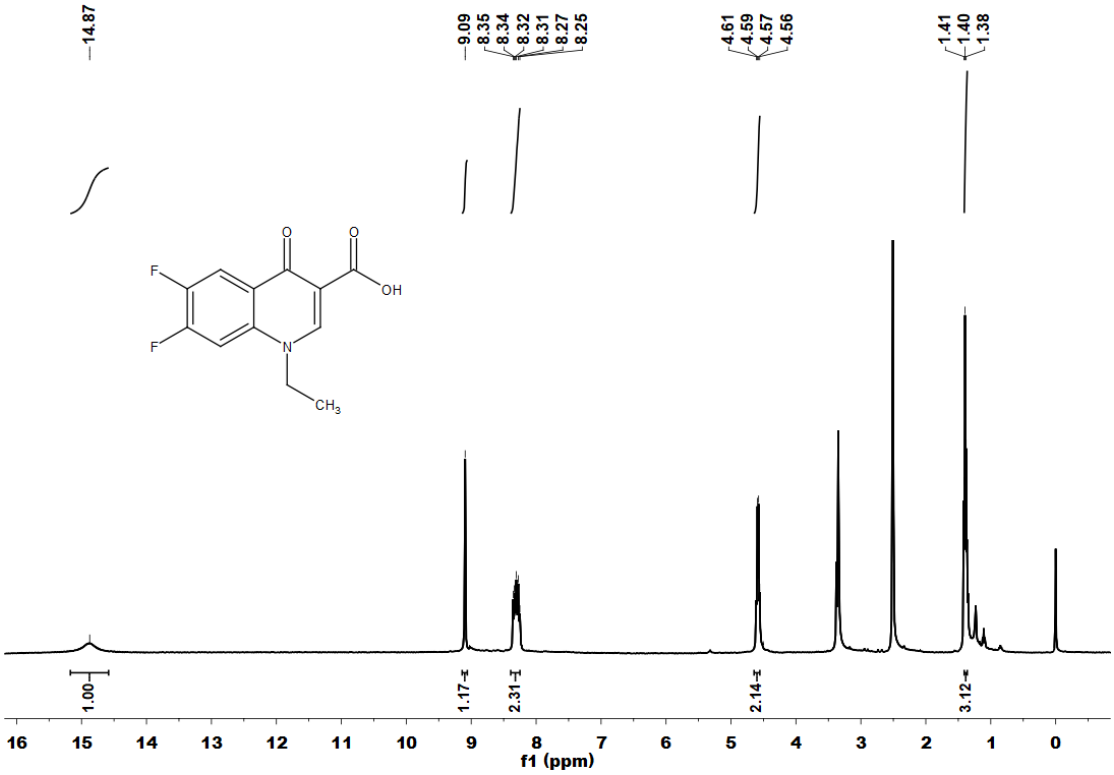
^{1}H NMR spectrum of **7**



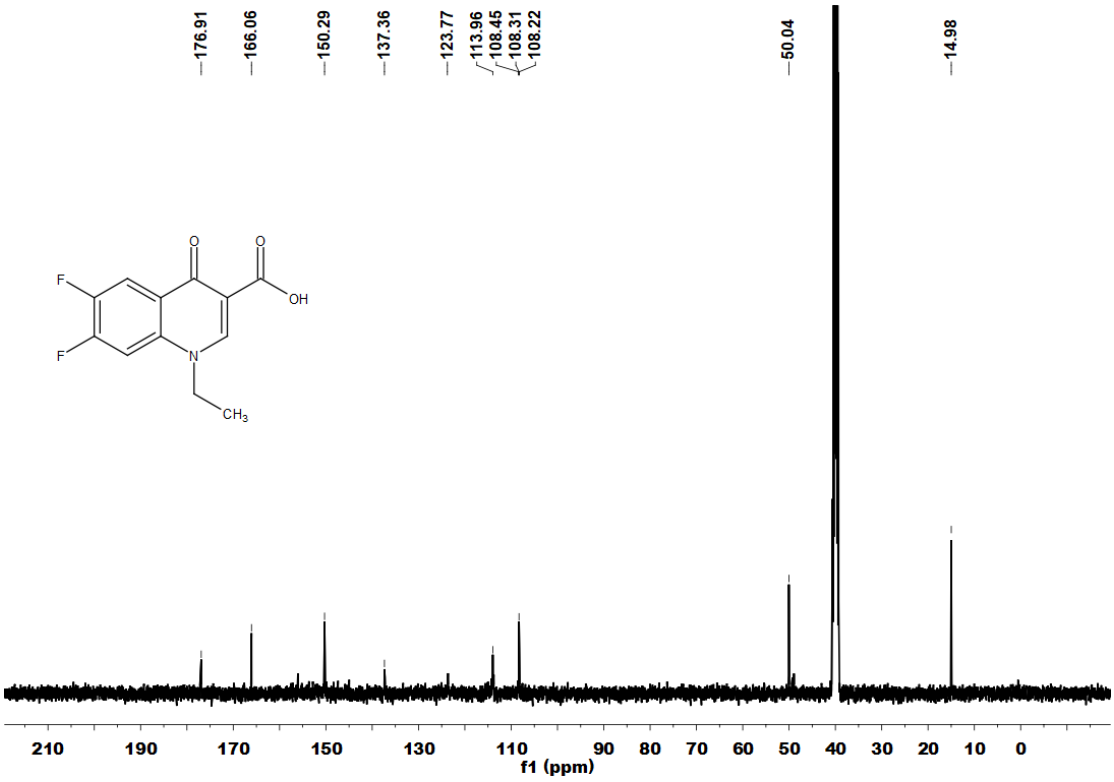
^{13}C NMR spectrum of **7**



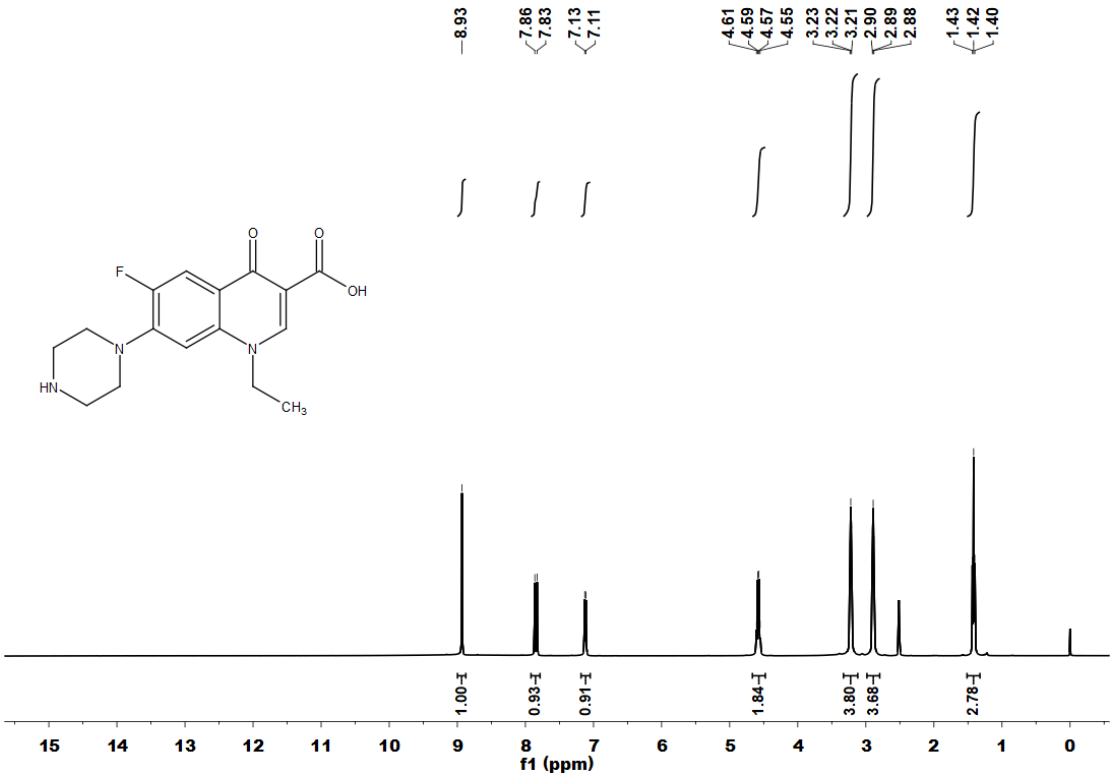
^{19}F NMR spectrum of **7**



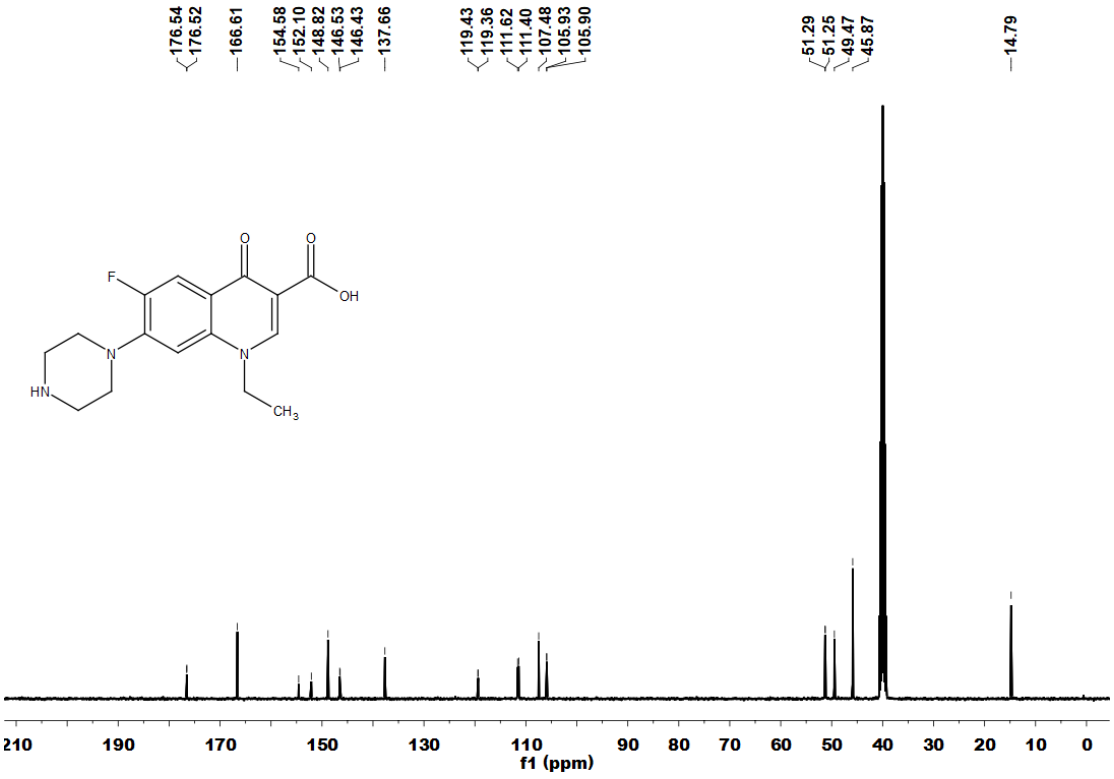
^{1}H NMR spectrum of **8**



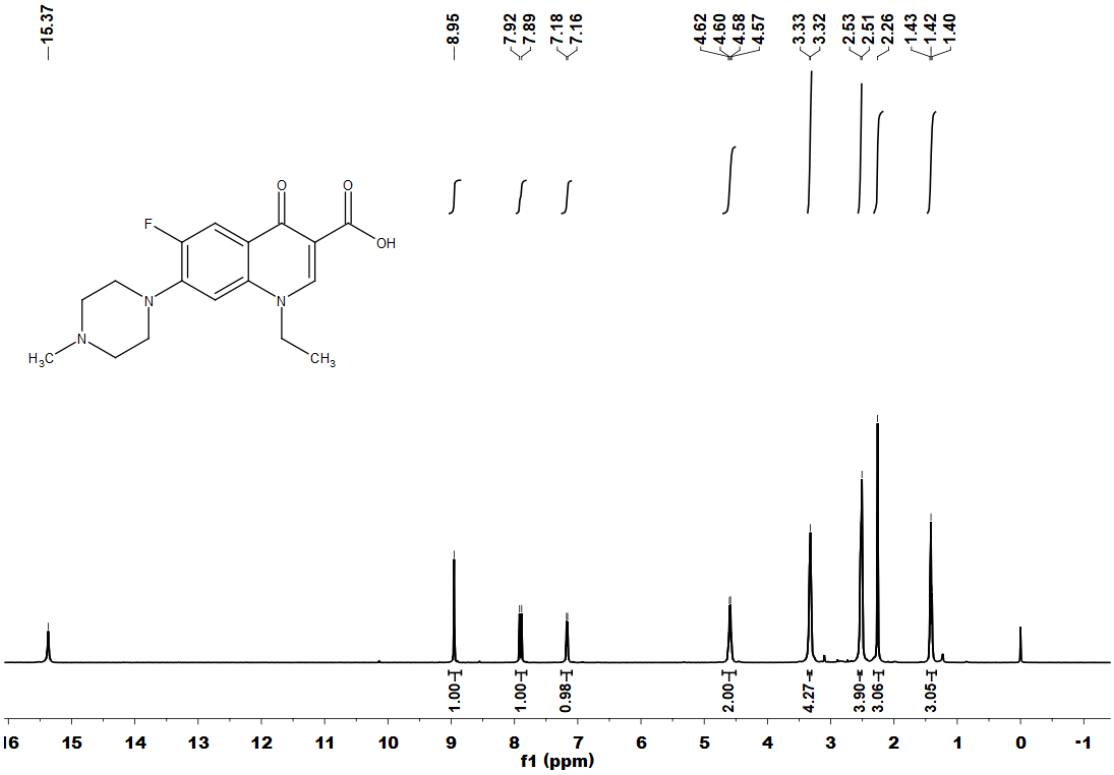
^{13}C NMR spectrum of **8**



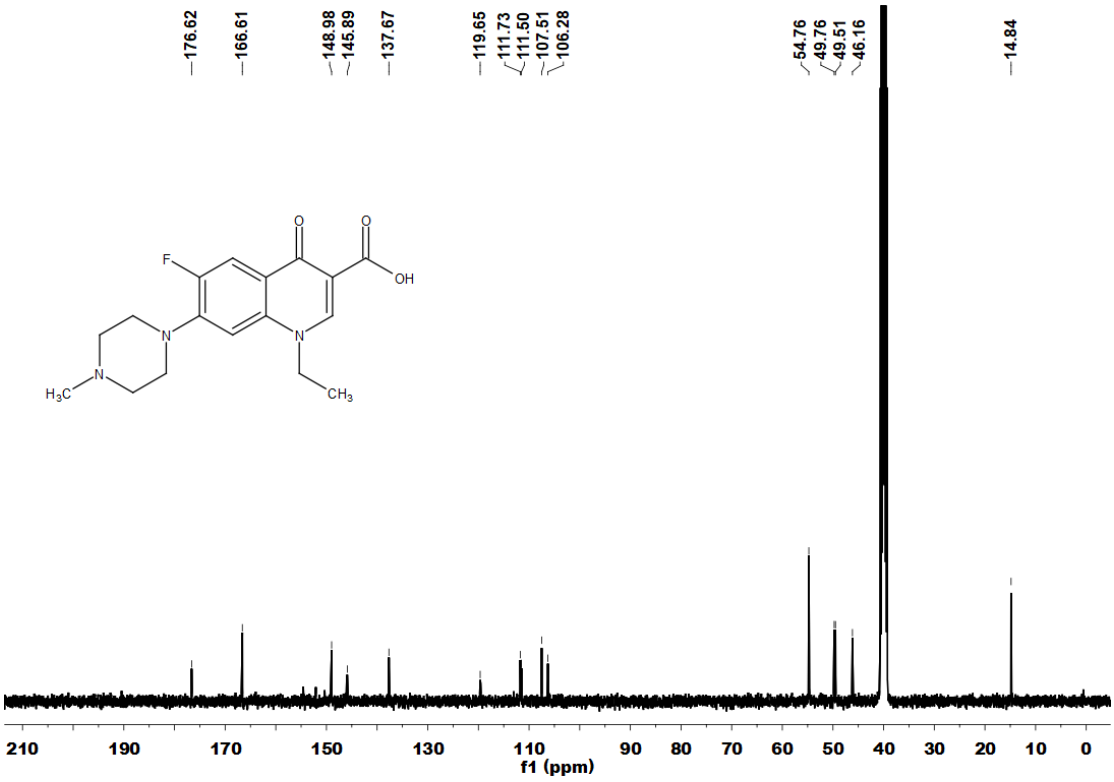
^{1}H NMR spectrum of **9**



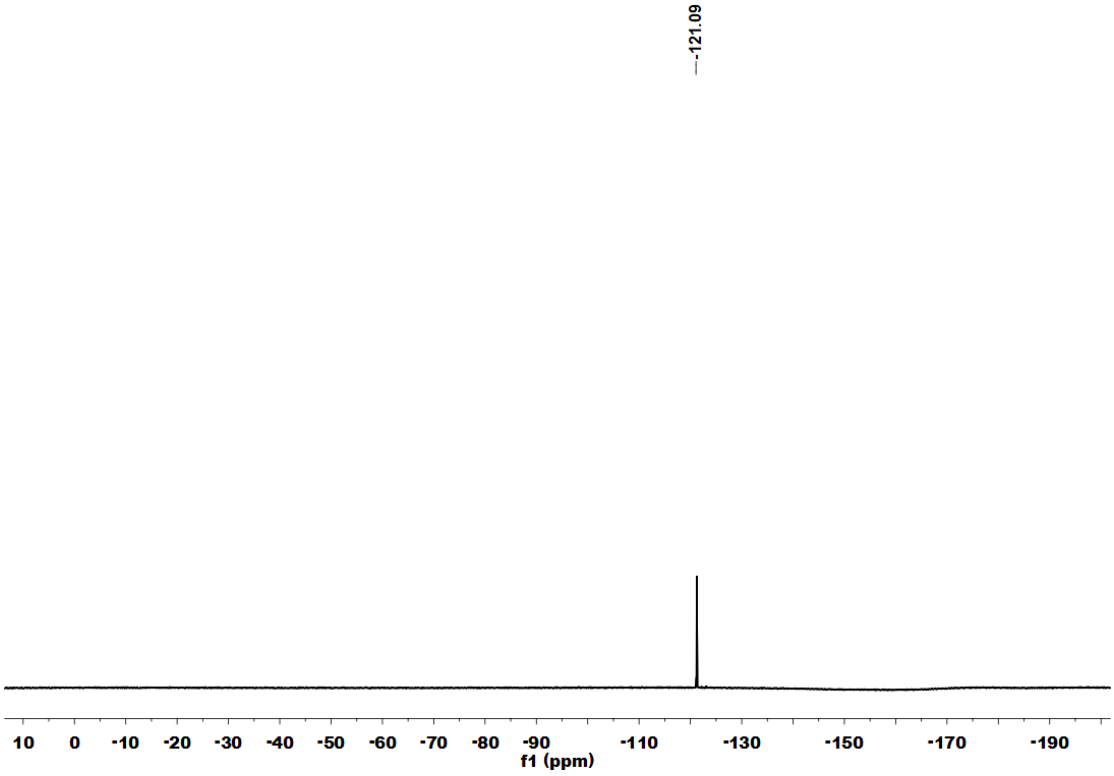
^{13}C NMR spectrum of **9**



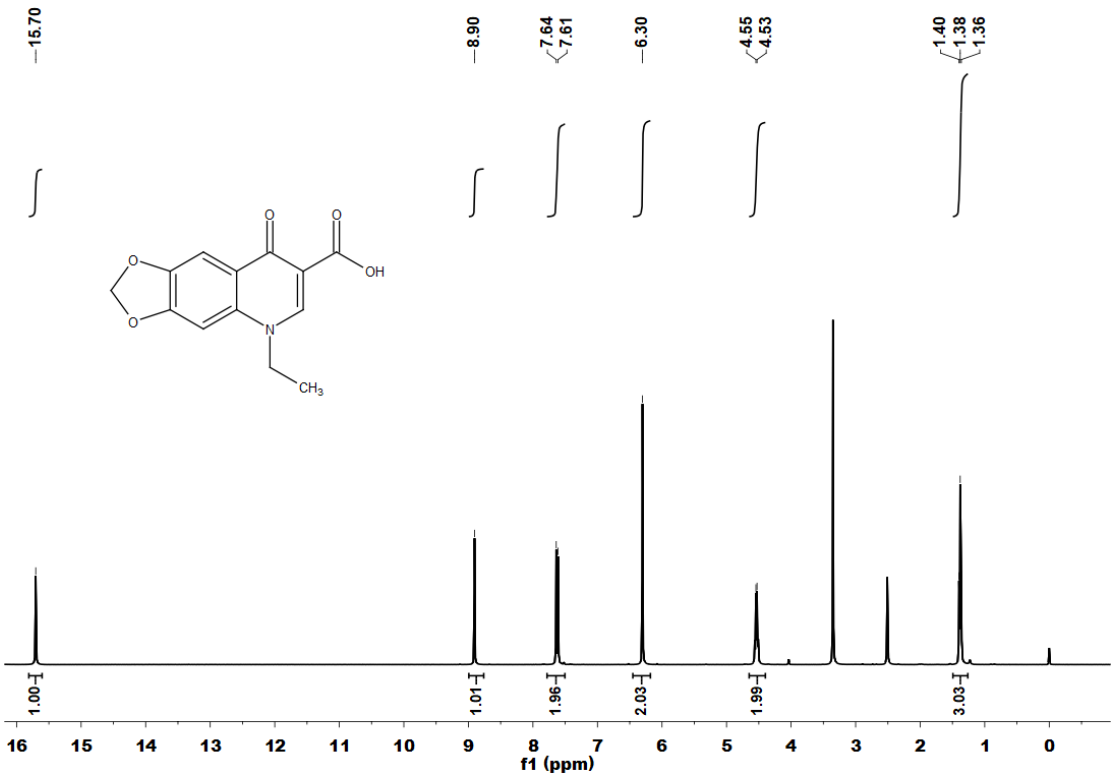
^{1}H NMR spectrum of **10**



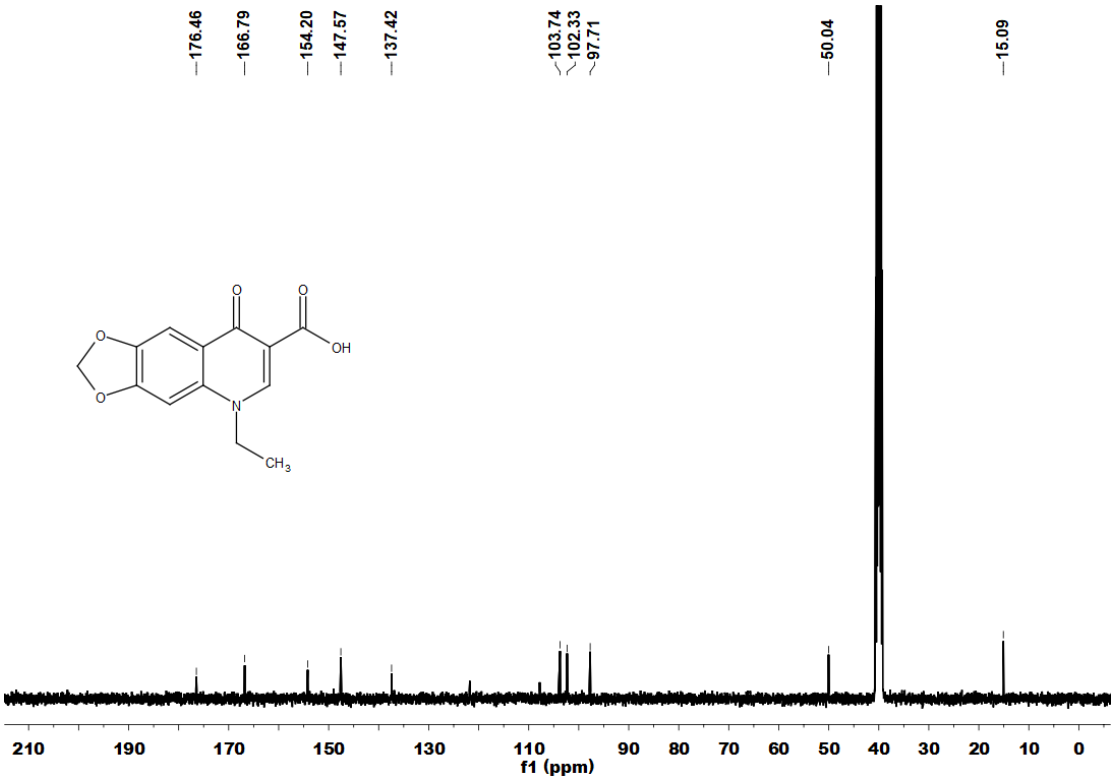
^{13}C NMR spectrum of **10**



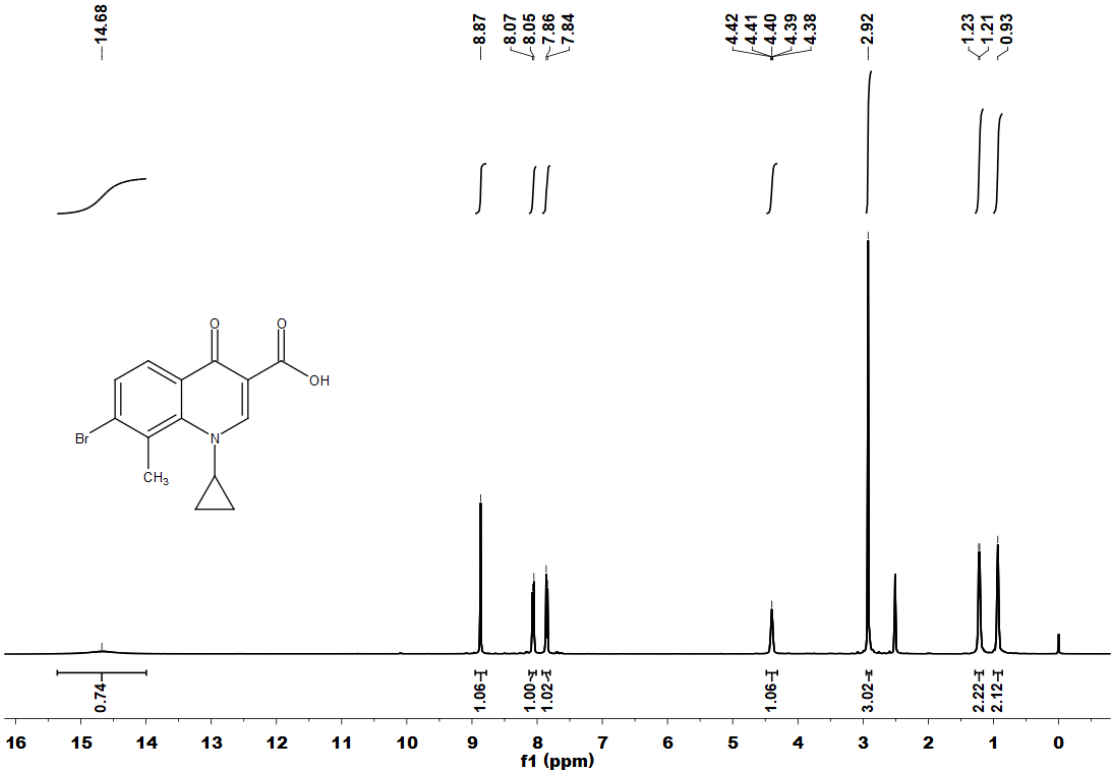
^{19}F NMR spectrum of **10**



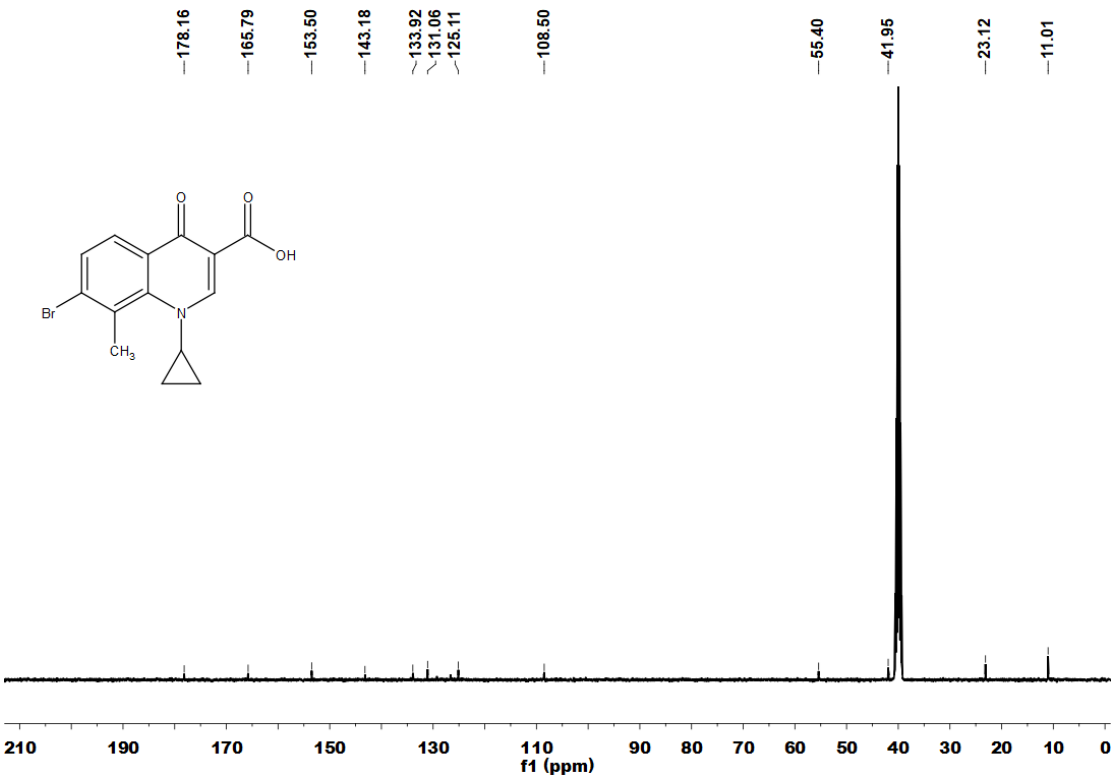
^{1}H NMR spectrum of **11**



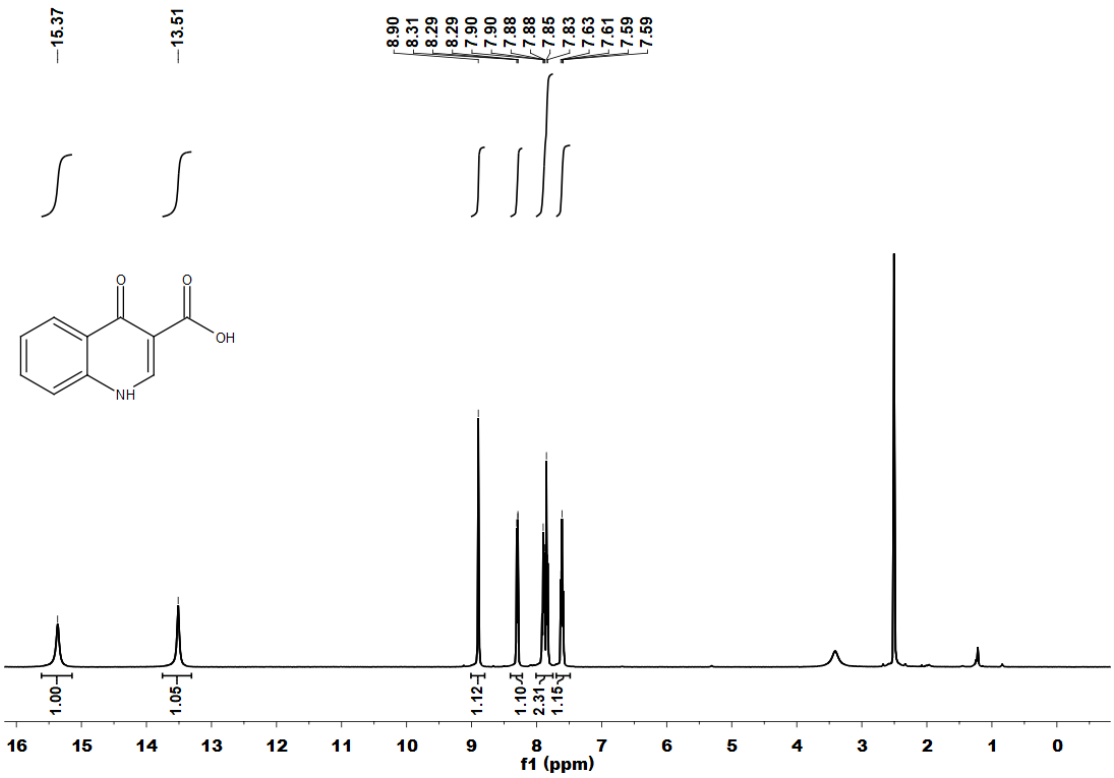
^{13}C NMR spectrum of **11**



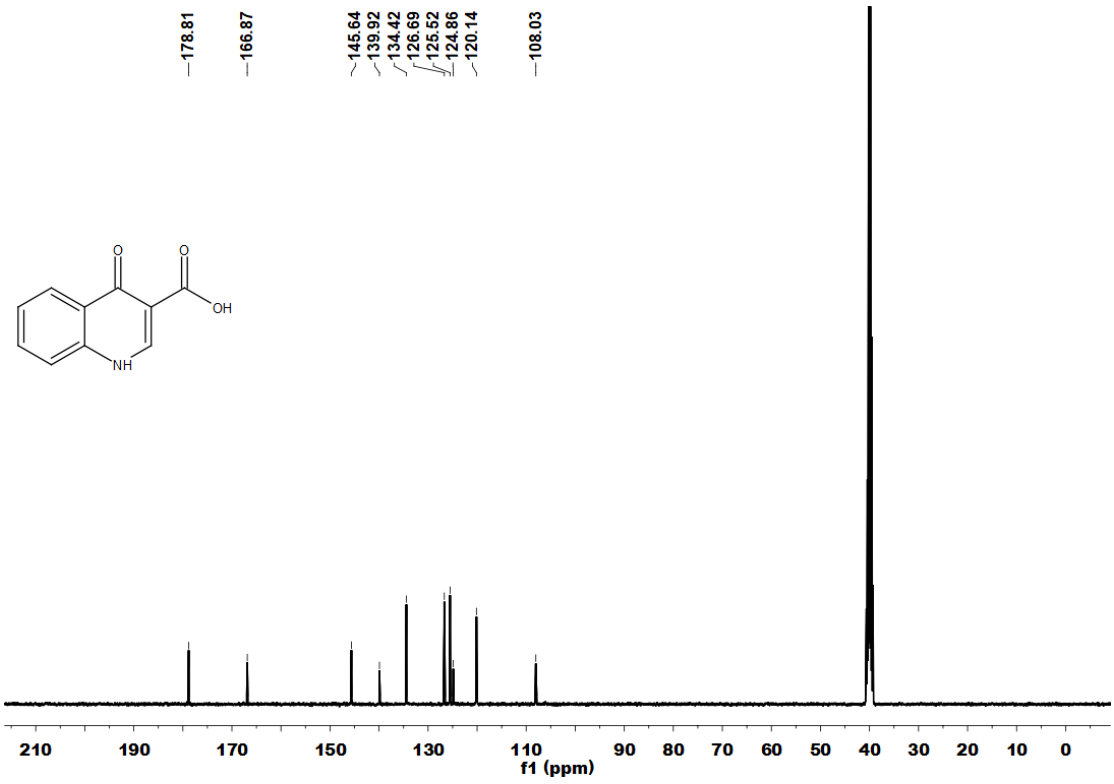
^{1}H NMR spectrum of 1**2**



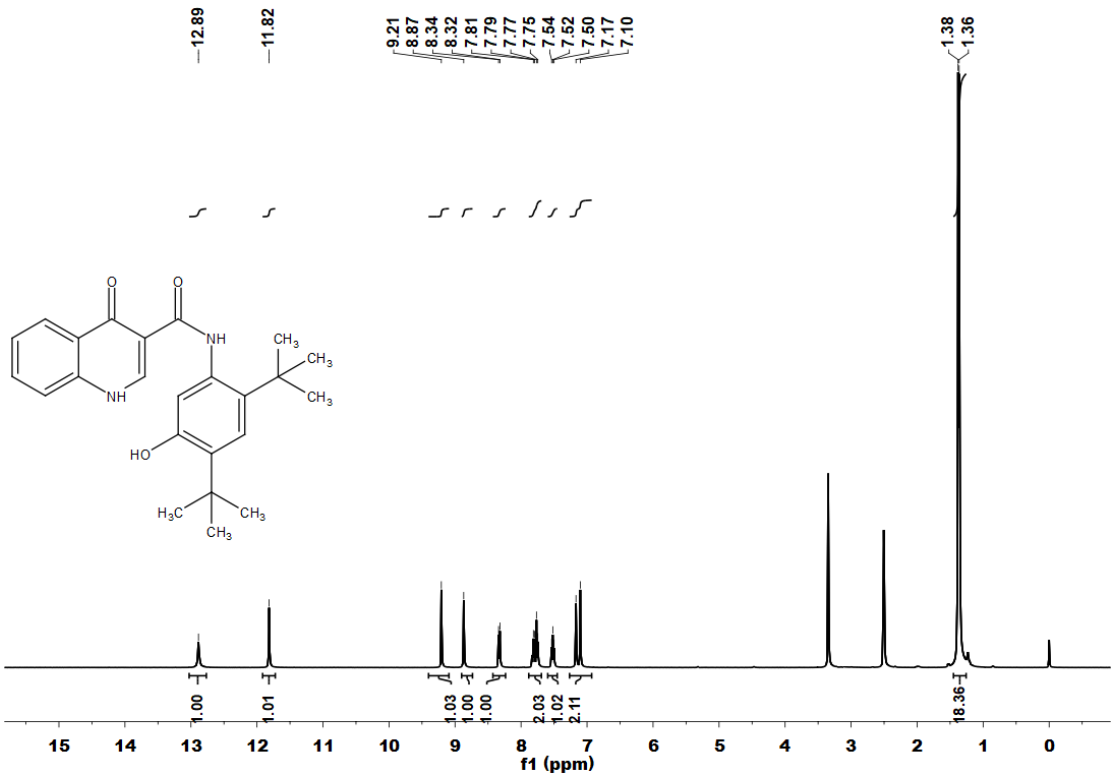
^{13}C NMR spectrum of 1**2**



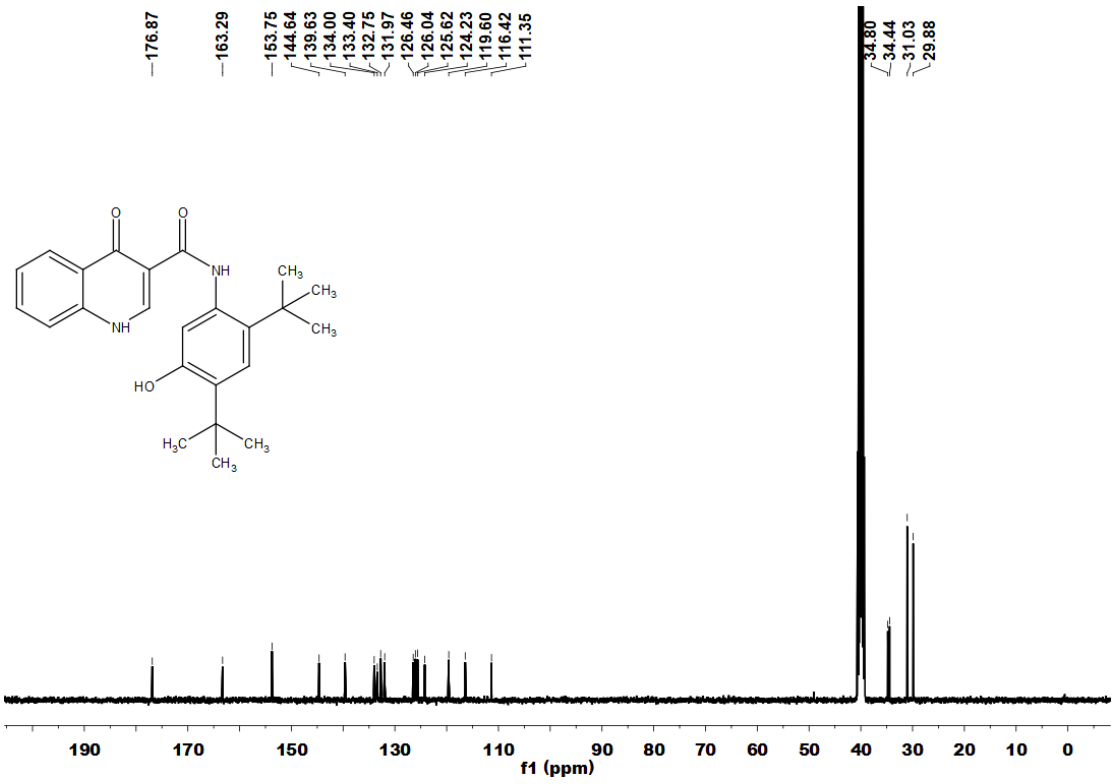
^{1}H NMR spectrum of **13**



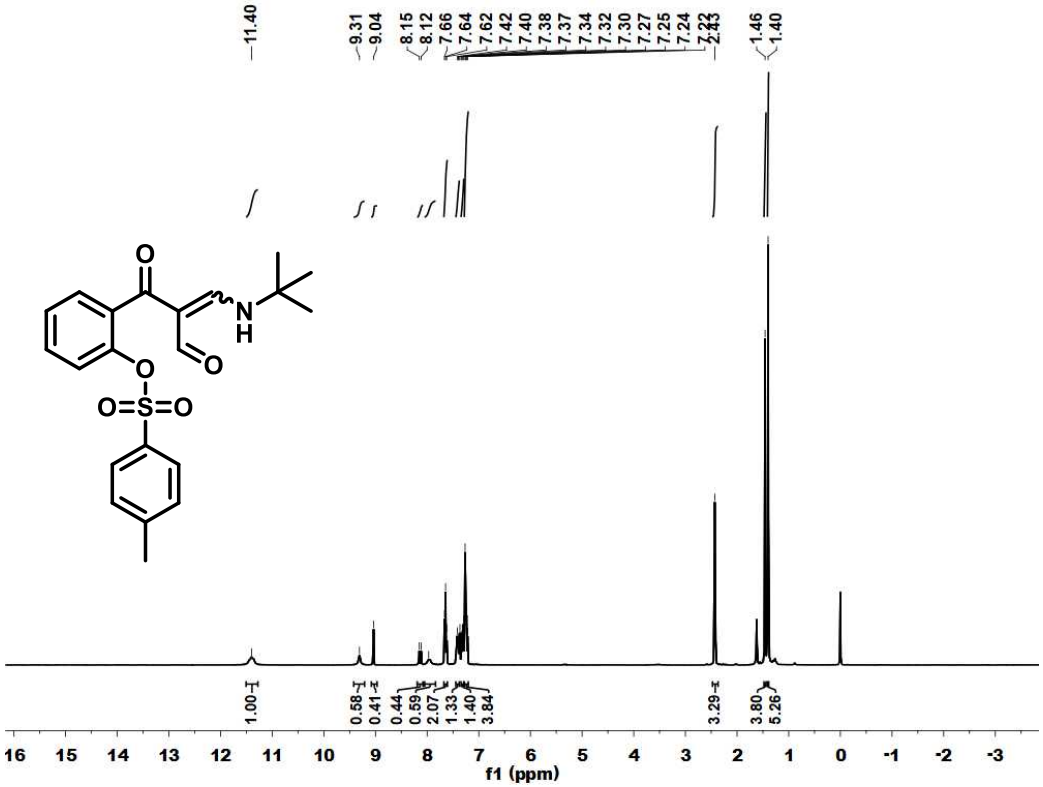
^{13}C NMR spectrum of **13**



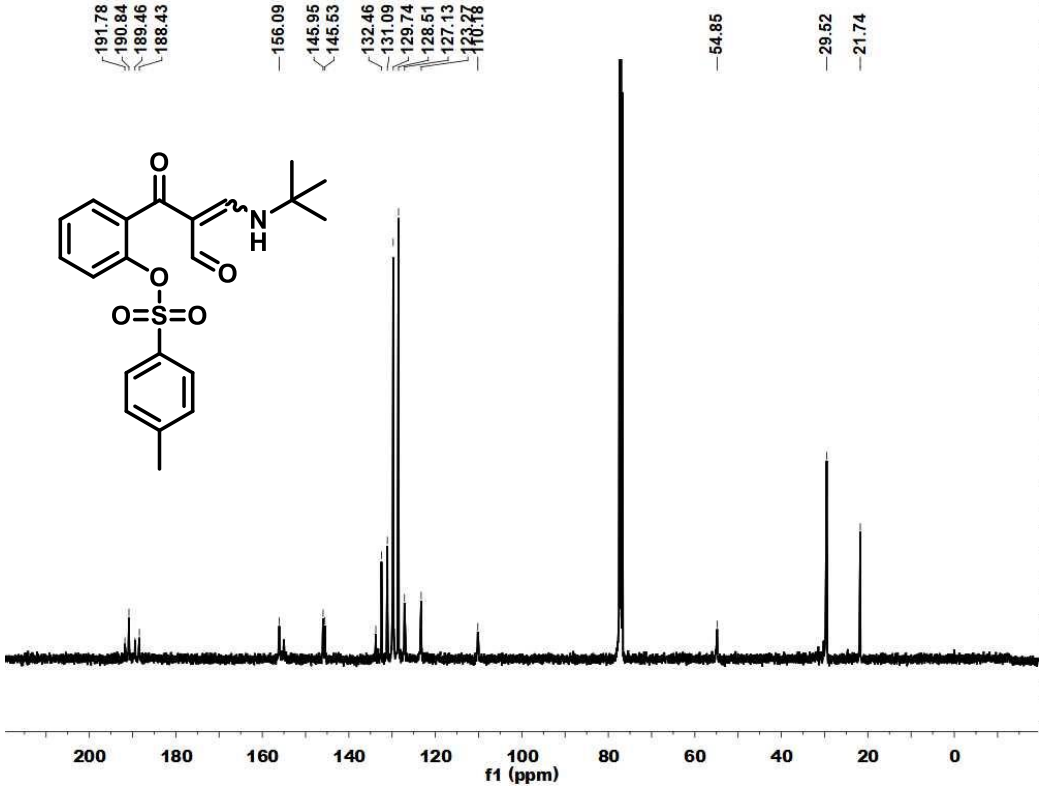
^{1}H NMR spectrum of **14**



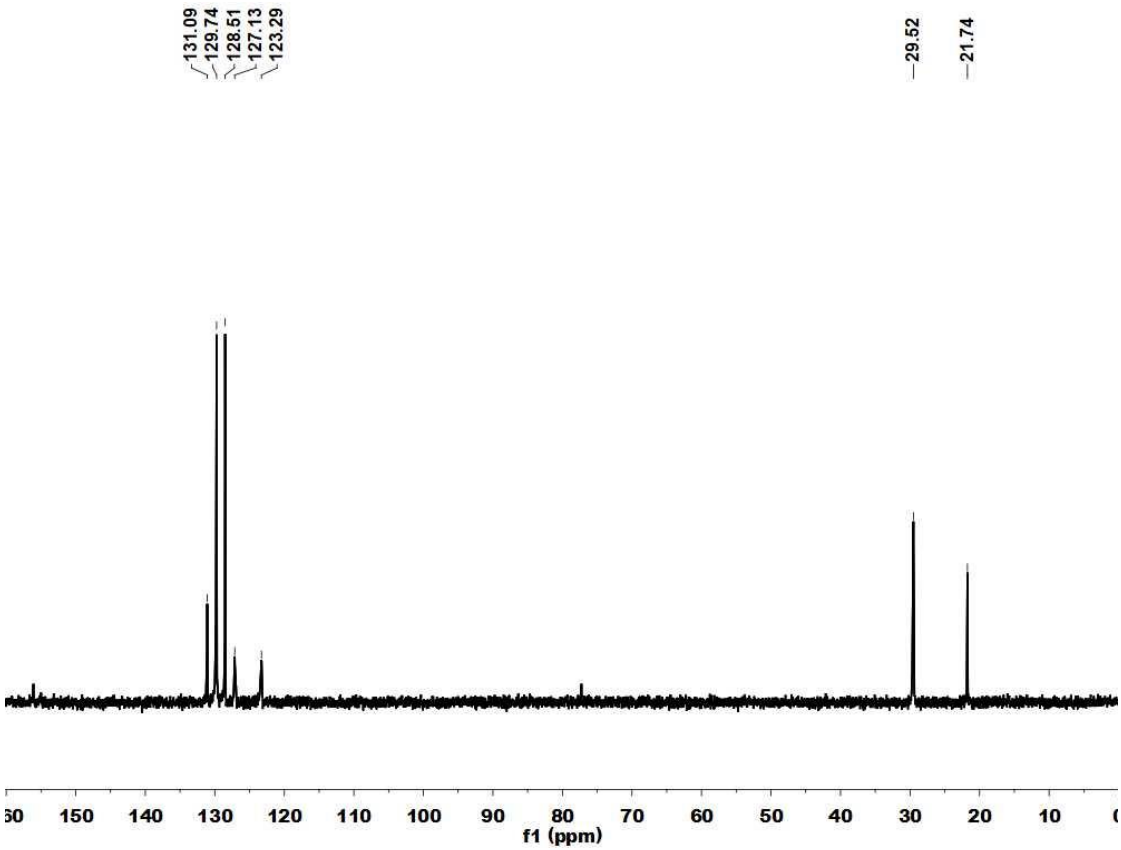
^{13}C NMR spectrum of **14**



^{1}H NMR spectrum of **15**



^{13}C NMR spectrum of **15**



DEPT 135˚ spectrum of **15**